LBA1 **Plenary Session**

Prospective randomized multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (ESOPEC trial).

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Background: The most effective multimodal approach for treatment of resectable locally advanced esophageal adenocarcinoma (EAC) is under debate. A prior ranking question is if neoadjuvant chemoradiation therapy or perioperative chemotherapy is superior. ESOPEC (NCT02509286) is a multicenter prospective randomized trial comparing neoadjuvant CROSS (41.4Gy plus carboplatin/paclitaxel) followed by surgery versus perioperative FLOT (5-FU/leucovorin/oxaliplatin/docetaxel) and surgery for the curative treatment of EAC. **Methods:** Patients with cT1 cN+ cM0 or cT2-4a cNany cM0 resectable EAC were eligible. The primary endpoint is overall survival (OS; 90% power; hazard ratio [HR] 0.645, 218 events needed; one sided significance level of 2.5%). Analysis is by intention-to-treat in all randomized patients. The effect of treatment on OS is estimated using Cox regression stratified by study site, and including N stage (N0, N+), and age as covariates. **Results:** Between Feb 2016 and Apr 2020, 438 patients from 25 sites in Germany were randomly assigned to two treatment groups (221 FLOT; 217 CROSS). Baseline characteristics (male sex 89.3%, median age 63 [range 30-86], cT3/4 80.5%; cN+ 79.7%) were well balanced between both arms. Neoadjuvant treatment was started in 403 patients (207 FLOT; 196 CROSS). Surgery was done in 371 patients (191 FLOT; 180 CROSS). R0 resection was achieved in 351 patients (180 FLOT; 171 CROSS). 90 days postsurgical mortality was 4.3% (3.2% FLOT; 5.6% CROSS). After a median follow up of 55 months, 218 patients had died (97 FLOT; 121 CROSS). Median OS was 66 (95% CI 36 – not estimable) months in the FLOT arm, and 37 (95% CI 28 – 43) months in the CROSS arm. The 3-year OS rates were 57.4% (95% CI 50.1 – 64.0%) for FLOT and 50.7% (95% CI 43.5 – 57.5%) for CROSS (HR 0.70, 95% CI 0.53-0.92, p=0.012). In 359 patients with available tumor regression status, pathological complete response was achieved in 35 (19.3%, 95%-CI 13.9 – 25.9%) in FLOT and in 24 (13.5%, 95%-CI 8.8 – 19.4%) in CROSS. **Conclusions:** Perioperative FLOT improves survival in resectable EAC compared to neoadjuvant CROSS. Funding: The trial was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation), project number 264590883. Clinical trial information: NCT02509286. Research Sponsor: DFG.

LBA2 Plenary Session

Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 NADINA trial.

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Background: Standard of care (SOC) for resectable, macroscopic stage III melanoma is therapeutic lymph node dissection (TLND) followed by adjuvant (adj) therapy with nivolumab (NIVO), pembrolizumab (PEM) or, in BRAFmut melanoma, dabrafenib + trametinib (DAB/TRAM). The recent phase 2 SWOG S1801 trial showed superior event-free survival (EFS) of neoadjuvant (neoadj) + adj PEM as compared to adj PEM (estimated 2y-EFS 72% vs 49%). Additional phase 2 trials demonstrated safety and high efficacy (77-80% 2y-EFS) of neoadj ipilimumab (IPI) 1 mg/kg + nivolumab (NIVO) 3 mg/kg, providing the rationale for testing neoadj IPI + NIVO against SOC in a phase 3 trial. **Methods:** In this investigator initiated, international phase 3 trial, resectable, macroscopic, nodal stage III melanoma pts, naive to ICI and BRAFi/MEKi, were randomized to receive 2 cycles of neoadj IPI 80mg + NIVO 240mg (q3w) followed by TLND, and in case of not achieving a major pathologic response (MPR) adj DAB/TRAM (150mg BID/2mg QD; 46 wks) or 11 cycles of adj NIVO (480mg; q4w; if BRAFwt) versus TLND followed by 12 cycles of adj NIVO (480mg; q4w). The primary endpoint EFS is defined as time from randomization until progression, recurrence or death due to melanoma or treatment, and was assessed using a Cox regression model. An interim analysis using a 2-sided alpha of 0.1% (Haybittle-Peto stopping rule) was planned per protocol after completing recruitment. **Results:** Between Aug 2021 and Dec 2023, 423 pts were randomly assigned; 212 pts to the neoadj arm and 211 to the adj arm. At data cutoff on January 12, 2024, with a median FU of 9.9 mos, significantly less events occurred in the neoadj arm vs the adj arm (28 vs 72), with HR 0.32 (99.9% CI 0.15-0.66, $p<0.0001$) and estimated 12-mo EFS rates of 83.7% (99.9% CI 73.8-94.8) vs 57.2% (99.9% CI 45.1-72.6) favoring the neoadj arm. In the subgroup of BRAFmut melanoma, estimated EFS rates were 83.5% and 52.1%, and in BRAFwt 83.9% and 62.4% for neoadj versus adj respectively. 58.0% of pts in the neoadj arm had an MPR, 8.0% a path partial-response (pPR), 26.4% a path non-response (pNR), 2.4% had progression before surgery and 5.2% were not reported (95% centrally reviewed). The 12-mo RFS rates according to path response were 95.1% for MPR, 76.1% for pPR and 57.0% for pNR. Systemic treatment related adverse events (AE) grade ≥3 were seen in 29.7% and 14.7% in the neoadj and adj arm; 1 pt died due to toxicity in adj arm (pneumonitis). Surgery related grade ≥3 AEs were reported in 14.6% and 14.4% respectively. **Conclusions:** NADINA is the first phase 3 trial that evaluates neoadj immunotherapy against SOC in melanoma, and is also the first phase 3 trial in oncology evaluating a neoadj regimen consisting of immunotherapy alone. Neoadj IPI+NIVO followed by response-driven adj treatment results in statistically significant improved EFS compared to adj NIVO and should be considered a new SOC treatment in macroscopic stage III melanoma. Clinical trial information: NCT04949113. Research Sponsor: Bristol Myers-Squibb; Australian Government.

LBA3 **Plenary Session**

Comparative effectiveness trial of early palliative care delivered via telehealth versus in person among patients with advanced lung cancer.

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Background: National guidelines recommend the early integration of palliative and oncology care for patients with advanced cancer, given robust evidence showing that this care model improves quality of life (QOL) and other important outcomes. However, most patients do not receive early palliative care (EPC) in the outpatient setting due to limited access and resources. To overcome these barriers, we conducted a large-scale comparative effectiveness trial of EPC delivered via secure video versus in person among patients with advanced non-small cell lung cancer (NSCLC) and their caregivers. **Methods:** Between 6/14/2018 and 5/4/2023, we enrolled 1250 patients with advanced NSCLC, diagnosed in the past 12 weeks, into a randomized trial of telehealth versus in-person EPC across 22 cancer centers in the US. Patients were randomly assigned to meet with a palliative care clinician every four weeks from enrollment through the course of disease either via video or in the outpatient clinic. Participants completed self-report measures at baseline and weeks 12 and 24. The primary aim was to evaluate the equivalence of the effect of telehealth versus in-person EPC on QOL at week 24, using regression modeling with an equivalence margin of ± 4 points on the Functional Assessment of Cancer Therapy-Lung (FACT-L, range = 0-136). We also compared rates of caregiver participation in EPC visits and patient-reported depression and anxiety symptoms (Patient Health Questionnaire-9; Hospital Anxiety and Depression Scale), coping (Brief COPE), and perceptions of prognosis (Perceptions of Treatment and Prognosis Questionnaire) between groups. Study recruitment ceased for two months at the onset of the COVID-19 pandemic. **Results:** Participants (mean age = 65.5 years; 54.0% female; 82.1% White) had a mean of 4.75 and 4.92 palliative care encounters by week 24 in the telehealth and in-person groups, respectively. Due to the pandemic, the in-person group had 3.9% of visits occur via video. QOL scores at week 24 for patients assigned to the telehealth group were equivalent to those receiving in-person EPC (adjusted means: 99.67 versus 97.67, $p < 0.043$ for equivalence). The rate of caregiver participation in EPC visits was lower in the telehealth versus in-person group (36.6% versus 49.7%, $p < 0.0001$). Study groups did not differ in depression and anxiety symptoms, use of coping skills, or perceptions of the goal of treatment and curability of their cancer. **Conclusions:** The delivery of EPC via video versus in-person visits demonstrated equivalent effects on QOL in patients with advanced NSCLC. The two modalities also did not differ across a range of patient-reported outcomes, though caregivers attended more in-person versus video visits. The findings underscore the considerable potential for improving access to and broader dissemination of this evidence-based care model through telehealth delivery. Clinical trial information: NCT03375489. Research Sponsor: Patient Centered Outcomes Research Institute; PLC-1609-35995.

LBA4 **Plenary Session**

Osimertinib (osi) after definitive chemoradiotherapy (CRT) in patients (pts) with unresectable stage (stg) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 LAURA study.

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Background: EGFR mutations occur in up to one-third of pts with unresectable stg III NSCLC. Consolidation durvalumab is standard of care (SoC) for pts who do not progress after concurrent CRT (cCRT), yet the benefit of consolidation immunotherapy specifically for EGFRm NSCLC remains uncertain, with limited data available. Osi, a 3rd-generation CNS-active EGFR-TKI, is recommended for EGFRm advanced/metastatic NSCLC and as adjuvant therapy for resectable EGFRm NSCLC. We report primary results from the global, double-blind, placebo (PBO)-controlled Phase 3 LAURA study (NCT03521154), assessing efficacy/safety of osi in unresectable stg III EGFRm NSCLC without progression after definitive CRT. **Methods:** Eligible pts: aged ≥18 years (≥20 in Japan), WHO PS 0/1, unresectable stg III EGFRm (Ex19del/L858R) NSCLC, had received definitive platinum-based cCRT/sequential CRT (sCRT) with no progression. Pts were stratified (cCRT vs sCRT; stg IIIA vs IIIB/IIIC; Chinese vs non-Chinese) and randomized 2:1 to receive osi 80 mg or PBO QD until progression (blinded independent central review [BICR]-confirmed)/discontinuation. Imaging, including brain MRI, was mandated at baseline, every 8 wks to wk 48, then every 12 wks, until progression by BICR. Open-label osi was offered after progression by BICR. Primary endpoint: progression-free survival (PFS; RECIST v1.1) assessed by BICR. Secondary endpoints included overall survival (OS) and safety. Data cut-off: January 5, 2024. **Results:** Overall, 216 pts were randomly assigned: osi n=143, PBO n=73. Baseline characteristics were generally balanced across osi/PBO arms: female 63/58%, stg IIIA 36/33%, IIIB 47/52%, IIIC 17/15%, Ex19del 52/59%. Osi significantly improved PFS by BICR vs PBO: HR 0.16; 95% CI 0.10, 0.24; $p<0.001$. Median PFS was 39.1 mo (95% CI 31.5, not calculable) for osi vs 5.6 mo (95% CI 3.7, 7.4) for PBO; 12-mo PFS rate was 74% (osi) vs 22% (PBO); 24-mo PFS rate was 65% (osi) vs 13% (PBO). Investigator-assessed PFS (HR 0.19; 95% CI 0.12, 0.29; nominal $p<0.001$) was consistent with PFS by BICR. PFS benefit was consistent across predefined subgroups. Interim OS analysis (20% maturity) showed a trend in favor of osi: HR 0.81; 95% CI 0.42, 1.56; p=0.530; 81% of pts (PBO arm) received osi after progression. All-causality AEs were reported in 98% vs 88% pts; ≥Grade 3 AEs in 35% vs 12%; serious AEs in 38% vs 15% for osi vs PBO, respectively. Radiation pneumonitis AEs (grouped term): 48% (osi) vs 38% (PBO), majority Grade 1/2. Any AEs leading to discontinuation were reported in 13% vs 5% for osi vs PBO, respectively. **Conclusions:** Osi after definitive CRT demonstrated a statistically significant and clinically meaningful improvement in PFS, for unresectable stg III EGFRm NSCLC, with no unexpected safety signals. These results establish osi as the new SoC for EGFRm NSCLC in this setting. Clinical trial information: NCT03521154. Research Sponsor: AstraZeneca.

LBA5 **Plenary Session**

ADRIATIC: Durvalumab (D) as consolidation treatment (tx) for patients (pts) with limited-stage small-cell lung cancer (LS-SCLC).

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Background: The standard of care (SoC) for pts with LS-SCLC is concurrent platinum-based chemoradiotherapy (cCRT) ± prophylactic cranial irradiation (PCI). ADRIATIC (NCT03703297), a phase 3, randomized, double-blind, placebo (PBO)-controlled, multicenter, global study, assessed D ± tremelimumab (T) as consolidation tx for pts with LS-SCLC who had not progressed after cCRT. Here we report results for D vs PBO from the first planned interim analysis (IA). **Methods:** Eligible pts had stage I–III LS-SCLC (stage I/II inoperable) and WHO performance status 0/1, and had not progressed after cCRT. PCI was permitted before randomization. Pts were randomized 1–42 days after cCRT to D 1500 mg + PBO, D 1500 mg + T 75 mg, or PBO + PBO every 4 weeks (Q4W) for 4 cycles, followed by D (D±T arms) or PBO Q4W until investigator-determined progression or intolerable toxicity, or for a maximum of 24 months (mo). The first 600 pts were randomized in a 1:1:1 ratio; subsequent pts were randomly assigned 1:1 to D or PBO. Randomization was stratified by stage (I/II vs III) and receipt of PCI (yes vs no). The dual primary endpoints were OS and PFS (blinded independent central review per RECIST v1.1) for D vs PBO. OS and PFS for D+T vs PBO were alpha-controlled secondary endpoints. **Results:** 730 pts were randomized, including 264 to D and 266 to PBO. Baseline characteristics and prior tx were well balanced between arms. Radiation schedule in the D vs PBO arms was once daily in 73.9% vs 70.3% of pts and twice daily in 26.1% vs 29.7%; 53.8% of pts in each arm received PCI. At this IA (data cutoff 15Jan2024), median (range) duration of follow-up for OS and PFS in censored pts was 37.2 (0.1–60.9) and 27.6 (0.0–55.8) mo, respectively. OS was significantly improved with D vs PBO (HR 0.73 [95% CI 0.57–0.93]; p=0.0104; median OS 55.9 [95% CI 37.3 – not estimable] vs 33.4 [25.5–39.9] mo; 24-mo OS rate 68.0% vs 58.5%; 36-mo OS rate 56.5% vs 47.6%). PFS was also significantly improved with D vs PBO (HR 0.76 [95% CI 0.61–0.95]; p=0.0161; median PFS 16.6 [95% CI 10.2–28.2] vs 9.2 [7.4–12.9] mo; 18-mo PFS rate 48.8% vs 36.1%; 24-mo PFS rate 46.2% vs 34.2%). Tx benefit was generally consistent across predefined pt subgroups for both OS and PFS. With D vs PBO, maximum grade 3/4 all-cause adverse events (AEs) occurred in 24.3% vs 24.2% of pts; AEs led to tx discontinuation in 16.3% vs 10.6% of pts and to death in 2.7% vs 1.9%. Any-grade pneumonitis/radiation pneumonitis was reported in 38.0% vs 30.2% of pts with D vs PBO (maximum grade 3/4 in 3.0% vs 2.6%). The D+T arm remains blinded until the next planned analysis. **Conclusions:** D as consolidation tx after cCRT demonstrated a statistically significant and clinically meaningful improvement in OS and PFS compared with PBO in pts with LS-SCLC. D was well tolerated and AEs were consistent with the known safety profile, with no new signals observed. These data support consolidation D as a new SoC for pts with LS-SCLC who have not progressed after cCRT. Clinical trial information: NCT03703297. Research Sponsor: AstraZeneca.

LBA105 Clinical Science Symposium

Results from the randomized phase 3 DREAMM-8 study of belantamab mafodotin plus pomalidomide and dexamethasone (BPd) vs pomalidomide plus bortezomib and dexamethasone (PVd) in relapsed/refractory multiple myeloma (RRMM).

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Background: Use of triplet/quadruplet therapies for 1L MM raises the need for novel combinations at first relapse, which belantamab mafodotin (belamaf) combos may address. In DREAMM-7, BVd led to a significant improvement in progression-free survival (PFS) and a strong trend in improved overall survival (OS) vs daratumumab-Vd in patients (pts) with ≥1 prior therapy. We report results from DREAMM-8 (NCT04484623), which tested a different belamaf combo (BPd) and met its primary endpoint of independent review committee–assessed PFS at a prespecified interim analysis. **Methods:** DREAMM-8 is a phase 3, open-label, randomized, multicenter trial evaluating the efficacy and safety of BPd vs PVd in RRMM pts who received ≥1 prior line of therapy (LoT), including lenalidomide. Pts were randomly assigned 1:1 to BPd (28-d cycles): belamaf 2.5 mg/kg IV (D1, C1), 1.9 mg/kg (D1, C2+) + pom 4 mg (D1-21, all C) + dex 40 mg (D1, QW, all C), or PVd (21-d cycles): pom 4 mg (D1-14, all C) + bortezomib 1.3 mg/m^2 SC (D1, 4, 8, 11 [C1-8]; and D1, 8 [C9+]) + dex 20 mg (day of and 1 day after bortezomib dose). **Results:** 155 pts were randomly assigned to BPd and 147 to PVd. With a median (range) follow-up of 21.78 mo (0.03-39.23), median PFS (95% CI) was not reached (NR; 20.6-NR) with BPd vs 12.7 mo (9.1-18.5) with PVd (HR, 0.52; 95% CI, 0.37-0.73; $P<0.001$). 12-month PFS rate (95% CI) was 71% (63-78%) with BPd vs 51% (42-60%) with PVd. ORR (95% CI) was 77% (70.0-83.7%) with BPd vs 72% (64.1-79.2%) with PVd; rate of complete response or better (95% CI) was 40% (32.2-48.2%) with BPd vs 16% (10.7-23.3%) with PVd. Median duration of response (95% CI) was NR (24.9-NR) with BPd vs 17.5 mo (12.1-26.4) with PVd. A positive trend favoring BPd was seen for OS (HR, 0.77; 95% CI, 0.53-1.14); follow up for OS is ongoing. Adverse events (AEs) were reported in >99% and 96% of pts in the BPd and PVd arms, respectively. Of pts treated with BPd, 89% had ocular AEs (CTCAE grade 3/4, 43%) vs 30% (grade 3/4, 2%) in the PVd arm. AEs were generally manageable, and broadly consistent with known safety profile of individual agents. **Conclusions:** The DREAMM-8 study demonstrated a statistically significant and clinically meaningful PFS benefit with BPd vs PVd in RRMM with >1 prior LoT. BPd also led to deeper and more durable responses, showed a favorable OS trend, and had a manageable safety profile. Clinical trial information: NCT04484623. Research Sponsor: GSK plc.

Additional baseline and safety data.

Baseline Characteristics	BPd (n=155)	PVd (n=147)
Prior LoT, median (range)	1 (1-6)	1 (1-9)
Prior antimyeloma therapy, n (%)		
Immunomodulator	155 (100)	147 (100)
Proteasome inhibitor	140 (90)	136 (93)
Anti-CD38 antibody	38 (25)	42 (29)
Safety	**(n=150)[a]**	**(n=145)[a]**
Grade 3/4 AEs, n (%)	136 (91)	106 (73)
Any SAEs; fatal SAEs, n (%)	95 (63); 17 (11)	65 (45); 16 (11)
AEs leading to discontinuation of any study treatment, n (%)	22 (15)	18 (12)

[a]Safety data were evaluated in the safety analysis set.

LBA500 **Oral Abstract Session**

A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy.

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Background: Prognosis of pts with early triple negative breast cancer (TNBC) is still poor and new effective treatments are needed. TNBC is the most immunogenic BC subtype, and this may account for sensitivity to immune checkpoint inhibitors. The A-BRAVE trial was designed to evaluate the efficacy of avelumab, an anti PD-L1 antibody, as adjuvant treatment for pts with early TNBC at high risk. **Methods:** This is a phase III, multicentric, randomized adjuvant study comparing 1 year of treatment with the anti PD-L1 avelumab vs observation for TNBC pts considered at high risk of relapse. Pts were enrolled after they completed standard treatment with curative intent including surgery and neoadjuvant/adjuvant chemotherapy. High risk was defined as: 1) invasive residual disease (breast and/or nodes) after neoadjuvant chemotherapy (Stratum A), 2) >pN2/any pT, pN1/pT2, or pN0/pT3 after primary surgery (Stratum B). Pts were randomly assigned (1:1, balanced for strata A and B) to Avelumab 10 mg/kg I.V. q2w for 1 year or observation. Co-primary endpoints were disease free survival (DFS) in the total population and in Stratum A. 474 pts were needed to detect, in the total population, an improvement from 60% to 73.6% 3-year DFS rate (HR 0.6; 90% power, 1-sided test, alfa 2%). 172 DFS events were required to perform the event-driven analysis. Assuming a proportion of 70-80% pts enrolled in Stratum A, the expected power to detect an HR 0.6 at alpha allocated in this subgroup is 70-79%. Overall survival was a secondary endpoint. **Results:** From June 2016 to October 2020, 477 pts were randomly assigned from 64 Italian and 6 UK centers. 11 pts (3 avelumab, 8 control) withdrew consent immediately after randomisation and are excluded from further analyses. 378 pts entered Stratum A (83%), of whom 99 (57 avelumab, 42 control) received further chemotherapy after surgery prior to enrollment in the trial. Efficacy results for the two co-primary DFS endpoints and the secondary OS endpoints are reported in the table. **Conclusions:** One year adjuvant avelumab versus control does not significantly improve DFS in high-risk TNBC patients. Nevertheless, the secondary enpoind OS was significanlty improved with avelumab vs control. RFS and DMFS will also be reported. A centralised collection of tumor tissue, plasma and feces has been performed and will allow a number of correlative studies. Clinical trial information: NCT02926196. Research Sponsor: Merck KGaA.

	Avelumab	Control	HR (95% CI)	p
	3-year survival % (95% CI)	3-year survival % (95% CI)		
DFS				
Total population	68.3 (61.9-73.8)	63.4% (56.8-69.3)	0.82 (0.61-1.11)	0.193
Stratum A (post-neoadjuvant)	66.9 (59.8-73.1)	61.0 (53.6-67.6)	0.81 (0.58-1.11)	0.194
OS				
Total population	85.2 (79.9-89.2)	78.2 (72.2-83.1)	0.66 (0.44-0.98)	0.041
Stratum A (post-neoadjuvant)	83.1 (77.1-87.8)	76.6 (69.6-82.1)	0.67 (0.44-1.03)	0.06

Clinical trial identification: EUDRACT 2016-000189-45. Legal entity responsible for the study: Department of surgery, oncology and gastroenterology, University of Padova. Funding: drug supply and financial support from Merck Kga.

LBA501 **Oral Abstract Session**

Rates of pathologic complete response (pCR) after datopotamab deruxtecan (Dato) plus durvalumab (Durva) in the neoadjuvant setting: Results from the I-SPY2.2 trial.

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Background: I-SPY2.2 is a multicenter phase 2 platform sequential multiple assignment randomized trial (SMART) in the neoadjuvant breast cancer setting that evaluates novel experimental regimens as first in a sequence (Block A) followed by standard chemo/targeted therapies (Blocks B/C) if indicated. The goal is to achieve a pCR after novel targeted agents alone or in sequence with standard therapies, with the optimal therapy assigned based on the tumor response predictive subtype (RPS). RPS incorporates expression-based immune, DNA repair deficiency (DRD), and luminal signatures with hormone receptor (HR) and HER2 status to subset patients into 6 subtypes: S1: HR+HER2-Immune-DRD-; S2: HR-HER2-Immune-DRD-; S3: HER2-Immune+; S4: HER2-Immune-DRD+; S5: HER2+/non-Luminal; S6: HER2+/Luminal. **Methods:** RPS S1, S2, S3, and S4 were eligible for assignment to Dato+Durva in Block A. Patients were followed by MRI during treatment (at 3, 6, and 12 weeks after start of Blocks A and B). Predicted responders by MRI and biopsy at the end of Block A or B have the option of going to surgery early; otherwise, they proceed to next treatment Block (B +/- C). Randomization to Block B includes a taxane-based regimen specific to the RPS, and options include S1: paclitaxel; S2 and S3: paclitaxel + carboplatin + pembrolizumab; S4: paclitaxel + carboplatin vs. paclitaxel + carboplatin + pembrolizumab. Patients who did not go to surgery after Block B proceeded to Block C (AC or AC + Pembrolizumab if HR-HER2-). The primary endpoint is pCR. Efficacy is evaluated within each RPS and HR+HER2- and HR-HER2- signatures. To estimate the arm's efficacy as a stand-alone therapy, we use a Bayesian covariate-adjusted model to estimate the pCR rate and compare the posterior distribution to a subtype-specific fixed threshold. This model uses pCR data when available and MRI data when pCR is not. To estimate pCR rate in the context of a multi-decision treatment regimen, we use a Bayesian model based on if and when a pCR occurred in the trial. The posterior is compared to a subtype-specific dynamic control generated from historical I-SPY data. **Results:** 106 patients were randomly assigned to the Dato+Durva arm between September 2022 and August 2023. The results for Dato+Durva as a stand-alone therapy are summarized in Table. After completion of Block A, 36 patients proceeded to surgery without completing Blocks B/C. **Conclusions:** Dato+Durva meets threshold for graduation within the RPS S3 subtype based on estimated pCR rate of 72% and warrants further investigation in a larger randomized controlled trial. Clinical trial information: NCT01042379. Research Sponsor: National Cancer Institute; P01CA210961; Quantum Leap Healthcare Collaborative.

Signatures	N	Estimated pCR Rate After Dato+Durva Alone (SD)	Subtype-Specific Threshold	P (>Thr)
RPS S1	25	0.02 (0.02)	0.15	0.00
RPS S2	23	0.11 (0.05)	0.15	0.20
RPS S3	47	0.72 (0.08)	0.4	>0.99
RPS S4	11	0.25 (0.11)	0.4	0.10
HR+HER2-	42	0.21 (0.06)	0.15	0.87
HR-HER2-	64	0.46 (0.06)	0.4	0.86

LBA502 **Oral Abstract Session**

A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial.

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Background: Triple-negative breast cancer (TNBC) is known for its high risk of early relapse and poor prognosis. Platinum agents have shown to increase pathological complete response (pCR) rates when added to neoadjuvant chemotherapy for TNBC. However, evidence regarding the survival benefit of platinum in this setting remains inconclusive. The PEARLY trial is a multicenter, randomized, open-label, phase 3 study designed to assess the efficacy and safety of carboplatin in combination with anthracycline/taxane therapy compared to standard anthracycline/taxane alone as either neoadjuvant or adjuvant treatment in early-stage TNBC. **Methods:** Patients with stage II or III TNBC were randomly assigned to either the carboplatin arm or the standard therapy arm, stratified by nodal status, institution, treatment setting (neoadjuvant *vs* adjuvant), and germline BRCA status. The standard therapy involved doxorubicin and cyclophosphamide (AC) followed by taxane treatment. The experimental arm included carboplatin in addition to taxane following AC. The primary endpoint was event-free survival (EFS), defined as disease progression or inoperable status for neoadjuvant therapy group, local or distant recurrence, occurrence of a second primary cancer, or death from any cause, while secondary endpoints encompassed overall survival (OS), invasive disease-free survival (IDFS), distant recurrence-free survival (DRFS), pCR rate, and safety. With a planned enrollment of 878 patients, the trial aimed for 80% power to detect a hazard ratio of 0.70 for EFS at a two-sided alpha level of 0.05, anticipating 248 EFS events over a 5-year follow-up period. **Results:** Between Jan 2016 and Jun 2020, 868 patients across 22 institutions in South Korea were enrolled. At a median follow-up of 51.1 months, carboplatin significantly improved EFS compared to the control arm (hazard ratio [HR], 0.68; 95% confidence interval [CI]: 0.50 to 0.93; p=0.017). The 5-year EFS rates were increased from 74.4% to 81.9%, demonstrating a 7.5% difference. Subgroup analysis showed consistent benefits across various patient categories. Secondary endpoints like IDFS and DRFS also favored carboplatin arm. OS data were immature, a total of 43 patients (10.2%) in the carboplatin arm and 57 patients (13.1%) in the control arm died (HR 0.66; 95% CI: 0.42 to 1.01). Grade ≥3 treatment-related adverse event rates were 74.6% (1 death due to infection) in the carboplatin arm and 56.7% (2 deaths due to infection and suicide) in the control arm. **Conclusions:** The addition of carboplatin to standard anthracycline followed by taxane therapy significantly improved EFS in patients with early-stage TNBC. The safety profile was consistent with the known expectations for each regimen. Clinical trial information: NCT02441933. Research Sponsor: Boryung; Hanmi; GC Corp.; Samyang Biopharm; Faculty research grant of Yonsei University College of Medicine for 2014 (6-2014-0188).

LBA503 **Oral Abstract Session**

ECOG-ACRIN EAZ171: Prospective validation trial of germline variants and taxane type in association with taxane-induced peripheral neuropathy (TIPN) in Black women with early-stage breast cancer.

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Background: Black women experience higher rates of TIPN compared to White women when receiving weekly paclitaxel (WP) for early-stage breast cancer. This disparity impacts health equity, as TIPN leads to more frequent dose reductions and higher recurrence rates in Black women. Conversely, disparities in TIPN by race are not seen in women receiving every three-week docetaxel (3D). Further, retrospective analyses have identified specific genotypes associated with differential risk of grade 2-4 TIPN in women of African ancestry receiving WP. The primary aim of EAZ171 was to prospectively validate germline predictors of TIPN in Black women receiving WP. Secondary objectives included comparing rates of TIPN and dose reductions in Black women receiving WP compared to 3D. **Methods:** Women with early-stage breast cancer who self-identified as Black and were planned by physician choice to receive (neo) adjuvant WP (80mg/m^2 x 12 doses) or 3D (75 mg/m^2 x 4-6 doses) were eligible. Genotyping determined germline neuropathy risk, defined as high (*FCAMR* homozygous wt or *SBF2* mutated) or low (variant allele in *FCAMR* and *SBF2* wt). Grade 2-4 TIPN by physician-reported CTCAE v.5 was compared between high vs. low risk genotypes, and between the WP vs. 3D arms at one year using Fisher exact tests with two-sided alpha of 0.1. Patient-rated TIPN was captured using PRO-CTCAE items, and patient-reported outcomes (PROs) assessed TIPN symptoms and functional interference (FACT/GOG-NTx, EORTC CIPN20). **Results:** 249 patients were enrolled between 6/27/19-3/31/22, including 121 receiving at least one dose of WP and 118 receiving a dose of 3D. Of those with genotype data, 91/117 (77.8%) in the WP arm and 87/118 (73.7%) in the 3D arm were classified as high risk. Physician-reported grade 2-4 TIPN was not significantly different in the high vs. low risk genotype groups with WP (47% vs. 35% p=0.27) nor with 3D (28% vs. 19% p=0.47). Grade 2-4 TIPN was significantly higher in the WP vs. 3D arm by physician-rated CTCAE (45% vs. 29% p=0.02) and PRO-CTCAE (40% vs. 24% p=0.03). Trends in worsening neuropathy scores were similar over time using the FACT/GOG-NTx and EORTC CIPN20 questionnaires, but were not significantly different between the two arms at 1 year. Patients receiving WP required more dose reductions due to TIPN (28% vs. 9% p<0.001) or due to any cause (39% vs. 25% p=0.02) than patients receiving 3D. **Conclusions:** In this prospective trial enrolling only Black women with breast cancer, germline variation did not significantly impact risk of TIPN with WP or 3D. However, 3D was more tolerable evidenced by less grade 2-4 TIPN and fewer dose reductions compared to WP. Given the disparate burden of TIPN and its potential impact on cure rates, this trial suggests docetaxel should be considered the preferred taxane for Black women with early-stage breast cancer. Clinical trial information: NCT04001829. Research Sponsor: National Cancer Institute; U10CA180794, U10CA180821, UG1CA189828, U10CA180868, UG1CA189859, UG1CA189997, UG1CA190140, UG1CA233196, UG1CA233320, UG1CA233330, UG1CA233339, UG1CA233341, and UG1CA239758.

LBA507 Oral Abstract Session

Prognostic utility of ctDNA detection in the monarchE trial of adjuvant abemaciclib plus endocrine therapy (ET) in HR+, HER2-, node-positive, high-risk early breast cancer (EBC).

