Background Maveropepimut-S (MVP-S, formerly DPX-Sur pivotac) is comprised of immunogenic T cell peptides from the cancer antigen, survivin, as well as a universal T helper peptide, A16L, and the innate immune activator, poly-dIdC, packed within the proprietary DPX® lipid-in-oil delivery platform. When combined with intermittent low-dose cyclophosphamide (CPA), and the immune checkpoint inhibitor, pembrolizumab, the proprietary DPX lipid-in-oil delivery platform elicits a sustained immune response that has been associated with clinical benefit in multiple tumor types. Here, we present translational analyses of immune cell infiltration and peripheral, cell-mediated immunity in advanced metastatic bladder cancer subjects (n=19) from this Phase 2 trial, NCT03836352.

Methods Survivin specific immune response was measured in PBMCs by IFN-γ ELISPOT (n=14) and MHC-Tetramer assay (n=13). Multiplex immunofluorescence (mIF) (n=5) was performed by Precision for Medicine. PD-L1 status (n=13) was analyzed using the 22C3 IHC assay at Covance. Gene expression analysis was performed using the NanoString IO360 panel (n=11).

Results Analysis of PBMCs by IFN-γ ELISPOT or MHC-tetramer assay demonstrates antigen-specific cell response in 71.4% (10/14) of evaluable patients, and in all five patients with measurable tumor responses. Baseline profiling of RNA signatures suggests that levels of B, T, and NK cells are higher in tumors of responding patients similar to previous MVP-S trials (DeCidE1; NCT02785250). Preliminary mIF also shows that one complete responder (RECISTv1.1) has a higher density of infiltrate, including CD8+ cells, at baseline. Grouped analysis of five on-treatment samples suggests higher immune resistance pathways such as TGF and CD71+ early erythroid cells, in non-responding patients, which has been linked to immune tolerance and suppression of T cells. 1 mIF of five paired pre- and on-treatment biopsies reveals higher levels of FoxP3+ (Tregs) in post-treatment tumour of non-responders whereas the reverse is observed in tissue of responders. PD-L1 staining of pre-treatment tumor tissue by IHC, shows (4/4) of evaluable responding patients had a CPS score of ≥1%.

Conclusions The combination of MVP-S, CPA, and anti-PD-1 therapy provides a renewed approach directly targeting the TAA survivin and imposing a limit on immune suppression with CPA along with checkpoint inhibition. The data herein show that the treatment of advanced metastatic bladder cancer with MVP-S plus CPA in combination with pembrolizumab elicits a strong survivin-specific immune cell response in addition to the clinical response as reported previously (AACR 2022). Taken together, the translational data demonstrate that this novel immune oncology approach leads to immune education that is correlated with improved disease control.

REFERENCE