Infiltration of tumor by T cells following treatment with DPX-Survivac and intermittent low dose cyclophosphamide (CPA) leads to clinical responses in advanced recurrent ovarian cancer (OvCa)

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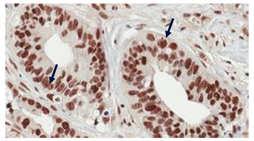
Abstract # 6075

DPX-Survivac: A novel T cell activating therapy

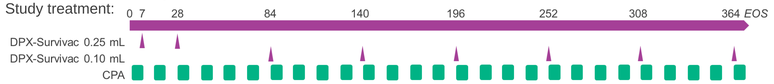
- Designed to elicit an effective immune response against survivin expressing tumors
- Unique mechanism of action (MOA) facilitates active and sustained uptake of target peptides by APC at the injection site
- APCs subsequently present the antigen in local lymph nodes generating *de novo* survivin-specific T cells
- T cells traffic to distant tumor sites and elicit effective tumor cell death
- DPX-Survivac is used in combination with intermittent low dose CPA which acts as an immunomodulator of T cell responses



Survivin-specific T cells detected by immunohistochemistry (IHC) in a subject with ovarian cancer

Study Design

- Multicenter Phase 2, ongoing in the United States and Canada
- Primary endpoints are ORR, DCR, and safety
- Secondary endpoints include cell mediated immunity, immune cell infiltration in paired biopsy samples, DOR, TTP, OS, and biomarker analyses
- Study treatment:



Baseline Characteristics

- 4 of 22 subjects remain active on study

Parameter		All n (%)
N	-	22
Age (years)	Median	58
	Range	38 - 78
Race	Caucasian	14 (63.6)
	Black / AA	0 (0.0)
	Asian	4 (18.2)
	Other	4 (18.2)
BRCA mutation status	Positive	4 (18.2)
	Negative	8 (36.4)
	Unknown	10 (45.5)
Stage at initial diagnosis	1-2	1 (4.5)
	3-4	21 (95.5)
Histology	High grade serous	21 (95.5)
	Carcinosarcoma	1 (4.5)
Prior lines of systemic therapy	1 - 2	10 (45.5)
	≥ 3	12 (54.5)
Prior therapy includes	Anti-VEGF	7 (31.8)
	PARP inhibitor	13 (59.1)
Sensitivity to most recent platinum	Sensitive	9 (40.9)
	Resistant/ refractory	13 (59.1)
Best response to most recent platinum	Unknown	2 (9.1)
	Progressive disease	5 (22.7)
	Stable disease	8 (36.4)
	Partial response	5 (22.7)
	Complete response	2 (9.1)
ECOG	0	12 (54.5)
	1	10 (45.5)

Safety

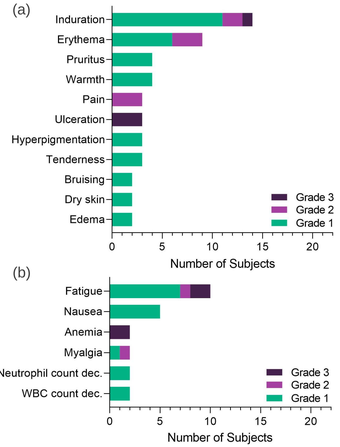


Figure 1: Treatment related (a) injection site reactions and (b) systemic AE occurring in 2 or more subjects

Translational Data

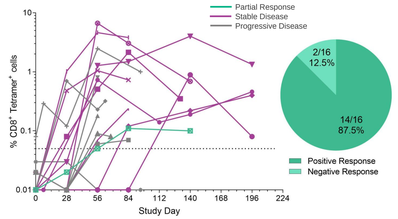


Figure 2: Increase in survivin-specific CD8⁺ T cell response was detected in PBMCs of 14/16 (87%) evaluable subjects as assessed by the *in vitro* MHC-tetramer assay.

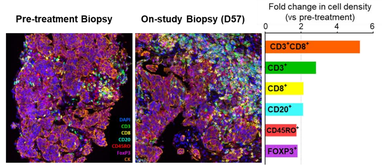


Figure 3: Fluorescence multiplex IHC analyses from a representative subject demonstrating a marked increase in tumor immune infiltration post-treatment (fold-change in the total tissue density).

