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 3.0 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 (HSCC), excluding SCC of salivary glands and skin
- Must have measurable disease (RECIST v1.1) within 4 weeks prior to randomization
- Must have received prior therapy with an immune checkpoint inhibitor (ICI) in the first-line setting for recurrent/metastatic disease with at least stable disease for at least 12 weeks (RECIST); prior combination immunotherapies are permitted, but patient must not have had any prior chemotherapy, cetuximab, or prior antiangiogenic treatment (see protocol for exception)
- No history of ≥ grade 3 immune-related AE on prior ICI therapy (see protocol for exception)
- No history of PD-L1 inhibitor-induced hyper-progression (defined per protocol)
- No prior carotid bleeding, tumors that invade major vessels, central lung metastases that are cavitary, 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 5.0 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)
  - 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
  - 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 followed by
  - Docetaxel 75 mg/m² IV day 1 followed by
  - Investigators choice of cisplatin or carboplatin
  - Cetuximab 250 mg/m² IV days 8 and 15 (days 1, 8, 15 of subsequent cycles)
  - 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 or C:** determined by Phase II outcome

Notes:

- See protocol for hydration and antiemetic guidelines
- If specific toxicity AEs occur, patient can switch from cisplatin to carboplatin per investigator discretion

Patient Enrollment

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

Protocol Information


Please Enroll Your Eligible Patients!
Phase II

Stratification Factors:
- P16/HPV (positive or negative determined by immunohistochemistry)
- PD-L1 (CPS Score ≥20% vs. <20%)
- Distant Metastases (M0 vs M1): determined by baseline imaging
- Disease progression pattern on first-line ICI: while on ICI versus after discontinuing ICI

Randomization

Arm A
Cetuximab 400 mg/m² on Cycle 1 Day 1, followed by Cetuximab 250 mg/m² on Cycle 1 Days 8 and 15 and Days 1, 8, and 15 of subsequent cycles, for a total of 6 cycles

Arm B
Chemotherapy² + Bevacizumab 15 mg/kg Day 1 each cycle x 6 cycles. Then proceed to Bevacizumab 15 mg/kg every 3 weeks until PD, intolerable toxicity or up to 2 years

Arm C
Bevacizumab 15 mg/kg Day 1 + Atazanavir 1200 mg Day 1 each cycle until PD, intolerable toxicity, or up to 2 years

Follow-up

1. Arm A and B: Chemotherapy consists of Docetaxel 75 mg/m² IV Day 1, Investigator Choice of Cisplatin 75 mg/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

Randomization

Arm A
Cetuximab 400 mg/m² Cycle 1 Day 1, followed by Cetuximab 250 mg/m² on Cycle 1 Days 8 and 15 and Days 1, 8, and 15 of subsequent cycles, for a total of 6 cycles

Arm B or C
As determined by the outcome of the phase II portion of the protocol

Follow-up

1. Arm A: Chemotherapy consists of Docetaxel 75 mg/m² IV Day 1, Investigator Choice of Cisplatin 75 mg/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