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GENITOURINARY TUMOURS, NON-PROSTATE

901O EV-103: Initial results of enfortumab vedotin plus pembrolizumab for locally advanced or metastatic urothelial carcinoma

C.J. Hoimes[1], J.E. Rosenberg[2], S. Srinivas[3], D.P. Petrylak[4], M. Milowsky[5], J.R. Merchan[6], M.A. Bilen[7], S. Gupta[8], A-S. Carret[9], N. Yuan[9], A. Melhem-Bertrandt[10], T. Flaig[11]

[1]Medical Oncology, Case Western Reserve University/University Hospitals, Cleveland, OH, USA, [2]Medical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA, [3]Medical Center, Stanford University, Palo Alto, CA, USA, [4]Medical Oncology, Yale Cancer Center, New Haven, CT, USA, [5]Medical Oncology, University of North Carolina, Chapel Hill, NC, USA, [6]Hematology and Oncology, University of Miami, Miami, FL, USA, [7]Oncology, Emory University Winship Cancer Institute, Atlanta, GA, USA, [8]Masonic Cancer Center, University of Minnesota, Minneapolis, MN, USA, [9]Clinical Development, Seattle Genetics, Bothell, WA, USA, [10]Clinical Development, Astellas Pharma USA, Northbrook, IL, USA, [11]School of Medicine, University of Colorado Cancer Center Anschutz Cancer Pavilion, Aurora, CO, USA

Background: Platinum-based chemotherapy remains the standard of care for patients (pts) with locally advanced or metastatic urothelial carcinoma (la/mUC). Despite the use of first-line (1L) PD-1/PD-1L inhibitors, 71–76% of pts who are cisplatin-ineligible do not respond. EV is an antibody-drug conjugate targeting Nectin-4, which is highly expressed in mUC. EV monotherapy data are encouraging; combination therapy may provide additional benefit. Here, we report initial data on a cohort of cis-ineligible pts receiving 1L EV + pembrolizumab.

Methods: This phase 1b study (NCT03288545) evaluated the safety/activity of EV + pembrolizumab. In the dose-escalation cohort, 1L or 2L pts received 1.0 or 1.25 mg/kg EV + 200 mg pembrolizumab. Cohort A pts received the recommended dose of 1.25 mg/kg EV + pembrolizumab as 1L therapy. In each 21-day cycle, EV was administered on Days 1 and 8 and pembrolizumab on Day 1. The primary endpoint was safety/tolerability; key secondary objectives: recommended EV dose, antitumor activity, DCR, DOR, PFS, and OS.

Results: As of 20 Feb 2019, 29 la/mUC pts (median 68 [51–90] y; 31% liver metastasis, 17% ECOG 2) have been treated with EV (1.25 mg/kg) + pembrolizumab in the 1L setting and completed at least 2 post-baseline scans or discontinued treatment. The most common treatment-emergent adverse events (AE) were fatigue (66%, 14% ≥Grade 3), decreased appetite (52%, 0% ≥Grade 3), alopecia (45%), and diarrhea (41%, 3% ≥Grade 3). Among AE of clinical interest, rash of any type occurred in 45% of pts (14% ≥Grade 3), peripheral neuropathy of any type in 52% (3% ≥Grade 3), and 17% experienced immune-mediated events that required systemic steroid treatment (10% ≥Grade 3). Overall, 2 pts (7%) discontinued treatment with EV + pembrolizumab due to AE (lipase increase,multi-organ failure). Preliminary confirmed ORR per RECIST 1.1 was 62% by investigators, including a 14% CR rate. The DCR was 90%.

Conclusions: In 1L cis-ineligible pts with la/mUC, EV + pembrolizumab demonstrates encouraging efficacy with a tolerable and manageable safety profile. Further evaluation of this combination is warranted. Updated data, including responses pending confirmation, will be available at the meeting.

Clinical trial identification: NCT03288545.

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