**METHODS SUPPLEMENTAL**

The following variables were selected from the SEER database: sex, age recode with single ages and 90+, marital status at diagnosis, year of diagnosis, type of reporting source, race and origin record, “primary site–labeled”, “ICD-O-3 Hist/behav, malignant”, “SEER historic stage A (1973-2015)”, “SEER Combined Summary Stage 2000 (2004-2017)”, “Combined Summary Stage (2004+)” and “Summary stage 2000 (1998-2017)”, “EOD10–Size (1988-2003)”, “CS Tumor Size/Ext Eval (2004-2015) and “Tumor size summary (2016+)”, “regional nodes examined (1988+)”, “regional nodes positive (1988+)”, “RX Summ--Surg Prim Site (1998+)”, “RX Summ--Surg Oth Reg/Dis (2003+)” and “Surgery of oth reg/dis sites (1998-2002)”, “RX Summ--Surg/Rad Seq”,” RX Summ--Systemic/Sur Seq (2007+)”, Reason no cancer-directed surgery, radiation record, chemotherapy record, “RX Summ--Scope Reg LN Sur (2003+)” and “Scope of reg lymph nd surg (1998-2002)”. Information regarding the follow-up and cause of death was obtained from SEER.

**Patient Characteristics**

Different age categorizations were used to analyze and identify potential age-dependent differences for localizations. We classified age as 0-17, 18-39, 40-64, and ≥65years. Other age categorizations that we used were <1, 1-2, 3-9, 10-17, 18-39, 40-65, ≥65years, and 0, 1, 2, 3, 4-9, 10-17, ≥18years. Marital status is categorized in SEER as single (never married), divorced, married, separated, widowed, unmarried or domestic partner, and unknown. We analyzed the data separately for patients ≤18years and >18years. The year of diagnosis was considered separately for the patients ≤18years and >18years but classified as 2000-2005, 2006-2010, 2011-2015, and 2016-2020.

**Primary tumor site**

The primary site of the tumor was categorized as head/neck PM, nPM, orbital, and head/neck NOS by using the SEER “primary site – labeled” and categorized as follows:

**PM**: parotid gland (C07.9), posterior wall of the nasopharynx (C11.1), lateral wall of the nasopharynx (C11.2), the anterior wall of the nasopharynx (C11.3), overlapping lesion of the nasopharynx (C11.8), nasopharynx NOS (C11.9), pharynx (C14.0), overlapping lesion of lip, oral cavity and pharynx (C14.8), nasal cavity (C30.0), maxillary Sinus C31.0), ethmoid sinus (C31.1), frontal sinus (C31.2), sphenoid sinus (C31.3), overlapping lesion of accessory sinus (C31.8), accessory sinus (C31.9), bones of the skull and face (C.41.0), cerebral meninges (C.70.0), meninges NOS (C70.9), frontal lobe (C71.1), temporal lobe (C71.2), parietal lobe (C71.3), ventricle NOS (C71.5), brain stem (C71.7), brain NOS (C71.9), pituitary gland (C75.1), pineal gland (C75.3).

**nPM**: external upper lip (C00.0), mucosa of upper lip (C00.3), commissure of lip (C00.6), base of the tongue NOS (C00.6), border of tongue (C02.1), anterior 2/3 of tongue NOS (C02.3), tongue (C02.9), upper gum (C03.0), lower gum (C03.1), gum NOS (C03.9), hard palate (C05.0), soft palate NOS (C05.1), uvula (C05.2), overlapping lesion of palate (C05.8), cheek mucosa (C06.0), retromolar area (C06.2), mouth NOS (C06.9), tonsil NOS (C09.9), oropharynx NOS (C10.9), posterior wall of hypopharynx (C13.2), hypopharynx NOS (C13.9), glottis (C32.0), supraglottis (C32.1), overlapping lesion of larynx (C32.8), larynx NOS (C32.9) mandible (C41.1), external ear (C44.2), skin other/unspecific parts of face (C44.3), skin of scalp and neck (C44.4).

**Orbit**: eyelid (C44.1), conjunctiva (C69.0), retina (C69.2), ciliary body (C69.4), lacrimal gland (C69.5), orbit NOS (C69.6), overlapping lesion of eye and adnexa (C69.8), eye NOS (C69.9).

