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MEETING ABSTRACTS

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August 8–10, 2024
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Editor: Ryan Gentzler, MD

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2024 ASCO Breakthrough Meeting Abstracts

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1 Rapid Oral Abstract Session

Therapeutic response and outcomes with uncommon breast cancer subtypes in the I-SPY trial 2010-2022. First Author: Alexandra Thomas, Duke Cancer Institute, Durham, NC

Background: Uncommon histologies are over-represented among high-risk breast cancer (BC) and denote an area with limited trial data and of significant unmet medical need. To better understand trial outcomes in this group and identify signals of tumor responsiveness, we report pathologic complete response (pCR) and early event-free survival (EFS) by disease subtype in the I-SPY2 trial. Additionally, the I-SPY2 trial currently utilizes a combination of tumor molecular signature and receptor status to determine response predictive subtype (RPS) first developed from 987 I-SPY2 patients [Wolf et al, Cancer Cell 2022]. We report disease response rates for those who received what is now known to be optimal RPS guided therapy. **Methods:** The I-SPY2 platform trial tests novel agents given neo-adjuvantly with a chemotherapy backbone in high-risk BC (HER2 positive, triple negative and high molecular risk estrogen receptor positive BC). Histologic images of research biopsies, local biopsy and surgical pathology reports were reviewed centrally by I-SPY pathologists. Receptor subtype distribution and pCR rates were summarized; and EFS was estimated using the Kaplan Meier method. Association between pCR and EFS was evaluated using the Cox proportional hazard model with significance assessed by the log rank test. **Results:** 144/2118 (7%) of I-SPY2 participants were identified with metaplastic (60), lobular (55), mucinous (9), micropapillary (8), neuroendocrine (4) and other (8) BCS. Tumor receptor status, pCR rate and EFS by tumor type are shown in the Table. For the full cohort, pCR was associated with better EFS (hazard ratio (95% CI): 0.12 (0.02 - 0.88), p = 0.01). Within metaplastic (metapBC) 11/32 (34%) and 5/28 (18%) patients had a pCR with or without checkpoint blockade, respectively. By RPS group, 9 of 18 (50%) (13 metapBC, 3 other, 2 lobular) in the HER2-Immune+ group who received RPS optimized therapy had a pCR. In this group 6/13 (46%) with metapBC had a pCR. In the HER2+ driven RPS groups, pCR rate in the HER+HER2orBasal was 88% (7/8) and 0% (0/3) in the HER2+Luminal. **Conclusions:** High pCR rates observed in metapBC and other among subsets of often difficult to treat BC subtypes support novel approaches and provide a roadmap for future study of uncommon BCs. Outcomes were improved when therapy matched RPS vulnerabilities. Participants presenting with uncommon BC subtypes will be prospectively identified in the I-SPY2.2 trial to further develop effective approaches for this group. Clinical trial information: NCT01042379. Research Sponsor: None.

	N	HR+/HER-	TNBC	HER2+	pCR, N (%)	N	3 year EFS (95% CI)
Lobular	55	46(84%)	3(5%)	6(11%)	8 (15%)	53	81% (70-93%)
Metaplastic	60	13(22%)	46(77%)	1(2%)	16 (27%)	57	66% (54-80%)
Micropapillary	8	5(62%)	1(12%)	2(25%)	2 (25%)	8	86% (63-100%)
Mucinous	9	8(89%)	0(0%)	1(11%)	0 (0%)	9	100%
Neuroendocrine	4	3(75%)	0(0%)	1(25%)	0 (0%)	4	100%
Other	8	3(38%)	4(50%)	1(12%)	3 (38%)	7	100%
Total	144	78(54%)	54(38%)	12(8%)	29 (20%)	138	76% (70-85%)

2 Poster Session

Updated efficacy of anti-TROP2 ADC ESG401 for first-line metastatic TNBC in phase 1b study. First Author: Fei Ma, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background: ESG401, a novel ADC comprising a humanized anti-TROP2 IgG1 monoclonal antibody conjugated to SN-38, with a Drug-Antibody Ratio of 8 and a stable cleavable linker, demonstrated preliminary efficacy and tolerability in the Phase Ia trial (Ma, ASCO 2023). This report presents updated results from the first-line mTNBC cohort of the Phase Ib trial and results from patients with brain metastases. **Methods:** Patients (pts) aged ≥18 years with confirmed local advanced/unresectable or metastatic TNBC, without prior metastatic treatment, received ESG401 (16 mg/kg IV on Day 1,8, and 15, with a 28-day cycle) until unacceptable toxicity, progressive disease, or consent withdrawal. **Results:** As of the cutoff date (Apr 7th, 2024), 24 pts in the cohort received ≥1 dose of ESG401. Median age was 53 years (range: 33-73), 33.3% were ECOG 0, 25.0% were de novo stage IV, 70.8% had visceral disease (8.3% brain, 33.3% liver, 50.0% lung). Updated efficacy results are shown in the Table. Thirteen pts (68.4% of 19 efficacy evaluable pts) remained on treatment, with the longest on-treatment duration being 10.3 mons. Median PFS has not been reached. Two pts in this cohort had brain metastases, with one achieving a complete intracranial response and an overall response of PR, and the other demonstrating overall PR with a -13.8% reduction in brain lesion size. Totally 16 pts with brain metastases were enrolled in the entire Phase Ia/1b trials, for these pts, the best overall intracranial response rate was 31%, with an intracranial disease control rate of 75%, while the corresponding overall response rate and disease control rate were 50% and 69%, respectively. The response of intracranial lesions to the treatment is consistent with that of extracranial lesions. The safety profile of ESG401 remained consistent with previous reports, showing no new or unexpected safety signals. **Conclusions:** ESG401 monotherapy demonstrates promising antitumor activity in 1L mTNBC pts, characterized by a high response rate and durable response. The ORR numerically exceeded that reported in the BEGONIA Study arm 7 in which pts with the same indication were treated with TROP-2 ADC and PD-L1 combination therapy. Additionally, ESG401 shows clear potential for treating HER2-negative breast cancer with brain metastases, including mTNBC and HR+/HER2- BC. These results support further clinical investigation of ESG401. Clinical trial information: NCT04892342. Research Sponsor: Shanghai Escugen Biotechnology Co., Ltd.

Clinical outcomes.

	All patients (N=19)[a]
ORR, n (%)	16 (84.2)
CR	1 (5.3)
PR	15 (78.9)
DCR, n (%)	19 (100)
CBR, n (%)	16 (84.2)
6-mo DoR rate, % (95% CI)	65.6 (26.0, 87.6)
9-mo PFS rate, %(95% CI)	73.3 (37.9, 90.6)

[a]Among 24 patients enrolled, 19 patients were evaluable for response assessment (defined as ≥1 on-study scan).

3 Poster Session

An artificial intelligence system for early prediction of breast cancer regression pattern during neoadjuvant chemotherapy. First Author: Yuhong Huang, Department of Breast Cancer, Cancer Center, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China

Background: Breast cancer exhibits diverse tumor regression patterns (TRP) following neoadjuvant chemotherapy (NAC). We aims to develop an artificial intelligence (AI) system utilizing longitudinal magnetic resonance imaging (MRI) for precise TRP prediction. **Methods:** This retrospective study involved 2249 breast cancer patients from 12 institutions. The dataset comprised a training cohort (n=1006) from institutions I and II, and an external validation cohort (n=1243) from institutions III-XII. We utilized a 3D U-Net model for automated tumor delineation, incorporating spatial habitat analysis and 3D ResNet-50 model for extracting imaging featur, to develop an AI system. **Results:** The 3D U-Net model showed significant accuracy, with Dice coefficients of 0.875 in the validation cohort. The AI system achieved areas under the curve of 0.912. It demonstrated robust performance across diverse molecular subtypes (accuracies: 80·68% to 87·87%) and tumor stages (accuracies: 80·16% to 84·98%) in the validation cohorts. **Conclusions:** Our study provides a noninvasive AI system for early TRP prediction in breast cancer, potentially assisting clinicians in adjusting NAC regimens and planning breast-conserving surgery. Research Sponsor: None.

4 Poster Session

Predictive analysis of breast cancer metastasis and identification of genetic markers using machine learning. First Author: Kovuri Umadevi, Government Medical College Nizamabad, Nizamabad, India

Background: The study devises a framework integrating machine learning (ML) paradigms with explainable artificial intelligence (XAI) to prognosticate the metastatic trajectory of breast cancer (BC) and delineate critical genomic indicators pertinent to metastasis. **Methods:** An examination was conducted on 98 initial BC specimens, which included 34 instances evolving into distant metastasis within a quintennial monitoring phase and 44 instances evincing no recurrence for a minimum pentad post-diagnosis. Genomic datasets underwent rigorous biostatistical scrutiny, followed by the implementation of an elastic net algorithm for feature discernment, thereby constraining the scope to a salient subset of genomic markers implicated in BC metastasis. An ensemble of advanced predictive models encompassing Light Gradient Boosting Machine (LightGBM), Categorical Boosting (CatBoost), Extreme Gradient Boosting (XGBoost), Gradient Boosting Trees (GBT), and Adaptive Boosting (AdaBoost) was deployed. Model efficacy was gauged through metrics such as accuracy, F1 score, precision, recall, the Area Under the Receiver Operating Characteristic Curve (AUC), and the Brier score. To elucidate the reasoning behind the ML predictions and to navigate the opacity inherent in such models, a SHapley Additive exPlanations (SHAP) approach was invoked. **Results:** The predictive acumen of the LightGBM model was superior, evidenced by a striking accuracy of 96% and an AUC of 99.3%. Parallel to biostatistical assessments, SHAP analysis leveraging XAI illuminated that augmented expression levels of specific genes, namely TSPYL5, ATP5E, CA9, NUP210, SLC37A1, ARIH1, PSMD7, UBQLN1, PRAME, and UBE2T (with statistical significance $p \leq 0.05$), correlated with an escalated risk of BC metastasis. Conversely, diminished expression of CACTIN, TGFB3, SCUBE2, ARL4D, OR1F1, ALDH4A1, PHF1, and CROCC ($p \leq 0.05$) was similarly associated with heightened metastatic susceptibility in BC. **Conclusions:** The insights garnered from this investigation may catalyze preventative strategies against BC progression and metastatic dissemination, thereby enhancing therapeutic efficacy through personalized intervention modalities for BC patients. Research Sponsor: None.

5 Poster Session

Evaluating interaction between tumor educated platelets and cancer stem cells on breast cancer subtypes. First Author: Aishwarya Guha, Chittaranjan National Cancer Institute, Kolkata, India

Background: Thrombocytosis has been reported to be responsible for poor prognosis of numerous malignancies. This swarm of platelets acts as foe for the body but as mate for the cancer cells by providing a protective shield around them, helping them to escape immunosurveillance process. A bidirectional interaction between platelets and tumor cells promote their conversion to an activated tumor educated platelet (TEP) state. The present report reveals the critical role played by TEPs to promote metastasis in BC subtypes by interacting with cancer stem cells (CSCs). **Methods:** Status of intra-tumoral and humoral TEPs ($CD41^+/CD62P^+$) was screened in luminal A (LumA) and triple negative (TNBC) BC subgroups. The impact of TEPs on $lin^-/CD44^+/CD24^-$ CSCs of both the categories *in-vitro,* was deciphered by performing mammosphere assay, clonogeneic and migration assays, with final validation in murine system. Effect on various genes and proteins related to stemness, metastasis and angiogenesis as a result of this interaction was elucidated by RT-PCR, flow cytometry and western blotting. **Results:** High percentage of TEPs in the peripheral blood is a potential biomarker and responsible for poor prognosis in BC subtypes. Both Lum A and TNBC patients had elevated TEP frequency, compared to healthy blood. Further, patients in the pre-carcinogenic stage had platelet count of $>$3.5 lakhs. Additionally, screening of breast tumor sections revealed intra-tumoral enrichment of TEPs, comparatively to a greater extent in TNBC than LumA, supporting their role in disease aggression. Also, a positive correlation was noted between TEP and CSC frequencies proving their synergistic interactions. Moreover, *in-vitro*, TEP influenced CSCs exhibited enormous clonogenic and tumorigenic potentialities. Their metastatic nature was confirmed by their enhanced migratory, invasive, angiogenic capacities with higher VIMENTIN and TWIST along with HIF1α, CD31 and MMP9 expression compared to E-CADHERIN. In line with *in-vitro* observations, *in-vivo* too, TEP~CSC produced metastatic colonies in murine lungs. Upon investigation, it was disclosed that it is through WNT-βcatenin-VEGFR2 axis that this mutual interdependency was functioning. **Conclusions:** This study advocates for the importance of TEPs as potential biomarker in BC diagnosis. Their alliance with vicious CSCs to promote disease advancement acquiesce them as a novel restorative agent. Research Sponsor: Council Of Scientific and Industrial Research; Chittaranjan National Cancer Institute.

6 Poster Session

Effect of impaired autophagic flux on breast carcinogenesis through the enhanced LC3-p62-NRF2 feedback loop. First Author: Mehreen Aftab, Indian Council of Medical Research- National Institute of Cancer Prevention and Research, Noida, India

Background: Breast cancer affects more women worldwide than any other type of cancer. Although some genes have been identified as potential causes, the exact molecular mechanism of the disease is still unknown. In our study, we aimed to investigate the role of NRF2 and the autophagy markers p62 and LC3 in breast cancer cell lines that have different Tp53 status using a new compound called 6,6'dihydroxythiobinupharidine (DTBN). In our previous research, we have shown that DTBN modulates key cellular signal transduction pathways that are relevant to disease biology, including cancer. Furthermore, we analyzed online databases to determine the correlation between NRF2, p62, LC3, and Tp53 in breast cancer patients. **Methods:** To evaluate the effect of DTBN on NRF2, p62 and LC3 in different types of breast cancer cell lines with varying TP53 status, we conducted molecular studies by inhibiting NRF2 activity. We synthesized the correlation between NRF2, p62, LC3 and TP53 expression and clinical parameters by analyzing TCGA and GEO datasets. **Results:** Our findings suggest that DTBN induces cell death and autophagy in all breast cancer cell lines, regardless of their Tp53 status. However, they also led us to hypothesize that NRF2 may hinder the sensitivity of cancer cells to DTBN-induced cell death and autophagy. To test this hypothesis, we inhibited NRF2 activity using an NRF2 inhibitor called brusatol. The results of the study indicate that the inhibition of NRF2 significantly increased cell death and autophagy in DTBN-treated cells. We observed a decrease in the expression of the autophagy marker p62, while an increase in the expression of another autophagy marker LC3. These findings suggest that the interaction between NRF2, LC3 and p62, which is activated in response to DTBN treatment, may serve as a potential anticancer drug target. We have validated the positive correlation between NRF2 and the autophagic gene p62 and LC3, in different Tp53 status breast cancer cell lines by analyzing TCGA and GEO data. **Conclusions:** Our study shows that high levels of Nrf2, LC3 and p62 expression are significantly associated with increased breast cancer cell proliferation and migration. This implies that patients with breast cancer have lower overall survival and a higher rate of recurrence. Our findings highlight the role of DTBN-induced NRF2 and LC3 expression and reduced p62 expression in breast cancer cells with varying Tp53 status. These results may represent a paradigm for better understanding the cancer cell response to therapies and designing more efficient combined anticancer therapies targeting NRF2, LC3 p62, and Tp53. Research Sponsor: None.

7 Poster Session

Multimodal analysis of methylation and fragmentomic profiles in plasma cell free DNA for differentiation of benign and malignant breast tumors. First Author: Thi Tuong Vi Van, Medical Genetics Institute, Ho Chi Minh City, Viet Nam

Background: Breast cancer ranks as the second leading cause of cancer-related mortality among women globally. Early detection of breast cancer is crucial for improving patient outcomes and reducing mortality rates. Liquid biopsy, which relies on circulating tumor DNA (ctDNA) shed by breast tumors into the bloodstream, presents a promising non-invasive approach for early breast cancer detection. However, accurately distinguishing between benign breast abnormalities and malignant tumors remains a significant clinical challenge, as misdiagnosis can lead to unnecessary invasive procedures. **Methods:** Herein, we employed a multimodal analysis approach, namely SPOT-MAS (Screen for the Presence of Tumor by DNA Methylation and Size), to profile alterations in methylation and fragment length patterns of cell-free DNA (cfDNA) from 169 breast cancer-confirmed patients and 99 patients diagnosed with benign breast lumps including cysts, fibroadenomas, and fibrocystic changes. A robust machine learning model was constructed using these signatures to differentiate between breast cancer patients and individuals with benign lesions. **Results:** Our genome-wide analyses identified distinct profiles of methylation changes, copy number alterations, and end motifs in cfDNA, enabling discrimination between breast cancer patients and individuals with benign conditions. Notably, we observed a significant enrichment of Thymine and Adenine at cfDNA cleavage sites in breast cancer patients. Moreover, our target sequencing analyses uncovered distinct methylation patterns in the regulatory regions of multiple genes, including hypermethylation in *GPR126* or hypomethylation in *TOP1* or *MAFB* in breast cancer cfDNA. Our multi-featured model achieved an AUC of 0.92 (95% CI: 0.88–0.97), a specificity of 97.44% and sensitivities of 57.14% and 61.70% for stage I and stage II–III patients, respectively. Furthermore, our multimodal assay effectively differentiated multiple molecular subtypes of breast tumors from benign lesions, achieving the highest sensitivity of 71.43% with Luminal A, followed by Luminal B, Triple Negative Breast Cancer (TNBC), Luminal B-HER2, and HER2 with sensitivities of 66.67%, 60%, 58.33% and 55.56%, respectively. **Conclusions:** Our findings demonstrate the potential of cancer-specific methylation and fragmentomic patterns in plasma cfDNA as novel biomarkers for accurately discriminating between breast cancer and benign lesions. This capability reduces the false-positive rate and helps avoid unnecessary biopsies in current clinical practice. Research Sponsor: Gene Solutions.

8 Poster Session

Research and analysis on the situation of diagnosis and treatment capabilities of breast cancer in China county. First Author: Xiang Tan, Anyue County People's Hospital, Ziyang, China

Background: 1. In 2016, 306,000 breast cancer cases were newly diagnosed in China, with one-third in rural areas. Breast cancer ranked second in incidence ($22.47/10^5$) among female cancers in Sichuan Province. 2. Health resources are unequally distributed in China, especially in Sichuan Province where 43.27% reside rurally. County hospitals play a vital role in rural patients' diagnosis, treatment, and referrals. **Methods:** This cross-sectional observational study surveyed 124 county-level hospitals that had treated breast cancer in 183 counties in Sichuan Province from December 2023 to January 2024. Outcomes include: 1) hospital level; 2) oncology certification; 3) availability of dedicated breast department and staffing; 4) breast cancer diagnosis and treatment technology; 5) pre-treatment TNM staging rate; 6) anti-neoplastic drugs and support Accessibility of medicines. **Results:** Out of 124 hospitals surveyed, 6 excluded for zero breast cancer cases in 2023. The remaining 118 hospitals revealed: 1) 78.81% tertiary, 93.22% public; 2) 75.42% with special outpatient qualifications, 57.63% with concurrent special antineoplastic drug designations, 17.80% with one qualification; 3) 57.63% with dedicated breast units, but only 16.1% with specialized breast cancer staff; 4) 31.36% with full breast imaging modalities, 78.23% lacking mammography; PET-CT and bone scan availability: 5.93% and 9.32%; 5) 71.19% with independent pathology, but only 30.65% providing comprehensive services; 6) Surgeries for breast cancer: 86.44% (44.07% breast conservation), radiation therapy availability: 39.83%; 7) AJCC TNM staging rate: 77.12%; 8) Antineoplastic accessibility: conventional chemotherapy (93.22%), anti-HER2 therapy (28.81%), endocrine therapy (47.46%), CDK4/6 inhibitors (26.27%, with 41.53% having only one); 9) Analgesics: 87.90% (morphine 94.92%, tramadol 88.98%, fentanyl patches 34.75%, oxycodone 46.61%); antiemetics (5-HT3 antagonists 69.49%, NK1 antagonists 72.88%, olanzapine 48.31%, metoclopramide 64.41%); medications for hematologic toxicity: 51.61%. **Conclusions:** Shortages exist in specialized breast care units and trained personnel among county hospitals in Sichuan, China. Special outpatient qualifications and antineoplastic prescription credentials concentrated mainly at tertiary centers. Enhancing imaging and histopathology capacities for breast cancer diagnosis is an urgent need. While conventional chemotherapies demonstrate good accessibility, anti-HER2 targeted therapies, endocrine therapies, and CDK4/6 inhibitors covered by national insurance have limited availability. Enhanced provision of new antiemetics and analgesics is needed. Research Sponsor: None.

Summary of diagnostic and treatment capacities for breast cancer in Chinese county-level hospitals.

Main parameters	Key findings
1. Hospitals	• Tertiary 78.81% • Public 93.22%
2. Oncology Accreditation	• Special outpatient qualifications 75.42% • Concurrent special antineoplastic drug designations 57.63%
3. Availability of dedicated breast units and staffing	• Dedicated breast units 57.63% • Specialized breast cancer staff 16.1%
4. Breast cancer diagnostic and therapeutic technologies	• Full breast imaging modalities 31.36%(PET-CT 5.93% and bone scan 9.32%) • Independent pathology 71.19% (Comprehensive pathology services 30.65%) • Breast cancer surgery 86.44% (conservation 44.07%) • Radiation therapy 39.83%
5. Pretreatment TNM staging rates	• AJCC TNM staging rate: 77.12%
6. Accessibility of antineoplastic and supportive medications	• Chemotherapy 93.22% • Anti-HER2 therapy 28.81% • Endocrine therapy 47.46% • CDK4/6 inhibitors 26.27% • Analgesics 87.90% • Antiemetics 100% • Medications for hematologic toxicity: 51.61%

9 **Poster Session**

Investigation of a tamoxifen-RACK7/KDM5C-IFN-I axis for ER$^+$ breast cancer immunomodulation. First Author: Marvin Angelo Esteban Aberin, Taiwan International Graduate Program in Molecular Medicine, Institute of Biomedical Sciences, Academia Sinica and National Yang Ming Chiao Tung University, Taipei City, Taiwan

Background: ER+ breast cancer patients generally have good prognosis. However, significant relapse rates (i.e., hormone drugs, Tamoxifen/TMX) and the poor response to immune checkpoint blockade (ICB) remain critical issues to be addressed. Thus, exploration of anti-ICB resistant mechanisms and alternative targets is needed to improve therapeutic efficacy. **Methods:** To investigate potential cross-resistant mechanisms between hormone and ICB therapy, ER+ cell lines T47D and MCF7 cells were chronically-treated with TMX for 6 months, and subjected to RNA-Seq and pathway enrichment analysis. Dysregulation of identified factors were validated via western blotting, RT-qPCR, and flow cytometry. Target factors were then inhibited or depleted by shRNA knockdown (KD) or small-compound inhibition. Identified ICB resistance mechanisms were further elaborated by in vitro co-culture assays, syngeneic mouse models, and immune-profiling of tumor microenvironment (TME). **Results:** Chronic exposure to TMX activates Type I interferon (IFN-I) signaling, induces IFN I-stimulated gene (ISG) expression, and downregulates the H3K4 demethylase and ISG repressor complex known as RACK7/KDM5C. Chronic TMX also upregulates CEACAM1, a well-known ligand for the immune checkpoint receptor TIM3. Results prompt us to evaluate whether loss of RACK7 combined with TMX treatment may modulate a lymphocyte-attractive (via IFN-I), but T-cell exhaustive (via CEACAM1-TIM3) TME. Indeed, in vitro treatment of TMX under RACK7-KD conditions triggers STING upregulation, TBK1 hyperphosphorylation, and a more pronounced activation of ISGs and CEACAM1. In vivo, TMX combined with RACK7-KD enhances tumor growth in the TS/A (ER+) syngeneic mouse model, while immune-profiling reveal that this combination promotes lymphocyte infiltration with a higher population of terminally exhausted CD8+ T-cells in the TME. **Conclusions:** Our data demonstrate that the TMX-induced activation of cGAS/STING pathway and RACK7 downregulation coordinately shape the IFN-I and immune checkpoint signaling axes in ER+ breast cancer. This TMX–RACK7–IFN-I regulatory network promotes a lymphocyte-attractive TME via IFN-I signaling activation, whereas induction of inhibitory ligands renders T-cells to be terminally-exhausted and unable to kill tumors. These findings highlight the potential use of TMX's STING-agonistic effect in re-shaping the "cold" breast cancer TME, and the use of combined TMX and anti-TIM3 or anti-CEACAM1 blockade to improve ICB therapy. Research Sponsor: None.

10 **Poster Session**

Investigation of the effect of macrophage and epithelial cell interaction in the progression of different subtypes of breast cancer. First Author: Banani Majumdar, The University of Burdwan, Purba Bardhaman, India

Background: In the realm of tumor progression, the immunosuppressive role of macrophages has been well-established. However, a significant lacuna persists concerning the mechanisms through which epithelial cells regulate macrophages. Furthermore, the precise manner in which macrophages modulate breast cancer cells remains unclear. Hence, the primary objective of the current investigation is to delve into the influence of macrophages on the progression of distinct subtypes of breast cancer. **Methods:** Human monocyte cell-derived macrophages (M0) were cultivated in the presence of conditioned media (CM) from various subtypes of breast cancer cells. Conversely, human luminal breast cancer cell line T47D, and basal cell line MDA MB 231 were cultured in the presence of CM from macrophages. **Results:** When macrophages were incubated with CM of T47D, they exhibited a spindle-shaped morphology with pseudopodia. Conversely, exposure to CM of MDA MB 231 induced macrophages to adopt a foamy, round shape with numerous filopodia. Flow cytometry analysis revealed that T47D-CM promoted a higher proportion of CD80+ cells, while MDA MB 231-CM led to an increase in both CD206+ and CD80+ cells. Moreover, both T47D and MDA MB 231-CM escalated the production of various cytokines including IL-1β, IL-2, IL-4, IL-5, IL-7, IL-12(p70), IL-13, IL-17, G-CSF, IFN-γ, and MIP-1β. Intriguingly, MDA MB 231-CM induced a significant increase in IL-6, GM-CSF, and TNF-α. Subsequent cultivation of cancer cells in the presence of macrophage-CM resulted in a marked proliferation of MDA MB 231 cells, while T47D cell proliferation decreased significantly. Correspondingly, there was a notable increase in apoptosis among T47D cells. Scratch wound healing assays revealed heightened migration of MDA MB 231 cells following treatment with macrophage-CM, whereas there was negligible alteration in T47D cell migration. Proteomic analysis unveiled dysregulation of 247 and 596 proteins in MDA MB 231 and T47D cells, respectively. Particularly noteworthy were three proteins—MDHM, H1.5, and LEG8—abundant in MDA MB 231 cells, yet scarce in T47D cells. These proteins have been implicated in promoting tumor growth across various cancer types. **Conclusions:** This study first time elucidates subtype specific role of macrophage in breast tumour. In triple-negative breast cancer, infiltrating macrophages induce an immunosuppressive effect, altering cytokine expression and fostering the expression of tumor-promoting factors in epithelial cells, thereby facilitating cellular proliferation and metastasis. Conversely, in luminal breast cancer, infiltrating macrophages exhibit a predominantly pro-inflammatory profile, resulting in minimal tumor-promoting effects. Key Words: Breast Cancer, Macrophage polarization, Conditioned Media, Cytokines, Proteomics. Acknowledgements, DBT – Govt of India, NIBMG, Kalyani. Research Sponsor: None.

11 **Poster Session**

Patient reported outcome measures at a large district general hospital post-mastectomy and implant based reconstruction. First Author: Danny Fraser, Basildon Hospital, Basildon, United Kingdom

Background: Breast reconstruction surgery for cancer can be a debilitating and life changing experience for patients, with complex affects on physical and mental health throughout the rehabilitation journey. We conduct a study on a cohort of patients undergoing this procedure, with focus on patient reported outcome measures. **Methods:** We reviewed all patients who underwent breast reconstruction surgery at our hospital from 2017 to 20223. Demographic, diagnosis, pre- and post-operative adjuvant treatment, and implant characteristics were collected. Psychosocial well being, physical wellbeing, satisfaction with breasts scales of the BREAST-Q were used. Independent t-test was conducted to find differences between PROMs for each group, and linear regression of age and implant size on each score. **Results:** 69 patients were contacted and 39 PROMS collected. The average age of patients was 57.6 years old. 40% were previous or current smokers and 40.8% had BMI$>$30. 29 had pre-pectoral placement and 40 sub-pectoral. 17 had smooth implants and 52 textured. The average size of implant was 330mm. Immediate reconstruction was associated with a lower psychosocial score (66.0vs86.9, p=0.02) compared to multi-stage implants. Sub pectoral placement was associated with a higher (75.7vs61.9 p=0.046) psychosocial score than pre pectoral placement. Textured surface was associated with lower physical score than smooth surface (34.7vs50.2 P=0.046). On linear regression, age was positively associated (p=0.007) with psychosocial score. **Conclusions:** These findings underscore the importance of personalized approaches in surgery, considering implant type, placement technique, and patient age. Surgeons should prioritize patient preferences and needs to optimize post-surgical satisfaction and well-being. Research Sponsor: None.

12 **Poster Session**

Utility of PET-CT for assessment of response to neo-adjuvant chemotherapy in breast cancer. First Author: Deepthi Valiyaveettil, Nizam's Institute of Medical Sciences, Hyderabad, India

Background: Response to neo-adjuvant chemotherapy (NACT) is associated with prognosis in non-metastatic breast cancer and can potentially inform further therapeutic options. The aim of this study was to correlate post NACT response on PET CT with pathological response. **Methods:** All patients who underwent pre- NACT (baseline) and post NACT PET CT imaging with F-18 FDG in a dose of 5-7 MBq/kg body weight with a minimum of 185 MBq given intravenously were retrospectively analyzed. Scan was performed on GE Discovery 710 whole-body PET scan with 128 slice CT. Relevant clinical and imaging related details were extracted from the treatment records. Post NACT PET response (PERCIST criteria) in the primary tumor and nodes was correlated with the pathological response on the post surgical specimen. Analysis was done using Microsoft Excel and SPSS v20 (IBM SPSS). **Results:** The median age was 49 years (range 30-76 years). 83.1% of patients had node positive disease on baseline PET imaging (not pathologically confirmed). Post chemotherapy PET showed complete metabolic response in the primary tumor and regional nodes in 56.3% and 74% of patients respectively. Two patients had progressive local disease. Pathological complete response rates post surgery in triple negative, Her2 neu positive and ER positive group was 50%, 34% and 12% respectively. The sensitivity, specificity, positive predictive value and negative predictive value is tabulated below. **Conclusions:** Overall FDG PET CT showed good specificity with limited sensitivity for post NACT response assessment in breast cancer. Our results suggest that post NACT PET CT may have limited utility for clinical decision making and at present its use cannot be recommended outside of a clinical trial. Research Sponsor: None.

Sensitivity, specificity, positive predictive value and negative predictive value of different subgroups.

Subgroups	Number	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Entire group (primary tumor response)	119	48.8%	85.9%	64.5%	76.1%
Entire group (nodal response)	119	63.6%	92.9%	94.2%	58.2%
Her 2neu positive (primary)	59	55.0%	84.0%	82.6%	58.3%
Her2neu positive (nodal)	59	68.8%	81.4%	57.9%	87.5%
ER positive, Her2 Neu negative (Primary)	25	80%	100%	100%	55.6%
ER positive, Her2 Neu negative (Nodal)	25	37.5%	66.7%	66.7%	37.5%
Triple negative (Primary)	34	68.8%	88.9%	84.6%	76.2%
Triple negative (Nodal)	34	50%	100%	100%	86.7%

13 **Poster Session**

Neoadjuvant treatment with trastuzumab and pertuzumab plus fulvestrant in older patients with HER2-positive, ER-positive early breast cancer. First Author: Juan Jose Celis, Sociedad Anticancerosa de Venezuela, Caracas, Venezuela (Bolivarian Republic of)

Background: The prevalence of breast cancer in older adults (≥70 years) is increasing and worse outcomes compared to younger patients could be explained by advanced presentation, late diagnosis, deterioration of organ function, and the presence of multimorbidities. Older patients are under-represented in clinical trials. Therefore, the risks and benefits of anticancer therapy should be carefully evaluated. The CREATE-X36 and KATHERINE37 trials enrolled few older individuals but did not show any new safety concerns, older patients should be considered for trastuzumab in case of residual HER2-positive disease following neoadjuvant systemic therapy; neoadjuvant endocrine therapy for at least 4-6 months is useful for older patients who are not immediately suitable for surgery and aromatase inhibitors are favored over tamoxifen in view of better response rate. Although adjuvant trastuzumab is beneficial regardless of age, anti-HER2 (neo)adjuvant strategies remain poorly investigated in patients age 65 years or older. Pertuzumab can be considered for high-risk individuals, but diarrhoea can be debilitating in older adults, similarly with adjuvant neratinib. Age is associated with increased cardiac toxicity rates with trastuzumab,80 with 15–40% of patients requiring early discontinuation, particularly patients who are age 80 years or older and have multimorbidities. **Methods:** Open-label, exploratory, phase 2 study done at one center in Venezuela. Patients were eligible if they had previously untreated, histologically confirmed, unilateral, invasive, cN0, HER2-positive, ER-positive breast cancer and older >70y. Patients were treated every 3 weeks with intravenous trastuzumab (8 mg/kg loading dose followed by 6 mg/kg) and intravenous pertuzumab (840 mg loading dose in the first cycle and then at 420 mg) and intramuscular fulvestrant (500 mg) every 4 weeks for four cycles. The coprimary endpoints were change from baseline in Ki67 expression at surgery and pathological complete response. **Results:** Between January, 2020, and June, 2023, we enrolled 12 patients. At baseline, geometric mean Ki67 expression was 42·9 and 12·1 at time of surgery (n=8; p=0·013). A clinical objective response immediately before surgery was achieved by 10 of 12 patients. At surgery, eight patients had a pathological complete response in breast and axillary nodes. The most frequent grade 3 adverse events was diarrhea (n=4), and stomatitis. No grade 4 or serious adverse events were recorded in the study and there were no deaths. **Conclusions:** The combination of fulvestrant, trastuzumab, and pertuzumab had a effect on the expression of Ki67 and pCR at surgery. Triple targeting of ER, HER2, could be an effective chemotherapy-free treatment strategy for older patiens. Further clinical testing and additional molecular characterisation is necessary. Research Sponsor: None.

14 **Poster Session**

Characterization of estrogen receptor mutant breast cancer in 3D cell culture. First Author: Olivia Mayer, Texas College of Osteopathic Medicine, Fort Worth, TX

Background: Breast cancer is a leading cancer in women worldwide. Many primary breast cancers are estrogen receptor positive (ER+) and responsive to anti-estrogenic therapies. These tumors can mutate estrogen receptors to survive, allowing the tumors to become more triple-negative-like and therefore more dangerous. Triple-negative breast cancer (TNBC) has been particularly challenging to treat due to its lack of estrogen (ER), progesterone (PR), and human epidermal growth factor (HER2) receptors. Due to the lack of treatment options, TNBC has a poor prognosis and contributes to a significant percentage of breast cancer mortalities. These ER mutants act more like TNBC, resulting in worse clinical outcomes. Current research on these ER mutants has been conducted using two-dimensional (2D), monolayer cell culture, which does not translate effectively in animal models, and ultimately, humans. Three-dimensional (3D) cell culture, which allows for the formation of spheroids, mimics actual tumors and provides results more consistent with tumor treatment in vitro. Due to the lack of research on these ER mutants in 3D culture, they must be characterized to determine baseline gene expression and behavior. After characterization, identifying changes resulting from drug treatment will be possible. **Methods:** Parental, ER+ MCF7-Luc cells, and daughter D538G and Y537S mutants were seeded at a density of 3000 cells/well in a low-attachment, round-bottomed 96-well plate. 48 hours and 7 days post-seeding, newly-formed spheroids were imaged. Using ImageJ analysis software, diameter, area, perimeter, circularity, aspect ratio, roundness, and solidity were determined. After 7 days in culture, spheres were collected for RNA extraction. Next, cDNA was synthesized, and qRT-PCR was performed to assess gene expression differences. **Results:** The wild-type ER+ spheres have smaller diameters, spherocity values closer to one, and are more compact. They express different levels of EMT markers from the controls, indicating alterations to signaling pathways. These 3D cultures vary in expression from the 2D cultures of the same cell lines. **Conclusions:** MCF-7 ER+ breast cancer cells aggregate more readily than ER+ mutants. The ER must be involved in signaling that promotes aggregation, as reduced ER signaling decreases the ability for spheroid formation. This phenomenon and the differences in gene expression may explain why mutants tend to behave in a more triple-negative manner. Cells cultured in 3D express some genes to different extents, confirming the importance of 3D culture for identifying future therapies – cells behave differently in different culturing contexts, 3D being more consistent with tumor behavior. Therefore, characterizing ER+ mutants prior to drug treatment studies is crucial to understanding how compounds affect cancer cells, as well as for identifying differences in various ER+ mutants for better treatment outcomes. Research Sponsor: University of Texas North Science Center.

15 **Poster Session**

Reviewing the recurrence rates in stage I-III HR or ER positive breast cancer in obese patients given multi-modal weight loss plan post-treatment with aromatase inhibitors. First Author: Matthew Joseph, UNTHSC Texas College of Osteopathic Medicine, Fort Worth, TX

Background: Aromatase inhibitors (AIs) in the treatment of endocrine recepter positive breast cancer stages I-III, poses significant challenges in the management of obesity. Obesity is not only associated with an increased risk of breast cancer incidence but also with higher rates of cancer recurrence and poorer treatment outcomes. Moreover, the use of AIs, while effective in reducing estrogen levels and preventing ER or HR positive breast cancer recurrence, may exacerbate weight gain and metabolic disturbances in obese individuals. Weight management strategies have experienced increased attention in breast cancer survivors in recent years, especially overweight or obese individuals. Novel data makes it possible to infer that obesity management activities and multimodal programs that incorporate dietary counseling and physical activity can reduce recurrence rates. **Methods:** Participants in this study were individuals with Stage I-III endocrine receptor positive breast cancer who had completed adjuvant therapy and had a BMI in the 40s or 50s, increasing risk of recurrence. Eligible patients were identified based on the start date for endocrine therapy. High-risk patients were then assigned to either the intervention or control group. Those in the intervention group received access to a dietician, along with informational pamphlets on physiology and weight loss strategies. Additionally, they were offered discounts to certain gyms or provided free access to fitness facilities. Both intervention and control groups were briefed about the study, with those in the intervention group encouraged to utilize the provided resources for weight management. **Results:** The evidence from our study will underscore the potential benefits of multimodal weight loss interventions in overweight or obese breast cancer survivors, particularly in improving anthropometric outcomes and enhancing overall quality of life. **Conclusions:** While the studies included in our analysis demonstrated reductions in body weight, BMI, and waist circumference, as well as improvements in quality of life measures, there remains a notable gap in understanding the impact of these interventions on breast cancer recurrence rates, especially in the context of endocrine-positive breast cancer treated with Aromatase Inhibitors (AIs). Research Sponsor: None.

16 **Poster Session**

COVID-19 infection impact on race and clinical outcome of patients with breast cancer: A nationwide analysis. First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide. Recent data showed the detrimental effects of COVID-19 infection on other neoplasm conditions, causing increased mortality rates and complications. However, limited information exists on the specific impacts of COVID-19 infection in patients hospitalized for breast cancer, as well as racial impact differences. **Methods:** We analyzed the 2020 U.S. National Inpatient Sample (NIS) to investigate the effects of COVID-19 infection on cases primarily admitted due to breast cancers. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariable logistic and linear regression analyses. The primary outcome was inpatient mortality, with secondary outcomes including system-based complications. Statistical significance was established at a p-value of 0.05. **Results:** We identified 25,559 patients with a primary discharge diagnosis of breast cancer. The mean age was 59.7 years; 99.28% were female. In the non-COVID group, Caucasians accounted for 60%, followed by African Americans (19%). However, in the COVID-19 group, African Americans predominated with 41%, followed by Caucasian (35%) (p-value = 0.05). Of these, 0.52% (85/25,559) had a concurrent diagnosis of COVID-19 infection. In a survey multivariable logistic and linear regression model adjusting for patient and hospital factors, COVID-19 infection was associated with higher in-hospital mortality (aOR 6.07; 95% CI (1.26, 29.13), p = 0.024), higher mean length of stay(b 5.22; 95% CI (2.08,8.36) p =0.001), acute respiratory failure (aOR 4.88; 95% CI (1.51, 15.77), p = 0.008), coagulopathy (aOR 8.38; 95% CI (2.19, 32.02), p=0.002) and SIRS (aOR 6.38; 95% CI (1.25, 32.50), p = 0.026). We observed non-significant, but increased, risks of acute kidney injury (AKI), shock, and sepsis, as well as total hospitalization costs in COVID-19-positive patients. **Conclusions:** In conclusion, our study underscores that COVID-19 infection is associated with higher in-hospital mortality and other clinical outcomes in breast cancer patients, as well as, a disproportionated impact against some races. Future longitudinal studies are warranted to comprehensively assess the causation of these clinical outcomes in this population. Research Sponsor: None.

18 **Poster Session**

Descriptive and content analysis of breast cancer vlogs on YouTube. First Author: Ari N. Meguerditchian, St. Mary's Research Centre, Montreal, QC, Canada

Background: Vlogs, or "video blogs," are personally-created experiential videos based on wide-ranging topics, usually posted to YouTube. Many women with breast cancer (BC) document their cancer experiences in YouTube vlogs. These may have the potential to serve as peer-to-peer support and provide community. This study provides a descriptive and content analysis of vlogs by women with BC. **Methods:** YouTube was searched in incognito mode in 11/2023 using the search terms "breast cancer vlog." A maximum of 10 videos/creator were included based on viewership and date created. Video characteristics collected included: title, length, number of views, likes, comments, and playlist inclusion. Videos were assessed for sponsorship, presence of explanation and discussion on BC, type of content, and themes. Creator characteristics included age, location, and engagement approaches. Descriptive and content analysis were performed to assess and analyze video content and potential areas where peer-to-peer support may be provided. **Results:** 90 vlogs by 13 creators were included, all originating from personal accounts. Mean video length, number of views, and number of comments were 21.4 minutes (SD 9.1), 266,780 (SD 534,465), and 1485 (SD 3422), respectively. 38.9% included hashtags. 12.2% included paid sponsorships. Most common filming location was at home (96.7%), followed by the hospital (31.1%), or in the car (21.1%). Home vlogs were most often set in the living room (44.3%), bedroom (33.0%), or kitchen (20.6%). 56.7% included visuals of treatment as well as physical findings. Creators addressed motivation for vlogging in 48.9%; the two most common reasons were wanting to build a community and helping others in a similar situation. In 46.7%, creators explicitly expressed emotion. Most common themes were treatment (85.6%), mental health (81.1%), side effects (72.2%), appearance (63.3%), and family relationships (36.7%). Subthemes included young age, finances, and the importance of online community support. Patient-directed advice was offered in 60.0%, mostly on treatment-related issues. In 56.7%, creators provided explicit treatment definitions. Chemotherapy was discussed in 70.0%; surgery in 57.8%, primarily mastectomy; radiation in 30.0%; general side effects in 71.1%. 24.4% were about a new diagnosis. When mentioned (44.4%), most common creator location was the USA. When mentioned (30.0%), most common age demographic was 20-29 years old. **Conclusions:** Vlogs by women with BC receive significant levels of engagement. The dedication to building community demonstrated by vlog creators, and the personal nature of their storytelling, advice, and suggestions, may make these vlogs a potential resource for peer-to-peer support. Research Sponsor: None.

19 **Poster Session**

Exploring depression risk among breast cancer survivors: A nationwide cohort study in South Korea. First Author: Hea Lim Choi, Severance Hospital (Yonsei University Medical Center), Seoul, South Korea

Background: With advances in early diagnosis and treatment, the population of breast cancer survivors globally continues to grow. Depression among these survivors poses a significant concern for their long-term survivorship and overall quality of life. This study aims to investigate the incidence of depression among breast cancer survivors and identify associated risk factors. **Methods:** We used the National Health Insurance Service database of Korea from 2010 to 2016 and examined 59,340 breast cancer survivors and 1:2 age-matched individuals without breast cancer to investigate the incidence of depression. Cox proportional hazards regression was used to calculate the hazard ratio (HR) and 95% confidence interval (CI). The risk of depression was assessed based on age, categorizing individuals as under or over 50 years old. We conducted 1-year, 3-year, and 5-year lag sensitivity analysis to demonstrate changes in risk over time. The study identified risk factors for developing depression through multivariable Cox regression, and Kaplan-Meier analysis was conducted to illustrate the incidence probabilities of depression in breast cancer survivors. **Results:** Breast cancer survivors exhibited a 39% increased risk of depression compared to individuals without breast cancer, and those under the age of 50 years facing higher risk than their older counterparts (HR 1.64, 95% CI 1.58-1.70 and HR 1.23, 95% CI 1.20-1.27, respectively). Chemotherapy (anthracycline and taxane) and endocrine therapy (tamoxifen and aromatase inhibitor) emerged as potential risk factors for depression among breast cancer survivors. Sensitivity analysis revealed a decreasing trend in depression risk over time, particularly among survivors aged older than 50 years. **Conclusions:** This study highlights a significant increase in depression risk among breast cancer survivors, particularly those under 50 years old. Specific treatments such as chemotherapy and endocrine therapy were identified as potential risk factors. These findings emphasize the necessity for targeted interventions and support strategies to address the heightened risk of depression in breast cancer survivors, ultimately improving their long-term well-being and quality of life. Research Sponsor: None.

TPS22 **Trials in Progress Poster Session**

OPERA-01: A randomized, open-label, phase 3 study of palazestrant (OP-1250) vs standard-of-care for patients with ER+, HER2- advanced or metastatic breast cancer after endocrine therapy and CDK4/6 inhibitors. First Author: Joohyuk Sohn, Division of Medical Oncology, Yonsei Cancer Center, Seoul, South Korea

Background: In estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2−) metastatic breast cancer (MBC), endocrine therapy (ET) plus a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i) is the standard-of-care (SOC) treatment in the first-line setting. However, patients develop resistance, most commonly due to acquired mutations in *ESR1*. Efficacy of available ET post CDK4/6i treatment is limited. Therefore, a significant unmet need exists for patients with ET-CDKi-resistant ER+, HER2− MBC to improve outcomes and delay time to chemotherapy. Palazestrant is an oral small molecule complete ER antagonist (CERAN) and selective ER degrader (SERD) that binds ER and completely blocks ER-driven transcriptional activity, irrespective of *ESR1* mutation status. In a phase 1/2 monotherapy study in heavily pretreated patients with ER+, HER2− advanced or MBC (NCT04505826), palazestrant showed a tolerable safety profile, favorable pharmacokinetics and encouraging antitumor efficacy in patients with and without *ESR1* mutation at the recommended Phase 2 dose of 120 mg once a day (qd) (Lin et al. ESMO 2023 MO382). **Methods:** OPERA-01 (NCT06016738) is a multicenter, randomized, open-label, phase 3 clinical trial comparing the efficacy and safety of palazestrant as a single agent to SOC ET (fulvestrant, anastrozole, letrozole, or exemestane) in patietns with ER+, HER2− MBC that relapsed or progressed on 1-2 prior lines of ET, including a CDK4/6i. Eligible patients are adults who have a confirmed diagnosis of evaluable ER+, HER2− inoperable locally advanced or MBC and an Eastern Cooperative Oncology Group performance status of 0 or 1. Prior treatments must include 1-2 prior lines of ET, last ET duration for $\geq$6 months; must have received CDK4/6i with ET and have disease progression during or within 28 days of completion of each line of prior treatment for MBC. No prior chemotherapy in the metastatic setting is permitted. In the dose selection part of the study, 120 patients are randomized to 90 mg qd or 120 mg qd palazestrant or SOC monotherapy. The dose selection will be conducted when 80 patients in both palazestrant arms have had an opportunity to be on treatment for 16 weeks. Overall, 510 patients, including patients from the dose selection part, will be randomized to palazestrant or SOC ET. The primary endpoint of progression-free survival will be assessed by blinded independent central review in patients with and without *ESR1* mutations in the intent-to-treat population. Secondary endpoints include overall survival, antitumor activity (objective response rate, clinical benefit rate, and duration of response), safety, patient-reported outcomes, and PK in patients with and without *ESR1* mutations. The study started recruitment in November 2023. Clinical trial information: NCT06016738. Research Sponsor: Olema Oncology.

23 Rapid Oral Abstract Session

An exploratory investigator-initiated trial via intrathecal or intracerebroventricular delivery of B7H3-specific allogeneic universal CAR-T cells in patients with recurrent high-grade gliomas. First Author: Xiaoyun Shang, T-MAXIMUM Pharmaceutical (Suzhou) Co., Ltd., Suzhou, China

Background: The MT027, developed by T-Maximum, is a B7-H3 (CD276)-directed genetically modified allogeneic T cell, targeting CD276-overexpressed tumor cells. Here, we reported a first-in-human, single-center, open-label investigator-initiated trial (IIT) via intrathecal or Intracerebroventricular delivery targeting recurrent high-grade glioma (ChiCTR2100047968). **Methods:** As of March 7, 2024, a total of 50 adult patients with recurrent high-grade glioma, B7H3+ expression, and KPS $\geq$40 were enrolled and administered at least one dose of MT027 (FAS), of whom, 32 received at least 3 doses (PPS1), 15 subjects with $\geq$3 doses and at least 1 efficacy visit (PPS2). 4 dose levels of 1.0, 1.5, 2.0, 2.5×10^7 cells per injection were administered once every 4 weeks. **Results:** The overall results demonstrated the favorable tolerability, safety, PK/PD characteristics, and preliminary efficacy. In FAS, the most common AE were fever and headache, without any CRS, ICANS, GvHD, or drug-related death. There were 4 cases (8%) of grade 3 AE or greater and 3 cases (6%) of SAEs. The copies of CAR in all groups reached 10000-100000 copy/ug, and persisted for $>$ 60 days after a single dose. After multiple doses, the MT027 CAR-T cell numbers maintained at a high level (median 8850 copies /μg (range: 200-385900)) and for a long time. The levels of IL6, TNF-α and IFN-γ in CSF increased significantly and maintained for a long time. The mOS was 13.54 m (95% CI: 7.45; 19.63) and 20.73 m (95% CI: 16.12; 25.34) in PPS1 and PPS2, respectively. The 12-month OS rate was 53.30% (95%CI: 37.5%-75.7%) and 84.60% (95%CI: 67.1%-100%) in PPS1 and PPS2, respectively (historical data: 14%). The objective response rate (ORR) was 33% and the disease control rate (DCR) was 80% in PPS2. **Conclusions:** In patients with relapsed high-grade glioma, the intrathecal or ICV administration of MT027 cell therapy was found to be safe and well-tolerated. The toxicity of grade 3 or above was 1/5 of similar products. The pharmacokinetics and pharmacodynamics of single-dose and multiple-dose treatments were stable. MT027 exhibited longer persistence in the body of the patients, and the cell numbers and cytokine responses induced in vivo were 1-2 orders of magnitude higher than those of similar products. MT027 cell therapy demonstrated the excellent efficacy in treating relapsed high-grade glioma, with significantly prolonged overall survival and higher objective response rate compared to the historical data and similar product data. Currently, we are preparing for the IND filing in US (expected in 2024) with the recurrent glioblastoma as the first indication. Clinical trial information: ChiCTR2100047968. Research Sponsor: None.

24 Poster Session

The candidate novel markers PIV and PILE score to predict survival outcomes and therapeutic response in patients with primary central nervous system lymphoma. First Author: Ling Duan, Capital Medical University, Beijing Tiantan Hospital, Beijing, China

Background: Recent studies highlighted the predictive value of easily measurable blood-based biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR), the monocyte-to-lymphocyte ratio (MLR), the platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation index (SII). Recently, a novel comprehensive marker that represents the pan-immune-inflammation value (PIV) has been proposed as a more reliable predictor of clinical outcomes. We aimed to investigate the prognostic significance of PIV and PILE score (a score based on PIV, lactate dehydrogenase (LDH), and Eastern Cooperative Oncology Group Performance Status (ECOG PS)), in patients with PCNSL. **Methods:** A total of 109 patients were enrolled. PIV was calculated as follows: (neutrophil count $\times$ platelet count $\times$ monocyte count)/lymphocyte count. The PILE score was calculated with the sum of individual values (for PIV $<$ median = 0, $\geq$ median = 1; for LDH $\leq$ upper limit of normal (ULN) = 0, $>$ ULN = 1; for ECOG PS $<$ 2 = 0, $\geq$ 2 = 1). The Kaplan–Meier method and Cox hazards regression models were used for survival analyses. The relationship between PIV, PILE, and therapeutic response was examined. **Results:** Pretreatment high PIV was confirmed to be an independent significant factor for overall survival (OS) in univariate (HR 3.990, 95%CI 1.778-8.954, $p < 0.001$) and multivariate (HR 3.047, 95%CI 1.175-7.897, p = 0.022) analyses. Baseline PIV was also associated with worse progression-free survival (PFS). Regarding OS, PIV showed a better predictive performance than other widely used systemic inflammation parameters. Significantly shorter OS and PFS were observed in the high PILE group (median OS: 25.60, 95% CI 15.60-NR vs. NR months, 95% CI 26.10-NR, p = 0.008; median PFS: 26.13, 95% CI 23.30-NR vs. 7.13 months, 95% CI 4.87-NR, $p < 0.001$). High PILE was associated with primary resistance to therapy (high PILE group: 21/42 patients, 50.00%; low PILE group: 5/45 patients, 11.11%; $p < 0.001$). A significantly lower response rate to initial treatment was found in patients in the high PILE group (23/42, 54.76%) as compared to patients in the low PILE group (7/45, 15.56%; $p < 0.001$). PILE was independently associated with therapeutic response to initial treatment (OR 0.17, 95% CI 0.05–0.46; $p < 0.001$). **Conclusions:** High PIV and high PILE were correlated with worse clinical outcomes in PCNSL patients, indicating that PIV and PILE might be a powerful predictor of prognosis and a potential predictive indicator for treatment response in PCNSL. Research Sponsor: None.

25 Poster Session

Unsupervised clustering of brain tumor leukocytes to reveal atypical lymphoid cell subsets. First Author: Ismaïl Hermelo, Prostate Cancer Research Center, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

Background: The brain tumor immune microenvironment (TiME) is characterised by suppression of tumor-infiltrating leukocytes. The lymphocyte niche activity is particularly downregulated within this TiME milieu. **Methods:** Here, using data-driven approaches in flow cytometry and RNA sequencing analysis, we aimed at dissecting leukocyte cell types infiltrating human brain tumor TiME. **Results:** Unsupervised clustering provided T lymphocyte subsets including double-negative ($CD3^+CD4^-$ $CD8^-$) T cells (DNT). Our DNT phenotype was validated with an independent dataset, suggesting DNT to be compatible with $\gamma\delta$ T cell phenotype. In our cohort, myeloid immune cell frequencies were associated with malignancy type as previously reported, while a gliosarcoma notably presented unexpectedly high lymphocyte frequencies. Consistently, double-positive ($CD4^+$ $CD8^+$) T cells (DPT) had higher frequency in the gliosarcoma than other tumors. The flow cytometry results were supported by transcriptome patterns and the activity of immune-related genes in these tumors. **Conclusions:** Our findings feature the benefit of data-driven approaches for brain TiME lymphocyte analysis, and show that primary brain tumors can entail atypical lymphocyte subsets like DNTs and DPT cells. Unbiased lymphocyte characterisation can potentially outline novel targets for immune checkpoint blockade therapy. Research Sponsor: Research Council of Finland.

26 Poster Session

Exploratory study of PD-1 inhibitors for recurrent meningioma. First Author: Yali Wang, Capital Medical University, Beijing Tiantan Hospital, Beijing, China

Background: Meningiomas are the most common primary intracranial tumor. Some patients still have poorly controlled conditions after multiple surgeries and radiotherapies. More effective treatment methods are urgently needed. Previous studies have suggested that meningioma may shape an inhibitory tumor immune microenvironment and achieve immune escape by expressing programmed cell death ligand 1 (PD-L1) and other factors. Immune checkpoint inhibitors (ICIs) such as PD-1 inhibitors have shown promising efficacy in cases, but large-sample studies are needed to confirm these findings. **Methods:** Recurrent meningioma patients were included and treated with PD-1 inhibitors until tumor progression or intolerance occurred. The efficacy evaluation of enrolled patients used the Response Assessment in Neuro-Oncology (RANO) criteria. The primary endpoint was progression-free survival at 6 months (PFS-6), and secondary endpoints were progression-free survival at 12 months (PFS-12) and overall survival (OS). Adverse events were also recorded. Regular imaging follow-ups were conducted, and clinical characteristics were collected for survival analysis. Peripheral blood lymphocyte subsets and cytokines were detected before and after treatment, and tumor paraffin sections were used for immunohistochemical detection of relevant molecular markers. **Results:** A total of 35 recurrent meningioma patients (10 grade I, 14 grade II, 11 grade III) were included. Among all grades of patients, the median PFS was 9 months, PFS-6 was 63.6%, and PFS-12 was 47.6%. In grade I patients, the median PFS was 14 months, PFS-6 was 83%, and PFS-12 was 67%. In grade II/III patients, the median PFS was 9 months, PFS-6 was 58.9%, and PFS-12 was 42%. Among all grades of meningioma patients, PFS was significantly correlated with Ki-67 index (P = 0.021) and tumor progression times (P = 0.019). In grade II/III meningioma patients, PFS was only correlated with tumor progression times (P = 0.012). Twenty-five patients had stable disease, and seven patients had disease progression, with no patient achieving partial or complete remission. There was no significant correlation between tumor mutation burden (TMB) and PFS. Further immunohistochemical analysis of tumor tissues in three recurrent high-grade patients revealed varying degrees of increase in local CD3+, CD4+, CD8+ and PD-1+ T lymphocytes after treatment compared to baseline. **Conclusions:** Our study suggests that PD-1 inhibitors may prolong PFS in recurrent meningioma patients (especially high-grade) with good drug safety, warranting further exploration. Recurrent meningiomas have an immunosuppressive tumor microenvironment, and PD-1 inhibitors may improve the immune status of tumor microenvironments. Clinical trial information: NCT04728568. Research Sponsor: None.

27 **Poster Session**

The use of adjuvant radiotherapy in resected adult intracranial atypical meningioma in United States: A SEER analysis. First Author: Jayson L. Co, London School of Hygiene and Tropical Medicine, University of London, London, United Kingdom

Background: It is unclear whether adjuvant external beam radiotherapy (EBRT) in atypical meningiomas after surgical resection provided overall survival advantage. Although meta-analysis were previously reported, there is heterogeneity in the included studies. With lack of prospective trial, we rely on observational data for management. This project aims to determine if the addition of adjuvant EBRT after resection compared to resection alone in atypical meningioma is associated with better prolonged survival among patients within United States. **Methods:** The National Cancer Institute Surveillance, Epidemiology and End Results database was queried for list of patients diagnosed with atypical meningioma from 2000 to 2020 according to International Classification of Disease (ICD) for Oncology, third edition with morphology codes 9539/0 and 9539/1.This was limited to intracranial location. Rate of dying among those receiving adjuvant EBRT after surgery for atypical meningiomas was compared to the rate of dying of those who had resection alone without adjuvant EBRT postoperatively. Other covariates included, age at diagnosis, gender, marital status, race, tumor laterality, tumor site, tumor, extent of resection and household median income. Chi-squared test was used to test the association between institution of adjuvant EBRT and other co-variates for categorical variable. Cox-proportional analysis was used to test the association between adjuvant EBRT and death. Observed survival was estimated using Kaplan-Meyer method. Survival curves were generated for both cohorts and log rank test was performed. **Results:** A total of 3,328 patients were included in analysis.1,004(30.17%) patients received adjuvant EBRT and 767(23.05%) died in the entire cohort. Rate of dying in the entire cohort is 43.84 per 1,000 person-years. Death rate for patients receiving adjuvant EBRT is 44.95 per 1,000 person-years, while patients who did not receive adjuvant EBRT had a death rate of 40.95 per 1,000 person-years. Patients aged 80 years or older, divorced and separated tend not to receive adjuvant EBRT, while patients with tumor size of 51-100mm and 101-200mm are more likely to receive adjuvant RT. Crude rate ratio among those patients receiving RT compared to the rate of those who did not receive adjuvant RT is 0.91 (95% CI: 0.76-1.07). Adjusting for possible confounders did not change the rate ratio between adjuvant EBRT compared to resection alone. Extent of resection did not modify the effect of adjuvant RT to death (likelihood ratio test-0.363). Survival analysis using Kaplan Meier curve showed no difference whether a patient received adjuvant EBRT or not (log rank test-0.238). **Conclusions:** There is no clear evidence on the survival benefit for use of adjuvant EBRT in resected atypical meningioma compared resection alone. This is true both in incomplete and completely resected atypical meningiomas. Research Sponsor: None.

28 **Poster Session**

Examining molecular landscape and drug sensitivity profiles of patient-derived xenografts from resected brain metastases. First Author: Aki Morikawa, University of Michigan, Ann Arbor, MI

Background: Brain metastases (BrMet) remain an unmet need. Preclinical models of BrMet are rare but can be a valuable tool to interrogate pathology and develop novel therapeutic approaches. We previously published molecular profiles and drug sensitivity screening using novel BrMet patient-derived xenograft (PDX) models established from resected BrMet from patients with breast cancer. We further expanded our study to include BrMet from other solid tumors. **Methods:** We ascertained the genomic profiles of thirteen novel non-breast BrMet PDX models from patients undergoing clinically indicated surgical resection of BrMet. We then conducted drug sensitivity screening on ex vivo organoids with a panel of over 350 drugs to interrogate drug responses. We also collected information on molecular alterations and clinical treatment history from matched source patient material to correlate molecular alterations between tissue and matched PDXs when available, as well as with drug response in PDXs. **Results:** The PDXs included tumors that commonly (lung and melanoma) and less commonly (ovarian and sarcoma) metastasize to the brain. We observed potentially targetable DNA alterations in the DNA damaging repair pathway (*ATM, BRCA, CHEK2)* and *ERBB2*. Using the drug sensitivity score 3 (DSS3), we assessed the sensitivity of the drugs tested. While the panel did not include the recently approved anti-HER2 targeted drugs, lapatinib (anti-HER2 TKI), and PARP inhibitors, e.g. olaparib and niraparib, were inactive against these PDXs. The three most active drugs among the BrMet PDXs were romidepsin, bortezomib, and triptolide, similar to what we observed previously for breast BrMet PDXs. When available, we correlated the DSS3 from the PDX testing with the drug exposure history and potentially actionable alterations reported in the matched source patient clinical samples. Interestingly, one case with CDKN2A/1B homozygous deletion had differential sensitivity against CDK inhibitors (highly active to dinaciclib but inactive to abemaciclib and palbociclib). **Conclusions:** We observed prevalent gene alterations associated with homologous recombination deficiency and HER2 among these non-breast BrMet PDX models, opening an opportunity for novel cross cancer approaches as these alterations are also reportedly linked to BrMet from breast cancer, these mechanisms may contribute to the propensity for BrMet. We also found that there are common drugs that are active across BrMet from different solid tumor types. To further explore the shared molecular features of BrMet across various solid tumors, we have established additional PDX models (near 100) from multiple solid tumors and plan to report on the molecular features. Research Sponsor: Breast Cancer Research Foundation; National Institutes of Health.

29 **Poster Session**

In-hospital outcome of central nervous system malignancy with COVID-19 infection: Analysis from National Inpatient Sample (NIS). First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Previous research highlights central nervous system (CNS) malignancy as significant contributors to disability-adjusted life-years. However, there's a lack of information on the impact of COVID-19 infection in hospitalized CNS malignancy patients. **Methods:** Using the 2020 U.S. National Inpatient Sample (NIS), we investigated the impact of COVID-19 infection affected patients primarily hospitalized for CNS malignancy. We calculated adjusted odds ratios (aORs) for specific outcomes using multivariable logistic and linear regression analyses. The primary outcome was inpatient mortality, with secondary outcomes including system-based complications. **Results:** We identified 37,385 patients diagnosed with CNS malignancy, averaging 53.6 years old, with 57.76% being female. Among them, 0.84% (315/37,385) were also diagnosed with COVID-19. After adjusting for patient and hospital factors, COVID-19 infection was linked to higher in-hospital mortality (aOR 4.12, 95% CI: 1.55, 10.89, p = 0.004), longer stays (Beta-coefficient 6.06, 95% CI: 2.97, 9.14, $p < 0.001$), increased total hospital costs (Beta-coefficient 11,855, 95% CI: 1,410, 22,301, p = 0.026), elevated risks of shock (aOR 3.96, 95% CI 1.03, 15.10, p = 0.018), acute respiratory failure (aOR 4.33, 95% CI: 1.83, 10.22, p = 0.001), and sepsis (aOR 3.96, 95% CI: 1.03, 15.10, p = 0.044). **Conclusions:** Our study reveals that COVID-19 infection is associated with higher in-hospital mortality and multiple adverse outcomes in patients hospitalized for CNS malignancy. Further longitudinal studies are necessary to thoroughly investigate the causality of these clinical outcomes in this population. Research Sponsor: None.

30 **Poster Session**

Bruton's tyrosine kinase inhibitor zanubrutinib-based regimens in relapsed/refractory primary diffuse large B-cell lymphoma of central nervous system. First Author: Yali Wang, Beijing Tiantan Hospital, Beijing, China

Background: Patients with relapsed/refractory primary central nervous system lymphoma (R/R PCNSL) usually have a poor prognosis. Ibrutinib-based regimens revealed promising efficacy but showed off-target effects and drug resistance in some cases. Here, we conducted a retrospective study to evaluate the efficacy and safety of regimens based on second-generation bruton's tyrosine kinase (BTK) inhibitor zanubrutinib in R/R PCNSL. **Methods:** We respectively reviewed 23 patients with R/R PCNSL treated with zanubrutinib in our center from Apr. 2021 to Jan. 2024. The primary end points were overall response rate (ORR) and progression-free survival (PFS). Secondary end points included complete response rate (CRR), disease control rate (DCR), overall survival (OS) and adverse events (AEs). Response was assessed according to International Primary CNS Lymphoma Collaborative Group criteria. The severity of AEs was graded using the NCI Common Toxicity Criteria, version 5.0. Validated next-generation sequencing (NGS) panels were used to analyze the mutational status of the BCR pathway genes or other solid tumor-related genes. **Results:** The median follow-up at the cutoff date (15 Jan 2024) was 17.0 months (range, 2-33 months). The ORR, CRR and DCR were 78.3%, 39.1% and 91.3%. The median PFS was 31.0 months, but the median OS was not reached. Compared to germinal center B-cell like (GCB) group, non-GCB group showed a better ORR (76.9% vs 66.7%) and CRR (46.2% VS 33.3%). Multivariate analysis revealed that overall response (vs. no response, HR=0.20, P=0.027), long duration of zanubrutinib ($\geq$6months vs. 2-5 months, HR=0.07, P=0.009) and refractory disease status (vs. relapse disease status, HR=0.12, P=0.014) were independent factors for longer PFS. The most commonly mutated genes are MYD88(15/17,88.2%), PIM1(9/17 52.9%), CD79B (8/17,47.1%), ETV6(7/17,41.2%), BTG1(5/17,29.4%) and GNA13(5/17,29.41%). The mutational status of MYD88/CD79B did not lead to any difference in PFS and OS. We obtained the Tumor Mutational Burden (TMB) information from 11 patients. The median TMB was 15.96 (range: 3.82-28.11) muts/Mb. Kaplan-Meier analysis demonstrated that PFS was significantly longer in patients with higher TMB ($\geq$15.96 muts/Mb) after zanubrutinib-based treatment(P=0.005). Grade $\geq$3 and serious treatment-emergent AEs (TEAEs) were not found. The most commonly TEAEs were hematologic toxicity (8/23,34.8%) and skin rash (5/23,21.7%). **Conclusions:** Our study demonstrates that zanubrutinib-based therapy is effective and safe for the treatment of R/R PCNSL. We advocate for the prolonged administration of zanubrutinib to maintain treatment response. Patients with higher TMB derive greater benefits from zanubrutinib-based regimens. Research Sponsor: None.

31 **Poster Session**

Implementation of hippocampal sparing whole brain radiotherapy in a resource-limited setting. First Author: David Dai-Wee Lee, University of Malaya, Kuala Lumpur, Malaysia

Background: Whole brain radiotherapy (WBRT) is a common treatment for brain metastases, but it often leads to cognitive decline due to hippocampal damage. Hippocampal avoidant technique has emerged to mitigate this cognitive toxicity. Our institution began hippocampal-avoidant WBRT (HA-WBRT) in 2021. We report our experience in implementing this technique in a resource-limited setting. **Methods:** We reviewed the medical records of patients who underwent HA-WBRT in our institution between January 2021 and March 2024. Clinical characteristics, treatment details, and dosimetry were reviewed. Hippocampal sparing was achieved using volumetric-modulated arc therapy (VMAT). **Results:** A total of 11 patients were included in the analysis. The median age was 57 years old, with a male-to-female ratio of 3:8. Most patients had metastatic breast cancer (7/11) followed by lung cancer (2/11). Among the breast cancer patients, 5 of them had HER2 positive subtype. Ten patients had good performance status (ECOG 0). Most patients (8/11) were treated with 20Gy in 5 fractions (with or without boost to tumor), and 3 patients with 30Gy in 10 fractions. The median time from CT simulation to treatment was 20.5 days. The target volume and organ-at-risk contouring were performed as per the AROMA trial (20Gy in 5 fractions) or RTOG 0933 study (30Gy in 10 fractions). The median beam-on time was 5.61 minutes. Nine patients completed WBRT with minimal acute toxicities. Two patients did not complete treatment due to a decline in performance status. Most patients were treated in multiple institutions thus, follow-up data was scarce. **Conclusions:** In our experience, HA-WBRT is feasible for suitable patients. Patients that benefit from this technique are younger, have good performance status, and have longer life expectancy e.g. breast primary. The challenges of implementing this treatment are a longer time for contouring and treatment planning, and longer treatment time compared with 2D or 3D WBRT. Long-term follow-up is needed to validate the benefit of this technique. Patient selection is key in implementing HA-WBRT in a resource-limited setting. Research Sponsor: None.

TPS32 **Trials in Progress Poster Session**

Exploratory phase I study of HF1K16 for the treatment of patients with refractory/recurrent advanced glioma. First Author: Ruofan Huang, Huashan Hospital, Fudan University, Shanghai, China

Background: Glioblastoma (GBM) is the most common primary and aggressive malignant brain tumor in adults. Almost all patients with glioblastoma eventually have disease relapse and the median overall survival (OS) remains at only 30 weeks for those recurrent GBM patients. However, very few therapies had been approved over the past two decades, emphasizing the need for novel treatments. It is now wildly acknowledged that the immune microenvironment in brain offers adequate opportunities to implement immunotherapy for the treatment. Since most recurrent tumors had previously been exposed to the genotoxic stress of irradiation and/or chemotherapy, it is predicted to resulted in a higher mutational load and more immunogenic. However, The limited success of T cell immunomodulatory approach for advanced glioma has prompted a deeper understanding of the brain tumor and the immune microenvironment. GBM tumors are well-appreciated to be a immunosuppressive and a hallmark of GBM immunosuppression is the appearance of circulating myeloid-derived suppressor cells (MDSCs) at higher levels. Our preliminary data suggests that HF1K16, a liposome ATRA (all trans retinoic acid) suspension, is capable of relieving immune suppression induced by MDSCs. Further, we recently completed a phase I dose escalation study which showed that HF1K16 is safe, well-tolerated with preliminary efficacy in brain tumor. Thus, we hypothesized that HF1K16 may reverse GBM-associated immune suppression and leading to an increase in TILs and improved survival. **Methods:** This is an advanced glioma-specific expansion arm for adult patients with prior confirmed brain tumor and failed standard treatment. We plan to enroll 20~30 evaluable patients. Key eligibility criteria include candidates age $\geq$ 18 years, Karnofsky performance status $\geq$ 60 with and at least one measurable lesion. The primary endpoint is determination of overall response rate (ORR), duration of response (DOR), disease control rate (DCR) and progression-free survival (PFS) according to RANO criteria. Secondary endpoints include longitudinal assessment of the peripheral immune response by changes in MDSC and T cell subsets and numbers. HF1K16 infusions were administered in 21-day cycles (q.o.d days 1-14). Prior to and during treatment, peripheral blood mononuclear cells were collected and analyzed with flow cytometry to monitor the changes in myeloid cell phenotype and T cell composition. The recruitment of patients is anticipated completed in 2024. Clinical trial information: NCT05388487. Research Sponsor: None.

