6000 **Oral Abstract Session**

Camrelizumab versus placebo combined with gemcitabine and cisplatin for recurrent or metastatic nasopharyngeal carcinoma: A randomized, double-blind, phase 3 trial.

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Background: Camrelizumab plus gemcitabine and cisplatin (GP) showed promising preliminary anticancer activity as first line (1L) therapy in patients (pts) with recurrent or metastatic nasopharyngeal carcinoma (R/M NPC) in a phase 1 trial (*W Fang et al; Lancet Oncol 2018*). Here, we compared the efficacy and safety of camrelizumab with placebo plus GP as 1L therapy for pts with R/M NPC in a phase 3 trial. **Methods:** Eligible pts with previously untreated R/M NPC were randomized (1:1) to receive either camrelizumab (200 mg on day 1) plus gemcitabine (1000 mg/m^2 on days 1, 8) and cisplatin (80 mg/m^2 on day 1) or placebo plus the same chemotherapy regimens intravenously Q3W for a maximum of 6 cycles, followed by maintenance therapy with camrelizumab or placebo. The primary end point was progression-free survival (PFS) per independent review committee (IRC). Secondary end points included investigator-assessed PFS, objective response rate (ORR), disease control rate (DCR), duration of response (DOR), overall survival (OS) and tolerability. This trial is registered with ClinicalTrials.gov, number NCT03707509. **Results:** From Nov 2018 to Nov 2019, 263 pts from 28 centers were randomized to camrelizumab plus GP (n = 134, camrelizumab arm) or placebo plus GP (n = 129, placebo arm). At data cutoff on Dec 31, 2020 (67.7% maturity), 178 IRC-assessed PFS events occurred, and the median follow-up was 15.6 months (range 1.3-25.5). The median PFS per IRC was 10.8 months (95% CI 8.5-13.6) in the camrelizumab arm and 6.9 (95% CI 5.9-7.9) in the placebo arm (HR 0.51 [95% CI 0.37-0.69]; one-sided $P < 0.0001$). Investigator-assessed PFS showed similar results. IRC-assessed ORR was 88.1% (95% CI 81.3-93.0) in the camrelizumab arm and 80.6% (95% CI 72.7-87.1) in the placebo arm, with a median DOR of 9.9 (95% CI 7.7-12.5) and 5.7 months (95% CI 5.2-6.9; HR 0.48 [95% CI 0.34-0.68]), respectively. The DCR was 96.3% (95% CI 91.5-98.8) in the camrelizumab arm and 94.6% (95% CI 89.1-97.8) in the placebo arm. 18-month PFS rate was 34.8% (95% CI 25.7-44.1) vs 12.7% (95% CI 6.8-20.5), respectively. OS benefit was observed in the camrelizumab arm vs placebo arm (median not reached vs 22.6 months; HR 0.67 [95% CI 0.41-1.11]). Grade ≥3 treatment-related adverse events (TRAEs) occurred in 93% of pts in the camrelizumab arm and 90% in the placebo arm. The most common grade ≥3 TRAEs were decreased white blood cell count (66% vs 70%), decreased neutrophil count (64% vs 65%), decreased platelet count (40% vs 40%), and anemia (39% vs 43%). None of the differences were statistically significant. The safety profile was as expected, with no new signals observed. **Conclusions:** Addition of camrelizumab to GP significantly prolonged PFS as 1L therapy for R/M NPC, with a manageable safety profile. These data suggest that first line treatment with camrelizumab plus GP could be a standard of care for R/M NPC. Clinical trial information: NCT03707509. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

6001 **Oral Abstract Session**

Cabozantinib versus placebo in patients with radioiodine-refractory differentiated thyroid cancer who have progressed after prior VEGFR-targeted therapy: Results from the phase 3 COSMIC-311 trial.

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Background: Cabozantinib (C), an inhibitor of VEGFR2, MET, AXL, and RET, showed clinical activity in patients (pts) with radioiodine (RAI)-refractory differentiated thyroid cancer (DTC) in phase 1/2 studies (Cabanillas 2017; Brose 2018). This phase 3 study (NCT03690388) evaluated the efficacy and safety of C vs placebo (P) in pts with RAI-refractory DTC who had progressed during/after prior VEGFR-targeted therapy for whom there is no standard of care. **Methods:** In this double-blind, phase 3 trial, pts were randomized 2:1 to receive C (60 mg QD) or P, stratified by prior lenvatinib treatment (L; yes, no) and age ($\leq$65, $>$ 65 yr). Pts with RAI-refractory DTC must have received L or sorafenib for DTC and progressed during or following treatment with $\leq$ 2 prior VEGFR inhibitors. Pts randomized to P could cross over to open-label C upon disease progression per blinded independent radiology committee (BIRC). The primary endpoints were objective response rate (ORR) in the first 100 randomized pts and progression-free survival (PFS) in all randomized pts. PFS and ORR were assessed by BIRC per RECIST v1.1. The study was designed to detect an ORR for C vs P (2-sided α = 0.01) and a hazard ratio (HR) for PFS of 0.61 (90% power, 2-sided α = 0.04). A prespecified interim PFS analysis was planned for the ITT population at the time of the primary ORR analysis. **Results:** As of 19 Aug 2020,125 vs 62 pts had been randomized to the C and P arms, respectively; median age was 66 yr, 55% were female and 63% received prior L. Median (m) follow-up was 6.2 months (mo). At the planned interim analysis, the trial met the primary endpoint of PFS with C demonstrating significant improvement over P (HR 0.22, 96% CI 0.13–0.36; p $<$ 0.0001). mPFS was not reached for C vs 1.9 mo for P; PFS benefit was observed in all prespecified subgroups including prior L (yes, HR 0.26; no, HR 0.11) and age ($\leq$65 yr, HR 0.16; $>$ 65 yr, HR 0.31). ORR was 15% for C vs 0% for P (p = 0.0281) but did not meet the prespecified criteria for statistical significance (p $<$ 0.01). A favorable OS trend was observed for C vs P (HR 0.54, 95% CI 0.27–1.11). Treatment-emergent adverse events (AEs) of any grade with higher occurrences in the C vs P arm included diarrhea (51% vs 3%), hand-foot skin reaction (46% vs 0%), hypertension (28% vs 5%), fatigue (27% vs 8%), and nausea (24% vs 2%); grade 3/4 AEs were experienced by 57% of pts with C vs 26% with P. Dose reductions due to any grade AEs occurred in 57% of pts with C vs 5% with P. Treatment discontinuations due to AEs not related to disease progression occurred in 5% of pts with C vs 0% with P. No treatment-related deaths occurred in either arm. **Conclusions:** C showed a clinically and statistically significant improvement in PFS over P in pts with RAI-refractory DTC after prior VEGFR-targeted therapy with no unexpected toxicities. C may represent a new standard of care in pts with previously treated DTC. Clinical trial information: NCT03690388. Research Sponsor: Exelixis.

6002 **Oral Abstract Session**

A phase II trial cohort of nivolumab plus ipilimumab in patients (Pts) with recurrent/metastatic salivary gland cancers (R/M SGCs).

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Background: R/M SGCs are a diverse group of malignant neoplasms arising from the major or minor salivary glands and have no standard treatment. The impact of combining PD-1/CTLA-4 checkpoint blockade in R/M SGCs is unknown. **Methods:** In a Simon's two-stage minimax phase II trial, pts with progressive R/M SGCs (any histology except adenoid cystic carcinoma (ACC)) were enrolled and treated with nivolumab 3 mg/kg every 2 weeks plus ipilimumab 1 mg/kg every 6 weeks (1 cycle = 6 weeks). Imaging, using RECIST v1.1 response assessment, was scheduled to be performed approximately every 12 weeks. The primary endpoint was best overall response (BOR = complete response [CR]+partial response [PR]) per RECIST v1.1. To detect a difference between an unacceptable BOR of 5% and a desirable BOR of 20% (one-sided type I error of 10%, power of 90%), at least 1 in the first 18 pts required an observed response. At least 4 responses of 32 total pts were needed to meet the primary endpoint. Treatment beyond progression of disease (PD) was allowed at the discretion of the investigator. A second cohort of pts with ACC was analyzed and reported separately. **Results:** From 7/25/2017-7/16/2020, 32 pts were enrolled and evaluable for the primary endpoint. There was 3 confirmed PRs in the first 18 pts, therefore enrollment of the second stage continued. BOR rate was 16% (5/32). Seven pts never reached a first disease assessment and were classified as non-responders: 5 due to clinical PD, 1 due to toxicity, and 1 pt withdrew. Four pts discontinued the trial for toxicities: pancytopenia (1), blurry vision (1), cardiomyopathy/hyperglycemia (1), and neutropenic sepsis (1), and mucositis (1). The 5 confirmed responders had regressions ranging from -66% to -100% in target lesions, with a duration of therapy ranging from 15.7 to 29.5 months (treatment ongoing for one as of 2/6/20). **Conclusions:** This cohort met its primary endpoint, and the responses observed were dramatic and durable. Paired biopsy and peripheral blood samples will be analyzed to elucidate insights into mechanisms of response and resistance to dual checkpoint blockade. Clinical trial information: NCT03172624. Research Sponsor: U.S. National Institutes of Health, Geoffrey Beene Cancer Research Center, Cycle for Survival, and the Overman Fund.

6003 **Oral Abstract Session**

Metronomic capecitabine as adjuvant therapy in locoregionally advanced nasopharyngeal carcinoma: A phase 3, multicenter, randomized controlled trial.

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Background: Patients suffering from locoregionally advanced nasopharyngeal carcinoma (NPC) commonly develop disease recurrence, despite a high rate of complete clinical remission after standard of care (concurrent cisplatin-radiotherapy, with or without induction chemotherapy). The benefit of additional adjuvant chemotherapy remains unclear. **Methods:** Patients with high-risk locoregionally advanced NPC (stage III to IVA, excluding T3-4N0 and T3N1), and with no locoregional disease or distant metastasis after definitive chemoradiotherapy, were eligible. They were randomly assigned (1:1) within 12 to 16 weeks after the last radiation dose to receive either capecitabine at a dose of 650 mg/m^2 twice daily for 1 year (metronomic capecitabine group) or observation (standard-therapy group). The primary end point was recurrence-free survival (RFS). The calculated sample size was 201 per group, with an 80% power (two-sided α 0.05) to detect a target hazard ratio (HR) of 0.52. **Results:** A total of 406 patients underwent randomization, comprising 204 in the metronomic capecitabine group and 202 in the standard-therapy group. After a median follow-up of 36 months (corresponding to 43 months when calculated from the start of standard therapy), the estimated 3-year RFS was 85.9% in the metronomic capecitabine group, as compared with 76.5% in the standard-therapy group (intention-to-treat population; HR 0.51, 95% confidence interval 0.32–0.81; $P = 0.003$). The incidence of grade 3 adverse events was 17.4% in the metronomic capecitabine group and 5.5% in the standard-therapy group; hand-foot syndrome was the most common adverse event related to capecitabine (9.0%). One grade 4 neutropenia occurred in the metronomic capecitabine group. Neither group sufferd from treatment-related deaths. During treatment, there was no clinically meaningful deterioration of health-related quality of life associated with the use of metronomic adjuvant capecitabine. **Conclusions:** The addition of metronomic capecitabine as adjuvant therapy to chemoradiotherapy significantly improved RFS in locoregionally advanced NPC, with a manageable safety profile and no compromise to quality of life. Clinical trial information: NCT02958111. Research Sponsor: Sun Yat-sen University Clinical Research 5010 Program, Pharmaceutical/Biotech Company.

	Metronomic capecitabine (%)	Standard therapy (%)	
Intention-to-treat population	n = 204	n = 202	P value
3-yr recurrence-free survival	85.9	76.5	0.003
3-yr overall survival	93.6	89.6	0.03
3-yr distant recurrence-free survival	90.5	82.1	0.008
3-yr locoregional recurrence-free survival	92.6	88.2	0.05
Safety population	n = 201	n = 200	
Completed the 1-year treatment period	74.1	–	
Any grade 3 adverse events	17.4	5.5	
Any grade 4 adverse events	0.5	0	

6005 **Oral Abstract Session**

Adjuvant capecitabine in locoregionally advanced nasopharyngeal carcinoma: A multicenter randomized controlled phase III trial.

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Background: We conducted a multicenter, randomized controlled phase III clinical trial (NCT02143388) to investigate the efficacy and toxicity of adjuvant capecitabine (AC) in addition to concurrent cisplatin and radiotherapy (CCRT) compared to CCRT alone in high-risk locoregionally advanced nasopharyngeal carcinoma (LANPC) patients. **Methods:** Eligibility criteria included AJCC/UICC 7^{th} ed TNM stage III-IVb and one of the following features: T3-4N2 or T1-4N3 or pre-treatment plasma EBV DNA concentration of $>$20,000 copy/ml or gross primary tumor volume (GTVnx) of >30 cm^3 or a maximum standard uptake value (SUVmax) of >10.0 by ^{18}FDG PET-CT within the primary tumor or multiple neck node metastases, with any larger than 4 cm. All patients were randomly assigned in a 1:1 ratio to receive CCRT (3-weekly cisplatin at 100 mg/m^2 for 2-3 cycles) followed by AC (1000 mg/m^2 bi-daily for 14 days every 21-day cycle for 8 cycles), or CCRT alone. The prescribed radiation doses were 68-72 Gy/30-32 fractions to the PTVnx, 60-68 Gy/30-32 fractions to PTVnd, 60-64Gy/30-32 fractions to $PTV_{high\text{-}risk}$, 54-58Gy/30-32 fractions to $PTV_{low\text{-}risk}$. Primary end point was failure-free survival (FFS). **Results:** Between Mar 2014 to Jul 2018, 180 patients were recruited (90 patients in CCRT+AC arm and 90 in CCRT alone arm). All patients completed RT and $\geq$2 cycles of concurrent cisplatin in both treatment arms (cumulative dose intensities for cisplatin were 200 mg/m^2 in both arms). 85 (94.4%) patients went on to receive AC, with 71 (78.9%) patients completing 8 cycles; 19 (22.4%) patients had dose reduction of AC. With a median follow-up of 44.8 mo, the 3-y FFS was significantly superior in the CCRT+AC arm than the CCRT arm for the intention-to-treat cohort (87.7% *vs* 73.3%; HR: 0.52 [95% CI: 0.29-0.77], $P = 0.037$). 3-year overall, distant metastasis-free and locoregional relapse-free survival were 92.6% *vs* 88.9% (HR [95% CI]: 0.66 [0.28-1.59]), 88.8% vs. 81.1% (HR: 0.67 [0.33-1.33]) and 91.5% *vs* 80.0% (HR: 0.50 [0.25-1.00]), respectively. Incidences of G3-4 acute toxicities were 57.8% (52 of 90) in CCRT+AC arm and 51.1% (46 of 90) in CCRT alone arm, with a higher incidence of hand foot syndrome (3.5% *vs* 0%), xerostomia (11.1% *vs* 3.3%), mucositis (23.3% *vs* 16.7%), and anemia (5.6% *vs* 2.2%) in the CCRT+AC arm. G3-4 late toxicities occurred in 13.3% (12 of 90) and 9.0% (8 of 89), respectively. **Conclusions:** The addition of capecitabine to CCRT conferred a superior disease control than CCRT alone in high-risk LANPC. Survivals in ITT and PP set. Clinical trial information: NCT02143388. Research Sponsor: National Natural Science Foundation of China [No. 81872469 and 82073330]; Wu Jieping Medical Foundation [No. 320.6750.19089 and 320.6750.17108]; Sun Yat-sen University Cancer Center 308 Program.

		ITT		PP	
Variable		CCRT+AC (*N* = 90)	CCRT alone (*N* = 90)	CCRT+AC (*N* = 71)	CCRT alone (*N* = 90)
FFS	Failure or death, *N* (%)	15 (16.7)	27 (30.0)	8 (11.3)	27 (30.0)
OS	3-y FFS, %	87.7	73.3	92.9	73.3
	Death, *N* (%)	8 (8.9)	12 (13.3)	3 (4.2)	12 (13.3)
DMFS	3-y OS, %	92.6	88.9	98.6	88.9
	Distant metastasis or death, *N* (%)	13 (14.4)	19 (21.1)	6 (8.5)	19 (21.1)
	3-y DMFS, %	88.8	81.1	94.3	81.1

6006 **Oral Abstract Session**

Association of pathological response to neoadjuvant pembrolizumab with tumor PD-L1 expression and high disease-free survival (DFS) in patients with resectable, locally-regionally advanced, head and neck squamous cell carcinoma (HNSCC).

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Background: Patients with resected HNSCC, with high-risk (positive margins, extracapsular spread [ECE]) or intermediate-risk pathological features have an estimated 1-year DFS of 65% and 69%, respectively. Immune checkpoint blockade improved survival of patients with recurrent/metastatic HNSCC, and preclinical models indicate radiotherapy (RT) synergizes with anti-PD-1. Therefore, we administered the PD-1 inhibitor pembrolizumab (pembro) pre- and post-surgery with adjuvant RT +/- cisplatin in patients with resectable, locoregionally advanced (clinical T3/4 and/or $\geq$2 nodal metastases) HNSCC (NCT02641093). **Methods:** Eligible patients received pembro (200 mg I.V. x 1) 1-3 weeks before resection. Adjuvant pembro (q3 wks x 6 doses) was administered with RT (60-66Gy) with or without weekly cisplatin (40mg/m2 X 6) for patients with high-risk and intermediate-risk features, respectively. The primary endpoint was 1-year DFS estimated by Kaplan Meier curves. Safety was evaluated by CTCAE v5.0. Pathological response (PR) to neoadjuvant pembro was evaluated by comparing pre- and post-surgical tumor specimens for treatment effect (TE), defined as tumor necrosis and/or histiocytic inflammation and giant cell reaction to keratinaceous debris. PR was classified as no (NPR, $<$ 20%), partial (PPR, $\geq$20% and $<$ 90%) and major (MPR, $\geq$90%). Tumor PD-L1 immunohistochemistry was performed with 22c3 antibody and reported as combined positive score (CPS). **Results:** Ninety-two patients were enrolled. Seventy-six patients received adjuvant pembro and were evaluable for DFS. Patient characteristics included: median age 58 (range 27 – 80) years; 32% female; 88% oral cavity, 8% larynx, and 3% human papillomavirus negative oropharynx; 86% clinical T3/4 and 65% $\geq$2N; 49 (53%) high-risk (positive margins, 45%; ECE, 78%); 64% (44/69 available) had PD-L1 CPS $\geq$1. At a median follow-up of 20 months, 1-year DFS was 67% (95%CI 0.52-0.85) in the high-risk group and 93% (95%CI 0.84-1) in the intermediate-risk group. Among 80 patients evaluable for PR, TE scoring resulted in 48 NPR, 26 PPR and 6 MPR. Patients with PPR/MPR had significantly improved 1-year DFS when compared with those with NPR (100% versus 68%, p = 0.01; HR = 0.23). PD-L1 CPS $\geq$ 1 was not independently associated with 1-year DFS, but was highly associated with MPR/PPR (p = 0.0007). PPR/MPR in PD-L1 CPS $<$ 1, $\geq$1 and $\geq$20, were estimated as 20, 55 and 90%, respectively. Grade $\geq$ 3 adverse events occurred in 62% patients with most common including dysphagia (15%), neutropenia (15%), skin/wound infections (10%), and mucositis (9%). **Conclusions:** PR to neoadjuvant pembro is associated with PD-L1 CPS$\geq$1 and high DFS in patients with resectable, local-regionally advanced, HNSCC. Clinical trial information: NCT02641093. Research Sponsor: Merck & Co., Startup funds, internal pilot grants.

6007 **Oral Abstract Session**

Primary results of the phase II CheckRad-CD8 trial: First-line treatment of locally advanced head and neck squamous cell carcinoma (HNSCC) with double checkpoint blockade and radiotherapy dependent on intratumoral CD8+ T-cell infiltration.

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Background: Inhibition of the PD-1/PD-L1 pathway is efficient in recurrent/metastatic HNSCC. Targeting the immune checkpoint CTLA-4 may be synergistic to radiotherapy. This trial studies feasibility and efficacy of combined PD-L1/CTLA-4 blockade concomitant to induction chemotherapy and radiotherapy. **Methods:** Patients with previously untreated stage III-IVB (AJCC 8^{th} edition) HNSCC were eligible for this multicenter phase II trial. Treatment consisted of a single cycle of cisplatin 30mg/m^2 d1-3, docetaxel 75mg/m^2 d1, durvalumab 1500mg fix dose d5 and tremelimumab 75mg fix dose d5. Patients with at least 20% increase of intratumoral CD8+ immune cell density or pathological complete response (pCR) in the re-biopsy (performed on d22-26) entered radio-immunotherapy (RIT) up to a total dose of 70Gy. Patients received further three cycles of durvalumab/tremelimumab (q4w, two concomitant and one subsequent) followed by eight cycles of durvalumab mono (q4w). Primary endpoint was a feasibility rate of patients entering RIT to receive treatment until at least cycle 6 of immunotherapy of ≥80% (i.e. dose limiting toxicity/DLT ≤20%; exclusion of patients with other reasons than DLT for treatment discontinuation; feasibility unacceptable if ≤65%). The calculated sample size was 57 patients to enter RIT. Main secondary endpoints were progression-free survival (PFS) and overall survival (OS). **Results:** Between Sep 2018 and Mai 2020, 80 patients were enrolled (one excluded). Median age was 60 years, 33 patients (42%) were current smokers, 43 patients (54%) had oropharyngeal tumors (53% p16 positive), 44 patients (56%) were stage IV. Median follow up was 12.5 months. After induction chemo-immunotherapy 41 patients had pCR and 31 an intratumoral CD8+ immune cell increase. Of 60 patients entering RIT (primary endpoint cohort), 10 received DLT and 4 discontinued for other reasons. The feasibility rate of the RIT cohort until cycle 6 was 82%, meeting the primary endpoint of ≥80% (95% confidence interval (CI), one-sided (lower boundary): 72%). The RIT cohort had a PFS rate at 1 year of 79% (CI 69-90%) and at 2 years of 73% (CI 61-87%) and an OS rate at 1 year of 89% (CI 81-98%) and at 2 years of 86% (CI 77-97%). The entire study cohort had a PFS rate at 1 year of 75% (CI 65-85%) and at 2 years of 68% (CI 58-81%) and an OS rate at 1 year of 86% (CI 78-95%) and at 2 years of 80% (CI 70-91%). Toxicity (treatment-related or un-related) ≥grade 3 appeared in 75 patients (95%) and mainly consisted of dysphagia (53%), leucopenia (48%) and infections (29%). DLT mainly consisted of hepatitis (10%). **Conclusions:** The trial met the primary endpoint feasibility. CD8+ T cell-based pathological patient selection after induction therapy identifies patients with promising PFS rates after chemotherapy-free RIT. Clinical trial information: nct03426657. Research Sponsor: AstraZeneca.

6008 **Oral Abstract Session**

Enhanced pathologic tumor response with two cycles of neoadjuvant pembrolizumab in surgically resectable, locally advanced HPV-negative head and neck squamous cell carcinoma (HNSCC).

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Background: We reported that one cycle of neoadjuvant pembrolizumab induced pathologic tumor response in >10% (pTR-any) and in >50% (pTR-2) of the resection bed in 44% and 22% of patients (pts) with surgically resectable HPV-negative, Stage III/IV HNSCC (*Clin Cancer Res* 2020). We hypothesized that two cycles of neoadjuvant pembrolizumab would induce pTR-2 in 50% of pts. Increasing the pathologic response rate may favorably impact clinical outcomes. **Methods:** Multi-institutional phase 2 trial where pts with locally advanced, HPV-negative HNSCC received two cycles of pembrolizumab (200 mg), given 42 and 21 days prior to surgery. Resected tumor was analyzed by two independent pathologists for pTR (tumor necrosis and/or giant cell/histiocytic reaction to keratinous debris) in the resection bed (primary tumor and/or lymph nodes). Additional definitions: pTR-1 (>10-49%) and major pathologic response (> 90%). The primary endpoint was pTR-2. A sample size of 26 pts was needed to detect a significantly higher pTR-2 rate of 50%, with 80% power using a one-sided alpha level of 0.05. Pts were followed for serious adverse events (AEs) for 30 days after surgery and for AEs of clinical interest for 90 days following the last dose of pembrolizumab. Pts underwent baseline blood collection and tumor biopsies to match with blood and surgical specimens obtained post-pembrolizumab. Planned correlatives included PD-L1 expression, immune function, and molecular signatures of activation in the pre- and post-treatment blood and tumor tissue. **Results:** Characteristics of 29 enrolled and treated pts were median age 62 (30-82) yrs, smoking history 62% (18 pts); clinical stage T_2 (n = 6), T_3 (n = 5), T_4 (n = 18) and $N_{0/1}$ (n = 17), N_2 (n = 12). All treated patients received two cycles of neoadjuvant pembrolizumab, which was tolerated well with only one (3%) grade 3 AE (rash) and no grade 4 AEs. The primary endpoint was evaluable in 25 pts, and not evaluable in 4 pts (one pt withdrew before surgery and in three pts, pTR review was pending). pTR-2 occurred in 44% (11 of 25 pts), and 4 (16%) of these pts had a major pathologic response including 1 (4%) pathologic CR at the primary site. **Conclusions:** Two (vs one) cycles of neoadjuvant pembrolizumab resulted in a two-fold increase in the frequency of pTR-2 (44% vs 22%). These data imply that the frequency of pTR to neoadjuvant pembrolizumab can be improved by increasing the number of cycles and the treatment interval. Clinical trial information: NCT02296684. Research Sponsor: Merck Inc.

6010 **Poster Discussion Session**

Updated report of a phase II randomized trial of transoral surgical resection followed by low-dose or standard postoperative therapy in resectable p16+ locally advanced oropharynx cancer: A trial of the ECOG-ACRIN cancer research group (E3311).

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Background: Definitive or postoperative chemoradiation (CRT) is highly curative for human papillomavirus-associated (HPV+) oropharynx cancer (OPC) but induces significant toxicity. As a potential deintensification strategy, we studied primary transoral surgery (TOS) and, in intermediate pathologic risk patients, reduced dose postoperative RT (PORT). **Methods:** E3311 is a phase II trial with randomization to reduced- or standard-dose PORT for resected stage III-IVa (AJCC7) intermediate pathologic risk HPV+ OPC, stratified by smoking history. Primary endpoints have been reported; we now present updated 3-year PFS and patient-reported outcomes (PRO), including head and neck-cancer specific quality of life (FACT-H&N) and swallowing perception and performance (MDADI). **Results:** Of 519 enrolled patients, 495 underwent TOS. The primary oncologic endpoint was 2-year PFS for 50 Gy (Arm B) or 60Gy (Arm C). Among 360 eligible and treated patients (ETP), Arm A (observation, N = 38) enrolled 11%, Arms B (N = 100) or C (N = 109) randomized 58%, and Arm D (66Gy + weekly cisplatin, N = 113) enrolled 31%. With 35.1 months median follow-up, 3-year PFS Kaplan-Meier estimate is 96.9% (90% CI [91.9%, 100%]) for Arm A; 94.9% (90% CI [91.3%, 98.6%]) for Arm B; 93.5% (90% CI [89.4%, 97.9%]) for Arm C; and 90.7% (90% CI [86.2%, 95.4%]) for Arm D. Recurrences and death without recurrence were 4 and 1 in Arm B, and 5 and one in Arm C. Smokers ($>$ 10 pack-years) did not have worse 3-year PFS in Arms B or C. Treatment arm distribution and outcome for ineligible patients who started adjuvant therapy mirrored the 360 ETP. A comparison combining arms B/C versus arm D in the proportion of patients stable/improved in FACT-H&N total score, from baseline to 6 months post-treatment as a pre-specified endpoint, was 56% vs. 38% (p value = 0.011, one-sided Fisher's exact test); however, underlying differences in treatment and risk may be confounding. An exploratory comparison between Arms B and C revealed improvement in FACT H&N (63% in Arm B vs. 49% in Arm C had a stable/improved score, p-value = 0.056). **Conclusions:** Primary TOS and reduced PORT retained outstanding oncologic outcome at 35 months follow up, with favorable QOL and functional outcomes, in intermediate risk HPV+ OPC. Clinical trial information: NCT 01898494. Research Sponsor: U10CA180820, U10CA180794, UG1CA189953, UG1CA232760, UG1CA233184, UG1CA233196, UG1CA233247, UG1CA233329, UG1CA233331, UG1CA233337, U10CA180863, Canadian Cancer Society #704970.

6011 **Poster Discussion Session**

Nivolumab, nabpaclitaxel, and carboplatin followed by risk/response adaptive de-escalated locoregional therapy for HPV-associated oropharyngeal cancer: OPTIMA II trial.

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Background: Despite the success of anti-PD-1 in recurrent/metastatic head and neck cancer, incorporation in the curative setting with induction therapy has yet to be investigated. Favorable prognosis of human papillomavirus associated (HPV+) oropharyngeal cancer (OPC) has led to interest in treatment de-escalation. OPTIMA 2 evaluated nivolumab (nivo) with nab-paclitaxel and carboplatin followed by risk/response adaptive de-intensified treatment for locoregionally advanced HPV+ OPC. We report the primary analysis and outcomes. **Methods:** OPTIMA 2 enrolled locoregionally advanced HPV+ OPC. Nivo, nab-paclitaxel, and carboplatin were administered for 3 cycles. High-risk (HR) included any of the following: T4, N2c-N3 (AJCC 7^{th} edition), $>$ 20 pack year smoking history, non-HPV16 subtype; All others were low-risk (LR). Arm A included LR with $\geq$50% post-induction shrinkage by RECIST received single-modality de-escalation with low-dose radiation (RT) alone (50 Gy) or transoral robotic surgery (TORS). Arm B included HR with $\geq$50% shrinkage or LR with $<$50% received intermediate-dose chemoradiation (CRT) to 45-50Gy. Arm C included all others and received regular dose CRT to 70-75Gy. Adjuvant nivo was administered for 6 months. The primary endpoint was deep response rate (DRR) $\geq$50% shrinkage to induction therapy. **Results:** From September 2017 until March 2020, 73 patients (pts) were eligible and started treatment. One pt died during induction. The DRR following induction was 70.8% (95% CI 60.3%, 81.3%). Median follow-up 23.1 months. Median age 61 (range 39-85), T4 12.3%, N2c/N3 19.2%, LR 47.9%, and HR 52.1%. De-escalated treatment was administered in 84.9%. Arm A N = 28, Arm B N = 34, and Arm C N = 10. 2-year progression free survival (PFS) for full cohort was 90.4% (95% CI = 79.3%, 95.7%). 2-year PFS for Arms A, B, and C were 96.3%, 85.8%, and 100.0% respectively. 2-year overall survival (OS) for full cohort was 93.3% (95% CI = 82.4%, 97.5%). 2-year OS for Arm A, B, and C were 96.0%, 91.9%, and 100.0% respectively. Among TORS (N = 9), pathologic complete response (pCR) rate was 66.7%. G-tube rates in Arms A, B, and C were 7.1%, 44.1%, and 75.0% respectively (p = 0.0001). Grade 4 toxicity in arms A, B, and C, were observed in 7.1%, 8.8%, and 10.0% of pts respectively. There were 3 local failures and no distant failures. **Conclusions:** Nivo/nab-paclitaxel/carboplatin followed by risk/response adaptive de-escalated treatment in locoregionally advanced HPV+ OPC demonstrates excellent survival outcomes with reduced toxicity and enteral feeding rates, including high risk disease. Induction chemoimmunotherapy demonstrates a high rate of deep clinical response and represents a promising de-escalation approach that incorporates anti-PD1 in the definitive setting. High pCR rate was observed following nivo/nab-paclitaxel/carboplatin. Clinical trial information: NCT03107182. Research Sponsor: Bristol Myers Squibb.

6012 **Poster Discussion Session**

Randomized trial of radiotherapy with weekly cisplatin or cetuximab in low risk HPV associated oropharyngeal cancer (TROG 12.01): A Trans-Tasman Radiation Oncology Group study.