**Head/neck NOS:** connective, subcutaneous, other soft tissue of the head, face, neck (C49.0)

**Granular tumor site**

To determine an optimal categorization of tumor sites we tested dividing the study cohort into more defined groups: orbit (C44.1, C69.0, C69.2, C69.4, C69.5, C69.6, C69.8, C69.9), parotid gland (C07.9), bones (C41.0, C41.1), ear (C30.1, C44.2), oral cavity (C00.0, C00.3, C00.6, C01.9, C02.1, C02.3, C02.9, C03.0, C03.1, C03.9, C05.0, C05.1, C05.2, C05.8, C06.0, C06.2, C06.9), skin/connective tissue (C44.3, C44.4, C49.0), pharynx (C09.9, C10.9, C11.1, C11.3, C11.3, C11.8, C11.9, C13.2, C13.9, C14.0, C14.8), larynx (C32.0, C32.1, C32.8, C32.9), nose (C30.0), sinuses (C31.0, C31.2, C31.2, C31.3, C31.8, C31.9), and brain (C70.0, C70.9, C71.1, C71.2, C71.3, C71.5, C71.7, C71.9, C75.1, C75.3).

**Histology**

Histology was taken from SEER “ICD-O-3 Hist/behav, malignant“ and categorized as RMS NOS (8900/3), alveolar (8920/3), embryonal (8910/3), pleomorphic adult type (8901/3), mixed type (8902/3), spindle cell (8912/3), and RMS with ganglionic differentiation (8921/3) as reported in SEER. We also have grouped these into alveolar, non-alveolar, and pleomorphic histology for further analysis.

**Tumor size**

Tumor size was divided into groups of ≤3cm, 3.1–5cm, >5cm, and unknown by taking SEER “EOD 10 – Size (1988-2003)”, “CS Tumor Size (2004-2015) and “Tumor size summary (2016+)”.

**Tumor Stage**

As reported in SEER, tumor stages were classified as local, regional, distant, and unknown/unstaged. Regional staged cases were sub-classified in a second analysis as “Regional by both direct extension and lymph node involvement”, “Regional by direct extension only”, “Regional lymph nodes involved only”, and Regional NOS. The data was derived from “SEER historic stage A (1973-2015)”, “SEER Combined Summary Stage 2000 (2004-2017)”, “Combined Summary Stage (2004+)” and “Summary stage 2000 (1998-2017)”. We excluded the unknown/unstaged from the multivariate analysis.

**Lymph Nodes**

We analyzed the pathologically examined lymph nodes by using “regional nodes positive (1988+)” and classified them into positive, negative, no examination, and unknown. The exact number of regional nodes positive was classified as reported in SEER. We used “regional nodes examined (1988+)” and classified it into yes, no, and unknown. The number of examined lymph nodes was classified as reported in SEER. Surgery of the lymph nodes was analyzed by using “RX Summ--Surg Prim Site (1998+)”, “RX Summ--Surg Oth Reg/Dis (2003+)”,and “Surgery of oth reg/dis sites (1998-2002)”.

**Treatment**

The chemotherapy status and radiation record were classified as reported. In addition, we used the SEER “Radiation record” to classify the radiation status into yes and no/unknown. Reason no cancer-directed surgery was classified as reported in SEER.

**RESULTS SUPPLEMENTAL**

**Year of diagnosis**

Between 2000 and 2020, 728 patients *≤*18 were diagnosed: 230 (32%) from 2000-2005, 178 (24%) from 2006-2010, 173 (24%) from 2011-2015, and 147 (20%) from 2016-2020 (table 1). Out of the 386 patients who >18 years, 78 (20%) were diagnosed from 2000-2005, 101 (26%) from 2006-2010, 90 (23%) from 2011-2015, and 117 (39%) from 2016-2020. For the majority (99%) the type of reporting source was the hospital or clinic (in- or outpatient) (supplemental table 1). The minority was laboratory only (hospital or private) (7 patients), in a physician’s office or at a private medical practitioner (4 patients), and radiation treatment or medical oncology center (2 patients).

**Prognostic effect of year of Diagnosis**

For pediatric patients from 2016-2020, DSS was 83.3%±7.84 (95%CI) and OS was 78.5%±8.82 (95%CI) (table 1). From 2000-2005, DSS was 74.2%±5.68 (95%CI) and OS was 74.2%±5.68 (95%CI). For the adult patients from 2016-2020, DSS was 38.3%±13.33 (95%CI) and OS 32.8%±12.15 (95%CI). From 2000-2006, DSS was 28.4%±3.24 (95%CI) and OS 27.4%±10.19 (95%CI).

