

Efficacy of cabozantinib (Cabo) in medullary thyroid cancer (MTC) patients with RAS or *RET* mutations: Results from a phase III study.

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Background: Cabo extends progression-free survival (PFS) in patients (pts) with progressive, metastatic MTC (Schöffski, *J Clin Oncol* 30, 2012). Mutations in the *RET* oncogene are associated with most hereditary cases and ~half of sporadic cases of MTC. RAS gene mutations have recently been identified in subsets of *RET* wild type (wt) cases. Therefore, we investigated the association of *RET* (a prospectively defined endpoint) and RAS mutations (a post hoc analysis) with efficacy outcomes in the phase 3 study of cabo in MTC. **Methods:** Pts enrolled into the double-blind, placebo-controlled phase III trial were evaluated for the presence of somatic and germline *RET* mutations using Sanger and next generation methods. A subset of pts determined to be *RET* wt (44 pts) or *RET* unknown (41 pts) were then evaluated for tumor-associated mutations in *KRAS*, *NRAS*, and *HRAS* in codons 12, 13, and 61 by next generation sequencing. Impact of *RET* and RAS gene mutation status was evaluated with respect to PFS and tumor response rate (RR) according to RECIST. **Results:** *RET* status was determined in 65% of the study pts (215/330), of which 79% harbored an activating mutation, and 21% were *RET* wt. All *RET* mutational subgroups (*RET* mutated, *RET* wt, and *RET* unknown) showed hazard ratios indicating PFS benefit from cabo treatment, and demonstrated RRs between 22% and 32%. However pts harboring a *RET* mutation had longer median PFS on cabo (60 wks) than pts with wt *RET* (25 wks, PFS difference p=0.0001). Also, pts with the poor prognosis mutation *RET* M918T showed a longer median PFS on cabo treatment (61 wks) than pts with any other *RET* mutation (36 wks, PFS difference p=0.009). Patients with hereditary MTC had similar PFS to those with sporadic disease, and the presence of the common *RET* polymorphism G691S had no effect on either PFS or RR. Sixteen of 85 tested pts (5% of total study pts) with wt or unknown *RET* status were found to harbor a RAS gene mutation. The RAS-mutated pts showed a similar RR (31%) and PFS (47 wks) as *RET* mutated pts (32% and 60 wks). **Conclusions:** While hazard ratios indicate PFS improvement for all *RET* subgroups on cabo, the extent of benefit may depend in part on *RET* genotype. Cabo treatment benefit is also seen in pts harboring a RAS mutation. Clinical trial information: NCT00704730.

A randomized, open-label, phase II study of afatinib versus cetuximab in patients (pts) with recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC): Analysis of stage 2 (S2) following crossover.

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Background: This open-label trial assessed the efficacy of the irreversible ErbB Family Blocker afatinib (A) vs cetuximab (C) in R/M HNSCC pts following failure of platinum-containing therapy. In Stage 1 (S1), A and C had confirmed objective response rates (RECIST 1.0) of 16.1% vs 6.5% by investigator review (8.1% vs 9.7% independent central review [ICR]; Seiwert TY, *et al.* MHNCS 2012. Abs 235). S2 data after crossover are presented. **Methods:** In S1, pts were randomized 1:1 to oral A 50 mg/day or IV C 250 mg/m²/wk (400 mg/m² IV loading dose) until progressive disease (PD) or intolerable drug-related adverse events (DRAEs). Pts could then crossover to the other treatment arm (S2), with treatment given until further PD or intolerable DRAEs. Tumor response in S2 (RECIST 1.0) was evaluated at 4 wks after crossover and every 8 wks thereafter. **Results:** 56% of pts crossed over into S2: 32 from A to C and 36 from C to A. Of these, 88% crossed over after PD and 12% after intolerable DRAEs. Baseline characteristics of S2 pts were similar in the A and C groups and treatment duration in S1 prior to crossover was comparable (A: 3.7 [0.2–15.7] months; C: 3.5 [0.0–12.5] months). Median treatment duration in S2 was 2.1 (0.0–7.6) months for A and 1.2 (0.0–9.9) months for C. Tumor size decreases of ≥30% were observed in 1 pt in each treatment group (ICR). The disease control rate (DCR) for A was 33% vs 19% for C and the median progression-free survival time was 9.3 wks for A and 5.7 wks for C (ICR). The most frequently reported DRAEs (≥20%) for A were rash/acne (56%), diarrhea (53%) and stomatitis (22%), and for C was rash/acne (44%). DRAEs of ≥Grade 3 were seen in 47% of pts treated with A and 16% of pts treated with C. 12 A-treated patients had dose reductions to 40 mg and 1 pt had a further dose reduction to 30 mg; no C-treated pts had dose reductions. **Conclusions:** R/M HNSCC pts seem to benefit from sequential therapy with A/C or C/A, especially when using A treatment after C failure. Cross resistance is not universally present and further investigation of sequential treatment is warranted. Clinical trial information: NCT00514943.

Sym004, a novel strategy to target EGFR with an antibody mixture, in patients with advanced SCCHN progressing after anti-EGFR monoclonal antibody: A proof of concept study.

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Background: Sym004 is a first-in-class drug mixture of two mAbs targeting non-overlapping epitopes on the EGFR. In preclinical models, Sym004 exhibited more pronounced EGFR internalization, degradation and tumor growth inhibition than cetuximab. Sym004 was investigated as monotherapy in palliative squamous cell carcinoma of the head and neck (SCCHN) patients (pts). **Methods:** SCCHN pts progressing after anti-EGFR mAbs for palliation were eligible. Documented clinical benefit (PR, CR or SD for at least 8 weeks according to RECIST) on an anti-EGFR mAb-containing regimen followed by disease progression during or within 12 weeks after treatment cessation was required. The primary endpoint of this multicentre single arm trial was centrally evaluated progression-free survival (PFS), estimated by median PFS and 24 week progression free rate. Secondary endpoints included objective tumor response, safety, biomarkers and pharmacokinetics. Pts received weekly iv infusions of 12 mg/kg Sym004 until disease progression. Tumor evaluation was performed week 6, 12 and every 8 weeks thereafter. **Results:** Based on the statistical hypothesis, 26 pts were included, of whom 23 had progressed while on anti-EGFR mAb treatment. One of 19 evaluable pts was HPV positive and no EGFRvIII mutation was detected in 21 evaluable pts. No anti-drug antibodies were detected. Independent central review of CT/MRI scans from 20 evaluable pts showed tumor shrinkage in 8 pts (% decrease in sum of the largest diameters: 6.5, 7.1, 9.6, 10.2, 11.3, 13.6, 16.7, 27.1) and 14 pts had SD as best overall response. Median PFS was 82 days (95% CI: 41, 140) and 24 week progression free rate was 12% (95% CI: 1, 39). During treatment 25/26 (96%) pts developed skin rash with \geq grade 3 reported in 11/26 (42%) pts. Hypomagnesemia \geq grade 3 was reported in 10/26 (38%) pts. Sym004 treatment resulted in a marked down regulation of EGFR in centrally reviewed biopsies from skin and tumors. **Conclusions:** Sym004 demonstrated clinical activity in heavily pretreated, predominately HPV negative pts with advanced SCCHN previously progressing on or after anti-EGFR mAbs. No unexpected toxicities were reported. Clinical trial information: NCT01417936.

A phase II-III study comparing concomitant chemoradiotherapy (CRT) versus cetuximab/RT (CET/RT) with or without induction docetaxel/cisplatin/5-fluorouracil (TPF) in locally advanced head and neck squamous cell carcinoma (LASCCHN): Efficacy results (NCT01086826).

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Background: This is the first phase III study directly comparing CRT vs CET/RT in LASCCHN. Primary endpoints of this study were to compare: 1) overall survival (OS) of induction vs. no induction arms; 2) Grade 3-4 in-field toxicity of CRT vs. CET/RT. Preliminary toxicity results of concomitant treatments (primary endpoint for this comparison) were reported at the 2012 ASCO meeting. Here we present response rate and survival data for the two concomitant treatments (CRT vs. CET/RT), irrespective of induction chemotherapy. **Methods:** Untreated patients with unresectable LASCCHN, stage III-IV, ECOG PS 0-1 were randomized to a 2x2 factorial design: *Arm A1:* CRT (2 cycles of cisplatin/5fluorouracil concomitant to RT); *Arm A2:* CET/RT; *Arm B1:* 3 cycles of TPF followed by the same CRT; *Arm B2:* 3 cycles of TPF followed by CET/RT. **Results:** A total of 421 patients were randomized: 261 received CRT (131 *Arm A1* + 130 *Arm B1*) and 160 received CET/RT (80 *Arm A2* + 80 *Arm B2*). 82% were male; median age was 60y; PS of 0 (79%) or 1 (21%). Stage was III (32%) or IV (68%). Sites of disease were: oral cavity 20%, oropharynx 57%, hypopharynx: 23%. No significant differences were observed in patients' characteristics distribution. At a median follow-up of 32.9 months, a total of 174 deaths occurred (204 required for final OS analysis). Data on activity and efficacy of CRT and CET/RT are shown in the Table. **Conclusions:** No significant differences were observed in response rate, progression free survival and OS between CRT and CET/RT. Pts are still being followed-up to assess OS of induction vs. no induction arms. Clinical trial information: NCT01086826.

	CRT	CET/RT	HR (95% CI)
Complete response	36%	39%	-
Partial response	47%	49%	-
Complete + partial response	83%	88%	-
Stable disease	9%	6%	-
Progressive disease	8%	6%	-
Median PFS (ITT analysis) – months	21.6	20.7	1.05 (0.80-1.39)
Median OS (ITT analysis)-months	44.7	44.7	0.86 (0.62-1.19)

Adjuvant chemotherapy with S-1 after curative treatment in patients with head and neck cancer (ACTS-HNC).

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Background: To establish the efficacy of adjuvant chemotherapy with S-1 (tegafur gimeracil oteracil potassium) after curative treatment in patients with advanced squamous cell carcinoma of the head and neck (SCCHN), we conducted a randomized phase III study to investigate whether S-1 is superior to UFT (uracil/tegafur). **Methods:** Patients with SCCHN who had received curative treatment and were confirmed to be tumor-free were randomly assigned to receive UFT (300 or 400 mg/day for 1 year) or S-1 (80, 100, or 120 mg/day for 1 year). The primary end point was disease-free survival (DFS). Secondary end points were overall survival (OS), relapse-free survival (RFS), and safety. We estimated that 500 patients were needed to establish the primary end point. **Results:** From April 2006 through November 2008, a total of 526 patients (262 assigned to UFT; 264 assigned to S-1) were enrolled. The 3-year DFS rate was 66.0% in the UFT group and 64.1% in the S-1 group (hazard ratio [HR], 0.87; 95% confidence interval [CI], 0.66 to 1.16; [log-rank], $P = .34$). The 3-year OS rate was 75% in the UFT group and 82.9% in the S-1 group (HR, 0.64; 95% CI, 0.44 to 0.94; [log-rank], $P = .022$). The 3-year RFS rate was 63.6% in the UFT group and 68.2% in the S-1 group (HR, 0.81; 95% CI, 0.60 to 1.09; [log-rank], $P = .16$). There were no significant differences in 3-year DFS or RFS; however, the 3-year OS was significantly better in the S-1 group. The incidence of the following grade 3 or 4 events was significantly higher in the S-1 group: oral mucositis/stomatitis (2.4%), leukopenia (5.2%), neutropenia (3.6%), and thrombocytopenia (5.0%). **Conclusions:** S-1 was not demonstrated to be superior to UFT in terms of 3-year DFS; however, 3-year OS was significantly better with S-1 than with UFT. Clinical trial information: NCT00336947.

E 1308: A phase II trial of induction chemotherapy (IC) followed by cetuximab with low dose versus standard dose IMRT in patients with human papilloma virus (HPV)-associated resectable squamous cell carcinoma of the oropharynx (OPSCC).

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Background: HPV is associated with 60-80% of OPSCC. E2399 results showed IC followed by (f/b) paclitaxel (P)/3D RT (70Gy) improved 2-yr progression-free (PFS) for HPV+ compared to HPV- OPSCC. We studied a regimen with 20% radiation dose reduction to 54Gy in HPV + OPSCC patients (pts) with a clinical complete response (CCR) to IC. **Methods:** Stage III/IVA,B resectable HPV+ OPSCC were included. Eligible pts received IC q3 week x 3 with P 90mg/m² days (D) 1,8, 15, cisplatin (CDDP) 75mg/m² D1, and cetuximab (C) 400 mg/m² D1, cycle 1 f/b C 250 mg/m² weekly. Primary tumor and involved nodal response to IC were determined independently. Pts received IMRT 54Gy/27 fxs with weekly C for CCR vs. 69.3Gy/33 fxs with weekly C if <CCR. Primary endpoint was 2-year PFS; secondary endpoints were toxicity, OS, response rate, QOL and correlative biomarkers. **Results:** From March 2010 to Oct 2011, 90 pts were enrolled (80 analyzable). Median age was 57 years, 95% men, 93% Caucasian, 91% PS 0, 46% never smokers, 84% not current smokers. Nodal stage: 39%-N2B, 29%-N2C, T stage: 23%-T1, 50%-T2, 16%-T3, 10%-T4. 96% received all 3 cycles of IC. Grade 3/4 toxicities included: rash (25%), neutropenia (11%). During CRT: oral mucositis (31%), dysphagia (17%), radiation dermatitis (8%). Response: Biopsy at primary site post-baseline measurements rendered 7/80 pts unevaluable (UE), 6/7 had investigator-reported CCR to IC. The centrally reviewed and investigator reported primary site CCR rate to IC was 63.8% (95% CI: 52.2%, 74.2%) and 71.3% (95% CI: 60.0%, 80.8%), respectively. Radiation: 73.8% (59/80 pts) received low dose IMRT/C to primary [54Gy (56), 52Gy (1), 40Gy (2)]. Best overall clinical response was 86% (CR +PR+SD) with 14% UE. Rate of post-treatment neck dissection in low dose vs other RT gp is 13.4% vs 22.2% (p value of 0.46), respectively. Median follow up is 11.8 months. **Conclusions:** Overall, IC with P, CDDP and C f/b low dose RT with C was well tolerated, with all pts responding and very low grade 3/4 toxicities. Data on PFS are premature. A 2 year PFS of 85% or better will be considered worthy of further study. Clinical trial information: NCT01084083.

Analysis of HPV and ERCC1 in recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN).

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Background: We studied the association of human papillomavirus (HPV) and excision repair cross-complementation group 1 (ERCC1) tumor expression with clinical outcomes in patients (pts) with R/M SCCHN. **Methods:** Archival baseline specimens were obtained from pts on ECOG trials: E1395, phase III trial of cisplatin/paclitaxel (CP) vs. cisplatin/5-FU (CF), and E3301, phase II trial of docetaxel/irinotecan. HPV DNA was detected by in situ hybridization (ISH) with a wide spectrum HPV probe. Tumor p16 status was defined as positive if immunohistochemical staining for p16 was strong and present in >80% of tumor cells. ERCC1 expression was measured (HistoRx PM-2000) and data analyzed using AQUA algorithms, after tissue was stained with ERCC1 ab (1:5000 HPA0297731, Sigma), and a wide-spectrum cytokeratin ab (Dako Z0622) for tumor mask. A prior determined cut point for nuclear staining was utilized. Fisher's exact test and log-rank test were used to compare categorical variables and survival. Stratified logistic regression and Cox regression model were used to estimate odds ratio (OR) and hazard ratio (HR), respectively, adjusting for potential confounding factors. p-values were two-sided. **Results:** Tissue was evaluable from 65 tumors (T) for HPV, 66 for p16 (E1395 and E3301), and 43 for ERCC1 expression (E1395). 11 T were HPV+ (12 p16+), and 54 were HPV-/p16-. HPV+ tumors were similarly represented in all treatment groups (p=0.58). Objective response rates (RR): 67% for HPV+, 22% for HPV- (p=0.013); 60% p16+, 22% p16- (p=0.05). RR rates were calculated excluding cases with unevaluable/unknown responses. HR for OS was 2.66 (HPV, p=0.02) and 2.27 (p16, p=0.04), favoring HPV+/p16+ pts. 18 T were ERCC1 high (H) and 25 ERCC1 low (L). HR for OS (H vs. L) was 1.96 (p=.11) RR: CF, 58% (L), 29% (H); CP, 33% (L), 56% (H). A test of ERCC1 by treatment interaction (p=0.12) suggested the effect of ERCC1 may be different for taxane vs. non-taxane regimens. **Conclusions:** This is the first study to show that HPV+/p16+ status is associated with a significant improvement in RR and OS among pts treated for R/M SCCHN. ERCC1 L was associated with a trend towards a better OS.

p16 expression as a human papillomavirus (HPV)-independent prognostic biomarker in non-oro-pharyngeal squamous cell carcinoma (non-OPSCC).

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Background: p16 is an important tumor suppressor and cell cycle regulator that is commonly lost in HPV-negative (-) and upregulated in HPV-positive (+) OPSCC. While the role of p16 expression in OPSCC as a surrogate marker of HPV infection and its association with prognosis are well established, its significance has not been studied in non-OPSCC including oral cavity, hypopharynx and larynx, where HPV infection is rare. We hypothesize that p16 expression is a prognostic biomarker of favorable outcome (progression-free and overall survival) in non-OPSCC. **Methods:** p16 expression in non-OPSCC from RTOG 0129, 0234 and 0522 was determined by immunohistochemistry (p16 mouse monoclonal antibody, prediluted, MTM-CINtech, 9518) and considered positive if >70% of the tumor cells demonstrated diffuse staining. The high risk HPV status in non-OPSCC from RTOG 0129 and 0522 was determined by in situ hybridization using a cocktail probe including HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 66. Hazard ratios from Cox models were expressed as positive/negative, stratified by trial, and adjusted for age, gender, T, and N stage. **Results:** p16 expression was positive in 14.1% (12/85), 24.2% (23/95) and 19.0% (27/142) of non-OPSCC from RTOG 0129, RTOG 0234, and RTOG 0522, respectively. HPV ISH was positive in 6.5% (6/93) and 6.9% (7/101) of non-OPSCC from RTOG 0129 and RTOG 0522, respectively. There was moderate agreement between p16 and HPV status ($\kappa=0.53$). The hazard ratios for p16 expression are 0.63 ($p=0.03$) and 0.56 ($p=0.01$) for PFS and OS, respectively. In 0522, there was no interaction between p16 status and two treatment arms (RT+cisplatin+/-cetuximab). In comparison of OPSCC and non-OPSCC, patients with p16(+) OPSCC have better PFS and OS than patients with p16(+) non-OPSCC, but patients with p16(-) OPSCC and non-OPSCC have similar outcomes. **Conclusions:** Similar to results in patients with OPSCC, patients with p16(+) non-OPSCC have better outcomes than patients with p16(-); however, the differential appears smaller than has been observed in HPV(+) OPSCC. Further studies are warranted to delineate the role of p16 expression as a prognostic biomarker in non-OPSCC and OPSCC. Clinical trial information: NCT00265941, NCT00047008, NCT00084318.

Multimodality determination of HPV status in head and neck cancers (HNC) and development of an HPV signature.

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Background: Determination of HPV status is prognostically important, and various testing modalities are commonly used. Discordant results are occasionally observed and a gold standard (for research purposes) is E6/E7 mRNA expression. We aimed to evaluate accuracy of multiple research HPV tests compared to p16 expression/anatomic site, and developed a new HPV signature that we hypothesize will capture HPV-related oncogenic processes independent for all HPV types. **Methods:** HNC samples from 136 patients were evaluated by: 1) nested E6 PCR (DNA) (Sotlar 2004), 2) qPCR for E6, E7 (HPV16), E6, L1 (HPV18) (mRNA), 3) p16 expression by IHC and/or mRNA. Results were correlated with anatomic site. A gene expression (GE) signature was developed based on Agilent 4x44Kv2 data and validated in a second cohort. In equivocal cases mutational status of TP53 was evaluated. **Results:** p16/CDKN2A expression was unreliable outside the oropharynx (OP) (81% false-positives in non-OP tumors, compared to 12% for OP tumors). Anatomic site as described by clinical reports was unreliable. In our cohort, 52 out of 77 OP (67.6%) were HPV positive by DNA and RNA based approaches, 3 only by DNA. DNA and RNA based approaches appeared to be similarly accurate and concordant in 97% of samples. The newly developed HPV-GE signature was highly accurate, and allowed to reconcile discrepant cases, suggesting that the DNA-based approach overcalled HPV(+) in 2 tumors while the RNA based approach underreported HPV status in two cases. Expression levels of E6/E7 mRNA showed extensive variability in HPV(+) samples. Interestingly the HPV-GE signature suggested continuous/overlapping biology for a minority of cases. Two tumors (1 supraglottis/HPV18, 1 oropharynx/HPV16) tested HPV(+) by DNA/RNA, p16/CDKN2A, and HPV-GE signature while at the same time having TP53 mutations. **Conclusions:** p16 should not be used outside the oropharynx and anatomic allocation may also be inaccurate. DNA and mRNA based approaches perform equally well and can be reconciled using the HPV-GE signature. The HPV-GE signature supports the hypothesis that HPV(+) and HPV(-) biology may overlap in a minority of cases.

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Clinical Science Symposium, Mon, 11:30 AM-1:00 PM

The Cancer Genome Atlas: Integrated analysis of genome alterations in squamous cell carcinoma of the head and neck.

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Background: Head and neck squamous cell carcinoma (HNSCC) is a leading cause of cancer death in worldwide. **Methods:** The Cancer Genome Atlas (TCGA) is conducting DNA, RNA and miRNA sequencing along with DNA copy number profiling, quantification of mRNA expression, promoter methylation, and reverse-phase protein arrays on surgically resected samples from previously untreated patients with HNSCC. We report for the first time the integrated genomic alterations for 279 HNSCC patients. **Results:** The demographics of 279 patients enrolled in the study show a median age of 61 years (range: 19-90); 27% female, and history of tobacco smoking in 80%. Over 30 sites of significant somatic copy number alteration were identified as well as 15 significantly mutated genes at the false discovery rate of <0.01, including: CDKN2A, TP53, PIK3CA, FAT1, MLL2, TGFBR2, HLA-A, NOTCH1, HRAS, NFE2L2, and CASP8. Evidence of the human papilloma virus (HPV) was observed by sequencing in up to 25% of samples. Integrated genomics data supported expected patterns including the predominant role of HPV type 16 infection in nonsmoking patients with tumors of the oropharynx which are wild-type for the tumor suppressor genes p16, Rb, and p53. In addition, striking atypical cases and viral infections will be presented as well as novel anti-correlation of HPV infection with focal copy number alterations including EGFR amplification and chromosome 11q. By contrast co-occurrence of HPV with focal deletions of TRAF3 and mutations of the oncogene PIK3CA will be described. Integrated tumor subtypes defined by gene expression, methylation, and miRNA will be presented in conjunction with associated mutations exclusive to tumor subtypes. For example, alterations of the “antioxidant response elements” transcription activators NFE2L2 and KEAP1 will be documented in association with the “classical” expression subtype of HNSCC, as has been shown in lung squamous cell carcinoma. By contrast, co-occurrence of CASP8 and HRAS will be documented in the “Basal” subtype. **Conclusions:** While, HNSCC is a heterogeneous tumor, coordinated tumor alterations are observed, including potentially targetable genes and pathways. Results presented on behalf of TCGA.

6010

Clinical Science Symposium, Mon, 11:30 AM-1:00 PM

Genomic profiling of kinase genes in head and neck squamous cell carcinomas to identify potentially targetable genetic aberrations in FGFR1/2, DDR2, EPHA2, and PIK3CA.

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Background: Development of targeted therapies in head and neck squamous cell carcinoma (HNSCC) has been limited due to the lack of validated, oncogenic genetic aberrations. We determined mutations and copy number (CN) events in kinases in a 120 patient cohort in order to identify new potential treatment targets. **Methods:** Fresh frozen tumor ($\geq 70\%$) and matched normal tissue from 120 patients with treatment-naïve, locoregionally advanced HNSCC were evaluated using targeted, massively parallel sequencing (Illumina HiSeq) for 60 cancer-relevant, targetable kinases (as well as PI3K related tumor suppressors). CN analysis was performed on the NanoString nCounter for 40 cancer relevant kinases. Mutations were modeled bioinformatically using the CHASM oncogenic driver prediction algorithm and reviewed for prior occurrence in COSMIC. **Results:** We identified somatic mutations in three potentially targetable receptor tyrosine kinases: 7 (5.8%) mutations were identified in DDR2, 3 (2.5%) mutations in FGFR2, and 4 (3.3%) mutations in EPHA2. Furthermore we identified multiple mutations in several PI3K family members including PIK3CA (N=22 (18.3%)) as well as PI3K related tumor suppressors (PTEN N=3 (2.5%)), INPP4B N=7 (5.8%)). Several mutations showed low CHASM scores consistent with oncogenic driver characteristics. We identified recurrent copy number aberrations in two kinases – FGFR1 (N=15 (13%), median CN:3.27 (3.03-15.662)), and EGFR (N=13 (11%), median CN: 3.73 (2.93-17.75)). Interestingly similar mutations/copy number events have been described in other cancer types including endometrial, and lung squamous cell carcinomas. **Conclusions:** We identified multiple novel mutations and copy number events in 45% of tumors: genetic aberration in FGFR1, FGFR2, DDR2, EPHA2, and the PI3K pathway are candidate oncogenic drivers that are potentially targetable. Results are corroborated by similar aberrations in other cancer types e.g. lung squamous cell carcinomas that are already being explored as therapeutic targets. Further validation and initiation of focused clinical trials in mutation pre-selected patients is indicated.

An epithelial-mesenchymal transition (EMT) gene signature to predict resistance to EGFR inhibition and AXL identification as a therapeutic target in head and neck squamous cell carcinoma.

Robert Cardnell, Lixia Diao, Jing Wang, David Bearss, Steven Warner, You Hong Fan, Uma Giri, Michael D. Story, John N. Weinstein, Kevin R. Coombes, Michelle D. Williams, The Cancer Genome Atlas Research Network, Ignacio Ivan Wistuba, Gordon B. Mills, Jeffrey Myers, William Nassib William, K. Kian Ang, John Heymach, Lauren Averett Byers; The University of Texas MD Anderson Cancer Center, Houston, TX; Tolero Pharmaceuticals, Inc, Salt Lake City, UT; The University of Texas Southwestern Medical Center, Dallas, TX; Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX; The Cancer Genome Atlas Research Network, Houston, TX

Background: Epithelial-mesenchymal transition (EMT) has been associated with EGFR inhibitor resistance in preclinical studies of head and neck squamous cell carcinoma (HNSCC). Recently, we developed an EMT signature that predicts EGFR inhibitor resistance in lung cancer. Using this signature, we explored the association between EMT and drug response in HNSCC, focusing on the tyrosine kinase Axl as a potential therapeutic target. **Methods:** We conducted an integrated molecular and drug response analysis in HNSCC. A 76-gene EMT signature previously developed and validated in lung cancer was tested in HNSCC cell lines (n>50) and patient tumors from The Cancer Genome Atlas (TCGA) (n=113) and a MDACC cohort (n=105). Reverse phase protein array (RPPA) and proliferation assays were used to measure protein expression and sensitivity to erlotinib and the Axl inhibitors SGI-7079 and TP-0930. **Results:** The EMT signature identified distinct epithelial and mesenchymal subsets of HNSCC among cell lines and patient tumors. RPPA experiments revealed higher protein levels of the receptor tyrosine kinase Axl, vimentin, and N-cadherin and lower expression of E-cadherin and beta-catenin in mesenchymal HNSCC (p-values <0.02). Elevated Axl expression was also associated with significantly shorter overall survival in patients with locally advanced HNSCC (p<0.001 in TCGA cohort; p=0.003 MDACC). Consistent with previous studies, mesenchymal HNSCC cells exhibited resistance to erlotinib (IC₅₀ >10 μ M); however, we discovered that mesenchymal HNSCC were highly sensitive to two Axl inhibitors, SGI-7079 and TP-0930 (IC₅₀s \leq 1.2 μ M and 0.2 μ M, respectively). **Conclusions:** Our EMT gene expression signature identified discrete epithelial and mesenchymal subgroups of HNSCC. Mesenchymal HNSCC cells expressed higher levels of Axl protein and exhibited sensitivity to Axl inhibition, but resistance to erlotinib. These results highlight differences in drug response between epithelial and mesenchymal cancers and support Axl as a potential therapeutic target and predictive marker of EGFR inhibitor resistance in HNSCC. (Funded in part by 5 P50 CA097007-10)

6012

Poster Discussion Session (Board #1), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Effect of PDL-1 expression on prognosis in head and neck squamous cell carcinoma.**

Maria Vasilakopoulou, Vamsidhar Velcheti, Theodoros Rampias, Clarence Sasaki, David Rimm, George Fountzilas, Amanda Psyrri; Yale University, New Haven, CT; Yale Cancer Center, New Haven, CT; Yale School of Medicine, New Haven, CT; Department of Pathology, Yale University School of Medicine, New Haven, CT; Hellenic Cooperative Oncology Group (HeCOG), Athens, Greece; University of Athens, Athens, Greece

Background: The recent demonstration that immunotherapeutic approaches may be clinically effective for cancer patients has renewed the interest for this therapeutic strategy. Engagement of programmed death-1 receptor (PD-1), expressed on activated T-cells, by its ligands, results in a negative regulatory effect, with inhibition of downstream cellular signaling events. Our aim was to investigate the expression and prognostic significance of immunoresistance molecule PDL-1 (the negative regulator programmed death-1-ligand 1) on an annotated HNSCC tissue microarray. **Methods:** A tissue array composed of 400 larynx cancers treated with surgery followed by radiotherapy was constructed. PDL-1 protein expression levels were assessed using automated quantitative protein analysis (AQUA). The objectives of this analysis were to determine the association of PDL-1 with efficacy outcomes (overall survival (OS), progression-free survival (PFS), and event-free survival (EFS)). The univariate and multivariate Cox proportional hazards models were used to evaluate the relationship between PDL-1 and event-time distributions. Event-time distributions were estimated by the Kaplan-Meier method and compared by the log-rank test. **Results:** Mean follow-up time for the entire cohort was 39.34 months. Two-hundred thirty eight of 400 cases had sufficient tissue for AQUA analysis. High tumor PDL-1 expression was associated with favorable outcome for OS (P=0.029) and trended towards improved DFS (P=0.06) at 5 years. In multivariable analysis, adjusting for well-characterized prognostic variables, PDL-1 expression status retained its prognostic significance for OS and there was again a trend for PFS (p=0.05). **Conclusions:** This paradoxical result is in accordance with reported studies in HPV-associated HNSCC where PD-1(+) T cells were associated with favorable clinical outcome. It is possible that PDL-1 detection may reflect a previous immune response against tumors. Further work will determine whether PD-1/PD-L1 blockade induces tumor regression in HNSCC.

6014

Poster Discussion Session (Board #3), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Postoperative detection of circulating EGFR transcripts as a surrogate marker for circulating tumor cells to predict tumor recurrence after adjuvant radio(chemo)therapy in locally advanced squamous cell carcinoma of the head and neck (LASCCHN).**

Inge Tinhofer, Robert Konschak, Carmen Stromberger, Ulrich Keilholz, Volker Budach; Department of Radiooncology CCM/CVK, Charite University Hospital, Berlin, Germany; Department of Hematology and Medical Oncology, Charitè, CBF, Berlin, Germany

Background: The prognostic role of circulating tumor cells (CTCs), occurring in up to 35% of LASCCHN patients, is still largely undetermined. In this prospective study we tested whether the detection of CTCs was associated with treatment outcome of adjuvant radio(chemo)therapy. **Methods:** Patients with LASCCHN (N=64) of the oropharynx (N=40), oral cavity (N=15), hypopharynx (N=3) or CUP (N=6) presenting after tumor surgery for adjuvant treatment were enrolled in this study. Peripheral blood samples were collected before start and at the end of adjuvant radio- (N=22) or radiochemotherapy (N=42). Transcripts of epidermal growth factor receptor (EGFR) were detected using RT-PCR. Samples positive in at least 2 of 3 PCR replicates were considered CTC-positive, according to previous studies. CTC detection was correlated with failure-free (FFS) and overall survival (OS). **Results:** CTCs were detected in blood samples from 21 of 64 patients (33%) whereas all 30 samples from healthy donors used as control were negative. The CTC+ and CTC- patient cohorts were comparable with relation to sex, age, smoking history, T and N stage, tumor localization, type of adjuvant treatment and the median follow-up for OS and FFS. Detection of CTCs before or after adjuvant treatment was not predictive for OS. However, the presence of CTCs at the start of adjuvant radio(chemo)therapy identified patients with reduced FFS (CTC- vs CTC+ [% of patients without relapse at 2 years]: 89% vs. 60%, HR: 0.30, 95% CI: .08-.92, p=.037). Multivariate Cox regression analysis revealed that the prognostic value of the CTC status was not influenced by the T and N stage and independent of whether the adjuvant treatment consisted of radio- or radiochemotherapy. **Conclusions:** Persistence of CTCs after tumor resection as detected by EGFR transcripts was established as an independent marker for tumor recurrence in LASCCHN. Postoperative detection of CTCs might prove useful for risk stratification in future clinical trials for optimization of adjuvant treatment, especially for the poor-prognosis group of CTC+ patients.

