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2022 ASCO® ANNUAL MEETING

UHN Princess Margaret Cancer Centre

UNIVERSITY OF TORONTO

PEmbrolizumab, Maveropepimut-**S**, and low-dose **C**yclophosphamide in advanced epithelial **O**varian cancer: Results from phase 1 and expansion cohort of **PESCO trial**

Ana Veneziani[1], Stephanie Lheureux[1], Husam Alqaisi[1], Gita Bhat[1], Ilaria Colombo[2], Eduardo Gonzalez[1], Sara Newton[1], Anthony Msan[1], Judy Quintos[1], Janelle Ramsahai[1], Robert C Grant[1], Neesha C. Dhani[1], Lisa Wang[1], Pamela Ohashi[1], Douglas Millar[1], Valerie Bowering[1], Amit M. Oza[1];

[1]Princess Margaret Cancer Centre, University Health Network, Toronto, Canada

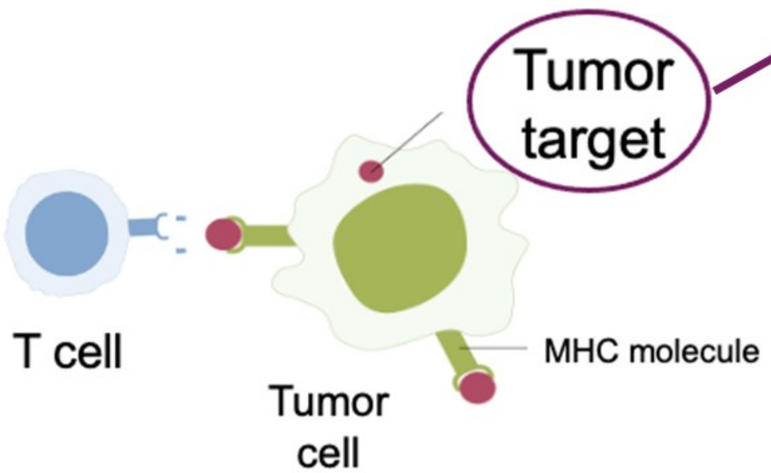
[2]Oncology Institute of Southern Switzerland

PRESENTED BY: Ana Veneziani, MD

Vaccine Development: Target Identification

Cancer immunotherapeutic:

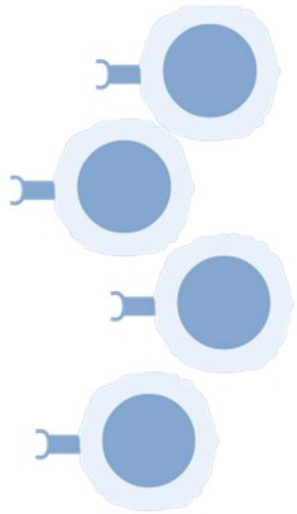
- Immunization against tumor target can boost T cells that recognize and destroy the tumor cells



Survivin

- Overexpressed in >90% of EOC.
- Plays a key role in apoptosis, proliferation, and angiogenesis.
- Correlates with progression and drug resistance.[1]

Vaccine



- **Maveropepimut-S (MVP-S),** formerly DPX- Survivac, leverages the DPX platform, a lipid-based delivery system, to educate a specific T cell-based immune response to 5 HLA-restricted peptides from survivin.

1.Berinstein NL, Karkada M, Oza AM, et al. *Oncoimmunology*, 2015.

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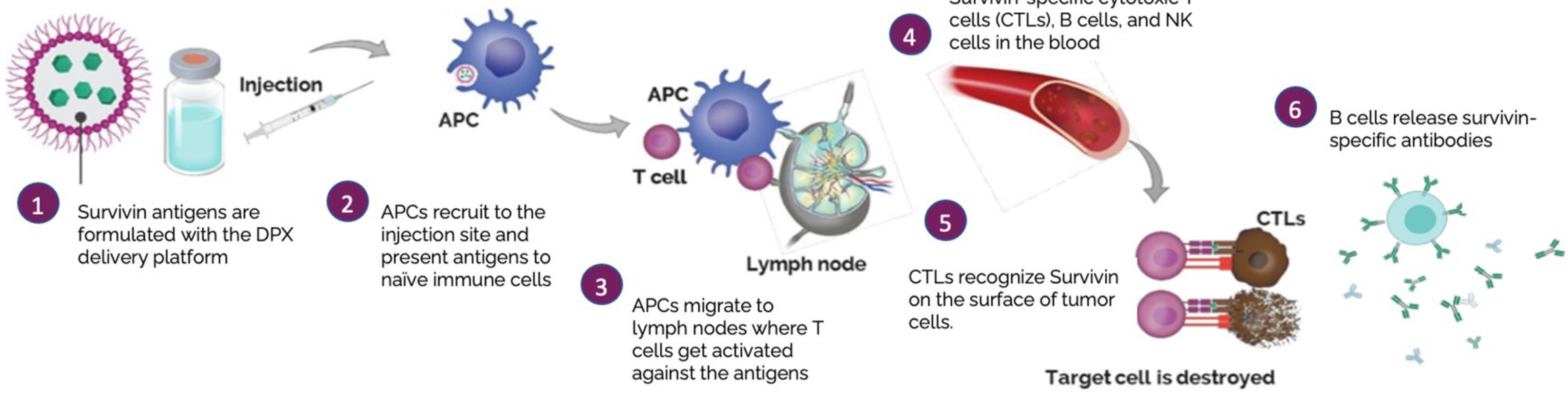
Background

- **MVP-S** incites a robust and persistent, survivin-specific immune response and promotes tumor T, B, and NK cell infiltration.
- Combination with Pembrolizumab and Cyclophosphamide:
  - Increase stimulation of effector T cells activity combined with T-regs inhibition.
- MVP-S shows clinical benefit in hematologic and solid cancers.



