

Identification of potential response predictors to maveropepimut-S (DPX-Survivac), a novel T cell activating immunotherapy, in patients with advanced recurrent ovarian cancer

Oliver Dorigo¹, Walead Ebrahimizadeh², Barry Kennedy², Lisa MacDonald², Stephan Fiset², Jeannine Villella³, Amit Oza⁴, Tanja Pejovic⁵, Prafull Ghatage⁶, Sharad Ghamande⁷, Diane Provencher⁸, Yogesh Bramhecha²

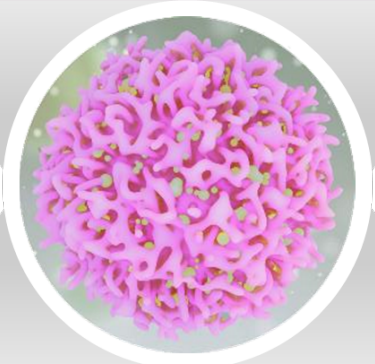
¹Stanford Cancer Institute, Stanford University, California, USA; ²IMV Inc., Nova Scotia, Canada; ³Lenox Hill Hospital/Northwell Health, New York, USA; ⁴Princess Margaret Cancer Centre, Ontario, Canada; ⁵Oregon Health & Science University, Oregon, USA; ⁶Tom Baker Cancer Centre, Calgary, Canada; ⁷Georgia Cancer Centre at Augusta University, Georgia, USA; ⁸Centre Hospitalier de l'université de Montréal, Quebec, Canada

Abstract # 353

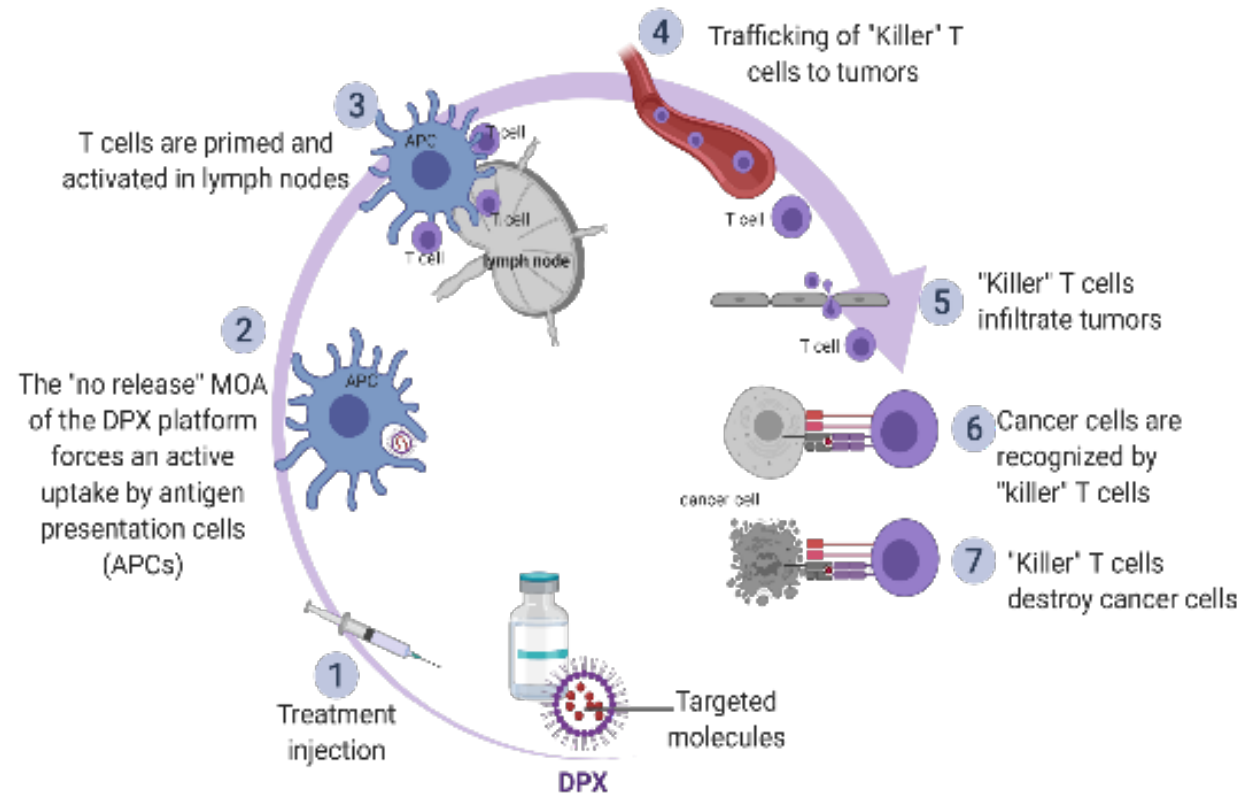


Maveropepimut-S (MVP-S) - Novel T Cell Activating Therapy

- Universal tumor-associated antigen
- Expressed in all 60 human tumor lines
- Confers resistance to chemotherapy & radiation
- Biomarker of poor patient prognosis