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Background: The excellent prognosis of patients with low risk HPV associated oropharyngeal squamous cell carcinoma has led to concerns about overtreatment and excessive toxicity with radiotherapy and cisplatin, leading to interest in de-intensification trials. We investigated whether cetuximab, an EGFR targeting antibody, when combined with radiotherapy would result in a decrease in symptom burden and toxicity with similar efficacy when compared to weekly cisplatin. **Methods:** TROG 12.01, a randomised, multicentre trial involving 15 sites in Australia and New Zealand enrolled patients with HPV associated oropharyngeal squamous cell carcinoma, AJCC 7^{th} edition Stage III (excluding T1-2N1) or stage IV (excluding T4 and/or N3 and/or N2b-c if smoking history $>$10 pack years and/or distant metastases). Patients were randomised (1:1) to receive radiotherapy (70Gy in 35 fractions) with either weekly cisplatin, 7 doses of 40mg/m^2 or cetuximab, loading dose of 400mg/m^2 followed by 7 weekly doses of 250 mg/m^2. The primary outcome was symptom severity assessed by the MD Anderson Symptom Inventory Head and Neck Symptom Severity Scale from baseline to 13 weeks post completion of radiotherapy using the area under the time-severity curve (AUC). Sample size was 170 evaluable patients to provide at least 90% power to detect an effect size of 0.5, using a 2-sided test at 0.05 level of significance. Trial was registered on ClinicalTrials.gov: NCT01855451. **Results:** Between 17^{th} June 2013 and 7^{th} June 2018, 189 patients were enrolled and 182 were evaluable, with 92 on cisplatin arm and 90 on cetuximab included in the main analysis. The median follow-up was 4.1 years (0.4 - 5.3). Analyses were performed in all eligible randomised patients that commenced treatment (modified intention-to-treat population). There was no difference in the primary endpoint of symptom severity; difference in AUC cetuximab – cisplatin was 0.05 (95%CI: -0.19, 0.30), p= 0.66. The T-score (mean number of $>$ grade 3 acute adverse events) was 4.35 (SD 2.48) in the cisplatin arm and 3.82 (SD 1.8) in the cetuximab arm, p= 0.108. The 3 -year failure-free survival rates were 93% (95% CI: 86-97%) in the cisplatin arm and 80% (95% CI: 70-87%) in the cetuximab arm (hazard ratio = 3.0 (95% CI: 1.2-7.7); p=0.015. The increase in failures in the cetuximab arm was evenly split between distant and locoregional failures. **Conclusions:** For patients with low risk HPV associated oropharyngeal cancer, radiotherapy and cetuximab had inferior failure-free survival without improvement in symptom burden or toxicity compared to radiotherapy and weekly cisplatin. Radiotherapy and cisplatin remains the standard of care. Clinical trial information: NCT01855451. Research Sponsor: National Health and Medical Research Council (Project Grant 1047673), Pharmaceutical/Biotech Company.

6014 **Poster Discussion Session**

TRYHARD, a randomized phase II trial (RTOG Foundation 3501) of concurrent accelerated radiation plus cisplatin (cis) with or without lapatinib (Lap) for stage III- IV Non-HPV head and neck carcinoma (HNC).

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Background: Chemoradiation (CRT) with cis or anti-EGFR Ab has been shown to improve survival of patients with stage III-IV HNC. Since Lap, a dual EGFR and HER2 inhibitor, has shown effectiveness with CRT in a pilot non-HPV HNC cohort, the RTOG Foundation launched a phase II trial to test the hypothesis that adding Lap to the RT-cis for frontline therapy of stage III-IV Non-HPV HNC improves progression-free survival (PFS). **Methods:** Patients with stage III-IV carcinoma of the oropharynx (p16-negative), larynx, and hypopharynx, having Zubrod performance of 0-1, and meeting predefined blood chemistry criteria were enrolled after providing consent. Patients were randomized (1:1) to 70 Gy (6 weeks) + 2 cycles of CDDP (q3 weeks) plus either Lap (1500 mg daily, Arm A) or placebo (Arm B) starting 1 week prior to RT and concurrent with RT and for 3 months post RT. PFS was the primary endpoint. The protocol specified 69 PFS events (142 patients) for the final analysis based on HR = 0.65, 80% power, 1-sided alpha 0.20, and one interim efficacy and futility analysis at 50% information. PFS rates between arms for all randomized patients were compared by 1-sided log-rank test (1-sided alpha 0.1803). Overall survival (OS) was a secondary endpoint. **Results:** From 10/'12 to 04/'17, 142 patients were enrolled, of whom 127 were randomized, 63 to Arm A and 64 to Arm B. Arms A vs B, respectively, were similar in baseline patient characteristics, radiation delivery, completing $\geq$ 70 Gy (85.7% vs. 82.8%) and cisplatin delivery, completing 200 (±5%) mg/m^2 (65.1% vs 70.3%), but dissimilar in Lap/placebo delivery (median dose, 87000 mg vs. 125250 mg). Median follow-up was 4.1 years for surviving patients. The final analysis suggests no improvement in PFS of adding Lap to CRT (HR [A/B]: 0.91, 95% confidence interval CI 0.56-1.46; *P*= 0.34; 2-year rates: 50.6%, CI 37.5-63.7% vs. 56.2% CI 43.0-69.4%), or in OS (HR: 1.06, CI 0.61-1.86; P = 0.58; 2-year rates: 71.8% CI 60.1-83.5% vs. 76% CI 64.5-87.4%), death within 30 days of therapy (3.3% vs. 3.4%), and overall treatment-related grade 3-5 adverse event rate (86.7% vs. 84.7%). Grade 3-4 mucositis rates on Arm A and Arm B were 21.7% vs. 23.7%, all grade dysphagia and rash rates were 43.3% vs. 59.3%, and 13.3% vs. 6.8%, respectively. **Conclusions:** The addition of Lap to the radiation-cisplatin platform did not improve progression-free or overall survival in unselected non-HPV HN. Thus, dual EGFR, HER-2 inhibition does not appear to enhance the effects of chemoradiation. Although we showed that accrual to a non-HPV HN specific trial is feasible, new strategies must be investigated to improve the outcome for this poor prognosis HN population. Research Sponsor: Novartis.

6015 **Poster Discussion Session**

Randomized phase II trial of ficlatuzumab with or without cetuximab in pan-refractory, advanced head and neck squamous cell carcinoma (HNSCC).

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Background: Cetuximab (C), an anti-EGFR monoclonal antibody (mAb), is approved for advanced HNSCC but benefits a minority. Crosstalk between the EGFR and hepatocyte growth factor (HGF)/cMet pathways is a known resistance mechanism. HGF is also immunosuppressive within the tumor microenvironment. A Phase I study confirmed the safety of C and ficlatuzumab (F), an IgG1 anti-HGF mAb, with preliminary efficacy and biomarker data suggesting that dual pathway inhibition may overcome tumor-intrinsic or immune cetuximab resistance. **Methods:** The primary objective of this phase II randomized, non-comparative trial was to evaluate the efficacy of F (20 mg/kg every 2 wks), with or without C (500 mg/m^2 every 2 wks), in pan-refractory, advanced HNSCC. Eligibility criteria included recurrent/metastatic HNSCC, performance status (PS) 0-1, C resistance (defined as progression on or within 6 months of exposure), and resistance to or ineligibility for platinum and anti-PD1 mAb. Randomization was stratified by HPV status and center. The primary endpoint was median progression-free survival (mPFS). An arm was deemed worthy of further study if the lower bound of the 90% 1-sided confidence interval (CI) excluded the historical control of 2 months. Secondary objectives included overall response rate (ORR) in the overall and HPV-stratified populations. A Bayesian continuous monitoring rule for futility was applied. **Results:** 60 patients were randomized and 58 treated between Jan 2018 and Dec 2020 (27 to F; 33 to FC). Baseline characteristics were balanced across major prognostic variables including age, PS, HPV status, platinum resistance, and PD1 mAb exposure. Median time since prior cetuximab was 3.5 months (range 0-48 months). Grade ≥3 adverse events attributed to F included: pneumonitis (2); edema (3); diarrhea (1); LFT elevation (1); rash (2); electrolyte abnormality (2). The Table presents efficacy data. The F arm stopped for futility after 26 evaluable subjects accrued. The FC arm completed accrual and met the primary endpoint; 32 evaluable subjects had mPFS of 3.6 months (lower bound 90% 1-sided CI: 2.3 months) and ORR of 19% (6/32). All responses were in HPV- subjects, including 2 complete (CR) and 4 partial responses (PR) to the FC combination and 1 PR to F monotherapy. The mPFS and ORR for the HPV- population (n = 16) on FC were 3.8 months and 38% (6/16). Mechanistic signaling and immune biomarkers are under analysis. **Conclusions:** The well-tolerated FC combination met the primary PFS endpoint in pan-refractory, advanced HNSCC with notable activity in HPV- HNSCC, warranting phase III investigation. Clinical trial information: NCT03422536. Research Sponsor: Aveo, U.S. National Institutes of Health.

	F (n = 26)	FC (n = 32)
Total Population		
ORR[a]	1PR/26 (4%)	2PR + 4CR/32 (19%)
mPFS[b]	1.8 (1.7)	3.6 (2.3)
HPV+		
ORR	0/10 (0%)	0/16 (0%)
mPFS	NE[c]	2.3 (1.9)
HPV-		
ORR	1PR/16 (6%)	2CR + 4PR/16 (38%)
mPFS	NE	3.8 (2.9)

[a]ORR: PR+CR/n
[b]mPFS: Months (lower bound of 90% 1-sided CI)
[c]NE = not evaluated.

6016 **Poster Discussion Session**

Phase II trial of soluble EphB4-albumin in combination with PD-1 antibody (pembrolizumab) in relapsed/refractory head neck squamous cell carcinoma.

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Background: EphB4 receptor tyrosine kinase and its ligand EphrinB2 are highly induced in head neck squamous cell carcinoma (HN SCC) tumor cells and vessels, particularly in HPV negative tumors. Each are predictors for poor survival with worse prognosis when both are induced. EphB4 provides tumor cell survival and EphrinB2 inhibits immune cell invasion. Soluble EphB4-Alb blocks bidirectional signaling, enhances immune cell recruitment alone and when combined with PD-1 antibody. **Methods**: A phase II trial of sEphB4-Alb combined with pembrolizumab accrued HN SCC patients after failure of one or more prior regimens. IHC positivity for p16 was used as a surrogate for HPV infection. Treatment regimen was sEphB4-Alb 10 mg/kg weekly IV infusion with pembrolizumab 200 mg IV infusion every three weeks. Study endpoints were toxicity, overall response rates (ORR) and overall survival (OS). Response to therapy was based on RECIST 1.1 criteria. Patient tumor samples were collected at baseline with a 2^{nd} biopsy at week 8 on therapy, for tissue analysis of PD-L1, EphrinB2 and other biomarkers. **Results**: Twenty-four patients were accrued to the phase II trial combination of sEphB4-Alb and pembrolizumab. Age, sex, prior treatment, HPV status, and response data are summarized in the table below. The most common toxicity was hypertension with 8 patients experiencing grade 3 HTN. No grade 4 or above toxicities were observed. Among HPV negative cases, partial and complete responses were observed in 6 of 14 patients (43%) with complete response (CR) observed in 3 of 6 responders. Additionally, rapid response was observed in 3 of 14 HPV negative patients. Response was associated with increase in immune markers on 2^{nd} biopsy. Median overall and progression-free survival in all patients was 12.6 months and 8.6 months, respectively. **Conclusions:** 1. sEphB4-Alb was well tolerated in combination with PD-1 antibody. 2. sEphB4-Alb was associated with increased immune response to tumor, when combined with PD-1 antibody. 3. sEphB4-Alb appears to have substantial activity (including complete remission) when combined with PD-1 antibody in relapsed/refractory HPV negative HN SCC. Clinical trial information: NCT03049618. Research Sponsor: Merck.

	sEphB4-Alb + PD-1 Ab N = 24
Age – median (range)	61 (31–79)
Male sex – no. (%)	19 (79)
Median prior regimens – no. (range)	1 (0–2)
Prior cetuximab – no. (%)	5 (21)
Response rates – no. (%)	
ORR	6 (25)
CR	3 (12)
HPV neg. – no. (%)	14 (58)
HPV neg. ORR (%)	6 (43)
HPV pos. – no. (%)	10 (42)
HPV pos. ORR (%)	0

6017 **Poster Discussion Session**

Efficacy of concurrent cetuximab (CTX) and nivolumab (NIVO) in previously untreated recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).

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Background: Current standard of care for patients (pts) with previously untreated R/M HNSCC that are incurable is either pembrolizumab (pembro) with/without chemotherapy depending on the Programmed Death-Ligand 1 (PD-L1) combined positive score (CPS). We evaluated the combination of CTX and NIVO for its efficacy. **Methods:** Pts were treated with CTX 500 mg/m2 IV on Day (D) -14 as a lead-in followed by CTX 500 mg/m2 IV and NIVO 240 mg/m2 IV on D1 and D15 every 28-D cycle (C). Pts with CTX infusion reaction or who did not receive C1D1 for any reason were non-evaluable and replaced. NIVO dose reduction was not allowed. **Results**: Fifty-four evaluable pts were analyzed. Median age was 62 (42-85). ECOG performance status at baseline was 0 (20, 37%), 1 (30, 56%), and 2 (4, 7%). Primary sites were oral cavity 19 (35%), oropharynx 22 (41%), hypopharynx 3 (6%), larynx 9 (17%), and unknown primary 1 (2%). p16 status is positive 22 (41%), negative 29 (54%), and unknown 3 (6%). PD-L1 CPS is < 1 in 6 (11%), >1 in 26 (48%), and unknown 22 (41%). Median follow up time for overall survival (OS) was 12.2 months. The most common grade 3 treatment-related adverse events (TRAEs) occurring in ≥ 2 pts were hypomagnesemia 2 (4%), hypophosphatemia 2 (4%), fatigue 4 (7%), and rash-acneiform 4 (7%). The only grade 4 TRAEs were hypomagnesemia in 1 (2%) and CTX infusion reaction in 1 (2%). The most common grade 3 immune-related adverse event (IRAE) occurring in ≥ 2 was fatigue 2 (4%). No grade 4 IRAEs is observed. Median progression-free survival (PFS) and OS were 7.8 and 14.5 months, while 1-year PFS and 1-year OS were 39% and 61%, respectively. There were no statistically significant differences in either PFS and OS based on tumor p16 or PD-L1 status. **Conclusions**: The clinical trial met its primary endpoint of 1-year OS. Our data indicate the combination of CTX and NIVO is safe and effective in pts with previously untreated incurable R/M HNSCC. Clinical trial information: NCT03370276. Research Sponsor: Lilly, Florida Health Department.

6018 **Poster Discussion Session**

A randomized phase II trial of diffusion-weighted MR imaging-guided radiotherapy plus chemotherapy versus standard chemoradiotherapy in locoregional advanced nasopharyngeal carcinoma.

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Background: We hypothesized that diffusion-weighted MR imaging (DWI) guided dose-painting radiotherapy (DP-RT) was associated with improved tumor control and survival compared with standard CT-based radiotherapy in locoregionally advanced nasopharyngeal carcinoma (NPC). The purpose of this randomized phase II trial was to compare the efficacy and toxicity of DWI guided DP-RT plus chemotherapy versus standard CT-based radiotherapy plus chemotherapy in locoregionally advanced NPC. **Methods:** Two hundred and fifty-six patients with stage III-IVa (8th AJCC) NPC were randomly assigned to receive DWI-guided dose-painting radiotherapy plus chemotherapy (DP-RT group, n = 128) or standard CT-based radiotherapy plus chemotherapy (CT-based RT group, n = 128). Patients in both groups received 3 cycles of induction chemotherapy followed by cisplatin-based concurrent chemoradiotherapy. In DP-RT group, subvolume GTVnx-DWI (gross tumor volume of nasopharynx in DWI) was defined as the areas within the GTVnx (gross tumor volume of nasopharynx) with an apparent diffusion coefficient (ADC) below the mean ADC (ADC $<$ mean). The dose to GTVnx-DWI was escalated to DT 75.2 Gy/32 Fx in patients with T1-2 disease, and DT 77.55 Gy/33 Fx in those with T3-4 disease, in 2.35 Gy per fraction. In CT-based RT group (n = 128), PGTVnx was irradiated at DT 70.4-72.6 Gy/32-33 Fx in 2.2 Gy per fraction. This trial is registered with chictr.org.cn, number ChiCTR1800015779. **Results:** Compared with standard CT-based radiotherapy, DWI-guided DP-RT significantly improved 2-year local recurrence-free survival (LRFS, 100% vs. 95.4%; P = 0.024), distant metastasis-free survival (DMFS, 97.9% vs. 90.6%; P = 0.006), disease free survival (DFS, 93.2% vs. 86.8%; P = 0.021), and overall survival (OS, 100% vs. 95.2%; P = 0.038). No statistically significant differences in acute and late toxic effects were observed. Multivariate analysis showed that dose painting (DWI-guided DP-RT vs CT-based RT without DP) was a significant independent prognostic factor for DMFS and DFS (P = 0.021 and P = 0.020, respectively). **Conclusions:** Diffusion-weighted MR imaging guided dose-painting radiotherapy plus chemotherapy is associated with a considerable survival benefit, without increasing toxicity, as compared with standard CT-based radiotherapy plus chemotherapy, among patients with locoregionally advanced nasopharyngeal carcinoma. Clinical trial information: ChiCTR1800015779. Research Sponsor: Cancer Foundation of China, and China Hunan Provincial Science and Technology Department.

6019 **Poster Discussion Session**

The 30 ROC trial: Precision intra-treatment imaging guiding major radiation reduction in human papillomavirus related oropharyngeal cancer.

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Background: Our previously published proof-of-concept trial using functional imaging to select patient with human papillomavirus (HPV) oropharyngeal carcinoma (OPC) for radiation de-escalation showed promising results. Here we report the outcome of a larger validation trial using the same paradigm where select HPV+ OPC patients received a definitive dose of 30Gy concurrently with chemotherapy and were subsequently observed. **Methods:** The trial enrolled patients who had p16+, T0-2, N1-N2c, M0 OPC by AJCC 7th TNM. Patients were required to have resection of the primary site (negative margin not required) or core biopsy of lymph node if unknown primary. In addition to standard positron emission tomography (PET), a pre-radiation dynamic ^{18}F-FMISO (fluoromisonidazole) PET was performed to identify hypoxia in gross nodal disease. Patients with evidence of hypoxia ($>$ 1.2 tumor to muscle standard uptake value on ^{18}F-FMISO) underwent repeat^{18}F-FMISO PET around 2 weeks into radiation. Patients without pre-radiation hypoxia or with resolution of hypoxia on ^{18}F-FMISO PET received 30Gy with 2 cycles of concurrent chemotherapy (cisplatin 100mg/m^2 or carboplatin AUC 1.25 x 4 with 5-fluorouracil 2400 mg/m^2). **Results:** From 11/2/17-1/4/21, 158 HPV+ OPC patients consented and were enrolled on trial. Patient characteristics were as follows: male (90%); ages 36-80 years; T-stage T0(26), T1(77), T2(55); N stage N1(19), N2a(15), N2b(95), N2c(29). Of the 114 patients with pre-treatment hypoxia, 24 had persistent hypoxia and received 70Gy. 128 patients were de-escalated to 30Gy and chemotherapy (86% cisplatin). 6 patients withdrew from trial [3 decided to receive standard of care; 3 refused ^{18}F-FMISO PET]. Acute mucositis rates were 11% grade 0, 59% grade 1, and 30% grade 2, respectively. Acute xerostomia rates were 92% grade 1 and 8% grade 2, respectively. Weight loss was infrequent and only 19% complained of grade 1 and 5% complained of grade 2 weight loss. Six patients experienced grade 3 adverse events (diarrhea (2), syncope (2), vasovagal (1), dysphagia (1)). No patients required PEG tubes. With a median follow-up is 12 months (range: 2 months to 40 months), the 1-year locoregional control, distant metastasis-free overall survival rates were 94%, 100%, and 100%, respectively. Among the 30Gy de-escalated patients, none failed in the primary site. 8 patients had recurrent nodal disease underwent successful salvage surgery of which no additional therapy was given to 4 patients. **Conclusions:** Major de-escalation to 30Gy using patient specific treatment response based on hypoxia resolution resulted in excellent locoregional control with significant toxicity reduction. Updated results along with detailed correlative analysis will be presented. Clinical trial information: NCT03323463. Research Sponsor: U.S. National Institutes of Health, Serra Mucositis Funds.

6020 **Poster Session**

Long-term follow-up of bintrafusp alfa, a bifunctional fusion protein targeting TGF-β and PD-L1, in advanced squamous cell carcinoma of the head and neck (SCCHN).

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Background: Bintrafusp alfa is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor (a TGF-β "trap") fused to a human IgG1 mAb blocking PD-L1. A previous report of an expansion cohort from a phase 1 study (NCT02517398) suggested that bintrafusp alfa had a manageable safety profile and early signs of clinical activity in patients with heavily pretreated, advanced SCCHN after a median follow-up of 86.4 weeks. Here we report long-term efficacy and safety for this cohort. **Methods:** Patients with advanced SCCHN that progressed/recurred after platinum therapy in the recurrent/metastatic setting, or $<$ 6 months after platinum therapy in the locally advanced setting, received bintrafusp alfa 1200 mg every 2 weeks until confirmed progressive disease, unacceptable toxicity, or trial withdrawal. The primary endpoint was confirmed best overall response assessed per RECIST 1.1 assessed by independent review committee (IRC); safety was a secondary endpoint. **Results:** As of May 15, 2020, 32 patients had received bintrafusp alfa for a median of 2.8 months (range, 0.5-29.9 months), no patient remained on treatment, and median follow-up to data cutoff was 41.7 months (range, 39.8-43.5 months). The objective response rate (ORR; 13%) was unchanged since the previous report; median duration of response (DOR) was increased at 21.4 months (95% CI, 5.5 months to not reached [NR]). While the clinical activity of bintrafusp alfa may be improved in patients with HPV-positive tumors (Table), outcomes were generally similar between PD-L1 subgroups ($\geq$1% vs $<$ 1% tumor cells). The overall safety profile was consistent with the previous report for this cohort, without grade 4 nor 5 treatment-related adverse events (TRAEs); no new TRAEs of grade 3 or that led to discontinuation of bintrafusp alfa were reported. **Conclusions:** With a median follow-up of over 3 years in patients with heavily pretreated advanced SCCHN, bintrafusp alfa showed sustained clinical activity and 3-year OS of 24.0%, which compares favorably to historical data. Clinical activity appeared to be greater in patients with HPV-positive tumors than those with HPV-negative tumors. The safety profile was manageable and consistent with earlier analysis. Further investigation of bintrafusp alfa in SCCHN and other HPV-associated cancers is ongoing. Clinical trial information: NCT02517398. Research Sponsor: Merck KGaA, Darmstadt, Germany, and GlaxoSmithKline.

	HPV-positive(n = 11)	HPV-negative (n = 20)	Overall (N = 32)
ORR per IRC (95% CI), %	27.3 (6.0-61.0)	5.0 (0.1-24.9)	12.5 (3.5-29.0)
Median DOR (95% CI), months	18.1 (5.5-24.7)	NR (NR-NR)	21.4 (5.5-NR)
Median progression-free survival (PFS) per IRC (95% CI), months	1.4 (1.2-19.6)	1.4 (1.2-4.0)	1.4 (1.3-4.0)
18-month PFS, %	27.3	17.5	21.3
24-month PFS, %	13.6	11.7	12.8
Median OS (95% CI), months	8.0 (2.9-NR)	9.1 (6.3-24.3)	9.1 (6.6-24.3)
18-month OS, %	45.5	43.0	44.0
24-month OS, %	45.5	30.7	36.0
36-month OS, %	34.1	18.4	24.0

6021 **Poster Session**

The association of skeletal muscle mass and cisplatin pharmacokinetics in head and neck cancer patients: The prospective PLATISMA study.

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Background: Locally advanced head and neck squamous cell carcinoma (HNSCC) is commonly treated with cisplatin-based chemoradiotherapy (CRT). Cisplatin is associated with severe toxicity, which negatively affects survival. In recent years, a relationship between low skeletal muscle mass (SMM) and toxicity has been described. This increased toxicity may be related to an altered cisplatin distribution and binding in the fat-free body mass, of which SMM is the largest contributor. This study aims to investigate the association between cisplatin pharmacokinetics and SMM in HNSCC patients. **Methods:** We performed a prospective observational study in HNSCC patients treated with CRT with cisplatin. Patients received standard-of-care chemotherapy with three cycles of cisplatin, at a dose level of 100 mg/m^2 per cycle. Quantitative data on body size descriptors including SMM, measured on computed tomography scans, and cisplatin pharmacokinetics (total and ultrafilterable plasma concentration) were collected, as well as data on toxicity. **Results:** 45 evaluable patients were included in the study. A large proportion of the study population had a low SMM (46.7%). The majority of patients (57.8%) experienced cisplatin dose limiting toxicities. Pharmacokinetic analysis showed a significant relationship between cisplatin pharmacokinetics and the body size descriptors SMM, weight, fat-free mass, and body surface area ($p< 0.005$). In a simulation, patients with a low SMM were predicted to reach higher bound cisplatin concentrations. The higher concentration of bound cisplatin could be seen as a reflection of the smaller volume of distribution, and could thereby explain the increased toxicity in patients with a low SMM. **Conclusions:** We found an association between cisplatin pharmacokinetics and SMM. Patients with a low SMM were predicted to reach higher bound cisplatin concentrations, which could be an explanation for the increased toxicity in this patient group. Clinical trial information: Trial NL7469 (NTR7711). Research Sponsor: Dutch Cancer Society.

6022 **Poster Session**

Anlotinib in radioiodine-refractory differentiated thyroid carcinoma: A subanalysis based on ALTER01032 study for patients with poor baseline characteristics.

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Background: Anlotinib (anlo), a multikinase inhibitor, has demonstrated a significant survival benefit in treating locally advanced or metastatic radioiodine-refractory differentiated thyroid carcinoma (RAIR-DTC) with a nearly 4 folds prolongation in median progression-free survival (mPFS) (HR = 0.21, $p < 0.0001$) compared with placebo in a randomized, placebo-controlled phase 2 study (ALTER01032, NCT02586337). Older age, bone metastasis, structural progression within a short time are generally indicated as negative prognostic factors for thyroid cancer. This subanalysis explored the outcomes of patients (pts) enrolled in ALTER01032 study with these poor baseline characteristics. **Methods:** 113 pts were enrolled, 76 in anlo arm and 37 in placbo arm. The primary endpoint is PFS. Pts with older age ($\geq$ 55), bone metastasis or radiographic documented disease progression within 3 months (mo) before enrollment were selected. The PFS and overall survival (OS) for these pts were estimated and compared. Since 64.9% pts in placebo arm received crossover treatment with open label anlo after progression while only 3 pts in anlo arm received post-study treatment, the penitential bias for OS from imbalance of subsequent treatment was adjusted by a two-stage estimation method. **Results:** The results of subanalysis were summarized in the table below. Pts with poor baseline characteristics showed higher risk of progression and death. Significant PFS prolongation was shown across all subgroups in pts received anlo compared with their counterparts who received placebo ($P < 0.05$). In pts with bone metastasis or structural progression within 3 mo, anlo treatment achieved significant OS benefit ($P < 0.05$). Also, in older pts, a trend of OS improvement was observed (HR = 0.85 (95% CI 0.37, 1.97)). Most pts in placebo arm received crossover anlo. After adjustment, a near-significant decrease of death risk was observed in older pts received anlo compared with those received placebo (HR = 0.48 (95% CI 0.20, 1.13)). **Conclusions:** This subanalysis showed anlo effectively improved both PFS and OS of pts with RAIR-DTC who have poor baseline characteristics above. Interestingly, although most pts in placebo arm received crossover anlo, they still have higher risk of death, indicating the importance of earlier treatment for these pts. Clinical trial information: NCT02586337. Research Sponsor: None.

Features	No. of pts (Anlo / Placebo)	mPFS for Anlo (mo)	mPFS for placebo (mo)	HR (95% CI), *P*-value	Crossover anlo n (%)	HR (95% CI) for OS, *P*-value	Adjusted HR for OS (95% CI), P- value
Older age	39/25	29.5	6.9	0.23 (0.12, 0.46), < 0.0001	19 (76.0)	0.85 (0.37, 1.97), 0.710	0.48 (0.20, 1.13), 0.0862
Bone metastasis	20/11	36.1	5.6	0.10 (0.03, 0.28), < 0.0001	7 (63.6)	0.16 (0.05, 0.51), 0.0005	0.04 (0.00, 0.30) < 0.0001
Progression within 3 mo before enrollment	45/23	NR	6.9	0.096 (0.045, 0.206), < 0.0001	17 (73.9)	0.35 (0.14, 0.86), 0.017	0.21 (0.08, 0.55), 0.001

6023 **Poster Session**

Toripalimab plus intensity-modulated radiotherapy for recurrent nasopharyngeal carcinoma: An open-label single-arm, phase II trial.

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Background: Toripalimab is a humanized immunoglobulin G_4 monoclonal antibody against programmed death 1 (PD-1). We aimed to investigate the efficacy and safety of toripalimab in combination with intensity-modulated radiotherapy (IMRT) for recurrent nasopharyngeal carcinoma (rNPC). **Methods:** We conducted a single-arm, phase II trial with rNPC patients who had biopsy-proven disease and were unsuitable for local surgery. Eligible patients received IMRT in combination with toripalimab administered via intravenous infusion of 240 mg once every 3 weeks for a maximum of seven cycles. The primary endpoint was the objective response rate (ORR). The secondary endpoints included safety profiles, progression-free survival (PFS). **Results:** Between May 2019 and January 2020, a total of 25 rNPC patients were enrolled (18 men [72.0%] and 7 women [28.0%]; median [IQR] age, 49.0 [43.5-52.5] years). With a median (IQR) follow-up duration of 14.6 months (13.1-16.2) months, 19 patients (79.2%) achieved an overall response, and disease control was achieved in 23 (95.8%) patients at 3 months post radiotherapy. The 12-month progression-free survival was 91.8% (95% CI 91.7% - 91.9%). The incidences of acute (grade $\geq$3) blood triglyceride elevation, creatine phosphokinase elevation, skin reaction, and mucositis were 1 (4.0%), 1 (4.0%), 2 (8.0%), and 1 (4.0%), respectively. The incidences of late severe (grade $\geq$3) nasopharyngeal wall necrosis, nasal bleeding, and trismus were 28.0%, 12.0%, and 4.0%, respectively. **Conclusions:** Toripalimab combined with IMRT was tolerable and showed promising antitumor activity in rNPC patients. Clinical trial information: NCT03854838. Research Sponsor: the Key-Area Research and Development of Guangdong Province.

6024 **Poster Session**

Afatinib and pembrolizumab for recurrent or metastatic head and neck squamous cell carcinoma (ALPHA Study): A phase II study with biomarker analysis.

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Background: Epidermal growth factor receptor (EGFR) pathway inhibition may synergize with anti-PD1 activity by inhibiting macrophage function, increasing antigen presentation, and augmenting T cell responses. Afatinib, an irreversible EGFR tyrosine kinase inhibitor (TKI), has been shown to enhance anti-PD1 activity in in vitro and animal studies. We thus hypothesized that adding afatinib to pembrolizumab may improve the treatment outcomes for patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC). **Methods:** The ALPHA study (NCT03695510) is a single-arm, phase II study with a Simon 2-stage design. Patients with platinum-refractory, recurrent, or metastatic HNSCC are eligible for the study. Afatinib (40mg, oral, daily) and pembrolizumab (200mg, every 3 weeks) are administered to eligible patients. The primary endpoint is the objective response rate (ORR). PD-L1 IHC testing (22C3), comprehensive genomic profiling (CGP, Roche Foundation Medicine One CDx), and targeted multiplexed gene expression profiling (Nanostring nCounter PanCancer Immune Profiling Panel) were applied for biomarker analysis. **Results:** From JAN 2019 to MAR 2020, 29 patients were enrolled in the study. Age: mean = 53.4 years old; M/F = 27/2. Tumor type: oral cavity: 19; oropharynx: 6, hypopharynx: 2, larynx: 2. PD-L1 TPS $>=$ 50: 7/29 (24.1%), CPS $>=$ 20: 8/29 (27.6%), TMB $>$ 10: 0/25 (0%). The common treatment-related adverse events (AEs; all grades, grade $>=$ 3) were skin rash (22/29, 4/29), diarrhea (17/29, 3/29), paronychia (13/29, 0/29), mucositis (9/29, 1/29), and weight loss (2/29, 0/29). One patient experienced grade 2 pneumonitis. Twelve patients had partial responses to the treatment (12/29, ORR: 41.4%). The data cut-off date was 11FEB2021. The median progression free survival (PFS) was 4.1 (95% confidence interval [CI], 1.9-6.3) months. The median overall survival (OS) was 8.4 (95% CI, 4.1-10.8) months. Patients with high PD-L1 expression had a higher response rate (TPS $>=$ 50: ORR = 0.71, CPS $>=$ 20: ORR = 0.63). EGFR amplification might also predict a higher response rate (ORR: 3/3, 100%). MTAP loss or mutation may predict a poor response to the treatment (ORR: 0/5, 0%), shorter PFS (HR: 4.21, [95% CI: 1.34-13.24], p = 0.014), and shorter OS (HR: 4.20 [95% CI: 1.32-13.41], p = 0.015). Nine patients underwent paired pre-treatment and post-treatment biopsies for gene expression analysis. The mRNA of HLA-A, HLA-B, CXCL13, CXCL9, and CD8A were elevated in the post-treatment biopsies. Three patients underwent post-progression biopsies for CGP study. One patient had a new MTAP mutation. **Conclusions:** Afatinib can modify tumor microenvironment and increase the clinical response rate in pembrolizumab-based therapy in HNSCC patients. PD-L1, EGFR amplification, and MTAP loss/mutation could be biomarkers for cancer immunotherapy. Clinical trial information: NCT03695510. Research Sponsor: Boehringer Ingelheim, Merck.