TPS33 **Trials in Progress Poster Session**

An investigator-initiated trial to evaluate safety and tolerability of YSCH-01 in patients with recurrent glioblastoma. First Author: Hafiz Khuram Raza, Shanghai Yuansong Biotechnology Co., Ltd., Shanghai, China

Background: Glioblastoma (GBM), accounting for 55% of primary malignant brain tumors, is characterized by its highly aggressive nature, poor prognosis, and high recurrence rate. Surgical resection is the primary treatment, yet recurrence is common, and survival rates remain dismal. Recurrent GBM lacks established interventions and standardized therapies. YSCH-01 is an oncolytic adenovirus, developed based on cancer-targeting gene-viro-therapy strategy (1), that has been incorporated with an interferon-like immune anticancer gene (L-IFN). Our preclinical studies have demonstrated significant tumor inhibition by YSCH-01 in both cell-line derived xenograft and patient-derived xenograft models (2). This investigator-initiated trial aims to evaluate the safety and efficacy of YSCH-01 in subjects with recurrent GBM. **Methods:** Six subjects with recurrent GBM are planned to be enrolled, receiving intracranial injections of YSCH-01 via Ommaya reservoir at a dosage of 5.0$\times$1010 VP, once every 3 weeks for a total of 5 administrations, with a dose-limiting toxicity (DLT) assessment period of 3 weeks. Ommaya reservoir implantation will precede drug administration by one day. Inclusion criteria specify pathology-confirmed recurrent GBM, age 18-75 years, expected survival $\geq$ 12 weeks, and Karnofsky Performance Status (KPS) score $\geq$ 50 points, with at least one enhanced lesion of $\geq$ 1 cm diameter. Safety will be evaluated based on DLT and adverse events (AEs) assessed using CTCAE 5.0. Efficacy will be assessed every 5 weeks using Response Assessment in Neuro-Oncology (RANO) criteria, with overall survival follow-up at 12 weeks for two years. Two of the planned six cases have been enrolled, completing the DLT period without DLTs. The trial is registered with Clinical Trial Registry under NCT05914935. Clinical trial information: NCT05914935. Research Sponsor: Investigator initiated trial (IIT) project on Hospital-Enterprise Cooperation; 2021-KY-16-03; Academician Expert Workstation Grants; 19R1002275468; Shanghai science and technology support project on biomedicine in the action plan of Science and Technology Innovation; 19431904200.

34 Rapid Oral Abstract Session

Phase Ib trial of durvalumab plus tremelimumab in combination with particle therapy in patients with advanced hepatocellular carcinoma with macrovascular invasion: DEPARTURE trial. First Author: Keisuke Koroki, Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

Background: The HIMALAYA trial established the combination of durvalumab and tremelimumab (STRIDE) as first-line treatment for advanced hepatocellular carcinoma (HCC). Carbon ion radiotherapy (C-ion RT) allows precise tumor targeting while sparing nearby normal tissue. Our strategy used C-ion RT to target a key tumor with macrovascular invasion (MVI) for disease management and potential MVI control, complemented by STRIDE. Recognising that C-ion RT stimulates immune responses, we posited that merging C-ion RT with STRIDE might enhance therapeutic effects. We present updated data of additional follow-up. **Methods:** This is a Phase Ib, multicenter study evaluating durvalumab with particle beam radiotherapy in HCC patients with MVI (Cohort A) and STRIDE (Cohort B). Both cohorts began with patients resistant to standard treatments. After safety confirmation, the study expanded to include therapy-naïve patients, totaling 15. C-ion RT begins after day 8 of the first cycle, following the initial drug dose. The relative biological effectiveness weighted dose is set at 60 Gy in four fractions over one week, targeting one representative intrahepatic nodule with MVI. The primary endpoint is adverse event rates, including dose limiting toxicity (DLT), with secondary endpoints on progression free survival (PFS) and overall survival (OS) (jRCT2031210046). This analysis of OS was conducted from the additional follow-up data from the primary analysis. **Results:** From July 2021 to January 2023, 15 advanced HCC patients were enrolled in our study (Cohort A: 3, Cohort B: 12). Four in Cohort B were systemic therapy-naïve. All cases confirmed MVI radiologically; with tumor invasion observed in the main portal vein for 4 patients and in the inferior vena cava for one. DLT evaluations in 3 from each cohort showed no incidents. While Cohort A had no adverse events, 4 patients in Cohort B (26.7%) experienced serious treatment-related adverse events. The median PFS was a significant 4.67 months (95%CI, 1.35–6.64). At the clinical cut-off date of March 31, 2024, 10 OS events were observed. The median OS was 10.4 months (95% CI, 5.6–15.2), and the 6- and 12-month OS rates were 66.7% and 46.7%, respectively. **Conclusions:** The safety of STRIDE in combination with particle therapy has been confirmed in advanced HCC with MVI. This combination, especially the irradiation of tumors with MVI using C-ion RT, holds promise in managing prognostic determinant tumors and potentially enhancing OS. Clinical trial information: jRCT2031210046. Research Sponsor: Astrazeneca.

36 Poster Session

Efficacy and safety of surufatinib plus toripalimab in previously treated advanced tumors progressing after immunotherapy. First Author: Panpan Zhang, Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Early Drug Development Centre, Peking University Cancer Hospital & Institute, Beijing, China

Background: Immunotherapy has resulted in significant and lasting clinical responses in non-small lung cancer (NSCLC), esophagus cancer, gastric cancer, colorectal cancer etc. However, most patients (pts) inevitably lose efficacy due to acquired resistance. This study (NCT04169672) aimed to investigate the efficacy and safety of surufatinib (a multi-kinase inhibitor of VEGFR1-3, FGFR1 and CSF1R) plus toripalimab (monoclonal humanized IgG4 programmed death 1 [PD-1] antibody) in pts with advanced solid tumors. Here, we reported the results from pts who bore different tumors and failed in previous treatments containing the checkpoint inhibitors. **Methods:** Eligible pts were 18~75 years old who had advanced solid tumors and received prior PD-1/programmed death-ligand 1 (PD-L1) antibody therapy for at least 3 months (m) before disease progression. Enrolled pts received surufatinib 250 mg orally once daily and toripalimab 240 mg intravenously every three weeks in a 21-day cycle. The primary endpoint was the objective response rate (ORR) per RECIST v1.1. Secondary endpoints include disease control rate (DCR), progression free survival (PFS), overall survival (OS) and safety. **Results:** As of data cutoff (Feb 28, 2023), a total of 28 pts were enrolled and received at least one dose of study treatment. Pts with PD-L1 combined positive score (CPS) $\geq$1 accounted for 67.9%. 9 pts were diagnosed with gastric cancer /gastroesophageal junction adenocarcinoma (GC/GEJ), 4 pts each with esophageal cancer, NSCLC or intestinal cancer, 2 pts with biliary tract cancer, 1 pt each with other 5 tumors. 39.3% of pts received $\geq$2 previous anti-tumor therapies. A variety of PD-1 antibodies were used before enrollment, which included tislelizumab (25.0%), sintilimab (17.9%), camrelizumab (14.3%), toripalimab (14.3%), pembrolizumab (7.1%), nivolumab (3.6%), etc. The median exposure duration was 4.1m for study treatment. In 27 tumor evaluable pts, the confirmed ORR and DCR were 7.4 % and 66.7%, respectively. In 28 intent-to-treat pts, the median PFS and OS were 3.94m (95% CI 1.38, 4.21) and 13.04m (95% CI 8.64, 21.59), respectively. The median survival follow-up duration was 20.90m (95% CI 16.10, 25.03). In 9 pts with GC/GEJ, the median PFS and median OS were 2.72m and 13.69m, respectively. Treatment related adverse events (TRAE) occurred in 89.3% of pts. Grade$\geq$3 TRAEs occurred in 39.3% of pts with blood pressure increased (10.7%) and liver injury (7.1%) reported most commonly. 28.6% of pts had immune-related adverse events, among which immune-related pneumonitis (7.1%) and immune-related diabetes (7.1%) reached G3. Two TRAEs led to surufatinib discontinuation. No deaths related to either surufatinib or toripalimab. **Conclusions:** Surufatinib plus toripalimab showed antitumor activity and a manageable safety profile in pts with advanced solid tumors progressing after immunotherapy, especially in GC/GEJ. Research Sponsor: Science and Technology Innovation – Biomedical Science and Technology Support Project; 20S11907500; HUTCHMED Limited.

37 Poster Session

Hypoxia-responsive synthetic gene circuits to improve safety and potency of CAR T cell therapy for solid tumors. First Author: Yannick Schreiber, Northwestern University, Evanston, IL

Background: Engineered cell therapies expressing a chimeric antigen receptor (CAR) in human T cells have demonstrated great promise for the treatment of hematological malignancies. However, unique challenges remain in translating the success of CAR T cell therapies to solid tumors, namely: (1) *specificity*: there are few truly unique antigens present on solid tumors, leading to off-target effects that damage normal tissue and pose safety risks; and (2) *suppression:* solid tumors develop microenvironments that are immunosuppressive and decrease T cell survival and tumor-directed cytotoxicity. To address these challenges and improve the safety and potency of solid tumor cell therapy, we engineered cells with synthetic genetic circuits containing a previously validated hypoxia biosensor (HBS) that responds to upregulation of the native HIF1α and HIF2α transcription factors by hypoxia, enabling the cells to sense and respond to the hypoxic tumor microenvironment ubiquitous among solid tumors. **Methods:** We evaluated CAR expression from circuit architectures containing the HBS promoter driving expression of both CAR and native HIF1α, HIF2α, as well as from circuit architectures containing the HBS promoter and our toolkit of synthetic transcription factors and promoters. Circuits were integrated into HEK293 cells via *PiggyBac* transposon vector to generate stable cell lines. Cells were subsequently cultured in normoxia (21% O_2) and hypoxia (1% O_2), and harvested for flow cytometric analysis to evaluate CAR surface expression across a three day time frame. **Results:** We identified novel circuits providing fast reporter output with minimal background signal under hypoxic conditions, and elucidated design rules that enable or restrict amplification of transgene in native HIF1α and HIF2α-containing circuits. We observed differences in CAR transgene expression in hypoxia between circuits containing HIF1α and HIF2α-mediated feedback, suggesting mechanistic differences in regulation of HIF1α and HIF2α when overexpressed. Additionally, we observed greatly amplified transgene expression in circuit topologies containing feedback mediated by our synthetic transcription factor and promoter toolkit compared to native HIF1α and HIF2α-containing circuits and cells constitutively expressing CAR. **Conclusions:** We present a new therapeutic technology that senses hypoxic environments and enables high-output sense and respond behaviors with therapeutic outputs. We envision that this technology will enable development of safer, more effective cell therapies for solid tumors, as well as provide new biological and mechanistic insights that can inform the future development of hypoxia-responsive cell therapies. Research Sponsor: NIH; Northwestern University McCormick School of Engineering.

38 Poster Session

Infusion-related reactions from immune checkpoint inhibitors: A proportional and network meta-analysis. First Author: Yu Fujiwara, Roswell Park Comprehensive Cancer Center, Buffalo, NY

Background: Immune checkpoint inhibitors (ICIs) have become the standard of care for the treatment of patients with solid tumors. Infusion-related reactions (IRRs) to ICIs have been reported in up to 20%, but the incidence varies among ICIs. Therefore, we aimed to report and compare the incidence of IRRs to each ICI therapy. **Methods:** We searched PubMed/MEDLINE, Embase, and Web of Science to identify phase 3 randomized controlled trials (RCTs) evaluating ICIs (CTLA-4, PD-1, PD-L1, and LAG-3 inhibitors) in solid tumors. We performed a random-effects model network meta-analysis to compare the odds ratio (OR) of IRRs by using RCTs comparing dual ICIs, ICI monotherapy, and placebo/observation. For a proportional meta-analysis, treatment arms evaluating ICI monotherapy, or dual ICIs, were selected to pool the incidence of IRRs. **Results:** A total of 25,250 patients from 47 phase 3 RCTs were included in the analysis. A network meta-analysis of treatment-related IRRs included 10 RCTs and showed that avelumab (OR 70.2, 95% confidence interval [CI]: 4.32-1140) and atezolizumab (40.72, 2.47-671.4) had a significantly higher risk of treatment-related IRRs compared with placebo/observation. Network ranking revealed that avelumab, atezolizumab, and relatlimab plus nivolumab were the top three therapies with risk of treatment-related IRRs. Proportional meta-analyses revealed that the pooled incidence of treatment-related IRRs was 5.39% for PD-1 plus CTLA-4 inhibitors, 8.25% for PD-L1 (avelumab: 13.1%, non-avelumab: 1.93%), 1.97% for CTLA-4, and 1.95% for PD-1 inhibitors. Results of immune-related IRRs were relatively consistent with those of treatment-related IRRs (Table). **Conclusions:** Avelumab has the highest risk of IRRs followed by atezolizumab and dual ICIs. This comparative study provides insight into the incidence of IRRs with ICI regimens. These results are useful in assessing which systemic therapies are responsible for IRRs, particularly when ICIs are combined with other agents. Research Sponsor: None.

	Treatment-related		Immune-related	
	Incidence (95 % CI) (%)	No. of RCTs	Incidence (95% CI) (%)	No. of RCTs
PD-1	1.95 (1.37-2.78)	21 (23 arms)	1.66 (1.19-2.31)	17
Nivolumab	3.00 (2.08-4.32)	13	-	-
Pembrolizumab	1.32 (0.78-2.23)	6 (8 arms)	1.60 (1.13-2.26)	16
Cemiplimab	0.56 (0.07-2.02)	1	-	-
Tislelizumab	0.94 (0.30-2.17)	1	-	-
Sintilimab	-	-	2.78 (0.76-6.96)	1
PD-L1	8.25 (4.62-14.33)	6	3.71 (1.05-12.31)	6
Avelumab	13.10 (8.51-19.63)	4	27.23 (22.88-31.92)	1
Non-avelumab	1.93 (0.22-14.72)	2	2.51 (1.38-4.52)	5
Atezolizumab	5.13 (3.16-7.81)	1	2.51 (1.38-4.52)	5
Durvalumab	0.58 (0.07-2.08)	1	-	-
CTLA-4 (Ipilimumab)	1.97 (1.21-3.22)	3	-	-
PD-1 + CLTA-4	5.39 (3.25-8.80)	3	1.58 (0.54-4.53)	3
Nivolumab + Ipilimumab	5.39 (3.25-8.80)	3	0.94 (0.25-3.47)	2
Pembrolizumab + Ipilimumab	-	-	3.55 (1.71-6.42)	1
PD-L1 + CTLA-4 (Durvalumab + Tremelimumab)	0.88 (0.18-2.56)	1	-	-
PD-1 + LAG-3 (Relatlimab + Nivolumab)	5.97 (3.68-9.07)	1	-	-

39 **Poster Session**

Association between the occurrence of immune-related adverse events and survival outcomes in patients with cancer treated with perioperative immune checkpoint inhibitors: A systematic review and meta-analysis. First Author: Taiga Komatsu, St. Luke's International Hospital, Chuo-KU, Japan

Background: Although multiple studies have revealed that the occurrence of immune-related adverse events (irAEs) is associated with better survival in patients with advanced cancer, the association in patients with early-stage disease in the perioperative setting remains unclear. We performed a systematic review and meta-analysis to evaluate this association in the neoadjuvant and adjuvant settings. **Methods:** We performed a database search in PubMed/MEDLINE and Embase to identify eligible articles up to March 2024. We included studies evaluating the association between the occurrence of irAEs and survival outcomes in patients with solid tumors receiving at least one ICI in the perioperative setting. Cancer type, ICI agent, the number of patients, and survival outcomes (hazard ratio [HR] with 95% confidence interval [CI]) were summarized. We performed a random-effect model meta-analysis of survival outcomes that contained HR and 95% CI information from more than two studies. **Results:** After screening 884 articles, we found 15 eligible articles of which four studies reporting only treatment-related adverse events without irAE information were excluded. Finally, 11 studies (Clinical trials: n=3, Cohort studies: n=8) analyzing the association between the incidence of irAEs and survival were identified. Melanoma, triple-negative breast cancer (TNBC), non-small cell lung cancer (NSCLC), and urothelial carcinoma were evaluated in seven, two, one, and one study, respectively. While ten studies defined the irAE group as any-type and any-grade irAEs, one study defined the irAE group as any-type and grade 2-5 irAEs. OS was evaluated in five studies (four studies for melanoma), of which two studies suggested that the occurrence of irAEs was associated with longer OS. A meta-analysis of three studies showed a tendency of the association between the occurrence of any-type and any-grade irAEs and longer OS (Pooled HR=0.69, 95% CI 0.47-1.00, p = 0.05). RFS was evaluated in eight studies (seven for melanoma), of which seven studies indicated the association between the incidence of any-type irAEs (any-grade: 6 studies, grade 2-5: 1 study) and longer RFS. A meta-analysis of five studies revealed a significant association between the occurrence of any-type irAEs (any-grade: 4 studies, grade 2-5: 1 study) and longer RFS (Pooled HR=0.52, 95% CI 0.41 - 0.67, $p < 0.0001$]); however, Funnel plot indicated a presence of publication bias. **Conclusions:** This study suggests an association between irAEs and longer survival from perioperative ICI therapy, particularly in patients with melanoma. The result should be cautiously interpreted given a possible presence of publication and immortal bias. Further prospective studies and individual patient data meta-analysis are needed to validate this result. Research Sponsor: None.

40 **Poster Session**

Use of a novel proteomimetic nanoplatform for simultaneous delivery of antigens with adjuvants to impact tumor growth in multiple tumor models. First Author: Max Mu Wang, Northwestern University, Chicago, IL

Background: Patient-specific cancer vaccines derived from tumor antigen have been explored as a promising therapeutic strategy, however, challenges delivering vaccine components in a coordinated fashion to elicit antitumor responses remain. To overcome these, we utilize a novel nanoplatform called the Protein-Like Polymer (PLP), which allows for sustained and targeted delivery of tumor antigens in conjunction with adjuvants. **Methods:** PLPs containing peptide antigens were synthesized via ROMP and characterized. A library of compounds with different sidechain linkage chemistries, degrees of polymerization (DP), and inclusion/exclusion of Oligo-ethylene glycol (OEG) were made to determine design rules for immune activation. Cell uptake and functional assays using payload-specific T Cells were conducted. Immunization in three independent tumor models was done to show generalizability. Ability of PLPs to co-deliver adjuvants was tested by electrostatically coupling small molecule STING agonist, 2'3' cGAMP. **Results:** Conjugating antigens to the polymer via a cleavable disulfide linkage, which reduces intracellularly in APCs, resulted in increased endosomal localization, higher levels of induced T cell proliferation, cytokine production, and expression of activation markers in CTLs and APCs. Incorporating a diluent amount of OEG side chains reduced enzymatic degradation while increasing immunogenicity and uptake. Additionally, increasing the DP, and therefore the density of antigen side chains, further improved vaccine efficacy and resistance to proteolysis. Antigen-PLP conjugates enhanced dendritic cell activation and T-cell response only when paired with cells from their cognate system, with no activity in immune cells not expressing receptors for the payload demonstrating antigen-specificity. Mice bearing established B16F10, MC38, or TC-1 tumors treated with PLPs containing gp100, adpgk, or E7 respectively all showed increased survival times, reduced tumor burden with corresponding changes in immune cell profiles, and immunological memory upon rechallenge. Impressively, mice treated with STING-PLP complexes had significantly smaller tumors vs control at day 14 (0.038g vs 0.76g; $p < 0.0001$) and allowed for subcutaneous administration of 2'3' cGAMP, which traditionally requires intratumoral injection. Studies on the effects of vaccinating with pools of neoantigens multiplexed onto one PLP are ongoing. **Conclusions:** This work validates the ability of PLPs to overcome major limitations in cancer vaccine development. The modularity of the platform allows for complex nano-architectures including systems capable of delivering challenging compounds, ie small molecule STING agonists, subcutaneously through electrostatic coupling, highlighting its potential to revolutionize cancer vaccinology. Research Sponsor: NIH.

41 **Poster Session**

Efficacy of combination of immune checkpoint inhibitors, chemotherapy, and targeted therapy in advanced/refractory cancer. First Author: Philip A. Salem, Salem Oncology Center, Houston, TX

Background: The treatment of advanced/refractory malignancies continues to pose a major challenge, and it is associated with poor outcome. It has been shown that in some cancers, the combination of chemotherapy (CT) with immune checkpoint inhibitors (ICIs), or CT with targeted therapy (TT), are superior to chemotherapy alone. Consequently, in our treatment program (ICTriplex), TT was added to CT plus ICIs. These three modalities have convergent efficacy with divergent toxicity. Our prior data were previously reported (1-3). **Methods:** Treatment with ICTriplex was highly personalized and was tailored to the individual patient and their specific cancer. It was designed based on diagnosis, prior therapy, and genomic profiling. Between March 2017 and January 2024, 56 patients (pts) with advanced malignancies were treated: 31 females and 25 males, with a median age of 58. Tumor types included: lung (12), pancreas (8), colorectal (8), biliary tract (5), breast (4), stomach (4), melanoma (3), ovary (3), sarcoma (3), cervix (2), glioblastoma (2), Hodgkin's (1), and thymoma (1). 43 pts received prior therapy: 14 received ICIs, 23 TT, and 42 CT. The agents used in ICTriplex were: 6 ICIs primarily nivolumab and pembrolizumab, 12 CT primarily taxanes, gemcitabine, and platinum, and 23 TT, primarily bevacizumab and erlotinib. Response was evaluated by both PET/CT and CT scans. A complete remission was achieved when metabolic activity completely resolved on PET/CT. Progression-free survival (PFS) and overall survival (OS) were calculated using the Kaplan-Meier estimator. **Results:** The overall response rate (ORR) was 88%. A complete remission (CR) occurred in 29 pts (52%), and a partial remission (PR) in 20 pts (36%). Of the 12 pts with lung cancer, 9 (75%) achieved CR and of these, 4 pts had brain metastases that completely resolved without radiation. Of the 8 pts with pancreatic cancer, 4 (50%) achieved CR. 4 of 5 pts with biliary tract cancer achieved CR. Toxicity was reasonable in all pts except for 3 who died from complications possibly related to ICIs. The median PFS was 11 months, and the median OS was 15 months. The achievement of CR and the PD-L1 + status, resulted in a statistically significant better PFS (p= 0.00; p= 0.02) and OS (p=0.00; p= 0.005). Patients with lung cancer showed a better PFS (p= 0.02) with the median at 19 months, and the median OS was 36 months. Potential predictors of unfavorable prognosis, such as receiving prior treatment, did not impact patients' clinical outcome. **Conclusions:** ICTriplex is a very effective treatment for advanced cancer that has become resistant to conventional therapy or with no available standard therapy. We strongly recommend this therapeutic approach for the treatment of such patients. 1. ASCO 2019 (e14254) 2. ASCO 2020 (e15150) 3. ASCO 2022 (e14590). Research Sponsor: None.

42 **Poster Session**

Surufatinib plus toripalimab in advanced soft tissue sarcoma (STS): Results from a multicenter, single-arm, basket study. First Author: Ying Cheng, Department of Oncology, Jilin Cancer Hospital, Changchun, China

Background: Soft tissue sarcomas (STS) are highly malignant despite their low incidence and prone to recurrence, with limited therapeutic options after failure of first-line treatment. Several antiangiogenic monotherapies have shown some efficacy but limited benefit. The open-label, multi-cohort, single-arm, basket study was performed to evaluate the efficacy and safety of the combination of surufatinib (a small-molecule inhibitor of VEGFR 1-3, FGFR1 and CSF-1R) with toripalimab (an anti-programmed death 1 [PD-1] antibody) for Chinese patients (pts) with advanced solid tumors. Here, we reported the results from the STS cohort. **Methods:** Pts with STS who had progressed on ≤ 2 lines of systemic chemotherapy, or were intolerant to standard treatment, or for whom there was currently no effective therapy were eligible. They received 21-day cycles of surufatinib 250 mg orally, once daily, plus toripalimab 240 mg intravenously, once every 3 weeks, until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) per RECIST 1.1. **Results:** As of data cutoff (Feb 28, 2023), a total of 20 pts (incl. 4 treatment-naïve pts) were enrolled and received the combination treatment (mean duration: 5.81 months [m]). Median (range) age was 50 (23-74) years, 10 pts were male, 17 pts were TNM stage IV. The pathological types include leiomyosarcoma (n=4, incl. 1 naïve patient), synovial sarcoma (n=4), alveolar soft part sarcoma (n=3, incl. 2 naïve pts), undifferentiated pleomorphic sarcoma (n=3), liposarcoma (n=2, incl. 1 naïve patient) and fibrosarcoma (n=1), malignant fibrous histiocytoma (n=1) and others (n=2). Seven (35%) pts had PD-L1 combined positive score of ≥ 1. The median follow-up duration was 27.14 m. Confirmed ORR and disease control rate (DCR) for 19 efficacy-evaluable pts was 10.5% and 68.4%, respectively; median duration of response was 7.05m. The median progression-free survival (mPFS) and median overall survival (mOS) was 2.69 m and 16.23 m for all dosed pts. For 16 previously treated pts, ORR and DCR was 6.3% and 62.5% respectively; median duration of response (DoR) was 7.13 m; mPFS was 2.65 m; mOS was 14.32 m. 18 (90%) pts experienced at least one treatment-related adverse event (TRAE), and 7 (35%) of them reported grade ≥ 3 TRAEs. The incidence of immune-related adverse events (irAEs) was 70%, only 2 pts had grade ≥ 3 irAEs, which were immune-related pancreatitis and immune-related diabetes. 2 pts were permanently discontinued due to TRAEs, which were grade 2 renal impairment and grade 3 hyperglycemia. No new safety signals were observed. **Conclusions:** Surufatinib plus toripalimab had a promising antitumor activity and a manageable safety profile in pts with advanced STS. Clinical trial information: NCT04169672. Research Sponsor: Science and Technology Innovation – Biomedical Science and Technology Support Project; 20S11907500; HUTCHMED Limited.

43 **Rapid Oral Abstract Session**

A phase Ib/II study of pacritinib, an interleukin 1 receptor associated kinase 1 (IRAK1) inhibitor, in patients (pts) with solid tumors harboring the 1q21.3 copy number amplification (CNA). First Author: Joline Si Jing Lim, Department of Haematology-Oncology, National University Cancer Institute, Singapore, Singapore

Background: The role of IRAK1 pathway in inflammatory and immune response is established in autoimmune diseases but less well-understood in cancer. Chromosome 1q21.3 CNA detected in plasma cell-free DNA was observed in pts with advanced solid tumors, and associated with IRAK1 upregulation. In preclinical animal models, IRAK1 upregulation promoted tumorigenesis, while its inhibition led to decreased tumor growth. Pacritinib is a JAK2/FLT3 inhibitor that is FDA approved for treatment in myelofibrosis, but also have known activity against IRAK1. We hypothesize that pacritinib may be effective in disease control of pts with plasma 1q21.3 CNA. **Methods:** A phase Ib/II clinical trial was designed to investigate the efficacy of pacritinib in pts with treatment (rx) refractory solid tumors harboring 1q21.3 CNA. Serial pt tumor and blood samples were collected and analyzed to elucidate the effect of IRAK1 inhibition on tumor microenvironment and systemic immune modulation. **Results:** 330 patients were screened, 1q21.3 CNA was detected in 30.1% of pts. Highest incidence of 1q21.3 CNA positivity was detected in breast cancer (39.8%), colorectal cancer (39.7%) and lung cancer (36.1%). 12 pts were commenced on rx over 3 dose levels (DL) (DL1: n=6, DL2: n=3, DL3: n=3). At DL1 (200mg BID), no DLTs were observed, but 2 pts had G3 transaminitis attributed to drug/disease, and 1 pt had intolerable G2 rash; decision was made for dose reduction. At DL2 (200mg OM, 100mg ON), no DLTs were observed. Reescalation to 200mg BID (DL3) was carried out with no DLT observed. Pacritinib at 200mg BD was declared the recommended phase II dose in pts with solid tumors. In the dose expansion cohort, 8 pts (4 colorectal cancer, 3 hepatobiliary [HPB] cancer, 1 lung cancer) have been enrolled thus far. No objective responses were observed. Within pts with HPB tumors, 1 pt with pancreatic cancer had a progression-free survival (PFS) of 25.0 weeks, and 1 pt with cholangiocarcinoma had a PFS of 15.9 weeks. Preliminary analysis of serial tumor biopsy samples suggest an expansion of CD8+ T cell population with pacritinib rx. Serial peripheral blood mononuclear cells analysis showed no significant trend in change in CD8+ T cell population, but a predominance of PD-1+ T cells with rx, and also an increase in CD4+ T cell population. In the myeloid cell population, there appears to be decrease in dendritic cell population, but no significant change in trend of macrophage was observed. **Conclusions:** Pacritinib at 200mg BID is safe and tolerable in pts with solid tumors. IRAK1 inhibition appears to modulate immune cell populations both in the tumor microenvironment and systemic circulation. Dose expansion is underway, with potential signal of disease control in HPB tumors. Clinical trial information: NCT04520269. Research Sponsor: National Medical Research Council.

44 **Poster Session**

An open-label single-center investigator-initiated exploratory clinical study in patients with refractory or recurrent solid tumors using SBRT as "in situ vaccination": R-ISV-FOLactis trial. First Author: Rutian Li, The Comprehensive Cancer Centre of Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China

Background: The immunotherapy of sarcomas remains a challenge. As a breakthrough tool for cancer immunotherapy, the therapeutic cancer vaccine is in rapid development. In situ vaccination can be realized by intratumoral immune injection and radiotherapy. We have developed a bifunctional engineered Lactococcus lactis (FOLactis) expressing an encoded fusion protein of fms-like tyrosine kinase 3 ligand (Flt3L) and OX40 ligand (OX40L). We hypothesized that intratumoral injection of "FOLactis" combined with SBRT will realize tumor control and the synergetic application of PD-1 mAb systematically will further improve the effect of immunotherapy. **Methods:** This exploratory clinical study is designed as an open-label trial aimed at treating patients with advanced solid tumors who are unresponsive or intolerable to standard treatment. Patients will be treated with SBRT, intratumoral injection of "FOLactis", and PD-1 blockade. The primary endpoint was the objective response rate (ORR) of target lesions after 3 months and 6 months. The secondary endpoint included the disease control rate (DCR) of target lesions, progression-free survival (PFS), overall survival (OS), etc. **Results:** From July 2022 to December 2023, 30 patients were eligible for this trial (63% were sarcomas). 53.3% and 33.3% had received radiotherapy or PD-1/PD-L1 mAb before respectively. The ORR and DCR of target lesions after 3 months were 27.6% and 93.1%, while these of systemic efficacy were 17.2% and 55.2%, respectively. In sarcomas, the ORR, DCR of target lesions were 11.1% and 88.9%, while these of systemic efficacy were 5.5% and 50%, respectively. Considering the deferred response in sarcomas, we also calculated the ORR after 6 months as the primary endpoint. The ORR, DCR of target lesions after 6 months were 56.3% and 100%, while these in sarcomas were 41.7% and 100%, respectively. Systemic median PFS were 2.87 months. Median PFS of target lesions and mOS has not reached. Among the evaluable target lesions, 6-month EFS was 50% in sarcomas (6/12) and 50% in all patients (8/16). Expression of $CD4^+$, $CD8^+$ T cells and dendritic cells was significantly increased between pre-treatment and post-treatment peripheral blood in responders. The most common treatment-related adverse events (TRAEs) were fever (83.3%), lymphocytopenia (53.3%), hypocalcemia (30%), neutrophilia (26.7%) and nausea (26.7%). Grade≥3 TRAE occurred in 11 patients, including lymphocytopenia (30%), fever (6.7%), leukopenia (3.3%), anemia (3.3%) and cardiac insufficiency (3.3%). **Conclusions:** In situ vaccination with"FOLactis", along with SBRT was tolerable and induced anti-tumor immunity, which would also augment systemic response when synergized with PD-1 mAb. This in situ vaccination is probably a promising option for advanced solid tumors. Clinical trial information: ChiCTR2200060660. Research Sponsor: the National Natural Science Foundation of China (82272852); the fundings for Clinical Trials from the Affiliated Drum Tower Hospital, Medical School of Nanjing University (2022-LCYJ-MS-09); the fundings for the development of new technology from the Affiliated Drum Tower Hospital, Medical School of Nanjing University (XJSFZJJ202025).

ABSTRACT WITHDRAWN

46 **Poster Session**

Development of multiplex digital PCR based droplex NSCLC panel test for detecting major mutations in patients with non-small cell lung cancer (NSCLC). First Author: Yun-Jeong Choe, Gencurix Inc, Seoul, South Korea

Background: Recently, in the treatment of non-small cell lung cancer(NSCLC) patient, immunotherapies and targeted therapies aimed at various genes have been developed. Next-Generation Sequencing(NGS) technology is currently known as the only method for detecting genetic alterations in many different genes simultaneously. However, this technology requires a substantial amount of DNA or RNA input from patients to obtain high-quality results in a clinical setting. We have developed a Droplex NSCLC Panel Test Kit based on multiplex digital PCR, which is known as ideal molecular diagnostic technique due to its simple workflow, minimal sample input, high sensitivity and specificity. In addition, it has a one-day TAT (Turn around time) and low costs compared NGS, resulting in a lower financial burden for patients. Recently, the development of non-invasive liquid biopsy diagnostics as an alternative to tissue biopsy is emerging important issue. The kit, applying a digital PCR platform, enables multiple mutation detection using plasma samples of blood. The digital PCR-based Droplex NSCLC Panel Test Kit is designed to detect over 170 key mutations in 11 genes, namely EGFR, ALK, ROS1, BRAF, MET, RET, KRAS, HER2, NTRK1, NTRK2, and NTRK3, using DNA and RNA extracted from NSCLC FFPET and plasma samples. **Methods:** The Droplex NSCLC Panel Test Kit consists of four Oligo Mixtures (OMs) for detecting mutations of 4 genes on DNA and two OMs for detecting 7 gene rearrangements on RNA. After extracting DNA and RNA from a single sample, cDNA synthesis from RNA is prioritized, followed by simultaneous execution of droplet generation, PCR processes, and data analysis. The kit test was based on QX600 droplet digital PCR system of Bio-rad with 6 fluorescent channels. To validate the analytical performance of the Droplex NSCLC Panel Test Kit for each type of sample, DNA and RNA samples were extracted from FFPET sections and plasma isolated from NSCLC patients. Each type of samples, contrived samples were manufactured and tested for analytical performance. **Results:** The results showed that DNA/RNA multiple mutations can be detected simultaneously on a 6-fluorescent channel system. The kit was highly sensitive for low-input sample in dilutions studies ranging from 5 to 20ng DNA or RNA for FFPET samples and plasma sample. The Digital PCR NSCLC panel test detected an analytical specificity of 100% and detection limit of 0.25% or higher for all genes included in the kit. **Conclusions:** We demonstrated that the performance of the Droplex NSCLC Panel Test is reliable and effective for the detection of above 170 clinically relevant mutations of 11 genes in FFPET and plasma samples of patients with NSCLC. Additionally, it will be necessary to evaluate the utility of the kit through further clinical studies with NSCLC patients, as well as expanding its compatibility to various digital PCR platforms. Research Sponsor: None.

47 **Poster Session**

Targeted degradation of undruggable proteins using a novel heterobifunctional proteomimetic platform. First Author: Max Mu Wang, Northwestern University, Chicago, IL

Background: Of the ~20,000 proteins in the human genome, only a subset can be modulated via traditional pharmacological approaches. "Undruggable" targets currently include proteins with pivotal roles in cancer pathogenesis. Our work aims to introduce a new paradigm for engaging these clinically relevant proteins using a modular platform we term the HYbrid DegRAding Copolymers (HYDRACs). HYDRACs multiplex targeting warheads with degradation inducers and have long circulation times plus high cell uptake. Preliminary studies on MYC and RAS, targets of great pharmaceutical interest, highlight the potential of this platform to revolutionize drug design. **Methods:** HYDRACs containing MYC or RAS targeting peptides randomly copolymerized with degrons were synthesized using ROMP. Fluorescent and biotin-tags were incorporated for use in uptake and pull-down assays. Viability following treatment with MYC-HYDRACs was performed in multiple cell lines with both cellular (MYC-independent lines) and polymer composition controls. Target engagement was assessed via immunoprecipitation and circular dichroism with protein degradation monitored by WB. Unbiased whole proteome analysis and RNAseq were done to confirm observed effects were selectively on-target. In vivo efficacy and biodistribution was assessed in tumor-bearing mice. **Results:** HYDRACs show high levels of cell uptake and antiproliferative effects at sub-micromolar concentrations in a formulation- and target-dependent manner. Cells treated with MYC-HYDRACs displayed reduced MYC protein levels, which were rescued by proteasome or neddylation inhibition. Swapping out the degron for various validated E3 ligase recruiters maintained MYC degradation, highlighting the "plug-and-play" nature of this approach. On-target activity was confirmed via RNAseq. Biophysical analysis showed strong HYDRAC-protein interactions, orthogonally supported by the presence of target protein following pull-down of biotin-terminated HYDRACs. Target protein degradation only occurred following treatment with an intact HYDRAC compound. Mice bearing MYC-CaP tumors showed delayed tumor growth following treatment with MYC-HYDRACs, with compound accumulation in the tumor for up to 72 h following a single injection. Generalizability was demonstrated against RAS, with RAS-HYDRACs capable of degrading KRAS across multiple different alleles, acting as a pan-KRAS degrader. **Conclusions:** We present a novel platform technology that addresses the challenges inherent to peptide delivery approaches. HYDRACs have the potential to dramatically alter the drug discovery landscape, allowing for the development of cancer-relevant target modulators for which there are no current viable therapies. We envision the HYDRAC platform as a generalizable approach to designing degraders of proteins of interest, greatly expanding the therapeutic armamentarium for TPD. Research Sponsor: NIH.

48 **Poster Session**

A phase II study of oral chlorophyllin in haemorrhagic cystitis secondary to radiation therapy for pelvic malignancies (CLARITY). First Author: Gagan Prakash, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India

Background: Chronic hemorrhagic cystitis (cHC) is seen in 5-15% of patients undergoing pelvic radiotherapy (pRT), often after a long cancer free survival. Hyperbaric oxygen therapy, the only modality with benefit proven in a randomized trial has limited utilization due of lack of availability, need of multiple sessions & cost. In this phase II study, we aimed to evaluate the efficacy & safety of Sodium-copper-chlorophyllin (CHL), a semi-synthetic mixture of sodium & copper salts of chlorophyll, in pRT-induced cHC. This study was based on our preclinical findings where CHL offered radioprotection & significantly reduced mortality & morbidity in mice exposed to lethal doses of whole-body radiation.A subsequent phase 1 trial in adult healthy volunteers established the recommended phase 2 dose. **Methods:** This was a prospective, single centre, single arm, interventional phase II clinical trial (NCT05348239). Adult patients with grades II-IV hematuria (CTCAE v5.0) following pRT received at least 3 months prior were eligible. All patients received oral CHL 750 mg OD for a maximum of 3 months. A Simon two-stage minimax design with a type 1 error of 2.5% & 80% power led to a sample size of 24 patients. The primary objective was the objective response rate (ORR), defined as the proportion of patients with complete response (CR) [resolution of gross hematuria] or partial response (PR) [decrease by at least one CTCAE grade of hematuria, but not complete resolution] from day 30-90 of starting the drug. At least seven objective responses were required to consider the drug for further development. **Results:** Thirty two patients were screened of whom 24 were enrolled, with median age of 63 (43-86) years. Indications for pRT included cervical (15), rectal (5) & prostate cancer (4). The median time from RT to cHC was 45 (4-216) months. At enrolment, 6 (25%), 17 (70.8%) & 1 (4.1%) patients had CTCAE grades 2, 3 & 4 hematuria respectively, majority being refractory. An objective response occurred in 20 patients (83.3%; 95% CI, 62-95%), (Stable=1, PR=10, & CR=10 as the best response).11 unrelated SAEs were observed in 8 patients. No treatment-related grade 4/5 adverse events were reported.No patient required angioembolisation, vesical artery ligation, or cystectomy.Proteomics studies indicated modulation of coagulation pathways and improved stem cell mediated regeneration and wound healing following chlorophyllin treatment. **Conclusions:** In this phase II study,oral CHL has shown objective & sustained response in cHC related grade II-IV hematuria following pRT. A randomized, placebo-controlled, phase III trial assessing the efficacy of oral CHL is now planned. Clinical trial information: NCT05348239. Research Sponsor: Department of Atomic Energy Government of India.

49 **Poster Session**

Effect of oncolytic Newcastle disease virus harboring PTEN gene on pancreatic adenocarcinoma growth through inhibition of PI3K/mTOR signaling and promotion of apoptosis. First Author: Hyun Jang, Libentech Co. LTD., Daejon, South Korea

Background: Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive and intractable cancer, warranting the need for more effective therapies. Cell proliferation, progression, and severity in PDAC are highly activated owing to KRAS mutations and low PTEN expression. **Methods:** A recombinant Newcastle disease virus (rNDV) harboring PTEN (rNDV-PTEN) was constructed to infect PDAC cells to artificially induce PTEN expression. The cancer killing effect of the rNDV-PTEN virus was observed in an in vitro assay, and $10^{7.0}$ pfu/dose(0.1 ml) of the rNDV-PTEN virus was inoculated through intravenous injection into a PANC-1 cell transplanted mouse to prove the tumor growth inhibition effect. Apoptotic signaling-related proteins were analyzed with Western blotting and qPCR assays based on the mRNA. During the treatment, biomarkers were also analyzed. **Results:** Factitious PTEN expression in KRAS-mutated PDAC cells following rNDV-PTEN infection lowered PI3K/AKT/mTOR signaling, induced PDAC cell death, and suppressed tumor growth. PTEN overexpression promoted apoptotic and autophagic signaling pathways in PANC-1 cells and orthotopic xenograft mice. rNDV-PTEN has substantial cancer cell-killing effects and inhibits tumor growth. rNDV-PTEN injection into animals did not elicit an immune response against rNDV and improved blood parameters, such as glucose, triglyceride, and total cholesterol levels. **Conclusions:** rNDV-PTEN showed a strong tumor-suppressive effect on PDAC, which was caused by an abnormally activated PI3K/AKT/mTOR signaling pathway due to KRAS mutations and PTEN loss. We also showed that rNDV-PTEN is relatively safe for use in cancer therapy. Further studies using patient-derived PDAC cells with the same genetic background, as well as more extensive animal safety tests, are required to demonstrate rNDV-PTEN as a PDAC therapeutic. However, PTEN gene-containing rNDV may be a very promising therapeutic candidate for pancreatic cancer treatment. Research Sponsor: None.

50 Rapid Oral Abstract Session

Multiinstitutional cohort study of patient outcomes in Child-Pugh (CP) B liver function treated with atezolizumab plus bevacizumab (A+B) for hepatocellular carcinoma (HCC). First Author: Amit Mahipal, University Hospitals Seidman Cancer Center, Case Western Reserve University, Cleveland, OH

Background: A+B is commonly used as first line systemic therapy in HCC patients with CP-B liver function, although in the IMbrave150 clinical trial, its efficacy was only assessed in patients with CP-A liver function. We evaluated outcomes in patients with CP-B liver function and compared to those with CP-A. **Methods:** We completed a multi-institution, retrospective review of patients with HCC from Mayo Clinic and University Hospitals Seidman Cancer Center, who had received A+B in the first line setting between March 2018 and November 2023. CP score was calculated at time of treatment, response was assessed, and progression free (PFS) and overall (OS) survival were determined using the Kaplan Meier method. **Results:** Among 322 patients with HCC, median age was 66.5 years, 78.6% were male, and 82.6% were white. Eighty-six patients (27%) had CP-B liver function, while 226 (70%) had CP-A and 10 (3%) had CP-C. Etiology of liver disease in patients with CP-B included hepatitis B in 7.0%, hepatitis C in 38.4%, alcohol use in 30.2%, and metabolic associated steatohepatitis in 20.9%. Median OS in patients with CP-B liver function was 6.4 months, while mOS was 21.6 months for those with CP-A ($p<0.0001$). Further stratifying, mOS in those with CP-B7 was 9.1 months, CP-B8 was 5.5 months, and CP-B9 was 4.0 months. 12-month OS in patients with CP-B was 32.4%, compared to 69.3% in CP-A. Median PFS was 4.8 months in those with CP-B and 8.9 months in those with CP-A. Median PFS in those with CP-B7, -B8, and -B9 was 6.4 months, 2.7 months, and 2.7 months, respectively. Among those with CP-B, 1 patient had a complete response, 17 (19.8%) had a partial response, 29 (33.7%) had stable disease, and 37 (43.0%) had progressive disease. Adverse events in CP-B patients included hypertension in 14.0% (grade 3 in 1 patient), bleeding in 16.3% (grade 3 or greater in 11.6%), fatigue in 38.4%, and an immune-related adverse event in 17.4% (grade 3 in 5.8%). **Conclusions:** Patients with advanced HCC and CP-B7 liver function may still benefit from A+B. Importantly, no additional safety risks were identified in this subgroup. Those with CP-B8 and CP-B9 have significantly worse survival than those with CP-B7 and the likelihood of benefit from systemic therapy is minimal. It is important for providers to address the impact of baseline liver function on expected outcomes in patient with HCC. Research Sponsor: None.

51 Poster Session

Reduced cardiovascular disease risk after gastrectomy for gastric cancer: Unexpected treatment benefits. First Author: Yeongkeun Kwon, Korea University College of Medicine, Seoul, South Korea

Background: The relationship between gastrectomy for gastric cancer and subsequent cardiovascular risk modifications has been noted, yet the direct consequences of such surgeries on cardiovascular incidences are not fully established. This study evaluated cardiovascular event rates among patients who received gastrectomy versus a matched general cohort. **Methods:** In a nationwide retrospective cohort analysis, we examined individuals diagnosed with gastric cancer who underwent gastrectomy (n=18,698), and a control group matched for demographics (n=81,787) from 2004 to 2008. Criteria for inclusion were patients devoid of any previous cancer diagnosis (except gastric cancer), myocardial infarction, or ischemic stroke. The primary outcome was the incidence of major adverse cardiovascular events (MACE) such as acute myocardial infarction (MI) or acute ischemic stroke, in patients with gastric cancer. **Results:** Within a seven-year observational window, 2.7% of the gastrectomy group (or 4.29 events per 1000 person-years) experienced new MAC). The gastrectomy group showed a significantly lower incidence rate of MACE compared to the matched control subjects (hazard ratio [HR] 0.65; 95% confidence interval [CI] 0.63–0.71; $P<0.001$), MI (HR, 0.68; 95% CI, 0.60–0.78; $P < 0.001$), and stroke (HR, 0.73; 95% CI, 0.66–0.79; $P<0.001$). In the subgroup analyses, no significant interactions were identified between the study groups and baseline variables. **Conclusions:** The study indicates a decreased risk of developing cardiovascular diseases post-gastrectomy for gastric cancer, as opposed to the general population. Beyond their significance for public health strategies aimed at cardiovascular risk management in gastric cancer patients, these findings empower both patients and healthcare providers with enhanced knowledge for making decisions about gastric cancer surgical options. Furthermore, this study lays the groundwork for future investigations into the metabolic effects of gastric cancer surgeries, notably their potential in lowering cardiovascular risk. Research Sponsor: None.

52 Poster Session

A phase I/II study of nanoliposomal irinotecan and carboplatin in patients with advanced or metastatic, poorly differentiated gastroenteropancreatic neuroendocrine carcinoma characterized by tissue and liquid next-generation sequencing. First Author: Nai-Jung Chiang, Department of Oncology, Taipei Veterans General Hospital, Taipei, Taiwan

Background: For locally advanced or metastatic gastroenteropancreatic neuroendocrine carcinomas (GEP-NECs), standard chemotherapy typically incorporates etoposide or irinotecan plus platinum agents. Herein, we initiate a phase I/II trial to apply Nal-IRI in combination with carboplatin as the 1st line treatment in patients with GEP-NECs to define the dose-limiting toxicity (DLT) and recommended phase II dose (RP2D). **Methods:** In the phase I part, traditional 3+3 design was applied. Enrolled patients would receive escalating dose of 60 (level -1), 80 (starting dose, level 0) or 100 (level 1) mg/m^2 salt-form nal-IRI plus carboplatin AUC=4 with maximum total dose of 600 mg on D1, every 21 days as a cycle. DLTs were evaluated during the first one cycle of treatment with tumor assessment every 6 weeks. Prophylaxis G-CSF was not allowed in the first cycle Paired testing of tissue (TBx) and liquid biopsy (LBx) was done by Illumina TSO500 platform before treatment. The second LBx would be repeated for confirmed partial responders when progression. **Results:** Totally 6 GEP-NEC patients with primary sites of colon in three, and each one in esophagus, ampulla of Vater and pancreas were enrolled to level 0. One patient had DLT of grade 4 neutropenia lasting for 3 days even under salvage G-CSF. Treatment-related adverse events showed grade 3/4 neutropenia (33.4%), grade 2 anemia (16.7%), grade 3 fatigue (16.7%), and grade 2 skin rash (16.7%). Four patients achieved confirmed partial response and 2 patients got stable disease, with the objective response rate of 66.7% (95% confidence interval: 22%-96%). After the data and safety monitoring board meeting, level 0 was decided as RP2D but not escalation to level 1 because of acceptable toxicity profiles and promising efficacies. Comprehensive genomic profiling showed that driver mutations were identified in three cases including two harboring *BRAF*^{V600E} mutation and one with *KRAS*^{G12D} mutation. The other three cases lacking driver mutation showed frequent copy number alteration including 1 with *MDM2* amplification (copy number 27) and a wild-type *TP53*. Homologous recombination deficiency (HRD), as determined by GIS score, was identified in a colon GEP-NEC who remained to be HRD-positive at progression but a higher TMB (from 4.7 to 10.2 Muts/Mb) and a higher *BRAF*^{V600E} mutation allele frequency (from 24.1% to 43.6%) in tumor tissue, compared to the baseline profiling. **Conclusions:** Based on current data, the RP2D is 80 mg/m^2 of nal-IRI (salt-form) and carboplatin of AUC=4, every 3 weeks. The extension phase II study in GEP-NEC is ongoing. Clinical trial information: NCT05385861. Research Sponsor: Taiwan Cooperative Oncology Group, National Health Research Institutes; PharmaEngine, Inc.; Illumina.

53 Poster Session

Deciphering the prognostic value of *FGFR2b/2c* isoform expression levels in advanced esophagogastric cancer through whole-transcriptome sequencing. First Author: Tadayoshi Hashimoto, Department of Gastroenterology and Gastrointestinal Oncology/Translational Research Support Office, National Cancer Center Hospital East, Kashiwa, Japan

Background: Fibroblast growth factor receptor (FGFR) isoform switching from *FGFR2b* to *FGFR2c* has been implicated in epithelial-to-mesenchymal transition and enhanced invasive potential in various malignancies and potentially be involved in resistance mechanisms to FGFR2b targeted therapy (e.g., bemarituzumab). This study sought to investigate the potential of respective *FGFR2* isoform expression evaluation utilizing whole-transcriptome sequencing (WTS) and its correlation with therapeutic efficacy and clinical outcomes in patients with advanced G/GEJ cancer. **Methods:** Patients with advanced G/GEJ cancer who received systemic therapy at the National Cancer Center Hospital East between May 2021 and September 2023, and were enrolled in the immunological profiling study (UMIN000019129) and MONSTAR-SCREEN-2 (UMIN000043899) were included. FGFR2 protein and RNA expression were assessed via immunohistochemistry (IHC) and WTS with Caris MI Profile, respectively. *FGFR2b* and *FGFR2c* isoforms were distinguished by the detection of their respective splice junctions using WTS data. The FGFR2b/(2b+2c) ratio was stratified into FGFR2b-dominat and -containing subtypes using the median value. The log-rank test was used to discern differences in overall survival (OS). **Results:** Among the 129 patients, 21 (16.3%) exhibited FGFR2-positivity by IHC (staining intensity 2+ or 3+≥1% membranous staining of tumor cells), and a significant correlation was observed between FGFR2 IHC status and RNA expression levels (TPM: transcript per million) in WTS (FGFR2-positive, median TPM=11.1; FGFR2-negative, median TPM=4.7; P=0.002). The distribution of FGFR2b/(2b+2c) ratio (median, 0.89) was: 10.9% ($0\leq x<0.2$), 5.4% ($0.2\leq x<0.4$), 7.0% ($0.4\leq x<0.6$), 12.4% ($0.6\leq x<0.8$), 43.4% ($0.8\leq x<1.0$), and 20.9% ($x=1.0$). Among 58 patients treated with 1st line therapy, no significant difference in treatment response was observed between the FGFR2b-dominat (67.9%) and FGFR2c-containing subtypes (53.3%) (P=0.259). Overall, the FGFR2c-containing subtype was associated with significantly shorter OS compared to the FGFR2b-dominat subtype (median OS, 10.1 vs. 17.9 months; hazard ratio, 1.72; 95% confidence interval, 1.03-2.86; log-rank P=0.037). **Conclusions:** Our findings underscore the substantial concordance between IHC and WTS analysis of FGFR2, the feasibility of distinguishing *FGFR2* isoforms using WTS, and the prognostic implications of *FGFR2c* isoform in patients with advanced G/GEJ cancer. Further analysis is warranted in patients receiving FGFR2b targeted treatment. Research Sponsor: Japan Agency for Medical Research and Development (AMED) under Grant Number 24ck0106890h0002.

54 Poster Session

Cryoablation versus transcatheter arterial chemoembolization for unresectable hepatocellular carcinoma with lenvatinib from a real-world study. First Author: Xiujuan Chang, Fifth Medical Center of Chinese PLA General Hospital, Beijing, China

Background: Hepatocellular carcinoma (HCC) is characterized by hypovascularity, the efficacy of transcatheter arterial chemoembolization (TACE) has been suboptimal. This study sought to evaluate and compare the efficacy and safety profiles of cryoablation (CRYO) plus lenvatinib (LEN) against TACE plus LEN for unresectable hepatocellular carcinoma (u-HCC) patients within a real-world clinical practice. **Methods:** A prospective study was conducted involving 234 patients with u-HCC who underwent treatment with LEN plus either CRYO or TACE at the Fifth Medical Center of the Chinese PLA General Hospital from October 2018 to May 2023. Treatment selection was determined through multidisciplinary discussions among a liver cancer board, weighing the pros and cons. The final decision was made by the patients and clinicians based on consensus. Clinical characteristics were balanced using propensity score matching (PSM). The primary endpoint was overall survival (OS), while secondary endpoints included progression-free survival (PFS), objective response rate (ORR), disease control rate (DCR), and adverse events (AEs). Tumor response was based on RECIST v1.1 and mRECIST by blinded independent imaging review, AEs by CTCAE v5.0. **Results:** In this study, 212 (90.6%) were male, with an average age of 56 years. 206 (88%) patients were infected with hepatitis B virus (HBV), and 178 (76.1%) and 77 (32.9%) patients were classified as Child-Pugh A and BCLC B. After PSM, the clinical characteristics were comparable between the CRYO plus LEN and the TACE plus LEN group. Over a median follow-up of 31.8 months, 124 patients (53%) died. The CRYO plus LEN group demonstrated similar OS (24.2 vs. 22.0 months, *P = 0.64*), PFS (8.7 vs. 11.9 months, *P = 0.48*), ORR (53.1% vs. 53.1%, *P = 1.00*), and DCR (86.5% vs. 78.1%, *P = 0.19*) compared to the TACE plus LEN group after PSM, with consistent results observed before PSM. The two groups exhibited comparable AEs. In addition to similar LEN-related AEs, the most common CRYO-related AEs included 50% elevated ALT, 50% elevated AST, and 38.5% fever, which were consistent with the TACE related AEs. Notably, the incidence of abdominal pain was higher in the TACE plus LEN group compared to the CRYO plus LEN group (7.5% vs. 0.8%, *P = 0.021*), while pleural effusion was more prevalent in the CRYO plus LEN group than that in the TACE plus LEN group (6.2% vs. 0, *P = 0.038*). **Conclusions:** The CRYO plus LEN group exhibited comparable efficacy and well-tolerated safety with TACE plus LEN for u-HCC patients within a real-world clinical setting. It offers a viable alternative for HCC characterized by hypovascularity, presenting a promising therapeutic approach in the clinical management of u-HCC. Clinical trial information: ChiCTR2200058643. Research Sponsor: None.

55 Poster Session

Effect of serum diamine oxidase activity derived from response to chemotherapy on adverse events and serum amino acid concentrations for esophageal cancer. First Author: Yuta Sato, Department of Gastroenterological Surgery and Pediatric Surgery, Gifu University Graduate School of Medicine, Gifu, Japan

Background: The relationship between activity of the small intestinal villi and the effectiveness of chemotherapy remains unclear. This study aimed to investigate how serum diamine oxidase (DAO) activity affects antitumor effects, adverse events, and amino acid absorption. **Methods:** We performed a single-center prospective cohort study that enrolled 50 patients with esophageal cancer (EC) receiving docetaxel, cisplatin, and 5-fluorouracil therapy. We determined the cut-off value of serum DAO activity contributing to a response to chemotherapy using a generalized additive model. Additionally, we compared adverse events, inflammatory markers, blood amino acid levels, and quality of life between the high and low DAO activity groups during chemotherapy. **Results:** The cut-off value of serum DAO activity at the first visit that contributed to a chemotherapy response was 6.5 units/L. Leukopenia and neutropenia of Grade $\geq$3 were significantly higher in the DAO low ($<$6.5 units/L) group (p = 0.044, 0.017, respectively). Interleukin-6 was significantly lower in the DAO high ($\geq$6.5 units/L) group at the first visit and at 4 weeks after the end of chemotherapy (p = 0.039, 0.011, respectively). Glutamine was higher in the DAO high group at all measurement points during chemotherapy. Fatigue was significantly lower in the DAO high group (p = 0.001). **Conclusions:** Serum DAO activity may be a predictor of the response to chemotherapy in patients with EC. The absorption capacity of amino acids was maintained in the group with high DAO activity, which may have contributed to the anti-inflammatory effect and provided a background for reducing adverse events. Clinical trial information: UMIN000048273. Research Sponsor: None.

56 Poster Session

Clinical determinants of survival in patients with stage II-III pancreatic cancer. First Author: Haruka Itakura, Stanford University School of Medicine, Stanford, CA

Background: We sought to identify the clinical determinants of overall survival (OS) in patients diagnosed with stage II-III pancreatic cancer not undergoing surgery. We curated a relatively homogenous cohort of patients who did not undergo surgical resection, but instead underwent chemotherapy in sequence with stereotactic body radiation therapy (SBRT) to examine the features that differentiated those with poor OS. **Methods:** In a retrospective study, we examined a cohort of 259 patients with stage II-III pancreatic cancer who underwent chemotherapy in sequence with SBRT without surgery at a single institution (Stanford Health Care). We conducted both univariate and multivariate Cox regression analyses to assess the relationships between OS and individual clinical and tumoral variables, including: age, sex, stage, Karnofsky performance status (KPS), body mass index, vessel involvement, tumor location, and biological equivalent dose [BED] of SBRT as potential determinants. **Results:** The study cohort consisted of 136 men (52.5%) and 123 women (47.5%) with a median age of 69 (range 38-94). Tumor histology was predominantly ductal adenocarcinoma (n=249, 96.1%), with tumor sites of involvement spanning: uncinate (n=35, 13.5%), head (n=160, 61.8%), body (n=59, 22.8%), and tail (n=5,1.9%). More patients had stage III (n=171, 66%) than stage II (n=88, 34%) disease, and their tumor resectability by NCCN criteria were rated as: unresectable (n=145, 56%), borderline (n=28, 10.8%), resectable (n=11, 4.2%), or unrecorded (n=75, 29%). Tumor progression was observed in local (n=71, 27.4%), regional (n=29, 11.2%), and distant (n=150, 57.9%) sites during the median follow up period of 17 months (range 15-18 months) from diagnosis and 12 months (10-13 months) from SBRT. Death (n=213, 82.2%) during this period was more common than survival (n=46, 17.8%). In univariate analyses, clinical features impacting OS included: KPS (hazard ratio [HR] 0.14, p=0.007); male sex (HR 1.44, p=0.01), pancreatic head tumors (HR 1.44, p=0.011), BED (HR 1.33, p=0.035), and age (HR 1.013, p=0.044). In the multivariate analysis, which incorporated only features significant in the univariate analyses, tumor location at the pancreatic head (HR 1.412, p=0.021) and male sex (HR 1.360, p=0.03) conferred the highest risks for poor OS, with BED bordering on significance (p=0.059) (Table). **Conclusions:** Among patients with stage II-III pancreatic cancer who underwent chemotherapy in sequence with SBRT, but not surgery, the most significant clinical determinants of poor OS were location of the tumor in the pancreatic head and male sex. Prioritizing additional disease monitoring and alternative therapies for this subset of patients at higher risk of poor survival may be warranted. Research Sponsor: Stanford Division of Oncology, Stanford Cancer Institute.

Multivariate Cox analysis.

Clinical variable	Hazard Ratio (HR)	P-value
Pancreatic head tumor	1.412	0.021
Male sex	1.360	0.030
BED-low	1.303	0.059
KPS	0.305	0.141
Age	1.005	0.443

57 Poster Session

Effect of TTYH3 on cholangiocarcinoma invasion, metastasis and lymph node metastasis through Wnt/β-catenin pathway. First Author: Yuwei Xie, Affiliated Hospital of Qingdao University, Qingdao, China

Background: Cholangiocarcinoma is a malignant tumor originating from the bile duct epithelium. Metastasis is an important factor affecting the prognosis of cholangiocarcinoma. To explore the role and mechanism of calcium-activated chloride channel protein Tweety homolog 3 (TTYH3) in cholangiocarcinoma metastasis. **Methods:** TTYH3 was overexpressed and knocked down in cholangiocarcinoma cells, and in vitro experiments were performed to clarify the biological function of TTYH3 in cholangiocarcinoma. Experiments on xenograft tumor mice model have shown that TTYH3 promotes tumorigenesis of cholangiocarcinoma cells. Analysis of the relationship between TTYH3 expression and patient prognosis and lymph node metastasis in cholangiocarcinoma tissue specimens. Exosomes were extracted from bile of patients with cholangiocarcinoma and bile duct stones, and the expression of TTYH3 in exosomes was compared. TTYH3 overexpressed exosomes were used to treat endothelial cells, and their function and mechanism in promoting lymphangiogenesis were analyzed. **Results:** In vitro experiments confirmed that TTYH3 promoted the migration and invasion of cholangiocarcinoma cell line QBC939. In vivo experiments confirmed that TTYH3 promotes the tumorigenesis of cholangiocarcinoma cells. TTYH3 promotes epithelial-to-mesenchymal transition of cholangiocarcinoma cells through the Wnt/β-catenin signaling pathway. TTYH3 promotes cholangiocarcinoma cell self-expression through positive feedback. TTYH3 is highly expressed in cholangiocarcinoma tissues. Patients with high TTYH3 expression have poor prognosis and a high incidence of lymph node metastasis. The TTYH3 protein content of bile exosomes in patients with cholangiocarcinoma is increased, which promotes the invasion and metastasis of cholangiocarcinoma cells, while also promoting lymphangiogenesis and increased permeability. TTYH3 promotes the uptake of exosomes by lymphatic cells and promotes lymphangiogenesis by regulating the influx of calcium ions and chloride ions in lymphatic cells. **Conclusions:** TTYH3 promotes the invasion and metastasis of cholangiocarcinoma cells through the Wnt/β-catenin signaling pathway, and exosome TTYH3 promotes lymphangiogenesis and lymph node metastasis. Research Sponsor: The study was supported by Taishan Scholars Program of Shandong Province; 2019010668; Natural Science Foundation of Shandong Province; ZR2021MH171, ZR2023MH243; Shandong Higher Education Young Science and Technology Support Program; 2020KJL005.

58 **Poster Session**

Correlation of enriched specific subset of immune cells nearby tumor associated macrophage (TAM) with pathologic complete response (pCR) of concurrent chemoradiotherapy followed by nivolumab in locally advanced rectal cancer (LARC). First Author: Mitsuho Imai, TR Supporting Office, National Cancer Center Hospital East, Kashiwa, Japan

Background: We previously reported tumor-infiltrating lymphocyte (TIL) dynamics predictive of pCR in microsatellite-stable (MSS) LARC. In the current analysis, we investigate whether an immune cell-to-cell spatial network may predict pCR in MSS LARC. **Methods:** VOLTAGE study is a phase I/II study to evaluate the efficacy of chemoradiotherapy (CRT) followed by nivolumab and subsequent surgery in LARC pts. H&E images and multiplex immunofluorescence (mIF) images containing a total of 35 markers for T cells, TAM, Myeloid-derived suppressor cells, and Dendritic cells were analyzed with the Lunit SCOPE platform (Lunit, Republic of Korea). The proportion of T cells among all DAPI-positive (-pos) cells in a 50-micrometer radius centered on the TAM cells was counted. **Results:** In the samples of MSS LARC pts gathered at baseline, pre-treatment (n=38), TIL density in tumor microenvironment (TME) analyzed by H&E images was significantly correlated with the proportions of CD8-pos, CD4-pos, and FOXP3-pos cells (coefficient [coeff] 0.635, 0.482, and 0.580, respectively), but loosely correlated with PDL1-pos, PD1-pos, and CTLA4-pos cells (coeff 0.255, 0.174, and 0.180, respectively). Interestingly, intratumoral TIL density was more strongly correlated with TAM markers such as CD68 (coeff 0.269), compared to stromal TIL density (coeff 0.086). pCR rate was 28.9% in all MSS LARC, with baseline TIL density in TME predicting pCR with area under the receiver operating characteristic curve (AUROC) of 0.636 (p = 0.101). Interestingly, the ratio of baseline PDL1-pos cell proportion nearby CD68-pos cells, over that in all TME area (hereafter referred to as 'TAM-PDL1-proximity score') showed the best predictive performance for pCR, with an AUROC of 0.768 (p = 0.005). At the optimal cutoff of 1.66 times TAM-PDL1-proximity score, pCR rates for pts $\geq$ the cutoff and $<$ the cutoff were 44% (11/25) and 0% (0/13), respectively (p = 0.006). **Conclusions:** PDL1-expressing immune cells nearby tumor associated macrophages before treatment is a promising predictive biomarker for pCR of neoadjuvant CRT followed by nivolumab in MSS LARC. Research Sponsor: Lunit, Inc.

59 **Poster Session**

Effect of deconvoluting single-cell transcriptomics on cellular programs regulated by cell-cell communication in colorectal cancer. First Author: Lujia Chen, University of Pittsburgh, Pittsburgh, PA

Background: Colorectal cancer (CRC) is the 3rd most common cancer. The consensus molecular subtypes among CRC tumors reflects the heterogeneity of composition and functional states of cells in the tumor microenvironments (TME), which in turn may underlie diverse behaviors of disease progression and responses to anticancer treatments. Cells within a TME communicate through intricate cell-cell communication (CCC) networks. The altered state of one cell can influence the states of other cells through ligand-receptor-mediated signal transduction. Gaining insight into the cellular states of cells and understanding their complex communications in a TME is vital for uncovering the heterogeneous mechanisms governing tumor growth, immune evasion, and therapy resistance. **Methods:** In this meta-analysis of eight single-cell cohorts encompassing 153 patients and 279 samples with more than 600,000 cells, we advance the understanding of CCC networks in CRC through a novel analytical framework. Employing hierarchical language modeling, we identify gene expression modules (GEMs) that mirror single-cell signaling states, crucial for deciphering the complexity of intercellular interactions. By applying causal discovery methods, we systematically uncover GEMs likely regulated by ligand-receptor signaling and cross-cell-type communication. We further validate the discovered CCC using spatial transcriptomic data by testing the spatial co-localization. **Results:** This analysis reveals nine cross-cell-type CCC programs, marked by highly correlated GEMs across various cell types, shedding light on the intricate CCC networks within the TME. The discovered CCC programs include malignant program, proliferation program, stromal interactions, stromal-myeloid interactions, innate immunity interactions, regulatory interactions, epithelial-lymphocyte interactions and exhaustion program. Each program is composed of GEMs from various cell types. Spatial transcriptomics further validate these findings by demonstrating the co-localization of GEMs within CCC programs in distinct spatial domains, emphasizing the spatial dynamics of tumor intercellular communication. We successfully construct the CCC subnetworks connected by ligand-receptor signaling. Our interactive website and analytical framework equip researchers with powerful tools to explore complex mechanisms, potentially uncovering novel drug targets and refining strategies for precision immunotherapies. **Conclusions:** This study provides an in-depth analysis of colorectal cancer by: *1)* Cataloging GEMs that precisely depict the transcriptomic processes unique to individual cell clusters or shared among multiple cell clusters. *2)* Presenting the CCC networks driven by ligand-receptor interactions within the TME supported by both single-cell RNA-seq data and spatial transcriptomic data. Research Sponsor: The National Library of Medicine; National Cancer Institute at the National Institutes of Health; R00LM013089, R01LM012011 and R01CA254274.

60 **Poster Session**

Predicting chemotherapy response in patients with advanced or metastatic pancreatic cancer using machine learning. First Author: Moonho Kim, Department of Hematology and Oncology, University of Ulsan College of Medicine, Gangneung Asan Hospital, Gangneung, South Korea

Background: When determining the initial chemotherapy regimen for advanced or metastatic pancreatic cancer, various factors must be evaluated. The decision between FOLFIRINOX and Gemcitabine/Nab-paclitaxel (GnP) is challenging, as patient survival hinges on the efficacy and toxicity profiles of these treatments, alongside individual patient characteristics and vulnerabilities.This study aims to guide the selection of an appropriate first-line chemotherapy regimen for advanced or metastatic pancreatic cancer by leveraging machine learning (ML) methods to predict survival outcomes. **Methods:** We conducted a retrospective analysis involving a cohort of 151 patients who underwent systemic chemotherapy for advanced or metastatic pancreatic cancer at Gangneung Asan Hospital in South Korea between 2019 and 2023. The initial data consisted of 17 types of demographic and clinical characteristics, as well as time-course of response and survival outcomes. The ML models predicting overall survival (OS) were developed using the XGBoost method. The minimal set of covariates resulting in the highest predictive performance during 5-fold cross validation were chosen as inputs to each model. **Results:** The median age of the patients was 66 years, with 62.3% being male. The ML models achieved the ROC-AUC of 0.81 when predicting OS after 12 months following the initial administration of FOLFIRINOX (n=61) or GnP (n=47). Five (peritoneal metastases, other metastases, bilirubin level, white blood cell counts, and retroperitoneal lymph node metastases) or four (age, tumor location, sex, and metastatic status) covariates were used to achieve the predictive accuracy for the two regimens, respectively. The median OS of the high versus low risk groups of FOLFIRINOX predicted by the ML models were significantly different (7 vs 18 months, $P < 0.01$), recording the hazard ratio (HR) of 2.79 (95% CI, 1.47-5.26). Similarly, the median OS of the high and low risk groups of GnP were significantly different (8 vs 16 months, $P < 0.001$, HR 3.50, 95% CI, 1.60-7.66). **Conclusions:** We developed the ML models that can compute the probability of OS based on the routinely collected data from patients with advanced or metastatic pancreatic cancer. To the best of our knowledge, this is the first ML solution aimed at aiding clinicians in the selection of the first-line chemotherapy regimen for pancreatic cancer. Research Sponsor: None.

61 **Poster Session**

^{68}Ga-FAPI-04 positron emission tomography/computed tomography (PET/CT) for detecting occult peritoneal metastasis in locally advanced gastric cancer: A single-center prospective cohort study. First Author: Qiancheng Hu Sr., The Department of Medical Oncology, Cancer Center, State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu, China

Background: Occult peritoneal metastasis (OPM) is a common finding in patients diagnosed with advanced gastric cancer. Preoperative diagnosis of OPM is crucial for developing treatment strategies and for evaluating the prognosis of patients with locally advanced gastric cancer. To evaluate the accuracy of ^{68}Ga-FAPI-04 PET/CT in diagnosing OPM in locally advanced gastric cancer. **Methods:** This was a prospective, observational, single-center, single-blind, cohort study. Patients with histologically proven locally advanced gastric or gastroesophageal junction adenocarcinoma on initial staging evaluation were recruited. Laparoscopic staging and cytological analysis of peritoneal washing served as reference standards for the final diagnosis. The primary outcome was the proportion of participants changing treatment strategy from curative to palliative treatment. **Results:** A total of 49 patients were recruited between November 2022 and July 2023. Nine of the 49 patients were diagnosed with OPM following ^{68}Ga-FAPI-04 PET/CT examinations. A total of 18.4% (n=9) of patients with locally advanced disease on initial staging evaluation by contrast-enhanced CT were upstaged to stage IV for peritoneal metastasis on ^{68}Ga-FAPI-04 PET/CT. The sensitivity of ^{68}Ga-FAPI-04 PET/CT in detecting OPM was 85.7%, and the specificity was 92.3%. The overall diagnostic accuracy of ^{68}Ga-FAPI-04 PET/CT was 91.8%. Based on ROC curve analysis, the area under the curve (AUC) was 0.893 (95% CI: 0.734–1). **Conclusions:** The findings of this study suggest a significantly additional value of ^{68}Ga-FAPI-04 PET/CT in detecting OPM. Thus, it would be useful to include ^{68}Ga-FAPI-04 PET/CT in the guidelines for staging locally advanced gastric cancer, instead of laparoscopic staging. Clinical trial information: ChiCTR2300067591. Research Sponsor: None.

62 Poster Session

The dynamic changes of circulating myeloid-derived suppressor cells (MDSCs) subsets in patients with colorectal cancer undergoing oxaliplatin-based chemotherapy. First Author: Dilafitria Fauza, Stem Cell and Cancer Institute, Jakarta, Indonesia

Background: Increased level of circulating myeloid-derived suppressor cells (MDSCs) have been associated with higher tumor stage, poorer survival, and poorer response to therapeutic agents in colorectal cancer (CRC). It has been reported that the common first-line chemotherapy involving combination with oxaliplatin mediated MDSCs depletion via induction of cell death. However, this phenomenon is yet to be further investigated since it only occurred in polymophonuclear MDSC (PMN-MDSC) subset, not in monocytic MDSC (M-MDSC). The present study aims to learn deeper on the dynamic changes of circulating MDSCs in response to oxaliplatin-based treatment in CRC patients. **Methods:** This was a prospective study that recruited 30 treatment-naïve patients with varying stage of CRC who were scheduled to receive oxaliplatin-based chemotherapy. Blood sampling was conducted prior and at several time points during and after chemotherapy. Multicolor flow cytometry assay was used to analyze the proportion of HLA-DR-, CD33+, and CD15+ (PMN-MDSC) and CD14+ (M-MDSC) cells within peripheral blood mononuclear cells (PBMCs). Other essential tumor biomarkers such as carcinoembryonic antigen (CEA) and tumor infiltrating lymphocytes (TILs) were assessed as well. As control, 14 healthy subjects were recruited. **Results:** Our result showed that circulating PMN-MDSCs was significantly higher in CRC patients compared to healthy subjects (p=0.003), whilst insignificant result was shown by M-MDSCs (p=0.890). Following chemotherapy, MDSCs level showed dynamic changes. Interestingly, a subgroup of CRC patients with decreased in both PMN- and M-MDSCs levels on D-14 chemotherapy were consistently showed a significant decreased of MDSCs level during and after therapy completion compared to baseline (p=0.0078). **Conclusions:** Circulating MDSCs level, particularly PMN-MDSCs in CRC patients was significantly higher compared to healthy subjects. Changes in both circulating PMN- and M-MDSCs levels at D-14 chemotherapy might have prognostic value in oxaliplatin-based chemotherapy. Research Sponsor: Stem Cell and Cancer Institute, PT Kalbe Farma Tbk.