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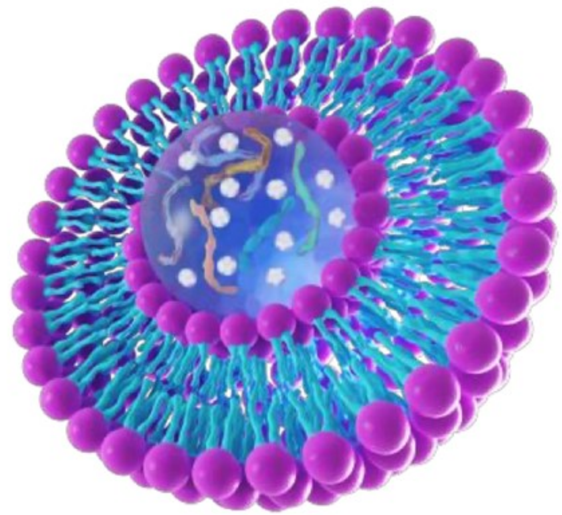
Background

- **Ovarian Cancer trials with Maveropepimut-S:**
  - **Phase I: Effect of CPA on the immunogenicity of MVP-S[1]**
    - 18 patients – Advanced OC with no PD post-chemotherapy.
    - Immune modulation with CPA enhanced the immunogenicity of MVP-S.
  - **Phase IB: MVP-S combined with CPA[2]**
    - 38patients – Stage IIC-IV recurrent OC
    - Safety confirmed. Signal of clinical activity.
    - Strong and sustained immune response across different dosing regimen
  - **Phase 2: MVP-S and CPA in recurrent epithelial OC (DeCidE trial)[3]**
    - 19 evaluable subjects - 5 PR + 10 SD.
    - Active immune response in majority of subjects tested, notably in responders and subjects with clinical benefit.



1. Neil Berinstein. J Clin Oncol 31, 2013 (suppl; abstr 3030)
2. Michelle Wilson. J Clin Oncol 32:5s, 2014 (suppl; abstr 5555)
3. Oliver Dorigo. J Clin Oncol 36, 2018 (suppl; abstr 5510)

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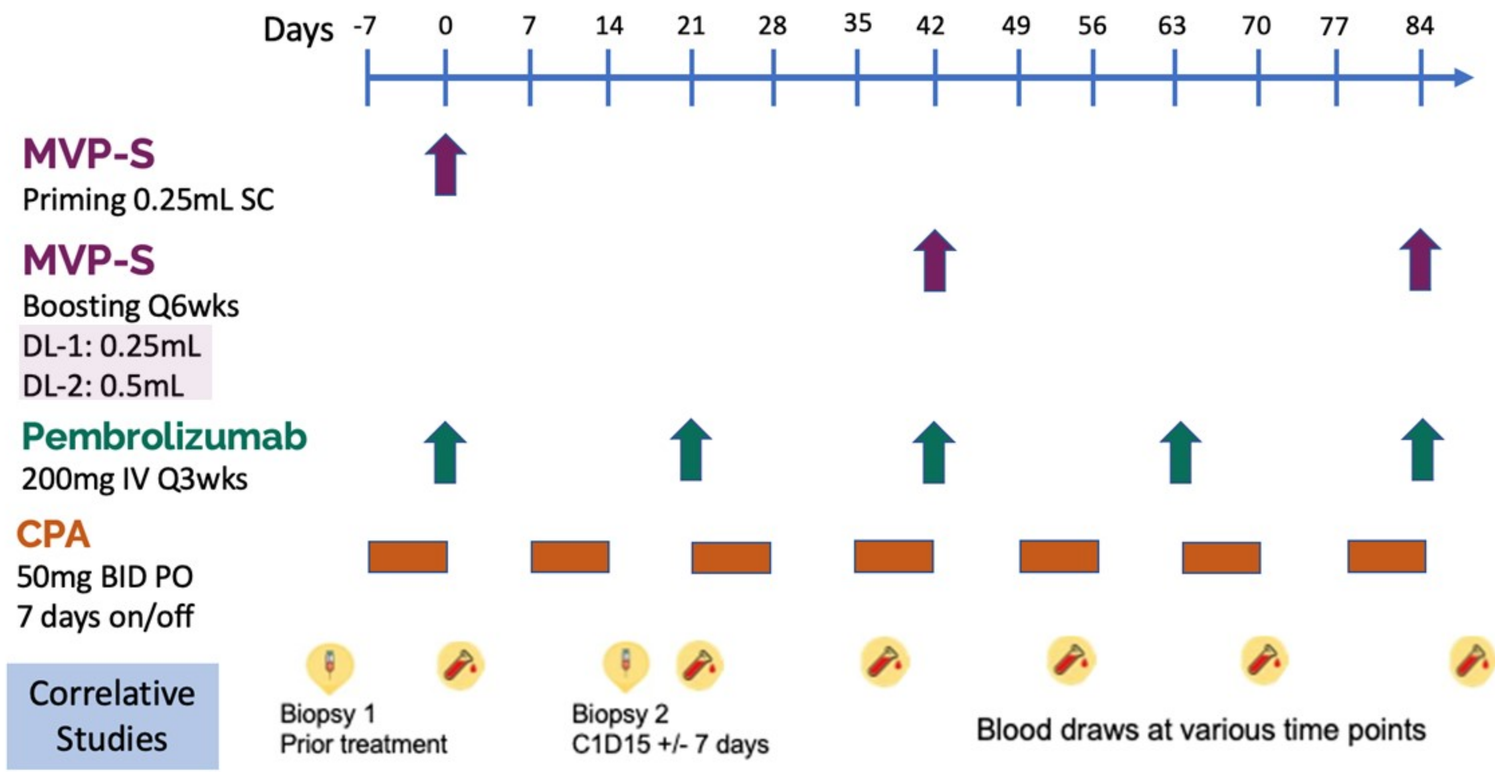
Study Design

Phase 1 Dose Escalation Cohort

Platinum-Resistant Epithelial Ovarian Cancer

• All histologies; Unlimited previous lines; Measurable disease; ECOG 0-1



RP2D

Phase 2 Dose Expansion Cohorts

Cohort A

Platinum-sensitive High-Grade Serous or Endometrioid cancer

No more than 4 prior lines of chemotherapy

Cohort B

Platinum-resistant High-Grade Serous or Endometrioid cancer

No more than 4 prior lines of chemotherapy

Cohort C

Other epithelial subtypes, irrespective of prior therapy and platinum free interval

Biostatistics

Phase I Dose Escalation Cohort

- 3 + 3 design.
- Sample size: 9-12 patients*.
- Evaluable for safety - at least one MVP-S and Pembrolizumab dose.
- Dose Level is safe if ≤ 1 DLT occur in 6 subjects.

