Safety and efficacy results of the combination of DPX-Survivac, pembrolizumab and intermittent low dose cyclophosphamide (CPA) in subjects with advanced and metastatic solid tumours (preliminary results)

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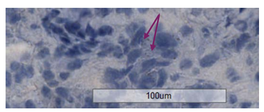
ABSTRACT #1208P

Background

DPX-Survivac is a novel and unique T cell activating therapy that generates *de novo* T cells against survivin. The oil-based product is administered by small-volume subcutaneous injection.

In Phase 1/1b maintenance studies in OvCa, it was shown that DPX-Survivac can generate a strong and specific T cell response against survivin and a long PFS interval has been observed in some subjects (> 7 years). In Phase 1b/2 studies the infiltration of tumours by survivin-specific T cells was correlated to tumour regressions. In all trials to date, DPX-Survivac shows a well-tolerated safety profile with the majority of events being grade 1 and 2 local site reactions.



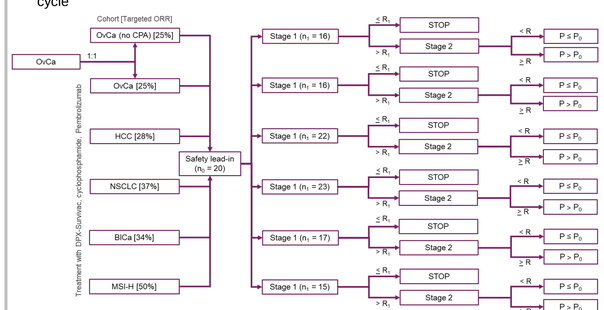
Survivin-specific T cells detected by immunohistochemistry in Phase 1b/2 OvCa trial subject

Pembrolizumab is a potent humanized immunoglobulin G4 (IgG4) monoclonal antibody (mAb) with high specificity of binding to the programmed cell death 1 (PD-1) receptor, thus inhibiting its interaction with programmed cell death ligand 1 (PD-L1) and 2 (PD-L2).

Intermittent low dose cyclophosphamide (CPA) is used as a "biological response modifier". Studies have shown that low does of CPA can have selective effects on the immune system that may augment the efficacy of immunotherapies.

Study Design

- Multicenter Phase 2 study, ongoing in Canada and the United States
- Primary objectives: objective response rate (ORR) using RECIST v1.1 and safety
- Secondary objectives: ORR, DoR, DCR, and PFS using iRECIST; overall survival; comparison of ORR for ovarian cancer treatment arms
- Exploratory objectives: changes in immune cell infiltration; assessment of potential biomarkers; peripheral levels of cell mediated immunity; patient reported outcomes
- Treatment: DPX-Survivac 2 x 0.25 mL SC q3w followed by up to 11 x 0.1 mL q9w; oral CPA 50 mg BID on alternating weeks; pembrolizumab 200 mg IV on day 1 of every three-week cycle



n = number of subjects; P = alternative hypothesis; P_0 = null hypothesis; R = minimal number of responders

Demographics

Table 1: Baseline subject demographics and disposition (N=15)

Parameter	Statistic	All n (%)	OvCa (+CPA)	OvCa (-CPA)	HCC	NSCLC	BlCa	MSI-H
N	-	15	4	4	2	2	2	1
Age (years)	Median	71	57	69	81	72	72	71
	Min, max	45-85	45-68	50-85	79-83	71-73	66-77	-
Sex	Male	5 (33.3)	0	0	2 (100)	1 (50.0)	2 (100)	0
	Female	10 (66.7)	4 (100)	4 (100)	0	1 (50.0)	0	1 (100)
Race n (%)	White	13 (86.7)	3 (75.0)	4 (100)	2 (100)	1 (50.0)	2 (100)	1 (100)
	Black or African American	1 (6.7)	1 (25.0)	0	0	0	0	0
	Asian	1 (6.7)	0	0	0	1 (50.0)	0	0
ECOG	0	10 (66.7)	3 (75.0)	3 (75.0)	2 (100)	1 (50.0)	0	1 (100)
	1	5 (33.3)	1 (25.0)	1 (25.0)	0	1 (50.0)	2 (100)	0
Number of previous lines of treatment	0	2 (13.3)	0	1 (25.0)	0	0	1 (50.0)	0
	1	4 (26.7)	1 (25.0)	0	1 (50.0)	1 (50.0)	0	1 (100)
	2	2 (13.3)	1 (25.0)	0	0	0	1 (50.0)	0
	3	2 (13.3)	1 (25.0)	0	1 (50.0)	0	0	0
	≥ 4	5 (33.3)	1 (25.0)	3 (75.0)	0	1 (50.0)	0	0
Receipt of Platinum?	Yes	11 (73.3)	4 (100)	3 (75.0)	0	2 (100)	1 (50.0)	1 (100)
	No	4 (26.7)	0	1 (25.0)	2 (100)	0	1 (50.0)	0
Receipt of Prior Checkpoint Inhibitor?	Yes (exposed)	3 (20.0)	0	0	0	2 (100)	1 (50.0)	0
	No (naïve)	12 (80.0)	4 (100)	4 (100)	2 (100)	0	1 (50.0)	1 (100)
Disposition	On treatment	13 (86.7)	4 (100)	4 (100)	2 (100)	1 (50.0)	2 (100)	0
	Discontinued	2 (13.3)	0	0	0	1 (50.0)	0	1 (100)
Reason for Discontinuation	Progression	1 (6.7)	0	0	0	1 (50.0)	0	0
	Withdrew consent	1 (6.7)	0	0	0	0	0	1 (100)