Sherene Loi, Stephen R. D. Johnston, Carlos L. Arteaga, Stephanie L. Graff, Sarat Chandarlapaty, Matthew P. Goetz, Christine Desmedt, Hironobu Sasano, Deli Liu, Vanessa Rodrik-Outmezguine, Anthony Sireci, Cynthia Sandoval, Helen H Won, Lacey M Litchfield, Nicholas C. Turner; Peter MacCallum Cancer Centre, Melbourne, Australia; The Royal Marsden NHS Foundation Trust, London, United Kingdom; UT Southwestern Simmons Comprehensive Cancer Center, Dallas, TX; Lifespan Cancer Institute, Legorreta Cancer Center at Brown University, Providence, RI; Memorial Sloan Kettering Cancer Center, New York, NY; Mayo Clinic, Rochester, MN; Laboratory for Translational Breast Cancer Research, Department of Oncology, KU Leuven, Leuven, Belgium; Tohoku University Hospital, Sendai, Japan; Eli Lilly and Company, Indianapolis, IN

Background: In monarchE (NCT03155997), 2 years of adjuvant abemaciclib + ET resulted in sustained improvement in invasive disease-free survival (IDFS; HR=0.680, 7.6% absolute benefit at 5 years) in patients (pts) with HR+, HER2-, node-positive, high-risk EBC. Here, we investigate the prognostic value of ctDNA detection and dynamics in pts from monarchE. **Methods:** Samples were analyzed from a selected pt subset (n=1397; abemaciclib + ET arm, n=685; ET arm, n=712), enriched for overall IDFS events compared to the total monarchE study population (IDFS event rate: 31% [433/1397] vs 18% [992/5637]). Pts had blood collected pre-study treatment (baseline) and at 3, 6, or 24 months. ctDNA detection was performed using the personalized, tumor informed Signatera ctDNA assay (Natera, Inc) and whole exome sequencing (WES) of matched primary tumor and normal required for assay design was performed. **Results:** Among 1397 pts, 65% (n=910) had sufficient plasma samples and WES performed, and all 910 had successful ctDNA assay testing. Among these 910 pts, the IDFS event rate was 27% (abemaciclib + ET, 23% [101/438]; ET alone, 31% [146/472]). Rates of ctDNA positivity (at baseline and any change from baseline) and associated IDFS events are shown in Table. Among pts with ctDNA positivity, 87% had an IDFS event in comparison to 15% with persistent ctDNA negative (-) status during the study. **Conclusions:** In a pt subset from monarchE enriched for IDFS events, ctDNA detection was relatively infrequent (<20%); however, its detection at any time during the 24 months of study therapy was adversely prognostic. As compared to pts who had remaining ctDNA positive (+), pts who had clearance of ctDNA on therapy had lower risk of IDFS events, but the event risk still remained clinically meaningful in these pts. Clinical trial information: NCT03155997. Research Sponsor: Loxo@Lilly.

	N (%)	IDFS Event (%)	Median Time from Earliest ctDNA Detection to IDFS Event in Months (range)
Overall ctDNA cohort	910 (100)	247 (27)	-
With IDFS event	247 (27)	247 (100)	-
Without IDFS event	663 (73)	0	-
ctDNA- (all timepoints)	758 (83)	115 (15)	-
ctDNA+ (any timepoint)	152 (17)	132 (87)	10 (0-48)
+ at baseline:	70 (8)	56 (80)	12 (0-43)
Cleared	24 (3)	10 (42)	19 (4-32)
Remained +	46 (5)	46 (100)	9 (0-43)
Became +	82 (9)	76 (93)	9 (0-26)

LBA509 **Rapid Oral Abstract Session**

Rates of pathologic complete response (pCR)after neoadjuvant datopotamab deruxtecan (Dato): Results from the I-SPY2.2 trial.

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Background: I-SPY2.2 is a multicenter phase 2 platform sequential multiple assignment randomized trial (SMART) evaluating novel experimental regimens in the neoadjuvant breast cancer setting. The novel therapy is given as first in a sequence (Block A), followed by standard chemo/targeted therapies (Block B/C) if indicated. The goal is to identify agents that lead to pCR after novel targeted agents alone, or in sequence with optimal therapy assigned based on the tumor response predictive subtype (RPS). RPS incorporates expression-based immune, DNA repair deficiency (DRD), and luminal signatures with hormone receptor (HR) and HER2 status to classify patients by subtype: S1: HR+HER2-Immune-DRD-; S2: HR-HER2-Immune-DRD-; S3: HER2-Immune+; S4: HER2-Immune-DRD+; S5: HER2+/non-Luminal; S6: HER2+/Luminal. **Methods:** RPS S1, S2, S3 and S4 were eligible for assignment to Dato in Block A. Patients (pts) were followed by MRI during treatment (at 3, 6 and 12 weeks after start of Blocks A and B). Predicted responders by MRI and biopsy at the end of Block A or B have the option of going to surgery early, otherwise they proceed to next treatment Block (B +/- C). Randomization to Block B includes a taxane-based regimen specific to the RPS, and options include S1: paclitaxel; S2 and S3: paclitaxel + carboplatin + pembrolizumab; S4: paclitaxel + carboplatin vs. paclitaxel + carboplatin + pembrolizumab. Patients who did not go to surgery after Block B proceeded to Block C (AC or AC + Pembrolizumab if HR-HER2-). The primary endpoint is pCR. Efficacy is evaluated within each RPS and HR+HER2- and HR-HER2- signatures. To estimate the arm's efficacy as a stand-alone therapy, we use a Bayesian covariate-adjusted model to estimate the pCR rate and compare the posterior distribution to a subtype-specific fixed threshold. This model uses pCR data when available and MRI data when pCR is not. To estimate pCR rate in the context of a multi-decision treatment regimen, we use a Bayesian model based on if and when a pCR occurred in the trial. The posterior is compared to a subtype-specific dynamic control generated from historical I-SPY data. **Results:** 103 pts were randomly assigned to the Dato arm between August 2022 and August 2023. All patients have proceeded beyond Block A; 33 went to surgery after Dato alone. The efficacy results for Dato as a stand-alone therapy are summarized in Table. **Conclusions:** Dato monotherapy was active, particularly in the HR-HER2- signature, but did not meet the pre-specified threshold for graduation in I-SPY 2.2. Clinical trial information: NCT01042379. Research Sponsor: National Cancer Institute; P01CA210961; Quantum Leap Healthcare Collaborative.

Signatures	N	Estimated pCR rate After Dato Alone (SD)	Subtype-Specific Threshold	P(>Thr)
HR+HER2-Immune-DRD- (RPS S1)	36	0.02 (0.02)	0.15	0.00
HR-HER2-Immune-DRD- (RPS S2)	11	0.14 (0.06)	0.15	0.37
HER2-Immune+ (RPS S3)	46	0.34 (0.09)	0.4	0.24
HER2-Immune-DRD+ (RPS S4)	10	0.31 (0.12)	0.4	0.21
HR+HER2-	53	0.09 (0.04)	0.15	0.10
HR-HER2-	50	0.29 (0.07)	0.4	0.06

LBA1000 **Oral Abstract Session**

Trastuzumab deruxtecan (T-DXd) vs physician's choice of chemotherapy (TPC) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) with prior endocrine therapy (ET): Primary results from DESTINY-Breast06 (DB-06).

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Background: T-DXd is approved for HER2-low (IHC 1+ or 2+/ISH-negative) mBC after ≥1 line of chemotherapy (CT). DB-06 (NCT04494425) evaluated T-DXd in pts with HER2-low or -ultralow (IHC 0 with membrane staining), HR+ mBC after disease progression (PD) on endocrine-based therapy and no prior CT for mBC. **Methods:** Pts with HER2-low or -ultralow, HR+ mBC were randomized 1:1 to T-DXd 5.4 mg/kg or TPC. Pts had no prior CT for mBC, with ≥2 lines of ET for mBC, or 1 line of ET for mBC if PD occurred ≤24 months (mo) of adjuvant ET or ≤6 mo of ET+CDK4/6i for mBC. Primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR) in HER2-low. Key secondary endpoints were PFS in intent-to-treat (ITT = HER2-low and -ultralow) and overall survival (OS). Other endpoints included objective response rate (ORR) and safety. **Results:** As of Mar 18, 2024, 866 pts (HER2-low, n=713; HER2-ultralow, n=153) were randomized; 90.4% had prior CDK4/6i. TPC group pts were selected for capecitabine (59.8%), nab-paclitaxel (24.4%) or paclitaxel (15.8%). T-DXd significantly improved PFS vs TPC in HER2-low (HR, 0.62 [95% CI 0.51, 0.74], P<0.0001; median, 13.2 vs 8.1 mo). ITT and HER2-ultralow results were consistent with HER2-low (Table). Median treatment duration was 11.0 mo (T-DXd) vs 5.6 mo (TPC). OS was immature at first interim analysis (HER2-low HR, 0.83 [95% CI 0.66, 1.05], P=0.1181; median follow up, 18.6 mo). Grade (Gr) ≥3 drug-related adverse events occurred in 40.6% (T-DXd) vs 31.4% (TPC). Adjudicated interstitial lung disease / pneumonitis occurred in 49 (11.3%; 0.7% Gr 3/4, 0.7% Gr 5) vs 1 (0.2% Gr 2) pts receiving T-DXd vs TPC. **Conclusions:** T-DXd showed a statistically significant and clinically meaningful PFS benefit vs TPC (CT) in HER2-low mBC. HER2-ultralow results were consistent with HER2-low. Safety was in line with known profiles. DB-06 establishes T-DXd as a standard of care following ≥1 endocrine-based therapy for pts with HER2-low and -ultralow, HR+ mBC. Clinical trial information: NCT04494425. Research Sponsor: This study is sponsored by AstraZeneca. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).

	T-DXd, HER2-low (n=359)*	TPC, HER2-low (n=354)*	T-DXd, ITT (n=436)	TPC, ITT (n=430)	T-DXd, HER2-ultralow (n=76)†	TPC, HER2-ultralow (n=76)†
mPFS (95% CI), mo¤	13.2 (11.4, 15.2)	8.1 (7.0, 9.0)	13.2 (12.0, 15.2)	8.1 (7.0, 9.0)	13.2 (9.8, 17.3)	8.3 (5.8, 15.2)
PFS HR (95% CI), P value	0.62 (0.51, 0.74), <0.0001	–	0.63 (0.53, 0.75), <0.0001	–	0.78 (0.50, 1.21)	–
12-mo OS rate, %	87.6	81.7	87.0	81.1	84.0	78.7
OS HR (95% CI), P value§	0.83 (0.66, 1.05), 0.1181	–	0.81 (0.65, 1.00)	–	0.75 (0.43, 1.29)	–
Confirmed ORR, %¤	56.5 (51.2, 61.7)	32.2 (27.4, 37.3)	57.3 (52.5, 62.0)	31.2 (26.8, 35.8)	61.8 (50.0, 72.8)	26.3 (16.9, 37.7)

*HER2-low status investigator assigned;
†subgroup analysis; HER2-ultralow status centrally confirmed;
¤by BICR;
§data immature.

LBA1001 **Oral Abstract Session**

Abemaciclib plus fulvestrant vs fulvestrant alone for HR+, HER2- advanced breast cancer following progression on a prior CDK4/6 inhibitor plus endocrine therapy: Primary outcome of the phase 3 postMONARCH trial.

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Background: The combination of CDK4/6 inhibitors (CDK4/6i) + endocrine therapy (ET) is the standard first line treatment for HR+, HER2- advanced breast cancer (ABC). While disease progression occurs in nearly all patients (pts) with ABC, the optimal treatment for pts who experience progression on a CDK4/6i + ET remains uncertain. Real-world evidence suggests that use of abemaciclib after disease progression on a prior CDK4/6i prolongs progression-free survival (PFS) in ABC; however, Phase 2 trials with other CDK4/6i have generated mixed results. Here we present the primary outcome analysis for the Phase 3 postMONARCH trial (NCT05169567) of fulvestrant + abemaciclib or placebo in pts with HR+, HER2- ABC following disease progression on prior CDK4/6i + ET. **Methods:** postMONARCH was a global, double-blind, placebo-controlled study with pts randomized 1:1 to abemaciclib + fulvestrant or placebo + fulvestrant. Eligible pts had disease progression on a CDK4/6i + AI as initial therapy for ABC or relapse on/after a CDK4/6i + ET as adjuvant therapy for early breast cancer. No other prior treatment for ABC was permitted. Primary endpoint was investigator-assessed PFS; secondary endpoints included PFS by blinded independent central review (BICR), overall survival (OS), objective response rate (ORR), and safety. Assuming a hazard ratio (HR) of 0.7, the study had ~80% power to detect superiority for abemaciclib, with a cumulative 2-sided type I error of 0.05. Kaplan-Meier method was used to estimate PFS curves and treatment effect was estimated using a stratified Cox proportional hazard model. **Results:** A total of 368 pts were randomized to abemaciclib + fulvestrant (n = 182) or placebo + fulvestrant (n= 186). Most pts (99%) enrolled directly after CDK4/6i + ET as initial therapy for ABC. Prior CDK4/6i was 59% palbociclib, 33% ribociclib, and 8% abemaciclib. At interim analysis, the study reached the pre-specified criteria for significantly improved investigator-assessed PFS with abemaciclib + fulvestrant compared to placebo + fulvestrant (169 events, HR = 0.66; 95% CI 0.48 – 0.91; p = 0.01). At primary analysis (258 events), the HR was 0.73 (95% CI 0.57 – 0.95), with PFS rates at 6 months of 50% vs 37% for the abemaciclib and placebo arms, respectively. Consistent effect was seen across major clinical and genomic subgroups, including pts with baseline *ESR1* or *PIK3CA* mutations. ORR was improved with abemaciclib compared to placebo (17% vs 7%, respectively, in pts with measurable disease). PFS according to BICR was also improved with HR = 0.55 (95% CI 0.39 - 0.77). OS remains immature (20.9% event rate). Safety was consistent with the known profile of abemaciclib. **Conclusions:** Abemaciclib + fulvestrant demonstrated statistically significant PFS improvement in pts with ABC progression on prior CDK4/6i-containing therapy. Clinical trial information: NCT05169567. Research Sponsor: Eli Lilly and Company.

LBA1002 Oral Abstract Session

Palbociclib plus exemestane with GnRH agonist vs capecitabine in premenopausal patients with HR+/HER2- metastatic breast cancer: Updated survival results of the randomized phase 2 study Young-PEARL.

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Background: The Young-PEARL study demonstrated improved progression free survival (PFS) (mPFS: 20.1 *vs.* 14.4 mo.) of exemestane plus palbociclib with ovarian function suppression (OFS) compared to capecitabine in premenopausal patients with HR+/HER2- metastatic breast cancer (mBC). Here we report updated survival outcomes with median follow-up of 54.8 months (data cutoff, November 30, 2023). **Methods:** Premenopausal women aged 19 years or older with HR+/HER2- BC who had relapsed or progressed during previous tamoxifen therapy were enrolled. One line of previous chemotherapy for mBC was allowed. The primary endpoint was PFS, which was defined as the time from C1D1 to disease progression or death. The key secondary endpoint was overall survival (OS). Other secondary endpoints included objective response rate (ORR) and toxicities. **Results:** 184 patients were randomly assigned to exemestane plus palbociclib with OFS (n=92) or capecitabine (n=92). Median age was 44.0 years (range, 28-58). Key efficacy and safety are shown in Table. Final analysis was conducted for 174 patients. The updated mPFS was 19.5 mo. (90% CI, 14.3-22.3) for exemestane + palbociclib + OFS compared with 14.0 mo. (90% CI, 11.7-18.7) for capecitabine (HR 0.75, *P*=0.04). mOS was 54.8 mo. (95% CI, 48.9-77.1) for palbociclib arm and 57.8 mo. (95% CI, 46.3-N/A) for capecitabine arm (HR 1.06, *P*=0.77). mPFS2 (from the date of 1st PD to 2nd PD) was significantly shorter in palbociclib arm than those of capecitabine arm (7.5 *vs.* 11.7 mo. *P*=0.02). Confirmed ORR based on the investigator assessments was 33.3% (95% CI, 23.6-43.1) for palbociclib and 33.7% (95% CI, 23.6-43.9) for capecitabine. Median treatment duration was 18.9 mo. (range 1.6-88.4) in palbociclib and 13.5 mo. (range 0.1-70.8) in capecitabine. In palbociclib arm, 86 (93.5%) experienced grade 3 or more TEAEs, mainly asymptomatic neutropenia (64.1%), compared to 41 (48.2%) patients with grade ≥3 TEAEs in the capecitabine arm, mainly Hand-Foot syndrome and neutropenia (18.8% for each). **Conclusions:** Young-PEARL study showed exemestane + palbociclib with OFS improves efficacy compared with capecitabine in terms of PFS, which did not lead to an OS benefit for patients with premenopausal HR+/HER2- mBC (median follow-up duration: 54.8 months). The overall safety profile of palbociclib and capecitabine continues to be manageable with longer follow-up. Clinical trial information: NCT02592746. Research Sponsor: None.

Summary of efficacy and safety results for palbociclib arm vs capecitabine arm in premenopuasal patients with HR+/HER2- mBC.

	Exemestane + Palbociclib + OFS	Capecitabine
Efficacy		
N	90	84
mPFS (90% CI) mo.	19.5 (14.3-22.3)	14.0 (11.7-18.7)
HR (90% CI)	HR 0.75 (0.57-0.98); *P*=0.04[a]	
mOS (95% CI) mo.	54.8 (48.9-77.1)	57.8 (46.3-N/A)
HR (95% CI)	HR 1.06 (0.72-1.57); *P*=0.77[b]	
Safety		
N	92	85
TEAEs	90 (97.8)	81 (95.3)
Grade ≥3	86 (93.5)	41 (48.2)

[a]One-sided, [b]Two-sided.

LBA1004 Oral Abstract Session

SACI-IO HR+: A randomized phase II trial of sacituzumab govitecan with or without pembrolizumab in patients with metastatic hormone receptor-positive/HER2-negative breast cancer.

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Background: Sacituzumab govitecan (SG) is a TROP2 antibody drug conjugate (ADC) with a topoisomerase I inhibitor payload (SN-38) approved for previously treated triple negative and hormone receptor-positive/HER2-negative (HR+/HER2-) metastatic breast cancer (MBC). Double-strand DNA breaks induced by SN-38 activate cGAS-STING, stimulating type I IFN production and T cell recruitment. SN-38 can upregulate MHC class-I and PD-L1 expression, enhance cytotoxic T cell effector functions and deplete regulatory T cells. To evaluate if SG synergizes with pembrolizumab (PD-1 inhibitor) we conducted a randomized, open-label phase 2 study comparing SG with or without pembrolizumab in HR+/HER2- MBC (NCT04448886). **Methods:** Eligible patients (pts) had unresectable locally advanced or metastatic HR+ (ER≥1% and/or PR≥1%), HER2- breast cancer treated with ≥1 prior endocrine therapy and 0-1 chemotherapy (CT) for MBC. Pts with brain metastases were eligible if locoregional therapy was completed and steroids discontinued ≥7 days before study therapy. Pts who received prior topoisomerase I inhibitor ADC, irinotecan or PD-1/L1 inhibitors were excluded. Pts were randomized 1:1 to Arm A [SG 10 mg/kg IV (D1, D8) + pembrolizumab 200 mg IV (D1), 21-day cycle] or Arm B (SG alone). The primary endpoint was progression-free survival (PFS); secondary endpoints included PFS in PD-L1+ pts (22C3 CPS ≥1), overall survival (OS), objective response rate (ORR) and toxicity (NCI CTCAE v5.0). Baseline and on-treatment biopsies were performed for correlative analyses. For this preliminary analysis, data were locked 1/12/24. **Results:** Between 03/2021-01/2024, 110 pts enrolled; 104 pts (52 Arm A; 52 Arm B) started study therapy and were included in the analysis. Median age was 57 yrs (range: 27-81); 102 pts (98.1%) were female. 80 pts (76.9%) received prior CDK4/6 inhibitor for MBC; 58 (55.8%) had no prior CT, 46 (44.2%) had 1 prior line of CT for MBC. At a median follow-up of 9.2 months (mo), median PFS was 8.4 mo in Arm A vs 6.2 mo in Arm B (HR 0.76, 95% CI 0.47-1.23, log-rank p=0.26); ORR 21.2% and 17.3%, respectively. OS data are immature with only 26 events to date; OS was 16.9 mo vs 17.1 mo (HR 0.65, 95% CI 0.30-1.41, log-rank p=0.28), respectively. The most frequent treatment-related toxicities (≥G2) in Arm A were neutropenia (67.3%), fatigue (36.5%), alopecia (36.5%), anemia (32.7%), leukopenia (26.9%), diarrhea (21.2%) and nausea (21.2%); in Arm B, neutropenia (59.6%), alopecia (38.5%), diarrhea (34.6%), nausea (32.7%), fatigue (32.7%) and anemia (21.2%). **Conclusions:** Addition of pembrolizumab to SG showed a non-significant trend toward improved PFS in unselected HR+/HER2- MBC at this preliminary time point. Final PFS and updated OS with further follow-up will be presented at the meeting. Exploratory outcome analyses by TROP2 and PD-L1 expression will be reported. Clinical trial information: NCT04448886. Research Sponsor: Gilead Sciences; Merck.

LBA2064 **Poster Session**

VAMANA: A phase 2 study of low-dose bevacizumab plus CCNU in relapsed/ recurrent glioblastoma.

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Background: There are limited systemic therapy options for recurrent glioblastomas (rGBM). CCNU and/or Bevacizumab are often used to treat rGBM not amenable to local therapy. The addition of Bevacizumab (10 mg/kg) to CCNU failed to improve overall survival in the EORTC 26101 study. The question is whether the failure was due to the high dose of Bevacizumab used in the study. High doses of Bevacizumab may lead to excessive pruning & destruction of blood vessels, hampering the delivery of CCNU. In vitro & in vivo studies showed that a lower dose of Bevacizumab (1-1.5 mg/kg) has the potential to normalize tumor vasculature leading to improved drug delivery & outcomes. To test this hypothesis, we conducted this study to evaluate the efficacy of low-dose Bevacizumab in combination with CCNU in rGBM. **Methods:** This was a phase 2 open-label, single-arm trial that included adults with rGBM with an ECOG PS 0-2 and adequate organ & marrow function. The participants received CCNU 110 mg/m^2 PO once a day, on day 1 of a 42-day cycle (max. 8 cycles) with Bevacizumab 1.5 mg/kg intravenously every 3 weeks (max.16 cycles). Appropriate anti-emetic prophylaxis was given. Treatment continued until disease progression, clinical deterioration, or development of intolerable side effects. Response assessment was done with MRI Brain +/- spine at 2 monthly intervals till disease progression. The modified RANO criteria were used for response assessment. Safety assessments were done on day 8 of cycle 1, & days 21 & 42 of each cycle. The primary end-point of this study was overall survival (OS) and secondary end-points were progression-free survival (PFS) & safety. A 6-month OS $\geq$ 40% was the signal to explore this regimen further and if the 6-month OS $<$20% it would be considered futile. Descriptive statistics were performed and the Kaplan-Meier method was used for time-to-event analysis. **Results:** Forty-six patients were enrolled in this study. The median age was 42 years (IQR 33-52.75) and 78.3% (36/46) were males. Most patients (76.1%, 35/46) had an ECOG PS of 1. The median follow-up duration was 15.27 months (95% CI 13.47-17.06). The median number of doses of Bevacizumab and CCNU were 4 and 2 respectively. Three (6.5%) patients completed all planned doses of Bevacizumab and CCNU. The objective response rate (ORR) was 15.2 % (7/46). The median OS was 6.133 months (95% CI 5.474-6.793). The 6-month OS was 57.1%. The median PFS was 3.267 months (95% CI 0.850-5.684). The most frequent grade 3 or higher toxicities seen were neutropenia (7/46, 15.2%), thrombocytopenia (5/46,10.8%), elevated ALT levels (3/46, 6.5%), anemia (2/46, 4.3%) and hyponatremia (2/46, 4.3%). **Conclusions:** This study demonstrates the efficacy of low-dose Bevacizumab in combination with CCNU in rGBM (the median OS exceeded the preplanned cut-off of 40%) with an acceptable toxicity profile and no new safety signals. This combination should be explored further in a phase III randomized study. Clinical trial information: CTRI/2020/07/026696. Research Sponsor: Neuro-Oncology Research Fund, Tata Memorial Centre; Unrestricted educational grant from Emcure Pharmaceutical limited.

LBA2509 Clinical Science Symposium

Atezolizumab in patients (pts) with tumor mutational burden (TMB)–high tumors from the TAPISTRY trial.

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Background: Studies have suggested that pts with TMB-high tumors could derive clinical benefit from atezolizumab, a PD-L1 inhibitor; however, these studies used inconsistent TMB cutoffs. We report efficacy and safety data of atezolizumab in adult and pediatric pts with TMB-high advanced/metastatic solid tumors from Cohort D of the TAPISTRY trial (NCT04589845), using two TMB cutoffs: ≥13 mutations [mut]/Mb and ≥16 mut/Mb. **Methods:** TAPISTRY is a phase II, global, open-label, multicohort basket trial evaluating the efficacy and safety of multiple therapies in pretreated pts with advanced/metastatic solid tumors. Pts in Cohort D had advanced unresectable/metastatic, PD-L1 inhibitor-naïve, TMB-high (≥13 mut/Mb) solid tumors. Atezolizumab was given every 21 days, at 1200 mg in pts ≥18 years old, and at ≥15 mg/kg (up to 1200 mg) in pts <18 years old. Tumor responses were assessed per RECIST v1.1. Primary endpoint: objective response rate (ORR) by independent review committee (IRC) in pts with TMB ≥16 mut/Mb. Secondary endpoints included ORR by IRC in pts with TMB ≥13 mut/Mb, duration of response (DoR), progression-free survival (PFS), overall survival (OS) and safety. **Results:** At data cut-off (Nov 9, 2023), 150 pts with TMB ≥13 mut/Mb were enrolled. In the safety-evaluable population (n = 148), median age was 63 years (range 11–86); 56% of pts were male, and 56% had received ≥2 prior lines of therapy (median 2; range 0–14). The efficacy-evaluable population included 129 pts with TMB ≥13 mut/Mb (TMB ≥16 mut/Mb; n = 111); the most common tumor types were colorectal (n = 40; 31%), breast, and gastroesophageal cancer (n = 11 each; 9%). Key outcomes are presented (Table). After a median follow-up of 9.8 months, ORR by IRC was comparable between pts with TMB ≥16 mut/Mb (22.5%) and pts with TMB ≥13 mut/Mb (20.2%). Responses were seen across a variety of tumor types. DoR 6- and 12-month event-free rates were 79% and 72%, respectively. Median PFS was short, suggesting fast disease progression in non-responders. Fatigue (22%) and anemia (20%) were the most common adverse events. Safety of atezolizumab was consistent with its known profile. **Conclusions:** Atezolizumab was well tolerated and led to antitumor activity in pts with TMB-high solid tumors. Responses were seen across a variety of tumor types. Clinical trial information: NCT04589845. Research Sponsor: F. Hoffmann-La Roche Ltd.

Efficacy	TMB ≥16 mut/Mb (n = 111)	TMB ≥13 mut/Mb (n = 129)
Objective response rate, n (%) [95% CI]	25 (22.5) [15.1–31.4]	26 (20.2) [13.6–28.1]
Complete / partial response	4 (3.6) / 21 (18.9)	4 (3.1) / 22 (17.1)
Stable disease / progressive disease / missing	37 (33.3) / 39 (35.1) / 10 (9.0)	43 (33.3) / 49 (38.0) / 11 (8.5)
Median DoR, months (95% CI)	NE (20.8–NE)	NE (20.8–NE)
Median PFS, months (95% CI)	2.8 (1.7–5.4)	2.7 (1.5–4.2)
Median OS, months (95% CI)	15.0 (9.1–21.5)	16.1 (9.1–21.4)
Safety, n (%)	**Safety-evaluable; n = 148**	
≥1 AE / Grade 3–5 AEs / serious AE	138 (93.2) / 60 (40.5) / 41 (27.7)	
≥1 TRAE	79 (53.4)	

(TR)AE, (treatment-related) adverse event.

LBA3501 Oral Abstract Session

Surgery versus thermal ablation for small-size colorectal liver metastases (COLLISION): An international, multicenter, phase III randomized controlled trial.

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Background: The standard of care for local treatment of patients (pts) with colorectal liver metastases (CRLM) is surgical resection. However, growing evidence suggests thermal ablation to be associated with a superior safety profile, lower costs, and shorter hospital stay, while rivaling surgical resection in terms of local control and overall survival (OS). This study aimed to explore the potential non-inferiority of thermal ablation compared to surgical resection for pts with small-size (≤3cm) resectable CRLM. **Methods:** In this multicenter, phase 3 Dutch Colorectal Cancer Group trial, pts aged 18 years and older with previously untreated CRLM were recruited from 14 centers in the Netherlands, Belgium and Italy. Pts with ≤10 CRLM, no extrahepatic metastases and ECOG 0-2 were stratified into low, intermediate and high disease burden subgroups and randomly assigned (1:1) to undergo surgical resection or thermal ablation. Though approach was left at the discretion of the operator, laparoscopic (+/- robot) resections and percutaneous ablations were favored over open procedures. To avoid drop-outs patients undergoing open procedures were randomized intra-operatively. The primary outcome was overall survival (OS) (log-rank; power 80%, 5% type I error rate; 1-sided). Secondary outcomes include distant and local tumor progression-free survival (PFS), local control, safety, length of hospital stay, quality of life and cost-effectiveness. **Results:** A total of 341 patients were enrolled; 299 were randomly assigned: 147 assigned to thermal ablation, 148 to surgical resection; 4 were excluded after randomization for not having the disease assessed. The trial was stopped at halftime for having met predefined stopping rules. After a median follow-up time of 28.8 months there was no difference regarding OS (HR 1.042; 95% CI, 0.689-1.576; p = 0.846) with a conditional probability of >90% to prove the hypothesis of non-inferiority. Procedure related mortality was 2.1% (n=3) for resection vs. 0% (n=0) for thermal ablation. The total number of adverse events (p = <0.001), the length of hospital stay (median 4 days [range 1-36] vs 1 day [range 1-44], p = <0.001) and local control also favored thermal ablation (HR 0.184; 95% CI, 0.040-0.838; p = 0.029). No differences were found regarding local (HR 0.833; 95% CI, 0.473-1.469; p = 0.528) and distant PFS (HR 0.982; 95% CI, 0.739-1.303; p = 0898). **Conclusions:** In conclusion, transitioning from surgical resection to thermal ablation as standard of care for patients with small-size (≤3 cm) CRLM would reduce complications, shorten hospital stay and improve local control, without compromising disease-free and overall survival. COLLISION is funded by a Medtronic-Covidien Investigator Sponsored Research grant. Clinical trial information: NCT03088150. Research Sponsor: Medtronic Covidien; 20130529.

LBA3502 **Oral Abstract Session**

Primary outcome analysis of the ORCHESTRA trial: A randomized phase III trial of additional tumor debulking to first-line palliative systemic therapy for patients with multiorgan metastatic colorectal cancer.

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Background: The phase-3, investigator-initiated, ORCHESTRA trial (NCT01792934) was conducted to prospectively evaluate overall survival (OS) benefit from tumor debulking in addition to standard palliative systemic therapy in patients with multiorgan metastatic colorectal cancer (mCRC). Local therapy of metastases is increasingly discussed as part of the treatment plan for patients with multiorgan mCRC in analogy to selected patients with oligometastatic disease for whom this is standard of care. Treatment decisions are made on a daily base in multidisciplinary teams (MDT) worldwide, but evidence of superiority for additional local therapy over systemic therapy alone based on a head-to-head comparison is lacking. **Methods:** Between May 2013 and May 2023, 454 patients were enrolled in 28 hospitals. Patients with multiorgan mCRC as described in Table, were eligible if at least 80% tumor debulking was deemed feasible by resection, radiotherapy and/or thermal ablative therapy at the start of first-line palliative systemic therapy according to the MDT. Upon clinical benefit after 3 or 4 cycles of respectively capecitabine or 5-fluorouracil/leucovorin and oxaliplatin ± bevacizumab, 382 patients were randomized 1:1 to continuation with systemic therapy alone in the standard arm or to tumor debulking followed by restart of the systemic therapy in the experimental arm. The primary endpoint was OS, from the date of inclusion to the date of death. Secondary endpoints included progression free survival (PFS) and treatment related adverse events. OS and PFS were analyzed by means of multivariable Cox proportional hazards regression analysis where the variables used in the randomization process were included as covariates. **Results:** 382 patients were randomized to either receive standard palliative systemic therapy in the standard arm (N=192) or to receive additional tumor debulking to palliative systemic therapy in the experimental arm (N=190). Baseline characteristics of patients were in standard arm versus (vs) experimental arm: median age 64 vs 64 years, male 69% vs 67%, >2 organs involved 38% vs 40%, baseline LDH >250 U/L 17% vs 16%, baseline CEA >200 ng/ml 5% vs 8%. At data cut-off on April 4th, 2024, a total of 153 OS events were observed in the standard arm and 155 OS events in the experimental arm. Median follow up was 32.3 months. Median OS in the standard arm was 27.5 months versus 30.0 months in the experimental arm (adjusted HR 0.88 [95% CI 0.70-1.10] p=0.225). Median PFS in the standard arm was 10.4 months versus 10.5 months in the experimental arm (adjusted HR 0.83 [95% CI 0.67-1.02], p=0.076). Details on local treatment modalities being applied, including rate of successful radical debulking and related adverse events, will be presented at the meeting. **Conclusions:** Additional tumor debulking to standard first-line palliative systemic therapy failed to improve overall survival for patients with multiorgan metastatic colorectal cancer. The increasing use of local therapies for patients with mCRC needs further consideration. Clinical trial information: NCT01792934. Research Sponsor: Dutch Cancer Foundation (KWF); ID0E4UAI7464; Roche Nederland; ID0EMVAI7465; Blokker-Verwer Foundation; ID0E2VAI7466.

Patients with Colorectal Cancer Metastases in at least Two Different Organs are Eligible If:	
1)	*More than one extrahepatic metastasis **OR***
2)	*More than five hepatic metastases not located in one lobe **OR***
3)	*Either positive para-aortal lymph nodes or celiac lymph nodes or adrenal metastases or pleural carcinomatosis or peritoneal carcinomatosis*

LBA3504 Oral Abstract Session

NEOPRISM-CRC: Neoadjuvant pembrolizumab stratified to tumour mutation burden for high risk stage 2 or stage 3 deficient-MMR/MSI-high colorectal cancer.

