

1281P - Phase 1b study of igrelimogene litadenorepvec plus pembrolizumab and pegylated liposomal doxorubicin in platinum-resistant ovarian cancer: preliminary safety and efficacy results

M.S. Block¹, V. Cervera-Carrascon^{2,3}, J. Clubb^{2,3}, N. Ojala², D.C.A. Quixabeira^{2,3}, T. Kudling^{2,3}, S.A. Pakola², V. Arias², M. van der Heijden², E. Jirovec², D. Adamo¹, M. Chisamore⁴, C. Kistler¹, S. Sorsa¹, A. Hemminki^{2, 3, 5}

1) Mayo Clinic Cancer Center, Rochester, Minnesota, United States. 2) Cancer Gene Therapy Group, Translational Immunology Research Program, University of Helsinki, Helsinki, Finland. 3) TILT Biotherapeutics Ltd, Helsinki, Finland. 4) Merck & Co., Inc., Rahway, NJ, USA. 5) Comprehensive Cancer Center, Helsinki University Hospital, Helsinki, Finland



Background

Platinum-resistant ovarian cancer is associated with poor outcomes and limited treatment options. Oncolytic viruses may enhance antitumor immunity through tumor-selective lysis and induction of immune responses, providing a strong rationale for combination with immune checkpoint inhibitors and chemotherapy.

Igrelimogene litadenorepvec (TILT-123) is an oncolytic adenovirus expressing TNF and IL-2 that is designed to promote T-cell trafficking towards the tumor and intratumoral T-cell activation (Fig. 1). TILT-123 has been studied in combination with pembrolizumab to augment antitumor immunity in the phase 1a of the same study demonstrating adequate safety and signs of efficacy (Block M.S. et al. Nature Communications, 2025)

Pegylated liposomal doxorubicin (PLD) remains a standard treatment option in platinum-resistant ovarian cancer and may further support immune-mediated tumor control in a non-overlapping fashion. Additionally, several studies have pointed to potential benefit after the combination of doxorubicin with oncolytic viruses.

The Phase 1b part of the PROTA (TILT-T563, NCT05271318) study evaluated TILT-123 in combination with pembrolizumab and PLD in patients with platinum-resistant ovarian cancer, with the objective of assessing safety, tolerability and preliminary antitumor activity.

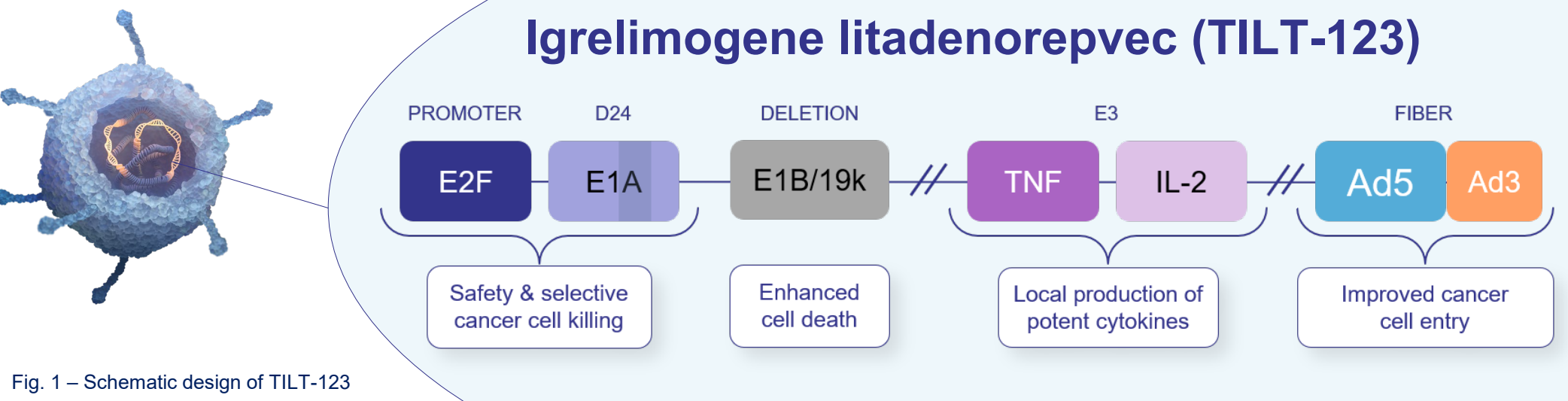


Fig. 1 – Schematic design of TILT-123

Methods

This phase 1b, open-label study enrolled ovarian, fallopian tube, or primary peritoneal cancer patients with up to one line of prior chemotherapy in the platinum resistant setting (not counting biological agents and targeted therapies including ADC);

Patients received a single intravenous dose (on day 1) and then intratumoral/intraperitoneal igrelimogene litadenorepvec combined with pembrolizumab (intravenously) and PLD (intravenously) (Fig. 2).