*Additional patients could be included for safety review or to confirm RP2D.

Phase 2 Dose Expansion Cohort B

- 10 patients;
- Signal of activity: 2/10 PR or SD for 12 weeks.

Objectives

Primary

- Efficacy:

Clinical Benefit and ORR by RECIST 1.1.

Secondary

- Safety and RP2D.
- ORR by iRECIST.
- PFS and OS.

Exploratory

- Immune response during treatment.
- Activity in other epithelial subtypes.

Time cut off for this analysis: April 20th, 2022.

Study Population

Characteristics	Phase I (N=16)	Cohort B (N = 10)	All (N = 26)
Age, median (range)	57y (36-77)	61y (49-78)	60y (36-78)
ECOG			
0	-	1 (10%)	1 (4%)
1	16 (100%)	9 (90%)	25 (96%)
Race			
White	15 (94%)	5 (50%)	20 (77%)
Asian	1 (6%)	3 (30%)	4 (15%)
Unknown	-	2 (20%)	2 (8%)
Histology			
HGSOC	11 (69%)	10 (100%)	21 (80%)
Non-HGSOC	5 (31%)	-	5 (20%)
Clear Cell	2	-	
Clear cell + Endometrioid	1	-	
Endometrioid + Sarcoma	1	-	
Mucinous	1	-	

Characteristics	Phase I (N=16)	Cohort B (N = 10)	All (N = 26)
BRCA mutation			
Positive	4 (25%)	-	4 (15%)
Negative	8 (50%)	10 (100%)	18 (69%)
Unknown	4 (25%)	-	4 (15%)
MMR status			
Proficient	8 (50%)	1 (10%)	9 (35%)
Deficient*	2 (13%)	-	2 (7%)
Unknown	6 (38%)	9 (90%)	15 (58%)
Prior treatment lines, median (range)	4 (1,7)	4 (2,4)	4 (1,7)

*MMR deficient: 1 Clear Cell Carcinoma and 1 HGSOC

Treatment Related Adverse Events: Phase 1 Dose Escalation

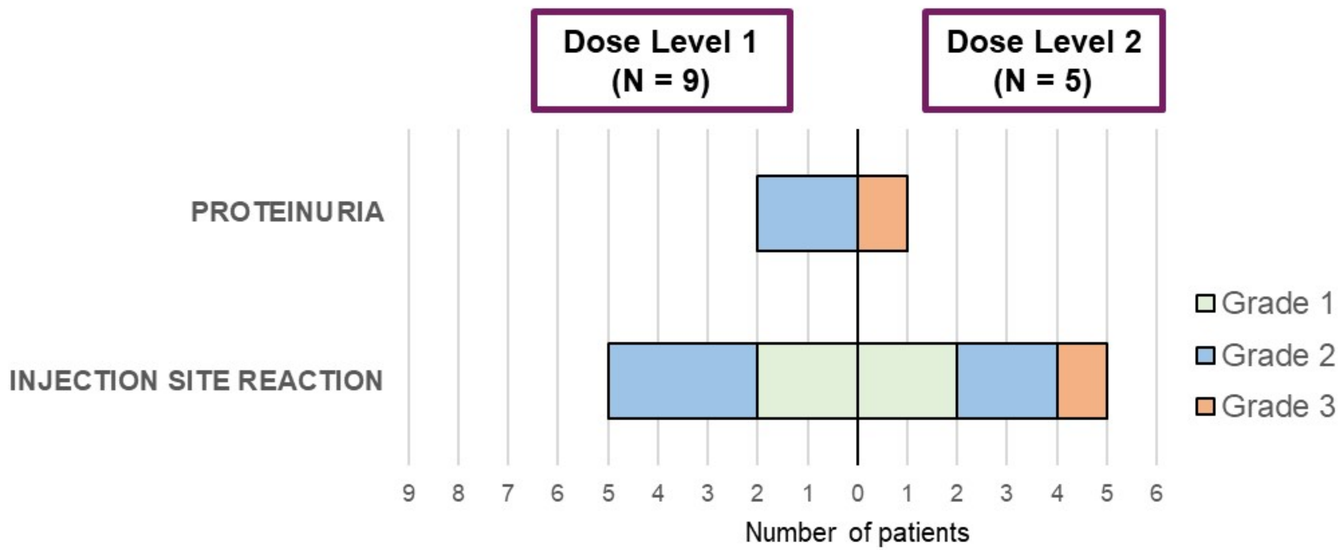
(CTCAE v4.03)

Dose Limiting Toxicities (DLTs)

- Grade 4 **non-hematologic** toxicity;
- ≥Grade 3 persistent **non-hematologic toxicity, laboratory value, or febrile neutropenia**;
- ≥Grade 2 **allergic or immune reactions**;
- ≥Grade 2 persistent **injection site skin ulceration** (> 1 wk.) that requires surgical intervention.

14 patients were evaluable for safety

- 3 Additional patients were enrolled to confirm the safety
- Nephritis (G3 proteinuria) and G3 ISR occurred in Dose level 2
- Dose Level 1 was selected as RP2D