6025 **Poster Session**

A phase 2 study of liposomal irinotecan with 5-fluorouracil and leucovorin in squamous cell carcinoma of head and neck or esophagus after prior platinum-based chemotherapy or chemoradiotherapy.

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Background: Liposomal irinotecan (nal-IRI) + 5-FU/LV has been approved and used in treating patients with metastatic pancreatic cancer after gemcitabine-based therapy through the NAPOLI-1 study result. This phase 2 trial evaluated the activity of NAPOLI-1 regimen in patients with squamous cell carcinoma (SCC) of head and neck (H&N) or esophagus that progressed on or recur after platinum-based chemotherapy or concurrent chemoradiotherapy. **Methods:** Patients with histologically confirmed SCC of H&N or esophagus whose disease progressed while on or progressed/recurred within 6 months after platinum-based chemotherapy or chemoradiotherapy, and unsuitable for further surgical or radiation intervention were eligible. Prior anti-EGFR or anti-PD1/anti-PDL1 treatment was allowed. The regimen consisted of nal-IRI 70 mg/m^2 (irinotecan free base) followed by LV 400 mg/m^2 and 5-FU 2400 mg/m^2, every 2 weeks. A Simon's 2-stage design was used with planned 30 evaluable patients in the first stage and 52 evaluable patients in total. The primary endpoint is objective tumor response. **Results:** From December 2018 to April 2020, 59 subjects were enrolled, including 16 with esophagus cancer and 43 with H&N cancer. Thirty-seven (63%) patients had metastatic disease at enrollment. The mean of treatment cycles were 5 (range, 1-21). Among the total 59 enrolled subjects, 53 subjects (14 esophagus cancer, 39 H&N cancer) were evaluable for objective tumor response. The disease control rate in esophagus cancer was 50% (7 SD, intent-to-treat (ITT) population 43.8%). For H&N patients, 1 CR, 4 PR, and 23 SD resulted in the response rate 12.8% (11.6% in ITT population) and disease control rate 72% (65% in ITT population). The median progression free survival (N = 59) was 2.5 months (esophagus/H&N: 1.5/2.7 months) and the median overall survival was 5.9 months (esophagus/H&N: 4.2/7.3 months). Seventy-eight percent of patients had ≥grade 3 treatment-related adverse events. The most frequent ≥grade 3 toxicities were decreased lymphocyte count (50.8%), decreased neutrophil count (42.4%), and decreased white blood count (33.9%). Only 3 patients (5%) had grade 3 diarrhea during the treatment period. **Conclusions:** This study showed the modest efficacy and manageable toxicity profile of nal-IRI+5-FU/LV in platinum-refractory locally advanced or metastatic H&N or esophagus cancer patients. Clinical benefits including complete tumor response were noted in H&N patients. The role of this regimen in selective patients and the efficacy of combination with immunotherapeutic agents warrant further explorations. Clinical trial information: NCT03712397. Research Sponsor: None.

6026 **Poster Session**

Preliminary results of the efficacy and safety of all-trans retinoic acid combined with low-dose apatinib in the treatment of patients with recurrent/metastatic adenoid cystic carcinoma of the head and neck.

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Background: There is no standard treatment for recurrent/metastatic adenoid cystic carcinoma of the head and neck (R/M ACCHN). Moreover, MYB and/or NOTCH1 mutation can lead to worse prognosis. Currently, anti-angiogenic targeted therapy is a relatively effective treatment option, but the accompanied toxicities may hinder the continuous medication. All-trans retinoic acid (ATRA) induces differentiation and promotes apoptosis, enhancing the cytotoxicity of anti-tumor agents; on the other hand, inhibits c-MYB and/or NOTCH1 expression. Apatinib is an oral tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor receptor 2. We reported the preliminary results of the efficacy and safety of ATRA combined with low-dose apatinib in patients with R/M ACC. **Methods:** In this exploratory study, patients with pathologically or histologically confirmed advanced, R/M ACC with measurable disease were screened. Patients who previously received anti-angiogenic therapy then withdrew due to toxicities could be recruited. ATRA was administered orally at a dose of 20 mg twice a day, and apatinib was administered orally at a dose of 250 mg once a day. The primary endpoint was objective response rate (ORR), as assessed according to the Response Evaluation Criteria In Solid Tumors v1.1. **Results:** Between March 2019 and April 2020, a total of 16 patients were enrolled. The median age was 53 years (range: 35-69), and 7 (44%) patients were male. Four (25%) patients received ATRA plus apatinib as the third-line therapy, while 12 (75%) received as the second-line therapy. Of 16 patients, 3 (19%) achieved partial response and 13 (81%) achieved stable disease (SD), with ORR of 19% and disease control rate of 100%, respectively. Among patients with SD, 12 (75%) showed tumor shrinkage (3%-28%) and 1 (6%) showed minor tumor enlargement (2%). The median follow-up time was 14.5 months (range: 8.1-22.1). Throughout the period, 5 (42%) patients developed disease progression. The 6-month and 12-month progression-free survival rates were 100% and 80%, respectively. Grade 3 adverse events included hand-foot syndrome (1 [6%]) and proteinuria (1 [6%]). No grade $\geq$4 adverse events occurred. **Conclusions:** ATRA combined with low-dose anti-angiogenic drug apatinib could be a potential treatment option for patients with R/M ACC, including those with pretreated advanced ACC after progression on or intolerance to other therapies. These encouraging results were worth further investigations, and a randomized phase 2 trial in ongoing (the Aplus study, NCT04433169). Research Sponsor: Jiangsu Hengrui Pharmaceuticals Co., Ltd.

6027 **Poster Session**

Mathematical predication models to optimize post-treatment surveillance in HPV-associated oropharyngeal cancer.

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Background: In this study we develop post-treatment imaging surveillance schedules for locally advanced oropharyngeal carcinoma (OPC) specific to the unique recurrence patterns of tumor stage and HPV status, using mathematical models. Current post-treatment imaging surveillance recommendations for OPC are not evidence based. The exception is the use of a positron emission tomography (PET) scan at 3 months post-treatment, after which practice across institutions diverge. An optimized and personalized surveillance schedule for OPC patients can minimize costs and diagnostic delays. **Methods:** A Markov multi-state model defining local and distant recurrences was trained using 2159 patients from the National Cancer Database. Patients from 2010-2015 treated at an academic or major cancer center with curative radiotherapy were included. Tumors must have been stage III to IVB (AJCC 7^{th} edition) with known p16/HPV status. Model performance was then successfully externally validated using the 2016 International Collaboration on Oropharyngeal cancer Network for Staging (ICON-S) study. Optimized radiographic surveillance schedules were created using this model, assuming a PET at month 3 and including 0 to 6 additional computed tomography (CT) scans of the neck and chest. Optimization was done for minimization of latency, defined as time between disease recurrence and radiographic discovery. **Results:** Model-selected schedules varied significantly from commonly utilized-surveillance schedules (such as imaging every 3 months within the first year from treatment) and showed lower mean diagnostic latency for every stage and HPV status (shown in Table). In the lowest risk cohort (Stage III HPV+), the optimized schedule had a sensitivity of 65% and latency of 3.1 months. In the highest risk group (Stage IVB HPV-), the optimized schedule had a sensitivity of 76% and latency of 1.9 months. **Conclusions:** Mathematical model optimization for HPV status and stage is feasible and produces non-intuitive results. These results could be used to inform surveillance if payors reimburse for fewer total scans. Across all cohorts, each added CT scan increases surveillance sensitivity and decreases latency. Incorporation of physical exam and direct visualization results into the model are still needed. Future steps include cost effectiveness research and prospective clinical trials. Research Sponsor: None.

Performance of optimized PET+6 additional CT scan surveillance strategies, divided by stage and HPV-status.

Cohort	Optimized Post-PET CT Scan Months	Sensitivity	Latency (months)	Latency (months) for Non-Optimized Post-PET CT Scans at Months 6,9,12,18,24,36
Stage III HPV+	8,13,18,23,28,33	.65	3.1	3.9
Stage III HPV-	6,9,12,15,19,23	.70	1.8	2.6
Stage IVA HPV+	7,11,15,19,23,31	.68	2.9	3.2
Stage IVA HPV-	6,10,14,18,23,30	.71	2.4	2.8
Stage IVB HPV+	6,9,13,18,23,30	.70	2.8	3.3
Stage IVB HPV-	6,9,12,16,20,24	.76	1.9	2.2

6028 **Poster Session**

Results from a phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with PD-L1 unselected metastatic second-line squamous head and neck carcinoma.

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Background: Eftilagimod alpha (efti) is a soluble LAG-3 protein that binds to a subset of MHC class II molecules to mediate antigen presenting cell (APC) activation and CD8 T-cell activation. The stimulation of the dendritic cell network and subsequent T cell recruitment with efti may lead to stronger antitumor responses in combination than observed with pembrolizumab alone. We hereby report results of the 2nd line metastatic squamous head and neck carcinoma (HNSCC) cohort (part C) of phase II trial (NCT03625323). **Methods:** Patients (pts) with HNSCC progressed on or after 1st line platinum-based therapy and unselected for PD-L1 expression were recruited into part C. The study used a Simon's 2-stage design (18 pts planned for stage 1 and 19 for stage 2), with objective response rate (ORR) by iRECIST as the primary endpoint (EP). Secondary EPs include tolerability, disease control rate (DCR), progression free survival (PFS), overall survival (OS), pharmacokinetics, pharmacodynamics and immunogenicity. Efti was administered as 30 mg subcutaneous injection every 2 wks for 8 cycles and then every 3 wks for 9 cycles with pembrolizumab (200 mg intravenous infusion every 3 wks for up to 2 yrs). Imaging was performed every 8 weeks. PD-L1 was assessed centrally (22C3 clone). The study was approved by ethics committees and institutional review boards. **Results:** In total 38 pts were enrolled. The median age was 62 yrs (range 37-84) and 89 % were male. The ECOG PS was 0 and 1 in 34% and 66%, respectively. Primary location at diagnosis was the oral cavity (29%), oropharynx (37%), hypopharynx (18%) and the larynx (16%). All PD-L1 subgroups (CPS < 1 %, ≥ 1 to ≤ 19; ≥ 20) were included. All pts were pre-treated with platinum-based chemotherapy. Pts received a median of 3.0 (range 1 – 21) pembrolizumab and 5.0 (range 1-31) efti administrations. Thirty-five (35) pts were evaluated for response (cut-off Jan 2021) with 4 (11 %) pts showing CR, 7 (20 %) pts PR, 3 (9 %) pts SD, 16 (46 %) pts PD with 5 (14 %) pts being not evaluable as per iRECIST. ORR was reported with 31.4 % (95 % CI 16.9 % - 49.3 %) and DCR 40 %Median PFS was 2.1 months and 35 % were progression free at 6 months. Median OS (46 % events) was 12.6 months. There were no adverse reactions leading to treatment discontinuation. The most common (> 10 %) treatment emergent adverse events were cough (18 %), asthenia (16 %), dyspnea (11 %), fatigue (13 %), diarrhea (11 %), hypothyroidism (11%), upper respiratory tract infection (11%) and back pain (11%). **Conclusions:** Efti in combination with pembrolizumab is safe and shows encouraging antitumor activity in platinum pre-treated 2nd line HNSCC patients. Clinical trial information: NCT03625323. Research Sponsor: Immutep S.A.

6029 **Poster Session**

Update on safety and efficacy of a phase 1/2 of SNS-301 added to pembrolizumab in patients with advanced squamous cell carcinoma of the head and neck (SCCHN).

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Background: The absence of infiltrating antigen-specific CD8+ T-cells at baseline is associated with low response rates to PD-1 blockade. SCCHN tumors often exclude effector T cells, and 2nd line response rates are low (13-18%). Highly immunogenic, antigen specific antitumor vaccines may expand intratumoral CD8+ T cells, potentially increasing durable response rates to PD-1 blockade. SNS-301 is a first-in-class, bacteriophage-based immune activating agent targeting human aspartate β-hydroxylase (ASPH), a tumor associated antigen overexpressed in multiple tumor types. SNS-301 is a self-adjuvanted vaccine consisting of λ-bacteriophage engineered to express an immunogenic fragment of ASPH fused to the phage gpD coat protein. The study objectives are to evaluate safety, immunogenicity and preliminary efficacy of SNS-301 added to pembrolizumab in patients (pts) not achieving tumor reductions on PD-1 blockade alone. **Methods:** Intradermal SNS-301 was combined with pembrolizumab in pts with locally advanced unresectable (LA) or metastatic/recurrent (met) SCCHN with a best response of stable disease (SD) or unconfirmed progressive disease (uPD) on ongoing PD-1 blockade $>$ 12 weeks. Pts provided pre and on-treatment biopsies to characterize the tumor microenvironment using Nanostring and multiplex immunohistochemistry (mIHC). Blood samples were collected to evaluate B and T cell responses using ELISA/ELISPOT assays. **Results:** As of February 4, 2021, 13 pts were enrolled. Median duration of PD-1 blockade was 48 weeks (range 14-114) at study entry. There were no DLTs & mostly Grade 1-2 unrelated adverse events. Only two related Grade 3 events were reported: rash & dehydration (also a serious adverse event). Ten pts were evaluable for efficacy: 1 pt with PD-L1 negative (neg) disease & SD on pembrolizumab monotherapy achieved a partial response (PR; -52% at 8 months), 4 pts achieved SD & 5 pts had progressive disease. Two of the pts with SD had long-lasting duration (8 & 10 months) of which the latter had PD-L1 neg disease. One pt with uPD at enrollment achieved SD for 4 months. Analyses of pre- & on-treatment biopsies from the PR pt demonstrated an increase in infiltrating CD8+ T cells, PD-L1 expression & PD-1/PD-L1 proximity measures. Nanostring analysis demonstrated increased gene expression signatures for immune cells in the PR pt that was concordant with the mIHC & clinical outcome. **Conclusions:** The combination of SNS-301 and pembrolizumab was well-tolerated and resulted in encouraging clinical efficacy in pts not expected to respond to PD-1 blockade alone. Translational data suggest cellular response to SNS-301 and transformation of a poorly inflamed tumor to an immunologically active tumor in a responding pt (PR). Based on these data, an additional cohort will start enrolling PD-1 blockade naïve pts with LA/met SCHNN in the front-line setting. Clinical trial information: NCT04034225. Research Sponsor: None.

6030 **Poster Session**

Expansion cohort validation of a clinical predictive model for head and neck cancer survival in patients treated with immune checkpoint inhibitors.

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Background: Immune checkpoint inhibitors (ICI) therapy is approved for patients (pts) with recurrent-metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). The majority of pts will die within two years of diagnosis. We have shown that pretreatment clinical characteristics may predict overall survival (OS). Here, we expand our analysis to a total of 201 pts. **Methods:** Between January 15,2016 and April 9, 2020, 201 pts with R/M HNSCC were treated with ICI as first, second line and beyond. Data on p16 status, hemoglobin (Hb), albumin, lactate dehydrogenase (LDH), neutrophil, platelet and lymphocyte count was recorded initially. OS was defined from the start of ICI to death. Progression Free Survival (PFS) was defined from the start of ICI to disease progression (PD) or death. A nomogram was created using the rms package to generate individualized survival prediction. **Results:** 201 pts were analyzed, sex: 154 male (77%), 47 female (23%), median age 61 (IQR: 55-68). ICI drug: pembrolizumab 100 (50%), nivolumab 91 (45%), ipilimumab+nivolumab 10 (5%). Line of therapy: First: 98 (49%), second and beyond: 103 (51%). Tumor site: oropharynx 84 (42%), oral cavity 45 (22%), others 72 (36%). p16 status: negative 132 (66%), positive 69 (34%). Laboratory values: Median neutrophil count: 4.58 (IQR: 3.43-6.47), Median lymphocyte count: 0.69 (IQR: 0.47-1.08), Median Platelet count: 229 (IQR: 187-300), hemoglobin (Hb) normal/low 101/100 (50%/50%), albumin: normal/low 156/45 (78%/22%), LDH: normal/high 124/77 (62%/38%). Overall response rate: 36 (18%). Median OS: 12 months (CI: 9.4-14.8), median PFS: 4 months (CI: 3.5-5.7). The variables associated with OS were neutrophil count (high) [HR 1.28 (1.08 – 1.51), *p=0.004*], lymphocyte count (high) [HR 0.75 (0.60 – 0.95), *p=0.015*], albumin (low) [HR 2.06 (1.37 – 3.10), *p<0.001*], hemoglobin (low) [HR 1.64 (1.14 – 2.35), *p=0.007*], LDH (high) [HR 1.78 (1.23 – 2.56), *p=0.002*] and p16 status (positive) [HR 0.58 (0.39-0.87), *p=0.009*]. Using the prognostic index of the chosen model, we stratified patients into three risk groups at the 33rd and 66th percentile. Median OS in the good risk group was 24 months (CI: 18.5-NR), average risk group 13.8 months (CI: 11-20), poor risk group 2.3 months (CI: 1.7-4.4). The discrimination of the model after internal validation was c-index of 0.72. **Conclusions:** A small percentage of R/M HNSCC pts treated with ICI have good long-term survival outcomes. In a larger cohort, we internally validated the utilization of a simple, inexpensive and widely accessible nomogram based on clinical and laboratory variables which can predict OS in this patient population. Research Sponsor: None.

6031 **Poster Session**

Adjuvant nivolumab following salvage resection in head and neck squamous cell carcinoma patients previously treated with definitive therapy: A single-arm phase II multi-institutional study.

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Background: Salvage surgery for locally recurrent head and neck squamous cell carcinoma (rHNSCC) results in local control rates of 33-50% but only 20-40% of patients achieve long-term survival necessitating additional therapy (Haque et al., Oral Oncol. 2019). Many patients are ineligible for re-irradiation and chemotherapy alone after salvage surgeryhas shown no survival benefit. The clinical activity and tolerability of immune checkpoint inhibitors has been demonstrated in metastatic HNSCC, but the benefit after salvage surgery (SS) has not been studied. Here we report the results of a multi-center phase II investigation of nivolumab, a PD-1 inhibitor, after SS in recurrent HNSCC (NCT03355560). **Methods:** HNSCC patients undergoing curative-intent SS were enrolled to receive 6 months of nivolumab beginning 4-11 weeks after surgery. All received radiation with or without chemotherapy as prior definitive therapy and had no other curative treatment options at the time of surgery. Key exclusion criteria included: distant metastatic disease, gross residual disease, or a history of immunodeficiency, autoimmunity, or pneumonitis. The primary endpoint was 2-year disease-free survival (DFS) measured by Kaplan Meier curves. Safety was evaluated by CTCAE v5.0. **Results:** 39 patients were enrolled. Median age was 68 years (range, 49-85). 12/39 (31%) were female. 34/39 (87%) were white. Disease sites included oropharynx 9/39 (23%), oral cavity 14/39 (36%), and larynx 16/39 (41%). P16 status was 26% (+), 48% (-), and 26% (unknown). 17/39 (44%) had high risk pathologic features (positive margins or extranodal spread) at time of SS. 28/39 (72%) patients experienced treatment-related adverse events (TRAE), the most common of which were fatigue (26%), hypothyroidism (10%) and acneiform rash (13%). Grade 3-4 TRAEs were rare, occurring in 3/39 (8%) patients and included diarrhea, oral pain, neck pain, productive cough, stridor, and COPD exacerbation. 3/39 (8%) required treatment discontinuation and there were no grade 5 events. The 2-year DFS was 60% (95%CI 0.39-0.91). 2-year overall survival was 74% (95% CI 0.54-1). In single-cell multiplex cytokine analysis, patients who relapsed following adjuvant nivolumab had a significantly higher proportion of peripheral blood CD8 T cells which displayed a polyfunctional cytokine profile. IFN-γ and Granzyme were the dominant CD8 cytokines in both responders and non-responders, however CD8 expression of MIP1a and TNF-α were significantly higher in patients who ultimately relapsed. **Conclusions:** Nivolumab after salvage surgery in rHNSCC is well tolerated and shows promising antitumor activity in this high-risk patient population with unmet need. Immunotherapy after salvage surgery should be studied in randomized clinical trials. Clinical trial information: NCT03355560. Research Sponsor: BMS.

6032 **Poster Session**

A phase III multicenter randomized clinical trial to compare cisplatin plus fluorouracil with or without docetaxel as the first-line induction chemotherapy for locoregionally advanced nasopharyngeal carcinoma: Long-term outcomes update.

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Background: A phase III multicenter prospective randomized controlled trial was conducted to compare cisplatin plus 5-fluorourcil with or without docetaxel as first-line induction chemotherapy in the patients with locoregionally advanced nasopharyngeal carcinoma (LANPC). Here, we report on the long-term outcomes and late toxicities of the trial (NCT01536223). **Methods:** Patients with newly diagnosed LANPC, stage III-IV disease, Karnofsky performance score≥70, without metastasis were eligible and randomly assigned 1:1 to TPF versus PF for three cycles. The primary end point was progression-free survival; local control, OS and advent events were important key secondary end points. The Kaplan-Meier method and the log-rank test were used to conduct and compare the survival curves in this study. **Results:** Two hundred ninety-nine patients were enrolled. 276 patients (138 TPF and 138 PF) were evaluable. Baseline characteristics were well-balanced between two groups, and the median age was 48 (range, 18-60 years). The ORR rates after induction chemotherapy and chemoradiotherapy were 90.6% and 9797.8% in TPF group and 87.0% ($P > 0.05$) and 97.8% ($P > 0.05$), respectively. The median follow-up was 99 months. For all patients, the 5- and 8-year OS and PFS were 76.9% and 74.9%, 72.3% and 69.1%, respectively. PF was associated with a similar PFS versus TPF (5-year PFS of 72.4% versus 73.2%, P =.747), and an equivalent OS at 5 years (79.2% and 79.1%, P = 0.519). Treatment-related grade 3 to 4 advent events were less frequent with PF compared with TPF. **Conclusions:** With prolonged follow-up, the survival outcomes in the PF group were not non-inferiority to those in the TPF group, but grade 3 to 4 advent events were less frequent. Clinical trial information: NCT01536223. Research Sponsor: None.

6033 **Poster Session**

Effect of neoadjuvant systemic therapy given during window trials on quality metrics in resectable head and neck squamous cell carcinoma.

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Background: Quality oncologic care, including negative surgical margin status, adequate lymph node yield and prompt initiation of adjuvant treatment, impacts disease control and overall survival in patients with mucosal head and neck squamous cell carcinoma (HNSCC). The aim of this study was to ascertain the effect of neoadjuvant systemic therapy given during window trials on oncologic quality metrics in patients with delayed definitive surgery for a HNSCC. **Methods:** Treatment-naïve patients with HNSCC participating in one of two window of opportunity clinical trials at UPMC from 2009-2019 were included. Neoadjuvant regimens consisted of one dose of cetuximab (n = 33) or anti-ErbB3 antibody (n = 9) within 28 days of surgery. Sociodemographic, clinical and tumor staging were recorded. The primary outcome was overall oncologic quality, as defined as a composite measure of negative margin status, adequate lymph node yield, completion of adjuvant therapy (if indicated) and time to initiation of adjuvant therapy within 6 weeks of surgery. Secondary outcomes were difference in clinical and pathologic stages and overall survival (OS). **Results:** A total of 42 patients with a mean age of 57.1 (±10.2) years and median follow-up of 58 months were analyzed. 29 patients had clinical stage IVA disease with 43% (18/42) oral cavity, 36% (15/42) larynx/hypopharynx and 21% (9/42) oropharynx primaries. All patients underwent surgery following neoadjuvant systemic therapy. In 30 patients (71%), all oncologic quality markers were achieved. Pathological downstaging occurred in 21% (9/42) of patients with 4 patients no longer meeting criteria for adjuvant treatment and were observed. 3 patients showed pathological upstaging. The 3-year OS were 76% (95% CI of 63.6-88.4), respectively. Patients with a pathologic downstage migration (64.9%, 95% CI of 49.9-79.8) had higher 5-year OS compared to those without (57.8%, 95% CI of 40.1-76.4, P = 0.046). **Conclusions:** Most patients receiving neoadjuvant systemic therapy on window trials prior to surgery met all oncologic quality markers. Importantly, even with brief window trial therapy pathologic downstaging was achieved and associated with significantly better overall survival. Research Sponsor: None.

6034 **Poster Session**

Phase II trial of combined durvalumab plus tremelimumab with proton therapy to boost the abscopal effect for recurrent or metastatic head and neck squamous cell carcinoma.

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Background: This phase 2 study investigated whether durvalumab plus tremelimumab with proton therapy improves objective response rate (ORR), overall survival (OS), and progression-free survival (PFS) in heavily treated recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) via boosting abscopal effect. **Methods:** Thirty-one patients who have previously received more than one chemotherapy regimen, including at least one platinum-based regimen and have at least two measurable lesions enrolled at Samsung medical center. Patients received durvalumab 1500mg intravenously (IV) in combined with tremelimumab 75 mg IV every four weeks for four cycles followed by durvalumab 1500mg every four weeks. After one cycle of durvalumab and tremelimumab combination, proton therapy was performed with a total dose of 25 Gy in 5-Gy daily fractions to one of the measurable lesions. We assessed the target lesion response outside the radiation field by RECIST criteria 1.1 to evaluate the abscopal effect. **Results:** Between March 2018 and July 2020, 31 patients were enrolled. The median age was 59 years, and median two prior chemotherapy regimens were administered. With 24.8 months of follow-up, the median number of cycles of immunotherapy was three. The ORR was 27.3%, including one complete response and five partial responses. Median OS was 6.4 months (95% CI, 1.0 to 11.8), and median PFS was 2.4 months (95% CI, 0.6 to 4.2). Median duration of response was 15.9 months (range 3.7 – 21.2). Grade 3 or higher adverse events were observed in 6 (27.3%) patients; anemia (n = 1), constipation (n = 1), electrolyte imbalance (n = 2), hyperglycemia (n = 1), pneumonia (n = 1). **Conclusions:** Combination of durvalumab/tremelimuab with proton therapy is well tolerable and shows encouraging anti-tumor efficacy in non-irradiated tumor lesions of heavily treated HNSCC patients. These results suggest that the combination of immunotherapy with proton therapy might enhance the abscopal effect. Clinical trial information: NCT03450967. Research Sponsor: AstraZeneca.

6035 **Poster Session**

Maintenance intervention to improve survival in patients with metastatic nasopharyngeal carcinoma who benefit from first-line treatment: A prospective multicenter randomized controlled clinical study.

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Background: The role of drug maintenance intervention in improving survival outcomes remains controversial.To investigate the safety and effect of Tegafur(S1) maintenance intervention in patients with metastatic nasopharyngeal carcinoma who benefit from the first-line treatment in a multicenter randomized controlled study, and to identify the related biological prognostic factors and guide the individualized treatment choice. **Methods:** Patients with metastatic nasopharyngeal carcinoma in the Fourth Affiliated Hospital of Guangxi Medical University and other cancer centers who met the inclusion criteria were randomly divided into maintenance therapy group: S1 maintenance therapy until disease progression or intolerance; Observation group: follow-up to disease progression. PFS, overall survival (OS) and adverse reactions of S1 maintenance therapy were compared between the two groups. The correlation between EBV-DNA, human serum amyloid A (SAA) and prognosis was evaluated. **Results:** Follow-up was conducted to May 2020, with a median follow-up of 19.8 months (6.1-51.3 months), 183 cases were evaluable (88 cases in S1 maintenance treatment group, 95 cases in observation group). Compared with the observation group, the S1 maintenance treatment group significantly increased patients' median PFS (16.2 months vs. 8.7 months, $P < 0.001$) and median OS (32.1 months vs. 18.2 months, $P < 0.001$). Reduced the risk of poor prognosis for PFS and OS (PFS: HR 0.305, 95%CI 0.211-0.441, < 0.001; OS: HR 0.363, 95%CI 0.238-0.553, $P < 0.001$). In the maintenance treatment group, the median S1 treatment lasted for 14 courses (4-58 courses), and the main adverse reactions were grade 1 skin pigmentation, oral mucositis, hand-foot syndrome, nausea, etc. No grade 4 toxic reaction occurred, and it was well tolerated. Compared with observation patients with negative EBV-DNA, observation patients with positive EBV-DNA had a higher risk of poor prognosis for PFS (HR 1.764, 95%CI 1.078-2.887, $P = 0.024$). The risk of poor prognosis in patients with positive EBV-NDA was significantly reduced by 61.1% (< 0.001) for PFS and 65.5% ($P = 0.001$) for OS ($P = 0.001$). Compared with the observation group with stable SAA expression, S1 maintenance therapy significantly improved the prognosis of patients. Patients with continuous decline in SAA had a 61.9% lower risk of poor prognosis in PFS ($P < 0.001$) and a 60.2% lower risk of poor prognosis in OS ($P = 0.007$). **Conclusions:** For patients with metastatic nasopharyngeal carcinoma who benefit from first-line treatment, maintenance therapy of S1 can significantly improve the survival prognosis and is well tolerated. Patients with positive EBV-DNA and continuous decline in SAA may benefit more from maintenance intervention. Clinical trial information: ChiCTR-IOR-16007939. Research Sponsor: Guangxi Natural Science Foundation(-China)Liuzhou City Science and technology research projects (China).

6036 **Poster Session**

Final analysis of a phase 1b, randomized, multicenter study of talimogene laherparepvec (T-VEC) plus pembrolizumab (pembro) combination for the treatment (Tx) of recurrent/metastatic squamous cell carcinoma of the head and neck (R/M HNSCC): MASTERKEY-232.

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Background: T-VEC, a genetically modified herpes simplex virus-1, is the first FDA- and EMA-approved oncolytic viral immunotherapy designed to enhance systemic antitumor immune responses. R/M HNSCC is a disease with considerable clinical complexity and poor prognosis. Pembro is a PD-1-specific humanized monoclonal antibody currently approved as first-line Tx for this disease, but there is an unmet need among many patients (pts). To meet this gap, the safety and preliminary efficacy of T-VEC plus pembro in pts with R/M HNSCC was evaluated in a phase 1b study (Harrington et al. *Clin Cancer Res*. 2020). Here, we present results of the final analysis of this study (NCT02626000). **Methods:** Eligible pts ($\geq$18 yrs) had ECOG-PS of 0 or 1; histologically confirmed R/M HNSCC of the oral cavity, oropharynx, hypopharynx, or larynx unsuitable for curative surgical resection or radiotherapy; platinum-refractory and with injectable tumors. Pts with known active CNS metastases and any systemic or local therapy 28 days before enrollment were excluded. T-VEC was injected intralesionally up to 8.0 mL of 10^6 PFU/mL according to lesion sizes on day 1; after 3 weeks, subsequent doses of $\leq$8.0 mL of 10^8 PFU/mL were given Q3W. Pembro was given intravenously at 200 mg Q3W. Pts were followed-up for 36 mos after the last patient was enrolled in the study. Key endpoints (irRECIST per investigator assessment) were objective response rate (ORR), best overall response (BOR), disease control rate (DCR), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety. **Results:** A total of 36 pts (80.6% male) were enrolled and treated: 28 (77.8%) had confirmed PD-L1-positive tumor (CPS $\geq$1), 5 (13.9%) were HPV-positive, 13 (36.1%) had metastatic disease, and 19 (52.8%) had prior lines of therapy in the R/M setting. At the final analysis, 7 pts (19.4%) completed the study, and 29 (80.6%) discontinued the study due to death. Safety profile was consistent with that at 1-yr analysis (Harrington et al. *Clin Cancer Res*. 2020). Confirmed ORR was seen in 16.7% (95% CI, 6.4–32.8). No patient had a complete response as their BOR, 6 (16.7%) had a partial response, 8 (22.2%) had stable disease, 6 (16.7%) had progressive disease, 6 (16.7%) were unevaluable, and 10 (27.8%) died before the first response assessment. The DCR was 38.9% (95% CI, 23.1–56.5). The median DOR was 45.9 mos (95% CI, 8.5–NE). The median PFS was 3.0 mos (95% CI, 2.0–5.8), and the median OS was 5.8 mos (95% CI, 2.9–11.4). **Conclusions:** The safety results at 3 yrs for T-VEC plus pembro in pts with R/M HNSCC were consistent with those of the 1-yr analysis. Although the response rate was consistent with that observed with pembro alone in historical HNSCC studies, the extended DOR in responding patients warrants further investigation. Clinical trial information: NCT02626000. Research Sponsor: Amgen.

6037 **Poster Session**

Interim analysis of IMMUNEBOOST-HPV: A multicenter, randomized, open label, phase II study evaluating the feasibility, and tolerance of neoadjuvant nivolumab in high-risk HPV driven oropharynx cancer.