64 Poster Session

i-Biomarker CaDx: A circulating miRNA-based multi-cancer detection test with generative and explainable AI for colorectal cancer. First Author: Alexandru Floares, Artificial Intelligence Expert, Cluj-Napoca, Romania

Background: Colorectal cancer (CRC), the second most deadly cancer, underscores the critical need for early detection to significantly improve treatment outcomes and survival rates. Colonoscopy, flexible sigmoidoscopy, and the fecal immunochemical tests (FIT), often fail to capture early disease, significantly decreasing the survival chance. Circulating miRNA is a promising non-invasive biomarker for various cancers, including CRC. The i-Biomarker CaDx (patent pending) is an innovative multi-cancer early detection and diagnosis platform, covering 32 cancer types with an impressive accuracy rate of 99-100%. This study focuses on the effectiveness of i-Biomarker CaDx for CRC, employing significant data collection and leveraging insights from Generative AI (GenAI) and Explainable Artificial Intelligence (XAI). **Methods:** We collected various available datasets (e.g. GSE106817, etc.) encompassing 305 colorectal cancer patients and a matching number of healthy controls. Microarray was employed to profile circulating miRNAs. We used various classification paradigms, e.g., decision trees, neural networks, etc. Hyperparameter optimization was conducted, and the best-performing classifiers were amalgamated in the final model, weighted by their respective efficacies. We assessed i-Biomarker CaDx's performance through cross-validation and independent test sets. The XAI provided detailed insights into miRNA variations associated with personalized diagnostic. GenAI integrated the test into the screening and early detection best practice workflows and performs Functional Analysis. **Results:** i-Biomarker CaDx shows exceptional diagnostic accuracy of 99-100%, surpassing conventional colorectal cancer diagnostic methods like colonoscopy, flexible sigmoidoscopy, and FIT. It can also be used for personalized treatment response monitoring. I-Biomarker effectively deciphers intricate miRNA relationships relevant to colorectal cancer using XAI. Thus, our analyses shed light on miRNA patterns and their associations with colorectal cancer, enhancing the understanding of the underlying molecular complexities of the disease. It goes further by explaining the personalized cellular and molecular mechanisms involved, and it will be integrated into the corresponding medical workflows. **Conclusions:** Our AI-powered multi-cancer early diagnostic platform demonstrates outstanding performance in detecting CRC, surpassing traditional diagnostic methods like colonoscopy, flexible sigmoidoscopy, and FIT. XAI allows for in-depth exploration of miRNA alterations and their impact on CRC, enriching our interpretations at both the population and individual levels. These findings underscore the substantial potential of i-Biomarker CaDx as a transformative, non-invasive diagnostic tool for CRC. Research Sponsor: None.

65 Poster Session

Safety analysis by treatment periods from EMERALD-1: A phase 3, randomized, placebo-controlled study of transarterial chemoembolization with durvalumab with/without bevacizumab in participants with embolization-eligible unresectable hepatocellular carcinoma. First Author: Masatoshi Kudo, Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan

Background: The global Phase 3 EMERALD-1 study (NCT03778957) primary endpoint was met: durvalumab (D) + bevacizumab (B) + transarterial chemoembolization (TACE) significantly improved progression-free survival vs placebos (pbos) + TACE (median 15.0 vs 8.2 mo; HR, 0.77; 95% CI, 0.61–0.98; p=0.032 [threshold 0.0435]) in participants (pts) with embolization-eligible unresectable hepatocellular carcinoma (uHCC) with a manageable safety profile. This post hoc, exploratory analysis assessed safety in the study's two treatment (tx) periods (pds): D-TACE (D-T) and D-B. **Methods:** Pts were randomized 1:1:1 to D+TACE, D+B+TACE, or pbos+TACE. In the D-T pd, pts received 1–4 TACE (cTACE or DEB-TACE [investigator choice]) plus D (1500 mg Q4W) or pbo for D. In the D-B pd, post-last TACE, pts received D (1120 mg Q3W) plus pbo for B, D (1120 mg Q3W) plus B (15 mg/kg Q3W), or pbos for D and B. Adverse events (AEs), start/end date, maximum/change in CTCAE grade, and causality were assessed in the D-T and D-B pds in pts who received any study tx in the arm to which they were randomized, until end of follow-up. **Results:** The Table shows duration of exposure (DoE). In the D+TACE, D+B+TACE, and pbos+TACE arms, AEs were reported by 144 (74.6%), 139 (72.0%), and 148 (74.0%) pts in the D-T pd and 133 (68.9%), 147 (76.2%), and 132 (66.0%) pts in the D-B pd; were possibly related (pos rel) to study tx in 59 (30.6%), 56 (29.0%), and 41 (20.5%) pts in the D-T pd and 76 (39.4%), 114 (59.1%), and 69 (34.5%) pts in the D-B pd; and were provoked by TACE in 72 (37.3%), 90 (46.6%), and 85 (42.5%) pts in the D-T pd and 16 (8.3%), 18 (9.3%), and 21 (10.5%) pts in the D-B pd, respectively. **Conclusions:** D+B+TACE had a manageable safety profile across the D-T and D-B pds, consistent with the individual agents and underlying disease. These data further support D+B+TACE as a new potential standard of care in embolization-eligible uHCC. Clinical trial information: NCT03778957. Research Sponsor: AstraZeneca.

	D+TACE D-T pd (n=193)	D+B+TACE D-T pd (n=193)	Pbos+TACE D-T pd (n=200)	D+TACE D-B pd (n=193)	D+B+TACE D-B pd (n=193)	Pbos+TACE D-B pd (n=200)
Median (range) DoE to D or pbo; to B or pbo, months	2.76 (0.2–30.8)	2.76 (0.2–25.3)	2.76 (0.9–26.1)	6.93 (0.7–45.5); 6.92 (0.7–45.5)	10.51 (0.3–38.1); 9.35 (0.3–36.5)	8.31 (0.7–43.0); 8.31 (0.7–43.0)
Any AE, n (%)						
Max Grade 3/4	29 (15.0)	29 (15.0)	26 (13.0)	36 (18.7)	60 (31.1)	22 (11.0)
Pos rel to study tx, max Grade 3/4*	4 (2.1)	6 (3.1)	4 (2.0)	10 (5.2)	38 (19.7)	8 (4.0)
With outcome of death	*9 (4.7)*	*6 (3.1)*	*5 (2.5)*	*6 (3.1)*	*16 (8.3)*	*6 (3.0)*
Pos rel to study tx*	*0*	*2 (1.0)†*	*1 (0.5)†*	*1 (0.5)‡*	*0*	*2 (1.0)‡*
Provoked by TACE	0	0	1 (0.5)	0	0	0
Leading to discontinuation of study tx	11 (5.7)	7 (3.6)	5 (2.5)	13 (6.7)	42 (21.8)	10 (5.0)
Pos rel to study tx*	*1 (0.5)*	*3 (1.6)*	*2 (1.0)*	*5 (2.6)*	*18 (9.3)*	*4 (2.0)*

*Excluding TACE. †Pos rel to D or pbo for D. ‡Pos rel to B or pbo for B.

66 Poster Session

Perioperative FLOT + immunotherapy for resectable gastric and gastro-esophageal junction cancer: A systematic review and meta-analysis. First Author: Lorenz Fort Estrada Revillas, St. Luke's Medical Center, Quezon City, Philippines

Background: The current standard of care for resectable gastric and GEJ cancers is perioperative chemotherapy with FLOT.Although its benefits in improving rates of pathologic complete response, increasing prospects of R0 resection, and improving survival have been proven, efforts to find novel strategies which can improve on its gains continue.The addition of an immune checkpoint inhibitor to FLOT has been a focal point of research in this field. This meta-analysis evaluated high-quality data from clinical trials to determine the efficacy of this chemoimmunotherapy combination. **Methods:** A systematic search of English-language articles on PubMed, Cochrane and Google scholar was done to identify randomized trials investigating the use of perioperative FLOT and immune checkpoint inhibitors in the treatment of resectable gastric and GEJ cancer. Quality of studies was assessed using the Revised Cochrane risk-of-bias tool for randomized trials. Inverse variance was the statistical method used with random effects as the analysis model in the production of the Forest plot and calculation of odds ratio at 95% CI. **Results:** Three RCTs (N = 1446), each with two arms, were included in the meta-analysis. The Phase II Dante Trial (N= 295)compared perioperative FLOT alone with perioperative atezolizumab + FLOT. The Phase III Keynote 585 trial(N=203) and the phase III Matterhorn trial (N=948) compared perioperative placebo + FLOT with perioperative pembrolizumab + FLOT, and perioperative Durvalumab + FLOT, respectively. Risk of bias and heterogeneity were low. Pooled results showed that in patients given perioperative FLOT + immunotherapy, there is statistically significant improvement in the rate of pathologic complete response (OR 2.60 95% CI 1.88-3.61, $p < 0.0001$). In terms of rate of R0 resection, there was no statistically significant difference between the two groups (OR 1.02 95% CI 0.75-1.38,p= 0.92). **Conclusions:** This analysis shows that adding immunotherapy to FLOT improves the rate of pathologic complete response, and maintains the high rate of R0 resection, in resectable gastric and GEJ cancers. Favorable results of pending survival outcomes from these trials may help re-shape the current standard of care in this field. Research Sponsor: None.

68 **Poster Session**

Navigating the future of pancreatic cancer treatment: Systematic review insights from immunotherapy clinical trials. First Author: Zouina Sarfraz, Fatima Jinnah Medical University, Lahore, Pakistan

Background: Pancreatic cancer remains a formidable challenge, being the seventh leading cause of cancer-related deaths globally. Despite advances in medical science, survival rates have not significantly improved, primarily due to late diagnosis and the limited efficacy of conventional treatments. This study investigates the potential of immunotherapy, offering a new horizon for treatment strategies. **Methods:** A systematic review was conducted, encompassing Phase I-III clinical trials that utilized immunotherapy in treating pancreatic cancer. Databases such as PubMed/Medline, CINAHL, Scopus, and ClinicalTrials.Gov were searched following PRISMA guidelines. A total of 29 completed trials and 106 ongoing studies were analyzed, focusing on survival rates, response to treatment, and adverse events. **Results:** Analysis of 29 completed clinical trials revealed that immunotherapy could extend the median OS in selected cohorts, with a notable trial showing an increase in OS from 6 to 13.6 months in patients receiving PD-1 blockers. Phase I trials demonstrated a cumulative OS of 13.6 months and a PFS of 5.1 months across various interventions. Ongoing studies, numbering 106, are exploring a wide range of immunotherapeutic agents, aiming to improve these outcomes further. Adverse events were consistent with expectations for immunotherapy, indicating a manageable safety profile. The most promising interventions appear to be combination therapies that include checkpoint inhibitors, showing an increase in the 5-year survival rate of up to 30% for patients undergoing adjunctive treatment post-surgery. **Conclusions:** Immunotherapy presents a potential paradigm shift in the treatment of pancreatic cancer. However, more robust clinical trials are necessary to fully understand its efficacy and safety. Future research should focus on identifying biomarkers for patient selection and exploring combination therapies to enhance treatment responses. The disparity in access to these therapies, especially in low- and middle-income countries, underscores the need for global efforts to make advanced treatments more accessible. Research Sponsor: None.

69 **Poster Session**

Circulating tumor DNA analysis in patients with esophageal cancer treated with neoadjuvant chemoradiotherapy followed by surgery. First Author: Mian Xie, Guangdong Provincial People's Hospital, Guangzhou, China

Background: The aim of this prospectively study is to investigate circulating tumor DNA (ctDNA) as a prognostic marker for survival in locally advanced esophageal squamous cell cancer (ESCC) patients treated with neoadjuvant chemoradiotherapy (nCRT) and surgery. **Methods:** Serial plasma samples were collected from 68 ESCC patients treated with neoadjuvant chemoradiotherapy before surgery. ctDNA was detected before treatment, after neoadjuvant chemoradiotherapy and after surgery by personalized, next-generation sequencing assay. Cox regression analyses were used to evaluate the prognostic significance of ctDNA for recurrence-free survival (RFS) and overall survival (OS). **Results:** ctDNA was detectable in 89.7%, 17.2%, and 6.9% of pretreatment, post-neoadjuvant chemoradiotherapy and post-surgery plasma samples, respectively. The conversion of ctDNA status from positive at baseline to negative at 4-6 weeks after neoadjuvant chemoradiotherapy was significantly associated with pathological complete response (pCR) (P = 0.02). Significant worse RFS was related to detectable ctDNA after neoadjuvant chemoradiotherapy (P = 0.008) or after surgery (P = 0.001). Detectable ctDNA at baseline (P = 0.01) and after surgery (P = 0.008) were associated with worse OS. In multivariate analysis, detectable postoperative ctDNA was significantly associated with RFS (P = 0.012) and OS (P = 0.025) after adjusting for other clinicopathological risk factors. **Conclusions:** ctDNA status is a strong prognostic factor of recurrence in locally advanced ESCC patients. Consequently, ctDNA could potentially improve pre- and post-treatment risk assessment and facilitate individual therapy for ESCC patients. Research Sponsor: None.

70 **Poster Session**

Clinical characteristics and outcomes in patients with early-onset locally advanced rectal cancer. First Author: Andrea Pretta, Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy

Background: Despite a reduction in both the incidence and mortality of CRC in the elderly population, recent studies have highlighted an increase in the incidence of early-onset CRC (EO-CRC). Clinical and prognostic data in this context are limited and conflicting. The aim of our study was to evaluate the clinical differences and outcomes of patients with early onset locally advanced rectal cancer. **Methods:** We retrospectively collected data from 305 patients affected by LARC treated in Italy at the Medical Oncology Units of the University Hospital of Cagliari, Istituto Nazionale dei Tumori Milan, and AOU Ospedali Riuniti Ancona. All patients underwent neoadjuvant chemoradiotherapy. The primary objective was overall survival (OS) while while secondary objectives were overall response rate (ORR) and major TRG. **Results:** Twenty five (8,2%) pts were EO-RC and 280 (91,8%) were LO-RC. In EO-RC the locations were distributed as follows: 9 (36%) lower rectum, 13 (52%) medium rectum, and 3 (12%) upper rectum. Pathologic responses were as follows: 3 (12%) TRG-0, 6 (24%) TRG-1, 10 (40%) TRG-2, and 6 (24%) TRG-3. While the radiological responses were as follows: 2 (8%) CR, 15 (60%) PR, 7 (28%) SD, and 1 (4%) PD. In LO-RC the locations were: 78 (27,8%) lower rectum, 153 (54,6%) medium rectum, and 49 (17,6%) upper rectum. Pathologic responses were as follows: 29 (10,4%) TRG-0, 60 (21,4%) TRG-1, 159 (56,8%) TRG-2, and 32 (11,4%) TRG-3. Radiological responses were as follows: 25 (8,9%) CR, 155 (61,4%) PR, 64 (22,9%) SD, and 19 (6,8%) PD. The 10 year overall survival was significantly higher in LO-RC patients compared to EO-CRC patients: 92.54% versus 70.83% (p = 0.0005). **Conclusions:** Compared to LO-RCs, EO-RC patients had more frequent low rectal tumors and higher rates of major pathological responses. Despite this, 10-year OS was found to be inferior in EO-RC. Further studies and insights will be necessary to better understand the biological and clinical characteristics of early-onset tumors. Research Sponsor: None.

71 **Poster Session**

Circulating tumor DNA for predicting radiographic and pathologic response to total neoadjuvant therapy in locally advanced rectal cancer: ENSEMBLE-1. First Author: Yoshinori Kagawa, Department of Gastroenterological Surgery, Osaka International Cancer Institute, Osaka, Japan

Background: Total neoadjuvant therapy (TNT) has dramatically shifted the treatment paradigm for locally advanced rectal cancer (LARC), prolonging survival with high rates of pathologic complete response (pCR) and introducing opportunities for nonoperative management (NOM). However, there is a need for robust predictive biomarkers of TNT efficacy, local cancer regrowth in NOM, and overall prognosis. Circulating tumor DNA (ctDNA) is a minimally invasive biomarker used to detect molecular residual disease (MRD) and predict recurrence in colorectal cancer after curative resection. The effectiveness of ctDNA MRD status specifically as a predictive biomarker for TNT was evaluated in the Phase II TNT study, ENSEMBLE-1 (jRCTs051200113), conducted in Japan. **Methods:** Patients with LARC undergoing TNT were enrolled in ENSEMBLE-1. Protocol treatment was defined as short-course radiotherapy (SCRT: 25Gy) followed by six cycles of CAPOX and total mesorectal excision (TME). NOM was allowed if a clinical complete response (cCR) was achieved after TNT. ctDNA was measured by SignateraTM (Natera, Inc.) at the following time points: baseline (pre-treatment), after SCRT, after 4 cycles of CAPOX, before TME, and post operatively at 4w, 12w, 24, 36 and 48w in the GALAXY trial (UMIN000039205). **Results:** A total of 30 patients were enrolled in the study. After completing TNT, TME and NOM were performed in 20 and 7 patients, respectively. ctDNA was measured in 26 patients (TME: 19 patients, NOM: 7 patients). ctDNA was detected in 100% (25/25) at baseline, 81% (21/26) after SCRT, 31% (8/26) after 4 cycles of CAPOX, and 45% (9/20) after TNT. The attached table shows the results of statistical analyses of the correlation between ctDNA status, clinical response, TME or NOM, and pathologic complete response (pCR). It was found that ctDNA status after SCRT and after 4 cycles of CAPOX was associated with cCR or non cCR (p=0.007 and p=0.007, respectively). Additionally, ctDNA status after TNT was associated with pCR or non pCR (p=0.029). **Conclusions:** Our study demonstrates that ctDNA-based MRD may predict TNT response in LARC patients. Negative ctDNA during treatment correlates with favorable responses and may be an aid in NOM decision making. Clinical trial information: jRCTs051200113. Research Sponsor: None.

Correlation with ctDNA, clinical response, treatment after TNT and pathological response.

	After SCRT (N = 26)	After 4 cycles of CAPOX (N = 26)	After TNT (N = 20)
Clinical Response cCR or non cCR	P = 0.007	P = 0.007	P = 0.157
Treatment after TNT NOM or TME	P = 0.101	P = 0.062	P = 0.479
Pathological response after TME pCR or non pCR	P = 0.095	P = 0.102	P = 0.029

Fisher's exact test was used to statistically examine the correlation between ctDNA MRD status and the factors at each timing.
cCR: clinical complete response, pCR: pathological complete response, SCRT: short-course radiation therapy, TNT: total neoadjuvant therapy, TME: total mesorectal excision.

73 **Poster Session**

Effect of pancreatobiliary reflux on macrophage-secreted IL-8, PI3K/NFκB pathway, and promotion of cholangiocarcinoma progression. First Author: Tingting Wu, Affiliated Hospital of Qingdao University, Qingdao, China

Background: Persistent pancreaticobiliary reflux (PBR) is associated with a high risk of biliary malignancy. This study aimed to evaluate the proportion of PBR in biliary tract diseases and mechanisms by which PBR promoted cholangiocarcinoma progression. **Methods:** Overall, 227 consecutive patients with primary biliary tract disease participated in this study. The amylase levels in the collected bile were analyzed. The mechanisms underlying the effect of high-amylase bile on bile duct epithelial and cholangiocarcinoma cells progression were analyzed. The source of interleukin-8 (IL-8) and its effects on the biological functions of cholangiocarcinoma cells were investigated. **Results:** The bile amylase levels in 148 of 227 patients were higher than the upper serum amylase limit of 135 IU/L. PBR was significantly correlated with sex, pyrexia, and serum gamma-glutamyl transferase (GGT) levels in the patient cohort. High-amylase bile-induced DNA damage and genetic differences in the transcript levels of the gallbladder mucosa and facilitated the proliferation and migration of bile duct cancer cells (HUCCT1 and QBC939 cells). The concentration of many cytokines increased in high-amylase bile. IL-8 is secreted primarily by macrophages via the mitogen-activated protein kinase pathway and partially by bile duct epithelial cells. IL-8 promotes the progression of HUCCT1 and QBC939 cells by regulating the expression of epithelial-mesenchymal transition-associated proteins and activating the phosphatidylinositol 3-kinase/nuclear factor kappa-B pathway. **Conclusions:** PBR is one of the primary causes of biliary disease. IL-8 secreted by macrophages or bile duct epithelial cells stimulated by high-amylase bile promotes cholangiocarcinoma progression. Research Sponsor: Taishan Scholars Program of Shandong Province; Natural Science Foundation of Shandong Province; ZR2023MH243; Shandong Higher Education Young Science and Technology Support Program.

74 **Poster Session**

Utility of radiomic features in predicting clinical outcomes in stage II-III pancreatic cancer. First Author: Haruka Itakura, Stanford University School of Medicine, Stanford, CA

Background: We identified computed tomography (CT)-derived radiomic features predictive of tumor progression within three months, then examined their ability to prognosticate overall survival (OS) along with clinical features in pancreatic cancer. We evaluated these features in patients with unresected pancreatic cancer who underwent stereotactic body radiation therapy (SBRT) in sequence with chemotherapy, but not surgery. **Methods:** In this retrospective study, we examined a cohort of 101 patients with stage II-III pancreatic cancer who underwent SBRT with sequential chemotherapy at a single institution (Stanford Health Care) between 1999-2020. From their pre-SBRT contrast-enhanced CT images with segmented tumors, delineating regions-of-interest, we extracted 900 radiomic (quantitative pixel-level imaging characteristic) features. In the first phase, we identified radiomic features that predicted rapid tumor progression within three months following SBRT. We divided the dataset into a training set (n = 53) for model development and a test set (n = 48) for evaluation. Using logistic regression with the Least Absolute Shrinkage and Selection Operator algorithm for feature selection and classification, we built a binary prediction model on the training set to identify patients at risk of progression within three months of SBRT. To fine-tune parameters, we performed five-fold cross-validation (CV) on the training set, repeating each set of parameters five times. We assessed model performance on the test set using the area under the curve (AUC). We selected the model with the best AUC, generating the predictive radiomic feature set. In the second phase, we conducted univariate and multivariate Cox regression analyses to assess the relationship between OS and individual clinical variables (age, sex, stage, vessel involvement, tumor location, performance status, body mass index, biological equivalent dose of radiation) and the radiomic feature set as high versus low risk. **Results:** Our cohort consisted of 48 men (mean age, 70 years ± 11 [SD]) and 53 women (mean age, 67 years ± 13 [SD]). From the first phase, 32 textural features comprised the radiomic feature set that best predicted rapid tumor progression, with mean AUCs of 0.852 (CV, n=53) and 0.814 (test, n=48). In the univariate Cox model, only the radiomic feature set was predictive of OS (hazard ratio, HR, 1.724, p=0.011). In the multivariate Cox model, radiomic features and age were significant predictors of OS, with HR of 1.819 (p=0.007) and 1.024 (p=0.024), respectively. **Conclusions:** CT-derived radiomic features predict rapid tumor progression following SBRT, confer nearly a twofold increase in mortality risk, and, along with patient age, enhance the identification of patients with stage II-III pancreatic cancer with poor OS. Research Sponsor: Stanford Division of Oncology, Stanford Cancer Institute.

	HR	P value
Radiomics - High Risk	1.82	0.007
Age	1.02	0.024
Pancreatic Head Tumor	1.45	0.102
BED - Low	1.31	0.224
Male	1.27	0.284

75 **Poster Session**

Prognostic impact of codon-specific KRAS mutational status on survival in patients with metastatic colorectal cancer treated with TAS-102 or regorafenib. First Author: Meng-Che Hsieh, Department of Hematology and Oncology, E-Da Cancer Hospital, Kaohsiung, Taiwan

Background: Previous study demonstrated KRAS (Kirsten rat sarcoma virus) codon G12 mutation as a potential biomarker of resistance in metastatic colorectal cancer (mCRC). Our study aimed to evaluate the prognostic impact of codon-specific KRAS mutational status on survival in patients with mCRC treated with TAS-102 or regorafenib. **Methods:** mCRC Patients treated with TAS-102 or regorafenib were retrospectively enrolled into our study. Patients were classified into KRAS G12 ($KRAS^{G12}$) mutation and no $KRAS^{G12}$ mutation according to extended RAS testing. Survival was estimated for comparison, stratified by KRAS mutational status and treatment. Kaplan-Meier curves were estimated for overall survival (OS). **Results:** A total of 183 patients were enrolled into our study, with 91 patients treated with TAS-102 and 92 patients treated with regorafenib. The median age was 63 years old in our cohort. Most patients were male (54%) with left side colon (85%). After extended RAS/RAF mutational testing, 28% patients had $KRAS^{G12}$ mutation, 50% had RAS/RAF^{WT}, 9% had $KRAS^{G13}$ mutation, 8% had $KRAS^{other}$ mutation, 3% had NRAS mutation and 2% had BRAF mutation. For patients treated with TAS-102 group, 20% patients had $KRAS^{G12}$ mutation, while for regorafenib group, 38% patients had $KRAS^{G12}$ mutation. The median OS of TAS-102 was 4.5 versus 11.3 months for $KRAS^{G12}$ mutation and no $KRAS^{G12}$ mutation, respectively (p= 0.013). The median OS of regorafenib was 10.5 versus 6.3 months for $KRAS^{G12}$ mutation and no $KRAS^{G12}$ mutation, respectively (p= 0.183). Furthermore, 34% patients with $KRAS^{G12}$ mutation received TAS-102, while 56% patients without $KRAS^{G12}$ mutation received TAS-102. For patients with $KRAS^{G12}$ mutation, the median OS was 4.5 m versus 10.5 months for TAS-102 and regorafenib group, respectively (p= 0.113). For patients without $KRAS^{G12}$ mutation, the median OS was 11.3m versus 6.3 months for TAS-102 and regorafenib group, respectively (p= 0.047). **Conclusions:** The prognostic impact of $KRAS^{G12}$ was divergent between mCRC patients treated with TAS-102 and regorafenib. Codon-specific KRAS mutational status should be taken into consideration before treatment. Research Sponsor: None.

76 **Poster Session**

Quantitative evaluation of oncogenic KRAS signaling and therapeutic effects of molecular-targeted drugs in living cells by single-molecule imaging. First Author: Ryoma Yokoi, Department of Gastroenterological Surgery, Gifu University Hospital, Gifu, Japan

Background: Oncogenic KRAS mutations pose challenges due to their constitutive activation and resistance to drugs in colorectal cancer. However, several aspects remain unresolved. Single-molecule imaging has revealed distinct behaviors of KRAS. Inactive KRAS wild-type (WT) molecules exhibit continuous lateral diffusion on the plasma membrane, while activated or oncogenic KRAS molecules display slower diffusion and transient trapping due to interactions with signaling molecules. These observations suggest that the overall signal intensity of KRAS within a cell is finely regulated by integrating short-term pulse signals during transient trapping. **Methods:** We conducted single-molecule observations of KRAS (WT, G13D, and G12D/C/V) in living colon cancer cells, both with and without molecular-targeted drugs, before and after EGF stimulation. We quantitatively analyzed their diffusional behavior to evaluate KRAS signaling and the therapeutic effects of molecular-targeted drugs. **Results:** The temporal fraction of trapped KRAS WT was highest at 2 minutes (6.4%) and decreased to pre-activation level (3.0%) at 5 minutes after EGF stimulation. Although the temporal fractions of trapped KRAS mutants were higher than those of KRAS WT both before stimulation (5%) and after stimulation (10%), their diffusional behaviors were mutation-specific. The temporal fraction of trapped KRAS G13D increased sharply, and those of KRAS G12D and G12C increased at a moderate rate, while that of KRAS G12V did not elevate after EGF stimulation. Cetuximab treatment significantly reduced the temporal fraction of trapped KRAS WT after stimulation, but only moderately decreased those of KRAS mutants. Notably, transient trappings of KRAS G12D and G12C were abrogated by KRAS inhibitors, and the combined therapy of KRAS inhibitors and cetuximab demonstrated additive effects. **Conclusions:** Our findings indicate that the mutation-specific diffusional behavior of oncogenic KRAS can be quantitatively assessed by single-molecule imaging. This method serves as a powerful tool to uncover the mechanisms underlying oncogenic KRAS signaling and evaluate the therapeutic efficacy of molecular-targeted drugs in living cells. Research Sponsor: COMIT Collaborative Research 2023.

77 Poster Session

Association of vitamin D deficiency with liver cirrhosis and hepatocellular carcinoma risk: A retrospective cohort study from the TriNetX US collaborative networks. First Author: Yuan-Tsung Tseng, Department of Medical Research, Tainan Municipal Hospital (Managed By Show Chwan Medical Care Corporation), Tainan, Taiwan

Background: Emerging evidence highlights the critical role of vitamin D in liver health, especially concerning the risk of liver cirrhosis and hepatocellular carcinoma (HCC). This investigation aims to explore the association between vitamin D deficiency and the prevalence of these liver diseases, contrasting outcomes between individuals with deficient and normal vitamin D levels. **Methods:** This cohort study utilized the US Collaborative Network within the TrinetX database, encompassing 63 medical institutions. It enrolled participants aged 20 years and older from 2011 to 2023. Vitamin D status was determined through serum 25-hydroxyvitamin D levels, categorizing deficiency as 20-30 ng/mL and normal levels as 30-80 ng/mL. Employing 1:1 propensity score matching, the study controlled for 32 characteristics, such as demographic information, health conditions, and medication use, to ensure equitable group comparisons. Additionally, a 1-year washout period was established. The primary aim was to assess the incidence of liver cirrhosis and HCC over a decade. **Results:** Analyzing data from over 1.86 million participants, the study ensured a balanced comparison across all variables. Participants had an average age of 50.6 years, with 66% identifying as white and 9% as black. Notably, vitamin D deficiency was significantly associated with an increased risk of liver cirrhosis (HR 1.16 [CI 1.11-1.21]) and HCC (HR 1.25 [CI 1.15-1.36]). Kaplan-Meier cumulative risk analysis further confirmed these elevated risks for both liver conditions in individuals with vitamin D deficiency compared to those with sufficient levels. **Conclusions:** This study confirms a significant association between vitamin D deficiency and a higher risk of liver cirrhosis and HCC, underscoring the importance of vitamin D in maintaining liver health. The findings support the potential of vitamin D level management as a preventive strategy against liver diseases. The implications of this research necessitate further exploration into the efficacy of vitamin D supplementation for liver disease prevention. Research Sponsor: None.

78 Poster Session

Comparative analysis of cirrhosis and hepatocellular carcinoma outcomes in Asian populations with non-alcoholic fatty liver disease (NAFLD) and metabolic dysfunction-associated steatohepatitis liver disease (MASLD): A five-year retrospective study. First Author: Yuan-Tsung Tseng, Department of Medical Research, Tainan Municipal Hospital (Managed By Show Chwan Medical Care Corporation), Tainan, Taiwan

Background: Metabolic Dysfunction-Associated Steatohepatitis Liver Disease (MASLD) represents the most up-to-date definition of Non-Alcoholic Fatty Liver Disease (NAFLD) for Asian populations, acknowledging that manifestations may differ across racial/ethnic groups. Due to metabolic and anthropometric differences, adapted criteria for MASLD have been proposed for Asian adults. This analysis aims to compare clinical outcomes between Asian patients diagnosed with MASLD and those with NAFLD. **Methods:** In this retrospective analysis, 48,189 Asian adults suspected of having MASLD were identified from the TriNetX global research network between January 1, 2010 and December 31, 2023. An equal number of patients (48,189) diagnosed with NAFLD were matched on a 1:1 basis with MASLD patients through propensity score matching. MASLD criteria were adapted to be Asia-specific, requiring a Body Mass Index (BMI) of $\geq$23 along with the presence of four aspects of metabolic dysfunction. Over a 5-year follow-up period, primary outcomes of cirrhosis and hepatocellular carcinoma (HCC) incidences were determined using Kaplan-Meier methods. Cumulative incidence curves depicted the rates of these events over time. Hazard ratios (HR) for the outcomes were calculated using Cox regression models to estimate the risk associated with MASLD. **Results:** Over 5 years, the cumulative incidence of cirrhosis (3.0% vs 3.0%, p=0.800) and HCC (1.3% vs 1.4%, p=0.695) were numerically lower in MASLD compared to NAFLD patients, respectively. Adjusted HRs for MASLD were: cirrhosis 1.00 (0.87-1.14) and HCC 0.86 (0.68-1.10). **Conclusions:** This study compared the clinical outcomes of MASLD and NAFLD in Asian populations and found no significant differences in identifying the risk of cirrhosis and hepatocellular carcinoma between the two diagnostic criteria. However, introducing the new term and diagnostic criteria of MASLD helps reduce the stigmatization associated with NAFLD, emphasizing the central role of metabolic dysfunction in disease occurrence. Although this study did not find significant differences between MASLD and NAFLD in predicting cirrhosis and hepatocellular carcinoma, the concept of Asian-specific diagnostic criteria remains important, highlighting that disease manifestations and risk factors may vary across different races and populations, necessitating personalized prevention and treatment strategies for specific populations. Future research should further explore the similarities and differences between MASLD and NAFLD in different Asian subgroups to optimize diagnostic criteria, improve the accuracy of risk prediction, and develop targeted interventions. Research Sponsor: None.

79 Poster Session

Comparative analysis of mortality and hospital expenditure in patients with gastroenterological cancer: Thailand and United States. First Author: Thanathip Suenghataiphorn, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Background: Concerns about rising health care cost and quality of care has been a major health issue worldwide. Gastrointestinal (GI) cancer accounts for one-quarter of the global cancer incidence. However, there are limited evidence, which demonstrates the differences in clinical outcome and economic burden of GI cancer when comparing between health care setting of developed and developing countries. **Methods:** Two data sources were analyzed: (i) The 2020 U.S. National Inpatient Sample (NIS) involving patients that were primarily discharged with gastroenterological cancer, and (ii) data at tertiary care center in Thailand used for this comparative study, with similar period and conditions. Participants were identified using relevant ICD-10 CM codes. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariate logistic and linear regression analyses. Participants are divided into those who experienced mortality and those who survived. We report crude mortality rates and expenditure outcomes. Statistical significance was established at a p-value of 0.05. **Results:** We identified 9,299 Thai records and estimated 216,859 US records with a primary diagnosis of GI cancer at discharge. Of these, 2.15% (200/9,299) of the Thai records and 3.82% (8,285/216,859) of the US records died. In a multivariate analysis, death during hospitalization is associated with higher length of stay (Thai: b = 18.10, 95% CI (16.71, 19.49), $p < 0.001$), (US: b = 3.38, 95% CI 3.38 (2.14, 4.63), $p < 0.001$) and higher hospitalization charges (Thai: b = 155,530.02 THB, 95% CI (141,805.10, 169,254.80), $p < 0.001$), (US: b = 46,882.44 USD, 95% CI (31,629.51, 62,135.37), $p < 0.001$). Subpopulation analysis revealed similar significant results. We observed higher increased length of stay in Thailand, whereas higher crude mortality rate and hospitalization charges was observed in the United States. **Conclusions:** In both Thailand and United States, mortality in patient with GI cancer is associated with increase in length of stay and higher hospitalization expenses. However, the magnitude of difference in each outcome differs between two countries. Future studies investigating health care costs, cultural role and clinical outcomes may provide insights for cost-reduction strategies, while maintaining or improving the current standard of care in this population group. Research Sponsor: None.

Number of hospitalizations, with total estimations and crude mortality rates.

	Thailand (Tertiary Center)		United States	
Type Of Cancer	Died	Total	Died	Total
Upper GI tract Cancer	42 (3.75%)	1,119	1,845 (5.19%)	35,539
Colon Cancer	27 (0.90%)	2,984	2,035 (2.54%)	80,114
Rectum Cancer	19 (0.89%)	2,145	644 (1.76%)	36,463
Pancreas and Biliary Cancer	38 (3.69%)	1,031	2,001 (4.64%)	43,094
Liver Cancer	74 (3.67%)	2,019	1,705 (8.06%)	21,141
Gastroenterological Cancer	200 (2.15%)	9,299	8,285 (3.82%)	216,859

80 Poster Session

Racial differences of secondary metastasis in patients with colon cancer: A United States population-based cohort study. First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Disparities in health outcomes exist among racial and ethnic groups in the United States, notably in patients with colon cancer. Metastasis is the primary cause of cancer morbidity and mortality. However, data on the metastasis risks and clinical outcomes on hospitalized individuals with colon cancer is still limited. Therefore, we aim to assess the association between metastatic colon cancer and racial differences. **Methods:** We analyzed the 2020 U.S. National Inpatient Sample (NIS) to explore patients who have colon cancer as the primary diagnosis. Additionally, we identified evidence of metastasis, as recorded by ICD-10-CM. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariable logistic and linear regression analyses. The primary outcome was racial differences in organ metastasis and secondary outcomes included mortality and length of stay. Statistical significance was established at p-value of 0.05. **Results:** We identified 80,130 patients with primary diagnosis of colon cancer at discharge. The mean age was 67.4 years; 49.7% were female. Caucasians accounted for 69.3%, with African Americans at 13.3% and Hispanics at 8.2%. 15% of the patients had liver metastasis, whereas 22% had lung metastasis. In a multivariate analysis adjusting for patient, COVID-19, chemotherapy usage and hospital factors, African Americans had higher risk of lung metastasis (aOR 1.22; 95%CI (1.07, 1.40), p = 0.003), higher risk of liver metastasis (aOR 1.51; 95%CI (1.31, 1.74), p = 0.021) and longer length of stay (b = 0.95; 95%CI (0.56, 1.33), p = 0.001). Hispanics also had higher risk of lung (aOR 1.22, $p < 0.05$) and liver metastasis (aOR 1.24, p = 0.021). We observed an increase in risk of metastasis and mortality but non-statistically significant in some parameters and races, as shown in table provided. **Conclusions:** In conclusion, our study revealed that racial difference is associated with higher risk of metastasis, as well as other outcomes. To establish a causal relationship between races, metastasis, and mortality in patients with colon cancer, further longitudinal research is necessary. Research Sponsor: None.

Adjusted odds ratio, adjusted for patient characteristics, hospital location and COVID-19 conditions.

Race	Lung metastasis	Liver metastasis	Mortality	Length of stay**
Caucasian	Baseline			
African American	**1.22 (1.07, 1.40)***	**1.51 (1.31, 1.74)***	1.08 (0.77, 1.52)	**0.95 (0.56, 1.33)***
Hispanic	**1.18 (1.00, 1.40)***	**1.24 (1.03, 1.50)***	1.02 (0.67, 1.56)	0.16 (-0.27, 0.61)
Asian	1.00 (0.77, 1.29)	0.83 (0.61, 1.12)	1.51 (0.82, 2.77)	0.59 (-0.02, 1.21)
Native American	1.00 (0.47, 2.13)	1.18 (0.52, 2.68)	N/A	0.06 (-1.45, 1.59)
Others	1.06 (0.82, 1.36)	1.07 (0.80, 1.44)	1.33 (0.70, 2.55)	0.32 (-0.29, 0.93)

*Denotes statistically significant at p-level.
**Length of Stay is expressed as beta-coefficient N/A denotes no subpopulation group.

81 Poster Session

Clinical outcome of patients hospitalized for pancreatic-biliary malignancy with comorbid acute decompensated heart failure: An analysis from National Inpatient Sample (NIS). First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Recent data suggest an association between cardiovascular disease burden and biliary cancer patients. However, the outcomes of hospitalized patients for biliary-pancreatic malignancy with concurrent acute decompensated heart failure (ADHF) are not well understood. Therefore, our objective is to assess the impact of ADHF on patients hospitalized for biliary-pancreatic malignancy. **Methods:** We used the 2020 U.S. National Inpatient Sample (NIS) to study patients hospitalized for biliary tract and pancreatic malignancy with concurrent acute decompensated heart failure (ADHF) identified by ICD-10 CM codes. Adjusted odds ratios (aORs) for predefined outcomes were determined via multivariable logistic and linear regression analyses. The primary outcome examined was inpatient mortality, while secondary outcomes included complications related to various body systems. **Results:** We identified 43,009 patients with a primary discharge diagnosis of biliary tract and pancreatic cancer. The mean age was 68.5 years; 49.4% were female. Caucasians accounted for 68%, followed by Hispanics (13%). Of these, 6.27% (3,699/43,009) had a concurrent diagnosis of heart failure. In the survey's multivariable logistic and linear regression analysis, accounting for patient and hospital confounding factors, ADHF demonstrated significant associations with higher in-hospital mortality (aOR 1.63; 95% CI 1.09, 2.44, p = 0.015). In addition, a significant association between ADHF and various adverse in-hospital outcome was observed including prolonged mean length of stay (Beta 1.45; 95% CI 0.67, 2.24, $p < 0.001$), increased mean total hospital cost (Beta 3,757; 95% CI: 2,641, 36,630, p = 0.024), elevated risk of shock (aOR 2.75; 95% CI: 1.77, 4.26, $p < 0.001$), higher risk of sepsis (aOR 1.71, 95% CI: 1.09, 2.68, p = 0.018), increased risk of acute respiratory failure (aOR 3.18, 95% CI: 2.25, 4.51, $p < 0.001$), and heightened risk of acute kidney injury (aOR 1.57; 95% CI: 1.24, 1.99, $p < 0.001$). **Conclusions:** Among patients hospitalized for biliary-pancreatic malignancy, concurrent ADHF is linked to increased mortality risk and various in-hospital adverse complications. Additional long-term studies are required for a comprehensive understanding of this association. Research Sponsor: None.

82 Poster Session

Effect of statin use on long-term survival after diagnosis of colorectal cancer: Emulating hypothetical target trials using a nationwide real-world database. First Author: Hyeong-taek Woo, Department of Preventive Medicine, Keimyung University School of Medicine, Daegu, South Korea

Background: Observational studies suggest that statin use after colorectal cancer (CRC) diagnosis is associated with improved survival. However, potential bias due to misalignment of time zero in observational studies may distort associations and therefore requires validation using robust epidemiological methods. We aimed to emulate a hypothetical randomized trial—a target trial—for estimating per-protocol effects of statin initiation in patients with incident colorectal cancer on long-term survival. **Methods:** To emulate a target trial using real-world data, we extracted information from 103,005 patients diagnosed with CRC between 2005 and 2015 from the Korean National Health Insurance (KNHI) database, encompassing health records for the entire Korean population. We excluded individuals who had been prescribed statins for at least 180 days before the CRC diagnosis or those with missing or incomplete demographic information. We set a 180-day grace period and compared the group that initiated statin treatment within 180 days after the CRC diagnosis with the non-statin group using the "clone-censor-weight" method. Patients' demographic and socioeconomic information, along with colorectal cancer treatment, were included as baseline covariates. Additionally, the Charlson Comorbidity Index (CCI) score was included both as a baseline covariate and as a time-varying covariate. Hazard ratios (HRs) for all-cause mortality and CRC-specific mortality within 60 months of baseline were calculated using pooled logistic regression models. **Results:** Among the 103,005 patients diagnosed with CRC, 88,516 were finally analyzed after the exclusion process. A total of 2,071 (2.3%) individuals initiated statin treatment during the grace period and 86,445 (97.7%) patients did not. Statin initiators, compared with statin noninitiators tended to be older (mean age: 65.7 vs. 62.6) and had a higher CCI score at baseline (mean CCI score: 1.38 vs.1.26). Individuals who initiated statin treatment did not reduce the hazard of all-cause mortality (The adjusted HR 1.01, 95% CI 0.98-1.04) and CRC-specific mortality (The adjusted HR 1.01, 95% CI 0.97-1.04). **Conclusions:** The results of the analysis after removing potential biases showed that statin was not related to improving survival in CRC patients. The study results conflict with those of previous observational studies but are consistent with the findings of other recently conducted target trial emulations. Research Sponsor: None.

83 Poster Session

First-line (1L) anti-PD-1 plus chemotherapy in HER2-negative advanced gastric cancer: Real-world evidence from a single Korean center. First Author: Joosung Gabriel Shim, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea

Background: The implementation of immune checkpoint inhibitor combinations as first-line (1L) treatment has shown promising outcomes and is now the standard of care for HER2-negative advanced gastric cancer. However, real-world evidence supporting this approach as 1L treatment remains limited. Here, we present an analysis of real-world outcomes, comparing 1L anti-PD-1 combined with doublet chemotherapy to the previous standard chemotherapy. **Methods:** Patient from January 2005 to August 2023 were retrospectively reviewed. The study defined the molecular epidemiology cohort (M cohort) as patients with results for HER2, Epstein-Barr virus (EBV), mismatch repair (MMR), or PD-L1. HER2-negative patients who received palliative first-line chemotherapy doublet regimens with or without PD-1 inhibitor were included. Survival analysis included progression-free survival (PFS) and overall survival (OS), as well as subgroup analyses for molecular subtypes. **Results:** Total 3,028 were enrolled in the M cohort. The incidence rates of HER2-positive, EBV-positive, and deficient Mismatch Repair (dMMR) were 20.0% (606/3028), 3.8% (93/2432), and 4.7% (126/2660), respectively. PD-L1 testing was conducted on 1,394 patients, with 54.3% (1634/3028) having a CPS (Combined Positive Score) of $\geq$10, and 47.6% (664/1394) having a CPS of $\geq$1. Among these patients 1,527 had received chemotherapy doublet, and 153 had received chemotherapy doublet with PD-1 inhibitor as their 1L treatment. During a median follow-up of 56.5 months (95% CI,49.9-66.2), patients who had received PD-1 inhibitor combination therapy showed improved PFS (7.1 vs. 6.1 months; Hazard Ratio [HR], 0.77; 95% Confidence Interval [CI], 0.64–0.93) and OS (18.1 vs. 14.6 months; HR 0.80; 95% CI, 0.63–1.01) compared to those without it. The benefits in PFS from PD-1 inhibitor combination therapy were particularly notable in patients with deficient MMR status (HR, 0.22 vs. 0.80 in those without PD-1 inhibitor combination; p for interaction $<$0.05) and in patients with signet ring cell carcinoma histology (HR, 0.58 vs. 0.92 in those without PD-1 inhibitor combination; p for interaction $<$0.05). **Conclusions:** We observed real-world efficacy of the combination of PD-1 inhibitor and chemotherapy doublet as 1L treatment for HER2-negative advanced gastric cancer, consistent with previous clinical trials. Research Sponsor: None.

Baseline characteristics.

Subgroup	IO+Doublet group, n/N	Doublet group, n/N	Hazard Ratio for PFS (95% CI)	P-interaction
Overall	153	1527		
Age at diagnosis				0.35
<65 yr	60/119	1063/1151	0.74 (0.59–0.91)	
≥65 yr	26/34	336/376	0.91 (0.61–1.36)	
Sex				0.72
Female	48/62	548/586	0.80 (0.60–1.08)	
Male	68/91	851/941	0.75 (0.58–0.96)	
Progression free survival	7.1 months	6.1 months	0.77 (0.64 - 0.93)	0.02*
Overall survival	18.1 months	14.6 months	0.80 (0.63 - 1.01)	0.98

*n, events. N, participants.

84 Poster Session

Systemic treatment post curative-intent intervention based on tumor-informed circulating tumor DNA result for oligometastatic colorectal cancer. First Author: Teerada Siripoon, Ramathibodi Hospital, Mahidol University, Ratchathewi, Thailand

Background: Local therapies potentially offer a curative approach for patients with oligometastatic colorectal cancer (CRC). The effectiveness of systemic chemotherapy following definitive local treatment in this setting is not well-defined. Tumor-informed circulating tumor DNA (ctDNA) might guide management strategies after curative-intent local treatment. **Methods:** This is a single institution retrospective study of patients with CRC who underwent curative-intent local therapy to an isolated site of metastatic disease and had post-intervention tumor-informed ctDNA (Signatera) testing. The study was approved by the institutional review board. Clinical characteristics, including ctDNA results, were collected and evaluated. Kaplan-Meier method and log-rank test were used to calculate and compare disease-free survival (DFS). Factors associated with DFS were analyzed using multivariate Cox proportional hazards model. **Results:** 45 patients were included with median age of 59 years, 62% being male, 91% white, and 53% with stage IV disease at diagnosis. 37% of the patients had RAS mutations, no patient had BRAF mutation, and 2.2% patient had mismatch repair deficient disease. Isolated liver metastases were present in 80% of patients, lung metastases in 11% and other sites in 9%. 44 patients received chemotherapy prior to definitive treatment, with a median treatment duration of 16 weeks. ctDNA tests were done prior to local therapy in 23 patients, with 14 cases (61%) testing positive. Definitive treatment included resection (58%), ablation (13%), radiotherapy (4%), and multimodality (25%). Post-definitive treatment chemotherapy was administered to 24 (53%) patients. ctDNA positivity following definitive therapy was observed in 10 patients (22%), which was associated with a poorer prognosis, with a median DFS of 5.3 months compared to 21.3 months for the ctDNA-negative group ($p<0.001$). These findings were confirmed on multivariate analysis. In patients who had negative ctDNA after definitive local treatment, median DFS was 14.9 months for those who received post-intervention chemotherapy versus 21.3 months for those without post-intervention chemotherapy (p=0.835). **Conclusions:** Patients with negative ctDNA results following definitive local therapy for isolated metastatic CRC have better prognosis. Post-intervention chemotherapy in this group of patients was not associated with improved DFS. ctDNA guided omission of post-intervention chemotherapy following curative-intent local treatment of oligometastatic CRC warrants further study. Research Sponsor: None.

DFS in ctDNA negative patients after definitive treatment.

	Recurrence	Median DFS (months)	P value	Hazard ratio (univariate analysis)
No additional chemotherapy (N=16)	8 (50%)	21.3 (12.3-NR)		
With additional chemotherapy (N=19)	9 (47.4%)	14.9 (8.4-NR)	0.835	1.11 (0.42-2.89)

85 **Poster Session**

Trends in megestrol acetate prescription among Korean patients with biliary-pancreatic cancer and their impact. First Author: Ju Won Kim, Korea University Anam Hospital, Seoul, South Korea

Background: Chemotherapy-induced anorexia poses a significant challenge for cancer patients, particularly in biliary tract cancer (BTC) and pancreatic ductal adenocarcinoma (PDAC), known for their poor response to treatment. Megestrol acetate (MA), a commonly prescribed appetite stimulant, is associated with concerns regarding thrombosis and polypharmacy. Understanding the trends in MA prescription and its cascade effects is essential for optimizing cancer care. **Methods:** We conducted a retrospective cohort study using data from the Health Insurance and Review Assessment Service (HIRA) database in South Korea. The study included patients diagnosed with BTC and PDAC between 2008 and 2017. Prescription trends for MA, thrombosis events, anticoagulant prescriptions, and total parenteral nutrition (TPN) were analyzed. Statistical analysis included Chi-square tests and Kaplan-Meier estimates. **Results:** In our analysis of 41,670 patients with BTC and PDAC between 2008 and 2017, MA prescriptions increased notably, with PDAC patients rising from 7.85% to 51.84%. TPN prescriptions remained consistently high, especially among patients prescribed MA. For instance, in 2008, 94.71% of BTC patients prescribed MA received TPN, compared to 70.34% without MA. Similarly, in 2017, 87.56% of those prescribed MA received TPN, compared to 61.63% without MA. Among BTC patients with long-term MA prescriptions, 16.34% received anticoagulants, compared to 4.92% without MA ($p<0.001$). Among PDAC patients, 18.3% with long-term MA prescriptions received anticoagulants, compared to 7.12% without MA ($p<0.001$). **Conclusions:** The study highlights the escalating trend in MA prescriptions among BTC and PDAC patients, along with increased thrombosis diagnoses and anticoagulant prescriptions. These findings underscore the importance of understanding and managing the cascade effects of MA use and associated polypharmacy in optimizing cancer care and improving patient outcomes. Research Sponsor: None.

86 **Poster Session**

Challenges of liquid panel in genomic profiling of esophageal squamous cell carcinoma (ESCC): Insights from an analysis of over 1000 cases. First Author: Ryuichi Morita, Gastoenterology and Hepatology, Kyoto Prefectural University of Medicine, Kyoto, Japan

Background: Genomic analysis of ctDNA from cancer patients can allow identification of actionable alterations of tumor without an invasive biopsy. ctDNA analysis has been reported to be superior for global summary of tumor heterogeneity and a short turnaround time compared to tissue analysis,however, there are potential issues including the detection sensitivity, threshold to determine TMB-H, and clonal hematopoiesis of indeterminate potential (CHIP). In order to elucidate the impact of ctDNA analysis on personalized cancer treatment, we decided to examine the genetic landscape and clinical outcomes of ESCC cohort registered in the C-CAT database. **Methods:** We retrospectively analyzed data from 1059 cases of ESCC registered in the C-CAT from June 2019 to February 2024. Clinical characteristics, TMB status, pathological gene variants, and time to treatment failure (TTF) of first-line treatment were examined. **Results:** The panels applied to eligible patients consisted of 925 tumor tissue panels (87.3%) and 134 liquid panels (12.7%). Pathological gene mutations were detected in 924 cases (99.8%) in tissue panels and 133 cases (99.2%) in liquid panels. The top 10 detected genes were *TP53* (93.4%), *CDKN2A* (57.8%), *CDKN2B* (45.5%), *CCND1* (43.9%), *FGF19* (41.0%), *PIK3CA* (29.0%), *NFE2L2* (28.3%), *BCL6* (16.5%), *NOTCH1* (13.5%), and *KMT2D* (12.2%). The detection rate for these genes excluding *NOTCH1* and *KMT2D* were significantly higher in tissue panels than in liquid panels ($P\leq0.01$). The median TMB was 5.00 Muts/Mb for both. In first-line treatment, the TTF for immune checkpoint inhibitors (ICIs) and chemotherapy was significantly longer in TMB-H ($\geqq$10 Muts/Mb) compared to TMB-L (3.1M vs. 1.9M, $P<0.01$) in patients evaluated by tissue panels, but it was not proven in patients evaluated by liquid panels (P=0.38). Furthermore, the results suggest that patients with *CDKN2A*, *CCND1*, and *FGF19* variants benefit more by adding ICIs to chemotherapy than patients without these variants and while the opposite was true for *BCL6* and *NOTCH1* and *KMT2D*. **Conclusions:** In this ESCC cohort, detection rates in the liquid panels were generally lower than in the tissue panels, suggesting that sufficient ctDNA could not be obtained in many cases. The appropriate patient selection for the liquid panels and the timing of blood collection should be discussed. Furthermore, the ideal threshold for determining TMB-H in the liquid panels needs to be further investigated. Research Sponsor: None.

87 **Poster Session**

The prognosis of pancreatic neuroendocrine tumors according to the WHO 2017 classification: The multi-center experience in Taiwan. First Author: Wei-Pang Ho, Department of Hematology-Oncology, Chang Gung Memorial Hospital at Linkou and Chang Gung University College of Medicine, Taoyuan City, Taiwan

Background: The occurrence of pancreatic neuroendocrine tumors (PanNETs) remains infrequent, there is an upward trend in their diagnosis. Our retrospective study, conducted in Taiwan, focuses on exploring the interplay between clinical characteristics, treatment modalities, and prognosis in PanNET cases. Particularly, we aim to assess the implications of the updated WHO classification system on prognosis. **Methods:** We conducted a retrospective analysis of 176 PanNET cases from Chang Gung Medical Foundation, encompassing Linkou, Taoyuan, and Tucheng Hospitals, spanning the years 2009 to 2022. Pathology reports for all cases were reevaluated by pathologists according to the WHO 2017 classifications. Clinical features and overall survival outcomes were documented. Additionally, we examined the prognosis of distinct subgroups categorized by the WHO 2017 classification and their respective treatments. **Results:** The 5-year survival rate for all patients in the cohort stood at 58.7%. Among these, individuals diagnosed with NET G1 exhibited the highest survival rate (n = 78, 83.1%), followed by those with NET G2 (n = 57, 55.0%), NET G3 (n = 25, 14.6%), and NEC (n = 16, 9.4%). Univariate analysis highlighted several significant prognostic factors, including age, absence of symptoms at diagnosis, tumor size, lymph node involvement, distant metastasis, higher Ki-67 index, and cellular morphology. Comparative analysis between the WHO 2017 and WHO 2010 classifications revealed both systems as significant independent predictors of overall survival in PanNET cases. Notably, the 95% confidence interval for the WHO 2017 classification (2.892–9.703) showed a slight improvement in prognostic precision compared to the WHO 2010 classification (3.696–10.067). Under the WHO 2010 classification, NET G3 and NEC were combined, with NEC presenting higher rates of distant metastases, lymph node involvement, and Ki-67 index. Further investigation revealed that patients receiving somatostatin analogs, chemotherapy, or targeted therapy exhibited improved survival rates, particularly notable in NET G3 and NEC subgroups. Furthermore, NEC patients displayed extended treatment durations and higher objective response rates to first-line chemotherapy compared to the NET G3 group. **Conclusions:** Our retrospective analysis has illuminated the interrelation between prognostic factors and the overall survival rate. Furthermore, the updated WHO 2017 classification elucidates the distinctions between G3 and NEC, thus influencing the selection of clinical interventions. Research Sponsor: None.

88 **Poster Session**

Impact of EOB-MRI on the outcome of patients with pancreatic cancer in real-world settings. First Author: Atsushi Oba, Division of Hepatobiliary and Pancreatic Surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Contrast-enhanced computed tomography (CE-CT) is a commonly used imaging modality for the preoperative detection of local extension and distant metastasis in patients (pts) with pancreatic cancer (PaC). There have been cases where surgical treatment was deemed unsuitable due to unexpected distant metastases discovered during surgery, which had not been detected by CE-CT. While studies have reported gadoxetate disodium-enhanced MRI (EOB-MRI) improves the detection of liver metastases, it is not clear whether adding EOB-MRI to CE-CT provides clinical benefits, e.g. improved outcomes through the early access to appropriate treatments by avoiding unnecessary surgery (open-close surgery) in pts with PaC. This study aimed to assess the effectiveness of adding EOB-MRI before surgical or non-surgical treatment on overall survival (OS) in pts with PaC in real world settings. **Methods:** This was a retrospective cohort study using a nationwide hospital-claims database in Japan. Pts aged $\geq$18 years diagnosed with PaC with a record of surgery, radiotherapy, or chemotherapy, who had an imaging modality were identified between January 1, 2011 to October 31, 2021. Pts were grouped into EOB-MRI and no EOB-MRI groups, and further grouped into surgery, no surgery and open-close laparotomy. OS was compared between propensity-score matched EOB-MRI and no EOB-MRI groups using the Cox regression model. **Results:** 39,624 pts were included in the study, of them, 4,477 (11.3%) underwent EOB-MRI prior to the initial treatment. 2,061 (46.0%) pts in EOB-MRI group underwent surgery, 2,346 (52.4%) had no surgery and 70 (1.6%) had open-close laparotomy. In 35,147 (88.7%) pts in no EOB-MRI group, 13,182 (37.5%) underwent surgery, 21,506 (61.2%) had no surgery, and 459 (1.3%) had open-close laparotomy. The OS results in subgroups are shown in the Table. **Conclusions:** In real-world settings, EOB-MRI performed prior to the initial treatment was associated with significantly higher OS than those without EOB-MRI in pts who did not undergo surgery, but there was no difference in OS in pts who underwent surgery. These results suggest that the early detection of micro hepatic metastases through EOB-MRI and multidisciplinary treatment that enables EOB-MRI may contribute to improved outcomes in pts with PaC. Clinical trial information: NCT06106568. Research Sponsor: None.

OS.

Crude	**No surgery**		**Surgery**	
Modality (N)	No EOB-MRI (21,506)	EOB-MRI (2,346)	No EOB-MRI (13,182)	EOB-MRI (2,061)
Death (%)	10,692 (49.7)	1,014 (43.2)	3,248(24.6)	443 (21.5)
Median survival time, days (95% CI)	420 (411–431)	553 (510–602)	NR (3,500–NR)	3,225 (2,823–NR)
Adjusted	**No surgery**		**Surgery**	
Modality (N)	No EOB-MRI (5,667)	EOB-MRI (1,889)	No EOB-MRI (5,172)	EOB-MRI (1,724)
Death (%)	2,579(45.5)	785 (41.6)	1,138 (22.0)	365 (21.2)
Median survival time, days (95% CI)	467 (445–491)	595 (528–662)	NR (3,500–NR)	NR (2,823–NR)
Hazard ratio (95% CI)	-	0.79 (0.73–0.85)	-	0.99 (0.88–1.11)
p-value	-	<.01	-	0.86

CI, confidence interval; NR, not reached.

89 **Poster Session**

Does liver cirrhosis affect outcomes in non-metastatic esophageal squamous cell carcinoma (ESCC) undergoing radiotherapy-based treatment? First Author: YuYang Hua, Department of Hematology-Oncology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiuang, Taiwan

Background: Liver cirrhosis frequently coexists with esophageal squamous cell carcinoma (ESCC), as both conditions share alcohol consumption as a common etiological factor. Surgical intervention is often contraindicated or associated with significant morbidity in patients with non-metastatic ESCC and liver cirrhosis. Consequently, radiotherapy-based therapy is commonly employed. This study aims to investigate prognostic factors for overall survival in such patients undergoing radiotherapy-based therapy. Additionally, we will evaluate predictors for the 90-day mortality rate, proposed as a measure to mitigate treatment-related toxicity and prevent unwarranted or excessive medical interventions. **Methods:** From January 2001 to December 2021, we conducted a retrospective review of the medical records of 1298 patients diagnosed with esophageal squamous cell carcinoma (ESCC). Within this cohort, we identified 103 patients with concomitant liver cirrhosis, diagnosed through abdominal ultrasonography, computerized tomography, and/or liver biopsy, as appropriate. Of these individuals, 78 patients with non-metastatic ESCC and liver cirrhosis were included in our analysis. We collected clinicopathologic parameters and examined their correlation with overall survival and the 90-day mortality rate. **Results:** Univariate analysis revealed several factors significantly associated with inferior overall survival: Child-Pugh classification B/C ($P<0.001$, compared to A), radiotherapy alone (P=0.03, compared to chemoradiotherapy), prothrombin time prolonged by $\geq$2 seconds (P=0.024), albumin levels $\leq$3.5g/dl ($P<0.001$), controlled/refractory ascites (P=0.01, compared to no ascites), and total bilirubin levels $\geq$1.5mg/dl (P=0.004). In multivariate analyses, albumin levels $\leq$3.5g/dl (P=0.001, odds ratio: 2.500) and total bilirubin levels $\geq$1.5mg/dl (P=0.019, odds ratio: 2.012) were identified as independent prognostic factors. Among the 78 patients receiving radiotherapy-based therapy, the 90-day mortality rate was 10.3% (n=8). Clinical 8th AJCC stage IVA (P=0.02), clinical T classification T3/4 (P=0.049), prothrombin time prolonged by $\geq$4 seconds (P=0.009), and albumin levels $\leq$3.5g/dl (P=0.027) were significantly correlated with higher 90-day mortality rate. The logistic model indicated that albumin levels $\leq$3.5g/dl (P=0.015, odds ratio: 16.129) and clinical 8th AJCC stage IVA (P=0.012, odds ratio: 17.544) were independently associated with higher 90-day mortality rate. **Conclusions:** In patients undergoing radiotherapy-based therapy for non-metastatic esophageal squamous cell carcinoma (ESCC) and liver cirrhosis, pretreatment hypoalbuminemia has been associated with increased 90-day mortality and unfavorable prognosis. Research Sponsor: None.

90 **Poster Session**

A potent and selective pan-RAS inhibitor, ADT-1004, targeting complex KRAS mutations for pancreatic cancer. First Author: Gary Piazza, Auburn University, Auburn, AL

Background: Pancreatic ductal adenocarcinoma (PDAC) is a challenging cancer with a 5-year survival rate of under 12%. More than 90% of PDAC cases involve KRAS mutations. $KRAS^{G12C}$ inhibitors recently developed have limited use because only 3% of PDAC express this mutation, highlighting the urgent need for pan-RAS inhibitors to address the complex mutation landscape in PDAC while avoiding resistance mechanisms. We synthesized and evaluated a novel pan-RAS inhibitor, ADT-1004, in mouse tumor models transplanted with mouse PDAC cell lines or patient-derived xenografts. ADT-1004 is an orally bioavailable prodrug of ADT-007, a highly potent and selective pan-RAS inhibitor (doi.org/10.1101/2023.05.17.541233). **Methods:** Human and mouse PDAC cell lines were utilized to evaluate *in vitro* growth inhibitory potency and selectivity of ADT-007. For *in vivo* experiments, KPC-Luc (1×10^5) and 2838C3-Luc (1.5×10^5) PDAC cells harboring the $KRAS^{G12D}$ mutation were injected into the pancreas of C57BL/6J mice. After one week, the mice were randomly divided into treatment groups (n = 7 per group) and received oral ADT-1004 at a dose of 40mg/kg body weight five times a week for 4 weeks. Tumor burden was assessed weekly by monitoring bioluminescence signals using the IVIS Xenogen imaging system. Four patient-derived xenografts from PDAC patients with $KRAS^{G12C}$, $KRAS^{G12D}$, $KRAS^{G12V}$, $KRAS^{G13Q}$ mutations were subcutaneously implanted in NSG mice by a small incision in the right flank. A week later, when the tumors reached a size of $100mm^3$ mice were randomized (n=7 per group) and treated orally with 40mg/kg of ADT-1004 five times a week for 6 weeks. Body weight and tumor size were measured twice weekly. **Results:** ADT-007 potently and selectively inhibited the growth of human and mouse PDAC cell lines. For example, the IC_{50} value pf ADT-007 for $KRAS^{G12C}$ MIA PaCA-2 PDAC cells was as low as 2 nM compared to 2500 nM for RAS^{WT} BxPC3 PDAC cells. Growth inhibition was dependent on activated RAS and associated with reduced GTP-RAS levels and MAPK/AKT signaling. ADT-1004 was well tolerated in mice at a dose up to 175 mg/kg bid orally with sustained plasma levels of ADT-007 far exceeding growth IC_{50} values. When administered orally at 40 mg/kg body weight, ADT-1004 displayed robust antitumor activity in mouse tumor models using patient or mouse derived PDAC cell lines with G12D, G12V, G12C, or G13Q KRAS mutations, causing significant inhibitory effects on ERK phosphorylation. **Conclusions:** ADT-1004 inhibited tumor growth of KRAS mutant PDA tumors by targeting activated RAS to disrupt downstream MAPK/AKT signaling. The results highlight the promise of ADT-1004 as a novel pan-RAS inhibitor and open new strategies for addressing the complex genetic landscape of PDAC and other RAS driven cancers. Research Sponsor: NIH NCI; R01CA254197.

91 **Poster Session**

Efficacy assessment of a novel pan-RAS inhibitor in KRAS-mutant and wild type colorectal 3D bioprinted organoid tumor tissue. First Author: Parmanand Ahirwar, CerFlux, Birmingham, AL

Background: Colorectal cancer (CRC) is the third leading type of cancer worldwide, with ~150,000 new cases in the US annually and a grim 14% 5-year survival for patients diagnosed at a late stage. A lack of treatment options leads to persistently poor prognosis for patients with advanced stage disease. KRAS mutations are well known drivers of CRC and other GI cancers. Multiple KRAS mutations occur in CRC, including G12D (34%), G12V (21%), G13D (20%), G12C (8%), and others (18%). Existing KRAS-targeted therapies have limited use in CRC, underscoring the need for pan-RAS inhibitors in treating CRC and other RAS driven cancers. Objective: Assess activity of ADT-007, our pan-RAS inhibitor, on wild-type (WT) and KRAS-mutant 3D bioprinted organoid tumor (BOT) tissue using our high-throughput *ex vivo* platform. **Methods:** Using previously established bioprinting protocols, WT and mutant BOTs were printed with HT29 and HCT116 cells, respectively. HT29 is an established human WT CRC cell line with known sensitivity to proteosome and survivin inhibitors. HCT116 is a $KRAS^{G13D}$ mutant human CRC cell line. 3 sets of BOTs were generated and acclimated for 24h. One set was treated for 72h with proteosome inhibitor Bortezomib, another with survivin inhibitor YM155, and the third with our novel pan-RAS inhibitor ADT-007. Dose response curves were generated from both conventional ATP luminescence readouts and high-content imaging. **Results:** BOT tissue microarchitecture was validated and $>$200 μm diffusion in BOTs was confirmed using high-content imaging. Differential response was quantified using Cell TiterGlo endpoint assay as well as advanced image processing of high-content live/dead nuclear stained images captured at multiple z-plains. ADT-007 IC_{50} was found to be substantially lower for mutant HCT116 compared to that for WT HT29 cell line BOTs, which was consistent with separately conducted *in vitro* and *in vivo* studies. **Conclusions:** A pan-RAS inhibitor, such as ADT-007 with high selectivity for cancer cells with activated RAS that is not limited to a specific KRAS mutant allele or RAS isozyme, could have broader use for CRC and other RAS-driven cancers. Further, due to their potential to replicate biophysical characteristics of a tumor and its microenvironment, BOT based precision and personalized medicine platforms can provide more accurate drug efficacy readout compared to *in vitro* cancer models. Research Sponsor: NIH/NCI; 1R43CA254493; NSF; TI-2321805.

92 **Poster Session**

CVM-1118: An oral anti-vasculogenic mimicry (VM) agent in combination with nivolumab in patients with unresectable advanced hepatocellular carcinoma (HCC)—A phase IIa study. First Author: Chia Jui Yen, Department of Oncology, National Cheng Kung University Hospital, Tainan, Taiwan

Background: CVM-1118 is a potent anti-tumor new chemical entity with multiple mechanisms of action including induction of apoptosis, cell cycle arrest, and inhibition of VM network formation. This study evaluated the anti-tumor effect and safety profile of CVM-1118 plus nivolumab in patients with progressive unresectable advanced HCC following the first-line therapy with TKIs. **Methods:** Eligible pts had unresectable advanced HCC and were refractory to prior systemic therapy (e.g., sorafenib, lenvatinib, regorafenib, and/or ramucirumab), with the exception of prior immunotherapy. Patients received oral CVM-1118 at 200 mg BID (400 mg daily) in combination with intravenous nivolumab at 240 mg Q2W in 28-day cycles. The primary endpoint of objective response rate was evaluated using mRECIST. The secondary endpoints were overall response rate (ORR) (per RECIST 1.1), progression free survival (PFS), disease control rate (DCR), and duration of overall response (DoR). **Results:** A total of 31 evaluable pts were enrolled (25 M/6 F; median age 65 y, range 44–80 y). All patients were Child Pugh A, BCLC stage B (13%, n=4) or C (87%, n=27) at the start of treatment. The median number of prior lines of therapy was 1 (range 1–2). The duration of CVM-1118 and nivolumab treatment ranged from 1.5–17.7 mos (median 3.1 mos) with 5/31 (16%) pts remaining on treatment for $\geq$ 5.2 mos (range 5.2–17.7 mos). The best ORR was 19.4% (mRECIST) (2 CR (6%), 4 PR (13%)), with remaining responses including 11 SD (36%) and 14 PD (45%). The DCR was 54.8% (95% CI 37.3–72.3%), the median PFS was 3.53 mos (95% CI 1.9–5.4 mos) and the median DoR was 12.1 mos (95% CI 5.2–16.1 mos). The most common treatment-related AEs ^{3} grade 3 included AST increased (12.9%), neutrophil count decreased (9.7%), anemia (6.5%), and WBC decreased (6.5%). As opposed to therapy with atezolizumab plus bevacizumab, gastrointestinal hemorrhage and hypertension were not observed in this study. Pharmacokinetics data demonstrated that CVM-1118 was rapidly metabolized to CVM-1125 in all pts following administration. On Day 1, the mean drug exposure of CVM-1125 was C_{max} 564 ng/mL and the $AUC_{0\text{-}24}$ was 2154 ng·hr/mL. Intersubject variability of drug exposure appeared to be high; the $T_{1/2}$ of CVM-1125 was ~1.7 hr. **Conclusions:** CVM-1118 combined with nivolumab demonstrated clinical activity in advanced HCC pts with a safety profile that appears favorable compared to atezolizumab plus bevacizumab. These data support further development of the combination of CVM-1118 and nivolumab in pts with unresectable advanced HCC. Clinical trial information: NCT05257590. Research Sponsor: TaiRx, Inc.

