**Purpose:**

- **Primary Objective:**
  - Response rate per RECIST 1.1
- **Secondary Objectives:**
  - PFS and OS
  - Grade 3/4 toxicities
- **Exploratory Objectives:**
  - Fresh tissue biopsies were requested for all patients treated at MDACC (pre- and on-treatment).
  - Immunophenotyping with IHC and flow cytometry (Morris et al, AACR 2016).
  - Serial blood samples were drawn on all patients.

**Methods:**

- All pts were required to be immunotherapy naïve; ≥ 1 prior metastatic treatment; presence or absence of PD-L1 expression. If HIV+, CD4 count > 300/uL.
- A Simon two-stage Phase II trial (Ho: p < .05, Ha: p ≥ .20) was conducted.
- Pts received Nivo (3 mg/kg) IV every 2 weeks. Optional pre-treatment and on-treatment tissue and plasma samples, and post progression (plasma samples only) were collected, including cfDNA.

**Results:**

- 39 pts consented; 37 patients are evaluable for toxicity and intent to treat (May 2015 - October 2015).
  - 2 pts were HIV+.
  - The median age is 56 years (range: 51-64); M:F is 11:28.
  - Median number of prior therapies: 2 (range 1-7).
  - Median number of cycles provided: 6 (range 1-23).
  - RR: ≥ CR’s; 7 PR’s resulted in an ORR of 24%.
  - Median PFS: 3.9M.
  - Grade 3 toxicities: Anemia (N=2) and rash, hypothyroidism, fatigue (N=1 each). No grade 4 toxicities were noted.

**Future Directions for Met SCCA:**

- **Clinical Trials**
  - Treatment naïve
    - InterAACT/ECOG EA#2133: Randomized phase II study of cytotoxic chemotherapy (NCT02051868) - International Rare Cancers Initiative (IRCI)
    - Refractory
      - ADXS11-001: Live listeria vaccine with fusion protein of HPV16/E7
      - Amendment of NCI9673 in development (ETA: Fall 2016)
  - HIV+ pts
    - HIV Consortium phase I study (NCT02408861)
- Continued clinical trial enrollment is crucial in the hopes of obtaining an FDA indication for the “rare” cancer of metastatic squamous cell carcinoma of the anal canal.

**Background:**

- Worldwide, it is estimated that SCCA will develop in > 27,000 patients (pts).
- 20% of pts will develop metastatic (met) disease for which there is no standard approach.
- We have previously demonstrated that > 90% of metastatic SCCA is associated with HPV.
- Nivolumab (Nivo), a monoclonal antibody targeting PD-1 on T cells, promotes immune-mediated anti-tumor activity of T cells against HPV-positive cells in vitro.
- We proceeded to conduct the first phase II trial of Nivolumab in previously treated met SCCA pts.

**Clinical Response:**

- **Pre-treatment: May 2015**
- **Post-treatment: June 2016**

**Conclusions:**

- There is an increased annual incidence of the HPV-associated malignancy, SCC of the anal canal.
- NCI9673 is the first prospective phase II trial to be completed in refractory metastatic SCCA.
- Single agent nivolumab was well tolerated and fulfilled the primary endpoint of response.
  - Note: No unexpected SAE’s were noted in HIV+ pts.
- Rapid enrollment was feasible via the NCI ETCTN and provided an opportunity for clinical trial development for a “rare” cancer.
- An amendment is underway to evaluate combination therapy.

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