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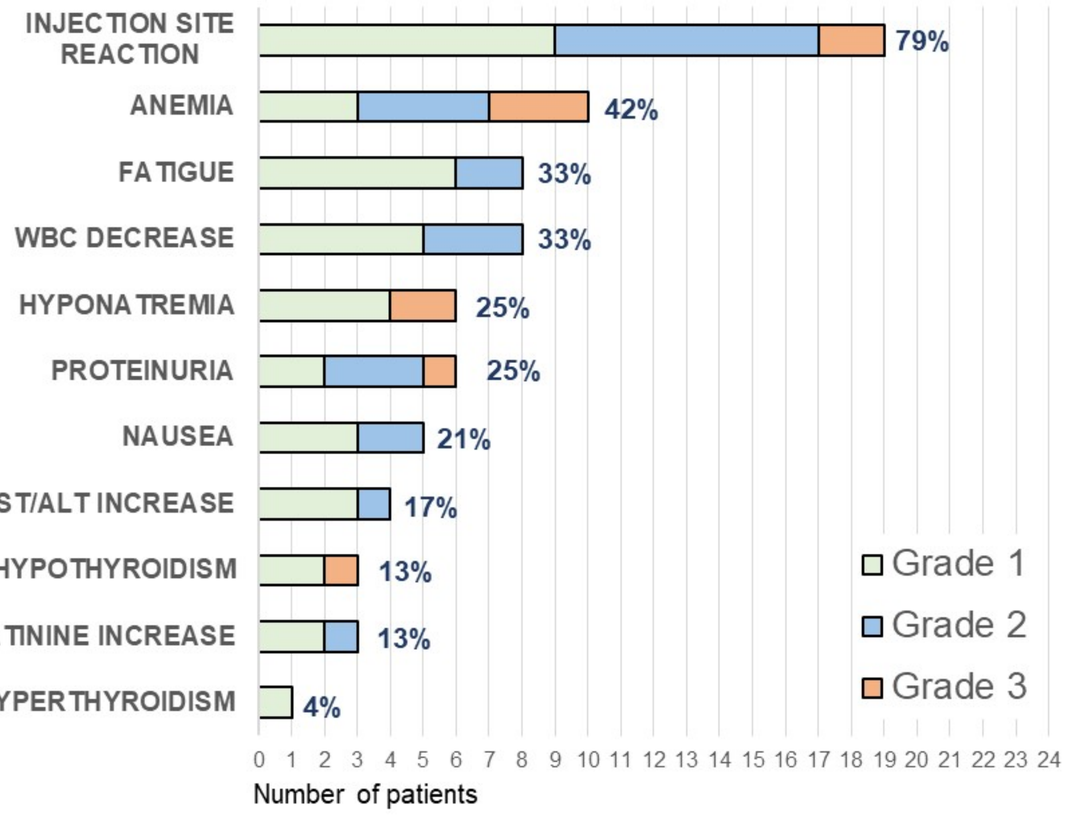
Treatment Related Adverse Events
(CTCAE v4.03)

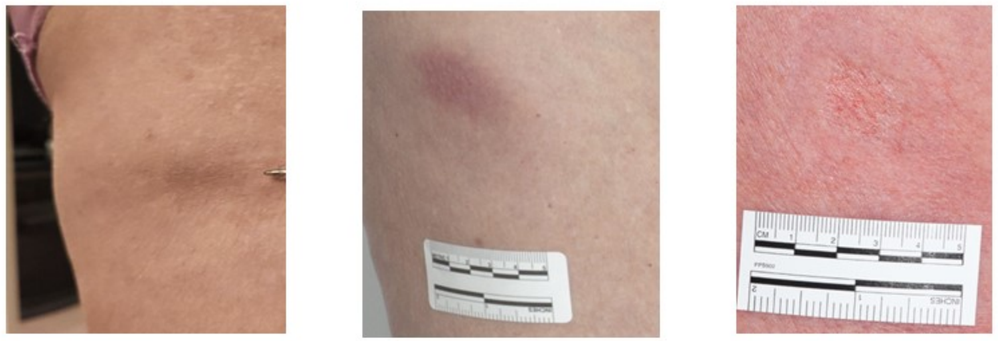
All Evaluable Patients (N=24)



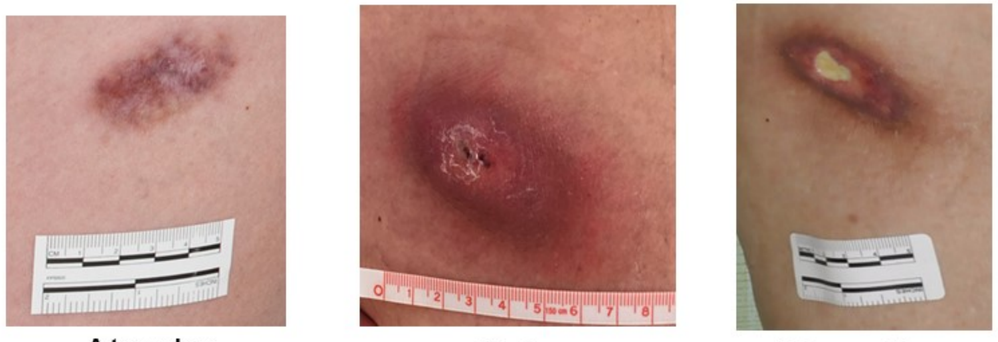
Events related to treatment occurring > 2 subjects or immune-related

Injection Site Reactions (ISR)