93 **Poster Session**

Association of aberrant expression of CD39 with the outcome of patients with cholangiocarcinoma. First Author: Bohao Zheng, Department of Biliary surgery, Zhongshan Hospital, Fudan University, Shanghai, China

Background: Cholangiocarcinoma is defined as a kind of malignant tumor originating from bile ducts. Due to the lack of effective diagnostic and treatment methods, the prognosis of cholangiocarcinoma is dismal. Accumulating evidence indicates that CD39 could promote the progression of several types of cancer. However, the biological function and the underlying mechanism of CD39 in cholangiocarcinoma have not been well investigated. **Methods:** Quantitative reverse transcription PCR (RT-qPCR), western blot (WB), and immunohistochemistry staining was used to evaluate the expression level of CD39 in cholangiocarcinoma. Kaplan-Meier and Cox hazard ratio regression analyses were implicated to evaluate the prognostic significance of CD39. Cell counting kit-8 (CCK-8) was carried out to evaluate the proliferative capacity, while transwell assay was used to detect the migration and invasion ability. In addition, B-NDG mice were used for the in vivo assay. The potential protein binding with the CD39 was identified through co-immunoprecipitation. **Results:** We observed that CD39 was aberrantly expressed in the tumor tissue and cholangiocarcinoma cell lines. Our analysis indicated that the high expression level of CD39 correlated with aggressive clinicopathological characteristics, and CD39 was identified as an independent poor prognostic factor in cholangiocarcinoma. In addition, our in vitro and in vivo data indicated that the knockdown of CD39 could suppress the proliferation, migration, invasion ability, and the epithelial-mesenchymal transition (EMT) process of cholangiocarcinoma. Opposite results were observed when CD39 was overexpressed. Mechanistically, CD39 could bind with Annexin A2 (ANXA2), which influences the phosphorylation level of ANXA2 at the Tyr24 site, thereby promoting the activation of PI3K/AKT signaling, which resulted in the biological change in cholangiocarcinoma. **Conclusions:** Our data indicated that CD39 was overexpressed in the tumor tissue. Meanwhile, CD39 was identified as an independent prognostic factor of poor overall survival for patients withcholangiocarcinoma. In terms of the biological role of CD39, our data indicated that CD39 promoted the progression and metastasis of cholangiocarcinoma through binding with ANXA2, and through activating the PI3K/AKT signaling. In brief, CD39 is a potential prognostic factor and therapeutical target for cholangiocarcinoma. Research Sponsor: National Natural Science Foundation of China; 82272772, 82072682, and 82303441; Natural Science Foundation of Shanghai Municipality; 21ZR1459100, and 22ZR1457900.

94 **Poster Session**

Pretreatment CT-based machine learning radiomics model to predict response in unresectable hepatocellular carcinoma treated with lenvatinib plus PD-1 inhibitors and interventional therapy. First Author: Changzhen Shang, Department of Hepatobiliary Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China

Background: Lenvatinib plus PD-1 inhibitors and interventional (LPI) therapy has demonstrated promising treatment effects in unresectable hepatocellular carcinoma (uHCC). However, biomarkers for predicting the response to LPI therapy remained to be further explored. The current study aimed to develop a radiomics model to noninvasively predict the efficacy of LPI therapy for uHCC. **Methods:** Clinical data of patients who were diagnosed with uHCC and accepted LPI therapy were collected in our institution. The clinical model was built by clinicopathological information. Nine machine learning classifiers were tested and the multilayer perceptron classifier with optimal performance was utilized as the radiomics model. The clinical-radiomics model was constructed by integrating clinical and radiomics scores. **Results:** 151 patients were enrolled in this study (2:1 randomization, 101 and 50 in the training and validation cohorts), of which three patients achieved complete response, 69 showed partial response, 46 showed stable disease and 33 showed progressive disease (evaluated by mRECIST criteria). The objective response rate (ORR), disease control rate (DCR), and conversion resection rate were 47.7, 78.1 and 23.2%, respectively. 14 features were selected from the initially extracted 1223 for radiomics model construction. The area under the curves of the radiomics model (0.900 for training and 0.893 for validation) were comparable to that of the clinical-radiomics model (0.912 for training and 0.892 for validation), and both were superior to the clinical model (0.669 for training and 0.585 for validation). Meanwhile, the radiomics model could categorize participants into high- and low-risk groups for progression-free survival and overall survival in the training and validation sets. **Conclusions:** The current study developed a novel and promising machine learning radiomics model, which could efficiently predict the efficacy of LPI therapy for uHCC, with comparable performance to clinical-radiomics model. Research Sponsor: None.

95 **Poster Session**

The correlation between L1CAM expression and outcomes in patients with metastatic colorectal cancer treated with first-line chemotherapy. First Author: Andrea Pretta, Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy

Background: L1CAM is a cell adhesion molecule and stem cell marker belonging to the immunoglobulin superfamily of cell adhesion molecules (IgCAMs). L1CAM may be aberrantly expressed in several types of human tumors. The aim of the present study was to evaluate the correlation between L1CAM expression and outcomes in patients with metastatic colorectal cancer. **Methods:** We retrospectively collected data from 51 mCRC pts treated between 2017 and 2022 at the Medical Oncology Unit of the University Hospital of Cagliari. Tumor samples were retrospectively tested for L1CAM immunohistochemical (IHC) expression with the aim of evaluating the correlation with clinical outcome in terms of overall survival (OS) and progression-free survival (PFS). The primary endpoint was the mOS while secondary endpoint was mPFS. The aim of the present analysis was to evaluate the role of L1CAM expression in tumor cells in predicting the clinical outcome of CRC patients treated with standard chemotherapy. Statistical analysis was performed with the MedCalc Statistical Sofware Version 14.10.2. **Results:** Median age was 70 ($\pm$13), 58.8% were males and 41.2% were females. 29.4% of pts had carcinoma of the right colon, 39.2% left colon and 31.4% rectum. Negative or weak L1CAM score 0 was observed in 39.2% patients; 43.1% pts showed a score 1+; 11.8% showed score 2+, and 5.9% showed score 3+. Positivity for L1CAM correlated with a worse prognosis. The median OS for pts not expressing L1CAM was 74.0 months versus 32.0 for patients expressing the biomarker ($p = 0.0021$). The mPFS for patients not expressing L1CAM was 21.0 months, vs 6.0 for patients expressing the biomarker ($p = 0.0066$). The same negative correlation on outcomes was shown based on the degree of L1CAM expression. A different L1CAM score corresponded to a different OS and PFS. Pts with score 0 showed a mOS of 74 months vs 37 and 18 months for scores 1+ and 2+/3+, respectively ($p < 0.0001$). Similar results were obtained with the mPFS: patients with score 0 showed a median of 21 months vs 8 and 2 months for scores 1+ and 2+/3+, respectively ($p = 0.0138$). **Conclusions:** L1CAM expression in cancer cells correlates with a worse prognosis in mCRC patients. Immunohistochemical evaluation of this biomarker could allow the identification of a subgroup of patients capable of benefiting from a targeted therapy. Research Sponsor: None.

96 **Poster Session**

Effects of *Aureobasidium Pullulans* produced β-1,3-1,6-glucan on CA19-9, sCD44, IgA and sCD209 in patients undergoing surgical resection of malignant pancreatic tumors. First Author: Samuel JK Abraham, Yamanashi University, Chuo, Japan

Background: Pancreatic cancer is a highly refractory tumor with poor prognosis, which aggressively progresses by suppressing the immunity. Surgical procedure related stress further weakens the immunity and aids cancer stem cell metastases, warranting immune enhancement strategies. AFO-202 strain of *Aureobasidium Pullulans* produced β-1,3-1,6 glucan (Nichi BRITE), having yielded immune enhancement in earlier studies, we evaluated its effects in patients undergoing surgical resection of malignant pancreatic tumors. **Methods:** 30 subjects in two groups were enrolled; control arm (n=15, "P" group) received a placebo, and treatment arm (n=15, "G" group) received Nichi BRITE 250mg/day, in three divided doses, for 22 days from the pre-operative day. Serum beta glucan specific IgA2 (BG-IgA), total IgA (IgA), sCD209, Serum Amyloid A (SAA), sCD44 and CA19-9 were evaluated at base line and at periodic intervals. **Results:** sCD44 significantly decreased 48.94% in "G" group and only 4.58% in "P" group ($p = < 0.0001$) on day 21. sCD209 on day 21 in "G" group increased by 54.68% ($p = 0.04$) against 15.03% in "P". BG-IgA at day 10 increased around 150% in "G", and only by 6% in "P". Total IgA, increased by 20.60% in "G" and only 5.73% in "P". SAA increased to 251.32% in "G" on day 21 and in "P" it decreased by 6.11%. Decreased sCD44 when correlated against Neutrophil to Lymphocyte Ratio (NLR), a significant positive correlation was in "G" (r statistic= 0.758; p-value =0.006; 95% CI= 0.2907~0.9335), but a negative correlation in "P". Pancreatic cancer marker CA19-9 decreased significantly in three months follow up in "G" (-86.02 U/ml) whereas it increased in "P" by +5.91 U/ml. Mean survival of Nichi BRITE group was 25.9 months against 22.3 months in "P" group. **Conclusions:** Administration of Nichi BRITE glucans to patients undergoing surgical resection of malignant pancreatic tumor was safe and it enhanced biomarkers of innate and adaptive immunity. Nichi BRITE significantly decreased the circulating cancer stem cell marker sCD44 implying a lesser recurrence risk, especially in patients with high NLR ratio who have a poor prognosis, and significantly reduced the CA 19-9 levels implying a better prognosis, making us recommend it as an adjuvant to patients undergoing surgeries for malignant tumors, and be included in the guidelines of clinical nutrition. Research Sponsor: GN Corporation Co. Ltd.

TPS97 Trials in Progress Poster Session

CHAPTER-GIST-101: A phase I study of pimitespib combined with imatinib in patients with imatinib-refractory gastrointestinal stromal tumor. First Author: Hidekazu Hirano, Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan

Background: Gastrointestinal stromal tumor (GIST) is soft-tissue sarcoma of the gastrointestinal tract. Most GISTs harbor mutations in *KIT* or *PDGFRA,* recognized as key drivers of GIST development and progression. Imatinib (IM), which inhibits KIT/PDGFRA tyrosine kinase, exerts significant clinical activity in GIST, but most GISTs develop resistance to IM, mainly due to secondary kinase-domain mutations in *KIT*. Therefore, standard therapies for patients (pts) with IM-refractory GIST have room for improvement. Heat shock protein 90 (HSP90) is one of the molecular chaperones. Many of HSP90's client proteins, such as KIT, PDGFRA, and BRAF, have been identified as cancer-related proteins required for tumor development, and their activation, especially in mutant forms, is dependent on HSP90.Therefore, HSP90 inhibitors have a potential to overcome IM-resistance. Pimitespib (PIMI) is a novel HSP90 inhibitor, approved in Japan for pts with fourth line GIST based on the results of the phase 3 study (CHAPTER-GIST-301). We reported at ESMO 2023 (1917MO) that PIMI effectively inhibited tumor growth in an IM-resistant xenograft model, and further enhanced the anti-tumor activity when given with IM, and that PIMI + IM was well tolerated with no dose-limiting toxicity and suggested preliminary efficacy in pts resistant to IM in a dose-escalation part (DEP) of CHAPTER-GIST-101 study. **Methods:** The CHAPTER-GIST-101 study (NCT05245968) is a global phase 1 study in pts with IM-refractory advanced GIST in the second-line setting, consisting of three parts: the DEP, its expansion part (ExP), and another DEP for Chinese pts. The DEP used a 3+3 design to determine the maximum tolerated dose of PIMI (120 mg/day or 160 mg/day, orally, on 5 days on/2 days off) in combination with IM (400 mg/day once daily) and the ExP is for the efficacy and safety with determined dose of 120 mg/day PIMI + IM. The ExP is a global, open-label, randomized, part evaluating the efficacy and safety of PIMI in combination with IM, PIMI monotherapy, and standard therapy sunitinib (SU) in each arm of 20 pts. Pts are randomized 1:1:1 to receive either PIMI 120 mg on 5 days on/2 days off with IM 400 mg once daily, PIMI 160 mg on 5 days on/2 days off followed by IM 400 mg once daily after discontinuation of PIMI, or SU 50 mg on 4 weeks on/2 weeks off. The primary endpoint is progression-free survival (PFS) by the independent radiological review. The secondary endpoints include investigator-assessed PFS, overall survival, objective response rate, disease control rate, duration of response, PK and safety. Exploratory pharmacogenomics analysis is also planned. After the DLT evaluation for the DEP, enrollment for the ExP began in March 2023 in Japan, Singapore, Taiwan and Australia, and for the DEP for Chinese pts is also ongoing in China to evaluate tolerability and efficacy of this combination. Clinical trial information: NCT05245968. Research Sponsor: None.

TPS98 Trials in Progress Poster Session

CORRECT-MRD I: A clinical validation study to predict recurrence in stage II-III colorectal cancer (CRC) using a bespoke circulating tumor DNA (ctDNA) assay to detect molecular residual disease (MRD). First Author: Yuichiro Tsukada, National Cancer Center Hospital East, Kashiwa, Japan

Background: Despite standard of care management with surgery ± adjuvant chemotherapy treatment (ACT), >30% of patients (pts) with resectable CRC recur. The presence of ctDNA in plasma after resection and after ACT, has been shown to be a strong prognostic factor for the risk of recurrence, suggesting that the presence of ctDNA in blood is molecular evidence of residual disease. As such, ctDNA analysis may enable post-surgical risk stratification for ACT decision-making, as well as detection of molecular recurrence during surveillance and subsequent early intervention. The CORRECT-I study aims to validate the association of post-definitive therapy and pre-recurrence follow-up ctDNA positivity with recurrence-free interval (RFI) in pts who have undergone complete surgical resection for stage II or III CRC. **Methods:** This study is a prospective, observational, multicenter study, which is open in Israel, Italy, Japan, Spain, and the UK. Pts must have pathologically confirmed stage II or III CRC, have undergone complete surgical resection, and have tissue available from the primary resection. Pts may not have started ACT prior to baseline blood draw post-surgery. Pts are asked to provide serial whole blood specimens for ctDNA analysis at a) post-surgical baseline, b) pre-recurrence follow-up visits (max 15 blood draws over max 5 years), and c) clinical recurrence. ctDNA will be analyzed with an NGS-based tumor-informed MRD assay that identifies somatic genomic alterations from DNA derived from the patient's tumor tissue and detects a selected subset of tumor-specific (bespoke) ctDNA in their blood. The primary objective of this study is to validate the association of post-definitive therapy and serial pre-recurrence follow-up ctDNA positivity with RFI, using a Cox proportional hazards regression analysis. Further objectives include the assessment of sensitivity and specificity of the ctDNA assay, the association between ctDNA at individual timepoints and RFI, ctDNA dynamics and RFI, and the time from ctDNA positivity to clinical recurrence. A multivariable model, including ctDNA, clinicopathological risk features, serial serum CEA assessments, and recurrence risk as determined by the Oncotype Colon Recurrence Score will be fit with RFI as endpoint. The primary analysis will be conducted when ≥30 histologic and/or radiographic confirmed cases of clinical recurrence have been observed. As of April 2, 2024, 158 pts of 400 have been enrolled. Research Sponsor: Exact Sciences.

TPS99 Trials in Progress Poster Session

Protocol amendment for ENSEMBLE study: A multicenter, randomized, phase III trial to test the superiority of consolidation irinotecan, capecitabine and oxaliplatin vs capecitabine and oxaliplatin following short course radiotherapy as total neoadjuvant therapy in patients with locally advanced rectal cancer—Changing the irinotecan dosage. First Author: Koji Ando, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background: Total neoadjuvant therapy (TNT) presents a promising approach for treating patients (pts) with locally advanced rectal cancer (LARC). TNT not only enhances outcomes for LARC pts but also contributes to improving their quality of life by offering non-operative management (NOM) for patients with complete clinical response (cCR) or near-complete clinical response (nCR). We are currently conducting a phase III trial, the ENSEMBLE study, which was presented at ASCO Breakthrough 2023. At this stage, we have modified the protocol for this study. Additionally, we are conducting translational research (TR) to establish clear criteria for NOM following TNT. **Methods:** In the ENSEMBLE study, the experimental treatment group received short-course radiotherapy (SCRT) (5×5 Gy) followed by six cycles of CAPOXIRI (capecitabine 800 mg/m2 [orally, twice daily, days 1-14], oxaliplatin 130 mg/m2 [intravenously, day 1], and irinotecan 200 mg/m2 [intravenously, day 1, every 3 weeks]). The standard-of-care group received SCRT (5×5 Gy) followed by six cycles of CAPOX (capecitabine 1000 mg/m2 [orally, twice daily, days 1-14], oxaliplatin 130 mg/m2 [intravenously, day 1, every 3 weeks]). However, the experimental treatment group experienced a higher rate of adverse events due to the high starting dose of irinotecan. After consulting the data and safety monitoring committee (DSMC), it was recommended to reduce the starting dose of irinotecan. **Results:** Enrollment for the ENSEMBLE study commenced in November 2022. By August 2023, severe adverse events necessitating emergency reporting had occurred in the experimental treatment group. In response to these adverse events, the DSMC was consulted, leading to the reduction of the starting dose of irinotecan to 150 mg/m2. Following this adjustment, no severe adverse events requiring emergency reporting were observed during the experimental treatment with CAPOXIRI. We are currently continuing the ENSEMBLE study to advance treatment options for LARC pts. The TR component of the ENSEMBLE study involves genomic profiling through whole genome plus RNA sequencing of tissue and blood samples, as well as circulating nucleic acid sequencing (cNAS). Additionally, all imaging data (MRI, CT, and colonoscopy) and clinical information are being collected to develop criteria for NOM. **Conclusions:** A starting dose of irinotecan at 150 mg/m2 appears to be feasible after SCRT in the ENSEMBLE study. Furthermore, the ENSEMBLE study aims to establish clear NOM criteria through deep learning with TR. Clinical trial information: NCT05646511/jRCTs031220342. Research Sponsor: None.

TPS100 Trials in Progress Poster Session

Observational study examining the feasibility of generating real-world evidence (RWE) for new drug applications from the clinical trials database (DB; RELIASE study). First Author: Hideaki Bando, Translational Research Support Office, Division of Drug and Diagnostic Development Promotion, Department for the Promotion of Drug and Diagnostic Development, National Cancer Center Hospital East, Kashiwa, Japan

Background: The extraction of the data that contributes to regulatory approval from real-world data (RWD) are difficult due to the lack of standardized data format as well as the extraction methodology. In addition, when RWE is used as an external control group, the similarity between internal and external control data has not been evaluated. **Methods:** In our 'REALISE' study, we will investigate the data extraction methodology as external control data of rare molecular subtype. We also elucidate the 'quality' and 'reliability' of RWD/RWE necessary for regulatory submissions. In addition, as most databases are not designed for regulatory use in the creation phase, we will investigate the retrospective methodologies to ensure reliability of RWD/RWE. We compare 'data quality' and 'data reliability' of ARCAD global DB (N=45,224), SCRUM-Japan registry (N=546), SCRUM-Japan observational study (N=14,325), and the Flatiron health RWD in Japan (N=650) and statistically analyze the differences and similarities among 4 databases. All analyses will be summarized descriptively. Similarity of patient characteristics and efficacy endpoints such as response rate, progression-free survival, overall survival, and all available endpoints will be evaluated by cancer type, treatment line, and standard treatment. For colorectal cancer, data extracted from the SCRUM-Japan registry, SCRUM-Japan observational study, and the Flatiron health RWD will be compared with data extracted from randomized controlled trials in the ARCAD global DB to examine the availability as an external control of RWD. The Kaplan-Meier method will be applied to estimate the survival distribution of time-to-event data. No imputation method for missing data will be used, and the frequency of missing data will also be summarized. We will also examine the methodology for extracting data with sufficient quality from the SCRUM-Japan observational study. In addition, if the reliability of RWD/RWE does not reach the required level, we will also examine the methodologies to retrospectively assure the reliability of the SCRUM-Japan observational study for regulatory submissions. Research Sponsor: Ministry of Health, Labour and Welfare.

The list of databases for the EALISE study.

	ARCAD global database	SCRUM-Japan Registry	SCRUM-Japan observational study	Flatiron Health Real-World Data study
Cancer type	Colorectal cancer	Solid tumors	Solid tumors	Gastrointestinal cancers (real-word data for breast cancer, with lung cancer and hematological malignancies under development)
Sample size (as of Jannuary 2024)	ARCAD global database: 45,224 cases from 63 trials ARCAD Asia database: 4,218 cases from 13 trials	546 cases	Total: 14,325 cases GI-SCREEN 2013-01-CRC: 3,641 cases GI-SCREEN 2015–01-Non CRC: 2,952 cases MONSTAR-SCREEN: 2,224 cases GOZILA Study: 5,508 cases	650 cases (Japan only)

101 Poster Session

Machine learning-based noninvasive diagnostic classifiers for the prediction of cancer tissue of origin using serum microRNAs. First Author: Andrew Zhang, Yale University, New Haven, CT

Background: Noninvasive multi-cancer early detection (MCED) with or without tissue of origin (TOO) has the potential to reduce cancer-related mortality by analyzing circulating cell-free nucleic acids and/or proteins in blood. Accurate prediction of TOO following a positive MCED test would guide selection of confirmatory tests, thereby expediting the definitive diagnosis and prompt initiation of the most appropriate treatment, tailored to the specific cancer type. Here, we report the development of machine learning-based diagnostic classifiers that predict TOO for 13 cancer types with high accuracy using serum microRNAs. **Methods:** Eight serum miRNA microarray datasets from GEO totaling 6,283 patients across 13 cancer types were used in this study. The patients were split, with an approximate 3:2 ratio, into a training (n=3,844) and a validation set (n=2,439). An ensemble of classifiers was constructed in the training set via the "one vs. rest" approach, thus one classifier for each cancer type. Random forest models with recursive feature elimination (RFE) selected the optimal set of miRNAs that was fed into support vector machine models to generate a prediction probability for each cancer type. The type with the highest probability was considered the predicted cancer type. The performance of these classifiers was evaluated in the validation set in two steps with the 1st using all cancer types and the 2nd using the top 2 or 3 cancer types from the 1st step to achieve a refined prediction. **Results:** RFE selected 426 miRNAs for building the 13 classification models. In the validation set comprising 2,439 patients across 12 cancer types, the classifiers correctly predicted cancer types for 1,922 (79%) samples based on the highest prediction probability. The accuracy increased to 92% and 95% based on top 2 and 3 predictions. In particular, based on top 3 predictions, the accuracy was >95% for bladder, breast, prostate, gastric, glioma and lung cancers, >85% for ovarian, liver and esophageal cancers, 78% for pancreatic cancer and sarcoma, and 67% for colorectal cancer. **Conclusions:** With 95% accuracy in narrowing TOO down to 3 organ sites, the miRNA-based TOO classifiers could be used clinically as a reflex test for the simple and highly accurate MCED screening models previously developed (*Cancers* 2022,14:1450; ESMO 2024). Together, they support the development of an inexpensive, accurate and noninvasive blood test for MCED with TOO. Research Sponsor: None.

102 Poster Session

Comprehensive validation of a cell-free DNA-based assay for multi-cancer detection: A Vietnamese longitudinal prospective cohort study of 9,024 participants. First Author: Le Son Tran, Medical Genetics Institute; Gene Solutions, Ho Chi Minh City, Viet Nam

Background: Blood-based multi-cancer early detection (MCED) has emerged as a promising method for enhancing early cancer detection efficiency and benefiting population health. However, the lack of evidence regarding their clinical utility across diverse populations has hindered their routine use. To address this, we conducted a comprehensive analytical and clinical validation of an MCED test, SPOT-MAS (Screening for the Presence Of Tumor by DNA Methylation And Size). **Methods:** Analytical validation was conducted on a retrospective cohort of 96 healthy and 169 cancer-confirmed individuals to determine the limit of detection, reproducibility, and potential interferents. Additionally, we launched a multi-center prospective study, named K-DETEK (ClinicalTrials.gov identifier: NCT05227261), to clinically validate the diagnostic performance. Our study recruited 10,027 asymptomatic individuals aged 40 years or older across 75 major hospitals in Vietnam, following them up for 12 months. **Results:** SPOT-MAS test demonstrated the capability to detect over 50% of cancer samples with 98% specificity at a tumor fraction of 0.049 (95% CI: 0.043-0.059). These results were consistent across intra- and inter-batch analyses. The test remained robust even with hemoglobin contamination up to 500 mg/dL and genomic DNA contamination of up to 100%. In the K-DETEK study, among 9,024 eligible participants, 43 (0.48%) showed a positive cancer signal. Of those, 25 were diagnosed with cancer through standard imaging and biopsy tests, with 21 matching tumor types with our predictions, resulting in a positive predictive value of 58.14% (95% CI: 43.33-71.62) and tumor-tissue-origin accuracy of 84%. 8,981 participants (99.52%) had a negative cancer signal, and 8,974 were confirmed cancer-free, indicating a negative predictive value of 99.92% (95% CI: 99.84-99.96). The test showed an overall sensitivity of 78.13% (95% CI: 61.25-88.98) and a specificity of 99.80% (95% CI: 99.68-99.87) for cases with tumors at all stages, with slightly lower sensitivity (74.05%, 95% CI: 56.64-87.32) for precancerous and early clinical stages. **Conclusions:** Our study represents the most comprehensive and largest validation study in Asia supporting the utility of SPOT-MAS as a multi-cancer blood test for early cancer detection. Its potential significance is underscored, particularly in low- and middle-income countries, emphasizing the need for accessible and effective screening tools. Clinical trial information: NCT05227261. Research Sponsor: Gene Solutions JSC.

103 Poster Session

A novel cell-free multi-omics approach for enhancing multi-cancer early detection. First Author: Thien-Chi Van Van Nguyen, Medical Genetics Institute, Ho Chi Minh City, Viet Nam

Background: While circulating tumor DNA (ctDNA)-based assays for multi-cancer early detection (MCED) have shown significant potential, their performance is hindered by the limited amount and inherent variability of ctDNA, particularly in cancer types with low ctDNA shedding. To enhance the accuracy of MCED, recent studies have focused on profiling cell-free RNA (cfRNA), which is secreted not only by tumor cells but also by other cell types to reflect the systemic tumor responses. Herein, we developed a novel cell-free multi-omics approach integrating cfDNA and cfRNA analyses from a single blood draw to improve the sensitivity of an MCED assay, especially for detecting low-shedding ctDNA cancer types. **Methods:** We recruited 535 healthy subjects and 287 patients across five cancer types (77 breast cancers, 102 colorectal cancers, 35 gastric cancers, 34 liver cancers, and 42 lung cancers). We established a multi-omics workflow to comprehensively profile cfDNA signatures (methylation, fragment length, motif ends, and copy number alterations), and cfRNA signatures (cfmRNA). Distinctive signatures were identified to differentiate cancers from healthy subjects and used for constructing robust machine learning classifiers. **Results:** We identified multiple significantly different features distinguishing cancer from healthy individuals, with 81% originating from cfDNA. Notably, cfmRNA features, accounting for 19% of total significant features, were mainly enriched in immune-related pathways, reflecting tumor-immune cell interactions. The cfDNA-based model achieved 81.2% accuracy, with highest performance in detecting liver cancer (100%) and 64%, 42%, and 36.4% for breast, colorectal, and gastric cancers, respectively, at 93% specificity. Combining cfDNA and cfRNA signatures increased sensitivity to 73%, 71%, and 46% for breast, colorectal, and gastric cancers. Overall, the multi-omic model achieved 85.6% accuracy and 72.7% sensitivity for detecting five cancer types at 92.6% specificity. **Conclusions:** The cell-free multi-omics approach holds potential for improving ctDNA-based MCED tests by simultaneously profiling both cfDNA and transcriptomic cfmRNA from a single blood draw. Validation on larger cohorts could lead to a paradigm shift in cancer screening practices. Research Sponsor: Gene Solutions.

104 Poster Session

A pan-tumor description of the genomic, transcriptomic, and immunological landscape of sodium-glucose cotransporter-2 (SGLT2) and association with clinical outcomes. First Author: Heng Tan, University of Miami/Jackson Memorial Hospital, Miami, FL

Background: SGLT2 has been identified as being overexpressed in a diverse set of cancers. Retrospective data has demonstrated a correlation between the use of SGLT2 inhibitors and a reduced incidence of lung cancer. We explored the association of SGLT2-coding gene *SLC5A2* with the transcriptomic, genomic, immunological landscape and outcomes in a subset of solid tumors. **Methods:** Breast ([N = 5623], HR+HER2- [6044] or TNBC [3040]), Colorectal carcinoma (CRC, 15425), NSCLC ([21603], Adenocarcinoma [AC, 8180] or Squamous Cell Carcinoma [SCC, 3579]), Pancreatic (Panc: 5488) and Prostate (PC: 5500) tumors were tested at Caris Life Sciences (Phoenix, AZ) with NextGen Sequencing on DNA (592 genes or whole exome) and RNA (whole transcriptome). PD-L1+ (22C3: TPS 1% for lung or SP142: 2+, 5% all other), Her2/Neu (+: ≥3+ and > 10%) and HR (ER or PR+: ≥1+ and ≥1%) expression was assessed by IHC. Mutations were defined as pathogenic SNVs/indels (-Mt). SLC5A2-H and -L expression (transcripts per million, TPM) was defined by cancer type as top and bottom quartile, respectively. Cell infiltration was estimated by QuantiSEQ. A transcriptomic signature predictive of response to immunotherapy was applied (T cell-inflamed). The Mann-Whitney U test was applied as appropriate ($p < .05$, adjusted for multiple comparisons). Real-world overall survival (OS) was obtained from insurance claims and Kaplan-Meier estimates were calculated for molecularly defined patients. **Results:** *SLC5A2* expression varied across cohorts (TNBC: 1.2 TPM, HR+HER2-BC: 1.7, CRC: 2.2, AC: 1.8, SCC: 1.3, Panc: 1.7, PC: 1.7, $p < .05$). *SLC5A2*-H had a higher prevalence of *FGF3* amplifications in HR+HER2- BC (17.4% -H v 10.4 -L), CRC (1.4 v .45) and PC (4.4 v .89, $p < .05$ all). KRAS-Mt was more prevalent in *SLC5A2*-L CRC (41% v 53) as was *BRAF*-Mt (6 v 14, $p < .05$ all). There was a lower prevalence of PDL1+ in *SLC5A2*-H for HR+HER- BC (14% -H v 24 -L), CRC (2 v 6), AC (47 v 68), SCC (50 v 66) and Panc (10 v 19, $p < .05$ all). All *SLC5A2*-H tumors had increased Neutrophil, B, NK cell infiltrate (Table) and an increased prevalence of T cell-inflamed tumors ($p < .05$, all). *SLC5A2*-H had longer OS v -L in CRC (HR .82 [.76-.88], $p < .001$), PC (HR .85 [.74-.99], p =.03), HR+HER2- BC (HR .79 [.68-.91], $p < .001$) and AC (HR .79 [.73-.85], $p < .001$). **Conclusions:** *SCL5A2*-H across all investigated tumors was associated with increased immune infiltrate and a T cell-inflamed phenotype in addition to improved survival in multiple cancer types. Future research on SGLT2 should delineate its role in cancer formation versus its association as a potential positive prognostic marker. Research Sponsor: None.

	TNBC		HR+HER2-		CRC		AC		SCC		Panc		PC	
SLC5A2 Quartiles	-L	-H	-L	-H	-L	-H	-L	-H	-L	-H	-L	-H	-L	-H
Neutrophil	2.6%	3.5	2.3	3.3	5.3	7.1	4.4	7.1	5.5	7.4	4.8	6.3	4.8	6.3
B cell	3.9	4.7	5.2	6.6	3.1	3.7	3.9	4.7	4.1	5.6	3.9	4.9	4.0	5.0
NK cell	2.8	3.9	2.8	3.7	2.9	4.1	2.3	3.2	2.1	3.2	2.4	3.1	3.7	4.9

105 Poster Session

Translating potential germline findings from tumour profiling into routine clinical care. First Author: Milita Zaheed, Prince of Wales Hospital, Sydney, NSW, Australia

Background: Tumor molecular profiling (TMP) provides an opportunity to identify heritable cancer predisposition. Molecular Screening and Therapeutics Study (MoST) (8000 patients, 2016-23) and Cancer Screening Program (CaSP) (23000 patients, 2023-25) are Australian research programs providing TMP for therapy matching in advanced cancer. Matched germline testing is resource-inefficient and is not performed . An integrated approach between TMP and cancer genetics is needed to improve familial cancer outcomes through prevention and early detection. **Methods:** In MoST, potential germline variants (PGV) in actionable cancer genes were investigated in blood DNA in a research setting. Positive cases were informed, and a genetics review for clinical testing recommended. In CaSP, germline follow-up recommendations are included in the Molecular Oncology Board (MOB) Report based on decision algorithms to inform clinicians of PGV needing clinical assessment. Cancer genetics clinics in Australia were surveyed regarding preferences for the return of genetic information from tumor profiling. A centralised precision care clinic was launched in March 2024 to investigate the implementation of returning PGV information from tumor-only profiling. **Results:** In MoST, 38% (140/367) of PGVs tested were positive in blood DNA. Of these, 44% were identified in the highest actionability genes: *BRCA1, BRCA2, PALB2,* Lynch Syndrome. The validation and return of results process was unsatisfactory; it was resource-heavy, timeframes were extended, DNA was sometimes unavailable, and communicating information to non-participating relatives of deceased participants was challenging due to a lack of established pathways. The systems design in CaSP has allowed the study to manage higher volume without a net increase in germline workforce. To date, 2372 patients have completed profiling with 173 MOB recommendations for PGV validations. Fifty-four cancer genetics staff nationally responded to the survey. Many (61%) were concerned about the increased uptake of TMP without a workforce to match germline testing demand (97%) and lack of funding assigned in a universal healthcare system (70%) being main concerns. Most (82%) supported a centralised service anticipating improved efficiency gain (71%), equity of access (77%) and streamlining of processes (71%). The stakeholders voiced a consistently high ($>$50%) demand for information regarding PGV in lower actionability genes. MOB recommendations were adapted to reflect 3 tiers of actionability The centralised clinic has reviewed 21 patients nationally to test 23 highest actionability variants. The average referral to review time is 2 weeks. **Conclusions:** Precision oncology can play a role in familial cancer prevention. Deliberate collaboration and integration between precision research and relevant specialised care can lead to resource-optimised, equitable delivery of quality care. Research Sponsor: Medical Research Future Fund; Omico.

106 Poster Session

Real-world insights from comprehensive genomic profiling across multiple cancer types. First Author: Ling-Jen Hung, Department of Hematology-Oncology, Chang Gung Memorial Hospital at Linkou and Chang Gung University College of Medicine, Taoyuan City, Taiwan

Background: This retrospective study was conducted to analyze tumor tissue profiling data to assess the potential of applying comprehensive genomic profiling (CGP) in patient care across diverse solid tumors. **Methods:** Patients with newly diagnosed or recurrent stage IIIB or IV lung adenocarcinoma with the null immunophenotype, esophageal, gastric, pancreatic, or bile duct cancer between January 2020 and July 2023 at two medical centers in Taiwan were included in the National Biobank Consortium of Taiwan project. The tumor samples were subjected to CGP using FoundationOneCDx, with therapeutic implications determined using OncoKB classification. **Results:** FoundationOneCDx testing of 574 patients was successful in 456 (79.4%) patients. Clinically actionable genomic alterations were detected in 21.1% (96/456) of the patients, including 17.5%, 2.9%, and 0.7% of patients at evidence levels 1, 2, and 3, respectively. Lung adenocarcinoma accounted for the largest proportion of samples with at least one actionable gene alteration (63.2%), followed by bile duct (26.9%), gastric (17.6%), esophageal (4.0%), and pancreatic (3.1%) cancer. Based on the CGP results, 43 patients (9.4%) received matched targeted therapy. The median overall survival of patients who received matched therapy or not was 26.1 months (95% confidence interval (CI), 16.7–35.5 months) and 10.6 months (95% CI, 8.1–13.1 months; hazard ratio, 0.28, 95% CI, 0.14–0.55, $p < 0.001$), respectively. **Conclusions:** This study provides comprehensive insights into genomic profiling across diverse cancers in Taiwan, highlighting the crucial role of CGP in identifying actionable genomic alterations and guiding effective therapeutic strategies in real-world practice. Research Sponsor: None.

107 Poster Session

Molecular tumor board: Real-world experience in a tertiary cancer centre in Singapore. First Author: Su Fen Ang, National Cancer Centre Singapore, Singapore, Singapore

Background: Genomic profiling is increasingly employed to support diagnosis and treatment of cancer. Our Molecular tumor boards (MTBs) serves as a collaborative platform for a multi-disciplinary team of oncologists, pathologists, scientists, bioinformaticians, genetic counsellors and research coordinators to discuss and match patients to the most relevant therapies and/or clinical trials. We report here the evaluation of our MTBs for year 2023 with the aim of identifying challenges and opportunities for successful implementation of precision oncology. **Methods:** Regular monthly MTBs were conducted to discuss molecular profiles from predominantly advanced-stage patients enrolled to the IMPACT study (Individualized Molecular Profiling for Allocation to Clinical Trials NCT02806388). Next-generation sequencing was performed either in-house using Oncomine or commercial FoundationOne panels. Additional tests such as whole transcriptome sequencing (WTS), immunohistochemistry (IHC) and fluorescent in-situ hybridization (FISH) were also performed where indicated. MTB recommendations were documented for follow-up and analysis. **Results:** A total of 102 out of 611 profiled patients were discussed in MTBs in 2023, with an average of 8.6 patients per month. Top 3 cancer types were gastrointestinal (32%), breast (18%) and lung (18%). 65/102 (63.7%) cases had MTB recommendations, of which 21 (20.6%) had multiple recommendations. Overall uptake rate for recommendations was 23.8% (29/122). **Conclusions:** MTB plays an important role in identifying therapeutic opportunities by factoring in patient variables, available data and physician experience while at the same time provides an avenue for further investigation to gather cumulative evidence. Frequent reasons encountered for not adopting the recommendations include: (1) insufficient sample to proceed with further investigations, (2) limited access to off-label treatments, and (3) additional considerations to participate in clinical trials. To fully realize the value of MTB, we will focus on (1) defining the molecular tests for efficient profiling, (2) crafting a route for special access to treatments and (3) increasing awareness and understanding of clinical trials. Research Sponsor: Duke-NUS Medical School Singapore; 08/FY2021/EX(SL)/102-A156(a); MOH-NMRC Singapore; OFIRG21nov-0083; MOH-NMRC Singapore; NMRC/OFLCG/002/2018; MOH-NMRC Singapore; MOH-CSAINV-19nov-000.

Summary of MTB recommendations.

Type of MTB recommendation	Number (% of total recommendations)	Implemented (% of number)	Lost to follow-up (% of number)
Treatment	23 (18.9%)	3 (13.0%)	3 (13.0%)
On-label	14 (11.5%)	3 (21.4%)	3 (21.4%)
Off label	9 (7.4%)	0 (0.0%)	0 (0.0%)
Trial	41 (33.6%)	9 (22.0%)	4 (9.8%)
Genomic biomarker-matched	21 (17.2%)	4 (19.0%)	3 (14.3%)
Non-genomic biomarker-matched	20 (16.4%)	5 (25.0%)	1 (5.0%)
Further Investigations	20 (16.4%)	5 (25.0%)	3 (15.0%)
No recommendation	38 (31.1%)	-	-

108 Rapid Oral Abstract Session

Patient-reported outcomes (PROs) from a randomized, phase 3 trial of enfortumab vedotin plus pembrolizumab (EV+P) versus platinum-based chemotherapy (PBC) in previously untreated locally advanced or metastatic urothelial cancer (la/mUC). First Author: Eiji Kikuchi, St. Marianna University School of Medicine, Kanagawa, Japan

Background: EV+P nearly doubled median progression-free survival and overall survival vs PBC in patients (pts) with previously untreated la/mUC in the phase 3 EV-302 trial. PROs are reported here. **Methods:** In EV-302 (NCT04223856) pts were randomized 1:1 to EV+P or PBC (gemcitabine with cisplatin or carboplatin). PRO assessments included the EORTC Quality of Life Questionnaire (EORTC QLQ-C30), and the Brief Pain Inventory Short Form (BPI-SF) completed at baseline, weekly for 12 weeks (wks), then every 3 wks through survival follow-up, inclusive of the time post-progression. Time to pain progression (TTPP) and mean change from baseline in worst pain at wk 26 using the BPI-SF were prespecified analyses statistically tested using a gatekeeping strategy. Mean change from baseline through wk 26 and time to confirmed deterioration (TTCD) of EORTC-QLQ-C30 and BPI-SF domains were prespecified descriptive analyses. TTPP and TTCD were assessed using Kaplan-Meier methods. **Results:** Of 886 pts randomized, 731 (376 received EV+P; 355 PBC) completed baseline PRO questionnaires. Compliance rates differed between arms and remained >70% through wk 29 for EV+P and through only wk 17 for PBC. Median TTPP was 14.2 months (mos) with EV+P and 10.0 mos with PBC (hazard ratio [HR]=0.92; 95% CI=0.72, 1.17; 2-sided p-value=0.48). The least squares (LS) mean reduction in worst pain at wk 26 was numerically greater with EV+P vs PBC (-0.61 vs -0.03, LS mean difference [95% CI]: -0.58 [-1.05, -0.11] [nominal 2-sided P = 0.015]). Pts with moderate to severe pain at baseline who were treated with EV+P (n=128, 34%) had a meaningful (>2 pt) improvement from baseline in BPI worst pain from wk 3 through 26. In EORTC QLQ-C30 Global Health Status/Quality of Life [GHS/QoL], EV+P demonstrated a transient worsening at week 3 (-6.3) that returned to baseline from weeks 4 through 26, while patients treated with PBC demonstrated deterioration from week 1 through week 17 (range -1.2 to -7.1) where scores returned to baseline. TTCD for EORTC QLQ-C30 GHS/QoL was 5.9 mos with EV+P vs 3.2 mos with PBC (HR = 0.98 [95% CI]: 0.79 – 1.2). **Conclusions:** Pts treated with EV+P have improved survival compared with PBC without detriment to quality of life and functioning, further supporting the value of EV+P for pts with la/mUC. Compliance, especially after progression, was lower than expected (particularly in the PBC arm) and may have impacted the results. Clinical trial information: NCT04223856. Research Sponsor: Seagen Inc., Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA., and Astellas, Inc.

109 Poster Session

Lenvatinib and pembrolizumab in patients with metastatic papillary renal cell carcinoma: A phase 2 pilot study. First Author: Ilya Tsimafeyeu, Bureau for Cancer Research - BUCARE, New York, NY

Background: Traditionally, metastatic papillary renal cell carcinoma (papillary mRCC) has been treated with tyrosine kinase inhibitors, resulting in a 23% objective response rate and a progression-free survival of 9 months (SWOG 1500 trial). Combinations of immunotargeted therapy have shown improved outcomes in clear-cell mRCC. This prospective pilot study aimed to evaluate the preliminary efficacy of combining lenvatinib with pembrolizumab in patients with papillary mRCC. **Methods:** At study entry in August 2021, patients with papillary mRCC types 1 or 2, multiple measurable lesions per RECIST 1.1 criteria, and no prior therapy for advanced disease were included. The primary endpoint was the objective response rate. The study employed Simon's two-stage design (Simon, 1989) to test the null hypothesis that the true response rate is 23% against a one-sided alternative. In the first stage, 5 patients were enrolled. If there were 1 or fewer responses among these initial 5 patients, the study would be halted. The null hypothesis would be rejected if 6 or more responses were observed in the entire cohort of 12 patients. This design yields a type I error rate of 0.05 and power of 0.8 when the true response rate is 63%. **Results:** As planned, 5 patients were enrolled in the stage 1. The median age was 57.4 years. Among them, 4 patients were diagnosed with papillary RCC type 2, and 3 patients had an unresected primary tumor. Additionally, 1 patient presented with brain metastases. The objective response rate was 100%, of which there was 1 complete and 4 partial responses. As of the last follow-up, the status of patients on therapy was as follows: i) three patients remained on therapy for more than 12 months; ii) one patient experienced disease progression after 14.3 months of treatment; iii) one patient who initially had an ongoing response developed grade 3 uncontrolled diarrhea after 5.5 months from the start of therapy. Despite the positive outcomes observed in stage 1 of the study, the enrollment was stopped. This decision was influenced by emerging results from the large phase 2 trial KEYNOTE-B61, as reported by Chung-Han Lee et al. (ASCO 2023). **Conclusions:** All patients responded to lenvatinib and pembrolizumab therapy. These results suggest promising efficacy of the combination in metastatic papillary RCC. Clinical trial information: KCRB01012021. Research Sponsor: None.

110 Poster Session

Prevalence of pathogenic or likely pathogenic germline mutations in patients with metastatic renal cell cancer. First Author: Atul Batra, Department of Medical Oncology, BRA-IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, India

Background: Data from the West suggests that 5-10% of patients with metastatic renal cell cancer (RCC) are known to harbor a pathogenic/likely pathogenic mutation in the RCC-associated genes. However, there are no data from the Indian subcontinent in this regard. **Methods:** This study was a prospective single-center cohort study conducted at a large tertiary care cancer center in northern India. Patients newly diagnosed with metastatic RCC were eligible to participate and, if willing, were offered pretest counseling and germline genetic testing. We performed whole exome sequencing on blood samples using next-generation sequencing on the Illumina platform. The frequency and spectrum of pathogenic/likely pathogenic (P/LP) variants were determined and classified using the ACMG guidelines, and clinical characteristics associated with mutation status were analyzed using a Fisher's exact test. **Results:** A total of 156 patients with metastatic RCC were enrolled in this study from October 2023 to February 2024. The median age at diagnosis was 44 years, and 67% were men. Histologically, 64% had clear cells, 12% had papillary, and 8% had unknown histology. In RCC-associated genes, 6 patients (3.8%) had P/Lp mutations, of which 4 had mutations in FH and 2 in VHL. Further P/LP variants in the non-RCC genes were detected in 12 additional patients (7.7%), of which 4 were in ATM, 2 in BRIP1, and one each in BRCA1, BARD1, PALB2, MUTYH, MSH6, and PMS2, respectively. The presence of germline P/LP mutation was associated with non-clear histology but not with age and sex. Patients with a P/LP mutation were more likely to have a family history of other cancers (most common, breast cancer) in first and second-degree relatives. **Conclusions:** 11.5% of patients with metastatic RCC were detected with germline P/LP variants, of which one-third had one of the RCC genes, and the rest had non-RCC gene mutations. Patients with mRCC should have access to germline genetic testing, and the gene panel for patients needs to be expanded to include genes previously classified as non-RCC genes. Research Sponsor: None.

111 Poster Session

Differences in the expression heterogeneity of ADC-related markers between primary tumors and metastatic lymph nodes in advanced urothelial cancers. First Author: Xingliang Tan, Department of Urology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in Southern China, Collaborative Innovation Center of Cancer Medicine, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, Guangdong, China

Background: The booming development of antibody–drug conjugates (ADCs), which represent a novel, effective and low-toxicity therapeutic approach, has dramatically improved clinical outcomes in urothelial cancers, especially those with advanced disease. However, previous studies focused less on the targeted genes expression pattern and heterogeneity in metastatic tissues, which are more critical to inhibit tumor progression. Here, we aimed to explore the expression of potential ADC-related genes, including HER2, HER3, Nectin4 and Trop2 in advanced urothelial cancers between primary tumors and metastatic lymph nodes (mLN) in pairs. **Methods:** A large cohort of 306 urothelial cancer patients (292 patients, pN+), including 65 renal pelvis, 38 ureter, 179 bladder and 24 urethral cancer patients (10 patients, pN+), from SYSUCC was enrolled. Paraffin-embedded primary tumors and corresponding mLN sections were subjected to immunohistochemistry (IHC) to detect ADC-related gene expression. HER2 IHC scores of 2/3+ were defined as high expression as previously described. HER3, Nectin4 and Trop2 were evaluated by H-scores (range 0-300, rank 0 to 3+) multiplied by the extent and intensity of the staining, and H-scores >15 were considered positive. **Results:** A total of 74.8% of advanced urothelial cancer patients were HER2 positive (1-3+), and 49.4% had high HER2 expression. High HER2 expression was detected in 33.8%, 42.2%, 56.5% and 50% of renal pelvis, ureter, bladder and urethral primary tumors, respectively. The rate of high HER2 expression in mLNs slightly decreased to 30.1%, 41.7%, 51.9% and 50%, and the concordance rate of HER2 expression between primary and mLNs was 71.9%. Similarly, 27.7%, 42.1%, 52%, and 66.7% of primary tumors were positive for HER3 expression; 72.3%, 89.5%, 77.7%, and 87.5% were positive for Nectin4; and 89.2%, 94.7%, 83.2%, and 95.8% were positive for Trop2 in renal pelvis, ureter, bladder and urethral cancers, respectively. Overall, 71.9%, 50.7%, and 65.3% of patients had consistent expression of HER3, Nectin4 and Trop2 in mLNs, respectively. Survival analysis indicated that the overexpression of HER2, HER3 and Trop2 in advanced urothelial cancers was associated with poor OS (p=0.001, 0.025 and 0.022, respectively). More importantly, we found that patients with higher HER2 expression in mLNs at primary sites had a worse prognosis (p=0.006). **Conclusions:** We first investigated the heterogeneity of ADC-related marker expression in primary urothelial tumors and mLNs in a large single cohort, especially in patients who underwent radical lymphadenectomy. Therapy targeting HER2-ADCs might show better homogeneity in advanced disease, but it is more recommended to detect IHC staining both in primary and metastatic tissues if possible. Research Sponsor: Natural Science Foundation of Guangdong Province, China.

112 Poster Session

Preliminary results of an open-label, single-arm, multi-center study on disitamab vedotin (DV) combined with torIpalimab and radiotherapy as bladder-preserving therapy in HER2 overexpression muscle-invasive bladder cancer (MIBC; DECIDING study-stage I). First Author: Ruiyun Zhang, Department of Oncology, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background: Cystectomy (RC) with or without (neo)adjuvant cisplatin-based chemotherapy [(N)AC] is standard in fit patients (pts) with MIBC. For those who decline or are ineligible for RC, trimodality bladder preservation therapy (TMT) is recommended. However, about 40% of MIBC pts are cisplatin-ineligible or refuse chemotherapy. A new bladder-preserving therapy is urgently needed. DV is an antibody-drug conjugate directed to HER2, which is highly expressed in urothelial cancer(UC). In a combined analysis of two phase II clinical trials, DV demonstrated a promising efficacy with a manageable safety profile in patients with HER2 overexpression (immunohistochemistry 3+ or 2+) locally advanced or metastatic UC who had progressed on at least one line of systemic chemotherapy (Xinan Sheng JCO 2023). Here, we introduce a prospective study on the safety and preliminary efficacy of Disitamab VEdotin Combined with torIpalimab and radiotherapy as blaDder-preservING therapy in HER2 overexpression muscle-invasive bladder cancer(DECIDING study-stage I). **Methods:** This was a two stage designed trial which planned to include 6 pts in stage I as safety introduction cohort and 45 pts in stage II as efficacy assessment expansion cohort. Major including criteria includes staging of cT2-T4aN0M0 MIBC, declining or ineligible for RC, HER2 overexpression, and ECOG PS 0/1. Pts receive DV 2.0 mg/kg and toripalimab 3.0 mg/kg in day1, every 14 days for 12 cycles. Radiotherapy performed simultaneously during drug treatment, with a total dose over 56 Gy/23 fx. CT/MRI, cystoscopy with biopsy and cytology were performed to evaluate response. Up to 6 pts were enrolled into stage I cohort. The primary endpoint were dose-limiting toxicity (DLT) in stage I. Secondary endpt were complete response (CR) rate at 3 months, (defined as negative urine cytology and no visible tumors on imaging and negative biopsies in the ITT population), CR rate at 12m and 24m, bladder-intact disease-free survival, cancer specific survival, and overall survival. **Results:** From 7/2023 to 8/2023, 6 pts of stage I cohort were enrolled. Median age 69 (60-79), 100% MIBC and declined RC, 3/6 and 3/6 of pts confirmed with HER2 IHC 2+ and 3+, respectively. All 6 pts completed first therapy. As of 28 days after first therapy, no DLTs in stage I. 1/6 of pts had grade 3 (Gr 3) TRAE (Hypertriglyceridemia), 2/6 of pts had Gr 2 TRAE (Hyperglycemia and Radiocystitis), and all 6 pts had Gr 1 TRAE(3/6 AST increased; 2/6 ALT increased, 2/6 rash, 1/6 GGT increased, 1/6 diarrhea, 1/6 pruritus, 1/6 nausea). **Conclusions:** DV combined with toripalimab instead of chemotherapy in TMT was well-tolerated in this early analysis. TRAE was consistent with prior trials and no DLTs in 28 days recived first drug therapy. Clinical trial information: NCT05979740. Research Sponsor: None.

113 Poster Session

Efficacy and biomarker analysis of neoadjuvant disitamab vedotin combined with immunotherapy in patients with muscle-invasive bladder cancer: A multi-center real-world study. First Author: Jiao Hu, Department of Urology, Xiangya Hospital, Central South University, Changsha, China

Background: Over half of the patients with muscle-invasive bladder cancer (MIBC) do not benefit from neoadjuvant chemotherapy due to cisplatin intolerance or resistance and have a poor prognosis. Antibody-drug conjugates (ADCs) have shown excellent clinical benefits in advanced MIBC in recent years, but there is a lack of studies using ADCs as neoadjuvant treatment. **Methods:** Patients with MIBC were eligible for inclusion criteria were included and received neoadjuvant RC48-ADC (disitamab vedotin) combined with toripalimab (n=79) or tislelizumab (n=23). The primary outcome was pathological downstaging, including complete pathological response (CR: pT0N0M0) and partial response (PR: pTa, Tis, and T1N0M0). The secondary outcome was disease free survival (DFS). Logistic regression and biomarker analyses were performed to identify efficacy predictors. **Results:** 102 patients from four hospitals were enrolled and evaluated for pathological staging. 84 patients (82.4%) had T2N0M0 tumors and 93 patients (91.2%) had pure urothelial carcinoma. 38 patients (37.3%, 95% CI: 27.9% - 47.4%) achieved CR and 77 patients (75.5%, 95% CI: 6.0% - 83.5%) achieved PR. The 1-year DFS rate was 97.4% (95% CI: 92.6% - 100.0%). Subgroup analysis showed that the clinical stage (P=0.001) and histological type (P=0.006) were independent efficacy predictors. However, there was no statistically significant difference between efficacy and HER2 status (P=1.000). Biomarker analysis showed that the enrichment of pathways, such as the extracellular matrix, angiogenesis, and lymphocyte chemotaxis, may be associated with better efficacy. **Conclusions:** Neoadjuvant RC48-ADC combined with immune checkpoint inhibitors showed promising efficacy in patients with MIBC, irrespective of HER2 expression. This study will expand neoadjuvant treatment strategies for patients who are intolerant to neoadjuvant chemotherapy. Research Sponsor: National Natural Science Foundation of China; 81902592; Hunan Province Young Talents Program; 2021RC3027; Changsha Natural Science Foundation; kq2208377; The Youth Science Foundation of Xiangya Hospital; 2022Q20; National Natural Science Foundation of China; 82070785; National Natural Science Foundation of China; 82303760; National Natural Science Foundation of China; 82373337; China Postdoctoral Innovation Talents Support Program; BX20230431; China Postdoctoral Science Foundation; 2023M733951; Hunan Natural Science Foundation; 2023JJ40946; Hunan Natural Science Foundation; 2024JJ2093; Hunan Province Young Talents Program; 2023RC3073.

Pathologic response.

	Overall (N=102)
Pathological response (%, 95% CI)	
CR	38 (37.3, 27.9 – 47.4)
PR	39 (38.2, 28.8 – 48.4)
SD	19 (18.6, 11.6 - 27.6)
PD	6 (5.9, 2.2 - 12.4)
CR response (%, 95% CI)	
CR	38 (37.3, 27.9 – 47.4)
Non-CR	64 (62.7, 52.6 – 72.1)
Binary response (%, 95% CI)	
Responder (CR + PR)	77 (75.5, 66.0 - 83.5)
Non-responder (SD + PD)	25 (24.5, 16.5 – 34.0)
DCR response (%, 95% CI)	
DCR	96 (94.1, 87.6 - 97.8)
Non-DCR	6 (5.9, 2.2 - 12.4)

CR: complete response; PR: partial response; SD: stable disease; PD: progression disease; DCR: disease control rate.

115 Poster Session

Neoadjuvant immunotherapy-driven bladder preservation for muscle-invasive bladder cancer: A multicenter, propensity score-matched cohort study. First Author: Luzhe Yan, Department of Urology, Xiangya Hospital, Central South University, Changsha, China

Background: Neoadjuvant immunotherapy-driven bladder preservation (Neoimmu-CMT), despite its prominence, is constrained in application due to the absence of robust clinical evidence. Currently, there is a lack of comparative studies on the efficacy of Neoimmu-CMT versus the traditional trimodal therapy (TMT) or neoadjuvant chemotherapy- driven bladder preservation (NAC-CMT). To address this gap, our study (ChiCTR2300069303) aims to assess Neoimmu-CMT's viability and identify suitable candidates through a multicenter, propensity score-matched analysis. **Methods:** The study included 163 patients from 14 hospitals, categorized into Neoimmu-CMT (n=97), TMT (n=30), and NAC-CMT (n=36) subgroups. PSM was utilized to mitigate baseline variability. Primary outcomes were disease-free survival (DFS), bladder-intact DFS (BI-DFS), and overall survival (OS). Univariate and multivariate Cox analyses were used to identify potential prognostic factors. Biomarker assessment comprised immunohistochemistry and single-cell RNA sequencing. **Results:** Post-PSM, Neoimmu-CMT significantly outperformed NAC-CMT in DFS (HR: 2.112, 95% CI: 1.247-3.576, P=0.005) and BI-DFS (HR: 2.329, 95% CI: 1.138-4.770, P=0.021), with a 2-year BI-DFS rate of 90.28% compared to NAC-CMT's 71.59%. However, Neoimmu-CMT and TMT showed no significant difference in DFS and BI-DFS, with Neoimmu-CMT marginally surpassing TMT in 2-year BI-DFS rates (86.42% vs. 80.89%). Clinical complete response to neoadjuvant treatment and lower clinical T stage were positive prognostic factors for Neoimmu-CMT. Biomarker analysis showed the tumor microenvironment immune phenotype closely relates to bladder preservation outcomes. **Conclusions:** Neoimmu-CMT is a promising bladder preservation strategy, comparable to TMT and superior to NAC-CMT. Its advancement could significantly broaden bladder preservation treatment options. Research Sponsor: National Natural Science Foundation of China; 81902592; Hunan Province Young Talents Program; 2021RC3027; Changsha Natural Science Foundation; kq2208377; The Youth Science Foundation of Xiangya Hospital; 2022Q20; National Natural Science Foundation of China; 82070785; National Natural Science Foundation of China; 82303760; National Natural Science Foundation of China; 82373337; China Postdoctoral Innovation Talents Support Program; BX20230431; China Postdoctoral Science Foundation; 2023M733951; Hunan Natural Science Foundation; 2023JJ40946; Hunan Natural Science Foundation; 2024JJ2093; Hunan Province Young Talents Program; 2023RC3073.

Prognostic factors of DFS.

	Univariable Cox DFS				Multivariable Cox DFS			
		95% CI				95% CI		
Variable	**HR**	**Lower**	**Upper**	**P value**	**HR**	**Lower**	**Upper**	**P value**
Neoadjuant therapy								
Immunotherapy	Reference				Reference			
Chemoimmunotherapy	0.660	0.222	1.967	0.456	0.769	0.255	2.323	0.642
ADC combined with Immunotherapy	0.967	0.189	4.936	0.968	1.283	0.224	7.359	0.780
Clinical T stage								
Low stage	Reference				Reference			
High stage	2.463	0.873	6.953	0.089	3.238	1.036	10.118	0.043
Response to neoadjuvant therapy								
cCR	Reference				Reference			
cPR	9.105	2.565	32.325	0.001	9.657	2.697	34.583	<0.001

116 Poster Session

Prognostic value and therapeutic response of neutrophil-to-lymphocyte ratio in penile cancer. First Author: Xingliang Tan, Department of Urology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in Southern China, Collaborative Innovation Center of Cancer Medicine, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, Guangdong, China

Background: Chronic inflammation mediated by poor genital hygiene is a well-recognized pathogenic trigger for penile squamous cell carcinoma (PSCC). The neutrophil-to-lymphocyte ratio (NLR) is a simple and reproducible factor reflecting the systemic inflammatory response and has been reported as an unfavorable indicator in PSCC. However, previous studies limited by small sample sizes, confounding prognostic features and without high-quality evidence to demonstrate the clinical significance of the NLR. **Methods:** A large cohort of 582 penile cancer patients who underwent radical inguinal lymphadenectomy with definitive pN stages were enrolled in this study. Univariate and multivariate Cox regression analyses were performed to investigate prognostic factors and inflammation-related markers in PSCC patients. More importantly, the propensity score matching (PSM) method was used to minimize the prognostic confounding clinicopathological features. Immunofluorescence was further used to investigate the correlation between tumor-infiltrating neutrophils, $CD8^+$ T cells and the NLR. **Results:** According to the ROC curve, the optimal cutoff value for the NLR was 3.0, and 226 (38.8%) PSCC patients had a high NLR. Survival analyses indicated that advanced pT, pN, pathological grade, lymphovascular invasion, high NLR, C-reactive protein (≥ 2.2 mg/L) and serum amyloid A (≥ 11.3 mg/L) were associated with poor PFS and CSS. After PSM to eliminate interference from clinical factors, pN and the NLR were found to be independent prognostic indicators in PSCC patients (both $p<0.001$). Cox multivariate regression analysis revealed that the HR for PFS was 1.64 (1.15–2.34) in the high NLR group and 1.56 (1.04–2.34) in the high NLR group (p=0.006 and 0.030, respectively). PSCC patients with high NLRs experienced shorter PFS after receiving cisplatin-based chemotherapy (p=0.037) and PD-1 immunotherapy (p=0.020). In addition, we found that the infiltration of tumor-associated neutrophils ($CD66^+$) and the $CD8^+$ T-cell ratio were positively correlated with the NLR. The development and formation of neutrophil extracellular traps (NETs) might contribute to chemoresistance and tumor progression in high-NLR PSCC patients. **Conclusions:** In this study, we demonstrated that the NLR is an effective, simple and independent prognostic indicator for PSCC. The NLR holds promise as a powerful tool to guide decision-making in clinical practice. Research Sponsor: Natural Science Foundation of Guangdong Province, China.

Univariate and multivariate analysis of clinicopathological factors associated with survival after PSM.

	PFS after PSM				CSS after PSM			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
Variables	**HR**	**P-value**	**HR**	**P-value**	**HR**	**P-value**	**HR**	**P-value**
Age (>55 vs ≤55)	0.85 (0.60 - 1.19)	0.350	1.21 (0.85 - 1.73)	0.283	0.95 (0.64 - 1.40)	0.790	1.42 (0.95 - 2.13)	0.087
BMI (>23 vs ≤23)	1.03 (0.92 - 1.14)	0.640	1.09 (0.97 - 1.23)	0.152	1.03 (0.93 - 1.15)	0.564	1.11 (0.98 - 1.25)	0.087
pT stage	1.17 (1.07 - 1.27)	**<0.001**	1.12 (0.95 - 1.31)	0.179	1.14 (1.03 - 1.26)	**0.013**	1.07 (0.89 - 1.28)	0.495
pN stage	2.22 (1.90 - 2.58)	**<0.001**	2.22 (1.89 - 2.60)	**<0.001**	2.22 (1.86 - 2.65)	**<0.001**	2.28 (1.89 - 2.75)	**<0.001**
Pathological grade	1.13 (1.04 - 1.24)	**0.006**	0.99 (0.85 - 1.17)	0.929	1.10 (0.99 - 1.23)	0.084	0.97 (0.81 - 1.17)	0.759
LVI/PNI (Yes vs No)	1.55 (1.06 - 2.27)	**0.023**	1.12 (0.76 - 1.66)	0.562	1.66 (1.09 - 2.55)	**0.019**	1.25 (0.81 - 1.94)	0.320
NLR (≥3.0 vs <3.0)	1.81 (1.27 - 2.56)	**<0.001**	1.64 (1.15 - 2.34)	**0.006**	1.81 (1.21 - 2.69)	**0.004**	1.56 (1.04 - 2.34)	**0.030**

PSM: propensity score matching; CSS: cancer specific survival; HR: hazard ratio; 95% CI: 95% confidence interval; LVI: lymphovascular invasion; PNI: perineural invasion; NLR: neutrophil-lymphocyte ratio.

117 Poster Session

Avelumab plus axitinib for first-line treatment of advanced renal cell carcinoma: A real-world ambispective RAVE-Renal study. First Author: Viacheslav Chubenko, St. Petersburg Clinical and Research Center of Specialized Types of Oncological Medical Care, St. Petersburg, Russian Federation

Background: In a phase 3 JAVELIN Renal 101randomized study, the combination of avelumab and axitinib demonstrated a significant improvement in progression-free survival (PFS; median 13.9 months) and objective response rate (ORR; 59.3%) among patients with metastatic clear-cell renal cell carcinoma (mRCC), leading to FDA approval as a first-line therapy. In our ambispective observational RAVE-Renal study, real-world data were gathered to assess the practical application and outcomes associated with the use of avelumab and axitinib in clinical settings. **Methods:** Patients were recruited from 13 sites, with data collected anonymously online. Key inclusion criteria were untreated mRCC and a minimum age of 18 years. Safety and efficacy assessments were conducted in all patients who received at least one dose of avelumab and axitinib. The primary endpoints included ORR and PFS, while secondary endpoints encompassed overall survival (OS) and the incidence of treatment-related adverse events (TRAEs). **Results:** At the time of data cutoff (February 03, 2024), a total of 125 patients were enrolled and treated. Median age was 61 years (range, 37-74). Patients were predominantly men (74.3%), previously nephrectomised (81.4%), had 2 and more metastatic sites (77.1%) including bone (24.3%), liver (15.7%), and brain (3%) metastases. IMDC risk was evaluated in 102 patients. Among these patients, 36 (35.3%) were categorized as having favorable risk, 50 (49%) as intermediate risk, and 16 (15.7%) as poor risk. The median number of avelumab infusions was 7 (range, 1-29). Table summarizes efficacy and safety data. **Conclusions:** The real-world study of first-line avelumab and axitinib therapy reveals comparable ORR and PFS to those observed in the pivotal clinical trial among patients with mRCC. The combination was well tolerated. Further follow-up of patients in the study is ongoing. Clinical trial information: KCRB01012022. Research Sponsor: None.

Summary of efficacy and safety data.

Follow-up, median, months	14.7
ORR*, %	44.3
Complete responses, n (%)	3 (2.5)
Partial responses, n (%)	51 (41.8)
Stable disease, n (%)	60 (49.1)
Disease progression, n (%)	8 (6.6)
PFS, median, months (95% CI)	15.0 (11.2-18.8)
1-year OS rate, %	71.2
All TRAEs, n (%)	99 (79.2)
Grade ≥3 TRAEs, n (%)	24 (19.2)

*Response was assessed in 122 patients (97.6%).

118 Poster Session

Changes in the treatment landscape of metastatic hormone-sensitive prostate cancer: A multicenter study. First Author: Fumihiko Urabe, Department of Urology, Jikei University School of Medicine, Minato-Ku, Japan

Background: A multicenter database was utilized to examine the current treatment landscape and clinical outcomes among patients with metastatic hormone-sensitive prostate cancer (mHSPC) following approval of upfront androgen receptor signaling inhibitors (ARSIs). **Methods:** We retrospectively analyzed patients with mHSPC who commenced treatment between February 2018 and June 2023. The Kaplan–Meier method was used to assess oncological outcomes, including time to castration-resistant prostate cancer (CRPC), progression-free survival 2 (PFS2, duration from initial treatment to tumor progression during second-line treatment), cancer-specific survival (CSS), and overall survival (OS). Cox regression analyses were performed to determine the impact of treatment choices on oncological outcomes. In addition, the incidence rate of adverse events was assessed. **Results:** In total, 829 patients were analyzed; 42.5% received ARSIs with androgen deprivation therapy (ADT), 44.0% received combined androgen blockade (CAB), and 13.5% received ADT alone. Analysis of annual treatment choice trends revealed an increasing preference for ARSIs with ADT. Kaplan–Meier curves and multivariate Cox regression analyses indicated higher rates of CRPC and shorter PFS2 in patients treated with CAB versus ARSIs with ADT. By contrast, CSS and OS were not significantly different between the ARSI with ADT group and the CAB group. Grade 3–4 adverse events occurred in 1.9% of patients receiving CAB and 6.0% of those receiving ARSIs with ADT. **Conclusions:** For patients with mHSPC, initial treatment with ARSIs in combination with ADT resulted in a longer time to CRPC and longer PFS2 compared to CAB. Although CAB and ADT alone were associated with fewer adverse events, ARSIs with ADT should be considered a first-line treatment option given its superior oncological outcomes. Research Sponsor: None.

119 Poster Session

PSA response and cabazitaxel outcomes stratified by prior docetaxel PSA response in metastatic castrate-resistant prostate cancer (mCRPC). First Author: Christopher Eing Wee, Cleveland Clinic, Cleveland, OH

Background: In the TheraP trial, both cabazitaxel and lutetium Lu 177 vipivotide textraxetan demonstrated similar overall survival (OS) in patients with mCRPC previously treated with docetaxel. We seek to identify predictors for cabazitaxel benefit by evaluating patients' cabazitaxel outcomes in the context of prior docetaxel outcomes. **Methods:** We identified patients who started cabazitaxel after January 2010 at our institution. Patients were included if they received docetaxel for mCRPC but excluded if they received docetaxel for hormone-sensitive disease, used taxane in combination with other agents (e.g. carboplatin), or received multiple courses of same taxane (e.g. "re-challenges"). For adequate assessment of PSA response, patients were only included if pre-chemo PSA was $>$ 20 ng/mL and had received at least two cycles of both taxanes. PSA response was defined as $>$50% decrease from baseline sustained for at least 3 weeks (PSA50). OS was calculated from time of cabazitaxel start to death from any cause. **Results:** Eighty patients were identified with a median age of 70 years at cabazitaxel start. Forty (50%) patients had a PSA50 with docetaxel, while only 18.8% had a PSA50 with subsequent cabazitaxel. Patients who had a PSA50 to docetaxel had a significantly higher chance of PSA50 to cabazitaxel (OR 5.29, 95% CI: 1.36, 20.53, p = 0.0162); the PSA50 rates on cabazitaxel were 30% and 7.5% between those that did and did not have a PSA50 to docetaxel, respectively. There were no significant differences in cabazitaxel median OS based on prior docetaxel PSA50. **Conclusions:** Patients who had PSA50 to docetaxel had a significantly higher chance to have a PSA50 to cabazitaxel. Prior docetaxel PSA50 could be considered when deciding whether to use cabazitaxel or an alternative agent for subsequent treatment. Research Sponsor: None.

Median # cycles		25^{th} – 75^{th} %ile
- Docetaxel	6	5, 8
- Cabazitaxel	5	3, 6
Median PSA at chemotherapy start (ng/mL)	ng/mL	
- Docetaxel	96.19	42.75, 298.35
- Cabazitaxel	166.46	94.27, 378.05
Median OS	Months	95% CI
- Docetaxel PSA50	10.16	8.81, 19.63
- No Docetaxel PSA50	8.28	6.64, 13.64

120 Poster Session

Detailed pathological characteristics and survival prognosis of patients with penile cancer from a high-capacity tertiary referral centre over a 20-year period. First Author: Zhicheng Liu, Department of Urology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in Southern China, Collaborative Innovation Center of Cancer Medicine, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China

Background: Penile cancer is a rare cancer that affects 0.1-1 per 100,000 men in developed countries. However, data on this cancer in developing countries, particularly in Asian populations, are lacking. A retrospective study is needed to determine the characteristics of penile cancer patients, tumor-related treatments, and prognosis. The objective of our study was to present statistical results that are applicable to an Asian population under the most recent staging system. Additionally, we aimed to report on the pathological characteristics and prognosis of a large sample of patients with penile cancer who underwent long-term follow-up with the standard extent of radical dissection. **Methods:** This study retrospectively analyzed clinical and pathological data from 1017 patients who were diagnosed with penile cancer at Sun Yat-sen University Cancer Center between October 2001 and October 2023. The primary study endpoint was overall survival (OS), and the secondary endpoint was progression-free survival (PFS). Survival curves were plotted using the Kaplan–Meier method, and differences were compared using the log-rank test. Univariate and multivariate Cox proportional risk models were used to analyze the factors associated with tumor survival. **Results:** The average follow-up time was 50 months (range: 0.6-232.8 months). The 5- and 10-year OS rates were 67.3% and 62.7%, respectively, and the 5- and 10-year PFS rates were 63.9% and 61.1%, respectively. After excluding 127 Tx patients and 23 TIS stage patients, the 10-year OS rates of pTa stage (29 patients), pT1 (305 patients), pT2 stage (217 patients), pT3 stage (271 patients), and pT4 stage (45 patients) patients were 96.3%, 80.1%, 61.7%, 55.4%, and 14.2%, respectively. A total of 690 patients underwent standard lymph node dissection. The 10-year OS rates of pN0 (376 patients), pN1 (111 patients), pN2 (78 patients), and pN3 (125 patients) patients were 92.7%, 62.5%, 48.1% and 31.3%, respectively. The results of the multifactorial analysis revealed that T stage (T4 stage versus Ta-T1 stage: HR=2.38, 95% CI: 1.00~5.66, P=0.05), pathological grade (G3~4 grade versus G1~2 grade: HR=1.63, 95% CI: 1.05~2.53, P=0.027), N stage (pN+ versus pN0: HR=14.11, 95% CI: 7.83~25.43, P$<$0.001), and white blood cell count (WBC$>$8.5: HR=1.71, 95% CI: 1.17~2.51, P=0.006) were independent prognostic factors in penile cancer patients. **Conclusions:** Patients with penile cancer had better long-term OS after standard lymph node dissection. The adverse factors were T stage, pathological grade, extent of lymph node metastasis, and preoperative WBC count. Identifying high-risk patients through preoperative evaluation can improve long-term survival rates. Radical lymph node dissection in the early stage has more curative value, and adjuvant therapy should be provided in patients with advanced-stage disease after surgery. Research Sponsor: None.

121 **Poster Session**

Single centre real world data on disease profile and outcome of 700 patients with penile cancer treated with curative intent at an Indian cancer centre.