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Background: The prognostic advantage of early stage deficient-MMR/MSI-High colorectal cancer (CRC) is lost after relapse. Hence, there is a clinical imperative to maximise the chance of cure in early-stage disease. Tumour mutation burden (TMB) is an emerging biomarker for response and clinical benefit to immunotherapy in the advanced setting. NEOPRISM-CRC (Neoadjuvant PembRolizumab In Stratified Medicine – ColoReCtal) is the first multicentre Phase II Trial to determine if neoadjuvant pembrolizumab is efficacious and safe, prospectively stratified to TMB. **Methods:** The trial population included patients (pts) with operable high-risk stage 2 or stage 3 dMMR/MSI-High CRC. Pts with tumours that were TMB high or medium ($\geq$6 mutations/Mb on FoundationOneCDx test) received 3 cycles of pembrolizumab (200mg every 3 weeks) and underwent surgery within 4-6 weeks of last cycle. Pts with TMB low tumours ($\leq$5 mutations/Mb) underwent surgery 4-6 weeks after 1 cycle of pembrolizumab. The primary end point was pathological complete response rate (pCR). Secondary endpoints included 3-year relapse free survival, overall survival, safety, and health-related quality of life. The trial also incorporated translational endpoints to explore relationships between possible predictive novel biomarkers and response to pembrolizumab in blood, tumour tissue and microbiome. We required 19 pts with TMB high or medium tumours to detect a pCR after 3 cycles of neoadjuvant pembrolizumab of 33% (minimum of 10%), with one-sided 5% significance level and 80% power (A'Hern single stage). The trial would be considered a success if ^{3}5/19 of those pts achieved pCR. To achieve this number, we aimed to recruit 32 patients in total. **Results:** The trial opened on 20th July 2022 and 32 pts were rapidly enrolled. The pCR primary endpoint analysis was performed on 1st March 2024. The primary endpoint was exceeded with the pCR in the intent to treat pts (N=32) as well as the pCR in evaluable tumours shown in Table 1. Median TMB was 42 mutations/Mb (4-82). There was only 1 TMB low tumour and no TMB medium tumours. In the TMB high-medium cohort there were 32 evaluable resected tumours as 1 pt had 3 synchronous primaries, and 1 pt did not undergo surgery due to toxicity as well as pt choice. There were no immune-related toxicities >Grade 3. At a median follow-up of 6 months (range 2-15), no pts have had disease recurrence. **Conclusions:** Neoadjuvant pembrolizumab for early stage deficient-MMR/MSI-High CRC is highly efficacious and safe. Longer follow up is needed to assess relapse free survival and translational biomarker work is ongoing. Clinical trial information: NCT05197322. Research Sponsor: Merck; 58807.

	All Patients N=32	TMB High or Medium N=31	TMB Low N=1
Intent-to-treat pCR rate (95% CI)	17/32 53% (35%-71%)	17/31 55% (36%-73%)	0/1 0% (0%-98%)
Evaluable tumours pCR rate (95% CI)	19/33 58% (39%-75%)	19/32 59% (41%-76%)	0/1 0% (0%-98%)

LBA3510 **Rapid Oral Abstract Session**

Overall survival (OS) of phase 3 CodeBreaK 300 study of sotorasib plus panitumumab (soto+pani) versus investigator's choice of therapy for *KRAS* G12C-mutated metastatic colorectal cancer (mCRC).

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Background: In CodeBreaK 300 (NCT05198934), soto+pani was superior to investigator's choice at the primary analysis of progression-free survival (PFS) in patients (pts) with chemorefractory *KRAS* G12C-mutated mCRC (Fakih et al. NEJM. 2023). OS data were immature at the PFS analysis. We now report the final OS analysis of CodeBreaK 300. **Methods:** Study procedures and eligibility criteria were previously reported. The PFS primary endpoint was tested at primary analysis. Key secondary endpoints included OS and objective response. Though the study sample size was not powered for OS, OS hypothesis testing using stratified log-rank test was planned when 50% of pts had observed events per protocol. Stratified Cox hazard ratio (HR) and Kaplan-Meier median estimates are provided. **Results:** In total, 160 pts were randomly assigned 1:1:1 to soto960+pani (n=53), soto240+pani (n=53), or investigator's choice of trifluridine/tipiracil, or regorafenib (investigator's choice; n=54). As of Dec 18, 2023, with a median follow-up of 13.6 months, 82 deaths had occurred with 24, 28, and 30 deaths in the soto960+pani, soto240+pani, and investigator's choice arms, respectively. Median OS (95% CI) was not reached for soto960+pani, 11.9 months (7.5, NE) for soto240+pani, and 10.3 months (7.0, NE) for investigator's choice. Hazard ratio (95% CI) was 0.70 (0.41, 1.18) for soto960+pani compared to investigator's choice and 0.83 (0.49, 1.39) for soto240+pani compared to investigator's choice. Updated ORR, DOR, and DCR are included in Table. No new safety signals were observed. **Conclusions:** While CodeBreaK 300 was not powered to detect a statistically significant difference in OS, the study showed a trend toward improved OS for patients randomized to soto960+pani. Together with PFS and response rates, these results support the use of soto960+pani as a potential SOC for pts with chemorefractory *KRAS* G12C-mutated mCRC. Acknowledgements: The authors thank the patients, investigators, and study staff who contributed to this study; The study was sponsored and funded by Amgen Inc.; Medical writing support was provided by Shubha Dastidar, PhD (CACTUS) and Christopher Nosala, PhD (Amgen Inc.). Clinical trial information: NCT05198934. Research Sponsor: Amgen Inc.

Efficacy.

	Soto960+Pani n=53	Soto240+Pani n=53	Investigator's Choice n=54
Median OS, months (95% CI)	NE (8.6, NE)	11.9 (7.5, NE)	10.3 (7.0, NE)
Hazard ratio (95% CI)	0.70 (0.41, 1.18)	0.83 (0.49, 1.39)	-
2-sided p-value	0.20	0.50	-
Median follow up, months	13.6	14.0	12.9
ORR, % (95% CI)	30.2 (18.3, 44.3)	7.5 (2.1, 18.2)	1.9 (0.0, 9.9)
Number of responders	1 CR, 15 PR	1 CR, 3 PR	1 PR
Median DOR, months (range)	10.1 (3.1, 12.9+)	NR[a] (5.6, 11.2+)	NR[a] (5.2, 5.2)
DCR, % (95% CI)	71.7 (57.7, 83.2)	69.8 (55.7, 81.7)	46.3 (32.6, 60.4)

CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; NR, not reported; NE, not estimable; ORR, objective response rate; PR, partial response.
[a]Kaplan-Meier median DOR was not estimated due to small numbers of responders.

LBA3511 Rapid Oral Abstract Session

Total neoadjuvant treatment with long-course radiotherapy versus concurrent chemoradiotherapy in local advanced rectal cancer with high risk factors (TNTCRT): A multicenter, randomized, open-label, phase 3 trial.

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Background: Distant metastases remain a common problem in locally advanced rectal cancer (LARC) patients who received neoadjuvant chemoradiotherapy (NCRT) and surgery. Previous researchers have demonstrated the survival benefits of total neoadjuvant treatment (TNT) using short-course radiotherapy with CAPOX and long-course radiotherapy (LCRT) with mFOLFIRINOX. This study aimed to explore the efficacy of TNT using long-course radiotherapy (LCRT) combined with CAPOX. **Methods:** In this phase 3, open-label, multicenter, randomized trial, eligible pts were diagnosed as stage II/III and had at least one high risk factor: cT4a-b (resectable), cT3c-d with extramural venous invasion, cN2; involved mesorectal fascia, or enlarged lateral lymph nodes. Pts were randomly assigned to either Arm A to receive TNT (LCRT with six cycles of neoadjuvant CAPOX (one cycle of induction CAPOX, two cycles of concurrent CAPOX, and three cycles of consolidation CAPOX) followed by total mesorectal excision (TME)) or Arm B to receive NCRT (LCRT with concomitant capecitabine, followed by TME and adjuvant CAPOX). Radiotherapy in both groups was administered at 50-50.4 Gy in 25-28 fractions. The primary endpoint was disease free survival (DFS). The secondary endpoints were pathological response complete (pCR) rate, overall survival (OS), metastasis-free survival (MFS) and post-operative 30-day morbidity. **Results:** (ITT) Between June 6, 2017, and Mar 5, 2024, 458 pts were randomly assigned to two Arms (232 in Arm A, and 226 in Arm B). At a median follow-up of 44 months (IQR, 24-57.25), the 3-yr DFS was significantly increased in Arm A (77.0% vs 67.9% in Arm A/B respectively, HR 0.623, 95% CI 0.435-0.892, p = 0.009). 3-yr MFS was also significantly higher in arm A: 83.0% vs 74.2% in arm B (HR 0.595, 95% CI 0.392-0.903, p= 0.013). A total of 56 OS events was reported, and the 3-yr OS was 90.3% vs 87.9% (HR 0.747, 95% CI 0.441-1.266, p = 0.276) in arm A/B, respectively. TNT and NCRT in both arms were well tolerated. Thrombocytopenia was the most frequent grade 3-4 hematological adverse event in Arm A, occurring in 24 (10.3%) of 232 pts. Until now, 27.5% of pts achieved pCR in Arm A, compared to only 9.9% in Arm B. (OR 3.436, [1.1.941-6.084], p= 0.0001). In Arm A and B, 13 and 2 pts achieved clinical complete response (cCR) and received watch-and-wait strategy, respectively. No significant difference in severe morbidity within 30 days post-operation were found between the two arms. **Conclusions:** TNT with LCRT combined with CAPOX significantly improve DFS, MFS and pCR compared to standard concurrent neoadjuvant chemoradiotherapy in LARC patients with high risk factors, with acceptable toxicities. Clinical trial information: NCT03177382. Research Sponsor: None.

LBA3512 **Rapid Oral Abstract Session**

Durable complete responses to PD-1 blockade alone in mismatch repair deficient locally advanced rectal cancer.

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Background: Early results have demonstrated that locally advanced mismatch repair deficient rectal cancers can become undetectable with PD-1 blockade alone and do not require chemotherapy, radiation, or surgery. Yet, the durability of this approach is unknown. **Methods:** We enrolled 47 mismatch repair deficient rectal cancers to a phase II study of 6-months of dostarlimab, a PD-1blocking monoclonal antibody. Co-primary endpoints were response rate that was previously met and the sustained clinical complete response rate, which has not yet been reported. A sustained clinical complete response was defined as complete pathologic response at surgery or no evidence of tumor by MRI, endoscopy, and digital rectal exam for at least 12 months following completion of therapy. If 13 or more patients achieved a sustained clinical complete response out of the first 30 patients, the study would be deemed successful. **Results:** All of the 41 patients who completed treatment achieved a clinical complete response. No patients required any additional therapy, and no patients experienced local or distant disease recurrence. Twenty patients achieved a sustained clinical complete response with a median follow-up of 28.9 months (95% CI 22.9 -37.1) from first treatment, which satisfied the second co-primary endpoint. No serious adverse events greater than grade 2 were observed. Ultrasensitive tumor-informed circulating tumor DNA levels and tumor bed biopsies normalized earlier than endoscopy, MRI or PET/CT. **Conclusions:** PD-1 blockade for 6-months alone yields durable recurrence-free responses in locally advanced mismatch repair deficient rectal cancer without the need for chemotherapy, radiation, or surgery. Clinical trial information: NCT04165772. Research Sponsor: GSK; National Cancer Institute; Stand Up to Cancer; Swim Across America.

LBA3557 Poster Session

A randomized study evaluating tailoring of advanced/metastatic colorectal cancer (mCRC) therapy using circulating tumor DNA (ctDNA): TACT-D.

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Background: Identifying non-responders to expensive salvage therapies with modest benefits and substantial treatment related adverse events (TRAEs) (e.g. regorafenib [Reg] or TAS102 [Tas] in mCRC) is key to precision care. Retrospective studies suggest that ctDNA changes at timepoints (4-10 weeks [wks] into therapy) before radiographic assessment may predict treatment outcomes. However, prospective studies assessing early ctDNA changes are lacking and clinical utility remains uncertain. **Methods:** TACT-D is a randomized study to validate early dynamic changes in ctDNA (ΔctDNA: change in either maximum variant allele frequency (maxVAF) or mean VAF in predicting treatment response/resistance. Patients (pts) with mCRC clinically eligible for Reg/Tas were randomly assigned 2:1 to either standard of care (SOC) or ctDNA arm. All pts had ctDNA sequencing by Guardant360 CDx assay on cycle 1 day 1 (C1D1) and C1D15. On SOC arm, pts were restaged at 8 wks. On ctDNA arm, ΔctDNA (C1D15 - C1D1) was run in real-time and increase in ctDNA (ΔctDNA $>$ 0) triggered early radiographic restaging. Therapy was continued for responders (RECISTv1.1 stable disease/response) and stopped for progression (non-responders). Co-primary endpoints were: 1) comparison of TRAEs among study arms and 2) association of ΔctDNA and objective response rate (RR). Key secondary endpoints were progression free (PFS) and overall (OS) survival. Study was powered (82%; 2-sided α = .05) to detect 30% decrease in toxicity. **Results:** Between 4/2019 and 8/2023, 100 pts were randomized; 80 evaluable had median age of 56 years, 46% were females, 44% and 56% received Tas and Reg, respectively. Baseline ctDNA levels (ρ 0.90) and ΔctDNA (ρ 0.68) using maxVAF (reported below) and mean VAF showed strong correlation (P $<$ .001). Median ΔctDNA for entire cohort was -47% with no significant difference by treatment arms (SOC -45% v Exp -58%, P = .79) and therapy (Tas -71 v Reg -44, P = .19). ΔctDNA increased in 18% pts. Grade 3/4 TRAEs (32% v 40%, P = .62) did not differ significantly between arms. No significant association was seen between ΔctDNA and RR (OR .88, P = 1.0), PFS (HR .99, P = .88) and OS (HR 1.00, P = .64). Notably, higher baseline maxVAF was strongly associated with response (median maxVAF: 21.8% in non-responders v 3.4% in responders), PFS (HR 1.02) and OS (HR 1.03) (all P $<$ .001). After adjusting for baseline maxVAF, ΔctDNA was found to be associated with both PFS (HR 1.87, P = .038) and OS (HR 3.55, P = .001). **Conclusions:** In the first prospective study of clinical utility of monitoring ctDNA in mCRC, baseline ctDNA was strongly prognostic for clinical benefit from salvage therapies in mCRC. Adjusted for this prognostic impact, ΔctDNA between C1D1 and C1D15 was predictive of clinical outcomes. Efforts are needed to establish novel signatures, optimal cutoffs/intervals for assessing ctDNA response in mCRC, tailored to pts and their therapy. Clinical trial information: NCT03844620. Research Sponsor: MD Anderson Cancer Center, Houston, TX; Guardant Health Inc., Redwood City, CA.

LBA3559 **Poster Session**

Encorafenib and cetuximab versus irinotecan/cetuximab or FOLFIRI/cetuximab in Chinese patients with *BRAF* V600E mutant metastatic colorectal cancer: The NAUTICAL CRC study.

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Background: *BRAF* V600E mutations are present in 8-12% worldwide of patients with metastatic colorectal cancer (mCRC) and linked with a poor prognosis. Encorafenib + cetuximab (E+C) was approved by the FDA and EMA for patients with *BRAF* V600E-mutant mCRC who received prior systemic therapy, based on data from the BEACON CRC study. **Methods:** This Phase II, multicenter, randomized, open-label, 2-arm study evaluated E+C vs irinotecan + cetuximab or FOLFIRI + cetuximab (control arm) in Chinese patients with *BRAF* V600E mutant mCRC whose disease progressed after 1 or 2 prior treatment lines in the metastatic setting. A safety lead-in initially conducted in 10 patients reported no DLTs. Eligible patients had mCRC and a *BRAF* V600E mutation in tumor tissue determined by a local assay before screening and centrally confirmed. Patients were randomly assigned to the doublet arm (E+C) or the control arm in a 2:1 ratio, respectively. Randomization was stratified by baseline ECOG performance status (0 vs 1) and prior use of irinotecan (yes vs no). The primary objective of the randomized phase was to compare the efficacy of E+C vs the control arm, as measured by PFS (assessed by blinded independent central review). Secondary objectives included PFS assessed by the investigator, ORR, DOR, DCR, TTR, OS, QoL, and safety and tolerability of E+C. Results of the randomized phase of the study are reported. **Results:** At data cut-off (19 Dec 2023), 65 patients were enrolled in the E+C arm and 32 in the control arm. Median patient age was 56 years, the primary cancer site was the left colon in 56.7% of patients, 48.5% had metastases to ≥3 organs, 56.7% had liver metastases, 77.3% received one prior metastatic treatment, and 22.7% received 2 prior metastatic treatments. Results are shown below for E+C vs the control arm, respectively. Median PFS assessed by BICR was 4.2 mo vs 2.5 mo (HR 0.37; 95% CI: 0.20, 0.68; P=0.0004). Median OS was 11.6 mo vs 8.2 mo (HR for death 0.55; 95% CI: 0.31, 0.99). Confirmed ORR was 24.6% (95% CI: 14.8, 36.9) vs 6.3% (95% CI: 0.8, 20.8). Treatment emergent adverse events (TEAEs) of grade 3 or higher occurred in 47.7% vs 51.9% of patients. Treatment-related grade 3 or higher occurred in 24.6% and 44.4% of patients. The most frequent TEAEs were anemia (30.8% vs 37%), vomiting (26.2% vs 33.3%), rash (24.6% vs 29.6%), weight loss (23.1% vs 18.5%), hypoalbuminemia (21.5% vs 22.2%), and melanocytic naevus (21.5% vs 0%). Three patient deaths were reported during treatment: unknown cause (n=1) and pneumonia (n=1) in the E+C arm and septic shock (n=1) in the control arm. **Conclusions:** Treatment with a combination of encorafenib and cetuximab is effective and well tolerated in Chinese patients with *BRAF* V600E mutant mCRC, resulting in a significantly longer PFS than standard therapies. These results are consistent with those previously reported in the BEACON study. Clinical trial information: NCT05004350. Research Sponsor: Pierre Fabre Laboratories.

LBA3606 **Poster Session**

Longitudinal circulating tumor DNA monitoring in predicting response to short-course neoadjuvant radiotherapy in locally advanced rectal cancer: Data from a phase III clinical trial (UNION).

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Background: The data presented here is from a multicenter, randomized, open-label, controlled Phase III clinical study evaluating the feasibility of short-course radiotherapy (shortRT) sequentially combined with camrelizumab and chemotherapy as neoadjuvant therapy (NAT) for locally advanced rectal cancer (LARC)(UNION). Our aim is to explore the value of circulating tumor DNA (ctDNA)-based minimal residual disease (MRD) in assessing the comparative efficacy of short-course and long-course chemoradiotherapy (CRT). **Methods:** A total of 244 plasma samples from 79 LARC patients, who underwent NAT prior to curative surgery, were collected at baseline (C1), on-NAT (C2), post-NAT (C3), and post-surgery (C4). Deep targeted panel sequencing of 556 cancer-related genes was performed. The changes in genomic features and ctDNA-MRD status during treatment were monitored, and the relationship between these changes and treatment response were explored. **Results:** During NAT, the ctDNA-MRD positivity rate showed significant declining trends. Patients with high baseline TMB tend to show a significant inclination towards major pathological response and tumor regression grade 0/1 after NAT, while there is no significant correlation observed between baseline ctDNA-MRD status and treatment response. Interestingly, compared to long-course radiotherapy, microsatellite instability is more pronounced after shortRT (P=0.042), and ctDNA negativity is significantly associated with pathological complete response (pCR) (P=0.022). Furthermore, both ctDNA clearance (P=0.049) and MRD clearance (P=0.015) after shortRT are significantly correlated with pCR. A risk scoring predictive model based on ctDNA-MRD was established, with achieving the highest C-index at the C2 time point. This model, combining MRD clearance and CEA, outperforms models using only MRD clearance (AUC=0.917, 95% CI=0.753 to 1.000) or only CEA (AUC=0.733, 95% CI=0.449 to 1.000), demonstrating superior performance in predicting pCR/non-pCR (AUC=0.983, 95% CI=0.937 to 1.000). **Conclusions:** These findings offers valuable insights into the dynamic landscape of NAT for LARC management and emphasize the potential of ctDNA-based MRD assessment as a valuable tool for tailoring treatment strategies. The differences observed between shortCRT and longCRT regimens underscore the need for personalized treatment approaches. Overall, our study contributes valuable insights into optimizing treatment decision-making and predicting treatment response in LARC patients, ultimately advancing the field of rectal cancer management. Research Sponsor: National Natural Science Foundation of China; Chinese Society of Clinical Oncology (CSCO)-Tongshu Oncology Research Fund.

LBA4001 **Oral Abstract Session**

Effect of chemotherapy/targeted therapy alone vs. chemotherapy/targeted therapy followed by radical surgical resection on survival and quality of life in patients with limited-metastatic adenocarcinoma of the stomach or esophagogastric junction: The IKF-575/RENAISSANCE phase III trial.

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Background: The IKF-575 trial investigates the long-standing question about the role of surgical intervention in limited-metastatic gastric / esophagogastric junction cancer after systemic induction therapy. **Methods:** Previously untreated patients (pts) with limited metastatic disease (retroperitoneal lymph node (RPLN) metastases only or a maximum of one incurable organ site that is potentially resectable or locally controllable with or without retroperitoneal lymph nodes) received 4 cycles of FLOT, + trastuzumab if Her2+ or + nivolumab if PD-L1 positive. Pts without progression after 4 cycles were randomized to receive additional FLOT (Arm B) or radical complete surgical resection of primary and metastases followed by the same treatment (Arm A). It was planned to randomize 176 pts for which 271 pts had to enrolled. The primary endpoint was overall survival in the ITT population using Kaplan-Meier estimates. Recruitment was stopped after enrollment of 183 patients (141 patients randomized) with minimal impact on statistical power, due to a slow enrollment rate. **Results:** The ITT comprised 139 pts (A, 67; B, 72): 20% had RPLN metastases only, 58% organ metastases only, and 22% had both. Surgery in Arm A (ITT) was performed in 91% of pts and R0-resection rate (primary) was 82%. 30-d and 90-d mortalities in the surgery population were 3% and 8%. At least 4 additional cycles of post-op or post-randomization chemotherapy were achieved in 42% of pts in Arm A vs. 71% of pts in Arm B. The primary endpoint ovrall survival was not met due to increased early mortality in the surgery Arm leading to crossing survival curves with OS 25%- and 75%-Quantiles being 10 vs. 14 months and 65 vs. 41 months for Arms A vs. B, respectively. Pts with RPLN metastases only seemed to benefit most from the surgical approach (mOS, 30 vs. 17 months; 5y OS 38% vs. 19%; still having increased early mortality), while pts showing no response to chemo (mOS, 13 vs. 22 months) or pts with peritoneal disease (mOS, 12 vs. 19 months) derived a detrimental effect. **Conclusions:** The IKF-575/RENAISSANCE trial is negative but informs future research. Future protocols should focus on pts with RPLN only disease and exclude non-responding pts or those with peritoneal disease. There is a need for strategies against the early mortality caused by chemotherapy interruption. Clinical trial information: NCT02578368. Research Sponsor: Deutsche Forschungsgemeinschaft (DFG); AL 1817/1-1, AL 1817/1-2.

LBA4002 Oral Abstract Session

Ramucirumab plus paclitaxel as switch maintenance versus continuation of oxaliplatin-based chemotherapy in patients (pts) with advanced HER2-negative gastric or gastroesophageal junction (GEJ) cancer: The ARMANI phase III trial.

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Background: In pts with HER2-negative advanced gastric/GEJ cancer and PD-L1 low/absent expression, platinum/fluoropyrimidine doublets are a standard first-line therapy. In this patient population, the outcomes are unsatisfactory and second-line therapy is given in only 40% of clinical trial patients. Switch consolidation maintenance may prolong the benefit of the initial strategy and delay clinical deterioration. Despite ramucirumab failing to prolong both progression-free survival (PFS) and overall survival (OS) in the first-line setting, paclitaxel plus ramucirumab is a standard second-line therapy and warrants investigation as a post-induction strategy. **Methods:** Pts with HER2-negative advanced gastric/GEJ cancer without disease progression after 3 months of initial oxaliplatin-based chemotherapy, stratified by site of origin (GEJ vs gastric), prior gastrectomy and peritoneal disease, were randomized 1:1 to ramucirumab 8 mg/Kg on days 1,15 plus paclitaxel 80 mg/sqm on days 1,8,15 every 28 days (arm A) vs CAPOX/FOLFOX at the same doses used in the last induction cycle, for additional 3 mos followed by fluoropyrimidine monotherapy maintenance (arm B). The primary endpoint was PFS, OS was a key secondary endpoint; quality of life, safety, and biomarkers were evaluated. A sample size of 280 pts achieved a 90% power to detect as significant at a 5% level (2-sided log-rank test) a median PFS increase from 4 to 6 mos (target HR=0.67). HRs were estimated by Cox models adjusting for stratification factors. Restricted Mean Survival Time (RMST) analysis was conducted in case of violation of proportional hazards assumption. **Results:** From Jan 2017 to Oct 2023, 280 patients were randomly assigned (144 arm A/136 arm B). Baseline characteristics were: male sex 67/61%, median age 64/66 years, PS 0 74/65%, GEJ 26/26%, prior gastrectomy 28/23%, peritoneal metastases 53/42%. At a median follow-up of 43.7 months (IQR 22.0-57.9), median PFS was 6.6 vs. 3.5 mos in Arm A vs. B (HR=0.63, 95%CI 0.49-0.81; P<0.001). 24-mos RMST analysis showed a statistically significant 2.4-mos average increment (p=0.002). Median OS was 12.6 vs. 10.4 mos in Arm A vs. B (HR=0.75, 95%CI 0.58-0.97; P=0.030). The frequency of grade ≥3 adverse events was 40.4% vs. 20.7% in arms A vs. B, respectively, mainly neutropenia 25.5/9.6%; febrile neutropenia 2.1/0%; hypertension 6.4/0%; venous thromboembolism 2.1/0%; peripheral neuropathy 5.7/6.7%. No treatment-related deaths were reported. **Conclusions:** Switch maintenance with paclitaxel plus ramucirumab after 3 months of oxaliplatin-based doublets may be a new strategy in patients with HER2-negative metastatic gastric/GEJ cancer who are non-eligible for initial immune checkpoint inhibitor-based regimens according to specific guidelines and regulatory approvals. Clinical trial information: NCT02934464. Research Sponsor: Eli Lilly and Company.

LBA4004 **Oral Abstract Session**

Early results of the PASS-01 trial: Pancreatic adenocarcinoma signature stratification for treatment-01.

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Background: Over 60% of patients with pancreatic ductal adenocarcinoma (PDAC) present with metastatic disease. Both modified FOLFIRINOX (mFFX) and gemcitabine/nab-paclitaxel (GnP) are first-line options in advanced PDAC, however have not been compared prospectively in North American patients. Moreover, biomarkers to guide selection are lacking. Basal-like and Classical subtypes are prognostic, but their predictive impact is unknown. Patient-derived organoids (PDOs) are now feasible to study for drug pharmacotyping. Expedient molecular profiling with additional PDO drug sensitivities could enable better precision choices in PDAC.
Methods: PASS-01 is a multi-center randomized phase II trial evaluating the benefit of 1st line mFFX vs GnP in de novo metastatic PDAC patients with ECOG PS 0-1, (germline BRCA1/2, PALB2 excluded) who have baseline tumor biopsies (bx) for whole genome/transcriptional sequencing (WGTS) and PDO generation/pharmacotyping with standard and novel drugs. The primary endpoint is the PFS of mFFX vs GnP (received at least 1 dose of assigned chemo, per protocol (PP)), 136 patients needed to reach 80% power to detect a difference in median PFS of 7 vs 5 months between mFFX and GnP at significance level of 0.3 in a 2-sided test. Secondary endpoints include: ORR, SAEs, OS, impact of RNA signatures and GATA6 expression on outcomes. Each patient is discussed at a molecular tumor board immediately following their 1st 8-week CT with the goal of recommending precision 2nd-line treatment options on progression.
Results: This trial accrued 160 pts between 09/20 and 01/24, 45% in Canada, 55% in US with 140 eligible for 1st line PFS, data lock Mar 1/24 (see table). Median PFS (PP) was 5.1 mo for GnP and 4.0 mo for mFFX (p=0.14). Best response PR/SD for GnP: 29/45% and 24/35% for mFFX. SAEs attributed to the study were 3% GnP, 13% mFFX and 0.7% bx. Median OS (ITT) was 9.7 mo with GnP and 8.4 mo with mFFX, p=0.04. Of 113 patients in the PP analysis with progression, 64 (57%) received 2nd-line treatment (GnP, n= 30, mFFX n=34) Of these, a correlate-guided approach was delivered in 32 (50%), including 21 (66%) receiving chemo and 11 (34%) receiving a targeted or immunotherapy regimen. Correlative studies are underway. Preliminary analysis shows >80% successful whole genomes and >72% RNA signatures. PP patients include 9 % *KRAS* wild-type and 21% Basal-like PDAC. PDO-drug models have been established in 50%.
Conclusions: Upfront multi-omic profiling of PDAC can be successfully incorporated into a multicenter randomized trial. While we have observed PP improved PFS and ITT longer OS favouring GnP in this cohort without gBRCA 1/2 or PALB2m, the benefit of chemo for advanced PDAC patients remains poor, with 43% unable to receive 2nd line, arguing strongly for the development of 1st-line biomarker selected strategies. Clinical trial information: NCT04469556. Research Sponsor: Stand Up To Cancer; CV6197; Lustgarten Foundation; Pancreatic Cancer Canada; Ontario Institute for Cancer Research.

N=140 (PP)	GnP n= 69	mFFX n= 71
Med age	64	62
ECOG PS 0/1	59/41	46/54
% liver mets	81	86
BL Ca-19-9 U/ml	1295	1677

LBA4008 Oral Abstract Session

Nivolumab (NIVO) plus ipilimumab (IPI) vs lenvatinib (LEN) or sorafenib (SOR) as first-line treatment for unresectable hepatocellular carcinoma (uHCC): First results from CheckMate 9DW.

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Background: First-line therapies based on programmed death ligand 1 (PD-L1) inhibitors are standard of care (SOC) in uHCC and demonstrate improved outcomes over SOR; however, prognosis remains poor and there is an unmet need for alternative therapies with long-term benefits. Second-line NIVO + IPI demonstrated clinically meaningful efficacy and manageable safety in SOR-treated patients (pts) with HCC in CheckMate 040, leading to its accelerated approval in the United States. We report first results from the preplanned interim analysis of the phase 3, open-label, randomized CheckMate 9DW trial evaluating the efficacy and safety of NIVO + IPI vs LEN or SOR as first-line therapy for pts with uHCC (NCT04039607). **Methods:** Adult pts with previously untreated HCC not eligible for curative surgical or locoregional therapies, Child-Pugh score 5–6, and ECOG performance status 0–1 were included. Pts were randomly assigned 1:1 to receive NIVO 1 mg/kg + IPI 3 mg/kg Q3W (up to 4 cycles) followed by NIVO 480 mg Q4W or investigator's choice of LEN 8 mg or 12 mg QD or SOR 400 mg BID until disease progression or unacceptable toxicity. NIVO was given for a maximum of 2 years. The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR) and duration of response (DOR) per blinded independent central review (BICR) using RECIST v1.1. **Results:** In total, 668 pts were randomized to NIVO + IPI (n = 335) or LEN/SOR (n = 333); among 325 pts treated in the LEN/SOR arm, 275 (85%) received LEN. After a median (range) follow-up of 35.2 (26.8–48.9) months (mo), median OS was 23.7 mo with NIVO + IPI vs 20.6 mo with LEN/SOR (HR, 0.79; 95% CI, 0.65–0.96; $P = 0.0180$) (Table), with respective 24-mo OS rates (95% CI) of 49% (44–55) vs 39% (34–45). ORR was higher with NIVO + IPI (36%) vs LEN/SOR (13%; $P < 0.0001$); complete response was observed in 7% of pts with NIVO + IPI vs 2% with LEN/SOR. Median DOR was 30.4 mo with NIVO + IPI vs 12.9 mo with LEN/SOR (Table). A summary of treatment-related adverse events (TRAEs) is shown in the Table. **Conclusions:** NIVO + IPI demonstrated statistically significant OS benefit vs LEN/SOR in pts with previously untreated uHCC, as well as higher ORR and durable responses with a manageable safety profile. These results support this combination as a potential new first-line SOC for uHCC. Clinical trial information: NCT04039607. Research Sponsor: Bristol Myers Squibb.

Efficacy	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Median OS (95% CI), mo	23.7 (18.8–29.4)	20.6 (17.5–22.5)
HR (95% CI); *P* value[a]	0.79 (0.65–0.96); 0.0180	
ORR,[b] n (%); 95% CI	121 (36); 31–42	44 (13); 10–17
P value[a]	< 0.0001	
Median DOR[b] (95% CI), mo	30.4 (21.2–NE)	12.9 (10.2–31.2)
Safety, n (%)	**(n = 332)**	**(n = 325)**
Any-grade/grade 3–4 TRAEs	278 (84)/137 (41)	297 (91)/138 (42)
Any-grade/grade 3–4 TRAEs leading to discontinuation	59 (18)/44 (13)	34 (10)/21 (6)

[a]Two-sided *P* value. [b]Per BICR using RECIST v1.1.