6015

Poster Discussion Session (Board #4), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Prognostication of survival from nasopharyngeal carcinoma by reduction of plasma Epstein-Barr viral DNA load at midpoint of radiotherapy course: A new paradigm of prognostication.**

Anthony T. C. Chan, Allen K.C. Chan, Brigitte Ma, Edwin Pun Hui, Frankie Mo, Katherine Chow, Linda Leung, Ka Wah Chu, Benny C.Y. Zee, Dennis YM Lo, Sing Fai Leung; Department of Clinical Oncology, State Key Laboratory of Oncology in South China, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, China; Department of Chemical Pathology, The Chinese University of Hong Kong, Shatin, Hong Kong; The Chinese University of Hong Kong, Prince of Wales Hospital, Sha Tin, Hong Kong; State Key Laboratory in Oncology in South China, Department of Clinical Oncology, The Chinese University of Hong Kong, Shatin, Hong Kong; Department of Clinical Oncology, Prince of Wales Hospital, Chinese University of Hong Kong, Shatin, Hong Kong; The Chinese University of Hong Kong, Hong Kong, China; Department of Clinical Oncology, The Chinese University of Hong Kong, Shatin, Hong Kong; Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong, China; Chinese University of Hong Kong, Shatin, Hong Kong; Department of Chemical Pathology, State Key Laboratory in Oncology in South China, The Chinese University of Hong Kong, Shatin, Hong Kong; Department of Clinical Oncology, Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong, China

Background: To test the hypothesis that prognostication of treatment outcome is feasible by biomarker response at mid-course of chemoradiotherapy (CRT)/ radiotherapy (RT), with respect to the plasma load of Epstein-Barr viral (EBV) DNA in nasopharyngeal carcinoma (NPC). **Methods:** 107 patients with stage IIB-IV NPC were prospectively studied. Plasma EBV DNA load was measured by quantitative PCR before therapy (pre-DNA), at completion of 4 weeks of CRT/RT (mid-DNA), and within 3 months of completion of therapy (post-DNA). The endpoints are post-DNA load, a recognized surrogate of survival, and clinical outcome. **Results:** 93% of patients had detectable EBV DNA before therapy (median load = 972 copies/ml). EBV DNA became undetectable in 55 (51%) patients at the end of week 4 of therapy. Detectable mid-DNA was associated with worse clinical outcome (median follow-up time, 6.2 years), for distant failure (HR 12.02, 95% CI 2.78-51.93; $P < 0.0001$), progression-free survival (HR 4.05, 95% CI 1.89-8.67, $P < 0.0001$), and overall survival (HR 3.29, 95% CI 1.37-7.90, $P = 0.0077$). About three-quarters of all failures were associated with detectable mid-DNA, whereas about one-third of all failures were associated with detectable post-DNA. Patients with detectable mid-DNA which disappeared after RT continued to sustain a less favourable prognosis than those with undetectable mid-DNA. Stratification by tumor stage (II, III, IV) has no significant prognostic effect. **Conclusions:** Unfavorable EBV DNA response at mid-course of radiotherapy/chemoradiotherapy is an adverse prognosticator for treatment outcome, is linked to majority of all failures, and discriminates outcome better than tumor stage. The data could provide a basis for trial design that addresses alteration of therapy intensity during the latter phase of chemoradiotherapy, and adjuvant therapy.

6016

Poster Discussion Session (Board #5), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Association of the 3'-untranslated region KRAS-variant with cisplatin resistance in patients with recurrent and/or metastatic head and neck squamous cell carcinoma.**

Joanne B. Weidhaas, Ju-Whei Lee, Robbert Slebos, Jason Howard, Jimena Perez, Jill Gilbert, Sunitha Nallur, Trupti Paranjape, Joaquin J. Garcia, Barbara Burtness, Arlene A. Forastiere, Christine H. Chung; Yale School of Medicine, New Haven, CT; Dana-Farber Cancer Institute, Boston, MA; Vanderbilt University, Nashville, TN; The Johns Hopkins University, Baltimore, MD; Johns Hopkins University, Baltimore, MD; Yale University, New Haven, CT; Mayo Clinic, Rochester, MN; Fox Chase Cancer Center, Philadelphia, PA; Eviti, Inc., Philadelphia, PA

Background: A germline mutation in *let-7* complementary site 6 (LCS6) within the *KRAS* 3'-untranslated region (rs61764370, the *KRAS*-variant: TG/GG) is known to associate with poor outcome and drug resistance in various cancers compared to the wild type allele (TT). We examine the prognostic significance of the *KRAS*-variant in recurrent/metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). **Methods:** The *KRAS*-variant was determined in 116 tumor DNA samples from HNSCC patients enrolled in 3 clinical trials and a tissue collection study using a previously validated PCR-based assay. **Results:** *KRAS*-variant status could be determined in 108/116 (93%) samples and an allele frequency of TG/GG was 28.7%. These results were correlated with patient demographics, p16/human papillomavirus (HPV) status and clinical outcome. There was no association between p16/HPV status and the *KRAS*-variant status (Fisher's exact test, $p=1.0$). The *KRAS*-variant was associated with poor progression-free survival in patients treated with cisplatin +/-cetuximab (log-rank $p=0.002$) but this association was not observed in docetaxel/bortezomib treated patients (log-rank $p=0.89$). **Conclusions:** *KRAS*-variant is a potentially promising biomarker of poor prognosis and a predictive biomarker of cisplatin resistance in R/M HNSCC. Prospective validation is warranted. Clinical trial information: NCT00003809.

6017

Poster Discussion Session (Board #6), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Assessment of early tumor response to induction chemotherapy (IC) in locally advanced squamous-cell carcinoma of head and neck (LASCCHN) with 18FDG PET-CT: A prospective trial.**

Ulisses Ribaldo Nicolau, Eduardo Nobrega Pereira Lima, Marclesson S. Alves, Thiago Bueno Oliveira, Victor Hugo Fonseca Jesus, Tadeu Ferreira Paiva, Loureno Cezana, Virgilio Sousa Silva, Paula Nicole Pinto, Gislaine Machado Porto, Antonio Cassio Assis Pellizzon, Genival Barbosa Carvalho, Luiz Paulo Kowalski; Hospital A.C. Camargo, São Paulo, Brazil

Background: Response to IC with triplet regimens adding taxanes to cisplatin and 5-fluorouracil (TPF), followed by chemoradiotherapy (CRT) for LASCCHN, is usually evaluated after 2 cycles of IC, based on bidimensional WHO or modified WHO criteria. Concerns regarding toxicity profile of TPF suggest a potential benefit of an early response evaluation approach that could select patients who would be spared from a toxic regimen and promptly started on an alternative treatment. The aim of this study is to assess the ability of evaluating early response after the first IC cycle based on a 40% decrease in standard-uptake value (SUV) measured by 18 FDG PET-CT on the 14th day. **Methods:** Patients with LASCCHN who underwent IC with TPF were prospectively evaluated. Staging procedure included locoregional and chest imaging, endoscopic examination and FDG PET-CT. At day 14 of first cycle, a second FDG PET-CT was performed and treating physicians were blinded for these findings. All cases were conducted according to the usual post-cycle 2 WHO or modified WHO criteria evaluation. Written informed consent was obtained from all recruited patients. **Results:** Between February 2010 and October 2012, 40 stage III/IV LASCCHN patients (34 oropharyngeal, 3 hypopharyngeal and 3 laryngeal) were recruited. With a median follow up of 11.4 months the actuarial 2 years overall (OS) and disease free survival (DFS) of all patients were 81.4% and 69.2%, respectively. Responders (any decrease of SUV) at day 14 PET CT had a better OS (90 vs. 27% - $p < 0,001$) and DFS (76 vs. 0% - $p < 0,001$) as compared to non-responders. Decrease of at least 40% in the SUV of primary tumor predicted a better DFS (100 vs. 51% - $p = 0,007$). **Conclusions:** These results suggest a potential role of early response evaluation with 18 FDG PET-CT in patients with LASCCHN undergoing IC. A SUV decrease of at least 40% predicts better DFS. An increase in the SUV predicts a poor prognosis.

6018

Poster Discussion Session (Board #7), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Positron emission tomography and stage migration for head and neck cancer.**

Noam Avraham VanderWalde, Ramzi George Salloum, Tsai-Ling Liu, Mark Christopher Hornbrook, Maureen Cecelia O'Keeffe-Rosetti, Debra Pearson Ritzwoller, Paul Arthur Fishman, Jennifer Elston Lafata, Amir H Khandani, Bhishamjit S. Chera; Department of Radiation Oncology, University of North Carolina At Chapel Hill, Chapel Hill, NC; Department of Health Policy and Management, Gillings School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC; Department of Health Policy and Management, Gillings School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC; Center for Health Research, Northwest/Hawaii/Southeast, Kaiser Permanente, Portland, OR; Center for Health Research, Northwest, Kaiser Permanente, Portland, OR; Institute for Health Research, Kaiser Permanente Colorado, Denver, CO; Group Health Research Institute, Seattle, WA; Social and Behavioral Health and Massey Cancer Center, School of Medicine Virginia Commonwealth University, Richmond, VA; Department of Radiology, Division of Nuclear Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC; Department of Radiation Oncology, University of North Carolina at Chapel Hill, Chapel Hill, NC

Background: Positron emission tomography (PET) is often used for the staging of head and neck cancer (HNC). The purpose of this study is to explore the association between the increased utilization of PET and stage/survival in the managed care environment. **Methods:** Adult patients diagnosed with HNC (n=958) between 2000-2008, at 4 integrated health systems (Group Health Cooperative, Seattle; Health Alliance Plan/Henry Ford Health System, Detroit; Kaiser Permanente Colorado and Northwest, Portland) were identified via tumor registries linked to claims data. We compared AJCC stage distribution, patient/treatment characteristics, and survival between pre-PET era (2000-2004) vs. PET era (2005-2008), and those with PET vs. those without, during the PET era. AJCC stage was grouped into stage I/II (localized), stage III/IVa/IVb (locally advanced), and stage IVc (metastatic). Ordered logistic regression estimated the effects of PET utilization on upstaging. Kaplan-Meier estimates described overall survival (OS) differences between PET users and nonusers in the PET era. Cox proportional hazards regression evaluated the effect of PET use on survival. **Results:** There was a non-significant increase in stage III/IVa/IVb (40% to 44%) with a decrease in stage I/II (58% to 52%) between pre-PET era and PET era (p=0.11). During the PET era, patients with PET were more likely stage III/IVa/IVb and less likely stage I/II compared to patients without PET (III/IVa/IVb: 62% vs. 29%, I/II: 35% vs. 68%). On multivariate analysis those who were staged with PET were twice as likely to have locally advanced disease (OR 2.091; p=0.006). There was no difference in stage IVc. Patients with PET scans were more likely to receive chemotherapy with radiation and less likely to receive no treatment. 3-year actuarial OS for patients (all stages) with and without PET was 81% vs. 77% (p=0.261). 3-year actuarial OS for patients staged III/IVa/IVb with and without PET was 58% vs. 41% (p= 0.001). **Conclusions:** HNC patients were more likely to be upstaged with the use of PET. There was an improvement in survival in stage III/IVa/IVb patients, but no difference in survival across all stages. This likely reflects selection bias and stage migration rather than improved outcomes among individual patients.

6019

Poster Discussion Session (Board #8), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Radiographic extracapsular extension (ECE) and treatment outcomes in locally advanced oropharyngeal carcinoma (OPC).**

Benjamin H. Kann, Michael Buckstein, Todd J. Carpenter, Ava Golchin, Richard Lorne Bakst, Krzysztof Misiukiewicz, Eric Michael Genden, Marshall R. Posner, Lale Kostakoglu, Peter M. Som, Vishal Gupta; Department of Radiation Oncology, Mount Sinai Medical Center, New York, NY; Department of Medicine, Hematology/Oncology, Mount Sinai Medical Center, New York, NY; Department of Otolaryngology, Mount Sinai Medical Center, New York, NY; Mount Sinai Medical Center, New York, NY; Department of Radiology, Mount Sinai Medical Center, New York, NY

Background: Pathologic ECE (pECE) of tumor through lymph node (LN) is a poor prognosticator for OPC and typically diagnosed upon surgical LN removal. At our institution, experienced radiologists routinely identify ECE on pretreatment CT. The prognostic value of radiographic ECE (rECE) is less clear and may prove clinically useful. In this study, we evaluate rECE as an independent prognosticator in OPC. **Methods:** Retrospective review of 185 patients with locally advanced OPC treated in our department from 2006-2012. 109 patients had accessible pretreatment CT reports clearly stating the presence or absence of rECE. Patients were treated with definitive concurrent chemoradiation therapy (CCRT) (30%), induction chemo then CCRT (47%), or surgery with adjuvant CCRT (14%) or RT (9%). Kaplan-Meier survival analysis compared these cohorts for locoregional control (LRC), distant control (DC), and progression-free (PFS) and overall survival (OS); log-rank tests were performed for significance. Multivariate analysis was conducted via cox-regression. **Results:** Median follow-up of the 109 patients was 31 months (range: 1-80 months). 61 patients had rECE(+) and 48 had rECE(-) scans. There was no significant difference between the cohorts in terms of median age, stage, treatment type, smoking history, or tumor HPV status. There was a difference in nodal stage with 83% of rECE(+) patients having N2-3 disease versus 67% of rECE(-) patients (p=0.02). On univariate analysis, there were differences between the rECE(-) versus rECE(+) cohorts in OS (4yr: 92% vs 72%, p=0.01), PFS (4yr: 92% vs 62%, p=0.002), and DC (4yr: 98% vs 76%, p=0.006), with no difference in LRC (4yr: 95% vs 91%, p=0.35). On multivariate analysis factoring in age, smoking history, stage, and treatment type, rECE presence was a negative predictor of OS (hazard ratio, 0.26; 95% CI, 0.07 to 0.95) and PFS (hazard ratio, 0.23; 95% CI, 0.06 to 0.81), with DC approaching significance (hazard ratio, 0.13; 95% CI, 0.02 to 1.05). **Conclusions:** While pECE is an established risk factor for locally advanced OPC, this study suggests that rECE may be an independent poor prognosticator of PFS, OS and DC with potential importance in guiding clinical management.

6020

Poster Discussion Session (Board #9), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Sorafenib in recurrent and/or metastatic salivary gland carcinomas (RMSGCs): An investigator-initiated phase II trial (NCT01703455).**

Laura D. Locati, Paolo Bossi, Enrico M. Civelli, Federica Perrone, Cristiana Bergamini, Barbara Cortelazzi, Pasquale Quattrone, Martina Imbimbo, Aurora Mirabile, Roberta Granata, Carlo Resteghini, Luigi Mariani, Davide Tosarello, Camilla Cassani, Alfonso Marchiano, Gabriella Saibene, Silvana Pilotti, Lisa F. Licitra; 1Head and Neck Medical Oncology Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 2Radiology Dept., Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Laboratory of Experimental Molecular Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 4 Pathology Dept., Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 5 Unit of Clinical Epidemiology and Trial Organization, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 6 Medical Scientific Liaisons, Bayer, Milan, Italy; 7 Data Management Office, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 8 Pharmacy, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

Background: Palliative chemotherapy is the standard of care for RMSGCs. However its activity is usually poor especially in adenoid cystic carcinoma (ACC), while in histotypes other than ACC (non ACC) the response, if any, is of short duration. Some preclinical and clinical evidence suggest a rationale for the employment of anti-angiogenetic agents in RMSGCs, such as sorafenib. **Methods:** Subjects with proven RMSGC not amenable to surgery and/or radiotherapy were enrolled to receive sorafenib at 400 mg BID q28 days until disease progression, unacceptable toxicity or consent withdrawal. Primary endpoint was response rate (RR) (CR+PR) according to RECIST; secondary objectives included RR according to CHOI criteria, disease control rate (DCR) and toxicity. 37 subjects were required to test the null hypothesis that RR will be $\leq 5\%$ versus the alternative that $RR \geq 20\%$ within a two stage Simon design. At least 4 responders were necessary to reject the null hypothesis. **Results:** 19 ACC and 18 non ACC subjects were accrued from September 2010 to September 2012. 21 patients had received at least one chemotherapy regimen for RMSGC. Overall 6 PRs according to RECIST were recorded corresponding to a RR of 16% (95% CI 6.2-32.0) (11% in ACC and 22% in non ACC). PR according to CHOI was observed in 10 cases (of which only 2 were concordant with RECIST); no response was reported in 15 cases while CHOI response was not evaluable in 12 patients. A dramatic necrotic evolution of the disease, which resulted in cavitation of metastatic lesions in one case, was observed in two patients with mucoepidermoid cancer (MEC). SD was 57% lasting a median of 7 months (range 2-15+ months). At a median follow up of 10 months (range 3-28+ months): 5 patients are still receiving sorafenib; 15 are no longer being treated and 17 have died. AEs were generally consistent with previous sorafenib studies, except for one G5 toxicity due to meningitis (probably related to necrosis of a local relapse) and one G3 aspergillus abscess. **Conclusions:** Sorafenib is the first anti-angiogenetic agent to demonstrate some activity in RMSGCs, particularly in MEC. Molecular analyses, typifying MEC and ACC are ongoing. Clinical trial information: NCT01703455.

6021 **Poster Discussion Session (Board #10), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM****Phase II study of dovitinib (TKI258) in patients with progressive metastatic adenoid cystic carcinoma.**

Patrick Michael Dillon, Chris Moskaluk, Paula M. Fracasso, Gina R. Petroni, Christopher Y. Thomas; University of Virginia, Charlottesville, VA; University of Virginia Health System, Charlottesville, VA; Wake Forest Baptist Medical Center, Winston-Salem, NC

Background: Adenoid cystic carcinoma (ACC) is an uncommon malignancy of secretory glands for which there is no standard systemic therapy. At least 90% of ACC tumors carry a t(6;9)(q22-23;p23-24) chromosome translocation that results in overexpression of the MYB oncogene that in turn upregulates FGF2 and other growth factors. Dovitinib is a multiple receptor kinase inhibitor that could potentially block autocrine activation of the FGFR and VEGFR-mediated angiogenesis. In a mouse model, dovitinib suppressed the growth of low passage ACC xenografts. **Methods:** In this open-label, single-arm trial, patients (n=21) with metastatic ACC that progressed in the last 6 months were treated with dovitinib 500 mg/d, 5-days on/2-days off. The primary endpoint was objective response rate using a two-stage design to test a null and alternative rate of 1% and 18%, respectively, with 90% power and type I error <5%. Secondary endpoints were progression-free survival, safety, quality of life, biomarker studies, and change in tumor growth rate. **Results:** All 21 patients (median age 54.3, range 29-74) had previous treatment with chemotherapy, radiotherapy or targeted agents. Median duration of treatment to date is 5.7 months (range 2-10 months) and is ongoing in 11 patients. Nine of 21 patients required dose reductions. Grade 3/4 drug-related adverse events included thromboembolism (4), hematuria (1), dehydration (1), pneumonia (2), hypertriglyceridemia (3), diarrhea (2), stomach pain (2), anxiety (1), transaminitis (3) and cytopenias (4). One death occurred unrelated to study drug. Among 19 evaluable patients, 2 had partial responses by RECIST criteria (1 with lung metastases and 1 with tracheal recurrence and stable bone metastases). Both experienced improvements in pain ratings and are free of disease progression at 8+ and 5+ months. Stable disease >6 months was observed in 9 patients while 6 others with shorter follow-up have not progressed. Four patients progressed early (<4 months) and two are too early to assess. **Conclusions:** Dovitinib produces objective partial responses and prolonged tumor stabilization with acceptable toxicity in patients with progressive ACC. Clinical trial information: NCT01524692.

A phase II study of dasatinib (BMS 354825) in recurrent or metastatic *ckit*-expressing adenoid cystic (ACC) and non-ACC malignant salivary glands tumors (MSGT).

Stuart J. Wong, Ezra E.W. Cohen, Theodore Karrison, David N. Hayes, Merrill S. Kies, Kevin J. Cullen, Tawee Tanvetyanon, Athanassios Argiris, Naoko Takebe, Dean Lim, Nabil F. Saba, Francis P. Worden, Jill Gilbert, Heinz-Josef Lenz, Albiruni R.A. Razak, John D. Roberts, Everett E. Vokes; Medical College of Wisconsin, Milwaukee, WI; The University of Chicago Medicine and Biological Sciences, Chicago, IL; The University of Chicago Medical Center, Chicago, IL; Lineberger Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Maryland, Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; University of Texas Health Science Center at San Antonio, San Antonio, TX; Investigational Drug Branch, Cancer Therapy Evaluation Program, Rockville, MD; City of Hope, Duarte, CA; Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; Vanderbilt University, Nashville, TN; University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA; Princess Margaret Hospital, Toronto, ON, Canada; Massey Cancer Center, Richmond, VA

Background: ACC is a rare disease, accounting for 1/3rd of MSGT, in which 90% of cases express the protein product of the *ckit* proto-oncogene. Dasatinib is a potent and selective inhibitor of five oncogenic PTKs/kinase families including *ckit*. We conducted a phase II study to determine the antitumor activity of dasatinib in ACC and non-ACC MSGT. **Methods:** In a two-stage design, adult patients (pts) with recent radiographic progressive, recurrent or metastatic ACC, + cKIT, were treated with dasatinib 70 mg PO BID. Pts with non-ACC MSGT of other histologic types, were treated as a separate cohort. Response was assessed every 8 wks by imaging using RECIST criteria. The study design stipulated enrollment of n=40 ACC patients (20 in stage I and 20 in stage II) and 25 non-ACC patients (14 in stage I and 11 in stage II). **Results:** Fifty-four pts were enrolled, 40 ACC and 14 non-ACC. One additional pt was a screen failure. Baseline data on 54 pts are: M:F = 28:26, median age 56.6 yrs (range 20-82), PS 0:1:2 = 24:28:2, prior radiation: chemotherapy = 44:21. The most frequent adverse events experienced (as % of pts, worst grade 2 or higher and at least possibly related to study drug) were: fatigue (28%), nausea (19%), headache (15%), lymphopenia (11%), dyspnea (11%), alanine aminotransferase increased (7%), anorexia (7%), vomiting (7%), alkaline phosphatase increased (6%), diarrhea (6%), and non-cardiac chest pain (6%). No grade 4 adverse events occurred and only 15 pts experienced a grade 3 adverse event (at least possibly attributed to study drug), primarily dyspnea (4 patients) and fatigue (3 patients). Significant cardiac toxicity was observed in one pt (grade 3 prolonged QT corrected interval). Among ACC pts, best response to dasatinib: 0 pts (0%) had PR, 21 pts (52%) had SD (range 2.8-13.8 months), 12 pts (30%) had PD, and 2 died prior to cycle 2. Median PFS was 4.8 mos. For 14 evaluable non-ACC pts, none had an objective response, triggering early stopping. 7 had SD (range 1.4-6.6 months), and 4 PD. **Conclusions:** Although there were no objective responses, dasatinib is well tolerated, with tumor stabilization achieved by 52% of ACC pts. Dasatinib demonstrated no activity in non-ACC MSGT. Clinical trial information: NCT00859937.

6023

Poster Discussion Session (Board #12), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**A phase II study of everolimus in patients with aggressive RAI refractory (RAIR) thyroid cancer (TC).**

Jochen H. Lorch, Naifa Busaidy, Daniel T Ruan, Pasi A. Janne, Sewanti Atul Limaye, Lori J. Wirth, Justine A. Barletta, Guilherme Rabinowits, Levi A. Garraway, Eliezer Mendel Van Allen, Nikhil Wagle, Glenn J. Hanna, Krzysztof Misiukiewicz, Margaret Suda, Tyler C Haddad, Catherine E Devine, Amy Williams, Ghulam Warsi, Marshall R. Posner, Robert I. Haddad; Dana-Farber Cancer Institute, Boston, MA; The University of Texas MD Anderson Cancer Center, Houston, TX; Brigham and Women's Hospital, Boston, MA; Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA; Massachusetts General Hospital, Boston, MA; Beth Israel Deaconess Medical Center, Boston, MA; Department of Medicine, Hematology/Oncology, Mount Sinai Medical Center, New York, NY; Medical Oncology, Dana Farber Cancer Institute, Boston, MA; Novartis, East Hanover, NJ; Novartis Pharmaceuticals, East Hanover, NJ; Mount Sinai Medical Center, New York, NY

Background: We present results of an open label phase II study of the mTOR inhibitor Everolimus in patients (pts) with RAIR TC. **Methods:** Pts with metastatic, incurable RAIR TC who had shown radiographic progression within 6 months prior to enrollment received Everolimus 10mg orally once daily. Responses were monitored by CT's every two months. The primary endpoint was progression free survival. Sequential biopsies were obtained in selected pts. **Results:** Enrollment to the differentiated TC (DTC) cohort finished in Jan 2013 and included 33 pts, among them 11 with Hurthle cell TC. Exploratory cohorts enrolled 10 pts with medullary [MTC] and 5 with anaplastic [ATC] with 2 added openings remaining for ATC. For the DTC cohort, median time on study to date is 10 months (mo) (<1-23+). 31 pts are evaluable at this time. PFS in the DTC cohort by Kaplan-Meier (K-M) analysis is 16.0 mo (95%CI 10-NR). Currently, disease stability for 6 and 12 mo or more was achieved in 18 and 10/31 pts, respectively, 11 pts remain on study. Median OS was not reached but 1 year survival by K-M analysis was 76%. One pt achieved a PR. 3 pts with DTC underwent sequential biopsies which revealed activation of autophagy while markers for apoptosis were not detected. Among 10 MTC pts, one achieved a PR and 9 pts had stable disease for 6 mo or more (6-33+). Among 5 ATC pts, 3 progressed, one has ongoing disease stability for 5 mo. One patient achieved a complete response that lasted for 18 mo and whole exome sequencing revealed somatic loss of function mutation affecting the Tuberous Sclerosis 2 (TSC2) protein, a negative regulator of mTOR activity [TSC2 (Q1178*) and FLCN (R17fs)]. Most common treatment-related adverse events were as anticipated and included fatigue, stomatitis and infections. Grade (gr) 3 events included infection 5, weight loss 3, leukopenia 3, thrombocytopenia 3, fatigue 3, hypophosphatemia 2, stomatitis 2, pneumonitis 1 and thrombosis 1pts. One pt had gr 4 hypercholesterinemia and one pt had gr 4 leukopenia. **Conclusions:** Everolimus has significant anti-tumor activity in pts with advanced TC. Activation of autophagy could account for high rate of disease stability. Sequencing may identify mechanistic basis and predictive markers for treatment response. Clinical trial information: NCT00936858.

6024

Poster Discussion Session (Board #13), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Phase II study of everolimus and sorafenib for the treatment of metastatic thyroid cancer.**

Eric Jeffrey Sherman, Alan Loh Ho, Matthew G. Fury, Shrujal S. Baxi, Sofia Haque, Brynna Lane Lipson, Sarah Kurz, James A. Fagin, David G. Pfister; Memorial Sloan-Kettering Cancer Center, New York, NY

Background: Everolimus is an oral inhibitor of the mammalian target of rapamycin (mTOR). Unpublished work from the Fagin lab shows that mTORC1 is also required for the growth promoting effects of the oncoproteins RET/PTC, RAS and BRAF in rat thyroid PCCL3 cells. Further work shows synergy of mTORC inhibitors with RET kinase inhibitors in medullary thyroid cancer cell lines. Sorafenib is an oral kinase inhibitor with in vitro activity against multiple targets, including RAF, RET, VEGFR1, and VEGFR2 that is compendium approved for the treatment of radioactive iodine-refractory (RAIR) and medullary (MTC) thyroid cancer. **Methods:** The study was a single institution, two-stage phase II design. Primary objective was response rate initiated on 9/21/2010. Eligible patients (pts) had progressive, RAIR/fluorodeoxyglucose (18-F)-avid, recurrent/metastatic, non-anaplastic, thyroid cancer; RECIST measurable disease; and adequate organ/marrow function. Sorafenib was given at 400 mg orally twice a day and Everolimus at 5 mg orally once daily. 41 patients were enrolled; 36 were eligible for the primary endpoint of response and 3 were evaluable for toxicity only at the data cutoff date of 1/10/13. Seventeen patients are still actively on study. Mutational analyses of tissue is ongoing. **Results:** Of the 41 eligible pts, demographics: female- 44% (18); median age-61 years (35-79). Grade 4-5 adverse events at least possibly related to drug: grade 4- Alanine Aminotransferase Increase (1 pt); grade 4- Hyperglycemia (1 pt); grade 4-Pancreatitis (1 pt). Histology and response data by partial response, confirmed and unconfirmed, (PR), stable disease (SD) and progression of disease (POD) are in the table below. The median time on treatment is 167 days (range 1 to 797 days) at the cutoff date of 1/10/2013. **Conclusions:** The combination of sorafenib and everolimus shows promising results, especially in the Hurthle cell and medullary subgroups where data from studies at Ohio State have suggested very poor response to sorafenib alone. Clinical trial information: NCT01141309.

Histology	No.	PR	SD	POD
Papillary	8	4 (50%)	3 (38%)	1 (13%)
Hurthle cell	9	6 (67%)	3 (33%)	0
Follicular	2	1 (50%)	1 (50%)	0
Poorly diff	8	4 (50%)	4 (50%)	0
Medullary	9	4 (44%)	4 (44%)	1 (11%)
Total	36	19 (53%)	15 (42%)	2 (6%)

6025

Poster Discussion Session (Board #14), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Re-differentiation of radioiodine-refractory *BRAF* V600E-mutant thyroid carcinoma with dabrafenib: A pilot study.**

Stephen M. Rothenberg, David G McFadden, Edwin Palmer, Gilbert H Daniels, Lori J. Wirth; Massachusetts General Hospital Cancer Center, Boston, MA; Massachusetts General Hospital Thyroid Unit, Boston, MA; Massachusetts General Hospital Department of Radiology, Boston, MA; Massachusetts General Hospital, Boston, MA

Background: Resistance to radioactive iodine is a leading cause of mortality in differentiated thyroid carcinoma. The MAPK pathway is a major determinant of iodine uptake into thyroid carcinoma cells. Mutations in BRAF activate this pathway, resulting in resistance to radioactive iodine. A pilot study using the MEK1/2 inhibitor, selumetinib, (Ho, ASCO 2012) increased radioiodine uptake in a subset of thyroid cancers. **Methods:** This is a single institution, single arm pilot study investigating the potential for the BRAF inhibitor dabrafenib to induce radioiodine uptake in metastatic, BRAF-mutant, radioiodine-refractory papillary thyroid carcinoma (PTC). The primary endpoint is increased radioiodine uptake demonstrated on a 4mCi 131-I whole body scan. Patients with increased uptake receive 14 additional days of dabrafenib followed by treatment with 150mCi 131-I. Secondary endpoints include safety and tolerability and clinical benefit as measured by decreases in serum thyroglobulin and objective response rate per modified RESIST 1.1. **Results:** To date, 7 patients have been enrolled. All had negative 131-I scans within 14 months of enrollment. No dose adjustments for toxicity have been needed. One patient developed reversible hypophosphatemia and a second developed a benign skin lesion. 3 of 5 evaluable patients developed radioiodine uptake after 28 days of dabrafenib, and new radioiodine-avid lesions were demonstrated in all three after receiving a therapeutic dose of 131-I. All three patients demonstrated increases in thyroglobulin levels during treatment with dabrafenib. **Conclusions:** This initial data suggests that a subset of patients with radioiodine-resistant BRAF-mutant PTC demonstrate new iodine uptake following treatment with dabrafenib. Reuptake may correlate with increases in thyroglobulin, suggestive of re-differentiation. It is not yet known whether increased uptake of radioactive iodine will translate into a radiographic response. Two patients failed to convert to radioiodine-sensitive disease; it is possible that BRAF inhibition was incomplete in these patients and/or determinants other than BRAF mutation status contribute to radioiodine sensitivity. Clinical trial information: NCT01534897.