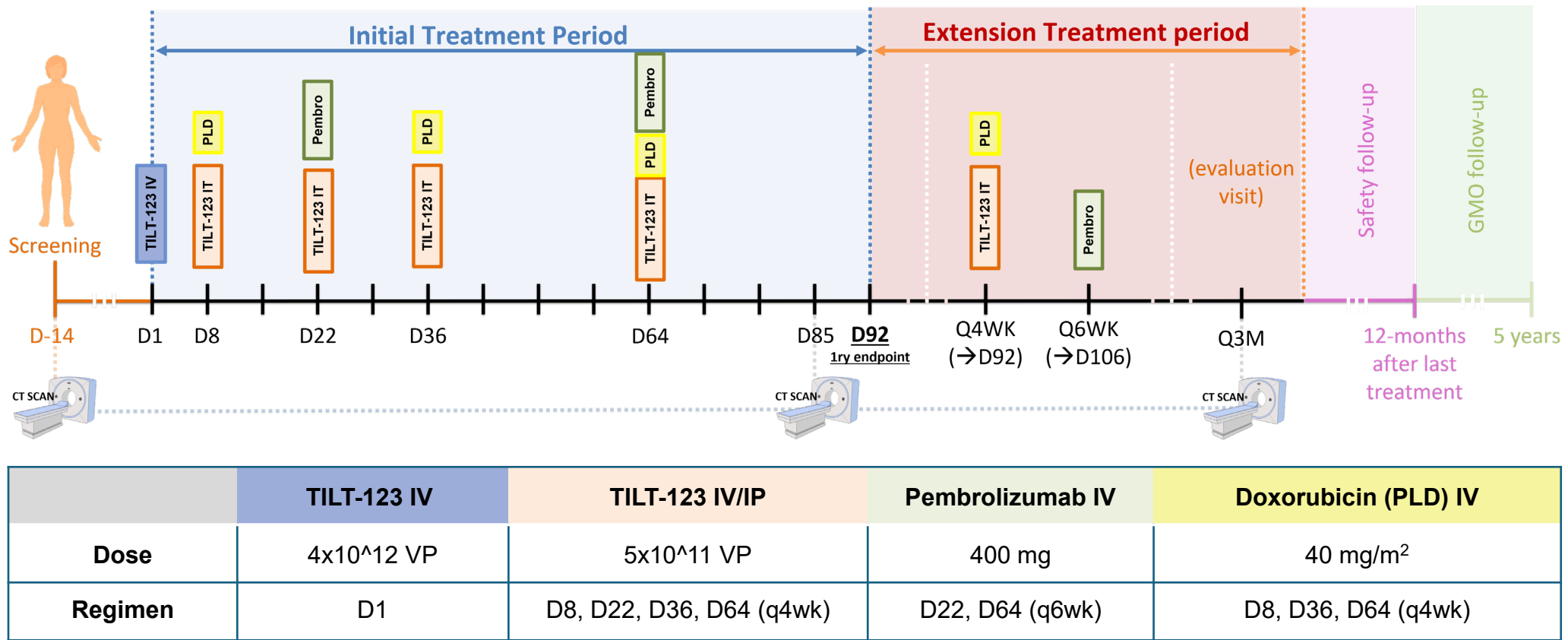


Fig. 2 – Schematic design of the TILT-T563 phase 1b trial and summary of treatments. TILT-123 doses are displayed in viral particles.

Primary endpoint was safety and tolerability. Secondary endpoints included overall response rate (ORR), duration of response (DoR), and disease control rate (DCR). Safety was evaluated by CTCAE criteria. Tumor assessments were made per RECIST v1.1.