LBA4014 Rapid Oral Abstract Session

Randomized phase II/III trial of gemcitabine plus nab-paclitaxel versus concurrent chemoradiotherapy with S-1 as neoadjuvant treatment for borderline resectable pancreatic cancer: GABARNANCE study.

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Background: No randomized controlled trials have compared systemic chemotherapy and chemoradiotherapy as neoadjuvant therapy for borderline resectable pancreatic cancer (BRPC). We attempted to determine which of the two could become established as standard neoadjuvant therapy for BRPC. **Methods:** This was an open-label, multicenter, randomized controlled phase II/III trial comparing two neoadjuvant treatments (UMIN-CTR 000026858): gemcitabine (GEM) plus nab-paclitaxel (nab-P) (group A, GEM 1000 mg/m^2 IV + nab-P 125 mg/m^2 IV on days 1, 8, and 15, 2 cycles) and concurrent chemoradiotherapy (50.4 Gy/28 fractions) with S-1 (80 mg/m2) on the irradiation days (group B). After the neoadjuvant therapy, patients (pts) underwent surgical resection if R0/R1 resection was judged as being possible, followed by postoperative adjuvant S-1 therapy for 6 months. The key eligibility criteria included patients aged 20 to 79 years with histologically proven adeno(squamous)carcinoma, centrally confirmed BRPC, PS 0-1, and no prior treatment for BRPC. The primary endpoint of the phase III part was overall survival (OS). A total of 110 pts (65 events) was required to detect a 17% difference in the 2-year OS [hazard ratio (HR) of 0.70] with a two-sided alpha level of 10% and power of 70%. **Results:** A total of 112 pts were randomly assigned to the trial treatments between June 2017 and December 2022 (group A/B: 56/56 pts). The median OS was 23.1 months in group A and 31.5 months in group B. No statistically significant difference in the OS was observed between the two arms (HR 0.758, 95% CI: 0.472-1.219, p = 0.2518), but a large late separation of the Kaplan-Meier curves was observed after 18 months. The difference in the 2-year OS between the groups was 14.6% (group A: 48.2%, group B: 62.8%); the separation continued until the end of the observed survival curves. A similar late separation in the PFS was seen after around 12 months, but the difference in the PFS was not statistically significant (median PFS: Group A, 12.6 months, Group B, 11.1 months; HR 0.805; 95% CI: 0.535-1.212; p = 0.2565). The R0 resection rate did not differ between the two groups (group A, 60.7%; group B, 57.1%). The tumor response rate was higher in Group A (group A, 16.1%; group B, 8.9%), but the pathological response rate was higher in group B (group A, 14.3%; group B, 30.4%). Neutropenia and thrombocytopenia were observed more frequently in group A, while anorexia was observed more frequently in group B. Both treatments were well-tolerated. **Conclusions:** A delayed survival advantage, in terms of both the OS and PFS, of concurrent chemoradiotherapy with S-1 was observed, without any additional toxicity burden. An updated analysis with longer-term efficacy/toxicity data is planned to verify the advantage of neoadjuvant chemoradiotherapy. Clinical trial information: UMIN-CTR 000026858. Research Sponsor: Japan Agency for Medical Research and Development; 15545308.

LBA4132 Poster Session

Phase II trial of BXCL701 and pembrolizumab in patients with metastatic pancreatic ductal adenocarcinoma (EXPEL-PANC): Preliminary findings.

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Background: Pancreatic ductal adenocarcinoma (PDAC) has limited therapeutic options and is thought to be a "cold" tumor that does not respond to immunotherapy, due to a tumor microenvironment (TME) consisting of a desmoplastic stroma and poor T cell infiltrate. BXCL701 is an oral synthetic dipeptide that competitively inhibits dipeptidyl peptidases DPP4, DPP8, DPP9 and fibroblast activation protein (FAP). BXCL701 exerts antitumor activity via inhibition of DPP8/9, which is associated with induction of proinflammatory cytokines, as well as inhibition of FAP, which disrupts tumor-stromal interactions. Preclinical xenograft models demonstrate synergy between BXCL701 and PD-1 blockade, reducing tumor growth and promoting an increase in intratumoral $CD4^+$ and $CD8^+$ T cells, macrophages and NK cells, with induction of host-protective immunity. **Methods:** This is a phase II trial of BXCL701 in patients with metastatic PDAC (mPDAC) following progression on 1 line of treatment for advanced disease and amenable to serial biopsies. BXCL701 is administered at 0.2 mg PO BID days 1-7 and 0.3 mg BID days 8-14 during cycle 1 (21 days) followed by 0.3 mg BID days 1-14 every 21 days in all other cycles, given with pembrolizumab 200 mg IV every 21 days (all cycles). The primary objective is to determine the 18-week progression-free survival rate ($PFS_{18weeks}$). We estimate that historical 2^{nd}-line $PFS_{18weeks}$ is 30% or less; using a Simon's two-stage (minimax) design, a type I error rate of 0.05 and power of 80% if the true rate is 50%, we will need 19 patients in stage 1 and 20 in stage 2 (39 total). There is a safety lead-in phase of 6 patients. We plan to enroll 43 patients to account for a predicted 10% drop out of unevaluable patients. Correlative pharmacodynamic studies include imaging mass cytometry to examine 36 markers of the PDAC TME in tissue biopsies, as well as blood-based analyses of *KRAS* circulating tumor DNA, circulating markers of fibrosis, and IL-6. Enrollment began in Q3 2023 (NCT05558982). **Results:** Six patients have enrolled, 3 women and 3 men, median age 57.5 (range 37-80). One patient was progression-free at 18 weeks and 1 patient had stable disease (SD) at 9 weeks, not yet evaluable for the 18-week landmark. Objective response rate is 16% and disease control rate is 50% (RECIST: 1 partial response, -41%, and 2 patients with SD, -18% and 0%). Three patients had significant reductions in CA19-9 from baseline (-100%, -73%, and -97%). Median PFS and overall survival have not been reached (NR, 95% CI 1.45 months-NR and 0.92 months-NR, respectively). There have been no serious treatment-related safety events. The safety lead-in will complete after the next patient completes the 6-week safety window (1 patient was unevaluable). **Conclusions:** BXCL701 plus pembrolizumab is well-tolerated and shows early signs of potential clinical activity in patients with mPDAC refractory to chemotherapy. Clinical trial information: NCT05558982. Research Sponsor: BioXcel; Merck.

LBA4143 Poster Session

Interim results of the randomized phase 2 cohort of study FW-2020-01 assessing the efficacy, safety and pharmacodynamics of CM24 in combination with nivolumab and chemotherapy in advanced/metastatic pancreatic cancer.

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Background: The novel monoclonal antibody CM24 blocks the activity of Carcinoembryonic Antigen Cell Adhesion Molecule 1 (CEACAM1), known to have key roles in cancer progression, immune evasion, and metastasis. We present the interim efficacy and safety data from the global multi-center, open label, randomized Phase 2 study (NCT 04731467) in patients (pts) with advanced/metastatic pancreatic ductal adenocarcinoma (PDAC) who progressed after 1st line therapy, treated with CM24, nivolumab (nivo) and chemotherapy vs. chemotherapy (CH). **Methods:** Patients with advanced/metastatic PDAC progressing after 1 prior line of systemic therapy including fluoropyrimidine/irinotecan or gemcitabine/nab-paclitaxel, having ≥1 measurable lesion, ≥18-year-old, ECOG ≤1 and adequate organ function were randomized 1:1 based on the class of prior CH received. Randomization was either to the experimental groups (EX) receiving CM24 (20mg/kg, q2wk), nivo (240mg/kg, q2wk) with one of the following CH regimens, liposomal irinotecan, 5 fluorouracil and leucovorin (Nal-IRI; q2wk) or gemcitabine/nab-paclitaxel (gem/nab; q1wk x3) or the control groups (C) with one of the CH regimens alone. This is a Bayesian design with an overall planned sample size of 60 pts with Overall Survival (OS) as the primary endpoint. Secondary endpoints include progression free survival (PFS), objective response rate (ORR) and disease control rate (DCR). An interim estimate of PFS HR, ORR and DCR based on data cut-off date of 21 Feb 2024 is reported. The analysis compares the EX vs. the respective C arm using log-rank test stratified by CH regimen. **Results:** A total of 63 PDAC pts were evenly randomized across the study arms. At data cut-off date, a total of 18 pts, 9 per treatment regimen remain on treatment. The median follow-up time for the Nal-IRI regimen is 6.3 months (95% CI: 5.5-8.4) and 5.2 months (95% CI: 4.0-6.7) for the gem/nab regimen. Median PFS ORR and DCR for the Nal-IRI EX arm were 3.8m (1.9-5.1; HR 0.70; p=0.213), 18.8% and 62.6%, and for the Nal-IRI C arm 1.9m (1.8-5.6), 6.3% and 40%, respectively (Table). Data for the gem/nab regimen and OS data for both regimens are not mature. Overall Grade ≥3 AE rate was 50% in the Nal-IRI EX arm and 13% in the C arm. The most common treatment-emergent grade ≥3 AEs EX vs. C were diarrhea (18.8% vs 6.7%), fatigue (18.8% vs 6.7%) and anemia (6.3% vs 0%). **Conclusions:** The interim analysis suggests that the combination of CM24/nivo/Nal-IRI/5FU/LV has a manageable safety profile with a longer PFS supported by higher ORR and DCR. OS Data continues to mature and will be reported once available. Clinical trial information: NCT04731467. Research Sponsor: Purple Biotech Ltd.

	CM24/Nivo+ Nal-IRI/5FU/LV	Nal-IRI/5FU/LV
	n=16	n=15
PFS, median (months), (95% CI)	3.8 (1.9-5.1)	1.9 (1.8-5.6)
3-mo PFS rate, %	64	40
PFS, HR, (95% CI)	0.70 (0.29-1.71)	
ORR, %	18.8	6.3
DCR, %	62.6	40.0

LBA4517 Rapid Oral Abstract Session

Perioperative sacituzumab govitecan (SG) alone or in combination with pembrolizumab (Pembro) for patients with muscle-invasive urothelial bladder cancer (MIBC): SURE-01/02 interim results.

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Background: SG is an antibody-drug conjugate composed of an anti-trophoblast cell surface antigen 2 (Trop-2) antibody coupled to SN-38 (a topoisomerase-I inhibitor) with US FDA-accelerated approval for locally advanced or metastatic urothelial carcinoma (mUC). A multicohort, open-label, phase 2 SURE study is evaluating neoadjuvant SG (SURE-01, NCT05226117) or neoadjuvant SG+pembrolizumab followed by adjuvant pembrolizumab (SURE-02, NCT05535218) in MIBC in a flexible design allowing a bladder-sparing approach. We report interim results from SURE-01. **Methods:** Pts with cT2-4N0M0 MIBC who were ineligible for or refused cisplatin-based neoadjuvant chemotherapy were planned to receive 4 cycles of neoadjuvant SG 10 mg/kg intravenously (IV) on days 1 and 8, Q3W, followed by radical cystectomy (RC). The trial included pre-post MRI imaging of the pelvis and ctDNA analysis. Pts with clinical complete response (cCR, defined with negative MRI, cystoscopy and ctDNA assays) refusing RC were offered redo transurethral resection of the bladder tumor (reTURBT) followed by observation in case no viable high-grade tumor in the bladder was found. The primary endpoint of the study is to assess the proportion of ypT0N0. The assumptions include a ypT0N0≤20% as H0 and ≥45% as H1 in a single-stage A'Hern's design. Secondary end points include event-free survival (EFS), cCR rate and OS. Treatment-related adverse events (TRAEs) and safety are assessed using standard criteria (CTCAE v5). Tumor samples underwent comprehensive genomic profiling assay. **Results:** From 03/22 to 11/23, 21 pts were enrolled. After the initial 8 pts the study was amended with SG at 7.5 mg/Kg dose due to a Grade 5 TRAE. Median age was 71y, 7 pts (33.3%) had a cT3-4N0. Ten pts (47.6%) had a mixed variant histology. All pts received at least 1 cycle of SG: Grade ≥3 TRAE occurred in 9 pts (42.5%), including one Grade 5 event (at 10mg/Kg dose). Toxicity was unrelated to *UGT1A1* polymorphism. Ten pts (47.6%) achieved a cCR. Sixteen pts are evaluable for final response at treatment completion: one pt had a disease progression and started palliative therapy, two did not undergo RC due to TRAE. Thirteen pts have undergone surgery (RC: N=10; reTURBT: N=3). ypT0N0-x response was achieved in 6/16 pts (37.5%), 7 (43.7%) an ypT≤1N0-x response. All pts with a residual disease revealed a ctDNA-negative test post-RC. Tumor samples from pts with cCR were enriched in *ARID1A* and *BRCA1/2* mutations vs nonCR: 40 vs 9%, 30 vs 18%; nonCR were enriched in *ERBB2* mutations vs cCR: 44 vs 10%. **Conclusions:** Observed ypT0N0-x responses after neoadjuvant SG showed promising activity in MIBC who have a high unmet need, with a potential to avoid RC. Reduced dose of SG was feasible and the data support the ongoing SURE studies in MIBC. Clinical trial information: NCT05226117; NCT05535218. Research Sponsor: Gilead Inc.; Merck Inc.

LBA5000 Oral Abstract Session

Cabazitaxel with abiraterone versus abiraterone alone randomized trial for extensive disease following docetaxel: The CHAARTED2 trial of the ECOG-ACRIN Cancer Research Group (EA8153).

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Background: The E3805 (CHAARTED) trial showed a significant survival benefit from early treatment with chemohormonal therapy (ADT + Docetaxel) in patients (pts) with high-volume metastatic hormone-sensitive prostate cancer (HSPC). However, most pts will develop castration-resistant disease (CRPC) and will require additional systemic therapy. We hypothesized that additional treatment with chemohormonal therapy in the CRPC setting will improve outcomes. **Methods:** EA8153 (CHAARTED2) is a prospective randomized phase II open label trial. Two hundred twenty-three (223) pts with metastatic CRPC previously treated with ADT + docetaxel for HSPC were randomized (1:1) to abiraterone/prednisone plus cabazitaxel 25 mg/m^2 for up to 6 cycles (n = 111) or abiraterone/prednisone alone (n = 112). Stratification factors included ECOG performance status (PS) of 0 vs. 1-2, time from initiation of ADT to development of CRPC of <12 vs. > 12 months, and presence vs. absence of visceral metastases. The primary trial endpoint is progression-free survival (PFS), defined as time from randomization to radiographic progression, symptomatic deterioration requiring discontinuation of treatment, or death. Key secondary endpoints include time to PSA progression (TTPP), overall survival (OS), and safety. **Results:** After a median follow-up of 47.3 (0-61.2) months, median PFS was longer for the cabazitaxel + abiraterone/prednisone arm vs. abiraterone/prednisone alone arm (14.9 months [95% CI 9.9-18.6] vs. 9.9 months [95% CI, 7.0-12.6], P = 0.049; hazard ratio [HR] 0.73, 80% CI 0.59-0.90). The advantage with the combination was more pronounced in patients < 65 years of age (15.6 vs. 9.8 months, P = 0.08), ECOG PS of 0 (20.9 vs. 10.1 months, P = 0.01), time to CRPC of < 12 months (12.9 vs. 5.1 months, P = 0.006), and absence of visceral metastases (18.1 vs. 10.1 months, P = 0.01). Median TTPP was also longer in the combination vs. the monotherapy arm (10 months [95% CI 8.5-13.5] vs. 6.1 months [95% CI 4.4-8], P = 0.002). No difference in OS was observed between the 2 arms in the interim analysis (25.0 vs. 26.9 months, P = 0.67). More grade >3 side effects were noted in the combination arm, as expected from use of cabazitaxel. **Conclusions:** The addition of cabazitaxel to abiraterone/prednisone significantly prolonged PFS in patients with metastatic CRPC who previously received ADT + docetaxel for HSPC compared to abiraterone/prednisone alone. No significant OS difference was noted between the two arms, but the study was not powered for this endpoint. Clinical trial: NCT03419234. Support: CA180820, CA180794, CA180799, CA180802; and Genzyme Corporation, a subsidiary of Sanofi S.A. Clinical trial information: NCT03419234. Research Sponsor: National Cancer Institute; CA180794; National Cancer Institute; CA180802; Genzyme Corporation, a subsidiary of Sanofi S.A.

LBA5002 Oral Abstract Session

A randomized, double-blind, placebo-controlled trial of metformin in reducing progression among men on expectant management for low-risk prostate cancer: The MAST (Metformin Active Surveillance Trial) study.

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Background: Active Surveillance (AS) involves vigilant monitoring of selected prostate cancer (PCa) patients, with radical treatment initiation upon significant disease progression. AS eligibility varies, generally including low-risk PCa men. Metformin, a widely-used oral hypoglycemic agent, is known for its excellent tolerability and efficacy in diabetes management. Extensive preclinical data suggested that metformin may slow PCa progression. The purpose of this study is to examine the effect of metformin on the rates of progression among men with low-risk localized PCa on AS. **Methods:** A randomized double blind placebo controlled trial was carried out in 14 centres across Canada.Eligible patients had biopsy-proven, low-risk, localized PCa diagnosed within the past 6 months, with a Gleason score of <6 observed in $\leq 1/3$ of the total cores, less than 50% positivity in any one core, a PSA level of ≤ 10 ng/ml, and a clinical stage between T1c-T2a. Additionally, they chose active surveillance as their primary treatment. Subjects that met eligibility criteria were randomly assigned (1:1) to receive metformin 850 mg BID or placebo for 3 years. All patients underwent repeat prostate biopsy at 18 and 36 months. The primary endpoint indicated was time to progression, defined as the earliest occurrence of primary PCa therapy (e.g., prostatectomy, radiation, hormonal therapy) or pathological progression ($>1/3$ of total cores involved, at least 50% of any one core involved, or Gleason pattern 4 or higher). **Results:** In our cohort of 407 patients, 204 were administered metformin, and 203 received a placebo. The median age of the overall cohort was 63 years. Out of the total 407 patients, 141 experienced disease progression. There was no statistically significant difference in progression-free survival (PFS) observed between patients treated with metformin and those receiving placebo ($p=0.63$). **Conclusions:** Despite tantalizing preclinical and epidemiological data, metformin consumption does not alter rates of progression among men with low risk PCa on AS. Clinical trial information: NCT01864096. Research Sponsor: None.

LBA5004 Oral Abstract Session

MANCAN2: A multicentre randomised controlled trial of self-help cognitive behavioural therapy (CBT) to manage hot flush and night sweats (HFNS) symptoms in patients with prostate cancer receiving androgen deprivation therapy (ADT).

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Background: Up to 80% of patients receiving ADT suffer HFNS which impacts quality of life (QOL) and potentially ADT compliance. Mitigation options are limited. Prior research has found self-help CBT, with minimal guidance, reduced HFNS due to ADT at 6 weeks. We tested the longer term impact of self-help CBT, guided and delivered by prostate Cancer Nurse Specialist (CNS) teams. **Methods:** MANCAN2 is a multicentre randomised controlled trial and process evaluation within UK prostate cancer units. Eligibility: localised/advanced prostate cancer; on ADT with $\geq$ 6 months further planned; HFNS Problem Rating Scale $\geq$ 2. Patients were randomised (1:1) in groups of 6 to 8 to treatment as usual (TAU) or CBT + TAU, by permuted block, stratified by site, cohort and treatment intent. CBT was a 4-week self-help intervention (booklet and relaxation audio) with pre- and post-intervention group workshops by the prostate CNS team. Primary objective: does adding CBT to TAU reduce 6 month HFNS Problem Rating Scale versus baseline (mixed linear regression). Secondary endpoints: 6 week HFNS Problem Rating Scale, HFNS frequency, HFNS beliefs and behaviours, QOL (EORTC QLQ-C30, symptoms (rating scales for anxiety, depression, mood and sleep) by mixed logistic regression), ADT compliance (chi-squared test). A 6 month mean HFNS Problem Rating Scale difference of $\geq$ 1.5 points was deemed clinically relevant, and required data from 111 patients (90% power, 5% type 1 error, 6 to 8 patients per group, intra-class correlation 0.01, anticipating 26% patient loss). **Results:** 162 patients were randomly assigned (81/arm) and 117 returned 6 month HFNS Problem Rating Scale data. Baseline characteristics were balanced. Mean CBT delivery adherence was 85%. 6 month mean HFNS Problem Rating Scale score was not significantly different for the TAU alone versus CBT + TAU (mean 4.08 vs 4.04, 95% CI for difference: -0.89, 0.80; p=0.97), although a difference was observed at 6 weeks (mean 4.47 vs 3.79, 95% CI: -1.26, -0.09; p=0.03). At 6 weeks, CBT patients had higher weekly HFNS frequency (median 54.2 vs 59.4, 95% CI: 0.22, 10.19; p=0.04), lower depression score (median 7.19 vs 6.19, 95% CI: -1.88, -0.12; p=0.03) and lower anxiety score (median 4.25 vs 3.39, 95% CI: -1.64, -0.08; p=0.03). CBT patients had more positive beliefs about openness and humour scores at 6 months (median 4.92 vs 4.59, 95% CI: -0.63, -0.03; p=0.03). There was no significant difference for other measures of HFNS beliefs and behaviours, quality of life, anxiety, mood, sleep quality and treatment compliance. **Conclusions:** Adding CBT to TAU in prostate cancer patients receiving ADT improved short-term HFNS severity but was not maintained at 6 months. Future research should investigate whether initial CBT benefit could be made sustainable in this setting. Clinical trial information: 58720120. Research Sponsor: National Institute for Health and Care Research; NIHR201542.

LBA5014 Rapid Oral Abstract Session

Blood-based markers of differential efficacy of bipolar androgen therapy and enzalutamide in the randomized TRANSFORMER trial.

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Background: Bipolar androgen therapy (BAT) for metastatic castration-resistant prostate cancer (mCRPC) is administered by alternating between supraphysiologic and near-castrate serum testosterone levels through intramuscular administration of testosterone cypionate 400mg given every 28 days together with ongoing androgen suppression. BAT is effective in a subset of patients, but evidence for predictive treatment selection is lacking. The goal of the study is to determine whether blood-based markers can be identified in the TRANSFORMER study, a randomized trial of abiraterone-pretreated mCRPC patients assigned to BAT or enzalutamide (Enza). **Methods:** We conducted whole genome and whole exome sequencing of circulating tumor DNA samples collected from the TRANSFORMER study. In this post-hoc biomarker study of a randomized trial, we sought to identify markers that predict preferential benefit from BAT or Enza in mCRPC patients progressing on abiraterone. We compared clinical or radiographic progression-free survival (PFS) and overall survival (OS) between BAT and Enza arms in subgroups defined by biomarker status and estimated treatment effects via the Cox regression model, stratified by duration of prior abiraterone treatment. To determine whether a molecular event is a predictive biomarker, we tested the interaction term of the dichotomized marker status by treatment arms. Statistical tests were two-sided, and p values $\leq$ 0.05 were deemed to indicate statistical significance. **Results:** We focused on somatic alterations implicated in androgen receptor (AR) signaling that can be detected at a relatively high frequency in blood samples. Whole genome sequencing and whole exome sequencing of cell-free DNA from 62 patients revealed tumor-specific AR pathway alterations, including AR point mutations and amplifications (33/62, 53.2%). In men with positive AR alterations detected in blood, BAT was more efficacious than Enza (median PFS 4.2 months vs. 2.9 months; hazard ratio [HR] 0.59[95% CI 0.25-1.37], P=0.22), while Enza was superior to BAT in those without AR alterations (median PFS 8.4 months vs. 3 months; HR 3.62[95%CI 1.44-9.1], P=0.006). We detected a significant interaction between AR alteration status and treatment types using PFS as the endpoint ($P_{\text{interaction}}$=0.002). The differential benefit is upheld with OS as the endpoint ($P_{\text{interaction}} <$0.001). In men with positive AR alterations, OS was longer with BAT compared with Enza (median OS 29.6 months vs. 24.1 months; HR 0.41[95% CI 0.16-1.03], P=0.058). In contrast, in men without AR alterations, OS was worse with BAT compared with Enza (median OS 19.3 months vs. NR; HR 4.38[95% CI 1.21-15.89], P=0.025). **Conclusions:** Metastatic CRPC patients progressing on abiraterone with AR alterations detected in blood may benefit preferentially from BAT. Routine liquid biopsy testing may enable further adoption of BAT. Research Sponsor: Brown Philanthrophy.

LBA5500 Oral Abstract Session

Final results of BrUOG 354: A randomized phase II trial of nivolumab alone or in combination with ipilimumab for people with ovarian and other extra-renal clear cell carcinomas.

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Background: Extra-renal clear cell cancer (CCC) are rare tumors that can arise from any organ. Gynecologic CCC can originate from the ovaries, endometrium, or cervix. Compared to serous carcinomas, ovarian CCC is associated with poorer outcomes to standard chemotherapy, warranting a focused evaluation for innovative therapies. We completed a two-stage two-arm phase 2 trial evaluating immunotherapy for extra-renal CCC and present the final results of treatment using nivolumab (N) monotherapy and in combination with ipilimumab (I) in this population. **Methods:** This is a randomized two-stage phase II study evaluating single-agent N (240mg IV every two weeks) or in combination with I (1mg/kg every six weeks) (N/I) in people with relapsed extra-renal CCC after at least one prior therapy (no prior immunotherapy). Measurable disease was required. In the first stage, volunteers were randomly assigned to N or N/I with stratification by tumor site (ovarian vs extra-ovarian). Treatment was continued until disease progression or unacceptable toxicity. Each arm was evaluated for overall response rate (ORR) separately at stage 1 using RECIST and iRECIST criteria. In January 2022, the N arm was closed, and subsequent volunteers were treated with N/I. The study completed enrollment in April 2023. **Results:** Between July 2018 and April 2023, 46 volunteers provided consent for the study and 44 were treated (14 N, 30 N/I). The median age was 57 (range, 18-75) years. Across the study, 75% were White, 9.1% Black, 4.5% were Asian, and 11.4% were Hispanic. All volunteers had a gynecologic primary, 36 (82%) with ovarian CCC. The median number of prior lines was 1 (range, 1-7). The Overall Response Rate (ORR) is 14.3% (2 Partial Responses) with N and 33% (4 Complete and 6 Partial Responses) with N/I. Four people continue on treatment with N/I as of December 2023. With a median follow up of 11.3 (range, 1.6-46.4) months, the median Progression-Free Survival is 2.2 (95% CI 1.2-3.4) months with N and 5.6 (95% CI 1.6-29.1) months with N/I. The median Overall Survival is 17 (95% CI 2.1-NR) and 24.6 (95% CI 5.9-NR) months, respectively. Serious treatment-related adverse events were recorded in 3 (21%) treated with N (all grade 3) and 14 (47%) treated with N/I (two of whom had grade 4 pancreatic enzyme elevations). No new safety signals were noted, and no treatment-related deaths were observed in either arm. **Conclusions:** Immunotherapy demonstrated important, meaningful, and durable activity in people with previously treated gynecologic CCC including four (12%) volunteers who achieved a complete response with N/I. N/I warrant further evaluation against standard treatment for people with ovarian CCC, given the historically chemotherapy-resistant nature of the disease. Clinical trial information: NCT03355976. Research Sponsor: None.

LBA5501 Oral Abstract Session

Atezolizumab versus placebo in combination with bevacizumab and non-platinum-based chemotherapy in recurrent ovarian cancer: Final overall and progression-free survival results from the AGO-OVAR 2.29/ENGOT-ov34 study.

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Background: Paclitaxel or pegylated liposomal doxorubicin (PLD) in combination with bevacizumab (bev) are standard treatment options in patients with relapsed ovarian cancer not candidates for platinum, but responses are usually short-lived. Recently, two trials have reported a numerical but non-significant advantage from the addition of atezolizumab (atezo) to chemo plus bev in the recurrent setting (ATALANTE, Kurtz JE et al., J Clin Oncol & NRG GY009, O'Cearbhaill et al, IGCS 2023). AGO-OVAR 2.29 investigated the efficacy of atezo in combination with bev and non-platinum-based chemo. **Methods:** AGO-OVAR 2.29 is a randomized, double blind, phase III trial evaluating the efficacy and safety of atezo plus bev and chemo in patients (pts) with recurrent ovarian cancer. Eligible patients had a 1st/2nd relapse within 6 months after completing platinum-based chemo or a 3rd relapse regardless of treatment-free interval. A fresh biopsy for central PD-L1 testing (VENTANA SP142 assay) prior to randomization was mandatory. All pts received weekly paclitaxel or PLD and bev until disease progression or intolerable toxicity and were randomized 1:1 to either atezolizumab 840 mg q14 days or placebo until progression or for a maximum duration of 24 months. Number of prior lines, planned chemo, prior bev and PD-L1 status served as stratification factors. Overall survival (OS) and progression-free survival (PFS) in the intention to treat (ITT) population were primary endpoints, both to be analyzed after observation of 391 deaths. Data cut-off (DCO) occurred on 26/01/2024. OS and PFS analysis is based on a multiple Cox regression with treatment arm and stratification factors as covariates. Safety is reported for pts who received at least one dose of study treatment. **Results:** 574 pts were randomly assigned to atezo (285) or placebo (289). 45.1% received PLD and 53.7% paclitaxel. 7 pts did not start study treatment. 36.1% of pts had received 3 prior lines and 72.5% prior bev. 25.8% were PD-L1 positive. At DCO 418 OS and 505 PFS events have occurred. Median OS was 14.3 months (mos) in the atezo and 13.0 mos in the placebo arm (HR 0.83, 95% CI 0.68-1.01; p=0.06) and PFS 6.3 mos for atezo vs 6.6 mos for placebo arm (HR 0.88, 95% CI 0.73-1.05; p=0.15). Similar HR were observed in PD-L1 positive and negative pts. In total, 580 SAE and 141 AESI were reported. AEs of ≥ grade 3 were reported in 71.5% in the atezo and 68.9% in the placebo arm. 63.7% of pts in the atezo and 51.4% in the placebo arm experienced serious AEs. **Conclusions:** The addition of atezo to chemo plus bev did not significantly improve OS or PFS in pts. with recurrent ovarian cancer who are no candidates for platinum. Safety was within the expected range. Translational research is ongoing. Clinical trial information: NCT03353831. Research Sponsor: F. Hoffmann-La Roche ltd.

LBA5505 **Oral Abstract Session**

Omission of lymphadenectomy in patients with advanced epithelial ovarian cancer treated with primary or interval cytoreductive surgery after neoadjuvant chemotherapy: The CARACO phase III randomized trial.

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Background: Lion trial demonstrated the lack of benefit of retroperitoneal pelvic and paraaortic lymphadenectomy (RPPL) in primary surgery in advanced epithelial ovarian cancer (AEOC) with clinically negative lymph nodes. As a consequence, the question of RPPL during interval cytoreductive surgery after neoadjuvant chemotherapy remains open. **Methods:** CARACO was a prospective multi-institutional phase III trial including patients with newly diagnosed AEOC FIGO III-IV, with no pre- and intra-operative suspicious lymph nodes, randomized intra-operatively to RPPL versus no-RPPL, stratified by surgical strategy (primary surgery, surgery after neoadjuvant chemotherapy). The primary endpoint was progression free survival (PFS). The target sample size was 450 evaluable patients, providing 80% power at 5% alpha based on the hypothesis of a 5 years PFS of 41%. **Results:** Between December 2008 and March 2020, 379 patients were randomly assigned to RPPL (n=181) or no-RPPL (n=187), 11 patients were excluded. Our required sample size was not reached because of a stop of inclusion after the publication of the Lion trial. The median number of removed lymph nodes in patients randomized to RPPL was 27 [IQR=19-36]. 75% of the patients were treated with neoadjuvant chemotherapy (244 patients treated with 3 or 4 cycles before interval surgery and 41 patients treated with 6 cycles before delayed surgery) and 83 patients treated with primary surgery followed with adjuvant platinum-based chemotherapy. The rate of surgery with no residual was 86% and 88% respectively in the No RPPL and the RPPL arm. Lymph node metastases were diagnosed in 49% of the patients in the RPPL arm, with a median of 3 involved lymph nodes [IQR=2-7]. After a median follow up of 9 years, median PFS in the no-RPPL arm and in the RPPL arm was 14.8 months and 18.5 months respectively (HR 0.98, 95%CI 0.78-1.22, p=0.86). Median OS was not significantly different: 48.9 months and 58.0 months in the No RPPL and RPPL arm respectively (HR 0.96, 95%CI 0.75-1.22 p=0.72). Results considering progression free and overall survival were not different in the subgroup of patients with a complete surgery or a neoadjuvant chemotherapy. Serious post-operative complications occurred more frequently in the RPPL arm: re-laparotomies 8.3% vs 3.2% [p=0.03], transfusion rate (34% vs 25%, p=0.05). Mortality within 60 days after surgery was similar between arms (1.1 vs 0.5% [p=0.54]) respectively. **Conclusions:** CARACO trial is the first randomized trial showing that systematic lymphadenectomy should be omitted in AEOC with clinically negative lymph nodes also in patients undergoing neoadjuvant chemotherapy and interval complete surgery. This surgical de-escalation allows to significantly reduce serious post operative morbidity. Clinical trial information: NCT01218490. Research Sponsor: French National Institue of Cancer (INCA).