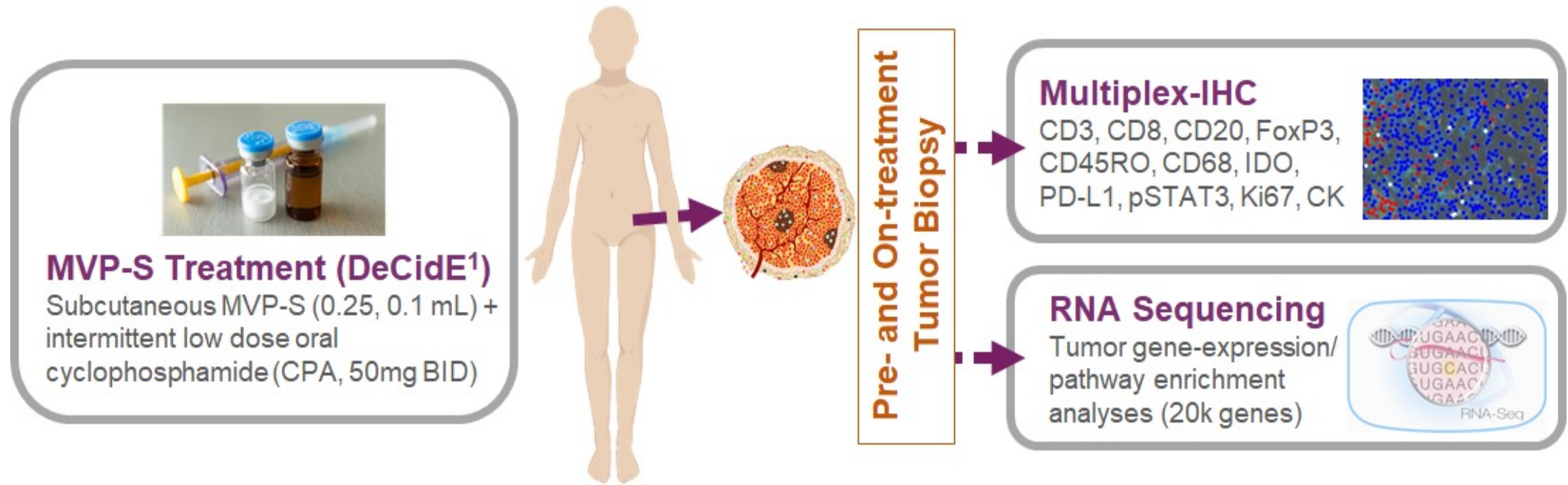


- Promotes cell proliferation
- Inhibit cell death & alter cancer metabolism
- Promote angiogenesis and adhesion
- Upregulated under hypoxia
- Downregulated when p53-deficient



- MVP-S combines DPX™, a lipid-based delivery platform with immunogenic T cell epitopes derived from the tumor associated-antigen survivin
- Elicits a robust immune response against survivin expressing tumors
- Unique mechanism of action facilitates active and sustained uptake of target peptides by Antigen Presenting Cells (APCs) at the injection site which then primes a *de novo* survivin-specific T cell response capable of trafficking to the tumor bed

Materials & Methods



Subjects with advanced, recurrent ovarian cancer were enrolled in the DeCidE¹-phase 2 study evaluating the safety and efficacy of MVP-S + intermittent low-dose CPA (N=22).

Tumor biopsies were subjected to multiplex immuno-fluorescence (mIF, Akoya Biosciences) and immunogenomics (RNAseq + WES; Personalis Inc.) analyses. RNAseq was performed using Illumina NovaSeq NGS platform with 300X mean coverage (>20k genes).

Data analyses performed by IMV Inc. and bPrescient Inc.

Higher pre-treatment T and B Cell Infiltration is Associated with Anti-tumor Clinical Activity of MVP-S + Intermittent Low-Dose CPA Treatment

