radiation treatment schedule remains unknown. The National Comprehensive Cancer Network (NCCN) guidelines recommend both hypofractionated radiotherapy (HFX) or CFX. We compared overall survival (OS) and treatment patterns among patients treated with HFX versus CFX for ESGC using a large national database.

Materials/Methods: We identified patients diagnosed with stage I-II (cT1-2N0M0) glottic cancer from 2004-2013 in the National Cancer Data Base. Patients were treated with either HFX (2.25Gy/fraction to 63-65.25Gy) or CFX (2.0Gy/fraction to 66-70Gy). Multivariable logistic regression was used to determine factors associated with the receipt of HFX versus CFX.

OS of patients receiving HFX versus CFX was compared using the log-rank test, multivariable Cox proportional-hazards regression, and propensity-score matching.

Results: 4,030 patients (39.5%) received HFX and 6,182 patients (60.5%) received CFX. Predictors for receipt of HFX included cT2 disease, recent year of diagnosis, and treatment at academic and higher-volume centers (all P<0.001). Patients treated with HFX increased from 22.1% in 2004 to 58.0% in 2013. HFX was associated with improved OS compared with CFX on univariable (5-year OS, 77.0% vs 73.5%; log-rank P=0.01), a finding confirmed on propensity-score matching. On subset analyses, an improvement in OS was borderline significant for patients with cT2 disease (5-year OS, 70.8% vs 64.5%; log-rank P=0.02).

Conclusions: HFX is associated with improved survival compared to CFX among patients treated with definitive radiotherapy for ESGC, particularly among patients with cT2 disease. HFX utilization increased over the study period; however, 40% of patients in our cohort did not receive HFX in the most recent year of our analysis.

(S028) Measurement of Circulating Tumors Cells in Squamous Cell Carcinoma of the Head and Neck and Patient Outcomes

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Purpose: Metastatic disease constitutes the greatest risk of death from cancer. It is known the circulatory system is an important means of dissemination of cancer cells. There are now accurate ways of detecting circulating tumor cells (CTCs) in blood samples, which may serve as a tool for personalized medicine. We report the outcomes of patients with squamous cell carcinoma of the head and neck whose circulating tumor cells were quantified using a novel technique.

Methods: Blood samples from 57 patients with stage I-IV squamous cell carcinoma of the head and neck were collected between 12/07/2009 and 02/02/2011. Surface-Enhanced Raman Spectroscopy (SERS) tagged with EGF was used to directly measure targeted CTCs in the presence of white blood cells. Due to technical error, the circulating tumor cells in six patients could not be quantified. Patients with metastatic disease, no follow-up, and those who were not treated at our institution were also excluded from the study leaving 48 patients for analysis.

Results: Median number of circulating tumor cells per 8 ml blood sample was 440 (range 0-5760). Median follow-up was 30.1 months (range 1.1-80.8 months). At the time of blood sample collection, a majority of patients had localized disease (N=42). Six had recurrent or persistent disease. Of patients with localized disease, a majority (N=34) were treated with concurrent chemoradiation. Of the patients with localized disease, 10 experienced disease progression. Six of these patients failed loco-regionally, 2 distantly, and 2 both loco-regionally and distantly. Five of failing patients had CTCs >1000. Three of the 4 patients who developed metastatic disease had CTCs >1000. All but one of the patients with recurrent disease experienced progression.

Conclusion: CTCs show promise as a means of identifying patients at greater risk of disease progression, allowing for the personalization of upfront therapy. Recurrent disease portends a poor prognosis.

(S029) Development of an Immune-Associated Molecular Signature Predicting Melanoma Survival

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Melanoma patients within AJCC sub-stages exhibit great variability in survival, underscoring the need for more accurate prognostic approaches. Aberrant promoter DNA methylation is a key feature of cancers, including melanoma. Identification of a DNA methylation signature, or CpG island methylator phenotype, has been useful in predicting prognosis, diagnosis and response to treatment in a variety of tumor types. The purpose of this study is to develop a DNA methylation based prognostic tool for melanoma patients, who currently exhibit great variability in survival even within AJCC sub-groups.

We used a discovery set of patient-derived melanoma cell lines (n=14) and sub-divided it into two groups, based on overall survival. We examined promoter methylation status of eighty candidate genes using bisulfite modification and Sanger sequencing. Candidate genes exhibiting differential methylation between the two survival groups were used to build a survival prediction score, methylLive, using a training cohort (n=72) of Stage III melanoma patients. In the independent validation cohort, consisting of melanoma patients from The Cancer Genome Atlas (n=473), a high methylLive score was associated with a significantly longer recurrence free survival, and longer overall survival in Stage I and II (p=0.0002, HR = 7.5), Stage IIIc (p=0.0007, HR = 4.8), Stage IIIa (p=0.01, HR = 4.4), and melanoma patients of all stages (p<0.0001). A high methylLive score was associated with an immunogenic transcriptional phenotype, activation of interferon signaling, and de-repression of melanoma antigens (p<0.001).

In this study, we define a methylation based melanoma survival prognostic score, methylLive, which can significantly improve stratification of patients with favorable and poor outcomes within melanoma AJCC sub-groups. For instance, methylLive identified Stage IIIC patients with high methylLive scores with 70% and 20% 10-year overall survival, providing significantly more information than the AJCC Stage IIIc 10-year survival of 24%. Improved prognostic accuracy can contribute to improved care of melanoma patients, and provision of most appropriate therapies.

(S030) Early SRS of Melanoma Brain Metastases in Patients Treated With Ipilimumab

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Background: Studies have suggested that radiation may enhance anti-tumor immune response through stimulation of tumor-specific antigen release. The optimal timing between radiotherapy and immunotherapy to maximize potential synergistic benefits has not been fully elucidated.

Material and Methods: We retrospectively analyzed 99 patients with metastatic melanoma between 2007-2014 who received ipilimumab therapy without brain metastases at time of immunotherapy. Patients subsequently developed brain metastases and were treated with stereotactic radiosurgery (SRS). Primary outcomes evaluated included intracranial disease control and overall survival (OS).

Results: With a median follow-up of 15.5 months, patients who received SRS within 5.5 months of their last dose of ipilimumab had significantly better intracranial control than those who received SRS after 5.5 months (median intracranial control of 8.43 months vs. 3.63 months; HR 0.46, 95% CI 0.25-0.86, p=0.02). OS was not different between the two arms. Pre-SRS circulating absolute lymphocyte count also predicted for treatment response as a baseline counts >1000/µL was associated with better intracranial control (HR 0.378, 95% CI 0.212-0.675, P=0.001).

Conclusions: We retrospectively observed that patients who received SRS for new brain metastases within 5.5 months after ipilimumab therapy had better intracranial disease control. Additionally, baseline circulating lymphocyte may be able to predict for SRS intracranial disease control.