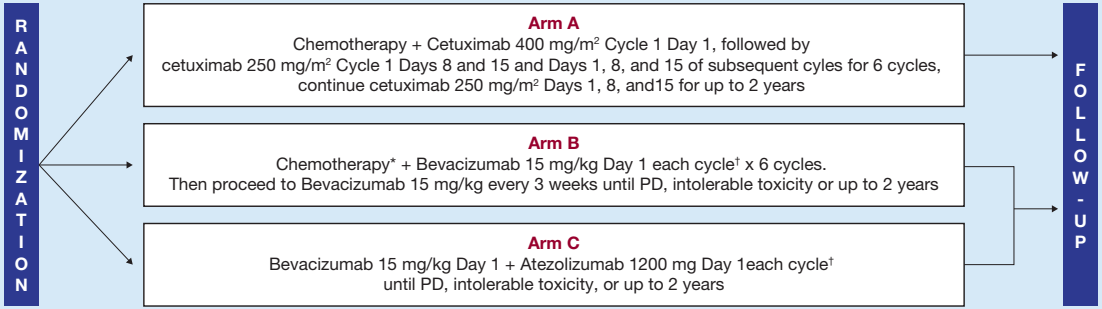
EA3202

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

Study Schema



Phase II accrual = 216 patients
*Arm A and B: Chemotherapy consists of Docetaxel 75 mg/m² IV Day 1, Investigator Choice of Cisplatin 75mg/m² IV Day 1 or Carboplatin AUC 5 IV Day 1
†One cycle = 21 days

For Phase III, patients will be randomized to Arm A (same as above), OR Arm B/C (as determined by the outcome of Phase II).
Phase III accrual = 214 patients

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Study Objectives

Primary Objectives

- Phase II: To evaluate progression-free survival (PFS)
- Phase III: To evaluate overall survival (OS)

Secondary Objectives

- To evaluate OS for the subset of patients with high PD-L1 expression, defined as Combined Positive Score (CPS) ≥ 20% on all study arms
- To evaluate the toxicity of each study arm

Refer to the protocol for imaging objectives (Section 2.3) and exploratory objectives (Section 2.4)

Eligibility Criteria*

Main Inclusion Criteria

- ≥ 18 years of age, ECOG PS 0–1, adequate organ and marrow function defined per protocol
- Histologically confirmed squamous cell carcinoma of the head and neck (HNSCC) (excluding SCC of salivary glands, Epstein-Barr Virus–associated nasopharynx and skin)
- Measurable disease (defined by RECIST v1.1); measurements must be obtained 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 first-line 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 are eligible if local therapies are not feasible
- Prior combination immunotherapies are permitted, but patient must not have had prior antiangiogenic treatment (e.g., bevacizumab, ziv-aflibercept, ramucirumab,

*When evaluating patients for this study, please refer to the full protocol for complete list of eligibility criteria.

sorafenib, sunitinib, pazopanib, regorafenib, lenvatinib, etc.)
  - Patients who received platinum/taxanes in the locally-advanced or recurrent/metastatic setting and did not progress for at least 4 months thereafter are eligible
  - Patients who received cetuximab in the locally-advanced setting and did not progress for at least 4 months thereafter are also eligible
- Must have PD-L1 expression ≥ 1% by CPS in the tumor and/or immune cells

Main Exclusion Criteria

- History of ≥ grade 3 immune-related adverse event on prior ICI therapy (except those that could be managed with steroids) and ICI could eventually be resumed
  - Patients who developed grade 3 endocrinopathies but are stable on hormone supplementation and/or a daily prednisone dose of ≤ 10 mg (or equivalent doses of another glucocorticoid) are permitted
- History of PD-1 inhibitor-induced hyper-progression, defined as 100% increase in tumor burden within 8 weeks (or 50% within 4 weeks) of initiating ICI and associated with clinical deterioration
- Uncontrolled hypertension, history of hypertensive crisis or hypertensive encephalopathy, or history of grade 4 thromboembolism
- History of coagulopathy or hemorrhagic disorders
- History of solid organ transplantation/stem-cell transplant

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Main Exclusion Criteria (cont)

- Uncontrolled pleural effusion, pericardial effusion or ascites requiring recurrent drainage procedures (once monthly or more)
- History of abdominal fistula, GI perforation, intra-abdominal abscess, or active GI bleeding within 6 months of randomization

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