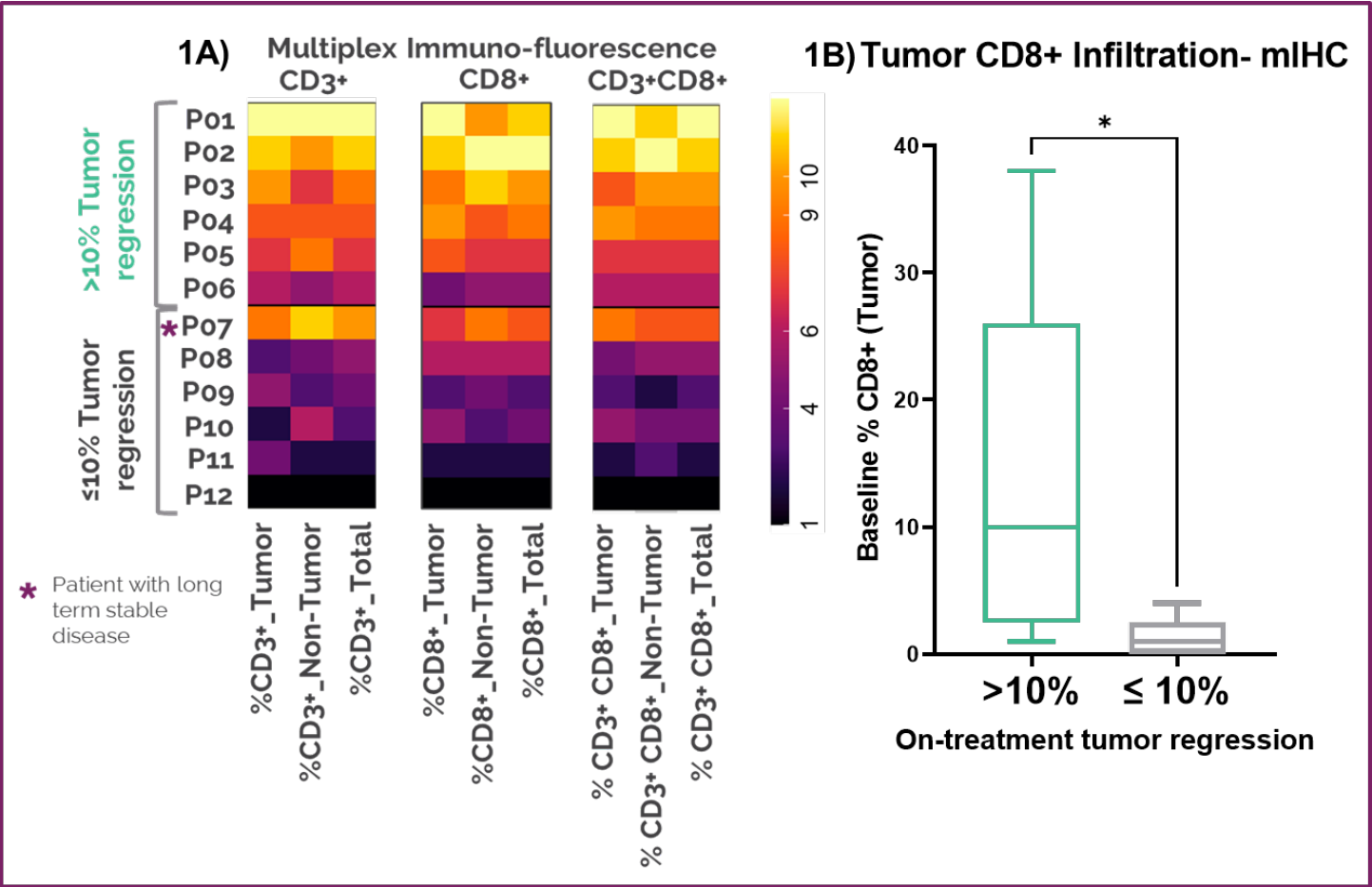


Figure 1A) Heatmap showing the rank-distribution of mlF features by on-treatment tumor regression status. Features are ranked from lowest (1) to highest with ties averaged.

Figure 1B) Box-plots representing significantly higher levels of pre-treatment CD8+ tumor infiltration in tumors of patients demonstrating >10% reduction in their target tumor lesion.

*Mann-Whitney U test ($p \leq 0.05$)

Higher pre-treatment T and B Cell Infiltration is Associated with Anti-tumor Clinical Activity of MVP-S + Intermittent Low-Dose CPA Treatment