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6037Background: Among HPV-positive Oropharyngeal Cancer (OPC) patients (pts), some has a less favorable prognosis (T4, N2/N3, smokers >10 pack-year [p/y]). We assume that neoadjuvant immunotherapy might improve their oncological outcomes, so we tested nivolumab (N) prior to ChemoRadiaTion (CRT). **Methods**: The study population is restricted to HPV positive OPC pts (both p16+ & HPV-DNA+) with advanced disease (T4, N2/N3) or a smoking history >10 p/y. Pts were randomly allocated 1:2 to receive either cisplatin-based CRT (n=20) or 2 cycles of N 240 mg followed by CRT (n=41). The Primary Endpoint (PE) is the rate of pts who can receive Full Treatment in Due Time (FTDT), according to these criteria: a) 2 N infusions on day 1 and on day 14-16 b) CRT started between days 28-37 after the 1st N infusion c) No RT break ≥1 week d) RT dose received >95% of theoretical dose e) Cisplatin dose received ≥200 mg/m^2 To achieve FTDT, all criteria are required in the Experimental Arm (EA) while only criteria c), d), and e) are required in the Control Arm (CA). In the EA, the trial was designed in 2 steps, with FTDT rate of 88% considered as inacceptable versus an alternative of 98%, a type I error of 0.10, and a type 2 error of 0.08. As per protocol, patient accrual was temporarily suspended after inclusion of 19 pts in the EA (1st step) and results were reviewed by an Independent Data Monitoring Committee (IDMC). To resume pts' inclusion, FTDT had to be achieved in 18 pts in the EA. **Results**: From 07/2019 to 09/2020, 30 pts were enrolled including 11 in the CA (demographics are summarized in table). 2 pts in the EA did not reach the PE. For the 1st patient, the cisplatin dose was <200 mg/m^2 due to grade 1 hearing loss and grade 2 tinnitus (1st cycle: 100 mg/m^2, 2nd cycle: 80 mg/m^2, no 3rd cycle). For the 2nd patient, CRT began at D38 due to logistical issues (maintenance of RT devices). As this delay was unrelated to N or to patient's condition, the IDMC considered that the inclusions could resume for the 2nd step. 7 N-related Adverse Events (AE) were reported in 4 pts including 3 serious AE (ankylosing spondylitis flare-up, colitis, diabetic ketoacidosis). **Conclusions**: Neoadjuvant N before CRT seems feasible for the treatment of OPC pts. The trial has reopened to inclusion as recommended by the IDMC. Clinical trial information: NCT03838263. Research Sponsor: Programme Hospitalier de Recherche Clinique en Cancérologie (PHRC-K) financé par le ministère de la Santé (Direction générale de l'offre de soins (DGOS)), Pharmaceutical/Biotech Company.

	CA	EA
Age		
Median	62	58
Min; Max	50-69	36-70
Sex		
Male	10 (91%)	14 (73.7%)
Female	1 (9%)	5 (26.3%)
ECOG		
ECOG 0	11 (100%)	17 (89.5%)
ECOG 1	0	2 (10.5%)
T-stage		
2	2 (18.2%)	5 (26.3%)
3	2(18.2%)	5 (26/3%)
4	7 (63.6%)	9 (47.4%)
N-stage		1 (5.3%)
0	2 (18.2%)	
1	7 (63.6%)	10 (52.6%)
2	2 (18.2%)	6 (31.6%)
3	0	2 (10.5%)
Tobacco consumption		
Non	3 (27.3%)	4 (21.1%)
Former	7 (63.6%)	14 (73.7%)
Current	1 (9.1%)	1 (5.3%)

6038 **Poster Session**

Use of cetuximab added to weekly chemotherapy to improve progression-free survival in patients with recurrent metastatic head and neck squamous cell carcinoma after progression on immune checkpoint inhibitors.

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Background: Immune checkpoint inhibitors (ICI) are currently approved in the treatment of patients (pts) with recurrent-metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). The majority of pts will progress on ICI. Little is known regarding the best treatment approach for this patient population. We previously showed that the combination of weekly carboplatin, paclitaxel and cetuximab was associated with reduced risk of grade 3/4 toxicities, which makes it an ideal regimen in this setting. Here; we report the outcomes of pts with R/M HNSCC who were treated with chemotherapy alone vs weekly chemotherapy plus cetuximab after progression on ICI. **Methods:** Between January 15th 2016 and April 9th 2020, 154 pts who progressed on ICI were analyzed. Among these pts, 64 had received subsequent systemic therapy and met the inclusion criteria. Progression Free Survival (PFS) was defined as the time elapsed between initiation of subsequent chemotherapy and tumor progression or death. Overall Survival (OS) was defined as the time elapsed between initiation of subsequent chemotherapy to death. Descriptive statistics and Cox regression were used to explore study variables. **Results:** 64 pts received subsequent chemotherapy after progression on ICI. 28 pts (44%) received a combination of weekly chemotherapy plus cetuximab. This regimen included carboplatin AUC 1.5, paclitaxel 45 mg/m^2, and cetuximab loading dose of 400mg/m^2 followed by weekly dose of 250 mg/m^2. 36 pts (56%) received chemotherapy alone without cetuximab. These regimens included capecitabine, afatinib, and gemcitabine, among others. Sex: 51 males (80%), 13 females (20%), age (median): 61 (IQR: 53-66), tumor site: oropharynx 32 (50%), oral cavity 11 (17%), larynx 8 (12%), other sites 13 (21%). P16 status: negative 36 (56%), positive 28 (44%). Prior ICI drug: pembrolizumab 34 (53%), nivolumab 26 (41%), ipilimumab + nivolumab 4 (6%). Median follow up: 9 months (IQR: 5-13). Overall response rate: weekly chemotherapy plus cetuximab 32%, chemotherapy alone 22% (p = 0.4). Pts who received chemotherapy alone had a median PFS of 3.2 months (CI: 2-5) vs 5.6 months (CI: 4.3-10.1) in the weekly chemotherapy plus cetuximab group. After adjusting for p16 status and prior ICI drug, PFS was improved in the group that received weekly chemotherapy plus cetuximab vs. chemotherapy alone (HR: 0.52; CI: 0.28-0.98; p = 0.042). Median OS was 10 months (CI: 8.5-NR) in the weekly chemotherapy plus cetuximab group vs 8.7 months (CI: 5.7-13.8) in the chemotherapy alone group (HR: 0.84; CI: 0.4-1.8; p = 0.8). **Conclusions:** Pts with R/M HNSCC who progressed on ICI experience longer PFS with the addition of cetuximab to weekly chemotherapy. Further investigation in a larger cohort of pts is needed to fully assess the impact on survival for this treatment combination. Research Sponsor: None.

6039 **Poster Session**

Adjuvant toripalimab or combined with S-1 in recurrent, previously irradiated head and neck squamous cell carcinoma treated with salvage surgery: A phase II clinical trial (The RePASS study).

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Background: The predominant pattern of failure for Head and Neck Squamous Cell Carcinoma (HNSCC) is locoregional disease. Salvage surgery remains the standard of care for operable disease. Re-irradiation after previous full course radiotherapy generally has been considered contraindicated. Since anti-PD-1 antibodies were efficacious and safety in recurrent/metastatic HNSCC, this study aimed to evaluate the efficacy and safety of adjuvant toripalimab (anti-PD-1 antibody) in recurrent, previously irradiated HNSCC treated with salvage surgery. **Methods:** This study was a single-arm, phase II study. Patients with HNSCC occurring in an area of previously irradiated and with at least one high risk factors after salvage surgery (1- positive margin; 2- extranodal extension; 3- rStaging T3-4/N2-3/T2N1) were enrolled. In the Stage I of 12 patients, patients received toripalimab 240mg once every 3 weeks until confirmed disease progression or unacceptable toxicity, for 12 months. In the stage II of 8 patients with PD-L1 CPS$\geq$1, patients received toripalimab combined with S-1, which was given orally at 25 mg/m^2, twice daily, on day 1 to 14, repeated every 21 days for 4-6 cycles. The primary endpoint was 1-year progression-free survival (PFS). We hypothesized a 1-year PFS of at least 56% and assumed a null hypothesis of 34%. A retrospective cohort of 16 patients was compared. **Results:** Between May 2019 and December 2020, 20 patients were enrolled. High-risk factors included ENE (35%), positive margin (25%), T3-4(30%) and T2N+(10%). Seventeen patients have PD-L1 CPS$\geq$1 and 3 patients have CPS $<$ 1. With a median follow-up of 11.2 months, estimated 1-year PFS and overall survival was 57.0% (95% confidence interval, 32%– 77%) and 79.2% (51%–91%). The primary PFS endpoint has exceeded the hypothesis and its median has not been reached. When compared to the retrospective cohort, the PFS was significantly better(p=0.001), even for Stage I patients(Median PFS: 5.1 vs 3.7 months, p=0.03). Stage II patients resulted a better PFS and OS compare to stage I (p=0.02 and p=0.002). For patients with CPS$\geq$1, 1-year PFS and OS was 79.1% (95% confidence interval, 51%–91%) and 91.7%(68%–99%), which were significantly better than patients with CPS $<$ 1 (p=0.001 and p=0.05). Adjuvant Toripalimab or combine with S-1 was well-tolerated with no grade 3-4 toxicity and dose interruption as a result of treatment-related adverse event only occurred in 2 patients. Flow cytometry revealed that patients with short PFS had fewer baseline overall count of B cells(p=0.09). **Conclusions:** Adjuvant Toripalimab or combined with S-1 after salvage surgery is efficacious and safety in recurrent, previously irradiated HNSCC, and a better PFS was observed in patients treated with combined therapy and with CPS$\geq$1. Further randomized trials are warranted. Clinical trial information: NCT04126460. Research Sponsor: Shanghai Junshi Biosciences.

6040 **Poster Session**

Update and external validation of a multivariable prediction model for tube feeding dependency for at least four weeks during chemoradiotherapy for head and neck cancer.

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Background: Patients who receive chemoradiation or bioradiation (CRT/BRT) for locally advanced head and neck squamous cell carcinoma (LAHNSCC) often experience high toxicity rates, which may interfere with oral intake, leading to (temporary) tube feeding (TF) dependency. International guidelines recommend gastrostomy insertion when the expected use of TF exceeds four weeks. In this study we aimed to update and externally validate a prediction model to identify patients in need for TF for at least four weeks, meeting the international criteria for prophylactic gastrostomy insertion. **Methods**: This retrospective multicenter cohort study was performed in four tertiary referral head and neck cancer centers in the Netherlands. The prediction model was developed using data from the University Medical Center Utrecht and the Netherlands Cancer Institute. The model was externally validated in patients from the Maastricht University Medical Center and Radboud University Medical Center. The primary endpoint was TF, initiated during or within 30 days after completion of CRT/BRT, and administered for at least four weeks. Potential predictors were retrieved from patient medical records and radiotherapy dose-volume parameters were calculated. **Results**: The developmental and validation cohort included 409 and 334 patients respectively. Multivariable analysis showed significant predictive value ($p < 0.05$) for adjusted diet at start of CRT/BRT, percentage weight change prior to treatment initiation, WHO performance status, tumor-site, nodal stage, mean radiation dose to the contralateral parotid gland, and mean radiation dose to the oral cavity. The area under the receiver operating characteristics curve for the updated model was 0.73 and after external validation 0.64. Positive and negative predictive value at 90% cut off were 80.0% and 48.2% respectively. **Conclusions**: This externally validated prediction model to estimate TF-dependency for at least four weeks in LAHNSCC patients performs well. This model, which will be presented, can be used in clinical practice to guide personalized decision making on prophylactic gastrostomy insertion. Research Sponsor: NUTRIM Graduate Programme.

6041 **Poster Session**

Racial and regional differences in incidence of oropharyngeal cancer in the United States during 2001 to 2017.

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Background: The incidence of human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma (OPSCC) has been reported to be increasing among both middle-aged and elderly adults in the United States. This study was to assess racial and regional differences in the incidence of OPSCC among adults in the US. **Methods:** We included 271,037 adult patients ≥ 20 years old diagnosed with potentially HPV-related OPSCC from the US Cancer Statistics 2001–2017 database which essentially covered the entire US population. Incidence of OPSCC was age- adjusted to the US standard population. Annual percentage change (APC) in the incidence was assessed across races/ethnicities and regions of residence. **Results:** Among these adults with potentially HPV-related OPSCC from 2001-2017, 5.3% were Hispanics, 83.0% were non-Hispanic Whites, and 9.2% were non-Hispanic Blacks, and 79.1% were male. Incidence of OPSCC increased from 3.9 per 100,000 in 2001 to 4.0 per 100,000 in 2017 (APC 0.43, 95% confidence interval (CI) 0.01, 0.85) in Hispanics, increased from 5.3 per 100,000 in 2001 to 8.6 per 100,000 in 2017 (APC 2.97, 95% confidence interval (CI) 2.71, 3.24) in non-Hispanic Whites, and decreased from 6.3 per 100,000 in 2001 to 5.1 per 100,000 in 2017 (APC -1.27, 95% confidence interval (CI) -1.56, -0.99) in non-Hispanic Blacks. The incidence increased from 5.8 per 100,000 in 2001 to 7.8 per 100,000 in 2017 (APC 1.94, 95% confidence interval (CI) 1.67, 2.21) in the South, increased from 5.0 per 100,000 in 2001 to 7.1 per 100,000 in 2017 (APC 2.13, 95% confidence interval (CI) 1.92, 2.34) in the Northeast, increased from 4.9 per 100,000 in 2001 to 6.3 per 100,000 in 2017 (APC 1.85, 95% confidence interval (CI) 1.53, 2.17) in the West, and increased from 4.9 per 100,000 in 2001 to 7.7 per 100,000 in 2017 (APC 2.79, 95% confidence interval (CI) -2.52, 3.07) in the Midwest. The incidence decreased from 0.9 per 100,000 in 2001 to 0.8 per 100,000 in 2017 (APC -0.81, 95% confidence interval (CI) -1.41, -0.20) among adults 20-44 years old, increased from 9.0 per 100,000 in 2001 to 12.7 per 100,000 in 2017 (APC 2.01, 95% confidence interval (CI) 1.66, 2.36) among adults 45-64 years old, and increased from 10.9 per 100,000 in 2001 to 16.7 per 100,000 in 2017 (APC 2.96, 95% confidence interval (CI) 2.75, 3.16) among adults 65+ years old. **Conclusions:** OPSCC incidence increased across racial/ethnic groups, regions, and age groups from 2001 to 2017, except that the incidence decreased among non-Hispanic Blacks and young people. Underlying causes for the decreasing trend in the incidence of OPSCC among certain groups need further investigation. Research Sponsor: U.S. National Institutes of Health, Center for Interdisciplinary Research in Women's Health, The University of Texas Medical Branch.

6042 **Poster Session**

Efficacy and toxicity of weekly paclitaxel, carboplatin, and cetuximab as induction chemotherapy or in cases of metastases or relapse for head and neck cancer in elderly or frail patients.

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Background: Standard of care treatments for locally advanced and metastatic head and neck squamous cell carcinoma (HNSCC) are not well tolerated, particularly in elderly or frail patients. One combination that has been studied in recent years is paclitaxel, carboplatin and cetuximab (PCC). Studies have shown this regimen yields promising results when used as an induction chemotherapy for locally advanced disease. PCC has also been studied in patients with metastatic or recurrent incurable disease, and has shown good response with tolerable toxicity rates, but there is a relative dearth of evidence surrounding its use. **Methods:** This retrospective observational study utilized EMR data analysis software to generate the cohort of adult patients that received PCC for HNSCC in 2014-2019 as well as demographic data. Chart review was used to gather details about the patients' tumors and clinical course. Modified RECIST response rates (MRRR), progression free survival (PFS) and overall survival (OS) were the primary end points calculated for the metastatic/recurrent group, and percentage of successful inductions (e.g., patients went on to definitive treatment, avoided surgery) and MRRR were used for the induction group. **Results:** There were 80 patients in the cohort. The average age was 65 (range 33-84) and the patients were 81% male. The most common tumor site was the tongue (25 patients), followed by tonsil (15), oropharynx (9), and larynx (7). 13 patients had p16 positive disease. Most patients had Stage IVA (36 patients), followed by IVB (20), and IVC (15); the remainder had stage III or below or unknown stage. The most common reasons patients did not receive cisplatin were performance status (13 patients), hearing loss (11), concern for nephrotoxicity (6) and age (5). 97.5% of patients experienced at least one adverse effect. The most common adverse effect was dermatologic (69%), followed by hematologic (51%), fatigue (41%) and gastrointestinal symptoms (41%). 53 patients (66%) experienced at least one dose interruption due to adverse effects. 11 patients (14%) stopped treatment due to toxicities. 58 patients received PCC for metastatic or recurrent disease. They had received a median of 1 line of systemic treatment prior; 72% had prior radiation, and 26% had prior salvage surgery. The MRRR was 22% (5 patients with complete response, 8 partial response, 15 stable, 27 progression). There was a 7.0 month mean PFS, and 17.3 month mean OS. Of the 22 patients who received PCC as induction, 86% (19) successfully reached their induction endpoint. The MRRR was 64% (8 patients with complete response, 6 partial response). **Conclusions:** PCC is a relatively well-tolerated combination with a very good induction success rate. More research is needed around alternate options for frail and elderly patients with HNSCC. Research Sponsor: None.

6043 **Poster Session**

Palbociclib (P) in patients (pts) with head and neck cancer (HNC) with *CDKN2A* loss or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study.

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Background: TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Results in a cohort of HNC pts with *CDKN2A* loss or mutation treated with P are reported. **Methods:** Eligible pts had advanced HNC, no standard treatment options, measurable disease, ECOG PS 0-2, and adequate organ function. Genomic testing was performed in CLIA-certified, CAP-accredited site selected labs. Pts received P at 125 mg orally once daily for 21 days, followed by 7 days off until disease progression. Pts matched to P had *CDKN2A* loss or mutation and no *RB*mutations. Simon 2-stage design tested the null disease control (DC) - defined as partial (PR), complete response (CR) or stable disease at 16+ weeks (SD 16+) - rate of 15% vs. 35% (power = 0.85; $\alpha = 0.10$). If $\geq$2 of 10 pts in stage 1 have DC, 18 more pts are enrolled. If $\geq$7 of 28 pts have DC, the null DC rate is rejected. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and safety. **Results:** 28 pts (64% male) with HNC with *CDKN2A*loss (20 pts) or mutation (8 pts) were enrolled from June 2016 to Sept 2019. All were eligible for efficacy and toxicity. Demographics and outcomes are summarized in Table. No objective response (OR) and 10 pts with SD16+ (9 with *CDKN2A* loss, 1 with mutation) were observed for a DC rate of 37% (95% CI: 21%, 50%); the null DC rate of 15% was rejected (p=0.005). 14 pts had at least one grade 3-5 adverse or serious adverse event (AE/SAE) at least possibly related to P with the most common being low WBC/platelets. Other grade 3-4 AEs included anemia, fatigue, hypocalcemia, and syncope. There was one pt with grade 5 respiratory failure likely due to extensive lung metastases and aspiration but P-related pneumonitis could not be ruled out. **Conclusions:** Monotherapy P demonstrated modest anti-tumor activity and clinically significant AEs in heavily pre-treated pts with HNC with *CDKN2A*loss or mutation. Additional study is warranted to confirm the efficacy of P in pts with HNC with *CDKN2A*loss or mutation. Clinical trial information: NCT02693535. Research Sponsor: Pfizer.

Demographics and efficacy outcomes (N=28).	
Median age, yrs (range)	**58 (33, 80)**
ECOG PS, %	
0	25
1	68
2	7
Prior systemic regimens, %	
1-2	25
≥3	75
DC rate, % (OR or SD16+) (95% CI)	37 (21, 50)
OR rate, % (95% CI)	0 (0, 12)
Median PFS, wks (95% CI)	9.4 (8.0, 20.3)
Median OS, wks (95% CI)	42.0 (22.9, 68.1)

6044 **Poster Session**

Capecitabine maintenance therapy after induction chemotherapy in newly diagnosed metastatic nasopharyngeal carcinoma: An open-label, randomized, controlled, phase trial.

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Background: Capecitabine maintenance therapy improves outcomes in various tumor types, but minimal data are available on the effect of capecitabine maintenance therapy in metastatic nasopharyngeal carcinoma (NPC). We aimed to investigate whether capecitabine maintenance therapy would prolong the progression-free survival (PFS) of newly diagnosed metastatic NPC, in comparison to best supportive care (BSC). **Methods:** This was an open-label, randomized, controlled, phase trial. Eligible patients for maintenance randomisation were aged 18-65 years old with newly diagnosed metastatic NPC at the Sun Yat-Sun University Cancer Center (SYSUCC), had completed 4 to 6 cycles of induction chemotherapy as per protocol and had achieved disease control to protocol treatment, including capecitabine. Patients were randomly assigned 1:1 to capecitabine maintenance (oral 1,250 mg/m^2/day on days 1-14 every 21 days) for up to 24 months with BSC or BSC alone. The primary endpoint was PFS. The secondary endpoints included overall survival, duration of response, objective response rate and adverse effects. Analyses were done by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT02460419 and is ongoing and no longer recruiting new patients. **Results:** Between May 16th, 2015, and January 9th, 2020, 140 metastatic NPC patients were screened, and 104 eligible patients were randomly assigned to capecitabine maintenance plus BSC (n = 52) or BSC alone (n = 52). After a median follow-up of 33.1 months (IQR, 21.5-50.7 months), median PFS was 35.2 months in the capecitabine maintenance group and 9.1 months in the BSC group (HR: 0.426; 95%CI: 0.248-0.731, P = 0.001). The most commongrade 3 or 4 adverse events during maintenance therapy were hand-foot syndrome (10.0%), nausea/vomiting (6.0%), fatigue (4.0%), and mucositis (4.0%). Totally 37 deaths occurred during follow-up, 14 (26.9%) in the capecitabine maintenance group and 23 (44.2%) in the BSC group. Overall survival data was immature. No deaths in the capecitabine maintenance group were deemed treatment related. **Conclusions:** Capecitabine maintenance significantly improved PFS in patients with newly diagnosed metastatic NPC who achieved disease control after induction chemotherapy compared to BSC and exhibited low grade and manageable toxicities. Clinical trial information: NCT02460419. Research Sponsor: None.

6045 **Poster Session**

Evaluation of radiomics as a predictor of tumor hypoxia and response to anti-PD-1 mab treatment (IO) in recurrent/metastatic HNSCC patients (R/M).

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Background: There is a great need for non-invasive predictors of the tumor microenvironment and the efficacy of anti-PD-1 mAb treatment (IO) in R/M HNSCC patients. We previously showed that lower tumor hypoxia was associated with increased efficacy with IO (*Journal of Clinical Oncol.* 38, no. 15_suppl (May 20, 2020) 6546) and now we evaluate the predictive value of radiomics in this same patient cohort. **Methods:** We studied radiomic signatures in a cohort of 36 patients with R/M HNSCC treated with IO. Treatment response was evaluated using RECIST 1.1. Patients were categorized as: Responders (R) ie CR, PR, SD and non-Responders (NR) i.e PD. As per our previous analysis (ref above) hypoxia was evaluated on archival FFPE samples via immunofluorescent imaging and defined by the ratio of percent area (% CAIX) / the mean intensity (Int) of carbonic anhydrase IX in tumor (%CAIX/Int). ImageJ software was used to determine %CAIX and Int. Feature extraction was performed on the pre-immunotherapy baseline CT scans. The lesions were segmented using 3D slicer v4.10.2 to create a volume of interest (VOI) for radiomic texture analysis (TA). A total of 400 features (10 histogram-based and 390 second-order texture features) were calculated from each extracted volume of interest (VOI). Radiomic features were obtained using a feature selection approach based on Least Absolute Shrinkage and Selection Operator (LASSO). Selected features were used to build a classification model, using XGboost, for prediction of tumor response to immunotherapy. Cross-validation was performed using the Leave One Out Cross Validation (LOOCV) approach for the XGBoost method to evaluate the robustness of the estimates and calculated accuracy, sensitivity, specificity and p-value. **Results:** Our patient cohort had a median age of 59, 69% male, 58% smokers. 61% received IO for platinum failure, 39% frontline. Primary site included 39% OC, 22% OPC (38% HPV positive), 17% Larynx, 5% hypopharynx, and 17% other. Radiomics applied to the primary HNSCC tumor highly predicted tumor hypoxia status with a sensitivity, specificity, and accuracy of 78%, 83%, and 81%, respectively, $p = 0.0001$. To predict response, we applied radiomics to both the primary HNSCC tumor and pathological lymph nodes; radiomics was also able to predict whether a patient would be a responder ($N = 8$) versus a non-responder ($N = 28$) to IO based on the pre-immunotherapy baseline CT scan. The sensitivity, specificity, and accuracy were 93%, 88%, and 92%, respectively, $p = 0.02$. **Conclusions:** Even in a small cohort, radiomics could predict response to IO and tumor hypoxia in R/M HNSCC patients. To our knowledge this is the first evaluation of this kind in this patient population. Further evaluation of radiomics as a predictor of efficacy with IO and the tumor microenvironment is warranted. Research Sponsor: U.S. National Institutes of Health.

6046 **Poster Session**

Refining TNM-8 M1 categories with anatomic subgroups for previously untreated de novo metastatic nasopharyngeal carcinoma.

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Background: The eighth edition TNM (TNM-8) classified de novo metastatic (metastatic disease at presentation) nasopharyngeal carcinoma (NPC) as M1 without further subdivision. However, survival heterogeneity exists and long-term survival has been observed in a subset of this population. We hypothesize that certain metastatic characteristics could further segregate survival for de novo M1 NPC. **Methods:** Patients with previously untreated de novo M1 NPC prospectively treated in two academic institutions (The University of Hong Kong [n = 69] and Provincial Clinical College of Fujian Medical University [n = 114] between 2007 and 2016 were recruited and re-staged based on TNM-8 in this study. They were randomized in 2:1 ratio to generate a training cohort (n = 120) and validation cohort (n = 63) respectively. Univariable and multivariable analyses (MVA) were performed for the training cohort to identify the anatomic prognostic factors of overall survival (OS). We then performed recursive partitioning analysis (RPA) which incorporated the anatomic prognostic factors identified in multivariable analyses and derived a new set of RPA stage groups (Anatomic-RPA groups) which predicted OS in the training cohort. The significance of Anatomic-RPA groups in the training cohort was then validated in the validation cohort. UVA and MVA were performed again on the validation cohorts to identify significant OS prognosticators. **Results:** The training and the validation cohorts had a median follow-up of 27.2 months and 30.2 months, respectively, with the 3-year OS of 51.6% and 51.1%, respectively. Univariable analysis (UVA) and multivariable analysis (MVA) revealed that co-existing liver and bone metastases was the only factor prognostic of OS. Anatomic-RPA groups based on the anatomic prognostic factors identified in UVA and MVA yielded good segregation (M1a: no co-existing liver and bone metastases and M1b: co-existing both liver and bone metastases; median OS 39.5 and 23.7 months respectively; $P = .004$). RPA for the validation set also confirmed good segregation with co-existing liver and bone metastases (M1a: no co-existing liver and bone metastases and M1b: co-existing liver and bone metastases), with median OS 47.7 and 16.0 months, respectively; $P = .008$). It was also the only prognostic factor in UVA and MVA in the validation cohort. **Conclusions:** Our Anatomic-RPA M1 stage groups with anatomical factors provided better subgroup segregation for de novo M1 NPC. The study results provide a robust justification to refine M1 categories in future editions of TNM staging classification. Research Sponsor: None.

6047 **Poster Session**

Outcomes and prediction of lethal recurrence after transoral robotic surgery for HPV+ head and neck cancer.

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Background: Increasing use of transoral robotic surgery (TORS) for human papilloma virus-related (HPV+) head and neck squamous cell carcinomas (HNSCCs) is likely to impact recurrence patterns and outcomes. Profiling HPV+ HNSCC recurrences after TORS and identifying features predictive of lethal outcome would facilitate tailoring adjuvant therapy and guide surveillance post-therapy. This study uses long term follow-up of patients at the first institution to bring TORS into clinical use to describe the recurrence patterns, distinguish outcomes associated with distinct patterns, and create a risk model for lethal recurrence. **Methods:** This retrospective cohort study at a single academic tertiary center analyzed 634 consecutive, treatment-naïve HPV+ HNSCC patients receiving TORS and neck dissection for clinical features at presentation and pathologic traits identified by surgical resection. The main outcomes were distant metastatic recurrence (DMR) and locoregional recurrence (LRR). Multivariate logistic regression with backward stepwise elimination was used to identify features associated with recurrence. **Results:** 6.5% of patients developed DMR at a median of 12.4 months after surgery and had a 5-year overall survival (OS) of 52.5% (95% CI, 33.9%-68.2%), whereas the 6.2% patients developing LRR alone had 5-year OS of 83.3% (95% CI, 66.2%-92.2%; P =.01). After recurrence, 5-year progression-free survival was 24.7% (95% CI, 11.4%-40.7%) for DMR cases and 85.7% (95% CI, 65.1-94.6%) for cases with LRR alone (P <.001). Comparing recurrent cases to recurrence-free controls showed DMR to be independently associated with positive surgical margins (AOR 5.7; 95% CI, 2.1-15.7) and advanced clinical stage at presentation (AOR 6.5; 95% CI, 1.9-23.0). Positive margins increased DMR risk by 4.2-fold and reduced 5-year disease-free survival (P <.001) in early-stage cases (Table), which comprised 95% of the cohort. By contrast, isolated LRR was associated with failure to receive indicated adjuvant therapy and was usually controllable by salvage therapy. **Conclusions:** Based on the largest single institution cohort reported to date, long term oncologic outcomes for HPV+ HNSCCs after TORS are excellent overall. While DMR is often fatal, LRR is salvageable with durable disease control. In addition to standard staging criteria, positive margins indicate substantially higher risk of DMR but not LRR. A risk model for DMR that incorporates margin status after TORS is relevant for guiding clinical trial design and whole-body surveillance. Research Sponsor: U.S. National Institutes of Health.

Risk model for DMR.

Advanced clinical stage	Positive margin	Total patients (N)	DMR absent (N)	DMR present (N)	Risk DMR (%)	Coefficient in model[a]	Adjusted odds ratio	95% CI	*P* value
No	No	270	244	26	9.6	-	[reference]	-	-
No	**Yes**	**20**	**12**	**8**	**40.0**	**1.8**	**6.3**	**2.3-16.7**	**<.001**
Yes	No	12	7	5	41.7	1.9	6.7	2.0-22.6	.002
Yes	Yes	0	-	-	-	-	-	-	-

a. Coefficient in logistic regression model. Intercept is -2.2.

6048 **Poster Session**

Ultra-sensitive detection and quantification of HPV DNA in the plasma of patients with oropharyngeal squamous cell carcinoma (OPSCC) enrolled in the OPTIMA 2 treatment de-escalation trial.

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Background: Human papillomavirus (HPV) infection is a primary factor driving the increasing incidence of OPSCC. As patients with HPV+ OPSCC show significantly improved treatment response and prognosis, there is an urgent need to de-escalate treatment of HPV+ OPSCC that optimizes oncologic control while minimizing treatment-related toxicity. Cell-free HPV DNA (cfHPV-DNA) from plasma specimens represents a promising noninvasive surrogate of disease burden in these patients. To enable cfHPV-DNA analysis as a strategy to monitor response to therapy and guide treatment de-escalation, we developed a highly sensitive assay for HPV16/18 detection and quantification in plasma, based on the SafeSEQ next-generation sequencing (NGS) technology. **Methods:** Longitudinal plasma samples were collected from patients with locoregional HPV+ OPSCC treated on our institutional de-escalation protocol of induction chemoimmunotherapy followed by risk/response stratified de-escalated locoregional therapy, OPTIMA 2 (NCT03107182). Neck CT or MRI was obtained for all patients at baseline and following induction chemoimmunotherapy; radiographic response to induction therapy was assessed per RECIST 1.1 criteria. cfHPV-DNA was quantified in plasma samples collected at baseline and at the end of induction therapy. Changes in cfHPV-DNA levels were correlated with radiographic response. **Results:** The SafeSEQ HPV assay demonstrates high analytical sensitivity, with ability to detect a single copy of HPV DNA. Replicate testing of contrived samples containing HPV 16/18 DNA at defined levels revealed robust quantitative detection across a dynamic range over 5 orders of magnitude. The assay showed a low level of background signal ($<$ 0.04 copies per sample) across 20 healthy donor samples, indicating high specificity. In plasma samples collected at baseline from patients enrolled in OPTIMA 2, cfHPV-DNA was detected at levels ranging from 1 to $>$ 30,000 copies/ml. A high correlation was observed between dynamic changes in patients' cfHPV-DNA levels and radiographic responses following induction therapy. Furthermore, in samples collected longitudinally during induction therapy, changes in cfHPV-DNA levels accurately tracked radiographic responses to therapy. **Conclusions:** We have developed a highly sensitive and specific cfHPV-DNA detection assay based on SafeSEQ NGS technology and have successfully applied it to monitor therapeutic response in HPV+ OPSCC patients. The assay exhibits robust quantitative detection of HPV across a broad range of levels, even when only a few copies are present, enabling high-resolution molecular monitoring. Prospective studies are underway to further evaluate the kinetics of cfHPV-DNA as a predictor of response to therapy in order to more precisely guide the management of patients with HPV+ OPSCC. Research Sponsor: Sysmex.

6049 **Poster Session**

The impact of tumor infiltrating lymphocytes (TILs) on disease progression in human papillomavirus (HPV)-related oropharyngeal squamous cell carcinoma.