Results

Out of eighteen screened patients, fourteen were enrolled (Fig. 3). Upon enrollment patients had received 2 (1-3) median prior therapies, 1 (0-2) in the resistant setting.

At data cutoff, the triplet regimen showed manageable safety, without unexpected toxicities. No dose-limiting toxicities were observed.

Adverse events aligned with known profiles of individual agents. Most were grade 1–2 events. The most common adverse events were nausea (10/14), fatigue (5/14), and chills (4/14). The total number of grade ≥3 treatment emergent adverse events (TEAEs) reported is 13 (Fig. 4).

	Total (%)
Number of patients	14
Sex	Female 14 (100.0%)
Median Age (years)	59
Age (years)	<65 10 (71.4%)
	≥65 4 (28.6%)
ECOG Performance Status	0 8 (57.1%)
	1 6 (42.9%)
Stage	IIIC 7 (50.0%)
	IIIB 1 (7.1%)
	IV 5 (35.7%)
Time since diagnosis	Median (months) 22.9
Histology	Epithelial ovarian c. 13 (90.9%)
	Fallopian tube c. 1 (9.1%)
BRCA1/2 Mutation	Negative 8 (57.1%)
	Positive 1 (7.1%)
	Negative 5 (45.5%)
HRD Score	Positive 2 (14.3%)

Fig. 3 – Summary of demographics from TILT-T563 patients. Unreported features were not included as separate rows in the table. Data cutoff 4.8.26

System Organ Class	Preferred Term	Grade	Related to TILT-123 n (%) f	Total N=14 n (%) f
Total TEAEs 8 (57.1%) 13				
Gastrointestinal disorders	Abdominal pain	3	0	2 (14.3%) 2
	Large intestinal obstruction	3	0	1 (7.1%) 1
	Oesophageal ulcer	3	0	1 (7.1%) 1
	Small intest. obstruction	3	0	2 (14.3%) 4
General disorders and administration site conditions	Fatigue	3	0	1 (7.1%) 1
	Injection site pain	3	1 (7.1%) 1	1 (7.1%) 1
Infections and infestations	Bacterial sepsis	5	0	1 (7.1%) 1
	Stoma site infection	3	0	1 (7.1%) 1
Nervous system disorders	Seizure	3	1 (7.1%) 1	1 (7.1%) 1

Fig. 4 – List of all TEAEs reported in TILT-T563. N = number of patients, n = number of patients experiencing a given TEAE. % = (n/N)*100, f = number of individual events. Data cut-off 4.8.26.

Encouraging antitumor activity was seen at data cutoff (4th September 2026) (Fig. 5). 9 patients were evaluable by RECIST1.1.

Overall response rate (ORR) is 44% (4/9); including 2 complete responses and 2 partial responses (all confirmed)

Disease control rate (DCR) is 77% (7/9).

Responses were durable with ongoing responses lasting from 9 to 21 months (median DOR/OS not available yet).

Patients that achieved disease control using RECIST 1.1 (disease stabilization, partial response or complete response) had a meaningful increase in survival ($p = 0.001$, Hazard ratio = 0,041 [0.006 to 0.278]) (Fig. 6). OS was 100% at cutoff

Out of 10 patients that were imaged at least twice, 8 showed a tumor change < +20% on measurable lesions (Fig. 7)

