identified from a single institutional database. Exclusion criteria included incomplete RT (<60 Gy). Staging was completed using AJCC 7th edition. The pT classification for this group was pT1 (15, 16%), pT2 (45, 47%), pT3 (24, 25%), and pT4 (11, 12%). The pN classification was pNX (4, 4%), pN0 (23, 24%), pN1 (19, 20%), pN2a (2, 2%), pN2b (36, 38%), pN2c (10, 11%), pN3 (1, 1%). The AJCC group stage was I (5, 5%), II (10, 11%), III (26, 27%), IVA (53, 56%), and IVB (1, 1%). Of the 95 patients, 85 (89%) patients had no or ipsilateral-only nodal involvement, and 59 (62%) received bilateral neck RT and 26 (27%) received unilateral neck RT. Ten (11%) patients had bilateral neck disease (pN2c) and all of them received bilateral neck RT. Prescribed radiation doses were 60-70 Gy to the postoperative bed and involved neck and 52-54 Gy to the elective neck in 30-33 fractions using simultaneous integrated boost. Chemotherapy was delivered to 41 (44%) patients. Neck dissection was performed in 90 (95%) patients, 55 (58%) in the ipsilateral neck and 35 (37%) in the bilateral neck. Survival outcomes were compared using Kaplan-Meier method with log-rank test.

Results: The median age was 55 (22-87). The unilateral RT group had less advanced pT ($p<0.001$), pN ($p=0.04$), and group stage ($p<0.001$) compared to the bilateral RT group. More bilateral neck dissections were performed in the bilateral RT group (45% vs. 15%, $p=0.014$). The median follow-up for living patients was 2.9 (0.5-16.9) years. Comparing the unilateral and bilateral RT groups, there was no difference local recurrence-free survival (2-year: 84% vs. 89%, $p=0.36$), distant metastasis-free survival (2-year: 66% vs. 88% $p=0.12$), or overall survival (2-year: 60% vs. 76%, $p=0.80$). The unilateral RT group had worse regional recurrence-free survival compared to the bilateral RT group (2-year: 62% vs. 89%, $p=0.001$). There were more failures in the contralateral neck in the unilateral RT group (23% vs. 5.7%, $p=0.01$). Of the 11 regional tumor recurrences that occurred in the unilateral RT group, 5 (45%) occurred in the contralateral neck and 1 (9%) occurred in the bilateral neck.

Conclusion: Omission of adjuvant elective neck RT to the contralateral neck in unselected patients with squamous cell carcinoma of the oral tongue was associated with a high risk of tumor recurrence in the contralateral neck.

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Human Papillomavirus in Sinonasal Squamous Cell Carcinoma

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Purpose/Objective(s): The role of Human Papillomavirus (HPV) in oropharyngeal cancers and its impact on survival has been well described. Whether HPV association is influential in other sub-sites of head and neck is not as well studied at this time. We investigated the patterns of HPV testing and its association with survival in sinonasal squamous cell carcinoma (SNSCC) utilizing the National Cancer Database (NCDB).

Materials/Methods: We selected all SNSCC cases between 2010-2016. HPV testing rates, clinicodemographic factors, treatments, and survival were analyzed. Multivariable regression was used to identify factors associated with HPV-positive tumors and overall survival.

Results: We identified 6010 SNSCC cases during the study period. Only 1274 (21.7%) cases were tested for high-risk HPV. Tested patients were slightly younger (median age 64 vs 66, $p < 0.001$) and less likely to have comorbidities (307, 22.9%, vs 1155, 25.6%, $p = 0.045$). No other clinicopathologic differences were identified. The majority of the tested cohort were male (818, 64.2%) and white (978, 76.8%). Approximately half were attributed to the nasal cavity (616, 48.4%) and paranasal sinuses (657, 51.6%). The majority were advanced stage (stage III-IV, 658, 63.4%). HPV-positive tumors comprised 28.1% (366) of the tested population. Among 34 hospitals that tested ≥60% of non-oropharyngeal squamous cell carcinomas for HPV, a similar proportion HPV-positive SNSCC was observed (27.9%, 19/68). Surgery, (305, 25.1%); followed by surgery and adjuvant radiotherapy (303, 24.9%) were the most common treatments. A minority (246, 20.3%) underwent surgery and chemoradiotherapy. In multivariable regression, younger age (<60, OR = 1.81, 95% CI = 1.39-2.36, $p < 0.001$) and nasal cavity location (compared to paranasal sinuses, OR = 2.00, 95% CI = 1.49-2.70, $p < 0.001$) were associated with higher rates of HPV-positive tumors. Five-year overall survival was 55.6% (95% CI = 50.9%-60.7%). In multivariable regression, HPV-positive tumors were associated with significantly improved overall survival (HR = 0.70, 95% CI = 0.50-0.98, $p = 0.04$); while older age, male sex, paranasal sinus location, advanced stage, and lymphovascular invasion were associated with worse outcomes.