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Background: In the head and neck, human papillomavirus-related oropharyngeal squamous cell carcinoma (HPV(+)OPSCC) has a better prognosis and more tumor infiltrating lymphocytes (TILs) compared to its HPV(-) counterpart. Within HPV(+)OPSCC, the prognostic value of TILs in the primary tumor and in metastatic lymph nodes is not well understood. **Methods:** This is a matched case-control study at a tertiary care center of HPV(+)OPSCC patients who underwent primary surgery between 05/2007–12/2016. Cases developed locoregional recurrence or distant metastases during follow-up, while controls did not during a similar duration of follow-up. Pairs were matched on age, American Joint Committee on Cancer (AJCC) 8th edition pathologic stage, sex, year of surgery, degree of adjuvant treatment, comorbidities, and smoking status. One representative H&E slide of the primary tumor and lymph node (when nodal disease was present) from each patient was independently reviewed by two pathologists (JG, MR) blinded to outcome, for tumor TILs (tTILs) density (defined as % TILs), presence/absence of desmoplastic stroma, and when stroma was present, for stromal TILs (sTILs) density (defined as relative crowding of TILs). The Brandwein-Gensler pattern of invasion (POI) score was used to grade the primary tumor. Interrater agreement was assessed using Cohen's *kappa*. Associations between TILs and time to disease progression were assessed using Cox proportional hazards regression models. **Results:** 41 case-control pairs (N=82) were included in the study: 38 (46%) were AJCC pStage I, 37 (45%) were pStage II, and 7 (9%) were pStage III; 22 (27%) underwent surgery alone, 15 (18%) underwent surgery with adjuvant radiotherapy, and 45 (55%) underwent surgery with adjuvant chemoradiation. Interrater agreement was fair for tTILs density in the primary tumor (k=0.24) and lymph node (k=0.23), moderate for desmoplastic stroma in the primary tumor (k=0.58) and lymph node (k=0.64), moderate for sTILs density in the primary tumor (k=0.58) and lymph node (k=0.48), and fair for the POI score (k=0.17). tTILs density $\geq$10% (HR 0.35, 95% CI 0.14-0.90, p=0.028) and a moderate/dense sTILs density (HR 0.15, 95% CI 0.04-0.68, p=0.014) in the primary tumor were significantly associated with decreased risk of disease progression. An aggressive POI score of III or IV was significantly associated with increased risk of disease progression (HR 4.00, 95% CI 1.34-11.96, p=0.013). None of the study measures in the lymph node were significantly associated with disease progression. **Conclusions:** In HPV(+)OPSCC, a higher density of tumor and stromal TILs and nonaggressive POI in the primary tumor specimen may indicate a lower risk of disease progression. TILs may serve as a powerful prognostic marker for the adaptive immune response to this disease. Research Sponsor: None.

6050 **Poster Session**

Endostar combined with intensity-modulated radiotherapy in low-risk local advanced nasopharyngeal carcinoma: A phase II, randomized, multicentric clinical trial.

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Background: A Phase II, randomized, prospective, multicentric trial was conducted to evaluate the efficacy and safety of Endostar plus radiotherapy in patients with low-risk local advanced nasopharyngeal carcinoma (NPC). This study reported the preliminary results of NCT02237924. **Methods:** From 09/2014 to 08/2016, patients with low-risk local advanced NPC were randomly treated with Endostar plus radiotherapy (ERT group, n=60) and concurrent chemoradiotherapy (CCRT group, n=60). Primary endpoint was the 5-year overall survival (OS) rate. The secondary endpoints were 3-year OS rate, progression free survival (PFS) rate, loco-regional recurrence free survival (LRRFS) rate and distance metastasis free survival (DMFS) rate. **Results:** After a median follow-up of 47 months, 3-year OS rate were 93.2% and 79.3% (p=0.032), 3-year PFS rate were 89.8% and 70.6% (p=0.011), 3-year DMFS rate were 93.2% and 80.7%, in two groups, respectively (P=0.042). 3-year LRRFS rate were 96.6% and 92.0% in two groups, respectively (but P=0.565). For short-term curative effects, CR rate were 71.2% and 60.0% for primary tumor, 74.6% and 63.3% for cervical lymph nodes, in two groups, respectively ($P < 0.05$). Moreover, the incidences of adverse events were significantly lower in ERT group compared with in CCRT group. The grade 3/4 Hyponatraemia (0 [0%] vs 3 [5%], p=0·04), the grade 1/2 vomiting (10 [16.7%] vs 52 [86.7%], p=0.000), dry mouth (45 [75.0%] vs 56 [93.3%], p=0.012), leukopenia (22 [36.7%] vs 42 [70.0%], p=0.000) and weight loss (30 [50.0%] vs 45 [75.0%], p=0.005). No patients died of treatment-related causes. **Conclusions:** OS, PFS, and DMFS rates can be improved, adverse events be reduced, with better tolerability, by Endostar plus radiotherapy, when compared to concurrent chemoradiotherapy for local advanced low-risk NPC. Clinical trial information: NCT02237924. Research Sponsor: National Natural Science Foundation of China.

Survival outcomes to treatment.

	Endostar + radiotherapy (n = 60)	Chemo-radiotherapy (n = 60)	Hazard ratio* (95% CI)	P value†
Overall survival				
Deaths	5(8.3%)	13(21.7%)		
patients with 3 years OS	93.2% (86.8-99.6)	79.3% (68.9-89.7)	0.342 (0.122-0.960)	0.032
Progression-free survival				
Failures	7(11.7%)	17(28.3%)		
patients 3 years PFS rate	89.8% (82.2-97.4)	70.6% (58.8-82.4)	0.362 (0.150-0.873)	0.018
Locoregional failure-free survival				
Locoregional failures	3(5.0%)	4(6.7%)		
without locoregional failure at 3 years	96.6% (91.9-99.9)	92.0% (84.4-99.6)	0.651 (0.146-2.911)	0.572
Distant failure-free survival				
Distant failures	4(6.7%)	11(18.3%)		
without distant failures at 3 years	93.2% (86.7-99.7)	80.7% (70.5-90.9)	0.325 (0.103-1.021)	0.042

6051 **Poster Session**

Phase I study of functionalized hafnium oxide nanoparticles (NBTXR3) activated by radiotherapy in cisplatin-ineligible locally advanced HNSCC patients.

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Background: The non-surgical standard of care (SOC) for the treatment of locally advanced head and neck squamous cell carcinoma (LA HNSCC) patients is concurrent chemoradiation with high dose cisplatin or cetuximab in case of contra-indication to cisplatin. However elderly patients, and those with poor performance status, comorbidities, and/or intolerance, may not benefit from these SOC treatments and represent a high unmet need. New approaches are thus needed to improve clinical outcomes without adding toxicity. NBTXR3, a novel radioenhancer, composed of functionalized hafnium oxide nanoparticles**,** is injected once intratumorally and activated by radiotherapy (RT).NBTXR3 increases the RT energy deposit inside tumor cells and subsequently increases tumor cell death compared to RT alone, while sparing healthy tissues. We present here the results of the dose expansion part of the phase I study evaluating NBTXR3 plus intensity modulated radiation therapy (IMRT) in this population. **Methods:** Patients with stage III-IVA or T3/T4 (AJCC/UICC TNM staging system 8th ed.) HNSCC of the oropharynx or oral cavity, ineligible to cisplatin or cetuximab and amenable for RT, received a single intratumoral injection of NBTXR3 and IMRT (70 Gy in 35 fractions /7 weeks). A classical 3 + 3 dose escalation design has tested four doses of NBTXR3, equivalent to 5, 10, 15, and 22% of baseline theoretical tumor volume. The RP2D established as 22% of baseline tumor volume is further tested in the dose expansion part. The primary endpoints of the dose expansion part are objective response rate (ORR) and complete response rate (CRR) of the primary tumor, by imaging according to RECIST 1.1. Safety is also evaluated. **Results:** As of August 13, 2020, 43 patients have been treated in the phase I dose expansion part. The median age was 70.7 years old (range: 50.7- 89.9), 70% of patients had cardiac disorder risk, 44% had gastrointestinal disorder risk and 44% metabolic and nutrition disorder risk. The median tumor volume was 42.8 mL (range: 1.3 - 222.3). At a median time of 7.8 months after NBTXR3 injection, the ORR of the primary lesion was 83.9% and the CRR 67.7% in the evaluable population for efficacy (N = 31). Three patients (7%) experienced at least one serious adverse event (AE) related to the injection procedure and/or NBTXR3 which represented less than 1% of all reported AEs. RT-related toxicity was as expected with IMRT. Three deaths due to AEs related to RT and other causes were reported. The recruitment is ongoing and updated efficacy and safety results will be presented. **Conclusions:** NBTXR3 intratumoral administration followed by IMRT may represent an option in elderly patients or patients with multiple comorbidities with LA-HNSCC who have limited therapeutic options. NBTXR3 activated by RT showed promising anti-tumor efficacy, supporting further evaluation in a phase III randomized trial. Clinical trial information: NCT01946867. Research Sponsor: Nanobiotix, SA.

6052 **Poster Session**

Inductive camrelizumab and apatinib for patients with locally advanced and resectable oral squamous cell carcinoma: A single-arm trial (Icemelting trial).

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Background: In patients with locally advanced oral squamous cell carcinoma (LAOSCC), major pathologic response (MPR) to induction therapy may translate into improved survival. The induction therapy using chemo-free drugs, such as the combination of anti-PD1 and anti-VEGFR drugs, has not been well issued in LAOSCC. **Methods:** A prospective single arm trial (NCT04393506) has been performed to evaluate the induction therapy of anti-PD1 and anti-VEGFR protocol in LAOSCC patients at clinical stage III and IVA. The patients received three cycles of intravenous Camrelizumab (PD-1 antibody, 200mg) on d1, d15, d29; and oral Apatinib (anti-VEGFR inhibitor, 250mg) daily, initiating on d1, ending on the 5th day before surgery. Radical surgery was planned on d42-d45. Post-operative radiotherapy was planned within 1.5 months after surgery, based on clinical and pathological stage. The primary endpoints were MPR and safety; primary tumors were assessed for the percentage of residual viable tumor that was identified on HE staining, and tumors with no more than 10% viable tumor cells were considered as MPR. This study has been approved by institutional ethics committee at Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine. **Results:** From April to December 2020, 21 patients were enrolled in this trial, and one patient withdraw from the trial at the beginning of treatment. The induction therapy was well-tolerated with no grade 3-4 toxicity or serve induction therapy-related AEs. One patient required surgery delay for 7 days due to unexplainable cTnI elevation. One patient put off Camrelizumab for 14 days due to grade 2 thrombocytopenia. One patient suspended Apatinib for 21 days due to grade 2 Hyperbilirubinemia. The induction therapy did not effect on the subsequent standard treatment. MPR rate was 40% (8/20), including 5% (1/20) pCR. Radiological evaluation of response to induction therapy showed 3 PR, 10 SD, 5 PD and 2 NA. Weak correlation was found between pathologic and radiological evaluation on induction therapy. Combined positive score (CPS) of PD-L1 expression in biopsy was evaluated in 19 patients; all 4 patients with CPS$\geq$ 20 had MPR, 3 out of 11 patients with 1$\leq$CPS $<$ 20 had MPR, and 1 out of 4 patients with CPS $<$ 1 had MPR. **Conclusions:** The chemo-free protocol of induction therapy using Camrelizumab and Apatinib is safe and well-tolerated for the patients with LAOSCC. The MPR rate is much higher using the anti-PD1 and anti-VEGFR protocol than the traditional induction chemotherapy protocol in LAOSCC. Clinical trial information: NCT04393506. Research Sponsor: Shanghai Municipal Commission of Health and Family Planning, Program of Shanghai Academic/Technology Research Leader.

6053 **Poster Session**

Neoadjuvant and adjuvant nivolumab and lirilumab in patients with recurrent, resectable squamous cell carcinoma of the head and neck.

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Background: Locoregional recurrence (LRR) is a major cause of death for patients (pts) with squamous cell carcinoma of the head and neck (SCCHN). With therapy options limited by prior treatment, surgery often represents the best chance for disease control. Emerging data suggests a role for neoadjuvant immunotherapy in upfront resectable SCCHN and the importance of NK cells in the tumor microenvironment. We hypothesized that dual immune checkpoint inhibition (anti-PD-1, nivolumab [N] and anti-KIR, lirilumab [L]) before and after salvage surgery would improve 1-year disease-free survival (DFS). **Methods:** Pts with operable LRR of SCCHN (any HPV or smoking status) with a disease-free interval of $>$ 8 weeks after curative intent therapy were eligible for this phase II trial. Pts received a single dose of pre-op N (240 mg) + L (240 mg) 7-21 days before surgery, followed by 6-cycles of adjuvant N+L on days 1, 15 (N alone) of a 28-day cycle (C) for C1-3; and on day 1 for C4-6. Primary endpoint was 1-year DFS; 37 DFS events among N = 54 pts provided 81% power to detect improvement in 1-year DFS from 57% to 67.5% (one-sided 10% Wald's test). Secondary endpoints: safety, radiologic response (RECIST v1.1) to pre-op N+L, and overall survival (OS). Correlatives included tumor sequencing, PD-L1 status, and immunoprofiling. **Results:** Between 3/15/18 and 5/29/20, N = 29 enrolled (stopped due to expiration of drug supply). Among 28 treated pts, median age: 66, 18% (5/28) women, 83% smokers; primary site: 10 oral cavity, 8 oropharynx (5/8 HPV+), and 10 larynx/hypopharynx. 96% (27/28) had prior HN radiation; 71% (20/28) prior chemotherapy. There were no delays to surgery. Grade 3+ adverse events: 11% (3/28); no deaths from treatment. At time of surgery, 96% (27/28) had stable disease radiologically with 3 showing regression, 4% (1/28) had disease progression. Pathologic response to N+L was observed in 43% (12/28): 4/28 (14%) major (tumor viability, TV $\leq$10%); 8/28 (29%) partial (TV $\leq$50%). PD-L1 CPS at surgery was similar regardless of pathologic response (p = 0.63). 68% (19/28) completed all 6-cycles of adjuvant N+L; N = 1 came off for toxicity. Ten pts (36%) recurred (local = 8, distant = 2). 5/28 (18%) had positive margins, of which 4 (80%) recurred; 4/28 (14%) declined to start adjuvant N+L, of which 3 (75%) later recurred. At median follow-up of 20.2 months, 1-year DFS70% (95%CI, 48-84%) and 1-year OS: 85% (95%CI, 65-94%). Median tumor mutational burden was 4 (range, 1-11). *TP53* was the most frequent alteration (78%, 21/27). CD39 expression by TILs and CD38 expression by circulating CD4/8+ T cells increased after N+L exposure ($p < 0.05$). **Conclusions:** Neoadjuvant and adjuvant N+L was safe and well tolerated. We observed a 43% pathologic response rate prior to salvage surgery, with a favorable 1-year DFS of 70% and 1-year OS $>$ 80% among previously irradiated pts. Further evaluation of this strategy is warranted (NCT03341936). Research Sponsor: Bristol Myers Squibb.

6054 **Poster Session**

Transoral robotic surgery for human papillomavirus-associated oropharynx squamous cell carcinoma: Recurrence and survival in the Veterans Affairs health system.

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Background: Most transoral robotic surgery (TORS) literature comes from single and multi-institutional studies at tertiary-care academic intuitions. Long-term outcomes for patients with HPV-mediated oropharyngeal squamous cell carcinoma (HPV-OPSCC) treated with upfront TORS in other hospital settings across the United States are largely unknown. We present long-term recurrence and survival outcomes from a novel Veterans Health Administration (VHA) longitudinal dataset that includes patient-level data. **Methods:** Retrospective analysis of national VHA patients with p16-positive OPSCC diagnosed between January 2010 and December 2016, treated with TORS primary tumor resection with neck dissection. Outcome measures included: Cancer-specific survival (CSS), progression free survival (PFS), overall survival (OS), recurrence, extranodal extension (ENE), positive surgical margin (PSM), and adjuvant therapy regimen. **Results:** One hundred sixty-one patients were included of whom 29 (18%) were low-risk [0-1 metastatic lymph nodes, negative margins]; 45 (28%) intermediate-risk [close surgical margins, 2 to 4 metastatic nodes, LVI or PNI, pathologic T3 or T4 tumor]; and 87 (54%) high-risk [PSM, ENE, and/or $\geq$ 5 metastatic nodes]. ENE was present in 41% of cases and 24% of cases had positive surgical margins. Median follow-up was 5.6 years (95% CI 3.0-9.3). The 5-year CSS rates for low, intermediate, and high-risk groups were: 100%, 90.0% (95% CI 75.4-96.1%), and 88.7% (78.3-94.2%). On univariable analysis, pathologic factors associated with inferior CSS were: pT3-T4 tumor category (HR 3.81, 95% CI 1.31-11; p = 0.01), presence of more than four metastatic lymph nodes (HR 3.41, 95% CI 1.20-11; p = 0.02), and ENE (HR 3.53, 95% CI 1.06-12; p = 0.04). Close or PSM were not associated with CSS (HR 0.67, 95% CI 0.21 – 2.14; p = 0.50). In the low-risk group, 48% avoided adjuvant therapy and although there were five recurrences, none died from cancer. The intermediate-risk group was treated with adjuvant radiation in 64% of cases, and chemoradiation in 29% of cases; and there were five locoregional recurrences and three distant recurrences. Adjuvant chemoradiation was used in 68% of high-risk cases. Of the seven total patients with distant recurrences, six died of their disease. **Conclusions:** Our findings in this national cohort of Veterans with HPV-OPSCC demonstrate that TORS followed by adjuvant therapy yields favorable survival outcomes. Tumor-category, ENE, and more than four nodal metastases were the strongest adverse features in our data, and surgical margins did not have a significant impact on survival. Further investigations with large cohorts and prospective clinical trials are needed to elucidate the true oncologic implications of high-risk features and to identify patients best suited for de-intensified treatment. Research Sponsor: U.S. Department of Defense. Grant Number: W81XWH-17-PCRP-PRA.

6055 **Poster Session**

Survival outcomes in primary head and neck adult sarcoma: A systematic review and meta-analysis.

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Background: Head and neck sarcomas (HNS) are rare entities and confer substantial morbidity and mortality. Yet, the optimal management of HNS remains unclear. This study aimed to describe the epidemiology of HNS and to identify the most favorable treatment approach. **Methods:** We performed a systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, using the PubMed (Medline), EMBASE, and Cochrane Library databases, queried from 1990 until present. Articles in the English language reporting on survival outcomes of adult primary HNS patients treated with curative-intent were included. All estimates were weighted based on sample size. Analysis of variance (ANOVA) and two-sample t-tests were used as appropriate. Meta-analyses were performed using random effects models. This study was registered with PROSPERO, CRD42021220970. **Results:** A total of 3652 articles were identified, with 42 articles reporting on 21228 patients, meeting inclusion criteria. Mean ± SD age was 56.7 ± 14.6 years with 14170 (67.0%) men and 6991 (33.0%) women. The most common locations included skin and soft tissues (n = 12749, 63.3%), bones of skull and face (n = 2256, 11.2%), and oral cavity (n = 1775, 8.8%). The most common histologies included undifferentiated pleomorphic sarcoma (n = 5065, 24.8%), osteosarcoma (n = 2578, 12.6%), Kaposi sarcoma (n = 2316, 11.3%), chondrosarcoma (n = 2141, 10.5%), and hemangiosarcoma (n = 2072, 10.1%). 5459 patients had early stage I-II disease (76.9%) whereas 1643 had late stage III-IV disease (23.1%). Most received surgery alone (n = 10968, 61.0%), 3917 (21.8%) received surgery and radiotherapy (RT), 2173 (12.1%) received definitive RT/chemoradiotherapy (CRT), 811 (4.5%) received surgery and CRT, and 98 (0.5%) received surgery and chemotherapy. Negative margins were achieved in 6081 (76.5%). Mean ± SD follow-up was 55.3 ± 42.8 months. Weighted mean, 2-, 5-, and 10-year overall survival (OS) were 78.5 months, 75.9%, 63.2%, and 54.9% respectively. There was no significant difference in mean OS (P = 0.674) or 5-year OS (P = 0.965) between patients who received surgery alone, multimodality treatment with surgery and RT/CRT, or definitive RT/CRT. Mean ± SD 5-year OS was significantly higher with negative margins (62.7 ± 20.8%) compared with positive margins (22.7 ± 19.1%; P = 0.001). Mean ± SD local recurrence rate (LRR) was 32.0 ± 13.0%. LRRs were 41.8% for definitive RT/CRT, 39.3% for surgery and CRT, 33.6% for surgery alone, 24.7% for surgery and chemotherapy, and 20.1% for surgery and RT (P = 0.126). **Conclusions:** In the largest HNS study to date, negative margins were associated with an improvement in OS. Multimodality treatment did not confer an OS benefit. Definitive RT/CRT may be associated with a higher LRR. Randomized trials are needed to establish the optimal treatment approach for HNS. Research Sponsor: None.

6056 **Poster Session**

A phase II study of PRV111 nanoengineered cisplatin patch as a neoadjuvant therapy for early-stage oral squamous cell carcinoma (OSCC).

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Background: OSCC is a devastating disease causing substantial morbidity and mortality. Despite advancements in the conventional therapeutic approaches, surgical resection often leads to permanent disfigurement, while radiotherapies and systemic platinum-based chemotherapy result in significant toxicities, affecting patient wellbeing and quality of life. Thus, development of novel therapeutic approaches is paramount to improve health outcomes and survival of patients with OSCC. Systemic toxicity is often dose limiting, but could be tentatively reduced by locoregional administration. We have developed PRV111, a nanotechnology based patch for local and regional delivery of highly concentrated potent cisplatin, designed to penetrate tumor tissue, reach and enter regional lymph nodes and avoid systemic circulation. Here we present the results of phase 1/2 CLN-001 trial, designed to improve efficacy and reduce toxicity by neoadjuvant treatment with PRV111. **Methods:** A phase 1/2, single arm, open-label CLN-001 (NCT03502148) study has enrolled 12 patients with confirmed OSCC; unknown nodal involvement, no distant metastasis, and tumor size $\leq$ 4.0 cm. Three weeks prior to surgery, patients were administered 1 cycle of standalone neoadjuvant PRV111, consisting of up to 4 treatment visits (each visit dose: $\leq$12mg of cisplatin, each patch loading dose: 2mg of cisplatin). The primary endpoints were safety, efficacy and tumor reduction in ~ 7 days by greater than 30%. Secondary endpoints included nanoengineered patch consistent and complete adhesion to mucosal surfaces and uniform drug release. Exploratory endpoints included immunogenesis/immunomodulation. **Results:** PRV111 successfully met all clinical primary endpoints, as well as safety and efficacy objectives. It caused over 70% tumor reduction in ~7 days with over 87% response rate across 10 subjects. No dose-limiting toxicities, serious adverse event, or systemic toxicities were reported and no locoregional recurrences were evident in 6 months. PRV111 induced ~15 times increase in tumor infiltrating lymphocytes compared with the initial biopsy. Concentrations of cisplatin found in the tumor and regional lymph nodes were over 300 and 100 times higher respectively as compared with IV cisplatin, with only negligible amount of cisplatin found in the blood. Grade 1 or 2 oral and tongue pain induced by the treatment were the most common adverse events. Furthermore, 97.5% successful patch performance was achieved across 182 patches used in the study. **Conclusions:** Adding neoadjuvent PRV111 to the care for patients with OSCC may improve the surgical outcome and increase event free survival. Given these encouraging results, future studies are needed to establish the application of this non-invasive platform in head and neck SCC and other epithelial cancers, including anal, colorectal, genitourinary, nasal, and skin. Clinical trial information: NCT03502148. Research Sponsor: U.S. National Institutes of Health, Other Government Agency, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.

6057 **Poster Session**

Impact of comprehensive geriatric assesment (CGA) in the treatment decision and outcome of older patients with locally advanced head and neck squamous cell carcinoma (LA-HNSCC).

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Background: Up to 24% of patients (pts) newly-diagnosed with LA-HNSCC are 70 years old (yo). NCCN guidelines recommend a geriatric assessment to guide treatment decisions in this pts population. Comprehensive geriatric assessment (CGA) of older HNSCC pts was implemented at our institution in 2018. We evaluated the impact of CGA in treatment decision and outcome and compare it to a control cohort with no CGA treated within the same institution. **Methods:** Retrospective single-institution analysis of two consecutively-treated cohorts of newly-diagnosed elderly LA-HNSCC pts treated at the Catalan Institute of Oncology: a cohort treated based on CGA between 2018-2020; and a control cohort with no CGA treated based on physician criteria following tumor board decision between 2016-2018. Pts demographics and disease characteristics were obtained from our in-site prospective database. Treatment received (standard, adjusted, palliative-intent, best supportive care [BSC]), treatment completion rate (TCR) an overall response rate (ORR) after conservative treatment were collected and compared for both cohorts using chi-square. **Results:** A total of 197 pts were included: CGA cohort =81; Control cohort=96. Baseline characteristics were similar between cohorts (Table). Pts in CGA cohort were classified as fit (F) 35 (34.7%), medium-fit (MF) 51 (50.5%) and unfit (UF) 15 (14.9%) according to CGA results. CGA changed final treatment decision following tumor board in 31 % of the cases. Pts were more likely to receive standard treatment in the CGA cohort when compared control (36 vs 21%; *p = 0.048*), with no differences observed in TCR (84% vs 86%; *p = 0.805*). In pts who underwent conservative treatment, ORR was similar between CGA and control cohort (73.9% vs 66.7 %; *p = 0.082*), respectively. Tumor progression was the major cause of death in both groups. **Conclusions:** Older pts with LA-HNSCC who underwent CGA were more likely to receive standard treatment than those who did not, supporting the relevance of CGA for clinical decision-making in this pt population. No differences were observed in CRR, TCR or death cause. In-deep survival analysis are on-going. Research Sponsor: None.

Cohorts characteristics.

	CGA cohort (n= 81)	Control cohort (n=96)
Median AGE (range)	80 (70-96)	77 (70-92)
Smoking Status: active/former/never: n (%)	23/ 45/ 32	31/ 40/ 29
Oral Cavity/Oropharynx/Larynx/Hypopharynx: n (%)	44/ 11/ 29/ 16	33/ 22 /37/ 8
Stage III / IV: n (%)	30 vs 70	21 vs 79
Treatment received: Standard(%) Adjusted(%) Palliative–intend treatment(%) BSC (%)	36: F 55; MF 38; UF 7 53: F 26; MF 63; UF 12 7: F 0; MF 33; UF 66.7 4: F 0; MF 33; UF 66.7	21: 75 PS ≤1; 25 PS ≥ 2 63: 57 PS ≤1; 43 PS ≥2 5: 60 PS≤1; 40 PS≥2 11: 10 PS≤1; 90 PS ≥2

6058 **Poster Session**

Survival (OS) and progression-free survival (PFS) results after induction chemotherapy (IC) followed by de-escalated chemoradiotherapy (RDCRT) for locally advanced (LA) HPV positive oropharynx cancer (HPVOPC.

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Background: HPVOPC has a significantly better prognosis and survival than HPV negative cancer resulting in overtreatment with significant acute and late toxicities and mortality. Radiation therapy is the single greatest determinant of toxicity. Studies to support reduction of radiation dose are a high priority. IC improves local regional control, reduces distant metastases, and may support radiotherapy de-escalation. Patients with T4, ECE, and N2c disease have poorer local regional control (LRC) and a higher rate of distant metastases (DM) and may be suitable for this option. **Methods:** Data was combined for the experimental arm of a previously reported Phase 3 trial (12 subjects, NCT01706939) and a continuation Phase 2 trial (20 subjects, NCT02945631). After informed consent subjects who were PCR+ HPVOPC, smoked $<$ 20 py, and were LA or functionally unresectable were treated with Taxotere, cisplatin and reduced 5-fluorouracil (mTPF) for 3 cycles and then assessed for response. Responders were treated with 5600 cGy and weekly carboplatin, and then followed for LRC, DM, PFS, OAS and toxicity. Data was analyzed as of 2/1/21. 85% LRC at 3 years was considered non inferior to standard of care chemoradiotherapy. An acceptable end point was predetermined to be 80% PFS and 85% LRC at 3 years in this LA population. **Results:** 32 subjects were entered and included in the analysis, all responded to IC and had RDCRT. 2 patients with non-HPV16 subtypes were initially entered, treated with IC, responded, and then were taken off study and excluded from the analysis due to non-HPV 16 subtype. They were treated with 7000 cGy and are alive and well. Poor risk factors (ECE, T4, N2c, Non-HPV16 subtype) were present in 72% of 32 subjects; 22 (69%) never smoked. At data cutoff with a median follow up of 50m (21-95m), 28/32 (87.5%) have LRC, 1/32 DM (3.1%), OS is 28/32 (87.5%) and PFS is 27/32 (84.4%). All 5 patients who recurred did so in the first 12m (median 8m); all had 1 or more poor risk factors and 1 is alive with disease 42m post recurrence. 2 year LRC, PFS and OS are 87.4% [95% CI: 69.8%, 95.1%], 84.4% [95% CI: 66.5%, 93.2%] and 90.6% [95% CI: 73.7%, 96.9%] respectively. There was no therapy-related mortality, generally rapid recovery from CRT and minimal long term consequences (to be reported). **Conclusions:** Induction with mTPF followed by RDCRT resulted in excellent LRC, PFS and OS in patients with LA HPV OPC and significant risk factors. These results compare favorably to standard of care and other dose de-escalation trials in high and low risk categories. This treatment paradigm is highly effective in a LA, high risk HPVOPC patients and is a reasonable treatment option to be compared to other de-escalation treatment plans in Phase 3 trials for this higher risk population. Clinical trial information: NCT02945631, NCT01706939. Research Sponsor: None.

6059 **Poster Session**

Prospective manipulation of the gut microbiome with Microbial Ecosystem Therapeutic 4 (MET4) in locoregionally advanced oropharyngeal squamous cell carcinoma (LA-OPSCC) undergoing primary chemoradiation (ROMA2).

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Background: Therapeutic manipulation of the gut microbiome in cancer patients (pts) is an area of active investigation. MET4 (NuBiyota) is an oral alternative to fecal transplant consisting of a mixture of human gut bacteria associated with immunotherapy (IO) response. We previously reported variation in IO-responsive taxa across stages in human papilloma virus related (HPV+) LA-OPSCC pts treated with chemoradiotherapy (CRT) (Oliva et al., ASCO 2020). ROMA-2 is the first interventional study evaluating the safety, feasibility and ecological effect of MET4, in combination with definitive CRT in HPV+ LA-OPSCC (NCT03838601). **Methods:** This is an investigator-initiated study of pts with HPV+ LA-OPSCC treated with standard of care CRT. MET4 is administered daily until week 4 of CRT or unacceptable toxicity. Stool samples are collected at baseline, week 4, week 8-10, and 2-months post CRT. Bacterial V4 16S rDNA was extracted from stool and sequenced. Microbiome analyses were conducted in R using DADA2, phyloseq and DESeq2. **Results:** As of February 11 2021, 25 pts have been enrolled. A total of 50 stool samples from the first 14 pts were collected (98% adherence) and analyzed. Baseline cohort characteristics: median age = 62.5 (range, 48-69); Stage I/II/III = 5/1/8; use of antibiotics = 1pt. 3 pts did not complete the 3-week course of MET4 treatment due to non-compliance (n = 1), withdrawal of consent (n = 1) and grade 2 diarrhea (n = 1). Other reported MET4-related adverse events (all grade 1) included bloating (n = 2), flatulence (n = 1) and belching (n = 1). No longitudinal changes in alpha-diversity were seen from baseline through follow up. Administration of MET4 resulted in a transient trend towards increased cumulative MET4 taxa relative abundance (RA) by week 4. Stage III patients demonstrated the lowest MET4 taxa RA at baseline, and the greatest increase in MET4 taxa RA from baseline to week 4. By week 4 the following taxa in all pts were increased compared to baseline: *Eubacterium hallii* (21.71 Log2Fold change[L2FC], padj $<$ 0.001) and *Parabacteroides johnsonii (*23.67 L2FC, padj $<$ 0.001). An increase in the following taxa was observed by weeks 8-10 compared to baseline: *Akkermansia muciniphilla* (3.75 L2FC, padj = 0.027), *Bacteroides fragilis* (6.73 L2FC, padj = 0.010), *Alistipes onderdonkii* (3.30 L2FC, padj = 0.049) and *Parabacteroides distasonis* (24.43 L2FC, padj $<$ 0.001). **Conclusions:** Manipulation of the gut microbiota in these pts was feasible and safe. MET4-induced ecological changes are heterogenous and vary by taxa. MET4 taxa implicated in IO-response were increased by week 4 and week 8-10. This increase was higher in pts with stage III disease. These data suggest that specific subgroups may benefit from combination IO therapy and may guide pt selection for further interventional clinical trial design. Clinical trial information: NCT03838601. Research Sponsor: Tumor Immunotherapy Program, Princess Margaret Cancer Center.

6060 **Poster Session**

Postoperative PET/CT for detection of early recurrence (ER) after surgery for squamous cell carcinomas (SCC) of the oral cavity (OC).