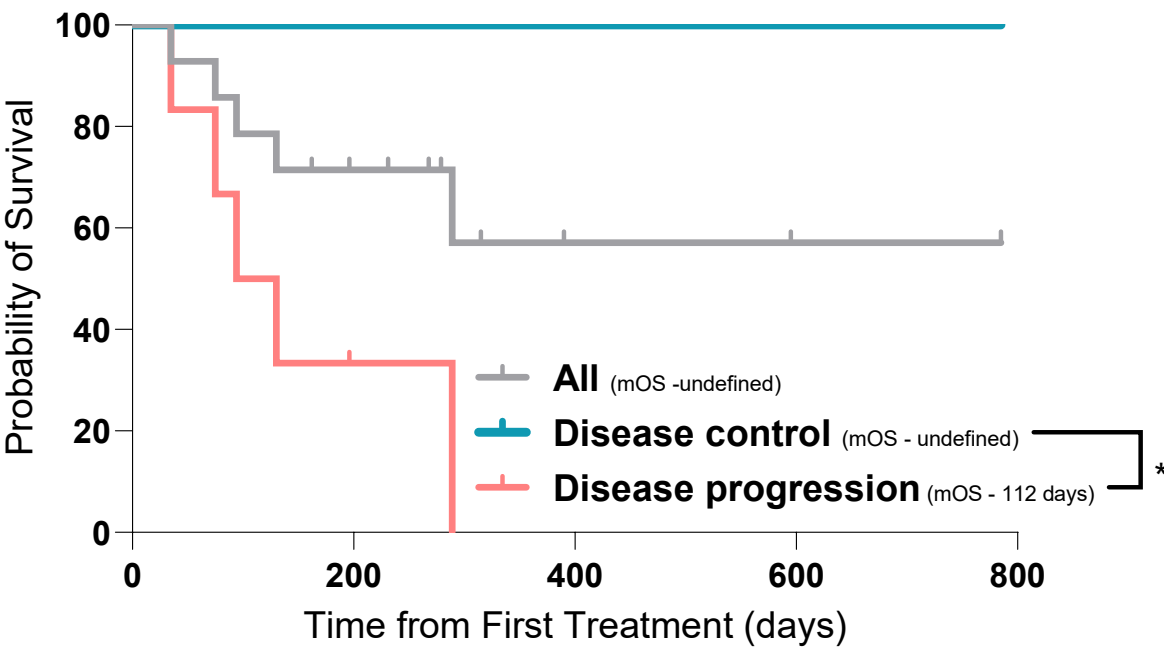


Fig. 6 – Overall survival data stratified by RECIST 1.1 (disease control or progression). Difference between groups assessed by Logrank (Mantel-Cox test) and hazard ratio by Mantel-Haenszel. Data cut-off 4.8.26

Patient case	Ovarian cancer type	Prior lines of therapy	Overall response by RECIST 1.1 (% tumor change from baseline)			Length of participation in trial
			Day 85	Best response	Last response	
301-19	Epithelial OVCa	2 (carboplatin + paclitaxel [niraparib] [olaparib], cisplatin)	PR (44%)	CR (100%) (21 mo)	CR (100%) (21 mo)	Ongoing
301-26	Serous OVCa	2 (carboplatin + paclitaxel [niraparib], carboplatin + gemtastine [bevacizumab])	PR (40%)	CR (40%) (9 mo)	CR (40%) (9 mo)	Ongoing
301-25	Epithelial OVCa	2 (nivolumab, carboplatin + paclitaxel [olaparib])	SD (22%)	PR (51%) (12 mo)	PR (51%) (12 mo)	Ongoing
301-13	Epithelial OVCa	1 (carboplatin + paclitaxel)	SD (29%)	SD (12 mo)	PD (12 mo)	Day 597
301-23	Fallop. tube. Ca	2 (carboplatin + paclitaxel + bevacizumab, carboplatin + gemtastine)	SD (12%)	SD (12 mo)	SD (12 mo)	Ongoing
301-24	Epithelial OVCa	1 (carboplatin + paclitaxel [niraparib])	SD (4%)	SD (4%)	SD (4%)	Day 85
301-27	Epithelial OVCa	2 (carboplatin + paclitaxel, letrozole)	SD (2%)	SD (2%)	SD (2%)	Day 92
301-15	Epithelial OVCa	2 (carboplatin + paclitaxel [niraparib], ELU001)	PD (46%)	PD (46%)	PD (46%)	Day 85
301-17	Epithelial OVCa	1 (carboplatin + paclitaxel + bevacizumab)	PD (59%)	PD (59%)	PD (59%)	Day 85
301-29	Epithelial OVCa	2 (carboplatin + paclitaxel, folate receptor alpha dendritic cells)	NE	NE	NE	Day 77
301-30	Not yet entered	3 (carboplatin + paclitaxel, carboplatin + gemtastine [bevacizumab], niraparib)	N/A	N/A	N/A	Day 83
301-20	Epithelial OVCa	2 (carboplatin + paclitaxel, gemtastine + bevacizumab)	N/A	N/A	N/A	Day 36
301-22	Epithelial OVCa	2 (carboplatin + paclitaxel [niraparib], let-123)	N/A	N/A	N/A	Day 35
301-28	Clear Cell OVCa	1 (carboplatin + paclitaxel)	N/A	N/A	N/A	Day 22

