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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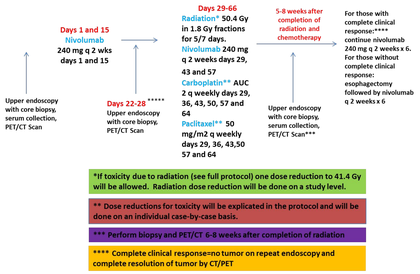
BACKGROUND

- Preoperative chemoRT is a standard of care in patients with locally advanced esophageal squamous cell carcinoma, as shown in the CROSS trial[1].
- Surgery is sometimes deferred in patients with clinical complete response (cCR) based on lack of overall survival benefit[2,3].
- Nivolumab has activity in advanced ESCC[4], 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 ×2, then concurrent chemoRT with nivolumab q2W x3. If no cCR, patient proceeds to esophagectomy, then adjuvant nivolumab q2W ×3; if cCR, patient has an option of no surgery but receives nivolumab q2W ×3.

Trial Schema

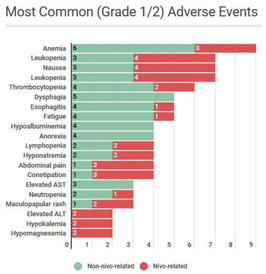


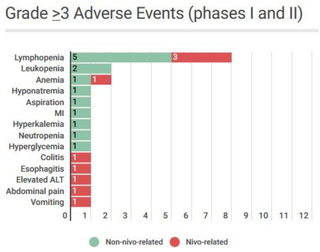
▲ Unacceptable Toxicity

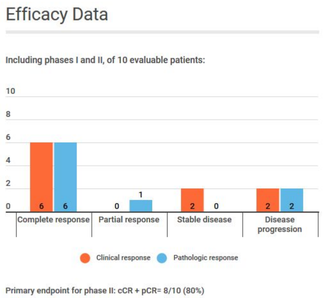
- Recurrent grade 3 or 4 hematologic toxicity (despite 1 prior dose reduction in chemotherapy)
- Any toxicity related to chemotherapy, RT, or treatment with nivolumab that results in a >2-week delay in chemoRT

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).
  - Two patients expired within 90 days of treatment (phase II).
    - Neither of these deaths were thought to be related to treatment.
  - 100% of patients had at least one AE; 83% of patients had at least one SAE







CONCLUSIONS

- ChemoRT with nivolumab is tolerable with manageable toxicities in locally advanced ESCC.
- Enrollment to the phase II portion ended because of slow accrual.
- Inquiry into modification of chemoRT regimen is merited given the two patients that expired in the phase II portion.
- For patients evaluable for efficacy, all who did not progress achieved a response and are alive, without evidence of disease (8 of 10 patients).
- More investigation is warranted to further evaluate the efficacy of this promising treatment regimen.

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