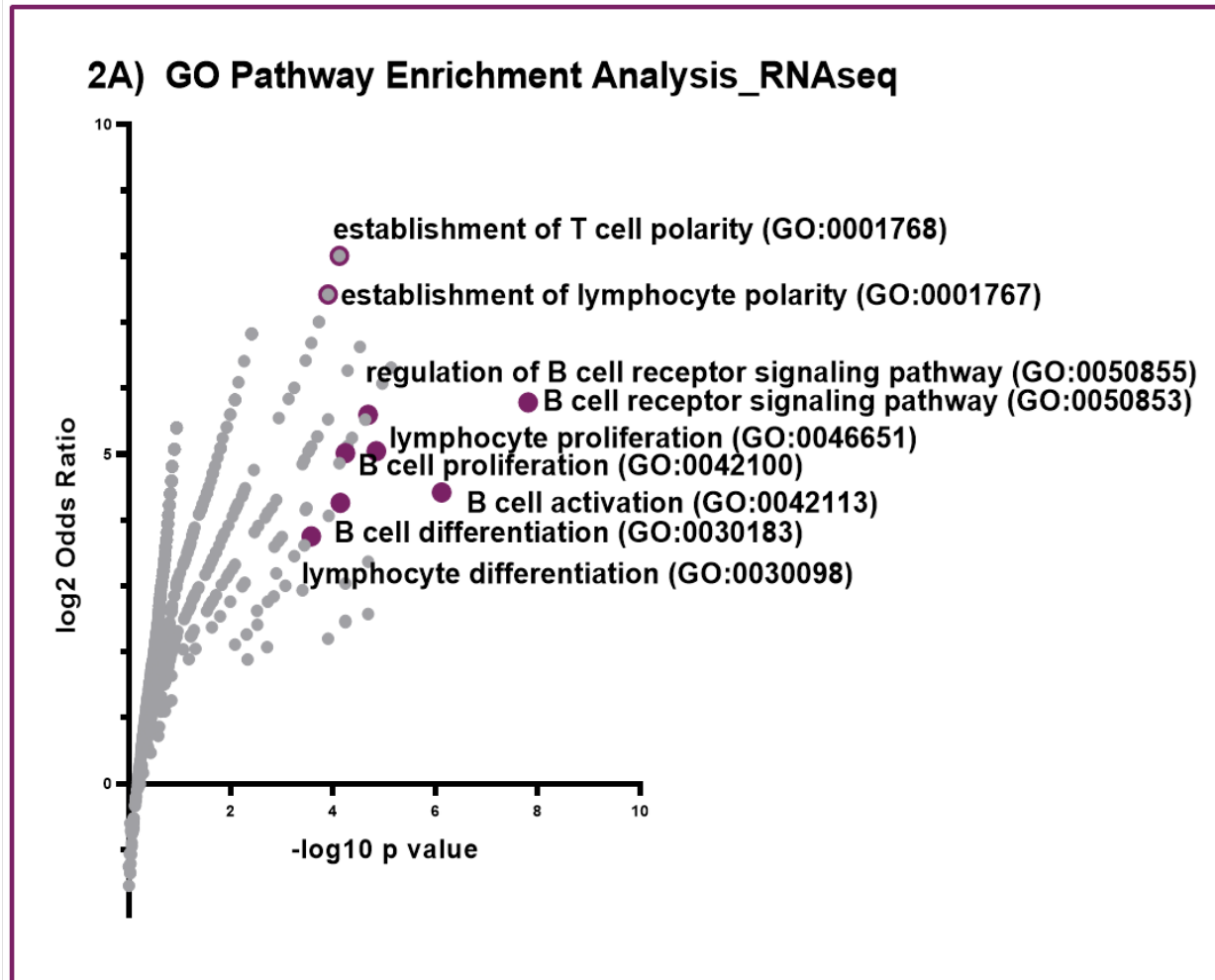
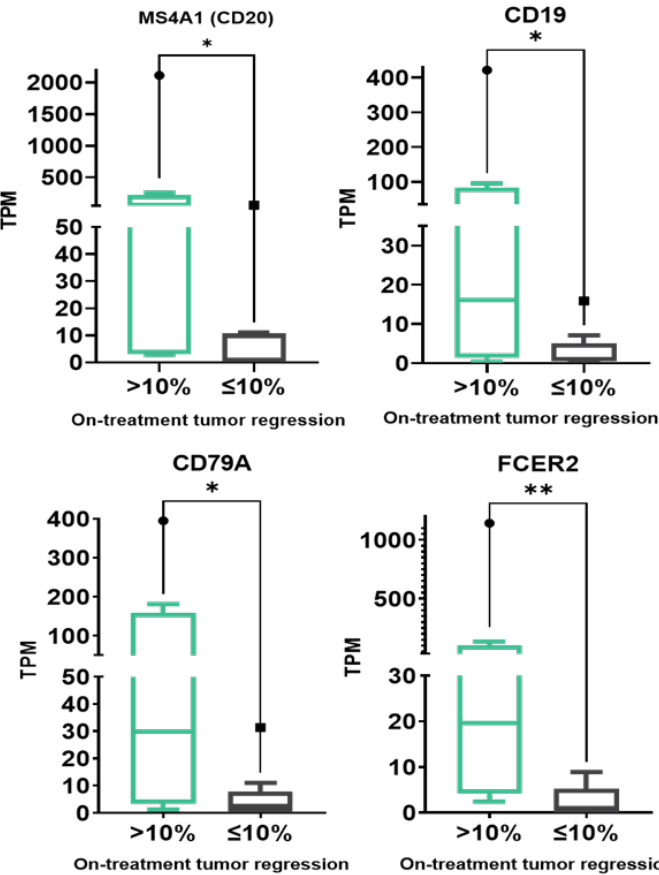


