Accrual goal = 82.
Cycle = 21 days.
*Stratify by disease stage (T3 vs T4a/T4b) and disease site involvement (orbit only vs skull base only vs both involved).
†Patients randomized to arm A will receive standard therapy (surgery followed by radiation ± chemotherapy). Patients randomized to arm B will receive neoadjuvant chemotherapy followed by surgery. Both arms A and B will receive postoperative radiation therapy.
‡Carboplatin with an AUC = 5 for patients who are ineligible to receive cisplatin.
§Patients with positive margins/positive extracapsular spread in lymph nodes will receive postoperative radiation therapy (66 Gy) and weekly concurrent therapy with weekly cisplatin at 40 mg/m². If patients have contraindications or cannot tolerate cisplatin, carboplatin at an AUC = 2 on a weekly basis for 6 weeks will be allowed.
AUC = area under the curve; BOS = base of skull; RT = radiation therapy.

Disease Eligibility Requirements
• Stage T3 and T4a (includes select T4b per protocol)
• N0 or N1-3
• Requiring resection of BOS, orbit, or both

**Study Schema**
Overall EA3163 Study Objective
To examine whether the addition of neoadjuvant therapy (docetaxel and cisplatin [or carboplatin]) can provide improved structure preservation and overall survival (OS) in patients with locally advanced NPNSCC.

Study Objectives
Primary Objectives
- Evaluate structure preservation rate
- Evaluate OS

Secondary Objectives
- Evaluate progression-free survival
- Examine the rate of structure preservation for the orbit (freedom from orbital exenteration)
- Evaluate site-reported p16 data and correlate with outcome
- Determine the accuracy of baseline/post-chemotherapy MRI and/or FDG PET/CT-based prediction of orbit and skull base preservation
- Determine the accuracy of baseline/post-chemotherapy MRI and/or FDG PET/CT-based prediction of 2-year overall survival

Eligibility Criteria*
Main Inclusion Criteria
- ≥18 years of age with stage T3 or T4a, histologically confirmed NPNSCC requiring orbital or skull base resection
  - Some patients with T4b disease deemed resectable by the treating surgeon can be included (see protocol for details)
- Measurable disease; MRI and/or PET/CT scans need to be performed within 2 weeks prior to randomization
- ECOG performance status of 0 or 1
- General physical condition compatible with the proposed chemotherapy and surgery

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.
Deemed surgically resectable by surgical teams at each institution and must have a determination of degree of anticipated structure preservation of orbit and skull base (Protocol Section 5.1.3 and Appendix III); must be determined prior to randomization

Adequate marrow and organ function ≤ 14 days prior to randomization

If prior history of squamous cell or basal carcinoma of the skin or in situ cervical cancer, must have been curatively treated

Use of effective contraception or abstinence

Main Exclusion Criteria

- Receiving investigational agents at time of randomization, or at any time while on study and during the 4 weeks preceding randomization
- History of allergic reactions attributed to compounds of similar chemical or biologic composition to docetaxel and/or both platinum-based chemotherapy agents
- Evidence of distant metastases or leptomeningeal disease
- Received previous irradiation for head and neck tumor, skull base, or brain tumors
- Uncontrolled intercurrent illnesses that in the investigator’s opinion will interfere with the ability to undergo therapy including chemotherapy
- History of a different malignancy, unless the disease has not progressed for ≥ 2 years
- Current peripheral neuropathy > grade 2 at time of randomization
- Any coexisting condition that would preclude full compliance with the study
- History of severe hypersensitivity reaction to docetaxel or other drugs formulated with polysorbate 80
- Pregnancy or breastfeeding