Tumour Infiltration

- On-treatment increase in diversity of tumour infiltrating T cells observed in biopsy samples

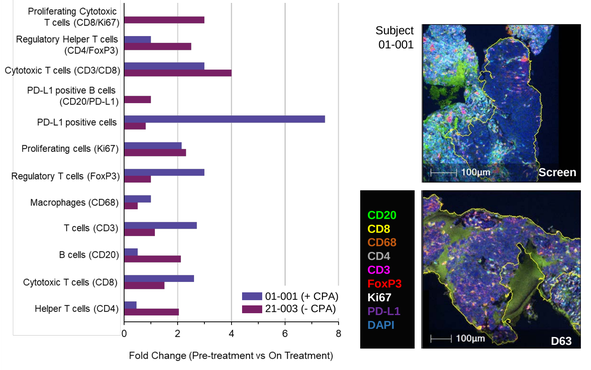


Figure 1: Treatment-induced increases in tumour immune infiltration demonstrated by multiplex IHC. Fold changes in pre-treatment and on-treatment (D56-D70) biomarker infiltration of two OvCa subjects (left) and representative images from one subject (right).

Safety

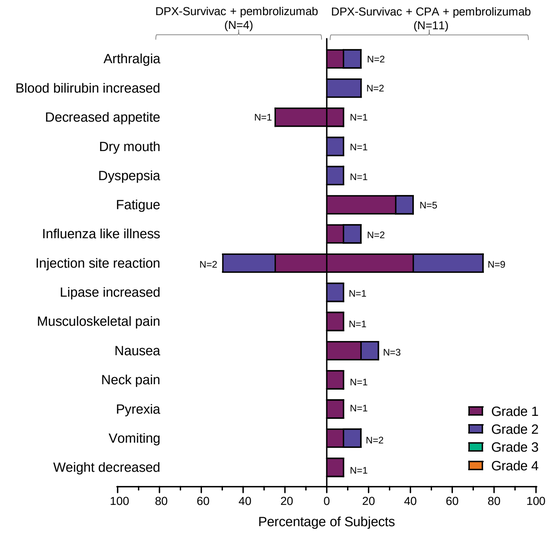


Figure 2: Treatment-related adverse events occurring in at lease one subject. AE are counted once per subject at the highest grade observed.

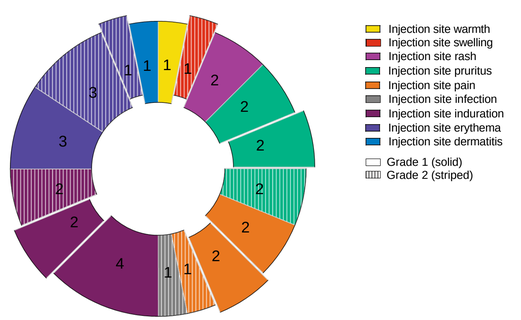


Figure 3: Summary of reactions occurring after injection with one or more doses of DPX-Survivac. Events are shown once per subject and at the highest grade observed. Pull outs represent events occurring in subjects not receiving CPA.

Response

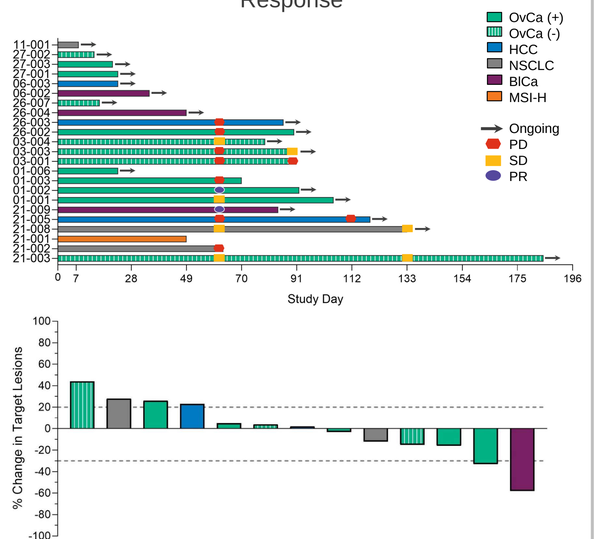


Figure 4: Duration of treatment (top) and waterfall analyses (bottom) of best on-study clinical response by RECIST v1.1 for evaluable study subjects.

Conclusions

- 23 subjects have been enrolled at time of cut-off in recurrent ovarian cancer, hepatocellular, non-small cell lung cancer, bladder cancer and MSI-H cancers
  - 19 subjects received DPX-Survivac, pembrolizumab, CPA and 4 DPX-Survivac with pembrolizumab
- Preliminary results from 1st on study scan show tumour reduction in subjects with ovarian, non-small cell lung and bladder cancer, with partial responses observed in 2 subjects to date
- T cell infiltration observed in subjects with tumour reduction after treatment
- Ovarian cancer subjects were randomized to treatment +/- CPA; tumour control and reductions are observed in both groups
- Treatments have been well tolerated with no Grade 3-4 events reported
- No irAE have been reported to date

Further Information

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Conflict of Interest: HC, EC, VC have no conflict of interest to declare. JS has stock or ownership interests in Abbvie, Abbott Laboratories, Bristol-Myers Squibb, Intuitive Surgical, Johnson & Johnson, Merck; a consultancy or advisory role with Tempus; and an other relationship with Dialectic Therapeutics. SF, LDM, YB, RC, GNR are all employees of IMV Inc.. MC is an employee of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.