6500 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Transoral robotic surgical resection followed by randomization to low- or standard-dose IMRT in resectable p16+ locally advanced oropharynx cancer: A trial of the ECOG-ACRIN Cancer Research Group (E3311).

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Background: ECOG-ACRIN 3311 examines reduced postoperative therapy in patients with "intermediate risk" p16+ oropharynx cancer (OPC) undergoing primary transoral surgical management. We report the primary endpoint of 2-year progression free survival (PFS) for patients randomized to 50Gy vs 60Gy without chemotherapy. **Methods:** Between December 2013 and July 2017, 82 credentialed surgeons performed transoral resection (TOS) for 519 OPC patients (cT1-2 stage III/IV AJCC7 without matted neck nodes); post-operative management was determined by pathologically assessed risk. Among 353 eligible and treated patients, Arm A enrolled 10% (N=37) for clear margins, 0-1 nodes, no extranodal extension (ENE)), Arms B (50Gy, N=102) or C (60Gy, N=104) randomized 58%, for clear/close margins, 2-4 + nodes, or ENE $\leq$1mm, while Arm D (N=110, 60-66Gy plus weekly cisplatin, 40 mg/m2, positive margin with any T stage, $>$4 + nodes, or $>$1mm ENE) enrolled 31%. Arm D assignment was based on $>$1mm ENE (76%), $>$ 4 nodes (27%), and/or positive margins (11%). Intermediate-risk patients were stratified by smoking history ($>$10 pk-yr). Of the 80 pts (15%) deemed ineligible, 28 had scans/labs not done per protocol, however treatment arm distribution for all patients mirrored that for the 353 pts eligible and treated. **Results:** Median follow-up was 31.8 months. 2 yr PFS for Arms A, B and C were 93.9% (90% CI=87.3%, 100%), 95.0% (90% CI=91.4%, 98.6%) and 95.9% (90% CI=92.6%, 99.3%) respectively, while Arm D was 90.5% (90% CI=85.9%, 95.3%). The regimen of TOS + low-dose radiation is considered worthy of further study, since the primary endpoint of the upper bound of the 90% CI (in the intermediate risk group) exceeding 85% was met. Of 17 progression events, 7 were locoregional. There were 10 distant recurrences: Arm A=1, Arm B=2, Arm C=4, Arm D=3. Grade III/IV treatment-related AE rates were 15%/2% during surgery, 13%/2% for Arm B and 25%/0% for Arm C. There were 2 treatment-related deaths (one surgical and one Arm D). **Conclusions:** Transoral resection of p16+ OPC is safe and results in good oncologic outcome, presenting a promising deintensification approach. For patients with low-risk disease, 2-yr PFS is favorable without post-operative therapy. For those with uninvolved surgical margins, $<$5 involved nodes, and minimal ($<$1mm) ENE, reduced dose postoperative RT without chemotherapy appears sufficient. Transoral surgery plus 50Gy should be compared to optimal non-surgical therapy in a phase III trial. Clinical trial information: NCT01898494. Research Sponsor: Eastern Cooperative Oncology Group, U.S. National Institutes of Health.

6501 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Equivalence randomized trial comparing treatment based on sentinel node biopsy versus neck dissection in operable T1-T2N0 oral and oropharyngeal cancer.

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Background: Although sentinel node (SN) biopsy is known to be accurate in operable oral and oropharyngeal cT1-T2N0 squamous cell carcinomas (OC), the oncological equivalence of a treatment based on SN compared to that based on neck dissection (ND) has to be evaluated. **Methods:** A prospective multicenter randomized medico economic study included patients with OC operated of primary tumor and systematic neck dissection in ND-arm (standard treatment) versus patients operated of primary tumor and SN biopsy only if negative or ND if SN biopsy positive (SN-arm, experimental treatment). Primary endpoint was neck-relapse-free survival at 2 years and 5 years. Hypothesis of equivalence was tested with a delta of 10%. Functional outcomes were assessed by comparing the length of the hospital stay, the number of physiotherapy prescriptions and dysfunctions in neck and shoulder scales during the 2 post-operative years. **Results:** Out of 307 included patients in 10 hospital centers, 279 evaluable cases showed a neck-relapse-free survival at 2 years and 5 years respectively of 89,6% (95%CI: 0.827; 0.938) and 89,6 %, (95%CI: 0.827; 0.938) in the ND-arm (14 neck relapses out of 139 patients) and of 90,7% (95%CI: 0.842; 0.946) and 89,4% (95%CI: 0.823; 0.938) in the SN-arm (13 neck relapses out of 140 patients). The survival difference between the two arms was less than the 10% expected interval, confirming the equivalence with p = 0.008. The median length of hospital stay was 7 days (ext. 3-30) in SN-arm and 8 days (ext. 2-94) in ND-arm (Wilcoxon's test, p = 0.001). The other functional outcomes were statistically worse in the ND-arm at the 2nd, 4th and 6th postoperative months. There was no more difference at 12 months and later. **Conclusions:** This study demonstrated the oncological equivalence of the SN approach compared to the ND approach in a multicenter study with a lower morbidity and care consumption in the SN approach during the 6 first post-operative months. Treatment based on sentinel node biopsy is established as a standard of care in OC. Clinical trial information: NCT02855723. Research Sponsor: French National Institute of Cancer.

6502 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Phase II/III trial of post-operative chemoradiotherapy comparing 3-weekly cisplatin with weekly cisplatin in high-risk patients with squamous cell carcinoma of head and neck (JCOG1008).

Naomi Kiyota, Makoto Tahara, Hirofumi Fujii, Tomoko Yamazaki, Hiroki Mitani, Shigemichi Iwae, Yasushi Fujimoto, Yusuke Onozawa, Nobuhiro Hanai, Takenori Ogawa, Hiroki Hara, Nobuya Monden, Eiji Shimura, Shujiro Minami, Takashi Fujii, Kaoru Tanaka, Takeshi Kodaira, Junki Mizusawa, Kenichi Nakamura, Ryuichi Hayashi, Head and Neck Cancer Study Group of Japan Clinical Oncology Group (JCOG-HNCSG); Medical Oncology and Hematology, Cancer Center, Kobe University Hospital, Kobe, Japan; Department of Head and Neck Medical Oncology, National Cancer Center Hospital East, Kashiwa, Japan; Jichi Medical University, Shimotsuke, Japan; Division of Head and Neck Medical Oncology, Miyagi Cancer Center, Natori, Japan; Cancer Institute Hospital, Tokyo, Japan; Department of Head and Neck Surgery, Hyogo Cancer Center, Akashi, Japan; Nagoya University, School of Medicine, Nagoya, Japan; Division of Clinical Oncology, Shizuoka Cancer Center, Shizuoka, Japan; Department of Head and Neck Surgery, Aichi Cancer Center Hospital, Nagoya, Japan; Otolaryngology-Head and Neck Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan; Saitama Cancer Center, Saitama, Japan; Department of Head and Neck Surgery, National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; Jikei University School of Medicine, Tokyo, Japan; Department of Otolaryngology, National Hospital Organization Tokyo Medical Center, Tokyo, Japan; Department of Head and Neck Surgery, Osaka International Cancer Institute, Osaka, Japan; Department of Medical Oncology, Kindai University Faculty of Medicine, Osakasayama, Japan; Department of Radiation Oncology, Aichi Cancer Center Hospital, Nagoya, Japan; Japan Clinical Oncology Group Data Center/ Operations Office, National Cancer Center Hospital, Tokyo, Japan; National Cancer Center Hospital, Tokyo, Japan; Department of Head and Neck Surgery, National Cancer Center Hospital East, Kashiwa, Japan

Background: The standard treatment for post-operative high-risk patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA-SCCHN) is chemoradiotherapy with 3-weekly cisplatin (CDDP) (100 mg/m^2, q3wk, 66 Gy/33Fr; 3-weekly CDDP+RT). However, one concern with 3-weekly CDDP+RT is insufficient CDDP compliance due to high-dose-related toxicities. Weekly CDDP+RT (40 mg/m^2, qwk, 66 Gy/33Fr; weekly CDDP+RT) is an alternative regimen with better compliance. Here, we conducted a phase II/III trial of weekly CDDP+RT in post-operative high-risk LA-SCCHN. **Methods:** This is a multi-institutional randomized phase II/III trial to confirm the non-inferiority of weekly CDDP+RT (Arm B) compared with 3-weekly CDDP+RT (Arm A). The trial enrolled pts aged 20-75 years with post-operative high-risk features (microscopically positive margin and/or extranodal extension) and ECOG-PS 0-1. Pts were randomized in a 1:1 ratio to Arm A or Arm B. Primary endpoint of phase II was the proportion of treatment completion and that of phase III was overall survival (OS). A non-inferiority margin of hazard ratio (HR) was set at 1.32. **Results:** Between Oct 2012 and Dec 2018, 261 pts were enrolled (Arm A 132 pts, Arm B 129 pts). At the planned second interim analysis in phase III with 76/161 events, the Data and Safety Monitoring Committee recommended terminating the trial and publishing the results because the statistical boundary for OS non-inferiority had met the pre-specified stop criteria. With a median follow-up of 2.2 years in all randomized pts, 3-year OS was 59.1% in Arm A and 71.6% in Arm B with a HR of 0.69 (99.1% CI, 0.374-1.273 [< 1.32], one-sided p for non-inferiority = 0.00272 $<$ 0.00433). 3-year RFS was 53.0% in Arm A and 64.5% in Arm B with a HR of 0.71 (95% CI, 0.48-1.06). Regarding acute adverse events, neutropenia ($\geq$ grade 3), increased creatinine ($\geq$ grade 2), hearing impairment ($\geq$ grade 2) and mucositis ($\geq$ grade 2) occurred in 48.8%, 8.5%, 7.8% and 55.0% in Arm A and 35.3%, 5.7%, 2.5% and 59.0% in Arm B, respectively. For compliance, median total dose of CDDP was 280 mg/m^2 (IQR, 250-299) in Arm A and 239 mg/m^2 (IQR, 199-277) in Arm B. Total radiation dose was 66 Gy (IQR, 66-66) in both arms. Proportion of treatment completion was 93.2% in Arm A and 86.8% in Arm B. **Conclusions:** Weekly CDDP+RT is non-inferior to 3-weekly CDDP+RT for post-operative high-risk LA-SCCHN pts and has a favorable toxicity profile. Weekly CDDP+RT should be considered the new standard treatment option for these pts. Clinical trial information: 000009125. Research Sponsor: National Cancer Center Research and Development Fund, Japan Agency for Medical Research and Develpmet Fund.

6503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Randomized phase II study of axitinib versus observation in patients with recurred or metastatic adenoid cystic carcinoma.

Bhumsuk Keam, Eun Joo Kang, Myung-Ju Ahn, Chan-Young Ock, Keun Wook Lee, Jung Hye Kwon, Yaewon Yang, Yoon Hee Choi, Min Kyoung Kim, Jun Ho Ji, Tak Yun, Byung-Ho Nam, Sung-Bae Kim; Seoul National University Hospital, Seoul, South Korea; Division of Medical Oncology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, Seoul, South Korea; Division of Hematology-Oncology, Department of Internal Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Department of Internal Medicine, Seoul National University Hospital, Seoul, South Korea; Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; Department of Internal Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, Seoul, South Korea; Department of Internal Medicine, Chungbuk Univeristy Hospital, Chungbuk University College of Medicine, Cheongju, South Korea; Department of Internal Medicine, Dongnam Institute of Radiological and Medical Sciences, Busan, South Korea; Department of Internal Medicine, Yeungnam University Hospital, Yeungnam University College of Medicine, Daegu, South Korea; Division of Hematology-Oncology, Department of Internal Medicine, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, South Korea; Rare Cancers Clinic, Center for Specific Organs Cancer, National Cancer Center, Goyang-Si, Gyeonggi-Do, South Korea; HERINGS, The Institute of Advanced Clinical and Biomedical Research, Seoul, South Korea; Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: Adenoid cystic carcinoma (ACC) does not respond to cytotoxic chemotherapy. Several anti-angiogenic agents were evaluated in single arm phase II trials. However, the role of chemotherapy is still controversial, because of natural stable disease course without chemotherapy and lack of randomized trial. We firstly conducted a randomized trial to evaluate the efficacy of axitinib compared to observation. **Methods:** In this multicenter, prospective phase II trial, we enrolled recurred, metastatic ACC patients who progressed within 9 months. Patients were randomly assigned either axitinib (5mg twice daily) or observation arm with 1:1 ratio. Crossover to the axitinib arm was permitted for patients in the observation arm who had disease progression. The primary endpoint was 6-month progression-free survival (PFS) rate. The secondary endpoints included objective response rate (ORR), overall survival (OS), PFS, duration of response and adverse events. **Results:** A total of 60 patients randomly allocated to axitinib (N=30) and observation arm (N=30) and response evaluation was conducted in 57 patients. With a median follow-up of 25.4 months, the 6-month PFS rate was 73.2% (95% confidence interval [CI], 54.8 to 88.1%) in the axitinib arm and 23.2% (95% CI, 9.3 to 41.1%) in the observation arm (hazard ratio, 0.19; 95% CI, 0.08 to 0.45; $P < 0.001$). Median PFS was 10.8 months in axitinib arm and 2.8 months in observation arm ($P < 0.001$). The ORR was 3.3% (95% CI, 0.1 to 17.2%) in the axitinib arm, and 0% (95% CI, 0 to 12.8%) in the observation arm. The disease control rate was 100% (95% CI, 88.4 to 100%) in the axitinib arm and 51.9% (95% CI, 32.0 to 71.3%) in the observation arm. After crossover, ORR of axitinib in the observation arm was 11.1% (95% CI, 2.4 to 29.2%). Median OS was not reached in axitinib arm, 28.5 months in observation arm ($P = 0.688$). The most frequently reported adverse events of axitinib were grade 1 or 2 oral mucositis and fatigue. Detailed data of adverse events and mutational profile data will be presented. **Conclusions:** In this first randomized trial in patients with recurred or metastatic ACC, axitinib significantly increased 6-month PFS rate compared to observation. Clinical trial information: NCT02859012. Research Sponsor: Adenoid cystic carcinoma research foundation.

6504 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Preliminary activity of tipifarnib in tumors of the head and neck, salivary gland and urothelial tract with HRAS mutations.

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Background: HRAS is a proto-oncogene overexpressed and mutated in some human carcinomas. Tipifarnib is a potent and highly selective inhibitor of farnesyltransferase, a critical enzyme for proper HRAS function. **Methods:** We report data from two phase 2 clinical trials investigating the activity of tipifarnib in HRAS mutant (HRASm) solid tumors: KO-TIP-001 (NCT02383927: Squamous carcinomas [SCC], thyroid and salivary gland tumors, among others) and IST-01 (NCT02535650: Urothelial carcinomas, UC).Primary endpoints were overall response rate (ORR, KO-TIP-001) and progression free survival (PFS) rate at 6 months (IST-01). All pts had RECIST v1.1. measurable disease at study entry. Pts receive a starting dose of tipifarnib of either 600 or 900 mg administered orally twice daily on days 1-7 and 15-21 of 28-day treatment cycles until progression of disease (PD) or unacceptable toxicity. **Results:** Proof of concept was achieved in studies KO-TIP-001 and IST-01. Based on preliminary efficacy results (Ho, et. al, ESMO 2018), KO-TIP-001 was amended to continue enrolling only in Head & Neck SCC (HNSCC) pts (Cohort 2) and other SCC pts (Cohort 3) with tumors carrying high HRASm variant allele frequency (VAF) $>$20%. As of 17 October 2019, 21 HNSCC pts meeting the high HRASm VAF criteria had been treated with tipifarnib of whom 18 were efficacy evaluable at data cut off. Pts had received a median of 2 prior systemic regimens. Ten objective responses were observed in 18 evaluable pts for an ORR of 56%. No responses were observed on last therapy prior to study entry. PFS on tipifarnib and on prior last therapy were, respectively, 6.1 and 2.8 months. In addition, 13 pts with recurrent/metastatic salivary gland tumors (SGT) were treated in KO-TIP-001 or in extended access programs. One objective response was observed in 12 (8%) evaluable pts and an additional 7 (58%) had stable disease as best response. Median PFS in SGT pts was 7 months. In IST-01, 224 UC pts were screened of whom 16 (7%) carried HRAS mutations and 15 of those were enrolled into the study. Five responses were observed in 12 evaluable UC pts (42%) and 3 additional pts had tumor size reduction. Median PFS was 5.1 months. **Conclusions:** Encouraging activity of tipifarnib was observed in HRASm solid tumors. Clinical trial information: NCT02383927, NCT02535650. Research Sponsor: Kura Oncology.

6505 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

KEYNOTE-048: Progression after the next line of therapy following pembrolizumab (P) or P plus chemotherapy (P+C) vs EXTREME (E) as first-line (1L) therapy for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).

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Background: 1L P vs E improved OS in PD-L1 CPS ≥20 and CPS ≥1 populations, and led to noninferior OS in the total population, with favorable safety; 1L P+C vs E had superior OS in CPS ≥20, CPS ≥1, and total populations with comparable safety in the phase 3 KEYNOTE-048 study (NCT02358031) in patients with R/M HNSCC. Neither P vs E nor P+C vs E improved PFS in the PD-L1 CPS ≥20, CPS ≥1, or total populations. Here, we present the progression after the next line of therapy (PFS2) to assess the effect of 1L P or P+C and subsequent anticancer therapy on patient outcomes. **Methods:** Patients with locally incurable R/M HNSCC and no prior systemic therapy in the R/M setting were randomly assigned 1:1:1 to P, P+C, or E. PFS2 was defined as time from randomization to objective tumor progression on next-line therapy or death from any cause. PFS2 was estimated using the Kaplan-Meier method as an exploratory outcome confined to those receiving subsequent therapy after 1L P. HR and 95% CIs were based on a Cox regression model with Efron's method of tie handling with treatment as a covariate (stratified by ECOG performance status [PS], HPV status, and PD-L1 for CPS ≥1 and total populations; by ECOG PS and HPV status for CPS ≥20 population). Data cutoff: Feb 25, 2019. **Results:** Of 882 (301 [P]; 281 [P+C]; 300 [E]) treated patients,422 (P: 148 [49.2%]; P+C: 115 [40.9%]; E: 159 [53.0%]) received subsequent anticancer therapy after 1L P, most commonly C (P: 135 [44.9%]; P+C: 88 [31.3%]; E: 102 [34.0%]); EGFR inhibitor (P: 59 [19.6%]; P+C: 37 [13.2%]; E: 19 [6.3%]); and immune checkpoint inhibitor (P: 6 [2.0%]; P+C: 12 [4.3%]; E: 50 [16.7%]); patients may have received more than one type of subsequent therapy. Median PFS2 is reported in Table. **Conclusions:** In patients with R/M HNSCC, longer median PFS2 was observed in the CPS ≥20 and CPS ≥1 populations for P vs E, and in the CPS ≥20, CPS ≥1, and total populations for P+C vs E. These data further support use of 1L P or P+C in patients with R/M HNSCC. Clinical trial information: NCT02358031. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Population	Treatment	Median PFS2, month	HR (95% CI)	24-mo PFS2 rate, %
CPS ≥20	P (n=133) vs E (n=122)	11.7 vs 9.4	0.64 (0.48-0.84)	27.0 vs 12.5
CPS ≥1	P (n=257) vs E (n=255)	9.4 vs 8.8	0.80 (0.66-0.96)	22.0 vs 9.9
Total	P (n=301) vs E (n=300)	9.0 vs 9.0	0.90 (0.75-1.07)	19.7 vs 11.4
CPS ≥20	P+C (n=126) vs E (n=110)	11.3 vs. 9.7	0.63 (0.47-0.84)	28.9 vs 12.0
CPS ≥1	P+C (n=242) vs E (n=235)	10.3 vs 8.9	0.66 (0.54-0.80)	23.7 vs 9.0
Total	P+C (n=281) vs E (n=278)	10.3 vs 9.0	0.74 (0.62-0.88)	21.4 vs 10.5

6506 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Low-cost oral metronomic versus intravenous chemotherapy in recurrent, inoperable and metastatic head and neck cancer: Phase III Metro-CIS study.

Nandini Sharrel Menon, Vanita Noronha, Vijay Maruti Patil, Sachin Babanrao Dhumal, Amit Joshi, Nilesh Sable, Suman Kumar, Abhishek Mahajan, Atanu Bhattacharjee, Shripad Dinanath Banavali, Kumar Prabhash; Tata Memorial Hospital, Mumbai, India; Tata Memorial Centre, Mumbai, NY, India; Tata Memorial Centre, Mumbai, India

Background: The NCCN preferred regimens for palliation in head and neck cancer, either EXTREME or KEYNOTE-048 are the only two regimens which have improved outcomes over chemotherapy, but they have limited applicability (1-3%) in low and middle-income countries due to the cost. Oral metronomic chemotherapy (OMC) has shown better outcomes than intravenous cisplatin; these results were obtained with a low incidence of adverse events and the cost of 1/100th of NCCN-preferred regimens in a Phase II study. **Methods:** This was a randomized Phase III non-inferiority open-label study. Adult patients with relapsed-recurrent or metastatic upfront palliatively treated squamous cell carcinoma of head and neck and ECOG PS 0-1 were eligible. Patients were randomized 1:1 between OMC (oral methotrexate 15 mg/m^2 weekly with celecoxib 200 mg once daily or intravenous cisplatin (IVC) 75 mg/m^2, 3-weekly for 6 cycles. CTCAE version 4.0 was used for adverse event recording. Response assessment (RECIST version 1.1) was performed every 2 months. EORTC QLQ-C 30 and EORTC QLQ -H&N 35 questionnaires were self-administered at baseline and 2-monthly thereafter. The primary endpoint was overall survival (OS) and was measured from the date of randomization to death. Assuming a 6-month OS in IVC arm of 40%, the non-inferiority margin of 13%, type 1 error of 5% (2-sided), type 2 error of 20% and lost-to-follow up rate of 20%, a total sample size of 422 subjects was required. Kaplan Meier method was used for the estimation of OS and progression-free survival (PFS). To determine non-inferiority the upper limit of 95% CI of difference between 6 months OS of the 2 arms had to be below 13%. **Results:** In the intention to treat analysis, the 6-months OS was 50.89% (95% CI, 43.3-57.97) and 62.26% (95% CI, 54.72-68.9) in the IVC and OMC arm respectively. The difference in 6-months OS between the 2 arms was - 11.37% (95% CI, -20.77 to -0.97). The median OS was 6.1 (95% CI, 5.33-6.93) versus 7.5 (95% CI, 6.5-8.8) months in IVC arm and OMC arm respectively (P= .026). The unadjusted hazard ratio for death was 0.773 (95% CI, 0.615-0.97, P= .026). The median PFS was 1.67 (95% CI, 1.47-2.03) versus 3.23 (95% CI, 2.57-4.13) months in IVC and OMC arms respectively ($P<$ 0.001). Any grade 3 or above adverse events were seen in 61 (30.2%) versus 37 (18.9%) patients in IVC and OMC arm respectively (P= .01). **Conclusions:** OMC improves outcomes in palliatively treated head and neck cancer and is a new standard of care in this setting, in addition to the EXTREME and KEYNOTE-048 regimen. Clinical trial information: CTRI/2015/11/006388. Research Sponsor: Tata Memorial Center Research Administration Council.

6507 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

TPExtreme randomized trial: Quality of Life (QoL) and survival according to second-line treatments in patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC).

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Background: TPExtreme trial comparing EXTREME regimen to the taxane-based TPEx confirmed the encouraging survival results of the TPEx regimen, despite lack of significant overall survival (OS) increase, with a significantly lower toxicity than the EXTREME regimen. Herein, the QoL and exploratory analyses of survival according to 2nd line treatments focusing on immunotherapy (IO) are presented. **Methods:** Randomized (1:1), open-label trial. Main inclusion criteria were R/M HNSCC not suitable for loco-regional treatment, age 18-70 years, PS $<$ 2, creatinin clearance $>$ 60ml/min, prior cisplatin $<$ 300 mg/m². 539 pts were enrolled over a period of 37 months (mo). QoL was evaluated with QLQ-C30 questionnaire at baseline, week(W)12, W18, W26 and analyzed by linear mixed model. The primary QoL endpoint was the Global Health Status score. 2nd line treatments were collected for 501 (93%) patients (pts), 256 in the EXTREME arm and 245 in the TPEx arm. **Results:** The percentage of QLQ-C30 questionnaires filled at baseline, W12, W18 and W26 were similar in the 2 arms, 89%, 52%, 43%, and 39% in the EXTREME arm and 91%, 59%, 40%, and 37% in the TPEx arm, respectively.. Higher scores of Global Health Status (p = 0.02), physical functioning (p = 0.009) and role functioning (p = 0.013) and lower scores of appetite loss (p = 0.041) were observed in the TPEx arm than in the EXTREME arm. No significant difference was observed for the other scores. In 2nd line treatment, 120 (47%) pts in the EXTREME arm and 109 (44%) in the TPEx arm received chemotherapy +/- cetuximab (CT); 41 (16%) pts in the EXTREME arm and 41 (17%) in the TPEx arm received IO, mainly anti-PD-1/PD-L1. 79% and 85% of these 2nd line treatments were given after progression in EXTREME and TPEx arms respectively. Median OS (95%CI) since randomization was 17.6 (15.2 – 19.5) mo with CT and 19.4 (13.4 – 22.3) mo with IO in the EXTREME arm vs 14.9 (13.0 – 16.3) and 21.9 (15.9 – 35.0) mo in the TPEx arm (interaction test p = 0.077) respectively. Median OS since start of 2nd line was 9.3 mo with CT and 8.3 mo with IO in the EXTREME arm, and 7.1 and 11.6 mo respectively in the TPEx arm. **Conclusions:** An improvement in the QoL of patients was observed in the TPEx arm compared to that of the EXTREME arm. Exploratory analysis showed that the taxane-based TPEx regimen followed by IO in 2nd line could provide interesting median OS for pts who need CT in 1st line, with less toxicity than EXTREME. This sequential treatment deserves to be compared to a strategy that starts with Platinum+5FU+pembrolizumab. Clinical trial information: NCT02268695. Research Sponsor: Merck SERONO, GORTEC.

6508 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Results of a randomized phase III study of dysphagia-optimized intensity modulated radiotherapy (Do-IMRT) versus standard IMRT (S-IMRT) in head and neck cancer.

Christopher Nutting, Keith Rooney, Bernadette Foran, Laura Pettit, Matthew Beasley, Laura Finneran, Justin Roe, Justine Tyler, Tom Roques, Audrey Cook, Imran Petkar, Shree Bhide, Devraj Srinivasan, Cheng Boon, Emma De Winton, Robert Frogley, Kathrin Mertens, Marie Emson, Emma Hall, on behalf of the DARS Investigators; Royal Marsden NHS Foundation Trust, London, United Kingdom; Belfast City Hospital, Belfast, United Kingdom; Weston Park Hospital, Sheffield, United Kingdom; Royal Shrewsbury Hospital, Shrewsbury, United Kingdom; Bristol Haematology and Oncology Centre, Bristol, United Kingdom; Institute of Cancer Research, London, United Kingdom; The Royal Marsden NHS Foundation Trust, London, United Kingdom; Norfolk and Norwich University Hospital, Norwich, United Kingdom; Cheltenham General Hospital, Cheltenham, United Kingdom; Guys and St Thomas NHS Foundation Trust, London, United Kingdom; The Royal Marsden Hospital and the Institute of Cancer Research, London, United Kingdom; Western General, Edinburgh, United Kingdom; Worcestershire Royal Hospital, Worcester, United Kingdom; Royal United Hospital, Bath, United Kingdom; Patient Advocate, London, United Kingdom; Boehringer Ingelheim, Vienna, Austria; The Institute of Cancer Research, London, United Kingdom

Background: Most newly diagnosed oro- & hypopharngeal cancers (OPC, HPC) are treated with (chemo) RT with curative intent but at the consequence of adverse effects on quality of life. CRUK/14/014 investigated if using Do-IMRT to reduce RT dose to the dysphagia/aspiration related structures (DARS) improved swallowing function compared to S-IMRT. **Methods:** Patients with T1-4, N0-3, M0 OPC/HPC were randomised 1:1 to S-IMRT (65 Gray (Gy)/30 fractions (f) to primary & nodal tumour; 54Gy/30f to remaining pharyngeal subsite & nodal areas at risk of microscopic disease) or Do-IMRT. The volume of the superior & middle pharyngeal constrictor muscle (PCM) (OPC) or inferior PCM (HPC) lying outside the high-dose target volume was set a mandatory mean dose constraint in Do-IMRT. Treatment allocation was by minimisation balanced by centre, use of induction/concomitant chemotherapy, tumour site & AJCC stage. Primary endpoint was mean MD Anderson Dysphagia Inventory (MDADI) composite score 12 months after RT with 102 patients needed to detect a 10 point improvement (assuming S-IMRT score of 72, standard deviation (SD) 13.8; 90% power, 2-sided 5% alpha). Patients were blind to treatment allocation. Secondary endpoints included local control. **Results:** 112 patients (56 S-IMRT, 56 Do-IMRT) were randomised from 22 UK centres from 06/2016 to 04/2018. Mean age was 57 years; 80% were male; 97% had OPC; 90% had AJCC stage 3&4 disease; 86% had concomitant chemotherapy only, 4% induction & concomitant and 10% no chemotherapy. 111/112 had RT doses as prescribed (1 patient died before RT). Median of the mean inferior PCM dose was S-IMRT 49.8Gy (IQR 47.1-52.4) vs. Do-IMRT 28.4Gy (21.3–37.4), $p < 0.0001$; superior & middle PCM dose was S-IMRT 57.2Gy (56.3–58.3) vs. Do-IMRT 49.7Gy (49.4–49.9), $p < 0.0001$. Do-IMRT had significantly higher MDADI scores: S-IMRT 70.3 (SD 17.3) vs. Do-IMRT 77.7 (16.1), $p = 0.016$. 3 local recurrences (1 S-IMRT, 2 Do-IMRT) have been reported. **Conclusions:** Do-IMRT reduced RT dose to the DARS and improved patient reported swallowing function compared with S-IMRT. This is the first randomised study to demonstrate functional benefit of swallow-sparing IMRT in OPC. Clinical trial information: 25458988. Research Sponsor: Cancer Research UK and the National Institute for Health Research.

6509 **Clinical Science Symposium, Fri, 8:00 AM-9:30 AM**

Evaluation of the correlation between antibiotic use and survival in patients with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC) treated with immune checkpoint inhibitors (ICIs).

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Background: Recent evidence suggests that treatment with systemic antibiotics (Abx) disrupts the intestinal microbiome and may be associated with decreased survival for patients receiving treatment with ICIs for advanced cancers, including R/M HNSCC. However, a potential confounder is that Abx use identifies a subgroup of patients with a worse prognosis. The FDA examined the association between Abx use and survival for ICIs and other drugs used for the treatment of patients with R/M HNSCC. **Methods:** Data submitted to the FDA from three randomized controlled trials with ICI as a single agent or with chemotherapy (ICI group) compared to chemotherapy and/or cetuximab (Control group) were pooled. The association between systemic Abx use within 30 days of initiating anticancer therapy and survival for the ICI and Control groups was evaluated using Kaplan-Meier (KM) estimates and compared using Cox proportional hazards regression models, controlling for ECOG performance status, line of therapy, HPV status, PD-L1 expression, and other important prognostic factors. **Results:** In the ICI and Control groups, 36% and 46% of patients received Abx, respectively. For the ICI group, the difference in KM-estimated median overall survival (OS) was 5.6 months based on receipt of Abx (hazard ratio [HR] 1.70). Abx had no impact on OS for the Control group. Similar trends were observed for progression-free survival (PFS). **Conclusions:** In this exploratory analysis, systemic Abx within 30 days of initiating treatment for R/M HNSCC was associated with decreased survival for patients treated with ICIs compared with patients who did not receive Abx. Use of Abx had no apparent difference in survival in the control group. Further examination of the association between Abx use and clinical outcomes for patients with R/M HNSCC treated with ICIs is needed. Research Sponsor: None.