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Background: Patients with ER after surgery and prior to postoperative radiation (RT) for SCC of the OC have aggressive biology and poor prognosis. After the introduction of a PET/CT simulator in our department, we incorporated post-operative PET/CT as part of RT planning. We hypothesized PET/CT would improve detection of macroscopic disease before postoperative RT. **Methods:** We reviewed the medical records of patients treated with postoperative radiotherapy between 2005 and 2019 for OC SCC. Clinicopathologic risk factors were recorded. Intermediate risk factors (IRFs) included pT3-4 disease, nodal disease, perineural invasion (PNI), lymphovascular invasion (LVI), and close ($<$ 5mm) surgical margins (SM); extranodal extension (ENE) and positive SM were considered high-risk factors (HRF). Patients were stratified into risk groups based upon the number and type of risk factors: 0-1 IRFs, 2 IRFs, $\geq$3 IRFs, and any HRF. Patients were considered to have ER if they had biopsy confirmed recurrence, or if the imaging or exam was sufficiently suspicious, after discussion with the head and neck team, to warrant treatment to definitive doses of RT (70 Gy). **Results:** Our cohort included 391 patients with SCC of the OCC who were treated with postoperative radiotherapy. 61% of patients were male, 35% had pT3-4 disease, 36% had pN2a-3 disease, 53% had PNI, 20% had LVI, 30% had ENE, and 14% had positive SM. The most common sites were oral tongue (46%), alveolar ridge (18%), and buccal mucosa (13%). 237 (61%) patients underwent postoperative PET/CT planning, and 165 patients (41%) were planned with CT only. Patients screened with post-operative PET/CT were more likely to be diagnosed with ER (46/237, 19.4%) than those simulated with CT only (6/154, 3.9%, $p < 0.0001$). Among patients simulated with PET/CT, 7%, 9%, 14%, and 35% of patients were diagnosed with ER for patients with 0-1 IRFs, 2 IRFs, $\geq$3 IRFs, and any HRF, respectively. Median follow-up was 4.1 years (95% CI 3.6 – 4.5). Among 52 patients with ER, 24 (49.0%) had local, 41 (83.7%) had regional, and 5 (10.2%) had distant recurrence. 17 (33%) of ER were biopsy proven. For patients with ER, 3-year freedom from locoregional recurrence, distant-metastasis free survival, and overall survival were 45.2% (95% CI 32% - 64%), 55% (95% CI 42% – 72%), and 43% (95% CI 30% - 61%), respectively. For patients without ER, use of postoperative PET/CT was associated with improved disease-free survival (HR 0.68, 95% CI 0.46 – 0.98, $p = 0.041$) and overall survival (HR 0.59, 95% CI 0.38 – 0.91, $p = 0.019$). **Conclusions:** Postoperative PET/CT may increase detection ER compared to CT simulation alone and improve risk stratification. Patients with ER are at high risk of locoregional failure, distant metastases, and mortality, despite salvage therapy. A prospective trial is underway at our institution to systemically study the role of PET/CT for detection of ER. Research Sponsor: U.S. National Institutes of Health.

6061 **Poster Session**

Impact of COVID19 pandemic on treatment outcome of locally-advanced head and neck squamous cell carcinoma (LA-HNSCC): IMPACCT study.

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Background: Treatment (ttm) of cancer patients (pts) was compromised during the first wave of COVID19 pandemic due to collapse of healthcare systems. Standard of care (SOC) for LA-HNSCC pts had to be adapted as operating rooms were temporarily unavailable, and to reduce risk of COVID19 exposure. The IMPACCT study evaluated the outcome of LA-HNSCC pts treated at the Catalan Institute of Oncology during the first semester of 2020 and compared it to a control cohort previously treated in the same institution. **Methods:** Retrospective single institution analysis of two consecutively-treated cohorts of newly-diagnosed HNSCC pts: from January to June of 2020 (CT20) and same period of 2018 and 2019 (CT18-19). Pt demographics and disease characteristics were obtained from our in-site prospective database. Ttm modifications from SOC as per COVID19-contingency protocol in CT20 for LA-HNSCC were collected. Chi-squared was used to compare variables and ttm response between cohorts. One-year recurrence-free survival (1yRFS) and overall survival (1yOS) of LA-HNSCC pts were estimated by Kaplan-Meier method and compared by Log-rank test. **Results:** A total of 306 pts were included: CT20=99; CT18-19=207. Baseline characteristics were balanced between cohorts (Table1). In pts treated with conservative ttm (non-surgical approach), persistence disease was higher in CT20 vs CT18-19 (26 vs. 10% p=0.02). Median follow-up of CT20 and CT18-19 was 6.8 months (IQR 5.1-7.9) and 12.3 (6.7-18.4), respectively. A trend towards lower 1yRFS and 1yOS was observed in CT20 vs CT18-19 (72 vs 83% p=0.06; 80 vs 84% p=0.07), respectively. Within CT20, 37 pts (37%) had one or more ttm modifications: switch from surgery to conservative ttm (n=13); altered radiotherapy fractionation (n=14); reduced cisplatin cumulative dose to 200mg/m2 (n=19); no adjuvant ttm (n=1). Pts who received modified ttm had no differences in 1yRFS vs those who did not (80 vs 66% p=0.31), but higher 1yOS was observed (97 vs 67% $p<0.01$). When stratified by stage, 1yOS difference remained significant in stage III/IVA (100 vs 61% $p<0.01$) but not in I/II (100 vs 77% p=0.28) or IVB (67 vs 50% p=0.54). **Conclusions:** COVID19 pandemic had a negative impact on ttm outcomes and survival in LA-HNSCC pts when compared to our historical cohort. Ttm modifications based on COVID19-contingency protocol did not compromise ttm efficacy in terms of RFS and was associated with better OS in Stage III/IVA. Research Sponsor: None.

Main pts characteristics.

	CT20=99	CT18-19=207	Chi-squared test p-value
Gender: (%) male	74	76	0.79
Age: median (IQR)	66 (57-76)	65 (57-75)	0.26*
Smoking status: (%) active/former/never	50/35/15	52/29/19	0.45
Location: (%) pharynx/larynx/oral cavity	27/29/44	31/36/33	0.12
Stage: (%) I-II/III-IVA/IVB/IVC	33/56/7/4	36/58/3/3	0.51
Treatment received: (%) surgical/conservative/palliative/best supportive care	42/51/3/4	56/38/1/5	0.07

* t-test comparison.

6062 **Poster Session**

Quality of life analysis of HPV-positive oropharyngeal cancer patients in a randomized trial of reduced-dose (rdCRT) versus standard (sdCRT) chemoradiotherapy: Five-year follow-up.

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Background: Human papillomavirus-positive oropharyngeal cancer (HPV OPC) portends a more favorable prognosis compared to HPV-negative cases. To prevent overtreatment, long-term morbidity and deterioration in functionality and quality of life (QoL), multiple studies have focused on de-intensification techniques for HPV OPC treatment. To this end, we prospectively assessed differences in patient reported QoL in locally advanced HPV OPC patients receiving rdCRTversus sdCRT)in a randomized trial using a sequential therapy plan. **Methods:** Patients were enrolled between December 2012 and February 2016; received 3 cycles of induction docetaxel, cisplatin, and 5-FU; and were randomized to sdCRT (70 Gy) or rdCRT (56 Gy) with weekly carboplatin. Patients were followed for Progression Free Survival (PFS), Overall Survival (OS), and changes in QoL as assessed by the MD Anderson Dysphagia Inventory (MDADI), MD Anderson Symptom Inventory (MDASI Head and Neck), Xerostomia Questionnaire (XQ), and the European Organization for Research and Treatment of Cancer Questionnaire (EORTC QLQ-C30) with the head and neck module (EORTC HN). A mixed model ANOVA was used to estimate changes from baseline QoL to that at each follow-up timepoint and to compare the difference in QoL changes between the treatment arms. **Results:** We randomized 20 HPV+ locally advanced (LA) patients (median age: 56.5 yrs) to rdCRT (12 subjects) or sdCRT (8 subjects). 70% had high risk features. At a median follow-up of 81.5 mos, PFS and OS were 87.5% and 83.3% for sdCRT and rdCRT, respectively with a median OS of 76 mos in both arms. One patient in the sdCRT arm developed an HPV negative retromolar trigone squamous cell cancer in the radiation field 7 yrs after therapy. Baseline QoL was identical in the 15 patients who completed the QoL modules. Patients receiving rdCRT hadsignificantly lower declines in QoL scores at 3-6 month follow-up. At 5 yrs, differences in QoL changes all favored the rdCRT arm (Table) and two QoL scales reached statistical significance ($P<0.05$). **Conclusions:** In HPV OPC patients, rdCRT resulted in comparable long-term survival and greater improvement in specific domains of QoL when compared to sdCRT. Our results support the need for a larger, long-term Phase 3 study in LA HPVOPC to assess these two treatments with respect to survival, QoL, and safety. Clinical trial information: NCT02945631. Research Sponsor: None.

Changes in QoL differences at 5 years comparing rdCRT vs sdCRT.

	rdCRT	sdCRT	P-value
MDADI	-0.75 [-14.62, 13.11]	-11.76 [-31.8, 8.27]	0.37
MDASI SI	-0.45 [-2.6, 1.7]	1.36 [-1.73, 4.44]	0.34
MDASI SS	0.06 [-1.22, 1.34]	1.57 [-0.28, 3.42]	0.18
XQ	1.55 [-0.57, 3.68]	4.69 [1.64, 7.75]	0.10
EORTC GHS	11.49 [-4.36, 27.35]	-23.94 [-46.84, -1.05]	0.01
EORTC FS	9.35 [-3.67, 22.36]	-8.16 [-26.92, 10.6]	0.13
EORTC SS	-7.76 [-18.16, 2.64]	15.19 [0.26, 30.12]	0.01
EORTC HN	-7.49 [-16.68, 1.71]	7.90 [-5.34, 21.15]	0.06

6063 **Poster Session**

Evaluating a clinically validated circulating tumor HPV DNA assay in saliva as a proximal biomarker in HPV+ oropharyngeal squamous cell carcinoma.

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Background: HPV genomic DNA in plasma and saliva has been widely studied, however more recently, circulating tumor human papillomavirus DNA (ctHPVDNA) has emerged as a reliable biomarker for surveillance in HPV+ oropharyngeal squamous cell carcinoma (OPSCC). A commercial assay for this biomarker distinguishes tumor-derived viral DNA (tumor-tissue modified viral DNA or TTMV) from other non-cancer associated sources of HPV DNA. The use of this technology has been previously described in plasma, but its utility in saliva is currently unknown. **Methods:** A prospectively collected and banked biospecimen repository was used to identify 46 patients with HPV+ OPSCC with paired pre treatment plasma and saliva samples. All samples were assessed for DNA integrity and TTMV using a clinically validated ddPCR-based assay (NavDx™; Naveris Inc, Natick, MA) to measure TTMV for HPV-16, -18, -31, -33 and -35 from frozen plasma and saliva samples. Retrospective chart review was performed to collect clinical and pathological data. Graphpad was used for statistical analysis. Spearman's r was used to correlate TTMV copies in saliva and plasma. Wilcoxon test was used to compare between sample types. Mann-Whitney test was used for categorical variables. **Results:** TTMV DNA was detectable in 43 of 46 plasma samples and in 44 of 46 saliva samples. One plasma sample failed quality control measures, one of each sample type had undetectable TTMV, and one of each type was indeterminate. Of 41 evaluable patients with paired samples, there were 38 (93%) males, 36 (88%) were stage I-II, 5 (12%) were stage III-IV (AJCC 8^{th}, clinical staging), and 25 (61%) had a history of smoking with a median of 37.5 pack years. TTMV was significantly enriched in saliva compared to plasma ($p<0.0001$), with median copy number 14,139 copies/ml (IQR=193,339.5) and 774.7 copies/ml (IQR=4,826.1), respectively. There was a significant positive correlation between plasma and saliva TTMV levels ($r=0.344$, $p=0.028$). There was no difference in overall stage for either specimen type. There was a trend in both sample types toward higher TTMV in patients with a history of smoking. Pack-year history was available for 38 (93%) patients in the final cohort. When grouping by pack-years, plasma TTMV approached significance ($p=0.058$) while high saliva TTMV was significantly associated with >10 pack-year history ($p=0.011$). **Conclusions:** This is the first study to demonstrate successful quantification of tumor-tissue modified HPV DNA in saliva. Compared to plasma, pre treatment saliva samples demonstrated significantly higher levels of TTMV. TTMV distinguishes ctHPVDNA from other sources of HPV. These data highlight the potential use of TTMV detection in saliva for early detection of HPV+ OPSCC as well as its potential role in local surveillance after treatment. More research is needed to elucidate the effects of smoking on TTMV levels. Research Sponsor: Naveris Inc.

6064 **Poster Session**

Quantitative immunofluorescence and mRNA analysis of immune-related biomarker groups in matched paired tumor samples from OPHELIA window study in head and neck squamous cell carcinoma (HNSCC).

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Background: Preclinical models suggest that PARP inhibitor-induced DNA damage can promote immune priming through a range of mechanisms including STING pathway activation. PARP inhibition also leads to adaptive upregulation of PD-L1 expression in preclinical models. To understand the distinct effects that different forms of DDR defects may have on tumor immunogenicity we decided to integrate genomic profiling with gene expression profiling and immunohistochemistry (IHC)/fluorescent assessments of PD-L1 expression, CD8 T-cell infiltration, and broad immune infiltrate, in order to define the overlap between DDR and immune-related biomarker groups and to build a deeper understanding of how DNA damage interfaces with antitumor immunity. **Methods:** 39 patients were enrolled in OPHELIA phase II trial in which pts were randomized 3:3:3:1 to Cisplatin (C) 60 mg/m2 on d1 followed by Olaparib (O) 75mg d 1-5 (Arm A), O 300 mg bid for 21-28 days (Arm B), no treatment (ARM C) or D 1500 mg on d1 followed by O 600 mg daily for 21-28 days (Arm D). PD-L1, STING, Ki67 and γ-H2AX were assessed using quantitative immunofluorescence (QIF). The GeneXpert (GX) closed system real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR) was used for quantitative assessment of CD274 (PD-L1), PDCD1LG2 (PD-L2), CD8A, and IRF1 multiplex mRNA panel in pre- and post-treatment samples. **Results:** Ki67 was decreased in 23 out of 29 (79.3%) available samples when assessed by QIF; 13 / 23 had a decrease of at least 25%. $\Delta\gamma$-H2AX did not differ among treatment groups. A significant increase was observed in PD-L1 and PD-L2 mRNA levels after treatment with D-O ($p = 0.023$ and $p = 0.016$, respectively). An increase trend in posttreatment CD8A mRNA was observed in 23 out of 29 cases in the three treatment arms ($p = 0.21$, ARM A; $p = 0.082$, ARM B; $p = 0.16$, ARM D). IRF1 mRNA and STING protein levels were not upregulated after olaparib- based treatment in the available paired treatment samples. **Conclusions:** This window study demonstrated a significant upregulation of PD-L1 mRNA, corresponding to our previous data of increased Combined Positive Score (CPS) in the D-O arm post-treatment. Our findings suggest that addition of D to O leads to PD-L1 upregulation. Dual blockade of PARP and PD-1 can boost immune response and antitumor activity in HNSCC. Clinical trial information: NCT02882308. Research Sponsor: Astrazeneca.

6065 **Poster Session**

Cisplatin and capecitabine induction chemotherapy in nasopharyngeal carcinoma.

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Background: Induction chemotherapy (IC) followed by concurrent chemoradiotherapy (CCRT) is now one of the standard treatment for locally advanced nasopharyngeal carcinoma (LANPC). Cisplatin/fluorouracil is one of the recommended IC regimens. Capecitabine is an oral fluoropyrimidine prodrug with higher concentrations of fluorouracil attained in the tumor cells after enzymatic conversions. We conducted this study to evaluate the feasibility, efficacy and safety of cisplatin and capecitabine (PX) IC followed by CCRT in LANPC. **Methods:** Newly diagnosed patients with LANPC (stage III-IVB according to 7^{th} edition of AJCC/UICC system [TNM-7] and stage III-IVA according to 8^{th} edition [TNM-8) were prospectively recruited from January 2015 to October 2019. They received induction PX (cisplatin: 80mg/m2 on day 1 + capecitabine: 1000mg/m2 twice daily from day 1 to 14 every 3 weeks for 3 cycles) followed by CCRT (cisplatin: 100mg/m2 every 3 weeks for a total of 2-3 cycles concurrent with intensity-modulated radiation therapy [IMRT]). IMRT with doses of 70Gy, 63Gy and 56Gy were delivered to 3 levels of planning target volumes (PTV) (high, intermediate and low risk) respectively and simultaneously in 35 fractions/7 weeks. Tumor response by MRI and CT was evaluated after completion of IC and 16 weeks after completion of CCRT according to RECIST v1.1. All adverse events were graded with NCI CTCAE v4.03. **Results:** One hundred and forty-five patients were recruited. The stage distributions according to TNM-8 were 82(56.6%) and 63(43.3%) for stage III and IVA, respectively. One hundred and thirty-seven patients completed 3 cycles of induction PX and 122 patients completed IMRT with 2 to 3 cycles of concurrent cisplatin. The median (interquartile range, IQR) tumor regression rates after 2-3 cycles of PX at the nasopharynx (NP) and the neck region (NK) were 51.2% (37.3%-66.5%) and 71.8% (56.7%-81.1%), respectively. At 16 weeks after CCRT, only one patient had residual disease. After a median follow-up of 33 months, 20 treatment failures and 8 deaths were observed. The estimated 2-year progression-free survival (PFS) and overall survival (OS) were 89.8% and 97.2%. The rates of grade 3/4 leukopenia, neutropenia, anemia, nausea/vomiting and electrolyte disturbance during IC were 6.2%, 15.9%, 6.9%, 4.1% and 9.0%, respectively. The corresponding rates were 45.1%, 24.6%, 27.5%, 2.8% and 11.3% during CCRT. Only 1 (0.7%) grade 3/4 hand-foot syndrome and 3 (2.1%) grade 3/4 diarrhea during IC were observed. The rates of grade 3/4 mucositis and dermatitis were 31.0% and 12.7%, respectively. There were no treatment-related deaths. **Conclusions:** Induction PX followed by CCRT was effective and well tolerated in patients with LANPC. Clinical trial information: NCT03427359. Research Sponsor: Shenzhen Key Medical Discipline Construction Fund (No. SZXK014) and Shenzhen Science and Technology program (Grant No: KQTD20180411185028798).

The SINTART 1 study: A phase II trial of induction chemotherapy (IC), surgery, photon-, proton-and carbon ion-based radiotherapy (RT) integration in locally advanced operable sinonasal epithelial tumors patients (pts).

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Background: Sinonasal epithelial tumors are rare diseases with several histotypes and poor prognosis. Multimodal approach including surgery is widely used, although no standard therapy has been established in prospective trials. This study assessed activity and safety of an innovative integration of multimodality treatment - IC, surgery and RT - modulated by histology, molecular profile and response to IC. **Methods:** Pts with untreated, operable squamous cell carcinoma (SCC), p53 wild type intestinal type adenocarcinoma (ITAC), sinonasal undifferentiated and neuroendocrine carcinoma (SNUC, SNEC) were enrolled in a single-arm, phase II, multicenter clinical trial from 2014 to 2018. Pts was treated with up to 5 IC cycles, whose regimen was selected according to histotype, followed either by curative radio-chemotherapy (CRT) (pts with ≥80% reduction of initial tumor volume (TV)) or surgery and adjuvant (C)RT. Photon and/or proton/carbon ion-based RT was employed according to disease site and stage. Primary endpoint was 5 years PFS, secondary endpoints were OS, IC ORR per RECIST 1.1 and safety. **Results:** Out of 39 enrolled pts, 35 pts were evaluable for primary endpoint. Two pts were only considered for safety analyses because definitive diagnosis on surgical specimen did not meet the study entry criteria; other two pts were screening failure due to inoperable disease. Five-year PFS was 38% (95% CI, 21 – 69), with a median PFS of 26 months. Five-year OS was 46% (95% CI, 28 – 75), with a median OS of 36 months. Responses to IC are reported in table. Globally, 15 pts avoided surgery. Overall treatment safety was in line with multimodality intensive head and neck cancer treatments (5% of pts with G3-4 adverse event during IC). One sudden cardiac death was recorded. At a median follow up of 27 months, 5 G3-4 RT related late adverse events have been recorded (1 G3 neurotoxicity, 2 G3 hearing impairment, 2 G3 xerostomia). Three-year PFS - OS for pts achieving PR/CR vs SD/PD to IC were 49.8% - 56.7% vs 43.2% - 53%, respectively. **Conclusions:** Treatment of advanced SNC with histology-driven IC followed by locoregional therapy tailored to response to IC was safe and showed survival rate similar to surgery containing case series. In the first prospective study, a surgery sparing multimodal approach proved feasible and effective in IC responsive pts. Clinical trial information: NCT02099175. Research Sponsor: Supported by Fondazione Regionale per la Ricerca Biomedica.

	all TYPES (35)	%	SCC (13)	SNUC (15)	ITAC (3)	SNEC (4)
IC scheme			TPF*	TPF*	PFL†	EP/AI‡
Response Rate	19	54	7 (54%)	9 (60%)	0	3 (75%)
≥80% TV Reduction	12	34	3	6	0	2
Complete Response	3	9	0	2	0	1
Partial Response	16	45	7	7	0	2
Stable Disease	14	40	6	4	3	1
Progressive Disease	2	6	0	2	0	0

6067 **Poster Session**

Comparative assessment of the eighth and seventh AJCC staging edition prognostic performance of patients with p16 positive oropharynx cancer.

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Background: The American Joint Committee on Cancer (AJCC) TNM staging system defines the anatomical extent of disease and serves as a guide for treatment and prognosis. The favorable prognosis of p16+ oropharyngeal squamous cell carcinoma (OPSCC) compared to p16 negative counterpart led to major updates in the AJCC 8th edition. Its prognostic performance, however, warrants further validation. **Methods:** We included patients diagnosed with p16+ OPSCC enrolled in a prospective registry (*Stiefel*) at The University of Texas MD Anderson Cancer Center between March 2015 and December 2018. Patients' stage at diagnosis was classified according to the AJCC 7th (AJCC-7) and 8th (AJCC-8) editions. Overall survival (OS) and progression-free survival (PFS) was defined as time from diagnosis to death or to progression or death, respectively. The Kaplan-Meier method was used to calculate 1- and 3-year survival probabilities. Differences between groups were compared using the log-rank test. Prognostic discriminative performance of each staging system was evaluated using Harrel's C-statistic. Survival differences between heavy ($>$ 10 pack-years [PY]) vs. light/never smokers ($\leq$ 10 PY) by AJCC-8 staging groups was assessed with the log-rank test. **Results:** Of 463 patients, the median follow-up was 34.7 months (2.3-169.74). Nearly 90% (N=413) of patients were down-staged from AJCC-7 to AJCC-8 with 69% of patients with IVA disease based on AJCC-7 (N=319) re-staged as stage I (N=196 [42%]), II (N=79 [17%]) or III (44 [10%]) according to AJCC-8. Over 60% (N=279) of patients were staged as I with AJCC-8. Compared to AJCC-7, AJCC-8 had improved prognostic ability (C-statistic, 0.58 for AJCC-7 vs. 0.63 for AJCC-8) and provided better discriminative survival probabilities at 1 and 3-year follow-up (Table). Similar results were observed for PFS. Smoking status did not impact OS when stratified by AJCC-8 staging groups: I, p=0.347; II, p=0.310; and III, p=0.532 for $>$ 10 vs. $\leq$ 10 PY. **Conclusions:** Our cohort validates that the AJCC-8 provides better prognostic discriminative performance when compared to AJCC-7, however, a disproportionate number of patients were classified as stage I. Smoking was not associated with survival within each staging group. Research Sponsor: Stiefel Oropharyngeal Research Fund.

Survival probabilities at 1- and 3-years follow-up according to the AJCC 7th and 8th edition staging systems.

AJCC	Staging	No. Total	No. Events	1-Year (95%CI)	3-Year (95% CI)	Log-rank
7th	I	17	1	100	93.3 (61.3-99.0)	p < 0.001
	II	29	5	89.1 (69.9-964)	85.4 (65.6-94.3)	
	III	54	5	94.3 (83.4-98.1)	90.2 (78.0-95.8)	
	IVA	319	59	92.0 (88.4-94.5)	81.6 (76.5-85.8)	
	IVB	19	7	94.1 (65.0-99.2)	60.1 (30.9-80.1)	
	IVC	25	11	59.4 (37.6-75.8)	50.9 (27.1-70.6)	
8th	I	279	38	93.4 (89.7-95.8)	85.7 (80.6-89.6)	p < 0.001
	II	94	20	91.4 (83.6-95.6)	80.5 (70.4-87.5)	
	III	65	19	90.2 (79.5-95.5)	71.5 (57.4-81.7)	
	IV	25	11	59.4 (37.6-75.8)	50.9 (27.1-70.6)	

6068 **Poster Session**

Pathologic and radiographic responses in a window of opportunity for durvalumab plus metformin trial for squamous cell carcinoma of the head and neck (HNSCC).

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Background: Durvalumab is a human monoclonal IgG1 antibody directed against programmed death-ligand 1 (PD-L1). PD-1/PD-L1 immune checkpoint inhibition (ICI) shows promise in HNSCC, but durable responses have been seen in only a fraction of patients. Metformin, a biguanide oral antihyperglycemic, has shown promise in altering immunity within the tumor microenvironment (TME) towards a stronger anti-tumor distribution of immune cells. We aimed to investigate the combined effect of metformin and durvalumab in patients with HNSCC. **Methods**: This was a single-center prospective phase 1, window of opportunity clinical trial in which previously untreated patients with any stage resectable HNSCC were randomized 3:1 to durvalumab + metformin (Arm A) or durvalumab alone (Arm B) during a four-week period between diagnosis and surgical resection. Six patients were included in a safety lead-in of durvalumab and metformin and an additional 32 patients were randomized. The primary endpoint was immune cell polarization. Here we report pathologic and radiographic effect. Pathologic effect was graded independently by two pathologists. Radiographic effect was evaluated using the immune-related Response Criteria (irRC). **Results**: Thirty-eight patients were enrolled (29 Arm A, 9 Arm B). Three patients withdrew consent prior to intervention (2 Arm A, 1 Arm B) and were excluded from analysis. AJCC 8^{th} edition staging was as follows: Stage I (n = 21), Stage II (n = 2), Stage III (n = 3), Stage IVa (n = 6), Stage IVb (n = 3). Primary tumor sites included the oropharynx (n = 20, all p16+), oral cavity (n = 11), larynx (n = 2), maxillary sinus (n = 1), and unknown (n = 1). Pathologic effect was observed in 55% (18/33) of evaluable patients: 60% in Arm A vs 37.5% in Arm B (p = 0.418). 40% of patients with involved lymph nodes had discordance of pathologic effect at the primary site versus lymph node. Radiographic response based on irRC among 30 evaluable patients included 1 CR, 1 PR, 24 SD, and 4 PD. There was a significant correlation between pathologic effect and radiographic disease control, defined as CR, PR, and SD (p = 0.021), but no correlation when looking only at radiographic responders (p = 0.925). No patients experienced Grade 3–4 treatment or immune-related adverse events or a delay in surgery due to trial participation. All patients remained resectable. **Conclusions**: Our data demonstrate that the study intervention was well-tolerated in HNSCC patients. There was a trend towards an increased proportion of pathologic responders in the group receiving metformin. Additional studies targeting the TME are needed to further elucidate whether synergistic effects between metformin and durvalumab were seen in this patient cohort. Clinical trial information: NCT03618654. Research Sponsor: Astra Zeneca.

6069 **Poster Session**

The efficacy and safety of anlotinib in neoadjuvant treatment in locally advanced thyroid cancer: A single-arm phase II clinical trial.

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Background: Surgery is the primary treatment for locally advanced thyroid cancer (TC). For some locally advanced TC, R0/R1 resection could not be achieved at initial diagnosis and neoadjuvant treatment would be an option. However, there is still little evidence regarding neoadjuvant treatment in locally advanced TC. **Methods:** This single-arm, phase 2 study investigated the efficacy and safety of Anlotinib (12mg orally daily, for two weeks on/on week off) for 2-6 cycles in patients with locally advanced TC in the neoadjuvant setting. Operable patients received surgery after neoadjuvant treatment. The primary endpoint was objective response rate (ORR). **Results:** A total of 13 patients were included and received an average of 3.5 cycles (range: 3-6 cycles) of Anlotinib treatment. 12 cases were papillary thyroid cancer, and 1 was follicular thyroid cancer. The ORR of Anlotinib was 76.9% with 10 partial response (PR), 2 stable disease (SD), and 1 progressive disease (PD). 8 PR and 1 SD patients received surgery after neoadjuvant treatment, of whom 8 had R0/1 resections and 1 had R2 resection. 2 PR patients refused to have surgery and the rest 2 patients were not operable. The R0/1 resection rate for intent to treat population was 61.5% and for per-protocol population was 72.7%. The maximum reduction in sum of tumor diameter was an average of 34.8% (range: 30.9%-45.5%) for PR patients. Most adverse events were grade 1 or 2. Common adverse events of all grade were hypertension (76.9%), hypertriglyceridemia (69.2%), proteinuria (53.8%), TSH increase (53.8%), cholesterol elevation (53.8%) and hand-foot syndrome (38.5%). The majority of adverse events discontinued after the neoadjuvant treatment stopped. **Conclusions:** Anlotinib demonstrated antitumor activity in the neoadjuvant treatment in locally advanced TC and the majority of patients achieved R0/1 resection. Adverse events were consistent with the known Anlotinib adverse event profile. These results suggest that Anlotinib neoadjuvant treatment represents a new option for locally advanced TC. Clinical trial information: NCT04309136. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

6070 **Poster Session**

Planned drug holiday in a cohort study exploring the effect of lenvatinib on differentiated thyroid cancer.

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Background: Lenvatinib is now available for unresectable radioactive iodine (RAI)-refractory differentiated thyroid cancer (DTC). However, toxicities are considerable and require frequent dose interruption and modification. Recently, planned drug holidays, which are dose interruptions in accordance with the timing of severe or intolerable adverse events, have been proposed to avoid severe adverse events due to lenvatinib (Tahara M.ESMO Open 2018). Our retrospective study demonstrated that progression-free survival (PFS) and overall survival (OS) were significantly longer in patients who used planned drug holidays than those who did not (Matsuyama C et.al, 2020 Annual Meeting of the Japan Association of Endocrine Surgeons). **Methods:** In this prospective observational study, patients with curatively unresectable and progressive RAI-refractory DTC were treated with lenvatinib in a real-world clinical setting. Lenvatinib was administered orally at a dose of 24 mg daily. Dose modification for toxicities were permitted. Primary endpoint was OS, and secondary endpoints were time to treatment failure (TTF), time to failure of strategy (TFS), PFS with clinical progressive disease, response rate, quality of life, safety, and patient reports. This study was registered with UMIN Clinical Trials Registry (UMIN000022243). **Results:** 262 patients were accrued. Of 255 evaluable, 153 were female; median age was 70 (range 27.0-88.0); histology was papillary thyroid carcinoma/follicular thyroid carcinoma/poorly DTC in 204/45/4; previous therapy was surgery/RAI/molecular targeted drug in 246/164/14; reason for initiation of lenvatinib was disease progression/unsuitable for RAI in 241/4. 1-year OS was 85.6% (95%CI: 80.6-89.4%); 1-year TTF rate was 74.9% (95%CI: 69.1-79.8%); 1-year TFS rate was 80.8% (95%CI: 75.4-85.2%); and 1-year PFS rate was 84.4% (95%CI: 79.3-88.4%). Overall response by RECIST was 3 (1.2%) in CR and 151 (61.9%) in PR. Most common grade 3 or 4 toxicities were hypertension (61.4%), hand foot syndrome (10.2%), fatigue (9.1%), anorexia (8.3%) and diarrhea (4.7%). Grade 5 toxicities occurred in 4 patients (fistula, hypoxia, respiratory failure, trachea stenosis). Of 253 patients evaluable for efficacy, 73 used planned drug holidays. TTF, TFS and PFS were significantly longer in patients who used planned drug holiday than those who did not (Table). **Conclusions:** Planned drug holiday for lenvatinib demonstrated significantly better clinical outcomes, including TTF, TFS and PFS, than daily oral administration. These data further support use of a planned drug holiday in RAI-refractory DTC patients receiving lenvatinib. Clinical trial information: 000022243. Research Sponsor: Eisai Co., Ltd.

Planned drug holiday	1-year TTF (95%CI)	1-year TFS (95%CI)	1-year PFS (95%CI)
yes (n = 73)	87.6% (77.6-93.4)	84.9% (74.4-91.3)	94.5% (86.1-97.9)
no (n = 180)	69.8% (62.4-75.9)	65.0% (57.5-71.5)	83.5% (77.2-88.3)
Log-rank test	p = 0.0049	p = 0.0017	p = 0.0190

6071 **Poster Session**

Predictive and prognostic biomarker identification in a large cohort of androgen receptor-positive salivary duct carcinoma patients scheduled for combined androgen blockade.

