

For Patients with Recurrent/Metastatic Head and Neck Cancer

EA3202 Available Through ECOG-ACRIN Cancer Research Group

A Phase II/III Trial of Chemotherapy + Cetuximab vs Chemotherapy + Bevacizumab vs Atezolizumab + Bevacizumab Following Progression on Immune Checkpoint Inhibition in Recurrent /Metastatic Head and Neck Cancers

Patient Population

See Section 3 for Complete Eligibility Details

- ≥ 18 years of age, ECOG PS 0-1, adequate lab values
- Must have histologically confirmed squamous cell carcinoma of the head and neck (HNSCC), excluding SCC of salivary glands, EBV-associated nasopharynx and skin
- Must have measurable disease (RECIST v1.1) within 4 weeks prior to randomization
- Must have disease progression after prior therapy with an immune checkpoint inhibitor (ICI) in the first-line setting for recurrent/metastatic disease (must have received ICI for at least 6 weeks); patients who have recurred/progressed within 12 weeks of ICI administered in the definitive setting for locally advanced disease will also be eligible if local therapies are not feasible
- No prior antiangiogenic treatment (see protocol for details); no history of ≥ grade 3 immune-related AE on prior ICI therapy (see protocol for exceptions); no history of PD-1 inhibitor-induced hyper-progression (per protocol)
- No prior carotid bleeding, tumors that invade major vessels, central lung metastases that are cavitory, prior history of bleeding related to the current H&N cancer, or history of gross hemoptysis within 3 months of randomization
- No history of coagulopathy/hemorrhagic disorders
- No uncontrolled hypertension, history of hypertensive crisis/hypertensive encephalopathy, or history of grade 4 thromboembolism
- Must have PD-L1 expression ≥ 1% by CPS in the tumor and/or immune cells
- No history of solid organ/stem cell transplant
- No uncontrolled pleural/pericardial effusion, or ascites requiring recurrent drainage procedures
- No significant cardiovascular disease (per protocol) within 3 months of randomization or unstable arrhythmia/angina at randomization
- No history of abdominal fistula, GI perforation, intra-abdominal abscess, or active GI bleeding within 6 months of randomization

Treatment Plan

See Section 5 for Complete Treatment Details

Cycle = 21 days

Phase II:

- **Arm A:** Day 1: cetuximab 400 mg/m² IV, docetaxel 75 mg/m² IV, investigators choice of cisplatin or carboplatin; cetuximab 250 mg/m² IV days 8 and 15 (days 1, 8, 15 of subsequent cycles)
 - ◇ Weekly dosing schedule is allowed (investigators discretion)
 - ◇ Repeat cycle every 3 weeks for 6 cycles
 - ◇ Then proceed to cetuximab (250 mg/m² IV weekly or 500 mg/m² IV biweekly) until progression, intolerable toxicity, or up to 2 years
- **Arm B:** Day 1: bevacizumab 15 mg/kg IV, docetaxel, investigators choice of cisplatin or carboplatin
 - ◇ Weekly dosing schedule is allowed (investigators discretion)
 - ◇ Repeat cycle every 3 weeks for 6 cycles
 - ◇ Then proceed to bevacizumab (15 mg/kg IV every 3 weeks) until progression, intolerable toxicity, or up to 2 years
- **Arm C:** Day 1: atezolizumab 1200 mg IV followed by bevacizumab 15 mg/kg IV
 - ◇ Repeat cycle every 3 weeks until progression, intolerable toxicity or up to 2 years

Phase III:

- **Arm A:** Cetuximab 400 mg/m² IV day 1, docetaxel 75 mg/m² IV day 1, investigators choice of cisplatin or carboplatin, cetuximab 250 mg/m² IV days 8 and 15 (days 1, 8, 15 of subsequent cycles)
 - ◇ Weekly dosing schedule is allowed (investigators discretion)
 - ◇ Repeat cycle every 3 weeks for 6 cycles
 - ◇ Then proceed to cetuximab (250 mg/m² IV weekly or 500 mg/m² IV biweekly) until progression, intolerable toxicity, or up to 2 years
- **Arms B/C** to be determined by Phase II outcome

Study Chair:

Aarti Bhatia, MD, MPH

Study Co-chair:

Jennifer M. Johnson, MD, PhD

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) <https://open.ctsu.org/open>

