353 IDENTIFICATION OF POTENTIAL RESPONSE PREDICTORS TO MAVEROPEPIMUT-S (DPX-SURVIVAC), A NOVEL T CELL ACTIVATING IMMUNOTHERAPY, IN PATIENTS WITH ADVANCED RECURRENT OVARIAN CANCER

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Background Epithelial ovarian cancer (OvCa) is the most lethal of gynecological malignancies. The high mortality is related to a late diagnosis with over 75% being at an advanced stage, high recurrence rates, and ultimately resistance to chemotherapy. Previous studies have consistently demonstrated a strong association between higher tumor T cell infiltration and improved survival in OvCa patients supporting the potential clinical utility of T cell activating immunotherapy approaches. Maveropepimut-S (MVP-S, formerly named DPX-Survivac) is a T cell activating immunotherapy which is a formulation of the proprietary drug delivery platform DPX™ with immunogenic T-cell epitopes derived from the tumor-associated antigen survivin. MVP-S in combination with intermittent low-dose cyclophosphamide has been shown to induce robust and durable antigen-specific T cell responses and anti-tumor clinical activity in recurrent OvCa patients. The current study presents translational data aimed at identifying tumor tissue-based predictive biomarkers for response to treatment with MVP-S.

Methods Baseline and on-treatment tumor biopsies were collected from patients treated with MVP-S primed with immune-modulating low dose cyclophosphamide. Multiplex-immunohistochemistry (mIHC, Akoya Biosciences) and RNA-seq analyses (Personalis Inc.) were used to analyze the tumor immune environment and identify potential response predictors to MVP-S.

Results Twenty-two patients with advanced, recurrent OvCa were enrolled in this study. mIHC analysis demonstrated that higher baseline CD3+CD8+ T cell infiltration in tumor tissue was significantly associated with anti-tumor clinical activity of MVP-S defined as >10% on-treatment tumor regression. Pathway enrichment analyses using the differentially expressed genes associated with anti-tumor clinical activity confirmed these findings. In addition, we identified B cell pathway genes to be significantly upregulated in patients with >10% on-treatment tumor regression. mIHC analyses of paired biopsies available for one subject with clinical response (PR) demonstrated that MVP-S treatment induced increased T and B cell infiltration in the on-treatment biopsy compared to the baseline biopsy. These findings suggest that immunogenic tumors are more susceptible to the MVP-S treatment, in line with its mechanism of action. Pathway enrichment analyses further revealed that upregulation of genes or pathways related to immune-suppression (e.g. WNT pathway) or immune evasion/exclusion (CD276, Arg2) were significantly associated with lack of anti-tumor activity indicative of potential mechanism of primary resistance.

Conclusions Collectively, these results provide insight for possible response predictors to MVP-S based therapy

Trial Registration NCT02785250

Ethics Approval The protocol and patient-informed consent form received approval by Institutional Review Boards. Written informed consent was obtained from all patients. REBs: Comite d'ethique de la recherche du CHUM (Montreal, Canada); Western Institutional Review Board 20161075 (Augusta, GA, USA); FWA #00002505 (NEW YORK, NY, USA); FWA00000161, IRB00000471 (Portland, Oregon, USA); University Health Network REB (Toronto, Canada); FWA00000935, FWA00000934 (Standford, CA, USA); Health Research Ethics Board of Alberta, (Edmonton, Canada)

http://dx.doi.org/10.1136/jitc-2021-SITC2021.353