First Author: Gagan Prakash, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India

Background: Globocan 2022 reported that there are close to 10000 newly diagnosed penile cancer (PeCa) patients annually in India, which contributes to around 27% of the world's burden of this disease. With the rarity of this male genitourinary cancer globally and absence of level I evidence on most aspects of the disease, real world data from a single Centre assumes importance and this retrospective study highlights the clinico-demographic profile, oncological outcome and surgical complications in patients treated with a curative intent. **Methods:** We retrospectively reviewed our prospectively maintained institutional database for patients with PeCa treated with curative intent from 2013 to 2021. Data was collected for demographic variables, clinico-pathological characteristics, post-operative complications and oncological outcomes. Descriptive data were expressed as mean / median / proportions. The Kaplan Meier method was used to calculate the cancer specific survival (CSS) of the patients, stratified by pN status. **Results:** From 2013 to 2021, 700 patients were treated for PeCa at our centre with curative intent, with a median age of 54 years (IQR 44-62) and a mean BMI of 24.1 kg/m^2. Around 40% of the patients had history of tobacco use. The clinico-pathological features and Clavian Dindo complication rates are summarized in the table. With a median follow-up of 42 months, the CSS for cN0 patients under observation for their groins was 97.3%.CSS for patients with pN0, pN1, pN2 and pN3 was 90.6%, 79.4%, 71.4% and 55%. Amongst pN3, 24.3% received adjuvant chemo alone, 23.7% received adjuvant RT/CTRT alone while 33.7% received both adjuvant chemo and RT.CSS of pelvic nodal pN3 patients was 35% compared to 71% of inguinal perinodal extension pN3. **Conclusions:** Our series, one of the largest reported from a single centre, highlights the real world oncological outcome of PeCa patients. We reemphasize the importance of addressing inguinal nodes early and adequately and the worser outcome of pN3 due to pelvic node involvement compared to pN3 due to extra nodal extension of inguinal nodes. Research Sponsor: None.

Clinico-pathological features of 700 patients with PeCa.

Variable	Total n=700
Treatment of the primary	
Wide local excision	52 (7.5%)
Circumcision	50 (7.2%)
Glansectomy	37 (5.3%)
Brachytherapy	12 (1.8%)
Partial penectomy	441 (63%)
Total penectomy	108 (15.4%)
Treatment of groins (n=1400)	
MILD/SILD	629 (44.9%)
IILD	381 (27.2%)
Observation	139 patients (19.8%)
Not performed	56 patients (8.1%)
pT stage	
<pT1	211 (30.1%)
pT2	294 (41.8%)
pT3	164 (23.4%)
pT4	0
NA	31 (4.5%)
pN stage (n=505)	
pN0	238 (47%)
pN1	62 (12.3)
pN2	12 (2.4%)
pN3	193 (38.2%)
pN3 because in inguinal ENE	126
pN3 because of pelvic nodal involvement	67
HPV status (p16)	
Positive	40 (5.7%)
Negative	93 (13.2%)
Data NA	567 (81%)
Complications with nodal dissection	
CDC 0	63.8%
CDC 1-2	13.1%
CDC 3a	19%
CDC 3b	4.5%

122 Poster Session

Restriction of YWHAB-mediated YAP cytoplasmic retention as a novel mechanism underlying stemness maintenance and chemo-resistance in peritoneal metastasis of ovarian cancer: A comparative proteomic study. First Author: Lin Qiu, Liaoning Cancer Hospital & Institute, Shenyang, China

Background: Ovarian cancer (OC) peritoneal metastasis (OCPM) is a significant cause of high mortality of OC. To investigate the mechanisms underlying OCPM stemness maintenance and resistance, we characterized proteomic alterations in residual OCPM tissues after neoadjuvant chemotherapy (NACT), and verified restriction of YWHAB-mediated YAP cytoplasmic retention as a novel important mechanism. **Methods:** Tumor specimens from HGSOC patients underwent proteomic analysis using TMT and REACTOME for pathway and GO analysis. The OVCAR3 cell line, derived from malignant ascites, and formalin-fixed samples were used for Immunohistochemistry. Ovarian cancer stem-like cells, including cisplatin-resistant cells, were cultured, and ALHD activity was measured by qPCR and ALDEFLUOR Kit. Western blot and Co-IP were used for protein analysis. Sphere formation and limiting dilution assays were performed in vitro and in vivo using BALB/c nude mice, and FACS quantified OCSCs. YWHAB-knockdown cells were created via plasmids, lentivirus, and transfection. Statistical tests included paired and unpaired t-tests, one-way ANOVA, and ELDA for limiting dilution. Data are shown as mean $\pm$ SD, with *p$<$ 0.05, **p$<$ 0.01, ***p$<$ 0.001 indicating significance. **Results:** TMT-based proteomics identified 324 differentially expressed proteins in post-NACT OCPM tissues, with 179 upregulated and 145 downregulated. Bioinformatics revealed novel targets in key pathways, including TUBB, VCP in Hedgehog, YWHAB in Hippo, TLA1/2, SPTA1 in MAPK, and FASN in NOTCH. YWHAB downregulation was confirmed in pPR OCPM tissues and cells, serving as a marker to differentiate pNR from pCR/pPR OCPM (AUC = 0.7673). YWHAB inhibition in pCR OCPM cells enhanced stemness, as seen in sphere formation, OCSC percentages, CD133 expression, ALDH activity, and tumorigenicity. It also induced cisplatin resistance. YWHAB inhibition reduced cytoplasmic YAP retention and increased nuclear YAP, enhancing transcriptional activity. YAP5SA expression negated the effects of YWHAB depletion on stemness and resistance in pCR OCPM cells. **Conclusions:** In summary, this study explored the potential mechanisms underlying OCPM stemness maintenance and resistance by employing proteomic analysis, and revealed a novel YWHAB-mediated mechanism. This finding indicates that YAP would an important target for eradicating YWHAB-restricted OCSCs in OCPM. Research Sponsor: National Natural Science Foundation of China, Youth Science Foundation Project; 82103056; Liaoning Province Science and Technology Department, Liaoning Province Applied Basic Research Project; 2022JH2/101300045; Liaoning Province "Xingliao Talent Plan" medical famous project, young medical famous project; TXMJ-QN-06.

123 Poster Session

Association between the non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) and risk of endometrial cancer among US adults: A population-based study. First Author: Penglin Liu, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing Maternal and Child Health Care Hospital, Beijing, China

Background: Endometrial cancer, as one of the metabolic-related malignancies, is becoming a significant public health concern worldwide. The non-high-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio (NHHR) has emerged as a comprehensive biomarker of various lipid-related metabolic disorders. However, the association of NHHR with endometrial cancer risk remains unclear to date. Therefore, we conducted this nationwide cross-sectional study to investigate the association of NHHR with the risk of endometrial cancer among US adults. **Methods:** Data were obtained from the National Health and Nutrition Examination Survey (1999–2018). Female participants who provided complete data on the NHHR and endometrial cancer were enrolled. The association of the NHHR with endometrial cancer was assessed by multivariate logistic regression analyses, adjusted by multiple potential confounders. Meanwhile, sensitivity analyses and subgroup analyses were conducted. **Results:** A total of 25,411 eligible participants were enrolled, including 214 (0.8%) women with endometrial cancer. The fully-adjusted multivariate logistic model showed a significantly positive association of NHHR with the endometrial cancer risk (odds ratio [OR] 1.15, 95% confidence interval [CI]: 1.05–1.25; *P*=0.003). Comparing the highest to the lowest quartile of NHHR, the fully-adjusted OR was 1.52 (95% CI: 1.02–2.28, *P* for trend=0.017). In subgroup analyses, the significantly positive association between NHHR and the risk of endometrial cancer was also found in non-obese women (OR 1.18, 95% CI: 1.04–1.35, P=0.012), women without diabetes (OR 1.15, 95% CI: 1.02–1.30, *P*=0.027), women with hypertension (OR 1.15, 95% CI: 1.03–1.28, *P*=0.012), women who use oral contraceptives (OR 1.16, 95% CI: 1.04–1.30, *P*=0.009) and in parous women(OR 1.15, 95% CI: 1.05–1.27, *P*=0.003). Additionally, in the sensitivity analysis by excluding participants with NHHR below 5% or above 95% in total cohort, the positive association of NHHR with endometrial cancer risk remained significant (OR 1.21, 95% CI: 1.03–1.42, P=0.018). **Conclusions:** This population-based study found that a higher NHHR correlated with an increased risk of endometrial cancer among the US population. Our findings suggested that NHHR might be a promising tool for the risk assessment of endometrial cancer. Prospective studies are necessary to further verify these findings. Research Sponsor: None.

Association of the NHH with endometrial cancer risk in total cohort.

	OR (95% CI)		
NHHR	**Model 1**	**Model 2**	**Model 3**
Continuous Values	1.17 (1.07–1.27)	1.15 (1.05–1.25)	1.15 (1.05–1.25)
Quartile Categories			
Q1	1	1	1
Q2	1.09 (0.72–1.66)	1.06 (0.70–1.60)	1.02 (0.65–1.58)
Q3	1.24 (0.83–1.85)	1.17 (0.78–1.76)	1.22 (0.80–1.86)
Q4	1.66 (1.13–2.43)	1.52 (1.04–2.22)	1.52 (1.02–2.28)
P for trend	0.004	0.016	0.017

124 Poster Session

Nationwide analysis of patients with ovarian cancer: Racial status and risk of metastasis. First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Literature review has found profound disparities in clinical outcomes, for patient with ovarian cancer. Metastasis is the primary cause of cancer morbidity and mortality. However, data on the metastasis risks on hospitalized individuals with ovarian cancer is still limited. Therefore, we aim to assess the association between metastatic ovarian cancer and racial differences using large database analysis. **Methods:** We analyzed the 2020 U.S. National Inpatient Sample (NIS) to explore patients who have ovarian cancer as the primary diagnosis. Additionally, we identified evidence of metastasis, as recorded by ICD-10-CM. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariable logistic and linear regression analyses. The primary outcome was racial differences in organ metastasis and secondary outcomes included mortality and length of stay. Statistical significance was established at p-value of 0.05. **Results:** We identified 19,789 patients with primary diagnosis of ovarian cancer at discharge. The mean age was 61.6 years. Caucasians accounted for 68.3%, with Hispanics at 11.1 % and African Americans at 9.7%. We found that 7% of the patients had liver metastasis. In a multivariate analysis adjusting for patient, COVID-19, chemotherapy usage and hospital factors, African Americans and Hispanics had higher risk of liver metastasis (aOR 1.95; 95%CI (1.32, 2.88), p = 0.001) (aOR 1.78; 95%CI (1.19, 2.66), p = 0.004). We also observed reduced length of stay for Asian Americans (b = -0.74; 95%CI (-1.31, -0.17), p = 0.011). We observed an increase in risk of metastasis and mortality but non-statistically significant in some parameters and races, as shown in table provided. **Conclusions:** In conclusion, our study revealed that racial difference is associated with higher risk of metastasis, as well as other outcomes. More studies following patients over time are needed to determine if race directly affects how ovarian cancer spreads and other clinical outcomes. Research Sponsor: None.

Adjusted odds ratio, adjusted for patient characteristics, hospital location and COVID-19 conditions.

Race	Liver Metastasis	Lung Metastasis	Mortality	Length of Stay**
Caucasian		**Baseline**		
African American	**1.95 (1.32, 2.88)***	1.11 (0.83, 1.43)	1.73 (0.86, 3.49)	0.49 (-0.20, 1.20)
Hispanic	**1.78 (1.19, 2.66)***	1.15 (0.86, 1.48)	0.52 (0.19, 1.43)	-0.20 (-0.77, 0.37)
Asian	1.05 (0.59, 1.89)	0.86 (0.57, 1.29)	0.72 (0.22, 2.28)	**-0.74 (-1.31, -0.17)***
Native American	0.60 (0.08, 4.36)	0.55 (0.22, 1.36)	N/A	-0.51 (-2.18, 1.15)
Others	1.48 (0.69, 3.16)	1.48 (0.84, 2.62)	0.88 (0.31, 2.46)	0.45 (-1.12, 2.02)

*Denotes statistically significant at p-level $<$ 0.05.
**Length of Stay is expressed as beta-coefficient.
N/A denotes no death in the subpopulation group.

125 Poster Session

Analysis of prognostic factors in uterine cervical malignancy treated with concurrent chemoradiation therapy: A retrospective study in two centers in Korea. First Author: Seung-Mi Lee, Department of Obstetrics and Gynecology, Kyungpook National University Hospital, Daegu, South Korea

Background: Cervical cancer is prevalent in most developing countries, and immune checkpoint inhibitors are very expensive to be standard treatment in limited-resource conditions. In these circumstances, concurrent chemoradiation therapy (CCRT) remains a preferred treatment. This study aims to evaluate prognosis and identify prognostic markers in cervical cancer patients treated with CCRT in Korea. **Methods:** This retrospective study utilized data from two centers (KNUH and KNUCH) January 2012 to September 2023. Disease stage was determined based on the FIGO 2018 system, including patients between stages IIB to IIIC-2. PET/CT assessed lymph node status. All patients received CCRT as the first-line treatment with cisplatin (40 to 60 mg/m^2) chemotherapy and EBRT with or without ICR, guided by gynecologic radiation oncologist. Pelvic MRI or CT within 5 months after CCRT was used to evaluate radiosensitivity, including the size of the residual primary cervical tumor. The primary endpoint was 5-year disease-free survival (DFS), determined via systemic imaging studies like concurrent chest and abdomen CT or PET/CT. Median DFS was evaluated using Kaplan-Meier survival analysis. Prognostic factors were stratified and analyzed using Cox's proportional hazard ratio regression. Multivariate analysis was conducted using only significant factors identified in the univariate analysis. Receiver operating characteristic curve and Youden's index were used to determine the cutoff value. **Results:** Ninety-seven patients were enrolled. The median DFS within 5 years was not reached; mean DFS was 41.5 months (95% CI=36.2–46.8). Multivariate Cox's proportional hazard regression identified two significant clinical factors for 5-year DFS; residual primary tumor size after CCRT and initial serum CA-125 level (p=0.001, p=0.007, respectively). The cutoff values were 1.85 cm for residual primary tumor size and 24.650 U/mL for CA-125 to predict the 5-year DFS rate (CR or NED vs. PR, SD, PD or recurrence). Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for residual tumor size (36.4%, 98.4%, 92.3%, 73.4%, respectively) and CA-125 (67.9%, 60.7%, 46.3%, and 79.1%, respectively). **Conclusions:** The size of the residual primary tumor or initial serum CA-125 level can be useful in predicting 5-year DFS rate after CCRT. Research Sponsor: None.

Baseline characteristics of the cohort in this study.

	N (%) or mean value
Age at diagnosis (yrs)	57.46$\pm$12.48 (27–81)
FIGO 2018 stage (n)	97 (100.0%)
IIB	24 (24.7%)
IIIB	6 (6.2%)
IIIC-1	44 (45.4%)
IIIC-2	23 (23.7%)
Histology (n)	97 (100.0%)
Squamous cell carcinoma	80 (82.5%)
Adenosquamous carcinoma or adenocarcinoma or undifferentiated* carcinoma	17 (17.5%)

*Cannot determine the histology between squamous cell carcinoma and adenocarcinoma due to poor differentiation.

126 **Poster Session**

Validation of FIGO 2018 staging for cervical cancer: Insights from a Japanese multicenter cohort. First Author: Kohei Hamada, Kyoto University Graduate School of Medicine, Kyoto, Japan

Background: The International Federation of Gynecology and Obstetrics (FIGO) updated its staging system for cervical cancer in 2018, introducing major changes such as the establishment of stage IIIC based on lymph node metastasis (LNM), which has been reported to provide a better reflection of prognosis. However, stage IIIC has been reported to be heterogeneous, with prognoses varying depending on LNM extent and local tumor factors. In Japan, where various imaging tests are extensively performed, this revision is expected to lead to numerous cases of stage migration due to LNM. However, there have been few reports on the impact of this revision in Japan. Therefore, this multicenter study aims to assess the validity of FIGO 2018 in a Japanese cohort, focusing on LNM, local tumor factors, and histological types. **Methods:** Using a unified registry for gynecological malignancies developed by The Japanese Society of Obstetrics and Gynecology, this study involved 1,468 cervical cancer patients treated between 2011 and 2019 across eight designated cancer treatment hospitals. The registry used the FIGO 2009 staging system, and patients with stage IA to IIIB disease were restaged according to the FIGO 2018. Stage IIIC cases were further classified into substages IIIC-T1, IIIC-T2, and IIIC-T3AB based on local tumor factors. **Results:** After restaging process, A total of 347 cases (27.6%) were upstaged to stage IIIC according to LNM. Survival analysis showed that stage IIIC had a poorer prognosis than stage II (HR, 2.09; 95% CI, 1.27-3.44; p=0.004), but a significantly better prognosis than stage IIIAB (HR, 0.46; 95% CI, 0.27-0.77; p=0.004). There was also a clear difference between subclasses stage IIIC1 and IIIC2, with IIIC2 having a worse prognosis (HR, 2.13; 95% CI, 1.23-3.67; p=0.007). A survival analysis focusing on stageIIIC1 subdivisions (T1, T2, and T3AB) showed varied prognosis among them. Furthermore, IIIC1-T1 and IIIC1-T2 had significantly worse prognoses compared to stages I and II (I vs IIIC1-T1, HR, 3.21; 95% CI, 1.64-6.30; p$<$0.001. II vs IIIC1-T2, HR, 1.82; 95% CI, 1.03-3.21; p=0.04), while the prognosis of IIIC1-T3AB was similar to stage IIIAB. In the analysis by histological type, there was little difference between IIIC1-T1 and IIIC1-T2 in squamous cell carcinoma, but there was significant difference between IIIC1-T1 and IIIC1-T2 in adenocarcinoma (HR, 5.12; 95% CI, 1.10-23.74; p=0.04). On the other hand, for IIIC2, prognosis was similar across T1, T2, and T3AB, all showing uniformly poor outcomes. **Conclusions:** We were able to concretely clarify the current situation in Japan and validate the usefulness of FIGO 2018. The comprehensive examination of LNM, local tumor factors, and histological type may further reinforce and complement FIGO 2018. Research Sponsor: None.

127 **Poster Session**

Exploration of the application of the sprayed γ-GGT fluorescent probe for visual imaging of epithelial ovarian cancer. First Author: Manlin Zhang, Liaoning Cancer Hospital & Institute, Shenyang, China

Background: To explore the feasibility, accuracy and related influencing factors of spraying γ -GGT fluorescent probe in visual imaging of epithelial ovarian cancer. **Methods:** This study employed a previously developed spray-type γ-GGT fluorescent probe in fresh ex vivo epithelial ovarian cancer tissues. The experimental group selected ovarian cancer lesions of varying sizes and observed fluorescence imaging after spraying different concentrations of the probe. The optimal imaging concentration and observation time were determined based on pathological results. The validation group then used the optimal parameters to image primary and metastatic lesions, normal tissue, and suspicious areas, confirming the probe's accuracy. Clinical data from patients, such as age and stage, were analyzed to identify factors affecting probe imaging. **Results:** A total of 16 cases of epithelial ovarian cancer were included in this study, 8 cases were in the experimental group and 8 cases were in the validation group, and the samples were collected from the primary ovarian lesions, omental metastases and peritoneal metastases. In the experimental group, 42 lesions of 3 different diameters were collected. The visible lesions were not found to have any changes in the imaging within 1min-1h after spraying the γ-GGT fluorescent probe, and the SBR value within 1min-1h was between 1.26-1.29, with no statistical difference ($P>0.05$), and the visible effect of 5 h was weaker or even invisible to the naked eye, and the best observation time was 1min-1h after spraying the γ-GGT fluorescent probe, and the SBR value of 1min-1h after spraying 10 μM of γ-GGT fluorescent probe was significantly higher than that of 1 μM and 5 μM ($P<0.05$), and the best visible effect was achieved by the naked eye, resulting in a minimum effective imaging concentration of 10 μM. A total of 27 points were collected from the lesion with a diameter of <0.3 cm and its surrounding normal tissues with a distance of 1 cm or tissues with a diameter of 1-1.5 cm with a height of suspicion but normal to the naked eye, and 26 of the 27 tissues were confirmed by pathology to be cancerous and 1 was non-cancerous, with a true positive rate of 96.3% and a false positive rate of 3.7%. The overall true positive rate of fluorescence imaging was 98.6%. Univariate analysis showed that there were significant differences in the level of preoperative γ-GGT and the SBR value of preoperative treatment (all $P<0.05$), and the results of multivariate analysis showed that preoperative treatment was an independent influencing factor for fluorescence imaging of γ-GGT fluorescent probe ($P<0.05$). **Conclusions:** This study tested the γ-GGT fluorescent probe for ovarian cancer imaging, finding 10 μM as the effective concentration and 1 minute to 1 hour as the optimal observation window. The probe's effectiveness is influenced by preoperative treatments. Research Sponsor: National Natural Science Foundation of China; 82103056; Liaoning Province science and technology plan project; 2022JH2/101300045; Liaoning Province "Xingliao Talent Program" Medical Masters Project, Young Medical Masters Project; TXMJ-QN-06.

128 **Poster Session**

TP53 mutation as predictive factor of platinum response in BRCA-mutated ovarian cancer: A prospective case-series analysis. First Author: Eleonora Lai, Medical Oncology Unit, University Hospital and University of Cagliari, Cagliari, Italy

Background: Platinum sensitivity (PS) is a prerequisite for first-line PARP inhibitors (PARPi) in locally advanced and relapsed high grade serous ovarian cancer (HGS-OC). BRCA mutations are predictive of PS and of response to PARPi. Notably, platinum and PARPi cytotoxic action is mainly related to p53-mediated inducted apoptosis. Therefore, the integrity of p53 machinery is crucial for platinum-related activity whereas the presence of p53 mutation is a fairly frequent event in ovarian cancer, especially in HGS-OC and in BRCA mutated. **Methods:** We prospectively analyzed 208 women with primary ovarian cancer undergoing surgery at the Department of Gynecologic Oncology, ARNAS G. Brotzu, Cagliari, Italy, between 2019 and 2023. Somatic NGS analysis was performed to detect BRCA and HRD mutations. TP53 mutations were classified according to according to hotspot, structural (missense/nonsense) and functional classification as "gain of function" (GOF) or "loss of function" (LOF), based on IARC TP53 database. Comparative testing with Fisher's exact test was used to examine TP53 mutation distribution and associations with clinicopathologic factors and PS. BRCA mutation status was further used to stratify the analysis. **Results:** Globally, we included 127 adult HGS-OC patients (pts). 84.2% had stage III-IV disease. TP53 mutation was found in 83.4% of pts. Somatic BRCA mutations were found in 28.3%. HGS-OC with somatic BRCA mutations had higher TP53 mutation frequency (88.8%) than BRCA WT (81.3%, p=0.1510). Employing the structural classification scheme, most harbored a missense TP53 mutation (76.5%). LOF TP53 mutations were found in 59.4% while GOF in 31.2%. No significant disparity was observed in the distribution of specific TP53 mutations within each classification scheme between cases with BRCA mutations and those without. As for BRCA mutated pts, TP53 WT were all PS. Among those p53 mutated, GOF mutations were associated with PS in 7 pts and platinum resistance in 3 pts; LOF mutations were associated with PS in 7 pts and platinum resistance in 12 pts. The difference in distribution of PS between functional categories of p53 mutations was significant (p=0.0291). As for BRCA WT pts, TP53 WT were all PS. Among TP53 mutated, GOF mutations were associated with PS in 14 pts and platinum resistance in 10 pts, whereas LOF mutations were associated with PS in 19 pts and platinum resistance in 25 pts, even if these findings were not statistically significant (p=0.2357). Of relevance, in 5 cases where LOF mutations of p53 was associated with null HIC p53 expression, pts were refractory to platinum-based chemotherapy. **Conclusions:** Even if preliminary, our data show that HGS-OC harboring TP53 null mutations are the poorest prognostic subgroup, especially in terms of PS. Further studies are needed to confirm our findings and the role of TP53 mutation as a biomarker of inherent or acquired platinum resistance. Research Sponsor: None.

129 Rapid Oral Abstract Session

PD-1 blockade with camrelizumab after chemoradiotherapy in nasopharyngeal carcinoma. First Author: Jun Ma, Department of Radiation Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China

Background: Approximately 30% of locoregionally advanced nasopharyngeal carcinoma (NPC) experience disease relapse despite definitive chemoradiotherapy. The programmed death-1 (PD-1) blockade camrelizumab has demonstrated considerable value in recurrent/metastatic NPC, while its role in locoregionally advanced NPC is worth exploring. **Methods:** We conducted a randomized, open-label, phase 3 trial to evaluate adjuvant camrelizumab in locoregionally advanced NPC after definitive chemoradiotherapy. Patients with T4N1M0 or T1-4N2-3M0 NPC who have undergone induction chemotherapy and concurrent chemoradiotherapy were randomized in a 1:1 ratio to receive adjuvant camrelizumab (200mg intravenously once every 3 weeks for up to 12 cycles; *Camrelizumab* group) or observation (*Standard-therapy* group). The primary endpoint was event-free survival (freedom from randomization to locoregional recurrence, distant metastasis, or death from any cause). The secondary endpoint included locoregional recurrence-free survival, distant metastasis-free survival, overall survival, safety, and quality of life. **Results:** A total of 226 patients were randomized to the *Camrelizumab* group and 224 to *Standard-therapy* group. At a median follow-up of 37 months, the 3-year event-free survival was 86.9% in the *Camrelizumab* group and 77.4% in the *Standard-therapy* groups (stratified hazard ratio, 0.61; 95% confidence interval [CI], 0.38 to 0.96; P = 0.03). Grade 3 or 4 adverse events were reported in 11.2% patients in the *Camrelizumab* group and 3.2% of those in the *Standard-therapy* group. The most common adverse event of grade 3 or 4 was leukopenia (4.9% and 1.4%, respectively). There was no meaningful deterioration in quality of life associated with the use of adjuvant camrelizumab. **Conclusions:** Adjuvant PD-1 blockade with camrelizumab significantly improved event-free survival, with mild toxicity, highlighting its compelling role in the management of locoregionally advanced NPC. (DIPPER,ClinicalTrials.gov numberNCT03427827). Clinical trial information: NCT03427827. Research Sponsor: None.

3-yr rate (%)	Camrelizumab (n = 226)	Standard therapy (n = 224)	P value
Event-free survival	86.9	77.4	0.03
Distant metastasis-free survival	93.3	86.3	0.032
Locoregional recurrence-free survival	93.7	88.0	0.041
Overall survival	96.3	92.8	0.79
Safety population	**n = 205**	**n = 221**	
Grade 3-4 AEs, n (%)	23 (11.2%)	7 (3.2%)	
Grade 5 AEs, n (%)	1 (<1%)	1(<1%)	

130 Poster Session

Effect of ZCRB1 on the glycolysis via PKM2-HIF1α axis and promotion of immune tolerance in nasopharyngeal carcinoma. First Author: Gengde Hong, Affiliated Cancer Hospital & Institute of Guangzhou Medical University, Guangzhou, Guangdong, China

Background: Nasopharyngeal carcinoma (NPC) is characterized by abundant lymphocyte infiltration. The failure of immune checkpoint inhibitors in NPC may be related to immune tolerance. **Methods:** Bioinformatics analysis was performed to identify the correlation between the *ZCRB1* mRNA level and immune cell infiltration in NPC tissues. Quantitative real time PCR and immunoblotting were used to determine the mRNA and protein expression, respectively. Functional experiments (CCK8, colony formation assay, cell migration assay and tumor xenograft) were used to explore the effect of ZCRB1 on the malignant phenotype in NPC cells. Glucose and lactate measurement assays as well as Seahorse XF glycolysis stress assay, were conducted to investigate the effects of ZCRB1 on glycolysis in NPC cells. RNA sequencing, QPCR and minigene analysis were used to confirm the splicing switch between PKM1 and PKM2. Luciferase assay was performed to detect the transcription activity of HIF1-α. Finally, correlation analysis between the ZCRB1 expression and glycolysis level was performed to in NPC samples. **Results:** The expression of ZCRB1 was negatively correlated with checkpoint-related genes and immune regulation-related gene sets in head and neck cancer. Likewise, in NPC, the expression of ZCRB1 was negatively correlated with lymphocyte infiltration, tumor immune microenvironment score and tumor-infiltrating CD4+ T cells, CD8+ T cells, and dendritic cells. Low expression of ZCRB1 was associated with better prognosis. Functional assays demonstrated that ZCRB1 significantly promoted NPC cells growth, clonogenicity, migratory capacity and glycolysis. Mechanistically, ZCRB1 was mainly involved in the hypoxic signaling pathway. Cells with ZCRB1 downregulation downregulated glycolysis-related genes and significantly reduced the transcriptional activity of HIF-1α. Moreover, minigene assays showed that the intron 9 region spliced by PKM in cells with ZCRB1 downregulation. Finally, bioinformatics analysis showed that the mRNA expression of ZCRB1 was positively correlated with the immune infiltration score significantly during glycolysis. **Conclusions:** ZCRB1 promotes the growth and migration of nasopharyngeal carcinoma cells and is associated with immune tolerance. Further, ZCRB1 accelerates the glycolysis via enhancing the transcriptional activity of HIF-1α through increasing PKM2 isoform splicing, providing a scientific basis for tumor metabolic reprogramming to reshape the immune microenvironment. Research Sponsor: National Natural Science Foundation of China (Grant No. 82372880).

131 Poster Session

Induction chemoimmunotherapy followed by radiotherapy in locally advanced head and neck squamous cell carcinoma: A real-world study. First Author: Yi Yang, Department of Radiation Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, Guangdong, China

Background: Patients with locally advanced head and neck squamous cell cancers (LAHNSCC) present poor prognosis despite multi-disciplinary comprehensive treatment, and novel treatment strategies are urgently needed. Recently, several phase II clinical trials reported encouraging pathological complete response rate of induction chemoimmunotherapy (IC+ICI) in LAHNSCC, suggesting potentially long-term survival benefits. Therefore, we conducted this real-world study to compare the efficacy of IC+ICI followed by radiotherapy (RT) versus induction chemotherapy (IC) followed by RT in LAHNSCC. **Methods:** We retrospectively included patients with LAHNSCC from Sun Yat-sen University Cancer center database treated with IC+ICI followed by RT or IC followed by RT between 1/2018-12/2021. Survival outcomes and adverse effects (AEs) were compared between the two groups. **Results:** A total of 262 patients were included: 128 (48.9%) in the IC+ICI group, and 134 (51.1%) in the IC group. Median age for the whole cohort was 60 (53–66) years, and the male-to-female ratio is 8.9:1. Most patients (84.4%) had stage IV disease. The median follow-up time was 26.7 (IQR 25.8-29.6) months. Marginally significant higher objective response rate (ORR) was observed in the IC+ICI group than that in the IC group (81.25% vs 72.39%, *P*=0.09). Patients in the IC+ICI group had significantly better results than those in the IC group in 2-year overall survival (OS; 88.9% vs. 71.5%, *P*<0.001), disease-free survival (DFS; 77.5% vs. 58.3%, *P*=0.005), locoregional relapse-free survival (LRRFS; 78.4% vs. 59.7%, *P*=0.009) and distant metastasis-free survival (DMFS; 87.5% vs. 64.6%, *P*<0.001). Multivariate analysis confirmed that combining immunotherapy in the induction stage was an independent prognostic factor for OS (HR 0.40, 95%CI 0.19-0.84), DFS (HR 0.45, 95%CI 0.28-0.72), LRRFS (HR 0.56, 95%CI 0.31-0.99), and DMFS (HR 0.37, 95%CI 0.19-0.73). The incidences of G3/4 AEs between the IC+ICI group and the IC group were comparable during the induction stage (6.25% vs 12.69%, P = 0.076) as well as the radiotherapy stage (14.06% vs 14.18%, P = 0.978). **Conclusions:** This study firstly reported that IC+ICI followed by RT was superior to IC followed by RT in long-term survival outcome in LAHNSCC. Research Sponsor: None.

132 Poster Session

Evaluation of prognostic factors for oral tongue squamous cell carcinoma: Significance of intratumoral tumor-infiltrating lymphocytes, lymph node ratio, and depth of invasion. First Author: Jongwon Lee, Korea University Hospital, Seoul, South Korea

Background: Oral tongue squamous cell carcinoma (SCC) is an aggressive malignancy with a variable prognosis. Identifying reliable prognostic factors is crucial for developing personalized treatment strategies and improving patient outcomes. This study examined the prognostic significance of clinicopathological factors in oral tongue SCC. **Methods:** A retrospective cohort study was conducted on 192 patients who underwent surgical resection at Asan Medical Center between 2010 and 2017. Clinicopathological data, including age at diagnosis, American Joint Committee of Cancer (AJCC) 8th edition stages, depth of invasion (DOI), extranodal extension (ENE), intratumoral and stromal (invasive front) tumor-infiltrating lymphocytes (TILs), lymphovascular invasion (LVI), margin status, metastatic-to-examined lymph nodes ratio (LNR), number of metastatic lymph nodes, perineural invasion (PNI), sex, size, tumor budding, tumor differentiation, tumor-to-stromal ratio (TSR), and worst pattern of invasion (WPOI) were analyzed. The total cohort, early-stage group, and late-stage group were analyzed separately. **Results:** Most variables showed significant associations with the survival rate. The multivariate Cox proportional hazard models for the total cohort showed significant results for intratumoral TILs, DOI grade, and LNR. However, other factors failed to show statistical significance. Intratumoral TIL was the only consistently potent factor for survival in all study groups. **Conclusions:** Our findings highlight the need for increased focus on the prognostic significance of intratumoral TILs. The DOI grade and LNR were also powerful prognostic factors, especially in late-stage tongue SCCs. Our data suggest that the prognostic significance of certain variables, such as the WPOI, may have been overestimated in the literature, thereby warranting a reassessment of the currently utilized prognostic markers in oral tongue SCC. Research Sponsor: None.

133 **Poster Session**

The prognostic value of deep learning-based percentage of tumour-infiltrating lymphocytes in nasopharyngeal carcinoma. First Author: Tianzhu Lu, Jiangxi Cancer Hospital, Nanchang, China

Background: To calculate the percentage of tumor-infiltrating lymphocytes (TILs) in nasopharyngeal carcinoma (NPC) using deep-learning (DL) algorithms based on digital pathology images and differentiate the outcome. **Methods:** We recruited 435 patients with primary non-metastatic NPC and 63 patients with de novo metastatic NPC received immunotherapy. TIL_{DL} percentage was calculated using the convolutional neural network model, and its ability to differentiate metastasis risk and independent prognostic value were analyzed using Kaplan–Meier survival and multivariate analyses (MVA). **Results:** The median follow-up time of the training and validation cohorts was 69, and 76 months, respectively. Kaplan–Meier survival analysis showed that the 5-year distant metastasis-free survival (DMFS) and overall survival (OS) of patients with high TIL_{DL} were significantly better than those of patients with low infiltration. MVA showed that TIL_{DL} degree is an independent prognostic factor for DMFS (training cohort: HR=0.197, 95% CI: 0.077-0.503, p=0.001; validation cohort: HR=0.119, 95% CI: 0.028-0.503, p=0.004) and OS (training cohort: HR=0.418, 95% CI: 0.200-0.873, p=0.020; validation cohort: HR=0.158, 95% CI: 0.048-0.520, p=0.002). The concordance index (C-index) of TIL_{DL} was higher than that of the immunohistochemical CD3+, CD8+ T-cell, and CD20+ B-cell densities in terms of the DMFS and OS prediction accuracy. In an immunotherapy cohort of de novo metastatic NPC (n=63), MAV revealed that high TIL_{DL} percentage were an independent prognostic factor for PFS (HR=0.368, p= 0.008). **Conclusions:** TIL_{DL} percentage exhibited discriminative capabilities regarding the risk of metastasis and mortality in non-metastatic NPC, and has potential to be a biomarker for dmNPC received immunotherapy. This model will help select patients with a high risk of metastasis and provides a reference for improved individualized treatment. Research Sponsor: Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences; 2020-PT320-004.

134 **Poster Session**

First implementation of artificial intelligence empowered all-in-one radiotherapy workflow for nasopharyngeal carcinoma. First Author: Guan-Qun Zhou, Department of Radiation Oncology, Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, China

Background: To establish an artificial intelligence (AI)-empowered All-In-One (AIO) workflow for providing one-stop radiotherapy to patients with nasopharyngeal carcinoma (NPC), and evaluate its feasibility and performance. **Methods:** The NPC-specific AIO workflow operates on a CT-integrated linac and integrates AI contouring and AI planning modules. A 3D U-net was employed for contours generation and 3D dose distribution. Knowledge-based planning approach and a protocol-based approach were used for plan optimization. MRI datasets with contours of primary gross tumors, CT datasets with contours of targets and organs at risk, and radiotherapy treatment planning datasets were collected from 877, 139, and 243 patients, respectively, for the training, validation, and testing of AI contouring and planning models. The NPC-specific AIO workflow underwent real-world clinical testing with an end-to-end evaluation involving 120 patients with NPC. The technical characteristics, implementation procedures and performance of AIO workflow were described and evaluated. **Results:** From March 2022 to October 2023, 120 patients with newly-diagnosed, non-metastatic NPC underwent AIO workflow, and 117 patients completed it in a median time of 23.2 min (range: 16.3 to 45.8 min). Median translation motions were 0.2 mm (CT scan to planning approval) and 0.1 mm (during beam delivery). AI-generated contours required little revision for clinical target volume (CTV1) and organs at risk (OARs), minor revision for cervical lymph nodes (GTVn) and clinical target volume (CTV2), with median Dice similarity coefficients (DSCs) of 0.98 and 0.94, respectively; more revision for GTVp, with a median DSC of 0.84. Of the 117 AI-generated plannings, 108 (92.3%) passed after initial auto-optimization. Volumes receiving $\geq$ 100% of the prescribed dose for all planning target volumes was $\geq$ 97.8%. Mean dosimetric parameters met dose constraints for all OARs except the thyroid and submandibulars. One patient died from acute renal failure after 10 fractions of radiotherapy. At week 12 after radiotherapy completion, 115 patients achieved complete response;1 had stable disease. Grade 3-4 acute effects were reported by 54 of 115 patients (36%). **Conclusions:** We successfully established an AI-empowered AIO workflow for initial radiotherapy of NPC, confirming its feasibility and safety for clinical application. Research Sponsor: None.

135 **Poster Session**

Infiltrating B-cell subtypes and associated hub genes in nasopharyngeal carcinoma identified from integrated single-cell and bulk-RNA sequencing data. First Author: Fangyan Zhong, NHC Key Laboratory of Personalized Diagnosis and Treatment for Nasopharyngeal Carcinoma, Jiangxi Cancer Hospital, Nanchang, Jiangxi, China

Background: Nasopharyngeal carcinoma (NPC) is associated with lymphocyte infiltration; however, the majority of research on NPC has focused on the role of T cells, with relatively little known about the roles of B cells and their subtypes. Therefore, we evaluated the prognostic value of CD20+ B cell density and B-cell subtypes along with their functional enrichment and hub genes in NPC. **Methods:** The prognostic value of CD20+ B-cell density for distant metastasis-free survival (DMFS), overall survival (OS), and progression-free survival (PFS) was explored by immunohistochemistry using multivariate analysis. Transcriptomic expression data from Gene Expression Omnibus (GEO) datasets were analyzed to identify B-cell subtypes and their functional enrichment in NPC tissues. Pseudotime trajectory analysis was performed to evaluate the B-cell differentiation trajectory and hub genes were identified using Cytoscape software. **Results:** Patients with NPC exhibiting a high infiltrating density of $CD20^+$ B cells showed significantly better 5-year DMFS, OS, and PFS compared to those of patients with a low infiltrating density. Naïve B cells, switched memory B cells, exhausted B cells, and plasma cells were identified as key B-cell subtypes infiltrating NPC tumors, with naïve B cells showing the highest infiltration levels associated with a better prognosis. Naïve B cells were closely associated with immune pathways and the hub genes were typical markers for T and B cells. **Conclusions:** A high infiltrating density of B cells showed strong prognostic value in patients with NPC. Naïve B cells may play an important role in tumor immunity for NPC. Research Sponsor: Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences; No. 2020-PT320-004.

136 **Poster Session**

Longitudinal tracing of on-treatment plasma Epstein-Barr virus DNA as a biomarker for real-time dynamic risk monitoring in patients with nasopharyngeal carcinoma: The EP-SEASON study. First Author: Ling-Xin Xu, Sun Yat-Sen University Cancer Center, Guangzhou, Guangdong, China

Background: Plasma Epstein-Barr virus (EBV) DNA is a biomarker for nasopharyngeal carcinoma (NPC). However, whether longitudinal on-treatment EBV DNA tracing would inform real-time recurrence risk in NPC remains to be elucidated. To address this issue, we conducted EP-SEASON (NCT03855020), a prospective cohort study of longitudinal on-treatment EBV DNA in EBV-positive NPC patients. **Methods:** Non-metastatic NPC with detectable pretreatment EBV DNA that received standard sequential chemo-radiotherapy were recruited. Serial EBV DNA in blood specimens were collected across pretreatment, 3-week after each induction chemotherapy (IC), every-week during radiotherapy (RT), within 1-week and 1-3 months upon RT completion. EBV DNA extracted from plasma was quantified by a real-time quantitative polymerase chain reaction assay targeting the *Bam*HI-W region of the EBV genome. Longitudinal changing patterns of EBV DNA and their clinical relevance were analyzed. **Results:** Between May 2019 and April 2021, a total of 1000 patients underwent per-protocol EBV DNA assessments and treatment; 248 and 752 patients received concurrent chemoradiotherapy (CCRT, $subcochort_{no\text{-}IC}$) and IC plus CCRT ($subcochort_{IC}$), respectively. Longitudinal changes and clearance rates of EBV DNA displayed unique patterns during IC and RT phases. Throughout IC and RT phases, the rate of EBV DNA clearance decreased with repeated IC cycles; interestingly, the rate re-rose upon the introduction of RT, and then dropped to low levels ($<$10%/week) after the 4^{th} week of RT (post-RT4w). Patients in $subcochort_{no^-IC}$ and $subcochort_{IC}$ also exhibited differential clearance patterns during RT, with the rate of clearance being higher in $subcochort_{no\text{-}IC}$ before the 2^{nd} week of RT (post-RT2w). Notably, despite the prognostic significance of EBV DNA at each timepoint ($P_{all} < 0.05$), longitudinal EBV DNA displayed a linkage changing map with dynamic recurrence risks: 3-year disease-free survival (DFS) rate steadily dropped with delayed EBV DNA clearance during IC; it re-rose at the 2^{nd} RT week upon EBV DNA clearance, followed by a sharp decrease at the 4^{th} RT week in $subcochort_{IC}$. In contrast, 3-year DFS rate continuously decreased with delayed EBV DNA clearance in $subcochort_{no\text{-}IC}$. Finally, we identified different phenotypes of whole-course circulating tumor DNA changing dynamics that showed distinct prognosis ($P < 0.05$). **Conclusions:** Longitudinal on-treatment EBV DNA tracing could forecast real-time risks and facilitate risk-adapted decision-making in NPC. Research Sponsor: Major Research Plan of the National Natural Science Foundation of China; National Postdoctoral Program for Innovative Talents; National Natural Science Foundation of China; Overseas Expertise Introduction Project for Discipline Innovation, 111 Project; Natural Science Foundation of Guangdong Province; Special Funding of China Postdoctoral Science Foundation; Cancer Innovative Research Program of Sun Yat-sen University Cancer Center.

137 Poster Session

Analysis of heterochromatin remodeling as a mechanism of radiotherapy (RT) resistance through molecular profiling of radioresistant (RR) head and neck (HNC) and prostate cancers (PCa). First Author: Evelyn Tan, National Cancer Centre Singapore, Singapore, Singapore

Background: Resistance to RT remains a clinical challenge, given our limited understanding of the molecular pathways underpinning radioresistance. Here, we investigated for mechanisms linked to RR using paired experimental and clinico-molecular HNC and PCa datasets for discovery and validation of novel pathways that may be enriched in RR cancers. **Methods:** For experimental data, we generated RR HNC (FaDu, HK1) and PCa (22Rv1, DU145) cell lines following high-dose X-irradiation (90 Gy in 45 fr). Genotypic characterization of RR and wildtype (WT) cells was performed by genomic and transcriptomic sequencing using WES (100X) and RNAseq (Illumina, CA), respectively, followed by functional characterization by western blot (WB) and immunofluorescence (IF). For clinico-molecular data, we utilized two prospectively recruited RT cohorts, consisting of 311 patients with HNC (n=158) and PCa (n=153). Tumor transcriptomes were profiled using RNAseq and Affymetrix ST array (ThermoFisher, CA), respectively. Comparative analyses of molecular profiles were first performed between RR and WT *in vitro* models to identify dysregulated pathways that were linked to radioresistance, and subsequently tested for association with disease-free survival (DFS) in the clinical cohorts. **Results:** Comparative genomic analyses between RR and WT HNC and PCa models revealed an abundance of acquired mutations in the RR compared with WT models, with a higher mutation count observed in PCa than HNC cells (SNV counts: 2,158 [DU145-RR] and 1,387 [22Rv1-RR] *vs* 396 [FaDu-RR] and 25 [HK1-RR], $P<0.0001$). Mutational signature analyses indicated a common enrichment of DNA mismatch repair-related mutational signatures (SBS3, SBS14, and SBS21) across the RR HNC and PCa models. Transcriptomic profiling revealed an upregulation of the *BAHD1* gene, which is involved in heterochromatin formation, across the 4 RR cell lines, corroborated by an enrichment of heterochromatin-related genesets. These results were consistent with functional characterization of RR versus WT cells by WB and IF indicating increased DNA repair capacity and heterochromatin response post-4 Gy irradiation. We further confirmed the dependency of the RR phenotype on the heterochromatin response with BAHD1 knockdown, resulting in reversal of these cellular responses. Finally, our results were supported by survival analyses indicating an inferior DFS post-RT in patients with HNC and PCa harboring a higher expression of heterochromatin-related geneset (HNC: $HR_{high\ vs\ low}$ 1.51*;* PCa: $HR_{high\ vs\ low}$ 1.37*).* **Conclusions:** Herein, by leveraging on paired experimental and clinico-molecular datasets, we have uncovered a novel BAHD1-dependent heterochromatin response that underpins resistance to RT in HNC and PCa, which may be amendable to systemic agents targeting chromatin remodeling. Research Sponsor: NCCS Cancer Fund; Duke-NUS Oncology Academic Program Goh Foundation Proton Research Program; Kua Hong Pak Head and Neck Cancer Research Program; National Medical Research Council Singapore Clinician Scientist Award.

138 Poster Session

Nivolumab combined with chemoradiotherapy sparing concurrent cisplatin in high-risk locoregionally advanced nasopharyngeal carcinoma (PLATINUM): A multicenter, single-arm, phase II clinical trial. First Author: Cheng Xu, Department of Radiation Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China

Background: Cisplatin-based concurrent chemoradiotherapy has long been regarded as the cornerstone of treatment for patients with locoregionally advanced nasopharyngeal carcinoma (LANPC) over two decades ago. However, the persistent issue of severe acute toxicities (54.0–61.0%) and late sequelae (9.2–11.4%) induced by concurrent cisplatin remains unresolved. **Methods:** In this single-arm, phase II clinical trial (PLATINUM study), patients with high-risk LANPC (T4N1M0 or T1–4N2–3M0) were recruited from 7 hospitals in China to receive intravenous nivolumab (360 mg once every 3 weeks for 3 cycles [Q3W x 3]) + induction chemotherapy (gemcitabine 1000 mg/m^2 + cisplatin 80 mg/m^2, Q3W x 3), followed by nivolumab (360 mg, Q3W x 3) + intensity-modulated radiotherapy (PGTVnx, 70Gy/33fx), and thereafter adjuvant nivolumab (480 mg, Q4W x 6). The primary end point was 3-year failure-free survival (FFS), defined as the time from enrollment to any disease failure or death. Secondary end points were overall survival, safety, and health-related quality-of-life (QoL) assessed by cellphone-based EORTC and FACT questionnaires. This trial was registered with ClinicalTrials.gov (NCT03984357). **Results:** Between April 2020 and October 2020, 152 patients (median [IQR] age, 49 [39–56] years; 18.4% women) were included. After a median follow-up of 43 months (92.6% alive patients $\geq$ 36 months), the 3-year FFS was 88.5% (95% CI, 83.4–93.8%) and the 3-year overall survival was 97.9%. Sixty (40.2%) patients had grade 3–4 acute treatment-related adverse events (trAEs) throughout treatment; 11 (7.2%) were associated with potential immunologic causes, mainly involving skin system (rash, 2.0%; dermatitis, 2.0%). A total of 123 patients completed all required treatment, including 6 cycles of adjuvant nivolumab, with an overall compliance rate of 80.9%. The incidences of grade 3–4 acute trAEs in the induction, radiotherapy, and adjuvant phases were 30.2%, 16.7%, and 6.0%, respectively; compliance rates, 95.4%, 96.5%, and 91.8%, respectively. Eight (5.2%) patients had grade 3–4 late trAEs, eg. hearing impaired (3.3%) and dry mouth (0.7%). No treatment-related death was observed. Patients had consistent worsening changes in general QoL from baseline between the radiotherapy and induction phases, except for the domains of global health status and physical function/well-being, which were more common during the radiotherapy phase. **Conclusions:** Nivolumab incorporated into induction chemotherapy followed by radiotherapy has a promising efficacy and low toxicity for high-risk LANPC patients. A phase 3 randomized clinical trial assessing PD-1 blockade plus this de-intensified radical chemoradiotherapy is underway (NCT04907370). Clinical trial information: NCT03984357. Research Sponsor: Chinese Society of Clinical Oncology-Bristol-Myers Squibb Immuno-Oncology Research Funding; Y-BMS2019-004; Bristol-Myers Squibb Company.

139 Poster Session

Safety, tolerability, and immunogenicity of WGc-043 in subjects with EBV-positive cancers: Results from an investigator-initiated trial. First Author: Xingchen Peng, West China Hospital, Sichuan University, Chengdu, China

Background: The Epstein-Barr virus (EBV) persists and spreads after infection in humans, leading to the occurrence and metastasis of a variety of cancers, posing great challenges in the treatment of cancer.. Conventional cancer therapies tend to have limited success and significant side effects. Therefore, there is an urgent need to develop more safe and efficient treatments such as innovative mRNA vaccines, which provide a new approach to cancer immunotherapy. WGc-043, an mRNA vaccine targeting EBV-positive tumor associated antigens, was evaluated for safety, tolerability, and immunogenicity in a prospective, single-center, investigator-initiated study. **Methods:** The study included 12 patients aged $\geq$18 with EBV-positive recurrent or metastatic nasopharyngeal carcinoma. Eligibility criteria included at least one measurable lesion, ECOG performance status 0-1, expected survival greater than three months, and no autoimmune disease. Participants were divided into three dose cohorts (25 μg, 50 μg, 100 μg) and received five administrations followed by optional continued monthly treatment of WGc-043 by intramuscular injection. The study assessed safety by adverse event monitoring, immune response based on the peripheral blood and tumor tissue sample analysis and efficacy according to imaging guidelines and irRECIST version 1.1. **Results:** The study results demonstrated that WGc-043 had a favorable safety profile with only grade 1 or 2 adverse events and fever (4/12) reported as the most common adverse event. Notably, two patients achieved partial response (PR) and five patients had stable disease (SD), highlighting the potential clinical efficacy of WGc-043. In addition, most (91.7%) subjects showed a significant reduction in plasma EBV DNA levels after administration. Immunogenicity analysis using IFN-γ ELISpot showed that 8 (66.7%) of the 12 enrolled patients developed strong specific immune responses against EBV-associated antigens, indicating that WGc-043 is a potent immunotherapy. **Conclusions:** This exploratory study underscores the safety and potential efficacy of WGc-043 as an mRNA vaccine for EBV-associated cancers, demonstrating its ability to induce specific immune responses and achieve substantial disease control in a challenging patient population, although further studies in larger clinical trials are needed. These results not only support the advancement of WGc-043 as a candidate for immunotherapy in EBV-positive cancers, but also highlight the translational potential of mRNA vaccine technology in the oncology landscape. Clinical trial information: NCT05714748. Research Sponsor: WestGene Biopharma Co., Ltd.

Response Category	Number of Subjects
Partial Response (PR)	2
Stable Disease (SD)	6
Progressive Disease (PD)	4
Total	12
Disease Control Rate (DCR)	66.67%
Objective Response Rate (ORR)	16.67%

140 Poster Session

Analysis of proliferating Treg cells as a predictor for immunotherapy response using systemic longitudinal immune profiling: Biomarker analysis of the phase 3 CONTINUUM trial. First Author: Saiwei Huang, Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, China

Background: The discovery of predictive biomarkers for immunotherapy is hindered by the lack of control groups in most translational studies, making it impossible to discern whether the identified biomarkers are merely prognostic or truly predictive for treatment outcomes. This study reported on prospectively designed biomarker analyses of the phase 3 CONTINNUUM trial (NCT03700476), the first trial that demonstrated prolonged event-free survival (EFS) with the addition of anti-PD-1 (aPD1) to chemoradiotherapy (CRT) in locoregionally-advanced nasopharyngeal carcinoma (LA-NPC). **Methods:** Mass cytometry was performed to generate a dynamic single-cell atlas on longitudinal peripheral blood mononuclear cell (PBMC) samples from 12 pairs of matched patients with or without relapse in the aPD1-CRT arm. The machine-learning algorithm CellCnn was applied to identify a cell subset that was most strongly associated with disease relapse, which was further confirmed by flow cytometry (n = 120). Single-cell RNA sequencing data from matched PBMC and tumor samples were analyzed and multiplex immunohistochemistry was performed on baseline tumor samples (n = 249) to verify the predictive value of the cell subset within tumors. **Results:** Baseline circulating regulatory T cells (Tregs), with a Ki67$^+$ proliferating phenotype, were found to display a higher frequency in LA-NPC patients who developed posttreatment relapse ($P < 0.001$), which was further validated by flow cytometry. The intratumoral Ki67$^+$ Tregs were also identified and correlated with an immunosuppressive tumor microenvironment. In patients with a low baseline level of Ki67$^+$ Tregs, additional aPD1 significantly improved EFS compared with CRT alone (log-rank P = 0.011, HR = 0.22, 95% CI: 0.06−0.79), while EFS was almost identical in both treatment arms in patients with high Ki67$^+$ Treg levels (log-rank P = 0.995, HR = 1.00, 95% CI: 0.49−2.05; interaction P = 0.047). This predictive value was further validated in datasets from two independent randomized trials in renal cancer. **Conclusions:** The frequency of Ki67$^+$ Tregs can serve as a reliable predictive tool in selecting patients who are more likely to benefit from immunotherapy, potentially informing individualized immunotherapy strategies. Research Sponsor: National Natural Science Foundation of China; 82172870, and 81930072; Natural Science Foundation of Guangdong Province; 2019B020230002.

141 **Poster Session**

A randomized, multicenter, phase II trial of camrelizumab (Cam) with and without metastasis-directed therapy (MDT) in recurrent/metastatic nasopharyngeal carcinoma (R/M-NPC). First Author: Xin Zhang, Radiation Oncology Center, Chongqing University Cancer Hospital, Chongqing, China

Background: To investigate the on- and off-target treatment responses of MDT when added to camrelizumab – an anti-programmed cell death 1 antibody in patients with R/M-NPC. **Methods:** We conducted an open-label, randomized, controlled, multicenter, phase II trial in 3 centers from China (NCT04830267). Patients with R/M NPC, without prior exposure to immune checkpoint inhibitors, who presented with ≥2 lesions, and at least 1 measurable lesion were screened and randomized 1:1 to either Cam (200 mg IV 2-weekly) alone or Cam plus MDT (Cam+MDT). Patients randomized to the MDT group must have 1 lesion that is amendable to MDT using stereotactic body radiotherapy (SBRT) prescribed to 27Gy in 3 fractions every other day between the first and second dose of Cam. Primary endpoint was off-target objective response rate (ORR) by RECIST v1.1. Secondary endpoints included on-target ORR, disease control rate (DCR), progression-free (PFS), overall survival (OS), and safety. **Results:** Between March 1, 2021, and August 16, 2023, 39 patients with R/M NPC were randomly assigned to receive either Cam alone (n=20) or Cam+MDT (n=19). 17/39 (44%) patients had oligometastatic disease (≤3 lesions); 18/39 (46%) had liver metastasis. Median duration of Cam was 4.1 mo (95%CI: 2.4-10.9) and 4.7 mo (95% CI: 2.3-11.0) in both treatment groups, respectively. Sites of MDT included lungs (8/19, 42%), followed by liver (4/19, 21%), bones (4/19, 21%), and lymph nodes (3/19, 16%); median SBRT target volume was 5.8 cc (IQR: 2.7-13.5). Off-target ORR did not differ between the treatment groups (26% *vs* 30%, *P*=0.51), although DCR was 74% in the Cam+MDT group compared with 60% in the Cam only group (*P*=0.37, Table). After a median follow up of 25.8 mo, median PFS was 9.3 mo (95% CI:6.2-NR) in the Cam+MDT group and 8.8 mo (95% CI: 3.3-NR) in the Cam group (P=0.75), and median OS was not reached in the Cam+MDT gorup (95% CI: 20-NR) and 13.7 mo (95% CI: 11-NR) in the Cam group. Interestingly, exploratory analyses suggest a longer OS with Cam+MDT for patients with >3 metastatic lesions (*HR* 0.228 [95% CI: 0.067-0.769]), and no liver involvement (*HR* 0.287 [95% CI: 0.068-1.208]). G3 and above adverse events were comparable between the treatment groups (14.3% *vs* 12.5%). **Conclusions:** We did not observe a difference for off-target ORR with the addition of MDT to Cam in patients with R/M-NPC, although DCR was higher with combinatorial treatment due to a higher proportion of stable disease. Interestingly, OS was prolonged with Cam+MDT in a subset of patients with >3 lesions and no liver involvement. Clinical trial information: NCT04830267. Research Sponsor: None.

Disease responses in the intention-to-treat population.

	Off-target			On-target
	Cam(n=20)	Cam+MDT (n=19)	P value	Cam+MDT (n=19)
Best overall response, No.(%)			0.51	
CR	0(0)	0(0)		1(5)
PR	6(30)	5(26)		12(63)
SD	6(30)	9(47)		5(26)
PD	8(40)	5(26)		1(5)
DCR, No.(%)	12(60)	14(74)	0.37	18(95)

142 **Poster Session**

Radiotherapy alone vs radiotherapy with concurrent chemoradiotherapy in patients with low-risk nasopharyngeal carcinoma: Updated results from a multicenter, open-label, non-inferiority, randomized phase III trial. First Author: Rui Guo, Department of Radiation Oncology, Sun Yat-sen University Cancer Center; Collaborative Innovation Center for Cancer Medicine; State Key Laboratory of Oncology in South China; Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangzhou, China

Background: There is limited evidence for the role of concurrent chemotherapy with use of intensity-modulated radiation therapy (IMRT) in low-risk stage II/T3N0 Nasopharyngeal Carcinoma (NPC) patients. We previously reported comparable 3-year failure-free survival-free survival (FFS) using radiotherapy alone compared with concurrent chemoradiotherapy in the low-risk patients. Here, we present the 5-year overall survival (OS) analysis and additional analysis. **Methods:** This multicenter, open-label, randomized, phase 3, noninferiority clinical trial was conducted at 5 Chinese hospitals, including 341 adult patients with low-risk NPC, defined as stage II/T3N0M0 without adverse features (all nodes <3 cm, no level IV/Vb nodes; no extranodal extension; Epstein-Barr virus DNA <4000 copies/mL), with enrollment between November 2015 and August 2020. This trial is registered with ClinicalTrials.gov, number NCT02633202. **Results:** In this randomized trial, patients were assigned to be treated IMRT alone (n=172) or with concurrent chemoradiotherapy (IMRT with cisplatin, n=169). With a median follow-up of 70.1 months, the IMRT-alone group had a similar 5-year overall survival (95.2% vs. 98.2%, hazard ratio, 2.27 [95%CI:0.70-7.40]; *P*=0.16), failure-free survival (86.2% *vs*. 88.4%, hazard ratio, 1.16 [95%CI:0.64-2.07]; p = 0.63). Hearing impairment (HI) data (assessed by The Hearing Handicap Inventory for Adult- Screening version (HHIA-S)) were collected from 86 patients in the IMRT-alone group and 81 patients in the concurrent chemoradiotherapy group. Among the patients, 45(26.9%) developed HI (IMRT-alone vs. CCRT: 20 [23.3%] vs. 25 [30.9%]), among which 36 (21.6%) had mind HI (IMRT-alone vs. CCRT: 15 [17.4%] vs. 21 [25.9%]). **Conclusions:** Radiotherapy alone provides comparable survival or disease control and less toxicity compared to CCRT in low-risk nasopharyngeal carcinoma. Clinical trial information: NCT02633202. Research Sponsor: the National Natural Science Foundation of China; 81930072; the National Natural Science Foundation of China; 82172870; the National Natural Science Foundation of China; 82172668; Natural Science Foundation of Guangdong Province; 2017A030312003; Key-Area Research and Development Program of Guangdong Province; 2019B020230002; Overseas Expertise Introduction Project for Discipline Innovation; 111 Project, B14035; Sun Yat-Sen University Clinical Research 5010 Program; 2016011; the National Key Research and Development Program of China; 2022YFC2505800.

143 **Poster Session**

HYPCON trial: A phase II randomized study evaluating hypofractionated versus conventional adjuvant radiation therapy in head and neck malignancies. First Author: Adrija Ghosh Jr., Radiation Oncology NCI-AIIMS, AIIMS New Delhi, New Delhi, India

Background: Hypofractionated RT has been established as standard of care at many cancer sites but there is limited data on use of hypofractionated RT for head and neck carcinomas (HNC). The HYPCON trial (CTRI/2023/02/049804) tested to reduce 10 fractions of PORT by delivery of hypofractionated PORT. **Methods:** Patients of HNC after radical surgery, with intermediate risk factors, were randomized based on site, T and N stage to either standard fractionation arm A (60Gy/30 fractions/6 weeks) or hypofractionated arm B (50Gy/20 fractions/4 weeks) in a 1:2 manner. The minimum sample size for the study was estimated based on a non-inferiority trial design as 120 considering a 10% clinical effectiveness margin and 5% attrition. Treatment allocation was done based on T stage, N stage & HNC subsite. Target delineation included tumour bed with adequate margins (CTV_P) and microscopic lymph nodal (CTV_N) basin at risk. Organ delineation included all DARS. A double arc swallowing-sparing IMRT was used in both arms. The primary endpoint was locoregional control (LRC) at 1 year. Compliance, RT time (RTT), overall treatment time (OTT), progression-free survival (PFS) and overall survival (OS) were calculated in all patients. Acute & late toxicities were recorded as per RTOG scale. **Results:** 135 patients were enrolled, 45 in Arm A & 90 in Arm B. Majority of patients (96.9%) had oral cavity primary. Most of patients 74.8 % had early-stage disease. Compliance to PORT was 91.1% in Arm A versus 100% in Arm B. Median RTT for Arm A was 43 days (25-73 days) and 28 days (25-43 days) for Arm B (p<0.0001). Median OTT in Arm A was 91 days (70-126 days) and 77 days (57-119 days) in Arm B (p<0.0001). Median follow-up was 12.7 (2.73-23.87) months. One year, LRC was 72.9% vs 91.6% (p=0.007); PFS was 70.6% vs 90.5% (p=0.009) and OS was 88.7% vs 94.5% (p 0.02) Arm A versus Arm B respectively. Grade 3 or higher acute toxicity was seen in 39% in Arm A and 31.1% in Arm B (p=0.374). Grade 3 or higher late toxicity events were noted in 29.2% and 32.2% in arms A and B respectively (p= 0.671). **Conclusions:** Hypofractionated PORT reduced RTT & OTT and was associated with improved treatment compliance, treatment outcomes (LRC, PFS, OS), and similar acute and late toxicity profile. This is the first study to demonstrate the superiority of hypofractionated compared to conventional PORT delivery for HNC. Clinical trial information: CTRI/2023/02/049804. Research Sponsor: None.

145 **Poster Session**

Effect of tumor-immune microenvironment (TIME) on disparate ascending (A) and descending (D) subtypes of nasopharyngeal carcinoma (NPC). First Author: Eugenia Li Ling Yeo, National Cancer Centre Singapore, Singapore, Singapore

Background: Endemic NPC is invariably linked to Epstein-Barr virus infection, and often presents as locoregionally-advanced (LA-) disease. Nonetheless, it is acknowledged that LA-NPC is clinically heterogeneous, with disparate clinical presentations of ascending (A) and descending (D) subtypes that are characterized by T3-4N0-1 and T1-2N2-3 disease, respectively. Here, we investigated the TIME between these distinct NPC phenotypes using whole transcriptome sequencing and digital pathology. **Methods:** We utilized a cohort of 111 patients with NPC from 2 institutions – NCCS (n=68) and JXCH (n=43) as test and validation datasets, respectively. Whole transcriptome profiling using RNAseq (Illumina, CA) was performed in the NCCS cohort, while spatial analyses of hematoxylin and eosin-stained whole slide images (WSIs) were undertaken in the NCCS cohort (35 A- and 33 D-subtypes), and validated in the JXCH cohort (26 A- and 17 D-subtypes). A customized pipeline was developed to analyze the spatial relationships between tumor-rich and immune-rich regions (tiles) within the WSIs. Mean distances between each tumor-rich and its nearest immune-rich tiles were computed for each WSI. Highest and lowest quartiles of the mean distances in the test cohort were used as thresholds to classify NPC tumors into 3 immune classes of differing immune cell density. **Results:** Transcriptomic profiling revealed an enrichment of immune-related genesets and differentially expressed genes in D- relative to A-subtype tumors. This corresponded to observations of higher overall immune, T and B cell scores in D- than A-subtypes by deconvolution analyses (ESTIMATE and CIBERSORT). Through spatial analyses of our WSIs, we defined three immune classes – immune-dense, -sparse, and -desert, which corresponded to mean distances of <88 μm, 88-208 μm, and >208 μm between tumour- to immune-rich tiles, respectively. D-subtype NPC had significantly more immune-rich regions compared with A-subtypes in both NCCS and JXCH cohorts (*P*=0.02 [NCCS]; *P*=0.01 [JXCH]). This corresponded to shorter median distances between tumor-rich to immune-rich tiles in D- than A-subtypes (103 μm vs 200 μm, *P*=0.01 [NCCS]; 123 μm *vs*250 μm, *P*=0.01 [JXCH]). Based on our novel spatial-based classification, we observed a higher proportion of immune dense tumors in D- than A-subtypes in the NCCS cohort, with only 3/33 (9%) D-subtypes being classified as immune desert. Using the same distance thresholds, we derived a consistent trend in the JXCH cohort, where a higher proportion of D-subtypes were classified as immune dense and sparse than A-subtypes (59% *vs* 31%, P=0.01). **Conclusions:** Our results support a model where the TIME delineates the biology underpinning the disparate clinical presentations of distinct A- and D-subtypes of LA-NPC. Research Sponsor: National Medical Research Council; NCCS Cancer Fund; Goh Cheng Liang Proton Therapy Research Fund; Kua Hong Pak Head and Neck Cancer Research Fund.

146 Poster Session

Hypomagnesemia as a predictor of the efficacy of combination EGFR-targeted drugs versus EGFR ADCs alone in HNSCC. First Author: Siqing Jiang, Hunan Cancer Hospital, Changsha, China

Background: EGFR-targeted drugs and ADCs in combination with EGFR-conjugated chemotherapy drugs can both cause hypomagnesemia. However, the predictive value of hypomagnesemia in response to treatment for head and neck squamous cell carcinoma (HNSCC) is unclear. **Methods:** This study retrospectively analyzed patients who participated in clinical trials of EGFR-targeted drugs and EGFR ADCs for HNSCC and solid tumors, from February 24, 2022, to March 25, 2024. The primary endpoint of the study was time to treatment failure (TTF). **Results:** This study conducted a retrospective analysis of 68 patients . All patients exhibited normal baseline serum magnesium levels prior to treatment, but following two cycles of treatment, varying degrees of hypomagnesemia were observed among them. Among the 46 patients who received 2 cycles of combination therapy with EGFR-targeted drugs, 33 were hypomagnesemia and 13 were normal serum magnesium, ORR [90.9%vs. 8.5%,(P=0.002)] (Table), TTF [151 days (95% CI: 212-380) vs. 87 days (95% CI: 52-230), HR 0.576 (95% CI: 0.270–1.230,P = 0.021)]. Among the 22 patients who received EGFR ADC alone for 2 cycles, 8 were hypomagnesemia and 14 were normal serum magnesium, ORR [37.5% vs.28.6%, (P=0.549)] (Table), TTF [97.5 days (95% CI: 68-300) vs. 108.5 days (95% CI: 60-160), HR of 0.877 (95% CI: 0.339–2.263; P = 0.547)]. **Conclusions:** The study demonstrates that, the occurrence of hypomagnesemia is associated with ORR and TTF following two cycles of combination of EFGR-targeted drugs, not observed in patients receiving EGFR ADCs as monotherapy in HNSCC. Research Sponsor: None.

Evaluation of efficacy compared with serum magnesium levels after 2 cycles of treatment in patients treated with combination EGF-targeted drugs and EGF ADCs alone.

Combination of EFGR-targeted drugs (n=46)

Efficacy evaluation after 2 cycles of treatment	Without hypomagn esemia (n=13) Grade 0	With hypomagnesemia (n=33) Grade 1 (≧0.5 mmol/L)	Grade 2 (0.5~0.4 mmol/l)	Grade 3 (0.4~0.3 mmol/l)	Grade 4 (<0.3 mmol/l)	*P* value
CR	0	0	0	0	0	
PR	5 (38.5%)	26 (78.8%)	4 (12.1%)	0	0	
SD	4 (30.8%)	3 (9.1%)	0	0	0	
PD	4 (30.8%)	0	0	0	0	
ORR	5 (38.5%)	30 (90.9%)				0.002

EGFR ADC drugs alone (n=22)

Efficacy evaluation after 2 cycles of treatment	Without hypomagn Esemia (n=14) Grade 0	With hypomagnesemia (n=8) Grade 1 (≧0.5 mmol/L)	Grade 2 (0.5~0.4 mmol/l)	Grade 3 (0.4~0.3mmo/l)	Grade 4 (<0.3 mmol/l)	*P* value
CR	0	0	0	0	0	
PR	4 (28.6%)	3 (37.5%)	0	0	0	
SD	6 (42.9%)	1 (12.5%)	0	0	0	
PD	4 (28.6)	3 (37.5%)	1 (12.5%)	0	0	
ORR	4 (28.6%)	3 (37.5%)				0.549

147 Poster Session

Impact of acute therapeutic toxicities on anxiety during radiotherapy among Chinese patients with newly diagnosed nonmetastatic head and neck cancer: A cross-sectional study. First Author: Fengyan Li, Department of Radiation Oncology, Sun Yat-sen University Cancer Center; State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine; Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangzhou, Guangdong, China

Background: Head and neck cancer (HNC) poses a significant threat to both psychological and physical health. This study aimed to depict the anxiety status of Chinese newly diagnosed nonmetastatic HNC patients during radiotherapy (RT) and to examine predictors of anxiety symptoms. **Methods:** Newly diagnosed nonmetastatic HNC patients who received RT at the Radiation Therapy Center of Sun Yat-sen University Cancer Center from August 23,2023 to August 24,2023 were recruited into this study. Using Zung Self-Rating Anxiety Scale (Zung SAS) to screen anxiety. Twenty-four common acute therapeutic toxicities (18 patient-reported and 6 clinician-rated) were assessed according to European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck 35 (EORTC QLQ-HN35) and Common Terminology Criteria for Adverse Events, fifth version (CTCAE V5.0). Chi-square (χ^2) test and multivariate binary logistic regression stepwise forward selection: likelihood ratio (LR) method were applied to identify factors associated with anxiety. **Results:** A total of 457 patients were included ultimately. Up to 29.10% of the patients showed varying degrees of anxiety and the average SAS standardized score was 45.66 $\pm$ 8.83. Chi-square test manifested that sex, annual household income, fatigue, anorexia, nausea, vomit, pain, dysphagia, sense problems (smell and taste), speech problems, trouble in social eating, trouble in social contact, sexual frustration, teeth problems, difficulty in opening mouth, xerostomia, sticky saliva, coughing, feeling ill, use of analgesics, use of nutritional supplements and weight loss were related to anxiety ($p < 0.05$). But multivariate logistic regression only demonstrated fatigue (OR = 3.696, 95% CI = 2.096-6.519), speech problems (OR = 3.247, 95% CI = 1.554-6.783), sexual frustration (OR = 2.029, 95% CI = 1.232-3.341), nausea (OR = 3.075, 95% CI = 1.807-5.234), feeling ill (OR = 2.283, 95% CI = 1.215-4.291), use of nutritional supplements (OR = 1.930, 95% CI = 1.136-3.280) and difficulty in opening mouth (OR = 3.007, 95% CI = 1.081-8.363) as independent predictive factors of anxiety. **Conclusions:** The Chinese newly diagnosed nonmetastatic HNC patients suffered greatly from anxiety during RT. This study identified the predictive contribution of sociodemographic and clinical characteristics and 24 common acute therapeutic toxicities to the vulnerability to anxiety, which can provide evidence and reference for medical staff to carry out psychological intervention. Research Sponsor: Basic and Applied Basic Research Foundation of Guangdong Province; 2024A1515030248; National Natural Science Foundation of China; 92259202; Cancer Innovative Research Program of Sun Yat-sen University Cancer Center; CIRP-SYSUCC-0010.