	ICI +Abx N = 372	ICI -Abx N = 666	Control +Abx N = 300	Control -Abx N = 349
Median OS, mo. (95% CI)	6.7 (5.6, 8.1)	12.3 (11.2, 13.6)	8.6 (7.2, 9.1)	8.8 (7.9, 9.7)
HR (95% CI)	1.70 (1.40, 2.00)		0.99 (0.70, 1.40)	
Median PFS, mo. (95% CI)	2.1 (2.1, 2.2)	3.5 (3.3, 3.6)	3.6 (3.5, 4.0)	4.5 (3.6, 4.9)
HR (95% CI)	1.48 (1.30, 1.70)		1.04 (0.73, 1.46)	

6511 **Clinical Science Symposium, Fri, 8:00 AM-9:30 AM**

Plasma-based tumor mutational burden (bTMB) as predictor for survival in phase III EAGLE study: Durvalumab (D) ± tremelimumab (T) versus chemotherapy (CT) in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) after platinum failure.

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Background: In NSCLC, bTMB assessed from circulating tumor DNA shows promise as a predictive survival biomarker for immunotherapy, but its value in R/M HNSCC is uncertain. We evaluated bTMB as a predictor of survival in R/M HNSCC. **Methods:** EAGLE (NCT02369874) was a randomized, open-label, phase 3 trial evaluating D (anti-PD-L1), or D+T (anti-CTLA-4), vs CT in R/M HNSCC. Patients (pts) with disease progression after platinum-based CT were randomized (1:1:1) to D (10 mg/kg intravenous [IV] every 2 weeks [Q2W]), D (20 mg/kg IV Q4W) + T (1 mg/kg IV Q4W for up to 4 doses, followed by D at 10 mg/kg Q2W) or CT. bTMB was assessed in pretreatment plasma samples using the Guardant Health OMNI platform. Association of somatic loss of function mutations with OS was assessed. **Results:** 736 intent-to-treat pts were randomized; 247 were evaluable for bTMB (BEP). bTMB expression was not linked to HPV status, PD-L1 status, age, gender, tumor location, or ECOG PS. Smoking and progression within 6 months on multi-modality CT in localized disease trended with higher bTMB. OS and PFS HRs were significantly improved for D or D+T vs CT in pts with high bTMB (≥16 mut/Mb) vs low (<16 mut/Mb; Table). The benefit of D or D+T vs CT in pts with high bTMB generally improved with increasing cutoff. 74 pts (27 D, 20 D+T, 27 CT pts) were bTMB high. 18-month OS rates were higher for D+T (22%; 95% CI 7%–42%) and D (33%; 95% CI 17%–51%) vs CT (0%; 95% CI 0%–0%) in pts with high bTMB. Pts with mutations in *KMT2D*, a HNSCC tumor suppressor gene, showed improved OS for D+T vs CT (HR 0.39; 95% CI 0.18–0.85). A trend of improved OS for D+T vs CT (HR 0.19; 95% CI 0.03–1.03) was also seen in pts with *ATM* mutations. **Conclusions:** This is the first retrospective analysis of a phase 3 trial to show bTMB may be predictive of outcomes for checkpoint inhibitors in R/M HNSCC. In pts with high bTMB, D or D+T improved OS hazards by at least 60%, vs CT at cutoffs ≥16 mut/Mb. Validation of bTMB as a predictive biomarker is ongoing. Clinical trial information: NCT02369874. Research Sponsor: AstraZeneca.

OS HRs (95% CI) for high versus low bTMB.

bTMB cutoff (mut/Mb)	D vs CT		D+T vs CT	
	High	Low	High	Low
≥8	0.63 (0.42–0.94)	1.04 (0.54–2.03)	0.68 (0.46–0.98)	1.34 (0.61–2.92)
≥12	0.65 (0.41–1.05)	0.75 (0.46–1.23)	0.61 (0.39–0.97)	0.98 (0.60–1.61)
≥16	0.39 (0.20–0.75)	0.91 (0.61–1.37)	0.40 (0.20–0.81)	0.92 (0.62–1.36)
≥20	0.40 (0.18–0.88)	0.81 (0.55–1.18)	0.41 (0.17–1.00)	0.84 (0.58–1.22)
≥24	0.26 (0.08–0.81)	0.82 (0.57–1.18)	0.29 (0.09–0.99)	0.83 (0.58–1.17)

6512 Poster Discussion Session; Displayed in Poster Session (Board #173), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Lenvatinib plus pembrolizumab combination therapy in patients with radioiodine-refractory (RAIR), progressive differentiated thyroid cancer (DTC): Results of a multi-center phase II international thyroid oncology group trial.

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Background: Lenvatinib is an approved therapy for patients with RAIR DTC. While the overall response rate (ORR) is high, few patients achieve a complete response (CR) and most patients eventually have progressive disease (PD). Combination lenvatinib and pembrolizumab is being explored in many different cancers, and this combination has been approved for advanced endometrial carcinoma. **Methods:** Patients with RAIR DTC with Response Evaluation Criteria in Solid Tumor (RECIST v1.1) measurable PD (<14 months (mo) prior to registration) were enrolled in this single-arm multicenter phase II study. Patients were excluded if they had received previous VEGFR-directed multikinase therapy. The lenvatinib starting dose was 20 mg/day orally and pembrolizumab was 200mg IV every 3 weeks. The primary endpoint was CR. ORR, progression-free survival (PFS) and safety graded by Common Terminology Criteria for Adverse Events v4.0 were secondary endpoints. **Results:** Thirty patients were enrolled. The median age was 62.5 years, and 53% of the patients were women. Seventy percent of patients had grade 3 adverse events (AEs) and 10 percent had grade 4 AEs. There were no treatment-related deaths. The most common > grade 3 AEs were hypertension (47%), weight loss (13%), maculopapular rash (13%), leukopenia (7%), diarrhea (7%) and oral mucositis (7%). Twenty-one patients (70%) required lenvatinib dose reduction. Of 29 evaluable patients, 18 (62%) had a partial response (PR) and 10 (35%) had stable disease (SD). The clinical benefit rate (ORR +SD) was 97%. Median time to tumor nadir was 7.4 mo (1.6-17.8 mo). Median PFS was not yet reached. The PFS at 12 months was 74%. Median time on therapy was 9.9 mo (3.2-18.9 mo). Fourteen patients are continuing therapy (7.6-18.9 mo). Six of these patients (43%) have not yet reached tumor size nadir. Three patients (10%) had > 80% target tumor shrinkage. **Conclusions:** Lenvatinib plus pembrolizumab is reasonably tolerated in patients with RAIR DTC. To date, there have been no documented complete responses. Combination lenvatinib plus pembrolizumab therapy has a high ORR in patients with RAIR DTC. Continuation of this study will help determine the depth and length of the responses. Clinical trial information: NCT02973997. Research Sponsor: Merck and Eisai, International Thyroid Oncology Group.

6513 Poster Discussion Session; Displayed in Poster Session (Board #174), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase II study of nivolumab (N) plus ipilimumab (I) in radioidine refractory differentiated thyroid cancer (RAIR DTC) with exploratory cohorts in anaplastic (ATC) and medullary thyroid cancer (MTC).

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Background: Treatment options for aggressive TC are limited. Pre-clinical data suggests efficacy of CTLA-4 plus PD-1 blockade in aggressive RAIR TC. **Methods:** This investigator initiated phase II study tested N (3mg/kg every 2 weeks) plus I (1mg/kg every 6 weeks) until disease progression or completion of 24 mo of treatment in RAIR differentiated TC including poorly differentiated TC (PDTC) with exploratory cohorts in anaplastic (ATC) and medullary TC (MTC). Radiographic response rate by RECIST v1.1 (CR+PR) was primary endpoint. At least 6 pts with disease response among n=32 DTC provided 84% power to distinguish between a 10% and a 25% RR (one-sided 9% binomial test). **Results:** Accrual is complete with n=32 patients with DTC, 10 with ATC and 7 with MTC enrolled between October 2017 and May 2019. Thirty-two DTC included: n=17 papillary, n=7 Hurthle, n=4 follicular TC, n=4 PDTC. Among n=49, median (range) age was 65 (30-88), 51% (25/49) were female. To date, in DTC, 3/32 achieved a PR (n=2 Hurthle and n=1 PDTC), 9.4% RR (.95CI:2%-25%). One near complete response has been observed. Among pts w ATC, 3/ 10 profound PR by RECIST occurred (30% RR, .95CI: 7%-65%). Among them, two remain without clear evidence of disease at 26 and 13 mo after treatment start. No PR's were observed in MTC. Most frequent grade 3-4 TRAEs were as expected and included increased lipase (n=8), increased serum amylase (n=4). There was an unexpected number of treatment related adrenal insufficiency (AI) (n=4) which was associated with long PFS (range 10.1—16.4+mo). **Conclusions:** N+I appears to have considerable activity in ATC. In unselected RAIR DTC, activity was low but responses were seen in PDTC and Hurthle cell TC. Exceptional responses with prolonged remissions were observed. Clinical trial information: NCT03246958. Research Sponsor: Bristol-Myers-Squibb.

6514 Poster Discussion Session; Displayed in Poster Session (Board #175), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Atezolizumab combinations with targeted therapy for anaplastic thyroid carcinoma (ATC).

Maria E. Cabanillas, Ramona Dadu, Renata Ferrarotto, Suyu Liu, Bryan M. Fellman, Neil D. Gross, Maria Gule-Monroe, Charles Lu, Horiana Grosu, Michelle D. Williams, Dzifa Yawa Duose, Saradhi Mallampati, Shannon Dervin, Edward Francis Mckenna, Rui Jennifer Wang, Mark Zafereo, Naifa Lamki Busaidy; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Department of Head and Neck Surgery, Houston, TX; Department of Thoracic/Head and Neck Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; Genentech, Inc., San Francisco, CA

Background: ATC is a rare/aggressive cancer with dismal outcome. Dabrafenib/trametinib is approved for BRAF-mutated ATC but pts eventually develop resistance. There are no approved drugs for pts with BRAF-wild type ATC. Better treatments (tx) are needed. **Methods:** ATC pts with PS $<$ 3 enrolled on a prospective trial at a single center, and tx was assigned by driver mutation: BRAF (cohort 1), RAS, NF1, or NF2 (cohort 2), or none of these (cohort 3). Cohort 4 with paclitaxel was exploratory for pts who did not qualify for 1-3. All pts received atezolizumab (A) IV + targeted therapy. Cohort 1 had run-in with vemurafenib (V) 960mg BID/cobimetinib (C) 60mg QD po for 28 days, followed by A 840mg Q2 weeks, at which time V dose was decreased to 720mg BID. Cohort 2: A + C (same doses as cohort 1); cohort 3: A 1200 mg Q3 weeks + bevacizumab 15 mg/kg q3 weeks. Pts unable to swallow used alternative drug preparation (ADP; crushed vemurafenib, suspension cobimetinib). Primary objective is to determine whether the tx in cohorts 1-3 leads to improved overall survival (OS). The trial was designed to enroll 36 pts but we are reporting early due to positive findings. Response rate (RR) was measured by RECISTv1.1. Median OS was estimated by Kaplan-Meier method. cfDNA and biopsy were obtained at baseline, course 2 and progression. Pts were allowed to undergo surgery and radiation while on trial. **Results:** From August 2017-January 2020, 34 ATC pts were enrolled in cohorts 1-3 and 9 in cohort 4. Cohort 3 closed early for futility. 3 pts had ADP. Median follow-up time was 7.51 mos (range: 0.43 – 27.37). Median OS in cohorts 1-3 was 18.23 mos (CI 10.45-NE) and 1-year OS was 67% (95%CI: 45%, 82%). See table. Response rate (RR) in cohort 1 was 71%: CR 1/17 (6%), PR 11/17 (65%), SD 4/17 (23%), 1 never restaged; in cohort 2 RR was 7%: PR 1/14 (7%), SD 7/14 (50%), PD 4/14 (29%), 2 died early. 8 (24% of cohort 1-3) pts had complete tumor resection after tx with VCA (n = 7) or CA (n = 1); all but 1 of these pts are alive. AEs as expected. cfDNA data will be reported at meeting. **Conclusions:** Atezolizumab + vemurafenib/cobimetinib for BRAF-mutated or + cobimetinib for NF1/2 or RAS-mutated ATC is effective, as evidenced by the long OS in these pts (13 mos $>$ historical control). A significant number of patients, particularly in cohort 1, were able to undergo complete tumor resection due to a favorable response to tx. Clinical trial information: NCT03181100. Research Sponsor: Genentech.

Female [N (%)]	**17 (50%)**	
Age, in yrs [median (range)]	66 (44-74)	
	N	Median OS in mos (95%CI)
Cohort 1	17	Not reached
Cohort 2	14	18.23 (4.47-NE)
Cohort 3	3	6.21 (4.11-11.99)
Cohort 4	9	4.44 (1.12-NE)
Cohort 1-3	34	18.23 (10.45, NE)

6515 Poster Discussion Session; Displayed in Poster Session (Board #176), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Concurrent cetuximab (CTX) and nivolumab (NIVO) in patients with recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): Results of phase II study.

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Background: While anti-Programmed Death-1 (anti-PD-1) inhibitors have efficacy, only some patients (pts) with R/M HNSCC achieve clinically significant benefits. We designed the study to determine the 1-year overall survival (OS) rate of concurrent CTX and NIVO in patients who had progressed on at least one prior treatment for their R/M HNSCC. **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 but withheld/discontinued based on adverse event (AE) severity. **Results:** Total 47 pts are enrolled. 2 pts are non-evaluable. 45 evaluable pts are analyzed. Median age is 64 (24-77). ECOG performance status at baseline is 0 (9, 20%), 1 (33, 73%), and 2 (3, 7%). Primary sites are oral cavity 10 (22%), oropharynx 24 (53%), hypopharynx 3 (7%), larynx 6 (13%), and unknown primary 2 (4%). p16 status is available in 33 (73%). Prior treatments before the study enrollment are: chemotherapy (CT) 42 (93%), no CT 3 (7%), radiotherapy (RT) 38 (84%), no RT 7 (16%), checkpoint inhibitors (CPI) 23 (51%), and no CPI 22 (49%). PD-L1 combined positive scores (CPS) is available in 30 (67%). Median follow up time for overall survival (OS) is 12.6 months. The most common grade 3 treatment-related AE (TRAE) occurring $\geq$2 are fatigue 6 (13%) and rash-acneiform 2 (4.4%). The only grade 4 TRAE is CTX infusion reaction in 1 (2.2%). The most common grade 3 immune-related AE (IRAE) occurring $\geq$2 is fatigue 3 (6.7%). No grade 4 IRAE is observed. The median progression-free survival (PFS) and median OS are summarized in Table. Pts with no prior exposure to CPI have favorable PFS and OS relative to pts with prior CPI (PFS: HR 0.49, 95% CI 0.25-0.97, p=0.04 and OS: HR 0.5, 95% CI 0.22-1.14, p=0.09). **Conclusions:** Our data suggest the combination of CTX and NIVO is active in pts without prior CPI exposure and overall well tolerated in all pts. These preliminary results support further evaluation of the combination in CPI naïve pts. Clinical trial information: NCT03370276. Research Sponsor: Eli Lilly, Bristol Myers-Squibb, James and Esther King Biomedical Research Program.

Survival analyses.

	Total (N=45)	Prior CPI (N=23, 51%)	No prior CPI (N=22, 49%)	PD-L1 CPS <20 (N=11, 24%)	PD-L1 CPS ≥20 (N=19, 42%)	PD-L1 CPS unknown (N=15, 33%)	p16+ (N=22, 49%)	p16- (N=11, 24%)	p16 unknown (N=12, 27%)
Median PFS (months)	3.4	3.1	6.0	2.1	5.2	3.6	3.1	3.1	7.9
1-yr PFS	19%	9%	32%	0%	29%	17%	11%	9%	48%
Median OS (months)	11.5	9.7	13.3	13.3	11.5	8.6	9.7	12.6	11.5
1-yr OS	44%	29%	60%	69%	40%	36%	37%	55%	47%

6516 Poster Discussion Session; Displayed in Poster Session (Board #177), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Combination of monalizumab and cetuximab in recurrent or metastatic head and neck cancer patients previously treated with platinum-based chemotherapy and PD-(L)1 inhibitors.

Roger B. Cohen, Jessica Ruth Bauman, Sebastien Salas, A. Dimitrios Colevas, Caroline Even, Didier Cupissol, Marshall R. Posner, Gautier Lefebvre, Esma Saada-Bouzid, Maureen Bernadach, Tanguy Y. Seiwert, Alexander T. Pearson, Franceline Calmels, Robert Zerbib, Pascale Andre, Federico Rotolo, Agnès Boyer-chammard, Jerome Fayette; University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; Fox Chase Cancer Center, Philadelphia, PA; CEPCM Assistance Publique des Hôpitaux de Marseille, Marseille, France; Stanford Cancer Institute, Stanford, CA; Gustave Roussy, Villejuif, France; Centre Val d'Aurelle, Montpellier, France; Hematology and Medical Oncology, Icahn School of Medicine at Mount Sinai, New York, NY; Centre Oscar Lambret, Lille, France; Centre Antoine Lacassagne, Université Côte d'Azur, Nice, France; Centre de Lutte Contre le Cancer J.Perrin, Clermont Ferrand, France; The University of Chicago Medicine, Chicago, IL; Section of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL; Innate Pharma, Marseille, France; Innate-Pharma, Marseilles, France; Centre Léon Bérard, Medical Oncology, Lyon, France

Background: Monalizumab is a first-in-class immune checkpoint inhibitor targeting Natural Killer Group 2A (NKG2A), which is expressed on subsets of Natural Killer (NK), gd T and tumor-infiltrating $CD8^+$T cells. NKG2A blockade promotes innate anti-tumor immunity mediated by NK and $CD8^+$T cells and enhances NK cell antibody-dependent cell-mediated cytotoxicity induced by cetuximab. In a Phase I study, the combination of monalizumab and cetuximab was well tolerated. In an initial expansion cohort 1 of 40 patients (pts) who had progressed after platinum-based therapy, we reported an overall response rate (ORR) of 27.5%, a 4.5 month median PFS and an 8.5 month median OS. In a subset of patients (n=18) previously treated with PD-(L)1 inhibitors (IO), corresponding results were 17%, 5.1, and 14.1 months, respectively (ESMO 2019). Here we present data from a second expansion cohort 2 (n=40) conducted specifically in the post-IO setting to independently confirm the cohort 1 results. **Methods:** Eligible patients had R/M SCCHN previously treated with platinum and a PD-(L)1 inhibitor. Pts received monalizumab 750 mg q2weeks and cetuximab according to the label until progression or toxicity. Cohort 2 was designed as a confirmatory multicenter single arm phase II study, with a pre-planned total of 40 patients. The primary endpoint was ORR assessed per RECIST 1.1. **Results:** As of January 31, 2020, 40 pts have been treated in cohort 2. Median follow-up is 7.3 months (range, 1.9-13.6+). Eight (8) pts have a confirmed partial response (PR); ORR is 20% [95% confidence interval: 11-35]. Median time to response is 1.6 months [1.6-5.3]. At the time of data analysis, 3 pts were still in PR and 3 pts had stable disease continue on treatment. PFS and OS are still immature. **Conclusions:** In pts previously treated with platinum and PD-(L)1 inhibitors, the combination of monalizumab and cetuximab demonstrated promising activity. The second extension cohort confirmed prospectively the ORR reported in cohort 1. A randomized phase III trial of monalizumab and cetuximab is planned in this platinum and IO-pretreated SCCHN population. Clinical trial information: NCT02643550. Research Sponsor: INNATE PHARMA, Pharmaceutical/Biotech Company.

6517 **Poster Discussion Session; Displayed in Poster Session (Board #178), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM**

Updated analysis of the inducible T-cell co-stimulatory receptor (ICOS) agonist, GSK3359609 (GSK609), combination with pembrolizumab (PE) in patients (pts) with anti-PD-1/L1 treatment-naïve head and neck squamous cell carcinoma (HNSCC).

Eric Angevin, Stefanie L. Groenland, Annette May Ling Lim, Juan Martin-Liberal, Victor Moreno, Jose Manuel Trigo, Christophe Le Tourneau, Matthen Mathew, Daniel C. Cho, Aaron Richard Hansen, David Vicente, Michele Maio, Antoine Italiano, Jessica Ruth Bauman, Michael Jon Chisamore, Helen Zhou, Catherine Elizabeth Ellis, Marc S. Ballas, Axel Hoos, Danny Rischin; Gustave Roussy Institut de Cancérologie, Villejuif, France; The Netherlands Cancer Institute–Antoni van Leeuwenhoek, Amsterdam, Netherlands; Linear Clinical Research and Sir Charles Gairdner Hospital, Nedlands, Australia; Vall d'Hebron Institute of Oncology (VHIO)-Cellex Center, Barcelona, Spain; START Madrid-FJD, Hospital Fundacion Jimenez Diaz, Madrid, Spain; Hospital Ramón y Cajal, Madrid, Spain; Department of Drug Development and Innovation (D3i), Institut Curie, Paris, France; Columbia University Medical Center, New York, NY; New York University Langone Medical Center, New York, NY; Princess Margaret Cancer Centre, Toronto, ON, Canada; Hospital Universitario Virgen Macarena, Sevilla, Spain; University Hospital of Siena, Siena, Italy; Institut Bergonie, Bordeaux, France; Fox Chase Cancer Center, Philadelphia, PA; Merck and Co., Kenilworth, NJ; GlaxoSmithKline, Collegeville, Upper Providence, PA; GlaxoSmithKline, Collegeville, PA; GlaxoSmithKline, Upper Providence, PA; Peter MacCallum Cancer Centre and the University of Melbourne, Melbourne, Victoria, Australia

Background: INDUCE-1 (NCT02723955) is a first-in-human study investigating GSK609, an IgG4 ICOS agonist non-T-cell depleting antibody, as monotherapy and combination therapy with anti-cancer agents that includes PE. A range of GSK609 dose levels (≥0.1–1 mg/kg) having biological and clinical activity were identified and evaluated in the expansion phase with GSK609 0.3 mg/kg selected as the dose for further investigation. Results from the HNSCC expansion cohorts (ECs) showed GSK609 has single agent activity in pts with relapsed/refractory disease, and early clinical activity in combination with PE in pts with anti-PD-1/L1 treatment-naïve disease (Rischin, et al. *Annals of Oncol* 2019;30 [Supplement_5]:v454–5). Updated results from the GSK609/PE HNSCC EC are presented. **Methods:** Eligible pts for the HNSCC EC had anti-PD-1/L1 treatment-naïve disease, ≤5 prior lines of therapy, measurable disease, and no active autoimmune disease. Pts received GSK609 0.3 mg/kg + PE 200 mg every 3 weeks (wks) until disease progression or unacceptable toxicity, up to 2 years (yrs)/35 cycles. Disease assessments were performed every 9 wks through wk 54 then every 12 wks thereafter. Pts were followed for survival and subsequent anti-cancer therapy. **Results:** As of 11 October 2019, 34 pts were enrolled and evaluable for efficacy analyses. The median age of this population was 61.5 yrs (range: 37–77); 85% were male; 53% received ≥1 prior line of therapy in the metastatic setting. ORR was 26% (95% CI: 12.9, 44.4; n = 9 with 4 complete and 5 partial responses); disease control rate was 68% (95% CI: 49.5, 82.6; n = 23). Among pts with PD-L1 IHC status by 22C3 pharmDx assay (n = 24; 71%), the majority of pts with a response or stable disease (SD) had PD-L1 CPS status < 20 (11 of 15 pts including 1 SD pt with CPS < 1). Median PFS was 5.6 months (95% CI: 3.9, 6,2). Median OS was not reached at time of analysis (95% CI: 8.2, NR); 6-month OS rate was 84% (95% CI: 66, 93). Treatment-related adverse events were reported in 66% of pts; the majority of events were Grades 1 or 2 with < 10% of pts experiencing ≥ Grade 3 events. **Conclusions:** This updated analysis with a more mature dataset shows promising clinical activity that supports further randomized investigation of GSK609 in combination with PE with an OS endpoint in HNSCC. Clinical trial information: NCT02723955. Research Sponsor: Study is funded by GlaxoSmithKline and in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

6518 Poster Discussion Session; Displayed in Poster Session (Board #179), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A prospective phase II open-label randomized controlled trial to compare mandibular preservation in upfront surgery to neoadjuvant chemotherapy followed by surgery in operable oral cavity cancer.

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Background: The study objective was to evaluate the non-Inferiority of survival and ability to preserve mandible with the use of neoadjuvant chemotherapy (NACT) in locally advanced oral cancers compared to upfront surgery alone without compromising survival. **Methods:** This study was a randomized, single centre, non-inferiority trial. Eligibility criteria included treatment naïve histologically confirmed cancer of the oral cavity; cancers requiring segmental resection for paramandibular disease without clinicoradiological evidence of bone erosion, clinical T2, T3 and T4, any N, M0 as per TNM (AJCC) 7th edition, age at least 18 years; and written informed consent. The patients were randomly assigned (1:1) to receive either upfront surgery followed by adjuvant treatment (Standard arm-SA) or receive two cycles of three drugs NACT (Docetaxel, Cisplatin, 5-Flurouracil) at three weekly interval (Intervention arm-IA). Depending on the response after two cycles, the patient would either receive an additional third cycle or undergo surgery followed by adjuvant treatment as decided by the tumour board. The primary endpoint was mandible preservation rate at 30% in the experimental arm. The secondary end points being Loco regional control and treatment related toxicity. **Results:** Between September 2010 and April 2013, 68 patients were enrolled and randomized to SA (34 patients) and IA (34 patients) with a median follow-up of 3.6 years (IQR 0.95- 7.05 years). Majority of the patients were T4 (n = 40, 58.8%) In the IA 28 patients had partial response (n = 28,82.4%), with a mandible preservation (Marginal Mandibulectomy) rate of 48% (n = 16/34). There were no close or positive margins in the IA. All patients received adjuvant treatment. The number of recurrences was similar in both the arms. All patients in the IA developed toxicities with the majority developing Grade III-IV toxicities (Grade III: 14, 41.2%, Grade IV: 11, 32.4%) (p = 0.739). The disease free survival (DFS) (p = 0.715, HR 0.911[0.516-1.607]) and overall survival (OS) (p = 0.747, HR 0.899[0.510-1.587]) were similar in both the arms. **Conclusions:** NACT seems to be a feasible option for mandibular preservation with acceptable toxicities in a select group of patients without compromising survival. However this needs to be tested in a larger phase III randomized trial. Clinical trial information: CTRI/2015/11/006396. Research Sponsor: Tata Memorial Centre Intramural Funds.

6519 Poster Discussion Session; Displayed in Poster Session (Board #180), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A multicenter phase II trial of the combination cisplatin/ docetaxel/durvalumab/tremelimumab as single-cycle induction treatment in locally advanced HNSCC (CheckRad-CD8 trial).

Markus Hecht, Antoniu-Oreste Gostian, Markus Eckstein, Sandra Rutzner, Jens von der Grün, Thomas Illmer, Matthias G. Hautmann, Thomas Brunner, Simon Laban, Gunther Klautke, Balint Tamaskovics, Axel Hinke, Benjamin Frey, Sabine Semrau, Arndt Hartmann, Claus Roedel, Wilfried Budach, Udo S Gaipl, Heinrich Iro, Rainer Fietkau; Department of Radiation Oncology, Universitatsklinikum Erlangen, Friedrich-Alexander-Universitat Erlangen-Nürnberg, Erlangen, Germany; Department of Otholaryngology - Head and Neck Surgery, Universitatsklinikum Erlangen, Friedrich-Alexander-Universitat Erlangen-Nürnberg, Erlangen, Germany; Institute of Pathology, Universitatsklinikum Erlangen, Friedrich-Alexander-Universitat Erlangen-Nürnberg, Erlangen, Germany; Department of Radiation Oncology, University Hospital Frankfurt, Goethe-Universität Frankfurt, Frankfurt Am Main, Germany; Medical Oncology Clinic Dresden Freiberg, Dresden, Germany; Department of Radiation Oncology, University Hospital Regensburg, Universität Regensburg, Regensburg, Germany; Department of Radiation Oncology, University Hospital Magdeburg, Otto von Guericke Universität Magdeburg, Freiburg, Germany; Department of Otolaryngology - Head and Neck Surgery, University Hospital Ulm, Universität Ulm, Ulm, Germany; Department of Radiation Oncology, Klinikum Chemnitz, Chemnitz, Germany; Department of Radiation Oncology, University Hospital Düsseldorf, Heinrich Heine Universität Düsseldorf, Dusseldorf, Germany; CCRC Cancer Clinical Research Consulting, Düsseldorf, Germany; Department of Radiation Oncology, University Hospital Frankfurt, Goethe-Universität Frankfurt, Frankfurt, Germany; Department of Radiation Oncology, University Hospital Düsseldorf, Heinrich Heine Universität Düsseldorf, Düsseldorf, Germany

Background: PD-1/PD-L1 inhibitors are efficient in head and neck squamous cell cancer (HNSCC). Combination with anti-CTLA4 agents may enhance anti-tumor activity compared to anti-PD-1/PD-L1 monotherapy in different tumor types. In the CheckRad-CD8 trial the typical induction treatment consisting of Cisplatin/Docetaxel was combined with Durvalumab/Tremelimumab. Patients with pathological complete response (pCR) in the re-biopsy after induction treatment or at least 20% increase of intratumoral CD8 density in the re-biopsy compared to baseline entered radioimmunotherapy with concomitant Durvalumab/Tremelimumab. **Methods:** In this prospective multicenter phase II trial, patients with HNSCC stage III-IVB received a single cycle of Cisplatin 30mg/m² d1-3, Docetaxel 75mg/m² d1, Durvalumab 1500mg fix dose d5 and Tremelimumab 75mg fix dose d5. Objectives of this interim analysis were to quantify the effect of the induction treatment on intratumoral CD8 density and the pCR rate and to generate safety data. **Results:** Between Sep 2018 and Dec 2019, 57 patients were enrolled. Median age was 59 years, 22 patients (37%) were current smokers, 27 patients (47%) had oropharyngeal tumors (52% p16 positive). The median pre-treatment intratumoral CD8 density was 335 CD8+ cells/mm². After induction treatment 27 patients (47%) had a pCR in the re-biopsy and further 25 patients (44%) had a relevant increase of intratumoral CD8+ cells (median increase by factor 3.0). Response according to RECIST criteria was CR in 1 (2%), PR in 19 (33%) and SD in 20 patients (35%) (17 patients not evaluable). Adverse events (AE) grade 3-4 appeared in 39 patients (68%) and mainly consisted of leucopenia (43%) and infections (28%). 6 patients (11%) developed grade 3-4 immune-related AEs. In multivariable analysis the intratumoral CD8 density was the only independently significant predictor of pCR (odds ratio 1.0013 per cell/mm², 95%-CI 1.00023-1.0023, p=0.017). 42 patients (74%) continued with Durvalumab/ Tremelimumab concomitant to radiotherapy. **Conclusions:** Single cycle induction treatment with Cisplatin/Docetaxel/Durvalumab/Tremelimumab is feasible and achieves a high pCR rate. CD8 density may have a predictive role for further treatment planning in locally advanced HNSCC. Clinical trial information: NCT03426657. Research Sponsor: Astra Zeneca.