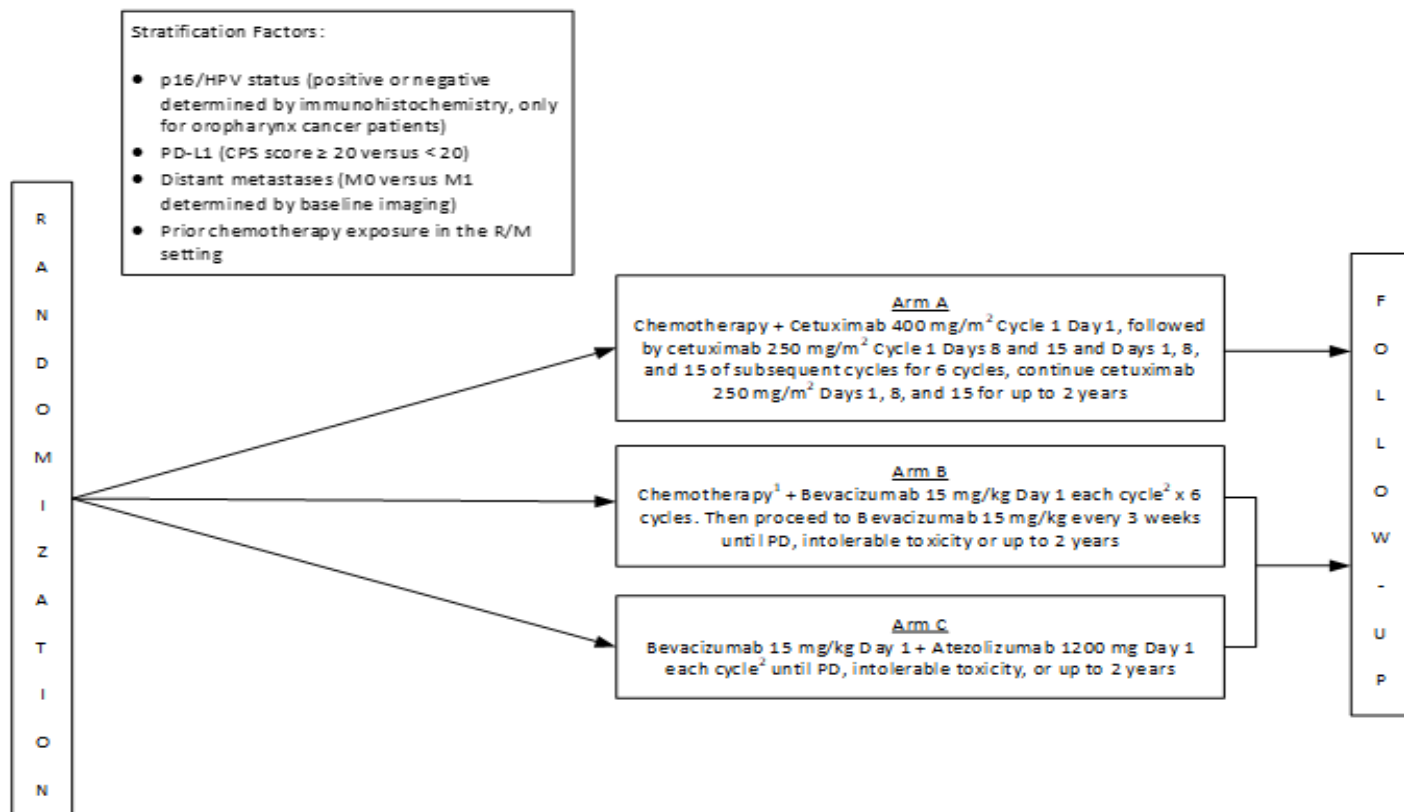
Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, <http://ecog-acrin.org> (Member Login)

Please Enroll Your Eligible Patients!

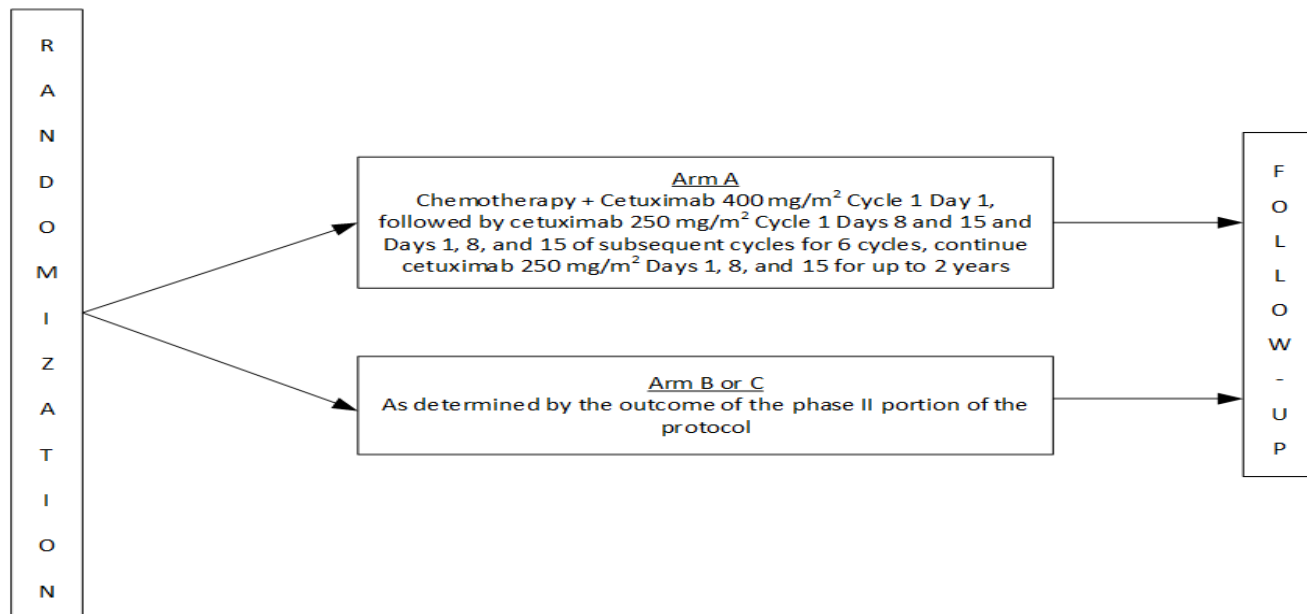
Schema

Phase II



1. Arm A and B: Chemotherapy consists of Docetaxel 75mg/m² IV Day 1, Investigator Choice of Cisplatin 75mg/m² IV Day 1 or Carboplatin AUC 5 IV Day 1. Please refer to Section 5.1 for more details
2. One cycle = 21 days

Phase III



1. Arm A: Chemotherapy consists of Docetaxel 75mg/m² IV Day 1, Investigator Choice of Cisplatin 75mg/m² IV Day 1 or Carboplatin AUC 5 IV Day 1. Please refer to Section 5.1 for more details
2. One cycle = 21 days

Phase III sample size = 214