LBA5515 Rapid Oral Abstract Session

AXLerate-OC/GOG-3059/ENGOT OV-66: Results of a phase 3, randomized, double-blind, placebo/paclitaxel-controlled study of batiraxcept (AVB-S6-500) in combination with paclitaxel in patients with platinum-resistant recurrent ovarian cancer.

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Background: Batiraxcept is an Fc-fusion protein engineered to have a 200-fold higher affinity than wild-type AXL for its activating ligand GAS6. Batiraxcept sequesters GAS6 and inhibits its interaction with AXL. The Phase 1b study demonstrated safety with batiraxcept in combination with paclitaxel. **Methods:** This was a global, placebo-controlled, double-blind, phase III trial (ClinicalTrials.gov identifier: NCT04729608). Patients with PROC were randomly assigned 1:1 to receive intravenous batiraxcept every 2 weeks (D1, 15 every 28 days) with once-a-week IV paclitaxel (D1, 8, 15 every 28 days) or placebo with paclitaxel until disease progression. The primary endpoint was progression-free survival as assessed by investigator-assessed progression-free survival and secondary endpoint was overall survival. The randomization was stratified by platinum-free interval (< 3 months, 3 to 6 months), prior lines (1 to 2, 3 to 4), and prior bevacizumab status (yes, no). Exploratory endpoints include objective response rate, duration of response, quality of life, clinical benefit rate, and pharmacokinetic and pharmacodynamic profile. **Results:** A total of 366 participants were randomly assigned, and analysis was performed based on intent-to-treat. There were 183 participants who had prior bevacizumab and 177 with no prior bevacizumab. Median PFS (mPFS) was 5.13 months in the batiraxcept + paclitaxel arm and 5.49 months in the control paclitaxel arm, hazard ratio (HR) 1.29 (CI, 1.01 to 1.64; p=0.98). Median OS with batiraxcept + paclitaxel was 14.29 months versus 14.39 months, HR 1.06 (CI 0.77 to 1.46; p=0.64). Objective response rates (ORRs) per RECIST 1.1 were similar in both arms: 25.1% with batiraxcept + paclitaxel versus 26.2% with control paclitaxel arm. An exploratory analysis of the 304 evaluable tumors found that 61 (20%) of tumors had high AXL expression by immunohistochemistry (IHC). In participants with high tumor AXL expression, median PFS was 5.78 months in the batiraxcept + paclitaxel arm and 3.71 months in the control paclitaxel arm, HR 0.55 (CI, 0.31 to 0.98; p=0.042). For high AXL expressing tumors, median OS was 17.8 months in the batiraxcept + paclitaxel cohort and 8.11 months in the paclitaxel cohort, HR 0.32 (CI, 0.14 to 0.73; p=0.006). **Conclusions:** The addition of batiraxcept to paclitaxel did not improve PFS or OS. However, in AXL high tumors, the PFS and OS were higher in participants who received batiraxcept with paclitaxel compared to paclitaxel alone. Clinical trial information: NCT04729608. Research Sponsor: Aravive.

LBA5516 Rapid Oral Abstract Session

A phase III randomized, double-blinded, placebo-controlled study of suvemcitug combined with chemotherapy for platinum-resistant ovarian cancer (SCORES).

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Background: Suvemcitug is a new-generation recombinant humanized anti-VEGF rabbit monoclonal antibody. In the previous P1b study, Suvemcitug demonstrated its favorable safety profile and efficacy signals when combo with chemotherapy in platinum-resistant ovarian cancer (PROC). SCORES is the first randomized, double-blind, placebo-controlled phase III clinical trial to confirm the efficacy of Suvemcitug combo with chemo in PROC, whether or not previously received antiangiogenic agents or PARP inhibitors. **Methods:** Eligible patients had progressed during platinum-based therapy or within 6 months after ≥4 cycles of platinum-based therapy with at least one measurable lesion. After the investigators chose chemotherapy (CT) (weekly paclitaxel 80 mg/ m^2 d1, 8, 15 & 22 q4w, pegylated liposomal doxorubicin 40 mg/ m^2 d1 q4w or topotecan 4 mg/m^2 d1, 8 & 15 q4w), patients were randomly assigned (2:1) to either Suvemcitug (1.5 mg/kg q2w) or placebo combine with CT until progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS) by blinded independent review committee (BIRC) according to the RECIST 1.1. Key secondary end point is the overall survival (OS). **Results:** A total of 421 patients were enrolled between June 2021 and June 2023 in China. As the data cut off of the primary efficacy analysis (8 December 2023), 197 PFS events (70.1%) in Suvemcitug arm and 111 PFS events (79.3%) in placebo arm had occurred with the median follow-up of 14.36 and 14.26 months, respectively. The median PFS by BIRC was 5.49 months in Suvemcitug arm versus 2.73 months in placebo arm (hazard ratio[HR] 0.46, $p<0.0001$). OS data are immature. 42.7% and 50.7% of patients are deceased in Suvemcitug arm or placebo arm respectively, and there is a trend of OS benefit trend: median OS 16.07 months vs. 14.88 months, HR 0.79, p=0.1244. Efficacy results are summarized below. Treatment-emergent adverse events (TRAEs) occurred in all patients in Suvemcitug arm, with the most common being neutrophil count decreased, white blood cell count decreased and platelet count decreased. No Suvemcitug-related grade 5 TEAE occurred. **Conclusions:** To the best of our knowledge, this is the first double-blinded phase III study demonstrated promising antitumor activity of anti-angiogenic agent in patients with PROC. The improvement in PFS, ORR and DCR gained by adding Suvemcitug to single-agent CT was observed with no new safety concern. Clinical trial information: NCT04908787. Research Sponsor: Shanghai Xianxiang Medical Technology Co., Ltd.

	Placebo+CT (N = 140)	Suvemcitug + CT (N = 281)
Median PFS by BIRC, month (95% CI)	2.73 (1.94, 3.75)	5.49 (4.93, 5.95)
Hazard Ratio (95% CI)	0.46 (0.35, 0.60)	
P value (Log-rank)	<0.0001	
Median PFS by investigator, month (95% CI)	2.46 (1.94, 3.65)	5.39 (4.80, 5.59)
OS, month (95% CI)	14.88 (11.43, 18.73)	16.07 (13.67, 18.53)
ORR by BIRC, %	12.1%	26.0%
ORR by investigator, %	8.6%	23.1%
DCR by BIRC, %	49.3%	76.5%
DCR by investigator, %	47.1%	75.1%

LBA6000 Oral Abstract Session

Adjuvant PD-1 blockade with camrelizumab in high-risk locoregionally advanced nasopharyngeal carcinoma (DIPPER): A multicenter, open-label, phase 3, randomized controlled trial.

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Background: Patients with high-risk locoregionally advanced nasopharyngeal carcinoma (NPC) often experience disease relapse even after receiving standard-of-care treatment, e.g. induction chemotherapy (IC) followed by concurrent chemoradiotherapy (CCRT). The benefit of PD-1 inhibitor as adjuvant treatment following IC+CCRT in locoregionally advanced NPC remains unclear. **Methods:** Patients with high-risk locoregionally advanced NPC (T4N1M0 or T1-4N2-3M0) who have received gemcitabine and cisplatin (GP) IC and CCRT were recruited at 11 centers in China. They were randomly assigned (1:1) within 2 weeks after the last radiation dose to receive intravenous camrelizumab (200 mg once every 3 weeks for 12 cycles; Camrelizumab Arm) or observation (Standard-therapy Arm). The primary endpoint was event-free survival (EFS). It is estimated that approximately 442 patients would provide 80% power to detect a hazard ratio (HR) of 0.52 with a log-rank test at a two-sided α level of 0.05. Quality of life (QoL) was assessed by EORTC-C30. **Results:** A total of 450 patients were randomly assigned to the Camrelizumab Arm (n=226) and the Standard-therapy Arm (n=224). After a median follow-up of 37 months (corresponding to 41 months when calculated from the start of standard therapy), the estimated 3-year EFS was 86.9% in the Camrelizumab Arm and 77.4% in the Standard-therapy Arm (intention-to-treat population; HR 0.61, 95% CI 0.38–0.96; P = 0.03). The incidence of grade 3-4 adverse events (AEs) was 11.2% in the Camrelizumab Arm and 3.2% in the Standard-therapy Arm, including grade 3-4 immune-related AEs in 8 (3.9%) patients in the Camrelizumab Arm. Reactive capillary endothelial proliferation was the most common adverse event related to camrelizumab (RECP, 87.8%, 4 (1.8%) patients had grade 3 RECP). Treatment-related deaths occurred in 1 (<1%) patients in the Camrelizumab group (subarachnoid hemorrhage) and 1 (<1%) patients in the Standard-therapy group (nasopharyngeal necrosis). During treatment, there was no clinically meaningful deterioration of health-related quality of life associated with the use of adjuvant camrelizumab. **Conclusions:** Adjuvant PD-1 blockade with camrelizumab significantly improved EFS in high-risk locoregionally advanced NPC, with mild toxicity and comparable quality of life. Clinical trial information: NCT03427827. Research Sponsor: Jiangsu Hengrui Pharmaceuticals.

3-yr rate (%)	Camrelizumab (n = 226)	Standard Therapy (n = 224)	P Value
Event-free survival	86.9	77.4	0.030
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)	
Immune-related	8 (3.9)	0	
Grade 5 AEs, n (%)	1 (<1%)	1(<1%)	
Immune-related	0	0	

LBA6015 Rapid Oral Abstract Session

PRGN-2012, a novel gorilla adenovirus-based immunotherapy, provides the first treatment that leads to complete and durable responses in recurrent respiratory papillomatosis patients.

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Background: Recurrent respiratory papillomatosis (RRP) is a rare, neoplastic disorder caused by chronic infection with human papillomavirus (HPV) type 6 or 11. Significant morbidity can occur due to airway obstruction and, although rare, transformation into malignant cancer. There are no approved therapeutics. RRP is currently managed with frequent ablative procedures that can lead to irreversible laryngotracheal scarring and disability. PRGN-2012 is a gorilla adenovirus-based gene therapy/immunotherapy designed to generate HPV6/11-specific T cell immunity. The FDA has granted PRGN-2012 Breakthrough Therapy Designation for the treatment of RRP recognizing that this single arm study can serve as pivotal to support a licensing application. **Methods:** This pivotal trial (NCT04724980) evaluates the safety and efficacy of PRGN-2012 in patients with RRP requiring a minimum of 3 surgeries in the 12 months prior to treatment. Eligible patients received 4 subcutaneous (SC) injections of PRGN-2012 at dose level (DL) 1 ($1x10^{11}$ Particle Units (PU) per injection; n=3) or DL2 ($5x10^{11}$ PU per injection; n=35) over 12 weeks. The primary endpoint was the rate of complete response (CR), defined as no requirement for surgery in the 12 months following completion of treatment. Other key endpoints include duration of response, change in extent of papilloma growth (anatomic Derkay score) and vocal function. **Results:** PRGN-2012 was well-tolerated, with no serious adverse events, grade $>$ 2 treatment-related adverse events, or early treatment discontinuations. The most common adverse events were injection-site reaction, fatigue, chills, fever, and myalgia. PRGN-2012 treatment at DL2 significantly ($p<0.0001$) decreased the requirement for surgery, with a median number of surgeries in the 12 month period decreasing from 4 (3-10) prior to treatment to 0 (0-7) surgeries post-treatment. Approximately 90% of patients experienced a decrease in the number of surgeries in the 12 months post-treatment compared to pre-treatment with PRGN-2012. The primary endpoint evaluation demonstrated a confirmed complete response in 17/31 (55%) of evaluable patients. The median duration of complete response has yet to be reached with a median follow up of 15 months (12 - 30) at the time of data cutoff (March 6, 2024). Additionally, PRGN-2012 treatment resulted in a significant reduction in Derkay score, improvement in vocal function and generation of HPV-specific immune responses. **Conclusions:** These data demonstrate the overall favorable safety profile and significant clinical benefit of PRGN-2012 in adult RRP patients. These findings support PRGN-2012 as a potential therapeutic option for this patient population where no FDA-approved therapeutics exist. Clinical trial information: NCT04724980. Research Sponsor: Precigen Inc.

LBA6018 Rapid Oral Abstract Session

Covalent FAPI PET enables accurate management of medullary thyroid carcinoma: A prospective single-arm comparative clinical trial.

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Background: Localizing medullary thyroid carcinoma (MTC) lesions is crucial for treatment decision, but the detection using the current imaging modalities is unsatisfied. Previously, we reported a ^{68}Ga-labeled targeted covalent radiopharmaceutical fibroblast activation protein inhibitor (^{68}Ga-TCR-FAPI), which demonstrated improved and sustained tumor targeting. This study aimed to head-to-head compare the ^{68}Ga-TCR-FAPI PET-CT and the currently approved ^{18}F-FDG PET-CT in detecting MTC. **Methods:** This was a prospective, single-center, open-labeled, single-arm comparative imaging trial. MTC patients with serum calcitonin>10 pg/ml and without targeted therapy were eligible. Serum calcitonin level, ^{68}Ga-TCR-FAPI PET-CT and ^{18}F-FDG PET-CT were acquired within a maximum interval of 30 days. Images were independently interpreted by 3 readers to calculate the patient-based and region-based detection rate. Quantitative PET parameters were calculated from the lesion ROI and compared between ^{68}Ga-TCR-FAPI and ^{18}F-FDG PET-CT. The accuracy of imaging findings was validated on lesions with histopathology or calcitonin-based follow-up. The primary outcome was patient-based detection rate, and the secondary outcome included region-based detection rates, metabolic parameters comparison and diagnostic accuracy. **Results:** 50 patients were enrolled between May 11th, 2023 and Feb. 1st, 2024. ^{68}Ga-TCR-FAPI exhibited significantly higher patient-based detection rate than ^{18}F-FDG PET-CT (98% vs. 66%, p=0.0002). Detection rates were also superior for ^{68}Ga-TCR-FAPI in head and neck (72% vs. 50%, p=0.0098), thorax (50% vs. 34%, p=0.0269), abdomen (28% vs. 10%, p=0.0077) and skeleton (54% vs. 16%, p<0.0001). On quantitative analysis, SUV_{max} was significantly higher in ^{68}Ga-TCR-FAPI PET-CT than ^{18}F-FDG PET-CT (11.71±9.16 vs. 2.55±1.73, p<0.0001). Diagnostic accuracy was substantially greater with ^{68}Ga-TCR-FAPI PET-CT than ^{18}F-FDG PET-CT (96.7% vs. 43.3%, p<0.0001) based on 60 histopathological validated lesions from 15 patients who underwent surgery. Notably, 60% (30/50) patients directly benefited from ^{68}Ga-TCR-FAPI PET-CT, with 66.7% (10/15) experiencing changes in surgical plans, and 100% (6/6) of the newly diagnosed MTC with R0 resection achieved biochemical cure at 1-month post-surgery. **Conclusions:** ^{68}Ga-TCR-FAPI PET-CT displayed higher detection rate, metabolic value and diagnostic accuracy than ^{18}F-FDG PET-CT in MTC patients, and should be integrated into MTC evaluation at initial diagnosis and persistent disease. Clinical trial information: NCT06084767. Research Sponsor: None.

Radioactivity in pathological proved MTC and non-MTC lesions.

	^{18}F-FDG			^{68}Ga-TCR-FAPI		
	MTC (n = 42)	Non-MTC (n = 18)	P Value	MTC (n = 42)	Non-MTC (n = 18)	P Value
SUV_{max}	3.56 ± 2.56	3.93 ± 2.89	0.623	14.54 ± 11.11	2.35 ± 1.63	< 0.0001
T/N ratio	2.36 ± 1.77	2.57 ± 1.63	0.679	8.16 ± 7.37	1.51 ± 0.91	< 0.0001

LBA6019 Rapid Oral Abstract Session

Phase 3 randomized study for evaluation of physician choice Rx versus best supportive care as second-line or beyond therapy in head and neck cancer with poor performance status.

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Background: Relapsed-recurrent head and neck squamous cell carcinoma (HNSCC) cancers have limited treatment options in the second line and beyond setting. Many of these patients have poor performance status (PS) and are subject to best supportive care (BSC). There is a lack of any level 1 evidence about the benefit of systemic therapy in HNSCC with poor PS. **Methods:** This was a randomized phase 3 superiority open-label multicentric study. Adult patients (age>=18 years) with relapsed-recurrent HNSCC, qualified to receive 2nd line or beyond systemic palliative therapy and had ECOG PS 2-3 were eligible. Such patients underwent central stratified random assignment 2:1 to either physician choice therapy either triple metronomic chemotherapy (tablet erlotinib 150 mg [fixed-dose] OD, capsule celecoxib 200 mg [fixed-dose] BD, and oral weekly methotrexate 9 mg/m2 orally or intravenous docetaxel [75 mg/m2 3 weekly]) or BSC. The chemotherapy was continued either till the progression of the disease or till the development of intolerable side effects. The primary endpoint was 6 month-overall survival (OS). The OS in the 2 arms was estimated using the Kaplan-Meier method and by log-rank test. A p-value of 0.05 was considered significant. Sample size: The 6-month OS assumed based on our previous data was 20%, we had assumed that it would increase to 50% in the intervention arm with a type 1 error of 5%, type 2 error of 20%, 2:1 allocation (1- BSC and 2-intervention) and 10% lost to follow up rate. The sample size required was 66. The events required for analysis were 47. **Results:** The study recruited 66 patients between 1st September 2022 to 27th December 2022 with 44 patients in physician choice therapy (PCT) and 22 in the BSC arm. The data was censored for analysis on 1st March 2024. The median age was 50 years (Range 25-75) with a predominantly male population (n=53;85%). The ECOG PS was PS 2 in 56 (84.8%) and PS 3 in 10 (15.2%) patients. The predominant site of primary was the oral cavity with 52 patients (78.8%). The previous number of systemic lines of therapy received were 1 in 41 (62.1%), 2 in 22 (33.3%), and >2 in 3 (4.5%) patients. Except for 2, all patients had a platinum refractory status (64;97%). The PCT was triple metronomic chemotherapy in 41 patients (93.2%; n=44) and docetaxel in 3 patients (6.8%; n=44). The 6-month OS was 9.09% (95% CI 1.56-25.1) in the BSC versus 53.8% (95% CI 37.9-67.2) in the PCT arm (P<0.0001). The median overall survival in PCT was 223.0 days (95% CI 129-283) versus 77.5 days (95%CI 58 -110) in the BSC arm. The corresponding hazard ratio was 0.333 (95%CI 0.187-0.593; P<0.0001). The data regarding adverse events will be presented at the conference. **Conclusions:** In this first-ever randomized study on poor PS HNSCC patients, warranting second-line and beyond therapy, the administration of systemic therapy led to a substantial improvement in OS. Clinical trial information: CTRI/2022/08/044733. Research Sponsor: None.

LBA6053 Poster Session

A phase III randomized, open-label study to establish the superiority of triple oral metronomic therapy (OMCT) used in addition to chemotherapy regimen (paclitaxel + carboplatin) over chemotherapy alone for the treatment of advanced unresectable head and neck cancer squamous cell cancer (HNSCC).

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Background: Advanced HNSCC has poor outcomes and limited treatment options, especially in resource-constrained settings. Immunotherapy is affordable for less than 5% of patients in lower-middle-income countries (LMICs). Triple OMCT, employing low-dose continuous chemotherapy, shows promise, but its safety and efficacy along with chemotherapy remain unproven. We aimed to assess whether the addition of OMCT to first-line chemotherapy can improve overall survival (OS) as compared to chemotherapy alone. **Methods:** This phase 3 randomized, prospective, open-label, superiority design study enrolled patients with advanced HNSCC who were planned for palliative intent platinum-based chemotherapy. The patients were stratified for the site of the tumor and ECOG PS, and were randomly assigned 1:1 to receive either triple OMCT (Erlotinib 150 mg OD, Celecoxib 200 mg BD and Methotrexate 9mg/m^2 once weekly) in addition to 3-weekly paclitaxel carboplatin (PC) chemotherapy (Arm A) or, PC chemotherapy alone (Arm B). Sample size calculation assumed no OS improvement with OMCT+PC (5% type I error, 80% type II error). The primary endpoint was OS, while secondary endpoints included PFS, quality of life (QoL) assessments, and safety. OS and PFS were analyzed via Kaplan-Meier and log-rank test; HR estimated via Cox proportional hazard models. QoL was assessed using EORTC QLQ-C30. The study was approved by Institutional Ethics Committee and registered with the Clinical Trials Registry India (CTRI/2022/10/046520). **Results:** Between Nov 02, 2022, and Dec 20, 2023, 238 patients were randomly assigned with 119 in each arm. Median age was 47 years, with 97.8% being males, and 78% of patients had ECOG PS 0-1. The median OS for patients in Arm A was 8.3 months (95% CI, 6.3-10.4) while it was 6.1 months (95% CI, 4.7-7.4), in Arm B (HR 0.63; 95% CI, 0.47–0.83; p=0.00011). The corresponding median PFS was 7.6 months (95% CI, 6.3-8.8) and 3.5 months (95% CI, 2.2-4.7) (HR, 2.79; 95% CI, 1.98-3.93; P<0.000). Significant differences in EORTC-C30 were found for the physical functioning domain between baseline and 1-month follow-up visit. PC chemotherapy combined with triple OMCT showed good tolerability, with common toxicities including fatigue (40.3%), and hyponatremia (25.4%), similar to the incidence observed with PC chemotherapy alone. **Conclusions:** This study demonstrates that the addition of triple OMCT to paclitaxel and carboplatin chemotherapy is an effective and safe treatment option for patients with advanced HNSCC in platinum-sensitive settings. This treatment option is particularly valuable in LMICs, where cetuximab and pembrolizumab are not feasible. Clinical trial information: CTRI/2022/10/046520. Research Sponsor: Indian Cooperative Oncology Network.

	Arm A	Arm B	Absolute Difference
6 months OS	75.5%	50.4%	25.1%
12 months OS	44.0%	25.5%	18.5%

LBA6054 **Poster Session**

Long term results of phase 3 randomized study evaluating the addition of low dose nivolumab to palliative chemotherapy in head and neck cancer.

Vijay Maruti Patil, Vanita Noronha, Nandini Sharrel Menon, Minit Jalan Shah, Zoya Ravish Peelay, Kavita Prakash Nawale, Priyanka Bhagyavant, Riddhi Sawant, Manali Kolkur, Kumar Prabhash; P.D. Hinduja Hospital, Mumbai, India; Tata Memorial Hospital, Tata Memorial Centre, Mumbai, India; Tata Memorial Hospital, Mumbai, India; Tata Memorial Centre, Mumbai, India; Cancer Research and Statistic Foundation, Dahisar, India

Background: The addition of low-dose nivolumab to metronomic chemotherapy (MC) improved 1-year overall survival in relapsed and refractory head and neck squamous cell carcinoma (HNSCC). However, sustained benefit over the long term is an important aspect of immunotherapy and it has never been studied in a prospective randomized study for low-dose nivolumab. **Methods:** This was an open-label randomized phase 3 superiority study. Adult patients (age= or >18 years), ECOG PS (0-1), relapsed -recurrent or newly diagnosed advanced HNSCC, and normal organ functions were eligible. Patients were randomly assigned 1:1 to oral metronomic chemotherapy consisting of methotrexate 9 mg/m2 weekly, celecoxib 200 mg twice daily, and erlotinib 150 mg daily, with (TMC-I) or without (TMC) with intravenous nivolumab 20 mg flat dose once-every-3-weeks. Systemic therapy was continued till the development of intolerable side effects or progression of disease. The primary endpoint was overall survival (OS). Landmark analysis was performed to compare OS between 2 arms. **Results:** The median follow-up was 32.5 months (95% CI 29.6-32.7). The 1 year, 2 year and 2.5 year OS were 20% (95%CI 11.9-29.7) versus 35.5% (95%CI 25-46.2) {Hazard ratio (HR)= 0.6534, 95%CI 0.4473 -0.956: P=0.028}, 5.3% (95%CI 1.7-12.3) versus 18.4 %(95%CI 10.7-27.8) {HR= 0.6318, 95%CI 0.4476 -0.8919: P=0.009} and 5.3% (95%CI 1.7-12.3) versus 17.1 % (95%CI 9.66.-26.3) {HR= 0.6379, 95%CI 0.4524 -0.8993: P=0.01} in the TMC and the TMC-I arms respectively. The benefit of the addition of nivolumab was independent of other factors like age, gender, ECOG PS, Site of malignancy, time to failure, PDL1 score, and previous exposure to platinum (Table). **Conclusions:** The addition of low-dose nivolumab to triple metronomic chemotherapy leads to a tripling of OS thus suggesting that even low-dose nivolumab has sustainable benefits. The benefit observed is irrespective of known prognostic factors in HNSCC. Clinical trial information: CTRI/2020/11/028953. Research Sponsor: Motivation for Excellence; Mumbai Oncology Association; NATCO Pharma Limited; INTAS Pharmaceuticals Limited.

Multivariate analysis for overall survival (OS).

Factor	Hazard Ratio	P Value
Arm		
TMC	Reference	0.001
TMC-I	0.525 (0.356-0.777)	
Age		
Non-Elderly	Reference-	0.315
Elderly	1.281(0.790 - 2.079)	
Gender		
Female	Reference	0.446
Male	0.781(0.413-1.476)	
ECOG PS		
0	Reference	0.705
1	1.154(0.55- 2.421)	
Site		
Non-Oral	Reference	0.562
Oral	1.121(0.635 - 2.306)	
Previous Platinum		
No	Reference	0.240
Yes	1.412(0.794 - 2.511)	
Tumor PDL1 score		
>50	Reference	
1-50	2.143(1.343 - 3.421)	0.014
0	1.652(0.881 - 3.097)	0.117
Unknown	1.125(0.565 - 2.243)	0.737
Time to failure on previous treatment		
<6 months	Reference	
6-12 months	0.816(0.254-2.624)	0.562
>12 months or upfront	1.200(0.670-2.153)	0.733

LBA6092 Poster Session

Long term results of a randomized phase III study of nimotuzumab in combination with concurrent radiotherapy and cisplatin versus radiotherapy and cisplatin alone, in locally advanced squamous cell carcinoma of the head and neck.

Vijay Maruti Patil, Vanita Noronha, Nandini Sharrel Menon, Minit Jalan Shah, Sarbani Laskar Ghosh, Ashwini Budrukkar, Monali Swain, Arun Balaji, Devendra Chaukar, Prathamesh S Pai, Pankaj Chaturvedi, Kumar Prabhash; P.D. Hinduja Hospital, Mumbai, India; Tata Memorial Hospital, Tata Memorial Centre, Mumbai, India; Tata Memorial Hospital, Mumbai, India; Tata Memorial Centre, Mumbai, India; Homi Bhabha National Institute, Mumbai, India

Background:: The addition of nimotuzumab to weekly cisplatin as a radiosensitizer had improved progression-free survival (PFS) in a phase 3 study in locally advanced head and neck squamous cell carcinoma (LA HNSCC). However, whether it leads to an improvement in long-term OS is unknown. Hence this analysis was performed to evaluate the efficacy (in terms of OS) and late-term adverse events of the addition of nimotuzumab to concurrent chemoradiation in LA HNSCC. **Methods:** This was an open-label, investigator-initiated, phase 3 randomized trial conducted from 2012 - 2018. 536 adult patients with LA HNSCC, fit for radical chemoradiation were randomly assigned. Primary sites in the nasopharynx, salivary gland, nasal cavity, and paranasal sinus were excluded. Randomized 1:1 to either radical radiotherapy (66-70 Gy) with concurrent weekly cisplatin (30 mg/m2) (CRT) or the same schedule of chemoradiation with weekly nimotuzumab (200 mg) (NCRT). The primary endpoint was a 10-year OS; the key secondary endpoint was late adverse events. Intent to treat analysis was performed. OS was defined as the time from randomization till death. Kaplan Meier method will be used for the estimation of OS. Landmark analysis was performed to compare 10 OS between the 2 arms. COX proportional hazard model will be used for the calculation of hazard ratio (HR). The adverse events between the 2 arms were compared using a Fisher's test. A p-value of 0.05 will be considered as significant. **Results:** The median follow-up was 8.86 years (95% CI 8.59-9.16). The primary site of the primary was the oropharynx (269,50.2%) and only 24 cases were HPV positive. The 10-year OS was 22.5% (95% CI 16.7-28.8) versus 33.5% (95% CI 27.6-39.4) in the CRT and NCRT arm respectively (Hazard ratio=0.811; 95%CI 0.664-0.995, P=0.044). The median OS was 2.78 years (95% CI 2.31-3.69) versus 3.69 years (95% CI 2.90-4.49) in the CRT and NCRT arm respectively (P value by log-rank test=0.04). The median OS in HPV negative oropharynx was 1.8 years (95% CI 1.51-2.09) versus 2.48 years (95% CI 1.79-3.16) in the CRT and NCRT arm respectively (P value by log-rank test=0.02; HR 0.724 95%CI 0.546-0.959). Long-term adverse events were captured in 380 patients. There was no statistically significant difference in late-term adverse events between the 2 arms and will be presented at the conference. **Conclusions:** The addition of nimotuzumab to weekly cisplatin leads to improvement in long-term overall survival in locally advanced HNSCC without any additional increase in late-term adverse events. These results are largely applicable in HPV-negative patients. Clinical trial information: CTRI/2014/09/004980. Research Sponsor: BIOCON limited (India); TRAC.

LBA6500 **Oral Abstract Session**

ASC4FIRST, a pivotal phase 3 study of asciminib (ASC) vs investigator-selected tyrosine kinase inhibitors (IS TKIs) in newly diagnosed patients (pts) with chronic myeloid leukemia (CML): Primary results.

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Background: We present primary results from ASC4FIRST (NCT04971226), the first study in CML comparing all current standard-of-care frontline TKIs with a novel agent, ASC, in newly diagnosed pts. ASC Specifically Targets the ABL Myristoyl Pocket (STAMP). **Methods:** Adults with CML were randomly assigned 1:1 to receive ASC 80 mg once daily or an IS TKI at standard label doses, stratified by ELTS risk category and prerandomization selected (PRS) TKI (imatinib [IMA] or second-generation [2G] TKIs), which was selected by investigators before randomization, accounting for pt preference. Pts diagnosed within 3 mo before enrollment with no prior treatment (Tx) except IMA/2G TKIs for ≤2 wk prior to randomization were eligible. Primary objectives were to demonstrate superior major molecular response (MMR) rate at wk 48 with ASC vs IS TKI and ASC vs IS TKI within the stratum of pts with IMA as PRS TKI (ASC^{IMA} vs $IS\ TKI^{IMA}$). The study is positive if either objective is met. Comparing MMR rate of ASC vs IS TKI at wk 48 within the stratum of pts with 2G TKIs as PRS TKI (ASC^{2G} vs $IS\ TKI^{2G}$) was an unpowered secondary objective. **Results:** Pts received ASC (n=201: ASC^{IMA}, n=101; ASC^{2G}, n=100) or IS TKI (n=204: $IS\ TKI^{IMA}$, n=102; $IS\ TKI^{2G}$, n=102 [nilotinib, 48%; dasatinib, 41%; bosutinib, 11%]). Median follow-up was 16.3 and 15.7 mo for ASC and IS TKI, respectively (cutoff: Nov 28, 2023). At cutoff, Tx was ongoing in 86%, 62%, and 75% of pts on ASC, IMA, and 2G TKIs, respectively, with pts most commonly discontinuing due to unsatisfactory therapeutic effect (6%, 21%, 10%) (Tx failure per ELN2020 [5%, 16%, 8%], MMR loss [0.5%, 0%, 0%], physician decision [0.5%, 5%, 2%]) and adverse events (AEs) (5%, 11%, 10%). MMR rate at wk 48 (per ITT) was superior with ASC (67.7%) vs IS TKI (49.0%) and with ASC^{IMA} (69.3%) vs $IS\ TKI^{IMA}$ (40.2%), meeting both primary objectives with high statistical significance; rate difference was 18.9% [95% CI, 9.6%-28.2%] and 29.6% [95% CI, 16.9%-42.2%], respectively, both with adjusted 1-sided $P<.001$. MMR rate at wk 48 was higher with ASC^{2G} vs $IS\ TKI^{2G}$ (66.0% vs 57.8%). *BCR::ABL1*^{IS} ≤1% rate at wk 48 was 87% with ASC vs 73% with IS TKI and 84% with ASC^{IMA} vs 62% with $IS\ TKI^{IMA}$. At wk 48, MR^4 and $MR^{4.5}$ rates were higher with ASC vs IS TKI (39% vs 21%; 17% vs 9%), ASC^{IMA} vs $IS\ TKI^{IMA}$ (43% vs 15%; 18% vs 5%), and ASC^{2G} vs $IS\ TKI^{2G}$ (35% vs 26%; 16% vs 13%). ASC had markedly favorable safety and tolerability vs IMA and 2G TKIs, with less grade ≥3 AEs (38%, 44%, 55%), half the rate of AEs leading to Tx discontinuation (5%, 11%, 10%), and less dose adjustments/interruptions to manage AEs (30%, 39%, 53%). Rate of arterial occlusive events was 1%, 0%, and 2%, respectively. **Conclusions:** ASC is the only agent to show a statistically significant superior efficacy and excellent safety and tolerability vs all current standard-of-care frontline Tx, with potential to be the therapy of choice for CML. Clinical trial information: NCT04971226. Research Sponsor: Novartis Pharma AG.

LBA6508 Oral Abstract Session

Multi-site randomized trial of a collaborative palliative and oncology care model for patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) receiving non-intensive therapy.

