p16 and high risk-HPV in node positive cutaneous squamous cell carcinoma of the head and neck were observed in clinicopathological factors based on p16 expression by immunohistochemistry. Detection of high-risk HPV subtypes was performed using HPV RNA in situ hybridization on a subset of 59 patients. Results were considered for these patients.

Conclusions: Although radiotherapy for painful bone metastases leads to a meaningful pain response, QoL does not improve after treatment. Initially, it remains stable followed by deterioration towards the end of life.

Proffered Papers: Clinical 12: Rare tumours

OC-0537
p16 and high risk-HPV in node positive cutaneous squamous cell carcinoma of the head and neck
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Purpose or Objective: The incidence of p16-overexpression and the role of human papillomavirus (HPV) in cutaneous head and neck squamous cell carcinoma (cHNSCC) is unclear. In the unknown primary setting, where cHNSCC is a potential putative site, p16 status is being used to guide management despite varying reports of its incidence in non-opharyngeal sites.

Material and Methods: 143 patients with cHNSCC lymph node metastases involving the parotid gland were evaluated for p16 expression by immunohistochemistry. Detection of 18 high-risk HPV subtypes was performed using HPV RNA in situ hybridization on a subset of 59 patients. Results were correlated with clinicopathological features and outcomes

Results: Median follow up time was 5.3 years. No differences were observed in clinicopathological factors based on p16 status. p16 was positive, intermediate and negative in 45 (31%), 21 (15%) and 77 (54%) of cases, respectively. No high-risk HPV subtypes were identified, irrespective of p16 status. p16 status was not prognostic for overall (HR 1.08 95% CI [0.85 - 1.36], p=0.528), cancer-specific (HR 1.12 95% CI [0.77 - 1.64], p=0.542) or progression-free survival (HR 1.03 95% CI [0.83 - 1.29], p=0.783). Distant metastasis free survival, freedom from locoregional failure and freedom from local failure were also not significantly associated with p16 status.

Conclusion: p16 positivity is common but not prognostic in cHNSCC lymph node metastases. High-risk HPV subtypes are not associated with p16-positivity, and do not appear to play a role in this disease. HPV testing, in addition to p16-status in the unknown primary setting may provide additional information in determining a putative primary site.

OC-0538
Tumor-related leukocytosis associated with poor radiation response and outcome in cervical cancer
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Purpose or Objective: To investigate the prognostic significance of tumor-related leukocytosis (TRL) in cervical cancer patients treated with definitive radiotherapy

Material and Methods: Between 1986 and 2012, 2,456 patients with uterine cervical cancer (FIGO stage IA-IIB 494, stage IIA-IIIB 1530, stage IIIA-IIIB 394 and stage IVA 38) who received definitive radiotherapy (62.6%) or platinum-based chemoradiotherapy (37.4%) consisting of EBRT and ICBT were retrospectively analyzed. TRL was defined as WBC count ≥9,000/μl on ≥2 occasions at the time of diagnosis and during the course of treatment. The neutrophil/lymphocyte ratio (NLR) was defined as the absolute neutrophocyte count divided by the absolute lymphocyte count. Locoregional failure free survival (LRFFS) and overall survival (OS) were compared between patients with or without TRL.

Results: Median age of all patients was 55 years (range, 21-87) and the median follow-up time was 65.1 months (range, 0.7-347.8). Among 2,456 patients included in this study, TRL was observed in 398 (16%) at the initial diagnosis. Patients in TRL(+) group were younger in age and had larger tumor, advanced FIGO stage and more common LN metastases (all p < 0.05). TRL (+) group showed relatively lower rate of complete remission (CR) (90% vs. 97%, p = 0.042). The 10-year LRFFS and OS for all patients were 84% and 78%, respectively. Compared to TRL(-) group, LRFFS and OS were significantly lower in TRL(+) group (10-yr LRFFS: 69% vs. 87%, p < 0.001; 10-yr OS: 63% vs. 81% p < 0.001). After propensity score matching by age, FIGO stage, tumor size, LN metastasis, histologic subtype and pretreatment hemoglobin (Pre Tx Hb), both groups were well matched. The LR control and OS rate of TRL (+) group was still significantly lower than those of TRL (-) group. In multivariate analysis, advanced FIGO stage, non-SqCCa, larger tumor size and TRL were identified as risk factors for LRFFS and OS (all p < 0.05). In addition, Pre Tx Hb, LN metastasis and high NLR (≥2.5) were also associated with poorer OS (all p < 0.05). Among patients with LRF (n=345), patients with TRL at the time of recurrence accounted for 26% and showed relatively poorer median OS (6 vs. 12 months, p = 0.001).

Conclusion: This study supports the aggressive nature and poor radiation response of cervical cancer with leukocytosis. Given the unfavorable features and higher probability of treatment failure, optimal therapeutic approach and careful monitoring for early detection of recurrence should be considered for these patients.
Material and Methods: Using the National Cancer Data Base, we identified stage II seminoma patients treated with orchietomy and either RT or MACT diagnosed from 1998-2012. Separately for stage IIA and IIB, factors affecting treatment modality (RT vs. MACT) were studied using a parsimonious multivariable logistic regression model. Propensity scores for treatment decision were incorporated into a multivariable Cox regression analysis of overall survival.

