Clinical correlations and long-term survival in PROTA: platinum-resistant or refractory ovarian cancer treated with an oncolytic adenovirus encoding TNF and IL2 in combination with pembrolizumab

Abstract #1203P

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DoD Study ID: OC220391

Background

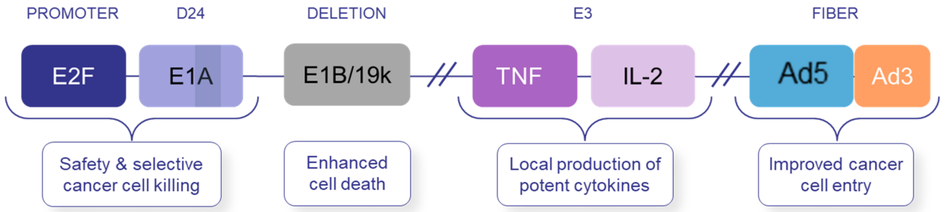

Figure 1 – Genetic structure of TILT-123 virus

- Platinum-resistant and refractory ovarian cancer present major therapeutic challenges, characterized by limited response rates to current treatments, particularly to immunotherapies including immune checkpoint inhibitors.
- TILT-123 (igrelimogene litadenorepvec) is an oncolytic adenovirus, engineered to improve T-cell therapies.
- In PROTA, phase 1a clinical trial, TILT-123 was evaluated in combination with anti-PD-1 pembrolizumab in patients with platinum resistant or refractory ovarian cancer.
- In this trial, 15 patients were treated with intravenous as well as intratumoral and/or intraperitoneal injections of TILT-123.

Trial design

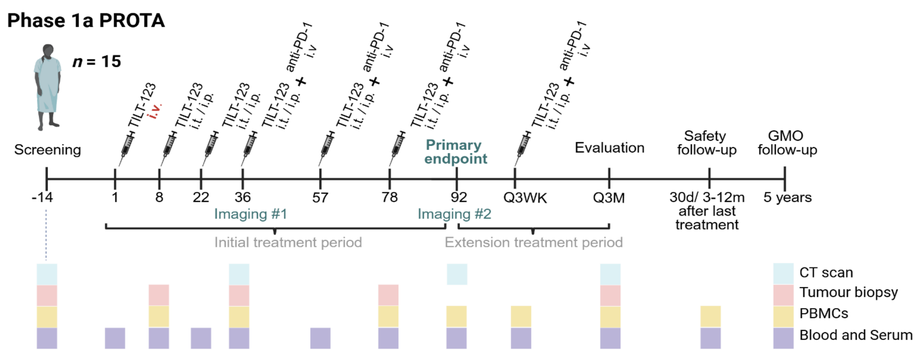

Figure 2 – Treatment schedule

	Virus i.v. dose (VP)	Virus i.t./i.p. dose (VP)	Pembrolizumab i.v. dose (mg)
Cohort 1	$3x10^{11}$	$1x10^{11}$	200
Cohort 2	$1x10^{12}$	$3x10^{11}$	200
Cohort 3	$2x10^{12}$	$3x10^{11}$	200
Cohort 4	$4x10^{12}$	$5x10^{11}$	200

Figure 3 – Dosing strategy for cohorts 1 to 4.

- On day 1: Patients receive an intravenous dose of TILT-123 ranging from $3x10^{11}$ to $4x10^{12}$ VPs.
- On days 8, 22, 36, 57, and 78: Patients receive intratumoral or intraperitoneal doses of TILT-123 ranging from $1x10^{11}$ to $5x10^{11}$ VPs.
- Every three weeks: Patients received 200mg intravenous doses of pembrolizumab at three-weeks intervals (Q3W) up to 2 years/35 cycles, starting on day 36.
- Samples collected included four tumor biopsies, seven serum samples, and five PBMC samples.