Fig. 5 – Summary of patients' prior lines of therapy and overall response (RECIST 1.1) by primary endpoint date, best response date and last response date. Four patients are still enrolled into the trial. Data cutoff 4.9.26

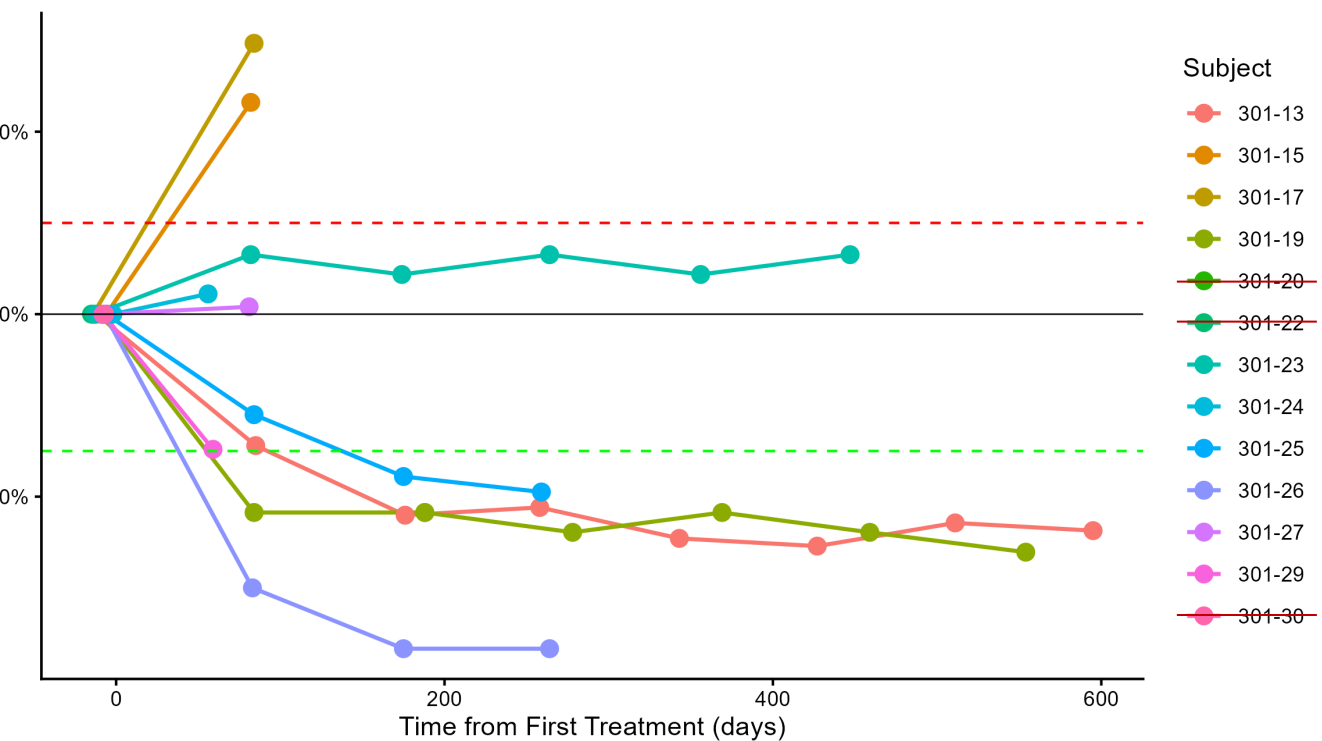


Fig. 7 – Spider plot representation of percentual change in tumor burden (change in sum of target lesion diameters as measured by CT imaging) compared to baseline. Data cut-off 4.8.26

Conclusions

TILT-123 combined with pembrolizumab and PLD demonstrated a **manageable safety profile** in patients with platinum-resistant ovarian cancer, with no dose-limiting toxicities observed.

The triplet regimen showed **encouraging preliminary antitumor activity**, achieving an overall response rate of 44% (4/9), including two complete responses, and a disease control rate of 77% (7/9) among RECIST-evaluable patients.

Responses were durable, and patients achieving disease control experienced significantly improved survival outcomes compared with patients with progressive disease.