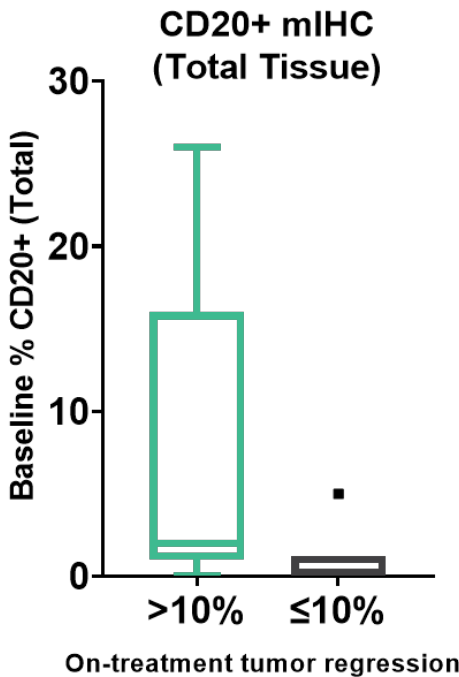
Figure 2A): Differential gene expression analyses identified 119 significantly upregulated genes in patients demonstrating >10% on-treatment tumor regression. Gene Ontology (GO) pathway enrichment analysis further indicated significant up-regulation of immune-related pathways highlighted in the figure

Higher pre-treatment T and B Cell Infiltration is Associated with Anti-tumor Clinical Activity of MVP-S + Intermittent Low-Dose CPA Treatment

2B) Tumor B Cell Infiltration: RNAseq



2C) Tumor B Cell Infiltration: mIHC



Box-plots representing significantly higher pre-treatment levels of representative B cell activation pathway genes (**2B**) as well as CD20+ staining (**2C**, mIF) in tumors of patients demonstrating > 10% reduction in their target lesion. *Mann-Whitney U test ($p \leq 0.05$).

MVP-S Induced Increased T and B Cell Infiltration in the On-treatment Tumor of a Patient with Clinical Response

65 y-o; high grade serous peritoneal cancer, stage 3c at diagnosis;
BRCA1/2 negative; 2 prior lines of therapy; platinum sensitive;
ECOG = 1; discontinued due to injection site reaction

Best RECIST Response: Partial Response (-57.8% at target lesion)

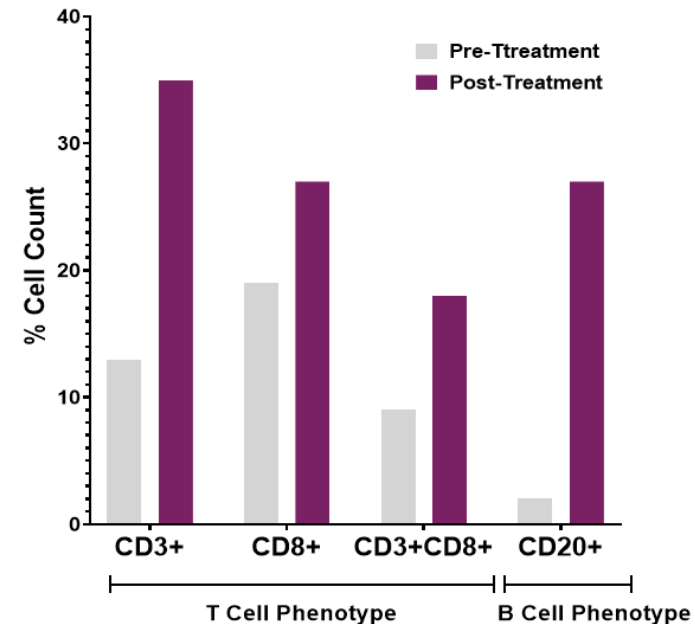
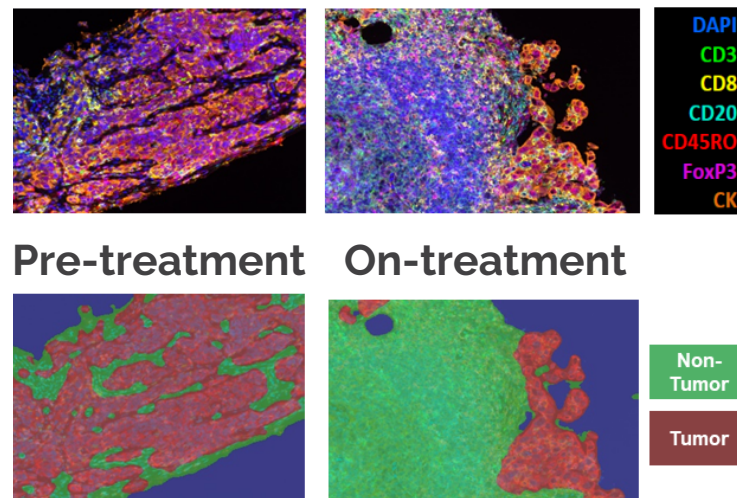


Figure 3) Multiplex immuno-fluorescence (mIF) analysis of paired tumor biopsies available for one patient with clinical response (PR) demonstrating marked increase in T cell and B cell infiltration on-treatment. Left panel: representative mIF images demonstrating multiple immune cell markers in the tumor and non-tumor regions.