**Lymph Nodes and tumor stage**

In 186 patients with lymph node examination, one node was examined in 57 patients (thereof 1 positive in 38 patients, no positive lymph nodes in 19 patients), two nodes in 16 (in 1 patient 1 positive, in 4 patients 2 positives, in 11 no positive lymph nodes), three nodes in 7 patients (in 1 patient 3 positives, in 6 no positive), four in 3 (in 1 patient 4 positives, in 2 no positives), five nodes were examined in 4 (in 1 patient 5 positives, in 3 patients no positives), and ≥6 nodes were examined in 30 patients (table 1). In 50 patients, aspiration of the regional nodes was performed (in 2 patients no positive aspiration, in 44 patients positive aspiration, in 4 patients positive nodes are documented but the number is unspecified). Overall, 123 patients (11%) reported positive lymph node involvement, 44 patients with one positive node, 6 with two positive nodes, 4 with three or four positive nodes, and 9 with five or more positive nodes. A positive aspiration of lymph nodes was reported for 44 patients (in the remaining 16 cases number of positive nodes is unspecified). For 69 (6%) patients pathological lymph node examination was negative. For 450 (40%) patients tumor stage was regional. Among these regional tumors, 79 were regional by both direct extension and lymph node involvement, 190 by direct extension only, and 29 by regional lymph node involvement only (table 1).

**Treatment**

**Chemotherapy**

Of 1114 patients, 1024 received chemotherapy, which accounts for 92% (supplemental table 1). For the remaining 90 patients, it is unclear whether they did not receive chemotherapy, or their status is unknown. As part of their initial treatment, 303 patients (27%) were administered systemic therapy after undergoing surgery, 22 patients (2%) received it before undergoing surgery, and 16 patients (1%) received it both before and after surgery. In one case, surgery was performed before and after systemic therapy and in another intraoperative systemic therapy was used. For 410 patients (37%) no systemic and/or surgical procedures were used. For the remaining 361 patients, no data is given, or the sequence is unknown.

**Radiotherapy**

As reported radiotherapy was conducted in 873 (78%) patients (supplemental table 1). 241 patients did not receive radiotherapy, or the information is unknown. Of those 873 irradiated patients 15 (1%) were irradiated before tumor excision and 393 (35%) after tumor excision. 5 Patients were irradiated before and after surgery. In one patient the sequence is unknown, but both were given. In the remaining 700 patients (63%) no radiation and/or cancer-directed surgery was performed. 849 patients (76%) received beam radiation. Two patients were treated with radioactive implants, one received radioisotopes, and five received a combination of beam radiation and implants/isotopes. 9 patients refused the radiotherapy and in 15 cases radiotherapy was recommended but it is unknown if administered. In the case of the remaining 233 patients, they either did not receive radiotherapy, the type of radiation was not specified, or the information was unknown.

**Surgery**

Tumor-directed surgery was performed in 485 out of 1114 patients, which accounts for 44% (supplemental table 1). For 582 cases surgical intervention was not recommended, for 14 patients surgery was contraindicated, for 3 patients surgery was not performed because the patient died before recommended surgery. Surgery was recommended for 26 patients, but for 21 of them, it was not carried out for unknown reasons. It is also unclear whether the remaining 5 patients underwent the surgical procedure. The status of the last 5 remaining patients is also unknown.

**Prognostic effect of treatment**

For patients receiving radiotherapy the 5-year DSS and OS were better than for patients not receiving radiotherapy (DSS was 63.5 %± 3.53 for receiving and 57.7% ± 6.86 for not receiving or unknown). For receiving chemotherapy versus not receiving, the cases without chemotherapy did significantly worse (DSS was 63.1 %± 3.24 for receiving and 53.6% ± 11.56 for not receiving or unknown; p<0.001 and OS 60.5% ± 3.14% and 43.3% ± 10.78; p<0.001). The analysis showed that systemic therapy which is applied after surgery is significantly associated with the highest 5-year DSS of 70.7%±5.49 (p<0,001) and OS of 68.2%±5.68 (p<0.001). In contrast, systemic therapy before surgery showed a 5-year DSS of 57.4%±22.54 and OS of 54.5±21.95. Radiation after surgery is associated with the highest 5-year DSS of 68.2%±4.9 (p<0.001) and OS of 65.5%±4.9 (p<0.001), followed by no radiation and/or cancer-directed surgery with DSS of 59.8%±3.92 and OS of 56.3%±3.92. The lowest 5-year DSS and OS showed radiation therapy applied before surgery with 45%±25.87 respectively. The patients with cancer-directed surgery had a 5-year DSS of 69.7%±4.31 and OS of 66.3%±4,51 while patients with not recommended surgery had a DSS of 56.6%±4.31 and OS of 53.7%±4.32.