TPS148 Trials in Progress Poster Session

Enfortumab vedotin and pembrolizumab as first-line treatment in recurrent or metastatic head and neck squamous cell carcinoma: A cohort of the EV-202 trial. First Author: Yoshitaka Honma, Department of Head and Neck, Esophageal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan

Background: Novel treatment strategies are needed to treat recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) given the poor durability of response and prognosis with standard therapy. In KEYNOTE-048, among patients with R/M HNSCC and PD-L1 combined positive score (CPS) $\geq$1, first-line (1L) treatment with pembrolizumab demonstrated a median overall survival (OS) of 12.3 months. Nectin-4 is widely expressed in a variety of solid tumors, including bladder cancers and HNSCC. Enfortumab vedotin (EV) is a Nectin-4–directed antibody–drug conjugate approved for use in previously treated (EV monotherapy) or 1L (EV + pembrolizumab) locally advanced or metastatic urothelial carcinoma (la/mUC). EV + pembrolizumab showed superior OS and progression-free survival (PFS) vs chemotherapy in 1L la/mUC. EV-202 is a multicenter, open-label, phase 2 study (NCT04225117) evaluating the efficacy and safety of EV in multiple tumor-specific cohorts. In the previously treated R/M head and neck cancer cohort, 11 of 46 patients (23.9%) had a confirmed objective response with EV monotherapy; median PFS was 3.9 months (Swiecicki P, et al. ASCO 2023. Poster #6017). We hypothesize that EV + pembrolizumab may demonstrate benefit as a 1L therapy in patients with R/M HNSCC and CPS $\geq$1. **Methods:** Patients in the R/M HNSCC cohort of EV-202 have histologically or cytologically confirmed HNSCC, an ECOG performance status 0 or 1, no prior systemic therapy administered in the R/M setting (with the exception of systemic therapy completed >6 months prior if given as part of treatment for locally advanced disease), and CPS $\geq$1. A total of 40 patients are expected to be enrolled. An interim analysis will be conducted when 20 patients are evaluable for tumor response; 5 responders will be needed to proceed. Of 40 total patients, 14 must demonstrate response to claim promising antitumor activity. Patients will receive EV 1.25 mg/kg intravenously on days 1 and 8 and 200 mg of pembrolizumab intravenously on day 1 of each 21-day cycle until discontinuation, for reasons including disease progression or toxicity. Disease assessments will be performed 9 weeks from the first dose and every 6 weeks thereafter until disease progression, start of subsequent anticancer therapy, death, consent withdrawal, loss to follow-up, or study end, whichever occurs first. The primary endpoint is investigator-assessed, confirmed ORR per RECIST v1.1. Secondary endpoints include investigator-assessed duration of response, disease control rate, PFS, OS, and safety/tolerability. Analyses will also be evaluated per iRECIST. Exploratory analyses will include pharmacokinetics, immunogenicity, quality of life, and assessment of biomarkers that may correlate with treatment outcome, including Nectin-4 expression. Recruitment for this cohort began in November 2023 and is ongoing. Clinical trial information: NCT04225117. Research Sponsor: Astellas, Inc. and Seagen, which was acquired by Pfizer in Dec. 2023.

TPS149 Trials in Progress Poster Session

Acute radiation morbidities and dosimetric evaluation of DARS structures: Results from the phase III randomized SWOAR trial. First Author: Aman Sharma, All India Institute of Medical Sciences (AIIMS), New Delhi, India

Background: The SWOAR is a phase III trial (ClinicalTrials.gov ID NCT05187091) evaluating sparing of dysphagia/aspiration related structures (DARS) & submandibular gland by IMRT. **Methods:** Patients with T1-4, N0-3, M0 of oropharynx, larynx and hypopharynx treated with radical RT were randomized to arm A (standard IMRT) or arm B (DARS IMRT) in 1:1 manner. Treatment allocation was done based on T stage, concurrent chemotherapy use (weekly 40mg/m^2) & subsite. A10-point improvement in MD Anderson Dysphagia Inventory (MDADI) composite score (primary end point of study) at 6 months post RT with SD of 17, power as 90% and two-sided alpha of 5% estimated sample size. SIB IMRT delivered dose of 66Gy (gross disease+0.5cm), 54Gy (gross disease+1cms+regional lymphatics) in 30 fractions. Acute radiation morbidities were scored by RTOG scoring criteria. Aspiration prevention assessment was done by PAS measured by FEES. **Results:** A total of 166 patients till date have been enrolled, 81 in Arm A & 85 in Arm B. Median age was 58 years, 73.4% had oropharyngeal primary, 89% had stage III-IV & received concurrent chemotherapy. Median composite MDADI scores pre-RT in Arm A was 70.5 (IQR 56.8-75.8) & 69.5 (56.8-75.8) in arm B. Post-RT median score dropped to 54.2 (48.8-60) in arm A & 54.8 (51.6-65.3) in arm B. Reduction in MDADI score pre & post RT in arm A was median 11.1 (0-21) & arm B was 7.9 (0-20) (p=0.28). Pre RT-PAS score was similar in both arms 1 (IOR 1-2), post-RT PAS in arm A was 1 (1-2) & arm B was 1 (1-1). Median of mean dose to SCM was 56.2Gy (46.8Gy-61.2Gy) vs 48.9Gy (36Gy-57.6Gy) p<0.003, MCM 58.5Gy (52.7Gy-63.1Gy) vs 56.2Gy (47.8-63.6) p=0.11, ICM 48.5Gy (46.8Gy-57.7Gy) vs 37.8Gy (26.5-62.4) p<0.001, base of tongue 60.5Gy (53.9Gy-64.3Gy) vs 53.9Gy (40.2Gy-62.4Gy) p=0.001,supraglottic larynx 57.7Gy (49.2Gy-64.4Gy) vs 60.5Gy (46.7-64.6) p=0.63, larynx 46.0Gy(42.4Gy-53.7Gy) vs 28.3Gy (21.5Gy-49Gy) p<0.001, cricopharyngeus 46.0Gy(43.6Gy-49.9Gy) vs 32.6Gy (27.3Gy-47Gy) p<0.001, esophageal inlet 44.6Gy (41.3Gy-47.9Gy) vs 27.2Gy (22.8Gy-39.1Gy) p<0.001, contralateral submandibular gland 52.8Gy (48.5Gy-57.2Gy) vs 40.4Gy (37.3-49.6) p<0.001, all arm A vs arm B respectively. Acute grade 3 occurred in 68.4% in arm A & 54.4% arm B, p=0.07. Acute grade 3 mucositis developed in 34.2% in arm A vs 16.7% arm B, p=0.009. **Conclusions:** Swallowing-sparing IMRT significantly reduced dose to contralateral submandibular gland & all the DARS structures (except middle constrictor muscle & supra glottic larynx). Dosimetric advantage gained by delivery of Swallowing-sparing IMRT resulted in significant reduction in development of acute grade III mucositis & showed a trend towards reduction in all acute grade III toxicities. Clinical trial information: NCT05187091. Research Sponsor: None.

150 Poster Session

In-training and private physicians' knowledge, attitudes, practices and perceived barriers on the utilization of low dose chest CT scan as lung cancer screening for high-risk patients in a tertiary hospital: Single center experience. First Author: Jesilyn Palec, Saint Gabriel Medical Center, Kalibo, Aklan, Philippines

Background: Lung cancer is the leading cause of cancer-related deaths worldwide. Aside from smoking cessation efforts and guidelines from all proficient panels, utilizing Low dose CT scan (LDCT) of the chest as lung cancer screening (LCS) has been poorly adopted. **Methods:** This was conducted after institutional review board approval. The respondents were handed hard copy or electronic consent forms and survey questionnaire depending on the platform of their choice. **Results:** Majority of the respondents were in-training female physicians with median age of 31 years old who specialized in Internal Medicine practicing between 1-5 years who catered to more than 10 patients per week in outpatient clinics. Nearly half of the respondents answered that the recommended frequency for lung cancer screening (LCS) for high-risk individuals is done bi-annually. Majority agreed that lung cancer screening is effective in decreasing lung cancer mortality and morbidity. Most respondents have initiated discussion about the risks and benefits of low dose chest CT scan (LDCT) as lung cancer screening among eligible high-risk patients. However, most of the respondents disagreed that lung cancer screening is cost effective. The top three perceived barriers on the utilization of Low dose chest CT scan as lung cancer screening reported in descending order revealed that it is not cost-effective, some forgets to screen patients and lung cancer screening has the potential to cause mental anguish or anxiety to patients. **Conclusions:** This study recommends conducting further studies exploring the socio-economic burden and impact assessment of lung cancer in the Philippines to enable translation of more meaningful strategies for local and national lung cancer screening access, health policies and financing. Promoting continuous lung cancer screening forums, lectures and information dissemination of annual LDCT of the chest among high risk patients will encourage and strengthen interdepartmental and multidisciplinary referral and collaboration in increasing earlier detection of lung cancer and decreasing related morbidity and mortality. Research Sponsor: None.

151 Poster Session

Disparities in self-reported pain control among cancer survivors. First Author: Marco Santos Teles, Rutgers New Jersey Medical School, Newark, NJ

Background: Cancer survivors often suffer from chronic pain. However, not all patients have access to medication and other pain management strategies, making pain control challenging. We aim to determine the association of sociodemographic factors with self-reported pain control in cancer survivors with cancer-related chronic pain. **Methods:** A cross-sectional analysis was conducted using data from the 2022 Behavioral Risk Factor Surveillance System survey. Cancer survivors who self-reported physical pain from cancer or treatment were included. Non-melanoma skin cancer survivors were excluded. The outcome of interest was pain control. Univariate analysis with chi-square and multivariable logistic regression were used to determine the sociodemographic characteristics associated with pain control. Models were adjusted for age, sex, marital status, income, insurance coverage, BMI, smoking status, and cancer site. **Results:** 1,670 cancer survivors with self-reported cancer-related chronic pain were identified. 9.2% were aged $<$ 40, 61.5% were female, and 71.6% were non-Hispanic white. 97.2% were insured, 50.5% earned $\geq$ \$50,000, and 27.6% were college graduates. 29.8% of survivors reported a history of breast cancer, followed by melanoma (6.3%), and lung cancer (6.1%). Young adults (age 18-39) reported significantly lower pain control compared to older survivors (52% vs. 77.7%, p $<$0.001). Non-Hispanic Black survivors reported the highest rates of pain control, followed by non-Hispanic white, and Hispanic survivors (87.7% vs. 77.5% vs. 60.6%, respectively, p= 0.013). Employed survivors reported significantly higher pain control than those out of the workforce (83.2% vs. 73.7%, p= 0.008, respectively). College graduates reported better pain control than those without a college degree (82.9% vs. 74.7%, p=0.009, respectively). There was no significant association between pain control and insurance coverage or income. On multivariate analysis, young adults had lower pain control than older adults (OR: 0.454; 95% CI: 0.219-0.942). Compared to non-Hispanic white survivors, being Hispanic was associated with worse pain control (OR: 0.324; 95% CI: 0.142-0.737); no significant association was found for non-Hispanic Black survivors (OR: 1.964; 95% CI: 0.851-4.631). Employment was associated with better pain control (OR: 1.997; 95% CI: 1.235-3.231). College degree attainment was not significantly associated with pain control on multivariate analysis (OR: 1.414; 95% CI: 0.934-2.142). **Conclusions:** Age, race/ethnicity and employment were associated with pain control among cancer survivors. Young adults, Hispanic and unemployed survivors were most likely to have poor pain control. Further research should elucidate the factors driving these relationships in order to achieve more equitable pain management in this population. Research Sponsor: None.

152 Poster Session

Health disparity viewed from public historic cancer mortality data in the US: Advocacy for gastrointestinal cancers, for tailored prevention measures, and for inter-agency population data harmonization. First Author: Tingting Zhang, HEAR2CARE.ORG, Spokane, WA

Background: We searched public datasets released by CDC to answer the question "Can we have a bird's-eye view of health disparity in cancer care in the US?" By looking into historic data, we hope to identify not only health disparity reflected by the different cancer mortality rates for major cancer types, but also signs of missing data. **Methods:** We analyzed 2016-2020 US Cancer Statistics (USCS) cancer burden data to assess cancer disparity as reflected by rates of death in different races or ethnicities. Since the 2022 AACR report on cancer in Asian Americans raised concerns, we then looked into the "Single Race 15" grouping for the underlying cause-of-death data in WONDER@CDC to count liver cancer deaths (ICD10: C22) 2018-2021 among 6 Asian minority groups with population data from 2021 Census ACS data. 2020 GLOBOCAN estimated liver cancer mortality data were also compared. With anecdotal stories suggesting immigrants may seek end-of-life care in the birth country to access culture-concordant services, we looked into how cancer deaths abroad was reported. **Results:** Gastrointestinal (GI) cancers emerged as an area of cancer health disparity from USCS data. 5 GI cancers (colon and rectum, pancreas, liver and bile duct, stomach, and esophagus) contributed to 1/4 of US cancer deaths, and cancers in the pancreas, liver and bile duct, and esophagus still have poor outcomes. Black non-hispanic Americans are more likely to die from cancers of colon/rectum or pancreas. All minority races or ethnicities are more likely to die from cancers in liver and bile duct, or stomach than white non-Hispanic Americans. Cancers in colon and rectum, liver and bile duct, or stomach also cause high numbers of death in US under-50 population. Liver cancer mortality of US East Asian alone groups shown in the table were lower than GLOBOCAN estimated ASR of 16.1, with the greatest discrepancy in the Chinese (9.1 vs 17.2). Difference between the Vietnamese and Asian Indians may reflect that liver cancer is #1 cause of death in Vietnam, or HepB infection is low in India. Census data excluded expat US citizens, and consulate reports of death abroad have neither cause of death nor race/ethnicity data. **Conclusions:** We identified gastrointestinal cancers as a focus for cancer health disparity advocacy. Divergent risks for liver cancer in Asian Americans call for tailored prevention measures. Cross-agency death abroad data harmonisation to include race/ethnicity information will complete views of cancer mortality data in US. Research Sponsor: None.

Liver cancer mortality in Asian groups.

	# of Death 2018-2021	Population in 2021	Crude Death Rate (CDR)	Male CDR	Female CDR
Asian Indian	495	4.4 mil	2.8	3.7	1.9
Chinese	1581	4.36 mil	9.1	12.8	5.8
Filipino	1003	2.96 mil	8.5	11.1	6.4
Vietnamese	1273	1.9 mil	16.8	26.8	7.8
Korean	738	1.45 mil	12.8	17.0	9.3
Japanese	426	743 k	14.3	16.9	12.4

CDR (Per 100k).

153 Poster Session

The challenge of colorectal cancer (CRC) screening in low and middle-income countries (LMIC): Acceptance, knowledge, and preferences in Brazil. First Author: Victor Filogonio, Federal University of Pelotas, Pelotas, Brazil

Background: Presenting an increasing incidence and high mortality rates, CRC is a challenge that many LMIC face and struggle to establish an effective screening strategy. Brazil is one of the few Latin American countries and LMIC that have a population-based CRC screening program, targeting ages 50-74 and performing a fecal occult blood test (FT) every 2 years and colonoscopy/sigmoidoscopy as a confirmatory test. **Methods:** We conducted a survey in patients visiting the primary care unit in the months of January and March 2024 in three distinct settings (Rural, Suburban, and Urban) aiming to estimate acceptance, knowledge, and preferences regarding FT and colonoscopy. Patients aged 50-74 were invited to join this study, excluding those with a history of CRC, and we used the integrated digital charting platform to set demographic variables. At the end of the survey, participants were invited to undergo CRC screening. Those who refuse to screen would select the main reason. **Results:** A total of 1,031 individuals responded the survey, which 52% were females and the median age was 62 years. A total of 763 (74%) accepted to undergo CRC screening with an overall preference for FT (72%) compared to colonoscopy (53,5%). FT acceptance remained somewhat constant in both gender subgroups (70-75%), and a lower colonoscopy acceptance in the male subgroup (46%). In the subdivided geographic setting groups, the rural population (12%) had the lowest knowledge score and the lowest overall acceptance rate (65%), ranking "No symptoms" as the main reason for not screening. The suburban and urban subgroups showed an equivalent overall acceptance rate (74-75%), ranking "Busy schedule" and "Healthy lifestyle" as the main reasons for not screening. **Conclusions:** Data suggests that an effective CRC screening depends on multiple factors. While literature sustains the weight of cost and long waiting times, this study contributes adding a new, more granular perspective. Efforts in patient education, and clarification of misconceptions and anxieties could prove to be an important step in the right direction. A closer contact between patient and healthcare provider could make the difference between screening or not. A leave of absence or mailed FT might be of great benefit for those with a busy schedule, while interaction with CRC survivors seems to drastically increase colonoscopy acceptance, an important intervention that should be encouraged and widespread. Although this study has its limitations due to sample size and geographic characteristics, it lays down a new layer in understanding the individuals and planning actions to prevent the advance of CRC in LMIC. Research Sponsor: None.

154 **Poster Session**

Opioid access barriers for cancer pain relief in Vietnam: A qualitative study. First Author: Trang Nguyen, University Medical Center Ho Chi Minh City, Ho Chi Minh, Viet Nam

Background: Although the World Health Organization designates opioids as an essential medication and recommends them as the cornerstone for managing moderate to severe cancer pain, their accessibility is severely restricted, particularly in low and middle-income countries. Despite Vietnam's early endeavors in the advancement of palliative care, including a revised opioid prescription policy in 2008, opioid use for cancer pain remains suboptimal, with oral morphine available only in a few major hospitals. To inform comprehensive strategies for improving opioid access, this study aims to explore the views of healthcare providers, regulators, cancer patients, and caregivers in Vietnam on the barriers to safely accessing opioids for cancer pain management. **Methods:** We conducted a qualitative, descriptive study and recruited five healthcare providers, six cancer patients and caregivers, and six regulators (i.e., policymakers in the Ministry of Health, heads or deputy heads of pharmacy, oncology, or palliative care departments) across Vietnam via purposeful sampling technique. Data were collected using semi-structured interviews, and the audio recordings were transcribed verbatim and subjected to inductive content analysis using a Framework Method. **Results:** Five categories of barriers were identified: 1) Patient-related barriers (fear of addiction and other side effects, morphine's association with impending death, negative administration experiences, religious beliefs); 2) Professional-related barriers (knowledge and experience deficit, fear of addiction and other side effects, concerns about opioid diversion and associated liabilities, lack of guidance, education, and training); 3) Medicine-related barriers (limited oral morphine availability, limited domestic pharmaceutical manufacturers and suppliers, supply interruptions, poor variety of opioid types and formulations, difficulties accessing parenteral opioids); 4) Services delivery barriers (scarce palliative and home care services); 5) Regulatory barriers (lack of information on opioid distribution channels, difficulties obtaining confirmation letters for patients' opioid usage needs, overly strict regulation enforcement). **Conclusions:** Barriers to opioid access for cancer pain control in Vietnam are multifactorial and mutually reinforcing, necessitating interdisciplinary solutions to overcome them. This approach should involve enhancing education about the appropriate use and management of opioids, along with current opioid policies for patients, communities, healthcare providers, and regulators; enacting and implementing policies mandating oral morphine availability at local health facilities; expanding palliative care services; utilizing telemedicine; and establishing an electronic opioid prescription monitoring system. Research Sponsor: Research Advancement Consortium in Health, Vietnam.

156 **Poster Session**

Resolving disparities in access to cancer care in LMIC-positive learning using a 10-year-old model. First Author: Dinesh Pendharkar, Sarvodaya Cancer Institute, Faridabad, India

Background: Despite significant advances in cancer diagnosis and treatment, there are wide disparities in access to cancer care, more so in low- and middle-income countries. The problem is multifactorial, such as patient-related, health system-related, socio-cultural-related to language and literacy, and socio-cultural-related to beliefs and stigma. These disparities extend across the cancer continuum, from diagnosis to end-of-life care. It is imperative to address these disparities. Here we report 10-year experience from an innovative access delivery model in one go, comprehensively addressing many of these challenges. **Methods:** Learning from the WHO framework of health system strengthening, a model that affects the major contributors to health system strengthening was developed. These include government-owned health departments, district hospitals, and physicians. Various regulations strengthened each of these components. The regulations were issued to create systems in district hospitals, train an alternative oncology workforce, and make oncology drugs available in the periphery. This measure allowed cancer-care-related services to be feasible in the existing peripheral health system. **Results:** In 2014, one of the states in India decided to initiate cancer care services in government-run district hospitals. One physician and two nurses from every district hospital were trained to offer cancer-related services locally from diagnosis to end-of-life, including cancer chemotherapy, under the 24 x7 mentorship of a senior oncologist. To date, more than 250 physicians and 500 nurses have been trained in this field. The program has been extended to eight states and 198 districts, covering an area of over a million square kilometers and a population of over 380 million. Data from only one district alone showed that nearly 7000 new patients availed of services (average 700 per year) with more than 17000 sessions of chemotherapy (Table). **Conclusions:** The majority of the world, including LMICs, is dependent on the services provided by government-run health institutions. The empowerment of government health systems appears to be the single most important factor in improving access to cancer care. This model of cancer cere delivery has consistently proven its robustness, replicability, and scalability. This finding deserves consideration for further research and expansion to other countries. Research Sponsor: None.

Cancer care services (year wise) provided by district hospital Ujjain.

Year	Chemotherapy	Palliative	Total IPD	Total OPD	New Patient
2014	253	-	253	388	217
2015	1144	162	1306	1807	477
2016	1057	164	1321	2026	589
2017	1924	132	2056	3770	658
2018	2361	271	2636	4244	764
2019	2403	447	2850	4255	798
2020	2726	693	3419	5336	735
2021	2148	565	2713	3889	642
2022	1530	1328	2858	4245	731
2023	1946	1255	3201	4796	789
Total	17492	5017	22613	34756	6400

157 Rapid Oral Abstract Session

Retrieval-augmented large language models for clinical trial screening. First Author: Jianqiao He, National University of Singapore, Singapore, Singapore

Background: Clinical trial screening is currently manual and laborious. We tested several large language models enhanced with retrieval-augmented generation (RAG-LLM) to assess their performance on this task. **Methods:** We extracted eligibility criteria of 184 oncology trials with FDA approval notifications between 8 January 2020 and 18 January 2024, as well as information on cancer staging and performance status scoring for the RAG-LLM vector database. A medical oncologist and 2 senior clinical trial coordinators developed a test set of 975 synthetic patient profiles which included primary site, stage, prior therapy, tumor mutations and one additional clinical feature. Each profile was paired with one of the 184 trials and annotated for ground-truth eligibility and the reason for it. This process was repeated for another validation set of 240 longer and more challenging profiles paired with 8 ongoing trials. We developed RAG-LLMs with 4 leading LLMs (Zephyr-7B, Med42, GPT 3.5, GPT4) and evaluated their accuracy in determining trial eligibility as well as retrieval-augmented generation assessment (RAGAs) metrics. A response was deemed accurate only if it correctly assigned both trial eligibility and the reason for assignment. **Results:** GPT4 performed best and achieved an accuracy of 95.18% and 80.00% on the test and validation set respectively with a mean inference time of 10.95 seconds. It also demonstrated the highest answer relevancy, context relevancy and faithfulness (Table). **Conclusions:** Our results demonstrate potential for RAG-LLMs to assist with trial screening at scale. Further evaluation in real-world cohorts utilizing electronic records and full protocol data with tracking of impact on trial enrolment can be explored within secure firewalls. Research Sponsor: Ryan Tan, MBBS, MRCP.

Performance of various AG-LLMs for clinical trial matching.

	Test set (n=975)		Validation set (n=40)[1]	
	Accuracy (base)	Mean Inference time in seconds (range)	Accuracy (base)	Accuracy (finetune)
Zephyr-7b[2]	39.18%	28.61 (3.47 - 44.34)	27.50%	27.50%
Med42[2]	48.10%	8.63 (2.12 - 45.67)	42.50%	57.50%
GPT3.5[3]	67.90%	1.92 (0.52 - 7.62)	52.50%	47.50%
GPT4[3]	95.18%	10.95 (1.64 – 102.86)	80.00%	N/E[4]

[1]200 of 240 profiles used for finetuning.
[2]Run on 2 x NVIDIA A100 80GB GPU.
[3]Run on google colab CPU through OpenAI API. Models gpt-3.5-turbo-0613 and gpt-4-1106 preview used.
[4]Not evaluated due to restricted access to finetuning for GPT4.

158 Rapid Oral Abstract Session

Effectiveness of using risk communication to help smokers with cancer quit smoking: A randomized controlled trial. First Author: William Ho Cheung Li, The Chinese University of Hong Kong, Sha Tin, Hong Kong

Background: Despite evidence that patients living with cancer who continue to smoke after diagnosis are at a higher risk for all-cause mortality and reduced treatment efficacy, many cancer patients continue to smoke. This study aimed to examine the effectiveness of using a brief risk communication approach to help smokers with cancer quit smoking. **Methods:** A randomized controlled trial was conducted on 528 patients who continued to smoke and were follow-up at five out-patient clinics in Hong Kong. A total of 268 subjects were randomly assigned to the intervention group that received health warnings on smoking, and 260 subjects were randomly assigned to the control group that received usual care. All subjects had follow-up telephone calls at 1week, 1 month, 3 months, 6 months and 12 months to assess smoking status. **Results:** The biochemically validated quit rate at the 6-month follow-up was higher in the intervention group than in the control group (5.2% vs 3.8%; OR 1.38, 95% CI 0.60–3.16). The rate of at least 50% self-reported reduction of smoking at 6 months, was higher in the intervention group than in the control group (16.8% vs 12.3%; OR 1.43, 95% CI 0.88–2.35).The results showed that many smokers diagnosed with cancer believed that it was too late to quit smoking. Many participants claimed that overcoming cigarette cravings was extremely difficult, and therefore felt that the barriers to quitting outweighed the perceived benefits. **Conclusions:** It is crucial to proactively implement novel and effective smoking cessation interventions for smokers with cancer. Importantly, it will help to improve the physical well-being and health-related quality of life of smokers with cancer and protect the public, especially vulnerable groups such as women and children, from exposure to second-hand smoke. This will ultimately save more lives, protect the environment, and boost sustainable development. Clinical trial information: NCT01685723. Research Sponsor: Food and Health Bureau, Hong Kong Government; 09100991.

159 Poster Session

Stereotactic centralized ablative radiation therapy: A novel methodology in treating bulky tumor and its technical realization. First Author: Jun Yang, Junxin Oncology, Garnet Valley, PA

Background: Bulky tumors pose significant challenges to traditional treatment modalities such as surgery, chemotherapy, and conventional radiotherapy. This study introduces a novel therapeutic approach named as Stereotactic-Core-Ablative-Radiation-Therapy (SCART), designed to deliver an ablative dose to a substantial core of the bulky tumor while quickly decreasing to a lower dose at the tumor periphery. **Methods:** A SCART-Treatment-Volume (STV) at the core of the GTV was predefined to administer an ablative radiation dose, aiming to induce DNA damage in cancer cells and potentially trigger biological cancer-killing effects. Utilizing Linac-based VMAT or Cyberknife techniques with 6MV photon beams, multiple radiation fields intersect and optimize at STV, generating an ablative dose at the STV. The dose rapidly diminishes to a safe level at the edge of GTV sparing the surrounding tissue. In the phase-1 trial, nineteen patients with 21 bulky tumors enrolled, receiving SCART at five dose levels (15GyX1, 15GyX2, 15GyX3, 18GyX3, 21GyX3, and 24GyX3), while maintaining the GTV's peripheral dose at 5Gy each fraction. **Results:** All patients completed treatment with average beam-on time of 8.9min and average treatment time of 18.5min. Mean follow-up time is 15.4 month. No grade-III or higher toxicity was observed. 7/19 patients still survive, with the overall survival of 40% at 30 months. Mean tumor volume shrinks by 60% between initial 301cc and post-SCART volumes of 118cc. Long-term follow-up revealed that 14/21 tumors achieved Partial Response, 2/21 Complete-Response, 3/21 Stable-Disease, and 1/21 Progressive-Disease, leading to an encouraging local control of 95%. **Conclusions:** SCART emerges as a safe and effective strategy for treating bulky malignant tumors, demonstrating excellent local control and overall survival. Multiple treatment courses were feasible. The results from phase-1 study suggest that SCART could revolutionize the treatment landscape for bulky tumors, offering a promising avenue for further exploration and application in clinical practice. Research Sponsor: None.

160 Poster Session

OncoGPT: An AI assistant for genomic-driven precision oncology. First Author: Samuel Ding, Boston Children's Hospital, Boston, MA

Background: Cancer patient's unique genomic profile can help oncologists select a course of precise personalized treatment for the subject. High throughput next-generation sequencing (NGS) technology allows us to identify genomic alterations simultaneously within a patient's tumor tissue and blood-circulating tumor DNA (ctDNA) in a single test, however, robust tool for accessing mutation-treatment matching is limited. **Methods:** OncoGPT was built on a cloud-based elastic computing platform. The NGS data analytical module consists of a cascade of computational algorithms for NGS data processing and gene variant calling. The interactive and univariate Cox proportional hazards models were used for mutation-treatment matching and prognostic effect analysis, respectively. Machine learning algorithms including decision tree, random forest, and neural network were trained and tested with novel features for tissue-of-origin (TO) classification across 8 caner types. **Results:** We built an AI-driven NGS data analytical platform by integrating computational models, matching algorithms and variant annotation databases to highly accurate achieve cancer-related gene mutations, copy number variation, and structure variants using NGS data from 35,122 tumors across 8 cancer types from three institutions. Next, an AI-driven TO classifier was developed and achieved a weighted F1 score of 0.926 for high confidence predictions ($\geq$ 0.9) on tumor samples. Furthermore, augmented AI matching algorithms were applied to match the optimal personalized treatment and provide prognostic prediction for cancer patients with significantly bett survival outcomes (hazard ratio (HR) = 0.326; 95% confidence interval (CI) = 0.213–0.565; P = $2.52\times10-5$). **Conclusions:** We have successfully developed an innovative intelligent system (OncoGPT) with AI capabilities to help accurately find actionable targets from patient tumor or blood ctDNA NGS sequencing data and precisely match individualized therapeutic and clinical trial options for patients. In addition, OncoGPT classified primary tumor sites across 8 different cancer types with high confidence predictions. We believe that OncoGPT would help clinicians make optimal treatment decisions for cancer patients through genomic-driven precision oncology. Research Sponsor: Boston Children's Hospital.

161 **Poster Session**

Voice-based depression assessment in patients with gynecological cancer. First Author: Nozomi Higashiyama, Kyoto University Graduate School of Medicine, Kyoto, Japan

Background: Although depression in patients with cancer can lead to a deterioration of treatment adherence and quality of life (QOL), diagnosis of depression in patients with cancer is difficult due to symptoms overlapping with side effects of cancer treatment such as fatigue. Traditional screening tools like the PHQ-9 questionnaire are underutilized in clinical practice. Recently, interest has grown in utilizing patients' voices to assess their mental well-being. This study aims to evaluate depression in patients with gynecological cancer and explore the usefulness of voice analysis as a depression detection tool. **Methods:** PHQ-9 scores were collected from 197 patients with gynecological cancer, with 28 cases undergoing longitudinal assessments at diagnosis, postoperatively, and during chemotherapy. Voice recordings were obtained from 70 patients at diagnosis, alongside serum samples from 22 patients. The PHQ-9 scores were compared across different treatment periods, with a specific focus on patients exhibiting a PHQ score of $\geqq$10, who can be diagnosed with Major Depressive Disorder (MDD). The provision of supportive care for MDD patients was also verified. A random forest model was developed from voice features obtained from 70 patients, with hyperparameter tuning and cross-validation to predict mild depression. Serum metabolites were comprehensively analyzed between depression prediction group and normal prediction group by the depression prediction model. **Results:** Mean PHQ-9 scores decreased over time since diagnosis; initially 6.50 $\pm$ 4.99 (mean $\pm$SD), postoperatively 6.18 $\pm$ 4.25, and during chemotherapy 4.88 $\pm$ 4.29. The frequencies of MDD also decreased over the clinical course; at diagnosis 24.3%, post-operatively 15.5%, and during chemotherapy 15.4%. Out of 17 cases of MDD during chemotherapy, only one (6.25%) received psychiatric intervention. All MDD cases during chemotherapy had PHQ-9 scores of 5 or higher, representing mild depression at diagnosis. Mild depression at diagnosis could be predicted with an AUC of 0.89 using voice features. Metabolites identified by the voice-based depression prediction model were associated with depression, such as xanthine, methionine, and taurocholic acid. **Conclusions:** Depression during chemotherapy is often not intervened. Patients with mild depression at diagnosis tend to develop MDD during chemotherapy. Voice-based mental health assessment at diagnosis is possibly a promising screening tool for depression during subsequent cancer treatment. Clinical trial information: UMIN000044266. Research Sponsor: None.

162 **Poster Session**

A scalable 3D spatial multi-omics method for high-plex morpho-molecular imaging of millimeter-thick tissues. First Author: Hei Ming Lai, Chinese University of Hong Kong, Hong Kong, Hong Kong

Background: Tissues are three-dimensional (3D). However, current histopathology only allows 2D and single-marker tissue views. **Methods:** We utilized tissue clearing, supramolecular histochemistry, light-sheet microscopy, and image processing algorithms to compile an end-to-end multi-modality pipeline for 3D digital pathology and oncology diagnostics development. **Results:** Our end-to-end solution allow parallelized, fully automated processing of formalin-fixed or paraffin-embedded tissues of 1cm^3 size. With a tissue-to-image time of 6 days, the whole intact tissue block can be non-destructively imaged with our newly developed 3D HnE (Hematoxylin-analogue & Eosin stain) and 4-plex immunohistochemistry (IHC). Deep and homogeneous penetration of staining was achieved such that all stained markers can be quantified as ground truth. The stained and cleared tissue can be recycled for subsequent FFPE 2D histology over multiple cycles for higher-plex imaging, and is also applicable to simultaneous survey of mRNA with multiplexed fluorescent in situ hybridization (FISH), post-translational modifications such as histone modifications via IHC, and glycosylation profiling with lectins. Image analysis readily allows high-dimensional clustering of cells based on their multi-modal biomolecular expression profiles, morphology, spatial locations, and neighborhoods. The method is applicable to a wide variety of human and murine tissues. **Conclusions:** Our 3D digital pathology platform enables maximal information extracted for precision diagnostics and advanced biomedical research. Research Sponsor: The Chinese University of Hong Kong.

163 **Poster Session**

Development and implementation of a digital health intervention (DHI) electronic patient-reported outcome measure (ePROM) platform to monitor patients with cancer. First Author: Matheus Soares Rocha, Thummi Global and Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil

Background: Cancer is heterogeneous diseases associated with a significant burden of symptoms and treatment-related adverse events. Digital Health Interventions (DHIs) emerge as promising tools for active/continuous monitoring of patients (pts). Evidence suggests that DHIs may enhance healthcare delivery and improve clinical outcomes by facilitating symptom detection and enabling more effective real-time informed decisions. We aim to develop and implement an electronic Patient-reported Outcome Measure (ePROM) platform to monitor pts undergoing cancer treatment. **Methods:** We developed ThummiOnco, a DHI ePROM platform designed for monitoring of pts during cancer treatment. It allows pts to report their symptoms (reported and graded according to the CTCAE), quality-of-life (QoL) (EORTC EQ-5D questionnaire), emotional state, treatment adherence (Morisky-Green questionnaire), Emergency Room (ER) visits and hospitalizations through a mobile application. Upon registration, pts consent to share their data with their medical team and provide essential demographic information such as age, sex, cancer type, and treatment regimen. A medical algorithm analyzes the collected data to generate instant personalized recommendations and guidance, including indicating the need of seeking emergency care in the case of serious high-grade or worrisome complaints. Patients also have the option to engage in real-time conversations with the medical team through an online chat feature. Treating physicians and the medical team can continuously access pts data real-time, through an online dashboard, enabling them to visualize information and statistics, address symptom alerts, and make informed management decisions. ThummiOnco is available at no cost to pts at https://thummi.global. **Results:** Between August 2021 and March 2024, ThummiOnco monitored 925 pts across 7 institutions in Brazil, encompassing both private and public health systems. The majority of pts (72%) were female, with 28% being male. The most frequently monitored cancer types were Breast Cancer (39%), Lung Cancer (7%) and Colon Cancer (6%). During this period, a total of 71.373 interactions were recorded, including 36.175 (51%) chat messages, 21.644 (30%) symptom reports, 10.597 (15%) emotional state reflections, 2.819 (4%) QoL assessments, and 138 (0.2%) ER registries. A total of 23 different symptoms were reported, with the most frequent being: fatigue (16%), joint pain (8%), and nausea (7%). 13.187 (61%) grade 1, 6.545 (30%) grade 2, and 1.912 (9%) grade 3 symptoms were registered. In total, the medical algorithm generated 1.921 recommendations for seeking emergency care. **Conclusions:** ThummiOnco's capacity to detect a wide range of symptoms and enable real-time informed decisions underscores its potential to enhance patient outcomes and healthcare service delivery. Research Sponsor: None.

164 **Poster Session**

Laser ablation of stage 4 buccal cancer: A paradigm shift in management. First Author: Rusy Bhalla, Orchid Center for Laser Surgery, Mumbai, India

Background: Laser ablation of soft tissue tumors is fast gaining ground in the field of Oncology. Conventional Oral cancer treatment is blamed most often for a radical dip in Quality of Life post-surgery and Radiotherapy. Mutilation, Mouth closure, inability to speak, eat or drink normally discourages patients to adopt surgery in early stages or even treatment as a whole. Laser technology uses controlled heat to burn the cancer affected tissues under sonography control. The new technique of Laser Ablation has removed the need for cutting of face and the need for radiotherapy. **Methods:** 54 patients were diagnosed with stage 4 inoperable cancer on clinical and radiological examination. Criteria for inoperability were size of tumor more than 3.5 cms and less than 5 cms, involvement of upper or lower Gingivo buccal sulcus with or without involvement of bone. Laser ablation was achieved by using 980mm diode laser. The margins of effective tumor ablation are assessed under sonography. The lymph nodes were laserised percutaneously under sonography control. Post operatively patients were administered chemotherapy by a standard cisplatin, paclitaxel and 5Fu 3 weekly for 6 cycles. **Results:** All patients showed a decrease in their swelling within 1 month of the procedure. There was an increase in appetite and well being within 2 weeks of the procedure. 47 (90%) patients had a total resolution of the tumor with laser and chemotherapy at 2 months. MRI scans done after 3 months showed a resolution of the original lesion with resolution of lymph nodes. 8 patients (9%) showed a recurrence in the operated area which did not settle on repeat laserisation. These patients underwent standard commando operation at other institutions. 41(75%) patients showed an MRI consistent with no active cancer at 8 months. All of these patients had a weight increase from 4 to 10 kgs compared from pre laser weight over this period. 13 (24%) patients showed a recurrence in neck lymph nodes after 8 months. Of these patients 8 (60%) patients showed a good response to laserisation of the affected node. Over all 80% of patients of stage 4 inoperable buccal cancer were in remission at 2 years with no sign of cancer on MRI scans. **Conclusions:** Laser ablation of oral cancer in late stage oral cancer should be offered as an alternative to patients not willing for a standard commando operation. Skill sets required for the same are different from conventional surgery. It involves a working knowledge of sonography and has a short learning curve. Research Sponsor: None.

165 **Poster Session**

Utilizing an automated cloud-based platform, Palantine Foundry, to generate and build large databases for clinical research applications. First Author: Quynh Nguyen, University of Texas MD Anderson Cancer Center, Houston, TX

Background: Academic institutions are adopting automated tools to help develop and maintain large databases. Leveraging advances in clinical data warehouses and artificial intelligence can potentially decrease resource utilization and the time required to conduct research by reducing intensive manual human curation of data. **Methods:** This research was performed as part of the institutional Data-Driven Determinants for COVID-19 Oncology Discovery Effort (D3CODE), IRB-approved protocol 2020-0348. Data were obtained from both structured and unstructured data sources within the MD Anderson electronic health record to validate a retrospective analysis for COVID-19 positive patients undergoing radiation treatments. Multiple data sources were identified, integrated and analyzed using the Syntropy Foundry platform, part of the Context Engine Data Management System at M.D. Anderson Cancer Center (MDACC) to include patient demographics, clinical notes, laboratory values, radiology reports, and oncology treatments. The platform allows real-time updating of these data-sources with integrated statistical packages to streamline rapid statistical analyses. We conducted a retrospective review of patients treated within 3 weeks of COVID infection between March 2020 and November 2022. Patient data was obtained using Foundry. Patients who tested positive for COVID-19 and had their treatment postponed were categorized as having a treatment delay. Patients who started radiation therapy and subsequently had an interruption in treatment due to contracting COVID-19 were categorized as having a treatment break. The Kaplan-Meier method was used to compare survival outcomes and was conducted within Foundry. **Results:** Syntropy Foundry helped develop a database comprising of 380 COVID-19 positive patients treated with radiation therapy between March 2020 through November 2022. It validated patient demographic information and research variables including patient age, histology, cancer stage, treatment plans, radiographic scans, recurrences, and follow up time that were separately performed manually. It reduced the time and human resources required to retrospectively collect and review these patient charts. **Conclusions:** Syntropy Foundry and ongoing efforts to leverage machine learning models to facilitate the interpretation of the large amount of accessible clinical data can potentially improve quality and reduce resources needed to generate large research databases. Future applications using artificial intelligence with Foundry to identify clinical recurrence and report patient outcome are under development. Research Sponsor: None.

166 **Poster Session**

Validating process mining in pediatric oncology: Demonstrating protocol adherence and variability in neuroblastoma treatment. First Author: Astrid van Barneveld, Princess Maxima Center for Pediatric Oncology, Utrecht, Netherlands

Background: Neuroblastoma is the most common extracranial tumor in children. The mortality rate for patients with metastatic disease is over 50%. In the Netherlands, 30 new patients are diagnosed annually. Current clinical treatment guidelines are complex and include multiple treatment arms consisting of chemotherapy, surgery, radiotherapy, and immunotherapy (IT). Although poor patient health and complications are known to cause adaptations to the otherwise standardized treatment regimen, the extent to which these variations occur is unknown. This study aimed to validate the use of process mining, a data-driven technique, to retrospectively examine protocol adherence and variability within current clinical guidelines based upon the GPOH-DCOG NBL2009 neuroblastoma treatment protocol. **Methods:** Data was extracted from electronic health records, as well as laboratory, pathology, and pharmaceutical databases, to create individual event logs for each patient. Process mining was performed using a fuzzy mining algorithm. The treatment courses for all neuroblastoma patients were mapped. Commonalities and variations were highlighted, and the throughput time for key treatment phases was calculated. Subsequently, conformance with protocol was determined. **Results:** Analysis of 70 patients treated between 2018-2022 showed 62 distinct treatment processes, revealing significant variations in patient care. Patients with high-risk disease showed the least variation (n=47, 42 variants). Notably, 17 variants were identified among 18 patients who died, indicating a highly personalized approach in the advanced stages of the disease. Subgroup analysis of 17 high-risk patients who received IT consisting of alternating cycles of anti-GD2 antibody and retinoic acid showed 6 variants. 12/17 patients (70.6%) completed the full IT regimen. Other treatment adjustments included shortened anti-GD2 infusions for two patients (5 and 8 days versus the prescribed 10 days, respectively), potentially indicating treatment toxicity. One patient received a 15-day infusion, exceeding the prescribed limit of 11 days. The recorded interval between the administration of anti-GD2 and retinoic acid was a median 5.5 hours (range: 60 seconds – 6.4 days), deviating from the prescribed interval of 24 hours and warranting further investigation. **Conclusions:** Process mining is a valuable tool for analyzing protocol performance and adherence in neuroblastoma treatment. Despite standardized treatment protocols, significant heterogeneity was observed in the treatment of neuroblastoma patients, especially those with poor prognosis. Throughput time analysis revealed variabilities in the IT regimen that warrant further investigation. This study underscores the potential of data-driven approaches to optimize treatment protocols and support evidence-based practices in clinical oncology. Research Sponsor: None.

TPS167 **Trials in Progress Poster Session**

Efficacy of a mountain craft training in improving resilience and psychological well-being and reducing fatigue in childhood cancer survivors. First Author: Joyce Oi Kwan Chung, The Hong Kong Polytechnic University, Hong Kong, Hong Kong

Background: This pilot study aims to determine the feasibility, acceptability, and preliminary efficacy of mountain craft training in improving resilience and quality of life and reducing fatigue and depressive symptoms in childhood cancer survivors (CCS). **Methods:** A randomised controlled trial. A sample of 40 CCS, aged 10 to 16, will be invited to participate in this study. Resilience scale, Center for epidemiologic studies depression scale; Paediatric Quality of Life Inventory; and Fatigue Scale – Child will be used to assess resilience, depressive symptoms, health-related quality of life and levels of fatigue, respectively. Participants in the intervention group will receive two 30-45 mins lectures on resilience, physical exercise, knowledge and skills in mountain craft; and a 4-day hiking programme on weekends over a 3-month period. Participants in the control group will participate in 4 day of leisure activities on weekends over a 3-month period. The main outcome measure: The participants' level of resilience at 6-month post intervention The Statistical Package for Social Sciences (SPSS) software (version 26.0) will be used to analyse the quantitative data. Pearson chi-square test or Fisher's exact test for categorical variables, and the independent sample t-test for continuous variables. The Generalised Estimating Equation (GEE) will be employed to determine the changes between the intervention and placebo control groups, the within-group (time) effects, and the interaction effects. Research Sponsor: None.

168 **Rapid Oral Abstract Session**

New approaches to active monitoring: Patient-reported outcomes and wearables utilisation in Waldenstrom macroglobulinemia. First Author: Kim Summers, Sanius Health, London, United Kingdom

Background: Waldenstrom macroglobulinemia (WM) is a rare haematological malignancy that has seen an emergence of novel targeted therapies. With a range of clinical features impacting quality of life (QoL), there is a need for disease-specific patient-reported outcomes (PRO), outside of existing measures with limited validity in WM. The aim of this work was to enrich understanding of the patient experience and identify potential WM-specific metrics, through wearable-captured physiological metrics and electronic-PROs (ePROs). **Methods:** Informed consent was provided by 79 patients with WM for the analysis of data from an FDA-cleared wearable smartwatch capturing activity, sleep, and heart rate, and a mobile app for patients to input daily ePROs. These ePROs included treatments taken, EQ-5D-5L, and disease symptoms (fatigue, weakness, numbness/tingling, breathlessness, difficulty concentrating/confusion, vision, rash, night sweats, dizziness/light-headedness, constipation, loss of appetite, diarrhoea, and vomiting). Data was integrated within a digital platform, and anonymised extracts analysed as a cohort and by treatment. **Results:** Patients had a mean$\pm$SD (range) age of 65$\pm$10 (43-88) years. 53% were female. As of the most recent self-reported treatment entry, 22% (17/79) reported Bruton tyrosine kinase inhibitor (BTKi) use. Completion rates over a 142-day snapshot for daily PROs was 60%, and 85% across wearable activity and sleep metrics (devices synced=58/79). A cohort mean EQ-5D-5L Score of 0.760$\pm$0.181 and Health State (0-100) of 74$\pm$18 was reported. The highest symptom severity scores (1-5) were 'fatigue' (1.9/5), 'weakness' (1.7/5), and 'numbness/tingling' (1.5/5), all other symptoms reporting a mean score of 1.4 or less. Increasing activity levels significantly correlated with decreasing symptom severity and increasing QoL scores ($p<0.05$). Lower symptom severity also correlated with higher total sleep durations, contrasting higher 'difficulty concentrating/confusion', 'dizziness/light-headedness', and 'usual activity impairment' scores with increasing levels of deep sleep. Breathing disturbance intensities (36.8 vs. 17.6, p=0.008) and nightly wakeup counts (1.9 vs. 1.6, p=0.038), tracked by wearables, were significantly higher in patients reporting BTKi treatment compared to the remaining cohort. **Conclusions:** Our data support the enrichment of knowledge around baseline physiological and QoL metrics for patients with WM, demonstrating the feasibility of a digital ecosystem of wearable-captured and ePRO metrics at a high data completeness level. Further work will ensure the generation of more population-representative outputs, through the expansion of the patient cohort, and a greater depth of insight into the impact of health events, disease complications, and therapeutic intervention on these remotely-tracked metrics. Research Sponsor: None.

169 **Rapid Oral Abstract Session**

Collaborative data sharing: The International Acute Myeloid Leukemia Consortium (INTERACT). First Author: Daisuke Tomizawa, National Center for Child Health and Development, Tokyo, Japan

Background: Outcomes for children and adolescents/young adults (AYAs) with acute myeloid leukemia (AML) remain suboptimal and are decidedly poor for patients with subtypes defined by high-risk features, including canonical genetic alterations and relapsed/refractory presentation. Due to their rarity, these subtypes are difficult to study within the existing clinical trials paradigm. Data sharing efforts aim to increase our understanding of rare cancer subtypes by pooling data from multiple sources. The INTERnational Acute myeloid leukemia ConsorTium (INTERACT) was established to pool and share data on pediatric and AYA patients with AML. **Methods:** In 2019, a data dictionary was created through an iterative, consensus-driven process that analyzed pre-existing clinical trials case report forms as the initial basis. By developing this standardized representation for data on patients with AML, data could be harmonized and integrated. A memorandum of understanding was signed in 2021, formally establishing INTERACT. An executive committee was convened to establish scientific priorities, facilitate ongoing data dictionary work, usher agreements with data contributors and review data requests submitted by investigators. In January 2024, the initial set of AML data was released on the Pediatric Cancer Data Commons (PCDC) data portal. **Results:** As of April 2024, the data dictionary includes 157 standardized data elements that were used to harmonize clinical data on 3,413 patients who participated in seven clinical trials conducted by four pediatric oncology cooperative groups across the United States, Europe, and Asia. Elements in the data dictionary include demographics, initial disease characteristics, genetic alterations, and survival status. Aggregate data can be freely explored using the publicly-available PCDC data portal (portal.pedscommons.org) and investigators seeking line-level access to data may submit a project request to the INTERACT executive committee for consideration. **Conclusions:** International collaborative data-sharing efforts will advance our understanding of pediatric and AYA AML by reducing barriers that constrain our study of AML to smaller cohorts of data. We hope that an early outcome of data sharing will be to increase our understanding of optimal treatments for patients with relapsed/refractory disease. Future goals of INTERACT include identifying data from additional studies to include, establishing relationships with new data contributors, and establishing working groups to advance the consortium's scientific and clinical trials goals. Research Sponsor: None.

170 **Poster Session**

Therapeutically targeting the CALR/CD47 pathway in MPN to reactivate natural immunosurveillance mechanisms within the body to enhance treatment outcomes. First Author: Ciro Roberto Rinaldi, University of Lincoln, Lincoln, United Kingdom

Background: MPNs are a group of related myeloid malignancies characterized by alterations in mature blood cell production/bone marrow environment and have a tendency to evolve into acute myeloid leukaemia. We demonstrated that CD47 blockade in combination with ruxolitinib, increased CALR expression enhancing cytotoxicity *in vitro*, promoting enhanced neoplastic clone clearance. With this study we describe a potential methodology for assessing effect of new compounds or combinations and the impact of modulating the immunoresponse upon myeloid malignant clones. **Methods:** Utilising HEL 92.1.7 and SET-2 cells (JAK2 mutated), Marimo cells (CALR mutated) and K562 cell line models; we will incubate with routine therapies (hydroxyurea, anagrelide, ruxolitinib) in combination with a range of anti-CD47 compounds (Anti-CD47 monoclonal antibodies, BET-1 inhibitors, SIRa inhibitor) and will determine the impact upon CD47 and CALR cell surface expression via flow cytometry. Monocyte derived macrophage (MDM) will be produced through Phorbol 12-myristate 13-acetate (PMA) differentiation of a monocytic Thp-1 cell line. Expression of macrophage cell surface markers (CD11b, CD14), as well as intracellular markers (CD68), will be detected by flow cytometry. MDM will then be polarized to either a pro-inflammatory M1, or anti-inflammatory M2 phenotype, with lipopolysaccharide/interferon gamma or interleukins 4 and 13, respectively. Co-culture experiments will then be undertaken to determine how different anti-CD47 therapy combination impact macrophage polarization and destruction of MPN cell lines. **Results:** We predict that CALR/CD47 levels on each cell line subtype will respond differently highlighting heterogeneity within MPNs and demonstrating the clear need for a more personalised immunotherapy approach. Alterations in JAK/STAT pathway and BET inhibition may hinder macrophage polarisation to the anti-tumorigenic M1 macrophage phenotype. We theorise that indirect co-culture of M1 macrophage with MPN suspension cells under different treatment modalities will enhance MPN cell death and decrease CD47 expression to a greater level than that which we expect to see in M2 polarised macrophage. We also anticipate that the M2 polarised macrophage, which dominate in the tumour microenvironment as MPN progresses, will fail to phagocytose MPN cells and may not be rescued by novel immunotherapeutics. **Conclusions:** Our group demonstrated the role of CD47 and CALR expression as a key mechanism and a potential target to enhance presentation of the cancer cell to the immune system, and we believe that understanding the interaction of CD47/CALR – macrophages, will drive new therapeutical approaches able to modulate the immune response and improve patients outcomes, potentially leading to complete MPN clone eradiation and cure. Research Sponsor: MORPHOSYS and GILEAD.

171 **Poster Session**

An observational study on the relationship between tyrosine kinase inhibitor treatment-free remission and cytotoxic T-lymphocytes in patients with chronic phase chronic myeloid leukemia. First Author: Tatsuro Jo, Japanese Red Cross Nagasaki Genbaku Hospital, Nagasaki, Japan

Background: Since the introduction of tyrosine kinase inhibitors (TKIs), the effectiveness of treating chronic phase chronic myeloid leukemia has seen remarkable improvement. A current challenge in TKI therapy is achieving treatment-free remission (TFR) safely. Numerous TKI-stop trials and translational studies have investigated factors influencing TFR, including TKI treatment duration, duration of deep molecular response (DMR), cellular immunity activation, and *bcr::abl1* transcript type. However, identifying reliable markers for achieving TFR safely remains uncertain. In this multicenter study, we focused on examining the association between TFR and cytotoxic T-lymphocytes (CTLs). **Methods:** Between June 2020 and March 2022, a total of 45 patients were enrolled: 38 patients with DMR for at least 1 year on TKIs (on TKI group) and 7 patients with DMR for at least 1 year after discontinuing TKIs (off TKI group). The study included 30 males, with a median age of 59 years (range: 29–87). Median TKI treatment duration was 7.7 years (range: 1.5–18.3), and median TKI cessation duration in the off TKI group was 4.9 years (range: 1.7–7.1). Molecular response and cellular immunity were monitored over 12 months post-consent for patients in the off TKI group and after TKI discontinuation for patients in the on TKI group. **Results:** During the observation period, 25 patients (65.8%) in the on TKI group maintained DMR, while 13 patients (34.2%) lost DMR. Conversely, all patients in the off TKI group sustained DMR. The median TKI treatment duration in the group maintaining DMR (9.45 years, range: 3.3–18.3, N = 32) significantly exceeded that in the group losing DMR (4.9 years, range: 1.5–11.9, N = 13) (P = 0.0048). Patients taking TKIs for over 7 years with a higher percentage of total memory CTLs than total effector CTLs maintained DMR. Conversely, patients losing DMR despite over 10 years of TKI treatment had a higher percentage of total effector CTLs than total memory CTLs. Among the 32 patients maintaining DMR, 19 exhibited a higher percentage of total effector CTLs than total memory CTLs, with 15 (78.9%) maintaining MR5 throughout the study. Furthermore, of the six patients maintaining DMR with relatively short TKI administration (median 5.5 years, range: 3.3–6.4), three displayed a higher percentage of total memory CTLs than total effector CTLs. Among the remaining three patients, two showed strong CTL activation, with one patient having an effector CTL clone over 30% and the other having a memory CTL clone over 30%. **Conclusions:** This study indicates that a sufficiently prolonged TKI treatment duration ($>$7 years) and maintaining deeper DMR ($\geq$ MR4.5, preferably MR5) are conducive to safely achieving TFR. Furthermore, a high percentage of total memory CTLs and intense CTL activation may serve as meaningful markers for TFR. Research Sponsor: Bristol Myers Squibb.

172 **Poster Session**

Outcome analysis of autologous stem cell transplantation in refractory and relapsed Hodgkin lymphoma: Insights from a North African single-institution study. First Author: Marouane Maaroufi, Department of Clinical Hematology and Pediatric Oncology, 20th August 1953 Hospital, Ibn Rochd University Hospital Center, Casablanca, Morocco

Background: The standard therapy for primary refractory or relapsed Hodgkin lymphoma (HL) involves the administration of high-dose chemotherapy followed by autologous stem cell transplantation (HDC/ASCT). Nevertheless, several risk factors may influence survival outcomes. We assessed outcomes of patients in this setting who underwent HDC/ASCT by performing survival analysis and studying prognostic factors affecting survival. **Methods:** We conducted a single-institution retrospective analysis of patients with relapsed/refractory HL who received HDC/ASCT between January 2018 and December 2022. Patients' status evaluation before ASCT was performed by Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) Scan and Computed Tomography (CT) Scan. The used conditioning regimen was BEAM (Carmustine, Etoposide, Cytarabine, and Melphalan). The primary endpoints were progression-free survival (PFS) and overall survival (OS). Survival analysis was performed using the Kaplan-Meier method, and survival differences between groups were assessed using the Log-Rank test. **Results:** Thirty-five patients diagnosed with relapsed/refractory HL were included in the study. Among them, 26 patients (74%) had refractory disease, while 9 patients (26%) relapsed following completion of first-line chemotherapy. All patients were treated with HDC/ASCT. Prior to ASCT, 30 patients underwent assessment using FDG-PET Scan, while CT Scan was employed for evaluation in 5 patients. Twenty-three patients (66%) were in complete remission, 8 patients (23%) were in partial remission, and 4 patients (11%) had progressive disease. With a median follow-up of 24.36 months after transplantation, 28 patients (80%) were in remission, 6 patients (17%) had disease progression, and one patients died of septic shock. The 2-year PFS and OS rates for the total population were 85.4% and 97.1%, respectively. Response to first-line chemotherapy did not have a substantial impact on prognosis, as evidenced by a 2-year PFS rate of 76.2% vs. 88.9% (p=0.88) and a 2-year OS rate of 100% vs. 96.2% (p=0.56) for patients with relapsed and refractory disease, respectively. The 2-year PFS and OS rates for patients receiving autograft during complete remission, partial response, and tumor progression were 93.8% vs. 87.5% vs. 50% (p=0.005), respectively; and 95.7% vs. 100% vs. 100%, respectively (p=0.77). Patients who had negative pre-transplant PET-Scans demonstrated a 2-year PFS rate of 92.9% vs. 64.8% for those with positive PET-scans (p=0.004). **Conclusions:** The findings of our study affirm the established practice of HDC/ASCT for individuals facing relapsed/refractory HL. The disease status at transplant and the pre-transplant PET-Scan status prove to be crucial factors in predicting patients' outcomes, while response to first-line chemotherapy did not influence prognosis. Research Sponsor: None.

173 **Poster Session**

In-hospital outcome of patients hospitalized for leukemia with comorbid acute decompensated heart failure: An analysis of National Inpatient Sample (NIS). First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Recent evidence found increase incidence of heart failure in leukemia patients, influenced by various factors such as the underlying disease and medication usage. Nevertheless, there remains a scarcity of data regarding the in-hospital outcome for individuals admitted for leukemia with comorbid acute decompensated heart failure. Thus, we aim to examine the impact of heart failure on clinical outcomes in leukemia patients. **Methods:** We utilized the 2020 U.S. National Inpatient Sample (NIS) to investigate patients admitted for leukemia with concurrent diagnosis of heart failure, identified through ICD-10 CM codes. Adjusted odds ratios (aORs) for predefined outcomes were determined using multivariable logistic and linear regression model, adjusting for comorbidities. The primary outcome assessed was inpatient mortality, while secondary outcomes included complications related to various body systems. **Results:** We identified 43,955 patients with a primary discharge diagnosis of leukemia. The mean age was 54.5 years; 49.7% were female. Caucasians accounted for 66%, followed by African Americans (13%). Of these, 11.86% (5,220/43,955) had a concurrent diagnosis of heart failure. In a survey multivariable logistic and linear regression model adjusting for patient and hospital factors, comorbid acute decompensated heart failure was associated with higher in-hospital mortality (aOR 1.57, 95% CI: 1.2, 1.94, $p < 0.001$), higher mean length of stay (Beta-coefficient 1.93; 95% CI: 0.65, 3.21, p = 0.003), mean total hospital cost (Beta-coefficient 9,472, 95% CI: 2,339, 16,604, p = 0.004), shock (aOR 2.41, 95% CI: 1.84, 3.15, $p < 0.001$), sepsis (aOR 1.71, 95%CI: 1.38, 2.12, $p < 0.001$), acute respiratory failure (aOR 2.37, 95% CI: 1.96, 2.87, $p < 0.001$), and acute kidney injury (aOR 1.57, 95% CI: 1.32, 1.85, $p < 0.001$). **Conclusions:** Our study revealed that hospitalized leukemia patients with concurrent heart failure experience higher risk of in-hospital mortality and various adverse in-hospital outcomes. Close monitoring of this factor during hospitalization is essential, and additional longitudinal research is warranted to fully understand this association. Research Sponsor: None.

174 **Poster Session**

Autologous bone marrow transplant in standard-risk newly diagnosed multiple myeloma: A systematic review. First Author: Andree Kurniawan, Internal Medicine, Faculty of Medicine, Pelita Harapan University, Jakarta, Indonesia

Background: Multiple myeloma (MM) is a hematological malignancy characterized by clonal proliferation of plasma cells. Bone marrow transplants in high-risk multiple myeloma have been a standard of care for newly diagnosed multiple myeloma (NDMM). Autologous bone marrow transplant (ABMT) has emerged as a promising therapeutic approach for standard risk of NDMM. We aim to review the existing literature on the efficacy of ABMT in standard-risk NDMM in comparison with non-transplant therapeutic approaches. **Methods:** We conducted a systematic search across PubMed, Google Scholar, Science Direct, and Embase for studies within the last 10 years. We included studies that compared ABMT with other therapies without any history of prior transplants in NDMM patients. We excluded studies that retrospective and case studies. We extracted firstly using PICO: standards risk NDMM, ABMT upfront therapy, progression-free survival, and toxicity. The quality of the study was assessed using the Newcastle-Ottawa scale or JADAD scale questionnaire. **Results:** Our search yielded 7 studies, with a total of 3728 patients in 7 randomized controlled trial studies. The endpoint was mainly progression-free survival (PFS), with others being response rates and stringent complete response (sCR). All studies consistently showed that ABMT yielded significantly better PFS and response rates in NDMM, with high-dose melphalan being the most common induction regime. ABMT resulted in relatively more severe toxic side effects compared to drugs only. However, the safety profile of ABMT is considered favorable, with manageable adverse events. Induction methods before ABMT include lenalidomide, bortezomib, dexamethasone, carfilzomib, and melphalan, with some studies reporting follow-ups on further maintenance therapy, mainly with lenalidomide. The effectivity of ABMT remains consistent regardless of the drugs used. **Conclusions:** ABMT is a favorable therapeutic approach for standard risk NDMM with manageable adverse effects and an acceptable safety profile. The effectivity of ABMT is regardless of the concomitant drug used. Research Sponsor: None.

175 **Poster Session**

Effect of iPSC-derived NK cells with site-specific integration of CAR19 and IL24 at the rDNA locus on anti-tumor activity and proliferation. First Author: Desheng Liang, Central South University, Changsha, Hunan, China

Background: The generation of CAR-NK cells using induced pluripotent stem cells (iPSCs) has emerged as a paradigm for manufacturing off-the-shelf cell products for universal immunotherapy. However, enhancing the potency, safety and multi-actions of CAR-NK cells is still full of challenges. **Methods:** Interleukin 24 (IL24) and CD19-specific chimeric antigen receptor (CAR19) were site-specifically integrated at the ribosomal DNA (rDNA) locus in human iPSCs by using TALENickases. The engineered iPSCs were differentiated into NK (CAR-iNK) cells by adopting a 38-day differentiation protocol followed by expansion using magnetic beads in vitro. **Results:** Compared with the CAR-iNK cells, IL24 armored CAR-iNK (CAR19-IL24-iNK) cells showed higher cytotoxic capacity and amplification ability in vitro. Meanwhile, CAR19-IL24-iNK cells inhibited tumor progression more effectively and exhibited better survival without significant side effects in the B-ALL (Nalm-6(Luc1))-bearing mouse model. Interestingly, RNA-sequencing analysis suggested that IL24 may enhance iNK cell function by attracting neutrophils and upregulating FAS and TNFSF10-related genes while exerting a direct effect on tumor cells. **Conclusions:** This study encourages the exploration of IL24 and other molecules to enhance antitumor properties of CAR-NK cells, suggesting a novel strategy to modulate tumor microenvironment while attacking tumor cells with the potential of promising off-the-shelf immunotherapy. Research Sponsor: None.

176 **Poster Session**

Molecular basis for JAK2 inhibition with type II compounds. First Author: Dafne Jacome, Tampere University, Tampere, Finland

Background: Upon prolonged exposure, the therapeutic efficiency of current clinical JAK2 inhibitors (type I inhibitors) can be attenuated, leading to drug resistance both in vitro and in vivo through non-genetic mechanisms. In contrast, type II inhibitors stabilize the inactive conformation of the kinase domain preventing the heterodimerization-mediated JAK2 activation. This confers efficacy to type I inhibitor persistent cells, improved efficacy against myeloproliferative neoplasms and other cancers such as B-cell acute lymphoblastic leukemia. Despite the advantages of type II JAK inhibitors, the discovery of type II inhibitor resistance mutation, L884P, in the kinase domain has hampered the further development of JAK2-targeted type II therapeutics. **Methods:** Here we use combination of protein-inhibitor binding assays, cell-based assays, X-ray crystallography, and computational tools to elucidate the resistance mechanism of JAK2-L884P mutation, to facilitate the development of type II inhibitors with activity against both wild-type and L884P mutated JAK2. **Results:** We have determined an atomic resolution crystal structure of JAK2-L884P mutant, revealing that mutation induces local changes in the structure but not in the ATP pocket. Furthermore, we have identified several type II compounds inhibiting. Interestingly, they show no major differences in potency in vitro against wild-type of L884P mutated JAK2. Selected compounds profiled in cell lines carrying wild-type or L884P-mutated JAK2, show differences in their cell viability, indicating that a resistance arises via allosteric effects. **Conclusions:** L884P mutation impacts the inhibitory potency of type II inhibitors via allosteric mechanism.Crystallographic analysis of our type II shortlisted compounds revealed that they differ in their binding modes and suggests that L884P-insensitive drugs can be developed. Preliminary cell-based experiments results confirm these findings. We will now focus on validating these observations with biomolecular simulations to clarify the molecular basis for the inhibitor resistance via L884P mutation. Our studies will facilitate the development of novel type II drugs against JAK2 in myeloproliferative neoplasms. Research Sponsor: Tampere University.

TPS177 **Trials in Progress Poster Session**

The role of P53 gene and p53 protein in non-Hodgkin malignant lymphoma. First Author: Gabriel Petre Gorecki, Titu Maiorescu University of Bucharest, Faculty of Medicine, Bucharest, Romania

Background: Background and study aim P53 gene mutations are the most common genetic abnormalities of cancer. They have been extensively studied in various mature B-cell malignancies, including chronic lymphocytic leukemia (CLL). In recent years, more attention has been paid to the importance of the p53-expressed protein in CLL, and a combination with low survival and non-response to classical conventional chemotherapy, due to mutations in the p53 gene, with progression to Richter Syndrome. Identifying different p53 gene mutations is very important because these mutations have an impact on the patient's clinical course in CLL. **Methods:** The frequency of p-53 protein expression in 85 patients diagnosed with CLL was analyzed by the Enzyme-Linked Immune-Absorbent Assay (ELISA) technique to investigate the relationship of this protein to the stage of the disease, as well as the impact on response to treatment and survival. Cell extracts $10^3 \times 10^3$/L in 100 μl lysis buffer were applied to ELISA plates coated with PAb 240 capture antibody. Clinical trial information: ISRCTN12539707. Research Sponsor: Individual Funding Source, Author Aurelian Udristioiu.

178 **Poster Session**

Cost-effectiveness of liquid biopsy for molecular profiling of newly diagnosed advanced non-squamous NSCLC in an Asian population. First Author: Aaron C. Tan, Division of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore

Background: Liquid biopsy is complementary to tissue biopsy for lung cancer profiling, yet evidence of the cost-effectiveness is limited. This could retard implementation and reimbursement in clinical practice. The aim of this study is to estimate the cost-effectiveness of profiling strategies that include liquid biopsy and to identify the optimal profiling approach for newly diagnosed advanced non-squamous non-small cell lung cancer (NSCLC) in an Asian population using Singapore as an example. **Methods:** A decision tree and partitioned-survival model was developed from the Singapore healthcare system's perspective to evaluate the cost-effectiveness of five molecular profiling strategies: either tissue or plasma next-generation sequencing (NGS) alone, a concurrent, and two sequential approaches. Model inputs were informed by local data or published literature. Sensitivity analyses and scenario analyses were undertaken to understand the robustness of the conclusions for decision making. The optimal strategy at different willingness-to-pay (WTP) thresholds was presented by cost-effectiveness acceptability frontier and the expected loss curve. **Results:** The sequential tissue-plasma NGS approach revealed an additional 0.0981 quality adjusted life years (QALYs) for an extra cost of S$3,074 over a 20-year time horizon compared to tissue NGS alone, resulting in an incremental cost-effectiveness ratio (ICER) of S$31,318/QALY and an incremental net monetary benefit of S$1,343 per patient. The findings were sensitive to the costs of pembrolizumab and osimertinib and the probabilities of re-biopsy after tissue NGS. Sequential plasma-tissue NGS and plasma NGS alone were more costly and less effective than alternatives. **Conclusions:** The sequential tissue-plasma NGS approach generated the highest net monetary benefit and was the optimal testing strategy when WTP was S$45,000/QALY. It retained superiority but understandably with a higher ICER when expensive, non-first line treatments were included. Overall, its routine clinical practice should be proactively considered for newly diagnosed advanced non-squamous NSCLC in an Asian population. Research Sponsor: None.

179 **Poster Session**

Integrating lifestyle medicine into cancer care: A new paradigm. First Author: Jasmin Hundal, Cleveland Clinic, Cleveland, OH

Background: Amid rising global cancer rates and obesity-related cancer risks, oncology must blend traditional cancer treatments with evidence-based lifestyle medicine (LM) to enhance patient outcomes. LM—evidence-based interventions in nutrition, exercise, sleep, avoiding substances, and social connection —emerges as a critical tool in the care spectrum. ASCO and ACS guidelines incorporating lifestyle interventions are limited, and existing ones have notable implementation gaps. This study advocates for integration of LM into cancer care. Such interventions, supported by growing research, offer significant promise in reducing cancer treatment side effects and improving outcomes, highlighting an urgent need for their incorporation into oncological protocols. **Methods:** The Department of Preventive Medicine at Cleveland Clinic Abu Dhabi (CCAD) launched an LM program at the Oncology Institute. Oncologists refer to LM physicians who assess patients using an LM-validated questionnaire. Cardiometabolic risk factors: body composition, waist circumference, lipid profile, hemoglobin A1c, high-sensitivity CRP, liver function, and liver elastography are tested at baseline and 3 months. Patients receive personalized LM treatment by certified physicians, dieticians, physiatrists, and psychologists, aimed at reducing treatment side effects and enhancing cancer outcomes while improving cardiometabolic health. Follow-ups at 6 weeks and 3 months post-intervention ensure progress tracking and reassessment. **Results:** Initiated in January 2021, it began as a pilot program for breast cancer patients and has since expanded to all cancer patients. To date, it enrolled 425 patients, evidencing sustainability and acceptance within the patient community. Referral rates from oncologists have shown a steady increase, reflecting the program's growing credibility and utility. Patient satisfaction levels are reported to be high. Preliminary outcomes indicate improvements in both physical and psychological health metrics, suggestive of the program's comprehensive impact. **Conclusions:** The pioneering oncology LM program at CCAD established a transformative model that seamlessly integrates LM into traditional oncology care and acts as a bridge to survivorship. By ensuring sustained access to lifestyle interventions from the point of diagnosis through post-treatment, the program aligns with the latest research and ASCO/ACS guidelines, pioneering a new standard in cancer treatment. It can effectively address cardiometabolic risks, including obesity, and reduce treatment-related adverse outcomes. This program demonstrates the feasibility and a replicable global model, one that merges evidence-based lifestyle practices with standard oncological care to create a unified approach that could be adopted by healthcare systems worldwide, marking a significant step in the evolution of patient-centered cancer care. Research Sponsor: None.

TPS180 **Trials in Progress Poster Session**

Stronger together: Implementing patient-reported symptom tool in routine cancer care in diverse Asia—A multi-national pilot feasibility study (PROMiSE-Pilot). First Author: Piyada Sitthideatphaiboon, King Chulalongkorn Memorial Hospital, Pathum Wan, Bangkok, Thailand

Background: Patients diagnosed with cancer often experience disease or treatment-related symptoms, which can be under-elicited and under-appreciated by clinicians during time-poor consultations. This is particularly challenging in Asia where structural disparities in healthcare access mean oncology services are often under-resourced. Five oncologists from Thailand, India, Singapore, Philippines and Australia formed a working group as part of ASCO Asia-Pacific Leadership Development Program (LDP-AP). Systematic symptom monitoring using patient-reported outcomes measures (PROM) was identified as a potential solution to improve care in diverse Asian settings. PROM has demonstrated improved outcomes in Western settings but its utility in resource limited Asian contexts is less well established. A study was developed to evaluate the feasibility of implementing PROM in routine outpatient care across diverse cultural contexts in Asia. **Methods:** PROMiSE-Pilot is a prospective, multi-centre, feasibility study of integrating PROM in routine outpatient care across Asia. The Edmonton Symptom Assessment Scale questionnaire (ESAS-r) was selected as the PROM tool. Clinicians in 4 hospitals in Singapore, Manila, Bangkok and Hyderabad will be invited to participate, and their patients will be invited to complete the ESAS-r on paper before each visit. The primary aim is to evaluate if proportion of patients who complete $\geq$5 of 10 items on ESAS-r is $\geq$85% (Clopper Pearson). Secondary aims include assessing proportion who complete $\geq$8 and all 10 items and perceived utility of ESAS-r evaluated through surveys adapted to measure patient and clinician satisfaction. Site-specific patient, clinician, administrative barriers and facilitators will be studied. A pragmatic approach to context-specific implementation was adopted with each site developing its own process map for delivering the pilot and adapting to local patient demographics (e.g. low literacy), cultural contexts and resources. Translated versions of ESAS-r were acquired where necessary. Recruitment commenced in March 2024 following ethics approval at 2 sites. 87 patient encounters have been captured from 5 participating clinicians in Singapore. 5 clinicians have agreed to participate in Bangkok. Target recruitment is 200 encounters per site. Multi-centre data will be presented at the Breakthrough congress. Clinicians from ASCO LDP-AP identified PROM as a low-cost but potentially high-value approach to improving quality of care in resource limited settings in Asia. Understanding the feasibility of such a tool is vital prior to consideration of wider scale adoption by stakeholders. This co-developed multi-national pilot additionally demonstrates the value of collaboration, our strength in diversity and a pragmatic model for investigator-initiated studies in Asia. Research Sponsor: None.