6026

Poster Discussion Session (Board #15), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**A phase II, multicenter, open-label, single-arm trial of famitinib in patients with advanced recurrent and/or metastatic nasopharyngeal carcinoma (NPC) after two previous treatment regimens.**

Yan Huang, Li Zhang, Jian-ji Pan, Guoqing Hu, Wu Gang, Jian ping Xiong, Chaosu Hu, Lizhu Lin, Hao Yu, Haoyuan Jiang; Sun Yat-sen University Cancer Center, Guangzhou, China; Fujian Cancer Hospital, Fuzhou, China; Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China; Wuhan Union Hospital, Wuhan, China; The First Affiliated Hospital of Nanchang University, Nanchang, China; Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai, China; The First Affiliated Hospital of Guangzhou Medical University of Chinese Medicine, Guangzhou, China; Department of Epidemiology and Biostatistics, Nanjing Medical University, Nanjing, China; Jiangsu HengRui Medicine Co., Ltd, Lianyungang, China

Background: Famitinib is an oral, small molecular multiple tyrosine-kinase inhibitor (TKI), targeting stem cell growth factor receptor (c-Kit), platelet derived growth factor receptor (PDGFR) and vascular endothelial growth factor receptor (VEGFR). So far, few target therapies show acceptable efficiency in advanced recurrent and/or metastatic nasopharyngeal carcinoma (RM-NPC) patients. The primary object of this study is to determine the safety and efficacy of famitinib in patients with RM-NPC. **Methods:** This study recruited histologically diagnosed RM-NPC patients who failed more than two lines of systemic chemotherapy. Other eligible criteria included ECOG PS \leq 2, adequate organ function and no prior exposure to other c-Kit, PDGFR or VEGFR TKIs. The patients received famitinib orally at a dose of 25 mg once daily until the disease progression or intolerable toxicity. **Results:** From May 2011 to Sep 2012, 58 patients (Simon's two-stage design, 28+30) were recruited at 8 sites in China. The clinical benefit rate (partial response or stable disease maintained \geq 12 weeks, tumor response was evaluated every 4 weeks) is 32.8%, including 5 PR and 16 SD patients. Median PFS was 3.2 months. The most frequently observed hematologic toxicities included thrombocytopenia, leucopenia and neutropenia; non-hematologic AEs were hypertension, proteinuria, and hand-foot syndrome. All adverse events were generally mild-to-moderate (grade 1/2) and manageable with supportive treatment; grade 3/4 incidence was relatively low. **Conclusions:** This phase II study shows that famitinib demonstrates substantial clinical benefits in patients with advanced RM-NPC and the drug-related adverse reactions were most predictable and tolerable, no special toxicity was reported. Biomarker analysis for responder and non-responder is still ongoing and will be present at the meeting. Clinical trial information: NCT01392235.

6027

Poster Discussion Session (Board #16), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Identification of a gene expression profile associated with progression-free survival (PFS) in relapsed or metastatic (RM) head and neck squamous cell cancer (HNSCC) patients (pts) treated with first-line cetuximab and platinum therapy.**

Paolo Bossi, Loris De Cecco, Federica Perrone, Barbara Cortelazzi, Maria Cossu Rocca, Siano Marco, Andrea Sponghini, Cristiana Bergamini, Laura D. Locati, Aurora Mirabile, Roberta Granata, Carlo Resteghini, Silvana Pilotti, Silvana Canevari, Lisa F. Licitra; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Laboratory of Experimental Molecular Pathology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; European Institute of Oncology, Milano, Italy; Kantonsspital, St. Gallen, Switzerland; Ospedale Maggiore della Carità, Novara, Italy

Background: First-line chemotherapy with platinum and cetuximab is usually offered to RM-HNSCC pts. In the Extreme trial a median PFS time of 5.6 months was reported. However, a small fraction of pts achieves a prolonged PFS (> than 12 months). Until now, no recognized predictive biological factor has been identified. **Methods:** A group of 14 pts treated with a first-line platinum and cetuximab with a PFS exceeding 12 months (long PFS) and a group of 26 pts with a PFS less than 5.6 months (short PFS) were selected. Tumor specimens of the recurrence (25 cases) or, if not available, of the primary tumor were collected. In order to identify molecular profiles deregulated between the 2 groups, a gene expression microarray analysis was performed using the Whole-Genome DASL assay and HumanHT-12_v4 BeadArray chips (Illumina). **Results:** The 2 groups were well balanced in regard to recognized prognostic factors (performance status, weight loss, prior radiotherapy, tumor grade, site of primary tumor, residual disease at primary tumor site). Mean PFS was 21 months in long (range 13-36) and 4 months in short PFS group (range 1-5). By class comparison analysis between the 2 groups, the expression pattern of 136 genes was found differentially expressed (FDR<0.05). In long PFS group, EGFR and genes associated to EGFR pathway including CDCP1 and EPGN were up regulated, as well as its ligand (EREG). Several members of the Kallikrein serine proteases gene family are present among the most upregulated genes in long PFS group, suggesting the involvement of extracellular-matrix remodelling. In addition to cellular morphology, pathways analysis showed an enriched modulation of genes belonging to cell-to-cell signalling, DNA replication/DNA repair and lipid metabolism. **Conclusions:** Our analysis suggests that a specific molecular signature may be associated with long and short PFS after platinum/cetuximab first line chemotherapy in RM-HNSCC pts. To our knowledge, it is the first study attempting to generate hypotheses in this field and further validation is required.

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Poster Discussion Session (Board #17), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Activity of cetuximab (C) in head and neck squamous cell carcinoma (HNSCC) patients (pts) with PTEN loss or PIK3CA mutation treated on E5397, a phase III trial of cisplatin (CDDP) with placebo (P) or C.**

Barbara Burtness, Ju-Whei Lee, Donghua Yang, Fang Zhu, Joaquin J. Garcia, Arlene A. Forastiere, Christine H. Chung; Fox Chase Cancer Center, Philadelphia, PA; Dana-Farber Cancer Institute, Boston, MA; Mayo Clinic, Rochester, MN; The Johns Hopkins University, Baltimore, MD

Background: Abnormalities in EGFR signaling targets are associated with C resistance but no biomarker of C resistance has been identified in HNSCC. We hypothesized that cases with loss of PTEN protein expression (PTEN null) or *PIK3CA* mutation would display C resistance in HNSCC. **Methods:** E5397 was a phase III trial of CDDP plus P or CDDP plus C and enrolled 117 eligible and evaluable pts. *PIK3CA* and PTEN were analyzed for 52 and 67 consented pts, respectively. PTEN expression (PTEN Cell Signaling Technology, Cat. 9559) was determined by automated quantitative analysis (AQUA) on the PM-2000 (HistoRx, New Haven) using a cutpoint generated in 5 HNSCC tissue microarrays, each consisting of HNSCC as well as positive (small intestine, median AQUA score 2833.2) and negative controls (breast and colon carcinoma, median AQUA score 205.5). A cutpoint of 570 provides 100% specificity, 100% sensitivity, and identified 30% of the HNSCCs as PTEN null, consonant with the literature. The 3 most common *PIK3CA* mutations (E542K and E545K in exon 9 and H1047R in exon 20) were determined by BEAMing (Inostics, Heidelberg, Germany). Response, overall survival (OS) and progression-free survival (PFS) were compared between PTEN null or *PIK3CA* mutated pts and all others. Log rank and multivariable Cox proportional hazards modeling were used to calculate p values. **Results:** 23/67 (34%) tumors were PTEN null and 2/52 (4%) had *PIK3CA* mutations (E542K and E545K). Both tumors with *PIK3CA* mutation had PTEN expression. No statistically significant differences in response, OS or PFS were noted in this small sample. However, among PTEN expressing/*PIK3CA* WT pts, median PFS increased to 4.2 months (m) for C (N=22) from 2.9 m for P (N=26) (Wald p=0.07), compared with 4.6 m for C (N=12) and 3.5 m for P (n=13) among the PTEN null/*PIK3CA* mutated (Wald p=0.60). **Conclusions:** The PTEN loss or *PIK3CA* mutation signature warrants further investigation as a predictor of C resistance.

PARTNER: A randomized phase II study of docetaxel/cisplatin (doc/cis) chemotherapy with or without panitumumab (pmab) as first-line treatment (tx) for recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN).

Lori J. Wirth, Shaker R. Dakhil, Gabriela Kornek, Rita Axelrod, Douglas Adkins, Shubham Pant, Paul E. O'Brien, Philip R. Debruyne, Kelly S. Oliner, Jun Dong, Bruce A. Bach; Massachusetts General Hospital, Boston, MA; Cancer Center of Kansas, Wichita, KS; Medizinische Universitaet Wien, Wien, Austria; Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA; Washington University School of Medicine in St. Louis, St. Louis, MO; University of Oklahoma Health Sciences Center, Oklahoma City, OK; Medical University of South Carolina, Charleston, SC; AZ Groeninge Hospital, Kortrijk, Belgium; Amgen, Inc., Thousand Oaks, CA

Background: PARTNER was a multicenter, randomized phase II estimation study evaluating 1stEline tx of R/M SCCHN with doc/cis ± pmab. **Methods:** Patients (pts) were randomized 1:1 to doc/cis with pmab (Arm 1) or doc/cis alone (Arm 2). Arm 1 received 9 mg/kg pmab on day 1 of each 21-day cycle, and all pts received 1stEline doc/cis both at 75 mg/m² on day 1 for up to 6 cycles. In Arm 1, pts could receive pmab monotherapy upon completion of 6 cycles of doc/cis until disease progression (PD). In Arm 2, pts could receive pmab as 2ndEline monotherapy upon PD. The primary endpoint was progression-free survival (PFS); secondary endpoints included overall survival (OS), objective response rate (ORR), and safety. HPV status was determined using p16 INK IHC. No formal hypothesis was tested. **Results:** Baseline characteristics were balanced between arms. Of 103 pts, HPV status was evaluable in 66 (64%); 29% were HPV positive. Efficacy results are shown (Table). Worst grade 3/4 adverse events (AEs) were 73% in Arm 1 vs 56% in Arm 2. **Conclusions:** Median PFS was increased in both arms over historical doublet cytotoxic chemotherapy. PFS and ORR were higher in the pmab arm in the overall population, in the HPV positive (n=19) group, and in the HPV negative (n=47) group. There was an increase in grade 3/4 AEs with this regimen. The crossover design, with 57% of Arm 2 pts receiving pmab as 2ndEline monotherapy, confounds interpretation of OS. Clinical trial information: NCT00454779.

All pts	Arm 1 (N = 52)	Arm 2 (N = 51)	HR (95% CI)
Median PFS, [#] mos (95%CI)	6.9 (4.7 – 8.3)	5.5 (4.1 – 6.8)	0.63 (0.40 – 1.00)
Median OS, mos (95%CI)	12.9 (9.4 – 18.5)	13.8 (11.8 – 22.9)	1.10 (0.71 – 1.72)
ORR, [#] % (95%CI)	44 (31 – 58)	37 (24 – 51)	
HPV negative	Arm 1 (N = 25)	Arm 2 (N = 22)	HR (95% CI)
Median PFS, [#] mos (95%CI)	7.3 (4.7 – 9.6)	5.3 (2.9 – 7.0)	0.53 (0.27 – 1.02)
ORR, [#] % (95%CI)	52 (32 – 72)	27 (9 – 46)	
HPV positive	Arm 1 (N = 6)	Arm 2 (N = 13)	HR (95% CI)
Median PFS, [#] mos (95%CI)	8.1 (3.9 – NE)	5.7 (4.5 – 6.8)	0.53 (0.16 – 1.71)
ORR, [#] % (95%CI)	67 (29 – 100)	54 (27 – 81)	

[#]Assessments by investigator review per modified RECIST 1.0. Pts with measurable lesions at baseline were included in the ORR analysis. HR: hazard ratio. NE: not estimable.

6030

Poster Discussion Session (Board #19), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Randomized phase II trial of cixutumumab (CIX) alone or with cetuximab (CET) for refractory recurrent/metastatic squamous cancer of head and neck (R/M-SCCHN).**

Bonnie S. Glisson, Jennifer Tseng, Shanthi Marur, Dong M Shin, Barbara A. Murphy, Ezra E.W. Cohen, Christopher Y. Thomas, Richard Willey, Jan Cosaert, William Nassib William, Nusrat Harun, J. Jack Lee, Robert I. Haddad; The University of Texas MD Anderson Cancer Center, Houston, TX; M. D. Anderson Cancer Center, Orlando, Orlando, FL; The Johns Hopkins University, School of Medicine, Baltimore, MD; The Winship Cancer Institute of Emory University, Atlanta, GA; Department of Medicine, Vanderbilt University Medical Center, Nashville, TN; The University of Chicago Medical Center, Chicago, IL; Wake Forest Baptist Medical Center, Winston-Salem, NC; ImClone Systems LLC, a wholly-owned subsidiary of Eli Lilly and Company, Bridgewater, NJ; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA

Background: Preclinical evidence supports clinical investigation of IGF-1R inhibitors alone, or combined with EGFR inhibitors, in SCCHN patients (pts). CIX and CET monoclonal antibodies block ligand binding to IGF-1R and EGFR, respectively. CIX mono and CIX+CET combo were studied in pts with chemotherapy-refractory R/M-SCCHN. **Methods:** This open-label phase II trial randomized 97 pts with R/M-SCCHN, ECOG PS 0-2 and disease progression following (<90 days) platinum-based chemotherapy, to CIX 10 mg/kg alone (Arm A) or with CET 500 mg/m² (Arm B) every 2 wks. Time to recurrence from last anti-EGFR exposure had to be >90 days; pts were stratified by prior CET exposure. Primary endpoint was median PFS (RECIST assessments every 8 wks). Efficacy endpoints in the CET-naïve patients, immunohistochemical analysis of 10 relevant markers on tumor specimens, and cytokine/angiogenic factor profiling of blood samples obtained serially through treatment were also examined. **Results:** 47 Arm A and 44 arm B pts were treated: median age: 60.0 y (35 - 81), PS 0/1/2: 17.6%/62.6%/19.8%, male (80.2%), tumors originating mainly from oropharynx (67.1%), supraglottic (9.9%) and oral cavity (13.2%), with 33% moderately and 36.3% poorly differentiated tumors, previous therapy: 98.9% chemotherapy and 82.4% radiotherapy indicating no baseline differences. Most common tx-emergent AEs were fatigue (55.3 vs. 61.4%), dermatitis acneiform (6.4 vs 63.6%), nausea (29.8 vs. 34.1%), weight decreased (25.5 vs. 29.5%), hyperglycemia (25.5% vs. 29.5%), vomiting (21.3 vs. 20.5%), and headache (17 vs. 25%). Efficacy: See Table. **Conclusions:** Targeting IGF-1R alone with CIX or co-targeting IGF-1R and EGFR with CIX and CET did not result in improved PFS compared to historical data with CET alone in patients with chemotherapy-refractory R/M-SCCHN. The results of this study do not support CIX single-agent activity in this patient population. Therapy on both arms was feasible. There was no apparent exacerbation of CET toxicity by concurrent CIX exposure. Clinical trial information: NCT00617734.

Endpoint	CIX	CIX+CET
Median PFS/OS months	1.9/5.3	2.0/5.5
6-month PFS	5.9%	15.3%
Clinical benefit (CR/PR/SD)	19% (2%/0%/17%)	38% (2%/7%/30%)

CRA6031 **Poster Discussion Session (Board #20), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**

Oral HPV infection in HPV-positive oropharyngeal cancer cases and their spouses.

Gypsyamber D'Souza, Neil D. Gross, Sara I Pai, Robert I. Haddad, Maura L. Gillison, Marshall R. Posner; Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Oregon Health & Science University, Portland, OR; The Johns Hopkins University, School of Medicine, Baltimore, MD; Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA; The Ohio State University, Columbus, OH; Mount Sinai Medical Center, New York, NY

The full, final text of this abstract will be available at abstract.asco.org at 7:30 AM (EDT) on Saturday, June, 1, 2013, and in the *Annual Meeting Proceedings* online supplement to the June 20, 2013, issue of *Journal of Clinical Oncology*. Onsite at the Meeting, this abstract will be printed in the Saturday edition of *ASCO Daily News*.

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Poster Discussion Session (Board #21), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**Differences in sexual practices and their role in gender, age, and racial disparities in HPV-positive HNSCC.**

Carole Fakhry, Kevin J. Cullen, Janice Bowie, Roland Thorpe, Gypsyamber D'Souza; Johns Hopkins University, Baltimore, MD; University of Maryland, Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD; Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Background: Human papillomavirus associated head and neck cancers (HPV-HNC) have been steadily rising in the U.S., while HPV-unassociated HNCs have declined due to reductions in tobacco use. The trend of increasing HPV-HNC has been attributed to the sexual revolution, but not well explored. Individuals with HPV-HNC tend to be younger, white, and male and HPV-HNC is strongly associated with sexual behaviors. **Methods:** This analysis included 2270 men and 2261 women from the 2009-10 National Health and Nutrition Examination Survey (NHANES) who answered a survey on demographic and behavioral risk factors. Participants also provided an oral rinse and gargle sample for HPV DNA analysis. Prevalence of sexual behaviors and oral HPV infection were calculated by gender, age cohort (18-29, 30-44, 45-59, 60-69), and race using NHANES sample weights to provide unbiased estimates for the US population. **Results:** Men (85%) and women (83%) were similarly likely to have ever performed oral sex, but men had more lifetime oral and vaginal sexual partners and higher oral HPV16 prevalence (each $p < 0.001$). Ever having performed oral sex was less common among 60-69 than 30-44 year old men (74% vs. 92%, $p < 0.001$) and women (71% vs. 91%, $p < 0.001$). Older individuals also had less lifetime sexual partners, but marginally higher oral HPV16 prevalence. Whites were more likely than blacks (90% vs 69%, $p < 0.001$) to have ever performed oral sex, to have more lifetime oral sex partners and higher oral HPV16 prevalence (each $p < 0.001$). Prevalence ratios of ever performing oral sex for men vs. women (PR = 1.03), 45-59 vs 60-69 year olds (PR = 1.25), and whites compared to blacks (PR = 1.32) were modest relative to more striking prevalence ratios for oral HPV infection and HPV-HNC (each PR > 1.5). **Conclusions:** There are significant gender, age-cohort, and racial differences in oral sexual practices in a representative sample of the U.S population. Although men, younger age-cohorts, and whites have higher exposures to sexual behaviors of interest, the magnitude of these behavioral differences does not appear large enough to explain the observed disparities in oral HPV infection and HPV-HNC.

6033

Poster Discussion Session (Board #22), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**A preliminary cost-effectiveness analysis of human papillomavirus vaccination in males for the prevention of oropharyngeal cancer.**

Donna M. Graham, Wanrudee Isaranuwachai, Steven Habbous, Claire de Oliveira, Geoffrey Liu, Lillian L. Siu, Jeffrey S. Hoch; Princess Margaret Cancer Center, Toronto, ON, Canada; Pharmacoeconomics Research Unit, Cancer Care Ontario, Toronto, ON, Canada; Ontario Cancer Institute, Princess Margaret Cancer Centre, Toronto, ON, Canada; Support, Systems and Outcomes Division, Toronto General Research Institute, Toronto, ON, Canada

Background: Many western countries have established female human papillomavirus (HPV) vaccination programmes for prevention of cervix cancer. Efficacy against additional HPV-related disease is proven in both sexes, but cost-effectiveness of male vaccination remains controversial. Projected figures suggest incidence and prevalence of oropharyngeal cancer (OPC) in North America will exceed that of cervix cancer by 2020 due to HPV-related cases. Two cost-effectiveness analyses evaluating male HPV vaccination have included OPC, with contrasting results. The Canadian government recommends, but does not fund, male vaccination. In order to assess the value for money of male HPV vaccination in Canada with respect to OPC, we performed a preliminary cost-effectiveness analysis. **Methods:** Following extensive literature review regarding HPV-related OPC in Canadian males, healthcare cost and clinical effectiveness estimates were obtained from published studies. A Markov model was used to compare potential costs and effectiveness of HPV vaccination against no vaccination among males aged 12 years old. A 3-month cycle length was used with a 'lifetime' time horizon. The outcome of the analysis was the incremental cost per quality-adjusted life-year (QALY). Sensitivity analyses were conducted on variables such as vaccine uptake rate and efficacy. **Results:** Assuming 99% vaccine efficacy and 70% uptake, the use of HPV vaccine produced 0.05 more QALYs and saved \$204 Canadian dollars (CAD) per person compared with no vaccine (QALYs and costs discounted at 5% per year). Assuming 50% vaccine efficacy and 50% uptake, use of HPV vaccine produced 0.01 more QALYs and saved \$43 CAD. Based on a population of 12 year old males of 192,940 in 2012, male HPV vaccination may potentially save \$8.3-39.4 million CAD for this cohort over its lifetime. **Conclusions:** Knowledge gaps exist regarding male HPV vaccination for OPC prevention. Due to practical limitations, including lack of identifiable precursor lesions in OPC, clinical trials to evaluate this issue may not be feasible. Without considering the effects of herd immunity, this preliminary analysis highlights potential savings from male vaccination.

Phase I study of weekly albumin-bound paclitaxel (ab-P) plus weekly cetuximab (Cet) plus intensity-modulated radiation therapy (IMRT) in patients with stage III/IVb head and neck squamous cell carcinoma (HNSCC).

Matthew G. Fury, Eric Jeffrey Sherman, Shyam S. Rao, Suzanne L. Wolden, Stephanie Smith-Marrone, Kenneth K. Ng, Boris Mueller, Daphna Y. Gelblum, Pinaki R. Dutta, James Lee, Ronglai Shen, Sarah Kurz, Nora Katabi, Sofia Haque, Nancy Y. Lee, David G. Pfister; Memorial Sloan-Kettering Cancer Center, New York, NY; Memorial Sloan-Kettering Cancer Center, Tarrytown, NY; Memorial Sloan-Kettering Cancer Center, Rockville Center, NY; Memorial Sloan-Kettering Cancer Center, Commack, NY

Background: There is a clinical need to improve the efficacy of standard Cet + concurrent RT for pts with stage III/IVb HNSCC. Taxanes have potent activity against HNSCC, and ab-P may offer therapeutic advantages in comparison with other drugs of this class. **Methods:** This was a single institution phase I study with a modified 3 + 3 design. 4 dose levels (DLs) of weekly ab-P were explored (30, 45, 60, and 80 mg/m²) during IMRT. Standard Cet (450 mg/m² loading dose followed by 250 mg/m² weekly) concurrent with IMRT (total dose, 70 Gy) was prescribed for all pts. The maximum-tolerated dose (MTD) would be exceeded if >2/6 pts experienced DLTs at a given dose level. NCI CTCAE v.3 was used, and DLT monitoring extended until 2 wks after IMRT. **Results:** 25 eligible pts (20M, 5F) enrolled, with median age 58 years (range, 46-84) and median KPS 90 (range 80-100). Primary tumor sites were oropharynx, 20 (10 HPV pos, 5 HPV neg, 5 not done); neck node with unknown primary, 2; and larynx, oral cavity, and maxillary sinus, 1 each. Two pts never received ab-P and were deemed inevaluable. At DL 1 (ab-P, 30 mg/m²), there was one DLT (g.4 pneumonia) among 6 pts. At DL2 (ab-P, 45 mg/m²), there were 2 DLTs (g.4 cerebrovascular accident; g.3 decrease in L. ventricle ejection fraction/CHF exacerbation) among 6 pts. At DL3 (ab-P, 60 mg/m²), there was 1 DLT (g.3 supraventricular tachycardia) among 6 pts. MTD was exceeded at DL4 (ab-P, 80 mg/m²) with 3 DLTS (g.3 neuropathy, g.3 dehydration, g.3 anemia) among 5 evaluable pts. For the entire study population, most common \geq g3 AEs were: lymphopenia 100%, functional mucositis, 56%, and pain in throat/oral cavity, 52%. There were no treatment-related deaths. Among 23 evaluable pts at a median follow up of 29 months, 2y PFS rate is 64% (95% CI: 41-80%) and 2y OS rate is 90% (95% CI: 66-97). **Conclusions:** The recommended phase II dose is ab-P 60 mg/m² weekly when given concurrently with IMRT and standard weekly Cet. This regimen merits further study as an alternative to IMRT + Cet alone for pts who require a non-platinum regimen. This study was approved and funded by the NCCN from general research support provided by Celgene, Inc. Clinical trial information: NCT00736619.

6035

Poster Discussion Session (Board #24), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**A phase III randomized trial of two cisplatin-based concurrent chemoradiation (CCRT) regimens for locally advanced head and neck squamous cell carcinoma (LAHNSCC).**

Cristina P. Rodriguez, David J. Adelstein, Lisa A. Rybicki, Panayiotis Savvides, Jerrold P. Saxton, Shlomo A. Koyfman, John Greskovich, Min Yao, Joseph Scharpf, Pierre Lavertu, Benjamin J. Wood, Brian Burkey, Robert Lorenz, Rod Rezaee, Chad Zender, Denise I. Ives; Oregon Health & Science University, Portland, OR; Cleveland Clinic, Cleveland, OH; Cleveland Clinic Foundation, Cleveland, OH; Case Comprehensive Cancer Center, University Hospital of Cleveland Medical Center, Cleveland, OH; Cleveland Clinic, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH

Background: Excellent outcomes have been reported using both single and multiagent CCRT in LAHNSCC. This trial compares a 5FU/cisplatin regimen to single agent cisplatin CCRT. **Methods:** Patients (pts) with previously untreated stage III-IV, M0, LAHNSCC of the larynx, oropharynx (OP), oral cavity or hypopharynx received definitive once or twice daily radiation (70-74.4 Gy) and were randomized between concurrent chemotherapy with either Arm A: cisplatin 100mg/m² on days 1, 22 and 43 or Arm B: cisplatin (20mg/m²/day) and 5-FU (1000mg/m²/day) as continuous 96 hour infusions weeks 1 and 4. ECOG performance status ≤ 1, and adequate renal, liver and marrow function were required for entry. The primary endpoint was recurrence free survival (RFS). **Results:** Between 2/2008 and 10/2011, 69 pts were enrolled. An accrual of 126 pts was planned in order to demonstrate an improvement in 2-year RFS from 55% to 75%. The study was closed prematurely when a scheduled interim analysis confirmed markedly better outcomes in both arms and the futility of further comparison. Pt and tumor characteristics were well balanced in both arms. OP cancer was diagnosed in 83% of pts; 86% of the OP cancers were HPV/p16+. With a median follow up of 29.4 months, 2 yr Kaplan-Meier outcome estimates were similar between arms (Table). Pts on Arm A experienced more nephrotoxicity (26% vs. 3%; p=0.007) and ototoxicity (11% vs. 0%; p=0.042), but less Grade ≥2 radiation dermatitis (43% vs. 68%; p=0.038), neutropenia <1000/mm³ (34% vs. 65%; p=0.012), and unplanned hospitalization (43% vs. 68% p=0.038). Treatment outcomes were inferior and feeding tube requirements greater in the HPV/p16 negative and actively smoking pts. **Conclusions:** Although these CCRT regimens produced similar outcomes, their toxicity profiles proved different and may serve to inform individual pt treatment. Tobacco use and HPV status had far greater impact on treatment outcomes than did the CCRT regimen. Clinical trial information: NCT00608205.

Outcome	All pts (N=69)	Arm A (N=35)	Arm B (N=34)	p (A vs. B)
RFS	89%	94%	85%	0.62
Overall survival	90%	96%	83%	0.07
Locoregional control	99%	100%	97%	0.94
Distant metastatic control	92%	94%	91%	0.86
Freedom from recurrence	91%	94%	88%	0.84

6036

Poster Discussion Session (Board #25), Sat, 1:15 PM-5:15 PM and
4:45 PM-5:45 PM**CAPRA: Safety, efficacy, and translational biomarkers of weekly everolimus, carboplatin, and paclitaxel as induction therapy for locally advanced head and neck squamous cell carcinoma (HNSCC).**

Eric Raymond, Christophe Le Tourneau, Michel Gatineau, Jean-Pierre Delord, Jérôme Fayette, Chantal Dreyer, Annemilai Tijeras-Raballand, Sebastien Albert, Muriel Granier, Benoist Chibaudel, Alexandra Hadengue, Nasredine Aissat, Khemaies Slimane, Sandrine J. Faivre; Hôpital Beaujon, Clichy, France; Institut Curie, Paris, France; Hôpital Saint-Joseph, Paris, France; Institut Claudius Regaud, Toulouse, France; Centre Léon Bérard, Lyon, France; Department of Medical Oncology, Beaujon University Hospital, Clichy, France; Département of Medical Oncology, Beaujon University Hospital, Clichy, France; Head and neck surgery department, Bichat University Hospital, Paris, France; GERCOR, Paris, France; Novartis Pharma SAS, Rueil-Malmaison, France

Background: The PI3K/mTOR pathway is activated in >50% of HNSCC with preclinical synergism between everolimus and carboplatin/paclitaxel. **Methods:** Patients (pts) with untreated locally advanced HNSCC with ECOG PS<2 received 9 consecutive weekly (w) cycles (cy) of CAPRA combining everolimus (30 mg/w at dose-level 1 then 50 mg/w at dose-level 2) with carboplatin (AUC2) and paclitaxel (60 mg/m²) followed by chemoradiotherapy. Endpoints were safety (CTCv3.0), antitumor activity (RECIST1.1), pharmacodynamic biomarkers on tumor biopsy. **Results:** A total of 50 pts with stage IV HNSCC (41 males, 9 females, median age 61) were enrolled. Among 7 patients included in the phase I, no dose-limiting toxicity was reported and the recommended dose (RD) of everolimus was 50 mg/w. Safety evaluation in 46 pts treated at RD for 325 cy and a mean number cy/pt of 7.1 (95%CI: 6.3-7.8) showed grade (Gr) 1-2 adverse events consisting of asthenia (50%), nausea/vomiting (28%), alopecia (26%), mucositis (24%), and constipation (20%). Hematological toxicities (Gr1-2/3-4) were neutropenia (35%/39%), anemia (61%/17%), and thrombocytopenia (54%/13%). Everolimus-related Gr3 toxicities were rashes (1pt), pruritus (1pt), dyspnea (1pt), hyperglycemia (2pts), and Gr1-2 hypercholesterolemia (23pts). There was no toxic death. Among 38 pts evaluable for antitumor activity, one pt experienced a complete response (2.6%), 29 pts a partial response (76.3%), and 8 pts a stable disease (21%) for an overall response rate of 79% (no progression reported). Interestingly, 20 major responses (>50% reduction tumor volume) were observed in large necrotic primary tumors/N3 involvement. Efficacy was not correlated to *KRAS/BRAF/PI3KCA/EGFR* mutations. Significant decreases of Ki67/p-S6K activities were observed in post CAPRA biopsies compared to baseline. **Conclusions:** Weekly everolimus with carboplatin/paclitaxel as induction regimen was well tolerated with 11% grade 3 and no grade 4/5 toxicity. Translational data showed direct effects of everolimus in tumors. CAPRA yields high rate of objective responses in patients with locally advanced HNSCC. Clinical trial information: NCT01333085.