Most common Adverse Event: Grade 1-2 ISR



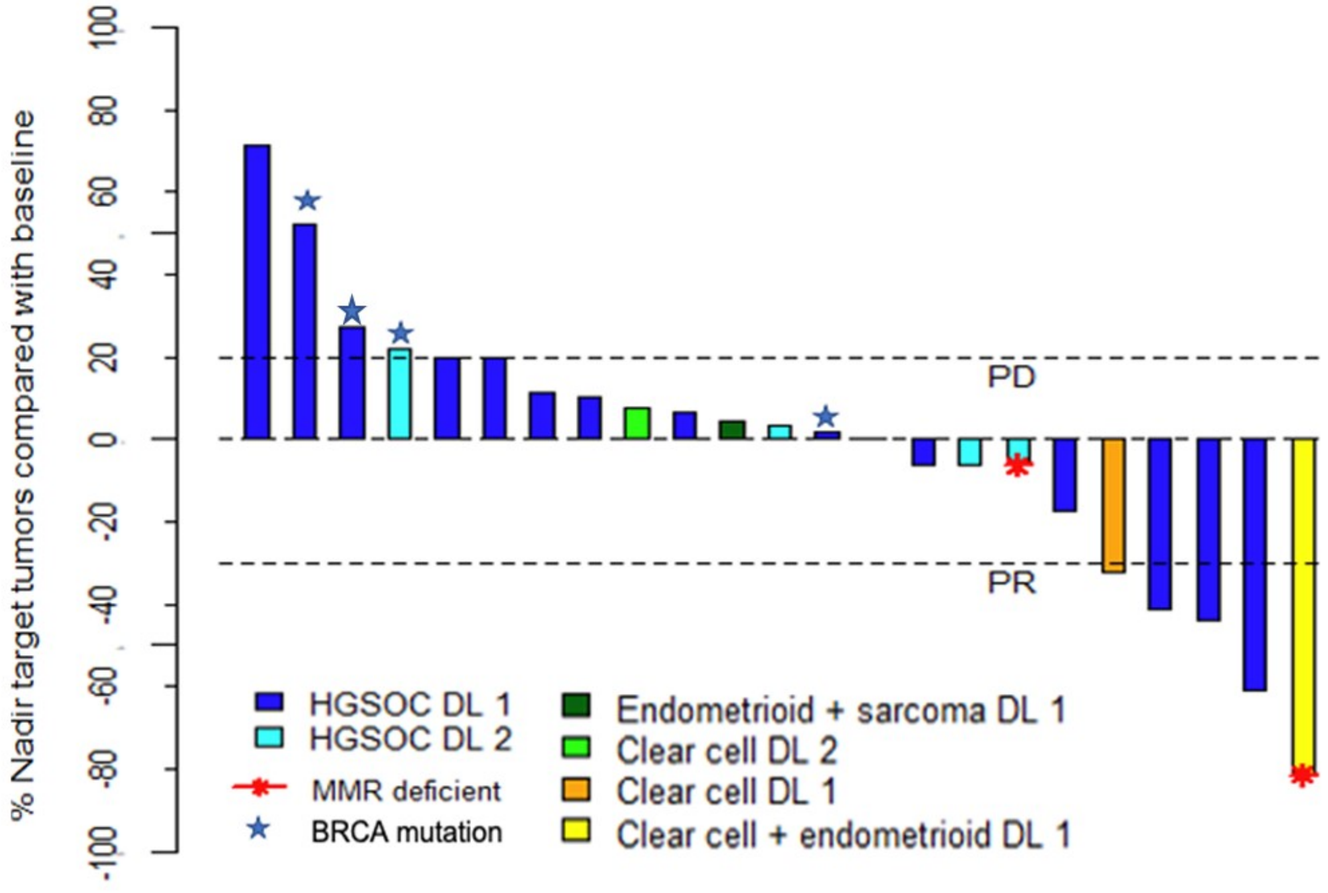
Induration | Erythema | Warmth



Atrophy | Pain | Ulceration

Best Overall Response – Target Lesions

All histologies (N=23)



- 23 patients were evaluable for efficacy.
- 4/23 patients: non-HGSOC histology.
- 3 Patients: Clear Cell Carcinoma.
  - 1/3 MMR deficient had CR.
- 4 BRCA mutations.
  - 3 PD and 1 SD.

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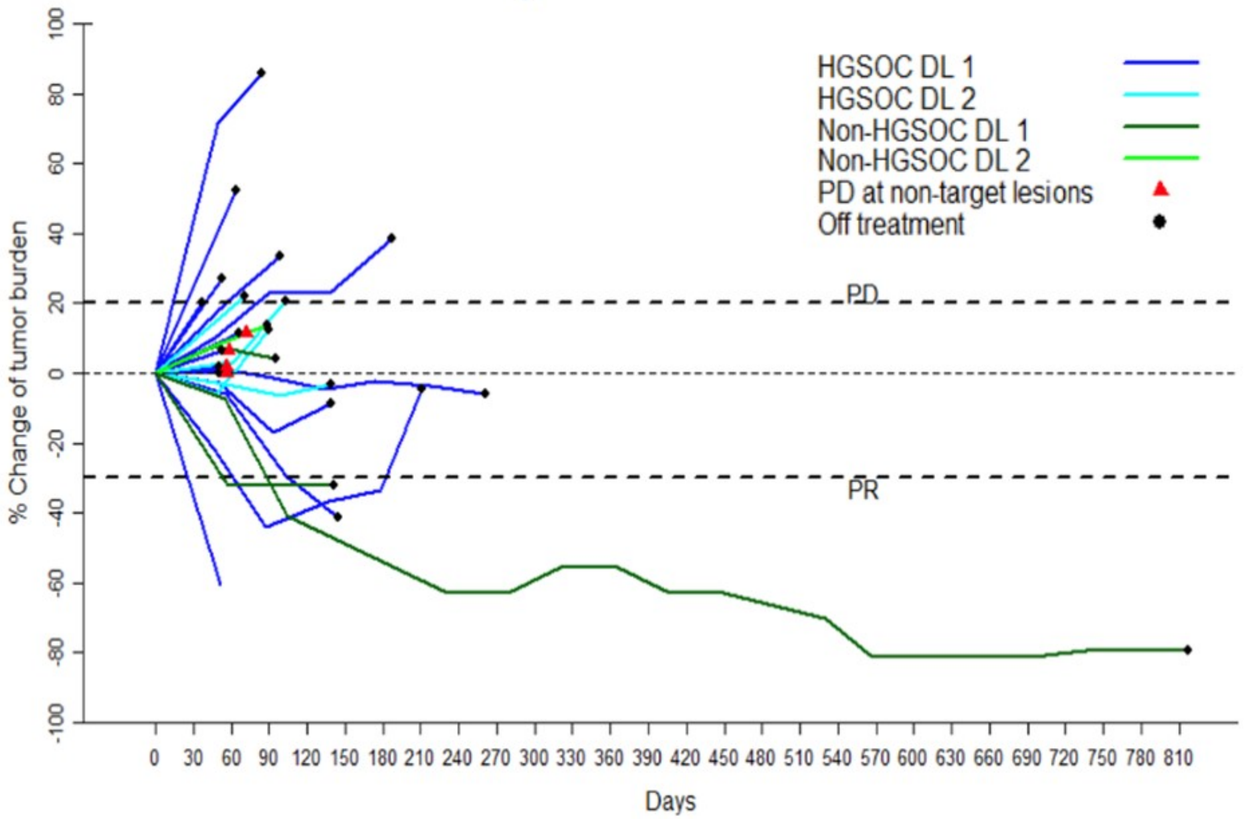
Best Overall Response – Target Lesions

