Protocol Title: An Open-Label, Randomized Phase III Study to Evaluate Enfortumab Vedotin vs Chemotherapy in Subjects with Previously Treated Locally Advanced or Metastatic Urothelial Cancer (Astellas EV-301)

Target Population: Previously Treated Locally Advanced or Metastatic Urothelial Cancer

Summary: The purpose of this study is to compare the overall survival (OS) of participants with locally advanced or metastatic Urothelial Cancer treated with Enfortumab Vedotin (EV) to the OS of participants treated with chemotherapy.

Key Inclusion Criteria:
- Histologically or cytologically confirmed Urothelial Carcinoma (i.e., cancer of the bladder, renal pelvis, ureter, or urethra).
  - Urothelial Carcinoma (transitional cell) with squamous differentiation or mixed cell types eligible.
- Must have radiographic progression or relapse during or after a checkpoint inhibitor (anti-PD1 or anti-PD-L1) for locally advanced or metastatic disease.
  - Locally advanced disease must not be amenable to resection with curative intent per treating physician.
- Must have received a platinum containing regimen (cisplatin or carboplatin) in the metastatic/locally advanced, neoadjuvant or adjuvant setting.
  - If platinum was administered in the adjuvant/neoadjuvant setting subject must have progressed within 12 months of completion.
- Radiologically documented metastatic or locally advanced disease at baseline.
- Archival tumor tissue sample should be available for submission to central laboratory prior to study treatment. If an archival tumor tissue sample is not available, a fresh tissue sample should be provided. If a fresh tissue sample cannot be provided, enrollment into the study must be discussed with the medical monitor.
- ECOG PS of 0 or 1.
- Adequate bone marrow, liver, renal, and coagulation function.

Key Exclusion Criteria:
- Preexisting sensory or motor neuropathy Grade ≥ 2.
- Active CNS metastases. Subjects with treated CNS metastases are permitted on study if the following are true:
  - CNS metastases have been clinically stable for at least 6 weeks prior to screening.
  - If requiring steroid treatment for CNS metastases, the subject is on a stable dose ≤ 20 mg/day of prednisone or equivalent for at least 2 weeks.
  - Baseline scans show no evidence of new or enlarged brain metastasis.
  - Subject does not have leptomeningeal disease.
- Ongoing clinically significant toxicity associated with prior treatment.
- Prior treatment with EV or other monomethyl auristatin E (MMAE)-based Antibody drug conjugates (ADCs).
- Received prior chemotherapy for Urothelial Cancer with all available study therapies in the control arm.
- Received > 1 prior chemotherapy regimen for locally advanced or metastatic Urothelial Cancer, including chemotherapy for adjuvant or neo-adjuvant disease if recurrence occurred within 12 months of therapy.
- Has known active Hepatitis B, Hepatitis C, or HIV infection (HIV 1 or 2).
- Has documented history of a cerebral vascular event, unstable angina, myocardial infarction, or cardiac symptoms consistent with NYHA Class III-IV within 6 months prior to the first dose of study drug.
- Has known active keratitis or corneal ulcerations.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT03474107

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