Conclusion: Currently only a minority of SNSCCs are tested for HPV. These data suggest that a sizable minority of SNSCC may be HPV related; and that HPV-positive tumors are associated with improved survival. Routine HPV testing, as currently recommended for oropharyngeal tumors, might be warranted in SNSCC as well. The impact of HPV association on survival of SNSCC needs further investigation.

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Hafnium oxide nanoparticles (NBTXR3) activated by radiotherapy for the treatment of frail and/or elderly patients with locally advanced HNSCC: a phase I/II study

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Purpose/Objective(s): Elderly and/or frail patients (pts) with head and neck squamous cell carcinoma (HSNCC) remain a challenging to manage and neglected population regarding clinical trials and data generation to support treatment choices. Despite representing 20% of the HNSCC population no consensus exists on what is the optimal treatment for these pts with locally advanced (LA) disease, vulnerable to treatment-induced toxicities with the current standard of care. New approaches are needed to improve clinical outcomes without adding toxicity. NBTXR3 hafnium oxide nanoparticles injected intratumorally may represent such an option. Otherwise inert; this first-in-class radioenhancer, augments the radiotherapy (RT) dose within tumor cells when activated by RT, increasing tumor cell death compared to RT alone. The results presented here demonstrate the feasibility and safety of NBTXR3 activated by RT in elderly/frail patients, a population with few therapeutic options.

Materials/Methods: Elderly/frail pts received a single intratumoral injection of NBTXR3 and intensity modulated radiation therapy (IMRT; 70 Gy/35 fractions/7 weeks). The study was a 3 + 3 dose escalation to test the NBTXR3 dose equivalent to 5, 10, 15, and 22% of baseline theoretical tumor volume, followed by a dose expansion. Primary endpoints include Recommended Phase 2 Dose (RP2D) determination and early dose limiting toxicities (DLT). NBTXR3 presence in surrounding healthy tissues and anti-tumor activity (RECIST 1.1) were also evaluated.

Results: Enrollment was completed at all dose levels: 5% (3 pts), 10% (3 pts), 15% (5 pts), and 22% (8 pts). No early DLT or SAE related to NBTXR3 or injection were observed. One G1 AE (asthenia; 22%) related

to NBTXR3 and four AEs (G2 oral pain, G1 tumor hemorrhage, asthenia, and injection site hemorrhage) related to injection were observed. RT-related toxicity was as expected with IMRT. The RP2D was determined to be 22%. CT-scan assessment demonstrated localization of NBTXR3 intratumorally without presence in surrounding healthy tissues. At a median follow-up of 231 days, 9/13 (2 unconfirmed) evaluable pts receiving doses ≥10%, achieved a complete response of the treated tumors. The final dose escalation safety and efficacy results will be presented herein.

Conclusion: NBTXR3 was well tolerated at all tested doses and demonstrated preliminary anti-tumor activity. A dose expansion phase at the RP2D is ongoing. These results highlight the potential of NBTXR3 as a novel treatment option for elderly/frail pts with LA HNSCC and address an unmet medical need.

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Definitive Radiotherapy for Elderly Patients with Locally Advanced Squamous Cell Head and Neck Cancer (LAHNSCC): A Single-Institution Experience

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Purpose/Objective(s): The elderly comprise an increasing percentage of patients with locally-advanced head and neck squamous cell carcinoma (LAHNSCC). In these patients, definitive treatment is often compromised due to concerns about medical comorbidities, performance status and the anticipated tolerance of treatment toxicities. We reviewed our experience with definitive management in our elderly (age ≥70) patients with LAHNSCC.