All histologies (N=23)

	Phase I (N=13)	Cohort B (N = 10)	All (N = 23)
Vaccine Doses, median (range)	2 (1,4)	1 (1,5)	**2 (1,5)**
Cycles, median (range)	4 (1,34)	3 (2,9)	**4 (1,34)**
Best Response			
Complete Response	1	0	1 (4%)
Partial Response	2	2	4 (18%)
Stable Disease	7	5	12 (53%)
Disease Progression	3	3	6 (27%)

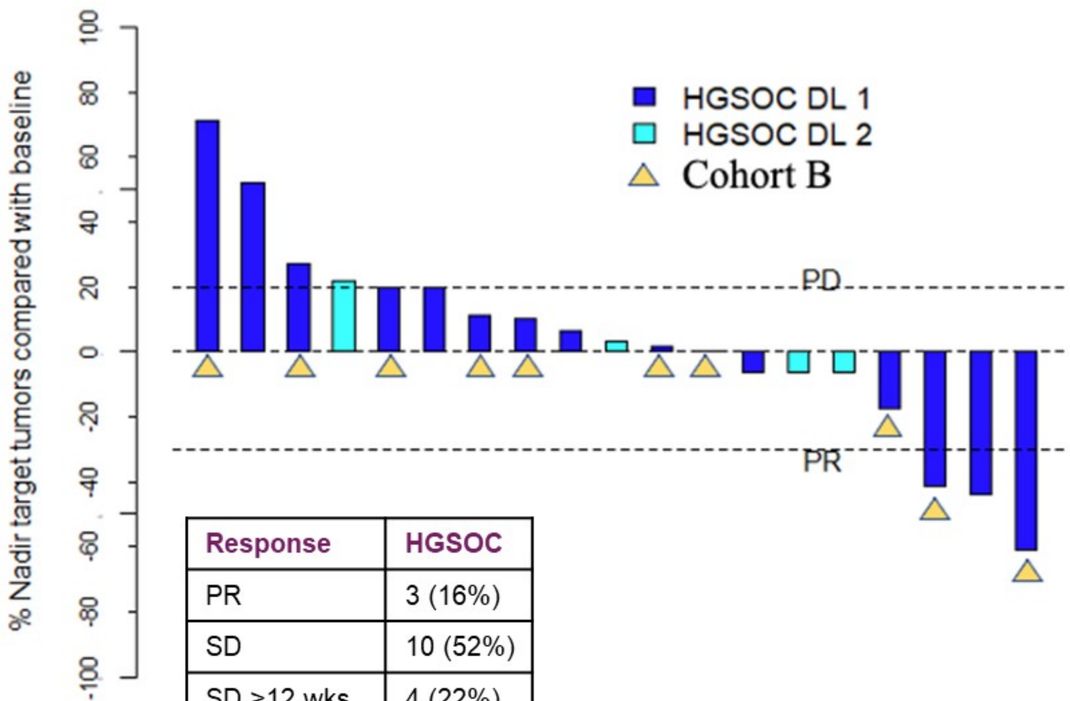
Response over time



Median follow-up: 12 months (range 5-27)

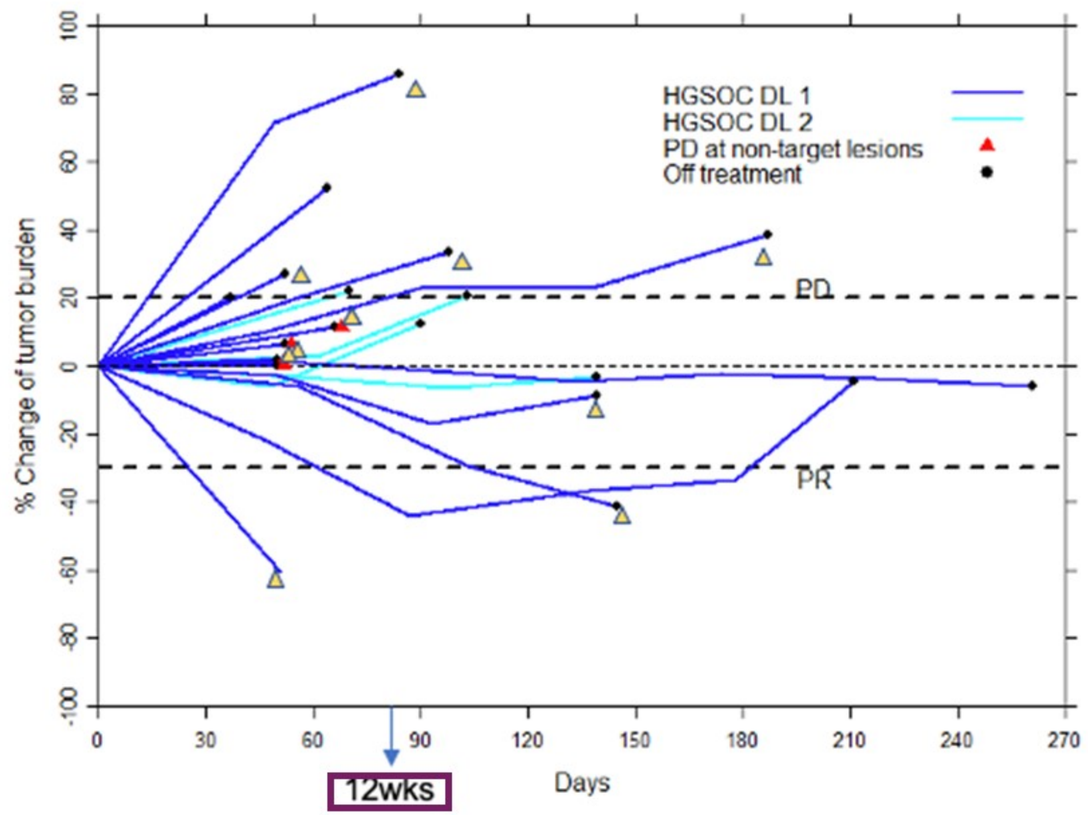
Best Overall Response – HGSOC

(N=19)



Response	HGSOC
PR	3 (16%)
SD	10 (52%)
SD >12 wks	4 (22%)
PD	6 (32%)