6521 Poster Discussion Session; Displayed in Poster Session (Board #182), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

GEM20110714: Final overall survival results of the phase III study of first-line gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma.

Shaodong Hong, Yan Huang, Yunpeng Yang, Gengsheng Yu, Jun Jia, Jiewen Peng, Qing Lin, Xuping Xi, Peijian Peng, Dongping Chen, Mingjun Xu, Xiaojun Lu, Li Zhang; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; Department of Medical Oncology, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University Cancer Center, Guangzhou, China; Jiangmen Central Hospital, Jiangmen, China; Dongguan People's Hospital, Dongguan, China; Zhongshan People's Hospital, Zhongshan, China; Shunde Hospital of Traditional Chinese Medicine, Foshan, China; Cancer Hospital of Hunan Province, Changsha, China; The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, China; The Affiliated Cancer Hospital of Guangzhou Medical University, Guangzhou, China; First Affiliated Hospital Of Gannan Medical University, Ganzhou, China

Background: GEM20110714, the first randomized, phase III study (NCT01528618) of systemic chemotherapy in recurrent or metastatic (R/M) nasopharyngeal carcinoma (NPC), reported significant reduction of disease progression with gemcitabine plus cisplatin (GP) versus fluorouracil plus cisplatin (FP; hazard ratio [HR], 0.55; 95% CI, 0·44–0·68; P < .001). This study establishes GP as the standard-of-care for first-line treatment of R/M NPC. We present the final overall survival (OS) analysis here. **Methods:** In this multicenter, open-label study conducted in China, patients who had an Eastern Cooperative Oncology Group performance status of 0 or 1 and R/M NPC were randomly assigned (1:1) to receive up to six cycles of either GP or FP once every 3 weeks. The primary endpoint was PFS, which has been previously reported; OS was a secondary endpoint. The final OS analysis was conducted with the data cutoff date of December 17, 2019. **Results:** After a median follow-up time of 64.4 months (95% CI, 61.1-67.6), 148 (81.8%) and 165 (91.2%) deaths occurred in the GP and FP arms, respectively. The estimated hazard ratio for OS was 0.723 (95% CI, 0.578 to 0.904; two-sided P = .004). The median OS was 22.1 months with GP versus 18.6 months with FP. The OS probabilities at 1, 3, and 5 years were 79.9% vs. 71.8%, 31.0% vs. 20.4%, and 18.5% vs. 7.6%, respectively. Un-predefined subgroup analyses based on baseline characteristics were consistent with the primary OS analysis. Postdiscontinuation systemic therapy use was similar: GP, 52%; FP, 57%. No new safety signals emerged. **Conclusions:** In patients with R/M NPC, GP is the first regimen to show significant improvement in OS in a phase III randomized study compared with a traditional chemotherapy regimen (i.e. FP). GP should be considered the standard treatment option for these patients. Clinical trial information: NCT01528618. Research Sponsor: None.

6522 Poster Discussion Session; Displayed in Poster Session (Board #183), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Development and validation of a gene expression-based signature predicting efficacy of induction chemotherapy in locoregionally advanced nasopharyngeal carcinoma: A multicenter cohort study.

Yuan Lei, Ying-Qin Li, Wei Jiang, Xiao-Hong Hong, Wen-Xiu Ge, Yuan Zhang, Weihan Hu, Ya-Qin Wang, Ye-Lin Liang, Jun-Yan Li, Lei Chen, Fangyun Xie, Wen-Fei Li, Yan-Ping Mao, Xu Liu, Yu-Pei Chen, Ling-Long Tang, Ying Sun, Na Liu, Jun Ma; Sun Yat-sen University Cancer Center, Guangzhou, China; Affiliated Hospital of Guilin Medical University, Guilin, China; South China Normal University, Guangzhou, China

Background: Induction chemotherapy (IC) followed by concurrent chemoradiotherapy is the mainstay treatment for patients with locoregionally advanced nasopharyngeal carcinoma (LA-NPC). However, some patients obtain little benefit and experience unnecessary toxicities from IC. We intended to develop a gene expression signature that can identify patients who will benefit from IC. **Methods:** We screened chemoresistance-related genes by comparing gene expression profiles of patients with short-term tumor response or non-response to IC (n = 95) using microarray analysis. Chemoresistance-related genes were quantified by digital expression profiling in a training cohort (n = 342) to obtain a gene signature. We then validated this gene signature in the clinical trial cohort (n = 187) and an external independent cohort (n = 240). **Results:** We identified 43 chemoresistance-related genes associated with the short-term tumor response to IC. In the training cohort, a 6-gene signature was developed that was highly accurate at predicting the short-term tumor response to IC (area under the curve [AUC] 0.87, sensitivity = 87.5%, specificity = 75.6%). We then apply the 6-gene signature to classify patients into the benefit group and the no-benefit group. In the benefit group, patients could benefit from IC in terms of failure-free survival (hazard ratio [HR] 0.54 [95% confidence interval 0.34-0.87]; p = 0.01), while patients in the no-benefit group could not (HR 1.25 [95%CI 0.62-2.51]; p = 0.53). In the clinical trial cohort, the developed 6-gene signature was also highly accurate at predicting the response to IC (AUC = 0.82; sensitivity = 87.5%; specificity = 71.8%). Additionally, IC conferred failure-free survival benefits only on patients in the benefit group (HR 0.37 [95%CI 0.18-0.75], p = 0.004) and not on those in the no-benefit group (HR 0.70 [95%CI 0.27-1.82]; p = 0.46). In the external independent cohort, similar results were observed. **Conclusions:** The 6-gene signature can help select patients who will benefit from IC and thus lay a foundation for a more individualized therapeutic strategy for LA-NPC patients. Research Sponsor: This study was supported by grants from the Key-Area Research and Development Program of Guangdong Province (2019B020230002), the National Natural Science Foundation of China (81930072; 81922057), the Natural Science Foundation of Guangdong Province (2017.

6523 Poster Discussion Session; Displayed in Poster Session (Board #184), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Network-meta-analysis of chemotherapy in nasopharyngeal carcinoma (MAC-NPC): An update on 8,221 patients.

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Background: Based on an individual patient data (IPD) network meta-analysis (NMA) of 20 randomized trials and 5,144 patients (pts), the MAC-NPC collaborative group has shown that the addition of adjuvant chemotherapy (AC) to chemo-radiotherapy (CRT) achieved the highest survival benefit in nasopharyngeal carcinoma (NPC; Ribassin-Majed JCO 2017). Here, we updated the meta-analysis with the addition of 8 trials. **Methods:** Trials of Radiotherapy (RT) with or without chemotherapy (CT) in patients with non-metastatic NPC were identified and updated IPD obtained. Both Western and Chinese medical literatures were searched. Overall Survival (OS) was the main endpoint. Fixed and random-effects frequentist NMA models were applied, network heterogeneity and consistency were evaluated. P-score was used to rank the treatments. R software - netmeta package was used to perform the analyses. Treatments were grouped in the following categories: RT alone (RT), induction chemotherapy followed by RT (IC-RT), induction chemotherapy without taxanes followed by concomitant chemoradiotherapy (ICtax(-)-CRT), induction chemotherapy with taxanes followed by concomitant chemoradiotherapy (ICtax(+)-CRT), concomitant chemoradiotherapy (CRT), concomitant chemoradiotherapy followed by adjuvant chemotherapy (CRT-AC) and RT followed by adjuvant chemotherapy (RT-AC). **Results:** Overall 28 trials and 8,214 pts were included. Median follow-up was 7.2 years. There was no heterogeneity in the NMA. There was inconsistency in the main analysis, which disappeared after the exclusion of 2 outlier trials. ICtax(+)-CRT ranked the best treatment for OS with a P-Score of 91%. Hazard ratio [HR, 95% Confidence Interval] for ICtax(+)-CRT was 0.75 [0.59-0.96] compared to CRT and 0.92 [0.69-1.24] compared to CRT-AC (second best treatment in raking with a P-Score of 85%; see league table below). When the 2 types of IC were merged, CRT-AC ranked the first followed by IC-CRT with P-Scores of 93% and 86% respectively, with a HR of 0.97 [0.84-1.14] for CRT-AC vs. IC-CRT. **Conclusions:** This IPD NMA of the treatment of locally advanced NPC demonstrates that the addition of IC or AC to CRT improves disease control probability and survival over CRT alone. Data on progression-free survival, locoregional and distant control will be presented at the meeting. Research Sponsor: french LNCC, PHRC.

ICtax(+)-CRT p-score = 91%			
0.92	CRT-AC		
[0.69-1.24]	p-score = 85%		
0.87	0.94	ICtax(-)-CRT	
[0.65-1.17]	[0.79-1.13]	p-score = 74%	
0.75	**0.82**	0.87	CRT
[0.59-0.96]	**[0.69-0.97]**	[0.74-1.02]	p-score = 45%

6524 **Poster Session (Board #185), Fri, 8:00 AM-11:00 AM**

Phase II study of consolidative intensity-modulated radiation therapy following first-line palliative systemic chemotherapy for de novo previously untreated metastatic (M1) nasopharyngeal carcinoma.

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Background: The prognosis of de novo previously untreated metastatic (M1) nasopharyngeal carcinoma (NPC) at diagnosis is poor, and the role of consolidative intensity-modulated radiation therapy (IMRT) to the primary tumor and the neck following first-line palliative chemotherapy remains unknown. We report a phase II study of consolidative IMRT after first-line chemotherapy in previously untreated M1 NPC. **Methods:** Consolidative IMRT was given in prospectively recruited patients whose previously untreated M1 NPC did not progress after 6 cycles of first-line chemotherapy with gemcitabine and cisplatin. The primary study objective was overall survival (OS). Secondary objectives included progression-free survival (PFS), local relapse-free survival (LRFS), regional relapse-free survival (RRFS), response and toxicity. **Results:** Sixty-nine consecutive patients were enrolled. Sixty-four (92.8%) patients received first-line chemotherapy, of which 8 (12.5%) developed progressive disease and another 8 (12.5%) did not receive IMRT despite non-progression to first-line chemotherapy. The remaining 48 patients whose disease controlled after chemotherapy received IMRT, including 18 (37.5%) who received concurrent chemoradiation. OS was significantly better in those who received IMRT (35.1 *versus* 14.2 months; $P < 0.001$), after a median follow-up duration of 3.40 years (range 0.43 years to 12.14 years). PFS, LRFS, and RRFS were also significantly longer in those who received IMRT. Multivariable analyses revealed that IMRT was the only prognostic factor of all survival end-points. Grade 3 adverse events were observed in 10 (20.8%) patients, mainly mucositis, dysphagia and desquamation. **Conclusions:** Consolidative IMRT was associated with an OS benefit and favorable tolerability among previously untreated M1 NPC patients who had non-progressive disease following first-line chemotherapy. These results support the rationale to further investigate IMRT as part of the initial treatment in this setting. Clinical trial information: NCT02476669. Research Sponsor: SK Yee Medical Foundation.

6526 **Poster Session (Board #187), Fri, 8:00 AM-11:00 AM**

Association between calcitonin and efficacy of anlotinib in medullary thyroid carcinoma: An analysis based on the ALTER01031 trial.

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Background: Calcitonin (Ct) is the most important biomarker for medullary thyroid carcinoma (MTC). In a randomized, placebo-controlled phase IIb trial (ALTER01031, NCT02586350) for MTC, anlotinib exhibited a strong capability not only in PFS prolongation but also in decreasing Ct level. This subanalysis explored the relationship between Ct level and anlotinib efficacy in this trial. **Methods:** Serum Ct of patients (pts) were tested at baseline and on week 6 (after 2 treatment cycles). Correlation between changes in Ct level and changes in target lesion diameters was explored. The influence of baseline Ct level on median PFS for anlotinib treated pts was estimated. Finally, pts in anlotinib arm were divided into two subgroups based on the percentage decline of Ct levels ($>$ 50% vs. $\leq$50%) at week 6. Median PFS (mPFS), median OS (mOS) and objective response rate (ORR) of two groups were compared. **Results:** 86 of 91 enrolled pts (58 in anlotinib arm and 28 in placebo arm) were recorded their serum Ct levels at baseline and no significant difference was observed between two arms (7990.0 ng/L vs. 10891.5 ng/L, $P = 0.192$). After 2 treatment cycles, the Ct level decreased to 4597.5 ng/L in anlotinib arm (n = 50) while increased slightly in placebo arm (12640.0 ng/L, n = 24, $P = 0.006$). For 49 pts in anlotinib arm who had complete assessments at baseline and week 6, roughly linear relationship was observed between Ct levels (X-axis) and target lesion diameters (Y-axis) in percent changes from baseline to week 6 ($y = 0.175x - 0.049$; $r = 0.352$, $P = 0.016$, excluding 3 outliers). Pts with less baseline Ct level ($\leq$ median value vs. $>$ median value) did not show more PFS benefit (17.7 vs. 22.4 months, $P = 0.802$). However, after 2 treatment cycles, a trend of better survival and higher response was observed in pts with high percentage decline of Ct level ($>$ 50%, n = 25) than those with low percentage decline ($\leq$50%, n =25) although without statistical difference (data presented in the table below). **Conclusions:** In ALTER01031, anlotinib showed a strong capability in rapidly decreasing serum Ct. Lower baseline Ct level does not mean better prognosis while a rapid Ct decrease may predict improved survival and treatment response to MTC pts received anlotinib. Clinical trial information: NCT02586350. Research Sponsor: None.

Percentage decline of Ct level	> 50% (events/ censored)	< 50% (events/ censored)	HR (95% CI)	*P* value
mPFS (months)	25.7 (10/15)	17.5 (15/10)	0.665 (0.304, 1.46)	0.302
OS (months)	not reached (5/20)	34.6 (10/15)	0.464 (0.169, 1.29)	0.149
ORR (%)	64	40		0.089

6527 **Poster Session (Board #188), Fri, 8:00 AM-11:00 AM**

Influence of Eastern Cooperative Oncology Group performance status (ECOG PS), tumor size and age on patient outcomes after anlotinib treatment: A subgroup analysis based on ALTER01031 trial for medullary thyroid carcinoma (MTC).

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Background: Anlotinib is a newly developed TKI achieved a nearly 2-fold PFS prolongation in a randomized, placebo-controlled phase 2b trial (NCT02586350) for MTC, the results of which were firstly published in 2019 ASCO annual meeting. This subanalysis examined the influence of baseline demographic (ECOG PS score, age) and tumor size on efficacy in this study. **Methods:** Kaplan-Meier method was applied to estimate the median PFS (mPFS) for subgroups of patients (pts) received anlotinib or placebo based on ECOG PS score (0 vs. 1), median tumor lesion diameter ($<$ 67 vs. $\geq$67mm) and age ($<$ 55 vs. $\geq$55 years old). **Results:** 91 eligible pts were randomly assigned in a 2:1 ratio to receive anlotinib or placebo. The numbers of pts in each subgroup were summarized in the table below. In placebo arm, mPFS did not differ significantly between pts with ECOG PS 0 and 1 (11.3 vs. 11.1months; HR = 0.895 [95% CI 0.347, 2.312], P = 0.821) or between pts with tumor lesion diameter $<$ 67mm and $\geq$ 67mm (7.0 vs. 11.1 months; HR = 1.168 [95% CI 0.463, 2.945], P = 0.737). Conversely, pts in anlotinib arm with ECOG PS 0 obtained more PFS benefits (34.6 vs. 14.0 months; HR = 0.331 [95% CI 0.163, 0.671], P = 0.002). Similarly, anlotinib treated pts with tumor lesion diameters $<$ 67mm achieved a longer mPFS (Not reached vs. 14.0 months, HR = 0.567 [95% CI 0.280, 1.147], P = 0.111). Consistent with that has been verified in differentiated thyroid cancer, high age predicted poor prognosis as mPFS were 14.3 months and 6.8 months in pts $<$ 55 and $\geq$ 55 years old respectively in placebo arm (HR = 0.322 [95% CI 0.116, 0.893], P = 0.007).). Anlotinib treatment exhibited PFS improvement to pts in both age groups but higher PFS prolongation was observed in pts $<$ 55 years old (22.4 vs. 14.0 months; HR = 0.720 [95% CI 0.321, 1.614], P = 0.381). **Conclusions:** This analysis showed that for pts in placebo arm, PFS was similar regardless of functional status (ECOG PS) or tumor size while older pts had higher progression risk. Treatment with anlotinib exhibited greater PFS benefits for pts with better functional status (ECOG PS = 0), younger age or lower tumor burden. These results indicated that it is reasonable to start anlotinib treatment at a relative earlier disease stage before the worsen of ECOG PS, increase of tumor size or ageing. Clinical trial information: NCT02586350. Research Sponsor: None.

Number of pts	ECOG PS (0/1)	Tumor lesion diameter (< 67/≥ 67 mm)	age (< 55/ ≥ 55)
Placebo	10/19	12/17	18/11
Anlotinib	25/37	34/28	38/24

6529 **Poster Session (Board #190), Fri, 8:00 AM-11:00 AM**

A phase II study on the efficacy and toxicity of cabozantinib in recurrent/metastatic salivary gland cancer patients.

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A phase II study on the efficacy and toxicity of cabozantinib in recurrent/metastatic salivary gland cancer patients. **Background:** Because c-MET and VEGFR are often overexpressed in salivary gland cancer (SGC), this study evaluated the efficacy and safety of cabozantinib in recurrent/metastatic (R/M) SGC pts. **Methods:** A single center, single arm, phase II study was conducted. Immunohistochemical c-MET positive (H-score $\geq$10) R/M SGC pts were included in 3 cohorts: adenoid cystic carcinoma (ACC), salivary duct carcinoma (SDC), and other SGCs. Objective growth or complaints due to the disease were required before inclusion in the ACC and other SGC cohort. No prior systemic treatments were required. Pts started 60 mg cabozantinib tablets OD. Primary endpoint was the objective response rate (ORR). A Simon two-stage design was used. In case of $\geq$1 objective response in the first 9 pts/cohort, 8 additional pts would be included in the cohort. **Results:** In total 25 pts were included from Sep. 2018 until premature closure due to severe toxicity in Nov. 2019. Median age was 56 years (range 49-72), prior treatments included: primary tumor resection (*n*=19), radiotherapy $\geq$50Gy (*n*=24), systemic therapy (*n*=10; adjuvant in 2 pts, palliative in 8 pts). Six pts had grade 3 (*n*=4), grade 4 (*n*=1), or grade 5 (*n*=1) wound/fistula complications, occurring at a median of 7.2 mths on cabozantinib (range 2.1-12.8). This resulted in a severe wound complication rate of 32% in 19 pts on treatment for $\geq$2 mths. Remarkably, 4 out of 6 pts developed this complication in the area exposed to high-dose Rx; 2/4 had a pre-existing fistula in this area. Median interval between Rx and start of cabozantinib was 71.3 mths (range 10.6-94.7). Other grade $\geq$3 adverse events in $>$1 pt were: hypertension (5 pts), diarrhoea (2 pts) and dehydration (2 pts). Current median follow-up is 6.8 mths. The ORR was 6% (1/17 pts) in the ACC cohort, 20% (1/5 pts) in the SDC cohort, and 0% (0/3 pts) in other SGC pts; median PFS is 12.6 mths (95% CI 6.8 – 18.4 mths), 9.0 mths (insufficient events for 95% CI), and 6.9 mths (95% CI 0 – 15.2 mths), respectively. Median OS is not reached in any cohort. **Conclusions:** This phase II study on cabozantinib in R/M SGC pts demonstrated severe wound and fistula complications in 32% of pts on treatment for $\geq$2 mths, mostly (4/6 pts) within the radiotherapy field. Because of this toxicity the study was closed prematurely. Furthermore, cabozantinib showed minimal clinical activity in SGC pts. Research funding: Ipsen Pharmaceuticals Clinical trial information: NCT03729297. Research Sponsor: Ipsen Pharmaceuticals.

6530 **Poster Session (Board #191), Fri, 8:00 AM-11:00 AM**

Pembrolizumab (P) or P + chemotherapy (C) versus EXTREME (E) as first-line (1L) therapy for recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): analysis of KEYNOTE-048 by disease state.

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Background: In the phase 3 KEYNOTE-048 trial (NCT02358031) in R/M HNSCC (N = 882), 1L P vs E showed superior OS in PD-L1 CPS ≥20 and CPS ≥1 populations, noninferior OS in the total population, no PFS benefit, and favorable safety; 1L P+C vs E showed superior OS in CPS ≥20, CPS ≥1, and total populations, no PFS benefit, and comparable safety. Results of P or P+C vs E in incurable recurrent only, metastatic only, and R/M subgroups are shown. The metastatic only and R/M subgroups were combined and classified as metastatic. **Methods:** Patients with incurable recurrent (local and/or regional node recurrent disease) or metastatic HNSCC were randomly assigned 1:1:1 to P, P+C, or E. OS and PFS were estimated using the Kaplan-Meier method. Hazard ratios and 95% CIs were based on a Cox regression model with Efron s method of tie handling with treatment as a covariate stratified by ECOG performance status, HPV status, and PD-L1 status. Data cutoff: Feb 25, 2019. **Results:** In the incurable recurrent only subgroup (n = 252), median OS was 11.5 vs 12.1 mo (P vs E) and 13.0 vs 11.1 mo (P+C vs E). In the metastatic subgroup (n = 620), median OS was 11.4 vs 9.7 mo (P vs E) and 13.0 vs 10.1 mo (P+C vs E). Median follow-up, OS, and PFS are shown in Table. Treatment-related adverse events (TRAE) in the incurable recurrent only subgroup: 49.4% (P), 94.7% (P+C), and 97.8% (E); grade 3-5 TRAEs rates: 16.0%, 78.7%, and 73.3%, respectively. TRAE rates in the metastatic subgroup: 61.6% (P), 96.4% (P+C), and 96.4% (E); grade 3-5 TRAEs rates: 17.6%, 69.5%, and 67.0%, respectively. **Conclusions:** P and P+C vs E were efficacious in the metastatic subgroup; in the relatively smaller subgroup of patients with incurable recurrent only HNSCC, the effect was less pronounced. Consistent with the total study population and regardless of disease state, the safety profile was favorable with P vs E and comparable with P+C vs E. These data further support use of 1L P or P+C in patients with R/M HNSCC. Clinical trial information: NCT02358031. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Disease State	Treatment	Median follow-up, mo	Median OS, mo	HR (95% CI) for OS	Median PFS, mo	HR (95% CI) for PFS
Incurable recurrent only	P (n = 82) vs E (n = 94)	11.5 vs 12.1	11.5 vs 12.1	1.09 (0.79-1.51)	2.6 vs 6.3	1.81 (1.32-2.49)
Incurable recurrent only	P+C (n = 76) vs E (n = 88)	13.0 vs 11.1	13.0 vs 11.1	0.92 (0.66-1.28)	4.8 vs 6.2	1.22 (0.88-1.70)
Metastatic	P (n = 216) vs E (n = 203)	11.5 vs 9.8	11.4 vs 9.7	0.73 (0.59-0.91)	2.3 vs 4.9	1.11 (0.90-1.36)
Metastatic	P+C (n = 201) vs E (n = 187)	13.0 vs 10.1	13.0 vs 10.1	0.66 (0.53-0.83)	5.0 vs 4.9	0.82 (0.66-1.02)

6531 Poster Session (Board #192), Fri, 8:00 AM-11:00 AM

Initial analyses of a phase I/II trial of durvalumab (D) plus tremelimumab (T) and stereotactic body radiotherapy (SBRT) for oligometastatic head and neck carcinoma.

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Background: PD-1/PD-L1 +/- CTLA-4 blockade in head-and-neck carcinoma (HNSCC) has shown signs of clinical activity. SBRT aims to reduce tumor burden and perhaps be immune-stimulatory. This analysis seeks to assess the safety and efficacy signal of the triple treatment combination (TTC) consisting of SBRT sandwiched between cycles of D (αPD-L1) and T (αCTLA-4) in oligometastatic (2-10) HNSCC. **Methods:** This is a single arm multi-institutional phase I/II trial (NCT03283605). D (1500 mg) and T (75 mg) were given for 4 monthly cycles, followed by monthly D. SBRT to 2-5 lesions was administered during cycle 2. The median prescribed and maximum SBRT doses were 40 Gy (range: 18-50) and 49 Gy (range:28-61), respectively, given in 3-5 fractions. Global health status was derived from EORTC QLQ C30 questionnaires. **Results:** At data cut-off (Dec 31, 2019), 20 patients were recruited, of which 16 had a study treatment and were analyzed. Table describes the patient characteristics. There were 1 CTCAE V5.0 Grade 2 and 1 Grade 3 (both GI) serious adverse event (SAE) attributable to D and T. Two patients had unrelated SAEs (1 Grade 3-hypercalcemia and 1 Grade 5-GI). The Grade 5 SAE was a gastric hemorrhage that occurred the night of the first D + T infusion. There was no Grade 3+ AE secondary to SBRT. Thus, SBRT did not add to the 2/16 patients who had D + T related SAEs. Global health status scores did not differ statistically between baseline (75) and cycle 3 (73). Of the 14 patients that received SBRT, 7 patients had RECIST target lesions untreated by SBRT. The best responses for these 7 patients were: 1 CR, 3 PR, and 3 SD. When SBRT treated lesions are included and analyzed per RECIST (n = 14), there were 9 PR, 3 SD and 2 PD. The estimated median progression free survival was 7.2 months. **Conclusions:** The first 16 evaluable patients demonstrated tolerable profiles to the TTC (D + T + SBRT) for the treatment of oligometastatic ($\leq$10 lesions) HNSCC. Best response rates were encouraging and could be due to the addition of SBRT during immunotherapy that served to either stimulate the immune system or annihilate slow responding or immunotherapy resistant lesions. Smaller overall tumor burden and 7/16 patients being treated in first line could also have contributed to better results. Clinical trial information: NCT03283605. Research Sponsor: AstraZeneca.

Covariate		n = 16
Gender	Female: Male	3: 13
Age	Median (Min, Max)	63.5 (42,84)
Rx lines prior to entering trial	0	7
	1	4
	2	5
	Prior immunotherapy	*2*
Treatment duration	Median months (Min, Max)	5.88 (0.13,13.3)
Total number of lesions	Median (Min, Max)	4 (2,8)
SBRT treated lesions	1	1
	2	11
	3	2

6532 **Poster Session (Board #193), Fri, 8:00 AM-11:00 AM**

HANNA: Real-world outcomes from an observational study with nivolumab in patients with recurrent or metastatic squamous cell carcinoma of the head and neck in Germany.

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Background: Nivolumab has demonstrated efficacy in clinical trials of recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN). As only limited real-world data are available, we describe the use of nivolumab and its outcomes in routine clinical practice. **Methods:** HANNA is a prospective, observational study of patients with R/M SCCHN treated with nivolumab in 56 hospitals and practices in Germany. In total, 385 patients will be followed for $\leq$ 5 years from treatment initiation until death, withdrawal of consent, loss of follow-up/record, or end of study. The primary objective is overall survival (OS). Secondary objectives include baseline characteristics, safety profiles, and quality of life (QOL) assessment. **Results:** By November 2019, data from 311 patients were available. Median follow-up was 3.5 months. Baseline characteristics were male, 81.7%; median age, 63 years; history of smoking, 73.3%; Eastern Cooperative Oncology Group performance status (ECOG PS) 0/1, 60.8%; ECOG PS 2/3, 29.6%. Location of primary tumor was oropharynx, 38.3%; hypopharynx, 20.9%; oral cavity, 22.8%; larynx, 11.6%; others, 6.4%. 55.6% of R/M SCCHN patients progressed $\leq$ 6 months after platinum-based therapy, whereas 43.4% were platinum-sensitive (progressed $>$ 6 months after platinum-based therapy). Nivolumab was received by 25.1% of patients as first therapy after platinum-based chemo- or radiochemotherapy, by 62.1% as second therapy, and by 12.9% as later line therapy. Median treatment duration was 4.6 months. OS at 1 year was 43.3%. 1-year OS for patients with ECOG PS 0 was 75.9%; ECOG PS 1, 41.2%; and ECOG PS 2, 27.3%. Platinum-sensitive patients had higher 1-year OS probability (51.6%). Drug-related adverse events (grade 1/2) and serious adverse events (grade 3/4) were observed in 28.9% and 10.0% of patients, respectively. Interim QOL data (per FACT-H&N and EQ-5D questionnaire) indicated a tendency toward stabilization or slight improvement. We will present an update of the data with longer follow-up (data cut March 2020). **Conclusions:** HANNA represents one of the largest real-world datasets for nivolumab in R/M SCCHN and comprises a more diverse set of patients than the phase 3 CheckMate 141 trial, including patients with higher ECOG PS, age, and platinum sensitivity. Outcomes from HANNA show that the improved OS, safety, and QOL seen with nivolumab in the real-world setting are consistent with the outcomes from CheckMate 141. Clinical trial information: NCT03114163. Research Sponsor: Bristol-Myers Squibb.

6533 **Poster Session (Board #194), Fri, 8:00 AM-11:00 AM**

Selection of patients for surveillance imaging after radiotherapy for squamous cell carcinoma of oral cavity and oropharynx.

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Background: NCCN guidelines do not recommend routine surveillance imaging for distant failure (DF) after definitive treatment of head & neck squamous cell carcinoma (SCC). We hypothesized that there exists a subset of patients with sufficiently high enough risk for DF to benefit from surveillance imaging. This study attempts to define high risk cohorts of oropharynx (OP) and oral cavity (OC) patients. **Methods:** A retrospective review was conducted of patients with SCC of the OP or OC at a single tertiary care institution from 1994-2019. Patients were staged according to AJCC 7th edition and included in this study if they completed definitive-intent treatment and received 60 Gray or higher of radiotherapy (RT). Local, regional, and distant failure were estimated with cumulative incidence. Univariable & multivariable risk factors for DF were identified with Fine & Gray competing risk regression. Significant variables were compiled to calculate a risk score. **Results:** 863 patients were included (676 OP/187 OC). OC patients were 60.4% male, median age 61, with median follow up of 77.5 months. Smoking status was 27.3% current, 44.4% former, 28.3% never, with 30 median pack years. Disease was 57.3% T1-2, 42.7% T3-4, 55.6% N0-2a, 44.4% N2b-3. 94.1% had surgery & 34.3% had concurrent systemic therapy. OP patients were 87.9% male, median age 58, 96.3% HPV+, with median follow up of 60.8 months. Smoking status was 20.9% current, 44.5% former, 34.6% never, with 20 median pack years. Disease was 67.9% T1-2, 32.1% T3-4, 29.9% N0-2a, 70.1% N2b-3. 11.5% had surgery & 87.3% had concurrent systemic therapy. Specifically, 52.2% of OP patients received concurrent cisplatin, 10.6% concurrent cetuximab, and 24.5% other systemic therapies. 11.7% of patients experienced DF, of which 77% failed in the lung. Within the OC cohort, nodal stage 2b or higher was the only predictive factor (HR 3.26, $p < 0.001$), conferring a 3 year risk of DF of 34% vs 10%. Within the OP cohort, a high risk cohort of 87 patients (12.9%) was identified with a 3 year incidence DF of 22%, compared to 10% or less in lower risk cohorts. This high risk cohort consisted of active smokers treated with definitive RT and either concurrent cisplatin or no concurrent therapy, with at least T3 and N2b disease, as well as any patients treated with definitive RT and concurrent cetuximab. **Conclusions:** We identified groups of OC & OP patients with greater than 20% risk of developing DF at 3 years, the majority of which occurred in the lung. Surveillance imaging of the chest should be considered for patients meeting these criteria. Research Sponsor: None.