Patient demographics

Patient ID	Cohort	Age	ECOG status at baseline	Time since diagnosis (months)	Cancer type	Histological Subtype	Number of previous systemic treatments	Platinum status	ICI status	Best Overall response RECIST 1.1	Best Overall response iRECIST	OS (days)	Serum anti adenovirus antibodies at baseline
302-05	1	60	1	63	Fallopian tube cancer	HGSOC	7	Resistant	Naive	PD	iUPD	85	Negative
302-06	1	70	1	282	Epithelial ovarian cancer	LGSOC	12	Resistant	Naive	SD	iSD	306	Positive
301-01	1	71	1	30	Primary peritoneal cancer	HGSOC	4	Resistant	Naive	SD	iSD	77	Negative
301-02	2	61	1	13	Epithelial ovarian cancer	HGSOC	3	Resistant	Naive	SD	iSD	434	Positive
301-03	2	72	1	148	Epithelial ovarian cancer	HGSOC	12	Resistant	Naive	SD	iSD	122	Negative
301-04	2	58	1	62	Epithelial ovarian cancer	HGSOC	7	Resistant	Refractory	PD	iUPD	93	Positive
302-07	3	66	1	26	Fallopian tube cancer	HGSOC	5	Refractory	Naive	SD	iSD	190	Negatie
301-05	3	78	0	15	Epithelial ovarian cancer	HGSOC	1	Resistant	Naive	SD	iSD	571	Positive
302-09	3	51	1	80	Epithelial ovarian cancer	HGSOC	8	Refractory	Naive	PD	iUPD	280	Positive
302-10	4	54	0	59	Epithelial ovarian cancer	HGSOC	11	Resistant	Naive	SD	iSD	548*	Positive
301-10	4	58	0	48	Fallopian tube cancer	HGSOC	5	Resistant	Naive	PD	iUPD	304	Negative
302-11	4	36	0	45	Primary peritoneal cancer	LGSOC	9	Resistant	Naive	N/A	N/A	138	Negative
301-11	4	69	0	36	Epithelial ovarian cancer	Mucinous carcinoma	4	Refractory	Naive	PR	iPR	518*	Negative
301-12	4	73	0	20	Epithelial ovarian cancer	Carcinosarcoma	3	Refractory	Naive	SD	iSD	151	Positive
302-12	4	71	0	76	Primary peritoneal cancer	HGSOC	8	Resistant	Naive	SD	iUPD	105	Negative

Table 1– Demographics of patients enrolled in cohorts 1 – 4

*Patients still alive (06th March 2025)

- A total of 15 patients were enrolled onto the trial; median age was 66 years.
- Prevalence of cancer types: epithelial ovarian cancer (60%), fallopian tube cancer (20%), primary peritoneal cancer (20%).
- 27% were platinum refractory and 73% were platinum resistant.

Antitumor efficacy and OS data

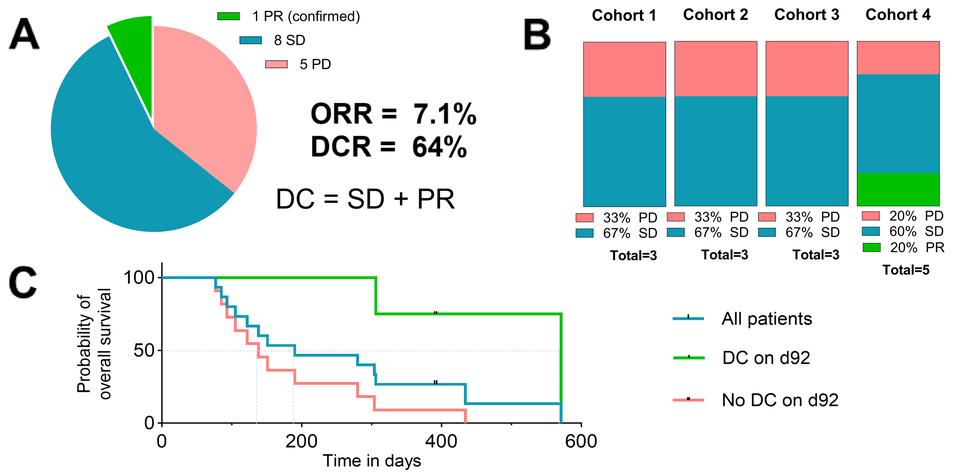

Figure 4 – Overall response rate, disease control rate, and overall survival summary for all patients.

A) Overall response rate (ORR) by RECIST1.1 included a confirmed PR, 8 SD, and 5 PD. Overall ORR was 7.1%, ORR in highest dose cohort was 20%, and exploratory disease control rate (SD+PR) was 64%.
B) RECIST1.1 response by dose cohort.
C) Kaplan-Meier graph showing overall survival for all patients, and comparisons between patients with and without disease control. Inter-group significance was calculated with log-rank test.

