A Phase I/II Multisite Study of Nivolumab and Carboplatin/Paclitaxel with Radiation Therapy (RT) in Patients with Locally Advanced Esophageal Squamous Cell Carcinoma (ESCC)

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BACKGROUND

- Preoperative chemoRT is a standard of care in patients with locally advanced esophageal squamous cell carcinoma, as shown in the CROSS trial1.
- Surgery is sometimes deferred in patients with clinical complete response (cCR) based on lack of overall survival benefit2,3.
- Nivolumab has activity in advanced ESCC, and adding it to chemoRT may improve outcomes.

METHODS

- This phase I/II study was designed to assess the safety, tolerability and efficacy of nivolumab added to chemoRT (6 weekly carboplatin AUC 2, paclitaxel 50mg/m², RT 50.4 Gy in 1.8 Gy fractions 5/7 days) for patients with TanyN1-3 or T3-4N0M0 ESCC. The phase I primary endpoint is "unacceptable toxicity" at 28 days after the last dose of chemotherapy. The phase II primary endpoints are cCR (endoscopy + PET/CT) and pCR rates for patients undergoing surgery. Nivolumab is given q2W (every 2 weeks) for 3 doses prior to esophagectomy, then adjuvant nivolumab q2W ×3. If no cCR, patient proceeds with chemoRT with nivolumab q2W x3. If no cCR, patient has an option of no surgery but receives nivolumab q2W ×3.

RESULTS

- From 7/20/2017 to 6/13/2019, 12 patients were enrolled in phases I (6) and II (6). Median age was 65.5y, 58% male/42% female, 58% white/25% asian/17% black.
- Including phases I and II, total enrollment evaluable for toxicity: 12 patients
- No unacceptable toxicities were observed.
- One patient had dose held due to weakness.
- Two patients required hospitalizations (dyspnea 1, colitis 1).
- One patient expired within 90 days of treatment (phase II).
- No unacceptable toxicities were observed.

CONCLUSIONS

- ChemoRT with nivolumab is tolerable with manageable toxicities in locally advanced ESCC.
- Enrollment to the phase II portion ended because of slow accrual.
- More investigation is warranted to further evaluate the efficacy of this promising treatment regimen.

REFERENCES


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