6534 **Poster Session (Board #195), Fri, 8:00 AM-11:00 AM**

Distinct transcriptional profiles in plasma exosomes associated with recurrence of nasopharyngeal carcinoma patients with standard treatment.

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Background: Nasopharyngeal carcinoma (NPC) is endemic with a high prevalence in Southern China, Asia,cetuximab and North Africa. Exosomes are small vesicles containing a wide range of functional proteins, mRNA and miRNA. In the progression of NPC, the tumor cells constantly release exosomes into the surrounding environment and also into the circulating blood. The aim of this study was to explore the association between RNA expression in plasma exosomes and prognosis of NPC patients after standard treatment. **Methods:** In this retrospective study, a total of 25 eligible NPC patients were included: 12 patients in the recurrence (R) subgroup and 13 patients in the no recurrence (NR) subgroup. RNA was extracted from the exosomes of plasma specimens which were collected at West China Hospital, Sichuan University. Gene expression profiles were conducted by using the RNA-sequencing platform. The DESeq2 package was used to analyze the differentially expressed genes (DEGs) between R and NR subgroups. The gene set variance analysis (GSVA) was performed to explore C5 gene sets enrichment related to the recurrence after standard treatment. **Results:** We observed 332 DEGs between R and NR subgroups, which include 125 up-regulated and 207 down-regulated genes (R vs. NR,|log2fold change|$>$1, $p<0.05$). Moreover, hierarchical clustering analysis of the 332 DEGs revealed that all samples clustered into two subgroups, with cluster 1 containing 82% (9/11) recurrence patients and cluster 2 containing 79% (11/14) no recurrence patients. Further, univariate Cox regression analysis showed that 293 out of 332 DEGs were significantly correlated with DFS ($p<0.05$), such as TRAM1, CAPN1, SAT1 and ACTB. GSVA and Log Rank test of survival data demonstrated that a total of 824 pathways/biological processes were significantly different between R andNR subgroups ($p<0.05$). Specifically, the top 9 pathways/biological processes, such lipoxygenase pathway, rough endoplasmic reticulum membrane and low density lipoprotein particle clearance, was mainly enriched in the NR subgroup ($p<0.001$). **Conclusions:** Profiling of plasma exosomes RNA in NPC patients reveals distinctive gene expression pattern between patients with or without recurrence. Further functional analysis revealed that top enriched 9 pathways/biological processes may correlate with a favorable prognosis and are worth investigating. Moreover, for the prognosis of patients with NPC, RNA expression of plasma exosomes may be a potentially valuable research object. Research Sponsor: the research and data on the evaluation method of stereotactic radiotherapy equipment (subject No: 2017YFC0113701), Research and development of tumor real-time monitoring molecular diagnostic products based on liquid biopsy -- a major science and technology project of guangdong province 2019B020232003;Dalian municipal Science and technology innovation projects (2018 j12sn063): a new method for the detection optical flow control chip peripheral blood tumor cells research Science and technology innovation project of Dalian City (No: 2018 j12sn063).

6535 **Poster Session (Board #196), Fri, 8:00 AM-11:00 AM**

Dendritic cell therapy with CD137L-DC-EBV-VAX in locally recurrent or metastatic nasopharyngeal carcinoma (NPC).

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Background: Epstein-Barr virus (EBV) is associated with non-keratinising (NK) NPC, a disease prevalent in Southeast Asia, and provides a potential target for dendritic cell (DC) vaccine therapy. CD137 ligand (CD137L) expressed on antigen presenting cells costimulates CD137 expressing T cells upon receptor/ligand interaction. CD137L signalling differentiates monocytes to CD137L-DC, a novel type of DC, which are more potent than classical DC in stimulating autologous T cells. Here, we explore the safety and efficacy of autologous CD137L-DC pulsed with EBV peptides spanning Epstein Barr nuclear antigen 1, latent membrane protein 1 (LMP1) and LMP2 (CD137L-DC-EBV-VAX) in patients with locally recurrent or metastatic NPC. **Methods:** In this single centre, phase I study, eligible patients (pts) with locally recurrent or metastatic NK-NPC and clinical benefit (CB) from their prior treatment (stable disease [SD], partial [PR] or complete response[CR]), underwent apheresis to isolate monocytes which were differentiated to CD137L-DC through CD137L agonist exposure. CD137L-DC were pulsed with EBV antigens during maturation to obtain CD137L-DC-EBV-VAX which was administered intradermally every 2 weeks (w) for up to 7 injections following site preconditioning with Tetanus and Diphtheria vaccine. **Results:** 14 pts were enrolled of which 2 progressed rapidly and did not begin treatment. Mean age was 58 years. Median lines of prior treatment for metastatic NPC was 1 (range 1-6), the most common being cisplatin and gemcitabine. 9 pts received 7 vaccine doses (range 2-7) with a mean administered cell count of $23.9x10^6$. CB was seen in 5 cases (42%) with 1 PR and 4 SD beyond 1 year. Median progression free survival (mPFS) was 26w (95% CI, 23-43). The lowest PFS (8w) was in a pt with 6 prior lines of treatment including a checkpoint inhibitor. Mean pretreatment neutrophil: lymphocyte ratio (NLR) was 3.4 and a value of less than 3 was associated with prolonged mPFS (42 *vs* 14w, $p = 0.01$). Enzyme linked immune absorbent spot (ELISPOT) analysis in 5 pts with CB showed a rise in interferon-γ secreting peripheral T cells prior to the 3^{rd} vaccine versus baseline. Treatment was well tolerated with only 4 cases of grade 1 related adverse events reported, most commonly injection site reaction (3pts). **Conclusions:** CD137L-DC-EBV-VAX is safe and exhibits promising efficacy when administered following CB from chemotherapy. A rise in activated peripheral blood mononuclear cells after 2 vaccinations in selected patients showing benefit suggests immunological correlates with efficacy. Clinical trial information: NCT03282617. Research Sponsor: National Medical Research Council (Singapore) - NMRC/BnB/0018c/2015.

6536 **Poster Session (Board #197), Fri, 8:00 AM-11:00 AM**

Cisplatin every three weeks versus weekly cisplatin or carboplatin with definitive radiotherapy for squamous cell carcinoma of the head and neck is associated with improved overall survival in a representative national population.

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Background: For patients with primary untreated locally advanced head and neck squamous cell carcinoma (PULA-HNSCC), high dose once every 3 weeks cisplatin (HDC; 100 mg/m^2) added to curative radiotherapy (RT) prolongs survival, but is associated with severe toxicities. Concurrent chemoradiation (CRT) with low dose weekly cisplatin (LDC; 30-40 mg/m^2), carboplatin (C), or RT alone is often substituted for HDC. We estimated and compared overall survival (OS) and acquired toxicities among Medicare beneficiaries treated with CRT using HDC, LDC, C, or RT. **Methods:** Patients diagnosed from 2004-2011 with PULA-HNSCC (stages III-IVB AJCC 6th and 7th editions) of the oropharynx (OPC), hypopharynx (HP), or larynx (L) who received definitive RT or CRT were identified using the linked SEER-Medicare database. An analytic cohort of patients receiving CRT with HDC, LDC, or C was constructed using well-established eligibility criteria. OS was estimated and compared between patients grouped by treatment received utilizing a multivariable stratified propensity scores weighted Cox regression model, including demographic and disease characteristics. Toxicities were compared using exact common odds-ratio and Fisher's tests. **Results:** We identified 1,335 patients that received RT: OPC (n = 731), HP (n = 174), or L (n = 430). Out of those, patients were treated with HDC (n = 264), LDC (n = 259), C (n = 353), or RT alone (n = 459). Median OS (years) was 5.61 (95% CI = 4.58-7.69) for HDC, 3.7 (95% CI = 3.1-4.79) for LDC, 3.1 (95% CI = 2.48-3.86) for C, and 1.36 (95% CI = 1.19-1.58) for RT, respectively. OS was significantly greater for HDC than for LDC (HR = 1.35, 95% CI = 1.06-1.72, p= 0.02), C (HR = 1.41, 95% CI = 1.12-1.76, p= 0.003), or RT (HR = 2.1, 95% CI = 1.68-2.61, p= $<$ 0.001). Treatment with HDC compared to LDC was not associated with increased prevalence of dysphagia or neutropenia. HDC was associated with hearing loss when assessed at 9-12 months post-diagnosis (p =0.03). **Conclusions:** In SEER-Medicare beneficiaries with PULA-HNSCC of the OPC, HP, or L, OS was significantly better for HDC than LDC when accounting for baseline clinical and demographic characteristics and propensity score weights. Toxicities were similar between regimens, except for an increased incidence of the late acute toxicity of hearing loss in HDC. A regimen of HDC improves OS, but needs to be carefully assessed against increased toxicity risk, with hearing loss in particular. Research Sponsor: None.

6537 **Poster Session (Board #198), Fri, 8:00 AM-11:00 AM**

Association of autoimmunity with survival in patients with recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) treated with immune checkpoint inhibitors (ICIs).

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Background: ICIs are associated with immune-related adverse events (irAEs) that occur as a consequence of enhanced immune response due to T-cell activation. The objective of this observational cohort study was to investigate the association between irAEs and disease outcome in pts with R/M HNSCC. **Methods:** 110 pts treated with ICIs were reviewed. Overall survival (OS) was calculated from the date of initiation of ICI to the date of death. To overcome guarantee-time bias, we calculated post-irAEs survival from the date of first irAE presentation in patients who developed irAEs or from the date of ICI initiation in pts without irAEs. **Results:** Primary site was the oral cavity (N = 51), oropharynx (N = 20), larynx (N = 29), hypopharynx (N = 1), paranasal sinuses (N = 5) and nasopharynx (N = 4). 41 (37.3%) had metastatic and 69 (62.7%) recurrent disease. 32 pts (29.1%) developed irAEs, with more common thyroiditis (N = 15, 13.6%). Of 100 pts with evaluable disease, 14 (14%) responded. 6/31 (19.4%) with irAEs vs. 8/69 (11.6%) without irAEs responded to ICI (p = 0.354). After a median follow-up of 16.4 months, 69 pts died. Median OS was 10 mo (95%CI, 6.7-13.4), 10 mo (95%CI, 5.6-14.5) for pts with recurrent and 10 mo (95%CI, 7.7-12.3) for pts with metastatic HNSCC (p = 0.966). Median OS was 17.9 mo (95%CI, 7.9-27.9) for pts with irAEs and 6.6 mo (95%CI, 3.3-9.9) for pts without irAEs (p = 0.001). Median post-irAEs survival was 16.3 (95%CI, 7.1-25.5) for pts with irAEs vs. 6.6 mo (95% CI, 3.3-9.9) for pts without irAEs (p = 0.020). Responders to ICI did not differ in median post-irAEs survival irrespective of whether they developed irAEs (p = 0.561), while among non-responders, those who developed irAEs had significantly longer median post-irAEs survival compared to those who did not (10 vs. 6 mo, respectively, p = 0.044). Multiviariate Cox proportional hazard models showed that independent favorable prognostic factors for post-irAEs survival were the development of irAEs (HR 0.54, 95%CI 0.30-0.97, p = 0.039) and response to ICI (HR 0.16, 95%CI 0.05-0.50, p = 0.002). **Conclusions:** The development of irAEs is a strong predictor of improved survival in patients with advanced HNSCC treated with ICIs. Research Sponsor: None.

6538 **Poster Session (Board #199), Fri, 8:00 AM-11:00 AM**

Immune checkpoint inhibitor in nasopharyngeal carcinoma: Multi-institution experience.

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Background: The current standard treatment for unresectable recurrent/metastatic (R/M) nasopharyngeal carcinoma (NPC) is cytotoxic chemotherapy but prognosis remains poor. Recent phase I-II trials of anti-PD-1 therapy (aPD-1) have demonstrated promising activity in R/M NPC, but the published experience is primarily limited to Epstein-Barr virus (EBV) positive tumors in the Asian population. Here we report our three institutional real-world experience with aPD-1 in patients (pts) with R/M NPC. **Methods:** A retrospective analysis was conducted after IRB approval at the Massachusetts General, Johns Hopkins, and University California San Francisco Hospitals. Demographic and clinical data was collected on pts with R/M NPC who received aPD-1 at the participating institutions. Objective response rate (ORR) was the primary outcome of interest and progression free survival (PFS) and overall survival were secondary outcomes. Univariate and multivariate analyses were conducted to assess association between clinicopathologic factors and outcomes, using logistic regression models. **Results:** A total of 36 pts were identified: 20 pts were treated with pembrolizumab and 16 with nivolumab. Median age was 50 (15-74). Twenty-nine (81%) were male. Twenty pts (56%) were Asian. Twenty-nine pts (81%) had EBV positive disease. Nine (25%) had aPD-1 as first-line therapy (1L). Molecular profiling results were available in 16 pts: TP53 mutation was the most common alteration (25%) and was limited to EBV negative tumors. Median total mutational burden (TMB) was 3/Mb (1-28). Median PD-L1 expression was 10% (0-90). Median follow up was 13.9 months (mos). Objective response was evaluable in all 36 pts: 9 pts achieved objective response (ORR 25.0%, 95% CI 12.1-42.2) with 2 complete responses: EBV positive vs. negative (27.6% vs. 14.2%, P=0.472), Asian vs. non-Asian (25% vs. 25%, P=1.000), and 1L vs. >1L (33.3% vs. 22.2%, P=0.511). Thirteen pts had stable disease (disease control rate 61.1%). Responses were seen in both TMB high (28/Mb) and low (1/Mb) tumors and no association with PD-L1 expression was observed. One-year survival rate was 81.3%. EBV positive pts had a trend towards better survival (84.8 vs. 66.7, P=0.640). Median PFS was 5.5 mos and not different between EBV positive vs. negative pts (5.6 vs. 4.0 mos, P=0.919). **Conclusions:** Our multi-institutional real-world experience with checkpoint inhibitor therapy in R/M NPC confirms that a similar degree of activity is seen as reported in the phase I-II experience in diverse races, but efficacy seems more prominent in EBV positive disease. Research Sponsor: None.

6539 **Poster Session (Board #200), Fri, 8:00 AM-11:00 AM**

Efficacy and tolerance of carboplatin-cetuximab in patients with metastatic or recurrent head and neck squamous cell carcinoma unfit for extreme regimen.

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Background: Head and neck squamous cell carcinoma (HNSCC) is the fourth cause of death by cancer in France. For metastatic patients, the standard first line treatment is the EXTREME regimen. However, a lot of these patients have a poor performance status (PS) and/or several comorbidities making them unfit for this regimen. We have treated them with carboplatin and cetuximab (simplified EXTREME regimen) since 2007. The aim of this study is to assess the efficacy and tolerance of this regimen in this frail population. **Methods:** We retrospectively reviewed the medical charts of all patients treated with simplified EXTREME regimen for recurrent or metastatic HNSCC in three French academic hospitals between 2007 and 2017. The primary endpoint was overall survival (OS) and secondary endpoints were progression free survival (PFS), overall response rate (ORR), identification of prognostic factors, and toxicity. **Results:** 103 patients were included with a median age of 63 y.o., 60% had a PS 0-1 and 40% a PS 2-3. With a median follow-up of 30.2 months, median OS was 7.2 months and median PFS 3.7 months. ORR was 39% and 24% of patients had disease stabilization. On univariate analysis, a PS of 2 or more was significantly associated with a worse OS (median OS 10.1 months if PS 0-1 versus 4.6 months if PS 2-3; HR = 1.68; 95%CI = 1.11-2.57; p = 0.01). Acute grade 3-4 hematologic and non-hematologic toxicity rates were 25.2% and 27.2%, respectively, with 11.8% of thrombopenia, 9.7% of neutropenia, 10% of skin toxicity, and 12.6% of asthenia. Patients with grade 1 or more skin toxicity had a higher ORR (HR = 3.44; 95%CI = 1.16-10.23; p = 0.03) and a prolonged OS (HR = 0.37; 95%CI = 0.23-0.58; $p < 0.0001$) and PFS (HR0.29; 95%CI = 0.19-0.47; $p < 0.0001$). During treatment, 29% of patients had a pain decrease, 13.5% a gain of weight, and 17.2% an improvement in PS. **Conclusions:** This is the largest cohort of patients treated with simplified EXTREME for HNSCC. Simplified EXTREME was well tolerated in this frail population with a high ORR. Patients with a good PS had prolonged survival. Interestingly, skin toxicity of any grade was significantly correlated with treatment efficacy. Research Sponsor: Merck Serono.

6540 **Poster Session (Board #201), Fri, 8:00 AM-11:00 AM**

Final results of the multicenter, open-label, randomized phase II trial PAZOTHYR evaluating continuous versus intermittent administration of pazopanib in radio-iodine-refractory thyroid cancers (NCT01813136).

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Background: Multikinase inhibitors (MKI) targeting angiogenesis, including pazopanib (P), have shown efficacy in progressive radioiodine refractory thyroid cancers (RAIR-TC) but are accompanied by adverse effects, leading to dose adjustments/interruptions. We aimed to investigate the efficacy and tolerance of a discontinuous scheme of pazopanib administration in this situation. **Methods:** This randomized phase II study enrolled RAIR-TC patients (pts) in first or second-line of MKI with documented disease progression within 12 months (m). After a 6-m pazopanib continuous induction phase, pts with stable disease (SD) or tumor response were randomly assigned in a 1:1 ratio to receive continuous pazopanib (CP) or intermittent pazopanib (IP) until progression and restart. They were stratified by best tumor response [stable disease vs. objective response] and prior MKI treatment [yes vs. no]). Primary endpoint was time to treatment failure (TTF) defined as time between randomization and permanent discontinuation of pazopanib (either for disease progression or intolerance); secondary endpoints included overall response rate (ORR), progression-free survival (PFS) and safety. **Results:** 168 pts (66.5 years median age; 51.8% female) were included and 100 pts randomized (CP: 50, IP: 50). The median number of metastatic sites was 2.0 (1-7) and 50 pts (29.8%) were pretreated with MKI. With a median follow-up of 31.3 m, we did not show any statistically significant difference in the TTF, 80% (66.0-88.7%)] of the pts being under P at 6 m after randomization in the IP arm *versus* 78% (63.8-87.2%) in the CP arm. Median TTF was 14.7 m 95% CI [9.3; 17.4] and 11.9 m 95% CI [7.5; 15.6] respectively (HR 0.79 [0.49-1.27]). The best response with P was 35.6% (95% CI [28.2; 43.6]) and the disease control rate was 89.4% 95% CI [83.5; 93.7]. Median time to progression under P was not statistically different between 2 arms (5.7m 95% CI [4.8;7.8] in the IP arm vs. 9.2m 95% CI [7.3; 11.1] in the CP arm (HR 1.36 [0.88; 2.12]). 36/100 pts (36%) experienced pazopanib-related grade 3/4 AEs (CP:17; IP: 19) mainly represented by gastrointestinal disorders, hypertension, cardiac disorders and asthenia. Five pazopanib-related deaths were reported (CP:1;IP: 4). **Conclusions:** The intermittent administration of pazopanib study did not significantly demonstrate superiority in efficacy or tolerance over continuous treatment. Continuous administration of MKI remains the standard in RAIR-TC. Clinical trial information: NCT01813136. Research Sponsor: PHRC11-089.

6541 **Poster Session (Board #202), Fri, 8:00 AM-11:00 AM**

A phase I/Ib study of lenvatinib and cetuximab in patients with recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).

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Background: Despite overexpression of EGFR in HNSCC, cetuximab monotherapy has limited benefit. Fibroblast growth factor receptor (FGFR) signaling is a known resistance mechanism to EGFR inhibition. Lenvatinib is a multi-targeted receptor tyrosine kinase inhibitor (RTKI) and has unique activity against FGFR 1,2,3, and 4. We are evaluating inhibition of EGFR and RTKs including FGFR through the combination of cetuximab and lenvatinib in patients (pts) with R/M HNSCC. **Methods:** In this phase I/Ib, single-institution study, pts with measurable disease per RECIST v1.1 that is incurable with surgery and radiation are eligible regardless of prior cetuximab therapy. The dose de-escalation phase included pts with HNSCC and cutaneous squamous cell carcinoma (cSCC) treated with standard cetuximab dosing and lenvatinib in 3 potential dose levels (DL): (0) 24mg, (-1) 20mg, (-2) 14mg oral daily in a standard 3+3 design. The primary objective was to determine the MTD of lenvatinib in combination with cetuximab. The expansion phase included an additional 5 pts with HNSCC treated at the MTD. Exploratory endpoints include ORR and PFS in HNSCC pts treated at the MTD. **Results:** 12 evaluable pts were treated on the dose de-escalation phase. There were no DLTs on DL 0; however, 3/6 pts were removed immediately following the 28-day DLT period due to toxicity that included extensive thrombotic events and athlerosclerotic disease. On DL -1, 0/6 pts (5 HNSCC/1 cSCC) had a DLT establishing lenvatinib 20mg daily as the MTD. 7 pts were enrolled onto the expansion phase; 4 are currently evaluable for response and 2 are unevaluable because of withdrawal due to a cetuximab reaction and required surgery. Of the 9 evaluable HNSCC pts treated with lenvatinib 20mg daily, 6 pts had a PR with a 67% ORR. For the 8 pts who have completed treatment, the median PFS is 3.6 months (range 1.6-10.4). Grade 3 AEs regardless of attribution included hypertension (3), oral mucositis (3) and oral cavity fistula (1). The most common AEs were acneiform rash (7), fatigue (6), and hypertension/hypothyroidism/oral mucositis (5 each). **Conclusions:** The MTD of lenvatinib 20mg daily with cetuximab appears to be active in R/M HSNCC with an impressive preliminary ORR, warranting further evaluation of the efficacy of this combination. Clinical trial information: NCT03524326. Research Sponsor: Eisai Pharmaceuticals.

6542 **Poster Session (Board #203), Fri, 8:00 AM-11:00 AM**

Clinical response and biomarker analysis of POLARIS-02 a phase II study of toripalimab, a humanized IgG4 mAb against programmed death-1 (PD-1) in patients with metastatic nasopharyngeal carcinoma.

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Background: Metastatic nasopharyngeal cancer (mNPC) patients progressed after standard therapy have limited treatment options. This study is to evaluate the clinical efficacy and safety of toripalimab in mNPC patients refractory to standard chemotherapy treatment (Clinical trial ID: NCT02915432). **Methods:** Patients receive 3 mg/kg toripalimab Q2W via IV infusion until disease progression, unacceptable toxicity, or voluntary withdrawal. Clinical response is assessed every 8 weeks according to RECIST v1.1. Tumor PD-L1 expression, plasma EBV titer and other biomarkers will be evaluated for correlation with clinical response. **Results:** From Dec 2016 to Feb 2019, 190 mNPC patients were enrolled from 17 participating centers in China. The median age was 46 years with 83% male. Patients were heavily pretreated with a median of 2 lines of prior systemic treatments. By the cutoff date of Jan 17, 2020, 97% patients experienced treatment related adverse events (TRAE). Most common TRAE included anemia, hypothyroidism, AST increased, proteinuria and fever. Grade 3+ TRAE occurred in 28% patients. Among 190 patients assessed by Independent Review Committee per RECIST v1.1, 6 CR, 33 PR and 40 SD were observed for an ORR of 20.5% and a DCR of 41.6%. The median DOR was 12.9 months. The median PFS and median OS were 1.9 months and 18.6 months respectively. PD-L1+ patients (n=48) had higher ORR than PD-L1- patients (n=134), 27.1% versus 19.4%. By tumor histology, ORR was higher in keratinizing NPC (n=8) than non-keratinizing NPC (n=168), 62.5% versus 19.0%. 144 patients had valid plasma EBV titer measured every 28 days during the study. An average drop of 101-fold plasma EBV titer from baseline was observed in patients with objective responses. Patients with 2-fold+ drop in plasma EBV titer on day 28 (n=60) went on to have 48.3% ORR and 76.7% DCR, whereas patients with less than 2-fold drop (n=88) had 5.7% ORR and 25.0% DCR. 14 responding patients who later developed progressive disease had at least 2-fold+ increase of plasma EBV tier 3-months (median) before radiographic identification of disease progression. **Conclusions:** Toripalimab demonstrated encouraging clinical activity with a manageable safety profile in mNPC patients refractory to standard chemotherapy. Patients with 2-fold+ drops in plasma EBV titer on day 28 from baseline had favorable clinical response of 48.3% ORR, which might be used as a predictive biomarker. Clinical trial information: NCT02915432. Research Sponsor: Shanghai Junshi Biosciences Co., Ltd.

6543 **Poster Session (Board #204), Fri, 8:00 AM-11:00 AM**

Phase I dose escalation of stereotactic body radiation therapy and concurrent cisplatin for re-irradiation of unresectable, recurrent head and neck squamous cell carcinoma.

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Background: For patients with unresectable, previously radiated, locoregionally recurrent head and neck cancer, stereotactic body radiation therapy (SBRT) has become an attractive option. The use of high daily doses of radiotherapy may overcome the inherent radioresistance of these recurrent cancers. Given the resistant and advanced nature of many of these cancers, the addition of chemotherapy to radiotherapy is typically recommended as a radiosensitizer. We therefore performed a phase I clinical trial in order to establish a maximum tolerated dose of SBRT with concurrent chemotherapy in locoregionally recurrent head and neck cancer. **Methods:** Major inclusion criteria were recurrence of previous squamous cell carcinoma of the head and neck in patients who had previously undergone radiotherapy to doses $\geq$ 45 Gy to the area of recurrence, $\geq$ 6 months prior to enrollment, and who were medically unfit for surgery, deemed unresectable, or refused surgery. Patients were treated with radiation therapy every other day for five fractions at three dose levels; 30 Gy, 35 Gy, and 40 Gy. Cisplatin was given prior to every SBRT fraction at a dose of 15 mg/m2. Patients were monitored for safety and tolerability for any grade 4 or greater toxicity (per CTCAE v4.0) that occurred within 3 months from the start of SBRT. Primary end point was maximum tolerated dose (MTD). **Results:** Twenty patients were enrolled and of those 17 patients were evaluable for the primary endpoint. Nine patients had a primary tumor in the oropharynx, four patients in the oral cavity, three in the neck, one in the larynx, and one simultaneously in the larynx and neck. Of the three patients that were not evaluable two withdrew consent, and one patient in the 30 Gy dose level died of unknown causes two weeks following completion of treatment. Due to safety concerns the 30 Gy dose level was expanded an additional three patients, and no further dose limiting toxicities (DLTs) were observed. At the 35 Gy and 40 Gy dose level there were no reported grade 4 or 5 adverse events (per CTCAE v4.0). There were 5 (27%) reported grade 3 toxicities and 12 (66%) grade 2 toxicities. **Conclusions:** This phase I study demonstrates that 40 Gy SBRT with concurrent cisplatin at a dose of 15mg/m2 is feasible, safe, and well tolerated. Patients continue to be followed for secondary outcomes of local control and overall survival. Clinical trial information: NCT02158234. Research Sponsor: H. Lee Moffitt Cancer Center Department of Radiation Oncology.

6544 **Poster Session (Board #205), Fri, 8:00 AM-11:00 AM**

INDUCE-1: Report on safety run-in cohorts combining Inducible T-cell co-stimulatory receptor (ICOS) agonist GSK3359609 (GSK609) with platinum+5-FU chemotherapy (5-FU/plat), with or without pembrolizumab (PE), for the treatment of advanced solid tumors.

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Background: The KEYNOTE-048 study (Burtness, at al. *Lancet* 2019;394:1915–28) led to approval of PE in combination with 5-FU/plat for first-line (1L) treatment of head and neck squamous cell carcinoma (HNSCC). The Phase I INDUCE-1 study (NCT02723955) has shown that GSK609±PE has a manageable safety profile in patients (pts) with advanced solid tumors (Hansen, at al. *Annals of Oncology* 2018;29[suppl_8]:viii404) and that GSK609 combined with PE has anti-tumor activity in pts with anti-PD-1/L1-naïve HNSCC (Rischin, et al. *Annals of Oncol* 2019;30[Supplement_5]: v454–5). To evaluate the safety of GSK609±PE in combination with 5-FU/plat, we initiated additional safety cohorts. **Methods:** Pts eligible for GSK609+5-FU/plat had a diagnosis of advanced selected solid tumors and ≤5 prior lines of systemic therapy. Pts eligible for GSK609+PE+5-FU/plat had a diagnosis of recurrent or metastatic 1L HNSCC deemed incurable by local therapies. 5-FU/plat was administered every 3 weeks (Q3W) for 4-6 cycles (Burtness, at al. *Lancet* 2019;394:1915–28); GSK609 24 or 80 mg ±PE 200 mg were administered Q3W for up to 2 years/35 cycles or until disease progression or unacceptable toxicity. **Results:** Twenty-nine pts were enrolled in the 5-FU/plat safety cohorts: 10 pts in the GSK609+5-FU/plat cohort and 19 pts in the GSK609+PE+5-FU/plat cohort. With GSK609+5-FU/plat, 9/10 (90%) pts experienced ≥ 1 adverse event (AE). Of 32 AEs of any grade, 9 were Grade ≥3 and 3 were serious AEs (SAEs). Two of the 3 SAEs were related to study treatment (oral mucositis and febrile pancytopenia). With GSK609+PE+5-FU/plat, 18/19 (94.7%) pts experienced ≥ 1 AE. Of 119 AEs of any grade, 24 were Grade ≥3 and 15 were SAEs. Of the 15 SAEs, 11 were related to study treatment (febrile neutropenia [n=4], colitis [n=2], diarrhea [n=1], vomiting [n=1], acute kidney injury [n=1], cardiac chest pain [n=1] and lung infection [n=1]). For all cohorts, no Grade 5 AEs were observed. For 10 pts evaluable for confirmed best overall response in all cohorts, 2 pts had partial response, 6 pts had stable disease and 2 pts were nonevaluable. No difference in GSK609 exposure was observed relative to GSK609 monotherapy. **Conclusions:** The safety profile of GSK609 in combination with 5-FU/plat±PE is manageable. Most AEs were Grades 1 or 2 and consistent with PE and chemotherapy toxicities. Continued follow-up to investigate long-term safety and efficacy of this combination is warranted. Clinical trial information: NCT02723955. Research Sponsor: Study is funded by GlaxoSmithKline and in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

6545 **Poster Session (Board #206), Fri, 8:00 AM-11:00 AM**

Radiomic response evaluation of recurrent or metastatic head and neck squamous cell cancer (R/M HNSCC) patients receiving pembrolizumab on KEYNOTE-012 study.