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Background: Patients suffering from recurrent or metastatic (R/M) salivary duct carcinoma (SDC) are often treated with combined androgen blockade (CAB). This treatment however frequently fails (response rates: 18-53%), resulting in a worse prognosis. Therefore, biomarkers that have prognostic value and can predict treatment response are urgently needed. **Methods:** mRNA from 77 R/M androgen receptor (AR) positive SDC patients treated with leuprorelin acetate combined with bicalutamide was extracted from pre-treatment tumor specimens. AR, Notch, Mitogen-Activated Protein Kinase (MAPK), Transforming Growth Factor beta (TGFβ), Estrogen Receptor (ER), Hedgehog (HH) and the Phosphoinositide 3-Kinase (PI3K) signaling pathway activities were calculated based on expression levels of relevant target genes. Besides this, 5-alpha reductase type 1 (*SRD5A1*) expression and Human Epidermal growth factor Receptor 2 (HER2) status were determined. Clinical benefit was defined as complete or partial response or stable disease $\geq$6 months. **Results:** Of the 7 signaling pathways, AR pathway activity was the best predictor of clinical benefit (AUC 0.67, 95%-CI 0.54-0.80). At a threshold of 47.8, 21% of the patients tested negative, with a negative predictive value of 93%. *SRD5A1* expression outperformed the signaling pathways regarding predictive value (AUC 0.78, 95%-CI 0.67-0.88). Fitting of a multivariable model led to the identification of *SRD5A1*, Notch and TGFβ as most predictive combination (AUC 0.82, 95%-CI 0.72-0.91). AR, Notch, HH and *SRD5A1* were also of prognostic importance regarding progression free survival and *SRD5A1* expression levels also for overall survival (median of 175.0 weeks for high versus 96.7 weeks for low expression). **Conclusions:** Our study revealed predictive and/or prognostic value of AR, HH, Notch and TGFβ signaling activities and *SRD5A1* expression in SDC patients treated with CAB. AR pathway activity can be used for identifying non-responders. Further clinical validation is required before implementation of these biomarkers in clinical practice. The observed role of *SRD5A1* expression in CAB response forms a rational basis for including SRD5A1-inhibitors in the treatment of SDC patients. Research Sponsor: None.

Pathway (mean [range])	Clinical benefit[1]	No clinical benefit[1]	Difference
AR	57.5 [31.7-71.9]	52.2 [29.6-71.9]	p = 0.013
Notch	68.1 [58.8-79.3]	64.0 [39.3-76.0]	p = 0.033
MAPK	63.0 [47.8-73.2]	65.4 [31.0-84.9]	p = 0.089
TGFβ	66.2 [49.2-74.5]	68.1 [57.5-78.5]	p = 0.34
ER	35.3 [11.3-45.3]	32.9 [16.7-44.9]	p = 0.068
HH	25.9 [11.3-38.9]	26.2 [5.7-35.0]	p = 0.59
PI3K	16.7 [6.5-32.9]	16.7 [6.5-28.8]	p = 0.86
***SRD5A1* expression[2]**	0.37 [-1.46-3.67]	1.45 [-1.46-2.39]	p = 0.001

[1]73 samples passed quality check for pathway analysis, 76 for *SRD5A1* expression analysis.
[2]Log transformed value of *SRD5A1* expression normalized to *HPRT1*.

6072 **Poster Session**

Clinical disease course and survival outcomes following disease recurrence in adenoid cystic carcinoma (ACC) with NOTCH signaling pathway activation.

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Background: ACC is a rare salivary cancer for which effective drug therapies remain lacking. The highest rates of disease recurrence are in patients with NOTCH pathway activation, which is reported in 10-20% of ACC tumors. Novel drugs targeting NOTCH signaling are under investigation in the recurrent and metastatic setting. To understand their clinical utility, there is an urgent need to better characterize the disease course and outcomes following current standard of care treatment from diagnosis and following recurrence. **Methods:** 120 patients with ACC underwent clinical review at a single UK Cancer Centre from 2017-19. Patients were retrospectively assessed for tumor NOTCH pathway activation using next generation sequencing (NGS) targeting *NOTCH1/2/3* genes (n = 98) and/or by immunohistochemistry (IHC) for the NOTCH1 intra-cellular domain (NICD1) (n = 87). To understand the disease course with NOTCH pathway activation, treatment data including surgery, radiotherapy and systemic therapies were extracted and presented as swimmer plots. Kaplan-Meier survival analysis was performed and a difference in survival with/without NOTCH activation was calculated with log rank test. Overall survival (OS) was calculated both from diagnosis and from first confirmed disease recurrence or metastasis, and recurrence free survival (RFS) calculated from diagnosis. **Results:** Of 120 patients, median age was 46 years (22-74 years). 114/120 patients (95%) had confirmed disease recurrence at clinical review. The primary site was major salivary gland in 58/120 (48%), the others were minor salivary. NOTCH1/3 activating somatic mutations were identified in 11% by NGS (11/98) and NICD1 diffuse nuclear staining was seen in 6% by IHC (5/87) for overall NOTCH activation in 11% (13/120). In NOTCH activated ACC, primary site was major salivary gland in 7/13 (54%), and non-pulmonary visceral/bone metastases were present in 6/13 (46%). Consistent with other reports, patients with NOTCH activation (n = 13) had shorter RFS (0.9 vs 3.6 years, $p = 0.11$) and significantly reduced OS from diagnosis (4.0 vs 16.3 years, $p < 0.0001$). Critically, as therapies targeting NOTCH signaling are being evaluated in recurrent/metastatic ACC, there was significantly reduced OS from time of first confirmed disease recurrence or metastasis (1.5 vs 9.6 years, $p < 0.0001$). This reduction in OS for NOTCH activation following recurrence was seen consistently whether patients were classified using NGS (1.9 vs 9.6 years, $p = 0.0009$) or NICD1 IHC (0.8 vs 8.5 years, $p < 0.0001$). **Conclusions:** This is the first study to report clinical outcomes for patients with NOTCH pathway activated ACC following disease recurrence. Although ACC is frequently considered an indolent disease, the short survival in this sub-group of ACC patients demonstrates the urgent need to develop effective drug therapies in this setting. Research Sponsor: The Ella Project (The Christie Charity), The Infrastructure Industry Foundation and Syncona Foundation, Pharmaceutical/Biotech Company.

6073 **Poster Session**

Selpercatinib efficacy and safety in patients with *RET*-altered thyroid cancer: A clinical trial update.

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Background: Selpercatinib, is a first-in-class, highly selective, CNS active and potent RET inhibitor approved in multiple countries for treatment of *RET*-fusion positive lung or thyroid cancers. Reported is an update of efficacy and safety results in *RET*-altered thyroid cancer, with a longer follow up (30 Mar 2020 data cutoff vs 16 Dec 2019) and additional enrolment. **Methods:** Patients (pts) with *RET*-mutant medullary thyroid cancer (MTC) and *RET*-fusion positive thyroid cancer (TC) were enrolled in the global (16 countries, 89 sites) Phase 1/2 LIBRETTO-001 trial (NCT03157128). The primary endpoint was objective response rate (ORR) per RECIST 1.1 by independent review committee (IRC). Secondary endpoints included duration of response (DoR), progression-free survival (PFS), clinical benefit rate (CBR; CR+PR+SD ≥16 weeks), and safety. The integrated analysis set (IAS, n = 143) includes efficacy evaluable MTC pts previously treated with cabozantinib and/or vandetanib (cabo/vande). The primary analysis set (PAS), a subset of IAS, is the first 55 enrolled pts. Cabo/vande naïve MTC pts (N = 112) and TC pts with prior systemic treatment (N = 22) were also analyzed. Safety population includes all pts who received ≥1 dose of selpercatinib (MTC N = 315; TC N = 42) by data cutoff. **Results:** For MTC patients, the ORR for IAS was 69.2%, in the PAS it was 69.1%, and 71.4% for cabo/vande naïve MTC pts. The ORR for TC pts (n = 22) was 77.3% (see table). Most treatment-emergent adverse events (TEAEs) were low grade; the most common (≥25% of MTC and/or TC pts treated with selpercatinib) were dry mouth, diarrhea, hypertension, fatigue and constipation for both MTC and TC pts, increased ALT/AST, peripheral edema and headache in MTC pts and nausea in TC pts. 4.8% of MTC and TC pts discontinued selpercatinib due to TEAEs but only 1.9% with MTC and none with TC discontinued due to treatment-related adverse events. **Conclusions:** In this updated analysis, selpercatinib continued to show marked and durable antitumor activity in pts with *RET*-altered thyroid cancers. Selpercatinib was well tolerated and no new safety concerns were identified. A global, randomized, phase 3 trial (LIBRETTO-531) evaluating selpercatinib compared to cabo/vande in kinase inhibitor naïve MTC pts is ongoing. Clinical trial information: NCT03157128. Research Sponsor: Eli Lilly and Company.

	PAS (n = 55)	IAS (n = 143)	Cabo/Vande naive (n = 112)	RET-Fusion TC (n = 22)
ORR % (95% CI)	69.1 (55.2, 80.9)	69.2 (61.0, 76.7)	71.4 (62.1, 79.6)	77.3 (54.6, 92.2)
CBR % (95% CI)	92.7 (82.4, 98.0)	90.9 (85.0, 95.1)	93.8 (87.5, 97.5)	100.0 (84.6, 100.0)
DoR, median (95% CI), months	NE (19.1, NE)	NE (19.1, NE)	21.95 (21.9, NE)	18.4 (10.1, NE)
Duration of follow-up median, months	17.45	10.05	9.26	20.27
Rate (%) PFS, > 12 months (95% CI),	82.3 (68.7,90.4)	76.9 (67.9, 83.7)	92.9 (84.5, 96.8)	68.6 (42.7, 84.6)

Clinical benefit rate, CBR; Complete response, CR; Not estimated, NE; Objective response rate, ORR; Partial response, PR; Progressive disease, PD; Stable disease, SD.

6074 **Poster Session**

Efficacy of selpercatinib after prior systemic therapy in patients with *RET* mutant medullary thyroid cancer.

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Background: Selpercatinib is a first-in-class, CNS active, highly selective, and potent RET kinase inhibitor which has demonstrated durable antitumor activity in patients (pts) with *RET* altered thyroid cancer and is approved in multiple countries for the treatment of *RET* fusion+ lung or thyroid cancers. As response rates to cancer therapy usually decline on subsequent lines of therapy, the efficacy of selpercatinib was examined in the context of the last prior therapy received before trial enrollment. **Methods:** Pts with *RET* mutant medullary thyroid cancer (MTC) previously treated with multikinase inhibitors (cabozantinib and/or vandetanib) were enrolled in the global LIBRETTO-001 trial (NCT03157128). This post-hoc exploratory intrapatient analysis, based on March 30, 2020 data cutoff date, was performed to compare the retrospective physician-reported objective response rate (ORR) from the last systemic therapy prior to enrollment, as reported in pts case reports, to ORR by independent review committee per RECIST 1.1 with selpercatinib treatment, with each patient serving as his/her own control. **Results:** Efficacy-evaluable pts, 64% male, 90% white with a median age of 58 years, received prior therapy for MTC (n = 143). Pts had a median of 2 (range 1-8) prior systemic regimens. The ORR on selpercatinib (69%) was markedly higher than for the last prior therapy (10%) received before enrollment. ORR improvements with selpercatinib were observed regardless of prior therapy: cabozantinib (66% vs 14%) or vandetanib (71% vs 12%). Fewer pts had progressive disease as their best overall response with selpercatinib (2/143; 1.4%) compared to last prior therapy (33/143; 23.1%). Notably selpercatinib achieved 62% ORR in pts that did not respond to their previous line of therapy prior to enrolment. This shift from non-responder to responder on selpercatinib therapy was consistent regardless of prior cabozantinib or vandetanib treatment, where pts achieved 57% and 61% ORR respectively when subsequently treated with selpercatinib. In contrast, only 3% of patients did not respond to selpercatinib after a previous response to the immediate prior therapy. Similarly, 5% and 2% of patients were non-responders on selpercatinib after a prior response with cabozantinib and vandetanib therapy respectively. **Conclusions:** Prior to selpercatinib, response with previous multikinase therapy was rare. By contrast, selpercatinib demonstrated robust efficacy regardless of response to or specific prior therapy in pts with *RET* mutant MTC. Clinical trial information: NCT03157128. Research Sponsor: Eli Lilly and Company.

6075 **Poster Session**

Phase Ib, international, dose-escalation study to evaluate the safety, pharmacokinetics (PK) and efficacy of ST-617 for the attenuation of oral mucositis (OM) in patients receiving chemoradiation (CRT) for head and neck (H&N) cancer.

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Background: OM is a common, painful, and costly toxicity associated with cytotoxic regimens used to treat H&N cancers, which may result in radiotherapy treatment interruptions to negatively impact tumor control. There are currently no approved interventions to successfully prevent or delay OM onset among patients being treated with radiation therapy, with or without concomitant chemotherapy (CRT). Oxidative stress is a critical event in OM's pathogenesis. Through its effect on Nrf2, ST-617 has marked antioxidative activity/properties. Supportive Therapeutics is developing ST-617, a dithioethione, for the attenuation of OM onset, duration and severity. The objective of this trial was to assess the safety, tolerability, PK, PD and efficacy of ST-617 in patients at high risk of severe OM (SOM). **Methods:** A dose escalation trial in which ST-617 administered as an oral suspension, 1-2 hours before the administration of daily RT fractions was performed at 9 study sites in South Africa and Australia. Eighteen patients with diagnoses of oral or oropharyngeal CA were enrolled (up to 6 pts/dose). Patients received concomitant cisplatin either weekly or tri-weekly. ST-617 was administered 3 days prior to CRT, and then continuing daily until the end of treatment. Safety outcomes, using CTCAE criteria (v 4.03) were used. Dose escalation occurred in the absence of toxicity. OM occurrence and severity were assessed by trained and validated evaluators using WHO, NCI-CTC and RTOG criteria; scores were centrally assigned. The primary efficacy endpoints included the incidence and duration of SOM (WHO grades 3 or 4) vs historical controls. PD tracking measured total ROS/RNS, GSH/GSSG, regulation in plasma and buccal epithelial cells. **Results:** 17 pts completed the 50, 100 and 150mg/day with no safety issues. No early dose limiting toxicity (DLT) or serious Adverse Event linked to ST-617 were observed. AEs observed were mainly nausea which is usually associated with CRT as expected. The 100 mg/day dose has been well tolerated with no grade 4 OM. No CRT dose interruptions or delays due to OM has been observed. Total ROS/RNS levels in plasma and buccal samples show significant decrease with increased ST-617 dosing from 50 to 100 mg/day. **Conclusions:** ST-617 administration was safe at all doses tested. The course and severity of patients treated with ST-617 compared favorably with historical controls. Mechanistic correlation between ROS/RNS levels was seen. A randomized, controlled, double blind trial is planned with the recommended dose of 100mg/day. Clinical trial information: 20180138. Research Sponsor: None.

6076 **Poster Session**

Randomized phase II study of sorafenib with or without everolimus in patients with radioactive iodine refractory Hürthle cell thyroid cancer (HCC) (Alliance A091302/ ITOG 1706).

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Background: HCC is a rare subtype of follicular cell thyroid cancer that has been poorly studied in the past. Recent genomic studies have shown the PI3K/Akt/mTOR pathway is frequently altered in HCC. In addition, a phase II study of sorafenib (S) and everolimus (E) showed promising data in HCC. A study to evaluate this was initiated through Alliance and the International Thyroid Oncology Group. **Methods:** Patients (pts) were randomized to either sorafenib and everolimus (SE) vs. sorafenib alone (S). Inclusion criteria included; (1) diagnosis of HCC (confirmed through central review), no prior S or E, refractory to radioactive iodine, progressive disease by RECIST over prior 14 months. Primary endpoint was a comparison of progression-free survival (PFS) between SE and S using a stratified 1-sided log-rank test with 0.20 significance level and a power of 80%. 28 events were needed at final analysis. Secondary endpoints consisted of overall survival (OS), confirmed response rate (RR), and adverse events. **Results:** 35 pts were randomized from 10/2014 to 9/2019, 34 of which were evaluable for analysis (17-SE; 17-S) because 1 patient cancelled prior to receiving treatment. Median age was 66.5 years and 74% were male. ECOG performance status (PS) was 0 (47%) and PS 1 (53%). 41% had prior systemic treatment for HCC. No significant differences in baseline characteristics were observed between treatment arms. Median follow-up in 22 alive patients was 39.2 months (range: 15.1-64.9). Seven (21%) patients remain on treatment. PFS was significantly improved in the SE arm as compared to the S arm (HR=0.65 (95% CI: 0.26, 1.57); median PFS: SE=24.7 months (95% CI: 6.1-no upper), S=10.9 months (95% CI: 5.5-no upper); stratified 1-sided p=0.1662). OS was similar between the arms (2-sided p=0.4138). Confirmed response rate was similar between arms as well (SE: 18% (3 partial response (PR) vs. S: 24% (3 PR, 1 complete response)); Fisher's exact p=1.00). Grade 3 adverse event (AE) rates (regardless of attribution) were similar between arms (SE: 77% vs. S: 77%; p=1.00). Each arm had 1 patient with at least one grade 4 AE (SE patient: cardiac arrest, tracheal obstruction, encephalopathy; S patient: mucositis oral) and no grade 5 AEs. **Conclusions:** PFS was improved with the addition of E to S in this small randomized multi-institutional phase II study done. Accrual was difficult, but these promising results suggest that this combination should be further studied. Support: U10CA180821, U10CA180882, U24CA196171; https://acknowledgments.alliancefound.org; Novartis/GSK; ClinicalTrials.gov Identifier: NCT02143726. Clinical trial information: NCT02143726. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

6077 **Poster Session**

Radiomics-based prediction of response to multikinase inhibitors in radioiodine-refractory differentiated thyroid cancer patients.

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Background: Antiangiogenic tyrosine kinase inhibitors (TKIs) represent the first-line treatment for radioiodine-refractory differentiated thyroid cancer (RR-DTC). Currently, no predictive factors for the activity of these drugs are available. We investigated whether radiomics may have a predictive role in this setting. **Methods**: We retrospectively identified patients (pts) affected by metastatic RR-DTC, treated with TKIs between July 2008 and January 2020 at our Institution, with availability of computed tomography (CT) scans at baseline and after at least 2 courses of TKI. Response to TKIs was evaluated according to RECIST v1.1. Pts with complete or partial response at the first radiological evaluation were considered responders (R), pts with stable or progressive disease non-responders (NR). A dedicated radiologist segmented the target lesions as regions of interest (ROIs). Radiomic features related to multiple categories (shape and size, first order statistics, textural features) were extracted from each ROI and computed using the PyRadiomics library v. 3.0. A semi-supervised form of principal component analysis estimated principal components that were then used for response classification through a k nearest neighbors (kNN) classifier. The quality of the model was assessed through train-validation-test split (55% of the data used as training set, 25% as validation set, 20% as test set), repeated 100 times. Performance of the predictive models was quantified with the mean Area Under the ROC Curve (AUC) obtained in the test set. **Results**: A total of 51 pts with metastatic RR-DTC who had received lenvatinib (n=37), sorafenib (n=4), axitinib (n=3), or vandetanib (n=7) were analyzed. Median age was 64.6 years, with a male prevalence (72.5%). Metastatic sites were lung (84.3%), bone (35.3%), brain (9.9%). Median time from TKI treatment start to the first radiological evaluation was 2.77 months, 24 pts (47%) were R (all partial responses) and 27 (52.9%) NR. In the radiomic analysis, 851 features were computed and 4-19 principal components were selected. Models' performance of prediction of early response to TKIs is presented in Table. For each value of AUC, the corresponding 95% confidence interval is reported in brackets. **Conclusions**: Radiomics predicted the response to TKIs of RR-DTC pts with an accuracy of 71%. Radiomics technique has the potential to enable clinicians to anticipate the probability of response to TKIs at baseline, directing toward the most suitable patient-tailored therapeutic path. Prospective studies may further validate these preliminary findings. Research Sponsor: None.

6078 **Poster Session**

A pooled analysis of response to selective RET inhibitors among patients with medullary thyroid cancer with M918T versus non-M918T RET mutations.

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Background: Medullary thyroid cancer (MTC) accounts for 1 to 2% of thyroid cancers in the United States; *RET* alterations occur in >95% of hereditary and 50% of sporadic forms. Up to 80% of patients with sporadic MTC have somatic M918T RET mutations, which is associated with poor prognosis (1). The tyrosine kinase inhibitors (TKIs) cabozantinib and vandetanib are approved to treat patients with MTC regardless of *RET* status; however, retrospective analyses have suggested that there may be greater benefit in patients with M918T mutations (1,2). Newly approved therapies selpercatinib and pralsetinib, developed for patients with *RET* mutations, have demonstrated higher response rates than previous first line therapies. In this analysis, we examine the differences in overall response rate (ORR) between patients with MTC with *RET* M918T non-*RET* M918T mutations. **Methods:** An analysis of ORR in patients with MTC with RET M918T mutations with non-M918T mutations was conducted using the efficacy populations used to support the approvals of pralsetinib and selpercatinib using the following groups: Patients who received prior cabozantinib or vandetanib (referred to as "previously treated"). Patients with no prior cabozantinib or vandetanib ("TKI naïve"). All patients regardless of prior therapy. **Results:** Exploratory analysis of ORR of pooled population of Selpercatinib and Pralsetinib in patients with MTC with RET M918T mutations and non-M918T mutations. [1] Prior vandetanib or cabozantinib. [2] No prior vandetanib or cabozantinib. Two groups of patients were analyzed (*RET* M918T mutation and *RET* non-M918T mutation), with subgroups with respect to prior treatment. Among all patients regardless of prior therapy, the ORR was similar between M918T non-M918T groups. Among previously treated patients, the ORR was lower in the M918T group vs. the non-M918T group, while in the TKI naïve group the ORR was higher in the M918T groups vs the non-M918T group although the 95% CIs overlap in both comparisons. **Conclusions:** There were no major differences in ORR among mutational subtypes in patients with MTC treated with *RET* inhibitors, regardless of prior therapy. ORR was similar between patients with M918T and non-M918T mutations. Additional experience in ongoing clinical studies may provide additional data regarding responses across specific mutation types. References: 1.Sherman SI et al "Correlative analyses of RET and RAS mutations in a phase 3 trial of cabozantinib..." Cancer. 2016;122(24):3856-3864. 2.Wells SA Jr et al "Vandetanib in patients with locally advanced or metastatic medullary thyroid cancer..." J Clin Oncol. 2012;30(2):134-41. Research Sponsor: None.

6079 **Poster Session**

Trastuzumab deruxtecan (T-DXd) in patients with human epidermal growth factor receptor 2 (HER2)-expressing salivary duct carcinoma: Subgroup analysis of two phase 1 studies.

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Background: T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and membrane-permeable topoisomerase I inhibitor payload. T-DXd has been approved for use in the US and Japan for both breast cancer and gastric cancer and has demonstrated safety and efficacy for additional solid tumors indications in the first-in-human (FIH) (J101; NCT02564900) and drug-drug interaction (DDI) (A104; NCT03383692) phase 1 studies. Here we present the combined subgroup analysis for salivary duct carcinoma. **Methods:** Patients (pts) with HER2-expressing salivary duct carcinoma after standard treatment or without any available standard treatment in both the FIH study and DDI study were included in this analysis. HER2 expression at enrollment was defined by IHC and/or amplification by ISH or NGS via local testing. A retrospective analysis of HER2 IHC and ISH of archived samples was conducted after enrollment by central laboratory per ASCO CAP guidelines. Pts with salivary duct carcinoma received T-DXd at 6.4 mg/kg and 5.4 mg/kg IV every 3 weeks in the FIH study and DDI study, respectively. RECIST version 1.1 was used for efficacy assessments by investigators. **Results:** Of 329 pts enrolled in both the FIH (289 pts) and DDI (40 pts) studies, a total of 17 pts with salivary duct carcinoma were pooled in this analysis: 8 pts with T-DXd at 6.4 mg/kg from FIH study and 9 pts with T-DXd at 5.4 mg/kg from DDI study. The sites of primary disease were parotid gland for 6 pts, submandibular gland for 4 pts, sublingual gland for 1 pt, and unknown for 6 pts. As for HER2 status by the central laboratory, 11 pts were IHC3+, 1 pt was IHC2+/ISH- and 5 pts had no available samples. Fourteen pts received HER2 targeted agents as a prior cancer therapy including trastuzumab. At data cutoff (FIH study: 1 Aug 2019; DDI study: 26 Sep 2018), the confirmed overall response rate was 47% (8/17) and the best overall response was PR in 8 pts and SD in 9 pts. Median duration of response and progression-free survival were 12.9 months and 14.1 months, respectively. Treatment-emergent adverse events (TEAEs) occurred in all 17 pts (grade $\geq$3, 64.7%); most common grade $\geq$ 3 TEAEs were decreased neutrophil count (8/17, 47.1%), decreased white blood cell count (6/17, 35.3%), anemia (2/17, 11.8%) and decreased platelet count (2/17, 11.8%). Three pts (3/17, 17.6%) had adjudicated drug related interstitial lung disease (Grade 1 for 2 pts and Grade 3 for 1 pt). Of these 17 pts, 7 pts (41.2%) experienced dose interruption and 3 pts (17.6%) experienced dose reduction due to TEAEs. Four pts (23.5%) discontinued treatment due to TEAEs. **Conclusions:** T-DXd showed promising antitumor activity in HER2-expressing salivary duct carcinoma with durable response. The safety profile was generally consistent with previous results in the other solid tumors. Clinical trial information: NCT02564900 and NCT03383692. Research Sponsor: Daiichi Sankyo Co., Ltd., Japan.

6080 **Poster Session**

Patient-reported outcomes (PROs) from a phase II trial of pembrolizumab for HPV-associated papilloma patients with laryngeal, tracheal and/or pulmonary involvement.

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Background: Recurrent respiratory papillomatosis (RRP) is caused by human papillomavirus (HPV) types 6 & 11. RRP proliferates in the respiratory tract impacting breathing, swallowing, and voice and carries a 1-4% risk of malignant transformation.There is no curative therapy for RRP. Given the tolerized host immune response against HPV, the safety and efficacy of pembrolizumab (pembro) as an alternative treatment for this patient population was evaluated in a phase II clinical trial. Patient reported outcomes (PROs) were assessed during the trial to capture the patient perspective of pembro as an alternative to surgery or in office procedures, both standard of care (SOC). **Methods:** RRP patients who had previously undergone >3 procedures in any year, or with known tracheal or pulmonary involvement prior to study entry were treated with pembro 200mg every 3 weeks. The primary endpoint of the trial was best 'overall response rate' (ORR) measured by an endoscopic-based disease burden score (lower score reflects better 'response') and/or RECIST 1.1, secondary endpoint included PROs. Twenty-one patients were required to assess the primary endpoint. Most of the QoL surveys used Likert scale to assess PROs ('never, sometimes, often, most of the time, always'). The percentage reporting 'never' having an issue with symptom or activity at baseline, 6 months, and at time of ORR (nadir disease burden score) is reported here. **Results:** Twenty-one patients were accrued. Median age (range) was 45 (19-68), 57% (12/21) were male and 67% (14/21) were white. Questionnaire completion rates were 100% at baseline, 90% at 6 months, and 85% at ORR. Improvement in: social interactions (less difficulty with: physical intimacy [38%,56%,65% reporting 'never' at baseline, 6 months, and at ORR respectively]), discussing disease diagnosis [19%,21%,39%]); personal feelings (less depression [14%,32%,33%], less anxiety [5%,16%,22%], less embarrassment [19%,37%,50%]), and work-related absences (less frequently fabricating reasons for work absence due to disease-related treatment [57%,78%,56%] and less utilization of family vacation or FMLA for disease treatment [29%,53%,56%]) were reported. At ORR, 72% (13/18) patients reported that IV infusion was not emotionally burdensome and 78% (14/18) reported it as the preferred treatment relative to their perceived experience with SOC surgery or in office procedures. **Conclusions:** PRO results show consistent benefit in key aspects of the patient experience with pembro over procedure based SOC further supporting its overall clinical benefit in patients with HPV-associated RRP. Clinical trial information: NCT02632344. Research Sponsor: MERCK, Other Government Agency.

6081 **Poster Session**

Molecular profiling and targeted agents in recurrent, metastatic salivary gland tumor (R/M SGT) patients (pts) treated at two academic centers.

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Background: Treatment selection based on actionable alterations (AAs) is an appealing strategy for pts with R/M SGT. The GEMS-001 study (NCT02069730) at Princess Margaret Cancer Centre (PM) and the Vall DHebron Institute of Oncology (VHIO) pre-screening program facilitate the identification of AAs for R/M SGT pts and treatment selection. **Methods:** We analyzed R/M SGT treated at PM and VHIO from 2015 to 2020. Clinicopathological features, molecular alterations and treatment modalities were correlated with outcomes. The primary endpoint was overall response rate (ORR) by RECIST 1.1. Clinical benefit rate (CBR) was defined by pts with partial response or stable disease $\geq$4 months. Clinical actionability of multigene panel testing (NGS) and immunohistochemistry (IHC) were assessed as per institutional molecular tumor boards or investigators. Pts were opportunistically matched to available therapies from each center. **Results:** In total 206 pts were enrolled. On IHC, HER2 overexpression was present in 9%, Androgen Receptor (AR) 33%, Estrogen/Progesterone Receptor (ER/PR) 11% and ALK overexpression 0%. On NGS, PIK3CA mutation (mut) was in 9%, NTRK fusion 6%, NOTCH1-3 mut 5%, HRAS mut 6%, ERBB2/3 alterations (alt) 4% and FGFR1-4 alt 3%. Up to 92 pts (45%) displayed at least 1 AA and 36 pts (18%) had $\geq$2 AAs. A total of 60 pts (29%) were matched to AAs. Of those matched, median age was 60 years (range 33-84), M:F 21:39, 95% ECOG$\leq$1 with a median number of prior treatment lines 0 (range 0-3), and their AAs included 26 AR, 9 HER2 or ERBB2 overexpression, 9 PIK3CA mut, 3 NTRK fusion, 3 FGFR1-3 alt and 10 other AAs (2 ER/PR overexpression, 2 EGFR mut, 1 c-kit mut, 1 BAP1 mut, 1 Non-V600 BRAF mut, 1 CDKN2A mut, 1 CHEK2 mut and 1 PTCH1 mut). Overall, ORR was 27% for the matched population. See table for outcomes. **Conclusions:** In our cohort, almost one third of the population received therapies matched to AAs. Our results suggest that targeted therapies have promising activity in pts with R/M SGT supporting comprehensive molecular and IHC profiling in treatment determination. Research Sponsor: None.

AA	ORR	CBR
NTRK	100%	100%
HER2	77%	56%
AR	23%	35%
PIK3CA	0%	67%
FGFR	0%	100%
NOTCH	0%	50%
Other	0%	44%

6082 **Poster Session**

Benefits of pembrolizumab in progressive radioactive iodine refractory thyroid cancer: Results of the AcSé Pembrolizumab Study from Unicancer.

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Background: AcSé Pembrolizumab is a Phase II, non-randomized parallel arm, open-label, multicentric study from Unicancer investigating the efficacy and safety of pembrolizumab monotherapy in different cohorts of patients with rare cancers (NCT03012620). Here we report the first results of pembrolizumab in the radioactive iodine refractory thyroid cancer cohort. **Methods:** Main inclusion criteria were progressive radioactive iodine refractory (RAIR) thyroid cancer (TC) resistant to standard treatment, age $>$ 18, ECOG PS$\leq$1. Patients received pembrolizumab 200 mg IV as a 30-minute infusion on Day 1 of every 21-day cycle for a maximum of 2 years. The primary endpoint was the confirmed objective response (OR) rate according to RECIST v1.1 by investigator. Secondary endpoints included duration of response, progression-free survival (PFS), overall survival (OS), and safety. **Results:** 43 patients (21 female, mean age 64.8 years; range 40-86) with TC (27 patients with differentiated TC (DTC) [papillary: 7; follicular: 14: oncocytic: 5 poorly differentiated: 1] and 16 patients with anaplastic TC (ATC)) were included from September 2017 to December 2020. The median number of previous systemic treatment lines was 2 (range, 0-7) in DTC and 2.5 (range, 1-4) in ATC. The median number of pembrolizumab cycles was 4 (range, 1-35). The median follow-up was 5.9 months (range: 22 days-22.9 months) for DTC and 2.7 months (range: 3 days- 24.4 months) for anaplastic TC. For DTC the best tumor response was partial response (PR) in 3 (11.1%) patients and stable disease (SD) in 5 (18.5%). Median duration of response was 2.5 months (range: 5 days-7.2 months). The median PFS was 2.6 months, the 6-month PFS was 16.9 %. The median OS was 12.7 months with a 6-month OS of 73.3%. For ATC the best tumor response was PR in 3 cases (18.8 %) and SD in 1 case (6.2 %). Median duration of response was 1.6 months (range: 2 days-7.2 months). The median PFS was 2.3 months, the 6-month PFS was 33.8 %. The median OS was 3.6 months with a 6-month OS of 32.9%. Treatment emergent adverse event included 9 Grade 1-2, 20 Grade 3 (3 being considered as related and 17 as not related) and 1 Grade 4 (sepsis, unrelated). Overall, the toxicity profile was similar to that observed in other cancers. **Conclusions:** The response rates observed under pembrolizumab is low in DTC and not negligible in ATC, but with a short duration of response. Clinical trial information: NCT03012620. Research Sponsor: La Ligue Nationale contre le Cancer, Other Government Agency, Pharmaceutical/Biotech Company.

