Protocol Title: Phase III Randomized Adjuvant Study of MK-3475 (Pembrolizumab) in Muscle Invasive and Locally Advanced Urothelial Carcinoma (AMBASSADOR) Versus Observation

Target Population: Stage II – III Bladder Urothelial Carcinoma

Summary: To determine disease free survival (DFS) and overall survival (OS) in all patients with Muscle-Invasive Bladder and Upper Tract Urothelial Carcinoma treated with adjuvant Pembrolizumab (MK-3475) vs observation.

PRE-REGISTRATION ELIGIBILITY CRITERIA:
- Histologically confirmed Muscle-Invasive Urothelial Carcinoma of the Bladder or Upper Tract.
  - Variant histology allowed as long as Urothelial Carcinoma is predominant (> 50%).
  - Pure Small-Cell Carcinoma is excluded.
- Paraffin tissue samples obtained by Transurethral Resection of Muscle-Invasive Bladder Tumor, Upper Tract Resection, Cystectomy / Nephrectomy / Ureterectomy, or Nephroureterectomy must be available.
  - Specimen submission is mandatory prior to registration as results are used for stratification.
- Must fit into 1 of the following 3 categories:
  1. Patients who received neoadjuvant chemotherapy and pathologic stage at surgical resection is ≥ pT2 and/or N+
  2. Patients who are not Cisplatin-eligible (according to ≥ 1 of the following criteria: ECOG Performance Status of 2, CrCl < 60 mL/min, Grade ≥2 hearing loss, Grade ≥ 2 neuropathy, or NYHA class III heart failure, and pathologic stage at surgical resection is ≥ pT3 or pN+)
  3. Patients that decline adjuvant Cisplatin-based or other systemic chemotherapy based on an informed discussion with physician and pathologic stage at surgical resection is ≥ pT3 or pN+
- Must have had radical surgical resection of their Bladder Cancer ≥ 4 weeks but ≤ 16 weeks prior to pre-registration.
- No invasive cancer at surgical margins AND no evidence of residual cancer or metastasis after surgery.
- No metastatic disease on cross-sectional imaging (according to RECIST 1.1 criteria).
- No current pneumonitis or prior history of non-infectious pneumonitis that required steroids within the previous 5 Years.
- No known active Hepatitis B or Hepatitis C.
- No postoperative/adjuvant systemic therapy.
- No prior treatment with any therapy on the PD-1/PD-L1 axis.

REGISTRATION ELIGIBILITY CRITERIA:
- Results of central PD-L1 testing available.
  - Q2 Solutions will forward the PD-L1 results to the statistical center and the statistical center will notify the site that the result is available.
  - Notification from the Alliance registration / randomization office will serve as a confirmation of this eligibility criteria.
  - After sites receive the confirmation e-mail from Alliance they can register the patient.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT03244384