Upregulation of Immuno-suppressive Genes/ Pathways Associated with Unfavorable Outcome

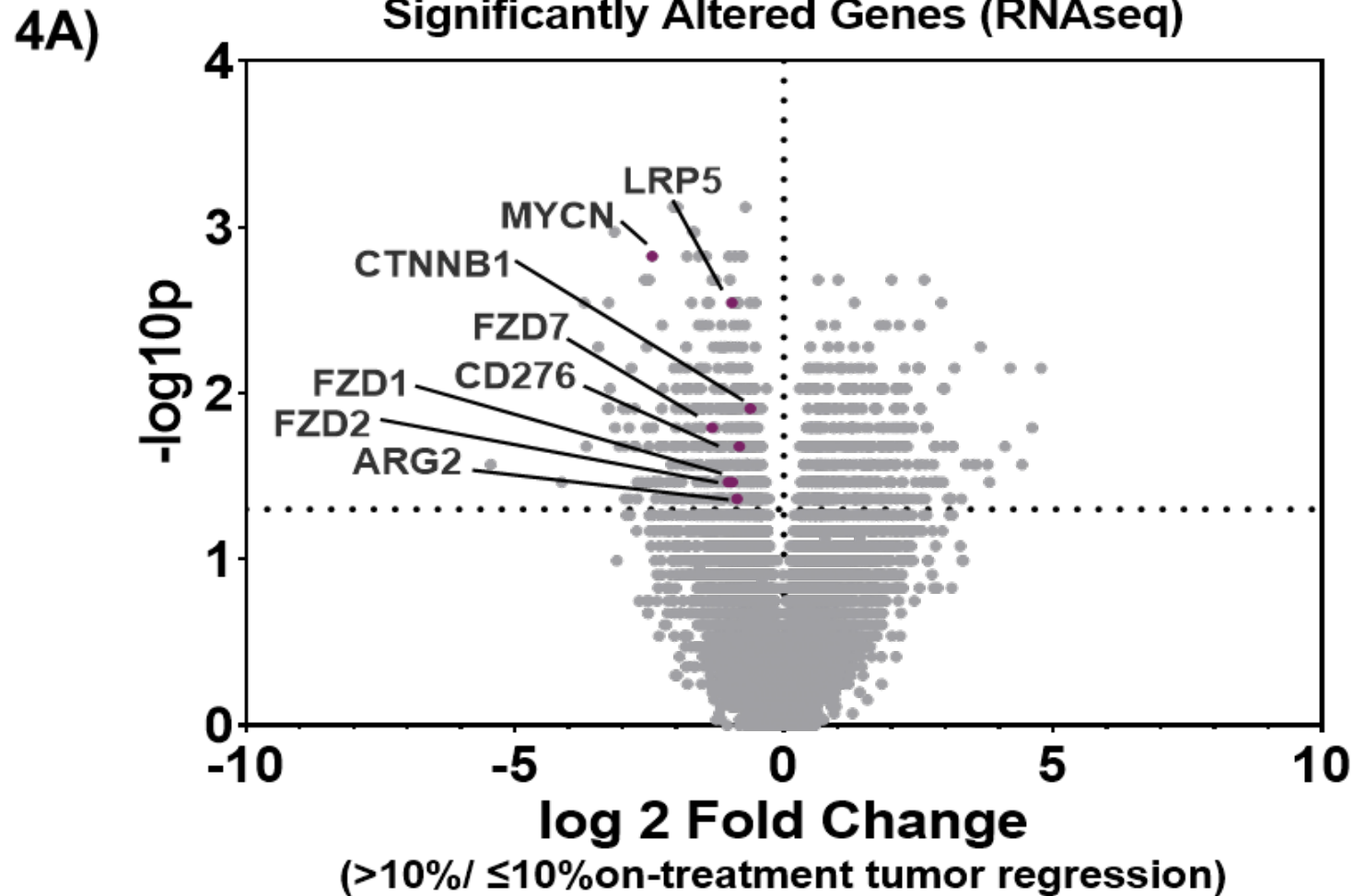


Figure 4A) Volcano plot representing the log2 fold-change of the mean expression of genes in the tumor of patients with >10% on-treatment tumor regression vs. those with ≤10% tumor regression. The $-\log_{10}$ probability (p) is calculated using Mann-Whitney U test.