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Background: Immunotherapy has become a standard of care in the treatment of R/M HNSCC, however only a subset of patients respond, highlighting the need for predictive and prognostic biomarkers. Radiomics is a non-invasive method to quantitatively analyze tumors through conventional imaging. **Methods:** The pre-treatment and first-on-treatment (after 8 weeks) computed tomography (CT) scans from 132 R/M HNSCC patients treated with single-agent Pembrolizumab (10mg/kg Q2W or 200mg Q3W IV) on the KEYNOTE-012 study were analyzed. Identified target lesions, per RECIST 1.1, were manually contoured, and radiomic features from the tumor and peritumoral region (3 mm expansion of the tumor) were extracted using PyRadiomics. All combinations of image filters and feature classes, not including shape descriptors of peritumoral region, were extracted. Feature space dimensionality was reduced by clustering features (hierarchical clustering using Pearson-based distance and complete linkage) and selecting the medoid of each cluster. Correlation with lesion-level response (LLR) at first-on-treatment CT and overall response (OR) was evaluated using concordance index (CI) with Benjamini-Hochberg multiple testing correction. **Results:** A total of 406 lesions were included (45 head & neck (HN), 207 lung, 57 liver, 86 lymph nodes (LN), 11 other). 3562 features were extracted from pre-treatment scans (2246 tumor, 1316 peritumor). Considering all lesion sites collectively, 27 of 110 feature clusters were significantly correlated with LLR (false discovery rate (FDR) < 0.05) but not with best overall RECIST response per patient on study. However, when grouped by organ, a number of feature cluster medoids were significantly associated (FDR < 0.05) with LLR (HN: 1, lung: 28, liver: 8, LN: 1) and OR (liver: 18). Feature clusters predictive of LLR and OR included descriptors of both tumor-specific and tumor/peritumoral gray-level intensity and texture (e.g. 74% tumor and 26% peritumoral features in clusters significantly associated with OR in liver). **Conclusions:** Tumor and peritumoral radiomic features at baseline correlate with LLR and OR to immunotherapy in R/M HNSCC. Despite significant heterogeneity in lesion site, both global and site-specific significant feature clusters could be identified. Research Sponsor: Merck.

6546 **Poster Session (Board #207), Fri, 8:00 AM-11:00 AM**

The impact of tumor hypoxia on the clinical efficacy of anti-PD-1 mAb treatment in recurrent/metastatic HNSCC patients (R/M).

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Background: Anti-PD-1 mAbs have changed the landscape of R/M HNSCC treatment, but physical, immunologic, and metabolic barriers present in the tumor microenvironment are likely drivers of low response rates. Hypoxia is a well-established feature of the tumor microenvironment and may act as a barrier to T cell infiltration and function. We evaluated the effect of hypoxia on the efficacy of anti-PD-1 mAb treatment in R/M HNSCC patients. **Methods:** We conducted a retrospective analysis of R/M patients treated with anti-PD-1 mAb that had consented to the UPMC Hillman tissue banking protocol (HCC 99-069). Pre-treatment archival FFPE samples were analyzed via immunofluorescent imaging for number of CD8+ T cells (CD8), Tregs, and the percent area (% CAIX) and mean intensity (Int) of carbonic anhydrase IX, a well-described marker of hypoxia. Tissue sections stained with PanCK, CAIX, CD8, Foxp3, and DAPI were imaged with an Olympus IX 83 microscope. ImageJ software and custom software plugins were used to determine %CAIX, Int, CD8, and Treg. PD-L1 by IHC was reported as a combined positive score (CPS) defining positive as CPS > 1. We compared non-responders (NR) i.e. PD to responders (R) i.e. PR or SD, and analyzed OS, PFS. All data were analyzed using GraphPad Prism software. Two-tailed unpaired t test was used when comparing 2 groups, 1-way ANOVA was used for multiple comparisons, and log-rank test was used for survival analysis. **Results:** The 36 patients included were 69% male, median age 59, 58% smokers. 61% were platinum failure. Primary site included 39% OC, 22% OPC (38% HPV positive), 17% Larynx, 17% other, 5% hypopharynx. Low % CAIX/Int, high CD8, and high CD8/Treg were all significantly associated with R. Patients with low % CAIX/Int (12 month OS Low: 75% vs. Mid: 17% vs. High:8%, $p = 0.02$) and high CD8/Treg had a significant increase in OS. Only high CD8 was associated with significantly higher PFS. Low %CAIX alone showed a non-significant trend towards increased R and no difference in PFS/OS. There was no difference in CD8, CD8/Treg, PD-L1 and Treg between %CAIX/Int groups. **Conclusions:** To our knowledge this is the first evaluation of tumor hypoxia as a predictive biomarker in anti-PD-1 mAb treated R/M HNSCC patients. Lower hypoxia by %CAIX/Int was associated with significantly increased response and OS. While further analysis in a larger dataset is needed to confirm, the lack of significant difference in CD8, Treg, PD-L1, and CD8/Treg between %CAIX/Int groups (Low, Mid, High) suggests that hypoxia may be an independent predictive marker. Research Sponsor: U.S. National Institutes of Health.

6548 **Poster Session (Board #209), Fri, 8:00 AM-11:00 AM**

Molecular biomarkers to identify patients (pts) who may benefit from durvalumab (D; anti-PD-L1) ± tremelimumab (T; anti-CTLA-4) in recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC) from HAWK and CONDOR studies.

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Background: Baseline tumor and germline biomarkers in R/M HNSCC were analyzed for predictive potential in pts benefitting from D or D+T. **Methods:** In HAWK (NCT02207530), 112 pts (PD-L1 tumor cells [TC]≥25%) received D (10 mg/kg Q2W for ≤12 m); in CONDOR (NCT02319044), 67 pts (PD-L1 TC < 25%) received D (10 mg/kg Q2W for ≤12 m), 133 pts received D+T (D 20 mg/kg Q4W, T 1 mg/kg Q4W for ≤12 m), and 67 pts received T (10 mg/kg Q4W [7 doses] then Q12W [2 doses] for ≤12 m) VENTANA PD-L1 (SP263) Assay determined PD-L1 status. Paired FFPE archival tumor and PBMC samples (as germline control) in the HAWK and CONDOR trials were evaluated by whole exome sequencing (WES). Tumor mutation burden (TMB) was number of somatic mutations/megabase. HLA class I types were obtained via WES of PBMCs (CONDOR only). HPV and neutrophil-to-lymphocyte ratio (NLR) were tested locally in CONDOR. Wilcoxon, log-rank tests, and COX-PH models were used. Pooled D & D+T data were analyzed unless noted. **Results:** 153 pts had paired evaluable FFPE tumor and PBMC samples (HAWK, n = 48; CONDOR, n = 105). TMB distributions were similar between studies (P= 0.43). TMB correlated with smoking (P= 0.02) but not HPV (P= 0.24), NLR (P= 0.66), or PD-L1 status (P= 0.43). Overall, high TMB (≥upper tertile) trended with longer OS vs low TMB in all evaluable pts (N = 153; 9.0 vs 5.6 m; HR = 0.70; 95% CI = 0.48-1.01); P= 0.06). In HAWK, there was no association of TMB with OS. In CONDOR, pts (D and D+T arms) with high TMB vs low had significantly longer OS (N = 76; 16.3 vs 5.3 m; HR = 0.53; 95% CI = 0.31-0.92). TMB and OS association was further assessed by increasing TMB cutoffs. Improved HRs trended with higher cutoffs; cutoffs ≥upper quartile significantly linked to OS.TMB was not associated with PFS or ORR. Pts with low PD-L1 and low TMB had worse OS compared to pts with high PD-L1 or high TMB. Pts with high NLR (≥median) and low TMB had significantly worse OS than pts with low NLR and high TMB (HR = 2.63, P< 0.001). Analysis of germline HLA alleles revealed significantly poorer survival for carriers of the HLA-B*15:01 allele (9.4%) (HLA-B variant status did not affect TMB and OS association in CONDOR). Germline HLA heterozygosity did not impact OS. Pts with mutations in *ATM* (5%), a DNA damage repair gene, also trended with prolonged OS. **Conclusions:** TMB is a possible predictive biomarker of IO HNSCC therapy. Combined analysis of NLR and TMB may provide additional PD-L1 data in assessing pts most likely to have long-term benefit. Clinical trial information: NCT002207530, NCT02319044. Research Sponsor: AstraZeneca.

6549 **Poster Session (Board #210), Fri, 8:00 AM-11:00 AM**

Overall survival modeling and association with serum biomarkers in durvalumab-treated patients with head and neck cancer.

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Background: Optimal patient selection for immunotherapy remains a challenge as most patients fail to respond. We aim to assess baseline factors for association with long-term survival from durvalumab treatment in patients with recurrent/metastatic head and neck squamous cell carcinoma (HNSCC)[1,2]. **Methods:** Pooled longitudinal tumor size, survival, and dropout data from four trials (1108: NCT01693562, CONDOR: NCT02319044, HAWK: NCT02207530, and EAGLE: NCT02369874) involving 467 HNSCC patients were used to develop tumor size-driven hazard models. A panel of 66 serum protein biomarkers at baseline and 4 relevant clinical markers from 346 out of 413 patients treated with durvalumab (all studies except 1108) were initially screened to select a pool of 21 candidate covariates. The criteria for dimensionality reduction comprised correlation strength between biomarkers and pharmacological hypotheses pertaining to a prior analysis[3] (inflammation, immunomodulation, tumor burden and angiogenesis). **Results:** The final tumor model highlighted that high tumor burden, elevated LDH and neutrophil-lymphocyte ratio were associated with faster tumor growth while patients with lower baseline tumor burden had an increase in net tumor shrinkage. For overall survival, the model suggested that high levels of immunomodulators (IL23, Osteocalcin), low inflammation (IL6, NLR), low tumor burden, and low angiogenesis factors (von Willebrand factor (vWF), plasminogen activator inhibitor-1 (PAI-1)) were associated with survival benefits for patients treated with durvalumab. Specifically, these patients had baseline serum IL23 $>$ 2.1 pg/mL and Osteocalcin $>$ 32 pg/mL or serum PAI-1 $<$ 229 pg/mL and serum IL6 $<$ 5.4 pg/mL which corresponded to a hazard ratio estimate (HR and 95%CI) of 0.36 (0.27- 0.47), logrank p-value: $2.3x10^{-14}$. The median (n, 95% CI) overall survival time for the patients with favorable biomarker profile was 14.6 months (n = 129, 11.2-21.4) vs. 4.4 months (n = 217, 3.6-5.3). **Conclusions:** Our results corroborate the prior hypothesis highlighting the prognostic value of inflammation, disease burden, tumor angiogenesis, and immunomodulatory factors on the clinical outcomes of HNSCC patients treated with durvalumab[3]. Collectively, we identified a serum biomarker profile of HNSCC patients with median survival times exceeding 1 year which may potentially be used for patient enrichment following further validation in prospective studies. References: [1]Yanan CPT 2017, [2]Baverel, 2018 ENA, [3]Guo, X, 2019 Asco P6048 Clinical trial information: NCT01693562, NCT02319044, NCT02207530, NCT02369874. Research Sponsor: AstraZeneca.

6551 **Poster Session (Board #212), Fri, 8:00 AM-11:00 AM**

CD3 and CD20 immune cell densities in primary tumors, lymph node metastasis, and recurrent disease samples of head and neck squamous cell carcinoma.

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Background: Immune cell (IC) infiltrates in primary tumors (PT) have been identified as prognostic markers in head and neck squamous cell carcinoma (HNSCC). IC densities may differ among PT, lymph node metastasis (LNM) and recurrent disease (RD) and by primary disease site (oral cavity- OC, oropharynx- OP, hypopharynx- HP, larynx- L). Here, we compare CD3 and CD20 IC densities in PT, LNM and RD in paired samples from different disease sites and determine the prognostic impact of IC infiltrates. **Methods:** Tissue microarrays with 425 PT, 198 LNM and 46 RD samples--each in triplicate--were stained immunohistochemically for CD3 and CD20 in the same slide. Immune cell densities per mm^2 were determined using a digital image analysis software (QuPath). Individual means were calculated from triplicates of each sample. IC infiltrates from different sample types (PT, LNM, RD) and primary tumor sites were compared using Kruskal-Wallis and Mann-Whitney-U tests. Paired samples were compared using Wilcoxon signed rank test. IC densities were classified as CD3 high/low and CD20 high/low for each primary tumor site using the individual median as a cut-off. Overall survival (OS) was calculated using the Kaplan-Meier method. P-values for each hypothesis were corrected using a false discovery rate of 5%. **Results:** CD3 and CD20 IC densities differed significantly by sample type (both $p<0.0001$) and primary site (CD3: $p=0.012$, CD20: $p=0.0017$). CD3 and CD20 densities were significantly lower in PT compared to LNM or in RD compared to PT and LNM. Paired samples ($n=172$) revealed a significantly higher CD3 and CD20 density (both $p<0.0005$) in LNM compared to PT, but no significant differences between PT and RD ($n=28$, $p>0.05$). CD3 densities were significantly higher than CD20 densities in all sample types. $CD3_{high}$ patients had the best prognosis in all sites except for OC ($q<0.05$) independent of CD20 status. In OC, CD3 density was not prognostic, but $CD3_{low}/CD20_{high}$ patients had the worst OS compared to $CD3_{low}/CD20_{low}$ and $CD3_{high}/CD20_{high}$ or even $CD3_{high}/CD20_{low}$ patients ($p=0.018$) who had the best prognosis. **Conclusions:** IC densities of CD3 and CD20 vary by sample type and primary site. Except for OC, in all sites the prognostic impact is determined by $CD3_{high}$, whereas in OSCC only the combination of CD3 and CD20 IC densities achieves a good prognostic value. Interestingly, $CD3_{low}/CD20_{high}$ patients have the worst overall survival in OC patients. Further work is needed to understand the interaction of B- and T cell infiltrates in the tumor, especially in OC. Research Sponsor: Clinician Scientist Program, Other Foundation.

6552 **Poster Session (Board #213), Fri, 8:00 AM-11:00 AM**

Correlation of tumor mutational burden (TMB) with CDKN2A and TP53 mutation in HPV-negative head and neck squamous cell carcinoma (HNSCC).

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Background: The tumor suppressors *TP53* and *CDKN2A* are commonly mutated or lost in HNSCC, impairing G1 checkpoints. This reduces ability to repair DNA damage arising from hypoxia, replication stress, and mutagen exposure, thus increasing TMB, a potential predictive biomarker for immunotherapy benefit. *TP53* mutations can be classified as loss-of-function (LOF) with or without dominant negative (DNE) activity, gain-of-function (GOF) and benign. We investigated whether specific categories of *TP53* mutation were associated with increased TMB, and whether these cooperated with *CDKN2A* mutation to elevate TMB. **Methods:** We analyzed 1010 HPV- HNSCC tumor samples (246 female) profiled with a 592-gene panel by Caris Life Sciences from 2015 to 2019. Predominant subsites were oral cavity (285), oropharynx (225) and larynx (153). TMB reflected all somatic nonsynonymous missense mutations detected. We report mean TMB per megabase (MB). Pathogenicity of *TP53* and *CDKN2A* mutations was determined according to American College of Medical Genetics (ACMG) guidelines. We also used four alternative methods of characterizing *TP53* mutations based on analysis of protein structure, public databases (IARC, ClinVar, InterVar), and publications (PMID: 25108461 and others) assessing structure-function relations. **Results:** 60% of cases had *TP53* mutations (*TP53*^{mut}) designated pathogenic by ACMG guidelines. Estimates of frequency of LOF/DNE mutations ranged from 30-42.8% of cases among the alternative classification methods. Damaging *CDKN2A* mutations were present in 20%. Average TMB per MB varied from 8.2/8.6 (females/males) in oral cavity cancers to 26.5/27.7 (females/males) in cancer of the lip. Mean TMB was typically higher in the presence of damaging LOF/DNE *TP53* mutations or *CDKN2A* mutations, but not *TP53* GOF mutations. Based on ACMG, for tumors with *TP53* and *CDKN2A* wild type (WT) TMB was 8.03, for those with *CDKN2A*^{mut}-only 9.82, for *TP53*^{mut}-only 10.56, and *TP53*^{mut}/*CDKN2A*^{mut} 17.6 ($p < 0.001$). For disruptive *TP53*^{mut} (Poeta algorithm), mean TMB for WT/WT was 8.67, for *TP53*^{mut} 11.31, *CDKN2A*^{mut} 17.9 and *TP53*^{mut}/*CDKN2A*^{mut} 15.83 ($p < 0.001$). **Conclusions:** Mutation of *TP53* and/or *CDKN2A* is associated with increased mean TMB relative to WT; mean TMB was highest for tumors bearing damaging mutations in both genes. GOF *TP53* mutation was not clearly associated with increased TMB. As TMB is evaluated as a predictive biomarker in the immunotherapy of HNSCC, specific *TP53/CDKN2A* mutational status should also be evaluated. Research Sponsor: Caris Life Sciences.

6553 **Poster Session (Board #214), Fri, 8:00 AM-11:00 AM**

Prognostic role of pre-treatment magnetic resonance imaging (MRI) radiomic analysis in patients with squamous cell carcinoma of the head and neck (SCCHN).

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Background: Emerging data suggest that radiomics can be used to predict outcomes in SCCHN. At present, only few data are available for pre-treatment MRI. **Methods:** Study population was retrieved from an ongoing multicenter, randomized, prospective trial (NCT02262221, HETeCo) evaluating health and economic outcomes of two different follow-up (FUP) strategies (intensive vs non-intensive) in effectively cured stage III-IV (VIII TNM ed.) SCCHN. We selected only patients with both pre- and post-contrast enhancement T1 and T2-weighted baseline MRI (b-MRI) and at least 2 years (2y) of FUP. A radiomic model was developed to identify high risk (HR) and low risk (LR) of disease recurrence. Radiomic features (RF) were extracted from the primary tumor in the b-MRI. The best RF combination was selected by Least Absolute Shrinkage and Selection Operator (LASSO). Ten-fold cross-validation was used to compute sensitivity, specificity and area under the curve (AUC) of the classifier. Kaplan-Meier (KM) curves were estimated for HR and LR, for both overall survival (OS) and disease-free survival (DFS) and log rank test was performed. Three years (3y)-DFS and OS were also estimated for the two groups. The radiomic risk class was used as a new variable in a multivariate Cox model including well established prognostic factors in SCCHN (TNM stage, subsite and HPV). **Results:** Out of 155 enrolled HETeCO patients, 98 baseline imaging were retrieved of which 57 b-MRI. Of these, 51 met the eligibility criteria (25 in intensive and 26 in non-intensive arm). Baseline patients' characteristics were: median age 66 yr (38-86); sex (M 42; F 9); median smoking history: 30 packs/y (1-100); 25 oral cavity (49%), 18 oropharynx (35%, 14 HPV+), 6 larynx (12%), 2 hypopharynx (4%). At a median FUP of 42 months (25-64), 45 (88%) patients are still alive. The recurrence rate was 20% (10/51, of which 2 distant). In total, 1608 RF were extracted. The sensitivity, specificity and AUC of the classifier were 90%, 76%, and 80%, respectively. The radiomic risk class was found to be an independent prognostic factor for both DFS and OS (p=0.01 and p=0.046, respectively). KM curves for DFS and OS were significantly different between HR and LR groups (p=0.002 and p=0.04, respectively). In HR vs LR, 3-y DFS and OS were: 78% [61-100%] vs 97% [90-100%], and 88% [75-100%] vs 96% [88-100%], respectively. **Conclusions:** Radiomics of pre-treatment MRI can predict outcomes in SCCHN. External validation of this preliminary radiomics-based model is currently ongoing. Research Sponsor: BRI (Bando Ricerca Istituzionale) 2018. This project has received funding (Fondi 5x1000 Ministero della Salute 2015) from Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy under grant agreement N. D/17/1SA (statement n. 511 on December, 21th, 2.

6554 **Poster Session (Board #215), Fri, 8:00 AM-11:00 AM**

HPV ctDNA analysis in unresectable recurrent/metastatic oropharyngeal cancer.

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Background: There is an increasing incidence of human papillomavirus associated (HPV+) oropharyngeal cancer (OPC). While HPV + portents improved prognosis, survival for patients with unresectable recurrent/metastatic (R/M) OPC remains poor. Extant data suggest that HPV ctDNA levels correlate with disease burden and treatment outcomes in patients with HPV + OPC in the primary setting but scant data exists in the metastatic setting. Objective: To develop a highly precise droplet digital (ddPCR) assay for quantification of plasma HPV ctDNA and to evaluate whether HPV ctDNA predicts treatment response in patients with HPV+ R/M OPC. **Methods:** Patients with HPV + R/M OPC starting systemic therapy were enrolled in a biorepository in which blood was collected prior to each cycle of therapy. PCR probes were created for the most common high-risk HPV subtypes, 16 and 18. HPV ctDNA was extracted from plasma and quantified with ddPCR. Percent change in HPV ctDNA was calculated after 1 and 2 cycles of treatment. Treatment response was assessed per standard of care or study protocol after 2-3 cycles of treatment. ROC curve analyses were performed. **Results:** A precise ddPCR assay was developed to identify plasma HPV ctDNA in 10 patients who underwent 16 distinct treatment courses. On ROC curve analysis, percent change in HPV ctDNA after 2 cycles of treatment was predictive of radiographic response (AUC 0.82, p = 0.03). The optimal cutoff point to optimize sensitive and specificity was identified as 30% change in HPV ctDNA (Table). Changes in HPV ctDNA after 1 cycle of treatment were also predictive of radiographic response (AUC 0.82, p = 0.05). **Conclusions:** Changes in HPV ctDNA may be predictive of treatment response in patients with R/M HPV + OPC. Furthermore, HPV ctDNA predicts response earlier than conventional imaging. While validation is needed, this assay shows promise in identifying poor responders who can be directed early towards clinical trials or alternative therapies. Research Sponsor: Internally funded by University of Michigan.

	Stable Disease or Partial Response	Disease Progression	
< 30% increase in HPV ctDNA	6	1	PPV 85.7% (95% CI 48-98%)
≥30% increase in HPV ctDNA	1	8	NPV 88.9% (95% CI 56-98%)
	Sensitivity 85.7% (95% CI 42-100%)	Specificity 88.9% (95% CI 52-100%)	

6556 **Poster Session (Board #217), Fri, 8:00 AM-11:00 AM**

Molecular correlates of response to preoperative olaparib alone or with cisplatin or with durvalumab in head and neck squamous cell carcinoma (HNSCC): A Hellenic Cooperative Oncology Group study.

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Background: Poly(ADP-ribose) polymerase (PARP) inhibitors drive increased DNA damage and tumor cell death, particularly in tumors with existing defects in DNA repair. Furthermore,they promote immune priming, through a range of molecular mechanisms. Foremost, among candidate intracellular pathways is STING (stimulator of interferon genes), an innate immune response activated by cytosolic DNA (perhaps a consequence of DNA damage) that can lead to enhanced interferon (IFN) production. PARP inhibitor-induced DNA damage also leads to adaptive upregulation of programmed death ligand 1 (PD-L1) expression. To this end, there is increasing rationale for testing PARP inhibitors alone or in combination with chemotherapy or PD1 checkpoint inhibitors in HNSCC. **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) orD 1500 mg on d1 followed by O 600 mg daily for 21-28 days (Arm D). Response was defined as tumor reduction noted on exam, imaging or pathology. Pretreatment biopsies were subjected to 310 gene OncoDNA NGS panel. Double Stranded Brakes/Repair (DSB/R) was measured by evaluating phosphorylation of histone H2AX by immunochistochemistry (IHC). In addition, IHC for PD-L1 (CPS) and STING was performed in paired pre- and post-treatment biopsies. **Results:** 17/36 pts in (O) treatment arms (6/11 evaluable pts Arm A, 9/11 evaluable pts Arm B, 2/11evaluable\ pts arm D) developed a response. One patient in D+O arm developed path CR. Low γH2AX staining at pretreatment biopsies was associated with progression (p=0.029). Higher PD-L1 expression (CPS≥1) was associated with disease progression (p=0.014). CPS PD-L1 was upregulated following (O) treatment. STING expression was not significantly upregulated post treatment in (O) treatment arms. Alterations in genes that have been previously reported to be associated with (O) sensitivity, namely DNA damage Response/Repair (DDR) genes and genes involved in chromatin remodeling (*CHK2, KMT2D, KMT2C, ARID2 and AJUBA*), were identified in responders. **Conclusions:** This window study demonstrated promising signs of activity of (O) in HNSCC, particularly in tumors with high expression of γH2AX and alterations in DDR or chromatin remodeling genes. Clinical trial information: NCT02882308. Research Sponsor: Preoperative Administration of Olaparib With Cisplatin or With Durvalumab or Alone or no Tratment in Patients Who Are Candidates for Surgery of Carcinoma of the Head and Neck. (OPHELIA).

6557 **Poster Session (Board #218), Fri, 8:00 AM-11:00 AM**

Exome scale liquid biopsy characterization of putative neoantigens and genomic biomarkers pre- and post anti-PD-1 therapy in squamous cell carcinoma of the head and neck.

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Background: The reduced scope, and number of genes profiled by typical liquid biopsy panels can result in missed biomarkers including neoantigens, which may change with treatment, as well as potentially undetected resistance mechanisms and pathways beyond the scope of targets typically captured by panels. To address these limitations, we used a whole-exome scale liquid biopsy monitoring platform, NeXT Liquid Biopsy, to analyze head and neck squamous cell carcinoma (HNSCC) patients that have received anti-PD1 therapy. Presently, we sought to (1) monitor neoantigen changes in cfDNA as a complement to tumor biopsy-derived neoantigens, (2) compare the impact of tumor escape mechanisms, including HLA-LOH, on neoantigens identified in tissue and cfDNA and (3) to identify novel biological signatures that combine information from both solid tumor and liquid biopsies. **Methods:** Pre- and post-intervention matched normal, tumor and plasma samples were collected from a cohort of 12 patients with HNSCC. Following baseline sample collection all patients received a single dose of nivolumab, followed by resection approximately one month later when feasible, or a second biopsy where resection was impractical. Solid tumor and matched normal samples were profiled using ImmunoID NeXT, an augmented exome/transcriptome platform and analysis pipeline. Exome-scale somatic variants were identified in cfDNA from plasma samples using the NeXT Liquid Biopsy platform. Data from these two platforms were compared with corresponding clinical findings. **Results:** Concordant somatic events were detected between plasma and tumor at pre- and post-treatment timepoints. Neoantigens predicted to arise from these somatic events were reduced in solid tumor post-treatment, but increased in cfDNA, when compared to pre-treatment timepoints. HLA LOH was identified in a number of subjects, likely resulting in reduced neoepitope presentation in those cases. Immune cell infiltration increased in the tumor following treatment, with no changes to the $CD8^{+}$/Treg cell ratio, suggesting consistent immunoregulation. **Conclusions:** Exome-wide neoantigen burden was reliably predicted from cfDNA, providing additional insight complementing data from solid tumor. Analyzing HLA LOH, and neoantigen burden from both solid and liquid biopsies together over the course of treatment creates a more comprehensive profile of therapeutic response and resistance mechanisms in HNSCC patients missed with typical liquid biopsy panels. Research Sponsor: Personalis, Inc.

6558 **Poster Session (Board #219), Fri, 8:00 AM-11:00 AM**

Association of radiation treatment failure in head and neck cancer with differential immune infiltrate.

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Background: Previously we have shown that PD-L1 expression is associated with treatment failure in Head and Neck Cancer (HNSCC) treated with radiation. We have further evaluated the effect of pre-treatment immune infiltrate on treatment failure following radiation. **Methods:** A total of 75 patients with HPV negative HNSCC treated with surgery and post-operative radiation were included in this study. Pre-treatment tumors were examined via RNA-Sequencing utilizing an Illumina platform. These data were then subjected to immune profiling utilizing publicly available software (xCell) to infer relative enrichment of immune cell infiltrate per sample. Each immune cell type detected at any level in at least 15 tumors was then evaluated for effect on loco-regional recurrence using Cox-regression analysis. Clinical variables included in this analysis include tumor stage, nodal stage and treatment site. Survival analysis was performed utilizing the method of Kaplan Meier, with log rank statistics used to test for significant comparisons. **Results:** The majority of HNSCCs analyzed in this study were from the oral cavity (65.3%), followed by the larynx and hypopharynx (28%) and oropharynx (6.7%). The total median dose of radiation delivered was 60 Gy (range: 36-79.2) and median follow up in living patients was 80.5 months (range: 7-190). On univariate analysis, no measured clinical variable was significantly associated with loco-regional recurrence (LRR). Similar to our previous studies in other HNSCC cohorts treated with radiation, PD-L1 expression was negatively associated with LRR ($p = 0.005$). Additionally, multiple immune cell infiltrates were negatively associated with LRR including: Th2 helper cells ($p = 0.007$), CD8+ central memory T cells ($p = 0.02$), immature dendritic cells ($p = 0.037$), CD4+ memory T cells ($p = 0.043$). In a multivariate model including these immune cell subsets, Th2 helper cells, CD8+ central memory T cells and immature dendritic cells remained significantly negatively associated with LRR following radiation. **Conclusions:** This analysis demonstrates the importance of pre-treatment immune infiltrate on outcomes in HNSCC and points to potential avenues to explore to augment response to radiation. Research Sponsor: NIH.

6559 **Poster Session (Board #220), Fri, 8:00 AM-11:00 AM**

Computerized features of spatial interplay of tumor-infiltrating lymphocytes predict disease recurrence in p16+ oropharyngeal squamous cell carcinoma: A multisite validation study.