6037

General Poster Session (Board #10A), Sat, 8:00 AM-11:45 AM

HPV prevalence in the different subsites of the oropharynx.*Per Attner; Karolinska University Hospital, Stockholm, Sweden*

Background: Oropharyngeal cancer patients are often reported as one group in articles and studies regardless that within the subsites of the oropharynx, there are differences regarding clinical features, treatment and HPV prevalence. To investigate these differences, we wanted to further analyze HPV prevalence in the different subsites of the oropharynx. **Methods:** We identified all patients diagnosed with oropharyngeal cancer in Stockholm County, Sweden, between 2000 and 2007, using the Swedish Cancer Registry, a registry unique in its reliability. Using the ICD 10 codes C01.9 (base of tongue cancer), C09.0-C09.9 (tonsillar cancer) and C10.0-C10.9 (oropharyngeal cancer) and C50.1-C50.8 (cancer of the soft palate). The two last subsites were grouped together into the group Other Oropharyngeal Cancer (OOC). We retrieved pre-treatment biopsies and tested for HPV-DNA using PCR, both with general primers and HPV16 specific primers. **Results:** We identified 474 patients diagnosed with oropharyngeal cancer in Stockholm County, Sweden between 2000 and 2007; 290 diagnosed with tonsillar cancer, 109 diagnosed with base of tongue cancer and 75 diagnosed with other oropharyngeal cancer. Of these 474 patients, pre-treatment biopsies for HPV-testing were available for 400 patients (236, 95 and 69, respectively). In the tonsillar cancer group, 185 biopsies were HPV-DNA-positive (79%), in the base of tongue cancer group 71 (75%) and in the other oropharyngeal cancer group 17 were positive (25%) **Conclusions:** Tonsillar and base of tongue cancer share some similarities and HPV prevalence is similarly high in both groups. Other oropharyngeal cancer (OOC) does not share the high HPV-prevalence and it would then be preferred that the sub-sites of the oropharynx are reported separately.

The results of first-line chemotherapy in 108 patients affected by recurrent or metastatic salivary gland malignancies (RMSGM).

Mario Airoidi, Massimiliano Garzaro, Luca Raimondo, Fulvia Pedani, Elisa Bellini, Oliviero Ostellino, Giuseppe Riva, Giancarlo Pecorari; 2nd Medical Oncology Division, A. O. Città della Salute e della Scienza di Torino, Turin, Italy; 1st ENT Division, Surgical Sciences Department, University of Turin, Turin, Italy

Background: Recurrent/metastatic salivary gland malignancies (RMSGM) are not manageable by means of surgery and/or radiotherapy; chemotherapy (CT) represents a palliative strategy without any curative purposes. In this abstract we report the results of CT in 108 cases of RMSGM. **Methods:** We enrolled 108 patients with radiologically documented progression of RMSGM. Five pts received cisplatin (DDP) 100 mg/sm d 1, q 3wks; 8 pts doxorubicin (DOX) 75 mg/sm d1, q 3wks; 30 pts vinorelbine (VNB) 30 mg/sm d. 1 and 8, q 3 wks; 9 pts DDP 60 mg/ sm + epirubicin (EPI) 60 mg/sm + 5-FU 600 mg/sm d.1, q 3 wks; 42 pts DDP 80 mg/sm d.1 + VNB 25 mg/sm d. 1,8 , q 3 wks, and 14 pts carboplatin (CBDCA) AUC 5.5 + paclitaxel (Taxol; TAX) 175 mg/sm d.1, q 3 wks. The maximum number of CT cycles was 6. **Results:** Patients characteristics were as follows: 65 males (60%) and 43 females (40%); median age: 57 yrs (range 20-74); 42 pts (39%) had ECOG PS=0 and 66 pts(61%) PS 1-2 (0-2); histological evaluation was as follow: adenocarcinoma 28 pts (26%), adenoid cystic carcinoma 63pts (58%), undifferentiated carcinoma 12 pts (11%) and malignant mixed tumors 5 pts (5%); the disease was local in 40 pts (37%), local + distant metastases in 30 pts (28%) and only metastatic in 38 pts (35%). **Conclusions:** DDP is the probably the most effective single drug scheme; our data suggest that VNB has superimposeable results with a better gastroenteric and renal toxicity profile. Single drug CT seems less effective than multi drug CT with DDP-based schemes. DDP+EPI+5-FU is as effective as DDP+VNB; CBDCA+TAX seems to have worse clinical outcomes than DDP combinations. The impact of CT on symptoms is quite good while on survival needs further investigations, moreover our data confirm the need of new biological target agents to improve clinical outcomes in RMSGM.

Drug	Pts No.	ORR%	NC%	mPFS (m)	mOS (m)
DDP	5	20	60	4	6
DOX	8	20	25	3	5
VNB	30	20	30	5	8
DDP+EPI+5-FU	9	33	22	7	9
DDP+VNB	42	33	33	7.5	10.5
CBDCA+TAX	14	14	45	5	8

Psychophysical functioning and quality of life in 94 patients affected by oropharyngeal cancer and treated with different therapeutic approaches.

Fulvia Pedani, Mario Airoidi, Massimiliano Garzaro, Riccardo Torta, Luca Raimondo, Giuseppe Riva, Antonella Varetto, Elisa Bellini, Laura Salonia, Giancarlo Pecorari; 2nd Medical Oncology Division, A. O. Città della Salute e della Scienza di Torino, Turin, Italy; 1st ENT Division, Surgical Sciences Department, University of Turin, Turin, Italy; Psycho-oncology Unit - San Giovanni Battista Hospital, Turin, Italy

Background: The treatment of oropharyngeal squamous cell carcinomas (OSCC) may heavily affect patient's quality of life (QoL). Aim of our study was the evaluation of the impact of different treatments on physical and psychological functioning and on QoL of patients affected by stage III-IV disease. **Methods:** The enrolled sample was composed by 94 OSCC patients divided into 3 subgroups based on treatment modalities: surgery + adjuvant radiotherapy (S + RT: 30 patients), exclusive concomitant chemoradiotherapy (CT + RT: 30 patients) and exclusive chemotherapy (CT) in 34 patients not suitable for surgery and/or radiotherapy. Psycho-oncological assessment included: Hospital Anxiety Depression Scale (HADS), Montgomery-Asberg Depression Scale (MADRS), Mini-Mental Adjustment to Cancer scale (MINI-MAC), EORTC QLQ C-30 questionnaire with the specific module Head and Neck 35 (H&N35). **Results:** The 60 patients primarily treated with S + RT or CT + RT presented superimposeable clinical and tumour characteristics while those treated with exclusive CT were affected by stage IV disease and in the 90% of cases underwent to previous treatment exclusive or combined treatment such as surgery, radiotherapy and chemotherapy. In the following table, data about physical and psychological functioning and on QoL of the 3 subgroups of patients are summarized. **Conclusions:** In stage III-IV OSCC treatments have a strong influence on QoL and coping styles. Patients treated with CT + RT were characterized by a lower percentage of self-reported anxiety and depression and higher EORTC Global QoL score. More than one third of patients treated with S + RT had overt symptoms of anxiety and depression. Stage IV patients treated with palliative CT had elevated level of anxiety, depression and low quality of life. Auto-evaluation is less effective in depression assessment. The role of concomitant psychological supportive care should be evaluated in these patients treated with different approaches.

	HADS Anxiety	HADS Depression	MADR Depression	EORTC Global QoL score
S + RT	33.3%	30.5%	40.1%	71.42
CT + RT	22.2%	13.9%	40.1%	76.05
CT	70.6%	67.5%	76.4%	49.04

6040

General Poster Session (Board #10D), Sat, 8:00 AM-11:45 AM

Validation of late oral health outcomes, an oral health subscale of the Vanderbilt Head and Neck Symptom Survey in post-radiation therapy head and neck cancer patients.

Leanne Kolnick, Jie Deng, Joel Brian Epstein, Cesar A. Migliorati, Julie Rezk, Mary S. Dietrich, Barbara A. Murphy; Department of Medicine, Vanderbilt University Medical Center, Nashville, TN; Vanderbilt University, School of Nursing, Nashville, TN; Oral Medicine Services, Otolaryngology and Head and Neck Surgery, City of Hope National Medical Center, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; Department of Diagnostic Sciences and Oral Medicine, College of Dentistry, University of Tennessee Health Sciences Center, Memphis, TN; Division of Dentistry, Dept of Oral and Maxillofacial Surgery, Vanderbilt University Medical Center, Nashville, TN; Department of Biostatistics, Schools of Medicine and Nursing, Vanderbilt University Medical Center, Nashville, TN

Background: The Vanderbilt Head and Neck Symptom Survey (VHNSS) version 2.0 oral symptom subscale was developed to address potentially overlooked and underreported oral health issues. We report the validation of questions pertaining to xerostomia (4 items), dental health (4 teeth), dentures (1 item) and trismus (1 item). **Methods:** Between May 2011 and April 2012, 50 patients treated with chemoradiotherapy for head and neck cancer completed the 50-item VHNSS survey, underwent an oral health assessment by a dentist, salivary flow and inter-incisal opening (IIO) measurements. **Results:** Patient reported “problems with dry mouth” correlated with unstimulated salivary flow rates (-0.43 , $p = 0.002$). “Cracked teeth” (-0.55 , $p = < 0.001$) or “difficulty chewing due to teeth” (-0.43 , $p = 0.004$) correlated with urgent or emergent dental care issues identified on exam. Using a cut off of >4 on any of four the dental questions, we were able to identify 83% of patients with urgent or emergent dental issues. The ROC curve was useful (0.89 , $p < 0.001$) for separating patients with and without urgent/emergent dental issues. “Limitations” in jaw movement correlated with IIO (-0.43 , $p = 0.002$). Small numbers of patients with dentures precluded meaningful analysis of this subsample. **Conclusions:** Clinically significant oral health issues pertaining to xerostomia, dental health and trismus may be identified using the oral health subscale of the VHNSS version 2.0. Patients who score > 4 on any of the teeth related items should be referred for immediate dental evaluation; and for trismus should be referred for physical therapy.

Evaluation of potential predictive markers of efficacy of dacomitinib in patients (pts) with recurrent/metastatic SCCHN from a phase II trial.

Marie-Lise Audet, Ghassan Allo, Xiaoduan Weng, Lucia Kim, Olguta Gologan, Suzanne Kamel-Reid, Lillian Siu, Francois Coutlee, Scott Andrew Laurie, Sebastien J. Hotte, Simron Singh, Eric Winqvist, Stephen K. L. Chia, Eric Xueyu Chen, Kelvin K. Chan, Patricia A English, Ian Taylor, Susan Quinn, Christine Mormont, Denis Soulieres; Centre Hospitalier Universitaire De Montréal, Hôpital Notre-Dame, Montreal, QC, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; University Health Network, Department of Pathology and Laboratory Medicine, Toronto, ON, Canada; Ottawa Hospital Cancer Centre, Ottawa, ON, Canada; Juravinski Cancer Centre, Hamilton, ON, Canada; Odette Cancer Centre, Sunnybrook Health Sciences Centre; University of Toronto, Toronto, ON, Canada; London Health Sciences Centre, London, ON, Canada; British Columbia Cancer Agency, Vancouver, BC, Canada; Princess Margaret Cancer Center, University Health Network, Division of Medical Oncology & Hematology, Department of Medicine, University of Toronto, Toronto, ON, Canada; Princess Margaret Hospital, Sunnybrook Odette Cancer Centre, Toronto, ON, Canada; Pfizer Inc., San Diego, CA; Pfizer Oncology, Groton, CT; Pfizer, Cambridge, MA; Pfizer Canada, Montreal, QC, Canada

Background: Dacomitinib is an irreversible pan-HER TKI with preclinical (EGFR^{vIII}+ cell lines, SCCHN xenografts) and clinical activity (phase II recurrent/metastatic SCCHN; Razak et al, *Ann Oncol* 2012). However, little is known about predictive markers of efficacy related to EGFR signalling in this setting. **Methods:** Of 69 pts treated with 1st-line dacomitinib in a phase II trial for recurrent/metastatic SCCHN, 48 pts had archival tumor specimens obtained before treatment and 13 had paired biopsies (days 0 and 7 of therapy, FFPE and snap frozen). EGFR^{vIII} and PTEN (IHC), HPV genotyping and human genomic mutations (Sequenom OncoCarta Panel – 19 genes, 238 mutations) were evaluated on archival tissue. IHC expression of AKT, CC3, EGFR, ERK, HER2, HER3, MET, Ki67, pAKT, pEGFR, pERK, pHER2 and pMET was evaluated in paired specimens. The presence/absence or expression level of these markers was correlated with response (RR)/clinical benefit (CB), PFS and OS. **Results:** In pts with archival tissue, no statistically significant difference was found in RR/CB or PFS based on HPV, EGFR^{vIII}, PTEN or presence of mutation. There was a trend to increased OS in HPV+ pts (HR 0.47, 95% CI 0.21–1.07, P=0.068). In paired biopsies, some expression variation was seen for cytoplasm AKT, membrane EGFR, nuclear ERK and pAKT. There was no correlation between basal expression of these markers and RR/CB or PFS. Variations in ratio to baseline of EGFR, pAKT, pERK and MET were qualitatively associated with RR/CB. No statistically significant correlations could be established for PFS, but there were interesting qualitative variations in the levels of expression of some molecules, eg, EGFR, pAKT. **Conclusions:** No predictive efficacy marker was identified. It cannot be determined if increased OS in HPV+ cases is due to prognostic or predictive effects. Paired biopsies demonstrated that dacomitinib was associated with variation in expression of multiple elements in signalling pathways linked to EGFR. Given the small number of paired biopsies, and large amount of data generated, descriptive study of cases is required. Further data will be presented at the meeting. Clinical trial information: 00768664.

6042

General Poster Session (Board #10F), Sat, 8:00 AM-11:45 AM

Role of adjuvant radiation in patients with squamous cell carcinomas of the oral cavity.

Steven Brad Maron, Bonnie Gould Rothberg, Michael Otremba, Benjamin Judson, Daniel Morgensztern; Yale School of Medicine, New Haven, CT

Background: Although surgery is the initial treatment of choice for patients with stage III squamous cell carcinoma (SCC) of the oral cavity (OC), the role of adjuvant radiotherapy (RT) remains undefined. We evaluated the differences in outcome according to stage subsets and use of adjuvant RT. **Methods:** The Surveillance Epidemiology and End Results (SEER) database was queried for patients with SCCOC, treated with surgery (S), RT, or both (SRT); older than 21 years; and diagnosed between 2004 and 2009. Patients with extracapsular lymph node extension or multiple primary cancers were excluded. Overall Survival (OS) rates were estimated by the Kaplan-Meier method and compared using log-rank testing as well as Cox proportional hazards. **Results:** Among the 1,051 patients meeting eligibility criteria, the most common treatment was SRT (49.1%), followed by S alone (28.9%), and RT alone (22.0%). The 5-year OS ranged from 33.3% in T3N1 to 52.8% in T1N1. Compared to S alone, the addition of RT improved 5-year OS in the entire cohort from 39.5% to 51.1% (HR 0.69, 95% CI 0.54-0.87, $p = 0.002$). This benefit, however, was significant only for stage T3N0 with a trend towards improvement in the T3N1 group. No significant benefit was observed in T1N1 or T2N1 disease (Table). **Conclusions:** Stage III SCC of the oral cavity is a heterogeneous disease with significant differences in survival according to its subsets. Adjuvant RT was associated with improved survival for patients with stage T3N0 disease but not T1N1 or T2N1. The benefit of RT in T3N1 cases did not reach statistical significance likely due to the small number of patients. If confirmed in prospective studies, further subdivision of stage III SCC of OC may be necessary, and the indication for RT may be restricted to patients with T3 disease.

Subgroup	Treatment (N)	5-year OS	HR (95% CI)	P value
T1N1	S (87)	51.6%	1.00	-
	RT (26)	38.7%	1.80 (0.90-3.57)	$p=0.10$
	SRT (133)	56.3%	0.80 (0.49-1.33)	$p=0.39$
T2N1	S (82)	33.1%	1.00	-
	RT (75)	34%	1.37 (0.88-2.15)	$p=0.16$
	SRT (195)	46.6%	0.74 (0.50-1.10)	$p=0.13$
T3N0	S (114)	40.6%	1.00	-
	RT (83)	18.3%	1.95 (1.32-2.89)	$p=0.0009$
	SRT (137)	52.8%	0.55 (0.36-0.84)	$p=0.006$
T3N1	S (21)	27.0%	1.00	-
	RT (47)	19.4%	1.05 (0.52-2.12)	$p=0.89$
	SRT (51)	49.6%	0.54 (0.26-1.14)	$p=0.11$

6043

General Poster Session (Board #10G), Sat, 8:00 AM-11:45 AM

Phase II randomized trial of radiotherapy (RT), cetuximab (E), and pemetrexed (Pem) with or without bevacizumab (B) in locally advanced squamous cell carcinoma of the head and neck (SCCHN).

Athanassios Argiris, James Ohr, Greg J. Kubicek, Uma Duvvuri, Dwight Earl Heron, Athanasios Panayotis Kotsakis, Christina Spencer, Seungwon Kim, Jennifer R. Grandis, Jonas Talmadge Johnson, Julie E. Bauman, Michael K. Gibson, Robert L. Ferris; University of Texas Health Science Center at San Antonio, San Antonio, TX; University of Pittsburgh, Pittsburgh, PA; University of Pittsburgh Cancer Institute, Pittsburgh, PA; University General Hospital of Heraklion, Department of Medical Oncology, Heraklion, Greece; University of Pittsburgh Eye and Ear Institute, Pittsburgh, PA; University of Pittsburgh Medical Center, Pittsburgh, PA

Background: We previously developed a novel regimen by the addition of Pem to RT and E (*Ann Oncol* 2011;22:2482). The current study evaluated PemE in the phase II setting and assessed the addition of B, an anti-VEGF monoclonal antibody, to PemE based on promising data with Pem/B (*JCO* 2011;29:1140) and E/B (*Ann Oncol* 2013;24:200) in recurrent/metastatic SCCHN. **Methods:** Patients (pts) with previously untreated stage III/IV SCCHN of the oropharynx, larynx or hypopharynx, performance status (PS) 0-1, no history of bleeding, and adequate laboratory parameters were randomized after stratification for PS, stage and site to: RT 2 Gy/day to 70Gy, E 250mg/m² weekly, after a loading dose of 400 mg/m² 1 week prior starting RT, and Pem 500mg/m² every 21 days x 3 cycles (arm A, PemE), or the same regimen plus B 15mg/kg every 21 days x 3 cycles during RT followed by B maintenance x 8 cycles (arm B, B-PemE), with antibiotic prophylaxis. The primary endpoint was progression-free survival (PFS) with a target of 64% at 2 years; planned sample size was 80. **Results:** 79 pts were randomized of whom 77 were eligible and analyzable (arm A/B:36/41); oropharynx 65/larynx 12; HPV+ 38/HPV- 15/HPV unknown 24; stage IV 54/stage III 23. 31 pts were enrolled in community centers. Treatment delivery of E and Pem was similar between arms: E, median number of doses 8 (range, 5-11); Pem 3 (2-3); and B 3 (1-3). 5 deaths occurred: 3 due to progression; 1 from unknown cause; 1 pt died from hemoptysis after bronchoscopy within 4 weeks of the 8th cycle of B leading to elimination of B maintenance after the 6th pt was enrolled. 9 pts (2 HPV+) progressed. With a median follow-up of 18 months, the 2-year PFS was 81% vs 87% and the 2-year overall survival (OS) was 96% vs 86% for arm A vs B. Grade 3/4 acute toxicities for arm A vs B (N=59) : dermatitis 3/1 vs 4/1; mucositis 13/2 vs 13/0; neutropenia 7/4 vs 7/3; rash 6/1 vs 8/1; fatigue 1/0 vs 3/0; weight loss 2/0 vs 5/0. **Conclusions:** Both regimens are feasible in academic and community practice settings with expected toxicities. Preliminary efficacy results are very promising and better than projected, however, the addition of B does not appear to improve outcomes. Clinical trial information: NCT00703976.

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General Poster Session (Board #10H), Sat, 8:00 AM-11:45 AM

Hospital variation in bronchoscopy and esophagoscopy rates during head and neck cancer diagnostic evaluation.

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Background: Hospital variation in bronchoscopy and esophagoscopy rates while diagnosing head and neck cancer may reflect professional uncertainty about the effectiveness of these procedures and a lack of clinical guidelines on best practices. Furthermore, high-volume hospitals have demonstrated better outcomes for select oncologic procedures. We examined the association between hospital case volume and diagnostic bronchoscopy and esophagoscopy rates. **Methods:** This retrospective cohort study used the 2006-2010 Michigan State Ambulatory Surgery Databases, capturing all outpatient surgical cases in Michigan. Eligible cases included head and neck cancer patients who underwent laryngoscopy, bronchoscopy, and/or esophagoscopy. The primary outcome measure was the likelihood that a patient who underwent laryngoscopy during head and neck cancer diagnostic workup also underwent either bronchoscopy or esophagoscopy. We used hierarchical, mixed-effect logistic regression to measure the association between the primary outcome and hospital case volume (<100, 100-999, or $\geq 1,000$ cases/hospital) while adjusting for patient-level variables such as age, sex, race, insurance status, and household income. **Results:** Of 17,828 head and neck cancer patients, 9,218 underwent diagnostic laryngoscopy. The 50 low-volume and 40 medium-volume hospitals performed significantly more concurrent bronchoscopies and esophagoscopies compared to the 2 high-volume hospitals (both $p < 0.001$). After adjusting for patient characteristics, medium-volume and low-volume hospitals respectively had 9.3-fold and 7.8-fold higher odds of performing esophagoscopy relative to high-volume hospitals ($p = 0.003$), although the association with bronchoscopy was no longer statistically significant. **Conclusions:** The proportion of head and neck cancer patients undergoing diagnostic laryngoscopy with concurrent esophagoscopy, but not bronchoscopy, varies significantly by hospital volume. A robust discussion of the comparative effectiveness of comprehensive and selective endoscopy will require further research into whether endoscopic volume correlates with tumor staging, survival, and other outcomes data.

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General Poster Session (Board #11A), Sat, 8:00 AM-11:45 AM

A phase II study of suberoylanilide hydroxamic acid (SAHA) in subjects with locally advanced, recurrent, or metastatic adenoid cystic carcinoma (ACC).

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Background: SAHA is a small molecule inhibitor of histone deacetylases (HDAC). Based on confirmed responses noted in 2 ACC patients treated with SAHA at our institution; we initiated this phase II trial. **Methods:** Patients with LA, recurrent or metastatic ACC and adequate organ function were eligible. Any prior number of chemotherapy regimens was allowed. Tumor tissue and blood were collected for correlative studies. SAHA was administered orally 400 mg daily for 28 days. The primary objective was to evaluate response rate (RR). Secondary endpoints included: time to tumor response (TTR); response duration (RD); progression-free survival (PFS); overall survival (OS); and adverse events (AE). 29 evaluable patients were needed in a Simon 2-stage optimal design to distinguish RR of at most 5% vs. at least 20%, with $\alpha = 0.15$ and power = 0.90. **Results:** 30 evaluable patients (overenrolled by 1) were accrued from at 5 different centers between August 2010 and June 2012. Median follow up among the censored patients is 3.8 months for PFS, and 7.2 months for OS. 19 patients were female, 24 were Caucasian, median age was 53 years (range 21-73); 21 patients had a performance status of 1; 20 patients were chemo-naïve. The median number of cycles completed was 5 (range 1-27+). Lymphopenia (n=5), hypertension (n=3), oral pain (n=2), thromboembolic events (n=2) and fatigue (n=2) were the only grade 3 AEs that occurred in more than 1 patient. 5 patients were dose reduced due to AEs. At the time of data cut-off, 9/30/2012, 1 patient with lung metastasis had a PR, with RD of 11.2+ months. TTR was 7.7 months. SD was the best response in 25 patients. Median PFS is 12.7 months (90% confidence interval lower limit: 3.7 months). Median OS has not been reached. There were 6 patients with PFS > 1 year. The correlative studies results will be presented. **Conclusions:** SAHA shows promise in the treatment of ACC. We are awaiting genomic analysis of the tumors to study the basis of clinical benefit (PR and SD) of SAHA in ACC. Future drug combination studies in ACC are being considered focusing on the epigenetic mechanism of SAHA. Supported by 5U01CA062487/19. Clinical trial information: NCT01175980.

Health care-associated infections (HAIs) in head and neck carcinoma (HNC) patients treated with chemotherapy (CT) and/or radiotherapy (RT).

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Background: HAIs are dangerous complications of HNC treatment. In lack of data we collected own data in a high volume HNCMOU, comparing them with those observed in other departments. **Methods:** HAIs recorded retrospectively among 2,288 hospital admissions at our HNCMOU observed from 2005 to 2009 were compared with 427 recent (2010-2012) hospital admissions. In the same period HAIs observed in ENT Surgical, Medical Oncology (MO) and Bone Marrow Transplantation (BMT) dept were recorded. **Results:** Between 2005 and 2009, 140 HAIs were observed in the HNCMOU: 49% Gram-, 35% Gram+, 16% fungi; 88% of *P. Aeruginosa* and all Enterobacteriaceae were sensible to meropenem and piperacillin/tazobactam, methicillin-resistant *S. aurei* (MRSA) were 42% (Table). In the last 3 years infections and resistances rates increased with a similar pattern of bacteria: among 212 HAIs (43% Gram-, 32% Gram+, 24% fungi) the majority (39%) involved respiratory tract, 89% of *P. aeruginosa* and 92% of Enterobacteriaceae were sensible to carbapenem and 89% and 51% were sensible to piperacillin/tazobactam. MRSA were 29%. We compared these data with HAIs occurred from 2005 to 2012 into other dept: most of HAIs in ENT Surgical dept were at surgical site (41%) due to Gram+ (45%), in BMT were sepsis (56%) due to Gram+ (51%) and in MO were urinary tract infections (39%) due to Gram – (70%). **Conclusions:** Gram- continue to represent the first cause of HAIs in HNC cancer patients treated with CT and/or RT, suggesting a peculiar pattern. This is paralleled by a rise in carbapenem resistance, while MRSA still represent a significant fraction.

Site	Gram + N 49 (35%)	Gram - N 69 (49%)	Fungi N 22 (16%)	Total 140
Respiratory tract	<i>S. aureus</i> 9 (15%)	<i>P. aeruginosa</i> 18 (30%)	<i>Aspergillus</i> species 2 (3%)	60 (43%)
	<i>Corinebacterium</i> species 3 (5%)	Enterobacteriaceae 16 (27%)		
	<i>S. pneumoniae</i> 3 (5%)	<i>H. influenzae</i> 6 (10%)		
	Others 3 (5%)			
Surgical	<i>S. aureus</i> 5 (13%)	<i>P. aeruginosa</i> 6 (15%)	<i>C. albicans</i> 9 (22%)	40 (29%)
	Others 6 (15%)	Enterobacteriaceae 5 (12%)	<i>C. species</i> 5 (13%)	
			<i>C. glabrata</i> 4 (10%)	
Blood	<i>S. epidermidis</i> 9 (26%)	Enterobacteriaceae 12 (34%)	<i>C. tropicalis</i> 2 (6%)	35 (25%)
	<i>S. aureus</i> 4 (12%)	<i>P. aeruginosa</i> 4 (11%)		
	Others 4 (11%)			
Other	<i>S. aureus</i> 4 (80%)	<i>G. vaginalis</i> 1 (20%)		5 (3%)

Cetuximab with or without sorafenib in recurrent/metastatic (R/M) squamous cell carcinoma of the head and neck (SCCHN).

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Background: For patients with R/M SCCHN, cetuximab, a monoclonal antibody against EGFR, is approved as a single agent and has a survival benefit when combined with chemotherapy. We hypothesized that addition of sorafenib, a multi-kinase inhibitor of targets including VEGFR, to cetuximab may have greater clinical benefit than cetuximab alone. **Methods:** This trial was designed as a blinded, randomized phase II, placebo-controlled study of cetuximab at 400 mg/m² IV on day 1 followed by 250 mg/m² IV weekly plus placebo bid (Arm A) or cetuximab at the same dose and schedule plus sorafenib 400 mg po bid (Arm B), each in 21 day cycles. After 19 patients were enrolled, the trial was amended to remove the placebo (and blinding) due to issues with placebo tablet solubility. Target sample size was 84 patients with 83% power to detect a 2-month increase in PFS, the primary study endpoint. Interim analysis was planned at midpoint, requiring hazard ratio < 1 to proceed to the second stage of study. Serum cytokine and tumor HPV ISH and p16 analyses were performed. **Results:** Of 56 patients (ages 26-74, 80% male) enrolled, 53 patients received treatment and 41 were evaluable for response. Of the patients who received therapy, 26 received cetuximab only (Arm A). For Arm A, the mean number of cycles delivered was 4.3 (range 1-16) and the mean for Arm B was 3.3 (range 1-11). The most common grade 3/4 AEs were fatigue (2 A, 1 B), hypertension (3 B), infusion reaction (both arms), and diarrhea (2 B). Arm A had 2 PRs and Arm B had 4 PRs. Median OS was 7 mo and 5.9 mo respectively. Median PFS was 3.1 mo for both arms. 24 patients had pre-treatment cytokine measurements. Of the 12 measured cytokines, high TGFB1 level was significantly correlated with inferior PFS (4.6 mo vs 1.6 mo), regardless of arm (p=0.015). 38 patients had tumors available for p16 staining (31 neg and 7 pos). 3 of 7 p16 pos were also HPV ISH pos. The p16 neg patients had significantly improved PFS (3.5 mo vs 1.6 mo) regardless of arm (p=0.032) but no difference in OS (p=1.0). **Conclusions:** Both arms demonstrated clinical activity although no significant difference was observed. However, a subset of patients with p16 neg tumors or low serum TGFB1 may have a greater benefit with cetuximab-based therapy. Clinical trial information: NCI-2012-02847.

Impact of obesity on survival in patients (pts) with early-stage squamous cell carcinoma (SCC) of the oral tongue.

Neil M. Iyengar, Amit Kochhar, Patrick Glyn Morris, Luc G. Morris, Xi Kathy Zhou, Alejandro Pino, Matthew G. Fury, David G. Pfister, Snehal G. Patel, Jay Boyle, Clifford Hudis, Andrew J. Dannenberg; Memorial Sloan-Kettering Cancer Center, New York, NY; Weill Cornell Medical College, New York, NY

Background: Obesity is a risk factor for several malignancies and an independent predictor of worse outcomes. In contrast, low body mass index (BMI) has been associated with increased risk of oropharyngeal cancers and poorer prognosis. In tongue SCC, impaired nutrition, smoking, and alcohol use impact BMI, and pre-diagnosis weight (wgt) loss negatively affects survival. The prognostic effect of obesity in tongue cancer is unknown. **Methods:** We conducted a single-institution, retrospective study of pts who underwent resection of T1/T2 SCC of the oral tongue. All pts underwent nutritional assessment prior to surgery. BMI was calculated from measured height and wgt at surgery and categorized as obese (≥ 30), overweight (25-29.9), or normal (18.5-24.9). The association between BMI and the primary endpoint, disease specific survival (DSS), was evaluated by Cox regression. The effect of BMI on the secondary endpoints, recurrence free survival (RFS) and overall survival (OS), was also assessed. **Results:** From 2000 to 2005, 155 pts (90 men, 65 women) of median age 57 (range 18-86) were included. Clinicopathologic characteristics were similar by BMI group. Obesity was significantly associated with adverse DSS compared with normal wgt in univariable (Table) and multivariable analyses (HR 2.87; 95% CI, 1.08-7.67; $p=0.04$). Obesity was also significantly associated with adverse RFS (HR 2.53; 95% CI, 1.12-5.74; $p=0.03$). Overwgt subjects may also have worse RFS (HR 1.74; 95% CI, 0.85-3.55; $p=0.13$). In pts without pre-diagnosis wgt loss ($n=94$), obesity was significantly associated with adverse OS (HR 2.70; 95% CI, 1.12-6.54; $p=0.03$). **Conclusions:** These data suggest that obesity is associated with a worse prognosis in tongue cancer, which may not have previously been appreciated due to confounding by pre-diagnosis wgt loss.

Characteristic (n)	Univariable		
	HR	95% CI	P
Age	1.03	1.00 - 1.06	0.02
BMI			
Normal (63)	Ref		
Overwgt (62)	1.34	0.59 - 3.06	0.49
Obese (30)	2.65	1.07 - 6.59	0.04
Stage			
T1 (109)	Ref		
T2 (46)	2.06	1.02 - 4.19	0.05
Nodal metastases			
No (100)	Ref		
Yes (55)	2.69	1.33 - 5.42	<0.01
Race			
Non-Black (151)	Ref		
Black (4)	5.87	1.76 - 19.55	<0.01
Smoking			
Never (65)	Ref		
Former (48)	1.24	0.55 - 2.78	0.60
Current (98)	0.97	0.40 - 2.34	0.94

Validation of the Vanderbilt Head and Neck Symptom Survey Version 2.0.