Response over time



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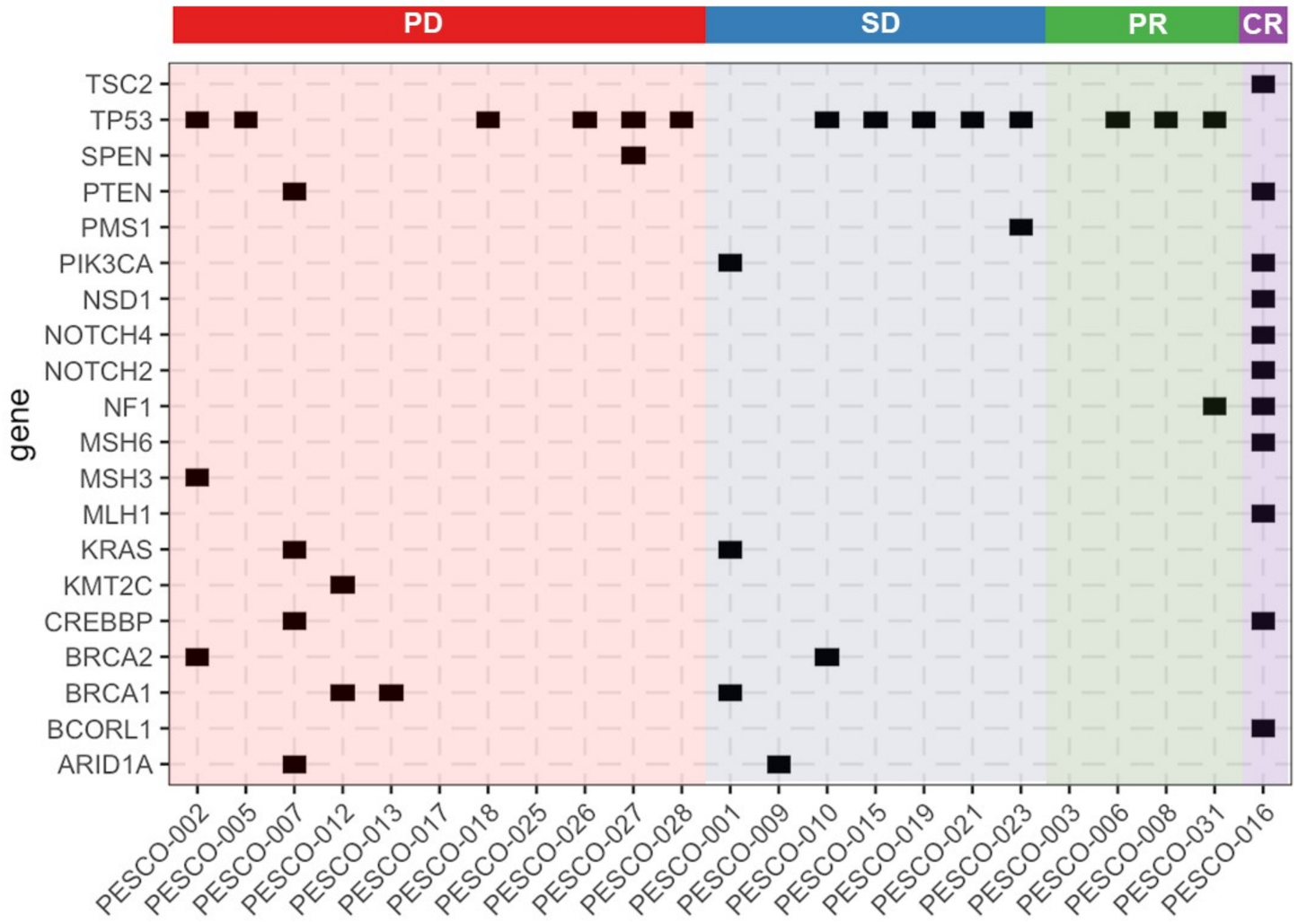
Ana Veneziani, MD.

Molecular Profiling and Best Response



- Tumor molecular profiling pre-treatment by NGS panel.
- Oncogenic mutations in 20 (87%) of 23 samples of all histologies.
- *TP53 mutation* in 14 patients (60%).
- 9 subjects with > 1 *mutation*.
- Complete responder is hypermutated.

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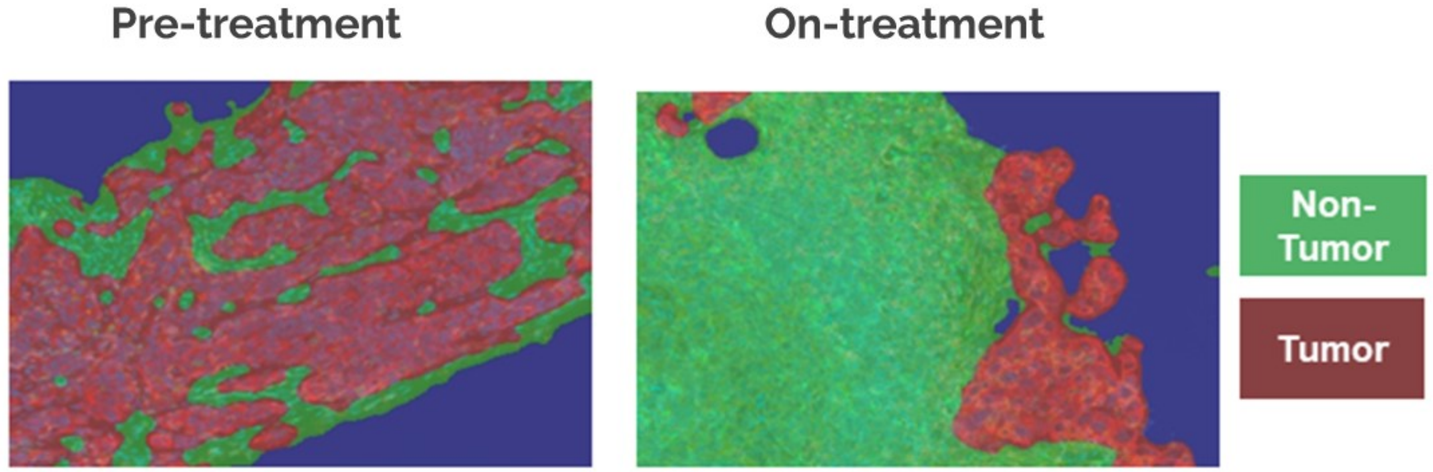
Previous Translational Studies with MVP-S

MVP-S induced immune response inclusive of T and B cells increase post treatment

- Robust, persistent, survivin-specific T cell responses.
- Infiltration of diverse survivin-specific T cell clones into tumor tissue.
- B cell infiltration into tumor on treatment.