181 **Poster Session**

A novel artificial intelligence-enhanced electrochemical method for rapid methylation detection in cfDNA: Advancing multi-cancer early diagnosis. First Author: Li-Yue Sun, Department of Health Management Centre, Zhongshan Hospital, Fudan University, Shanghai, China

Background: The detection of methylation in circulating free DNA (cfDNA) has become a pivotal approach for the early screening and diagnosis of cancer. Traditional methods, face challenges including high detection limits, inconvenience, and elevated costs. Our prior work developed a rapid, cost-effective, and sensitive electrochemical methylation detection method for multi-cancer early detection (MCED), yet it couldn't identify the tissue of origin (TOO). We aimed to enhance this method by integrating traditional tumor biomarkers with artificial intelligence (AI) algorithms for improved cfDNA methylation detection and rapid TOO determination. **Methods:** A training cohort of 626 individuals was analyzed, including 173 colorectal cancer (CRC) patients, 49 patients with hematological tumors, 273 patients with other types of tumors, and 131 healthy controls. This analysis utilized electrochemical detection, carcinoembryonic antigen (CEA), and carbohydrate antigen 19-9 (CA19-9). We evaluated the diagnostic performance of these markers using ten types of AI algorithms. The optimal algorithm was selected to construct diagnostic models for CRC and hematological tumors. These models were then validated in an external cohort comprising 100 cancer patients. **Results:** In the training cohort, the logistic algorithm outperformed others, achieving AUC of 0.915 for CRC, 0.850 for hematological tumors, and 0.860 for other tumors. Based on these results, we opted to utilize the logistic algorithm for the development of diagnostic models for CRC and hematological tumors. The CRC model surpassed the performance of the electrochemical adsorption rate (AUC = 0.817) in CRC, though it showed limited efficacy for hematological tumors (AUC = 0.544) and other tumor types (AUC = 0.806). Conversely, the hematological tumors model achieved its highest performance in hematological tumors (AUC = 0.833), with commendable results for CRC (AUC = 0.831) and other cancers (AUC = 0.799) as well. In the validation cohort, the CRC model accurately identified 32 out of 35 CRC patients, and 17 of these were also detected by the hematological tumors model. Among the hematological tumors patients, 18 out of 20 positive with the hematological tumors model, and 15 were detected by the CRC model. For the remaining 45 patients with various other cancer, 22 tested positive with the CRC model and 28 with the hematological tumors model. **Conclusions:** Integrating machine learning with electrochemical cfDNA methylation detection and tumor markers provides a powerful approach for accurate cancer detection and TOO determination, promising to improve early diagnosis and personalized treatment strategies. Research Sponsor: National Natural Science Foundation of China; 82302640; Guangdong Medical Scientific Research; B2023038; Guangzhou Science and Technology Plan Project; 2023A04J1129.

182 **Poster Session**

Mortality and economic cost in common primary cancer admitted with COVID-19: Analysis of NIS 2020. First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Recent data showed the detrimental effects of COVID-19 infection on various conditions, resulting in a wide range of health disparities and worsening outcomes, as well as an increased burden of cost. However, limited information exists on the impacts of COVID-19 infection on the most commonly admitted with primary cancer, regarding clinical and economic impact. **Methods:** We analyzed the 2020 U.S. National Inpatient Sample (NIS) to investigate the effects of COVID-19 infection on cases primarily admitted with the most common admitted with primary cancer, using relevant ICD-10 CM codes. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariable logistic and linear regression analyses. The primary outcome was inpatient mortality, with secondary outcomes including the cost of hospitalization and length of stay. Statistical significance was established at a p-value of 0.05. **Results:** We estimated 919,104 hospitalizations with a primary discharge diagnosis of cancer conditions. Of these, 0.54% (4,985/919,104) had a concurrent diagnosis of COVID-19 infection and 46.1% were female. The mean age was 63.6 years old and Caucasians dominated the majority of the records (69.7%), followed by Hispanics (13.1%). In a multivariable logistic and linear regression model adjusting for patient and hospital factors, COVID-19 infection was associated with higher in-hospital mortality for all cancer conditions and other outcome. The txable denotes all-type and subpopulation analysis. **Conclusions:** In conclusion, our study encompasses all most common admitted primary cancer conditions and shed light how COVID-19 infection is associated with higher in-hospital mortality, prolonged hospital stays, and increased economic burden in various condition. Future longitudinal studies are warranted to comprehensively assess the long-term health sequelae in this population. Research Sponsor: None.

Adjusted odd ratios and beta-coefficient for each outcome, stratified by subpopulation groups.

Conditions	Estimated Hospitalization	Mortality	Length of Stay**	Charges	Costs
Lower Colon Cancer	116,605	**6.50 (3.60, 11.73)***	**4.75 (2.51, 6.99)***	**41,561 (3,044, 80,078)***	**6,634 (589, 12,680)***
Lung and Bronchus Cancer	103,334	**5.39 (3.01, 9.64)***	**5.51 (2.59, 8.43)***	37,389 (-9,847, 84,626)	**10,683 (784, 20,581)***
Leukemia	43,996	**2.87 (1.61, 5.10)***	2.34 (-1.99, 6.67)	2,561 (-103,233, 108,356)	6,925 (-27,997, 41,849)
Lymphoma	39,976	**3.01 (1.45, 6.24)***	3.28 (-0.10, 6.66)	22,660 (-51,201, 96,522)	306 (-13,841, 14,453)
Kidney Cancer	39,849	N/A	**4.89 (0.62, 9.17)***	2,953 (-25,437, 31,344)	547 (-5,418, 6,513)
Total	919,104	**3.86 (3.15, 4.72)***	**5.96 (4.93, 6.98)***	**52,443 (34,209, 70,677)**	**13,907 (9,015, 18,800)**

N/A denotes no deaths in subpopulation group, * denotes significant level at $p < 0.05$, **denotes beta-coefficient.

183 **Poster Session**

Addressing ovarian cancer research gaps in under-resourced settings using individual initiatives: The OVANORDEST pilot project in Morocco. First Author: Khalid El Bairi, Faculty of Medical Sciences, University Mohammed VI Polytechnic, Ben Guerir, Morocco

Background: In Morocco, ovarian cancer (OC) is a neglected women's cancer. To bridge this gap, early-career cancer researchers might develop and engage in individual initiatives to enhance research outcomes. In this perspective, I recently launched the OVANORDEST project as an individual initiative. This plan outlines a three-step strategy designed to promote OC research, highlighting specific milestones. This abstract presents the findings from the initial feasibility study, which focuses on real-world evidence, implementing inexpensive precision medicine approaches, supporting women in oncology, and enhancing meta-research. **Methods:** Initially, a bibliometric study was conducted to find research gaps in the field of OC in Morocco. A 16-year real-world retrospective study was conducted at the Hassan II Oncology Center (October 2005-June 2020). To implement precision medicine approaches, quality evidence on several potentially inexpensive blood-based biomarkers such as Pan-Immune Inflammation-Value (PIIV) were explored using a PROSPERO-registered umbrella systematic review and then investigated in an original cohort. Cox regression analyses were applied to identify the effects of different biomarkers on survival outcomes. Meta-research was developed by publishing two special thematic issues and one edited book on OC biomarkers. The project also included a mentorship program designed to empower women oncologists. **Results:** A total of 258 patients with OC were included. Most patients had advanced FIGO stages at diagnosis. The median overall survival (OS) for the entire cohort was 32 months, with a median progression-free survival (PFS) of 14.6 months. CA-125 positivity, advanced disease stage, and presence of residual disease after surgery were prognostic factors that adversely affected survival. In the multivariable analysis after adjustment for the FIGO stage, high PIIV was an independent predictive factor of OS (HR= 1.83; 95% CI: 1.18-2.84, p=0.007). Two specialized thematic issues were published alongside a book dedicated to ovarian cancer biomarkers. Additionally, careers of a group of women oncologists were boosted and a local patient advocacy group was supported in adopting supportive strategies for patients. **Conclusions:** Engaging early-career cancer researchers through individual initiatives in under-resourced settings may considerably improve research outcomes. In this context, I propose that sharing this experience, which has been successfully applied in Morocco, could empower health systems and facilitate the generation of research outputs in low- and middle-income countries. Research Sponsor: None.

184 **Poster Session**

Cross-sectional study on the current status of county-level cancer prevention and treatment capabilities in the four southwestern provinces of China. First Author: Chi Du Sr., Dujiangyan People's Hospital, Dujiangyan, China

Background: Lung cancer (LC) stands out as the most prevalent form of cancer in China, and it is also the primary cause of cancer-related mortality. Notably, 42.3% of newly diagnosed cancer patients are identified at the grassroots level each year. In response, the Chinese government is actively promoting tiered diagnosis and treatment approaches. This study aims to evaluate the current state of county-level cancer prevention and treatment capabilities in China, offering suggestion for policy and the standardized pathway development. **Methods:** A cross-sectional study was conducted in 470 district and county (city) hospitals across four provinces in southwest China: Sichuan, Yunnan, Guangxi, and Guizhou, from December 2023 to March 2024. The study was initiated by 13 hospitals, and all participating physicians signed informed consent forms. All analyses were conducted by SPSS 22.0. **Results:** Of the 470 county-level hospitals in China, 151 have a permanent population of over 500,000. 146 counties (198 hospitals) have established cancer specialties. There are 74 medical linear accelerators and 33 cobalt-60 treatment machines. Among them, 63.6% are tertiary hospitals, and 94.9% are public hospitals. 37.4% of hospitals have linear accelerators, and 16.7% have cobalt-60 treatment machines. 89.8% perform TNM staging, 79.1% perform radical surgery, 96.4% perform chemotherapy, 83.2% perform endocrine therapy, 97.5% perform targeted therapy, 87.3% perform immunotherapy, 54.8% perform interventional therapy, and 34.0% perform radiotherapy. Additionally, 56.8% conduct multidisciplinary diagnosis and treatment (MDT), and 37.0% provide palliative care. 83% hospitals have pathology departments, and 46.0% have established cancer centers. 79% hospitals can perform routine pathological diagnosis, and 17.0% can perform genetic testing in-hospital. Imaging departments have conducted CT plain scans in 96.4% of cases, CT enhancements in 87.7%, MRI plain scans in 84.1%, and MRI enhancements in 72.3%. Fibro-bronchoscopy was carried out in 87.2% of cases, and gastrointestinal endoscopy in 84.2%. Morphine injection was accessible in 84.8% of cases, oxycodone in 64.5%, and tramadol in 86.8%. Non-steroidal analgesics were accessible in 88.3% of cases. **Conclusions:** In the southwestern areas of China, the penetration rate of oncology expertise is 31.1%. Most medical institutions offering oncology specialties are tertiary public hospitals. The average number of radiotherapy machines per county or district is 0.16. The development of surgery, oncology, and the imaging is well. Radiotherapy is still in developing, and the genetic testing capacity in-hospital is insufficient. The application of TNM staging is satisfactory. Accessibility to analgesic and anti-inflammatory drugs is well, but the construction of county cancer centers still needs improvement. Research Sponsor: None.

185 Poster Session

Illness uncertainty, coping, and quality of life in patients with advanced cancer and family caregivers: A dyadic study. First Author: Ting Guan, Syracuse University, Syracuse, NY

Background: Illness uncertainty is prevalent among patients with cancer and their family caregivers. While the relationship between illness uncertainty, coping, and quality of life (QOL) has been explored individually for patients or caregivers, it remains largely unexamined within patient-caregiver dyads. Guided by Mishel's Uncertainty in Illness Theory, this study examined the relationships between illness uncertainty, coping, and QOL among patients with advanced cancer and family caregivers. **Methods:** This cross-sectional study analyzed the data from a randomized clinical trial that examined the effects of a dyadic-based intervention on psychological outcomes for patients with advanced cancer and family caregivers. Illness uncertainty, coping, and QOL were measured using the shorten version of the Mishel Uncertainty in Illness Scale for Adult, the Brief Cope, and the Functional Assessment of Cancer Therapy, respectively. The actor-partner interdependence mediation model was used to achieve the aim. **Results:** This study included 484 patient-caregiver dyads, with patients diagnosed with advanced breast (32.4%), lung (29.1%), colorectal (25.4%), and prostate cancer (13.0%). Patients' avoidant coping mediated the relationship between their own illness uncertainty and QOL ($p < .001$). Caregivers' active coping and avoidant coping mediated the relationship between their own illness uncertainty and QOL ($p < .001$). Notably, caregivers' illness uncertainty was positively associated with patients' avoidant coping ($b = 0.113$; $p < .01$). **Conclusions:** This study is one of the first to use a dyadic approach to investigate the relationships between illness uncertainty, coping, and QOL in advanced cancer patients and caregivers. Our findings highlight the importance of viewing patient-caregiver dyads as the unit of care. These findings support targeted interventions offered to both patients and family caregivers to manage their illness uncertainty and improve their QOL. Giving the effect of caregivers' uncertainty on patients' coping, healthcare professionals should advocate for additional psychosocial supports for family caregivers. Clinical trial information: NCT00709176. Research Sponsor: National Cancer Institute; CA107383.

186 Poster Session

Enhancing awareness and efficacy of palliative care consultation through educational intervention among healthcare professionals in a tertiary hospital: A promotional education study. First Author: Youn Seon Choi, Korea University Guro Hospital, Seoul, South Korea

Background: Palliative Care Consultation (PCC) has demonstrated efficacy in augmenting patient quality of life, diminishing hospitalization durations, lowering medical costs, and improving survival outcomes. Despite its benefits, there still remains low awareness of PCC in Korea, with healthcare professionals (HPs) treating terminal cancer patients often lacking knowledge about it. Thus, we aimed to assess the awareness of PCC among HPs in a tertiary hospital, subsequently implementing targeted educational interventions to ascertain their impact through a survey. **Methods:** Face-to-face instructional session focusing on PCC was administered to HPs by palliative care professional. The datasets from pre- and post- education questionnaires of a cohort comparing 120 participants were subjected to analysis. Utilizing t-test, we evaluated the statistical significance of score variations observed before and subsequent to the educational intervention. **Results:** Within the participants, 61.7% of the HPs reported having experience with PCC. Preliminary survey results indicated that 11.8% were "Completely unaware" of PCC, while 37.8% possessed "unaware". The mean scores demonstrated an improvement in knowledge of PCC from 18.04 pre-education to 19.84 post-education. (*P=0.003*). **Conclusions:** Through promotional education, an enhancement in knowledge levels regarding PCC was observed. Emphasizing sustained concern in CPC is essential to ensure that palliative care recipients receive appropriate care at the optimal time. Research Sponsor: None.

187 Poster Session

Association of peripheral edema with immune checkpoint inhibitors: A systematic review. First Author: Kazuya Tsuchiya, 374th Medical Group, The United States Air Force, Yokota Hospital, Japan, Tachikawa City, Japan

Background: Immune checkpoint inhibitors (ICIs) are widely used to treat patients with cancer but immune-related adverse events occasionally disrupt treatments and affect their quality of life. Peripheral edema from ICI therapy appears rare but can occur due to increased peripheral vascular permeability. Thus, we aimed to report the incidence and outcomes of peripheral edema from ICIs. **Methods:** Medline, Embase, and Web of Science were searched to identify phase 3 randomized controlled trials (RCTs) reporting the incidence of peripheral edema in patients treated with ICIs. We calculated the incident rate of peripheral edema based on treatment patterns (monotherapy and combination therapy) and ICI subtypes (PD-1, PD-L1, and CTLA-4 inhibitors). We also performed a systematic review to identify articles reporting treatment outcomes of peripheral edema from ICIs. **Results:** Overall, 60 RCTs comprising 22,590 patients were identified for the incidence analysis. Treatment-related peripheral edema (Grade 1-5) occurred in 2.8% from ICI monotherapy (n = 195/6969; PD-1 inhibitors: 2.2% [n = 104/4694], PD-L1: 3.7% [n = 58/1557], CTLA-4: 4.6% [n = 33/718]), 5.0% (n = 112/2257) from ICI with chemotherapy, and 8.7% (n = 205/2349) from ICI with molecular-targeted therapy. Grade 3-5 treatment-related peripheral edema occurred in 0.3% of patients treated with ICI monotherapy (Table). For treatment outcomes of peripheral edema, a systematic review identified 19 studies (17 case reports/series,1 phase 1/2 clinical trial, 1 pharmacovigilance study) comprising 40 patients with immune-related peripheral edema. In total, 82.5% (n = 33/40) of cases received glucocorticoid treatment, and 55.0% (n = 22/40) required a high dose (≥ 1 mg/kg/day) of prednisone. ICI was discontinued in 77.5% (n = 31/40) due to peripheral edema (permanent discontinuation in 35% [n = 14/40]). **Conclusions:** Peripheral edema occasionally occurs in patients treated with ICIs but its occurrence often requires glucocorticoid administration, which may impact cancer treatment outcomes. Research Sponsor: None.

	Treatment-related				Any-cause			
Peripheral edema	N of patients	N of RCTs	Grade 1-5 N (%)	Grade 3-5 N (%)	N of patients	N of RCTs	Grade 1-5. N (%)	Grade 3-5 N (%)
ICI monotherapy	6969	21	195 (2.8)	21 (0.3)	3354	10	213 (6.4)	3 (0.1)
PD-1	4694	15	104 (2.2)	14 (0.3)	1946	6	124 (6.4)	3 (0.2)
PD-L1	1557	4	58 (3.7)	1 (0.1)	1092	4	88 (8.1)	0 (0)
CTLA-4	718	3	33 (4.6)	6 (0.8)	316	2	1 (0.3)	0 (0)
Dual ICI	684	2	0 (0)	0 (0)	429	2	34 (7.9)	3 (0.7)
PD-1 + CTLA-4	313	1	0 (0)	0 (0)	256	1	27 (10.5)	2 (0.8)
PD-L1 + CTLA-4	371	1	0 (0)	0 (0)	173	1	7 (4.0)	1 (0.6)
ICI + chemotherapy	2257	7	112 (5)	4 (0.2)	4086	10	549 (13.4)	10 (0.2)
PD-1	866	3	77 (8.9)	2 (0.2)	1816	4	266 (14.6)	3 (0.2)
PD-L1	1391	4	35 (2.5)	2 (0.1)	2270	6	283 (12.5)	7 (0.3)
ICI + molecular-targeted therapy	2349	7	205 (8.7)	4 (0.2)	986	4	142 (14.4)	4 (0.4)
PD-1	1025	3	52 (5.1)	2 (0.2)	587	2	72 (12.3)	1 (0.2)
PD-L1	1324	4	153 (11.6)	2 (0.2)	399	2	70 (17.5)	3 (0.8)

188 Poster Session

Efficacy and safety of low-dose versus standard-dose immune checkpoint inhibitor as monotherapy in patients with solid tumors: A meta-analysis and systematic review. First Author: Yu Qian, Hubei Cancer Hospital, Wuhan, China

Background: Immunotherapy is a novel anti-cancer therapy with different mechanisms compared with chemotherapy. Several studies have reported that low dose of immune checkpoint inhibitors (ICIs) is effective. However, it is unknown whether the efficacy of low-dose immunotherapy is inferior to that of standard dose immunotherapy. We aimed to compare the existing randomized clinical trials on the efficacy of immunotherapy at low dose and standard dose as a single agent for patients with solid tumors. **Methods:** We searched PubMed, EMBASE, and the Cochrane Library for randomized clinical trials with the clinical outcomes of low dose and standard dose of programmed cell death-1 (PD-1)/programmed cell death ligand 1 (PD-L1) inhibitor as monotherapy until November 30, 2023. The low dose is defined as lower than the dose approved by FDA. The hazard ratio (HR) and 95% confidence interval (CI) of overall survival (OS) and disease control rate (DCR) were collected. The Stata 15.0 software was used to analyze the data. **Results:** Twenty-two studies with 3226 patients with five ICIs for 22 solid tumors were included. There is no difference in OS (HR 1.12, 95% CI = 0.97-1.31; $p > 0.05$), ORR (Odds ratio (OR) 0.92, 95% CI = 0.76-1.11; $p > 0.05$) and DCR (OR 0.83, 95% CI = 0.65-1.06; $p > 0.05$) for patients with low dose and standard dose of PD-1/PD-L1 inhibitors. **Conclusions:** Our results suggested that PD-1/PD-L1 inhibitor as monotherapy with a low dose may be as effective as standard dose for patients with solid tumors. The regular dose-response relationship may not be appropriate for ICIs. Further work is needed to explore the optimal dose of ICIs based on the comprehensive consideration of efficacy, safety, and economic assessment. Research Sponsor: None.

189 **Poster Session**

Unveiling the impact: Exploring malnutrition rates in patients with cancer and its association with anticancer treatments. First Author: Roshini Pradeep, Midwestern University GME Consortium Residency Program, Cottonwood, AZ

Background: Malnutrition is a common cause of morbidity and mortality in patients with cancer. Malnutrition is seen in 40 to 80% of patients with cancer. Recent literature has shown loss of lean body mass in cancer population can be an independent factor for poorer outcomes. Anorexia, the loss of appetite has been either secondary to the disease itself or as a side effect of treatment. The mechanism of anorexia development is due to physiologic alteration in metabolism during carcinogenesis. Hence, it becomes important to screen for malnutrition in all patients with diagnosis of cancer. **Methods:** This single-center cohort study, conducted between January 15, 2024, and February 9, 2024, involved 106 patients receiving outpatient oncology care. Patients aged 18 to 90 years who consented to participate were administered the Mini Nutritional Assessment (MNA) questionnaire at the oncology registration desk. Exclusion criteria included patients with a dietician and those with pure nonmalignant hematological diagnoses. Data analysis comprised identifying patients at risk of malnutrition (8-11 points) or malnourished (0-7 points) using the MNA scale, followed by retrospective chart review. Primary outcomes focused on identifying prevalent cancer types among malnourished or at-risk patients, while secondary outcomes included comparing malnutrition proportions among different treatment groups and assessing gastrointestinal tract metastases and common causes of malnutrition. **Results:** The data encompassed 106 patients, among whom 29 (27.3%) were identified as at risk of malnutrition, while 9 (8.4%) were malnourished. Notably, a majority of at-risk or malnourished patients (60.5%) were classified as overweight or obese. The most prevalent cancers among these patients were breast cancer (26.3%), genitourinary cancer (23.6%), and gastrointestinal cancer (18.4%). Chemotherapy use was noted in 16 (42.1%) patients, immune checkpoint inhibitor treatment in 12 (31.5%), and a combination of both in 7 (18.4%). Gastrointestinal metastasis was observed in 5 (13.1%) patients. Among those at risk of malnutrition, the primary contributing factors identified were tumor impact and location (63.1%), diarrhea (18.4%), and fatigue (18.4%). **Conclusions:** The study underscores the significant prevalence of malnutrition risk among cancer patients, emphasizing the importance of systematic screening during outpatient oncology follow-ups. Research Sponsor: None.

190 **Poster Session**

Validation of a tagalog version of the EORTC PATSAT-C33 and EORTC OUT-PATSAT7 patient satisfaction questionnaires for patients with cancer undergoing outpatient radiotherapy. First Author: Michelle Regina Castillo, University of the Philippines, Philippine General Hospital, Manila, Philippines

Background: The satisfaction of cancer patients with their care significantly impacts their quality of life. Beyond specific cancer treatments, the delivery of care plays a vital role. Evaluating patient satisfaction with care is increasingly important in oncology due to the prolonged and intensive nature of cancer management. Discussions often focus on medical aspects, neglecting administrative and psychosocial concerns. Patient-centered care involves assessing satisfaction, which reflects perceived quality. Patient satisfaction is now recognized as a key indicator of care quality. **Methods:** The EORTC developed tools like PATSAT-C33 and OUT-PATSAT7 to assess satisfaction with cancer care. These instruments, translated into Tagalog using a "forward-backward" translation procedure in accordance with the EORTC QOL Study Group guidelines, were validated among Filipino cancer patients undergoing radiotherapy. The tools encompass dimensions like doctors' skills, information exchange, nurses' responsiveness, and care organization. They showed reliability and validity comparable to the original versions. **Results:** Construct, criterion, and factorial validity were assessed, indicating the tools measure intended constructs effectively. The multi-item scales of EORTC PATSAT-C33 and EORTC OUT-PATSAT7 have good to excellent internal consistency. A value between 0.8 - 0.9 represents good reliability, whereas a Cronbach alpha of $\geq$0.9 represents excellent reliability. Criterion validity was confirmed by comparing them with a validated Filipino satisfaction scale. Each dimension identified in the original study applies to Filipino cancer patients, suggesting the tools' applicability across populations. **Conclusions:** Despite some demographic biases in the study sample, the translations proved valid and reliable. These Tagalog versions are recommended for use with native Tagalog-speaking Filipino cancer patients. Further studies with larger sample sizes may enhance reliability. Research Sponsor: None.

Reliability of the Filipino translations of EOTC PATSAT-C33 and EOTC OUT-PATSAT7.

Scale	# of items	Item #	Cronbach alpha
EORTC PATSAT-C33			
Doctors technical skills	3	1-3	0.902
Doctors information exchange	3	4-6	0.919
Doctors affective behavior	4	7-10	0.910
Radiotherapy technicians information exchange	3	11-13	0.931
Radiotherapy technicians affective behavior	4	14-17	0.951
Coordination	4	18-21	0.948
Interaction with healthcare professional	7	22-28	0.944
Family involvement	1	29	N/A
Access/parking	1	30	N/A
Access/way	1	31	N/A
Environment	1	32	N/A
Overall care	1	33	N/A
EORTC OUT-PATSAT7			
Convenience	3	35-37	0.924
Transition	3	38-40	0.935
Continuity	1	34	N/A

191 **Poster Session**

Accuracy of gravity based automatic infusion system applied to chemoport for intravenous infusion. First Author: Jonggwon Choi Jr., Konyang University Hospital, Seo-Gu, South Korea

Background: When a vesicant drug is administered to the peripheral vein, a gravity drip method rather than an peristaltic infusion pump is recommended. In addition, it is reported that the gravity based pump has less particle generation than the peristaltic pump that injects fluid through constant peristaltic movement. However, it is pointed out that the disadvantage of gravity based pump is that the rate of administration can easily change according to the change in the location of the injection site. We evaluate the accuracy of new gravity based pump (pressure-sensitive speed control fluid injection device, Accudrip made by Hanvit MD) at various injection rates and hanging heights common to hospital settings. **Methods:** The accuracy and safety of the intravenous (IV) flow controller were evaluated for patients receiving IV chemotherapy in the oncology department. It was verified whether the accurate injection rate could be maintained even in various fluid heights, fluid amounts, and types of anticancer drugs that could affect the injection rate. Various anticancer drugs, including immune checkpoint inhibitor, were mixed with 250 ml/500 ml of normal saline and administered for 30 min/60 min, and glucose 500 ml/1000 ml was administered for 60 min/120 min to measure accuracy, each progressed 25 times. Medical staff were surveyed on the ease and limitations of medical practice for each peristaltic infusion pump and new gravity based pump. In addition, side effects occurring in patients during fluid administration were recorded. **Results:** The mean degree of error in the estimated end time of gravity based automatic infusion system was 3.09% (2.09 ~ 4.10). The error of the gravity based automatic infusion system was statistically significant depending on the patient age (p=.001) and the infusion time (p=.016), but the degree of error according to the type of fluids (p=.302) and fluid concentration (p=.844) was not statistically significant. Among the subjects of the study, nurses' satisfaction with the application of gravity based pump was 4.10 ($\pm$0.62) out of 5, and among the general characteristics of nurses, age (p$<$.078), and working department (p$<$.91) did not show a statistically significant difference, but work experience (p $<$.021) showed a statistically significant difference. **Conclusions:** The accuracy of Gravity based automatic infusion system was determined because the degree of error in the expected end time of infusion was not significant according to the infusion variable. In a survey of nurses who have used gravity based pump directly, it was found that the ease of use and satisfaction were similar to those of the conventional peristaltic pump. These findings will contribute greatly to the precise drug administration (over or under-administration) and minimization of adverse events in real-world hospital settings. Research Sponsor: None.

192 **Poster Session**

PRO-WAVE1: Monitoring patient reported outcomes (PROs) in prostate cancer through Wave Health, a novel ePRO health platform. First Author: Matthew David Lashey, Treatment Technologies and Insights, Inc., El Segundo, CA

Background: It is well established that the monitoring and evaluation of PROs in cancer patients has a positive impact in both quality of life and overall survival [Basch E., JAMA 2017]. In parallel, the widespread use of electronic devices such as smart phones in the general population have increased significantly over recent years [Statista, 2023], representing a unique opportunity to operationalize ePROs. However, there is uncertainty about the feasibility and applicability of these technologies in certain patient population such as prostate cancer (PC) patients. PRO-WAVE1 aims to determine the acceptability, engagement and satisfaction of the Wave Health patient app and healthcare provider portal, enhanced for PC patients. **Methods:** 98 patients across 8 sites in Spain enrolled in the study, and 82 of those patients actively engaged with the Wave Health App over a 13-week period. Each week, patients completed validated ePRO questionnaires (generating 93.3% compliance) consisting of: a weekly symptom review (WSR), FACT-P and CHLT-30-Dkspa. A report summary of the patients' WSR was generated for care team view in the Wave Health Connect platform – specifically to conduct weekly check ins on patients. Further, an optional in-app feedback survey was administered once patients completed the study to measure overall app satisfaction, information usefulness, reduction in anxiety, and effectiveness of communication with medical teams. **Results:** In addition to unusually high compliance and perceived usefulness, there was a particularly high response rate for an optional end of study survey (78%), whereby 64 patients who completed the feedback survey reported remarkable experiences, including: 90% reported being satisfied with the app to track their activities and keep their medical team informed; 95% of patients described the information provided by Wave Health as "useful"; 6 in 10 patients indicated that using Wave Health helped them feel less anxious about their treatment experience; 75% of patients reported that Wave Health helped them track their health and keep their medical team informed. Correspondingly, patients without a caregiver rated the platform higher than those with a caregiver across all areas (information useful/relevancy, communication with care team, likeliness to recommend and overall satisfaction). Additionally, 90% of HCPs positively perceived the platform's impact on the quality of communication with patients. **Conclusions:** The high levels of patient compliance, satisfaction, perceived usefulness, and anxiety reduction associated with the app, along with the high HCP perceived usefulness of the portal, underscore the opportunity to enable better treatment management between HCPs and patients - particularly for those without caregivers. A larger study with a comparator arm will help further evaluate impact on costs and clinical outcomes. Research Sponsor: Bayer AG.

193 **Poster Session**

Acupuncture for patients with cancer in a palliative care team in Japan: A prospective case series study. First Author: Shoko Masuyama, Morinomiya University of Medical Sciences Acupuncture Information Center, Osaka, Japan

Background: In the joint guideline of the Society for Integrative Oncology and ASCO, acupuncture is recommended for general or musculoskeletal pain from cancer, chemotherapy-induced peripheral neuropathy, and other conditions. However, Japanese acupuncture needles are thinner and less stimulating than those used in other countries. To assess whether adding Japanese-style acupuncture to usual palliative care alleviates subjective symptoms in hospitalized cancer patients, we conducted a prospective case series study at an urban core hospital in Japan. **Methods:** Acupuncture treatment was administered to participating cancer patients once or twice a week, for a maximum of six sessions over three weeks. Each treatment session lasted approximately 30 minutes. Patients in the study continued to receive standard care. The main outcome measure was the change in the 10 cm visual analog scale (VAS) for the primary subjective symptoms immediately after treatment. We regarded a reduction in VAS of 20% or more as a minimal clinically important difference (MCID). The protocol of the study was approved by the Clinical Research Ethics Committee of Osaka General Medical Center (CRB5180013). **Results:** During the study period, 83 cancer patients gave written consent to receive acupuncture treatment. The mean age was 66.1 years (SD 10.7), with 66% of patients in stage 4, and 70% using opioids. Significant reductions in VAS scores for subjective symptoms were observed immediately after treatment for pain (1st session: from 5.4 to 3.9 on average, $P<0.001$; 2nd: 4.9 to 3.4, $P<0.001$; 3rd: 3.9 to 2.6, $P<0.001$; 4th: 4.7 to 2.8, P=0.002), edema (2nd: 5.5 to 3.7, $P<0.001$), paresthesia (2nd: 6.2 to 4.6, P=0.005), nausea (1st: 6.5 to 3.9, P=0.012; 2nd: 3.3 to 2.0, P=0.008), stiffness (1st: 6.8 to 3.1, P=0.011; 2nd: 4.3 to 2.8, P=0.022), and breathing difficulty (1st: 5.9 to 3.2, P=0.012). However, there was no significant improvement in malaise across any sessions. The maximum percentages of patients experiencing symptom relief beyond MCID in pain, edema, paresthesia, nausea, stiffness, and breathing difficulty were 67%, 75%, 60%, 80%, 88%, and 83%, respectively, across the treatment sessions for each symptom. There was no significance in odds ratios for age, sex, previous acupuncture experience, or opioid use associated with clinically meaningful pain reduction. All recorded adverse events were mild and transient. **Conclusions:** The symptom relief observed in this study is only a short-term effect immediately after treatment and includes non-specific effects such as the placebo effect. Future research should explore the specific effects of acupuncture using an exploratory trial design. However, determining the appropriate control group for acupuncture trials remains controversial. At least from a clinical perspective, acupuncture may be a possible option for palliative care for cancer patients, including in Japan. Research Sponsor: None.

194 **Poster Session**

Identifying risk factors associated with self-reported lower quality of life (QoL) in individuals with PTEN hamartoma tumor syndrome. First Author: Terralyn Schmidt, Pten Hamartoma Tumor Syndrome Foundation, Hampton Cove, AL

Background: PTEN Hamartoma Tumor Syndrome (PHTS) is a multisystem disorder that affects various organs and systems in the body, presenting with a range of clinical manifestations. Individuals with PHTS face elevated risks of cancer and neurological symptoms, along with significant physical and psychological challenges, which underscores the need for ongoing research and the development of effective management strategies. The purpose of this study is to identify risk factors that are associated with a lower self-reported quality of life in individuals with PHTS using quantitative data from the PTEN Hamartoma Tumor Syndrome Foundation's patient registry surveys. **Methods:** Spearman correlation analysis of survey answers from 232 registry members in the foundation revealed negative correlations between quality of life and clinical features such as autism spectrum disorder (-.20**) and cancer diagnoses (-.21**). **Results:** This suggests that the more severe and penetrant cases of PHTS on the spectrum of variability face challenges that negatively impact quality of life. Additionally, 72.6% of participants reported that reducing cancer risk is a top priority. **Conclusions:** The findings highlight the need for healthcare providers to anticipate the need for extra care and psychosocial attention for individuals with PHTS who have an autism diagnosis, and to provide education and counseling about cancer prevention strategies to those with a heightened cancer risk. Research Sponsor: None.

Spearman correlates of reported patient quality of life (n = 62 - 203).

	Quality of Life
Gender (Female)	-.14
Income	.46***
Diagnosis, Autism	-.20**
Diagnosis, Cancer	-.21**
Number, Cancer Diagnoses	-.30*
PHTS Syndrome	
BRRS	.05
Cowden Syndrome	-.01
Cowden-like Syndrome	.03

*p ≤ .05, **p ≤ .01, ***p ≤ .001.

195 Rapid Oral Abstract Session

Efficacy and safety of olomorasib (LY3537982), a second-generation KRAS G12C inhibitor (G12Ci), in combination with pembrolizumab in patients with *KRAS* G12C-mutant advanced NSCLC. First Author: Yutaka Fujiwara, Aichi Cancer Center Hospital, Aichi, Japan

Background: While immunotherapy (IO) is established as the cornerstone of first-line treatment for *KRAS*-mutant NSCLC, outcomes remain suboptimal. Further progress may be achieved with the addition of targeted therapy to IO, an established first-line paradigm in some other cancer types (RCC), but historically challenging in NSCLC. Here, we study pembrolizumab plus olomorasib, a potent and highly selective second-generation inhibitor of GDP-bound KRAS G12C, in NSCLC patients treated on LOXO-RAS-20001, a phase 1/2 study of olomorasib in *KRAS* G12C-mutant solid tumors (NCT04956640). **Methods:** Patients (pts) with advanced *KRAS* G12C mutant NSCLC (tissue or plasma) in any treatment line, including prior KRAS G12Ci and/or prior IO were eligible. Dose escalation of olomorasib plus pembrolizumab followed a mTPI-2 method. Safety was evaluated across all pts dosed with the combination. Antitumor activity per RECIST v1.1 was studied in all pts who had ≥1 post-baseline response assessment (PBRA) or had discontinued before the first PBRA. **Results:** As of 30 October 2023, 50 pts with advanced NSCLC received 50-150 mg BID PO olomorasib plus 200 mg Q3W pembrolizumab. Median age was 66 yrs (range, 42-83), median number of prior systemic therapies was 2 (range, 0-8), and 34% had received a prior KRAS G12Ci. During escalation, 2 of 6 ptstreated at 150 mg BID developed grade ³3 LFTs, precluding further evaluation of this dose. In 44 pts treated at 50 or 100 mg BID, TRAEs ≥10% (related to olomorasib and/or pembrolizumab) were diarrhea (30%), ALT increased (20%), AST increased (18%), fatigue (14%), nausea (14%) and pruritus (11%); grade 3 TRAEs in ≥10% of pts were diarrhea (16%); pneumonitis was seen in 3 pts (grades 2/3/4). TRAEs led to olomorasib dose reduction in 14% of pts, olomorasib dose hold in 27%, and pembrolizumab dose hold in 18%. Due to TRAEs, 9% of pts discontinued olomorasib or pembrolizumab and 9% discontinued both. 27 pts remain on treatment, and 17 discontinued treatment (10 due to PD, 4 due to AE). Among the 30 efficacy evaluable KRAS G12Ci-naïve pts (60% IO pre-treated, 60% chemotherapy pre-treated), at a median follow-up of 6 months (95% CI, 4-7) ORR was 63% (15 PR, 4 unconfirmed PR pending/ongoing; 95% CI, 44-80) and DCR was 93% (28/30; 95% CI, 78-99); the median PFS was not estimable (95% CI, 5-NE); ORR was 75% (9/12) in PD-L1 ≥50%, 56% (10/18) in PD-L1 <50%/unknown (3 pts PD-L1 unavailable). In 9 first-line pts, ORR was 78% (6 PR, 1 unconfirmed PR pending/ongoing; 95% CI, 40-97) and DCR was 100%. **Conclusions:** Olomorasib (50 or 100 mg BID) in combination with pembrolizumab demonstrated favorable safety and antitumor activity in pts with *KRAS* G12C-mutant advanced NSCLC, supporting further development in first-line NSCLC. A global, registrational study investigating this combination in first-line NSCLC is currently enrolling (SUNRAY-01, NCT06119581). Clinical trial information: NCT04956640. Research Sponsor: Eli Lilly and Company.

196 Rapid Oral Abstract Session

Accuracy of detecting residual disease after neoadjuvant chemoradiotherapy for esophageal squamous cell carcinoma (preSINO trial): A prospective multicenter diagnostic cohort study in Asia. First Author: Zhigang Li, Department of Thoracic Surgery, Section of Esophageal Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China

Background: The benefit of standard esophagectomy in patients with clinical complete response (cCR) after neoadjuvant chemoradiotherapy (nCRT) is disputable and the alternative of active surveillance should be studied. PreSANO study demonstrated that clinical response evaluations (CREs) are accurate to detect residual tumor after nCRT in patients with mainly adenocarcinoma, however, its applicability to esophageal squamous cell carcinoma (ESCC) is unknown. The preSINO trial (NCT03937362) aimed to assess the accuracy of CREs based on bite-on-bite biopsy, endoscopic ultrasonography with fine needle aspiration (EUS-FNA) of suspected lymph nodes, PET-CT in patients with ESCC, and to provide a basis for organ-sparing strategy of ESCC in Asia. **Methods:** Patients were eligible when they were planned for nCRT (CROSS regimen) followed by standard surgery. Patients received the first CRE (bite-on-bite biopsies) 4-6 weeks after completion of nCRT. Patients with locoregional residual tumor and without distant metastases underwent immediate surgery. In patients with a cCR at CRE-1, a second CRE (CRE-2) was done 10-12 weeks after completion of nCRT using PET-CT, bite-on-bite biopsies and EUS-FNA of suspicious lymph nodes. All patients underwent surgery irrespective of the outcome of CRE-2, in the absence of distant metastases. Circulating tumor DNA (ctDNA) analyses based on tumor-informed assay were performed at baseline and CREs for exploratory analysis. Primary endpoint was the accuracy of CREs for detecting TRG3-4 or TRG1-2 with ypN+ residual tumor. A false-negative rate (FNR) of 19.5% was considered acceptable according to the study protocol. **Results:** From Aug 20, 2019, to Jan 15, 2023, 309 patients were included of whom 250 patients underwent nCRT plus surgery. Eighteen of 133 patients with TRG3-4 or TRG1-2 with ypN+ residual tumor were not detected by bite-on-bite biopsies and EUS-FNA (FNR: 13.5%). Sensitivity, specificity, negative predictive value and positive predictive value of detecting any residual tumor were 82%, 93%, 69% and 97%, respectively. PET-CT detected interval distant metastases in 13 (5%) of 268 patients prior to surgery. Postoperative distant recurrence rate among patients with ctDNA-positive and ctDNA-negative during CREs were 15.1% (11/73) and 3.3% (2/59), respectively. **Conclusions:** Bite-on-bite biopsies and EUS-FNA for lymph nodes were accurate for detecting locoregional residual disease after nCRT in patients with ESCC. Post-nCRT ctDNA-positive during CREs may indicate an increased risk of long-term distant metastasis, potentially serving as a diagnostic tool to identify patients who would benefit from postponement of surgery and additional systemic therapy. The long-term follow-up results of this trial will further answer this question. Clinical trial information: NCT03937362. Research Sponsor: Shanghai Chest Hospital; YJXT20190202.

197 Rapid Oral Abstract Session

Assessing the efficacy and safety of a novel, registration-free, CT-guided percutaneous transthoracic needle biopsy navigation system (RC120): A multicenter, prospective, single-arm clinical trial. First Author: Caicun Zhou, Shanghai Pulmonary Hospital, School of Medicine, Tongji University, Shanghai, China

Background: Current optical and electromagnetic navigation systems for CT-guided percutaneous transthoracic needle biopsies (PTNB) have limitations. They require surface markers on the patient and intraoperative registration. Specific patient positioning during biopsies is required. Our team developed a new navigation system that addresses these issues. It doesn't rely on patient surface markers or intraoperative registration, and it provides more flexibility in patient positioning during biopsies. Our research evaluates the effectiveness and safety of this system. **Methods:** A single-arm prospective study was conducted, including participants aged 18-80 years prepared for percutaneous lung core biopsy at two clinical centers in China. The primary endpoint was the success rate of biopsies within 2 needle adjustments. The secondary endpoint was the success rate of biopsies within a single needle adjustment. Safety endpoints were defined by the occurrence of adverse events. The number of CT scans patients underwent during the procedure was used to assess radiation dosage. Follow-up was conducted on subsequent pathological and molecular diagnoses. **Results:** The study included 98 patients from two sites, with a median age of 64 years. Most participants were males, accounting for 72.45% (71 out of 98). The primary endpoint was achieved with a biopsy success rate of 98.98%, requiring a maximum of two needle adjustments. The secondary endpoint was met, demonstrating a biopsy success rate of 97.96% with a maximum of one needle adjustment. The overall success rate was 98.98%, with a 95% confidence interval (CI) of 94.45% to 99.97%, significantly exceeding the target value of 85% ($P < 0.0001$). The median number of CT scans was 3, ranging from 3 to 12. The average duration of the procedure was 18.0 minutes. Regarding safety endpoints, the two most common adverse events were hemorrhage in the lesion (14 instances, 29.17%) and pneumothorax (8 instances, 16.67%). Other adverse events included elevated blood pressure (5 instances, 10.42%), hemoptysis (4 instances, 8.33%), and other common adverse events such as cough, constipation, anemia, and bloody sputum, each occurring twice. There were 9 other less common adverse events, each occurring once. These adverse events are common in PTNB and can be attributed to the puncture operation itself, not our navigation system. **Conclusions:** Our new registration-free navigation system proved to be an effective, efficient, safe, and well-utilized system for assisting percutaneous lung biopsies in clinical practice. Clinical trial information: ChiCTR2300072197. Research Sponsor: Shanghai Simple Touch Technology; Key projects of the National Natural Science Foundation of China; 82141101; Collaborative innovation project of Shanghai Municipal Health Commission; 2020CXJQ02; National Natural Science Foundation of China; 82102766; Shanghai Key Clinical Specialty Construction Project of Shanghai Municipal Health Commission; The establishment and application of a multidisciplinary collaborative diagnosis and treatment system of Shanghai Municipal Health Commission; Key Cultivation project of Shanghai Pulmonary Hospital; fkzr2001; The key discipline of oncology of Shanghai Pulmonary Hospital; Shanghai Pulmonary Innovation Research Group Project; FKLY20001.

198 Poster Session

A phase 2, open-label, single-arm study evaluating the combination of pembrolizumab (pembro), lenvatinib, and chemotherapy in patients (pts) with metastatic non-small cell lung cancer (NSCLC) harbouring a targetable mutation who experienced disease progression on standard tyrosine kinase inhibitors (TKIs). First Author: Hoi Wai Chan, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong, Hong Kong

Background: Pts with metastatic NSCLC harbouring a targetable mutation who progressed on standard TKIs often receive chemotherapy as the next line of treatment. We report efficacy and safety of a novel combination of pembro, lenvatinib and chemotherapy for these pts. **Methods:** This was a phase 2, open-label, single-centre, single-arm study enrolling pts with metastatic NSCLC with sensitizing EGFR, ALK or ROS1 mutation who progressed on standard TKIs. Eligible pts had measurable disease, no untreated brain metastasis and ECOG PS ≤1. Pts received pembro 200 mg, pemetrexed 500 mg/m^2 and carboplatin AUC 5 every 3 weeks for 4 cycles plus lenvatinib 8 mg QD. The maintenance regimen without carboplatin was continued as tolerated for up to 2 years. The primary endpoint was objective response rate (ORR) by independent radiology review (IRR) as per RECIST 1.1. The secondary endpoints were PFS, overall survival (OS) and safety. **Results:** At the data cutoff date (2nd February 2024), 24 pts were screened and 19 were enrolled: median age 64 years (range 29–77); 10 (53%) female. Four pts were excluded at screening due to untreated brain metastasis. All enrolled pts were evaluated for safety while 15 pts were evaluable for response. All pts had adenocarcinoma with targetable mutation: EGFR mutation in 18 (95%) pts and ALK fusion in 1 (5%) pt. The median follow-up time was 11.3 months. Treatment was ongoing in 8 pts on the date of analysis, while 6 pts permanently discontinued due to disease progression and 1 pt permanently discontinued due to a treatment-related adverse event (TRAE). The ORR was 40% (6/15, 95% CI 19.8%–64.3%). All responses were partial responses. The median PFS was 11.9 months (range 3.5–20.3). The OS was not reached. TRAEs of any grade (Gr) occurred in 74% (14/19) of the pts. Most of the TRAEs were Gr 1–2, which occurred in 63% (12/19) of the pts. The most common TRAEs were hypothyroidism (31.6%), nausea (26.3%), neutropenia (26.3%), thrombocytopenia (26.3%), anorexia (21.1%), hypertension (15.8%), anaemia (10.5%), pruritus (10.5%) and rash (10.5%). G1 diarrhoea was reported in 1 pt (5.3%) and G1 adrenal insufficiency in 1 pt (5.3%). Gr 3 TRAEs were neutropenia in 2 pts, anaemia in 1 pt and thrombocytopenia in 1 pt. The only Gr 4 TRAE was thrombocytopenia. No treatment related death was observed. **Conclusions:** The combination of pembro, lenvatinib and chemotherapy demonstrated a favourable ORR and safety in treating metastatic NSCLC pts with a targetable mutation who progressed on standard TKIs. Clinical trial information: NCT04989322. Research Sponsor: Research Grants Council, University Grants Committee, Hong Kong; 17126819.

199 **Poster Session**

Intracranial outcomes of 1L selpercatinib in advanced *RET* fusion-positive NSCLC: LIBRETTO-431 study. First Author: Minji Uh, Loxo@Lilly, Indianapolis, IN

Background: Selpercatinib is a highly selective and potent CNS active *RET* inhibitor approved for treatment of advanced *RET* fusion-positive (*RET*+) NSCLC. Treatment or prevention of CNS disease is critical in *RET*+ NSCLC patients (pts), who have nearly a 50% lifetime prevalence of brain metastases (mets) (Drilon et al. JTO 2018). LIBRETTO-431 is the first study to compare intracranial (IC) efficacy of a targeted therapy to chemo/IO in pts with oncogene driven NSCLC. **Methods:** LIBRETTO-431 (NCT04194944) is a randomized, open-label, phase 3 trial comparing 1L selpercatinib vs chemotherapy (cisplatin/carboplatin + pemetrexed) +/- pembrolizumab. As previously reported, the study met its primary endpoint of PFS by blinded independent central review (BICR) at the pre-planned interim analysis. IC analyses included CNS and non-CNS PD, IC PFS and IC responses by BICR per RECIST 1.1 in all pts who had a baseline and one or more post-baseline CNS scans (CNS-evaluable) and were designated to receive pembrolizumab if randomized to the control arm (CNS-pembro population). Adverse events were evaluated in the CNS safety population. **Results:** A total of 192 of 261 pts enrolled were CNS-evaluable (selpercatinib: 120, control: 72). Baseline characteristics were generally balanced with the selpercatinib arm having a slightly lower proportion of pts with BICR-assessed baseline brain mets (21% vs 25%) and prior CNS radiotherapy (RT; 6% vs 10%) compared to the control arm. Selpercatinib delayed CNS PD as evidenced by a lower 12 mo cumulative incidence rate (CIR) for CNS PD, as well as delaying non-CNS PD compared to control in pts with and without brain mets (Table). In pts with measurable brain mets at baseline (n=29), median time to IC response per RECIST 1.1 was similar between selpercatinib and control (1.4 mo [range: 1.2-2.9] vs 1.6 mo [range: 1.2-2.9]); however, as previously reported the IC response rates were higher (82% vs 58%) and more durable (12 mo DOR rate 76% vs 63%) with selpercatinib vs control (Zhou et al. NEJM 2023). IC responses to selpercatinib were more common in pts without prior CNS RT (14/15, 93%) than with prior CNS RT (3/6, 50%). **Conclusions:** Selpercatinib delayed IC progression in advanced *RET*+ NSCLC pts with or without baseline brain mets and achieved higher IC response rates compared to chemotherapy + pembrolizumab. LIBRETTO-431 is the first study to demonstrate IC efficacy improvement of a targeted therapy vs chemo/IO in a biomarker selected NSCLC population. These data further support selpercatinib as the preferred 1L regimen in pts with advanced *RET*+ NSCLC. Clinical trial information: NCT04194944. Research Sponsor: Loxo@Lilly, a wholly owned subsidiary of Eli Lilly and Company.

Cumulative incidence rates at 12 mo.

	Site of PD	Selpercatinib 12 mo CIR	Control 12 mo CIR	Cause-specific HR for first event (95% CI)
Pts without brain mets at baseline (n=150)	CNS PD	1%	15%	0.17 (0.04 - 0.69)
	non-CNS PD	20%	36%	0.45 (0.15 -1.36)
Pts with brain mets at baseline (n=42)	CNS PD	26%	33%	0.61 (0.19 - 1.92)
	non-CNS PD	22%	34%	0.48 (0.27 - 0.84)

200 **Poster Session**

Preliminary analysis of PD-1 inhibitors combined with chemotherapy as neoadjuvant therapy for local advanced non-small cell lung cancer (NSCLC). First Author: Hongru Li, Fujian Provincial Hospital, Fuzhou, Fujian, China

Background: The benefits of neoadjuvant immunotherapy and chemotherapy for resectable NSCLC suggest that this combined treatment may provide more surgical opportunities and survival benefits for potentially resectable locally advanced NSCLC. **Methods:** We retrospectively collected data from 28 patients with stage III EGFR/ALK/ROS wild-type NSCLC. Eligible patients received 2-8 cycles of neoadjuvant chemo-immunotherapy (squamous carcinoma: PD-1 inhibitor combined with albumin-bound paclitaxel and cisplatin/carboplatin; adenocarcinoma: PD-1 inhibitor combined with pemetrexed and carboplatin), followed by re-evaluation for surgery. Afterwards, patients underwent surgery after downstaging, with some receiving adjuvant immunotherapy maintenance for one year. Primary endpoints included major pathological response (MPR), pathological complete response (pCR), progression-free survival (PFS), and overall survival (OS). **Results:** All 28 patients were male, with 7 (25%) in stage IIIA, 10 (35.7%) in IIIB, 4 (14.3%) in IIIC, 2 (7.14%) in IVA, and 2 (7.14%) in IVB. There were 22 cases of squamous cell carcinoma, 4 of adenocarcinoma, 1 of large cell lung cancer, and 1 of lymphoepithelioma-like carcinoma. 23 patients (82.1%) completed neoadjuvant treatment and underwent resection, achieving 100% R0 resection rate (23/23); 5 patients did not undergo surgery, 3 of whom received combined radiochemotherapy due to disease progression, 1 delayed surgery due to immunotherapy associated myocardial damage, and 1 died from massive hemoptysis and hemorrhagic shock. The objective response rate (ORR) was 60.7%, 95%CI [40.6-78.5%] and the disease control rate (DCR) was 85.7%, 95%CI [67.3-96.0%]. Among the 23 patients who underwent surgery, the pCR was 60.9%, 95%CI [38.5-80.3%], MPR was 4.3%, 95%CI [0.1-21.9%], clinical downstaging rate was 50%, 95%CI [30.6-69.4%] and pathological downstaging rate was 86.9%, 95%CI [66.4-97.2%]. 17 patients (77.3%) underwent lobectomy, and 5 (22.7%) underwent bilobectomy with a median blood loss of 100 ml, IQR [55.0-100]. There were no surgery-related deaths. Postoperatively, one patient developed chylothorax, one had a lung infection, and the two improved after conservative treatment. 11 patients (47.8%) received post-surgery immunotherapy maintenance, and 2 of them (8.7%) developed immune-related pneumonia. As of April 7, 2024, the median follow-up time was 21.5 months (95%CI: 17-34 Mo), At 12 months。 PFS rate was 82.1% (95%CI: 69.1-97.6%); OS rate was 96.3% (95%CI: 89.4-100%). **Conclusions:** Neoadjuvant immunotherapy combined with surgery for unresectable locally advanced NSCLC may benefit patients and significantly extend survival. Research Sponsor: Natural Science Foundation of China; the Natural Science Foundation of Fujian Province; Fujian Provincial Medical Science and Technology Innovation Joint Fund.

201 **Poster Session**

Outcomes of EGFR, ALK, ROS1, BRAF, MET, and RET mutated non-small cell lung cancer with brain metastases (NSCLC BM). First Author: Xiaoyan Li, Beijing Tian Tan Hospital, Capital Medical University, Beijing, Fengtai District, China

Background: Non-small cell lung cancer (NSCLC) is a leading cause of brain metastases. Advances in gene-directed therapies have shifted the focus away from traditional platinum-based chemotherapies. Key targeted mutations in NSCLC include EGFR, ALK, BRAF, MET exon skipping, RET fusions, and ROS1 rearrangements. This retrospective study aims to explore overall survival (OS) and progression-free survival (PFS) in NSCLC BM patients with these gene mutations. **Methods:** In this retrospective study, conducted by the Department of Medical Oncology at Beijing Tiantan Hospital and the First Medical Center, PLA General Hospital, we reviewed 1526 patients with NSCLC brain metastasis from 2010 to 2022. Data collected included molecular marker status, systemic therapies, and dates of progression. The analysis focused on determining OS and PFS from the time of brain metastasis diagnosis to the last follow-up or death. Statistical analysis used the Cox proportional hazards model. **Results:** The study reviewed 1526 patients, identifying the following mutation distribution: EGFR mutations in 628 patients, ALK rearrangements in 207 patients, ROS1 rearrangements in 64 patients, BRAF mutations in 31 patients, MET exon skipping in 55 patients, and RET fusions in 42 patients. Significant variations in median OS (mOS) and median PFS (mPFS) were observed across these mutation groups. Patients with EGFR and ALK mutations demonstrated longer mOS and mPFS. Patients with RET and ROS1 mutations also showed better outcomes compared to those with BRAF and MET mutations. **Conclusions:** This study highlights the importance of molecular mutations in NSCLC BM as prognostic indicators and therapeutic targets. EGFR and ALK mutations were associated with more favorable outcomes, emphasizing the need for personalized medicine in managing NSCLC BM. The study suggests further research focused on specific mutation types is crucial to refine treatment strategies and improve patient care. Research Sponsor: Beijing Natural Science Foundation; 7242007.

202 **Poster Session**

Differential expression in potential therapeutic target protein by treatment in small cell lung cancer with and without transformation. First Author: Saori Murata, Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan

Background: Small cell lung cancer (SCLC) is a disease with a poor prognosis. Besides combination strategy with immune checkpoint inhibitors (ICIs) and cytotoxic agents, antibody-drug conjugates (ADCs) and bispecific T-cell engagers (BiTE) are being developed. These drugs target tumor-associated surface protein. Whether prior treatment affect the transition of protein expression has not been fully investigated especially in the era of ICIs. The purpose of this study is to evaluate changes in protein expression in SCLC tissues before and after treatment. **Methods:** We included patients diagnosed with SCLC by surgery or biopsy and underwent re-biopsy after treatment (non-transformed group) at the National Cancer Center Hospital between 2014 and 2023. Patients who were initially diagnosed with non-small cell lung cancer and underwent transformation to SCLC (transformed group) were also included. Tissues were obtained by surgery, bronchoscopy, or CT-guided biopsy with an interval of at least 100 days. We investigated clinicopathological features in paired specimens focusing on DLL3, ASCL1, NEUROD1, POU2F3, and YAP1, which have been reported to be expressed in SCLC, as well as tumor-associated surface proteins potentially related to novel drug development. **Results:** Fourteen non-transformed group cases and 9 transformed group cases were included. Of these, pathology specimens were evaluable in a total of 15 cases: 9 for the non-transformed group and 6 for the transformed group. The median age was 68 years, 11 (73%) were male, 11 (73%) were smokers, 8 (53%) were in clinical stages I-IIIA, 1 (7%) in stages IIIB and 6 (40%) in stage IV. Among the transformed group, 4 of them were treated by Osimertinib before transformation. Progression free survival from first-line therapy was 298 days (255-446) vs. 314 days (245-NA) and overall survival was 1239 days (567-NA) vs. NA days (517-NA), respectively for non-transformed group and transformed group. For both these group of cases, we have evaluated several protein expressions as described above. The transition of these proteins within each group is presented in the conference. **Conclusions:** In this study, we focused not only on proteins already reported to be expressed in SCLC, but also on proteins that are potential new therapeutic targets and evaluated changes in protein expression. Research Sponsor: None.

Patient characteristics.

		All n=15	Non-transformed n=9	Transformed n=6
Age, median		68	68	61
Sex (Male)		11 (73%)	8 (89%)	3 (50%)
Smoking		11 (73%)	9 (100%)	2 (33%)
Surgery		5 (33%)	3 (33%)	2 (33%)
Driver mutation	ND	6 (40%)	6 (67%)	0 (0%)
	Negative	4 (27%)	3 (33%)	1 (17%)
	EGFR	5 (33%)	0 (0%)	5 (83%)
Osi before biopsy		4 (27%)	0 (0%)	4 (67%)
ICI before biopsy		2 (13%)	1 (11%)	1 (17%)

TKI: tyrosine kinase inhibitors, ICI: immune checkpoint inhibitors, Osi: Osimertinib.

203 Poster Session

Feasibility of pretreatment FDG PET radiomics in predicting circumferential margin involvement for esophageal cancer after neoadjuvant concurrent chemoradiotherapy. First Author: Wei-Chih Shen, Artificial Intelligence Center, Chung Shan Medical University Hospital, Taichung, Taiwan

Background: Involvement of circumferential resection margin (CRM) proves to be a valuable factor in predicting prognosis for patients with esophageal cancer. This study aimed to explore the feasibility of using pretreatment ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) in predicting CRM involvement for patient received neoadjuvant concurrent chemoradiotherapy (CCRT). **Methods:** We retrospectively enrolled patients with esophageal cancer who received neoadjuvant CCRT followed by radical surgery between October 2013 and July 2023. All patients received FDG PET/CT examinations before CCRT. The maximum standardized uptake value (SUV_{max}) within a tumor was identified, and the metabolic tumor volume (MTV) was calculated by using a fixed SUV threshold method (50 % of SUV_{max}). Descriptive features and five groups of radiomic features (Gray Level Co-occurrence Matrix [GLCM], Gray Level Dependence Matrix [GLDM], Gray Level Run Length Matrix [GLRLM], Gray Level Size Zone Matrix [GLSZM], and Neighboring Gray Tone Difference Matrix [NGTDM]) were further calculated to describe the heterogeneity of the FDG uptakes within MTV. The CRM involvement status was defined by the Royal College of Pathologists (RCP). Tumor presence at or within 1 mm of the cut margin was considered CRM positive. Finally, we used the area under the receiver operating characteristic curve (AUC) to evaluate the predictive performance of radiomic features for CRM. The significance level was set to 0.05. **Results:** A total of 71 cases of esophageal tumors, encompassing data from 70 patients were included. Of the 70 patients, 94% were male with a mean age 58 years across the entire cohort. Sixteen tumors were proved as CRM positive (16/71, 22.5%). Finally, 2 descriptive features and 10 radiomic features were selected that can effectively predict CRM status. These ten radiomic features exhibit robust predictive power for CRM status, demonstrating significance across various discretization bin number. The best performing feature is Skewness (AUC=0.716, p-value$<$0.0001). **Conclusions:** This preliminary result revealed that CRM involvement for esophageal cancer tumors could be predicted by using radiomic features. Future studies are warranted for clinical application. Research Sponsor: None.

Predictive performance of radiomic features for circumferential resection margin involvement.

Categories	Features	AUC	p-value
Descriptive	Kurtosis	0.690	0.003
	Skewness	0.716	0.000
GLCM	Cluster Shade	0.656	0.015
	Joint Average	0.315	0.004
	Sum Average	0.320	0.007
	Autocorrelation	0.309	0.004
GLDM	High Gray Level Emphasis	0.313	0.004
GLRLM	Short Run High Gray Level Emphasis	0.325	0.009
	High Gray Level Run Emphasis	0.317	0.005
	Long Run High Gray Level Emphasis	0.319	0.007
GLSZM	High Gray Level Zone Emphasis	0.316	0.006
	Small Area High Gray Level Emphasis	0.347	0.027

204 Poster Session

Dietary pattern and the corresponding gut microbiome in response to immunotherapy in Thai patients with advanced non-small cell lung cancer (NSCLC). First Author: Piyada Sitthideatphaiboon, Faculty of Medicine, Chulalongkorn University and The King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Background: Gut microbiota is considered a key player modulating the response to immune checkpoint inhibitors (ICI) in cancer. The effects of dietary pattern on this interaction is not well-studied. **Methods:** A prospective multicenter cohort of 95 patients with advanced non-small cell lung cancer (NSCLC) undergoing ICI therapy were enrolled. Stool shotgun metagenomic sequencing was performed. Three-day dietary patterns before ICI were assessed. Patients were categorized as hyperprogressive disease (HPD) if they exhibited a time to treatment failure of $<$2 months. All others were categorized as non-hyperprogressive disease (non-HPD). The correlation between dietary patterns, gut microbiome, and response to ICI therapy was analyzed. **Results:** In the multivariate analysis, high abundance of *Firmicutes unclassified* and the Ruminococcaceae family correlated with significantly diminished progression-free survival (PFS) with HR of 2.40 [*P*=0.006] and 4.30 [*P*=0.005], respectively. More specifically, within the subset of NSCLC patients treated solely with ICI therapy, high abundance of *Intestinimonas* and the Enterobacteriaceae family were associated with reduced PFS with HR of 2.61 [*P*=0.02] and HR 3.34 [*P*=0.005], respectively. In dietary pattern analysis, HPD group showed increased consumption of cholesterol, sodium, and fats beyond recommended levels compared to non-HPD group. This group also displayed a tendency towards higher food pattern scores characterized by significant intake of fat and dairy products. **Conclusions:** Our study revealed distinct association between the gut microbiome composition and treatment outcomes. Based on these findings, the overall composition of diet may play a pivotal role in ICI therapeutic outcomes. Research Sponsor: the National Research Council of Thailand (NRCT); N35A660426; Rachadapisek Sompote Matching fund; RA-MF-04/67; the National Research Council of Thailand; N35E660102.

Univariate and multivariate analyses of PFS.

	Univariate		Multivariate	
Variables[a]	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (<60/≥60)	1.43 (0.75 – 2.76)	0.28		
Gender (male/female)	0.85 (0.42 – 1.70)	0.64		
ECOG PS (≥2/0-1)	1.10 (0.34 – 3.56)	0.88		
Smoking (ever/never)	0.74 (0.39 – 1.41)	0.36		
Histology (SQ/non-SQ)	1.49 (0.63 – 3.56)	0.37		
Brain metastasis (yes/no)	0.48 (0.21 – 1.07)	0.07	0.42 (0.18 – 1.01)	0.05
Liver metastasis (yes/no)	1.94 (0.75 – 5.01)	0.17		
PD-L1 expression (negative/positive)	1.20 (0.60 – 2.38)	0.61		
Line of ICI (later/first)	1.93 (0.99 – 3.72)	0.05	1.29 (0.63 – 2.61)	0.49
Type of ICI (single/combo)	1.59 (0.86 – 2.94)	0.14		
Received antibiotics (yes/no)	0.87 (0.35 – 2.20)	0.77		
Abundance of *Firmicutes unclassified* (above/below median)	2.04 (1.13 – 3.69)	**0.02***	2.40 (1.28 – 4.50)	**0.006***
Abundance of Alphaproteobacteria family *(GGB6612)* (above/below median)	3.92 (1.16 – 13.24)	**0.03***	1.27 (0.29 – 5.51)	0.72
Abundance of Ruminococcaceae family *GGB9730_SGB15291* (above/below median)	4.72 (2.01 – 10.81)	**<0.0001***	4.30 (1.56 – 11.83)	**0.005***

[a]Category after the slash (/) was set as a reference category.

205 Poster Session

Efficacy and safety analysis on the combination of camrelizumab with nab-paclitaxel and cisplatin-based chemotherapy in first-line treatment of advanced or metastatic esophageal squamous cell carcinoma. First Author: Xiaofeng Cong, Jilin University, Changchun, China

Background: Nab-paclitaxel has indicated good efficacy during the multi-line esophageal squamous cell carcinoma (ESCC) treatment. Our study summarized the efficacy and safety of the first-line combination treatment of camrelizumab with nab-paclitaxel and platinum in advanced or metastatic ESCC patients. This could provide evidence of the positive effects of using nab-paclitaxel. **Methods:** We included patients with advanced or metastatic ESCC who received camrelizumab in association with nab-paclitaxel and cisplatin for 3-6 cycles as first-line therapy. The patients were recruited from the First Hospital of Jilin University between August 2021 and December 2023. The primary endpoint was the objective response rate (ORR), while the secondary endpoints were progression-free survival (PFS), overall survival (OS), disease control rate (DCR), PFS, and OS rates at 12, 18, and 24 months, including safety. **Results:** 43 patients were included in this study, they were assessed based on the therapeutic effect, with 72.1% [95% CI,58.1%-86.1%]ORR and 100% DCR. The median PFS was 25.5 months, and the median OS was not achieved. The OS rates were 96.8%, 86.4%, and 78.6% at 12 months, 18 months, and 24 months, respectively. In contrast, the PFS rates were 90.1%, 75.8%, and 68.3%, respectively. Grade 3 or above treatment-related adverse reactions (TRAEs) occurred in nine patients (20.9%). No patient developed severe grade 5 TRAEs. **Conclusions:** During the first-line treatment of advanced or metastatic ESCC, applying nab-paclitaxel in associated with camrelizumab and cisplatin -based therapy showed a positive effect. Therefore, the results exhibit an extension of OS and PFS with manageable safety and no new TRAEs. Research Sponsor: None.

206 Poster Session

Programmed cell death ligand 1 (PD-L1) inhibitors versus programmed cell death 1 (PD-1) inhibitors for the first-line therapy of extensive-stage small cell lung cancer: A propensity score-matched study. First Author: Yaru Tian, Department of Radiation Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China

Background: Addition of programmed cell death ligand 1 (PD-L1) inhibitors or programmed cell death 1 (PD-1) inhibitors to etoposide-platinum (EP) chemotherapy has become the standard first-line regimen for ES-SCLC. The clinical efficacy and safety between the two types of immune checkpoint inhibitors (ICIs) remain controversial. We conduct the retrospective study and propensity score-matched analysis to explore the potential differences between them. **Methods:** Patients diagnosed with ES-SCLC and treated by EP plus PD-L1 or PD-1 inhibitors at Shandong Cancer Hospital between March 2019 and November 2022 were reviewed retrospectively. According to PD-L1 or PD-1 inhibitors, they were divided into two groups. Propensity score matching (1:1) was performed to balance the baseline characteristics of the two groups. The baseline characteristics and adverse events between the two groups were compared using the chi-squared test. The survival curves of overall survival (OS) and progression-free survival (PFS) were plotted by the Kaplan-Meier method and differences were analyzed by the log-rank test.The primary endpoints were OS and PFS. **Results:** As a result, 448 patients were analyzed in this study. 264 patients received PD-L1 inhibitors plus EP and 184 received PD-1 inhibitors plus EP. The median follow-up was 17.6 months. The median OS and PFS was 20.4 months and 7.8 months in the overall population. Before propensity score matching, the median OS was 20.1 months in PD-L1 inhibitor plus EP group and 20.7 months in PD-1 inhibitor plus EP group, respectively (HR 1.043, 95%CI 0.776-1.401; *p*= 0.781). The median PFS was 7.6 months in the PD-L1 inhibitor plus EP group and 8.5 months in PD-1 inhibitor plus EP group (HR 1.099, 95%CI 0.886-1.364; *p*= 0.390). After propensity score matching, the median OS and PFS were 20.4 months and 7.8months in PD-L1 inhibitor plus EP group, and those were 20.1 months and 8.6 months in PD-1 inhibitor plus EP group. There was no significant difference in OS and PFS between PD-L1 inhibitors plus EP and PD-1 inhibitors plus EP in the matched population (HR 1.104; *p*= 0.578 and HR 1.072; *p*= 0.602, respectively). The overall adverse events were comparable in the two groups. Only ≥3 grade neutropenia was more frequent in the PD-L1 inhibitors plus EP group (77.7% vs 69.0%, *p*= 0.040). **Conclusions:** In conclusion, the overall efficacy and safety profile was similar between PD-L1 inhibitors and PD-1 inhibitors for the first-line treatment of ES-SCLC. Research Sponsor: National Natural Science Foundation of China; Natural Science Foundation of Shandong; ZR2022LZL008.

ABSTRACT WITHDRAWN

208 **Poster Session**

Delayed addition of PD-1/PD-L1 inhibitors into chemotherapy on the outcomes for patients with extensive-stage small cell lung cancer: A propensity score-matched study. First Author: Shuangqing Lu, Shandong Cancer, Jinan, China

Background: Immunotherapy in combination with chemotherapy has become the first-line treatment for extensive-stage small cell lung cancer (ES-SCLC). However, some patients failed to undergo simultaneous immunotherapy at the time of initial chemotherapy, and whether this will have an impact on the efficacy of immunochemotherapy has not been fully explored. **Methods:** Between January 2020 and December 2022, the study included 416 patients diagnosed with ES-SCLC and receiving first-line immunotherapy, divided into two groups: delayed-IO (administering PD-1/PD-L1 inhibitors at 2-4 Cycles of chemotherapy) and early-IO (administering PD-1/PD-L1 inhibitors concurrent with first-cycle chemotherapy). Propensity score matching (PSM, 1:1) was performed to balance the baseline characteristics of the two groups. The primary endpoints were OS and PFS. Calculations were performed using the Kaplan-Meier method and comparisons were made using the log-rank test. **Results:** Mainly due to the fact that PD-L1/PD-1 inhibitors were not included in the medical insurance, which was difficult for patients to afford and the poor physical condition of some patients, taking into account the safety of the patients themselves, 72 patients in the delayed-IO group (2 cycles of chemotherapy: 41; 3 cycles: 16; 4 cycles: 15), and 344patients were included in the early-IO group. The median OS and PFS were 24.00 months and 8.75 months in the delayed-IO group, and those were 18.59 months and 7.57 months in the early-IO group, respectively, before PSM. There was no significant difference in OS and PFS between the two groups (HR 0.72; P = 0.054 and HR 0.86; P = 0.281, respectively). After PSM, there were 72 patients in each of the two groups. The median OS in the delayed-IO group and the early-IO group was 24.00 months and 18.79 months, respectively (HR 0.60, 95% CI 0.38-0.97; P = 0.037). Median PFS was 8.75 and 6.49 months in the two groups, respectively (HR 0.69, 95% CI 0.48-0.99; P = 0.044). There was a statistically significant difference between the two groups. The overall adverse event profile was comparable between the two groups. **Conclusions:** Our findings suggest that administering PD-1/PD-L1 inhibitors at 2-4 Cycles of chemotherapy was superior to administering PD-1/PD-L1 inhibitors concurrent with first-cycle chemotherapy in patients with ES-SCLC, while the safety profile of both was similar. Research Sponsor: Shandong Province Natural Science Foundation innovation and development joint fund project; ZR2022LZL008; Natural Science Foundation of Shandong; ZR2021QH245.