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Background: Patients with AML and high-risk MDS receiving non-intensive chemotherapy have substantial quality of life (QOL) impairments and often do not engage in timely discussions with their clinicians about their end-of-life (EOL) care preferences. Yet interventions to optimize EOL care delivery and QOL for this population are lacking. **Methods:** We conducted a multi-site randomized clinical trial of a collaborative palliative and oncology care model compared to usual care in 115 adult patients with AML and high-risk MDS receiving non-intensive therapy at two tertiary care academic hospitals. Patients with a new diagnosis or relapse/ refractory disease were eligible to participate within 30 days of initiating therapy. Patients assigned to the intervention met with a palliative care clinician monthly in the outpatient setting and a minimum of twice weekly during every hospital admission. Patients assigned to usual care were seen by palliative care only upon request. We used Natural Language Processing methods to interrogate the Electronic Health Record (EHR) with a validated algorithm to collect documented EOL care preferences. The primary outcome was to compare time from documentation of EOL care preferences to death between the study arms. Secondary outcomes obtained from the EHR include rates of documentation of EOL care preferences, hospitalization, and hospice utilization at the EOL. Patient-reported secondary outcomes include discussions with clinicians about EOL care preferences, QOL (Functional Assessment of Cancer Therapy – Leukemia), and psychological distress (Hospital Anxiety and Depression Scale) at 3 months after enrollment. **Result:** We enrolled 51.8% (115/222) of eligible patients. The rate of documented EOL care discussions in the EHR was higher among intervention patients vs. usual care (96.5% vs. 68.4%, $P<0.001$). Overall, 61.7% (71/115) of patients died, and those receiving the intervention had a longer time from documentation of EOL care preferences to death (41 days vs. 1.5 days, $P<0.001$). Intervention patients were more likely to report discussing their EOL care preferences with their clinicians (56.9% vs. 14.0%, $P<0.001$), and less likely to be hospitalized in the last 30 days of life (70.6% vs. 91.9%, $P=0.031$). There was no difference in hospice utilization at the EOL. At 3 months, patients assigned to the intervention reported better QOL (138.6 vs. 125.5, $P=0.010$), but no difference in depression or anxiety symptoms compared to those assigned to usual care. **Conclusions:** Palliative care significantly improved rates of discussion and documentation of EOL care preferences, reduced hospitalization at the EOL, and improved QOL in patients with AML and high-risk MDS. Clinical trial information: NCT03310918. Research Sponsor: MGH ECOR Research Scholar Grant; Leukemia and Lymphoma Society.

LBA7000 **Oral Abstract Session**

Tolerability and efficacy of BrECADD versus BEACOPP in advanced stage classical Hodgkin lymphoma: GHSG HD21, a randomized study.

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Background: We hypothesized that therapy with the novel BrECADD regimen (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) guided by positron emission tomography after two cycles (PET2) could improve the treatment of advanced-stage classical Hodgkin lymphoma (AS-cHL). The HD21 trial aimed at demonstrating superiority over the intensified BEACOPP regimen (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) in terms of treatment-related morbidity (TRMB) and non-inferiority (NI) in terms of progression-free survival (PFS). This is the first report of the final confirmative analysis of the HD21 trial. **Methods:** HD21 is an international, open-label, randomized phase III trial including AS-cHL patients 18-60 years at diagnosis. Patients were randomized to receive individualized 4 or 6 cycles of either BEACOPP or BrECADD guided by PET2 results. The co-primary endpoints included TRMB and PFS, which had been successfully established recently. Testing for superiority was planned with mature follow-up of four years. An adjusted alpha level of 0.047 was required to cross the efficacy boundary for superiority. The trial was conducted in accordance with ICH-GCP (NCT02661503) and supported by a research grant from Takeda Oncology. **Results:** The ITT (intention-to-treat) cohort for the efficacy analysis consisted of 1482 patients, of which 742 were randomized to receive BrECADD and 740 to BEACOPP. Median age was 31.1 years (range 18 to 60), 44% were female. PET2 was negative in 424 (57.5%) and 426 (58.2%) patients for BrECADD or eBEACOPP, respectively, and these were scheduled for 4 treatment cycles. With median follow-up of 48 months, 4y-PFS was 94.3% for BrECADD (95%-CI 92.6-96.1), and 90.9% for BEACOPP (95%-CI 88.7-93.1). The hazard ratio was 0.66 [95% CI 0.45-0.97], p=0.035). PFS benefit of BrECADD was driven by a reduction in early treatment failures, i.e., primary progression within 3 months (5 vs. 15) or early relapse between months 3 and 12 (11 vs. 23) and observed across all investigated subgroups. PET2-negative patients in the BrECADD group showed a 4-year PFS of 96.5%. 4-year OS was 98.5% for BrECADD and 98.2% for BEACOPP. Analyses of gonadal function demonstrated significantly higher follicle stimulating hormone recovery rates after one year in both men (67% vs. 24%) and women (89% vs. 68%) with higher birth-rates in the BrECADD group (n=60 vs. n=43). **Conclusions:** BrECADD is significantly more effective than BEACOPP and is associated with an unprecedentedly high 4-year PFS, reducing the risk of progression, relapse or death by a third. Together with an abbreviated treatment duration of only 3 months for the majority of patients and a favorable tolerability, treatment with PET2-individualized BrECADD sets a new benchmark for the treatment of adult patients with AS-cHL. Clinical trial information: NCT02661503. Research Sponsor: Takeda Oncology.

LBA7003 **Oral Abstract Session**

Tucidinostat plus R-CHOP in previously untreated diffuse large B-cell lymphoma with double expression of MYC and BCL2: An interim analysis from the phase III DEB study.

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Background: Epigenetic dysregulation is commonly correlated with the pathogenesis and development in diffuse large B-cell lymphoma (DLBCL). Tucidinostat, a subtype-selective histone deacetylase (HDAC) inhibitor, has shown promising efficacy in combination with R-CHOP in DLBCL patients with double expression of MYC and BCL2 (DE) in exploratory studies. **Methods:** We conducted a randomized, double-blind, placebo-controlled, phase III trial (DEB) to evaluate the efficacy and safety of tucidinostat plus R-CHOP in comparison with R-CHOP in previously untreated DLBCL patients with DE. Patients were randomly assigned in a 1:1 ratio to receive six cycles of either tucidinostat plus R-CHOP (tucidinostat group) or placebo plus R-CHOP (placebo group). Patients who achieved complete response (CR) after combination therapy received either tucidinostat or placebo as maintenance treatment with a maximum duration of 24 weeks. The primary endpoint was investigator-assessed event-free survival (EFS), and the key secondary endpoint was the complete response rate (CRR) evaluated at the end of combination treatment. An interim analysis was pre-defined to be conducted when CRR was obtained and the number of EFS events reached at least 60% of the total events required for entire study. **Results:** Between May 21, 2020, and July 25, 2022, 423 patients were enrolled and randomly assigned, 211 to the tucidinostat group and 212 to the placebo group. At data cutoff of this interim analysis (January 10, 2023), the median follow-up time was 13.9 months (95% CI, 12.9 - 15.4). A total of 152 EFS events (68.5% of the planned total) were observed, with 64 (30.3%) in the tucidinostat group and 88 (41.5%) in the placebo group. The 24-month EFS rate was 58.9% (95% CI, 48.9-67.6) in the tucidinostat group and 46.2% (95% CI, 35.7-56.1) in the placebo group. The hazard ratio (HR) between the two groups was 0.68 (95% CI, 0.49-0.94), with a p-value of 0.018. At the completion of combination treatment, the CRR in the tucidinostat and placebo groups were 73.0% (95% CI, 66.6-78.5) and 61.8% (95% CI, 55.1-68.1), respectively. The adjusted difference in CRR was 11.1% (95% CI, 2.3-20.0; P=0.014). The safety profiles of both groups were as expected, with no new safety findings. The incidence of ≥ grade 3 hematologic adverse events was generally higher in the tucidinostat group than the placebo group, but most patients were able to tolerate and complete the planned treatment cycles. No significant cardiac toxicity, hepatotoxicity, or nephrotoxicity were observed in both groups. **Conclusion:** The DEB study is the first phase III trial to show that combining tucidinostat with R-CHOP regimen is a feasible and efficacious novel approach in previously untreated DLBCL patients with DE. Tucidinostat plus R-CHOP could be a new frontline treatment option in this patient population. Clinical trial information: NCT04231448. Research Sponsor: None.

LBA7005 Oral Abstract Session

Brentuximab vedotin in combination with lenalidomide and rituximab in patients with relapsed/refractory diffuse large B-cell lymphoma: Results from the phase 3 ECHELON-3 study.

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Background: Despite recent advances, there remains a need for novel therapies for pts with R/R DLBCL. BV, an anti-CD30 antibody-drug conjugate, has shown efficacy and safety when combined with lenalidomide (len) and with rituximab (R) in heavily pretreated populations (Bartlett 2022; Ward 2022). The double-blind, global phase 3 ECHELON-3 study (NCT04404283) compared BV with R+len (R2) vs R2 in pts with R/R DLBCL who are ineligible for HSCT or CAR T-cell therapy. Here, we present results from the interim analysis (IA) for overall survival (OS). **Methods:** Pts with R/R DLBCL received BV+R2 or placebo+R2 (randomized 1:1). Pts received BV (1.2 mg/kg) or placebo q3w, R (375 mg/m^2) q3w, and len (20 mg) qd. The primary endpoint was OS in the intent-to-treat population. Secondary endpoints were investigator-assessed progression-free survival (PFS), objective response rate (ORR), and complete response (CR) rate. The preplanned IA was performed at 134 OS events with a prespecified efficacy boundary of 2-sided P=0.0232. **Results:** 230 pts were randomized: 112 to BV+R2 and 118 to R2; all but 2 pts (both in R2 arm) received ≥1 dose of study drug. Median age was 71 yrs (range, 21-89), 56.5% were male, and 10.9% had an ECOG of 2. Median prior lines of therapy was 3 (range, 2-8); 29% had prior CAR T-cell therapy and 68% were CD30- (<1% CD30 tumor expression). At median follow-up of 16.4 months (mos) (range, 0.1-31.5) (cut-off: January 22, 2024), median OS was 13.8 mos (95% CI: 10.3-18.8) with BV+R2 vs 8.5 mos (95% CI: 5.4-11.7) with R2 (HR 0.629; 95% CI: 0.445-0.891; P=0.0085); OS benefit was consistent across key subgroups. Median PFS was 4.2 mos (95% CI: 2.9-7.1) with BV+R2 vs 2.6 mos (95% CI: 1.4-3.1) with R2 (HR 0.527; 95% CI: 0.380-0.729; P<0.0001). ORR was 64.3% (95% CI: 54.7-73.1) with BV+R2 vs 41.5% with R2 (95% CI: 32.5-51.0; P=0.0006); CR rate was 40.2% vs 18.6%, respectively. In CD30+ vs CD30- subgroups, ORR/CR was 72.2%/38.9% vs 60.5%/40.8% with BV+R2, respectively, and 50.0%/26.3% vs 37.5%/15.0% with R2, respectively. Efficacy analysis including cell of origin will be presented. The safety profile of BV+R2 was tolerable vs R2: Grade (Gr) ≥3 treatment-emergent adverse events (TEAEs) were 88% vs 77%, serious TEAEs were 60% vs 50%, and Gr 5 TEAEs were 12% vs 8%, respectively. Most common TEAEs were neutropenia (46% vs 32%), anemia (29% vs 27%), and diarrhea (31% vs 23%). Rates of peripheral neuropathy for BV+R2 vs R2 were 31% vs 24% (all Gr) and 6% vs 2% (Gr 3). Median treatment duration was 3.6 mos with BV+R2 vs 2.0 mos with R2. **Conclusions:** Treatment with BV+R2 triplet, compared to R2, demonstrated statistically significant and clinically meaningful improvements in all key efficacy outcomes including OS in high-risk subgroups, with manageable safety. This triplet regimen represents a novel treatment option for pts with heavily pretreated R/R DLBCL. Clinical trial information: NCT04404283. Research Sponsor: This study was sponsored by Seagen Inc., which was acquired by Pfizer Inc. in Dec. 2023.

LBA7074 **Poster Session**

HDAC I/IIb selective inhibitor purinostat mesylate in relapsed and refractory diffuse large B-cell lymphoma: A single agent phase IIa trial.

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Background: Relapsed/refractory diffuse large B-cell lymphoma (r/r DLBCL) has a poor prognosis. Double-expressor (DEL) or TP53 abnormal r/r DLBCL patients(pts) are associated with even worse outcomes. Class I and IIb histone deacetylases (HDACs) are overexpressed in DLBCL and have been identified as a therapy target. Purinostat Mesylate (PM) is a high selective HDAC I/IIb inhibitor. Phase I dose-escalation trial of PM (1.2, 2.4, 4.0, 6.0, 8.4, 11.2, 15 mg/m^2) by i.v was conducted in 29 hematologic malignancies at day 1, 4, 8, 11 of a 21-day cycle. PM was generally well tolerated with no DLTs. 61.1% (11/18) ORR was observed in r/r lymphoma pts. Based on these data, we conducted a phase 2a to further explore efficacy and safety of PM and mechanism of actions. **Methods:** This randomized, multicenter, open-label, phase 2a study was conducted from Nov.2022 to the present(NCT05563844). Key eligibility include r/r DLBCL pts with prior therapy including anti-CD20 antibody and anthracycline-based chemotherapy; ECOG≤2. Thirty pts were randomized 1:1 received PM at 8.4 and 11.2 mg/m^2 on Day 1, 4, 8, 11 of a 21-day cycle. Pts continued to receive PM until disease progression or unacceptable toxicity. Primary outcome was ORR and safety. Multiple cell lines and PDX mouse models were used to evaluate the PM activity and mechanism of action in vitro and in vivo. ATAC-seq, bulk RNA-seq, and scRNA-seq from both PDX models and pts were investigated for the activated immune response of PM. **Results:** Thirty patients were enrolled and 28 patients were evaluable. The ORR (20/28) was 71.4% (95%CI:51.3-86.8) with 5 CR and 15 PR. Fifteen pts at 8.4 mg/m^2 achieved an ORR of 66.7%(95%CI:38.4-88.2) with 1 CR and 9 PR. Thirteen pts at 11.2 mg/m^2 achieved ORR of 76.9%(95%CI:46.2-95.0) with 4 CR and 6 PR. As of the data cut off in Feb. 2024, 7 pts remained on treatment and the longest treatment has lasted 17 cycles. Median PFS was 4.3m (95%CI:2.8-8.5), OS were immature. In subgroup analyses, 7 DE DLBCL pts obtained 42.9%(3/7) ORR and 11 pts with TP53 abnormal by FISH or NGS test achieved 45.5%(5/11) ORR. Fifteen pts with non-DE or without TP53 abnormal achieved ORR of 86.7%(13/15). The most frequently reported Grade≥3 TRAE were thrombocytopenia, neutropenia, lymphocytopenia. No PM-related death was reported. PM monotherapy showed stronger and superior antitumor effects in DE DLBCL and TP53 mutations PDX models than selinexor and R-CHOP. PM significantly down-regulates the proteins c-MYC, EZH2, and mutated P53. ATAC-seq, bulk RNA-seq and scRNA-seq revealed that PM can stimulate the proliferation and activation of cytotoxic T cells and NKT cells, up-regulate the expression of B-cell tumor MHC I and II and inhibit tumor cell immune escape. **Conclusions:** This study further supports the recommended dose 11.2 mg/m^2 PM as the phase 2b for r/r DLBCL. Currently, the phase 2b, open-label, multicenter study has enrolled in 37 sites in China. Clinical trial information: NCT05563844. Research Sponsor: Chengdu Zenitar Biomedical Technology Co., Ltd, Chengdu, Sichuan, China; Sichuan Province "14th Five-Year Plan" Life and Health Major Science and Technology Project (2022ZDZX0027).

LBA8002 **Oral Abstract Session**

BEAT-meso: A randomized phase III study of bevacizumab (B) and standard chemotherapy (C) with or without atezolizumab (A), as first-line treatment (TX) for advanced pleural mesothelioma (PM)—Results from the ETOP 13-18 trial.

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Background: The currently approved frontline TXs for PM are the combination of ipilimumab/nivolumab or platinum plus pemetrexed. The addition of B to C has been shown to improve overall survival in a randomized clinical trial. While combined immunotherapy or single agent immunotherapy with C is superior to C alone, there is potential for a synergistic triple combination of C, B, and immunotherapy. **Methods:** BEAT-meso (NCT03762018) is an international open-label, 1:1 randomized phase III trial, stratified by histology and stage. The objective is to determine the efficacy and safety of adding A (1200 mg, Q3W until progression) to B (15mg/kg, Q3W until progression) and standard C (4-6 cycles of carboplatin AUC5 with pemetrexed 500 mg/m^2, Q3W), as first-line TX for advanced PM. The trial is designed to detect an increase in the median overall survival (OS, primary endpoint) with the addition of A, aiming for a hazard ratio (HR) of 0.708, at 2.5% 1-sided alpha and 82% power (284 deaths, sample size 400 patients (pts)). In the pre-specified interim efficacy analysis (80% of the events, 01/2023), boundary was not crossed, and the trial continued to completion. Secondary endpoints include progression-free survival (PFS), objective response rate (ORR), disease control rate, duration of response (DoR), adverse events (AEs) assessed by CTCAE v5.0 and symptom-specific and global quality of life (QoL). **Results:** Between 04/2019 and 03/2022, a total of 400 pts was randomized, 200 per arm. The median age was 70 years, 79% were male, 50% were former smokers, 65% had ECOG performance status 1 and 78% had epithelioid histology. At a median follow-up of 35 months (m) (as of 1/09/2023), median OS was 20.5m [95% CI: 17.5-23.3] in the ABC and 18.1m [15.7-20.9] in the BC arm (deaths: 145 & 150; $HR_{ABC\ vs\ BC}$=0.84; [0.66 - 1.06], 2-sided stratified p=0.14, ITT final analysis). PFS was significantly longer in ABC with median 9.2m [8.1-10.9] vs 7.6m [6.9-8.3] in BC (HR=0.72; [0.59 - 0.89], 2-sided stratified p=0.0021). Histology shows a significant TX interaction for both PFS and OS. The OS HR is 0.51 [0.32-0.80] for non-epithelioid and 1.01 [0.77-1.32] for epithelioid (interaction p=0.012). In an exploratory analysis, post-progression OS was significantly different between the two arms, adjusted for post-progression TX (HR=0.76; [0.58 - 0.99]). The ORR was 55% in ABC and 49% in BC (p=0.27), while median DoR was 8.2m [6.8-9.7] in ABC and 5.6m [4.8-7.0] in BC (p=0.0041). Global QoL change was not significantly different between the two arms. Grade≥3 TX-related AEs occurred in 55% of pts in ABC and 47% of pts in BC (grade 5: 7 and 1 pt, respectively). **Conclusions:** The significant increase in median PFS with the addition of A did not translate into a significant increase in median OS. ABC demonstrated superiority over BC in non-epithelioid cases. Clinical trial information: NCT03762018. Research Sponsor: ETOP IBCSG Partners Foundation; MO40388.

LBA8007 **Oral Abstract Session**

Clinical outcomes with perioperative nivolumab (NIVO) by nodal status among patients (pts) with stage III resectable NSCLC: Results from the phase 3 CheckMate 77T study.

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Background: In CheckMate 77T, perioperative NIVO showed statistically significant EFS improvement vs neoadjuvant (neoadj) chemo followed by adjuvant (adj) placebo (PBO) in pts with stage (stg) II or III resectable NSCLC. We report clinical outcomes by baseline (BL) stg III N2 status, a subgroup with poor historical 5 y survival (26%–36%; Goldstraw *J Thorac Oncol* 2016). **Methods:** Adults with resectable stg IIA–IIIB (N2; AJCC v8) NSCLC were randomized to neoadj NIVO 360 mg Q3W + chemo (4 cycles [cyc]) followed by adj NIVO 480 mg Q4W (13 cyc) or neoadj PBO Q3W + chemo (4 cyc) followed by adj PBO Q4W (13 cyc). Primary endpoint: EFS per BICR. Exploratory analysis: efficacy and safety in pts with BL clinical stg III N2 or non N2 disease (dz). **Results:** BL characteristics were generally similar between pts with stg III N2 (NIVO, 91; PBO, 90) and non N2 dz (55; 57), and between treatment (tx) arms, except a higher percent of pts with N2 dz had NSQ histology and ECOG PS 0 (both arms). Pts with N2 dz had improved EFS with NIVO vs PBO (HR 0.46; 1 y EFS 70% vs 45%) and higher pCR (22.0% vs 5.6%; median f/u 25.4 mo; Table). Pts with non N2 also had EFS benefit with NIVO vs PBO (HR 0.60; 1 y EFS 74% vs 62%) and higher pCR (25.5% vs 5.3%; Table). Surgical feasibility was similar between pts with N2 and non N2 dz and numerically higher with NIVO vs PBO. Of pts with N2 dz, 77% (NIVO) vs 73% (PBO) had definitive surgery (pneumonectomy 1% vs 14%; R0 resection 86% vs 86%); of pts with non N2 dz, 82% vs 79% had definitive surgery (pneumonectomy 13% vs 9%; R0 resection 84% vs 87%). Tumor downstaging postsurgery was seen in most pts with stg III dz and was deeper with NIVO vs PBO: 61% vs 50% (N2; 33% vs 14% to ypT0), 87% vs 76% (non N2; 27% vs 11% to ypT0). Of all pts with stg III dz, nodal downstaging postsurgery was 52% (NIVO) vs 45% (PBO); 46% vs 36% to ypN0. Grade 3–4 TRAEs occurred in 34% (NIVO) and 26% (PBO) of pts with N2; 29% and 21% of pts with non N2 dz. **Conclusions:** In this exploratory analysis, perioperative NIVO showed clinical benefit vs PBO in pts with stg III NSCLC, regardless of N2 status. Over half of pts with stg III dz had nodal downstaging with NIVO; majority downstaged to ypN0. This first comprehensive analysis by nodal status among pts with stg III dz from a global phase 3 study of perioperative immunotherapy further supports perioperative NIVO as a tx option for pts with resectable NSCLC. Clinical trial information: NCT04025879. Research Sponsor: Bristol Myers Squibb.

	Stage III N2		Stage III Non N2	
	NIVO n = 91	PBO n = 90	NIVO n = 55	PBO n = 57
Median EFS, mo	30.2	10.0	NR	17.0
(95% CI)	(26.9–NR)	(8.1–15.1)	(24.2–NR)	(10.6–NR)
HR	0.46		0.60	
(95% CI)	(0.30–0.70)		(0.33–1.08)	
1 y EFS, %	70	45	74	62
pCR, %	22.0	5.6	25.5	5.3
(95% CI)	(14.0–31.9)	(1.8–12.5)	(14.7–39.0)	(1.1–14.6)
MPR, %	29.7	11.1	41.8	12.3
(95% CI)	(20.5–40.2)	(5.5–19.5)	(28.7–55.9)	(5.1–23.7)
EFS (pts with no pCR) HR (95% CI)[a]	0.58 (0.37–0.89)		0.75 (0.41–1.36)	

NR, not reached.
[a]HRs were not generated for pts with pCR because < 10 pts with N2 or non N2 NSCLC had pCR with PBO.

LBA8010 **Rapid Oral Abstract Session**

Neoadjuvant nivolumab (NIVO) + chemotherapy (chemo) vs chemo in patients (pts) with resectable NSCLC: 4-year update from CheckMate 816.

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Background: The phase 3 CheckMate 816 study established neoadjuvant NIVO + chemo as a standard of care for eligible pts with resectable NSCLC. Here, we report the 4-year survival update from this study, representing the longest follow-up among all global phase 3 studies evaluating neoadjuvant or perioperative immunotherapy-based treatments. **Methods:** Adults with stage IB (≥ 4 cm)–IIIA (per AJCC v7) resectable NSCLC, ECOG PS ≤ 1, and no known *EGFR*/*ALK* alterations were randomized 1:1 to receive NIVO 360 mg + chemo Q3W or chemo alone Q3W for 3 cycles, followed by surgery. Event-free survival (EFS) and pathologic complete response (pCR; both per blinded independent review) were primary endpoints and were both statistically significant. Overall survival (OS) was a key secondary endpoint. Exploratory analyses included efficacy by pCR status and extent of resection. **Results:** At the 23 Feb 2024 database lock (median follow-up, 57.6 mo), NIVO + chemo continued to improve EFS vs chemo (median, 43.8 mo vs 18.4 mo; HR [95% CI], 0.66 [0.49–0.90]); 4-year EFS rates were 49% vs 38%. EFS favored NIVO + chemo vs chemo regardless of whether pts had lobectomy or pneumonectomy (Table), with 56%–57% vs 40%–43% of pts without disease recurrence at 4 years. NIVO + chemo also continued to show OS improvement vs chemo (HR [98.36% CI], 0.71 [0.47–1.07]; P = 0.0451; median OS was not reached [NR] in both arms, and the significance boundary was not met at this interim analysis). An OS improvement of 13% was sustained over time for NIVO + chemo vs chemo; 4-year OS rates were 71% vs 58%. Pts in the NIVO + chemo arm who had pCR continued to have improved OS vs those who did not (HR [95% CI], 0.08 [0.02–0.34]); 4-year OS rates, 95% vs 63%); a similar trend was seen in the chemo arm, although few pts had pCR with chemo (n = 4). No new safety signals were observed at this update. Additional survival analyses in pt subgroups and by ctDNA levels will be presented. **Conclusions:** In this 4-year analysis from CheckMate 816, neoadjuvant NIVO + chemo sustained EFS and OS separation vs chemo over time and demonstrated the long-term survival benefit of having pCR in pts with resectable NSCLC. These data provide the first understanding of the long-term benefits of neoadjuvant immunotherapy when added to chemo, reinforcing neoadjuvant NIVO + chemo as a standard of care, and providing a benchmark to assess the benefits of all perioperative immunotherapy-based treatments. Clinical trial information: NCT02998528. Research Sponsor: Bristol Myers Squibb.

	NIVO + chemo			Chemo			
	n	Median EFS, mo (95% CI)	4-year EFS rate, %	n	Median EFS, mo (95% CI)	4-year EFS rate, %	HR (95% CI)
Overall	179	43.8 (30.6–NR)	49	179	18.4 (14.0–26.7)	38	0.66 (0.49–0.90)
In pts with surgery by extent of resection[a]							
Lobectomy	115	NR (38.1–NR)	56	82	24.9 (13.9–58.0)	43	0.59 (0.39–0.90)
Pneumonectomy	25	NR (19.4–NR)	57	34	19.6 (13.8–52.3)	40	Not calculated[b]

[a]Pts with surgery (NIVO + chemo, n = 149; chemo, n = 135).
[b]Too few events (< 10 per arm) to calculate HR.

LBA8035 **Poster Session**

IMpower010: Final disease-free survival (DFS) and second overall survival (OS) interim results after ≥5 years of follow up of a phase III study of adjuvant atezolizumab vs best supportive care in resected stage IB-IIIA non-small cell lung cancer (NSCLC).

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Background: IMpower010 (NCT02486718) met its primary endpoint of significant DFS improvement with atezo vs BSC after adj chemotherapy in resected NSCLC in the PD-L1 TC ≥1% and all-randomized stage II-IIIA populations, leading to worldwide approval of adj atezo for PD-L1 TC ≥1% or PD-L1 TC ≥50% stage II-IIIA NSCLC. At OS IA1, a trend favoring atezo was seen in the PD-L1 TC ≥1% stage II-IIIA population. Here we report findings from the DFS FA and OS IA2. **Methods:** The IMpower010 study design has been previously described (Felip *et al*, *Lancet* 2021). The primary DFS and secondary OS endpoints were tested hierarchically: DFS in the PD-L1 TC ≥1% (SP263) stage II-IIIA, then in the all-randomized stage II-IIIA, and then in the intent-to-treat (ITT; stage IB-IIIA) populations, followed by OS in the ITT population. Secondary endpoints included 3- and 5-y DFS and DFS in the PD-L1 TC ≥50% (SP263) stage II-IIIA population. OS in the ITT population could only be formally tested if the significance boundary for DFS in that population was crossed. **Results:** At the DFS FA and OS IA2 (clinical cutoff date: Jan 26, 2024), with a minimum follow-up of 60 mo, DFS and OS for the PD-L1 TC ≥1% and TC ≥50% stage II-IIIA populations were consistent with previously observed benefit; the difference in median (m) DFS between arms in the PD-L1 TC ≥1% population was 31.2 mo (Table). In the ITT population, the significance boundary for DFS was not crossed and OS was similar between arms, although data were immature. The safety profile of atezo was consistent with prior analyses. **Conclusions:** These results provide the first cancer immunotherapy data with ≥5 y of follow-up from a Phase III study in resectable NSCLC. Although the statistical boundary for the ITT population was not crossed, DFS benefit with adj atezo continues to translate into a positive OS trend vs BSC in the PD-L1 TC ≥1% and TC ≥50% stage II-IIIA populations. These results further support the use of adj atezo in PD-L1–selected populations. Clinical trial information: NCT02486718. Research Sponsor: F. Hoffmann-La Roche, Ltd.

	PD-L1 TC ≥1% stage II-IIIA		PD-L1 TC ≥50% stage II-IIIA		All-randomized stage II-IIIA		ITT (stage IB-IIIA)	
	Atezo n=248	BSC n=228	Atezo n=115	BSC n=114	Atezo n=442	BSC n=440	Atezo n=507	BSC n=498
3-/5-y DFS, %	62.7/ 53.2	52.1/ 42.7	74.9/ 65.1	53.2/ 44.5	59.3/ 49.3	52.6/ 44.4	61.4/ 52.0	55.5/ 46.5
mDFS, mo	68.5	37.3	NR	41.1	57.4	40.8	65.6	47.8
HR	0.70[a,b]		0.48[b]		0.83[a,b]		0.85[a]	
95% CI	0.55, 0.91		0.32, 0.72		0.69, 1.00		0.71, 1.01	
*P*value[c]	—		—		—		0.07[a]	
3-/5-y OS, %	82.1/ 74.8	78.9/ 66.3	89.1/ 82.7	77.8/ 65.3	78.7/ 69.8	79.7/ 68.6	79.3/ 70.9	81.1/ 69.8
mOS, mo	NR	87.1	NR	87.1	NR	NR	NR	NR
HR[b]	0.77[a]		0.47		0.94[a]		0.97[a]	
95% CI	0.56, 1.06		0.28, 0.77		0.75, 1.19		0.78, 1.22	

NR, not reached. [a]Stratified analysis. [b]Not formally tested at this analysis. [c]2-sided.

LBA8050 Poster Session

Radiation therapy (RT)-free pembrolizumab plus chemotherapy (P+C) for PD-L1 TPS ≥50% locally advanced non-small cell lung cancer (LA-NSCLC): Primary analysis from multicenter single arm phase II study (Evolution trial; WJOG11819L).

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Background: Standard of care for unresectable LA-NSCLC is chemoradiation therapy (CRT) followed by durvalumab (D). Survival curves of P monotherapy/P+C for PD-L1 TPS ≥50% stage IV NSCLC suggested possible comparable survival to CRT for stage III patients (pts). Moreover, some studies of neoadjuvant C+immunotherapy (I) for stage III pts have demonstrated high pathological complete response and major pathological response rates, implying potentially outstanding efficacy of C+I for earlier stage. We thus hypothesized P+C without RT in PD-L1 ≥50% LA-NSCLC pts provides a comparable efficacy to CRT followed by D while avoiding CRT-induced severe toxicities. **Methods:** This is a phase II study conducted by West Japan Oncology Group. P with platinum plus pemetrexed (PEM) (non-squamous) or P with carboplatin plus nab-paclitaxel (squamous) was administered every 3 weeks without RT. After four cycles of induction P+C, P with PEM (non-squamous) or P alone (squamous) was continued until progression or 2 years. The primary endpoint was 2 year-PFS rate (threshold/expected: 20%/45%). **Results:** Between May 2020 and February 2022, 21 pts were enrolled. Median age was 73 (range, 53-89). Stage IIIA/B/C included 11 (52%)/7 (33%)/3 (14%), respectively. Histologic subtypes were 14 (67%) adenocarcinoma, 5 (24%) squamous cell carcinoma, and 2 (10%) others. Median follow-up period was 29.9 (range, 0.3-44.2) months. Median number of P administrations was 30 (range, 1-35). The primary endpoint was met with 2-year PFS rate of 67% (90% CI: 46-83%). At the time of data cut-off, 13 (62%) of 21 pts were still progression-free. Median PFS and OS were not reached. Two-year OS rate was 85%. Centrally reviewed tumor response: 8 (38%) CR; 9 (43%) PR; 3 (14%) SD; and 1 (5%) NE were confirmed, resulting in overall response rate (ORR) of 81% and disease control rate of 95%. ORRs/2-year PFS rates of PD-L1 TPS 50-79% and 80-100% were 67%/56% and 92%/75%, respectively. Non-hematological AEs ≥grade 3 were observed in 11 (52%) pts, including: 2 (10%) pneumonitis; 2 (10%) pneumonia; 1 (5%) diarrhea; 1 (5%) ALT elevation; and 1 (5%) acute heart failure. There was one (5%) grade 5 AE (pneumonia). **Conclusions:** RT-free P+C provided long-lasting responses in approximately two-thirds of pts. Higher PD-L1 TPS cases achieved higher RR, including some CRs and higher 2-year PFS rate. To confirm our hypothesis that RT-free P+C can be a less toxic curative option in selected LA-NSCLC pts with PD-L1 TPS ≥50%, further data is warranted. Clinical trial information: NCT04153734. Research Sponsor: Merck Investigator Studies Program (MISP).

