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Phase II trial of pembrolizumab (P) in combination with sEphB4-HSA (B4) in previously treated metastatic urothelial carcinoma (mUC)

S. Sadeghi[1], D.I. Quinn[1], T. Dorff[2], S.K. Pal[2], S. Groshen[3], D. Tsao-Wei[3], P.N. Lara[4], R. Parikh[5], M.E. Devitt[6], M. Parikh[4], A. Jackovich[7], N.J. Vogelzang[8], E.F. Burgess[9], R. Dreicer[6], I. Siddiqi[10], I. Gill[11], P. Gill[1]

[1] Medicine, USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA, [2] Oncology, City of Hope Comprehensive Cancer Center, Duarte, CA, USA, [3] Oncology, USC - University of Southern California - Keck School of Medicine, Los Angeles, CA, USA, [4] Oncology, University of California Davis Cancer Center, Sacramento, CA, USA, [5] Oncology, University of Kansas, Westwood, KS, USA, [6] Medicine, University of Virginia Cancer Center, Charlottesville, VA, USA, [7] Medicine, Rutgers University, New Brunswick, NJ, USA, [8] Comprehensive Cancer Centers of Nevada, US Oncology Research c/o Comprehensive Cancer Crts of NV, Las Vegas, NV, USA, [9] Medical Oncology Department, Levine Cancer Institute, Charlotte, NC, USA, [10] Pathology, USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA[11] Urology, USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA

Background

EphrinB2 (B2) expressed in mUC is a gatekeeper blocking immune cell (IC) traffic. Blocking B2 with B4 facilitates IC traffic into the tumor and may be synergistic with PD1/PDL1 treatment (tx). This trial investigated the safety and efficacy of B4 + P in mUC.

Methods

Patients (pts) with mUC previously treated with platinum chemotherapy (PC) were eligible. Prior PD1/PDL1 was excluded. Tx consisted of P 200mg IV q3 weeks + B4 10mg/kg IV weekly in a 21 day cycle until progression (PD) or unacceptable toxicities (tox). Response was measured q6 weeks using RECIST 1.1. Primary endpoint was overall survival (OS), secondary endpoints were progression free survival (PFS) and duration of response (DOR), and objective response rate (ORR). Pts who did not complete 1 cycle of tx or did not get the first imaging were inevaluable for response. Tumor tissue for all evaluable pts were tested for B2 by Immunohistochemical (IHC) staining.

Results

69 pts enrolled between 12/2016 - 09/2020. Median age 67, male/female 58/11, prior lines of tx 1/1+ 63/6. Sites of disease at baseline: nodes 43 (62%), lungs 24 (35%), liver 16 (23%), bone 9 (13%). ECOG 0 39 (57%) vs. 1 30 (43%). Bellmunt risk groups 0/1/2-3 were 41/43/16%. 23% upper tract primary. Among all enrolled at a median follow up 25.4 mo (range 1.3-48.3), the median OS was 14.4 mo (95% CI 6.4, 21.4). The ORR was 38%, median PFS 4.0 mo (95% CI 2.3, 5.5) and median DOR 8.0 mo. Among 62 evaluable pts ORR was 42% (95% CI 30-55, 9 CR, 17 PR), 40 pts expressed B2 (65%). Among B2+ pts ORR was 57.5% (95% CI 42-74, 8CR, 15 PR), median OS 15.3 mo (95% CI 12.0- NE), PFS 6.5 mo (95% CI 26-12.8), DOR 27 mo (range 10.4, NE). Median cycles of tx 5 (range 1-36). 6 pts still on tx, 5 pts off tx without PD. 36 (52%) off tx due to PD, 4 tox 1 grade (G) 3 arthralgia, 1 G3 edema, 1 G3 abdominal pain and 1 G3 supraventricular tachycardia, 4 died on tx (1 organ failure attributed to P, 1 aspiration pneumonia, 2 decline in health status). Hypertension was the most common tox attributed to B4, 72% all G, 42 % G3-4. Other tox ≥10%: fatigue, anorexia, nausea, headache, proteinuria, hyperuricemia, rash, ↑AST, anemia.

Conclusions

B4 + P is well tolerated and may have synergistic efficacy in mUC. B2 was expressed in the majority of pts and predicted for improved tx outcome.

Clinical trial identification

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Legal entity responsible for the study

USC.

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Disclosure

All authors have declared no conflicts of interest.