Detection of virus in tumors

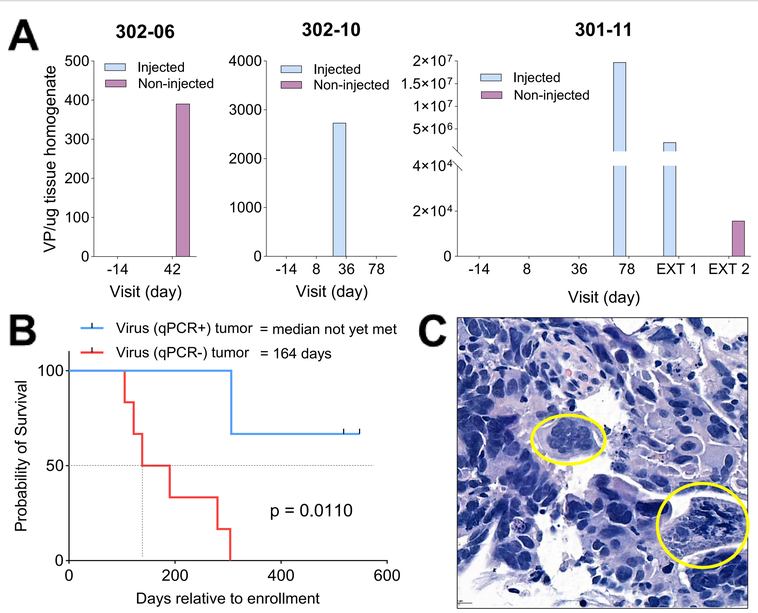

Figure 5 – Detection of TILT-123 DNA in tumors is associated with longer overall survival

A) qPCR analysis of tumor biopsies with primers targeting the IL-2/IRES region of TILT-123 demonstrating positivity in three patients.
B) Kaplan-Meier including overall survival for patients with virus positive versus virus negative tumors. Inter-group significance was calculated by log-rank test.
C) Hematoxylin and eosin staining of a tumor biopsy collected from patient 302-10 on day 36, demonstrating cytopathic effect as determined by a pathologist.

Clinical data

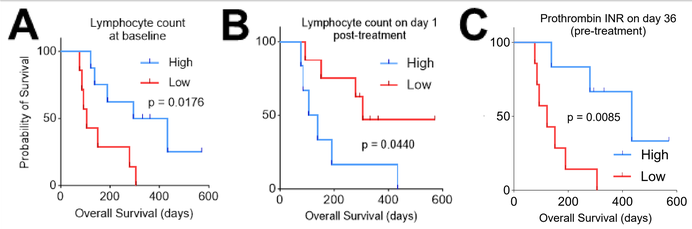

Figure 6 – Lymphocyte count at baseline and post-treatment, and prothrombin INR levels correlate with overall survival

A) A ≥median baseline lymphocyte count correlates with longer overall survival (369 days vs. 105 days, p = 0.0176).
B) Greater transient lymphocyte drop after therapy also links to longer overall survival (306 days vs. 121 days, p = 0.0262).
C) A ≥median prothrombin INR on day 36 correlates with overall survival (434 days vs. 122 days, p = 0.0085).

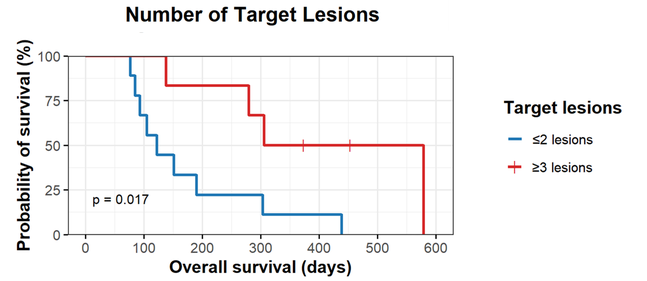

Figure 7 – Target lesion count correlates with longer overall survival

A) Patients with more than or equal to 3 RECIST 1.1 target lesions achieve longer overall survival (log-rank).

Conclusions

- ✓ **Median overall survival was 190 days overall, and 545 days in patients with disease control by day 92. 6 patients (40%) were alive after 300 days.**
- ✓ **Overall response rate was 20% in the highest dose cohort.**
- ✓ **Lymphocyte re-distribution from circulation may act as a marker of treatment benefit.**
- ✓ **Longer OS correlated with slower coagulation, and higher target lesion counts. These results may help identify patients likely to benefit from combined TILT-123 and pembrolizumab.**
- ✓ **A phase 1b is ongoing (NCT05271318).**

This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

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The presenting author has no COI to declare.