Germán Corredor, Cheng Lu, Can Koyuncu, Kaustav Bera, Paula Toro, Pingfu Fu, Shlomo A. Koyfman, Deborah Chute, David J. Adelstein, Wade Thorstad, Justin A. Bishop, Farhoud Faraji, James Lewis Jr., Anant Madabhushi; Case Western Reserve University, Cleveland, OH; Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH; Cleveland Clinic, Cleveland, OH; Wash U in St. Louis, St. Louis, MO; UT Southwestern Medical Center, Dallas, TX; University of California, San Diego, San Diego, CA; Vanderbilt University Medical Center, Nashville, TN; Case Western Reserve University, Louis Stokes Cleveland Veterans Administration Medical Center, Cleveland, OH

Background: While overall, patients with p16+ oropharyngeal squamous cell carcinoma (OPSCC) have a favorable prognosis, subsets of patients experience disease recurrence (DR) and death despite aggressive multimodality treatment. Aside from routine staging criteria, there are no biomarkers of tumor behavior routinely employed in OPSCC to identify patients at higher risk of DR. In this study we sought to evaluate whether the interplay between tumor-infiltrating lymphocytes (TILs) & cancer cells, in both stromal and epithelial compartments from digitized H&E-stained slides, can predict DR in OPSCC patients. **Methods:** OPSCC resected specimens from 354 patients (66 with DR) were retrospectively collected from 3 different sites. 107 (16 DR) patients from site 1 formed the training set and 247 (50 DR) patients from sites 2 & 3 formed the independent validation cohort. Computerized algorithms automatically identified 4 types of nuclei (TILs & non-TILs in both stromal & epithelial regions), defined clusters for each nuclei type based on cell proximity, and used network graph concepts to capture measurements relating to the arrangement of these clusters. The top 10 features determined by a statistical selection method (LASSO) were used to train a Cox regression model that assigns a risk of DR to each patient on the training set. The median risk score was used as threshold for stratifying patients on the validation set into low and high-risk of DR. Survival analysis was used to evaluate the stratification given by the trained model. **Results:** Patients identified by the TIL interplay model as high risk for DR had statistically worse disease specific survival. Univariate analysis yielded an HR=2.49 (95% CI: 1.22-5.07, p=0.04) for site 2 and HR=3.62 (95% CI: 1.39-9.43, p=0.03) for site 3. Multivariate analysis controlling the effect of different clinical variables is shown in the attached table. **Conclusions:** We introduce a prognostic model based on the automated quantification of the interplay between tumor microenvironment cells that is able to help distinguish OPSCC patients with higher DR risk from those who will experience longer disease-free survival. Research Sponsor: U.S. National Institutes of Health.

	p-val site 2	HR site 2	p-val site 3	HR site 3
O-stage (8th ed) 1,2 vs. 3,4	0.88	1.07 (0.45-2.52)	0.11	2.78 (0.80-9.60)
T-stage (8th ed) 1,2 vs. 3,4	0.11	1.93 (0.86-4.37)	0.96	1.03 (0.31-3.49)
N-stage (8th ed) 0,1 vs. 2,3	0.01	2.75 (1.31-5.74)	0.90	1.07 (0.34-3.34)
TIL interp. Low vs. High	0.02	2.81 (1.15-6.87)	0.05	3.45 (0.99-12.07)

6560 **Poster Session (Board #221), Fri, 8:00 AM-11:00 AM**

Prognostic value of radiological extranodal extension detected by computed tomography for predicting outcomes in head and neck squamous cell cancer patients treated with radical chemoradiotherapy.

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Background: As per the AJCC 8th edition ENE/ECS is the most important predictor for N staging of HNSCC and is one of the key predictor of outcomes. Because ENE/ECS is based on pathological findings after surgery and it is difficult to predict outcomes for locally advanced squamous head and neck cancer (LASHNC) treated radically with CCRT. We hypothesized that ENE assessed by CT imaging (rENE) may directly correlate with outcomes in LASHNC treated radically with CCRT. **Methods:** This open-label, investigator-initiated, phase 3, randomized trial was conducted from 2012 to 2018. Adult patients with LASHNC who were fit for radical chemoradiation were randomized 1:1 to receive either radical radiotherapy (66-70 grays) with concurrent weekly cisplatin (30 mg/m^2) (CRT) or the same schedule of CRT with weekly nimotuzumab (200 mg) (NCRT). 536 patients were accrued,182 were excluded due to non-availability DICOM CT scan, 354 patients were analysed for rENE (based on 6 criterion for metastasis and 3 for rENE). Near equal distribution of patients was achieved in CRT arm (170 patients) and NCRT arm (184 patients). There were 181 (51.1%) oropharynx and 173(48.9%) larynx and hypopharynx patients. We evaluated association of radiological ENE and clinical outcomes.The endpoints were disease-free survival (DFS), duration of locoregional control (LRC), and overall survival (OS). **Results:** There were 244(68.9%) patients with radiologically metastatic nodes, out of which 140(57.3%) had rENE. There was no significant association between rENE and CRT (p value 0.3) or NCRT (p value 0.412). The median follow-up was 33.0 months (95%CI 30.7-35.2 months). Complete response was achieved in 204 (57.6%) cases, PR/SD in 126(35.6%) cases and PD in 24(6.8%) cases. rENE positive patients had poor overall 3-year survival (46.7%), poor DFS (48.8%) and LRC (39.9%) than rENE negative cases (63.6%, 87%, 60.4%). rENE positive cases had 1.71 times increase chances of incomplete response than rENE negative cases. Overall stage, clinical positive node, response, rENE and site were the only significant factors for predicting OS, DFS and LRC. **Conclusions:** In conclusion, pre-treatment rENE can be regarded as an independent prognostic factor for survival (OS, DFS, LRC) in patients with LASHNC treated radically with CCRT. Pre-treatment rENE is not only associated with CCRT response but is also associated with poor prognosis and hence rENE, as an imaging biomarker, can stratify responder's vs non-responders. Clinical trial information: CTRI/2014/09/004980. Research Sponsor: This study was funded by Biocon Ltd, Science and Engineering Research Board grant EMR/2015/001591, and by the Tata Memorial Center Research Administration Council.

6561 **Poster Session (Board #222), Fri, 8:00 AM-11:00 AM**

Immune functional portraits of head and neck cancer using next generation sequencing.

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Background: The addition of biomarkers as companion diagnostics and Next Generation Sequencing (NGS) have dramatically increased therapeutic efficacy and have aided precision medicine development. The unique genomic profile and tumor microenvironment (TME) composition of each patient can be ascertained through NGS. Using TCGA and Geo datasets, we characterized head and neck cancers (HNC) according to the cellular and functional state of their TME and conducted a pilot validation study using prospectively collected HNC tumors. **Methods:** To stratify the TME of HNC tumors into molecular functional portraits, we analyzed the sequencing data of 1,486 HNC tumor samples and 143 controls (normal, oral leukoplakia) from TCGA and GEO data sets. For the prospective pilot study, resected tissue from oropharyngeal carcinomas independent of HPV status were processed for whole exome (WES) and RNA-seq (n = 6; HPV-positive = 1). **Results:** To characterize the cellular composition and functional state of HNC tumors and their TMEs, we created 26 separate molecular signatures related to functional processes such as immune checkpoint inhibition, immune infiltration, immunosuppression, and stromal activities represented by angiogenesis and mesenchymal stromal cells. Unsupervised clustering of these signatures delineated tumors into 4 types: immune infiltration with increased stromal signatures (type A), immune infiltration with decreased stromal signatures (type B), no immune infiltration with increased stromal signature (type C), and no immune infiltration and decreased stromal signatures (type D). Most HPV-positive tumors were type B (p = 1e-27) and associated with increased survival compared to the HPV-negative tumors (types C and D; p = 3e-05). Type B HPV-positive tumors had reduced *FAT1* and *TP53* mutations, whereas type B HPV-negative tumors had increased *caspase 8* mutations/loss. In the validation cohort, actionable mutations were found in *PI3KCA* and *TSC2* in types A and B HPV-negative tumors. Moreover, while the HPV-positive tumor was classified as type C, we identified a *caspase 8* homozygous deletion and absence of *FAT1* and *TP53* mutations, supporting the TCGA and GEO analysis. **Conclusions:** Exome and transcriptome analyses with cellular deconvolution from bulk RNA-seq enrich tumor characterization by including major TME components, providing a comprehensive biomarker profile for precision therapy and clinical decision making. Our prospective analysis identified TME parameters comparable with the large datasets and revealed targetable genomic alterations. Research Sponsor: None.

6562 **Poster Session (Board #223), Fri, 8:00 AM-11:00 AM**

Detection of somatic mutations in saliva of patients with oral cavity squamous cell carcinoma.

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Background: Oral cavity squamous cell carcinoma (OCSCC) frequently presents as clinically advanced disease with poor prognosis. When diagnosed at early stages, survival rates approach 80%, underscoring the need for validated, cost-effective detection methods. OCSCC is driven by the serial acquisition of genetic alterations. Tumor-defining somatic mutations are attractive biomarkers and hence their presence in saliva may be associated with malignancy as shown in a few proof-of-concept studies, including our previous work. Based on this premise, we present a low-cost, accurate, next generation sequencing (NGS) test with high clinical utility aimed at detecting mutations in the saliva for early diagnosis and potential screening of OCSCC. **Methods:** We have designed a custom NGS panel that covers exons of 7 most frequently mutated genes in OSCC. This minimal gene set derived from the analysis from 3 public datasets, predicted incidence of at least one somatic aberration in 89% of patients. We recruited 91 treatment-naïve OCSCC patients and profiled DNA from tissue and matched pre-operative saliva using this test. We also tested DNA from 12 subjects with premalignant lesions with high-grade oral dysplasia and matched saliva. **Results:** Using stringent variant calling criteria, at least one somatic variant was detected in 88 (96%) of the 91 primary tumors. 90.9% of the matched saliva were concordant, with only a minor decrease in early stage disease. Tumor-specific mutations ($\geq$5% AF) in driver genes were detected in 10 (83.3%) dysplastic lesions, suggesting that driving clonal events may occur early in disease development. Interestingly, in 3 matched saliva of the dysplastic samples, the same mutations were detected. To ensure a variant is not a false positive call, we performed a vigorous multistep analytical validation of this saliva-based test: (i) independent re-sequencing of 24 saliva confirmed 94% reproducibility; (ii) no functionally relevant variants were detected in saliva from 12 of 13 healthy subjects without history of tobacco and alcohol usage; (iii) reproducibility, sensitivity, and specificity were confirmed using a positive control with 7 loci at 0.25% AF across 8 independent saliva sequencing runs and a certified negative control and was found to be on par with droplet digital PCR. **Conclusions:** These data highlight the feasibility of saliva-based testing for early diagnosis of OCSCC and premalignant lesions. Research Sponsor: Tata Centre for Development (TCD) at University of Chicago, Philanthropic - Jill and Ozzie Giglio.

6563 **Poster Session (Board #224), Fri, 8:00 AM-11:00 AM**

18 FDG PET/CT prediction of treatment outcomes in patients with p16-positive, non-smoking associated, locoregionally advanced oropharyngeal cancer (LA-OPC) receiving deintensified therapy: Results from NRG-HN002.

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Background: To determine the negative predictive value (NPV) of 12-14 week post-treatment PET/CT for 2-year progression-free survival (PFS) and 2-year locoregional control (LRC) in NRG-HN002, which is a two-arm phase II trial for patients with low-risk, non-smoking associated p16-positive LA-OPC randomized in a 1:1 ratio to reduced-dose IMRT with or without cisplatin. **Methods:** PET/CT scans were reviewed both centrally and locally by participating institutions. Tumor response evaluations for primary site, right neck, and left neck were carried out using a 5-point ordinal scale ('Hopkins Criteria'). Overall scores were then assigned as 'Negative,' Positive,' or 'Indeterminate.' Patients who had a 'Negative' score for all three evaluation sites were given an overall score of 'Negative.' The endpoints were NPV for LRC and PFS at 2 years testing NPV $\leq$ 90% vs $>$ 90% (1-sided alpha 0.10 and 76% power). **Results:** There were 316 patients enrolled, of whom 306 were randomized and eligible. Of these, 131 (42.8%) patients consented to a post-therapy PET/CT, and 117 (89.3%) patients were eligible for PET/CT analysis. The median time from end of treatment to PET/CT scan was 94 days (range 52-139). The rates of 2-yr PFS and LRC in the analysis subgroup were 91.3% and 93.8%, respectively. Based on central review, post-treatment scans were negative for residual tumor for 115 patients (98.3%) and positive for 2 patients (1.7%). The NPV for 2-year LRC was 94.5% (90% lower confidence bound [LCB] 90.6%; p = 0.07). NPV for 2-year PFS was 92.0% (90% LCB 87.7%; p = 0.30). Similar NPV results were obtained based on analysis of local reviews. **Conclusion:** Within the context of deintensification with reduced-dose radiation, the NPV of a 12-14 week post-therapy PET/CT for 2-year LRC is statistically $>$ 90%, similar to that reported for patients receiving standard chemoradiation. However, in this study, there was not enough evidence to conclude that the NPV of a 12-14 week post-therapy PET/CT for 2-year PFS is $>$ 90%. Grant acknowledgement: This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U24CA180803 (IROC), UG1CA189867 (NRG Oncology NCORP) from the National Cancer Institute (NCI). This project is funded, in part, under a Grant with the Pennsylvania Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations or conclusions. Clinical trial information: NCT02254278. Research Sponsor: U.S. National Institutes of Health.

6564 **Poster Session (Board #225), Fri, 8:00 AM-11:00 AM**

Computational discovery of non-mutational tumor-restricted antigens reveals evidence of immunoediting in head and neck squamous cell carcinoma.

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Background: We previously identified 107 expression-based tumor antigens (EbTAgs) defined as genes with negligible expression in healthy tissue and overexpression in cancer. EbTAgs present novel targets for the adaptive anti-tumor immune response and exhibit evidence of immunoediting in highly immune infiltrated oral cavity tumors. To detail the landscape of EbTAgs in head and neck squamous cell carcinoma (HNSC) and further elucidate EbTAg immunoediting, we compared the expression EbTAgs in the context of tumor immune infiltration among four HNSCC subtypes: oral cavity (OC), HPV+ oropharyngeal (HPV+OP), HPV- oropharyngeal (HPV-OP), and laryngeal/hypopharyngeal (LH). **Methods:** Upper quartile FPKM gene expression values of all protein coding genes were calculated for all HNSC samples using RNAseq data from The Cancer Genome Atlas (TCGA). TCGA HNSC tumors were divided into subtypes and analyzed for EbTAg expression. Individual tumor sample immune infiltrate was determined using unsupervised clustering of 14 immune cell signature ssGSEA scores for the HNSC dataset as a whole and for each subtype. **Results:** LH tumors expressed significantly more EbTAgs than other subtypes ($p=0.0014$), specifically HPV+OP ($p=0.0008$, Tukey's test). Immune clustering analysis showed that LH tumors were significantly more likely to be in the low than the high immune cluster whereas the reverse was true for HPV+OP tumors ($p<0.0001$). Hypothesizing that EbTAg expression was a function of tumor immune infiltration rather than HNSC subtype, we compared EbTAg expression between tumors in low and high immune clusters of the entire HNSC dataset as well as of each HNSC subtype. Significantly more EbTAgs were expressed in low immune tumors compared to high immune tumors of the HNSC dataset ($p<0.0001$). Similarly, significantly more EbTAgs were expressed in low immune tumors compared to high immune tumors of the OC, OP-all tumors, and HPV+OP datasets ($p=0.0003$, $p<0.0001$, $p=0.0006$) with a trend of more EbTAgs in the immune low versus high tumors in the HPV-OP and LH datasets ($p=0.12$, $p=0.095$). **Conclusions:** EbTAg expression in TCGA HNSC samples correlates with tumor immune infiltration resulting in lower expression under greater immunological pressure. These results reinforce the hypothesis that EbTAgs undergo immunoediting and are immunologically relevant. Exploration of EbTAgs as antigenic targets of modular vaccines or adoptive T-cell therapy as well as biomarkers of immune checkpoint inhibition therapy response is warranted. Research Sponsor: U.S. National Institutes of Health.

6565 **Poster Session (Board #226), Fri, 8:00 AM-11:00 AM**

Does sinonasal cancer survival differ based on human papillomavirus status?

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Background: The sinonasal tract is a lesser known "hot spot" for the human papillomavirus (HPV), compared with the oropharynx. Additionally, unlike the oropharynx, the role of HPV tumor status in the survival and overall prognosis of the sinonasal tract and other non-oropharyngeal head and neck cancer sites remains inconclusive. Understanding differences in survival based on HPV status could be useful clinically, as it has been for HPV-positive oropharyngeal disease. This study examined whether there are survival differences in sinonasal cancer based on HPV status. **Methods:** This study included adult sinonasal cancer cases diagnosed between 2010 and 2015 in the National Cancer Database. A multivariable Cox proportional hazards model estimated the association between sinonasal cancer HPV status (HPV-positive, HPV-negative) and all-cause mortality while controlling for covariates (sex, age, race/ethnicity, insurance status, urban/rural, county-level household income, county-level percentage without high school diploma, comorbidity score, stage, histology, facility type, and treatment). A second multivariable proportional hazards model stratified HPV-positive tumor status by high-risk HPV (16, 18, 26, 31, 33, 35, 36, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, and 85) vs. low-risk HPV (6, 11, 32, 34, 40, 42, 44, 54, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87, and 89) and compared their all-cause mortality to HPV-negative patients. **Results:** There were 1,750 sinonasal cancer patients included in this study, and 484 (27.7%) had HPV-positive disease. Among patients with HPV-positive disease, 75.6% had high-risk types. Mortality risk among all HPV-positive patients combined was 23% lower than HPV-negative patients (aHR = 0.77; 95% CI 0.64, 0.93). After stratifying by high-risk vs. low-risk HPV, high-risk HPV positive patients had 30% lower mortality risk than HPV-negative patients (aHR = 0.70; 95% CI 0.57, 0.88) while risk of mortality did not significantly differ between low-risk HPV-positive patients and HPV-negative sinonasal cancer patients. **Conclusions:** Sinonasal cancer shows differential survival based on HPV status, and sinonasal cancer patients positive for high-risk HPV had a significantly greater survival advantage than low-risk strains and those with HPV negative disease. HPV status might yet play a role in prognostication of sinonasal cancer, if future studies confirm these findings. Research Sponsor: None.

6566 **Poster Session (Board #227), Fri, 8:00 AM-11:00 AM**

Combination of tumor multinucleation and spatial arrangement of tumor-infiltrating lymphocytes to predict overall survival in oropharyngeal squamous cell carcinoma: A multisite study.

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Background: Oropharyngeal squamous cell carcinoma patients can have major morbidity from current treatment regimens, necessitating accurate identification of patients with aggressive versus indolent tumors. In this study, we sought to evaluate whether the combination of computer extracted features of tumor cell multinucleation (MN) and spatial interplay of tumor-infiltrating lymphocytes (TILs) is prognostic of overall survival (OS) in OPSCC patients. **Methods:** OPSCC specimens from 688 patients were retrospectively collected from 3 different sites. 141 patients from site 1 formed the training set (D1) and 322 patients from site 2 and 225 patients from site 3 formed the independent validation cohort (D2, n = 547). A machine learning (ML) model was employed to automatically calculate a Multinucleation risk index (MNI), which is the ratio of the number of MN to the number of epithelial cells, to each patient. A separate ML model was also used to capture measurements related to the interplay between TILs and tumor cells (SpaTIL), which were then used to compute a risk score using a Cox regression model. The median value of both the MNIs and the SpaTIL risk scores in D2 were used to identify patients as either low- or high-risk. A definitive label was assigned to each patient by combining the class labels obtained from the MNI and SpaTIL models using a logical AND operation. **Results:** In D2, the patients with high-risk scores had statistically significantly worse survival in univariate analysis. The univariate analysis yielded an HR = 1.91 (95% CI: 1.25-2.93, p = 0.0027) for D. Multivariate analysis controlling the effect of different clinical variables is shown in the table. **Conclusions:** We presented a computational pathology approach to prognosticate disease outcome in OPSCC by combining features relating to density of multinucleation and spatial arrangement of TILs and validated the approach on a large multi-site dataset. With additional validation the approach could potentially help identify OPSCC patients who could benefit from de-escalation of therapy. Research Sponsor: U.S. National Institutes of Health.

	p-val	HR
Age (< 56)	0.18	1.32 (0.88 - 1.97)
O-stage (8th ed) 1 2 vs 3 4	0.28	1.32 (0.80 - 2.20)
T-stage (8th ed) 1 2 vs 3 4	0.024	1.69 (1.07 - 2.67)
N-stage (8th ed) 0 1 vs 2 3	0.995	1.00 (0.65 - 1.54)
MNI + SpaTIL Low vs High	0.018	1.62 (1.09 - 2.4)

6567 **Poster Session (Board #228), Fri, 8:00 AM-11:00 AM**

Machine learning guided adjuvant treatment of head and neck cancer.

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Background: A combined analysis of the EORTC 22931 and RTOG 95-01 trials confirmed that patients (pts) with head and neck squamous cell carcinoma (HNSCC) and positive margins or extracapsular extension (ECE) benefit from adjuvant chemoradiotherapy (CRT), but the best treatment of pts with other risk factors is unclear. We hypothesized that deep learning models could identify the margin/ECE negative pts who benefit from CRT. **Methods:** We abstracted pts from the NCDB diagnosed from 2004-2016 with resected HNSCC who received radiotherapy (RT). We reserved 20% of pts for validation and used the remaining 80% for feature selection and model training. Features were chosen based on independent significance in a Cox proportional hazards model, and included demographics, tumor stage, site, grade, RT dose, and receipt of chemotherapy. HPV status was included, and imputed when unknown. We generated survival predictions with DeepSurv (DS), random survival forest (RSF), and neural network multitask (NNM) models. We consider CRT to be recommended by a model if predicted survival is longer with CRT than RT. We calculated the median overall survival (mOS) difference and hazard ratio (HR) for receipt of treatment in line with model recommendations. This was repeated with inverse probability of treatment weighting (IPTW) to account for confounding. As a comparator, we used the intermediate risk factors in the EORTC (T3-4 except T3N0 larynx, N2-3, LVI, deep nodes with oral / oropharynx cancer) and RTOG (2 involved nodes) trials as decision rules. **Results:** 36,831 pts from the NCDB met the inclusion criteria. 92% had T3-4 or node positive disease, and 40% received CRT. RTOG, EORTC, DS, NNM, and RSF models recommend CRT for 32%, 74%, 63%, 61%, and 35% of pts. The concordance index in the validation set was 0.696, 0.692, and 0.699 for DS, NNM, and RSF. Treatment according to model recommendations in the validation cohort was associated with a mOS benefit of 18.4 months (7.6 to 29.3, 95% CI) for DS, 20.5 months (8.8 to 32.2, 95% CI) for NNM, and 5.8 months (-6.6 to 18.3, 95% CI) for RSF. Similar results were seen with IPTW. **Conclusions:** Machine learning models can predict benefit from CRT in margin/ECE negative pts, and outperform treatment according to EORTC or RTOG inclusion criteria in this cohort. External validation of these models is warranted. Research Sponsor: None.

	HR (95% CI)	p-value	HR, IPTW (95% CI)	p-value
RTOG	0.94 (0.87 – 1.01)	0.10	0.84 (0.70 – 1.00)	0.06
EORTC	0.91 (0.84 – 0.98)	0.01	0.88 (0.74 – 1.04)	0.13
DS	0.85 (0.79 – 0.92)	< 0.01	0.81 (0.68 – 0.95)	0.01
NNM	0.83 (0.77 – 0.90)	< 0.01	0.79 (0.67 – 0.93)	< 0.01
RSF	0.89 (0.83 – 0.97)	< 0.01	0.81 (0.68 – 0.97)	0.02

6568 **Poster Session (Board #229), Fri, 8:00 AM-11:00 AM**

Association of sarcopenia with higher toxicity and poor prognosis in nasopharyngeal carcinoma.

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Background: Given the growing evidence that sarcopenia is associated with toxicity and survival in various cancers, we investigated its significance in patients with nasopharyngeal carcinoma (NPC) receiving concurrent chemoradiotherapy (CCRT). **Methods:** In this retrospective analysis, we studied 862 NPC patients who had received CCRT between 2010 and 2014. Sarcopenia was determined using routine pre-radiotherapy computed tomography (CT) simulation scans at the third cervical (C3) vertebral level. Receiver-operating characteristic (ROC) curve analyses were used to determine the optimal cutoff values. Propensity score matching (PSM) was applied to develop comparable cohorts of patients with or without sarcopenia. **Results:** A total of 862 patients were included as the primary cohort, and 308 patients were matched and regarded as the matched cohort. In the primary cohort, the five-year overall survival (OS), locoregional recurrence-free survival (LRFS), and distant metastasis-free survival (DMFS) rates for the sarcopenia group vs. non-sarcopenia group were 78.2% vs. 93.6% (P <0.001), 89.4% vs. 87.9% (P = 0.918), and 82.5% vs. 89.0% (P = 0.007), respectively. Univariate and multivariate survival analyses revealed that sarcopenia was an independent predictor of OS (P <0.001 and P <0.001) and DMFS (P = 0.009, P = 0.034). Patients with sarcopenia experienced significantly higher rates of treatment-related toxicities compared with patients without sarcopenia (P= 0.032). In addition, patients with sarcopenia also experienced significantly worse treatment response than those without sarcopenia (P = 0.004). Similar results were found in a PSM cohort. **Conclusions:** The current findings support that sarcopenia is a promising indicator for predicting clinical outcomes in NPC patients receiving CCRT. A simple and rapid analysis on CT simulation images can provide information about the therapeutic toxicity and survival prognosis, consequently guiding personalized multi-modality interventions during CCRT. Research Sponsor: National Natural Science Foundation of China (Nos. 81772877, 81773103, 81572848).

6569 **Poster Session (Board #230), Fri, 8:00 AM-11:00 AM**

SNOW: Sitravatinib and nivolumab in oral cavity cancer (OCC) window of opportunity study.

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Background: Sitravatinib (receptor TKI against TYRO3, AXL, MERTK and VEGF family of receptors) is predicted to increase M1-type tumor-associated macrophages (TAMs) and decrease MDSCs in the tumor microenvironment. SNOW is a window-of-opportunity study evaluating the immunogenic and antitumor effects of preoperative sitravatinib and nivolumab in patients (pts) with OCC. Early results demonstrated the combination was safe and active (Oliva et al, SITC 2019). Biomarker analyses and updated results are presented. **Methods:** Pts with untreated T2-4a, N0-2 or T1>1cm-N2 OCC are eligible. All pts receive oral sitravatinib 120mg daily from day (D) 1 up to 48h pre-surgery and 1 dose of Nivolumab 240mg on D15. Surgery planned between D23-D30. Standard of care adjuvant radiotherapy given based on clinical stage. Tumor pictures, fresh tumor biopsies, blood samples taken at baseline, D15 and pre-surgery. Tumor flow cytometry and multiplex immunofluorescence staining performed on all biopsies to study changes in immune-cell populations. Tumor whole-exome sequencing (WES) performed on baseline biopsies. **Results:** As of Jan 31st 2020, 10 out of 12 planned pts were enrolled. Study treatment was well-tolerated: only 1 pt had grade (G) >3 toxicity (hypertension) and 1 pt required surgery delay due to G2 thrombocytopenia. None had intraoperative complications. 1 pt had wound infection and tracheostomy bleeding 11 days post-surgery, possibly-related to study drugs. All pts had tumor reduction, 9/10 had pathological downstaging, including 1 complete response (Table). All had clear margins with no extranodal extension; none required adjuvant chemotherapy. All pts are alive with no recurrence (median follow-up= 69 weeks). Lower % of MDSCs and increased % of M1-TAMs and M1:M2 ratio trend was seen at D15 and pre-surgery, with stronger effect in major responders. Best responders (Pts S1-S2) had higher % of PD-L1+ TAMs at baseline. Tumor WES revealed an HRAS G12D mutation in pt S2 and a BLM mutation (DNA repair) in pt S6 (no downstaging). **Conclusions:** Pharmacodynamic analyses support the antitumor and immune effects of sitravatinib and nivolumab in OCC. Immune pathological response assessment and transcriptomics are on-going. Clinical trial information: NCT03575598. Research Sponsor: Tumor Immunotherapy Program, Princess Margaret Cancer Centre, Pharmaceutical/Biotech Company.

Pt	S1	S2	S4	S6	S7	S8	S9	S10	S11	S13
Primary tumor	Alveolus	Alveolus	Tongue	Tongue	Floor of the Mouth	Tongue	Alveolus	Tongue	Tongue	Gingiva
PD-L1 CPS	79	90	34	100	<1	7	27	*	*	*
Clinical stage	T4aN2b	T4aN2b	T3N1	T3N1	T4aN2c	T2N0	T4aN0	T2N2b	T3N0	T4aN0
Pathological stage	ypT0N0	ypT4aN0**	ypT2N0	ypT3N1	ypT4aN0	ypT1N0	ypT3N0	ypT1N2a	ypT1N1	ypT2N0

* Pending **Only residual tumor in bone

6573 **Poster Session (Board #234), Fri, 8:00 AM-11:00 AM**

Phase I trial of hafnium oxide nanoparticles activated by radiotherapy in cisplatin-ineligible locally advanced HNSCC patients.

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Background: The standard of care non-surgical approach for locally advanced head and neck squamous cell carcinoma (LA HNSCC) patients (pts) is concurrent chemoradiation with high dose cisplatin or cetuximab in case of contra-indication. Older age is a contra-indication to cisplatin, and cetuximab might not improve survival in older pts. It is therefore urgently needed to develop new treatment options for elderly pts with LA HNSCC. NBTXR3 are hafnium oxide nanoparticles that can enhance the efficacy of radiotherapy (RT) by increasing locally the deposited dose. In this phase I clinical trial we aimed to evaluate the feasibility and safety of NBTXR3 administered as intratumoral (IT) injection prior to RT in LA HNSCC elderly pts. **Methods:** Pts with stage III-IV LA HNSCC of the oropharynx or oral cavity ineligible for platinum-based chemoradiation received a single IT injection of NBTXR3 into a selected primary tumor and intensity modulated RT (IMRT; 70 Gy/35 fractions/7 weeks) [NCT01946867]. A 3+3 dose escalation design, tested NBTXR3 dose levels equivalent to 5, 10, 15, and 22% of baseline tumor volume, followed by a dose expansion at the Recommended Phase II Dose (RP2D). Primary endpoints included RP2D determination, and early dose limiting toxicities (DLT). NBTXR3 intratumoral bioavailability and anti-tumor activity (RECIST 1.1) were also evaluated. **Results:** Enrollment was completed at all dose escalation levels: 5% (3 pts), 10% (3 pts), 15% (5 pts), and 22% (8 pts). No early DLT or SAE related to NBTXR3 or injection were observed. The median follow-up from NBTXR3 administration is 7.6 months. One AE (Grade 1) related to NBTXR3 and four AEs (Grade 1-2) related to the injection were observed. RT-related toxicity was as expected with IMRT. CT-scan assessment showed a good dispersion of NBTXR3 throughout the injected tumor and not in surrounding healthy tissues. The RP2D was determined to be 22%. Preliminary efficacy was evaluated in pts who received the intended dose of NBTXR3 and RT. A complete response of the injected lesion was observed in 9/13 (69%) evaluable pts at doses $\geq$10% (2 unconfirmed) and an overall complete response in 5/13 (38%) evaluable pts at doses $\geq$10%. Preliminary safety and efficacy data of the dose expansion cohort at the RP2D will also be presented. **Conclusions:** NBTXR3 activated by RT was well tolerated at all tested doses and demonstrated promising preliminary anti-tumor activity. Recruitment is ongoing in the dose expansion cohort. These results demonstrate that further testing of NBTXR3 in this population is warranted. Clinical trial information: NCT01946867. Research Sponsor: Nanobiotix, SA.

6574 **Poster Session (Board #235), Fri, 8:00 AM-11:00 AM**

DURTRERAD: A phase II open-label study evaluating feasibility and efficacy of durvalumab (D) and durvalumab and tremelimumab (DT) in combination with radiotherapy (RT) in non-resectable locally advanced HPV-negative HNSCC—Results of the preplanned feasibility interim analysis.