LBA8069 **Poster Session**

Overall survival following heterogeneous FDG-guided dose-escalation for locally advanced NSCLC in the international phase III NARLAL2 trial.

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Background: The survival and loco-regional control for patients (pts) with locally advanced non-small cell lung cancer (LA_NSCLC) treated with radiotherapy (RT) are dismal despite adjuvant Durvalumab. However, there have been concerns about dose escalation for these pts since the unexpected result of the dose-escalation trial RTOG0617. A novel approach is therefore warranted to escalate the dose to the tumor. A possible approach is to use the principle from stereotactic body radiotherapy (SBRT) with inhomogeneous dose distribution. SBRT has demonstrated excellent local control in early-stage lung cancer. The international multicenter NARLAL2 (novel approach to RT for LA_NSCLC) phase III trial on dose escalation, randomized pts with LA_NSCLC between standard 66 Gy/ 33 fractions (F) versus heterogeneous FDG-PET driven dose escalation, aiming at mean dose to GTV-tumor$_{PET}$ 95 Gy/ 33 F and mean dose to GTV-node$_{PET}$ 74 Gy/ 33 F while strictly respecting dose to organs at risk. We here present the data on overall survival (OS) 1 year after the end of recruitment. **Methods:** Pts aged ≥18 years with LA_NSCLC were recruited from seven institutions in Denmark and Norway. Eligibility criteria included ECOG PS 0-1, histological or cytological confirmed NSCLC stage IIB-IIIB, signed informed consent, and a clinically acceptable plan for RT with conventional 66 Gy/ 33 F. PET-CT and brain MR were part of staging. Pts were randomly assigned to either treatment group (1:1, stratified for center and histology). The trial aimed to have iso-lung toxicity within the treatment arms by creating two RT plans (before randomization) for each patient (one for each treatment arm) with matching mean lung dose and lung V_{20Gy}. The follow-up (FU) were scheduled weekly during RT, every 3rd month for 2 years, and every 6th month for another 3 years after randomization. At FU visit a CT-scan and toxicity scoring were performed. All interim analyses were passed without interventions (toxicity and OS). The trial's primary endpoint was time to loco-regional failure from randomization. Secondary endpoints included OS, acute, and late toxicity. The sample size calculations requested 350 pts to be enrolled in the study. Recruitment of the pre-planned number of pts finalized in March 2023. The trial was registered with ClinicalTrials.gov (NCT02354274). **Results:** From January 2015 to March 2023, 350 pts were randomized: 177 and 173 pts in standard and escalated arms respectively. The two groups were well-balanced regarding age, gender, stage, and PS. The dose to GTV-tumor was 66.5 Gy [66.2, 67.1] (median [IQR]) in the standard arm and 88.1 Gy [84.9, 90.4] in the escalated arm. Median OS were 35.8 months (m) and 51.6 m for pts treated in the standard and escalated arm, respectively ($p = o.36$). Median FU time 50.8 m (reverse Kaplan-Meier). **Conclusions:** Dose escalation is safe in the NARLAL2 setting with respect to OS. Clinical trial information: NCT02354274. Research Sponsor: None.

LBA8500 Oral Abstract Session

Sacituzumab govitecan (SG) vs docetaxel (doc) in patients (pts) with metastatic non-small cell lung cancer (mNSCLC) previously treated with platinum (PT)-based chemotherapy (chemo) and PD(L)-1 inhibitors (IO): Primary results from the phase 3 EVOKE-01 study.

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Background: In pts with mNSCLC who progress on PT-based chemo and IO, doc is standard of care, but outcomes remain poor. SG, a Trop-2-directed antibody drug conjugate, showed durable response and tolerable safety in pretreated mNSCLC. We report results from the phase 3, randomized, open-label EVOKE-01 study comparing SG vs doc. **Methods:** Pts with mNSCLC with disease progression after PT-based chemo and IO were randomized 1:1 (stratified by histology, best response to last prior IO, and prior treatment for actionable genomic alterations [yes/no]) to receive SG (10 mg/kg IV, days 1 and 8) or doc (75 mg/m^2 IV, day 1) in 21-day cycles until progression or unacceptable toxicity. The primary endpoint was overall survival (OS); key secondary endpoints were investigator assessed progression-free survival (PFS) and objective response rate (ORR), patient-reported outcomes (PROs), and safety. **Results:** As of Nov 29, 2023, 603 pts were randomized. Median (range) age was 65 (31–84) yrs; 55% had 1 prior therapy line. The study was not statistically significant for OS. A numerical improvement in OS, favoring SG, was seen (HR 0.84 [95% CI, 0.68–1.04; 1-sided P = 0.0534]) including in pts with squamous and nonsquamous histology. PFS and ORR are shown in the Table. A clinically meaningful difference in median OS favoring SG (3.5 mo) was seen in pts without response to last prior IO. PROs were improved with SG vs doc. Grade ≥3 treatment-emergent adverse event (TEAE) incidence was 66.6% (SG) and 75.7% (doc). Treatment-related AEs led to discontinuation in 6.8% (SG) and 14.2% (doc). **Conclusions:** Although statistical significance was not met, SG showed numerical improvement in OS vs doc. Results were consistent across all major subgroups including histology. Clinically meaningful improvement in OS was noted in pts without response to prior IO. SG was better tolerated than doc; observed safety was consistent with the known profile. Clinical trial information: NCT05089734. Research Sponsor: Gilead Sciences, Inc.

	SG N=299[a]	Doc N=304[a]
Median OS, mo (95% CI)	11.1 (9.4–12.3)	9.8 (8.1–10.6)
HR (95% CI), 1-sided *P*	0.84 (0.68–1.04), 0.0534	
Median PFS, mo (95% CI)	4.1 (3.0–4.4)	3.9 (3.1–4.2)
HR (95% CI)	0.92 (0.77–1.11)	
ORR, % (95% CI)	13.7 (10.0–18.1)	18.1 (13.9–22.9)
Median TTD shortness of breath domain, NSCLC-SAQ, mo	2.8 (2.2–4.0)	2.1 (1.6–2.9)
(95% CI)	0.75 (0.61–0.91)	
HR (95% CI)		
Median TTD NSCLC-SAQ total score, mo (95% CI)	3.1 (2.5–3.9)	2.7 (2.1–3.5)
HR (95% CI)	0.80 (0.66–0.97)	
Median OS by best response to last IO subgroups, mo (95% CI)		
HR (95% CI)		
Non-responsive (SD/PD) n=383	11.8 (9.6–12.5)	8.3 (7.0–10.6)
	0.75 (0.58–0.97)	
Responsive (CR/PR) n=219	9.6 (8.1–14.4)	10.6 (8.9–12.8)
	1.09 (0.76–1.56)	
TEAE, %	**N=296[b]**	**N=288[b]**
Any grade	99.7	97.9
Grade ≥3	66.6	75.7
Leading to discontinuation	9.8	16.7
Leading to death	3.4	4.5

[a]Intent to treat; [b]All treated; TTD, time to deterioration.

LBA8503 **Oral Abstract Session**

Lorlatinib vs crizotinib in treatment-naïve patients with advanced *ALK*+ non-small cell lung cancer: 5-year progression-free survival and safety from the CROWN study.

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Background: Lorlatinib, a brain-penetrant, 3rd-generation ALK tyrosine kinase inhibitor, demonstrated improved progression-free survival (PFS) and intracranial (IC) activity vs crizotinib in the phase 3 CROWN study in treatment-naïve patients (pts) with advanced *ALK*+ non-small cell lung cancer (NSCLC). We report long-term efficacy and safety outcomes from the CROWN study after 5 years of follow-up. **Methods:** 296 treatment-naïve pts with advanced *ALK*+ NSCLC were randomized 1:1 to receive lorlatinib 100 mg once daily (n = 149) or crizotinib 250 mg twice daily (n = 147). In this post hoc analysis, we present investigator-assessed efficacy outcomes, safety, and biomarker analyses. Formal statistical testing was not performed. **Results:** As of October 31, 2023, 74 of 149 pts (50%) vs 7 of 142 pts (5%) were still receiving lorlatinib vs crizotinib. With a median duration of follow-up for PFS (95% CI) of 60.2 months (57.4-61.6) in the lorlatinib and 55.1 months (36.8-62.5) in the crizotinib arm, median PFS (95% CI) was not reached (NR; 64.3-NR) with lorlatinib and 9.1 months (7.4-10.9) with crizotinib (HR, 0.19; 95% CI, 0.13-0.27). 5-year PFS (95% CI) was 60% (51-68) with lorlatinib and 8% (3-14) with crizotinib. Median time to IC progression (95% CI) was NR (NR-NR) with lorlatinib and 16.4 months (12.7-21.9) with crizotinib (HR, 0.06; 95% CI, 0.03-0.12). In pts without baseline brain metastases in the lorlatinib arm, only 4 of 114 developed brain progression, occurring within the first 16 months of treatment. Efficacy outcomes by baseline brain metastases are shown in the Table. Grade 3/4 adverse events (AEs) occurred in 77% of pts with lorlatinib and in 57% of pts with crizotinib. Treatment-related AEs led to treatment discontinuation in 5% and 6% of pts in the lorlatinib and crizotinib arms, respectively. Safety profile was consistent with that observed in prior analyses. Emerging new *ALK* mutations were not detected in circulating tumor DNA collected at the end of lorlatinib treatment (n = 31). **Conclusions:** After 5 years of follow up, the median PFS in the lorlatinib arm has yet to be reached, corresponding to the longest PFS ever reported in advanced NSCLC. Coupled with prolonged IC efficacy and absence of new safety signals, these results indicate an unprecedented improvement in outcomes for pts with advanced *ALK*+ NSCLC. Clinical trial information: NCT03052608. Research Sponsor: Pfizer.

	With Baseline Brain Metastases		Without Baseline Brain Metastases	
	Lorlatinib (n = 35)	Crizotinib (n = 38)	Lorlatinib (n = 114)	Crizotinib (n = 109)
PFS				
Median (95% CI), months	NR (32.9-NR)	6.0 (3.7-7.6)	NR (64.3-NR)	10.8 (9.0-12.8)
HR (95% CI)	0.08 (0.04-0.19)		0.24 (0.16-0.36)	
5-year PFS (95% CI), %	53 (35-68)	Not estimable	63 (52-71)	10 (5-19)
Time to IC progression				
Median (95% CI), months	NR (NR-NR)	7.2 (3.7-11.0)	NR (NR-NR)	23.9 (16.4-30.8)
HR (95% CI)	0.03 (0.01-0.13)		0.05 (0.02-0.13)	

LBA8505 **Oral Abstract Session**

Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory *EGFR*-mutated, advanced non-small cell lung cancer (NSCLC): Primary results, including overall survival (OS), from the global, phase 3, randomized controlled PALOMA-3 trial.

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Background: Amivantamab (ami) plus lazertinib (laz) demonstrated antitumor activity in *EGFR*-mutated advanced NSCLC. Subcutaneous (SC) ami administration takes ≤7 mins and has low infusion-related reaction (IRR) rates. PALOMA-3 (NCT05388669) evaluated SC ami+laz vs IV ami+laz for pharmacokinetics (PK), efficacy, and safety among pts with *EGFR* Ex19del or L858R-mutated advanced NSCLC and disease progression on osimertinib and platinum-based chemotherapy. **Methods:** SC ami at 1600 mg (2240 mg, ≥80 kg) was manually injected weekly for the first 4 weeks, then every 2 weeks; IV ami was given at the approved dose of 1050 mg (1400 mg, ≥80 kg). Laz was orally dosed at 240 mg daily. Co-primary PK noninferiority endpoints were trough concentration (C_{trough} on Cycle [C] 2 Day [D] 1 or C4D1) and C2 area under the curve (AUC_{D1-D15}). Key secondary endpoints were objective response rate (ORR; noninferior) and progression-free survival (PFS). OS was a predefined exploratory endpoint. Prophylactic anticoagulation was recommended for the first 4 months (mo) of treatment. **Results:** In total, 418 patients (pts) were randomized (SC, n = 206; IV, n = 212); 416 received ≥1 dose. Overall, median age was 61 years, 67% were female, 61% Asian, and median 2 prior lines. At a median follow-up of 7.0 mo, PALOMA-3 met both co-primary endpoints. Geometric mean ratios (GMRs) comparing SC ami+laz vs IV for C_{trough} were 1.15 (90% CI, 1.04–1.26) for C2D1 and 1.43 (90% CI, 1.27–1.61) for C4D1. GMR for C2 AUC_{D1-D15} was 1.03 (90% CI, 0.98–1.09). ORR was 30.1% (95% CI, 24–37) in the SC arm and 32.5% (95% CI, 26–39) for IV (relative risk, 0.92; *P*= 0.001), meeting the noninferiority criteria. Median duration of response (DoR) was longer for SC ami+laz vs IV (median, 11.2 vs 8.3 mo among confirmed responders). A favorable PFS trend was observed for SC ami+laz over IV (median, 6.1 vs 4.3 mo; HR, 0.84; *P*= 0.20). OS was notably longer for SC ami+laz vs IV (HR, 0.62; 95% CI, 0.42–0.92; nominal *P*= 0.017). At 12 mo, 65% were alive in the SC arm vs 51% for IV. IRRs were ~5-fold lower in the SC arm: 13% vs 66% for IV, primarily grade 1-2 (0.5% vs 4% grade ≥3, respectively). Overall, 81% received prophylactic anticoagulants, with VTE reported by 9% in the SC arm vs 14% for IV. Across both arms, VTE incidence was 10% for pts who received prophylactic anticoagulants vs 21% for pts who did not. Severe bleeding risk was low among all pts receiving anticoagulants (1% grade ≥3). **Conclusions:** SC ami demonstrated noninferior PK and ORR compared to IV. Unexpectedly, DoR, PFS, and OS were longer in the SC arm vs IV, suggesting that the route of administration or formulation may affect outcomes. The safety profile was improved for SC ami, with lower IRR and VTE rates. Prophylactic anticoagulation can be safely implemented and reduces VTE risk. Clinical trial information: NCT05388669. Research Sponsor: Janssen Global Services LLC.

LBA8509 Clinical Science Symposium

KRYSTAL-12: Phase 3 study of adagrasib versus docetaxel in patients with previously treated advanced/metastatic non-small cell lung cancer (NSCLC) harboring a $KRAS^{G12C}$ mutation.

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Background: Adagrasib (ADA) is a potent covalent inhibitor of $KRAS^{G12C}$ with favorable properties such as long half-life (23 h), dose-dependent pharmacokinetics, and brain penetrance. In the phase 1/2 KRYSTAL-1 trial, ADA demonstrated deep and durable responses with promising PFS and OS in patients (pts) with previously treated *KRAS*^{G12C}-mutated NSCLC. Here, we report the primary analysis from KRYSTAL-12 (NCT04685135), a randomized, open-label phase 3 trial of ADA compared with docetaxel (DOCE) in pts with *KRAS*^{G12C}-mutated locally advanced or metastatic NSCLC who had previously received a platinum-based chemotherapy, concurrently or sequentially with anti-PD-(L)1 therapy. **Methods:** Pts with *KRAS*^{G12C}-mutated locally advanced or metastatic NSCLC, previously treated with platinum-based chemotherapy and anti-PD-(L)1 therapy, were randomized 2:1 (stratified by region [non-Asia Pacific vs Asia Pacific] and sequential vs concurrent chemoimmunotherapy) to receive ADA (600 mg BID orally; tablet formulation) or DOCE (75 mg/m^2 Q3W IV), with the ability to crossover to ADA upon disease progression (assessed by real-time blinded independent central review [BICR]). No washout period was required between prior anti-PD-(L)1 therapy and study treatment. Primary endpoint was PFS assessed per BICR according to RECIST v1.1. Secondary endpoints included ORR by BICR, duration of response (DOR), OS, 1-year OS rate, and safety. **Results:** In total, 301 pts were randomized to ADA and 152 to DOCE. Baseline characteristics were generally similar between treatment arms. With a median follow-up of 9.4 mo (data cutoff 31 Dec, 2023), the primary endpoint of PFS was significantly improved with ADA over DOCE (HR 0.58 [95% CI, 0.45–0.76]; $P < 0.0001$; median PFS 5.49 vs 3.84 mo). ORR by BICR was also significantly higher with ADA compared with DOCE (31.9% [95% CI, 26.7–37.5] vs 9.2% [95% CI, 5.1–15.0]; odds ratio 4.68 [95% CI, 2.56–8.56]; $P < 0.0001$); median DOR was 8.31 (95% CI, 6.05–10.35) vs 5.36 (95% CI, 2.86–8.54) mo, respectively. Treatment-related adverse events (TRAEs) were reported in 94.0% of pts treated with ADA and 86.4% with DOCE; grade ≥3 TRAEs occurred in 47.0% and 45.7% of pts, respectively. TRAEs led to discontinuation of ADA in 7.7% of pts and DOCE in 14.3%. Additional efficacy and safety analyses, including subgroup analyses, will be presented. **Conclusions:** In the phase 3 KRYSTAL-12 trial, ADA demonstrated a statistically significant and clinically meaningful improvement in PFS and ORR over DOCE in pts with previously treated *KRAS*^{G12C}-mutated NSCLC. Safety profile of ADA was consistent with previous reports and with no new safety signals. These results further support ADA as an efficacious treatment option for pts with previously treated *KRAS*^{G12C}-mutated locally advanced or metastatic NSCLC. Funding: Mirati, a Bristol Myers Squibb Company. Acknowledgements: KRYSTAL-12 was sponsored by Mirati, a Bristol Myers Squibb Company. Third-party medical writing support, under the direction of the authors, was provided by Flaminia Fenoaltea, MSc, of Ashfield MedComms, an Inizio company, and was funded by Mirati, a Bristol Myers Squibb Company. Clinical trial information: NCT04685135. Research Sponsor: Mirati Therapeutics, Inc.

LBA8511 Clinical Science Symposium

KROCUS: A phase II study investigating the efficacy and safety of fulzerasib (GFH925) in combination with cetuximab in patients with previously untreated advanced KRAS G12C mutated NSCLC.

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Background: Fulzerasib (GFH925), a KRAS G12C inhibitor, showed substantial efficacy in previously treated NSCLC patients (pts) as monotherapy. Activation of epidermal growth factor receptor (EGFR) is identified to be one of the dominant mechanisms for KRAS inhibition resistance. Preclinical evidence showed synergistic activity in KRAS G12C mutant NSCLC modeling using fulzerasib in combination with cetuximab. Here we report the first results for a KRAS G12C inhibitor combined with an anti-EGFR antibody in NSCLC pts as front-line treatment. **Methods:** KROCUS (NCT05756153) was an open-label, single-arm, multi-center, Phase II study with the primary objective to evaluate the efficacy of fulzerasib in combination with cetuximab in pts with previously untreated advanced NSCLC harboring KRAS G12C mutation. Secondary objectives included safety/tolerability, pharmacokinetics and biomarkers. Pts were enrolled to receive fulzerasib (oral, 600 mg BID) and cetuximab (intravenous, 500 mg/m^2, every two weeks [Q2W]) combination treatment in a 28-day cycle. **Results:** As of Jan. 30, 2024, a total of 27 pts (median age: 68 yrs old; 55.6% female) were treated, 11 (40.7%) with baseline brain metastases. Of 20 pts who had at least one post-treatment tumor assessment, ORR was 80.0% (95% CI: 56.3, 94.3, including one CR), of whom eight pts had ≥ 50% tumor shrinkages in the target lesions. Disease control rate (DCR) was 100% (95% CI: 83.2, 100.0). Five out of seven pts (71.4%) with brain metastases achieved PRs. Nine pts with baseline PD-L1 expression tested (six TPS≥1% and three TPS <1%) all achieved PRs. The overall safety profile of the combination was favorable. Treatment-related adverse events (TRAEs) of any grade occurred in 21 (77.8%) pts. 5 pts (18.5%) experienced G3 TRAEs and no G4 or 5 TRAEs. Three pts (11.1%) had dose reduction/interruption with fulzerasib due to TRAEs but no pts discontinued treatment while one pt (3.7%) had dose reduction/interruption and three (11.1%) discontinued cetuximab due to TRAEs. Table 1 shows the most common TRAEs or G3 TRAEs. **Conclusions:** The preliminary data from ongoing KROCUS study has demonstrated very promising efficacy and favorable safety profile of fulzerasib + cetuximab in the first line setting of KRAS G12C mutated NSCLC. More data will be generated to provide clinical evidence supporting this combination as a potential frontline therapy. Clinical trial information: NCT05756153. Research Sponsor: Zhejiang Genfleet Therapeutics Co., Ltd.

TRAEs occurred in > 2pts or G3 TRAEs.

	All G/G3 (N = 27) n (%)
Rash*	15 (55.6)/ 1 (3.7)
Asthenia	5 (18.5)/ 1 (3.7)
Nausea	4 (14.8)/0
ALT increased	3 (11.1)/0
AST increased	3 (11.1)/0
Infusion related reaction	2 (7.4)/1 (3.7)
Electrocardiogram QT prolonged	1 (3.7)/1 (3.7)
Skin fissures	1 (3.7)/1 (3.7)
Ulcerative keratitis	1 (3.7)/1 (3.7)

*Grouped Terms: dermatitis acneiform, rash, perioral dermatitis, and rash pustular.

LBA8598 **Poster Session**

Safety and anti-tumor activity of BAY 2927088 in patients with *HER2*-mutant NSCLC: Results from an expansion cohort of the SOHO-01 phase I/II study.

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Background: *HER2* (*ERBB2*) mutations have been reported in approximately 2-4% of patients (pts) with NSCLC, with exon 20 insertions being the most common. BAY 2927088 is an oral, reversible tyrosine kinase inhibitor that potently inhibits mutant *HER2* and mutant *EGFR* in preclinical models. Encouraging objective responses were observed in pts with NSCLC harboring a *HER2*-activating mutation and treated with BAY 2927088 in the dose-escalation/backfill part of the Phase I/II SOHO-01 trial (NCT05099172). More recently the FDA has granted Breakthrough Therapy designation for BAY 2927088 for previously treated pts with advanced NSCLC and activating *HER2* mutations. Here we report the safety, anti-tumor activity, and longitudinal circulating tumor DNA (ctDNA) data in a cohort of pts treated with BAY 2927088 from the expansion part of this trial. **Methods:** Pts with advanced NSCLC harboring a *HER2*-activating mutation and who experienced disease progression after at least 1 systemic therapy, but naïve to *HER2*-targeted therapy, were enrolled and received BAY 2927088 at 20 mg twice daily. Plasma samples were collected at baseline and several on-treatment time points for longitudinal ctDNA profiling using next-generation sequencing (NGS; Oncomine Precision Assay). **Results:** As of February 19, 2024, 34 pts were treated with BAY 2927088, with a median follow-up of 8 months. Median age was 62 years, 68% were female, 74% had never smoked, and 53% had received ≥2 lines of systemic anti-cancer therapy. Median duration of treatment with BAY 2927088 was 7.1 months (range 0.2-9.2). Treatment was ongoing in 17 pts (50%). Ten pts had a dose reduction, 8 had dose interruptions, and 3 discontinued study treatment due to a drug-related adverse event. The most common adverse events were diarrhea (85%; mainly grade 1-2) and rash (47%; grade 1-2). In 33 pts evaluable for efficacy, responses were observed in 23 (objective response rate 70%; 95% CI 51.3, 84.4) and 5 (15%) had stable disease for a disease control rate of 82% (95% CI 64.5, 93.0). Responses were rapid (median time to response 5.7 weeks) and durable (median duration of response not reached). Median progression-free survival was 8.1 months (95% CI 4.4, not evaluable). In a subset of 20 pts with successful paired (baseline, on-treatment) blood NGS and detectable *HER2* ctDNA at baseline, 19/20 (95%) had a decrease in ctDNA and 1 pt with progressive disease had an increase in ctDNA; 15/20 (75%) had no detectable ctDNA after 6 weeks of treatment (including 3/4 pts with stable disease). **Conclusions:** BAY 2927088 led to rapid, substantial, and durable responses in pts with pretreated *HER2*-mutant NSCLC. The safety profile was consistent with previously reported data. These data support the further clinical development of BAY 2927088 in pts with *HER2*-mutant NSCLC. Clinical trial information: NCT05099172. Research Sponsor: Bayer AG.

LBA8612 **Poster Session**

Subcutaneous amivantamab and lazertinib as first-line treatment in patients with *EGFR*-mutated, advanced non-small cell lung cancer (NSCLC): Results from the phase 2 PALOMA-2 study.

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Background: Amivantamab (ami), an EGFR-MET bispecific antibody with immune cell-directing activity, is approved as an intravenous (IV) formulation. IV ami + lazertinib (laz), a 3rd-generation EGFR TKI, demonstrated superior progression-free survival (PFS) in patients (pts) with treatment-naïve, advanced *EGFR*-mutated NSCLC vs osimertinib (Cho *Ann Oncol* 2023). Subcutaneous (SC) ami substantially reduced infusion-related reactions (16% vs 67%) and administration time (≤7 mins vs 2–4 hours) vs historical IV experience (Minchom *JCO* 2023). PALOMA-2 (NCT05498428) evaluated the efficacy, safety, and pharmacokinetics (PK) of first-line SC ami+laz. **Methods:** Cohorts 1 and 6 enrolled pts with treatment-naïve, *EGFR* Ex19del or L858R-mutated advanced NSCLC. Prophylactic anticoagulation for the first 4 months (mo) of treatment was recommended in cohort 1 and mandatory in cohort 6. SC ami was administered by manual injection in the abdomen at 1600 mg (≥80 kg: 2240 mg) weekly for the first 4 weeks and every 2 weeks thereafter. Laz was dosed orally at 240 mg daily. The primary endpoint was objective response rate (ORR) as assessed by the investigator per RECIST v1.1. **Results:** As of 6 Jan 2024, 68 and 58 pts were enrolled in cohorts 1 and 6, respectively. Overall, median age was 59 years, 60% were female, and 68% Asian. The median follow-up was 10 mo for cohort 1 and 6 mo for cohort 6. ORR (confirmed responses) in cohort 1 was 68% (95% CI, 55–79) by investigator and 72% (95% CI, 60–82) by independent central review. ORR in cohort 6 was 64% (95% CI, 49–78) and 73% (95% CI, 58–85), respectively. At data cutoff, 40/46 responders in cohort 1 and 29/29 responders in cohort 6 were receiving ongoing treatment. Best overall response rates (includes unconfirmed responses) were 81% (95% CI, 70–89) for cohort 1 and 76% (95% CI, 61–87) for cohort 6. Median time to response was 2 mo (range, 1.4–5.3). Median duration of response, PFS, and overall survival were not estimable. Administration-related reactions (ARRs) were reported in 13 (19%) pts in cohort 1 and 6 (11%) pts in cohort 6, all grade 1–2. EGFR- and MET-related AEs were primarily grade 1–2. Total of 71% of pts in cohort 1 and 100% in cohort 6 received prophylactic anticoagulation. Venous thromboembolic events (VTE) were reported in 18% and 7% of pts in cohorts 1 and 6, respectively. There were no dose reductions or discontinuations due to VTE. Rate of bleeding was 2% among pts receiving anticoagulation. Mean ami concentrations on cycle 2 day 1 were 328 μg/mL (n=49) in cohort 1 and 371 μg/mL (n=41) in cohort 6, consistent with historic IV levels. **Conclusions:** SC ami+laz showed a response rate similar to historic IV ami+laz in first-line *EGFR*-mutated NSCLC, with an improved safety profile that included significantly lower ARR rates. Further, prophylactic anticoagulation can be safely implemented and reduced incidence of VTE. Clinical trial information: NCT05498428. Research Sponsor: Janssen Research & Development.

LBA9501 Oral Abstract Session

Phase 3 study (PIVOTAL) of neoadjuvant intralesional daromun vs. immediate surgery in fully resectable melanoma with regional skin and/or nodal metastases.

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Background: PIVOTAL (NCT02938299) is an open label, randomized, multicenter, phase 3 trial evaluating Daromun as a neoadjuvant intralesional therapy for resectable, locally advanced Stage III melanoma. Daromun, a combination of two antibody-cytokine fusions (L19IL2 and L19TNF) showed efficacy in a phase 2 study (NCT02076633) in unresectable melanoma patients (pts). **Methods:** PIVOTAL was run at 22 sites in 4 EU countries. Pts were 1:1 randomly assigned to receive up to 4 weekly intratumoral injections of Daromun followed by surgery (week 5 to 8; treatment arm) or surgery alone within 4 weeks from randomization (control arm). Each weekly administration of Daromun (13 Mio IU of L19IL2 and 400 μg of L19TNF) was distributed among all injectable tumor lesions. Cutaneous melanoma pts with skin and/or LN metastases amenable to complete surgical resection were eligible. Prior anti-tumor treatments including surgery, radiation therapy (RT) and systemic therapies were allowed. Any approved adjuvant treatment post-surgery during follow-up was equally allowed. Pts with uveal or mucosal melanoma, metastatic melanoma with unknown primary, or distant metastases at screening (ruled out by PET/CT) were not eligible. **Results:** From 07/2016 to 08/2023, 127 pts were randomized to the treatment and 129 to the control arm. Most pts had received previous treatments, including surgery, systemic therapy or RT (Table). The study's primary endpoint was relapse-free survival (RFS), assessed by investigators and confirmed by retrospective Blinded Independent Central Review (BICR) of PET/CT scans. The primary outcome analysis shows an HR between the RFS of the treatment and control arm of 0.59 [95% CI 0.41-0.86; log-rank p=0.005] as per BICR assessment and 0.61 [0.41-0.92; p=0.018] as per investigator assessment (power = 85%; two-sided α = 0.05). Median RFS was 16.7 mo. in the treatment and 6.9 mo. in the control arm as per BICR. Moreover, distant metastasis-free survival (DMFS) was significantly improved by the neoadjuvant treatment, with an HR of 0.60 [0.37-0.95; p=0.029]. Complete pathological responses (pCR) after surgery were recorded in 21% of treatment arm pts. The safety profile of Daromun was characterized mostly by low-grade, local adverse events (14% grade 3 TEAEs). Systemic AEs were limited and of low grade (no autoimmune TEAEs and no drug-related death recorded). **Conclusions:** The analysis of the primary efficacy endpoint RFS and of secondary endpoints DMFS, pCR and safety show that neoadjuvant Daromun is an effective and safe therapeutic option for resectable, locally advanced melanoma pts. Clinical trial information: NCT02938299. Research Sponsor: Philogen S.p.A.

		Treatment Arm (N=127) Pts (%)	Control Arm (N=129) Pts (%)
Prior surgery	None	12 (9.4)	10 (7.7)
	1	19 (15.0)	28 (21.7)
	2	44 (34.6)	45 (34.9)
	≥3	52 (40.9)	46 (35.7)
Prior RT	No	120 (94.5)	125 (96.9)
	Yes	7 (5.5)	4 (3.1)
Prior systemic therapy	No	84 (66.1)	87 (67.2)
	Yes	43 (33.9)	42 (32.8)

LBA9503 Oral Abstract Session

Combination of encorafenib and binimetinib followed by ipilimumab and nivolumab versus ipilimumab and nivolumab in patients with advanced *BRAF*-V600E/K-mutated melanoma: The primary analysis of an EORTC randomized phase II study (EBIN).

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Background: The benefit of an induction treatment with targeted therapy (TT) with BRAF+MEK inhibitors prior to a combined immunotherapy (IT) with ipilimumab (ipi) + nivolumab (nivo) in patients (pts) with advanced BRAF-V600E/K mutant melanoma is still unclear. **Methods:** EBIN is an international randomized controlled phase II trial comparing upfront IT (arm A: nivo [3mg/kg] + ipi [1mg/kg] q3w x4 followed by nivo 480 mg q4w) with the sequential approach (arm B: 3 months induction with TT with encorafenib 450 mg QD + binimetinib 45 mg BID orally, followed by IT using the same regimen as in arm A), total treatment [Tx] duration in both arms: 2 years. In arm B, pts were allowed to be rechallenged with TT after progression. Pts with measurable BRAF-V600E/K unresectable stage III/IV melanoma, except pts with uveal melanoma, untreated or symptomatic brain or leptomeningeal involvement were randomly assigned 1:1 to arm A or B. Prior Tx for advanced melanoma was not allowed but adjuvant Tx completed at least 6 months before randomization was permitted. The primary objective was to show superiority of arm B in progression-free survival (PFS) using the log-rank test stratified by stage and lactate dehydrogenase (LDH) with a 1-sided alpha error set at 5%. The study had a power of 80% to detect a HR of 0.65. The study planned to randomize 135 pts in each arm. **Results:** All 136 pts randomized to arm B and 131 out of 135 in arm A started protocol Tx. At baseline, 170 (63%) pts had stage M1c, 129 (48%) had LDH above upper limit normal (ULN), 74 (27%) had a liver metastasis, and 19 (7%) received adjuvant therapy. The median follow-up was 21 months. In arm B, 135 (99%) pts were free of progression at week 12, when the end of TT was scheduled. In the intention-to-treat population, there was no evidence of a longer PFS in arm B (HR = 0.87, 90% confidence interval [CI] 0.67-1.12, p = 0.36). In a prespecified subgroup analysis, the HR for arm B vs arm A was 2.09 (95% CI 0.96-4.53), 0.74 (95% CI 0.43-1.29), 0.86 (95% CI 0.54-1.37), and 0.46 (95% CI 0.21-1.03) in pts with stage III with LDH≤ULN or M1a, M1b/M1c with LDH≤ULN, ULN < LDH≤2ULN, and LDH > 2ULN, respectively (p-value for interaction 0.045). In a post-hoc subgroup analysis, pts with ≥3 metastatic sites or a sum of target lesions ≥10cm at baseline did not have a longer PFS in arm B but in pts with liver metastasis the Tx HR was 0.48 (95% CI 0.28-0.80, p-value for interaction 0.008). The objective response rate was 53% in arm B and 45% in arm A. Complete response rate was 12% in arm B and 10% in arm A. Grade ≥3 adverse events occurred in 58% of pts in arm B and 51% in arm A. **Conclusion:** The EBIN trial shows there is no difference in PFS between the two treatment arms for unselected patients but supports the hypothesis that patients with very high LDH and those with liver metastases benefit from the sequential approach. Clinical trial information: NCT 03235245. Research Sponsor: BMS; Pierre Fabre.