209 **Poster Session**

Effect of heterozygosity loss of HLA-I on immune evasion and promotion of non-small cell lung cancer brain metastasis and immunotherapy resistance. First Author: Jiefei Han, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Background: HLA-I play a crucial role in T cell recognition and killing of tumor cells as well as in PD-1/PD-L1 immunotherapy. Loss of heterozygosity (LOH) of HLA-I alleles has been found to be common in lung cancer patients and influences immune escape during tumor evolution. This study aims to explore the incidence of HLA-I LOH in intracranial metastases of advanced non-small cell lung cancer patients with brain metastasis and its impact on the efficacy of immunotherapy. **Methods:** A total of 29 patients with non-small cell lung cancer brain metastasis were included in this study. All enrolled patients underwent either percutaneous biopsy or surgical resection of intracranial metastases and had tissue specimens from the primary lung lesions. Whole-exome sequencing was performed on all primary/metastatic lesions to determine HLA-I typing/LOH and calculate tumor mutation burden (TMB). Additionally, we assessed the expression levels of CD8 T cells in the tumor immune microenvironment. Among the enrolled patients, 20 received PD-1/PD-L1 treatment. **Results:** Among the enrolled patients, 82.8% (24/29) had heterozygous HLA-I typing, with HLA-I LOH present in 25% (6/24) of patients' primary lesions and 58.3% (14/24) in brain metastatic lesions. Analysis of TMB in different lesions revealed a median TMB of 7.8 mut/Mb in lesions with intact HLA-I and 11.4 mut/Mb in lesions with HLA-I LOH. Notably, the median TMB in brain metastatic lesions with HLA-I LOH was 13.2 mut/Mb, higher than that in HLA-I LOH primary lung lesions (10.1 mut/Mb). Immunohistochemistry demonstrated that CD8 T cell expression levels were lowest in brain metastatic lesions with HLA-I LOH and highest in intact HLA-I primary lung lesions. Among patients who received immunotherapy, four cases exhibited inconsistent lesion responses, with stable or regressing primary lesions but progressive intracranial metastases. Survival analysis revealed that patients with HLA-I LOH in brain metastases had significantly lower PFS compared to those without (4.1 months vs. 6.9 months, $P < 0.05$), with no significant difference in OS. **Conclusions:** This study indicates that the incidence of HLA-I LOH in brain metastases of lung cancer is higher than that in primary lung lesions, accompanied by higher TMB, possibly due to the ineffective presentation of tumor antigens resulting in the accumulation of mutations in lost HLA-I. Moreover, tumors with HLA-I LOH have reduced levels of CD8 T cell infiltration, suggesting impaired tumor antigen presentation impedes immune cytotoxicity. These phenomena contribute to the poorer efficacy of immunotherapy in such patients. In conclusion, HLA-I LOH may be one of the important mechanisms of immune escape in lung cancer brain metastases. Research Sponsor: None.

210 **Poster Session**

A comprehensive meta-analysis of tissue resident memory T cell shaping non-small-cell lung cancer immune microenvironment and patient prognosis. First Author: Aidan Shen, Terasaki Institute for Biomedical Innovation, Los Angeles, CA

Background: Tissue-resident memory T cells (T_{RM}) are a specialized subset of long-lived memory T cells that reside in peripheral tissues. However, the impact of T_{RM}-related immunosurveillance on the tumor-immune microenvironment (TIME) and tumor progression across various non-small-cell lung cancer (NSCLC) patient populations is yet to be elucidated. **Methods:** Our comprehensive analysis of multiple independent single-cell and bulk RNA-seq datasets of patient NSCLC samples generated reliable, unique T_{RM} signatures, through which we inferred the abundance of T_{RM} in NSCLC. A machine learning model was developed to prognosticate survival, tested in multiple independent NSCLC cohorts. Model performance was corroborated through Kaplan-Meier survival plots, receiver operating characteristic (ROC) curves, principal component analysis, and t-SNE analyses. **Results:** We discovered that T_{RM} abundance is consistently positively correlated with CD4+ T helper 1 cells, M1 macrophages, and resting dendritic cells in the TIME. In addition, T_{RM} signatures are strongly associated with immune checkpoint genes and the prognosis of NSCLC patients. A T_{RM}-based machine learning model to predict patient survival was validated and an 18-gene risk score was further developed to effectively stratify patients into low-risk and high-risk categories, wherein patients with high-risk scores had significantly lower overall survival than patients with low-risk. The prognostic value of the risk score was independently validated by the TCGA dataset and multiple independent NSCLC patient datasets. Notably, low-risk NSCLC patients with higher T_{RM} infiltration exhibited enhanced T-cell immunity, nature killer cell activation, and other TIME immune responses related pathways, indicating a more active immune profile benefitting from immunotherapy. However, the T_{RM} signature revealed low T_{RM} abundance and a lack of prognostic association among lung squamous cell carcinoma patients in contrast to adenocarcinoma, indicating that the two NSCLC subtypes are driven by distinct TIMEs. **Conclusions:** Altogether, this study provides valuable insights into the complex interactions between T_{RM} and TIME and their impact on NSCLC patient prognosis. The development of a simplified 18-gene risk score provides a practical prognostic marker for risk stratification. Keywords: Tissue resident memory T cell, non-small-cell lung cancer, prognosis, tumor immune microenvironment, machine learning. Research Sponsor: National Institutes of Health, United States (NIH); R01 DK119795; National Institutes of Health, United States (NIH); R35 GM122465.

211 Poster Session

Real-world outcomes with lurbinectedin in second-line and beyond for small cell lung cancer in Korea. First Author: Joosung Gabriel Shim, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea

Background: Small-cell lung cancer (SCLC) accounts for approximately 10~15% of all lung cancers and is characterized by a strong tendency for early metastasis, and a poor prognosis. Most patients are diagnosed with extensive disease, with only one-third presenting with earlier-stage disease amenable to potentially curative multimodality therapy. Before the advent of lurbinectedin in 2020, only few options existed for treating patients with SCLC that had progressed after first-line therapy. The sole available second-line option for metastatic SCLC was topotecan, which is associated with hematological toxicities and only modest efficacy. Although lurbinectedin has been added to the arsenal against metastatic SCLC, real-world data on its efficacy has been scarce due to its recent implementation. In this study, we investigated the demographics and clinical outcomes of metastatic SCLC patients treated with lurbinectedin in Korea. **Methods:** Patients with metastatic SCLC who had failed first-line therapy were identified (n=51) at Yonsei Cancer Center, Seoul, Republic of Korea, and received lurbinectedin at a starting dose of 3.2mg/kg. Efficacy data, including investigator-assessed tumor response, progression data, survival, and demographic information, were recorded. **Results:** A total of 51 patients were treated with lurbinectedin at a single center in Korea. Thirty-four patients were eligible for assessment. The median age of diagnosis was 68. The overall objective response rate and disease control rate were 20% and 47%, respectively. For patients treated with lurbinectedin in the second-line therapy, the ORR and DCR were 12% and 15% respectively, while the ORR was 18% and DCR was 29% for patients in beyond third-line of therapy. The median progression-free survival was 1.8 months (95% CI 0.38 to 2.08), and the median overall survival was 2.8 months (95% CI 0.55 to 2.70). A patient group with a history of smoking showed prolonged overall survival and disease control rate. The most common adverse effects related to lurbinectedin were anemia (55%), leukopenia (53%), nausea (35%), loss of appetite (25%), general weakness (19%), neutropenia (12%), dizziness (6%), alopecia (6%), phlebitis (3%), thrombocytopenia (3%), pneumonia (3%). **Conclusions:** The real-world data of lurbinectedin in SCLC patients suggests that it is still a viable option in this disease area with dismal prognosis. Research Sponsor: None.

Overall objective response.

	Total	Smoking	
	(n=34)	Never (n = 6)	Former or current (n = 28)
Objective response rate (ORR)	7 (20)	2 (6)	5 (15)
ORR (2nd line)	4 (12)	1 (3)	4 (12)
ORR (>3rd line)	6 (18)	1 (3)	1 (3)
Disease control rate (DCR)	16 (47)	2 (6)	14 (41)
DCR (2nd line)	5 (15)	1 (3)	5 (15)
DCR (>3rd line)	10 (29)	1 (3)	9 (26)
Best overall response			
CR	0 (0)	0 (0)	0 (0)
PR	7 (20)	2 (6)	5 (15)
SD	9 (26)	0 (0)	9 (26)
PD	18 (54)	4 (12)	14 (41)
NE	0 (0)	0 (0)	0 (0)

212 Poster Session

Hospitalization outcome of patients with lung cancer with COVID-19 infection: NIS 2020 analysis. First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer-related deaths globally. Recent data showed the detrimental effects of COVID-19 infection on other neoplasm conditions, causing increased mortality rates and complications. However, data on the precise effects of COVID-19 on hospitalized individuals with lung cancer are scarce. **Methods:** We analyzed the 2020 U.S. National Inpatient Sample (NIS) to investigate the effects of COVID-19 infection on cases primarily admitted due to lung and bronchus cancer. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariable logistic and linear regression analyses. The primary outcome was inpatient mortality, with secondary outcomes including system-based complications. Statistical significance was established at a p-value of 0.05. **Results:** We identified 103,334 patients with a primary discharge diagnosis of lung and bronchus cancer. The mean age was 68.9 years; 50.5% were female. In the non-COVID group, Caucasians accounted for 75%, followed by Hispanics (12%). Of these, 0.36% (374/103,334) had a concurrent diagnosis of COVID-19 infection. In a survey multivariable logistic and linear regression model adjusting for patient and hospital factors, COVID-19 infection was associated with higher in-hospital mortality (aOR 5.39; 95% CI (3.01, 9.64), $p < 0.001$), higher mean length of stay (b 5.51; 95% CI (2.59, 8.43) $p < 0.001$), mean total hospital cost (b 10,683; 95% CI (784.32, 20,581.93) p = 0.034), shock (aOR 4.37; 95% CI (1.96, 9.91), $p < 0.001$), acute respiratory failure (aOR 2.23; 95% CI (1.30, 3.85), p = 0.004), mechanical ventilation usage (aOR 3.12; 95% CI (1.46, 6.66), p = 0.003) and acute kidney injury (aOR 2.71; 95% CI (1.54, 4.74), $p < 0.001$). We observed non-significant, but increased, risks of sepsis, SIRS, and coagulopathy in COVID-19-positive patients. **Conclusions:** In conclusion, our study underscores that COVID-19 infection is associated with higher in-hospital mortality and other major clinical outcomes in lung cancer, as well as increased economic burden and cost of stay. To definitively establish causal relationships between the observed factors and the reported clinical outcomes in this population, further longitudinal research is necessary. Research Sponsor: None.

213 Poster Session

Racial impact of secondary metastasis in patients with lung cancer: Evidence of US hospitals in 2020. First Author: Thanathip Suenghataiphorn, Griffin Hospital, Derby, CT

Background: Lung cancer patient often encounter disparities in health outcomes, especially in difference racial and ethnic groups. Metastasis is the primary cause of cancer morbidity and mortality. However, data on the metastasis risks and clinical outcomes on hospitalized individuals with lung cancer is still limited. Therefore, we aim to assess the association between metastatic lung cancer and racial differences. **Methods:** We analyzed the 2020 U.S. National Inpatient Sample (NIS) to explore patients who have lung cancer as the primary diagnosis. Additionally, we identified evidence of metastasis, as recorded by ICD-10-CM. Adjusted odds ratios (aORs) for specified outcomes were calculated through multivariable logistic and linear regression analyses. The primary outcome was racial differences in organ metastasis and secondary outcomes included mortality and length of stay. Statistical significance was established at p-value of 0.05. **Results:** We identified 103,335 patients with primary diagnosis of lung and bronchus cancer at discharge. The mean age was 68.9 years; 50.5% were female. Caucasians accounted for 74.3%, with African Americans at 12.1% and Hispanics at 4.6%. 10% of the patients had brain metastasis, whereas 14% had bone metastasis. In a multivariate analysis adjusting for patient, COVID-19, chemotherapy usage and hospital factors, African Americans had higher risk of brain metastasis (aOR 1.18; 95%CI (1.02, 1.37), p = 0.002), higher risk of bone metastasis (aOR 1.16; 95%CI (1.02, 1.33), p = 0.025), higher risk of mortality (aOR 1.21; 95% CI (1.01, 1.45), p = 0.039) and longer length of stay (b = 0.85; 95%CI (0.55, 1.16), p = 0.001). Hispanics also had higher risk of brain (aOR 1.36, $p < 0.05$) and prolonged length of stay (b 0.79, $p < 0.005$). We observed an increase in risk of metastasis and mortality but non-statistically significant in some parameters and races, as shown in table provided. **Conclusions:** In conclusion, our study revealed that racial difference is associated with higher risk of metastasis, as well as other outcomes. Further longitudinal research is necessary to establish a causal relationship between races, metastasis, and mortality in patients with lung cancer. Research Sponsor: None.

Adjusted odds ratio, adjusted for patient characteristics, hospital location and COVID-19 conditions.

Race	Brain Metastasis	Bone Metastasis	Mortality	Length of Stay**
African American	**1.18 (1.02, 1.37)***	**1.16 (1.02, 1.33)***	**1.21 (1.01, 1.45)***	**0.85 (0.55, 1.16)***
Hispanic	**1.36 (1.12, 1.66)***	1.21 (0.99, 1.49)	1.11 (0.83, 1.48)	**0.79 (0.28, 1.31)***
Asian	0.96 (0.74, 1.24)	**1.26 (1.01, 1.57)***	1.17 (0.86, 1.60)	0.20 (-0.28, 0.69)
Native American	1.59 (0.88, 2.85)	1.40 (0.80, 2.43)	2.02 (0.98, 4.16)	0.13 (-1.10, 1.37)
Others	1.04 (0.77, 1.42)	1.08 (0.80, 1.44)	1.05 (0.66, 1.67)	0.46 (-0.12, 1.06)

*Denotes statistically significant at p-level < 0.05.
**Length of Stay is expressed as beta-coefficient.

214 Poster Session

Efficacy and safety of 1L selpercatinib in *RET* fusion-positive NSCLC: LIBRETTO-431 East Asian subgroup analysis. First Author: Ying Cheng, Jilin Cancer Hospital, Changchun, China

Background: In prior studies, the efficacy and safety of selpercatinib, a selective RET inhibitor, was consistent in *RET*+ NSCLC pts across geographies. As previously reported, LIBRETTO-431 met its primary endpoint of improved PFS by blinded independent central review (BICR) at the pre-planned interim analysis. Here we report the efficacy and safety from LIBRETTO-431 in pts from East Asia, a majority of the study population. **Methods:** LIBRETTO-431 (NCT04194944) is a randomized, open-label phase 3 trial comparing 1L selpercatinib vs control (platinum/pemetrexed +/- pembrolizumab). Geography (East Asia vs non-East Asia) was a stratification factor. BICR-assessed PFS, ORR and DOR were examined in pts from East Asia randomized with investigator's intent to treat with pembrolizumab (ITT-pembro) if assigned to control. AE data were collected for all pts from East Asia who received at least one dose of selpercatinib or control (n=140). **Results:** Of 142 randomized pts from East Asia, 116 were included in the ITT-pembro population (selpercatinib: n=75, control: n=41). Baseline characteristics were well balanced, however the selpercatinib arm had slightly more pts from East Asia vs the control arm (58% vs 49%). In ITT-pembro pts from East Asia, with a median follow up of 19.4 mo and 21.2 mo in the selpercatinib and control arms respectively, the median PFS was not yet reached with selpercatinib (95% CI: 16.4-NE) vs 11.1 mo (95% CI: 7.0-16.8) with control. At 12 mo the PFS rate was 72.8% with selpercatinib vs. 41.7% with control. The ORR was 86.7% (95% CI: 76.8-93.4) with selpercatinib vs 61.0% (95% CI: 44.5-75.8) with control. Similar results were observed in pts from East Asia in the overall ITT population. The most common AEs reported in pts from East Asia on selpercatinib included elevated AST (73.6%), elevated ALT (70.3%), hypertension (60.4%), increased blood bilirubin (52.7%) and diarrhea (44.0%) while those reported with control included anemia (61.2%), elevated AST (49.0%), leukopenia (49.0%), neutropenia (44.9%) and elevated ALT (42.9%). A summary of safety data for selpercatinib vs control in pts from East Asia is presented in the table. **Conclusions:** LIBRETTO-431 is the first randomized study to report efficacy and safety of a RET inhibitor in pts from East Asia. Consistent with the results in the overall population, selpercatinib demonstrated superior PFS compared to chemotherapy + pembrolizumab in 1L pts from East Asia. These data support early comprehensive genomic testing and the use of selpercatinib as the preferred 1L regimen in *RET*+ NSCLC pts across geographies. Clinical trial information: NCT04194944. Research Sponsor: Loxo@Lilly, a wholly owned subsidiary of Eli Lilly and Company.

Summary of safety.

	Selpercatinib n = 91	Control n = 49
Median time on treatment, mo (standard deviation)	16.6 (± 7.8)	9.7 (± 7.9)
≥1 dose adjustment, n (%)	79 (86.8)	32 (65.3)
Grade ≥3 AE, n (%)	70 (76.9)	25 (51.0)
AE leading to treatment discontinuation, n (%)	11 (12.1)	1 (2.0)
Fatal AE on treatment or within 30 days of last dose, n (%)	2 (2.2)	0 (0.0)

215 Poster Session

Precision medicine-based platform to guide the treatment of EML4-ALK driven lung cancers and other NSCLC in real time. First Author: Sofia Diana Merajver, University of Michigan Rogel Cancer Center, Ann Arbor, MI

Background: Lung cancer (LC) is the top cause of cancer-associated mortality worldwide, with a 10-year overall survival rate of 5%. Although most LCs are smoking related, in the US, 25% of non-small cell LC (NSCLC) are diagnosed in persons with little or no smoking history. Fusions involving anaplastic lymphoma kinase (ALK) are the oncogenic driver in ~3–7% of NSCLC. While inhibitors targeting the kinase domain of ALK (TKIs) have proven extremely effective, inevitably, resistance develops with limited treatment options beyond second line TKIs. Additionally, NSCLCs without identified molecular alterations have even more limited tumor specific treatment options. **Methods:** We developed a precision medicine-based platform (PMP) to screen patient-derived, minimally cultured, organoid material (PDM) directly from resections with curated panels of drugs. PDM collected during clinically indicated procedures is plated in 3D-culture to generate patient-derived organoids (PDOs) and screened with drugs tailored to each tumor type. PDOs are screened at therapeutically relevant doses, drawing from pharmacokinetic data for each drug. We have optimized an assay to rapidly screen for EML4-ALK fusions and can perform next-generation sequencing in real time (~7 days) to integrate with drug screening results. Our organoid cultures retain the full spectrum of tumor microenvironment present in the original sample. **Results:** To date, we have analyzed 83 cases, including 8 EML4-ALK NSCLC. We have demonstrated the ability to produce high quality data from low input samples (biopsies). In one EML4-ALK NSCLC we were able to collect PDM from two distinct anatomic spaces (pleural effusion and peritoneal fluid) and screen with the same panel of drugs, with nearly identical results, highlighting the reproducibility and consistency of our assay. Screening of EML4-ALK tumors which have progressed to second or higher line TKIs, demonstrate sensitivity to earlier generation ALK TKIs, a known phenomenon. Characterization of tumors with unknown clinical drivers identifies that ~1/3 tumors which have no actionable or hypothetically prioritized variants, and they exhibit particularly poor response to chemotherapies. Our results recapitulate known resistance/progression in samples previously exposed to therapy, demonstrating a strong negative predictive value. Longitudinal assessment is being tracked to robustly assess positive predictive value (PPV). **Conclusions:** Our PMP captures robust and reproducible results that are consistent with known clinical pathogenesis. Moving forward, we are collecting longitudinal data from enrolled patients in parallel with clinical trials to demonstrate the PPV of our PMP. We additionally strive to demonstrate reproducibility to obtain Clinical Laboratory Improvement Amendments approval and to deliver results to patients and physicians to help guide clinical care. Research Sponsor: Richard Tam Foundation.

TPS216 Trials in Progress Poster Session

LIBRETTO-432: A phase 3 study of adjuvant selpercatinib or placebo in stage IB-IIIA *RET* fusion-positive (*RET*+) NSCLC. First Author: Theresa Bayt, Eil Lilly and Co, Indianapolis, IN

Background: Around 30% of NSCLC patients (pts) present with stage IB-IIIA disease. Standard treatment options are definitive locoregional therapies w/wo chemotherapy (CT) and/or immunotherapy, followed by surveillance until disease recurrence. Targeted therapies are standard for metastatic NSCLC with driver alterations and recent Phase III trial data has emerged in support of their use in the adjuvant setting for stage IB-IIIA (ADAURA and ALINA). *RET* is a key oncogenic driver in NSCLC and a promising target for adjuvant targeted therapy. Selpercatinib, a highly selective, potent and CNS active RET inhibitor, recently demonstrated longer PFS than platinum-based CT as 1L treatment in pts with *RET*+ advanced NSCLC (Zhou et al. NEJM 2023). LIBRETTO-432 is a Phase 3, global, multicenter, randomized, double-blind, controlled trial evaluating efficacy and safety of adjuvant selpercatinib v Placebo in pts with *RET*+ Stage IB-IIIA NSCLC following completion of definitive therapies with curative intent, and other adjuvant therapy if indicated (NCT04819100). **Methods:** Pts (n≈170) will be randomized (1:1) to selpercatinib BID [160mg ≥50kg; 120mg <50kg], or Placebo, in continuous 28-day cycles for a maximum treatment duration of 3y. Stratification factors include disease stage (IB/II/IIIA) and prior definitive therapy. Treatment will continue until disease recurrence/progression, unacceptable toxicity, or another protocol-defined reason. Crossover is allowed for Placebo pts who experience disease recurrence/progression. Key eligibility criteria include age ≥18 y; histologically confirmed Stage IB/II/IIIA NSCLC; *RET*+ tumor by PCR/NGS; prior definitive locoregional therapy with curative intent (surgery, radiotherapy) for Stage IB/II/IIIA NSCLC; and ECOG performance status 0-1. Maximum time allowed from definitive therapy completion to randomization is 26 w. Key exclusion criteria are evidence of other known oncogenic drivers; SCLC; and disease recurrence/progression following definitive therapy. Primary endpoint is investigator-assessed event-free survival (IAEFS) in the primary analysis population (pts with Stage II-IIIA). EFS is defined as time from randomization until locoregional disease recurrence with histopathological confirmation, distant disease recurrence per RECIST v1.1 or histopathological confirmation, or death. Gated secondary endpoints include IAEFS in the overall population (pts with Stage IB-IIIA) and OS in both primary analysis and overall populations. Non-gated secondary efficacy endpoints include BICR-assessed EFS, BICR and investigator-assessed time to distant disease recurrence in the CNS, and PFS on next line of treatment. Recruitment is ongoing, with enrollment across ~170 sites and 30 countries. Results from this trial will further inform the value of RET inhibition and genomic testing for adjuvant NSCLC pts. Clinical trial information: NCT04819100. Research Sponsor: Loxo Oncology Inc.

TPS217 Trials in Progress Poster Session

A single-arm, exploratory study of disitamab vedotin (DV) combined with camrelizumab and platinum-based chemotherapy as first-line treatment in patients with HER2 expressing locally advanced or metastatic esophageal squamous cell carcinoma (ESCC). First Author: Meihong Wu, Department of Oncology, The First Affiliated Hospital of Naval Medical University, Shanghai, China

Background: Esophageal cancer (EC) is one of the most common cancers worldwide with esophageal squamous cell carcinoma (ESCC) being the predominant histological subtype. PD-1 blockades combined with chemotherapy are now standard-of-care in first-line setting for patients with ESCC. HER2 expression, prevalent in an estimated 7.6% to 28.5% of ESCC cases, correlates with diminished overall survival, suggesting HER2-targeted therapy as a potential novel approach. To our knowledge, there is currently no clinical trial regarding anti-HER2 therapy in ESCC. Clinical evidence has suggested the potential synergistic anti-tumor effect of Disitamab Vedotin (DV) with PD-1 inhibitors in HER2-expressing gastric or gastroesophageal junction (G/GEJ) cancers. This single-arm, exploratory study aimed to evaluate the safety and preliminary anti-tumor activity of DV combined with camrelizumab and platinum-based chemotherapy in ESCC. **Methods:** This is a single-arm, exploratory study (NCT06055153). Approximately 20 patients will be enrolled in this study, phase 1 will initiate with a 3+3 dose-escalation scheme (2.5mg/kg to 2.0mg/kg) to identify dose-limiting toxicities (DLTs) and establish a safe dosage of DV. The expansion cohort will subsequently evaluate this dose for both efficacy and safety. The study population will included both male and female patients over the age of 18 with histologically confirmed ESCC, and locally advanced unresectable, recurrent unresectable or metastatic EC verified by imaging examination. This group also includes those patients who have experienced relapse or progression more than six months post the conclusion of last therapeutic regimen. Required HER2 expression levels in tumor specimens range from IHC 1+ to 3+. According to RECIST v1.1, participants must have at least one measurable lesion, an ECOG performance status of 0 or 1, and a minimum expected survival of 12 weeks with suitable organ function. Treatment protocol includes intravenous administration of DV (either 2.5 mg/kg or 2.0 mg/kg on day 1), Camrelizumab (200 mg on day 1), and Cisplatin (75mg/m2) or Nedaplatin (75mg/m2) on a 21-day cycle, continued until disease progression or the advent of unacceptable toxicity. The primary outcomes for evaluation are DLT for safety and the objective response rate (ORR) for efficacy. Adverse events will be monitored in accordance with the CTCAE 5.0 criteria. Secondary endpoints encompass progression-free survival (PFS), overall survival (OS), disease control rate (DCR), duration of response (DoR), and time to response (TTR). Clinical trial information: NCT06055153. Research Sponsor: None.

TPS218 Trials in Progress Poster Session

SUNRAY-01, a pivotal, global study of olomorasib (LY3537982) in combination with pembrolizumab with or without chemotherapy for 1L treatment in *KRAS* G12C-mutant advanced NSCLC. First Author: Makoto Nishio, Department of Thoracic Medical Oncology, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Mutations in *KRAS* are among the most frequent oncogenic drivers with the G12C variant found in ~13% of NSCLC. Outcomes for *KRAS* G12C-mutant NSCLC may be improved by combining *KRAS* G12C inhibitors with current 1L standard of care (SOC). Olomorasib is a potent and highly selective second-generation inhibitor of *KRAS* G12C, which delivers >90% sustained target occupancy in preclinical models. In the LOXO-RAS-20001 phase 1/2 study, olomorasib in combination with pembrolizumab demonstrated preliminary efficacy and a favorable safety profile.[1] **Methods:** SUNRAY-01 (NCT06119581) is a pivotal, global, phase 3 study in 1L advanced *KRAS* G12C-mutated NSCLC designed to seamlessly 1) optimize the dosing of olomorasib in combination with 1L SOC, and then 2) compare efficacy and safety of olomorasib plus SOC with placebo plus SOC. In the open-label randomized dose optimization (pembrolizumab plus olomorasib 50 mg vs 100 mg BID) and single arm safety lead-in (olomorasib plus pembrolizumab, pemetrexed, platinum), the optimal dose of olomorasib for combination therapy will be determined before the phase 3 study (parts A and B) is opened for enrollment. In part A, 384 participants with PD-L1 expression ≥50% are randomized (1:1) to pembrolizumab plus olomorasib or placebo. In part B, 552 participants are randomized (1:1) to pembrolizumab, pemetrexed, platinum plus olomorasib or placebo regardless of PD-L1 expression. Allocation of participants with PD-L1 expression ≥50% to either part A or part B will be at the discretion of the investigator. The primary objective is to compare efficacy based on PFS per RECIST v1.1 by blinded independent central review. Secondary endpoints include OS, ORR, DOR, DCR, TTR, PFS2, safety and tolerability, and patient-reported outcomes. Eligible participants (≥18 years) must have a *KRAS* G12C mutation in tumor or blood and known PD-L1 expression (0-100%), stage IIIB, IIIC, or IV NSCLC not suitable for curative intent radical surgery or radiation therapy, measurable disease per RECIST v1.1, and an ECOG PS 0-1. Participants can be enrolled based on local KRAS and PD-L1 testing results. Participants should not have received prior systemic therapy for advanced or metastatic NSCLC, however 1 cycle of SOC treatment prior to enrollment is allowed if immediate treatment is clinically indicated. Participants with asymptomatic (lesions ≤1.5 cm) or previously treated radiographically stable brain metastases are eligible. Key exclusion criteria include history of pneumonitis/interstitial lung disease and clinically significant active cardiovascular disease or malabsorption syndrome. The study opened for enrollment in December 2023. Reference: 1. Murciano-Goroff et al. 2023 *Cancer Res* 83 (8 Suppl): CT028. Clinical trial information: NCT06119581. Research Sponsor: Eli Lilly and Company.

TPS219 **Trials in Progress Poster Session**

REZILIENT3: Phase 3 study of zipalertinib plus chemotherapy in patients with previously untreated, advanced nonsquamous non-small cell lung cancer (NSCLC) harboring epidermal growth factor receptor (*EGFR*) exon 20 insertions (ex20ins) mutations. First Author: Makoto Nishio, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Despite recent advances, tolerable and effective treatments for patients with NSCLC harboring *EGFR* ex20ins mutations are needed, particularly in the first-line setting where platinum-based chemotherapy remains the standard of care. Zipalertinib (CLN-081/TAS6417), an oral tyrosine kinase inhibitor (TKI) of EGFR with broad activity against *EGFR* mutations, showed encouraging antitumor activity in heavily pretreated patients with *EGFR* ex20ins–mutant NSCLC, leading to 'Breakthrough Therapy' designation by the U.S. Food and Drug Administration in January 2022. Data suggest that combining EGFR TKIs with chemotherapy can improve antitumor efficacy versus chemotherapy or TKI treatment alone in patients with *EGFR*-mutated nonsquamous NSCLC. REZILIENT3 is a pivotal phase 3 study designed to compare the efficacy and safety of zipalertinib plus first-line standard-of-care platinum-based chemotherapy versus chemotherapy alone in previously untreated patients with nonsquamous NSCLC harboring *EGFR* ex20ins mutations. **Methods:** This randomized, controlled, open-label, phase 3 study (NCT05973773) will be conducted in two parts. Part A (safety lead-in) will confirm the safety of zipalertinib 100 mg twice daily as the recommended dose in combination with chemotherapy in patients with locally advanced or metastatic nonsquamous NSCLC harboring *EGFR* ex20ins mutations or other uncommon single/compound *EGFR* mutations. In Part B (randomized part), patients with *EGFR* ex20ins mutations and at least one measurable lesion (per Response Evaluation Criteria in Solid Tumours, version 1.1) will be randomized 1:1 to zipalertinib plus chemotherapy or chemotherapy alone, stratified by Eastern Cooperative Oncology Group performance status (0/1), brain metastases (yes/no), and geography (Asia/rest of world). Zipalertinib will be administered orally at a starting dose of 100 mg twice daily (pending confirmation in Part A). Chemotherapy (pemetrexed 500 mg/m² plus cisplatin 75 mg/m² or carboplatin area under the curve 5 mg/mL/min) will be administered intravenously on Day 1 of each cycle (carboplatin/cisplatin for four cycles). Patients randomized to chemotherapy alone will be allowed to cross over to zipalertinib monotherapy after documented progressive disease. The primary endpoint in Part B is progression-free survival assessed by blinded independent central review. Secondary endpoints include overall survival, investigator-assessed progression-free survival, objective response rate, duration of response, disease control rate, safety, intracranial efficacy endpoints, and quality of life. Part A is anticipated to enroll between 6 and 12 patients, while Part B is estimated to enroll approximately 260 patients. Enrollment started in June 2023. Clinical trial information: NCT05973773. Research Sponsor: Taiho Oncology, Inc.

220 **Poster Session**

Prognostic and immunological significance of tertiary lymphoid structures in nasopharyngeal carcinoma. First Author: Daofeng Huang, Department of Radiation Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China

Background: Tertiary lymphoid structures (TLSs) are ectopic lymphoid tissues found in non-lymphoid organs, characterized by the presence of $CD20^+$ B cell follicles adjacent to a T cell zone. Their presence has been associated with improved survival in various tumor types. However, the role of TLSs in nasopharyngeal carcinoma (NPC) remains unclear. In this study, we investigated the prognostic and immunological significance of TLSs in NPC patients. **Methods:** The investigation involved a discovery cohort (n = 145) comprising NPC patients diagnosed at Sun Yat-sen University Cancer Center between July 2010 and December 2016, with pretreatment primary tumor samples collected. An independent validation cohort included 150 NPC patients with gene expression profiles, among whom Hematoxylin & Eosin (H&E)-stained slides were available for 95 patients. The primary endpoint of this study is overall survival, defined as the duration of time from diagnosis until death from any cause. The presence of TLSs was assessed on H&E and CD20-stained slides. Analyses of tumor-infiltrating immune cell subsets, differentially expressed genes, and BCR/TCR clonotypes were performed to explore the association between TLSs and the anti-tumor immune response. A molecular definition of TLSs was proposed and assessed for its prognostic value across multiple cohorts. **Results:** The presence of TLSs was independently associated with a favorable overall survival (hazard ratio [HR], 0.26; 95% confidence interval [CI], 0.07-0.94; log-rank p = 0.04), surpassing the significance of B cell density in multivariate analysis (HR, 0.83; 95% CI, 0.38-1.79, log-rank p = 0.63). These findings were corroborated in the independent validation cohort. TLSs positively correlated with multiple immune-related pathways and a higher proportion of functionally mature immune cells. Notably, the counts of BCR and TCR clonotypes showed a significant positive correlation with the TLSs score. We proposed a TLSs gene signature and demonstrated its prognostic relevance across multiple cohorts, including patients treated with immune checkpoint blockade. **Conclusions:** TLSs exhibit heightened immune activity and indicate improved survival outcomes in NPC patients. A TLSs gene signature was proposed and demonstrated its prognostic relevance across multiple cohorts, indicating potential guidance for treatment decisions in cancer. Research Sponsor: National Natural Science Foundation of China; 82172870; National Natural Science Foundation of China; 81930072; Natural Science Foundation of Guangdong Province; 2017A030312003; Overseas Expertise Introduction Project for Discipline Innovation; B14035; Guangdong Basic and Applied Basic Research Foundation; 2020A1515110078; Guangzhou Basic and Applied Basic Research Project; 202102020184.

221 **Rapid Oral Abstract Session**

The impact of HRD mutation on survival in patients with *KRAS*-mutated advanced pancreatic cancer: A real-world database study. First Author: Yusuke Kawanaka, Department of Medical Oncology, Kindai University Faculty of Medicine, Osakasayamashi, Japan

Background: Advanced pancreatic ductal adenocarcinoma (PDAC) is associated with a poor prognosis. Prior studies indicate that homologous repair deficient (HRD+ve) PDAC patients (pts) have improved survival and greater response to platinum agents, but the optimal treatment for these population is still unclear. Here, we evaluate the survival impact of HRD mutations in *KRAS*-mutated PDAC, which represent 90% of cases, in a real-world setting. **Methods:** We retrospectively reviewed all pts diagnosed with *KRAS*-mutated PDAC from Jun 2019 to Dec 2021, who were registered in the Center for Cancer Genomics and Advanced Therapeutics (C-CAT), the cancer registry with comprehensive genomic profiling (CGP) data. Pts were stratified with the presence or absence of HRD mutations identified through Foundation One, including *ATM*, *ATR*, *BRCA1*, *BRCA2*, *BRIP1*, *CHEK2, FANCA*, *PALB2*, and *RAD51*. We analyzed the prevalence of co-alterations and the impact of HRD status on survival. Pts with a history of systemic therapy for curative intent were excluded from the survival analysis. **Results:** In 2251 PDAC cases (HRD+ve 232pts, HRD-ve 2019pts) enrolled, we found that HRD+ve PDAC had a significantly lower incidence of *TP53* mutation ($p<0.001$), *CDKN2A* mutation ($p<0.046$), and *CDKN2A* loss ($p<0.046$). Survival analysis was performed in 823 pts (HRD+ve 92pts, HRD-ve 731pts). HRD+ve pts had significantly longer overall survival (OS, 28.8m vs 23.5m, P=0.030). In the first line setting, HRD+ve pts had exhibited a markedly extended time-to-treatment failure (TTF; [HRD+ve, 19pts vs. HRD-ve, 177pts]; 7.6m vs. 5.4m; p=0.026) and OS ([HRD+ve, 30pts vs. HRD-ve, 239pts]; 28.8m vs. 23.5m; p=0.019) when treated with mFOLFIRINOX (mFFX), but not when treated with gemcitabine plus nab-paclitaxel (GA; [HRD+ve, 34pts vs. HRD-ve 276pts]; OS, 29.3m vs 26.3m; p=0.34; TTF, 5.2m vs. 5.2m; p=0.80). In the second line setting, there were no differences in TTF between HRD+ve and HRD-ve irrespective of these regimens. Among HRD+ve PDAC pts, pts who having received mFFX tend to have better survival compared to those who did not (46pts vs. 46pts; OS, 31.7m vs 26.3m; p=0.09). **Conclusions:** Our analysis has identified a unique profile in HRD+ve PDAC, underscoring the importance of platinum-based chemotherapy in the initial treatment to enhance survival, which highlights the practical clinical benefits of routine CGP for pts with *KRAS*-mutated PDAC. Research Sponsor: None.

222 **Rapid Oral Abstract Session**

Predictive and pharmacodynamic biomarkers for combination therapy in stage III-IV melanoma: A Simon phase II trial (NCT03999749). First Author: Teruyuki Mizutani, NYU Langone Medical Center, New York, NY

Background: The evaluation of biomarkers that predict response and immune-related adverse events (irAEs) is crucial for optimizing melanoma treatment with Immune checkpoint inhibitors (ICIs). We report predictive and pharmacodynamic biomarkers for response and irAEs using high-dimensional flow cytometry in a phase II trial combining nivolumab (3 mg/kg), ipilimumab (1 mg/ml), and the IL-6 receptor inhibitor tocilizumab (4 mg/kg) in unresectable/advanced melanoma patients. **Methods:** We analyzed serum and blood from melanoma patients at baseline, weeks 7 and 37, categorized them by irAE severity and clinical response. Patients were categorized based on the severity of irAEs (grades 3-5) (TOX), the absence of toxicity or grades 1-2 irAE (NT), clinical benefit (CB), and non-clinical benefit (NCB). Immune monitoring regimen included ELISA for IL-6, gp130, IL-23, osteopontin, and Luminex oncological panel (LXSAHM-22). We employed multi-parametric flow cytometry panels to examine myeloid cells, cytotoxic T cells, and checkpoint protein expression on immune cells. We processed ~1 million PBMCs per sample using various antibodies, with data acquisition performed via Sony's ID7000 cytometer. The data underwent quality control, normalization PBMCs per patient, concatenation, dimensionality reduction, and clustering in FlowJo. **Results:** Among the 70 patients administered treatment, we observed a best overall response rate of 57%. Grade 3-5 irAEs occurred in 22% of patients by week 24. Patients manifesting irAEs exhibited notably higher baseline Th17 cell counts (NT=181$\pm$18 vs. Tox=311$\pm$49, $p<0.01$) and CD26+ Naive CD4 T-cell populations (NT=5838$\pm$801 vs. Tox=9632$\pm$1343, $p<0.04$), suggesting their potential role as predictive markers for toxicity. Additionally, *in vitro* investigations led us to identify CD26 co-stimulation as a preliminary step in TH17 cell differentiation. Key pharmacodynamic markers included a significant elevation in Treg cells (NCB=1286$\pm$71 vs. CB=1492$\pm$95, p=0.02) and reduction in serum gp130 levels (NCB=104$\pm$5 vs. CB=83$\pm$5 ng/ml, $p<0.01$) at week 7 in addition to IL-6 (NCB=7.5$\pm$1.5 vs. CB=4.6$\pm$1.1 pg/ml, $p<0.01$) and osteopontin (NCB=95$\pm$15 vs. CB=25$\pm$3 ng/ml, $p<0.01$) by week 37 when compared to baseline. **Conclusions:** Our findings suggest that Th17 cells can serve as a toxicity biomarker for combination therapy with ipilimumab, nivolumab and tocilizumab. Circulating Treg cells and serum osteopontin have emerged as promising pharmacodynamic biomarkers. Clinical trial information: NCT03999749. Research Sponsor: None.

223 **Poster Session**

Validation of a chemotherapy toxicity prediction model in older adults with cancer in Taiwan. First Author: Chieh-Ying Chang, Department of Hematology-Oncology, Chang Gung Memorial Hospital at Linkou and Chang Gung University College of Medicine, Taoyuan City, Taiwan

Background: The Cancer and Aging Research Group (CARG) model is established for predicting chemotherapy-related toxicities in older patients; however, its applicability has not been validated in Taiwanese or non-solid tumor populations. Due to biopsychosocial distinctions in the Taiwanese demographic and inherent disparities between lymphoma and solid tumors, a modified CARG (mCARG) was assessed for its toxicity prediction capabilities. **Methods:** In this study, 337 consecutive patients aged $\geq$65 years with solid tumors (N=258) or lymphoma (N=79), slated for first-line chemotherapy, were recruited from a single medical center in Taiwan between 2018 and 2021, with follow-up until December 31, 2021. Patients were categorized into low-, medium-, and high-risk groups based on mCARG, excluding the cancer-type parameter from the original CARG variables. Validation of mCARG involved receiver operating characteristic (ROC) curves, and individual mCARG variables were analyzed using univariate analysis for their impact on chemotherapy toxicities and overall survival. **Results:** This study included 337 patients (mean age, 70 years; 160 female [47%]; 177 male [53%]) classified as low-(N=112, 33.2%), medium-(N=106, 31.5%), and high-(N=119, 35.3%) risk. Toxicities of grades $\geq$3 were 41.1%, 50.0%, and 71.4% ($P<0.001$), respectively. ROC was 0.665 (95% CI: 0.608–0.722), indicating satisfactory discrimination. However, the lymphoma subgroup exhibited no significant differences in toxicity risk levels (70.0%, 74.1%, and 81.0%; P=0.39). Among mCARG variables, age $\geq$72 years (P=0.008), polychemotherapy (P=0.009), decreased hemoglobin ($P<0.001$), falls (P=0.008), and inability to walk one block (P=0.01) were associated with toxicities. One-year overall survival rates were 80.6%, 69.4%, and 57.2%, respectively, in ascending-risk groups, with high-risk groups showing decreased survival (P=0.001). **Conclusions:** This prognostic study validated the mCARG model in a heterogeneous cancer cohort in Taiwan but failed to do so in the lymphoma subgroup. Although unable to predict all toxicities, mCARG could offer insights into patient survival among older individuals with cancer. Research Sponsor: National Science and Technology Council.

224 **Poster Session**

Tissue of origin detection for cancer tumor using low-depth cfDNA samples through combination of tumor-specific methylation atlas and genome-wide methylation density in graph convolutional neural networks. First Author: Nhu Nhat Tan Doan, Gene Solutions, Ho Chi Minh City, Viet Nam

Background: Cell free DNA (cfDNA)-based assays hold great potential in detecting early cancer signals yet determining the tissue-of-origin (TOO) for cancer signals remains a challenging task. Here, we investigated the contribution of a methylation atlas to TOO detection in low depth cfDNA samples. **Methods:** We constructed a tumor-specific methylation atlas (TSMA) using whole-genome bisulfite sequencing (WGBS) data from five types of tumor tissues (breast, colorectal, gastric, liver and lung cancer) and paired white blood cells (WBC). TSMA was used with a non-negative least square matrix factorization (NNLS) deconvolution algorithm to identify the abundance of tumor tissue types in a WGBS sample. We showed that TSMA worked well with tumor tissue but struggled with cfDNA samples due to the overwhelming amount of WBC-derived DNA. To construct a model for TOO, we adopted the multi-modal strategy and used as inputs the combination of deconvolution scores from TSMA with other features of cfDNA. **Results:** Our final model comprised of a graph convolutional neural network using deconvolution scores and genome-wide methylation density features, which achieved an accuracy of 69% in a held-out validation dataset of 239 low-depth cfDNA samples. **Conclusions:** In conclusion, we have demonstrated that our TSMA in combination with other cfDNA features can improve TOO detection in low-depth cfDNA samples. Research Sponsor: The study was funded by Gene Solutions.

225 Poster Session

Early circulating tumor DNA (ctDNA) changes during treatment with immune checkpoint inhibitors (ICI) as a predictor of clinical outcomes in patients (pts) with advanced stage melanoma/skin cancer. First Author: Vincent T. Ma, University of Wisconsin Carbone Cancer Center, Madison, WI

Background: ctDNA monitoring has shown promising results in predicting relapse in resected solid tumors. Its role in treatment response assessment and predicting survival outcomes in the unresectable or metastatic disease setting merits further investigation. In our study, we attempt to assess the role of early ctDNA changes in predicting disease response, progression, and overall survival outcomes in pts with advanced stage melanoma/skin cancer treated with ICI therapy. **Methods:** A retrospective analysis using a personalized, tumor-informed ctDNA assay (Natera) on prospectively collected plasma samples from pts with unresectable stage III/IV melanoma/skin cancer treated with anti-PD-1 based therapy at the University of Wisconsin (Madison) was performed. Baseline ctDNA levels were assessed prior to the start of treatment and at 3-4 weeks (i.e. prior to the second treatment dose). A logistic regression model was used to evaluate the odds of overall disease control [complete response + partial response + stable disease, per RECIST version 1.1] based on the change in ctDNA levels (decrease vs increase) between both time points. Cox proportional hazard models were used to investigate the effects of ctDNA level change on progression free survival (PFS) and overall survival (OS). **Results:** 46 pts were evaluated. 82% melanoma, 14% Merkel cell carcinoma, 2% skin adenocarcinoma and 2% squamous cell carcinoma. 77% were treated with dual ICI (anti-PD-1 based) therapy and 23% with anti-PD-1 monotherapy. Median follow up was 12.1 months. Median change in ctDNA levels from baseline were -4.83 MTM/mL among pts with ctDNA decrease and +37.39 MTM/mL among pts with ctDNA increase. A qualitative decrease in ctDNA level was associated with overall disease control (OR 65.00, 95% CI 11.88-587.89, $p<0.0001$), longer PFS (HR 0.08, 95% CI 0.03-0.22, $p<0.0001$), and longer OS (HR 0.17, 95% CI 0.05-0.54, p=0.0008) compared to an increase in ctDNA level from baseline to 3-4 weeks after starting ICI therapy. Median PFS was not reached (NR) and 1.63 months; and median OS was NR and 5.57 months among pts with ctDNA decrease and ctDNA increase, respectively. **Conclusions:** We found that early ctDNA dynamics after 3-4 weeks of ICI initiation in pts with advanced melanoma/skin cancer appears to be a candidate strategy to predict treatment response, risk of progression, and potentially long-term survival. Larger prospective studies are warranted to validate the utility of ctDNA in treatment monitoring. Research Sponsor: None.

226 Poster Session

Prognostic value of immuno-nutritional status in patients with cancer treated by immune checkpoint inhibitors. First Author: Ming-Chun Kuo, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan

Background: The treatment efficacy of immune checkpoint inhibitors (ICIs) may relate to tumor factors or host factors, such as systemic inflammation status or nutritional status. In this study, we investigated the prognostic value of immuno-nutritional status in cancer patients treated by ICIs, and develop nomogram models for predicting overall survival (OS). **Methods:** We used Chang Gung Research Database to retrospectively evaluate cancer patients who received ICIs during January 2015 to December 2021. Patients had double cancer or received only one cycle of ICI were excluded. All patients were divided into a training cohort and a validation cohort. The training cohort was used to analyze the risk factors and develop nomogram models. The models were validated by the validation cohort. The univariate analysis, stepwise multivariate analysis, receiver operator characteristics (ROC) analysis were used to find out the independent risk factors. The calibration plot were used to evaluate the reliability of the models. **Results:** All patients (3219 cases) could be categorized into lung cancer (22.1%), genitourinary cancer (14.9%), upper gastrointestinal tract cancer (8.1%), colorectal cancer (3.1%), hepatocellular carcinoma (24.6%), pancreatobiliary cancer (3.8%), head and neck cancer (12.9%), melanoma (4.0%), breast cancer (1.9%) and lymphoma (0.5%). 80.2% of patients received anti-PD1, 19.8% of patients received anti-PD-L1. In training cohort, the cut-off value was set for neutrophil-to-lymphocyte ratio (NLR), total lymphocyte count (TLC), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), systemic inflammation index (SII), prognostic nutrition index (PNI) and hemoglobin-albumin-lymphocyte-platelet (HALP) score. The above risk factors showed significant difference in median OS in validation cohort respectively (Table). The multivariate analysis demonstrated that NLR, PNI and HALP score were independent risk factors in predicting OS. The hazard ratio were 1,439 (95% CI 1.149-1.801), 0.689 (95% CI 0.549-0.865) and 0.784 (95% CI 0.626-0.982) respectively. **Conclusions:** We developed nomogram models to investigate the immuno-nutritional status and predict the OS of cancer patients who received ICIs therapy. High NLR, low PNI and low HALP score were associated with worse OS. Research Sponsor: Chang Gung Medical Research Program (CMRP).

Prognostic factors of OS in cancer patients who received ICIs therapy.

	Training cohort (n=1287)		Validation cohort (n=1932)			
	Cut-off value	AUC		mOS (months)	HR	95% CI
NLR	4.10	0.6174	NLR high	6.37	1.758	1.567-1.971
			NLR low	10.29		
TLC	1.04	0.6123	TLC high	8.97	0.732	0.653-0.821
			TLC low	7.17		
LMR	2.94	0.6356	LMR high	10.24	0.623	0.553-0.702
			LMR low	7.13		
PLR	20.35	0.5766	PLR high	6.00	1.677	1.480-1.899
			PLR low	9.10		
SII	864.75	0.5839	SII high	7.02	1.428	1.274-1.601
			SII low	9.17		
PNI	46.31	0.6323	PNI high	11.37	0.437	0.378-0.506
			PNI low	5.67		
HALP score	17.15	0.6104	HALP high	8.87	0.571	0.498-0.653
			HALP low	5.14		

227 Poster Session

Long-term survival after metasectomy in patients with bone or soft-tissue metastases from renal cell carcinoma. First Author: Takashi Higuchi, Kanazawa Red Cross Hospital, Kanazawa, Japan

Background: Renal cell carcinoma (RCC) is reported to be associated with long-term survival, and surgical resection is now recommended in patients with metastatic lesions. This study evaluated the long-term outcome of surgery for bone or soft tissue metastases from RCC. **Methods:** Between 1993 and 2014, 58 patients (46 men and 12 women) underwent surgery, excluding palliative surgery, for bone or soft tissue metastatic lesions from RCC at our institution. These patients were retrospectively evaluated for factors associated with prognosis by using the log-rank test and Cox proportional hazards analysis. **Results:** The patients' mean age was 60 years, and the mean follow-up period was 52 months. The surgical sites included the spine (33 patients), limb bone (10 patients), pelvis (8 patients), thoracic bone (4 patients), and soft tissue (3). The surgical procedures were total en bloc spondylectomy (TES) in 33 patients, wide excision in 13 (6 of them were also treated with prosthesis), and curettage and bone grafts in 12 (4 of them were treated with internal fixation). The 3-, 5-, 10-, and 15-year overall survival (OS) rates were 75%, 62%, 48%, and 25%, respectively. According to the surgical methods, the 5-year OS was 64% for TES, 62% for wide excision, and 46% for curettage and bone grafts. According to the surgical site, the median survival time was 127 months for the spine, 140 months for the limb bone, and 54 months for the pelvis. In multivariate analysis, preoperative lung metastasis and the pathological type, except for clear cell carcinoma, were independent risk factors for poor prognosis. However, age, performance status, Motzer classification, and abnormal blood test results were not significant risk factors. **Conclusions:** Our findings suggest that the surgical resection of bone and soft tissue metastatic lesions from RCC is a favorable option for improving prognosis even in patients with unfavorable conditions such as an advanced age or poor performance status. Now that treatment outcomes for renal cell carcinoma are improving, bone metastases can be treated with surgery. Research Sponsor: None.

228 Poster Session

Osteosarcoma patient-derived orthotopic xenograft (PDOX) models for identification of novel and effective therapeutics. First Author: Takashi Higuchi, Kanazawa Red Cross Hospital, Kanazawa, Japan

Background: Osteosarcoma is the most common malignant primary tumor of bone and mainly occurs in young generations. Due to the heterogeneity, rarity, poor response rate to systemic therapy, and metastatic potential of osteosarcoma, individualized precision medicine and novel drug discovery are greatly needed. Toward this goal, we have established the patient-derived orthotopic xenograft (PDOX) mouse model with surgical orthotopic implantation for all major cancers. The PDOX models recapitulate human tumors better than subcutaneous-transplanted xenografts including patient-derived xenograft (PDX). Metastasis is observed to a greater extent in PDOX models due to the intact histology and correct-organ tumor micro-environment of the orthotopically implanted tissue. Therefore, the PDOX model is highly predictive of drug efficacy and useful for identifying effective drugs for tumors in which new drugs are difficult to develop. **Methods:** We have reported 18 osteosarcoma PDOX studies evaluating approved and experimental drugs since 2017. The present report reviews our research group's experience with the osteosarcoma-PDOX model, and the power of the PDOX models to identify effective therapeutics. **Results:** Effective treatment for drug-resistant osteosarcoma includes regorafenib, as monotherapy, and temozolomide-irinotecan, trabectedin-irinotecan, sorafenib-everolimus, sorafenib-palbociclib, and olaratumab-doxorubicin-cisplatin, as combinations. Experimental therapy with recombinant methioninase, tumor-targeting S. typhimurium A1-R, or combinations of these agents and other drugs have shown surprising efficacy in the recalcitrant-osteosarcoma PDOX models. **Conclusions:** Owing to the high concordance of drug efficacy between patients and their corresponding PDOX models, these models provide improved and personalized treatment options for patients with osteosarcoma. The patient does not need to suffer from the potential drug toxicity and morbidity of ineffective chemotherapies. In an era of growing promise of new treatment and precision medicine, PDOX models can offer a unique opportunity to provide specific and individualized therapy and novel therapeutic options for osteosarcoma patients. Research Sponsor: None.

229 Poster Session

Non-invasive minimal residual disease detection of liver cancer using circulating tumor DNA features and α-fetoprotein: A prospective study. First Author: Yinyin Chang, Clinical Laboratories, Shenyou Bio, Zhengzhou, China

Background: Liver cancer hasahigh recurrence rate of 50%-70% for early-stage patients. Minimal residual disease (MRD) is closely correlated with cancer early recurrence. Here, we developed SeekInCure, a non-invasive assay to detect MRD and predict the prognosis of liver cancer patients after radical surgery. **Methods:** 32 liver cancer patients undergoing radical surgery were prospectively enrolled. 8 mL peripheral blood was collected from each patient before and after surgery, respectively. SeekInCure assay, which integrated the protein tumor marker (AFP) and cancer genomic hallmarks: copy number aberration, and fragment size from ctDNA to calculate a score (P_{HCC}), was utilized to detect the cancer signal in each blood sample. MRD status determined by P_{HCC} value was correlated with the clinical outcome (OS) and the benefit of treatment after radical surgery. **Results:** Out of the 32 liver cancer patients, 78.1% (25/32) were at early stages (Stages I/II: 65.6%/12.5%), and 59.4% (19/32) received systemic treatment after surgery. MTB- patients (12.5%, 4/32) showed better overall survival (OS) than MTB+ patients (87.4%, 28/32) with a high hazard ratio (HR) value of 1.19. After radical surgery, 23 HCC patients were MRD-, including 4 MTB- patients remaining negative; meanwhile, 9 out of 28 MTB+ patients remained MRD+. The OS of MRD- patients was significantly better than that of MRD+ patients (HR 5.67; 95% confidence interval (CI), 1.33 ~ 24.20; P = 0.008). Moreover, the OS of MRD- patients with and without systemic treatment showed no significant difference (P = 0.930). **Conclusions:** This prospective study demonstrated the potential clinical value of ctDNA in detecting MRD status to predict the prognosis in early-stage liver cancer patients and to identify patients who may benefit from avoiding overtreatment. This strategy requires validation in independent prospective studies. Research Sponsor: None.

230 Poster Session

Bitter taste receptors as prognostic markers in adrenocortical carcinoma. First Author: Jehad Yasin, The University of Jordan, Amman, Jordan

Background: Adrenocortical carcinoma (ACC) is a rare malignant neoplasm of the adrenal gland. Progressive forms of this cancer carry a dismal prognosis with 5-year survival rates $< 40\%$. As such, predictors of stage progression and prognostic biomarkers are a must. Taste 2 receptors (TAS2Rs) are localized on the surface of bitter receptor cells. Recent evidence has shown their role as prognostic biomarkers in multiple cancers, such as breast, prostate, and head and neck squamous cell carcinoma. The aim of this study was to elucidate the role of TAS2Rs in ACC. **Methods:** Differentially expressed genes (DEGs) based on high and low expression groups of TAS2R genes were identified through the 'DESeq2' package on R. Subsequent Gene Set Enrichment Analysis (GSEA) was performed using the 'TCGAbiolinks' package on R and Enrichr online tool. Immune infiltration analysis was conducted using TIMER2.0 and CIBERSORT. Survival analysis with an optimal expression cutoff for overall survival (OS) and a median cutoff for disease-free survival (DFS) based on The Cancer Genome Atlas Adrenocortical carcinoma (TCGA-ACC) data was executed using the 'survival' and 'survminer' R packages and GEPIA2 online tool. **Results:** Analysis of the TCGA-ACC cohort revealed OS estimates that indicated worse survival in patients with higher TAS2R14, TAS2R19, TAS2R20, and TAS2R30 expression (Table). Further analysis produced consistent results, demonstrating that elevated expressions of TAS2R14 and TAS2R19 are correlated with decreased DFS, with Hazard Ratios (HR) of 2.60 (p = 0.0046) and 2.20 (p = 0.022), respectively. Furthermore, the F-test and stage plots have shown consistent upregulation of selected TAS2R genes across stages I–IV ($p < 0.05$). RNA-seq analysis revealed 1170 common (579 down-regulated, 591 upregulated) DEGs between high and low TAS2R14 and TAS2R19 expression groups. GSEA showed upregulated genes in high expressers have relations to hedgehog signaling, epithelial to mesenchymal transition, TGF-B signaling, and organization of the extracellular matrix. On the other hand, down-regulated genes showed functions in metabolic reprogramming, chemokine receptor binding, MHC protein complex, and chemokine-mediated inflammation. GSEA on co-expressed genes showed pathways related to ferroptosis, autolysosome activity, and iron homeostasis and metabolism. Immune infiltration analysis revealed significantly increased CD4+, naïve and plasma B cell infiltration with higher TAS2R14 and TAS2R19 expression ($Rho > 0.25$, $p < 0.05$), in addition to increased M1 macrophage infiltration with higher TAS2R19 expression (Rho = 0.28, $p < 0.05$). **Conclusions:** TAS2R genes are potentially involved in modulating carcinogenic processes, including stage progression, metastasis and invasion, immune regulation, and metabolic processes. This modulation may explain the poorer prognostic outcomes in ACC patients with elevated TAS2R expression. Further validation in external cohorts is necessary to confirm these results. Research Sponsor: None.

Univariate cox proportional hazards egression model (overall survival).

Gene	Hazard Ratio (HR)	P Value	95% Confidence Interval
TAS2R14	5.71	0.0044	(4.51,6.91)
TAS2R19	3.61	0.0025	(2.78,4.44)
TAS2R20	2.30	0.0306	(1.55,3.06)
TAS2R30	2.16	0.0434	(1.41,2.91)

The association between TAS2R gene expression and ACC patient survival, where a HR greater than 1 suggests a harmful effect of the gene on survival. P-values indicate the statistical significance of these associations, with values less than 0.05 considered statistically significant.

231 Poster Session

Factors predicting long-term survival of hepatocellular carcinoma in developing country. First Author: Sunee Neesanun, Department of Medical Oncology, Sawanpracharak Hospital, Nakhon Sawan, Thailand

Background: Hepatocellular carcinoma (HCC) is a common cancer globally, especially in Asian Pacific countries with survival time limit. Previous data on long-term survival (LS) in HCC patients has been limited. This study aims identifying factors that predict LS for HCC patients treated in hospitals with restricted access to advanced therapies. **Methods:** This study utilized a retrospective cohort design, analyzing electronic medical records of patients diagnosed with HCC at Sawanpracharak Hospital from October 2018 to September 2022. LS for HCC was defined as survival for two years or more. Univariable and multivariable with stepwise backward regression analyses were employed to identify independent prognostic factors. **Results:** The analysis included 398 HCC patients, with 75 (18.84%) classified as long-term survivors (LS HCC). Stepwise backward regression identified that ALP levels <172 U/L were associated with a significantly increased likelihood of LS (OR = 3.667, 95% CI 1.443-9.317, p=0.006). Additionally, curative surgery/RFA treatment (OR = 1.941, 95% CI 1.128-3.342, p=0.017) and Albumin >3.5 g/dL (OR = 9.898, 95% CI 1.160- 84.438, p=0.036) were significant positive predictors. ECOG performance status (3-4 vs 2 vs 0-1) and AJCC stage (early vs locally vs advance) also emerged as significant factors, with better performance status (OR = 8.723, 95% CI 1.046-72.741, p=0.045) and AJCC stage 3 and 4 (OR 0.200 95% CI= 0.075-0.532, P= 0.001 and OR = 0.204, 95% CI 0.0547-0.760, p=0.018 respectively) associated with LS. Notably, alcohol consumption was associated with a decreased likelihood of LS (OR = 0.399, 95% CI 0.171-0.929, p=0.033). The model demonstrated good discriminative ability with an AUC of 0.912. **Conclusions:** Lower ALP levels, curative treatment, higher albumin levels, better ECOG performance status, earlier AJCC stage, and abstinence from alcohol consumption were all associated with a significantly increased likelihood of LS HCC. The high AUC of the model suggests its potential for predicting long-term survival in this patient population. Research Sponsor: None.

Multivariable with stepwise backward elimination regression analysis for long-term survival HCC.

	Multivariable		
	OR	95% CI	P value
ECOG			
3-4			
2	2.891	0.331-25.240	0.337
0-1	8.723	1.046-72.741	0.045
Alcohol, n (%)	0.399	0.171-0.929	0.033
Surveillance, n (%)	0.463	0.192- 1.117	0.087
AJCC			
1A-2 (early)	Ref		
3 (locally advance)	0.200	0.075-0.532	0.001
4 (advance)	0.204	0.055-0.760	0.018
Curative treatment	1.941	1.128-3.342	0.017
Albumin			
<2.5	Ref		
2.5-3.5	5.249	0.606-45.432	0.132
>3.5	9.898	1.160-84.438	0.036
ALP < 172	3.668	1.443-9.317	0.006
AUC 0.912			

232 Poster Session

Anti-tumor effect of zartoprofen, a non-steroidal anti-inflammatory drug, targeting PPARγ (peroxisome proliferator-activated receptor gamma) on chondrosarcoma. First Author: Takashi Higuchi, Kanazawa Red Cross Hospital, Kanazawa, Japan

Background: Peroxisome proliferator-activated receptor gamma (PPARγ) plays a central role in the differentiation of adipocytes. Anti-tumor effects by activating PPARγ have been reported on chondrosarcoma. We revealed that zaltoprofen, a non-steroidal anti-inflammatory drug (NSAID), could activate and induce PPARγ in chondrosarcoma cells. We report antitumor effects of zaltoprofen targeting PPARγ on chondrosarcoma. **Methods:** PPARγ activation by zaltoprofen was assessed with luciferase assay. Human chondrosarcoma cells and PPARγ-silencing cells established with shRNA were subjected to the anti-tumor analyses, western blotting, RT-PCR, and zymography. For *in vivo* study, chondrosarcoma cells were subcutaneously inoculated into nude mice. Zaltoprofen was administered to mice (30 mg/kg/day). Tumors were pathologically assessed. We obtained tumor tissue specimens from a patient who underwent several surgeries for recurrent spinal chondrosarcoma. The patient was administered zaltoprofen as a therapeutic agent for algia the tumor remained stable for more than 2 years. Pathological analyses were performed on the specimen before and after administration of zaltoprofen). **Results:** Zaltoprofen significantly increased PPARg activation (EC_{50} 47.3 uM). Treatment with 200–400 uM zaltoprofen significantly inhibited cell viability and induced PPARγ protein and mRNA expression in chondrosarcoma cells. Zaltoprofen (400 uM) significantly decreased the cell proliferation, migration, invasion, and MMP2 expression in control cells, whereas these were significantly increased in PPARγ-silencing cells. Also, zaltoprofen (400 uM) induced p21, p27, and p53 expression in control cells, whereas these effects were canceled in PPARg-silencing cells. Upregulation of KROX20 followed by CEBP-α and −β, all of which were reported to induce PPARγ in normal adipose tissue, were detected after zaltoprofen administration. Tumor growth was significantly inhibited in mice administered zaltoprofen. Apoptotic indices in the TUNEL-labeled area were significantly larger and Ki-67 positive cells were significantly lower in tumor specimens from mice administered zaltoprofen. Patient's specimens revealed that PPARγ expression was stronger and MMP2 expression was weaker in post-administration specimens. **Conclusions:** Zaltoprofen suppressed tumor progression by inhibiting cell proliferation, migration, and invasion with induction of PPARγ expression in chondrosarcoma cells. The suppressing effect on tumor progression by zaltoprofen was also observed *in vivo*. Zaltoprofen induced PPARγ expression and MMP2 downregulation in clinical specimens with expected antitumor effects. This is the first study demonstrating that one of the NSAIDs, zaltoprofen, may act as an antitumor agent by targeting PPARγ for chondrosarcoma. Research Sponsor: JSPS KAKENHI; 17K16682.

233 **Poster Session**

Potential for boron neutron capture therapy (BNCT) with ASCT2-targeted boron agents. First Author: Kenichiro Eza, Department of Neurosurgery, Osaka Medical and Pharmaceutical University, Takatuki, Japan

Background: Boron Neutron Capture Therapy (BNCT) is a cutting-edge particle irradiation technique that utilizes the nuclear reaction triggered by the irradiation of non-radioactive boron-10 with thermal neutrons, selectively annihilating tumor cells that have incorporated boron. In the clinical arena, Boronophenylalanine (BPA), a phenylalanine compound targeting amino acid receptors, has been the cornerstone of BNCT. While BNCT has been effective against malignant gliomas, its dependency on BPA uptake has illuminated the existence of inherent resistance within specific cells, tissues, and cancer types. This study pivots towards the Alanine-serine-cysteine transporter 2 (ASCT2)—a transporter distinct from LAT1—investigating its potential as a gateway for the development of innovative boron carriers, with the aim of expanding the clinical applicability and effectiveness of BNCT. **Methods:** This research embarked on in vitro investigations to evaluate boron accumulation in F98 and C6 rat glioma cells, and 9L rat gliosarcoma, following 24 hours of exposure to BPA and GluB-2 (10 μg B/ml each). Complementary in vivo studies involved the intravenous administration of these compounds to an F98 rat brain tumor model, with the subsequent measurement of boron distribution at 2.5, 6, and 24 hours post-administration. The efficacy of these treatments was then ascertained through neutron irradiation experiments, gauging therapeutic outcomes via the survival periods of the subjects. **Results:** In vitro findings highlighted that GluB-2 facilitated a significantly higher intracellular boron concentration compared to BPA in F98 cells (p=0.02, Student's t-test). In vivo results indicated that the apex of boron biodistribution in tumors was achieved at 2.5 hours post-BPA treatment and at 6 hours post-GluB-2 treatment, with GluB-2 securing a superior maximum intratumor boron concentration. Survival analysis revealed a mean survival of 28.0$\pm$2.5 days for the neutron alone group, 37.7$\pm$5.0 days for the group receiving BPA IV + BNCT at 2.5 hours, 55.1$\pm$19.9 days for the group treated with GluB-2 IV + BNCT at 6 hours, and 25.3$\pm$1.4 days for the untreated group. Remarkably, the group treated with GluB-2 demonstrated significantly prolonged survival compared to the BPA-treated group ($p<0.001$, log-rank test). **Conclusions:** Combining BNCT with GluB-2 showed superior efficacy over BPA. Further research is needed to optimize boron concentration timing and ASCT2 expression levels, yet GluB-2 presents a promising advancement in BNCT, potentially transforming malignant brain tumor treatment. Research Sponsor: None.

234 **Poster Session**

Effect of ac4C acetyltransferase NAT10 on tumor progression via ATF4/ASNS mediated asparagine biosynthesis in osteosarcoma. First Author: Yutong Zou, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China

Background: Osteosarcoma is the most common primary malignant bone tumor in children and adolescents, characterized by high malignancy, high mortality, and high disability rates. Investigating the mechanism of osteosarcoma progression, identifying new targets, and developing effective therapy are of great significance for improving patient clinical outcomes. NAT10-mediated ac4C modification is widely present in mRNA and plays important roles in multiple biological processes of mRNA. NAT10 and ac4C modification also play a crucial role in the occurrence and development of malignant tumors such as bladder cancer, esophageal cancer, and breast cancer. **Methods:** Through RNA-seq and functional screening, NAT10 was identified as the potential therapeutic target. The biological functions of NAT10 and ac4C modification in osteosarcoma were explored *in vivo* and *in vitro*. Downstream target of NAT10 was identified through acRIP-seq combined with RNA-seq. The ac4C modification of downstream target gene were detected using RIP-qPCR and its regulatory effect on mRNA stability was explored using RNA half-life analysis. Drug screening was performed using FDA-approved drugs and a small molecule compound library to identify NAT10 inhibitors. The efficacy of inhibitors in osteosarcoma treatment is validated through *in vivo*, *in vitro* experiments and patient-derived tumor xenograft (PDX) models. **Results:** Functional screening targeting RNA modification regulatory factors demonstrated that inhibiting NAT10 significantly reduced the proliferation, migration and invasion of osteosarcoma cells. NAT10 knockout significantly inhibited the proliferation and metastasis of osteosarcoma cells, as well as the malignant progression *in vivo*. The acRIP-seq and RNA-seq revealed that ATF4 is a downstream target gene regulated by NAT10 in osteosarcoma. NAT10 promoted ac4C modification of ATF4 mRNA, enhanced the stability of ATF4 mRNA, and ATF4 promoted the transcription and expression of ASNS. ASNS catalyzes the synthesis of asparagine (Asn), thereby promoting the malignant progression of osteosarcoma. Drug screening identified Paliperidone and AG-401 as potential inhibitors of NAT10. Through cell functional experiments, orthotopic osteosarcoma models, organoids model, and PDX models, it was demonstrated that Paliperidone and AG-401 can inhibit the malignant progression of osteosarcoma. **Conclusions:** NAT10 was highly expressed in osteosarcoma and associated with patient prognosis. Through ac4C modification, NAT10 regulated the synthesis of asparagine mediated by ATF4/ASNS, providing materials for protein and nucleotide synthesis in tumor cells, thus promoting the malignant progression of osteosarcoma. Paliperidone and AG-401 were identified as potential NAT10 inhibitors and targeting NAT10 could be a promosing strategy in osteosarcoma treatment. Research Sponsor: The National Natural Science Foundation of China.

235 **Poster Session**

The single cell transcriptional landscape of fibrosarcoma. First Author: Juan Wang, The First Hospital, Jilin University, Changchun, Shandong, China

Background: Fibrosarcoma (FS) is a relatively uncommon subtype of soft tissue sarcoma, which predominantly occurs in the extremities and girdles of elderly individuals. FS are famous for its high recurrence and metastasis rate. However, the current treatment regimens have shown poor efficacy in treating these progressive lesions. Therefore, a deep understanding of the tumor microenvironment characteristics of fibrosarcoma is needed to develop more effective drugs.Therefore, a deeper understanding of the tumor microenvironment characteristics of fibrosarcoma is needed for further development of therapeutic drugs. **Methods:** We performed single-cell transcriptome sequencing for the first time on 6 patients bearing with FS. Bulk-seq data of soft tissue sarcoma was downloaded from public database including TCGA and GEO for prognostic analysis. What' s more, a cohort of 54 FS patients was retrospectively collected for protein detection. **Results:** The tumor microenvironment landscape was characterized by the presence of malignant fibroblast, diverse macrophages, limited T-cell presence, and high levels of vascular infiltration. The expression of siglec15 was significantly upregulated in the malignant cells. And the prognostic significance of siglec15 was confirmed by the TCGA public database. What's more, the high expression of siglec15 protein was negatively related to overall survival of fibrosarcoma patients from our institution. We also explored the interactions among different cell subtypes, especially the interactions between malignant cells and endothelial cells, as well as macrophages and endothelial cells, which not only promote tumor progression but also inhibit T-cell infiltration and function. **Conclusions:** In total, our work has uncovered the low T cell infiltration landscape of FS. The primary reason of insufficient immune infiltration may be due to the blockage of T cell extravasation caused by the interaction between endothelial cells, malignant cells and macrophages. Research Sponsor: None.