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Background: DURTRERAD is a randomized phase II study evaluating feasibility and efficacy of durvalumab (anti-PD-L1) vs. durvalumab and tremelimumab (anti-CTLA-4) in combination with radiotherapy as primary treatment for locally advanced HPV negative HNSCC**.** (NCT03624231). Concurrent chemo-RT with a platinum-based regimen is considered the standard treatment, although efficacy and long-term toxicity are not satisfactory. Combining immunotherapy with RT might result in improved efficacy with limited long-term toxicity. **Methods:** The phase II study planned to enroll 120 pts, 60 pts (1:1) in each treatment arm. Treatment with DT (1500mg/75 mg, arm DT),or D (1500mg, arm D) both in combination with RT (70Gy) was considered to be feasible if less than 10% of the patients treated will discontinue treatment due to on-treatment toxicities. A first interim analysis for feasibility and efficacy was planned after randomisation of 20 patients. **Results:** So far 23 patients have been screened, 16 patients have been randomised and started their allocated treatment, 10 in arm D and 6 in arm DT. Of 10 patients in arm D 1 patient stopped infusional treatment due to immune related toxicity. Out of 6 patients in the DT arm, however, 5 patients stopped treatment due to treatment related AEs, 2 pts due to immune related toxicity with one Grade 5 AE. Three patients stopped due to non-immune related AE. The grade 5 AE prompted the interim analysis, which revealed non-feasibility as well as safety-issues of the DT+radiotherapy combination . As a result, the DT arm was prematurely terminated. **Conclusions:** Even though in the recurrent/metastatic setting DT was not associated with increased toxicity, DT in combination with RT was not feasible in our poor prognostic, vulnerable patient cohort of advanced HPV negative unresectable HNSCC, warranting early disclosure of these results. No increase in toxicity was observed in the D monotherapy arm, and the trial continued with D monotherapy in combination with RT. Clinical trial information: NCT03624231. Research Sponsor: AstraZeneca.

6575 **Poster Session (Board #236), Fri, 8:00 AM-11:00 AM**

Dose and volume de-escalation for HPV-associated oropharyngeal cancer: Long-term follow-up of the OPTIMA trial.

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Background: Human papilloma virus (HPV) associated oropharyngeal cancer is associated with a favorable prognosis, but standard multimodality treatment is associated with substantial treatment related toxicity. A de-escalation treatment paradigm that optimizes oncologic outcomes while reducing toxicity is needed. We sought to further expound on our published OPTIMA data with long-term follow-up and additional pts subsequently treated using the OPTIMA treatment paradigm. **Methods:** Long-term follow-up of our institutional de-escalation OPTIMA trial (NCT02258659) and retrospective review of additional patients treated subsequently per OPTIMA outline was performed. Pts were classified as low-risk (LR) ($\leq$T3, $\leq$N2B, $\leq$10PYH) or high-risk (HR) (T4, $\geq$N2c, $>$ 10PYH). Pts received induction chemotherapy (IC) of 3 cycles of dose dense carboplatin and nab-paclitaxel (OPTIMA) or paclitaxel (subsequently treated). LR with $\geq$50% response received low-dose radiotherapy (RT) to 50 Gy. LR with 30-50% response or HR with $\geq$50% response received intermediate-dose chemoradiotherapy (CRT) to 45Gy. All others received full-dose CRT to 75Gy. **Results:** 108 pts consented and 107 were treated (61 on study; 46 subsequently) from October 2014 through November 2019. 1 pt transferred care post-enrollment. Median follow-up was 36 months (interquartile range 17-45). Median age was 63 years (range 33-84) and 95% were male. 47% were LR and 53% were HR. $\geq$50% tumor shrinkage occurred in 78/107 (73%) of pts overall, and 37/51 (73%) among LR; 41/56 (73%) among HR. 82% of pts received de-escalated (C)RT. Overall, 94% of pts were alive at last follow-up (98% LR; 89% HR). 3 pts (2 HR and 1 LR) developed disease recurrence (2.7%), with 2 local recurrences and 1 distant recurrence. Likelihood of G-tube placement was 3% in low-dose RT, 35% in intermediate-dose CRT, and 84% in full-dose CRT. **Conclusions:** IC followed by risk-adapted dose and volume de-escalated treatment for HPV+ oropharyngeal cancer demonstrates excellent oncologic and functional outcomes with long-term follow-up. Supported by Celgene, Alinea benefit supported by Grant Achatz/Nick Kokonas, and National Cancer Institute of the National Institutes of Health (NIH) through Grant Number P30 CA14599. Clinical trial information: NCT02258659. Research Sponsor: Celgene, U.S. National Institutes of Health, Alinea benefit supported by Grant Achatz/Nick Kokonas, and National Cancer Institute of the National Institutes of Health (NIH) through Grant Number P30 CA14599.

6576 **Poster Session (Board #237), Fri, 8:00 AM-11:00 AM**

Single-cell multiplexed proteomics to identify novel polyfunctional CD8+ T cell signatures induced by nivolumab in head and neck cancer patients after salvage surgery.

Shuchi Gulati, Sulsal Haque, Sarah Palackdharry, Aubrey Steele, Casey Allen, Vinita Takiar, Muhammad Kashif Riaz, Maria Lehn, Roman Jandarov, Chad Zender, Yash Patil, Alice L Tang, Brian Cervenka, Ammar Sukari, Misako Nagasaka, Trisha Michel Wise-Draper; University of Cincinnati Medical Center, Cincinnati, OH; Metro Health-University of Michigan Health, Grand Rapids, MI; University of Cincinnati Cancer Institute, Cincinnati, OH; University of Cincinnati, Cincinnati, OH; Division of Biostatistics and Bioinformatics, University of Cincinnati, Cincinnati, OH; Department of Oncology, Karmanos Cancer Institute/Wayne State University, Detriot, MI; Barbara Ann Karmanos Cancer Institute, Detroit, MI; University of Cincinnati Cancer Center, Cincinnati, OH

Background: Immune checkpoint inhibitors (ICIs) are FDA approved for use in head and neck squamous cell cancer (HNSCC), however, only ~20% patients achieve a response. Identification of biomarkers of response or toxicity remains a challenge. Polyfunctional T-cells, or T-cells producing multiple cytokines, have been recognized as contributors to durable immunity against various cancers. However, their role has not been studied prospectively in HNSCC patients receiving ICIs. To look for an early predictor of response, we used single-cell functional proteomic profiling (IsoPlexis) on blood samples pre- and post- first dose of nivolumab (nivo) in patients on our phase-II study of locally recurrent HNSCC (NCT03355560). **Methods:** HNSCC patients who failed definitive radiation +/-chemotherapy and were subsequently treated with curative intent salvage resection were enrolled to receive 6 months of nivo beginning 4 to 11 weeks after surgery. Blood samples were collected before and after the first dose of nivo. Peripheral blood mononuclear cells were isolated, enriched for CD8+ T cells and using the 32-plex IsoCode technology, single-cell cytokine signals were captured and polyfunctional strength of CD8+ T cells was evaluated across four groups (effector, stimulatory, regulatory, inflammatory). A comparison analysis was performed between pre- and post- nivo treatment and between patients who relapsed (non-responders) vs those who did not (responders). **Results:** Thirty-three of 39 planned patients have been enrolled, of which 28 are evaluable and 5/28 (18%) developed recurrence. Median age is 68 years (range 51-85), 9/28 (32%) patients are female, 26/28 (93%) are white, disease sites include oropharyngeal 6/28 (21%), oral cavity 11/28 (39%) and larynx 11/28 (39%). Samples were evaluated at a median follow up of 5.9 months from enrollment. Single-cell analysis demonstrated a strong upregulation of polyfunctional human CD8+ T cell subsets in responders. Polyfunctional Strength Index (PSI) was enhanced in CD8+ T cells across the responders' samples, composed largely of effector cytokines (granzyme-β, IFN-γ, MIP-1α, perforin, TNF-α). **Conclusions:** Single-cell functional proteomic analysis revealed significantly upregulated polyfunctional profiles and an increase in effector cytokines in patients who responded to nivo. This data provides important insights into PD-1 inhibitor triggered T-cell activity and may be used to predict response to ICIs in HNSCC patients using a blood test. Clinical trial information: NCT03355560. Research Sponsor: BMS.

6577 **Poster Session (Board #238), Fri, 8:00 AM-11:00 AM**

Nivolumab (Nivo) and ipilimumab (Ipi) in combination with radiotherapy (RT) in high-risk patients (pts) with locally advanced squamous cell carcinoma of the head and neck (LA SCCHN).

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Background: Immune checkpoint inhibitors (ICI) are the standard of care in recurrent/metastatic SCCHN but their role in the curative therapy setting with RT is under study. We evaluated the novel approach of combining Nivo, a PD-1 inhibitor, and Ipi, a CTLA-4 inhibitor, in lieu of chemotherapy, with concurrent RT in pts with high-risk LA SCCHN. **Methods:** We enrolled newly diagnosed, chemotherapy eligible pts with AJCC 7^{th} edition stage IVA-IVB SCCHN of the oral cavity, oropharynx (OP), hypopharynx, and larynx. HPV+ OP were T4, N2c or N3 OP. Nivo (3 mg/kg every 2 weeks IV x 17 doses) and Ipi (1 mg/kg every 6 weeks x 6 doses) were administered starting 2 weeks prior to the start of RT. RT was prescribed to a dose of 70 Gy delivered in 2 Gy/fraction/day using VMAT. The primary objective was safety of combination ICI with RT. Secondary objectives included 1-year progression-free survival (PFS), overall survival, and correlative studies. **Results:** 24 pts were enrolled; median age of 60 (range 48-77); 20 were male; 16 oropharynx (14 HPV+), 2 hypopharynx, and 6 larynx; AJCC 7^{th} edition stage IVA (23), IVB (1). Grade 3 acute in-field adverse events (AEs) occurred in 17/24 (71%) of patients during concurrent ICI-RT (9 mucositis, 6 dysphagia, 5 dermatitis, 4 odynophagia, 1 dysphonia); there were no grade 4/5 AEs during ICI-RT. During ICI maintenance 5 pts developed in-field ulcerations at the primary site detected at an average of 3 months post RT; 1 of them died of bleeding due to erosion into the carotid artery with no evidence of active cancer; 4 additional pts developed in-field necrosis. 7 pts discontinued ICI treatment at $>$ 3 months post-RT: 1 due to immune AE, 5 due to in-field ulcerations, 1 due to persistent mucositis without ulceration. 4 pts (17%) had grade 3 immune AEs: 1 elevation of lipase, 1 colitis, and 2 rash. There were no grade 4/5 immune AEs. The median follow-up is 16 months (range, 6.3-30.6). 21 of 24 pts (87.5%) are alive with no evidence of disease progression. 2 pts recurred at distant sites: 1 had a solitary lung lesion at 11 months and was treated with RT; 1 in mediastinal lymph nodes at 9 months and was treated with chemo-RT. Locoregional control remains at 100%. **Conclusions:** RT plus dual ICI combination was feasible and resulted in no locoregional relapses so far in 24 high-risk LA SCCHN pts. Longer follow-up is needed to fully assess PFS and locoregional control as well as post-treatment in-field ulceration/necrosis that may be attributed to the potent radiosensitizing effect of dual PD-1 and CTLA-4 blockade. Clinical trial information: NCT03162731. Research Sponsor: Bristol Myers Squibb.

6578 **Poster Session (Board #239), Fri, 8:00 AM-11:00 AM**

Prospective, longitudinal digital activity monitoring before and after treatment of low-risk oropharyngeal squamous cell carcinoma: A feasibility study.

Gary Brandon Gunn, Renata Ferrarotto, Faye M. Johnson, Diana Bell, Richard Cardoso, Jason Michael Johnson, M. Laura Rubin, Ying Yuan, Steven J. Frank, Clifton David Fuller, David Ira Rosenthal, Michael Elliot Kupferman, Ryan Goepfert, Amy Clark Hessel, Kate A. Hutcheson, Neil D. Gross; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; UT MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Department of Head and Neck Surgery, Houston, TX

Background: Given the expected excellent prognosis of low-risk oropharyngeal squamous cell carcinoma (OPSCC), consideration of long-term toxicity and functional outcomes has become increasingly important. Activity monitors (e.g. FITBIT) are imperfect but have been shown to have reasonable validity in healthy adults. Here we aimed to test the feasibility of using medical grade longitudinal digital activity monitoring to better define objective functional outcomes after treatment of low-risk OPSCC. **Methods:** This prospective, observational parallel cohort study included patients with previously untreated stage I-III (AJCC 7) OPSCC eligible for standard of care single-modality treatment with either Intensity-Modulated Proton Therapy (IMPT) or TransOral Robotic Surgery (TORS). Objective Actigraph accelerometer data (Actigraph, Pensacola, FL) were collected continuously for 1 week at baseline, 3, 6 and 12 months after treatment along with subjective patient-reported outcome (PRO) measures. **Results:** Forty-four patients (34M, 10F) enrolled with median age 59 years (range: 42-78). Baseline, 3 and 6 month activity data were available for 40 patients (91%): 16 IMPT and 24 TORS. There was a significant decrease in mean percent of day performing moderate to vigorous physical activity (MVPA) (-0.78, 0.021) mean number of steps/minute (-1.1, $p = 0.035$), and mean kcals/day (-115.9, $p < 0.001$) from baseline to 3 months after treatment for the overall cohort. A significant decrease in mean kcals/day (-82.2, $p = 0.004$) persisted for the overall cohort at 6 months with no significant difference between groups. **Conclusions:** Longitudinal digital activity monitoring is feasible before and after treatment of low-risk OPSCC. This approach may offer objective functional endpoints for future de-escalation trials. Similar short-term decreases in objective activity measurements were observed after IMPT and TORS. Long-term (12 month) activity data and correlations to subjective PRO measures will be available at the time of presentation. Clinical trial information: 02663583. Research Sponsor: Philanthropy, U.S. National Institutes of Health.

6579 **Poster Session (Board #240), Fri, 8:00 AM-11:00 AM**

Risk of chronic opioid use after radiation for head and neck cancer: A systematic review and meta-analysis.

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Background: Opioid overuse is a major international public health concern. The prevalence and risk factors for chronic opioid use (COU) in radiation-induced head and neck pain are poorly understood. The aim of this study was to estimate the rates of COU and to identify risk factors for COU in head and neck cancer (HNC) patients undergoing curative-intent radiotherapy (RT) or chemoradiotherapy (CRT). **Methods:** We performed a systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, using the PubMed (Medline), EMBASE, and Cochrane library databases, queried from dates of inception until present. COU was defined as persistent opioid use $\geq$3 months after treatment completion. Studies in the English language that reported on COU in HNC patients who received RT/CRT were included. Meta-analyses were performed using random effects models. Heterogeneity was assessed using the I^2 value. **Results:** A total of 134 studies were identified, with 7 retrospective studies (reporting on 1841 patients) meeting inclusion criteria. Median age was 59.4 years (range 56.0-62.0) with 1343 (72.9%) men and 498 (27.1%) women. Primary tumour locations included oropharynx (891, 48.4%), oral cavity (533, 29.0%), larynx (93, 5.1%), hypopharynx (32, 1.7%), and nasopharynx (29, 1.6%). 846 (46.0%) patients had stage I/II disease and 926 (50.3%) had stage III-IV disease. 301 (16.3%) patients had RT alone, 738 (40.1%) received CRT, and 594 (32.3%) underwent surgery followed by adjuvant RT/CRT. The proportion of HNC patients who received radiotherapy and developed COU was 40.7% at 3 months (95% CI 22.6%-61.7%, I^2= 97.1%), 15.5% at 6 months (95% CI 7.3%-29.7%, I^2= 94.3%) and 7.0% at 1 year. There were significant differences in COU based on primary tumor sites ($P < 0.0001$), with the highest rate (46.6%) in oropharyngeal malignancies. Other factors associated with COU included history of psychiatric disorder (61.7%), former/current alcohol abuse (53.9%), and start of opioids prior to radiation treatment (51.6%). There was no significant difference in the proportion of COU by gender ($P = 0.683$), disease stage (I/II vs III/IV; $P = 0.443$), or treatment received (RT, CRT, or adjuvant RT/CRT; $P = 0.711$). **Conclusions:** A significant proportion of patients who undergo radiotherapy for head and neck cancer suffer from COU. High-risk factors for COU include an oropharyngeal primary tumour, history of psychiatric disorder, former/current alcohol abuse, and pre-treatment opioid use. New strategies to mitigate opioid use are needed. Research Sponsor: None.

Upfront DPYD genotyping and toxicity associated with fluoropyrimidine-based concurrent chemoradiotherapy for oropharyngeal carcinomas.

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Background: The combination of carboplatin and 5-fluorouracil (5-FU) is effective when used concurrently with radiotherapy for locoregionally advanced oropharyngeal carcinomas (Calais et al. 1999). DPYD polymorphisms can be associated with an increased risk of severe toxicity to fluoropyrimidines (Deenen et al. 2016). Upfront screening for the DPYD*2A allele is available in the province of Québec, Canada since March 2017. This study aimed to determine the effect of upfront genotyping on grade $\geq$3 toxicities. **Methods:** The studied population included all consecutive cases of oropharyngeal carcinomas treated with 5-FU based chemoradiotherapy one year before and after the implementation of upfront DPYD*2A genotyping. All patients were treated at the Centre Hospitalier de l'Université de Montréal (CHUM) between March 2016 and April 2018. Clinical data were extracted from chart review. Extended screening for 3 supplemental at-risk DPYD variants was also retrospectively performed in August 2019. **Results:** 181 patients were included in the analysis (87 patients before and 94 patients after DPYD*2A screening implementation). 91% of patients (n = 86) were prospectively genotyped for the DPYD*2A allele. Of those screened, 2% (n = 2/87) demonstrated a heterozygous DPYD*2A mutation. Those two patients received cisplatin-based treatment and thus avoided 5-FU toxicities. Extended genotyping of DPYD*2A-negative patients later allowed for the retrospective identification of 6 additional patients with alternative DPYD variants (two c.2846A > T and four c.1236G > A allele mutations). **Conclusions:** The DPYD*2A, c.2846A > T and c.1236G > A polymorphisms are associated with an increased risk of G3-4 toxicity to 5-FU, as well as higher hospitalization rates. Upfront DPYD genotyping can identify patients in whom fluoropyrimidine-related toxicity should be avoided. This represents an interesting addition in terms of pharmacovigilance. Research Sponsor: None.

Adverse events of interest are summarized in the table below.

	Pre-DPYD*2A screening	Post-DPYD*2A screening	*p*	DPYD-mut (non-DPYD*2A) (n = 6)	DPYD WT (n = 78)	*p*
Grade ≥3 toxicity	71%	62%	0.18	100%	60%	0.046
Mucositis	54%	47%		100%	44%	
Dysphagia	39%	26%		66%	23%	
Radiation-induced dermatitis	15%	14%		0%	14%	
Neutropenia	8%	9%		17%	9%	
Hospitalization	29%	21%		33%	23%	
Enteral feeding	41%	30%		50%	32%	

6582 **Poster Session (Board #243), Fri, 8:00 AM-11:00 AM**

A novel multiple-catheter implantation method for advanced head and neck cancer.

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Background: We previously developed a super-selective intra-arterial chemotherapy (iaCT) approach for head and neck cancer (HNC), by which, an intra-arterial catheter is retrogradely inserted via either the superficial temporal artery (STA) or occipital artery (OA) and connected to a subcutaneous reservoir. As a result, since this approach overcomes the need for frequent fluoroscopy sessions, the infusion frequency can be increased and the therapeutic effectiveness improved. However, since the anticancer effect is limited to the region supplied by the selected blood vessel, it is often difficult to control an advanced HNC by single-catheter iaCT. Subsequently, a novel multiple-catheter implantation method (MCIM) for super-selective iaCT has been developed using, both, the STA and OA. **Methods:** A total of 21 patients with stage III or IV HNC were enrolled in this study and treated via MCIM for iaCT between 2009 and 2017. The catheters were super-selectively placed in the tumor-feeding arteries after having entered the STA or OA. The first catheter was introduced into one of the target branches. Next, a second catheter was introduced into another target branch. If a third catheter was required, the procedure was repeated. The extra-arterial portions of the catheters were subcutaneously connected to an implanted juxta-mastoidal infusion reservoir. **Results:** The response rate was 100%; particularly, 20 cases of complete response and 1 of partial response were confirmed. Although the partial responder underwent salvage surgery and two complete responders ultimately died (due to either delayed recurrence or brain metastases), the other 18 patients have been living cancer-free for 2-9 years. **Conclusions:** The MCIM method allows to expand the infusion region while maintaining the main advantages of super-selective iaCT. As a consequence, due to the lack of need for patient confinement in the catheter room and for frequent fluoroscopy sessions, patients' mental and physical distress, medical expenses, and treatment time are all ultimately reduced. Research Sponsor: None.

6583 **Poster Session (Board #244), Fri, 8:00 AM-11:00 AM**

Neoadjuvant nivolumab (N) plus weekly carboplatin (C) and paclitaxel (P) in resectable locally advanced head and neck cancer.

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Background: Despite multimodality standard therapy, patients (pts) with resectable locally advanced squamous cell carcinoma of the head and neck (LA SCCHN) are at high risk for recurrence. Pts with pathologic complete response (pCR) or major pathologic response (MPR) to neoadjuvant chemotherapy have improved overall survival. PD-1 checkpoint inhibitors are approved in combination with platinum-based chemotherapy in the 1st-line treatment of recurrent/metastatic SCCHN. We hypothesize the addition of N to wkly carboplatin C and P will increase the pCR rate at the primary site compared to historical controls. **Methods:** This is an investigator-initiated trial for pts with newly diagnosed (AJCC 8^{th}) stage III-IV HPV- (oral cavity (OC), oropharynx (OP), hypopharynx (HP), and larynx (L) or stage II-III HPV+ OP SCCHN without distant metastasis who are surgical candidates. Neoadjuvant chemo starting d1 is C AUC 2 IV wkly x 6 plus P 100 mg/m2 IV wkly x 6 plus N 240 mg IV q 2 wks x 3 with surgery on wk 8. The primary endpoint is pCR at the primary site. To estimate pathologic response, the resected pathology specimens are cut $>$1 section/cm. Using the Aperio Digital scanning system, slides are imaged, and then annotated by at least 2 pathologists for viable tumor vs. treatment effect with areas automatically calculated to yield the percentage of viable tumor. Our primary endpoint will be reached if 11/37 planned pts have a pCR at the primary site. **Results:** From 11/17-12/19, 27 pts received the study regimen and had surgery (1/27 had an unknown primary; thus, inevaluable for the primary endpoint). Of 27 pts, median age was 59 (46-83), women 31%, HPV+ 15%, OC 73%, OP 19%, HP 7%, L 4%; stage III 33%, stage IVA 67%. Gd 3 toxicities were in 37% pts; 1 pt febrile neutropenia, 3pts anemia, 1pt diarrhea, 1pt cellulitis and 1pt rash. Four pts had gd 3-4 neutropenia. Dose reductions were in 2 pts, and 4 pts had 1 wkly dose dropped. All 27 pts went to surgery, none with PD by CT; all with negative margins. One pt died with rapid recurrence; no other recurrences (median f/u 13 mos). Our primary endpoint was met; 11/26 (42%) pts (excluding pt with unknown primary) had a pCR at the primary site. 9/23 (39%) HPV- pts, had a pCR. MPR or pCR was 18/26 (69%) and in HPV- pts, 15/23 (65%). 2/11 pts had microscopic residual disease in 1 LN each. **Conclusions:** The combination of N and wkly PC was well tolerated. The primary endpoint of pCR at the primary site in $>$ 11/37 pts was met with the 27^{th} pt. Accrual continues. Exploratory outcomes assessing markers of immune bias in tumor tissue and plasma are in process. Clinical trial information: NCT03342911. Research Sponsor: Bristol-Myers Squibb.

6584 **Poster Session (Board #245), Fri, 8:00 AM-11:00 AM**

RAS-mutated sporadic medullary thyroid cancer: A single-center experience.

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Background: Activating *RAS* mutations are recognized as important drivers in sporadic medullary thyroid cancer (sMTC), with a reported prevalence between 0-43%. However, few studies have looked at correlations between *RAS*-mutated sMTC and clinicopathologic features. **Methods:** Patients with sMTC diagnosed between 1992 – 2019 with NGS testing for *RET* and *RAS* mutations seen at a tertiary cancer center were retrospectively evaluated. The objective was to analyze demographic and clinical features among patients with *RAS*-mutated sMTC and to evaluate associations between these features and overall survival (OS). Analyses were performed to correlate patient demographics and pathologic staging with treatment characteristics, disease course, and OS. **Results:** We identified 42 patients (50% female) with *RAS*-mutated sMTC out of 218 pts with sMTC. Median age at diagnosis was 50 years (range 24-78 years). 26 (62%) patients had stage IV disease at time of diagnosis. 28 (67%) of patients had *HRAS* mutations and 14 (33%) had *KRAS* mutations. *HRAS Q61R* was the most common *HRAS* mutation type (n = 19, 45%). Median follow-up time was 64 months (range 23-274 months) during which 11 (26%) patients died. The median OS was 16.2 years, with 5- and 10- year OS of 88% and 73% respectively. Of the 20 (48%) patients who received systemic therapy, 79% had stage IV disease and tended to be older (median age 54). Median time from diagnosis to initiation of systemic therapy was 33 months. Factors associated with worse OS included distant metastases at diagnosis, shorter time interval between diagnosis and treatment, and Ctn/CEA doubling times $<$ 6 months. *HRAS Q61R* mutations were associated with a better prognosis, with 100% 10-year OS compared with 10-year OS of 39% and 51% (p = 0.02) for other *HRAS* and *KRAS* mutations respectively. **Conclusions:** At a tertiary cancer center, patients with *RAS*-mutated sMTC had a 10-year OS rate of 73%, with significantly worse OS in patients with *HRAS/KRAS* mutations other than *HRAS Q61R*. In comparison, prior studies have reported 10-year OS rates between ~71-90% in sMTC and 10-year OS rates as low as 56% for more aggressive *RET M918T* sMTC mutations. The findings here are consistent with other studies that have suggested patients with *RAS*-mutated sMTC are at intermediate risk for aggressive disease, though there are limited data on OS rates in *RAS* or RAS-/RET- sMTC. Future research comparing outcomes between various *RAS* mutations and in comparison to *RET+* and RAS-/RET- patients is needed, especially as systemic therapy use in *RAS*-mutated sMTC evolves. Research Sponsor: None.

6585 **Poster Session (Board #246), Fri, 8:00 AM-11:00 AM**

ELLA01-1: A study to determine the utility of TP53 mutations as a prognostic biomarker in adenoid cystic carcinoma.

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Background: TP53 mutations are reported in 5% of patients with adenoid cystic carcinoma (ACC). Whilst TP53 mutations are associated with adverse clinical outcomes across multiple tumour types, their prognostic significance in ACC is unknown. We sought to determine the utility of TP53 mutations as a prognostic biomarker in a prospective cohort of ACC patients. **Methods:** From April 2017 to September 2019, 146 patients with ACC were prospectively recruited to an ethically approved study. DNA was extracted from archival FFPE samples and underwent targeted next generation sequencing (Qiagen GeneRead DNAseq Targeted Panel V2 n = 134; Foundation Medicine; n = 12). Clinical, pathological and outcome data were collected on all patients and Kaplan-Meier survival analysis was performed to test for survival differences between TP53 mutated and wild-type ACC. **Results:** 146 ACC patients (mean age 48 years, range 16-79) underwent DNA extraction and next generation sequencing for TP53 mutations. The primary site was major salivary gland in 47% and minor salivary gland in 48% (other 5%). Analysis was successful in 122/146 patients (84%). Recurrent or metastatic disease was present in 94% (115/122) at study entry. TP53 alterations were identified in 9% (11/122), most frequently within the DNA binding domain (9/11). Non-pulmonary visceral metastases were seen more frequently in TP53 wild-type than in TP53 mutated ACC (44% vs. 10%; p = 0.042), and other clinical parameters were balanced between groups. During follow-up from diagnosis (median follow up 6.6 years), death occurred in 45% of patients with TP53 mutation and in 23% with TP53 wild-type ACC (p = ns). In TP53 mutated ACC, median overall survival was significantly shorter (5.3 vs. 16.3 years), and 10-year survival rate significantly lower (42% vs. 82%) than TP53 wild-type ACC (log-rank p = 0.013). **Conclusions:** In this cohort of patients with ACC, TP53 mutations were seen with a higher frequency than previously reported. This may be explained by the high frequency of recurrent or metastatic disease at study entry. TP53 mutation was associated with a statistically significant reduction in overall survival in patients with recurrent and metastatic ACC. These findings suggest that stratifying by TP53 status may be of clinical value to inform follow-up strategy in addition to established clinical, pathological and genomic biomarkers. Research Sponsor: The Christie Charity, University of Manchester, Syncona Foundation, Infrastructure Industry Foundation.

6586 **Poster Session (Board #247), Fri, 8:00 AM-11:00 AM**

Recurrent or metastatic salivary gland tumor (MSGT) patients treated with selinexor, a first in class selective exportin-1 (XPO1) inhibitor.

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Background: MSGT are rare with limited systemic treatments. This single institution, prospective study in recurrent or metastatic (RM) MSGT involved 2 phases: genomic profiling followed by treatment with either genomically-matched or unmatched therapy. Here we present the results of the unmatched arm for patients (pts) treated with S an oral selective inhibitor of XPO1 that leads to activation of tumor suppressor proteins and retention of oncoprotein mRNAs in the cell nucleus, inducing cancer cell apoptosis. **Methods:** Patients (pts) with RM-MSGT had archived paraffin embedded tumor samples profiled with targeted next generation sequencing, immunohistochemistry for androgen receptor (AR) and fluorescent in-situ hybridization for HER-2 and ALK. If no actionable mutations were identified or if no matched agents were available, pts with progressive disease could receive S (60mg given twice weekly Q28 days). The study had a simon-2 stage design; 1 partial response in the first 18 pts treated with S, would trigger an additional 7pts to receive S in stage 2. **Results:** Between July 2014 and April 2019 85 pts were enrolled on study: 73 had sequencing which identified 41 with no actionable mutations and 32 with actionable mutations. 18 pts (10F/8M, median age 61 years [40-79]) were treated with S and included adenoid cystic (n = 8), salivary duct (n = 4), acinic cell (n = 2) and other subtypes (n = 4). Of these 18, 4 pts had actionable aberrations: AR amplification (n = 2), mutations in SMARCB1 (n = 1) and CDKN2A (n = 1). 13pts were treatment naïve, 3pts and 2pts received 1 and 2 or more lines of treatment respectively prior to enrollment: androgen deprivation therapy (n = 2), chemotherapy (n = 3), early phase clinical trials (n = 3). The median number of cycles of S received were 3 (range: 1-19). The best response by RECIST was SD in 13pts (72%) (SD $>$ 6 months (range: 6-18 months) in 5pts (28%); tumor reduction measured in 7pts (39%)), no PRs, PD in 3pts (17%), and 2pts (11%) were not evaluable for response due to insufficient duration of treatment coming off early due to toxicity. The median PFS (95% CI) was 7.6 (3.5-NA) months and the median OS (95% CI) was 15.4 (7.3-NA) months. The most common drug-related toxicities were grade 1-2 fatigue 14pts (78%), nausea 13pts (72%) and dysguesia 10pts (56%). 5 (28%) pts had a dose reduction and 6 (33%) in total had a dose interruption due to toxicity. **Conclusions:** Single agent antitumor activity was limited and the side effect profile was tolerable. No specific genomic aberration was associated with response to S. Clinical trial information: NCT02069730. Research Sponsor: Karyopharm.

6587 **Poster Session (Board #248), Fri, 8:00 AM-11:00 AM**

Radioiodine (RAI) in combination with durvalumab for recurrent/metastatic thyroid cancers.