LBA9512 Rapid Oral Abstract Session

Individualized neoantigen therapy mRNA-4157 (V940) plus pembrolizumab in resected melanoma: 3-year update from the mRNA-4157-P201 (KEYNOTE-942) trial.

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Background: mRNA-4157 is a novel, mRNA-based individualized neoantigen therapy designed to increase endogenous antitumor T-cell responses by targeting unique patient (pt) tumor mutations. In the primary analysis of the Ph 2 mRNA-4157-P201 (KEYNOTE-942) trial (median planned follow-up, 23 mo), pts with completely resected high-risk stage IIIB–IV cutaneous melanoma receiving mRNA-4157 + pembrolizumab (pembro; combo) had prolonged recurrence-free survival (RFS) and distant metastasis-free survival (DMFS) vs pembro alone (Weber JS, et al. *Lancet.* 2024). **Methods:** Pts were assigned 2:1 to mRNA-4157 (1 mg IM, max 9 doses) + pembro (200 mg IV, max 18 cycles) or pembro alone. The primary endpoint was investigator-assessed RFS; secondary endpoints were DMFS and safety. This planned supportive analysis was triggered when the last randomized pt had ≥2 y follow-up. Translational subgroup analyses were also reported. HLA genotypes were analyzed by exome sequencing of DNA from PBMC. RFS and DMFS were not formally tested; nominal 2-sided p-values are descriptive. **Results:** With an additional year follow-up (data cutoff, 03 Nov 2023; median [range], 34.9 [25.1–51.0] mo) after primary analysis, minimal new events occurred. RFS benefit in the combo vs pembro arm was maintained with 49% risk reduction in recurrence and/or death (HR [95% CI], 0.510 [0.288–0.906]; 2-sided nominal p-value 0.019). The 2.5-yr RFS rate of combo treatment (tx) vs pembro alone was 74.8% vs 55.6%. Combo tx also produced clinically meaningful, sustained improvement in DMFS vs pembro alone (HR [95% CI], 0.384 [0.172–0.858], 2-sided nominal p-value 0.0154). OS favored combo vs pembro alone; 2.5-y OS rate was 96.0% vs 90.2% (HR [95% CI], 0.425 [0.114–1.584]). RFS benefit of combo vs pembro was maintained in TMB high (HR [95% CI], 0.564 [0.253–1.258]), TMB non-high (0.571 [0.245–1.331]), PD-L1 positive (0.471 [0.226–0.979]), PD-L1 negative (0.147 [0.034–0.630]), and ctDNA negative (0.207 [0.091–0.470]) subgroups; ctDNA positive HR was not estimable. No significant associations between individual HLA alleles and RFS were observed in either tx arm. Maximal heterozygosity at HLA class I genotype loci (A, B, C) improved RFS vs homozygosity for ≥1 locus in the pembro arm (HR [95% CI], 0.425 [0.179–1.01]) but not combo arm (1.252 [0.498–3.146]). mRNA-4157 was well tolerated and combo tx had a safety profile consistent with previous analysis with no potentiation of immune-related AEs. **Conclusions:** The current analysis with ~3 y median follow-up showed durable and meaningful long-term RFS and DMFS benefit with mRNA-4157 + pembro vs pembro alone. A trend for improved OS with combo tx was also observed. HLA and translational subgroup results suggest mRNA-4157 + pembro may benefit a broader pt population vs pembro alone. Clinical trial information: NCT03897881. Research Sponsor: Moderna, Inc., in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

LBA9513 **Rapid Oral Abstract Session**

Combination or sequence of vemurafenib, cobimetinib, and atezolizumab in high-risk, resectable melanoma (NEO-TIM): Primary results.

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Background: Adjuvant immune checkpoint blockade (ICB) and target therapy (TT) improve outcomes of patients (pts) with high-risk resectable melanoma. Prospective neoadjuvant (NAT) clinical trials with TT or ICB are now running in a subgroup of high-risk melanoma pts with pooled overall promising preliminary results of high rates of pathologic complete responses (pCRs, 30–50%) and early data of positive correlation between pCR and relapse-free survival (RFS). We aimed to conduct a randomized, non-comparative phase II trial to define the role of NAT plus adjuvant TT and ICB, given in combination or sequence, in pts with high risk surgically resectable melanoma. **Methods:** 95 pts with resectable, RECIST measurable stage IIIB/IV, BRAF-mutant melanoma were randomized 1:1 in arm A and arm B, respectively, to receive NAT vemurafenib (V) and cobimetinib (C) for 6 weeks or NAT triplet combination (V and C plus atezolizumab (A), followed by complete lymph node dissection (CLND). Patients with BRAF wild-type melanoma were included in Arm C with NAT C and A. All pts had 17 cycles of A 1200 mg IV q3w post-CLND. Primary endpoint is pCR centrally/independently determined defined as residual cancer burden 0. Secondary endpoints are RFS, Overall Survival (OS), Pathological Overall Response Rate (pORR), Safety, Biomarkers analyses. Results: At data cut-off Dec 15, 2023, 29% of pts were female, median age was 59 yrs, 60% had a clinical stage IIIC, and median f/u was 17 months (IQR: 10-22). The Major Pathological Response (defined as pCR/near-pCR) was reached in 13 (45%), 10 (34%) and 13 (36%) pts in arm A, B and C, respectively. Five (17%), 4 (14%) and 6 (16%) pts did not receive surgery, and 1 (3%) patient of arm B is still under evaluation of pathological respose rate (pRR). At 12 months,RFS was 78%, 86% and 82% in arm A, B and C, respectively. Nearly 19% of pts treated in arm C were discontinued before surgery due to PD, AEs or patient's withdrawn consent, 7% and 14% in arm B and A, respectively, due to comorbidities and AEs. G3-G4 toxicity was observed in 38%, 24% and 22% of pts in arm A, B and C. **Conclusions:** Pts treated with TT upfront had highest response to NAT but the pts who received IO as NAT had a better RFS. Clinical trial information: NCT04722575. Research Sponsor: Roche.

Biomarkers analysis is ongoing.

	ARM A n = 29	ARM B n = 29	ARM C n = 37
pRR			
MPR	45%	34%	36%
pORR	66 %	55%	41%
pCR	28%	24%	22%
near-pCR	17%	10%	14%
pPR	21%	21%	5%
pNR	17%	28%	43%
Missing	17%	14%	16%
Waiting	0%	3%	0%

LBA9516 Rapid Oral Abstract Session

Phase III randomized trial evaluating tilsotolimod in combination with ipilimumab versus ipilimumab alone in patients with advanced refractory melanoma (ILLUMINATE 301).

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Background: There are limited treatment options for advanced melanoma that has progressed during or after immune checkpoint inhibitor therapy. Intratumoral (IT) immunotherapy may improve tumor-specific immune activation by promoting local tumor antigen presentation while avoiding systemic toxicities. The Phase 3 ILLUMINATE-301 study (NCT03445533) evaluated tilsotolimod, a toll-like receptor 9 agonist, with or without ipilimumab in patients with anti-programmed death-1 (PD-1)-advanced refractory melanoma. **Methods:** Patients with unresectable Stage III–IV melanoma that progressed during or after anti-PD-1 therapy were randomized 1:1 to receive 24 weeks of tilsotolimod plus ipilimumab or 10 weeks of ipilimumab alone. Nine IT injections of tilsotolimod were administered to a single designated lesion over 24 weeks. Intravenous ipilimumab 3 mg/kg was administered every 3 weeks from Week 2 in the tilsotolimod arm and Week 1 in the ipilimumab arm. The primary endpoint was efficacy measured using objective response rate (ORR; independent review) and overall survival (OS). **Results:** A total of481 patients received tilsotolimod plus ipilimumab (n = 238) or ipilimumab alone (n = 243). ORRs were 8.8% in the tilsotolimod arm and 8.6% in the ipilimumab arm, with disease control rates of 34.5% and 27.2%, respectively. Median OS was 11.6 months in the tilsotolimod arm and 10.0 months in the ipilimumab arm (hazard ratio (HR) 0.96 [95% confidence interval (CI) 0.77–1.19]; P = 0.7). Grade ≥3 treatment-emergent adverse events occurred in 61.1% and 55.5% of patients in the tilsotolimod and ipilimumab arms, respectively. **Conclusion:** Adding tilsotolimod to ipilimumab did not improve response or OS in patients with PD-1 refractory advanced melanoma. However, the results represent the largest prospective dataset reported to date on using ipilimumab in this setting and are a valuable addition to the knowledge base. Clinical trial information: NCT03445533. Research Sponsor: None.

LBA9519 **Poster Session**

Ipilimumab and nivolumab plus UV1, an anticancer vaccination against telomerase, in advanced melanoma.

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Background: The combination of ipilimumab (IPI) and nivolumab (NIVO) remains a standard of care for patients with advanced melanoma, especially those with poor prognostic factors, albeit with a significant risk of toxicity. Therapeutic cancer vaccines are ideally positioned to improve outcomes without significantly increasing toxicity. UV1 is a therapeutic cancer vaccine generating T-cell responses against the universal cancer antigen telomerase. In a Phase I trial in melanoma (N = 30), UV1 plus pembrolizumab demonstrated a tolerable safety profile, a complete response rate of 33%, median PFS of 18.9 months, and 2-year OS rate of 73.3%. Recently, results from a randomized Phase II trial indicated a longer overall survival and a higher response rate for previously treated patients with advanced mesothelioma receiving UV1 in combination with IPI-NIVO (1). **Methods:** In this Phase II, open-label, multicenter study, we randomly assigned treatment-naïve patients with unresectable or metastatic melanoma (stage IIIb-IIId or IV) to IPI 3mg/kg + NIVO 1mg/kg for 4 cycles, followed by NIVO 480 mg as maintenance, with or without 8 intradermal injections of 300 μg UV1 (+GM-CSF). The primary endpoint was progression-free survival (PFS) assessed by blinded independent central review (BICR) according to RECIST 1.1. Secondary endpoints included overall survival (OS), objective response rate (ORR), duration of response, and safety. **Results:** A total of 156 patients underwent randomization; 78 patients were assigned to the IPI-NIVO-UV1 arm and 78 patients to the IPI-NIVO arm. The median age was 60, 48% had M1C or D disease, 38% had LDH >upper limit of normal, and 42% had a positive BRAF mutation status. With a minimum follow-up of 18 months, the 12-month PFS rate was 57% in both arms (HR 0.95, 95% CI 0.59-1.55, p value 0.845). The ORR was similar with IPI-NIVO-UV1 compared to IPI-NIVO, at 60% vs 59%, respectively (Odds ratio 1.12, 95% CI 0.58-2.16, p value 0.867). The 12-month OS rate was 87% and 88%, respectively (HR 1.15, 95% CI 0.60-2.20, p value 0.674). The occurrence of grade >3 adverse events was similar in both treatment arms. **Conclusion:** UV1 did not improve on outcomes of IPI-NIVO, in terms of PFS. Longer follow-up is required for the accurate assessment of OS. No significant toxicity increases were observed with the addition of UV1. Data from a biomarker driven cohort are awaited. 1. Helland et al, Eur J Cancer 2024. Clinical trial information: NCT04382664. Research Sponsor: Ultimovacs ASA.

LBA9584 **Poster Session**

Quality of life with neoadjuvant ipilimumab (IPI) and nivolumab (NIVO) versus adjuvant nivolumab in resectable stage III melanoma: 36-week data from the phase 3 NADINA trial.

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Background: Neoadjuvant (neoadj) ipilimumab (IPI) + nivolumab (NIVO) showed improved event-free survival compared to adjuvant (adj) NIVO, but at the cost of increased immune related toxicity (irAEs). In the PRADO trial, impairment of health-related quality of life (HRQoL) was predominantly driven by the extent of the surgery and not by irAEs. To evaluate the effect of neoadj IPI+NIVO on HRQoL, we report the 36w HRQoL outcomes from the phase 3 NADINA trial. **Methods:** Eligible patients (pts) with resectable, macroscopic stage III melanoma were randomly assigned to receive 2 cycles of neoadj IPI+NIVO followed by a therapeutic lymph node dissection (TLND; w6) and only in partial- or non-responders, 1y of adj systemic treatment; or TLND (w0) followed by 12 cycles adj NIVO. EORTC QLQ-C30 questionnaires (qtn) were digitally collected at baseline, w6, w12 and thereafter q12w. The unadjusted HRQoL scores (scale 0-100) were assessed for pts who completed 39w of follow-up (FU) on January 12, 2024. **Results:** 261/423 randomized pts had 39w FU at data cutoff. 81% completed the qtn at BL, with thereafter an average compliance of 80%. QLQ-C30 data were available for 107 pts in the neoadj arm and 103 in the adj arm. Physical-, role-, emotional functioning, and pain were comparable between the neoadj and adj arm across all timepoints (Table), as were fatigue and the summary score. A numerical trend towards worsening of physical-, role functioning, and pain was seen at w6 for the adj arm and at w12 for the neoadj arm, representing the post-surgery QoL timepoints. **Conclusion:** Using fully digitalized data collection, this first HRQoL analysis of neoadj vs adj immunotherapy in stage III melanoma showed comparable results between the neoadj and adj arms. Physical-, role functioning, and pain were impaired in both groups at the first post-surgery timepoint. Clinical trial information: NCT04949113. Research Sponsor: Bristol-Myers Squibb; Australian Government.

Outcome	Arm	Baseline	Week 6	Week 12	Week 24	Week 36
Physical functioning (Mean, 95% CI)	Neoadj	91.8 (89.1-94.5)	87.2 (84.0-90.5)	78.2 (74.2-82.2)	87.7 (84.3-91.1)	87.7 (84.2-91.2)
Physical functioning (Mean, 95% CI)	Adj	94.1 (92.0-96.2)	84.1 (80.7-87.5)	83.7 (80.1-87.4)	91.6 (88.9-94.3)	90.9 (87.5-94.2)
Role functioning (Mean, 95% CI)	Neoadj	90.2 (86.5-93.9)	77.3 (72.0-82.7)	66.3 (60.4-72.2)	79.2 (74.0-84.5)	82.6 (77.8-87.5)
Role functioning (Mean, 95% CI)	Adj	88.7 (85.0-92.3)	65.9 (59.7-72.1)	74.6 (69.3-79.9)	82.9 (77.2-88.6)	81.9 (76.2-87.7)
Emotional functioning (Mean, 95% CI)	Neoadj	76.3 (73.0-79.6)	83.0 (80.0-86.0)	82.0 (79.0-85.0)	86.8 (84.1-89.5)	85.9 (82.6-89.2)
Emotional functioning (Mean, 95% CI)	Adj	73.1 (69.4-76.9)	81.9 (78.7-85.2)	77.4 (73.5-81.4)	80.7 (76.8-84.6)	81.1 (77.0-85.2)
Pain (Mean, 95% CI)	Neoadj	8.7 (6.1-11.4)	18.0 (13.6-22.4)	25.5 (21.1-30.0)	13.2 (9.1-17.3)	12.0 (7.8-16.1)
Pain (Mean, 95% CI)	Adj	9.2 (6.5-12.0)	24.9 (20.4-29.4)	17.9 (13.1-22.7)	13.5 (9.0-17.9)	13.1 (8.4-17.7)

LBA12004 **Oral Abstract Session**

Alliance A222001: A randomized, double-blind, placebo controlled phase II study of oxybutynin versus placebo for the treatment of hot flashes in men receiving androgen deprivation therapy.

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Background: Hot flashes are among the most common adverse events impacting quality of life reported by patients receiving androgen deprivation therapy (ADT) for the treatment of prostate cancer. Oxybutynin is an effective therapy for reducing frequency and severity of hot flashes in women. Pilot information supports that this drug may also benefit men with hot flashes related to ADT. **Methods:** Patients with prostate cancer receiving a stable regimen of ADT with at least 28 hot flashes per week were randomized to receive either oral oxybutynin 2.5 mg twice a day, oxybutynin 5 mg twice a day, or matching placebo doses for 6 weeks. The primary endpoint was the change in patient-reported hot flash scores (determined by multiplying the number of hot flashes by the mean hot flash severity [grade 0: none, 1: mild, 2: moderate, 3: severe, and 4: very severe]) from baseline to 6 weeks, as measured by a daily hot flash diary. A total of 87 patients provided 76% power to reject the null hypothesis of no between-arm mean difference in hot flash score reduction from baseline to 6 weeks, when comparing each oxybutynin arm to the combined placebo arms. This was based on a two-sided contrast estimated from a generalized linear mixed model, α= 0.10, intraclass correlation of 0.50, population standardized mean difference of 0.50, and 10% missing data rate. **Results:** 88 patients were accrued between 10/28/21 and 12/02/23. Six patients cancelled before starting treatment and one was ineligible, leaving 81 analyzed patients with a median age of 68. Baseline characteristics were balanced between arms with patients reporting an average of 10.15 (SD = 5.55) hot flashes per day and an average daily hot flash score of 18.23 (SD = 13.48) at enrollment. On average, patients on the placebo arm, low dose oxybutynin arm, and high dose oxybutynin arm had reductions of 2.15, 4.77, and 6.89 hot flashes/day, respectively. Compared to placebo arm patients, high dose oxybutynin arm patients had a greater reduction in hot flashes/day ($p < 0.001$), as did low dose oxybutynin arm patients (p = 0.02). Daily hot flash scores for the same three protocol arms reduced by an average of 4.85, 9.94, and 13.95 points, respectively. Compared to placebo arm patients, high dose oxybutynin arm patients had a greater reduction in daily hot flash scores (p = 0.002), as did low dose oxybutynin arm patients (p = 0.07). No treatment-related grade 3+ adverse events occurred. The most commonly reported oxybutynin-related grade 2 adverse event was dry mouth. **Conclusions:** Oxybutynin is superior to a placebo for the management of hot flashes in men associated with androgen deprivation therapy and appears to be well tolerated. Support: UG1CA189823; https://acknowledgments.alliancefound.org. Clinical trial information: NCT04600336. Research Sponsor: Alliance; 1UG1CA189823.

LBA12006 Oral Abstract Session

Primary outcomes of the enhanced, EHR-facilitated cancer symptom control (E2C2) cluster-randomized, stepped wedge, pragmatic trial.

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Background: Symptom burden and functional decline are prevalent, inconsistently treated, and associated with adverse health outcomes in patients with cancer. Symptom monitoring with electronic patient-reported outcome measures (ePROMs) has yielded mixed results due, in part, to care teams' variable bandwidth and resourcing for symptom management. The collaborative care model (CCM) offers a validated means to address these issues and potentially improve clinical and health services outcomes. Capturing ePROMS through the electronic health record (EHR) for use in CCM delivery provides a potentially scalable approach to manage symptoms at the population level. **Methods:** E2C2 is a cluster-randomized, population-level, stepped wedge pragmatic trial that compares a bundled, EHR-facilitated, CCM-based intervention to improve control of SPPADE symptoms (Sleep interference, Pain, impaired Physical function, Anxiety, Depression, and Energy deficit/fatigue) with usual care. All patients, regardless of cancer type or stage, treated in the medical oncology clinics of a multi-state health system, were assigned to one of fifteen clusters. Control and intervention conditions monitored SPPADE symptoms with Epic EHR administered 11-point numerical rating scales (NRSs). Moderate and severe symptoms were defined as 4-6/10 and >7/10, respectively. The intervention added EHR clinician decision support; automated delivery of symptom self-management information; and options to address severe symptoms with a dedicated symptom care manager. The primary outcome was post-baseline SPPADE scores assessed using multivariate regression of six cluster-period mean SPPADE symptom scores against E2C2 exposure, fixed cluster and secular time effects. **Results:** From March 2019 to January 2023, 50,559 patients were assigned to E2C2 clusters and 40,295 completed at least one ePROM. At first assessment, participants' mean age was 63.3 years; 58% were female; 26% were rural, and the prevalences of moderate or worse symptoms were fatigue 42%, impaired function 34%, sleep disturbance 34%, anxiety 27%, pain 26%, and depression 23%. The intervention significantly reduced mean composite SPPADE symptom scores, $p < 0.001$, among all patients, as well as those with >1 moderate or worse symptom. All mean symptom scores were lower in the intervention group, with the largest effects detected among patients with fatigue -0.2 (-0.4, -0.07), anxiety -0.14 (-0.2, -0.03), and depression -0.1 (-0.2, -0.002). **Conclusions:** In this large cluster-randomized trial, an EHR-facilitated, bundled intervention that scaled CCM-based surveillance and management of SPPADE symptoms significantly reduced population-level symptom burden, particularly for fatigue, anxiety, and depression. This study provides real world evidence and the foundation for future national efforts aimed at controlling symptoms in patients with cancer. Clinical trial information: NCT03892967. Research Sponsor: National Cancer Institute; 1UM1CA233033.

LBA12007 **Oral Abstract Session**

Results from a randomised, open-label trial of a multimodal intervention (exercise, nutrition and anti-inflammatory medication) plus standard care versus standard care alone to attenuate cachexia in patients with advanced cancer undergoing chemotherapy.

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Background: Cancer cachexia arises from the interaction between the host and the tumour, triggering an inflammatory response that leads to weight and appetite loss, diminished physical activity, reduced treatment efficacy and survival. Combining interventions to address inflammation, weight loss, and physical activity is proposed as an effective strategy. Building on a promising pilot study, we conducted the MENAC (Multimodal Exercise Nutrition Anti-inflammatory Cachexia) trial to comprehensively evaluate this approach in patients with lung and pancreatic cancer undergoing systemic anti-cancer treatment (SACT). **Methods:** MENAC was an investigator-initiated, multicentre, open label, randomised phase 3 trial conducted at 17 sites in 4 countries. Patients with stage III or IV lung or pancreatic cancer receiving SACT with non-curative intent were randomly assigned (1:1) to a multimodal intervention consisting of nutritional counselling plus fish oil containing oral nutritional supplements, physical exercise [endurance and strength] and non-steroidal anti-inflammatory drugs [NSAIDs]) versus standard care. Randomisation was stratified by country, cancer type and stage. Primary Objective: To assess differences between arms in change in body weight. Secondary Objectives: To assess differences in muscle mass (measured by CT L3 technique) and physical activity (assessed through step counts using ActivPAL activity meter) between arms. Assessments were conducted at basline (pre-randomisation) and at endpoint (after 6 weeks). **Results:** From May 2015 to February 2022, 212 patients were enrolled (105 to multimodal treatment, 107 standard care). Over 6 weeks, weight stabilised in patients assigned to multimodal treatment compared with those assigned to standard care (mean weight change [SD] 0.05 kg [3.8] *vs* – 0.99 kg [3.2], respectively) with a mean difference in weight change of -1.04, 95 % CI -2.02 to -0.06, p=0.04. There was no conclusive difference in muscle mass (mean change [SD] -6.5cm^2 [10.1] *vs* -6.3cm^2 [11.9], p=0.93) or in mean step counts [SD] (-377.7 [2075] *vs* -458 [1858], p=0.89). There were 28 and 24 reported SAEs in the intervention and control arm respectively, no SUSARs were reported. **Conclusions:** A multimodal cachexia intervention stabilised weight compared to standard care at six weeks. There was no difference in physical activity or muscle mass between trial arms. Clinical trial information: NCT02330926. Research Sponsor: Wereld Kanker Onderzoek Fonds (WKOF) as part of the World Cancer Research Fund International grant programme; The Liasson Committee for Education, Research and Innovation in central Norway; ECRIN, the European Clinical Research Infrastructure Network; Rising Tide Foundation for Clinical Cancer Research; Marie Curie and Pancreatic Cancer UK; CIHR- Canadian Institute for Heath Research; Abbot provided the Oral Nutritional Supplement; Pronova BioPharma provided n-3 polyunsaturated fatty acid capsules; CIHR- Canadian Institute for Heath Research; Alberta Cancer Foundation.

LBA12014 Rapid Oral Abstract Session

Preventive effect of naldemedine for opioid-induced constipation in patients with cancer starting opioids: A multicenter, double-blinded, randomized, placebo-controlled, phase 3 trial.

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Background: A peripherally acting μ-opioid receptor antagonist (PAMORA), such as naldemedine, could alleviate OIC in cancer patients. However, the evidence of PAMORA on OIC prevention in cancer patients starting opioid analgesia is limited. This clinical trial aimed to confirm the preventive effect of naldemedine for OIC in cancer patients who start daily strong opioid administration compared with placebo. **Methods:** We conducted a multicenter, double-blinded, randomized, placebo-controlled trial between July 2021 and May 2023 with four academic hospital in Japan (jRCTs031200397). Patients with cancer starting regular strong opioid for the first time for cancer pain, and age 20 years or older were included. The eligible patient was randomly assigned to the naldemedine (Symproic 0.2 mg) or placebo group in a 1:1 ratio. The protocol treatment period was 14 days after the start of naldemedine (or placebo) and the naldemedine group had Symproic at 0.2 mg once a day after breakfast for 14 days. The placebo group had the placebo once a day after breakfast for 14 days. The primary endpoint was the proportion of patients with a Bowel Function Index (BFI) of less than 28.8 on Day 14. We conducted the safety assessments with the number of all adverse events occurring during the protocol treatment period using the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 Japanese translation of Japan Clinical Oncology Group. **Results:** Of the 103 patients were assessed for eligibility, 99 patients were randomly assigned on a 1:1 basis to receive naldemedine (n = 49) or placebo (n = 50). The BFI score at Day 1 was 18.3±19.8 with naldemedine group and 18.2±20.0 with placebo. The proportion of patients with a BFI of less than 28.8 on Day 14 was significantly greater with naldemedine group (64.6% [31 of 48 patients]; 95% CI, 51.1% to 78.1%) than with placebo (17.0% [8 of 47 patients]; 95% CI, 6.3% to 27.8%) with a difference of 47.6% (95% CI, 30.3% to 64.8%, $p < 0.0001$). There was no statistical difference in the proportion of adverse events; abdominal distention, abdominal pain, diarrhea, bowel obstruction, and nausea. However, there was a significantly lower proportion of vomiting in patients treated with naldemedine. During the treatment period, none of patients treated with naldemedine had diarrhea, nausea, or vomiting as adverse events causally related to protocol treatment (0.0% [0 of 48 patients] v.s 34.0% [16 of 47 patients]. **Conclusions:** Naldemedine is a valuable option with proven efficacy in preventing OIC in cancer patients starting regular strong opioids. Clinical trial information: 031200397. Research Sponsor: Grant for Research Advancement on Palliative Medicine, Japanese Society for Palliative Medicine.

LBA12082 Poster Session

Randomized double-blind placebo-controlled trial evaluating pregabalin for chronic cough in patients with lung cancer.

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Background: Chronic cough is a distressing symptom that detracts from the quality of life (QoL) of patients with cancer. Developing effective therapies for cough is an unmet need, with no approved medicines available. Neuromodulators like pregabalin may act centrally as cough suppressants. **Methods:** Randomized double-blind placebo-controlled study in the Department of Medical Oncology at Tata Memorial Hospital (Mumbai, India) in patients with locally advanced/metastatic non-small-cell lung cancer (NSCLC) with at least 2 weeks history of moderate or severe cough. Patients had ECOG PS 0-2, and creatinine clearance $>$ 60 mL/min. Randomization was 1:1 to pregabalin 300 mg orally daily or matching placebo, both administered for 9 weeks. Primary endpoint was the difference in cough severity as measured by Visual Analog Scale (VAS) after 9 weeks treatment with pregabalin versus placebo. Secondary endpoints included cough severity on day 7 and week 9 measured by VAS, and Manchester Cough in Lung Cancer Scale (MCLCS); side-effects, and QoL assessed by EORTC QLQ C30 and LC13. Means of the change from baseline scores were calculated for patients in each arm, and compared between two arms by independent samples Mann Whitney U test. $P < 0.05$ was considered significant. **Results:** Between Jul 2022 and Dec 2023, we enrolled 166 patients: 83 to each arm. Median age was 56 years (IQR, 47-62.5); 112 (67.5%) were male, and 149 (89.8%) had metastatic NSCLC. Baseline cough severity was grade 2 in 127 (76.5%) and grade 3 in 37 (22.6%); median cough duration was 163 days. The therapy (pregabalin/placebo) was well tolerated in both arms, with no difference in grade $>$ 3 toxicities between the two arms; P=0.908. Systemic cancer-directed therapy was started in 95.2% and 91.4% of patients in the pregabalin and placebo arms, respectively; P=0.328. By week 9, subjective improvement in cough was reported by 45 (57%) patients in pregabalin arm, and 40 (52.6%) patients in placebo arm; P=0.846. The mean VAS score (in mm) decreased from 71.58 at baseline, to 45.32 at day 7, and 19.73 by week 9 in the pregabalin arm; corresponding values in the placebo arm were 71.74, 46.23, and 21.18, respectively; P=0.530. Cough assessment by mean MCLCS scores showed a similar decrease throughout the course of the study, with no statistically significant differences between the two arms (Pregabalin-Baseline: 27.63, Day 7: 23.49, Week 9: 17.39; Placebo-Baseline: 27.28, Day 7: 23, Week 9: 17.34); P=0.455. There was no significant difference in QoL between the two arms. Mean LCCO (cough symptom question on QLQ LC13) score decreased from 75.9 (baseline) to 54.2 (day 7) to 36.4 (week 9) in pregabalin arm, vs 66.3, 54, and 31.4, respectively, in placebo arm; P=0.150. **Conclusions:** Pregabalin does not lead to a significant decrease in cough in patients with lung cancer. Systemic cancer-directed therapy is the most effective antitussive therapy for cancer-induced cough. Clinical trial information: CTRI/2020/11/029275. Research Sponsor: Tata Memorial Center Research Administrative Council; ACG Associated Capsules Pvt Ltd.

LBA12134 Poster Session

A randomized trial to assess the effect of oral cryotherapy in the prevention of mucositis in patients with head and neck cancer receiving chemo-radiotherapy.

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Background: Oropharyngeal mucositis is a common toxicity seen in patients with HNSCC on concurrent chemoradiation (CTRT). Oral cryotherapy is effective in preventing oral mucositis in patients on 5FU-based therapy. The effect of oral cryotherapy on mucositis in patients with HNSCC receiving CTRT is not known. Hence, we conducted this study to assess the efficacy of oral cryotherapy. **Methods:** This was an open-label, randomized study that included adults with HNSCC on adjuvant/radical CTRT, an ECOG PS 0-2, without baseline mucositis or contraindications to oral intake. The patients were randomized 1:1 to the oral cryotherapy (CRYO) arm or control (CONT) arm. All patients in the CRYO arm received oral cryotherapy in the form of ice chips within the first 5 fractions of radiotherapy (RT), and till the end of CTRT or till the development of grade 3 or higher mucositis. Patients were asked to keep ice chips in the mouth, 30 minutes before the start of RT. Once the ice melted, they were asked to swirl the melted ice water in their mouth and gargle with it before swallowing/spitting it. This procedure was repeated for 20-30 minutes until the start of RT and for 10 minutes after RT for the day. The same procedure was followed during chemotherapy (CT) infusion, on other days this procedure was repeated 5-7 times/day. Patients in the CONT arm received CTRT and toxicities were managed as per the institutional standards. Patients were evaluated for mucositis and other toxicities of CTRT (CTCAEv5.0) at baseline and weekly intervals during CTRT and at the first follow-up visit 10-12 weeks after completion of CTRT. The primary endpoint was the incidence of grade 3-5 mucositis at any time during CTRT and up to 3 months after completion. Secondary endpoints were QoL and compliance. Descriptive statistics were performed. The incidence of grade 3 or higher mucositis and other toxicities were compared between the arms using the Chi-Square test. **Results:** 128 patients were enrolled in the study, 64 in each arm. The median age was 59 years (IQR 40-58.75). Most of the patients were males, 93.75% and 85.9% in the CRYO and CONT arms respectively. Most of the patients had ECOG PS 1, 65.6% and 68.75 % in the CRYO and CONT arm respectively. Most patients (40/64, 62.5%) in both arms received concurrent cisplatin as the radiosensitizer. More patients in the CONT arm (23/64 patients, 35.9%) developed grade 3 or higher mucositis as compared to the CRYO arm (17/64 patients, 26,6%), but this was not statistically significant (p=.340). There was no statistically significant difference in the incidence of grade 3 or higher dysphagia, anemia, neutropenia, rise in creatinine, hyponatremia, or radiation dermatitis between the 2 arms. There were no new safety signals noted with the use of cryotherapy. **Conclusions:** Although cryotherapy reduced the incidence of grade 3-5 mucositis, it was not significant and its efficacy was not established. Clinical trial information: CTRI/2020/07/026657. Research Sponsor: None.