Materials/Methods: From our IRB-approved registry, all patients age ≥ 70 years with AJCC 7th (and earlier) edition stage III-IV, M0 LAHNSCC who were treated with definitive radiotherapy (RT) with or without systemic therapy between 1993 and 2019 were identified. A similar cohort of patients ages 60-69 was also identified for comparison. Chemotherapy added to RT was indicated for T3-4 or N2-3 per AJCC 7th edition or if extracapsular extension (ECE) was found on surgical pathology. Univariate (UVA) analyses were performed to assess association with pretreatment Charlson comorbidity index, Karnofsky Performance Status (KPS), chemotherapy delivered, and RT dose. Cumulative incidence of recurrence was defined using Fine and Gray regression with death as a competing event. Overall (OS) and progression-free survival (PFS) were analyzed using the Kaplan-Meier method.

Results: There were 126 elderly patients identified with a median age of 73.4 years, and median follow up of 36.3 months. There were 224 patients age 60-69 years identified, with a median age of 64 years and a median follow up of 47.4 months. The mean RT dose in 2 Gy-equivalent fractions was 69.3 Gy for the elderly and 69.5 Gy for patients age 60-69. Tumor primary site was hypopharynx, larynx and oropharynx in 10%, 33%, and 57% of the elderly patients, and 1%, 9% and 90% in those age 60-69. HPV status was positive in 69 (55 %) elderly patients and in 190(85%) patients ages 60-69. Systemic therapy was indicated in 113 (90%) patients from the elderly cohort and in 199 (89%) patients age 60-69 years. 87 (69%) of the elderly were given systemic therapy; 66 of these (76%) were given platinum-based chemotherapy and 21 (24%) received Cetuximab. 195 (87%) of the 60-69 year olds were given systemic therapy; 171 of these (88%) received platinum-based chemotherapy and 24 (12%) received Cetuximab. The 2-year cumulative incidences of recurrence for patients ages 60-69, 70-79 and ≥80 were 13.9%, 24.9% and 30.3%, respectively (p=0.0133). Median PFS and OS for the elderly cohort were 58.3 and 67.5 months, respectively. Charlson comorbidity index score 2-3 vs. 0-1 (HR 2.08, 95% CI 1.04-4.18; p=0.038) was predictive for recurrence in the elderly patients.

Conclusion: Compared to younger patients, elderly patients received less aggressive treatment and experienced higher recurrence rates. Overall, favorable results were still likely after definitive RT in elderly patients. Age alone should not preclude curative-intent management.

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Radical Reduction of Radiation Therapy Dose Prescription for Elective Treatment Areas in Human Papillomavirus (HPV) - Associated Oropharyngeal Carcinoma (OPC)

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Purpose/Objective(s): In March 2017, we implemented a new radiation guideline to allow substantial dose reduction to elective treatment regions in patients with HPV-associated OPC receiving definitive chemoradiation. We then prospectively followed the patients for treatment outcomes.

Materials/Methods: We applied routine de-escalated radiation dose to most elective regions to 30 Gy in HPV-associated OPC patients treated with concomitant chemotherapy, mostly high-dose cisplatin (excluding cetuximab), while continued treating grossly visible disease to 70 Gy. Patients were treated to 30 Gy for the elective treatment regions (15 fractions of 2 Gy), followed by cone-down of 40 Gy to a total of 70 Gy to all sites of gross disease. Some patients also received an intermediate dose of 50 Gy in a small field immediately adjacent to the 70 Gy region.

Results: From March 2017 to December 2018, a total of 199 consecutive HPV-positive OPC patients received concurrent chemoradiation with 30Gy elective nodal irradiation. The median age was 60 years and 47% of them were never smokers. Seventy percent of the patients had T1-T2 primary disease, 25% T3-T4, and 5% unknown primary. Sixteen percent of the patients had bilateral nodal disease. Eighty percent of them received high-dose cisplatin. During a median follow up of 13 months, there was no regional recurrence within the 30Gy elective nodal region. No patient had local recurrence at the primary disease site and 2 patients (1%) developed regional nodal recurrence within the high-dose 70 Gy fields at 9 month and 16 months post therapy. Both patients received salvage neck dissection and had no evidence of disease at last follow up. Five patients (2.5%) had distant metastases but remained alive, and 6 patients (3%) died from causes unrelated to their cancer. When restricting to a subset of the cohort treated through March 2018 with a longer median follow up of 18 months, there remained the same 2 (2%) regional failure in the high-dose fields and no failure within 30 Gy elective regions.