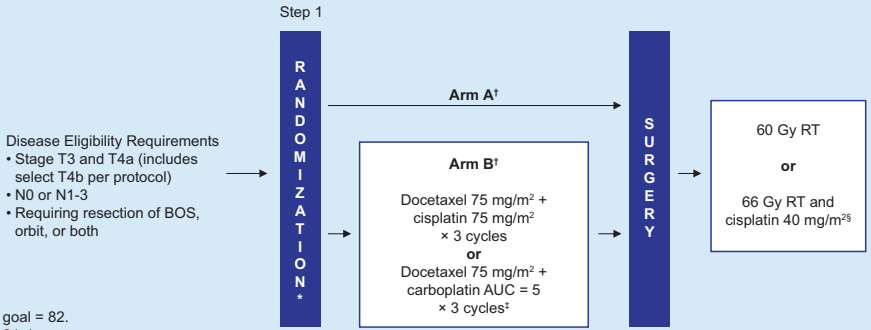
EA3163

Phase II Randomized Trial of Neoadjuvant Chemotherapy Followed by Surgery and Post-Operative Radiation Versus Surgery and Post-Operative Radiation for Organ Preservation of T3 and T4a (and Selected T4b) Nasal and Paranasal Sinus Squamous Cell Carcinoma (NPNSCC)

Study Schema



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.

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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

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