A clear improvement in terms of clinical benefit was observed between Phase 1a and Phase 1b. Besides the PLD addition, **moving to an earlier treatment line could be critically improving the outcome** (Ph1a median prior lines = 7, Ph1b median prior lines = 2).

Presenting author disclosure statement:

Institutional research support from Alkermes, Bristol-Myers Squibb, Genentech, Merck, nference, Perspective Therapeutics, Pharmacocycles, Regeneron, Sorrento, TILT Biotherapeutics, and Transgene.

We thank the patients and staff at:



We thank the collaborators:

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

We thank the funding bodies including:

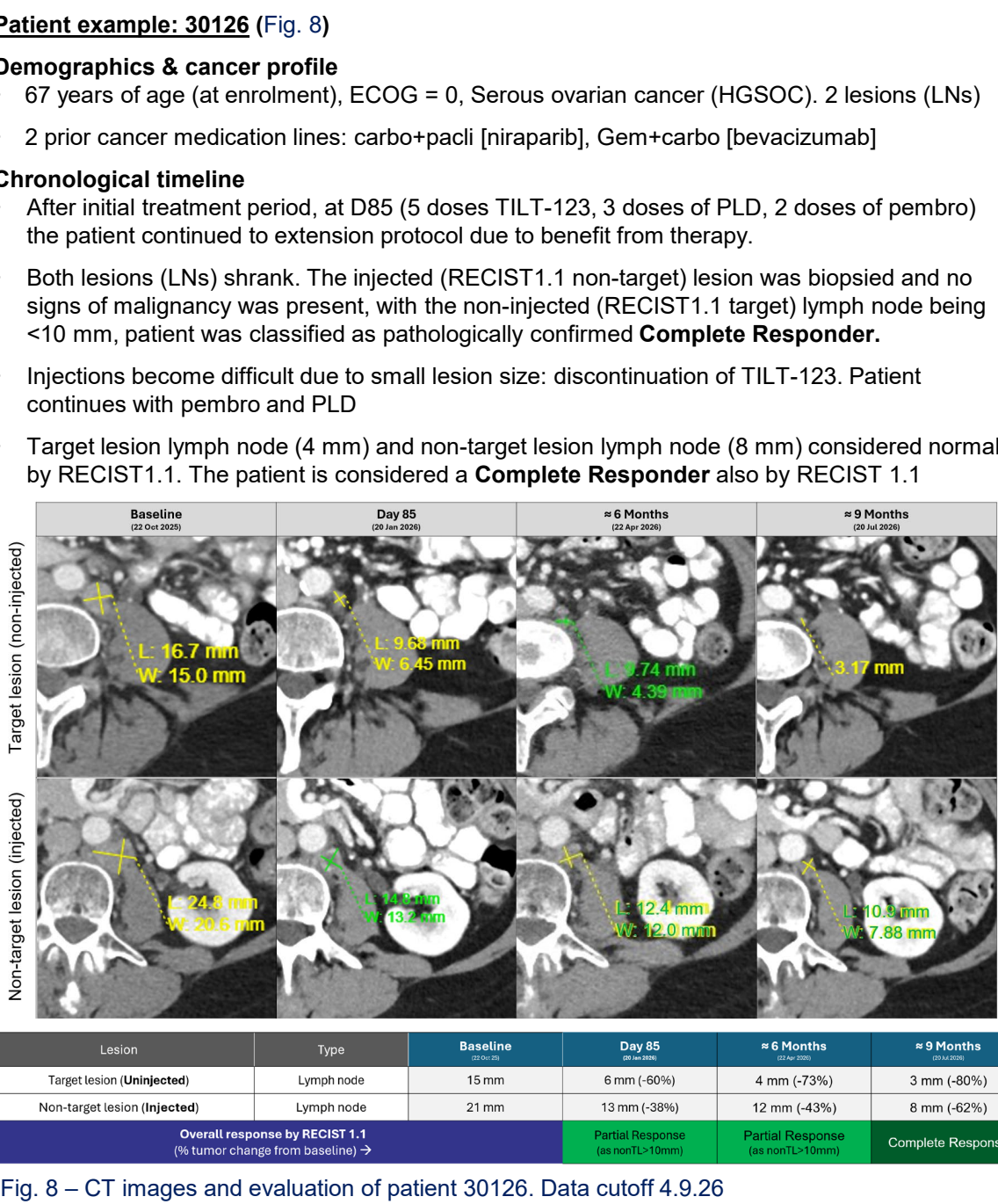


Fig. 8 – CT images and evaluation of patient 30126. Data cutoff 4.9.26

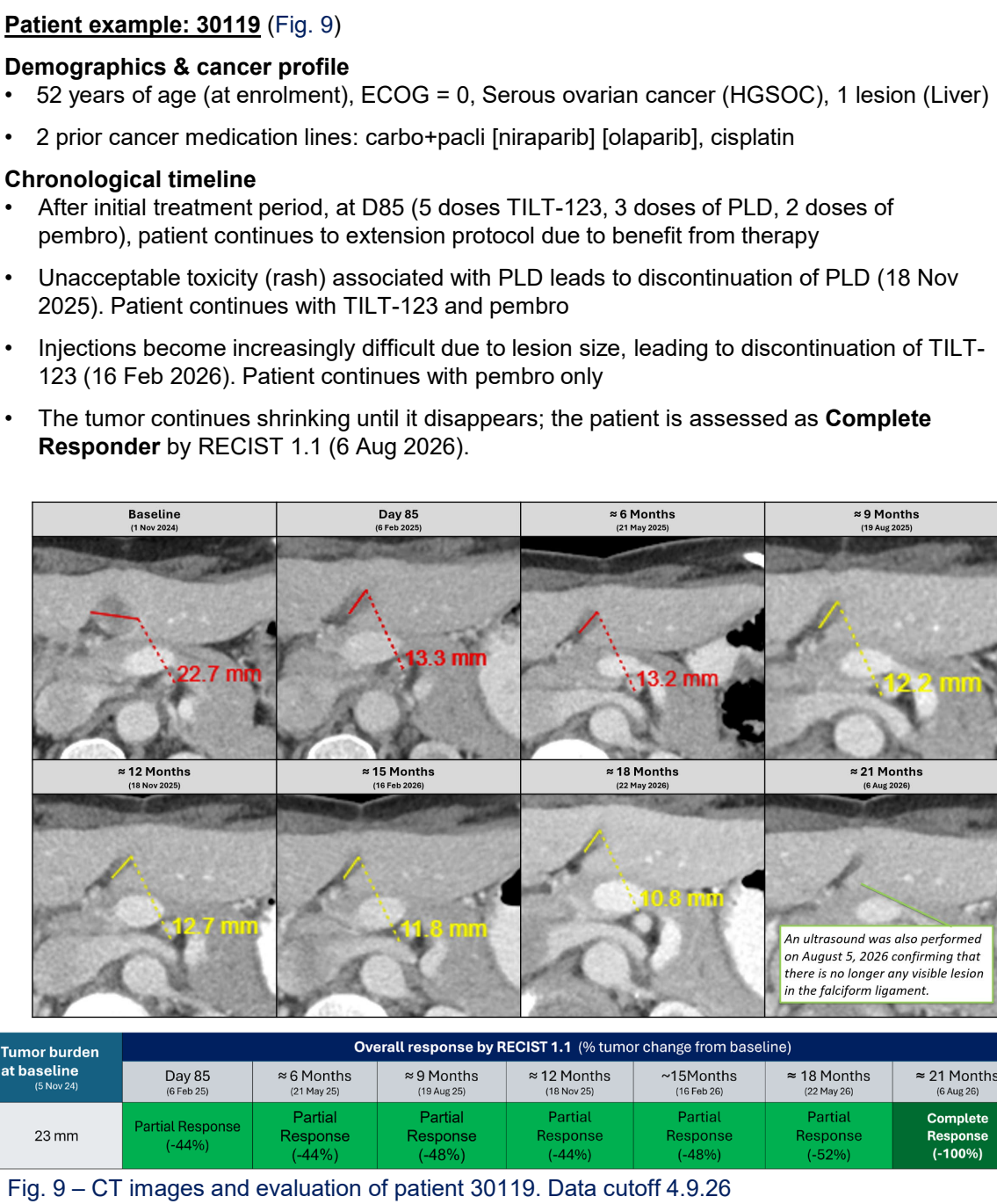


Fig. 9 – CT images and evaluation of patient 30119. Data cutoff 4.9.26