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Background: We previously reported the development and preliminary testing of the Vanderbilt Head and Neck Symptoms Survey version 2.0 (VHNSS 2.0) for assessment of symptom burden in head and neck cancer (HNC) patients who are undergoing or completed primary or adjuvant radiation based therapy (Cooperstein et al., *Head and Neck*, 2012, 24(6): 797-804). In addition to expanding items on existing domains, version 2.0 includes new domains such as dental health, mucosal sensitivity, and joint range of motion. Herein we report the results of initial validation of the instrument. **Methods:** 159 unique patients with HNC completed the 50 item VHNSS 2.0 as a part of one of three supportive care studies. Since each of these studies was prospective and longitudinal with repeated application of the VHNSS 2.0, we chose to utilize the first complete questionnaire for each patient for this analysis. **Results:** Patient characteristics: median age 57 (range 28-81 years), male 74.8%, Caucasian 91.8%, T3 or T4 46.5%, N2 or N3 66%, Site: pharynx 57.9%, oral cavity 15.1%, larynx 11.3%, 15.7%. Analysis identified 10 distinct clusters with 3 single items. The internal consistency of the clusters was good to excellent. Cronbach's alpha coefficient, a statistical measure of reliability is shown in the Table. **Conclusions:** The VHNSS 2.0 is a robust, reliable measure of acute and late toxicities in patients undergoing radiation for HNC. These results provide a platform for administering appropriate interventions, which would ultimately provide for effective management of adverse oral health outcomes.

Symptomatic clusters	# of items per cluster	Cronbach's alpha
Mouth pain	6	.90
General pain	3	.94
Swallow solid	8	.92
Swallow liquid	2	.70
Nutrition	4	.83
Mucous	4	.95
Dry mouth	5	.92
Taste/smell	6	.92
Voice	3	.89
Teeth	4	.75
Hearing	1	—
Trismus	1	—
Neck/shoulder ROM	1	—

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General Poster Session (Board #11F), Sat, 8:00 AM-11:45 AM

Recombinant adenoviral human p53 gene combined radio- and chemotherapy after a tumorectomy in treatment of laryngeal carcinoma in advanced stage.

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Background: To investigate the benefits of post-surgery using recombinant adenoviral human p53 gene (rAd-p53) combined with radio- and chemo-therapy in treatment of laryngeal carcinoma in advanced stage. **Methods:** A total of 61 patients with a stage III or IV laryngeal cancer, 51 males and 10 females with an average age of 63.2, were randomly divided into three groups: G1, G2 and G3. The 18 G1 patients received no treatment after surgery. The patients in G2 (21 patients) and G3 (22 patients) received rAd-p53 followed by radio-and chemo-therapy, and only radio- and chemo-therapy, respectively. The rAd-p53 was injected into the surgery wound bed at a dose of 2×10^{12} viral particles (VP) once per 3 days for 5 times. Radiotherapy was given at a total dose of 63-67 Gy in 7 weeks. The chemo-regimen included 5-Fu 500 mg/m² from day 1 to day 5 and DDP 30 mg / m² from day 1 to day 3 in a treatment course of 21days for two courses. **Results:** All the study patients were followed up for at least 3 years. One patient in G2 lost to follow up. The local control rates (no recurrence) at 3 years were 38.9% (7/18), 75.0% (15/20), and 54.5% (12/22) for G1, G2, and G3, respectively. The 3-years progress free survivals (PSF) were 38.9%, 50.0%, and 45.0% for G1, G2, and G3, respectively. The 3-years overall survivals (OS) were 38.9%, 65.0%, and 45.0% for G1, G2, and G3, respectively. The three efficacy endpoints of G2 were significantly better than both G1 and G3. These efficacy measures of G3 were significantly higher than G1. **Conclusions:** Post-surgery chemo- and radiotherapy is necessary to increase the local control rate, prolong both PRF and OS. The rAd-p53 gene therapy can farther increase the efficacy measures.

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General Poster Session (Board #11G), Sat, 8:00 AM-11:45 AM

Neoadjuvant erlotinib, erlotinib-sulindac, or placebo: A randomized, double-blind biomarker modulation study in operable head and neck squamous cell carcinoma (HNSCC).

Julie E. Bauman, Neil D. Gross, William E. Gooding, William Denq, Sufi M. Thomas, Lin Wang, Simion I. Chiosea, Brian L Hood, Melanie S Flint, Mai Sun, Thomas P. Conrads, Robert L. Ferris, Jonas Talmadge Johnson, Seungwon Kim, Athanassios Argiris, Lori J. Wirth, Jill Siegfried, Jennifer R. Grandis; University of Pittsburgh Cancer Institute, Pittsburgh, PA; Oregon Health & Science University, Portland, OR; University of Pittsburgh, Pittsburgh, PA; University of Pittsburgh Eye and Ear Institute, Pittsburgh, PA; University of Texas Health Science Center at San Antonio, San Antonio, TX; Massachusetts General Hospital, Boston, MA

Background: The epidermal growth factor receptor (EGFR) and cyclooxygenase-2 (COX-2) pathways are upregulated in HNSCC. Crosstalk potentiates growth, proliferation and invasion. Preclinical models show synergistic anti-tumor effects from dual blockade. We evaluated biomarker modulation in paired tumor specimens from a 3-arm phase 0 trial of erlotinib, a small molecule EGFR inhibitor; erlotinib + sulindac, a non-selective COX inhibitor; vs. placebo. **Methods:** Patients (pts) with untreated stage II-IVb HNSCC were randomized 5:5:3 to neoadjuvant erlotinib 150 mg daily (Arm 1, n = 19), erlotinib + sulindac 150 mg twice daily (Arm 2, n = 16), or placebo (n = 12). Pts were treated for 7-14 days. Tumor specimens were collected pre- and post-treatment. The primary endpoint was change in Ki-67 proliferative index. We hypothesized an ordering in Ki-67 down-modulation, with Arm 2 > Arm 1 > placebo. A Jonckheere-Terpstra test evaluated trend; a Wilcoxon test was applied to pairwise contrasts. We prepared tissue microarrays for IHC, to explore pharmacodynamic modulation of 21 EGFR and COX-2 pathway constituents including EGFR, Src, STAT3, Akt, EP2 and EP4. **Results:** From Dec 2005 – Dec 2008, 48 pts enrolled; 28 tumor pairs were evaluable for biomarker modulation. Class toxicities of EGFR inhibition, including acneiform rash and diarrhea, were observed on Arms 1 and 2. Compared to placebo, Ki-67 was reduced by erlotinib (p = 0.0005) or by erlotinib-sulindac (p = 0.0001). There was a trend in ordering of Ki-67 down-modulation, with greater effect from the addition of sulindac (exact Jonckheere-Terpstra, Arm 1 vs. 2, p = 0.003). Among 21 protein candidates tested for association with Ki-67, only low baseline p-Src correlated with greater Ki-67 reduction in both erlotinib groups ($R^2 = 0.312$, p = 0.024). **Conclusions:** Relative to placebo, brief neoadjuvant treatment with erlotinib or erlotinib-sulindac significantly decreased the proliferative index in operable HNSCC. Sulindac enhanced Ki-67 down-modulation. Efficacy studies of dual EGFR-COX inhibition are justified. Baseline p-Src warrants further study as a resistance biomarker for anti-EGFR therapy. Clinical trial information: NCT01515137.

Predictive values of (18)f-FDG PET standardized uptake value for adjuvant chemotherapy in patients with nasopharyngeal carcinoma.

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Background: Concurrent chemoradiotherapy (CCRT) with or without adjuvant chemotherapy is the mainstay of treatment for locally advanced nasopharyngeal carcinoma (NPC). However the benefit of adjuvant chemotherapy has been controversial and search for adequate predictive factors is warranted. We conduct this study to evaluate the predictive values of mean standardized uptake value (SUV) measured in [(18)F]-fluorodeoxyglucose positron emission tomography ((18)F-FDG PET) for adjuvant chemotherapy in patients with locally advanced NPC. **Methods:** From January 2004 and July 2010, Data collection were performed in 108 NPC patients who underwent (18)F-FDG-PET before CCRT and adjuvant chemotherapy. The SUV was recorded for the primary tumor. All patients received intensity modulated radiotherapy. Concurrent chemotherapy was composed of cisplatin 100mg/m² triweekly. Adjuvant chemotherapy was consisted of 3 cycles of cisplatin 75 milligrams/m² and fluorouracil 1000 milligrams/m² for 4 days. **Results:** The median follow-up was 41 months. The optimal cutoff value was 8.35 for SUV. 63.8% of patients had lower SUV (n=69), and 36.2% had higher SUV (n=39). Patients with a lower SUV had a significantly better 3-year overall survival (OS), disease-specific survival (DDS), and distant relapse-free survival (DRFS), but showed no difference in local relapse-free survival. Multivariate analysis showed only stage, SUV and adjuvant chemotherapy were significant in terms of overall survival. In patients with higher SUV, those receiving adjuvant chemotherapy had significantly higher 3-year OS, DDS, and DRFS compared with those without adjuvant chemotherapy. However, in those with lower SUV, there was no difference of OS, DDS and DRFS between patients with and without adjuvant chemotherapy. **Conclusions:** SUV of (18)F-FDG-PET for primary tumor could identify NPC patients who benefit from adjuvant chemotherapy.

	OS(%)	P	DDS(%)	P	DRFS(%)	P	LRFS(%)	P
Lower SUV (with vs without adjuvant chemotherapy)	95.1 vs 90.7	0.534	100 vs 95.1	0.308	95.7 vs 94.1	0.887	84.5 vs 90.5	0.541
Higher SUV (with vs without adjuvant chemotherapy)	88.2 vs 58.9	0.026	88.2 vs 58.9	0.026	85.2 vs 50.9	0.086	88.0 vs 65.5	0.098

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General Poster Session (Board #12A), Sat, 8:00 AM-11:45 AM

Clinical outcomes of transoral robot-assisted supraglottic laryngectomy: An experience of a French cooperative evaluation group of transoral robotic surgery.

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Background: Transoral, minimally invasive organ preservation surgeries are being increasingly used for laryngopharyngeal carcinomas to avoid the toxicities of combined chemotherapy and radiation therapy regimens. This study investigates the efficiency, safety, and functional outcomes of transoral robot assisted surgery (TORAS) for supraglottic laryngectomy. **Methods:** Experience of TORA supraglottic laryngectomy for patients with supraglottic carcinomas is presented in a multicentric study of a case series with planned data collection between 2009 and 2012. **Results:** Eighty-six of 262 patients underwent TORA supraglottic laryngectomy for supraglottic carcinomas. Thirty-three percent of patients were started an oral diet within 24 hours. For 77% of the other patients, the median use of a feeding tube was 8 days (0-10 months). Nine percent of them had a definitive percutaneous gastrostomy feeding. For 87% of patients no tracheotomy was performed, for 23% of the others patients, the median use of tracheotomy was 8 days, 3% of them had a definitive tracheotomy. Aspiration was observed in 22% of the patients in the postoperative course and was responsible for the death of one patient. Sixteen percent of the patients had a postoperative bleeding. Fifty percent of the patients received adjuvant radiation therapy based on pathology results. **Conclusions:** TORA supraglottic laryngectomy is a safe procedure with good functional outcomes and fast recovery but adverse events are possible. Consequently this technique needs a good selection of the patients to reduce the risk of postoperative complications.

Squamous cell carcinoma of the oral cavity (SCCOC) in young patients: The Dana Farber Cancer Institute experience.

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Background: Young patients (\leq age 45) with SCCOC and limited tobacco and alcohol exposure represent a distinct clinical entity with a poor prognosis. These patients are poorly characterized. We report our institution's experience treating these patients over the past decade. **Methods:** Patients \leq 45 years with SCCOC treated between 2001 and 2012 were identified retrospectively. Patient characteristics and treatment were recorded. **Results:** A total of 99 patients were identified (34 F and 65 M). Median age at diagnosis was 34 and 38 years, respectively (range 14 to 45 years). Thirty one (91.2%) women were never or former smokers with fewer than 10 pack-years, as compared with 50 (76.9%) men ($p = 0.07$). In women, 33 (97.1%) reported minimal to no alcohol use, compared with 52 (80%) men ($p = 0.02$). Oral tongue was the primary site in the majority of patients (30 F, 58 M). Surgical resection was the primary treatment modality (30, 88.2% F vs. 44, 68% M). Post-op radiation or chemoradiation was applied depending on stage and pathological findings. Stage: 53/99 (53.5%) presented with stage I or II disease and 46/99 (46.5%) had stage III or IV disease. Males on average had more advanced stage disease at presentation (33/65, 50.8%). Four of 7 women and 4 out of 18 men tested positive for human papilloma virus (HPV). Seven women (20.6%) and 13 (20%) men demonstrated evidence of local or locoregional recurrence with a median time to recurrence of 5 years and 0.67 years (range 1-10 and 0.08-11), respectively. Second primaries were rare (2, 5.88% F vs. 0, 0% M). Two women (5.9%) and 9 men (13.9%) died from recurrent disease. Overall, 4 (30.8%) women with stage III, IV disease demonstrated recurrence vs. 6 (18.2%) men ($p = 0.35$). **Conclusions:** In our experience, young patients with SCCOC have high cure rates that do not appear to be inferior to other sites in the head and neck area. Men and women are equally affected. Further clinical and genomic characterization for this group of patients is warranted.

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General Poster Session (Board #12C), Sat, 8:00 AM-11:45 AM

Use of gene expression signature to discriminate oropharyngeal cancers according to HPV16 status.

Haitham Mirghani, Catherine Ory, Nicolas Ugolin, Furrat Amen, Joel Guigay, Jean Lacau Saint Guily, Sylvie Chevillard, Roger Lacave; Head and Neck oncology Institut Gustave Roussy, Villejuif, France; Commissariat Energie Atomique, Fontenay Aux Roses, France; Institut Gustave Roussy, Villejuif, France; Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France; Hopital Tenon, University Paris 6, APHP, Paris, France; Hospital Tenon, APHP, Paris, France

Background: Strong evidence supports the hypothesis that high-risk human papillomavirus (HPV), particularly HPV16, is a causative agent for an increasing subset of oropharyngeal squamous cell carcinomas (OPSCC). These tumors have distinct oncogenic mechanisms and a more favorable prognosis than tobacco induced OPSCC. Although these differences emphasize the need for a specific therapeutic approach, HPV status is still not used to guide treatment. A better understanding of the molecular profile related to HPV16 induced OPSCC may help to develop personalized treatments. **Methods:** To identify an HPV16-related molecular signature, we compared the gene expression profile of 15 transcriptionally active HPV16-positive and 15 HPV16-negative OPSCC. The study was conducted in two steps. First, a learning set of 16 OPSCC comprising 8 HPV16-positives and 8 HPV16-negatives OPSCC was analyzed in order to identify the signature. Potentially confounding factors of stage, sex and tobacco consumption were equally distributed in both groups. Secondly, the robustness of this signature was further confirmed by blind case-by-case classification of an independent set of 14 OPSCC. **Results:** We identified a signature composed of 224 genes which discriminates HPV16-induced OPSCC from their tobacco induced counterparts. After the viral status was revealed, 13 out of 14 tumors were correctly classified according to tumor etiology, 1/14 was undetermined and none were misclassified. Interestingly, deregulated genes in HPV16-positive tumors are principally involved in innate immunity, in cell cycle regulation through the TP53/RB/E2F pathway, and autophagy through mTOR regulation. Well known targets of E6 and E7 proteins are also found to be deregulated. **Conclusions:** Our results demonstrate that a set of selected genes can distinguish OPSCC according to etiology. These genes shed light on HPV16 induced carcinogenesis since specific molecular pathways are deregulated. Further investigations are required for a better understanding of the differing natural histories and biological properties of these tumors. These properties may be exploited as a target of novel therapeutic agents in HPV-related OPSCC.

6056

General Poster Session (Board #12D), Sat, 8:00 AM-11:45 AM

Radiotherapy (RT) potentiation with weekly (q1w) or standard every 3 weeks (q3w) cisplatin chemotherapy (CT) for locally advanced head and neck squamous cell carcinoma (HNSCC).

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Background: Q3w CT is standard RT potentiation for HNSCC but its toxicity requires to look for new treatment's modalities. The aim was to explore if q1w CT could be a safe and effective alternative. **Methods:** Patients (pts) treated by chemoradiation (CT-RT) for a HNSCC were retrospectively included. Study population was first described. Then overall (OS) and progression-free survival since the RT onset were performed. Survival distributions were estimated by Kaplan-Meier method and compared between CT groups using the Log-Rank test. Prognostic effect of CT group was explored using Cox model. **Results:** 266 pts treated between January 2004 and December 2008 were included: 170 and 96 pts respectively received q1w and q3w CT. At diagnosis, 46% had oropharynx lesions, 20% larynx, 17% hypopharynx and 14% oral cavity. 70% pts experienced surgery, 39% CT induction and a median dose of radiation of 64 Gy without any significant difference between CT groups. However, median age at diagnosis was significantly different between q1w and q3w CT (58 vs 54, $p < 0.001$) as well as alcohol consumption (79% vs 68, $p = 0.047$), stage at diagnosis (30%-60% stage III-IV vs 13% -80%, $p = 0.003$), IMRT use (4% vs 13%, $p = 0.011$) and median weight before RT (66 kg vs 71kg, $p = 0.014$). Q3w CT was more toxic than q1w in terms of weight loss (87% vs 75%, $p = 0.012$), renal failure (50% vs 35%, $p = 0.022$), worse CT plan completion (42% vs 66%, $p < 0.001$). Moreover, grade 3/4 toxicities, such as mucositis (34% vs 13%, $p < 0.001$) and dermatitis (7% vs 1%, $p = 0.012$), were more frequent. More pts needed parenteral nutrition (10% vs 2%, $p = 0.008$), analgesics (91% vs 70%, $p < 0.001$), secondary hospitalization (31% vs 8%, $p < 0.001$), RT interruption ≥ 3 days (8% vs 2%, $p = 0.037$) and had long-term toxicities (24% vs 12%, $p = 0.014$). With a median follow-up of 42 months 95% CI [36.8-48.8], a trend in favour of q3w CT was found: 2-years OS of 83% (95% CI [73-90]) vs 74% (95% CI [66-80]), $p = 0.089$. However, after adjustment on prognostic factors CT group was not significantly associated with OS nor with PFS. **Conclusions:** Q1w RT-CT is safer than q3w and may be as efficient. Follow-up data will be updated to reinforce efficacy results.

Induction chemotherapy (IC) with docetaxel/cisplatin/5-fluorouracil (TPF) followed by cisplatin-containing concomitant chemoradiotherapy (CRT) in fit patients with locally advanced head and neck cancer (LAHNC): The CONDOR study—A study of the Dutch Head and Neck Society.

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Background: Standard treatment for patients (pts) with LAHNC is concomitant CRT containing cisplatin. In general 70% of the pts receive all planned cisplatin cycles. TPF IC is associated with survival benefit, but has never been studied in combination with standard CRT. We aimed to determine if TPF followed by cisplatin-containing CRT, in 2 different schedules, was feasible. **Methods:** In this multicenter randomized phase II trial LAHNC pts, PS 0-1, were treated with maximal 4 TPF courses (T 75 mg/m², P 75mg/m² and F 750 mg/m² day 1-5) and thereafter randomized between P 100 mg/m² on days 1, 22, 43 combined with conventional RT (arm A) or P 40 mg/m²weekly, maximally 6, combined with accelerated RT (arm B). Primary endpoint was feasibility, defined as receiving $\geq 90\%$ of the planned total radiation dose. Based on power analysis 70 pts were needed. **Results:** Following an interim-analysis, the study was early terminated after inclusion of 65 pts because only 32% of pts could be treated with the full cisplatin dose during CRT after TPF. 81,5% of pts was male, median age was 56 yrs and PS was 0 in 79% and 1 in 21%, primary site: oral cavity (23%), oropharynx (57%), hypopharynx (12%), larynx (8%). 3 pts did not start TPF; 6/62 pts were not randomized after TPF, due to death (1), toxicity (3) or severe PD (2). RR after TPF was CR 4%, PR 64% and SD 28% in the randomized pts. 27 pts were randomized in arm A and 29 in arm B. 97% of the pts received at least 90% of the planned total radiation dose. However, in arm A only 6 of the 27 pts (22%) and in arm B 12 of the 29 pts (41%) received the total planned chemotherapy part of the CRT. Most common grade 3-4 toxicity during TPF was febrile neutropenia (18%),and during CRT arm A vs arm B dehydration (26% vs 14%), dysphagia (26% vs 24%), mucositis (22% vs 57%) and creatinin increase (19% vs 3%). After a median follow-up of 21 (7-42) months 66% of the pts was still alive. **Conclusions:** After TPF IC cisplatin-containing concomitant CRT is not feasible in LAHNC, because the total planned dose of cisplatin could only be administered in 32% of the pts due to severe toxicity. Clinical trial information: NCT00774319.

Acupuncture for dysphagia after chemoradiation therapy in head and neck cancer: A randomized sham-controlled study.

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Background: Dysphagia is a common side effect following chemoradiation (CRT) in pts with head and neck cancer (HNC). The purpose of this pilot trial was to assess the feasibility of recruiting HNC pts and to collect preliminary data on the efficacy and safety of acupuncture on dysphagia-related QOL. **Methods:** Pts were eligible if diagnosed with stage III-IV HNC, without evidence of distance metastasis, receiving curative-intent CRT. Pts were randomized to 12 sessions of either active or sham acupuncture, once every two weeks, over 24 weeks from during CRT to 20-week post-CRT. All study personnel and the pts were blinded; the treating acupuncturists were not. MDADI and other questionnaires were measured at baseline (end of CRT), end of acupuncture, and at six months follow-up (12-month post-CRT). Data were analyzed by repeated-measures ANOVA adjusting for baseline. **Results:** Accrual was completed in December 2011. Among 42 pts enrolled, 35 (83%) received at least 8 sessions of acupuncture, and 28 (67%) received all 12. Six pts withdrew due to time constraints. No serious side effects were observed. The mean MDADI total scores improved from baseline in both treatment arms [64.5 (SE+2.4) vs. 71.4 (SE±3.1), $p = 0.048$; 64.5 (SE±2.4) vs. 77.8 (SE±3.0), $p < 0.001$]; the difference in improvement was not significant ($p = 0.12$). The median feeding tube duration did not differ between active and sham treatments ($n = 39$, median 125 days vs. 147 days, $p = 0.93$). **Conclusions:** Acupuncture is a safe and feasible treatment for HNC pts. There were improvements in QOL parameters from end of CRT to the time points examined that did not differ between the two arms. Efficacy of acupuncture to improve swallowing-related QOL in HNC pts may require more frequent or longer duration of treatment. Clinical trial information: NCT00797732.

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General Poster Session (Board #12G), Sat, 8:00 AM-11:45 AM

A phase II study of radiation therapy (RT), paclitaxel poliglumex (PPX), and cetuximab (C) in locally advanced head and neck cancer (LA-HNC).

Seung Shin Hahn, Jeffrey Bogart, Chung Taik Chung, Jack Hsu, Robert Kellman, Michael Andrew Lacombe, Jung-AH Kim, Stephen L. Graziano, Dena Martin, Ajeet Gajra; SUNY Upstate Medical University, Syracuse, NY; Upstate Medical University, Syracuse, NY

Background: RT + cisplatin in LA-HNC showed a survival benefit over RT alone, but with significant toxicity. Addition of C to RT demonstrated survival benefit without increased RT-related toxicity. PPX consists of paclitaxel linked to a biodegradable, water-soluble polymer of glutamic acid. PPX has a radiation enhancement factor of ≈ 8 in a radiocurability murine model. This study addresses the combined use of intensity modulated RT (IMRT), PPX, and C in patients with LA-HNC. **Methods:** Eligible patients had untreated stage III/IV squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx, larynx, or unknown primary, ECOG PS 0-1, and adequate bone marrow function. Patients received C 400 mg/m² day 1 and 250 mg/m² weekly for 7 weeks. PPX was administered at 40 mg/m² weekly for 7 weeks. IMRT began on day 8 consisting of 69.96 Gy delivered in 2.12 Gy daily. **Results:** 38 patients with LA-HNC are included in this report and evaluable for response. 24 (63%) had CR and 14 (37%) had PR. HPV status is 21+, 11- and 8 unknown. Pre-therapy, 36 patients had nodal disease, 9 underwent neck dissection post-treatment and 1/9 patients had microscopic involvement by cancer. Locoregional tumor control occurred in 36/38 (95%) patients with two patients developing locoregional recurrence after completion of therapy. Two patients have died from metastatic disease and two patients are alive with distant metastases. Two additional deaths were unrelated to therapy (sudden cardiac death and COPD exacerbation with respiratory failure). The majority of adverse events (AEs) were grade 1/2 and consistent with known toxicities of individual agents. The most common grade 3 AEs were mucositis (n=28), radiation dermatitis (n=15), dehydration (n=8) and cetuximab rash (n=9). The median overall survival and progression free survival have not been reached. Updated numbers will be presented. Overall survival rate is 34/38 (89%) by intent-to-treat analysis, with a median follow up of 13 months. **Conclusions:** The combination of IMRT, PPX, and C is tolerable and shows promising clinical activity in patients with LA-HNC. An expansion cohort of HPV negative patients on this protocol is in progress. Clinical trial information: NCT00660218.

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General Poster Session (Board #12H), Sat, 8:00 AM-11:45 AM

Organ preservation with daily concurrent chemoradiotherapy using retrograde superselective intra-arterial infusion for stage III, IV oral cancer: Analysis of therapeutic results in 112 cases.

Kenji Mitsudo, Toshiyuki Koizumi, Toshinori Iwai, Hideyuki Nakashima, Senri Oguri, Mitomu Kioi, Makoto Hirota, Iwai Tohnai; Department of Oral and Maxillofacial Surgery, Yokohama City University School of Medicine, Yokohama, Japan; Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Tokyo Medical University, Tokyo, Japan; Department of Oral and Maxillofacial Surgery, Yokohama City University Graduate School of Medicine, Yokohama, Japan

Background: Retrograde superselective intra-arterial chemotherapy for oral cancer has the advantage of delivering a high concentration of the chemotherapeutic agents to the tumor bed, it can be used to provide daily concurrent chemoradiotherapy for patients with advanced oral cancer. The purpose of this study was to evaluate the therapeutic results and rate of organ preservation in 112 patients of stage III or IV (M0) oral cancer treated with retrograde superselective intra-arterial chemotherapy and daily concurrent radiotherapy. **Methods:** Between August 2006 and July 2011, 112 patients with stage III or IV oral squamous cell carcinoma underwent intra-arterial chemoradiotherapy. Catheterization from the superficial temporal and occipital arteries was performed. And treatment consisted of superselective intra-arterial chemotherapy (docetaxel, total 60 mg/m², cisplatin, total 150 mg/m²) and daily concurrent radiotherapy (total 60 Gy) for 6 weeks. **Results:** The median follow-up for all patients was 46.2 months (range, 10–90 months). The median follow-up for living patients was 49.7 months (range, 36–90 months). After intra-arterial chemoradiotherapy, primary site complete response was achieved in 98 (87.5%) of 112 cases. Thirty patients (26.8%) died. Using the Kaplan-Meier method, 3-year, and 5-year survival rates were 74.6% and 71.3%, respectively, while 3-year, and 5-year local control rates were both 79.3%. Grade 3 or 4 toxicities included mucositis in 92.0%, neutropenia in 30.4%, dermatitis in 28.6%, anemia in 26.8%, and thrombocytopenia in 7.1%. Grade 3 toxicities included dysphagia in 72.3%, nausea/vomiting in 21.4%, fever in 8.0%, and renal failure occurred in 0.9%, no patients died as a result of treatment toxicity. **Conclusions:** Retrograde superselective intra-arterial chemotherapy and daily concurrent radiotherapy for Stage III, IV oral cancer provided good overall survival and local control rates, thus preserving organs and contributing to patients' QOL.

Is there an interaction between epidermal growth factor receptor (EGFR) inhibition and p16-status in patients (pts) with oropharyngeal squamous cell cancer: A retrospective analysis.

Tobenna Igewonu Nwizu, Lisa A. Rybicki, Deborah Chute, Cristina P. Rodriguez, Shlomo A. Koyfman, John Greskovich, Jerrold P. Saxton, Joseph Scharpf, Robert Lorenz, Brian Burkey, Benjamin J. Wood, Mumtaz Khan, Samer Al-khudari, Aaron P. Hoschar, Denise I. Ives, Joanna Bodmann, David J. Adelstein; Cleveland Clinic Foundation, Cleveland, OH; Oregon Health & Science University, Portland, OR; Cleveland Clinic, Cleveland, OH; Cleveland Clinic, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH

Background: Conflicting data exists about whether EGFR inhibition is more or less effective in pts with p16 positive or negative oropharynx cancer (OPC). We update results from two institutional clinical trials in pts with locoregionally advanced head and neck squamous cell carcinoma (LRA HNSCC) given chemoradiotherapy either with or without the oral EGFR inhibitor gefitinib (G), with specific attention to the subset of pts with p16-defined OPC. **Methods:** Between 1996-2000, 44 pts with LRA HNSCC were treated on a Cleveland Clinic IRB-approved protocol using concurrent cisplatin, fluorouracil and radiation without G (G- cohort). Between 2003-2007, 60 similar pts were treated using the same chemoradiotherapy regimen with the addition of G 250 mg daily for 2 years beginning on day 1 of radiation (G+ cohort). Available biopsy material from 64 OPC pts (23 G-, 41 G+) was retrieved and tested by immunohistochemistry for p16 (as a surrogate for human papillomavirus) positivity. Kaplan-Meier outcome projections were compared using the log-rank test. **Results:** With a median follow-up in excess of 7 years for all pts, survival and patterns of failure did not differ between the two trials. The 5-year overall survivals (OS) were 68% vs. 64% (p=0.73) and relapse-free survivals (RFS) 65% vs. 63% (p=0.85) in the G+ and G- cohorts respectively. OPC was more frequent in the more recently treated G+ cohort (68% vs. 53%). Excluding 14 pts for whom tumor was unavailable, OPC p16-positivity was also more frequent in the G+ cohort (74% vs. 63%). As expected, outcomes in the p16+ OPC pts were significantly better than in the p16- OPC pts including OS (66% vs. 58%, p=0.049) and RFS (69% vs. 56% p=0.027). However, in comparing the G+ and G- cohorts, the use of G did not significantly alter any survival outcome or pattern of failure in either the p16+ or p16- OPC pts. **Conclusions:** Although the retrospective nature of this analysis limits the strength of our conclusions, in the definitive management of LRA HNSCC, we could identify no effect of oral EGFR inhibition on any outcome. In subset analysis there was also no differential impact found in either the p16+ or p16- OPC pts. Clinical trial information: NCT00352105.

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General Poster Session (Board #13B), Sat, 8:00 AM-11:45 AM

Effect of early detection of recurrent disease by FDG PET/CT on management of patients with squamous cell cancer of the head and neck (HNSCC).