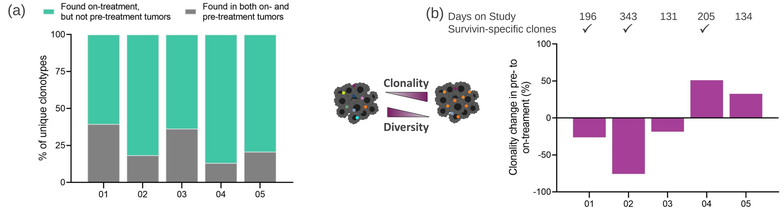


Figure 4: (a) Analysis of the TCRβ repertoire (5 subjects with stable disease) demonstrating the % of unique clonotypes found in the on-treatment tumor. (b) On-treatment change in clonality of the TCRβ repertoire, suggestive of early epitope spreading. Time on study and detection of survivin specific clones to date in day 56 samples are denoted with a check.

Conclusions

- Strong translational data link the observed clinical benefits with the unique MOA of DPX-Survivac; 87% of subjects showing survivin-specific effector immune response
- DPX-Survivac induced infiltration of survivin-specific T cell clones in tumors as early as day 56
- DPX-Survivac and intermittent low dose CPA shows promising clinical activity in recurrent, platinum resistant patients that warrants additional testing in advanced recurrent OvCa

Case Studies

76 y-o; high grade serous OvCa, stage 3c at diagnosis; BRCA1/2 negative; 5 prior lines of therapy, including bevacizumab and PARPi; refractory to last platinum; ECOG = 1; ongoing on study

(a)

Study Day	% Change at Target Lesions[a]	Non-Target Lesion[a]	RECIST
D56	-28.0	Pathologic	SD
D140	-34.5	Non-pathologic	PR
D196	-37.9	Non-pathologic	PR
D252	-21.7	Non-pathologic	PD[b]

[a] 2 target lesions: L dependent and L lateral pleural nodules
1 non-target lesion: Porta hepatis lymph node
[b] Progression at 1 target lesion, patient will undergo surgery and continue study due to clinical benefits

(b)

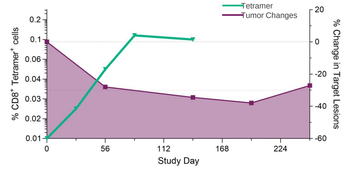


Figure 5: (a) Summary of RECIST v1.1 response showing changes from baseline. (b) Survivin-specific CD8⁺ T cells detected in PBMCs by *in vitro* MHC-tetramer assay plotted against the longitudinal % change in the target lesions.

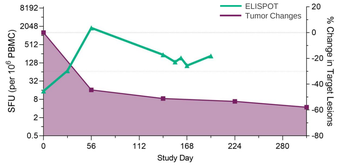
65 y-o; high grade serous peritoneal cancer, stage 3c at diagnosis; BRCA1/2 negative; 2 prior lines of therapy; platinum sensitive; ECOG = 1; discontinued due to injection site reaction

(a)

Study Day	% Change at Target Lesions[a]	Non-Target Lesions[a]	RECIST
D56	-44.4	Pathologic	PR
D140	-51.1	Pathologic	PR
D224	-53.3	Pathologic	PR
D308	-57.8	3/5 non-path	PR

[a] 2 target lesions: R external iliac and R deep inguinal lymph nodes
5 non-target lesions: all lymph nodal

(b)



(c)

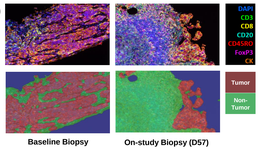
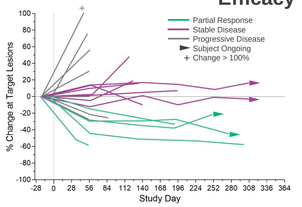


Figure 6: (a) Summary of RECIST v1.1 response showing changes from baseline. (b) Survivin-specific T cells detected in PBMCs by *ex vivo* IFN-γ ELISPOT plotted against the longitudinal % change in the target lesions. (c) Fluorescence mIHC analyses demonstrating marked increase in tumor immune infiltration post-treatment. The bottom panels highlight the tumor and non-tumor areas based on the cytokeratin staining (analysis by Akoya Biosciences).

Efficacy



- Efficacy demonstrated in both platinum sensitive and platinum resistant/refractory subjects (2 PR and 3 PR)
- Efficacy demonstrated in subjects with and without prior exposure to PARPi (2 PR and 3 PR) or bevacizumab (3 PR and 2 PR)

Figure 7: Spider plot depicting the on-study target lesion responses and preliminary sub-group analysis of best target lesion response.

Further Information

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ClinicalTrials.gov Identifier: NCT02785250

Study sponsored by IMV Inc.

Thank you to the study participants and their families as well as the study teams at Stanford University (O. Dorigo), Princess Margaret Cancer Centre (A. Oza), Oregon Health & Sciences University (T. Pejovic), and Georgia Cancer Center (S. Ghamande).