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Background: Immune checkpoint blockade (ICB) has limited efficacy for radioiodine-refractory thyroid cancer. The high incidence of autoimmune thyroid disease and ICB-induced hypothyroidism suggests that loss of T cell tolerance to thyroid protein epitopes is common and can be activated by ICB to induce immune responses. We hypothesize that RAI can enhance presentation of thyroid protein immunogens and putative neoantigens in thyroid cancers to amplify the effectiveness of ICB. We studied the safety and efficacy of RAI plus the anti-PD-L1 agent durvalumab (durva) in recurrent/metastatic (R/M) patients (pts). **Methods:** Pts. had at least one RAI-avid tumor on the most recent RAI scan or one tumor on FDG PET with an SUVmax $<$ 10. RECIST measurable disease was required. Any number of prior therapies was allowed. Pts were treated with durva 1500 mg IV every 4 weeks with recombinant human TSH (rhTSH)-stimulated RAI (100 mCi) administered in Cycle 1. Treatment beyond progression was allowed. The primary objective was to assess safety. Durva related dose limiting toxicities (DLTs) were monitored for 6 weeks after the first dose. Since no durva DLTs were observed in the first 6 pts, per protocol rules the trial accrued 11 pts total. Secondary objectives were assessing best overall response (BOR) per RECIST and progression-free survival (PFS). **Results:** 11 pts (7 female) were enrolled. Eight had prior drug therapy. No DLTs or $>$ Grade 3 durva related adverse events (AEs) were observed. The most common non-laboratory AEs (regardless of attribution) were cough (7), hypertension (7), pain (6), edema (5), and fatigue/nausea/diarrhea/arthralgia/dry skin/dyspnea/edema (4 each). As of 2/6/20, 2 had partial response, 7 stable disease, and 2 progression of disease as BOR. Six pts had tumor regression. Four pts received treatment for $>$ 6 months. Six are still on treatment. Analyses of research biopsies (bxs) (8 had pre-treatment bxs, 6 had an additional on-treatment bx) will be presented. **Conclusions:** Durva plus RAI is safe and well tolerated. The preliminary efficacy signal in this small cohort is promising. Understanding how RAI plus PD-L1 targeting impacts the tumor immune microenvironment may guide how RAI should be evaluated in future ICB trials. Clinical trial information: NCT03215095. Research Sponsor: AstraZeneca, U.S. National Institutes of Health.

6588 **Poster Session (Board #249), Fri, 8:00 AM-11:00 AM**

Effect of ARMS-qPCR on detection sensitivity of earlier diagnosis of papillary thyroid cancers with worse prognosis determined by BRAF V600E and TERT promoter mutation coexisting.

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Background: Co-existing of *BRAF* V600E and *TERT* promoter C228T/C250T mutation has been extensively related to prognosis in thyroid cancer. Our study aimed to establish a more sensitive method for mutation detection and explore the correlation more in-depth. **Methods:** *BRAF* and *TERT* promoter mutation status of 250 papillary thyroid cancer was detected by both Amplification Refractory Mutation System quantitative PCR (ARMS-qPCR) and Sanger sequencing to compare the sensitivity. The associations between the mutation status and the clinicopathological features were analyzed. **Results:** ARMS-qPCR displayed higher sensitivity than Sanger (*BRAF* V600E: 75.2% vs. 52.4%, $p< 0.001$; *TERT* promoter C228T/C250T: 12.0% vs. 3.6%, $p= 0.001$; Co-mutation (9.6% vs. 3.2%, $p= 0.005$). Both methods indicated that patients with *BRAF* V600E and *TERT* promoter co-mutation were higher in age at diagnosis (ARMS-qPCR: 51.0 ± 14.2 vs. 40.2 ± 12.6, $p <0.001$; Sanger: 64.3 ± 7.1 vs. 40.5 ± 12.6, $p <0.001$), and the recurrence rate (16.7% vs. 3.1%, $p= 0.014$; 50.0% vs. 2.9%, $p< 0.001$), besides, the co-mutation group were related to more advanced TNM stage ($p< 0.001$; $p< 0.001$) and higher MACIS score (5.1 ± 1.5 vs. 4.2 ± 0.7, $p= 0.006$; 6.6 ± 1.1 vs. 4.2 ± 0.8, $p< 0.001$). In addition, compared with the co-mutation results of Sanger, it seems that ARMS-qPCR has identified an earlier stage of group, which were younger (43.3 ± 10.1 vs. 66.4 ± 6.1, $p< 0.001$), and with smaller tumor (1.8 ± 1.5 vs. 4.0 ± 1.3, $p= 0.002$), as well as lower recurrence rate (0.0% vs. 50%, $p= 0.007$). Besides, the newly identified group were lower in MACIS score (4.2 ± 0.8 vs. 6.9 ± 0.7, $p= 0.002$) and with lower TNM stage ($p= 0.001$). **Conclusions:** Patients with *BRAF* V600E and *TERT* promoter C228T/C250T co-mutation have a worse prognosis. Using ARMS-qPCR, the more sensitive method could identify earlier stages of patients with a potentially worse prognosis. Research Sponsor: National Science Foundation of China.

	ARMS-qPCR Co-Mut			Sanger Co-Mut			ARMS-qPCR(+)		
	+(n = 24)	-(n = 226)	*p*	+ (n = 8)	- (n = 242)	*p*	Sanger + (n = 8)	Sanger-, (n = 16)	*p*
Age at diagnosis ± SD	51.0±14.2	40.2±12.6	**< 0.001**	66.4±6.1	40.4±12.5	**< 0.001**	66.4±6.1	43.3±10.1	**< 0.001**
Size(cm) ± SD	2.5±1.8	1.8±1.0	0.057	4.0±1.8	1.8±1.0	**< 0.001**	4.0±1.3	1.8 ±1.5	**0.002**
Recurrence, n (%)	4(16.7)	7(3.1)	**0.014**	4(50.0)	7(2.9)	**< 0.001**	4(50.0)	0(0.0)	**0.007**
MACIS score ± SD	5.1±1.5	4.2±0.7	**0.006**	6.9±0.7	4.2±0.8	**< 0.001**	6.9±0.7	4.2±0.8	**< 0.001**
TNM stage, n (%)			**< 0.001**			**< 0.001**			**0.001**
I+II	23(95.8)	225(99.5)		7(87.5)	241(99.6)		6(87.5)	17(100.0)	
III+IV	1(4.2)	1(0.4)		1(12.5)	1(0.4)		1(12.5)	0(0.0)	

TPS6589 **Poster Session (Board #250), Fri, 8:00 AM-11:00 AM**

Phase III LEAP-010 study: first-line pembrolizumab with or without lenvatinib in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).

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Background: The PD-1 inhibitor pembrolizumab is currently approved as first-line monotherapy for patients with R/M HNSCC whose tumors express PD-L1 combined positive score (CPS) $\geq$1. In a phase 1b/2 trial (NCT02501096) of pembrolizumab plus lenvatinib (multikinase inhibitor of VEGFR 1-3, FGFR 1-4, PDGFRa, RET, and KIT) in solid tumors, the combination demonstrated promising anti-tumor activity and a manageable safety profile in patients with HNSCC. LEAP-010 (NCT04199104) is a randomized, double-blind, placebo-controlled, phase 3 study that will evaluate the efficacy and safety of first-line pembrolizumab with or without lenvatinib in patients with PD-L1–positive R/M HNSCC. **Methods:** Key eligibility criteria include histologically confirmed R/M HNSCC incurable by local therapies, PD-L1–positive tumor (CPS $\geq$1) as determined by central laboratory, measurable disease as assessed by blinded independent central review (BICR) per RECIST v1.1, and ECOG performance status (PS) 0 or 1. Patients will be randomly assigned 1:1 to pembrolizumab plus lenvatinib or pembrolizumab plus placebo. Randomization will be stratified by PD-L1 status defined by tumor proportion score ($<$ 50% vs $\geq$50%), human papillomavirus status for oropharynx cancer (positive vs negative), and ECOG PS (0 or 1). Patients will receive intravenous pembrolizumab 200 mg every 3 weeks for 35 cycles (~2 years) and oral lenvatinib 20 mg or placebo once daily; patients may continue to receive lenvatinib or placebo after pembrolizumab treatment is complete. Treatment will continue until BICR-verified disease progression or unacceptable toxicity. Pembrolizumab retreatment (second course) for 17 additional cycles will be allowed for eligible patients who stop pembrolizumab and subsequently experience BICR-verified disease progression. These patients could have stopped treatment with stable disease, partial response, or complete response or after 35 cycles of pembrolizumab for reasons other than disease progression or toxicity. Tumor imaging assessment will be performed at week 6, then every 6 weeks until 1 year, and thereafter every 9 weeks. Primary end points are objective response rate and progression-free survival, assessed by BICR per RECIST v1.1, and overall survival. Secondary end points are duration of response and safety and tolerability. Recruitment is ongoing; planned enrollment is ~500 patients. Clinical trial information: NCT04199104. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; and Eisai Inc., Woodcliff Lake, NJ, USA.

TPS6590 **Poster Session (Board #251), Fri, 8:00 AM-11:00 AM**

Single-arm study of bimiralisib in head and neck squamous cell carcinoma (HNSCC) patients (pts) harboring *NOTCH1* loss of function (LOF) mutations.

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Background: Effective targeted therapies are needed for HNSCC that is lethal despite recent advances with immunotherapy. A major challenge to personalize treatment is that most genomic alterations are in tumor suppressors, including *NOTCH1* that is mutated in ~20% of HNSCC. We recently published that HNSCC cell lines harboring *NOTCH1* LOF mutations undergo cell death *in vivo* and *in vitro* following PI3K inhibition, in contrast to *PIK3CA* mutant cell lines that merely undergo cell cycle arrest when exposed to the same drugs. Based on these results we initiated a novel genomic biomarker-driven phase II clinical trial treating *NOTCH1* mutant HNSCC pts with the dual PI3K/mTOR inhibitor bimiralisib (PQR309). **Methods:** The primary objective is to determine the objective response rate (ORR) of recurrent/metastatic HNSCC harboring *NOTCH1* LOF mutations to bimiralisib. Pts who have already received standard platinum chemotherapy and immunotherapy will receive bimiralisib orally twice per wk unless progression or intolerable toxicity occurs. Tumors will be evaluated using RECIST q 6 wks. A Simon's optimal two-stage design is used. To have 80% power to detect an ORR of 30%, (one-sided α = 0.05, β = 0.20) 10 pts will be enrolled in the first stage. If $\leq$1 pts respond, the trial will be closed for futility. If $\geq$2 pts have an OR, the study will enroll an additional 19 pts in the second stage. The null hypothesis (ORR $\leq$ 10%) will be rejected if $\geq$ 6 in 29 pts have an OR. Seven pts have enrolled. The algorithm for determining *NOTCH1* mutation function is based on the patterns of mutations in HNSCC vs. leukemia where mutations are activating. It may be difficult to determine whether *NOTCH1* mutations are homo- or heterozygous due to normal cell contamination. Therefore, levels of activated NOTCH1 in pretreatment tumors may be assessed by IHC with an antibody against activated NOTCH1 (NICD). In parallel with the trial, to further confirm *NOTCH1* LOF, we can use site-directed mutagenesis to re-create *NOTCH1* mutations from trial pts that will then be introduced into NOTCH1-null cell lines to assay for NICD and growth inhibition with culture on NOTCH1 ligand. All pts will have serial collection of blood for pharmacokinetics and for ctDNA to examine clonal evolution associated with acquired resistance. Samples with high *NOTCH1* mutation ctDNA VAF will be analyzed by WES and compared with pretreatment tissue. In the second stage, IHC and WES may be performed on pre- and post-treatment (day 15 and progression) tissue to examine pharmacodynamics and mechanisms of resistance. Clinical trial information: NCT03740100. Research Sponsor: PIQUR.

TPS6591 **Poster Session (Board #252), Fri, 8:00 AM-11:00 AM**

INDUCE-3: A randomized, double-blind study of GSK3359609 (GSK609), an inducible T-cell co-stimulatory (ICOS) agonist antibody, plus pembrolizumab (PE) versus placebo (PL) plus PE for first-line treatment of PD-L1-positive recurrent/metastatic head and neck squamous cell carcinoma (R/M HNSCC).

Aaron Richard Hansen, Thomas S. Stanton, Min Hee Hong, Ezra E.W. Cohen, Hisham Mohamed Mehanna, Michael Jon Chisamore, David Turner, Sapna Yadavilli, Kelly Bell, Carlos Baccan, Rosalida Leone, Helen Chen, Helen Zhou, Catherine Elizabeth Ellis, Marc S. Ballas, Axel Hoos, Danny Rischin; Princess Margaret Cancer Centre, Toronto, ON, Canada; St Joseph Hospital, Santa Rosa, CA; Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Yonsei University Health System, Seoul, South Korea; Moores Cancer Center at University of California, La Jolla, CA; Institute of Head and Neck Studies and Education, Institute of Cancer and Genomic Sciences, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; Merck and Co., Kenilworth, NJ; GlaxoSmithKline, Collegeville, PA; GlaxoSmithKline, Collegeville, Upper Providence, PA; GlaxoSmithKline, Stockley Park, Middlesex, United Kingdom; GlaxoSmithKline, Upper Providence, PA; Peter MacCallum Cancer Centre, Melbourne, Australia

Background: Pembrolizumab as part of first-line treatment for patients (pts) with R/M HNSCC has improved survival. However, in order to further improve outcomes in this population investigation of rational combinations targeting different mechanisms that cancers exploit to evade the immune system is required. ICOS, a member of the CD28/B7 immunoglobulin receptor superfamily, provides a co-stimulatory signal augmenting T-cell proliferation, cytokine production, cytotoxic function and survival. GSK609 is a humanized IgG4 antibody selected for its potent agonist activity and non-depleting properties. The rationale for targeting ICOS with GSK609 plus PD-1 blockade with PE is supported by preclinical and clinical evidence (Rischin, et al. *Annals of Oncol* 2019;30[Supplement_5]:v454–5). INDUCE-3 trial (NCT04128696) will explore if the addition of GSK609 to PE improves outcomes of pts with R/M HNSCC. **Methods:** INDUCE-3 uses a 2-in-1 adaptive design that has the option to seamlessly expand from an initial Phase 2 to a Phase 3 study. Pts (n = 600) will be stratified by PD-L1 status and HPV status (oropharynx only) then randomly assigned in a 1:1 ratio to receive GSK609 plus PE or PL plus PE, every 3 weeks until progression, unacceptable toxicity, or up to 35 cycles. GSK609 plus PE will be assessed for superiority versus PL plus PE in overall survival (OS) and progression-free survival (PFS) per RECISTv1.1 as dual primary endpoints; secondary endpoints include PFS per immune-based RECIST; milestone OS; safety and tolerability; time to deterioration in patient-reported physical function and pain. Efficacy and patient-reported outcome endpoints will be assessed in the PD-L1 combined positive score (CPS) $\geq$1 and $\geq$20 populations. Key eligibility criteria are aged $\geq$18 years; locally incurable R/M HNSCC of the oral cavity, oropharynx, hypopharynx, or larynx; no prior systemic therapy in the R/M setting; PD-L1 CPS $\geq$1 by central testing; measurable disease per RECIST v1.1 and ECOG PS 0/1. Recruitment is ongoing in countries across the globe. Funding: Study is funded by GlaxoSmithKline and in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Clinical trial information: NCT04128696. Research Sponsor: GSK.

TPS6592 **Poster Session (Board #253), Fri, 8:00 AM-11:00 AM**

CCTG HN.10: A phase II single-arm trial of elective volume adjusted de-escalation radiotherapy (EVADER) in patients with low-risk HPV-related oropharyngeal squamous cell carcinoma (NCT03822897).

Scott Victor Bratman, Eric Berthelet, James B. Butler, John R de Almeida, Irene Karam, Ur Metser, Robert Anton Olson, Craig Pochini, John Waldron, Eugene Yu, Andrea McNiven, Winson Y. Cheung, Marc Gaudet, Sarah Hunter, Bingshu E. Chen, Wendy R. Parulekar; Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada; BC Cancer, Vancouver, BC, Canada; Cancer Care Manitoba, Winnipeg, MB, Canada; Department of Otolaryngology-Head & Neck Surgery/Surgical Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada; Sunnybrook Health Science Centre, Toronto, ON, Canada; Joint Department of Medical Imaging, University Health Network, Toronto, ON, Canada; BC Cancer Agency, Vancouver, BC, Canada; Eastern Health, St. John's, NL, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Radiation Medicine Program Princess Margaret Cancer Centre, Toronto, ON, Canada; Ottawa Hospital Research Institute, Ottawa, ON, Canada; Canadian Cancer Trials Group, Kington, ON, Canada; Canadian Cancer Trials Group, Kingston, ON, Canada

Background: Treatment for HPV positive(+) oropharyngeal squamous cell carcinoma (OSCC) is highly effective but associated with significant short and long term treatment related morbidity. We hypothesize that decreasing the regions of elective nodal irradiation (ENI) in the neck will lead to less toxicity and better quality of life/functional outcomes while maintaining high disease control rates in patients with favourable prognosis HPV+ OSCC. **Methods:** HN.10 is a Canadian Cancer Trials Group phase II trial with a primary objective to evaluate the efficacy of primary definitive radiotherapy (RT) or chemoradiotherapy (CRT) utilizing volume reduced ENI as measured by 2-year event-free survival (EFS) in patients with low-risk HPV+ OPSCC. Secondary objectives include to evaluate overall survival, local control, regional control, locoregional control, out-of-field regional control, distant metastasis free survival, early and late toxicities of treatment, subjective swallowing functions, quality of life, utilization of healthcare resources, work productivity, and prognostic biomarkers. An imaging and biospecimen bank will be compiled as part of trial conduct. Key eligibility criteria include: pathologically proven diagnosis of HPV+ OPSCC; HPV association determined locally by either p16 immunohistochemistry or direct detection of HPV DNA sequences (e.g. by PCR or in situ hybridization) performed on a core needle or surgical biopsy specimen of the primary tumour or involved cervical lymph node; clinical stage T1-3 N0-1 M0 (UICC/AJCC 8th Ed.); fit for radiotherapy +/-chemoradiotherapy. Statistical Design: The primary endpoint is 2-year EFS. Assuming 2-year EFS to be 91% (Ha) for low-risk HPV-related OPSCC with standard treatment, and that the experimental treatment will be considered as ineffective if the 2-year EFS is $\leq$ 85% (H0), with one-sided alpha of 0.1, a sample size of 100 patients will have 80% power to detect a 6% difference of 2-year EFS. With 3 years of accrual and 2 years of follow-up, the total duration of this study will be 5 years. A total of 304.7 person-years of follow-up is needed for the final analysis. The null hypothesis (H0) will be rejected when the observed survival rate is 88.85% or higher (i.e. if there are 18 or fewer EFS events observed). Conduct to Date: Study activation February 20, 2019. Enrollment as of January 29 2020: 23. Clinical trial information: NCT03822897. Research Sponsor: CIHR Project Scheme.

TPS6593 **Poster Session (Board #254), Fri, 8:00 AM-11:00 AM**

The AIM-HN and SEQ-HN study: A pivotal study evaluating the efficacy of tipifarnib in patients with head and neck squamous cell carcinoma (HNSCC) with *hras* mutations (AIM-HN) and the impact of *hras* mutations on response to first line systemic therapies for HNSCC (SEQ-HN).

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Background: *HRAS* mutations define a unique molecular subset of ~ 5% of HNSCC. Evidence suggests that these tumors respond poorly to standard systemic therapy but the impact of *HRAS* missense mutations on clinical outcomes has not been formally characterized. Tipifarnib is a potent and selective inhibitor of farnesyltransferase, a critical enzyme for *HRAS* activity. Phase 2 Proof of concept for tipifarnib in *HRAS* mutant HNSCC was recently achieved in study KO-TIP-001 (NCT02383927, Ho et. al. ESMO 2018). **Methods:** The AIM-HN and SEQ-HN Study (KO-TIP-007, NCT03719690) is an ongoing international, multicenter, open-label, 2 cohort (AIM-HN and SEQ-HN), pivotal trial designed to determine the Overall Response Rate (ORR) of tipifarnib in patients (pts) with *HRAS* mutant HNSCC (AIM-HN). SEQ-HN will retrospectively investigate how the ORR to first line treatment compares between the accrued *HRAS* mutant pts to matched-case control *HRAS* wild type (wt) HNSCC pts. Information on subsequent lines of therapy for *HRAS* mutant and wt pts will also be collected. AIM-HN will enroll at least 59 pts (oral cavity, pharynx, larynx, sinonasal, nasopharyngeal, or unknown primary) who are refractory or have relapsed from at least one prior line of systemic platinum-based therapy and have measurable disease by RECIST 1.1. AIM-HN pts must have tumors with >35% *HRAS* mutant variant allele frequency (VAF) or >20% VAF if serum albumin is >3.5 g/l. AIM-HN pts will receive treatment with tipifarnib at 600 mg bid on days 1-7 and 14-21 of 28-day cycles. Using Simon's Two-Stage Minimax design, if true ORR is > 30%, the study will have 80% power to detect ORR > 15% at 0.025 significance level. Both interim (after first 31 pts) and final analysis, 2-sided 95% CI on ORR, will be performed on the modified intent to treat population. The SEQ-HN observational cohort will enroll ~225 control pts who will receive standard of care treatment. A subset of SEQ-HN pts will be matched to the *HRAS* mutant AIM-HN pts according to defined patient characteristics and compared for responses to therapy. Clinical trial information: NCT02383927. Research Sponsor: Kura Oncology.

TPS6594 **Poster Session (Board #255), Fri, 8:00 AM-11:00 AM**

Randomized, phase II study of ficlatuzumab with or without cetuximab in patients with pan-refractory, recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC).

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Background: Patients with pan-refractory R/M HNSCC, with clinical resistance to cytotoxic therapy, anti-EGFR molecular targeting, and immunotherapy, have poor survival. An established tumor-intrinsic resistance mechanism to cetuximab, an anti-EGFR IgG1 monoclonal antibody (mAb), is activation of the hepatocyte growth factor (HGF)/cMet pathway, which converges with the EGFR network at both the PI3K/Akt and MAPK nodes allowing for reciprocal compensation. Moreover, over-expression of HGF in the tumor microenvironment is immunosuppressive. Convergent data suggest that HGF/cMet pathway inhibition concurrent with EGFR blockade may overcome cetuximab resistance. We previously reported a Phase I study of ficlatuzumab, a humanized anti-HGF IgG1 mAb, with cetuximab in cetuximab-resistant R/M HNSCC. The combination showed promising safety, overall response rate (ORR) and progression-free survival (PFS). Preliminary biomarker analyses showed that high circulating cMet was associated with poor PFS whereas serum Veristrat, a proteomic classifier associated with worse prognosis in the setting of anti-EGFR monotherapy, was not. An increase in total peripheral T cells, particularly the $CD8^+$ subset, was associated with treatment response while progression was associated with expansion of a unique myeloid population. We designed a follow-on randomized phase II trial evaluating ficlatuzumab with or without cetuximab in pan-refractory, R/M HNSCC with signaling and immune correlatives. **Methods:** This is a multicenter phase II trial with a randomized, non-comparative, two-arm design (ficlatuzumab 20 mg/kg with or without cetuximab 500 mg/m^2 every 2 weeks) in patients with pan-refractory R/M HNSCC. Key eligibility criteria include: R/M HNSCC; cetuximab resistance (progression during or within 6 months of cetuximab-radiation or palliative cetuximab); platinum resistance; prior exposure to anti-PD1 mAb; ECOG 0-1; consent to baseline research biopsy. The primary objective is to evaluate the efficacy of each arm as measured by PFS. To test the hypothesis that either regimen improves historical PFS from 2 to 3.33 months requires 66 eligible patients. Key secondary endpoints are ORR and survival. Mechanistic biomarkers include tumor HGF/cMet pathway activation, tumor and peripheral immune profiles, soluble cMet, and serum Veristrat. Thirty-five of 66 subjects have enrolled at 6 centers. A Bayesian continuous monitoring rule for futility has not been triggered for either arm. Clinical trial information: NCT03422536. Research Sponsor: Aveo.

TPS6595 **Poster Session (Board #256), Fri, 8:00 AM-11:00 AM**

Window-of-opportunity trial of nivolumab with or without the IDO inhibitor BMS-986205 in patients with resectable squamous cell carcinoma of the head and neck (SCCHN).

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Background: Indoleamine 2,3-dioxygenase (IDO1) catabolizes tryptophan to kynurenine and is highly expressed in multiple malignancies including SCCHN. Elevated IDO1 activity may contribute to an immunosuppressive tumor microenvironment and compromise therapeutic responses to immune checkpoint therapy. We designed a window-of-opportunity trial to test whether the IDO inhibitor BMS-986305 improves treatment responses and T cell function in SCCHN patients treated with nivolumab. **Methods:** Patients with previously untreated, resectable, pathologically confirmed SCCHN are eligible. Primaries of the oral cavity, oropharynx, larynx, hypopharynx, or nasal cavity/paranasal sinuses must be AJCC 8^{th} edition stage II or higher (M0). Stage I oropharyngeal cancers with lymphadenopathy are also eligible. Patients are randomized 3:1 to receive either A) nivolumab 480 mg IV x 1 plus BMS-986205 100 mg PO daily starting a week prior to nivolumab and continuing for 4 more weeks (total of 5 weeks) or B) nivolumab 480 mg IV alone for 4 weeks. At the 5^{th} week of treatment patients are assessed for response with physical exam and repeat CT scans for tumor volumes: if there is greater than 10% reduction in volume of either primary tumor or lymph node metastases, patients will be considered responders and receive another cycle of their originally assigned treatment, i.e. nivolumab 480 mg IV for a second dose +/- BMS-986205 100 mg PO daily for an additional 4 weeks followed by surgery in week 9. If tumor volume is stable or progression is noted in either the primary site or lymph nodes, patients are considered non-responders followed by definitive surgery in week 5 (i.e. after only one cycle of treatment). The primary endpoint of this study is the response rate after cycle 1 (using the criteria defined above). The projected sample size is 48 patients (36 in arm A and 12 in arm B). Secondary endpoints include safety, pathologic treatment effect and metabolic and molecular correlates of treatment in the tumor microenvironment. Clinical trial information: NCT03854032. Research Sponsor: Bristol Myers Squibb.

TPS6596 **Poster Session (Board #257), Fri, 8:00 AM-11:00 AM**

ROMAN: Reduction in oral mucositis with avasopasem manganese (GC4419)–Phase III trial in patients receiving chemoradiotherapy for locally advanced, nonmetastatic head and neck cancer.

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Background: Approximately 70% of patients receiving intensity-modulated radiotherapy (IMRT) plus cisplatin for locally advanced head and neck cancer (HNC) develop SOM, defined as WHO Grade 3 or 4, which limits patients' ability to eat solids (Gr 3) or liquids (Gr 4, requiring enteral nutrition). An RT-induced burst of superoxide initiates oral mucositis (OM) development. GC4419, a superoxide dismutase mimetic, interrupts this process by converting superoxide to H2O2. It showed promising reduction of SOM in a published open-label Phase 1b/2a trial (IJROBP 1 Feb 2018). In a subsequent randomized, double-blind placebo-controlled trial in 223 patients receiving IMRT/cisplatin for HNC (ASCO 2018), 90 mg of GC4419 administered M-F prior to IMRT demonstrated statistically significant reduction in SOM duration (p=0.024, median 1.5 days @ 90 mg vs. 19 days placebo) and meaningful reductions @ 90 mg in SOM incidence (43% vs. 65%) and severity (incidence of Grade 4, 16% vs. 30%). The safety results were acceptable and consistent with the known toxicities of IMRT/cisplatin.
Methods: 335 patients at multiple centers in the U.S. and Canada with locally-advanced, nonmetastatic head and neck cancer (oral cavity/oropharyngeal) receiving 70 Gy IMRT (>50 Gy to > 2 oral sites) plus cisplatin (40 mg/m2 qwk x 6-7, or 100 mg/m2 q3wk x 3) are being randomized (double-blinded) 3:2 to 90 mg of GC4419 or placebo, M-F before each RT fraction. Enrollment is stratified by cisplatin schedule and treatment setting (definitive vs. post-op). OM by the WHO scale will be assessed twice weekly during RT & weekly for 2 weeks post RT. The primary efficacy endpoint is incidence of SOM through the end of IMRT. Secondary efficacy endpoints include severity (incidence of Grade 4 OM through the end of IMRT), & days of SOM (days from first to last SOM for all patients, with patients never developing SOM having 0 days of SOM by definition). Days of SOM for the subset developing SOM will be analyzed descriptively. Patients will be followed for one year post IMRT for tumor progression/recurrence and for two years for survival. Clinical trial information: NCT03689712. Research Sponsor: Galera Therapeutics, Inc.

TPS6597 **Poster Session (Board #258), Fri, 8:00 AM-11:00 AM**

A phase II open-label, multicenter, study to evaluate the efficacy and safety of rivoceranib in subjects with recurrent or metastatic adenoid cystic carcinoma.

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Background: Adenoid cystic carcinoma (ACC) is a rare salivary gland malignancy, also found in other secretory gland sites (tracheobronchial tree, esophagus, breast, lungs, prostate, uterine cervix and vulva). Initial disease is typically treated with surgical resection and radiation, but recurrent or metastatic disease remain to be a significant challenge. There is no standard systemic therapy option for advanced ACC, although recent studies with tyrosine kinase inhibitors have shown moderate objective response and disease stabilization rates. Rivoceranib (also known as apatinib) is a potent selective inhibitor of VEGFR-2 and has been evaluated in a single arm phase II study of 59 recurrent or metastatic ACC patients in China and has demonstrated an (ORR) of 47.1% and disease control rate of 98.1. **Methods:** This is a phase II, open-label, multicenter[HGJ3], single arm clinical trial of oral rivoceranib (700 mg daily) in patients with recurrent or metastatic ACC of any anatomic site, not amenable to curative surgery or radiotherapy to confirm activity of rivoceranib. Subjects must have at least one evaluable lesion by RECIST v1.1 and have evidence of disease progression within the 6 months prior to study entry. Fifty-five subjects will be enrolled at 7 US sites and 4 South Korean sites. The primary endpoint is ORR assessed by investigators with a target ORR of 25% to detect a difference of 15% from the historical ORR of 10% at 1-year (this achieves 80% power with a 5% significance level). Secondary endpoints include overall survival, disease control rate, progression free survival at 6, 12 and 24 months and time to progression. Exploratory objectives include correlation between ORR and the presence of MYB/MYB-L1 fusion, pharmacokinetics evaluation, and patient-reported quality of life assessments by FACT-G. This study is open and enrolling at the time of submission. References: 1. Tchekmedyian V, Sherman EJ, Dunn L, et al. Phase II Study of Lenvatinib in Patients With Progressive, Recurrent or Metastatic Adenoid Cystic Carcinoma. Journal of clinical oncology: official journal of the American Society of Clinical Oncology 2019;37:1529-37. 2. Zhu G, Zhang L, Li R, Dou S, Yang W, Zhang C. Phase II trial of apatinib in patients with recurrent and/or metastatic adenoid cystic carcinoma of the head and neck: Updated analysis. Journal of Clinical Oncology 2018;36:6026. Clinical trial information: NCT04119453. Research Sponsor: Elevar therapeutics.