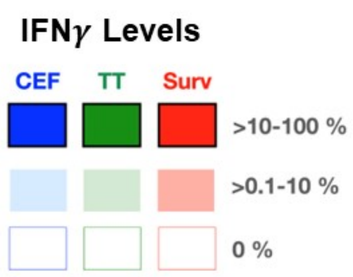


DeCide Ovarian Trial –SITC 2021

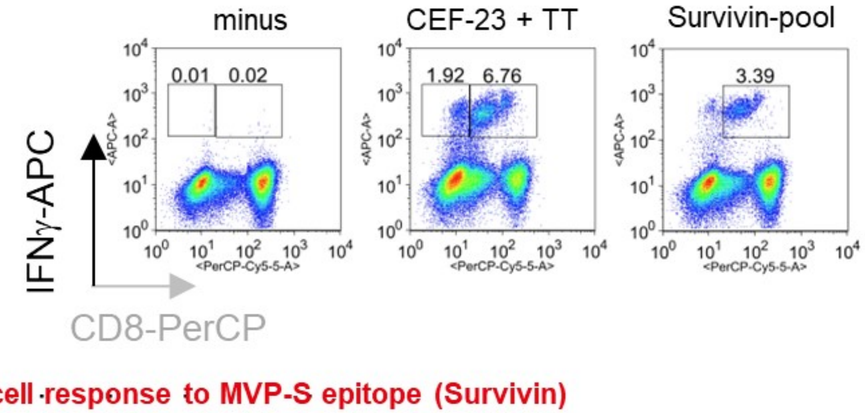
MVP-S epitope-specific T cell re-stimulation assay from PBMC: IFNγ levels (12 patients)

Patients were not screened for HLA matching

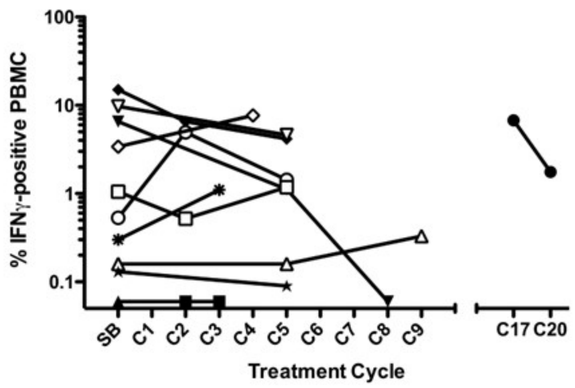
Correlation between immune and clinical responses



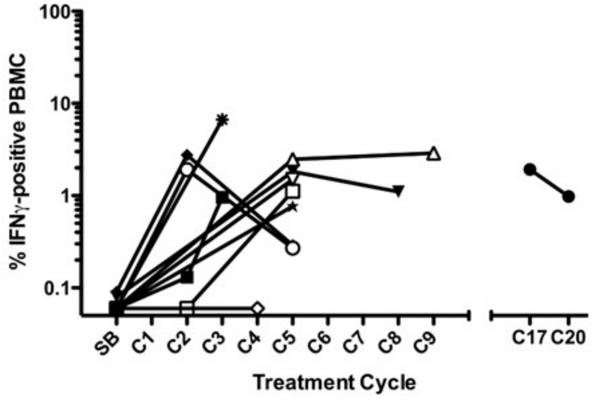
Re-stimulation Peptide pools Complete responder (Cycle 17)



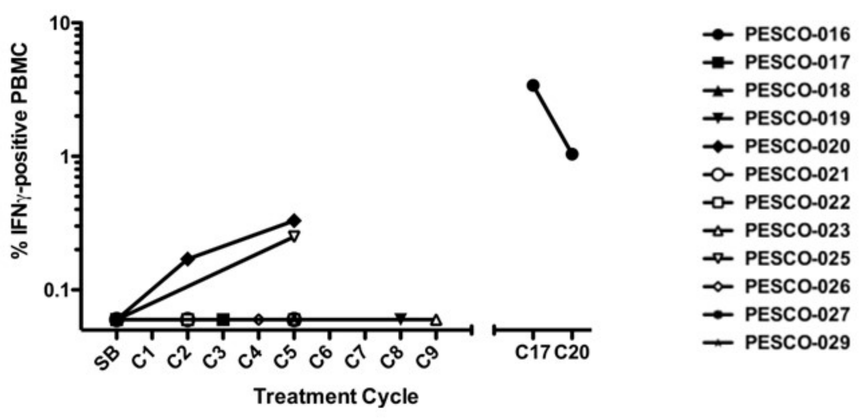
Memory response to CEF[1] epitope



CD4 T cell response to T helper epitope



CD8 T cell response to MVP-S epitope (Survivin)



1. CEF: Cytomegalovirus, Epstein-Barr virus, and Influenza virus
2. TT: T helper

Conclusions

- Combination of Pembrolizumab, Maveropepimut-S, and low-dose Cyclophosphamide was generally well tolerated.
  - The most common toxicity was Injection Site Reaction.
  - No AEs were qualified as DLT per protocol definition.
- Efficacy endpoint in the Phase 2 Expansion Cohort B was met:
  - Signal of activity: At least 2 PR or SD for 12 weeks
  - Cohort B: 2 PR and 3 SD, 2 of them for more than 12 weeks.
- Patients were not screened for HLA match.
  - Immune responses against survivin were detected.
  - Complete responder had a high and long-lasting response against Survivin.
- Low or negative immune responses.
  - HLA types or defects in CD8 T cell responses.
- Further analyses will explore if these results warrant a cohort with HLA matching.

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Acknowledgments

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