Lale Kostakoglu, Reza Fardanesh, Eric Genden, Srikar Rao, John Doucette, Peter M. Som, Vishal Gupta, Krzysztof Misiukiewicz, Marshall R. Posner; Department of Radiology, Mount Sinai Medical Center, New York, NY; Department of Otolaryngology, Mount Sinai Medical Center, New York, NY; Mount Sinai Medical Center, New York, NY; Department of Radiation Oncology, Mount Sinai Medical Center, New York, NY; Department of Medicine/Hematology/Oncology, Mount Sinai Medical Center, New York, NY

Background: Despite the increasing cure rates a substantial fraction of HNSCC patients (pts) will present with locoregional and/or distant relapse within 3 years of definitive therapy. The prognosis of HNSCC pts after failure of first-line therapy has been poor but recent changes in the biology of HNSCC, advances in surgical techniques and radiotherapy; and new drugs may lead to improved salvage therapy. Notably, the success of these developments are implicitly dependent on early diagnosis disease. Our objective was to compare the efficacy of surveillance FDG-PET/CT to that of high resolution CT (HRCT) and physical exam (PE/E) for detection of early relapse in HNSCC after completion of primary treatment. **Methods:** A retrospective analysis of FDG-PET/CT, neck HRCT and PE/E was performed in 99 curatively treated HNSCC pts during post-therapy surveillance (PTS) to compare the performance characteristics of the tests in the detection of early recurrence or metachronous cancer. **Results:** A total of 19/99 (20%) pts had recurrence during a median follow-up of 21mo (range:9-52). Median time to first PET/CT was 3.5mo. The median time to radiological recurrence was 6 mo (range:2.3-32). PET/CT detected more disease recurrences or second primaries and did so earlier than HRCT and PE/E. Sensitivity, specificity, PPV and NPV for detecting locoregional and distant recurrence or metachronous cancer : 100%, 87.3%, 56.5% and 100% for PET/CT vs. 61.5%, 94.9%, 66.7% and 93.8% for HRCT vs. 23.1%, 98.7%, 75% and 88.6% for PE/E. In all 19 pts with a true positive PET/CT there was a significant management change prompting either salvage or definitive surgery or initiation of systemic therapy. Of the 14 recurrent pts treated with curative intent, 11 were alive with no evidence of disease at a median follow up of 31.5 mo. **Conclusions:** FDG-PET/CT has a high sensitivity in the early detection of relapse or second primary cancer in HNSCC, associated with significant management implications. Given improvements in therapy and changes in HNSCC biology, appropriate modifications in the current recommended algorithms of the NCCN for PTS may be required to engage effective salvage or definitive therapies.

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General Poster Session (Board #13C), Sat, 8:00 AM-11:45 AM

A blood-based epigenetic test for early detection of nasopharyngeal carcinoma (NPC).

Yew-Oo Tan, Eduard M. Alfanta, Ramon Antonio B. Lopa, Elaine Hsuen Lim, Hwee Yong Whang, Karmen Wong, Philip Jordan, Emily Corfield, Matthew Salter, Megan Field, Alexandre Akoulitchev, Thomas Kwok Seng Loh, Boon C. Goh, Wen Son Hsieh; Singapore Oncology Consultants, Singapore, Singapore; Philippine General Hospital, Manila, Philippines; Epitech International Pte Ltd, Singapore, Singapore; Oxford Biodynamics Limited, Oxford, United Kingdom; National University Health System, Singapore, Singapore

Background: NPC is highly curable in early stages but 70% of NPC patients are diagnosed with advanced disease due to lack of effective screening. Genetic and epigenetic alterations involved in the pathogenesis of NPC are known. The higher order chromosomal structures reflecting aberrant transcriptional states of these genes can be measured via techniques such as chromosome conformation capture. Detection of these changes in peripheral blood may provide an accurate test for the early cancer detection. **Methods:** Blood samples have been collected from 84 patients with histologically confirmed NPC and 100 matched controls. Samples from 45 NPC patients and 68 controls have been analyzed. Fourteen genes known to be dysregulated in NPC were investigated. Potential higher order juxtaposition sites in the candidate genes were predicted using pattern recognition software. PCR primer sets were designed around the chosen sites to screen potential markers. Twenty-two markers showing predictability between NPC and control samples were analysed for optimal reproducibility using alternative primer sets. The optimal sets of markers were then tested amongst the complete set of samples. The dataset was processed by re-sampling using the synthetic minority oversampling technique. The overall sample was split into two groups (66% training set and 34% test set) in the classification. **Results:** Sixteen markers from 7 candidate genes were found to be optimal in differentiating between NPC and control samples in the first 103 samples. Using the multilayer perceptron (MLP) classification, the following results were obtained: Sensitivity 88.9%, 95% CI (79.2% - 98.6%); Specificity 72.7%, 95% CI (58.9% - 86.5%); PPV 72.7%, 95% CI (58.9% - 86.5%); NPV 88.9%, 95% CI (79.2% - 98.6%). The accuracy of the test was similar in detection of stage I and II NPC versus that of stage III or IV NPC. **Conclusions:** Using a PCR-based method to detect alterations in the cancer epigenome, the feasibility of developing a blood test of potential utility in early diagnosis of NPC was demonstrated. Analysis of larger numbers of patient samples and optimization of markers are ongoing. The performance characteristics of the test in the total population of 184 samples will be presented.

Treatment-associated mortality in head and neck cancer: Analysis of phase III trials.

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Background: Chemoradiotherapy is an accepted standard for patients with locoregionally advanced squamous cell carcinoma of the head and neck (SCCHN). Although acute and long-term toxicities of this approach are known, little is known about early mortality associated with curative-intent treatment. **Methods:** We reviewed 45 phase III trials of curative-intent radiotherapy in SCCHN published from 2000-2012 for adequate reporting of early mortality defined as deaths during and within 3 months of therapy, regardless of attribution. We estimated pooled proportions of deaths during prescribed therapy using a random effects model of radiotherapy alone (RT), concurrent chemoradiotherapy (CCRT) and induction chemotherapy (IC) regimens. The relative risk of death during CCRT vs. RT and CCRT/IC vs. RT were estimated. **Results:** Although all trials reported early mortality statistics, definitions had wide variability, and only 34 trials (75%) met adequate reporting characteristics. Ten trials excluded enrolled patients who died prior to initiating therapy. Of studies reporting early mortality statistics, crude frequency of death during prescribed therapy was 2.7% (308/11362). The pooled estimated rates of death observed during RT alone was 1.7% (SE: 0.3, $I^2=89.2%$) from 29 studies, while 2.8% (SE: 0.4, $I^2=64.9%$, 19 studies) and 3.1% (SE: 0.5, $I^2=53.5%$, 9 studies) for CCRT and IC regimens, respectively. The pooled relative risk for death in CCRT compared to RT treatment was 1.08 (95%CI: 0.78, 1.48, $p=0.63$, $I^2=0$, 15 studies). The relative risk for death in CCRT or IC therapy compared to RT was 1.06 (95%CI: 0.77, 1.45, $p=0.72$, $I^2=0$, 15 studies). When reported, most early deaths were attributed to infectious complications or cardiovascular events. **Conclusions:** Early death remains an uncommon but important complication of curative-intent radiotherapy in SCCHN that necessitates consistent reporting. Despite strict eligibility criteria and protocol-defined care, treatment-associated death occurs with all regimens, though no clear increase was observed with CCRT/IC regimens over RT alone. Early mortality should be considered during treatment planning, particularly for patients with considerable comorbidities.

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General Poster Session (Board #13E), Sat, 8:00 AM-11:45 AM

An open-label single-arm, phase II trial of zalutumumab, a human monoclonal anti-EGFR antibody, in patients with platinum-refractory squamous cell carcinoma of the head and neck.

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Background: Treatment for patients with platinum-refractory metastatic squamous cell carcinoma of the head and neck (SCCHN) is limited. Cetuximab has been approved in the US in this patient population based on a phase II trial that demonstrated 13% response rate (RR) and 5.9 months median OS. A recently conducted phase III trial of zalutumumab, a human monoclonal IgG1k antibody against EGFR, versus best supportive care showed significant increase in PFS. Here, we present the results of a companion phase II trial in the same patient population. **Methods:** Patients with platinum-refractory recurrent or metastatic SCCHN received weekly infusions of zalutumumab starting at a loading dose of 8mg/kg. The dose was then reduced to 4mg/kg and individually titrated by increments of 4mg/kg every 2 weeks based on skin rash evaluation up to a maximum of 16mg/kg aiming at a grade 2 skin rash. Primary objective was OS. The analysis was based on the intent-to-treat principle and OS was estimated using the Kaplan-Meier method. **Results:** Between January 2008 till August 2011 90 patients were enrolled in 57 centers in the United States, Europe and South America. 23% of patients had WHO PS 2 and 74% had distant relapse metastases. Grade 3-4 adverse events (AEs) related to zalutumumab were observed in 19% of the patients and included skin rash (5%), hypomagnesemia (4%) and pneumonitis (1%). Infusion-related reactions occurred in 33% of patients. The frequency of all-cause grade 3-4 AEs was 62% and included infections (14%), gastrointestinal disorders (12%), hypokalemia (6%), dyspnea (9%) and anemia (6%). Two deaths secondary to cardiac arrest in a patient with history of myocardial infarction, and respiratory acidosis in a patient with a pleural effusion and hypomagnesemia were deemed related to zalutumumab. CR was observed in one (1%) patient and PR in four (5%) patients. The median PFS was 8.6 weeks (95% CI [8.0, 10.4]) and the estimated median OS was 5.3 months (95% CI [4.1, 7.1]). **Conclusions:** Zalutumumab showed reasonable efficacy in platinum-refractory recurrent or metastatic SCCHN patients and dosing titration based on skin rash evaluation was feasible. Clinical trial information: NCT00542308.

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General Poster Session (Board #13F), Sat, 8:00 AM-11:45 AM

Genetic profiling of advanced RAI-resistant differentiated thyroid cancer and correlation with axitinib response.

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Background: The VEGFR inhibitor axitinib has demonstrated compelling antitumor activity in advanced RAI-resistant differentiated thyroid cancer (DTC). Biomarkers predicting which patients may benefit from axitinib are unavailable. We aimed to describe molecular markers in DTC that correlate with clinical outcome to axitinib. **Methods:** Pretreatment FFPE thyroid cancer blocks from patients treated with axitinib were collected and genomic DNA was isolated. The OncoCarta Mutation Panel was used to test for 238 mutations. Copy number of *VEGFR1-3* and *PIK3CA* was determined using qPCR. Genomic DNA was analyzed for coding regions of *VEGFR1-3* with custom primers. Clinical response to axitinib, including best response (BR) (RECIST) and progression free survival (PFS), was ascertained from corresponding patients. Fisher's exact test and logistic regression models were used to correlate BR with molecular findings. Cox proportional hazards regression was used to correlate PFS with molecular defects. **Results:** A total of 22 pathology samples (11 primary, 11 metastatic) were identified. In patients with 2 samples (n = 4), results were concordant and only included once for analysis. Of 18 specimens, 4 tumors (22%) harbored *BRAF* V600E mutations, 2 (11%) had *KRAS* mutations (G12A, G13D) and 2 (11%) had *HRAS* mutations (Q61R, Q61K). One sample with mutated *KRAS* also had a *PIK3CA* (H1047R) mutation. qPCR showed increased copy numbers of *PIK3CA* in 6 (33%) tumors, *VEGFR1* in 0 (0%) tumors, *VEGFR2* in 4 (22%) tumors, and *VEGFR3* in 6 (33%) tumors. *VEGFR* sequencing showed a possibly damaging non-synonymous SNP in *VEGFR2* (G539GR) in 2 samples (11%), a possibly damaging SNP in *VEGFR3* (E350VE) in 1 sample (6%), and a potentially novel mutation in *VEGFR2* (T439IT) in 2 samples (11%). No significant relationship was seen between BR or PFS and the presence of molecular defects. **Conclusions:** While DTC is genetically heterogeneous, primary and metastatic lesions showed identical alterations. Molecular evaluation of DTC specimens did not predict clinical response to axitinib but data were limited by small sample size. We did identify molecular changes in *VEGFR* that should be further explored. This study was supported by Pfizer, Inc.

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General Poster Session (Board #13G), Sat, 8:00 AM-11:45 AM

Phase II trial of everolimus and erlotinib in patients with platinum-resistant recurrent and/or metastatic head and neck squamous cell carcinoma.

Erminia Massarelli, Lawrence E. Ginsberg, Heather Lin, Hai T. Tran, J. Jack Lee, Michelle D. Williams, George R. Blumenschein, Charles Lu, Merrill S. Kies, Vassiliki Papadimitrakopoulou; Department of Thoracic Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Diagnostic Radiology, The University of Texas M.D. Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Head and neck squamous cell carcinoma (HNSCC) is characterized by epidermal growth factor receptor (EGFR) overexpression but treatments targeting EGFR have met with limited clinical success. We hypothesized that everolimus (EV), an mTOR inhibitor, potentiates the activity of erlotinib (ER), an EGFR tyrosine kinase inhibitor, in platinum-resistant recurrent and/or metastatic HNSCC. **Methods:** This single-arm two-stage phase II clinical trial evaluated EV 5 mg and ER 150 mg orally daily in patients (pts) with platinum-resistant recurrent and/or metastatic HNSCC. Primary endpoints were response rate and 12-week progression-free survival (PFS). Plasma biomarkers by multianalyte profiling (Luminex Corp) and ELISA at baseline (20 pts), 4 weeks (18 pts) and 12 weeks (16 pts) as well as p16 expression in baseline tumor tissue (29 pts) were assessed in correlation with clinical results. **Results:** Of the 36 evaluable pts (median age 61 years, 29 males, 19 with oropharynx primaries, 15 with ≥ 2 lines of chemotherapy, 17 with prior cetuximab), 3 (8%) achieved partial response at 4 weeks, one of which was confirmed at 12 weeks, while 27 (75%) pts achieved disease stabilization at 4 weeks, 11 of which were confirmed at 12 weeks. The 12-week PFS was 49%, median PFS was 11.9 weeks and median overall survival (OS) was 10.25 months. Grade 3 toxicities included mucositis (17%), fatigue (14%), skin (8%), diarrhea (8%), and 5 pts withdrew from trial secondary to toxicity. High neutrophil gelatinase-associated lipocalin (NGAL) levels at baseline were associated with worse OS (HR 4.59; 95% CI 1.36, 15.46; $p=0.014$) and at 4 weeks with worse PFS (HR=12.29; 95% CI 1.26, 119.87; $p=0.03$) and OS (HR=6.21; 95% CI 0.95, 40.62; $p=0.057$). High carbonic anhydrase-9 (CA-9) levels at 4 weeks were associated with worse OS (HR=1.18; 95% CI 1.001, 1.41; $p=0.049$), while decreased CA-9 levels at 4 weeks were associated with better PFS ($p=0.77$). **Conclusions:** Efficacy for the combination of EV and ER is reasonable however plasma markers of tumor invasion and hypoxia are associated with worse outcomes, and further biomarker analysis may define subsets of pts with significant therapeutic benefit. Clinical trial information: NCT00942734.

The association between severe treatment-related lymphopenia and progression-free survival in patients with newly diagnosed squamous cell head and neck cancer.

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Background: Severe treatment-related lymphopenia (TRL) occurs in 50% of glioblastoma and pancreatic cancer patients and is associated with early death from tumor progression. We sought to determine if similar findings were seen in head and neck squamous cell carcinoma (HNSCC). **Methods:** Eligible patients for this retrospective study had: 1) HNSCC cancer diagnosed in 2007-2009, 2) good performance status, 3) platinum-based chemoradiation, and 4) follow-up at Johns Hopkins. Serial total lymphocyte counts (TLC), overall survival (OS) and progression-free survival (PFS) were analyzed accounting for known prognostic factors. **Results:** Fifty-six adults met eligibility criteria: median age: 57 years, female: 21%, HPV+: 61%, surgery prior to chemoradiation: 16%, stage IVA-IVB: 77%, T stage 3-4: 40% and N stage 2b-3: 56%. Changes in TLC are shown below (Table). 14/56 patients (25%) had tumor recurrence and 9 (16%) died of their tumor. HPV+ patients had longer PFS ($p=0.01$) and OS ($p=0.006$) than HPV- patients. 10/22 HPV- patients had disease progression and 7 died. HPV- patients who developed grade III-IV TRL two months after beginning chemoradiation had a strikingly higher hazard rate for disease progression than those whose TLC remained higher (multivariate analysis HR 6.2, 95%CI: 1.1-35.2; $p=0.039$). Too few events occurred in the HPV+ cohort for analysis. **Conclusions:** TLCs were normal before chemoradiation. However, two months after chemoradiation ~60% of patients had severe TLC regardless of HPV status. HPV- patients with severe TRL were much more likely to have disease progression than those without TRL. Prospective studies are needed to confirm these findings which are similar to those reported in other cancers. Preservation of the immune system during chemoradiation may be important to improving PFS and OS.

	Median TLC: Baseline	Median TLC: 2 months post-RT	% with TLC <500: 2 months post-RT
Overall	1,660	448	61%
HPV- (n=22)	1,770	550	36%
HPV+ (n=34)	1,610	320	76%

A randomized, multicenter, open phase II study of cetuximab with docetaxel, cisplatin as induction chemotherapy in unresectable, locally advanced head and neck squamous cell carcinoma (LA-HNSCC).

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Background: In this randomized phase II trial, we investigated the efficacy and safety of cetuximab in induction chemotherapy and followed by concurrent chemoradiotherapy (CCRT) in LA-HNSCC. **Methods:** Patients were randomized to receive 3 cycles of docetaxel (75 mg/m²) and cisplatin (75 mg/mg²) every 3 weeks with or without cetuximab (CDP vs. DP). CCRT was given as a definitive treatment. Patients in CDP arm received CCRT with weekly cetuximab (250 mg/m²) and cisplatin (30 mg/m²), while patients in DP arm received CCRT with weekly cisplatin. Primary endpoint was objective response rate (ORR) after induction chemotherapy. **Results:** 92 patients were randomized to receive either CDP (48) or DP (44). The median age was 59 years (range 29 – 73 years). The location of primary disease included oropharynx (41), hypopharynx (24), larynx (13) and oral cavity (14). 40 of the 48 patients in CDP arm and 40 of the 44 patients in DP arm completed 3 cycles of chemotherapy. Reason for incompleteness in CDP arm included hypersensitivity (1), septic shock (1), skin rash (1), seizure (1), arterial thrombosis (1), unexplained death (1), unsatisfactory response (1), and withdrawal of informed consent (1). ORR to chemotherapy in CDP arm and DP arm was 81% (4 CR and 35 PR) and 82% (4 CR and 32 PR), respectively. 3 patients were not evaluable for response in CDP arm due to unexplained early death (1), septic shock (1), and hypersensitivity reaction after the first dose of cetuximab (1). CCRT completion rate after the completion of CDP and DP was 80% and 85%, respectively. Median PFS and OS were not reached in either arm, with a median follow-up time of 33 months. CDP arm showed 70% and 88% of PFS and OS rate, while DP arm showed 56% and 74% of PFS and OS at 3 years, when intend-to-treat analysis was performed. If we limited to the patients who received 3 cycles of CDP or DP, we saw 78% and 59% of 3-year PFS rate, respectively and 94% and 73% of 3-year OS rate, respectively. **Conclusions:** Addition of cetuximab during induction and CCRT phase may compromise completion rate of 3 cycles of induction chemotherapy but does not compromise completion of CCRT and shows promising survival data. Clinical trial information: NCT00623558.

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General Poster Session (Board #14B), Sat, 8:00 AM-11:45 AM

Significance of myeloid-derived suppressor cells in squamous cell carcinoma of the head and neck.

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Background: Patients with advanced stage squamous cell carcinoma of the head and neck (SCCHN) have less than 50% 5-year survival rate. Human papillomavirus (HPV)-associated SCCHN in oropharyngeal sites have shown better prognosis. Little is known about the role of myeloid-derived suppressor cells (MDSCs) in immune suppression or tumor progression in the setting of SCCHN. Our objective is to evaluate the clinical significance of MDSCs in subjects with SCCHN, HPV-positivity, and advanced cancer staging. **Methods:** Thirty-three subjects with SCCHN and 10 healthy donors were enrolled in this prospective cohort study. Fresh blood was collected at the time of surgical resection of SCCHN in a tertiary academic center between August 2011 and January 2013. Peripheral blood mononuclear cells (PBMCs) were obtained using Ficoll Hypaque. MDSCs were immunophenotyped as CD14⁻CD33⁺CD11b⁺ by flow cytometry. HPV status was determined by in situ hybridization. Frequencies of MDSCs in blood of different cohorts were evaluated. **Results:** Thirty-three subjects (ages 34-83 years, 25 males) with SCCHN were enrolled. Increased numbers of CD14⁻CD33⁺CD11b⁺ cells of total leukocytes were found in HPV-associated SCCHN (median 26.6%, n=11) compared to HPV-negative SCCHN (16.3%, n=19). Interestingly, 3 subjects who previously had HPV-positive SCCHN but with no evidence of disease had 6.24% (n=3) CD14⁻CD33⁺CD11b⁺ cells of leukocytes which was higher than healthy donors (3.55%, n=10). Subjects with advanced cancer stages (III-IV) had higher levels of MDSCs (26%, n=19) compared to those with a lower grade (I-II, 15.5%, n=11) regardless of HPV status. Three subjects were lost to follow up. Of the remaining subjects, the overall median follow time was 3 months and subjects who were found to have recurrence, regional or local metastasis had higher frequencies of MDSCs in the blood (26.35%, n=4) compared to those with no evidence of disease (18.5%, n=26) at the time of surgery. **Conclusions:** This study suggests there is an accumulation of MDSCs in peripheral blood of patients with SCCHN, particularly in HPV-associated SCCHN. Further, increased levels of MDSCs in the peripheral blood are related to more advanced cancer stage and poor clinical outcomes.

Evaluating the cost-effectiveness of low-level laser therapy (LLLT) in head and neck cancer patients submitted to concurrent chemoradiation.

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Background: Oral mucositis (OM) is a main factor for increasing treatment costs in head and neck squamous cell carcinoma (HNSCC) patients (pts) treated with chemoradiation (CRT). This study was designed to estimate the cost-effectiveness of LLLT to prevent oral mucositis in HNSCC patients submitted to CRT. **Methods:** From June 2007 to Dec 2010, 94 patients with HNSCC of nasopharynx, oropharynx and hypopharynx entered a prospective, randomized, double blind, placebo-controlled, phase III trial (47 LLLT (LG) and 47 placebo (PG)). CRT consisted of conventional RT 70.2 Gy (1.8Gy/d, 5 times/wk) + concurrent cisplatin 100 mg/m² every 3 wks. The LLLT used daily was a diode InGaAlP (660nm-100mW-4J/cm²). OM evaluation was done by WHO and OMAS scale. The resources used by patients in both groups were documented during the trial. Unit costs for procedures were obtained from a public reference list (SIGTAP / SUS) as of Jan 2012 and unit costs for drugs were based on ex-factory prices. The cost per laser session was US\$ 34.00 (exchange rate from Brazilian currency to US dollar = 1.95) for the baseline analysis. Costs of RT, chemotherapy, fluconazole and chlorhexidine 0.12% were equivalent in both groups and therefore not included in the analysis. Hospitalization rates associated with the treatment of oropharyngeal or oral mucositis were not documented in the study and were estimated according to previously published data. **Results:** Under the perspective of the Brazilian public healthcare system (SUS), total costs were higher in PG than LG on opioide use (LG= US\$ 29.45; PG= US\$143.72, gastrostomy (LG= US\$ 41.69; PG= US\$107.22) and hospitalization (PG= US\$ 63.59). In LG costs were higher with laser therapy (US\$ 1,549.50). The total incremental cost associated with the use of LLLT was US\$ 1,306.61 per patient. The incremental cost-effectiveness ratio (ICER) was US\$ 3,838.16 per case of grade 3 and 4 mucositis avoided when compared with no treatment. **Conclusions:** Our results indicate that laser group had a smaller morbidity during treatment and LLLT is cost-effective when compared to placebo under a threshold of at least US\$ 4,000 per avoided mucositis case. Clinical trial information: NCT01439724.

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General Poster Session (Board #14D), Sat, 8:00 AM-11:45 AM

Single nucleotide polymorphisms (SNPs) of hypoxia-related and DNA repair genes associated with toxicity and clinical outcome in head and neck squamous cell carcinoma patients treated with cetuximab plus radiotherapy.

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Background: One of the standard therapy in inoperable head and neck squamous cell carcinoma (HNSCC) patients is cetuximab plus radiotherapy. However, the efficacy of this treatment varies greatly among individuals. In an attempt to identify predictive markers to determine the patients most likely to benefit from this treatment, we examined the potential effect on outcome and skin toxicity according to single SNPs in hypoxia-related genes and DNA repair genes. **Methods:** Sixty-one patients enrolled between May 2006 and August 2011 and diagnosed with HNSCC were included. Data on epithelitis, mucositis and folliculitis were collected in accordance with WHO criteria. SNPs were analyzed in HIF-1 α , HIF-2 α , HIF-1 β , VHL, FIH-1, XRCC1 and XRCC5 in DNA obtained from paraffin-embedded tumor tissues by allelic discrimination in an ABI PRISM 7500 Sequence detection system. Results were correlated with time to progression (TTP), overall survival (OS) and toxicity. **Results:** The median of TTP and OS were better in patients with mucositis severe vs mild (17 vs 7 months, $p=0.03$, and 26 vs 12 months, $p=0.016$, respectively) and in those with folliculitis severe vs mild (10 versus 7 months, $p=0.01$, and 26 vs 10 months, $p<0.001$, respectively). Patients with HIF-1 α CT/TT had better OS than those with HIF-1 α CC or wild type (28 versus 13 months, $p=0.035$). Patients with XRCC5 GG/AA genotypes had longer TTP than patients with XRCC5 AG (11 versus 7 months, $p=0.035$). **Conclusions:** Our findings indicate that the presence of severe skin toxicities, as well as SNPs in HIF-1 α and XRCC5, are associated with interindividual differences in outcome among HNSCC patients.

Association of polymorphisms in genes related to cell cycle (*ERP29*, *LEF1*, *MCC* and *PTCH1*) and DNA transcription factors (*IKBKAP* and *ZNF415*) with base of tongue squamous cell carcinoma risk.

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Background: Recently, we found 6.609 genetic single nucleotide polymorphisms (SNPs) with distinct frequencies between base of tongue squamous cell carcinoma (BTSCC) patients and controls. The study was performed using high-resolution DNA microarrays genotyping (Affymetrix). The SNPs identified never have been previously described with BTSCC risk. Some SNPs of interest were located in genes related to cell cycle (*ERP29*, *LEF1*, *MCC* and *PTCH1*) and DNA transcription (*IKBKAP* and *ZNF415*) and they were selected to validation process. **Objective:** Validate the SNPs *ERP29* c.*293A>G (rs7114); *LEF1* c.*1213A>G (rs2107028) and g.127267A>G (rs4245926); *MCC* c.*5077A>G (rs7033); *PTCH1* g.27369025G>A (rs16909856) and g.27369324G>A (rs16909859); *IKBKAP* c.3214T>A (rs3204145) and *ZNF415* c.*443A>G (rs3814) associated to BTSCC risk. **Methods:** Genomic DNA from 49 BTSCC patients and 49 controls was genotyping by TaqMan assays (Applied Biosystems). The differences between groups were analyzed by logistic regression model. Power analysis (PA) was used to verify the effect of sample size on the results obtained. **Results:** Eight SNPs identified by Affymetrix were validated by TaqMan assays. The frequencies of *ERP29* c.*293AG+GG (30 vs 11%, $P=0.03$; PA=65%), *LEF1* c.*1213AA+AG (95 vs 80%, $P=0.02$; PA=61%) and g.127267AA+AG (93 vs 78%, $P=0.02$; PA=56%), *MCC* c.*5077AA+AG (85 vs 64%, $P=0.008$; PA=67%), *PTCH1* g.27369025GG+GA (90 vs 73%, $P=0.005$; PA=58%) and g.27369324GG+GA (90 vs 73%, $P=0.008$; PA=58%), *IKBKAP* c.3214TT+TA (90 vs 72%, $P=0.01$; PA=62%) and *ZNF415* c.*443AA+AG (59 vs 41%, $P=0.02$; PA=43%) were more common in patients than in controls. Individuals with these genotypes were at 2.9(CI95%: 1.1-8.4), 3.9 (CI95%: 1.4-11.2), 4.0 (CI95%: 1.2-14.7), 3.5 (CI95%: 1.2-11.9), 5.0 (CI95%: 1.7-16.9), 4.5 (CI95%: 1.5-15.2), 4.1 (CI95%: 1.4-12.9), and 3.9 (CI95%: 1.2-13.7)-fold increased risks for BTSCC than others, respectively. **Conclusions:** Our data present for the first time evidence that inherited abnormalities in *ERP29*, *MCC*, *LEF1*, *PTCH1*, *IKBKAP*, and *ZNF415* genes may be important determinants of BTSCC. Financial support: FAPESP and FINEP.

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General Poster Session (Board #14F), Sat, 8:00 AM-11:45 AM

Phase I/II trial of crolibulin and cisplatin in solid tumors with a focus on anaplastic thyroid cancer: Phase I results.

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Background: Anaplastic thyroid cancer (ATC) is one of the most aggressive of all solid tumors, with a median survival of 3-5 months. Chemotherapy has not impacted local control or survival. Crolibulin (CRO) is a microtubule destabilizing agent that disrupts vascular endothelial cells, and in turn, blood flow to the tumor. Preclinical studies showed synergism with cisplatin (CIS). The phase I portion of this phase I/II study, designed to assess the safety and tolerance of CRO and CIS in patients with solid tumors, has completed accrual. **Methods:** Patients with advanced solid tumors, ECOG \leq 1, and adequate organ function were treated on a dose escalation schema with CIS (75-100 mg/m²) IV day 1 and CRO (13-20 mg/m²) IV days 1, 2, 3 (21-day cycles). CIS and CRO were continued until unacceptable toxicity or progressive disease (PD), with an option to continue CRO alone if toxicity was CIS-related. **Results:** Between Jan 2011 and Jan 2013, 21 patients were enrolled and assigned CIS/CRO (mg/m²) at 75/13 (6), 75/20 (3), and 100/20 (12). Diagnoses were as follows: ATC (16), urothelial carcinoma (2), prostate carcinoma (2) and mesothelioma (1). Patients received a median of 2 cycles of CIS/CRO (range: 1-6). Presently, four remain on CIS/CRO and one on CRO alone. The most common grade (G) 3 toxicities were: lymphopenia (33%), hyponatremia (29%), anemia (19%), hypertension during infusion (14%), and hypophosphatemia (9%). There were two G4 toxicities: elevated lipase and thrombocytopenia; and one G5 toxicity of laryngeal hemorrhage related to tumor erosion. There were two dose-limiting toxicities: G3 pancreatitis at dose level (DL) 1 and laryngeal hemorrhage at DL3. Eight ATC patients were treated at DL3. Of these, one (13%) had RECIST 1.1 complete response (CR) and one (13%) had stable disease (SD). Three (38%) had PD, and three are not yet evaluable. The CR has been on study for > 12 months and remains on CRO alone. **Conclusions:** CIS plus CRO deserves further evaluation as a regimen for ATC. The MTD of CIS/CRO is 100 mg/m² IV day 1 and 20mg/m² IV days 1, 2, 3 every 21 days. This combination is well tolerated, with toxicity primarily related to CIS. The phase II portion of this trial will compare CIS/CRO versus CIS in ATC patients. Clinical trial information: NCT01240590.

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General Poster Session (Board #14G), Sat, 8:00 AM-11:45 AM

Induction chemotherapy (CT) with docetaxel, cisplatin, and fluorouracil (TPF) followed by concomitant cisplatin plus radiotherapy in locally advanced nasopharyngeal cancer (NPC): Results after 06 years.

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Background: In squamous cell carcinoma of head and neck cancer, TPF induction CT improved survival over cisplatin plus fluorouracil (Posner MR: *NEJM*, vol357, Oct 2007). The main objective of this study is to evaluate the activity and safety of TPF in patients (pts) with locally advanced NPC followed by concomitant cisplatin plus radiotherapy (cCTRT). **Methods:** Pts with undifferentiated NPC were enrolled from December 2006–December 2012 and received 3 cycles of TPF (docetaxel 75 mg/m² and cisplatin 75/m² day 1, plus fluorouracil 750 mg/m² days 1–5, every 4 wks) with G-CSF days 1–5 post CT. CT was followed by cCTRT with cisplatin 40 mg/m²/wk and radiotherapy (65–70 Gy) starting 4–6 wks after the third cycle of CT. The primary endpoint was overall response rate (ORR) after induction CT and after cCTRT. Secondary end points were safety, disease free survival (DFS), and overall survival (OS). **Results:** 42 pts have been enrolled (26 M/16 F). UICC 1997 classification: n=9 stage II, n=10 stage III, n=23 stage IV. Median age is 37 yrs (range 18–64). Evocative clinical signs are cervical nodes n=20, rhinologic n=13, otologic n=5, and neurologic n=4. All pts were evaluated for safety and 38 for response. TPF well tolerated with main toxicities grade 3–4 (WHO) were neutropenia 36%, thrombocytopenia 32%, anemia 18%, diarrhea 6%, and mucositis 18%. Four pt died from sepsis that was probably treatment-related. ORR was 90% with an 71.4% (n=27) complete response (CR) rate, 23.6% (n=9) partial response (PR), and 5.2% (n=2) stable disease. No pts progressed after induction CT. Main toxicity during cCTRT was neutropenia grade 3–4 in 9%, mucositis grade 3 in 45% and grade 4 in 4%. Late toxicities were xerostomia grade 3 in 50%. At treatment completion, CR and PR rates were 79% and 20%; 2 pts had stable disease. At a median follow up of 72 months (range 7–72), 8% of pts have shown recurrence or progressive disease. DFS and OS rates at 72 months were 65% and 70%, respectively. **Conclusions:** TPF followed by cCTRT appears to be an active and feasible regimen with a manageable safety profile and may be a promising therapeutic option for pts with high stage NPC.