Upregulation of Immuno-suppressive Genes/ Pathways Associated with Unfavorable Outcome

4B)

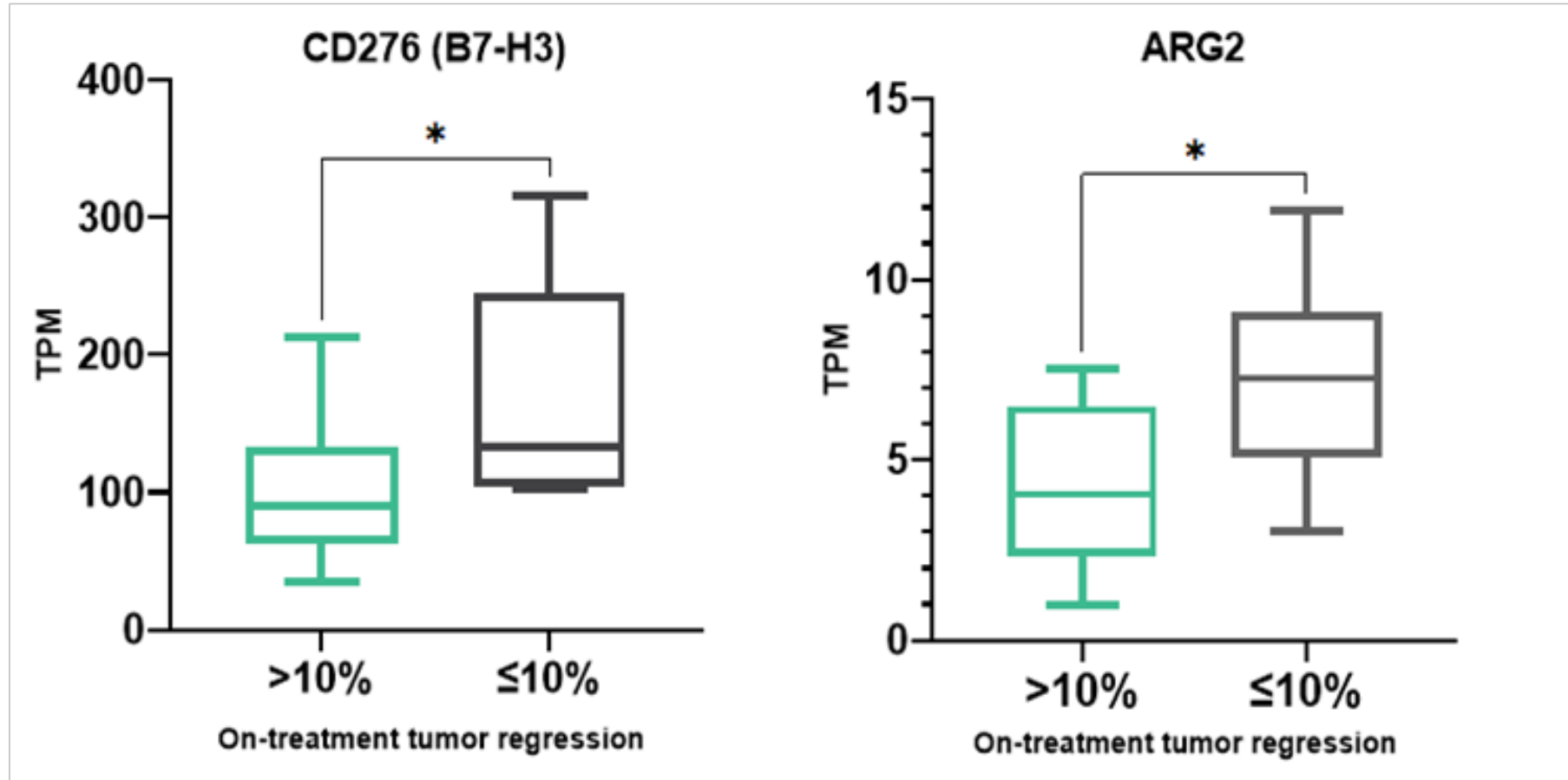
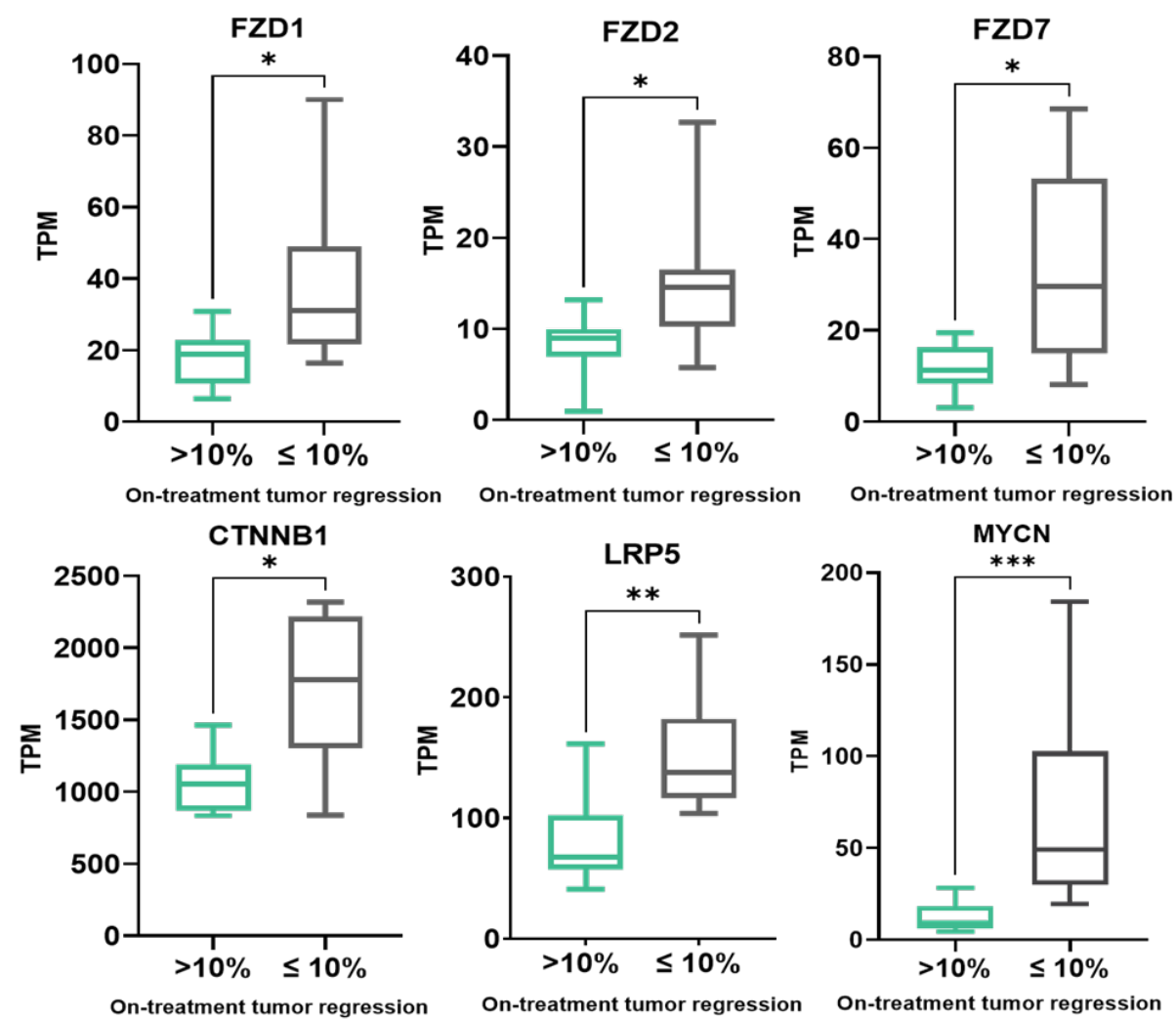