Results: Analysis included 2,437 patients (IIA=960, IIB=812, IIC=665). Median follow-up was 65 months (IQ range 34-106). Rates of RT utilization by stage were: IIA=78.1%, IIB=54.4%, IIC=4.2%. Rates of MACT utilization by stage were: IIA=21.9%, IIB=45.6%, IIC=95.8%. Median RT dose was: IIA=30.9 Gy (IQR 25.5-35.5) and IIB=35.5 Gy (IQR 31.1-36.0). For both IIA and IIB patients, later year of diagnosis, treatment at an academic facility, and pathologic assessment of lymph node(s) were associated with increased use of MACT vs. RT. Also predictive for preferential use of MACT were Charlson-Deyo comorbidity score of 1+ and non-private insurance for IIA patients, and T stage of 2+ for IIB patients. Unadjusted 5-year survival by stage was: IIA=97.1% (95% confidence interval [CI] 96.1-98.1), IIB=93.9% (95% CI 92.1-95.7), IIC=92.6% (95% CI 90.6-94.6). log-rank p=0.006. Factors predicative of improved survival on multivariable analysis included age<40, private insurance, and comorbidity score of zero. For IIA patients, overall survival was improved with RT compared to MACT with a 5-year survival of 99.0% (95% CI 98.2-99.8) vs. 93.0% (95% CI 89.0-97.0). This advantage persisted on multivariable analysis with a HR of 0.22 (95% CI 0.08-0.64, p=0.005) and propensity adjusted HR of 0.28 (95% CI 0.09-0.86, p=0.027). For IIB patients, 5-year survival was 95.2% (95% CI 92.8-97.6) for RT and 92.4% (95% CI 89.2-95.6) for MACT (log-rank p=0.041). This was not statistically significant on multivariable analysis with a HR of 0.74 (95% CI 0.32-1.70, p=0.475) and propensity adjusted HR of 0.77 (95% CI 0.33-1.80, p=0.549). An unadjusted Kaplan-Meier plot by stage and treatment is given in Figure 1.

Conclusion: In the largest cohort of stage II seminoma patients evaluated to date, we have identified numerous factors predictive for treatment selection and overall survival. We have shown a survival advantage for stage IIA patients treated with RT compared to MACT, while no such survival advantage was seen for stage IIB patients.

OC-0540
IOERT after gross total resection combined with EBRT in extremity sarcoma: a pooled analysis
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Purpose or Objective: In 2009 we reported promising first results of a European pooled analysis which evaluated the use of intraoperative radiation therapy (IORT) in the treatment of soft tissue sarcomas. However, comparison of these results with non-IORT series seemed difficult, mainly because of the inclusion of grossly incomplete resected lesions, patients treated without additional external beam radiation therapy (EBRT) and comparatively short follow-up. Therefore we re-analyzed our data limited to the patients who received IOERT preceeded or followed by EBRT after gross total resection with extended follow-up.

Material and Methods: Three European expert centers participated in the current analysis. Patients with gross incomplete resection, missing documentation of EBRT or primary lesions outside the extremities were excluded, leaving 259 patients for analysis. Median age was 55 years and median tumor size 8 cm. 80% of the patients presented in primary situation with 81% of the tumors located in the lower limb. Stage at presentation was I:9%, II:47%, III:39%, IV:5%. Most patients showed high grade lesions (FNCLCC grade 1:9%, 2:34%, 3:58%, predominantly liposarcoma (31%) and MFH (27%). IOERT was applied to the tumor bed with a median dose of 12 Gy using a median electron energy of 8 MeV. IOERT was preceeded (17%) or followed (83%) by EBRT with a median dose of 45 Gy in all patients. 37% of the patients received additional chemotherapy.

Results: Median follow up was 63 months. Surgery resulted in free margins (R0) in 71% while 29% suffered from microscopic positive margins (R1). We observed 27 local failures, transferring into a 5-year local control rate of 86%. Univariate analysis revealed primary vs recurrent situation and resection margin as significant factors for local control but only resection margin (5-year LC rate 94% vs 70%, HR 3.8) remained significant in multivariate analysis. Distant failure was found in 70 patients, resulting in a 5-year distant control rate of 69%. Factors with significant impact on distant control in univariate analysis were histology, grading, resection margin and stage IV prior/at IOERT, but only grading and stage IV remained significant in multivariate analysis. Actuarial 5-year rates of FFTF and OS were 61% and 78%, respectively. Significant factors for overall survival were only grading and stage IV prior/at IOERT (uni- and multivariate). Secondary amputations were needed in 14 patients (5%) resulting in a final limb-preservation rate of 95%. Good functional outcome was achieved in 81%.

Conclusion: Combination of IOERT and EBRT after limb sparing surgery resulted in encouraging local control and overall survival with excellent rates of preserved limb function in this unfavourable patient group. Our analysis identified resection margin as most important factor for local control while overall survival was mainly influenced by grading and stage IV prior/at IOERT.

OC-0541
Long-term results of the AIEOP MH-89 protocol for pediatric Hodgkin lymphoma
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