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General Poster Session (Board #14H), Sat, 8:00 AM-11:45 AM

Outcomes for stage IVA squamous cell carcinoma of the oral cavity according to staging subtypes.

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Background: Patients with locoregionally advanced squamous cell carcinoma of the oral cavity (SCCOC), defined as stages III to IVB without T4b, are treated similarly and combined for enrollment into most clinical trials. There are several combinations of tumor (T) and lymph node (N) categories for stage IVA. We evaluated the differences in outcomes according to subtypes of patients with stage IVA SCCOC. **Methods:** The Surveillance, Epidemiology, and End Results (SEER) database was queried for patients with stage IVA SCCOC diagnosed between 1988 and 2007. Patients were subdivided according to tumor (T) and lymph node (N) status. Overall survival (OS) was estimated by the Kaplan-Meier method and compared by using log-rank test. Cox proportional hazard regression models were used for multivariate analyses. **Results:** Among the 3,904 patients meeting inclusion criteria, most patients underwent surgery, either alone (24%) or with radiation (59%). There was a significant difference in outcomes according to AJCC subsets (T4aN0, T4aN1, T1N2, T2N2, T3N2 and T4N2), with 5-year OS ranging from 15.8% in T4aN2 to 41.3% in T4aN0 (HR 2.3; 95% CI 2.03-2.62, $p < 0.001$). Since the 5-year OS was similar for patients with T1N2-T2N2 and T3N2-T4aN2, these groups were further subdivided according to the T (T1-2 or T3-4a) and N2 subsets. The 5-year OS was significantly different according to the subgroups, ranging from 11.8% in T3-4aN2c to 37.5% in T1-2N2a (Table). The stage subgroups remained independent predictors for survival after adjusting for age, gender, race and treatment. **Conclusions:** Stage IVA SCCOC is a heterogeneous disease with significant differences in outcomes according to its subsets. If these findings are confirmed in additional studies, further subdivision of stage IVA may be warranted.

Stage	Patients	5-year OS	Median OS	HR, 95% CI, p value
T4aN0M0	1,474	41.3%	39 m	1
T4aN1M0	367	26.1%	19 m	1.55 (1.36-1.76, $p < 0.001$)
T1-2N2aM0	102	37.5%	26 m	1.31 (1.04-1.64, $p = 0.024$)
T1-2N2bM0	742	32.4%	24 m	1.20 (1.08-1.33, $p < 0.001$)
T1-2N2cM0	195	25.3%	17 m	1.58 (1.34-1.87, $p < 0.001$)
T3-4aN2aM0	71	15.8%	16 m	1.90 (1.47-2.44, $p < 0.001$)
T3-4aN2bM0	566	20.0%	15 m	1.81 (1.62-2.02, $p < 0.001$)
T3-4aN2cM0	345	11.8%	12 m	2.30 (2.03-2.62, $p < 0.001$)

Phase II trial of concomitant hyperfractionated-accelerated radiotherapy (HART) with cisplatin (Cis) plus cetuximab (Cet) for locoregionally advanced inoperable squamous cell carcinoma of the head and neck (LA SCCHN): Feasibility and 2-year OS.

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Background: To report the mature data of a prospective phase II-trial to investigate the feasibility, efficacy and safety of combination therapy with Cis, Cet and HART in LA SCCHN. **Methods:** Patients (pts) with stage III or IV, M0 SCCHN were enrolled and treated with an initial dose of Cet (400 mg/m²), followed by weekly dose of 250 mg/m² before HART, which started with a prescribed dosage of 2.0 Gy per day for three weeks followed by 1.4 Gy twice daily to a total dosage of 70.6 Gy to the gross tumor volume. Cis 40 mg/m² was administered weekly for 6 weeks. **Results:** From February 2007 through November 2010, 74 pts were enrolled, 68 pts with a median age of 56 years (range 37 to 69 years) were evaluable. 50% had oropharyngeal SCC. Of these, 65 pts (96%) received > 90% RT dosage, 50 pts (74%) > 90% Cet dosage and 56 pts (82%) > 4 cycles Cis 40 mg/m². 3D-CRT was used in 72% and 28 patients are currently still being followed up. The most common grade >3 toxicities were mucositis (59%) and dysphagia (52%). Cet-related grade >2- toxicities included dermatitis (15%) within the radiotherapy portals. Nine (14%) pts were missing for response evaluation (e.g. withdrawal of consent). Complete remission rate [(p)CR] was observed in 23/68 (34%) including with 16 pts (24%) who reached a CR of the primary tumor but a selective lymph node dissection was performed 6-8 weeks after end of radiation treatment for residual neck disease. Furthermore, partial remission (PR) was achieved in 29/68 (43%), so an overall response (OR) of 52/68 (77%) was reached. No change/stable disease occurred in 3/68 pts (4%), progressive disease (PD) occurred in 1 pt (1%) and 3 pts (4%) have died due to disease progression. The 2-year overall survival and disease-free survival were 64.2% and 45.3%, respectively. **Conclusions:** Combination therapy of LA SCCHN consisting of HART-Cis-Cet is an highly active regimen. The addition of Cet to weekly Cis and daily RT was well tolerated and resulted in encouraging local disease control and survival rates. Clinical trial information: 2005-000355-15.

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General Poster Session (Board #15B), Sat, 8:00 AM-11:45 AM

Progression-free survival (PFS) as a measure of efficacy for anti-EGFR antibodies in recurrent/metastatic (R/M) squamous cell carcinoma of head and neck (SCCHN).

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Background: Anti-epidermal growth factor receptor (EGFR) antibodies show promise in treatment of SCCHN. Since the approval of cetuximab as a first-line treatment in R/M settings, other EGFR inhibitors have failed to achieve FDA approval due to failures to achieve survival benefits, despite significant improvements in PFS. **Methods:** We analyzed aggregate data from all published phase III clinical trials using EGFR monoclonal antibodies as first-line treatment in R/M SCCHN, to investigate PFS as a surrogate endpoint to overall survival (OS). **Results:** The limited data indicate a linear relationship between PFS and OS with a constant difference between them of 5 months. This estimate has a confidence interval of variability about an estimated mean, and a prediction interval of variability around an estimate for a single patient. The meta-analyzed (fixed effect) estimate of the relative risk of mortality is 0.63 and the standard error is 0.094 and is statistically significant. **Conclusions:** Approval of cetuximab in SCCHN was based on significant benefit to OS observed in the Extreme study, in which controls were notably prohibited from crossover at progression. Panitumumab showed comparable benefit in PFS, though expected OS endpoints were not achieved, possibly due to over-performance of standard arms benefiting from improved second line treatment (including Cetuximab) and crossover at progression. Though not included in our analysis, Zalutumumab also showed improvement in PFS as a second line therapy. We propose that PFS be considered as a surrogate endpoint for OS in SCCHN trials, in light of new second line therapies and improved survival outcomes seen over the past decade.

Phase III trial	Authors	Treatment	Patients	Median OS (months)	Median PFS (months)
ECOG	Burtness, et al. JCO 2005	C + cetuximab vs. C + placebo	117	9.2 vs. 8.0	4.2 vs. 2.7
Extreme	Vermorken, et al. NEJM 2007	CF + cetuximab vs. CF	442	10.1 vs. 7.4	5.6 vs. 3.3
Spectrum	Vermorken, et al. ESMO 2010	CF + panitumumab vs. CF	657	11.1 vs. 9.0	5.8 vs. 4.6

C, platinum; CF, platinum + fluoruracil.

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General Poster Session (Board #15C), Sat, 8:00 AM-11:45 AM

Specific detection of Epstein-Barr virus microRNAs in plasma samples from nasopharyngeal carcinoma patients: Correlation with tumor mass assessed by MRI.

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Background: Epstein-Barr virus (EBV) microRNAs of the BART family can be detected in the plasma of at least a fraction of nasopharyngeal carcinoma (NPC) patients. Our aim was to investigate the specificity of plasma BART detection in NPC patients and the correlation with viral DNA load and/or clinical characteristics. **Methods:** Hsa miR484 and 4 miR-BARTs (ebv-miR BART 2-5p, 5, 9 and 18) were assessed by RT-PCR following RNA extraction in 37 plasma samples including 20 NPC, 8 non-NPC head and neck squamous cell carcinoma (SCC) patients and 9 healthy EBV carriers. EBV DNA copy numbers (viral load) were measured in the same samples. To explore correlations of BART concentrations with tumor mass, MRI-based volume analysis was designed and performed on a subset of 13 patients with non metastatic NPC. In addition, longitudinal variations of BART concentrations were studied in 9 NPC patients for whom we had sequential plasma samples. **Results:** The cellular hsa miR-484 was detected in all plasma samples with a slightly higher average concentration in plasma samples from NPC and SCC patients. On the other hand, the miR-BARTs were undetectable or at a very low level in samples from SCC patients and healthy carriers contrasting with a high level in most NPC patients. There was an overall positive correlation between EBVDNA copy numbers and plasma concentrations of each miR-BART. However substantial amounts of plasmatic miR-BARTs were observed in several patients for whom no plasma EBV DNA was detected. Their concentration was apparently not correlated to the initial tumor volume but their longitudinal variations were parallel with clinical evolution in all but one case. **Conclusions:** To a large extent, detection of plasma miR-BART-2-5p, 5, 9, and 18 is specific of NPC patients. Their concentration does not seem to correlate with tumor mass, at least in localized NPC patients. In a fraction of patients without initial detection of plasma EBV DNA, the kinetics of plasma BARTs may provide informations on early tumor response under treatment and may have prognostic value.

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General Poster Session (Board #15D), Sat, 8:00 AM-11:45 AM

Multicenter, open-end, randomized controlled study using P53 gene recombinant adenovirus injection (rAd-p53) combined with chemotherapy for orofacial carcinoma (OFC): Phase IV clinical trial—Progress report and conclusion.

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Background: The gene therapy product (Gendicine, rAd-p53) had pre-market studies done around 1998 indicated its efficacy in the treatment of squamous cell nasopharyngeal carcinoma in multi-modality treatment regimen. Gendicine has been used successfully in treating over 40 cancer types since then. With the advancement in optimization of combined treatment methods over the years, there was a need for a medium term efficacy study. This report summarizes our phase IV study. **Methods:** Patient selection, intervention and allocation were done according to GCP and supported by statistical analysis. Orofacial cancer (OFC) patients of advanced stages (III/IV) from multiple hospitals (n=30) in China were recruited for this open-end, randomized, controlled study (2009.7--2012.06). The 2 groups were rAd-p53+chemotherapy (GT+CT) (n=743) and CT alone (n=232). Patient exclusion rate were 20.81% (n=128) and 13.9% (n=28) respectively. Virus particles were delivered intra-tumorally at a dose of 10^9 (tumor cell/cm² tumor area) x area x100 (virus multiplicity of infection, MOI), every 3d totally 10 times on d 1-28 inclusive. In synchrony with GT, 5-fluorouracil (5-FU, 250 mg/m²/d), on d 7-11 and d 25-29 along with carbocisplatin (KP, 400 mg/m²/d, i.v.), and with methotrexate (MTX, 50mg/m² /d) on d 7, 14, 25, 32 were administered. The control group received 5-FU, KP and MTX. **Results:** For advanced OFC treated with GT+CT, the efficacy and QoL were significantly ($p<=0.001$) improved, the result was in accordance with our phase II/ III studies. **Conclusions:** This study proved rAd-p53 when used as an adjunct is safe and efficacious. The side-effect was mostly self-limiting low-grade to mild fever. The combined treatment modality had complete remission (CR) improved by 21.38%, relief ratio (RR) by 11.53% and clinical benefit ratio by 20.82% over GT-CT. Long-term follow-up will be continued.

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General Poster Session (Board #15E), Sat, 8:00 AM-11:45 AM

Predictive biomarkers in a phase II trial of weekly carboplatin (CBDCA), paclitaxel (P), and cetuximab (C) induction and chemoradiation (CRT) in patients (pts) with resectable stage III/IVa,b head and neck squamous cell carcinoma (HNSCC): Eastern Cooperative Oncology Group E2303.

Amanda Psyrris, Ju-Whei Lee, Maria Vasilakopoulou, Eirini Pectasides, Barbara Burtness, David Rimm, Harold J. Wanebo, Arlene A. Forastiere; University of Athens, Athens, Greece; Dana-Farber Cancer Institute, Boston, MA; Yale University, New Haven, CT; Fox Chase Cancer Center, Philadelphia, PA; Department of Pathology, Yale University School of Medicine, New Haven, CT; Landmark Medical Center, Woonsocket, RI; Eviti, Inc., Philadelphia, PA

Background: We studied the addition of C to a sequential regimen of weekly CBDCA and P followed by CBDCA-P-radiation in pts with locally advanced resectable HNSCC. Tissue-based biomarkers may aid in pt selection for such approaches. **Methods:** Sixty-three eligible pts with operable stage III/IV HNSCC participated in E2303, an Eastern Cooperative Oncology Group (ECOG) phase II trial of induction chemotherapy with weekly C, P and CBDCA x 6 followed by CRT with concurrent weekly C, paclitaxel, carboplatin. A tissue microarray was constructed and b-catenin, E-cadherin, Epidermal Growth Factor Receptor Variant III (EGFRVIII), insulin-like growth factor-1 receptor (IGF1R), NF-kappa b, p53, PI3Kp85, PI3Kp110a, PTEN, NRAS, and pRb protein expression levels were assessed using automated quantitative protein analysis (AQUA). For each marker, time-to-event distributions (OS, PFS, and EFS) were estimated by Kaplan-Meier estimates and compared using log-rank tests. Multivariable Cox proportional hazards models were used to estimate hazard ratios and test for significance, with primary site (oropharynx vs. non-oropharynx), disease stage (III vs. IV), and other important markers adjusted in the model. All p-values are two-sided. A level of $p < 0.05$ is considered statistically significant. **Results:** Based on the continuous scale, pRb tended to association with EFS ($p=0.05$). On multivariable analysis, low pRb level was a significant predictor for improved EFS ($p=0.048$). Our pRb data analysis was based on 32 pts with marker data available. **Conclusions:** pRb level is a potential predictive biomarker for response to cetuximab. HPV E7 oncoprotein binds and degrades pRb; therefore, low pRb protein level might be a surrogate marker for HPV association. Large prospective studies will be required to determine the association between pRb, HPV status and response to cetuximab in HNSCC.

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General Poster Session (Board #15F), Sat, 8:00 AM-11:45 AM

Clinical utility of CT and FDG PET/CT in assessing the neck in node-positive head and neck cancer after chemoradiotherapy.

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Background: Concurrent chemoradiotherapy has been widely accepted to treat locoregional advanced head and neck cancer, but the need for subsequent neck dissection remains controversial. Our objective was to determine whether CT or fluorodeoxyglucose (FDG) PET/CT is superior in the evaluation of persistent nodal disease after chemoradiotherapy in patients with node-positive head and neck squamous cell carcinoma (HNSCC). **Methods:** Study entry criteria included node-positive HNSCC treated with concurrent chemoradiotherapy, a local complete response, and post-treatment CT and FDG PET/CT studies 11 weeks after chemoradiotherapy. Fifty-eight patients with 68 node-positive necks were eligible. Nodes larger than 1 cm (minor axis), or with central necrosis on CT, or any visually hypermetabolic nodes on FDG PET/CT were considered clinically positive. Regardless of PET/CT findings, necks with positive CT were subjected to neck dissection, whereas those with negative CT were observed without neck dissection. **Results:** Seventeen necks showed positive CT, 13 and 4 of which underwent neck dissection and fine needle aspiration cytology, respectively, resulting in pathologic evidence of persistent nodal disease in 5 necks. Four of 51 necks with negative CT developed regional recurrence. Diagnostic accuracy of CT and PET/CT is shown in table. In general, the negative predictive value (NPV) was equivalent between CT and FDG PET/CT, whereas FDG PET/CT was better than CT in the specificity and accuracy. **Conclusions:** In patients with HNSCC, both CT and FDG PET/CT after chemoradiotherapy have a high NPV for excluding residual regional disease and avoiding unnecessary neck dissection. Although the NPV is similarly high, PET/CT has superior utility compared with CT because the number of false positive findings is less in PET/CT than CT.

Variable	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
CT	56%	80%	29%	92%	76%
PET/CT	44%	95%	57%	92%	88%
P value	P = 1	P < 0.01	P = 0.35	P = 1	P < 0.05

Carboplatin (C), cetuximab (Cet), and everolimus (E) in recurrent or metastatic squamous cell carcinoma of the head and neck (RMSCCHN). Results of a phase Ib study.

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Background: Platinum-based therapy in combination with Cet is the standard first line systemic therapy in RMSCCHN. Preclinical studies suggest that mTOR inhibitors may restore sensitivity to EGFR inhibitors in resistant cell lines, and that in combination with Cet may augment anti-tumor activity. We conducted a phase Ib trial of C, Cet and E for untreated RMSCCHN. **Methods:** Patients received C at AUC=2 on a 3 weeks on 1 off schedule with Cet weekly at a fixed dose and E at escalating dose levels of 2.5, 5.0, 7.5 and 10 mg daily using a 3+3 design. After 4 cycles of therapy patients without disease progression continued on maintenance Cet and E until disease progression or intolerable toxicity. Patients had previously untreated RMSCCHN not amenable to surgery or radiotherapy, age \geq 18 years and an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0-2. **Results:** After IRB approval, the study enrolled 18 patients with RMSCCHN between February 8, 2011 and Jan 25 2013. One patient was a screen failure. Four had an anaphylactic reaction to Cet and were excluded from the analysis. A total of 13 patients received E (M/F: 92%); median age 65 (44-75yrs). Two of six patients treated at dose level 1 (E-2.5 mg/day) experienced dose limiting toxicity (DLT) with grade 3 hyponatremia and nausea. Additional 7 patients were treated with de-escalated dose of E (2.5 mg QOD). No DLTs were observed at this dose level. Salient clinically relevant Grade >2 toxicities included: leukopenia (23%), neutropenia (15%) hyponatremia (18%), hyperglycemia, nausea, rash, hypokalemia, urinary infection, bacteremia, (each 8%). Dose reductions of C were necessary for a total of 18/61 delivered cycles of therapy. A response rate (RR) of 62.5% with all responders having partial responses (PR) was observed. The PFS was 7.8 months. **Conclusions:** The MTD of E in combination with Cet and C is estimated at 2.5 mg QOD. Though this is less than the commonly utilized dose of E, the regimen was associated with encouraging response rate and PFS Clinical trial information: NCT01283334.

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General Poster Session (Board #15H), Sat, 8:00 AM-11:45 AM

Nimotuzumab with concurrent chemoradiotherapy in patients with locally advanced head and neck cancer (LASCCHN).

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Background: Nimotuzumab is a humanized monoclonal antibody targeting EGFR receptors. Unlike other anti-EGFR monoclonal antibodies, it has demonstrated to be safe and effective when combined with chemotherapy or/and radiotherapy. We evaluated safety and efficacy of concurrently administering nimotuzumab with chemo-radiotherapy in patients with locally advanced inoperable squamous cell carcinomas of head and neck region in a usual health care setting. **Methods:** Open-label single-arm study. Patients of age 18 years and above with histologically confirmed squamous cell cancer of head and neck region in an inoperable stage (stage III & IV) having an ECOG ≤ 2 were included in the study. Informed consent was obtained from all the patients. The patient were administered injection cisplatin (30 mg/m² IV) and nimotuzumab (200 mg IV) weekly for six weeks along with radiotherapy of 6600cGy over 33 fractions. Patients were evaluated based on RECIST criteria 24 weeks after the last cycle of chemotherapy. **Results:** Fifty seven patients were enrolled in the study. Mean age of the patients was 51yr (29 yr-79 yr). Most common site of cancer was oral cavity 32 (56.14%). Fourty six (80.70%) patients completed 6 cycles of therapy. ORR was 80.7%, 34 with CR (59.6%), 12 with PR (21%), 8 with SD (14%), 3 with PD (5.2%). Most common adverse event seen was mucositis (33%) but there was no grade III or IV adverse event. **Conclusions:** Addition of anti-EGFR monoclonal antibody (nimotuzumab) is safe and efficacious based on the loco-regional response and confirms the available phase II data. The long-term survival benefits based on this encouraging response rate needs to be further evaluated especially in patients with inoperable LASCCHN.

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General Poster Session (Board #16A), Sat, 8:00 AM-11:45 AM

Are three drugs better than two and does docetaxel trump paclitaxel in induction therapy for locally advanced oral cavity cancers?

Vanita Noronha, Vijay Patil, Amit Joshi, S Juvekar, Bharatsinha Baburao Bhosale, Bhavesh Poladia, Sushmita Rath, Pankaj Chaturvedi, D. Chaukar, P. S. Pai, A. K. Dcruz, Kumar Prabhash; Tata Memorial Hospital, Mumbai, India; Tata Memorial Centre, Mumbai, India

Background: A variety of regimens have been used for induction chemotherapy in locally advanced head & neck cancers. Cisplatin & 5 FU drug combination is inferior to the combination of taxane & these 2 drugs. However, often in clinical practice at our center giving TPF is difficult in view of logistics & tolerance issues. In such scenarios we prefer to use 2 drug combination of platinum & taxane. However no study has addressed whether when the 2 drug combination includes taxane, is it still inferior to the 3 drug combination and which the taxane of choice is. **Methods:** This is a retrospective analysis of prospectively collected data of patients undergoing induction chemotherapy in oral cavity cancers from 2010-2012. We chose for analysis those patients who had a baseline scan and a follow-up scan done within 2 weeks of completion of the second cycle of induction chemotherapy. Response was scored in accordance with RECIST 1.1. Data was analyzed using SPSS, version 16. Chi-square analysis was done to compare response rates between regimens. **Results:** Two hundred & forty five patients were indentified. The median age was 45 years (24-70 years), 208 (84.9%) were male patients & in 154 patients (62.9%) had primary in buccal mucosa. The regimen received were TPF 22 (9%), TP (Docetaxel + cisplatin) 97 (39.6%), PP (paclitaxel+cisplatin) 89 (36.3%), TC (Docetaxel+ carboplatin) 16 (6.5%) & PC (paclitaxel + carboplatin) 21 (8.6%). The overall response rates (RR) were CR, PR,SD & PD in 4 (1.6%), 56 (22.9%), 145 (59.2%) & 40 (16.3%). On comparison, 3 drug regimen (TPF) had 50% RR as against 22% RR with 2 drug regimen ($p=0.004$). On comparison for taxane, docetaxel containing regimens had 30.3% RR as against 17.2% RR with paclitaxel containing regimens ($p=0.018$). There was no statistically significant difference in RR between patients receiving carboplatin or cisplatin. **Conclusions:** TPF had better RR than a 2 drug taxane-containing regimen and docetaxel leads to a better RR than paclitaxel for induction chemotherapy in locally advanced oral cavity cancers.

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General Poster Session (Board #16B), Sat, 8:00 AM-11:45 AM

Proton beam therapy combined with selective intra-arterial infusion chemotherapy for locally advanced tongue cancer.

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Background: The standard treatment for locally advanced tongue cancer is surgery. However, the patient's quality of life is lost. As a newly non-operative treatment, we report the efficacy and toxicity of proton beam therapy combined with selective intra-arterial infusion chemotherapy (PBT-IACT) for locally advanced tongue cancer. **Methods:** Between February 2009 and August 2012, 45 cases of stage III-IV(M0) squamous cell carcinoma of the tongue (28 men and 17 women) were treated by PBT-IACT at Southern TOHOKU Proton Therapy Center. Median age was 58 years (range:24-83 years), and clinical stage III/IVA/IVB were 11/32/2 respectively. In case of surgery, the patients required subtotal or total resection of the tongue. Initially, 2 courses of systemic chemotherapy and prophylactic whole neck irradiation (36Gy/20fr.) were performed. Subsequently, for gross tumor targets, PBT (33Gy/15fr.) and IACT were administered via the superficial temporal artery by continuous infusion of cisplatin with sodium thiosulphate. For PBT, 1 or 2 portals of 210 MeV proton beam were arranged in optimal angles to avoid overdosing the risk organ. Systemic chemotherapy was performed only for age of 70 years or younger. **Results:** The median follow-up was 27 months (range:8-48 months). Over all survival (OS), disease-free survival (DFS), and local control (LC) rates at 2 years were 88%,78%, 80%, respectively. LC of cervical lymph node metastases at 2 years was 86%. As the early toxic event, grade 3 mucositis (32/45) and blood/bone marrow toxicity (22/45) were observed. Within 6 months after this therapy, mandibular osteomyelitis occurred in 1 case. **Conclusions:** PBT-IACT appeared to be safe and has a good LC rate for locally advanced tongue cancer. Furthermore, it is not inferior to surgery and can be one of the new effective treatment options for locally advanced tongue cancer.

Relationship between level of lymph node metastasis (LNM) and survival in head and neck squamous cell carcinoma (HNSCC).

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Background: Evidence from small cohorts suggests that level of LNM predicts survival in patients with HNSCC. This study sought to investigate the prognostic value of level of LNM in a large populational database and contrast it with the current AJCC classification of lymph node involvement. **Methods:** SEER registry was queried for patients with stage I-IVB HNSCC of oral cavity (OC), oropharynx (OP), larynx (LAR) and hypopharynx (HP) diagnosed from 2004 to 2009 (N=39,699, median follow-up 2.3 years). Each anatomic group was divided into 3 subgroups based on level of LNM (no LNM, LNM to levels 1-3, 4 or 5), and 4 subgroups based on AJCC classification (N0, N1, N2, N3). Overall survival (OS) in each subgroup was computed (Kaplan-Meier method) and compared (log-rank test). Concordance statistics (C-index) were used to assess the accuracy of LNM classification by level vs AJCC in predicting OS. **Results:** Both AJCC and level of LNM-based classifications predicted OS in patients with OC, LAR, and HP cancers. For OP, neither AJCC nor level of LNM-based classification predicted OS as expected (lower OS for N0 vs N1/2 or levels 1-3/4) (Table). The performance of level of LNM-based classification was comparable to AJCC N staging for OC, LAR and HP. **Conclusions:** Level of LNM is a prognostic factor for OC, LAR and HP HNSCC. Classification by level of LNM reached similar accuracy as AJCC N staging in predicting OS for OC, LAR and HP. Neither classification is satisfactory for OP, illustrating the need to refine the staging system in this subgroup.

HR (CI)	OC (n=12,081)	OP (n=12,831)	LAR (n=12,763)	HP (n=2,024)
LNM level				
1-3 vs 0	2.63 (2.44-2.82)	0.72 (0.67-0.77)	2.10 (1.94-2.28)	1.14 (0.99-1.31)
4 vs 0	3.26 (2.75-3.86)	0.91 (0.80-1.03)	2.73 (2.36-3.15)	1.18 (0.94-1.48)
5 vs 0	3.92 (3.19-4.82)	1.03 (0.91-1.16)	2.78 (2.36-3.28)	1.28 (1.02-1.59)
C index	0.61 (0.57-0.64)	0.54 (0.50-0.57)	0.58 (0.54-0.61)	0.52 (0.35-0.69)
AJCC				
N1 vs. N0	2.31 (2.10-2.54)	0.74 (0.68-0.81)	1.89 (1.70-2.10)	1.13 (0.96-1.33)
N2 vs. N0	3.17 (2.92-3.45)	0.75 (0.70-0.81)	2.52 (2.31-2.74)	1.16 (1.00-1.34)
N3 vs. N0	3.11 (2.28-4.23)	1.14 (0.97-1.35)	2.77 (2.15-3.56)	1.53 (1.11-2.10)
C index	0.61 (0.57-0.64)	0.54 (0.50-0.57)	0.58 (0.54-0.61)	0.52 (0.35-0.69)

6088

General Poster Session (Board #16D), Sat, 8:00 AM-11:45 AM

miRNA analysis between malignant and benign tissue and circulating exosomes (CE) in patients (pts) with tongue squamous cell carcinoma.

Guilherme Rabinowits, Ludmila Flores, Anne M. O'Neill, Kristen Stevenson, Irene M. Ghobrial, Victoria Vergara, Vickie Y Jo, Sigitas Jonas Verselis, Nicole Grace Chau, Jochen H. Lorch, Robert I. Haddad; Dana-Farber Cancer Institute, Boston, MA; Brigham and Women's Hospital, Boston, MA

Background: The identification of a specific miRNA pattern in HNSCC is challenging given the heterogeneity of this disease and different methodologies used in prior studies. Here we chose to group pts according to primary tumor location and used Nanostring as a larger miRNA platform. **Methods:** CE-miRNA was isolated from 500ul of plasma collected in Heparin/EDTA tubes. Samples were pretreated with Pacific Hemostasis Thromboplastin D. Supernatant was treated with ExoQuick. Exosomal pellet was resuspended in 1ml of QIAzol Lysis Reagent. Formalin fixed paraffin embedded (FFPE) samples were deparaffinized and digested with proteinase K. miRNA from plasma and FFPE were isolated with miRNeasy Mini Kit. Samples were processed by Nanostring Technology. In this analysis, only tongue cancer pts were selected due to availability of paired tumor and benign tissue miRNA in conjunction with CE from the same pts and others with tongue cancer. **Results:** 21 HNSCC pts and 32 age-matched controls have enrolled to date. For homogeneity we analyzed only patients with tongue cancer (n=9): 8 males, median age 55.5 years (range 24-64), all had stage IVA tongue cancer (6 base of tongue), 6 HPV/p16 positive. Nine pts received chemoradiation; 4 also had surgery; 8 had clinical and radiological complete response. Of the 800 miRNAs tested 62 were overexpressed and 15 were suppressed in the tumor compared to benign tissue in the same pts. Of those overexpressed and suppressed in tumor tissue, 4 (miR23a-3p; miR150-5p; miR199a-5p; miR203) had a post/pre treatment average ratio (PPTAR) less than 1, while 4 (miR720; miR1253; miR145-5p; miR1283) had PPTAR greater than 1, respectively on CE of pts. miR150-5p was suppressed and miR1283, miR145-5p and miR1253 were overexpressed on CE of control samples compared to pre treatment samples of pts. **Conclusions:** Of the 800 miRNAs, 8 appear to correlate with treatment response. The average levels of 4 of those miRNA mirror the average levels of tumor tissue miRNA and is in an inverse relationship with benign tissue and control blood samples, suggesting this may be a unique signature for tongue cancer. This observation needs to be validated in larger studies.

A comparative study of the response and toxicities in locally advanced head and neck cancer patients treated with paclitaxel, cisplatin, 5-FU versus docetaxel, cisplatin, 5-FU as neoadjuvant chemotherapy followed by concurrent chemoradiation.