Figure 4B) Box-plots representing significantly higher pre-treatment levels of known immuno-suppressive genes (CD276, Arg2) in the tumor of patients with negligible anti-tumor activity (≤10% tumor regression).

Upregulation of Immuno-suppressive Genes/ Pathways Associated with Unfavorable Outcome

4C) WNT-β-Catenin Signaling Genes



Box-plots representing significantly higher pre-treatment levels of known signaling pathway (Figure 4C, representative WNT-β-Catenin signaling intermediates) in the tumor of patients with negligible anti-tumor activity (≤10% tumor regression).

Conclusion

- **Potential biomarkers for MVP-S response in ovarian cancer were identified by comprehensive integrated analysis**
 - Higher levels of T and B cell tumor infiltration was associated with anti-tumor activity,
 - MVP-S treatment induced strong increase in T and B cell tumor infiltration compared to the pre-treatment levels in a patient with durable clinical benefit underscoring the importance of these biologies,
- **Differential gene expression analysis of pre-treatment tumors also identified genes and pathways enriched in non-responding patients**
 - Immunosuppressive genes are overexpressed in non-responders as compared to responders,
 - Known mechanisms of primary resistance to immunotherapies such as WNT- β - Catenin signaling is also enriched in non-responders,
- **These findings suggests that immunogenic/ inflamed tumors are more susceptible to the MVP-S treatment.**

Contact Information

Corresponding Author: ybramhecha@imv-inc.com

ClinicalTrials.gov Identifier: NCT02785250

Study sponsored by IMV Inc.

Sincere acknowledgement to all study subjects and their families as well as teams of all the participating institutions across the USA and Canada.