6083 **Poster Session**

NTRK, RET, BRAF, and *ALK* fusions in thyroid fine-needle aspirates (FNAs).

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Background: Receptor tyrosine kinase (RTK) fusions may be targeted by small molecule inhibitors to treat various advanced tumors, including thyroid cancer. Clinical trials have studied selective inhibitors of *ALK, BRAF, NTRK* and *RET*, leading to several FDA-approved therapies. The Afirma Genomic Sequencing Classifier (GSC) classifies cytologically indeterminate thyroid nodules as molecularly benign or suspicious. The Xpression Atlas reports 905 genomic variants and 235 fusion pairs on GSC Suspicious, Suspicious for Malignancy (SFM), and Malignant FNA samples at the time of diagnosis. Here we report the prevalence of these fusion genes in real-world clinical practice. **Methods:** We analyzed anonymized data from 50,644 consecutive Bethesda III-VI nodule FNA samples submitted to the Veracyte CLIA laboratory for molecular testing using whole transcriptome RNA sequencing (RNA-Seq). Gene pairs are listed alphabetically. **Results:** 32,080 Bethesda III/IV nodules were classified as GSC Benign and 278 were Parathyroid Classifier positive. No *ALK*, *BRAF, NTRK1/3,* or *RET* fusions were identified among these samples. Among 16,594 Bethesda III/IV GSC Suspicious FNAs, 3% (n = 529) were positive for *ALK*, *BRAF, NTRK1/3 or RET* fusions. Among the 1,692 Bethesda V/VI FNAs, the proportion of positive nodules was 8% (n = 135). Among these combined cohorts of Bethesda III/IV GSC Suspicious and Bethesda V/VI, the most common gene fusions observed for each of the 5 studied RTK genes was: *ETV6/NTRK3* (n = 164, 72% of *NTRK3* fusions), *CCDC6/RET* (n = 104, 55% of *RET*), *BRAF/SND1* (n = 32, 20% of *BRAF*), *ALK/STRN* (n = 20, 37% of *ALK*), and *NTRK1/TPM3* (n = 14, 50% of *NTRK1*). *BRAF* showed the highest diversity of fusions, with 80 gene partners. Different gene partners with *RET, ALK, NTRK1,* and *NTRK3* numbered 25, 11, 9, and 5, respectively. **Conclusions:** Whole-transcriptome RNA-seq on small sample thyroid FNA specimens can identify clinically relevant *ALK, BRAF, NTRK,* and *RET* fusions across Bethesda categories. The prevalence ranges from 3% in Bethesda III/IV Afirma GSC Suspicious specimens to 8% among Bethesda V/VI specimens. Future studies need to determine if detection of precision medicine candidates by pre-operative FNA can optimize initial treatment, predict response to treatment, and prioritize selective targeted therapy should systemic treatment be needed. Research Sponsor: Veracyte.

Number and prevalence of selected receptor tyrosine kinase gene fusions among 50,644 thyroid FNA samples by Bethesda category.

RTK gene	AUS/FLUS(III) N = 39464	FN/SFN(IV) N = 9488	SFM(V) N = 837	Malignant(VI) N = 855
ALK	29 (0.07%)	22 (0.23%)	3 (0.36%)	0 (0.00%)
BRAF	88 (0.22%)	47 (0.50%)	15 (1.79%)	13 (1.52%)
NTRK1	16 (0.04%)	8 (0.08%)	2 (0.24%)	2 (0.23%)
NTRK3	126 (0.32%)	67 (0.71%)	21 (2.51%)	15 (1.75%)
RET	86 (0.22%)	40 (0.42%)	40 (4.78%)	24 (2.81%)
Any	345 (0.87%)	184 (1.94%)	81 (9.68%)	54 (6.32%)

AUS/FLUS- atypia or follicular lesion of undetermined, FN/SFN-follicular and Hürthle cell neoplasm or suspicious for same.

6084 **Poster Session**

Treatment patterns and systemic therapy outcomes for patients with salivary duct carcinoma and adenocarcinoma NOS.

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Background: Salivary duct carcinoma (SDC) and adenocarcinoma, not otherwise specified (Adeno-NOS) are rare and aggressive subtypes of salivary gland cancers. Biomarker studies revealed targetable alterations such as androgen receptor (AR) and HER2 overexpression; nevertheless, chemotherapy (CT) remains the cornerstone treatment of patients (pts) with locally advanced or metastatic disease based on limited efficacy data. We sought to describe the treatment patterns and outcomes of SDC and Adeno-NOS pts. **Methods:** We retrospectively collected clinicopathological, treatment, and outcomes data of SDC or Adeno-NOS pts that were seen at MD Anderson from 1990-2020. AR positivity was defined by IHC staining in $\geq$ 10% of tumor cells, and HER2 by IHC 2+ or 3+ scores. Overall response rate (ORR) was assessed by an independent radiologist per RECIST v1.1. Recurrence-free survival (RFS) and overall survival (OS) from diagnosis were estimated using log-rank test. A multivariable cox regression model was performed to estimate the hazard-ratio (HR) of risk factors on pts outcomes. **Results:** 200 pts were included, 110 had SDC and 90 Adeno-NOS. Most pts (61%) presented with locoregional disease (stage III-IVB), while 13% had distant metastasis (IVC). AR was positive in 77% of cases, and HER2 in 47%. In the curative setting (N=174), 98% pts underwent surgery and 90% radiotherapy (RT); 15 pts with stage IVA-B disease had aggressive trimodality therapy including surgery, RT, and systemic therapy. Overall, 55% pts recurred. The mRFS and 5-y RFS rate were 24 mos (95%CI, 16-43) and 34.5%, respectively. For pts with IV-A-B stage, trimodality therapy was associated with an improved OS in comparison to surgery and/or RT (39 mos vs NA, p=0.04). In the metastatic setting, 82 pts received $\geq$1 line of systemic therapy; the preferred 1st line regimen was platinum/taxane with or without trastuzumab (50%). Table summarizes the ORR and mPFS to each therapy line. ORR and PFS was higher for HER2-targeted therapy (1st line: 47% and 11 mos; 2nd line 29% and 6 mos; respectively); only 10 pts received androgen blockage. At a median follow-up of 7.5 y, the mOS was 5 ys and the 5-y OS rate was 50%. In multivariate analysis, higher T and N stages (HR 2.1 and 3.8, $p<0.05$), and positive margins (HR 2.0, p=0.003) were associated with worse RFS; older age (HR 1.03, p=0.003), and higher TNM stage (HR 1.78, p=0.006) were associated with worse OS. HER2 expression was not prognostic. **Conclusions:** This study validates prognostic factors in SDC and adeno-NOS and is the largest series to report outcomes to palliative systemic therapy per treatment line, providing a benchmark for future studies in these diseases. Aggressive trimodality therapy may improve outcomes of pts with stage IVA-B disease. Research Sponsor: Research funds from Klaus pharma.

TPS6085 **Poster Session**

Encorafenib and binimetinib with or without nivolumab in treating patients with metastatic radioiodine refractory BRAF V600 mutant thyroid cancer.

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Background: Differentiated thyroid cancer is the most common endocrine malignancy and has a high frequency of actionable molecular aberrations including BRAF V600E mutations (45%), RET fusions (10%), and NTRK fusions ($<$ 2%). FDA approved systemic therapies for metastatic radioiodine refractory differentiated thyroid cancer (RR-DTC) include multikinase inhibitors (Lenvatinib and sorafenib), NTRK inhibitors (larotrectinib and entrectinib for NTRK fusion+ cancers), and RET inhibitors (selpercatinib and pralsetinib for RET fusion+ cancers). Previous phase II clinical trials showed clinical efficacy with first and second generation BRAF inhibitors in patients with BRAF mutant RR-DTC. BRAF inhibitors have not yet been FDA approved for treatment of BRAF mutant RR-DTC. Effective therapeutic options for patients with BRAF mutant RR-DTC remains an important unmet clinical need. BRAF mutant thyroid cancers often show elevated expression of PD-L1. Additionally, BRAF inhibition results in increased expression of PD-L1 in thyroid cancer. This clinical trial seeks to evaluate the safety and efficacy of encorafenib plus binimetinib with or without nivolumab in patients with BRAF mutant metastatic RR-DTC. Encorafenib and binimetinib are highly selective and potent oral inhibitors of BRAF and MEK, respectively. Nivolumab is a potent inhibitor of the immune co-inhibitory receptor programmed cell death protein 1 (PD-1). **Methods**: This is a phase II, single institution, open-label, randomized clinical trial evaluating the combinations of (Arm 1) encorafenib 450 mg/day + binimetinib 45 mg twice daily and (Arm 2) encorafenib 450 mg/day + binimetinib 45 mg twice daily + nivolumab 480 mg I.V. every 4 weeks in patients with metastatic BRAF mutant RR-DTC. The trial will enroll 20 patients in each arm and treatment will be given in 28 day cycles for up to 2 years. Eligible patients must have metastatic/unresectable BRAF mutant RR-DTC, an ECOG performance status of 0-1 and adequate bone marrow, liver and kidney function. Patients with CNS metastases are included if the metastases have been treated and remained stable or are asymptomatic and $\leq$10 mm in diameter. Patients may be systemic therapy naïve or have previously been treated with multikinase inhibitors. Prior therapy with BRAF, MEK or immune checkpoint inhibitors is exclusionary. The primary endpoint is confirmed objective response rate (ORR) determined by RECIST v1.1 with restaging imaging every 12 weeks. Secondary endpoints include progression free survival, overall survival, and safety/tolerability (CTCAE v5.0). Arms 1 and 2 will be evaluated independently and are not powered for direct comparison. The trial design includes continuous toxicity monitoring with a Pocock-type stopping boundary. This clinical trial is in progress and 3 patients have been enrolled. Clinical trial information: NCT04061980. Research Sponsor: Bristol Myers Squibb and Pfizer.

TPS6086 **Poster Session**

Phase II multicenter randomized trial to assess the efficacy and safety of first line nivolumab in combination with paclitaxel in subjects with R/M HNSCC unable for cisplatin-based chemotherapy (NIVOTAX): A TTCC study.

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Background: Nivolumab is the standard of care for patients (pts) with R/M HNSCC in the platinum-refractory setting. Up to 20% of R/M HNSCC pts are ineligible for cisplatin-based CT due to poor performance status and/or comorbidities. ERBITAX (weekly cetuximab + paclitaxel) is a recommended regimen for this patient population according to the Spanish Society of Medical Oncology guidelines. Preclinical data suggests a role for paclitaxel as immuno-modulator, mainly by increasing tumor infiltrating CD8+ (Galluzzi L., et al 2015). NIVOTAX trial aims to evaluate efficacy and safety of nivolumab + paclitaxel vs ERBITAX as first-line treatment for R/M HNSCC pts with platinum-refractory disease or ineligible for platinum-based chemotherapy. **Methods:** NIVOTAX (NCT04282109) is a randomized, open-label, multicenter, phase II trial sponsored by the Spanish Group of Head and Neck Cancer Treatment (TTCC) including R/M HNSCC pts not amenable for curative-intent therapy, previously untreated for R/M disease and not candidates for cisplatin-based chemotherapy. Population is distributed in 3 Groups: 1= Platinum-refractory; 2=Platinum-sensitive but unable to receive cisplatin due to: Karnofsky performance status (KPS) 70% and/or major comorbidities (renal/heart failure, grade $\geq$2 hearing loss) and/or previous allergic reactions to platinum compounds; 3= Platinum-sensitive but cumulative cisplatin dose received $\geq$225 mg/m^2 for locally-advanced disease. Pt are stratified according to: KPS (70% vs 80-100%); PD-L1 by Combined Positive Score (CPS $\geq$1 vs $<$ 1); and HPV positivity (HPV+ oropharynx vs HPV-/non-oropharyngeal). 141 Pt are being randomized 2:1 to NIVOTAX (nivolumab 240 mg q2 weeks + weekly paclitaxel at 80 mg/m^2 up to 12 weeks followed by maintenance nivolumab 480 mg/ q4 weeks) or ERBITAX (weekly 250 mg/m^2 plus paclitaxel 80 mg/m^2 up to 12 weeks followed by maintenance cetuximab 250 mg/m^2 weekly). Both arms will be continued up to a maximum of 24 months. Primary end-point is to evaluate treatment efficacy in terms of 2-year overall survival (2-y OS). It is assumed that 2-y OS in the NIVOTAX arm will be at least 26% (10% gain when compared to the expected 16% 2-y OS rate in this pt population). Secondary objectives include progression free survival (PFS), overall response rate, disease control rate, duration of response, 6m PFS, 5y-OS and safety profile. Response endpoints will be assessed using RECIST 1.1 criteria. As of February 12, 2021, 64 pts have been randomized. Planned safety data review for the first 10 pts treated with NIVOTAX regimen did not show any unexpected AE. Clinical trial information: NCT04282109. Research Sponsor: Bristol-Myers Squibb.

TPS6087 **Poster Session**

The AIM-HN Study: A pivotal study evaluating the efficacy of tipifarnib in patients with recurrent or metastatic head and neck squamous cell carcinoma with *HRAS* mutations.

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Background: Head and neck squamous cell carcinoma (HNSCC) accounts for more than 830,000 new cancer cases each year worldwide. The prognosis for recurrent and/or metastatic (R/M) HNSCC patients remains poor with an estimated median overall survival (mOS) of 7-15 months in the first line setting and 5-8 months in the second line setting and beyond. Approximately 4-8% of HNSCC tumors are driven by gain-of-function mutations in the *HRAS* (m*HRAS*) proto-oncogene. Tipifarnib is a potent and selective farnesyltransferase inhibitor that disrupts HRAS function by blocking required protein membrane localization, and subsequent cellular growth and survival. Data from a prior phase 2 study (RUN-HN; NCT02383927) of tipifarnib in R/M m*HRAS* HNSCC patients in the second line plus setting demonstrated encouraging efficacy, with an objective response rate (ORR) of 55% and mOS of 15.4 months for patients with mHRAS variant allele frequency (VAF) $\geq$ 20%, providing support for pursuing a pivotal trial in this patient population. **Methods:** AIM-HN (NCT03719690) is a global, open-label single-arm pivotal study evaluating the efficacy and tolerability of tipifarnib in second line plus R/M m*HRAS* HNSCC patients. The primary objective is to determine the ORR in patients with a m*HRAS* VAF $\geq$ 20% (High VAF population), as assessed using RECIST v1.1 by Independent Review Facility. Key secondary objectives include the ORR for patients of all VAF levels, and the duration of responses for both VAF$\geq$ 20% and all VAF levels. Key inclusion criteria include: histologically confirmed head and neck cancer of squamous histology not amenable to local therapy with curative intent; known tumor missense *HRAS* mutation (with VAF determined and available) detected by Next Generation Sequencing; ECOG performance status of 0-1; measurable disease by RECIST v1.1; and adequate organ function. Key exclusion criteria include: salivary gland, thyroid, (primary) cutaneous squamous or non-squamous histologies; intolerable Grade 2 or $\geq$ Grade 3 neuropathy or unstable neurological symptoms within 4 weeks of Cycle 1 Day 1; or active, uncontrolled infections requiring systemic therapy. Tipifarnib is administered at a dose of 600 mg, orally with a meal twice a day for 7 days in alternating weeks (Days 1-7 and 15-21) of 28-day cycles until discontinuation criteria are met. All patients are being followed for safety through the End of Treatment visit, roughly 30 days after treatment discontinuation or immediately before the administration of another anticancer treatment, whichever occurs first. Upon therapy discontinuation, all patients are being followed approximately every 12 weeks for survival status, and the use of subsequent therapy. The IDMB last reviewed data in October 2020 and recommended the trial continue as planned. AIM-HN is continuing to enroll patients globally. Ho et al, *JCO*, accepted. Clinical trial information: NCT03719690. Research Sponsor: Kura Oncology.

TPS6089 **Poster Session**

CMP-001-007: Open-label, phase 2 study of intratumoral CMP-001 + pembrolizumab in patients with recurrent or metastatic head and neck squamous cell carcinoma.

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Background: PD-1 blockade ± chemotherapy has recently become a primary systemic therapy recommended by NCCN guidelines for patients (pts) with recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). However, most pts still do not respond to treatment, indicating a large unmet need for pts with unresectable disease. CMP-001 is a toll-like receptor 9 (TLR9) agonist comprising a CpG-A oligodeoxynucleotide packaged in a virus-like particle that can induce type I interferon secretion from tumor-associated plasmacytoid dendritic cells, promoting a Th1-like chemokine milieu in the tumor microenvironment and inducing an antitumor CD8+ T-cell response. In a phase (ph) 1b study in pts with metastatic melanoma, intratumoral (IT) injection of CMP-001 + intravenous (IV) pembrolizumab (pembro) reversed PD-1 blockade resistance, induced responses in injected and noninjected lesions, and had an acceptable safety profile (Milhem et al, SITC 2020). This combination is therefore being tested in pts with HNSCC. **Methods:** CMP-001-007 (NCT04633278) is an open-label, multicenter, ph 2 study designed to investigate the efficacy and safety of CMP-001 + IV pembro in adult pts with histologically or cytologically confirmed R/M HNSCC considered incurable by local therapies. Eligible pts have undergone a pretreatment tumor biopsy, received no prior systemic therapy in the R/M setting, and have primary tumor locations of oropharynx, oral cavity, hypopharynx, or larynx. In addition, pts must have PD-L1-positive tumors (combined positive score $\geq$1), known tumor human papillomavirus (HPV) status (for oropharyngeal cancer), and measurable disease per RECIST v1.1 with $\geq$1 lesion amenable to IT injection. Pts with primary tumors in the nasopharynx are excluded. Enrolled pts will receive CMP-001 10 mg once weekly for 7 doses and every 3 weeks (Q3W) thereafter. The first dose may be administered subcutaneously or via IT injection, with all subsequent doses administered IT. All pts will also receive pembro 200 mg IV Q3W after the CMP-001 injection. Treatment continues until unacceptable toxicity or disease progression. The primary endpoint is investigator-assessed objective response rate (ORR) per RECIST v1.1. Secondary endpoints include safety, duration of response (DOR), progression-free survival (PFS), overall survival, and effects of HPV infection and PD-L1 expression on ORR, DOR, and PFS. Exploratory endpoints include analyses of baseline and changes from baseline in tumor or serum biomarkers related to TLR9, immune checkpoints, and potential predictors of response, as well as serum concentrations of CXCL10 and CMP-001. Refer to clinicaltrials.gov/ct2/show/NCT04633278 for the most current information on enrolling sites. Clinical trial information: NCT04633278. Research Sponsor: Checkmate Pharmaceuticals.

TPS6090 **Poster Session**

The BURAN study of buparlisib (AN2025) in combination with paclitaxel compared to paclitaxel alone, in patients with recurrent or metastatic head and neck squamous cell carcinoma.

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Background: Buparlisib (AN2025) is a 2,6-dimorpholino pyrimidine derivative oral pan-class I PI3K inhibitor. The PI3K signaling pathway is one of the most frequently altered pathways in HNSCC. A previous randomized, double-blind, placebo-controlled phase II study (BERIL-1)assessed patients with recurrent/metastatic HNSCC after PD on or after platinum-based chemotherapy in the metastatic setting. Patients assigned 1:1 to receive second-line oral buparlisib or placebo, plus intravenous weekly paclitaxel in 28-day cycles. Median PFS 4.6 months buparlisib arm, 3.5 months placebo arm (hazard ratio 0.65 [95% CI: 0.45–0.95], nominal one-sided p=0.011). Median OS 10.4 months buparlisib arm, 6.5 months placebo arm (hazard ratio 0.72 [95% CI: 0.49-1.04], nominal one-sided p=0.041). Best ORR buparlisib arm 39%, placebo arm 14%. Safety in buparlisib arm was manageable and comparable to placebo arm. (Soulieres, Lancet Oncology). Results suggest that buparlisib in combination with paclitaxel could be effective treatment following failure of platinum-based chemotherapy. **Methods:** The treatment algorithm for HNSCC was recently modified with inclusion of anti-PD-1/PD-L1 agents that provide a survival advantage, defining an unmet need after their use. The BURAN study is initiated as a confirmatory study to define activity in this setting. Methods: A multicenter, randomized, open-label phase III trial evaluating efficacy and safety of daily buparlisib (100 mg) in combination with weekly paclitaxel (80 mg/m^2), compared to weekly paclitaxel alone, in patients with refractory, recurrent, or metastatic HNSCC, progressing after prior anti PD-1/anti PDL-1 therapy either as monotherapy or with a platinum-based regimen (in combination or sequence), and no more than two prior lines of treatment. 483 patients will be randomized 2:1, to receive either buparlisib in combination with paclitaxel or paclitaxel alone, stratified according to historical HPV status. Primary Objective: OS of buparlisib in combination with paclitaxel compared to paclitaxel alone. Secondary Objectives: Comparative PFS, ORR, and DoR, by Investigator and Independent Radiological Review Committee. Efficacy in subgroups of patients by randomization strata. Effect on symptoms and health related QOL. Efficacy related to biomarkers, microbiome analysis. Pharmacokinetics (PK) of buparlisib in combination with paclitaxel. Safety Objective: Comparative safety and tolerability. Primary analysis is OS in the ITT population, once 383 events have occurred, to demonstrate a 20% reduction in risk of death. Survival follow-up is to a maximum of five years. Trial opened December 12, 2020; X patients currently enrolled. Clinical Trial registry number: NCT04338399. Clinical trial information: NCT04338399. Research Sponsor: Adlai Nortye USA Inc.

TPS6091 **Poster Session**

TrilynX: A phase 3 trial of xevinapant and concurrent chemoradiation for locally advanced head and neck cancer.

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Background: Concurrent chemoradiotherapy (CRT) is the standard of care for previously untreated patients with locoregionally advanced squamous cell carcinomas of the head and neck (LA-SCCHN). Xevinapant (Debio 1143) is an orally available antagonist of inhibitor of apoptosis proteins with the potential to enhance the antitumor activity of platinum-based chemotherapy and radiotherapy. The radiosensitizing effect of xevinapant is mediated through caspase activation and TNF, IFNγ, CD8 T cell-dependent pathways. Three-year follow-up results from a randomized Phase 2 study showed significant improvements of xevinapant versus placebo in addition to standard chemoradiation (CRT) for locoregional control (LRC) rate at 18 months, PFS and OS. The addition of xevinapant was well tolerated, manageable and did not jeopardize backbone therapy [1, 2]. **Methods:** TrilynX is a multinational, Phase 3, double-blind, placebo-controlled, randomized clinical study assessing the efficacy of xevinapant in combination with concurrent CRT compared with placebo in combination with CRT for LA-HNSCC. Adult patients with newly diagnosed, pathologically proven, treatment-naive LA-SCCHN will be enrolled. Study population will include hypopharynx, larynx and p16-negative oropharyngeal. Other eligibility criteria: ECOG PS 0 or 1, AST and ALT $\leq$ 3.0 x ULN, total bilirubin $\leq 1.5 \times$ ULN, and eligible for definitive CRT. Approximately 700 eligible patients will be randomly assigned to receive oral xevinapant at 200 mg per day on days 1 to 14 of 3-week cycles or placebo for three cycles in combination with cisplatin (100 mg/m^2, q3w) for three cycles, and concomitant standard fractionation intensity-modulated radiotherapy (70 Gy/7 weeks). The concurrent CRT period will be followed by a monotherapy period consisting of further three cycles of xevinapant or placebo. The primary endpoint is Event Free Survival (EFS) assessed by a Blinded Independent Radiological Committee (BIRC). An interim analysis will occur when 279 EFS events as assessed by the BIRC are observed. The primary analysis will occur once 429 EFS events are observed. TrilynX has ~90% power to detect the expected hazard ratio benefit of 0.73. Secondary end-points include OS, PFS, LRC, ORR, HRQL, and safety. Data driven design, patients will be followed up for a minimum of 60-months. PK sparse sampling is performed to assess exposure-response relationships with efficacy and safety. Biomarkers of response and resistance will be explored. TrilynX started in August 2020 and it is ongoing. References: [1] X. Sun et. al, Lancet Oncol; 21(9): 1173-1187, 2020. [2] J. Bourhis et al., Ann Oncol; 31 (suppl 4): LBA39, 2020. Clinical trial information: NCT04459715. Research Sponsor: Debiopharm Internation SA.

TPS6092 **Poster Session**

First-in-human phase I/II trial of PRGN-2009 vaccine as monotherapy or with bintrafusp alfa in patients with recurrent/metastatic (R/M) human papillomavirus (HPV)-associated cancers (HPVC) and as neoadjuvant/induction therapy in locoregionally advanced (LA) HPV oropharyngeal (OP) and sinonasal (SN) squamous cell cancer (SCC).

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Background: R/M HPVC (cervical, anal, oropharyngeal, etc.) are incurable by current therapies. For newly diagnosed LA HPV-OPSCC standard-of-care (SOC) is radiotherapy ± chemotherapy (C/RT) or surgery ± adjuvant C/RT, with considerable risk of relapse. Newly diagnosed LA SNSCC treatment follows the OPSCC paradigm, and detection of HPV appears to confer improved prognosis. Neoadjuvant PD-1 immune checkpoint blockade (ICB) before surgery may improve RFS and is being evaluated in a multicenter phase III clinical trial (Keynote-689). PRGN-2009 (P) is a novel gorilla adenovirus vaccine containing 35 non-HLA-restricted epitopes of HPV 16 and 18 shown to induce HPV specific responses (preclinical models). Bintrafusp alfa (BA) is a bifunctional fusion protein targeting TGF-β and PD-L1 with promising activity in HPVC. This trial will evaluate the safety and activity of P/ P + BA in patients with previously treated R/M HPVC and as neoadjuvant/induction therapy before SOC surgery or C/RT in newly diagnosed LA HPV-OPSCC and HPV-SNSCC. **Methods:** This is a first-in-human, investigator-initiated, single-center phase I/II trial. Pts with previously treated (incl. ICB) R/M HPVC are eligible for Phase I: P dose escalation arm (3+3 design, 6-12 patients) testing 2 dose levels ($1x10^{11}$, $5x10^{11}$ viral particle units, SC Q2W three times, then Q4W), and combination arm (10 patients) testing P (recommended phase 2 dose (RP2D), same schedule) + BA (1200 mg IV Q2W). Treatment (both arms) will continue until disease progression, unacceptable toxicity, decision to withdraw. Primary endpoint is safety. Secondary endpoints include ORR (RECIST 1.1), PFS, and OS. For Phase II, patients with newly diagnosed stage II/III (AJCC Cancer Staging Manual, 8th ed.) HPV-OPSCC and stage II/III/IVA/IVB HPV-SNSCC planned for SOC C/RT or surgery will be eligible for two treatment arms of 20+2 patients each (sequential): P arm and P + BA, to evaluate the treatment activity. All patients will have pre-treatment biopsy, receive two cycles of the study treatment at the NCI Clinical Center two weeks apart, followed by post-treatment biopsy and SOC treatment (at the referring institution) 4 weeks after the first study treatment. Primary endpoint is post-treatment $\geq$2-fold increase in tumor-infiltrating CD3+ cells. Secondary endpoints include RFS, OS. Exploratory endpoints for both arms include analyses of immune subsets, soluble factors, and HPV-specific immune responses in peripheral blood and tissue where available, and in Phase II sequencing (exome, scRNA), immune spatial profiling with multiplex immunofluorescence, and salivary HPV DNA. Clinical trial registry: NCT04432597. Clinical trial information: NCT04432597. Research Sponsor: U.S. National Institutes of Health.

TPS6093 **Poster Session**

NRG Oncology HN006: Randomized phase II/III trial of sentinel lymph node biopsy versus elective neck dissection for early-stage oral cavity cancer.

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Background: Since patients with early-stage oral cavity cancer (OCC; T1-2N0M0; AJCC 8th ed) have a 20-30% rate of occult nodal metastases despite clinical and radiographic assessment, standard of care treatment includes elective neck dissection (END). Many patients have comprehensive surgical management of the regional cervical nodal basin even though the majority of those necks (70-80%) will not contain disease. Assessment of draining first echelon lymph nodes by sentinel lymph node (SLN) biopsy (Bx), a less invasive surgical procedure, may provide an alternative to END, while potentially reducing morbidity and cost. A decisive clinical trial comparing SLN Bx versus END can focus the HNC clinical and research community and resources on establishing the standard of care for management of the neck in early-stage OCC. **Methods:** In order to address the efficacy of SLN Bx in this population, we recently activated an international multi-institutional phase II/III prospective trial randomizing patients to two surgical arms: SLN Bx and END. PET/CT is an integral imaging biomarker in this trial. A node-negative PET/CT study with central read is required before randomization. Patients with a positive PET/CT central result will remain in a registry to compare imaging findings with final neck pathology. Given the current evidence available regarding morbidity for SLN Bx versus END, the phase II will determine if patient-reported neck and shoulder function and related QOL at 6 months after surgery using the Neck Dissection Impairment Index (NDII) shows a signal of superiority of SLN Bx compared to END. A total of 228 randomized patients with negative PET/CT for potential evaluation of shoulder-related morbidity with difference in 6-month NDII scores (minimum important difference ^{3}7.5; one-sided a = 0.10; 90% power) will serve as the "Go/No-Go" decision to move forward into phase III. The phase III portion is a non-inferiority (NI) trial with disease-free survival (DFS) as the primary endpoint (NI margin hazard ratio 1.34 based on a 5% absolute difference in 2-year DFS; one-sided alpha 0.05; 80% power, and an interim look for efficacy at 67% of the events based on an O'Brien-Fleming boundary). The NDII at 6 months after surgery is a hierarchical co-primary endpoint for the phase III. Target accrual of phase III is 618 PET/CT negative patients, including those randomized in phase II (297 DFS events required for the final analysis). In addition to radiotherapy and imaging credentialing, quality assurance will include central pathology review of all negative SLN Bx cases and surgeon credentialing through an education course and SLN Bx and END case review by the surgical co-chairs. A surgical quality assurance working group will review all trial SLN Bx and END outcomes. As of 02/15/21, 7 patients have been screened and 6 of the planned 228 randomized patients in phase II have been enrolled. Clinical trial information: NCT04333537. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

TPS6094 **Poster Session**

Trial in progress: A phase I/II trial of novel MDM2 inhibitor alrizomadlin (APG-115), with or without platinum chemotherapy, in patients with p53 wild-type salivary gland carcinoma.

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Background: Salivary gland carcinoma is a rare tumor that accounts for 6% of all head and neck cancers. This histologically and anatomically heterogeneous malignant tumor type is largely resistant to platinum and other chemotherapies but commonly has wild-type *TP53* based on next-generation sequencing analysis. Alrizomadlin is a novel, orally active, small molecular agent that binds to MDM2, restoring p53 tumor suppressor function and inducing apoptosis in tumor cells retaining wild-type p53. Preliminary clinical evidence suggests promising antitumor activity and a favorable safety profile for alrizomadlin in the treatment of solid tumors (Rasco 2019). **Methods:** This US multicenter open-label trial is evaluating alrizomadlin with or without platinum chemotherapy in adults with histologically documented wild-type *TP53* salivary gland carcinoma, including primary or metastatic lesions, an ECOG performance status 0-1, and a life expectancy of at least 12 weeks. In addition, subjects need to have measurable disease by computed tomography according to RECIST v1.1, with radiographic disease progression within the prior 12 months, high-grade status with or without metastases, and/or not amenable to curative treatment. An initial randomized phase (Part 1) will be followed by a single-arm phase (Part 2). Treatment arms include a cycle length of 21 days, and the study is using a time-to-event continual reassessment method. In Part 1 (42 patient target), patients are randomly allocated (in a 1:2 ratio) to one of two arms: single-agent alrizomadlin at a starting dose of 150 mg (Arm A) or at a starting dose of 150 mg with concomitant IV carboplatin administered at starting AUC = 4.5 (Arm B). Based on overall response rate (ORR; complete or partial response after Cycle 2) and safety profile, the most promising treatment arm will be advanced to Part 2, which has a target enrollment of 20 patients. Study endpoints are (1) dose-limiting toxicity (DLT), which is defined by the rate of drug-related grade $\geq$ 3 adverse events (by NCI CTCAE v5.0) over the first 2 cycles (6 weeks) of study treatment; (2) maximum tolerated dose based on these DLTs; and (3) ORR by RECIST v1.1 observed at up to 12 months. As of January 27, 2021, 11 of 42 patients had been enrolled in Part 1. Internal study identifier APG-115SG101. Clinical trial registration: NCT03781986. Clinical trial information: NCT03781986. Research Sponsor: Ascentage Pharma Group Corp Limited (Hong Kong); University of Michigan NCI Cancer Center Support Grant (P30CA046592), Ann Arbor, MI.