Background and Rationale

• Metastatic urothelial carcinoma (mUC) is an aggressive malignancy with 5-year survival rates of <5%.1

• PK parameters (AUC, Cmax, Tmax, Ctrough)

• Enrollment is ongoing in North America and planned in Europe, Latin America, Asia-Pacific, and Israel

• Historically confirmed, including UC originating from the renal pelvis, ureter, bladder, or urethra

Disitamab Veddoted Proposed Mechanism of Action

DISITAMAB VEDOTIN

Proposed mechanism of action of an antibody-drug conjugate directed to HER22

Study Design

PHASE 2

• OPEN-LABEL

• MULTICENTER

Eligibility

Key Inclusion Criteria

• Histologically-confirmed, locally advanced, unresectable or metastatic urothelial carcinoma, including UC originating from the renal pelvis, ureter, bladder, or urethra

• HER2-expression status determined by central laboratory to be HER2+ or HER2-low

• Cohorts A and B only:

• Patients must have received only 1 or 2 lines of prior systemic therapy for LA/mUC, including 1 line of platinum-containing therapy with or without a PO-D-1 inhibitor, with progression within 12 months of completing last dose, is allowed

• No prior systemic therapy for LAMUC (unadjuvant or adjuvant systemic chemotherapy with or without a PO-D-1 inhibitor, with progression within 12 months of completing last dose, is allowed)

• Must be eligible for treatment with chemotherapy for the current line of mUC

• Must be eligible for treatment with chemotherapy for the current line of mUC

• Prior anti-HER2 agents or HER2-directed therapy

• Peripheral sensory or motor neuropathy ≥ Grade 2

Assessments

• Tumor response assessments will be performed according to RECIST v1.1

• cORR and cPR per RECIST v1.1 by BOR and investigator assessment will be evaluated in the Response Evaluation analysis set; corresponding 95% CI using the Clopper-Pearson method will be presented

• Blood samples will be collected for PK and ADA analysis and will be summarized using descriptive statistics

• For Cohorts A and B, the patient reported outcomes will be assessed

• Safety assessments will include monitoring and recording of AEs (including SAEs), concomitant medication, changes in laboratory test results and vital signs, ECOG PS, ECGs, and cardiac ejection fraction results. All severity will be graded using CTCAE v5.0

Key Exclusion Criteria

• Known hypersensitivity to DV or pembrolizumab (Cohort C only)

• Prior anti-HER2 therapy during the 2 weeks of study start

• Toxicity from previous treatment that has not returned to Grade 0 or 1 (exception: alopecia)

• Prior MMAE-directed ADC or HER2-directed therapy

• Other malignant tumors within 3 years of treatment except the following

• Truete prostate cancer (treated with definitive intent) ≥1 year prior to first diagnosis

• Malignancies that can be cured following treatment

Study Treatment

• Cohort A will evaluate DV as a monotherapy for HER2-positive tumors (IV, Q2W)

• Cohort B will evaluate DV as a HER2-low tumors (IV, Q2W)

• Cohort C will evaluate DV (IV, day 1 of each 6-week cycle) for treatment-naïve HER2-positive or HER2-low tumors

References