Diptirani Samanta, Surendra nath Senapati, Kirti Ranjan Mohanty, Saroj Das; Acharya Harihar Regional Cancer Centre, Cuttack, India; Acharya Harihar Regional Cancer Centre, Cuttack, Odisha, India

Background: To evaluate the response and toxicity of docetaxel, cisplatin, 5-FU vs paclitaxel, cisplatin, 5-FU as neoadjuvant chemotherapy (NACT) followed by concurrent chemoradiation (CTRT) with weekly cisplatin in locally advanced head and neck cancer. **Methods:** 40 locally advanced head and neck cancer patients who satisfied the eligibility criteria were randomized. 21 patients received three cycles of NACT i.e paclitaxel (175 mg/m²) on d1, cisplatin (30 mg/m²) and 5-FU (600 mg/m²) d2-d4 (TCF) and 19 patients received three cycles of NACT docetaxel (75 mg/m²) on d1, cisplatin (30 mg/m²) and 5-FU (600 mg/m²) d2-d4 at three week intervals, followed by concurrent weekly cisplatin 30 mg/m² along with conventional external beam radiation of total tumor dose dose 66 Gy. Response was assessed after NACT and again after six weeks, three months and six months of completion of chemoradiation. Toxicities were assessed after each cycles of NACT and also weekly during CTRT and thereafter. **Results:** Two weeks after completion of NACT complete response (CR) in TCF was 4.76%, partial response (PR) 80.9% and no response 9.5%. However in DCF, CR was 15.78 % PR was 73.68%. 10.52% patientd died due to toxicity. With a median follow up of seven months, in TCF CR was 57.14%, PR 33.33% and no response was 4.76%, whereas in DCF CR was 78.94%, PR 10.52% and death 10.5%. On evaluation of toxicities during NACT, patients in DCF had more significant neutropenia and in TCF more incidence of neuropathy. During CTRT, in TCF grade II and III mucositis was 54%, grade II neutropenia 5.6%, and grade II anemia 5.3%. In DCF mucositis grade II and III was 49.0%, neutropenia grade II 18.7% and anemia grade II was 7.4%. Late toxicities included were comparable in both arms. **Conclusions:** With a median follow up of 7 months, the CR in DCF was 78.94%, superior than TCF i.e 57.14%. Neutropenia was significant in DCF and neuropathy was high in TCF. In CTRT mucositis was the commonest toxicity observed in both TCF and DCF which was not statistically significant.

6090

General Poster Session (Board #16F), Sat, 8:00 AM-11:45 AM

Long-term disease control of ≥ 2 years achieved with cabozantinib in subjects with metastatic medullary thyroid carcinoma on a phase I study.

Ezra E.W. Cohen, David S. Hong, David G. Pfister, Ravi Salgia, Barbara Burtness, Roger B. Cohen, Douglas Wilmot Ball, Raneeh Mehra, Milan Mangeshkar, Yifah Yaron, Frauke Bentzien, Razelle Kurzrock; The University of Chicago Medicine and Biological Sciences, Chicago, IL; The University of Texas MD Anderson Cancer Center, Houston, TX; Memorial Sloan-Kettering Cancer Center, New York, NY; The University of Chicago, Chicago, IL; Fox Chase Cancer Center, Philadelphia, PA; The Johns Hopkins University, School of Medicine, Baltimore, MD; Exelixis, Inc, South San Francisco, CA; University of California, San Diego, San Diego, CA

Background: Metastatic medullary thyroid cancer (MTC) carries a median survival of about two years (Modigliani et al. 1998; Roman et al. 2006). Cabozantinib inhibits three primary pathways implicated in MTC pathogenesis and progression: MET, vascular endothelial growth factor receptor-2 (VEGFR2), and RET. A phase I study was initiated in September 2005 in patients (pts) with advanced solid tumors. **Methods:** 85 pts, including 37 with MTC were enrolled to evaluate safety, pharmacokinetics, and to determine maximum-tolerated dose (MTD). Once the MTD of 140 mg freebase (equivalent to 175 mg malate salt) was determined, 20 metastatic or locally advanced MTC pts were enrolled in an MTD expansion cohort. 10/37 MTC pts achieved a confirmed partial response (cPR) (Kurzock et al. 2011). We report here on long-term disease control (DC), defined as cPR or progression-free at ≥ 24 months (m), in the MTC cohort. **Results:** After a minimum follow-up period of 52 m, 11 of 37 pts (30%) experienced DC, and have remained progression-free for > 24 m. Time from diagnosis and time since development of metastatic disease was similar in patients with (11) or without (26) long term DC. As of 04 Dec 2012, 5 of these 11 pts remain on treatment for a median time of 55 m (53-73m). A best response of cPR was associated with long-term benefit: 4/5 pts continuing on treatment achieved cPR, one achieved SD. The adverse event profile of cabozantinib was generally predictable and adverse events were managed with symptomatic treatment and dose modifications. The median final dose for pts with long-term DC was 60 mg (range 20-140), with a median number of dose reductions of 2 (range 0E4). Reasons for dose reductions in two or more pts experiencing long-term DC included diarrhea (7), palmar-plantar erythrodysesthesia syndrome/rash (6), mucositis/stomatitis (3), anorexia (3), nausea (2), and vomiting (2). **Conclusions:** Treatment with cabozantinib demonstrates long-term DC in a cohort of pts with metastatic MTC. Cabozantinib offers an important new treatment option for patients with progressive, metastatic MTC. Clinical trial information: NCT00215605.

Comparison of patient performance between PEG/no PEG placement in head and neck cancer patients during chemoradiotherapy treatment.

Robin Metcalfe-Klaw, Hasan Husaini, Cathy L Lazarus, Louis Benjamin Harrison, Bruce Culliney, Zujun Li, Mark L Urken, Adam Jacobson, Daniel Buchbinder, Mark Persky, Theresa Tran, Michael Pitman, Catherine Concert, Daisy Maria Palacios, Bridget Bennett, Mahesh Kumar, Kenneth Hu; Beth Israel Medical Center, New York, NY; Beth Israel Medical Center, New York, NY; New York Eye and Ear Infirmary, New York, NY

Background: Many head and neck cancer patients suffer from side effects of chemoradiotherapy that can result in reduced oral intake, and weight loss. To prevent this malnutrition they often undergo preventative percutaneous endoscopic gastrostomy (PEG) placement. We aim to determine whether PEG placement is necessary for successful patient performance during treatment. **Methods:** We compared 2 groups: patients that underwent PEG (Gp-1=P) (n=20), and those that did not undergo PEG (GP-2=NP) (n=47). All patients were treated with chemoradiotherapy. All were assessed at baseline (BL), and wk 5 of tx. WHO variables including weight loss, mucositis, dysphagia, and odynophagia ratings, along with patient-rated modified “distress thermometers”, were analyzed. **Results:** Patients with no PEGs had higher weights at BL (NP=193 vs P= 171, p=0.073) and at wk 5 (NP=179 vs P= 160, p=0.056). Weight loss in these groups were 8.09 % - P (p=0.000), 8.25% - NP (p=0.000) respectively from BL - wk 5. The median distress level of each group was 0-P and 1-NP at BL (p=0.302) and 6-P and 3-NP at wk 5 (p=0.086). 27 patients had a distress level of ≥ 4 at wk 5. Of these 27, 12 were PEG’d and 15 were not (p=0.008). 86 % of patients in the PEG group had distress ≥ 4 and 44 % in the NP group had distress levels ≥ 4 . Patients that underwent PEG had slightly higher odds (NS) of associating their distress to nausea, fatigue and/or eating than patients that were not PEG’d. The wk 5 WHO toxicity scale assessment showed 15 PEG’d patients had Grade 1 (n=5), Grade 2 (n=9) & Grade 3 (n=1) dysphagia and 28 NP patients had Grade 1 (n=23) & Grade 2 (n=5) dysphagia (CHI square =11.66, p=0.009). **Conclusions:** Patients that underwent PEG placement before or during treatment performed worse in every assessment (weight loss, distress thermometer & toxicity scale) as compared to the no PEG group. Patients who have a normal or above average BMI are candidates to be monitored for PEG placement. However, both groups examined were able to complete treatment without significant treatment breaks. Close multidisciplinary monitoring and more intensive supportive care are needed when determining need for PEG placement during treatment.

Sequential TKI treatments for iodine-refractory differentiated thyroid carcinomas.

Christelle de la Fouchardiere, Marie-Helene Massicotte, Isabelle Borget, Maryse Brassard, Mederic Claude-Desroches, Anne Laure Giraudet, Christine Docao, Francoise Bonichon, Cecile Chougnet, Sophie Leboulleux, Eric Baudin, Martin Schlumberger; Centre Léon Bérard, Lyon, France; Institut Gustave Roussy, Villejuif, France; Institut Gustave Roussy, Villejuif, France; Endocrinology Service, Department of Medicine, Centre Hospitalier Universitaire de Québec, Université Laval, Québec, QC, Canada; Radiology Department, Institut Universitaire de Cardiologie et de Pneumologie de Québec, Québec, QC, Canada; Nuclear Medicine Service, Hôpital René Huguenin, Institut Curie, Saint-Cloud, France; Centre Hospitalier Régional Universitaire de Lille, Lille, France; Institut Bergonié, Bordeaux, France

Background: Tyrosine kinase inhibitors (TKI) are currently used to treat patients with advanced iodine-refractory differentiated thyroid cancers (DTC) but none has been approved by the FDA or the EMA until now. Sometimes, patients are treated with off-label TKI when a clinical trial is not available or in second- and third-line therapy. **Methods:** We hereby report the efficacy of “off-label” sorafenib and sunitinib treatments as first-, second- and third-line therapy in metastatic DTC patients from the French TUTHYREF (TUmeurs THYroïdiennes REfractaires) network. Primary endpoints were progression free survival (PFS) and tumor response according to sequential TKI treatment. Secondary endpoint was organ-specific metastatic site analysis. **Results:** 45 patients with advanced iodine-refractory DTC treated with off-label TKI were included in this study (26 men, mean age: 62 years). 22 had papillary, 10 had follicular and 13 had poorly DTC. 24/45 patients were treated with two and 3/45 with three lines of TKIs. Sorafenib was the most frequently used (57%) followed by sunitinib (21.5%) and vandetanib (21.5%). Partial response (PR) rate was of 29% in the 21 patients who received first-line sorafenib therapy whereas PR was observed in 57% of the 7 first-line sunitinib patients. There was no PR with second- (n=24) and third-line (n=3) treatments. However, median progression free survival (PFS) was similar in second- as compared to first-line sorafenib or sunitinib treatment (6.7 vs. 7.6 months, HR 0.85 (95CI 0.45-1.61) p=0.6). Liver metastases were the most responsive to treatment (n=7; mean of -30%), followed by lung (n=57; mean of -19%) and lymph node (n=43; mean of -13%) metastases. Bone (n=14) and pleural (n=9) lesions were the most refractory to treatment (mean of -1% and -5%, respectively). **Conclusions:** Due to the small number of patients, we could not recommend a specific treatment sequence (sorafenib then sunitinib) over another (sunitinib then sorafenib). But TKI therapy appears to be beneficial in refractory DTC patients even in second- and third-line therapy, with similar PFS and stable disease as best response. Bone and pleural metastases were the most refractory and liver lesions the most responsive to treatment.

6093

General Poster Session (Board #17A), Sat, 8:00 AM-11:45 AM

Survival and prognostic factors of radioiodine refractory pulmonary metastatic differentiated thyroid carcinoma (DTC).

Johanna Wassermann, Marie-Odile Bernier, Jean-Philippe Spano, Charlotte Lepoutre-Lussey, Jean-Marc Simon, Fabrice Ménégaux, Catherine Hoang, André Aurengo, Laurence Leenhardt; Department of Nuclear Medicine, Pitié-Salpêtrière University Hospital, Paris, France; Department of Medical Oncology, Pitié-Salpêtrière University Hospital, Paris, France; Department of Radiotherapy, Pitié-Salpêtrière University Hospital, Paris, France; Department of Endocrine Surgery, Pitié-Salpêtrière University Hospital, Paris, France; Department of Pathology, Pitié-Salpêtrière University Hospital, Paris, France

Background: The challenging key point of management of radioiodine refractory DTC patients is to define those who could benefit from experimental drugs in clinical trials. **Methods:** We reviewed clinical and pathological data of patients with refractory pulmonary metastatic DTC treated in our center from 1990 to 2011. Survival was estimated with the method of Kaplan-Meier. Associated prognostic factors were studied in Cox model based analyses. **Results:** Among 167 pulmonary metastatic DTC, 46% (n=76) met a criterion of radioiodine refractory disease: at least one metastases without I131 uptake: 61% (n=46); progressive disease despite I131: 22% (n=17) and absence of complete response despite a cumulated dose >600mCi: 17% (n=13). There were 63% of female (n=48) and the median age was 64 years (range 18-87). The initial treatment was total thyroidectomy in 92% (n=70), lymph node dissection in 71%, (n=54) and radioiodine therapy in 100% of patients. Pathological features were papillary histology in 61% (n=46), follicular histology in 29% (n=22) and poor differentiated histology in 10% (n=8). pT stage was 1ab, 2, 3, and 4 in 11%, 13%, 63% and 13% respectively, pN stage after lymph node dissection was 0, 1a and 1b in 33%, 7% and 60% respectively. Metastasis were present at diagnosis in 45% (n=34) of cases. The refractory feature was established at the time of diagnosis and in the follow-up in 18% and 82% of cases respectively. When the disease was considered as refractory, the median overall survival was 5.5 years. The refractory feature at the initial diagnosis was the only independent prognostic factor correlated with poor survival (p<0.001). **Conclusions:** Patients who are considered as radioiodine refractory at the initial diagnosis of DTC have poor prognosis and should be considered for clinical trials in case of progression.

6094

General Poster Session (Board #17B), Sat, 8:00 AM-11:45 AM

Combination lapatinib and capecitabine in advanced, incurable squamous cell carcinoma of the head and neck (SCCHN).

Jared Weiss, David N. Hayes, Kenneth M. Algazy, Arati Suvas Desai, Brenda Horn, Sara Gulino, Dale Flowers, Diane Frazee, Arthur M. Feldman, Arthur P. Staddon, Juneko E. Grilley-Olson, Roger B. Cohen, Corey J. Langer; Lineberger Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC; Abramson Cancer Center of the University of Pennsylvania, Philadelphia, PA; Abramson Cancer Center at Penn Presbyterian Medical Center, Philadelphia, PA

Background: In an era of increasing use of platinum-based induction chemotherapy and chemoradiotherapy, most metastatic/recurrent SCCHN patients (pts) have received multiple chemotherapeutic agents prior to being diagnosed with incurable disease, at which point PS is often poor, pts are often refractory to multiple agents, and standard therapies (Tx) are unacceptably toxic and inconvenient. **Methods:** We conducted a phase II study of 44 pts with metastatic/recurrent SCCHN with a primary endpoint of median OS. Pts received capecitabine 1,000 mg/m² BID for 14/21 day cycles, with lapatinib at 1,250 mg daily for a total of four cycles. In the absence of disease progression or unacceptable toxicity, pts received maintenance Tx with lapatinib. Prior exposure to any chemotherapy other than capecitabine and lapatinib was allowed, as long as it was as part of therapy delivered with curative intent. **Results:** 36 of 44 planned patients are assessable at this time. 69% had prior resection, 75% prior radiation and 61% prior chemotherapy, of whom 18 (50%) had received prior platinum. Median age was 62, 11 pts (31%) had PS 0, 22 pts (61%) pts had PS1 and 3 pts (8%) had PS2. Median number of cycles given was 4; 14 pts have gone on to maintenance Tx. The most common grade 3-4 adverse events have included dehydration, diarrhea, and hand-foot syndrome, each occurring in 11% of pts. 2 patients did not have RECIST evaluable disease. Of the remaining 34 patients, 6 pts had PR and 1CR, for an ORR of 21% (24% in assessable pts). As of 1-31-13, 20 pts are alive, 2 are lost to followup, and 14 are deceased. **Conclusions:** The combination of capecitabine and lapatinib is tolerable and active in metastatic/recurrent head neck cancer, including pretreated patients. OS data, not yet mature, will be required to determine if this regimen is worthy of further testing. Clinical trial information: NCT01044433.

6095

General Poster Session (Board #17C), Sat, 8:00 AM-11:45 AM

Survival in patients with HPV-positive oropharynx squamous cell carcinoma with distant metastases.

Katharine Andress Rowe Price, Scott H. Okuno, Joaquin J. Garcia, Julian R. Molina, Kerry D. Olsen, Jan C. Kasperbauer, Daniel L. Price, Yolanda I. Garces, Daniel Ma, Michelle A. Neben-Wittich, Shastin E. Shull, Robert Leonard Foote, Eric J. Moore; Mayo Clinic, Rochester, MN

Background: Prognosis for patients (pts) with locally-advanced, HPV-positive oropharynx squamous cell carcinoma (HPV+OPSCC) is significantly better than for pts with HPV-negative head and neck squamous cell carcinoma (HNSCC). Historic survival of pts with metastatic HNSCC is 6-9 months with palliative therapy. However, the prognosis and survival of pts with HPV+OPSCC with distant metastases is not known. **Methods:** Pts with HPV+OPSCC with distant metastatic disease were identified from databases from the departments of surgery, radiation, and medical oncology. Demographic and clinical data was abstracted from the medical record. All pts had confirmed HPV/p16+ disease. **Results:** Fifteen pts with metastatic HPV+ OPSCC were identified. The median age was 57 years (range 42-78, 15 male). The median pack-year smoking was 0 (range 0-120). Primary site included 10 tonsil and 5 tongue base. At diagnosis, one pt had stage III and 14 had stage IV disease (IVA: 9, IVB: 2, IVC: 3). T- and N-stage included T1 (1), T2 (10), T3 (3), T4 (1) and N1 (1), N2a (1), N2b (9), N2c (3), N3 (1). Extracapsular extension was seen in 8 pts, absent in 2, and unknown in 5. Seven pts had lymph node (LN) involvement at level IV/V. Initial therapy for locally-advanced disease included surgery followed by adjuvant radiation (RT) in 1 pt and chemoRT in 8, and definitive chemoRT in 3 pts. Three pts were metastatic at initial diagnosis. Of 6 pts with an isolated metastatic site, 3 pts are alive > 2 years from diagnosis of metastasis (median 1.97 years, range 0.49-2.29). Palliative therapy included surgery (3), RT (9), platinum chemo +/- cetuximab (8), cetuximab alone (2) or with a taxane (2). The most common sites of metastasis included bone (6), lung (5), and LNs (5). The 1-year survival rate after diagnosis of metastatic disease was 92%. The median time to diagnosis of metastatic disease after definitive therapy was 0.47 years (95% CI 0.19-1.29); 75% of pts who developed metastatic disease did so within 1 year of definitive therapy. Of note, 2 of the 15 pts developed a secondary immune-mediated malignancy (melanoma and non-HIV associated Kaposi's sarcoma). **Conclusions:** The survival of pts with metastatic HPV+OPSCC is significantly better than that of historic controls.

Superselective intra-arterial chemotherapy for oral cancer by subcutaneous implantation of an intra-arterial catheter and an infusion reservoir: A new chemotherapy method to improve the quality of life and curative effect.

Masatoshi Ohmae, Iwai Tohnai, Itsuro Kato, Mitsuhiro Nakazawa; Rinku General Medical Center, Izumisano, Osaka, Japan; Department of Oral and Maxillofacial Surgery, Yokohama City University School of Medicine, Yokohama, Japan; Oral and Maxillofacial Surgery II, Osaka University Graduate School of Dentistry, Suita, Japan

Background: We have developed a superselective intra-arterial chemotherapy (iaCT) approach for oral cancer, in which intra-arterial catheter is retrogradely inserted via the superficial temporal artery (STA) and/or occipital artery (OA). This approach increases chemotherapy efficiency but remarkably decreases activities of daily living (ADL) because the catheter penetrates the skin over the approaching artery (STA/OA). **Methods:** This study assessed our new outpatient iaCT approach involving implantation of an intra-arterial catheter connected to a subcutaneous infusion reservoir. We included 10 patients who had oral cancer treated using outpatient iaCT: tongue carcinoma, 7; cheek mucosal carcinoma, 1; upper gingival carcinoma, 1; palatal carcinoma, 1. In this approach, the STA or OA or both were percutaneously dissected out, a catheter was inserted, and the catheter tip was superselectively placed in the tumor-feeding artery. The extra-arterial catheter portion was implanted through a subcutaneous tunnel and was connected to a subcutaneous infusion reservoir implanted around the mastoid process. The patients were discharged after catheterization, and the chemotherapeutic agent was intra-arterially administered at the Outpatient Chemotherapy Center of Rinku General Medical Center once or twice a week. Intra-arterial infusion was repeated 6 times per course. **Results:** The response rate was 100%, i.e., 8 cases of CR and 2 of PR; patients with PR underwent surgery. Their ADLs were scarcely disturbed except for ambulatory visits. **Conclusions:** In this approach, the catheter is completely implanted subcutaneously; therefore, usual catheter-related issues (e.g., infection, catheter fall out) rarely occur. Because this leads to very good ADLs, outpatient chemotherapy can be safely performed. Consequently, the quality of life (QOL) improves and medical expenses decrease. Our new outpatient iaCT approach improves QOL of and curative effects for oral cancer patients if the ambulatory convenience and the performance status are good.

TPS6097

General Poster Session (Board #17E), Sat, 8:00 AM-11:45 AM

Phase II study of de-intensification of radiation and chemotherapy for low-risk HPV-related oropharyngeal squamous cell carcinoma.

Bhishamjit S. Chera, Bahjat F. Qaqish, Mark C Weissler, David N. Hayes, Carol G. Shores, Alan Monroe, Roger F. Anderson, Justin Wu, Juneko E. Grilley-Olson, Jared Weiss, Trevor Hackman, Adam M Zanation, William M. Mendenhall, Robert J Amdur; Department of Radiation Oncology, University of North Carolina at Chapel Hill, Chapel Hill, NC; The University of North Carolina at Chapel Hill, Chapel Hill, NC; Department of Otolaryngology/Head and Neck Surgery, University of North Carolina at Chapel Hill, Chapel Hill, NC; Lineberger Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC; Penrose - St. Francis Health Services, Colorado Springs, CO; Rex UNC Health Care, Raleigh, NC; University of Florida Proton Therapy Institute, Jacksonville, FL; Department of Radiation Oncology, University of Florida, Gainesville, FL

Background: The prognosis is excellent for low-risk human papillomavirus (HPV) associated oropharyngeal squamous cell carcinoma (OPSCC). Current standard chemoradiotherapy (CRT) regimens cure most patients but cause significant acute (mucositis) and long-term toxicities (xerostomia and dysphagia). Toxicity is primarily determined by the dose of radiotherapy and the intensity of chemotherapy. The aim of this study is to evaluate the pathological complete response (pCR) rate of low-risk HPV-associated OPSCC after de-intensified CRT. **Methods:** The major inclusion criteria are: 1) T0-T3, N0-N2c, M0, 2) HPV or p16 positive, and 3) ≤ 10 pack-years smoking history. Patients receive 60 Gy of intensity modulated radiotherapy (IMRT) with concurrent weekly intravenous cisplatin (30 mg/m²). CT scans are obtained 4 to 8 weeks after completion of CRT to assess response. All patients have a surgical resection of any clinically apparent residual primary tumor or biopsy of the primary site if there is no evidence of residual tumor and a selective neck dissection to encompass at least those nodal level(s) that were positive pre-treatment, within 4 to 14 weeks after CRT. Longitudinal assessments of quality of life (EORTC QLQ-C30 & H&N35, NDII), patient reported outcomes (PRO-CTCAE, EAT-10), and swallowing evaluations (modified barium swallow) are obtained prior to, during, and after CRT. The primary endpoint of this study is the rate of pCR after CRT. The null hypothesis is that the pCR rate for de-intensified CRT is at least 87%, the historical rate (based on the reported 3-year local regional control rate of 87% in the RTOG 0129). Power computations were performed for N=40, with a type I error of 14.2% if the true pCR rate is 0.87. The study will be done in 3 stages with 15+15+10 patients with interim analyses at 15 and 30 patients. The trial will be stopped if the pCR rate is $\leq 9/15$ and $21/30$. The null hypothesis will be accepted if the pCR rate is $\geq 33/40$. Clinical trial information: NCT01530997.

TPS6098

General Poster Session (Board #17F), Sat, 8:00 AM-11:45 AM

Phase II study of dalantercept, a novel inhibitor of ALK1-mediated angiogenesis, in patients with recurrent or metastatic squamous cell carcinoma of the head and neck.

Antonio Jimeno, Lori J. Wirth, Marshall R. Posner, Roger B. Cohen, Jared Weiss, Elizabeta C. Popa, Nabil F. Saba, Kenneth F. Grossmann, Ammar Sukari, Ezra E.W. Cohen, Athanassios Argiris, Carolyn H Condon, Dawn Wilson, Ty McClure, Marat Alimzhanov, Scott Pearsall, Kenneth M. Attie, Matthew L. Sherman, Shuchi Sumant Pandya; University of Colorado, Denver, Aurora, CO; Massachusetts General Hospital, Boston, MA; Mount Sinai Medical Center, New York, NY; Abramson Cancer Center of the University of Pennsylvania, Philadelphia, PA; Lineberger Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC; Weill Cornell Medical College, New York, NY; Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; Karmanos Cancer Institute, Wayne State University, Detroit, MI; The University of Chicago Medicine and Biological Sciences, Chicago, IL; University of Texas Health Science Center at San Antonio, San Antonio, TX; Acceleron Pharma, Cambridge, MA

Background: Despite advances in the treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN), the prognosis remains poor with a need to develop novel therapeutic strategies. Targeting angiogenesis in SCCHN is an active area of clinical research. Activin receptor-like kinase 1 (ALK1) is a type 1 receptor in the TGF- β superfamily which is selectively expressed on activated endothelial cells. ALK1 binds bone morphogenetic proteins (BMP) 9 and 10 (ligands for ALK1) and is primarily involved in the maturation stage of angiogenesis. Dalantercept is a human ALK1-Fc receptor fusion protein that binds BMP9/10 and acts as a ligand trap. In preclinical tumor models, dalantercept demonstrated a decrease in tumor vascularization and delayed tumor growth. In a completed phase I study, dalantercept demonstrated anti-tumor activity in patients with advanced solid tumors including SCCHN. **Methods:** An open label, multi-center, multiple dose, phase II study to evaluate dalantercept in patients with advanced SCCHN is ongoing. Dalantercept is being administered every three weeks via SC injection in a total of 45 patients to assess safety, tolerability, and efficacy. 13 patients were enrolled at the 0.6 mg/kg dose level. To date, 6 out of 30 planned patients have received dalantercept at the 1.2 mg/kg dose level. Key inclusion criteria are tumors arising from the oral cavity, oropharynx, hypopharynx, or larynx, at least one prior platinum-containing regimen, ECOG performance status \leq 1, and measurable disease. Exclusion criteria include prior anti-angiogenesis therapy, significant pulmonary, cardiovascular, or bleeding risk. The primary efficacy endpoint is RR. Secondary endpoints include PFS, OS, TTP, DOR, DCR, and PD biomarkers on tumor and serum specimens including BMP9/10 and ALK1 expression. Clinical trial information: NCT01458392.

TPS6099

General Poster Session (Board #18A), Sat, 8:00 AM-11:45 AM

Seamless phase II/III trial design with survival and PRO endpoints for treatment selection: Case study of RTOG 1216.

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Background: Clinical trial results from phase II trials to select an experimental treatment arm for separate phase III trial comparison can require years. Cancer clinical trials also now aim at both survival and PRO/functional outcomes, especially in head and neck (HN) studies. We developed a unique seamless phase II/III trial design to save on sample size and trial duration. The initial multi-arm phase II trial selects the most effective regimen among multiple experimental arms by first comparing each of the new treatments to a common control arm, using chosen endpoints, such as progression free survival. The winner will be tested for overall survival in the phase III study. **Methods:** We propose a phase II/III design to test the efficacy of experimental arms of postoperative radiation (RT) + docetaxel or RT + docetaxel + cetuximab in patients with HN squamous cancer. These are compared to the control arm of RT + cisplatin in the phase II part. Only one arm will be selected to go on to phase III depending on efficacy (PFS), PRO and safety outcomes. One experimental arm must be sufficiently better than the common control arm and the winner not having increased toxicity or functional cost to be selected for phase III inclusion. If not, the trial is halted for futility. Patients in the phase II selected arm and the control arm are included in phase III testing. Group sequential method is used to design each component. Separate interim efficacy and futility analyses are built in such that each endpoint can be monitored as in separate phase II, III trials. Once sample sizes are derived, operating characteristics for the seamless II/III design are evaluated through simulations under the null and various alternative hypotheses. Savings on sample size and time are compared to typical separate phase II and III designs and to the design testing only the arm of RT + docetaxel + cetuximab in phase II. **Conclusion:** The phase II/III RTOG 1216 HNC trial offers cost effectiveness, operational efficiency and scientific innovation.

TPS6100

General Poster Session (Board #18B), Sat, 8:00 AM-11:45 AM

Pharmacodynamic study of neoadjuvant vemurafenib (VEM) in patients (pts) with BRAF mutated, locally advanced papillary thyroid cancer (PTC).

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Background: BRAF mutations are found in 40% of pts with newly diagnosed PTC but much more prevalent in recurrent PTC, ranging from 78-86%, suggesting they play an active role in tumor progression. Activating mutations in BRAF result in constitutive activation of MEK and subsequently ERK. ERK mediates activation of nuclear transcription factors coordinating expression of genes involved in proliferation and survival of malignant cells. PTC usually has an excellent prognosis, especially in younger pts and in pts who respond to the only effective treatment: surgery followed by radioactive iodine (RAI). However, more advanced stage disease at diagnosis, older age, and lack of RAI avidity are associated with a high rate of recurrence and distant metastasis, imparting a worse overall survival. Long-term outcomes depend highly on initial surgery outcome. Pts at highest risk of recurrence and death are those with gross residual disease after surgery and macroscopic tumor invasion. VEM is an inhibitor of the activated form of the BRAF serine-threonine kinase enzyme. The drug is FDA approved for the treatment of advanced melanoma and is currently being studied in a phase 2 trial in metastatic BRAF-mutated PTC. This is a neoadjuvant trial to determine if pharmacodynamic changes in the tumor correlate with response to drug. **Methods:** Pts with primary or recurrent BRAF mutated PTC who are planned for surgical resection are eligible. Pts will undergo baseline core biopsy prior to starting VEM 960mg bid. After 56 days of treatment they will undergo surgery and post-treatment specimen will be collected. Pts with widely metastatic PTC may continue VEM. The primary endpoint is to determine whether changes in ERK phosphorylation responses after treatment with VEM correlate with clinical response at day 56 in pts with locally advanced, BRAF mutated PTC. Secondary endpoints include assessments of safety of neoadjuvant VEM, response by RECIST, rate of surgical complications, persistent disease at the surgical site at 1 year, and mechanisms of resistance to VEM. The trial began enrolling pts in December 2012, with a total of 22 pts planned. This trial has no sponsor. Clinical trial information: NCT01709292.

TPS6101

General Poster Session (Board #18C), Sat, 8:00 AM-11:45 AM

Potential of cetuximab by inhibition of Tregs in metastatic squamous cell cancers of head and neck.*Gautam Gopalji Jha, Jeffrey S Miller; University of Minnesota, Minneapolis, MN*

Background: There are few effective treatment options for patients with metastatic squamous cell cancers of head and neck (HNSCC). The only significant advance in the last few decades has been approval of cetuximab, a monoclonal antibody directed against the overexpressed epidermal growth factor receptor (EGFR). Despite its high specificity for EGFR, cetuximab as single-agent has resulted in response rates of only 13% and PFS of less than 2 months. Recent evidence suggests that cetuximab may induce tumor cell killing through an immune-mediated ADCC and not through blockade of EGFR signaling. Cetuximab binds EGFR on tumor cells making them targets for natural killer (NK) cell-mediated lysis. The effectiveness of cetuximab is limited by the tumor mediated immune-suppression that inhibits NK and other effector cells. This local and possibly generalized immune suppression is primarily mediated by regulatory T cells (Tregs) which inhibit NK cells and other effector cells. HNSCC tumors are highly immunosuppressive and characterized by marked and persistent elevation of inhibitory Tregs. The myelosuppression and immunosuppression caused by cyclophosphamide is dose dependent, and at lower doses cyclophosphamide has been shown to selectively deplete Tregs, restore NK cell activity and paradoxically induce auto-immunity. **Objectives:** To assess potentiation of clinical response by tracking PFS, OS and HRQOL and immune augmentation in tumor biopsies and blood samples. **Methods:** The current pilot study (n=15) will assess the hypothesis that Tregs, which are elevated in HNSCC, can be suppressed with cyclophosphamide and that this suppression can lead to improved anti-tumor responses mediated by cetuximab. **Eligibility:** Metastatic HNSCC progressed on initial chemotherapy or not a candidate for platinum **Treatment:** Daily oral cyclophosphamide 50 mg bid and weekly cetuximab (SOC). Patients will have blood collected for immune monitoring at weeks 0, 3, 6, 12 and pre and post treatment biopsies at week 0, 6. T cell subsets, NK cell function, Tregs, MDSC will be assessed at tumor site and in blood for immune response. Restaging CT scans will be done pretreatment and at weeks 6, 12. Clinical trial information: NCT01581970.