Clinical and Translational Evaluation of Lifileucel in Patients with Metastatic Undifferentiated Pleomorphic Sarcoma and Dedifferentiated Liposarcoma

Memorial Sloan Kettering Cancer Center

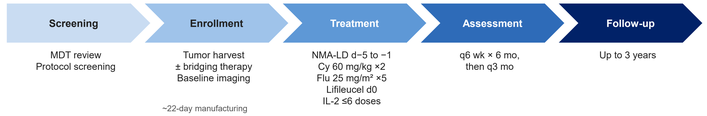
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Background

- Metastatic UPS and DDLS have median overall survival under 2 years and few options after first-line chemotherapy.
- TILs are present in, and can be expanded from, both histologies.
- Lifileucel is an autologous TIL therapy FDA-approved in melanoma. We tested it in UPS/DDLS (NCT05607095).

Methods



Eligibility

- Unresectable/metastatic DDLS or UPS
- ≥1 prior systemic therapy
- ≥1.5 cm lesion for harvest, plus a target lesion
- ECOG 0–1, adequate organ function

Endpoints

- **Primary:** feasibility (≥6/10 infused); safety (grade ≥3 TRAE)
- **Secondary:** ORR, DCR, DOR (RECIST 1.1)
- **Exploratory:** blood, TIL product, harvest and on-treatment biopsy profiling

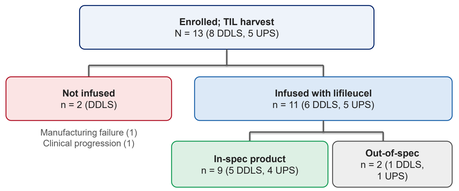
Correlatives

- Bulk TCRseq of serial blood and TIL product; scRNAseq + V(D)J of blood, TIL product, harvest and on-treatment biopsy. Clonality = 1 − Pielou evenness. Expanded clones: ≥2-fold, Fisher's exact p<0.05.

Feasibility and safety

Characteristic	N = 13[1]
Age at consent	
Median (Q1, Q3)	58 (50, 62)
Min, Max	43, 66
Sex	
Female	4 (31%)
Male	9 (69%)
Diagnosis	
DDLS	8 (62%)
UPS	5 (38%)
N treatment lines	
1	2 (15%)
2	6 (46%)
3	2 (15%)
4	1 (8%)
>5	2 (15%)

[1] n (% enrolled); percentages may not total 100 due to rounding



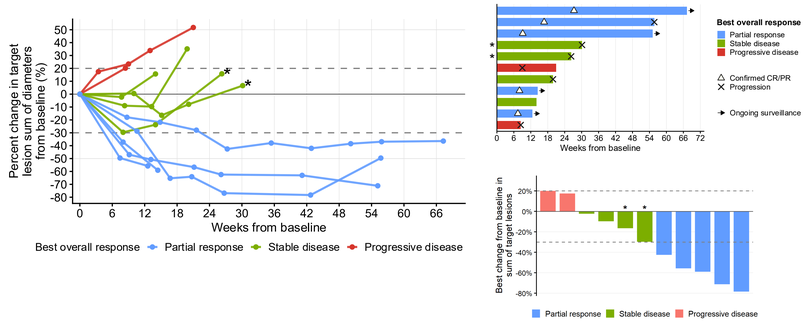
Safety (infused, n = 11)

- All had expected grade 4 cytopenias from lymphodepletion
- Most common grade ≥3 non-hematologic TRAE: febrile neutropenia (36%)
- 1 patient: grade 4 pulmonary infection and hemorrhage after TIL harvest
- No treatment-related grade 5 events; 1 death from progressive disease

Efficacy

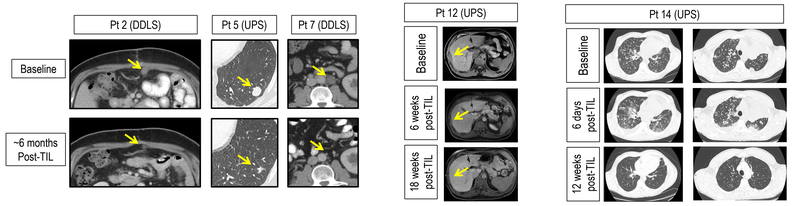
Patient	Age (y)	Sex	Diagnosis	Prior treatment lines (n)	Prior checkpoint inhibitor (Y/N)	Lifileucel infusion (Y/N)	Target SOD (mm)	IL-2 doses (n)	Best overall response	DoR++ (weeks)	DoSD (weeks)
5	**66**	**M**	**UPS**	**7**	**Y**	**Y**	**114.7**	**2**	**PR**	**46**	**55.1**
7	**51**	**M**	**DDLS**	**2**	**N**	**Y**	**115.3**	**2**	**PR**	**39**	**55.7**
2	**43**	**F**	**DDLS**	**2**	**N**	**Y**	**39.0**	**5**	**PR**	**40**	**67.3**
12	**49**	**M**	**UPS**	**2**	**Y**	**Y**	**82.8**	**5**	**PR**	**6.4**	**14.4**
14	**50**	**M**	**UPS**	**7**	**Y**	**Y**	**239.8**	**3**	**PR**	**5.1**	**12.6**
13	45	M	UPS	3	Y	Y	141.0	3	SD		14
4	62	M	DDLS	1	Y	Y	70.3	6	SD		19.9
9	66	M	DDLS	2	N	Y	161.6	2	PD		
10	50	M	DDLS	2	Y	Y	177.6	6	PD		
* Infused with out of spec product:											
1	60	M	UPS	2	N	Y	96.9	6	SD		26.3
8	66	F	DDLS	1	Y	Y	78.6	6	SD		30.1
Uninfused product:											
6	61	F	DDLS	3	N	N					
11	58	F	DDLS	4	N	N					

++ Data cutoff 30 Oct 2026: 4/5 PRs ongoing. DoSD, duration of stable disease. UPS, undifferentiated pleomorphic sarcoma; DDLS, dedifferentiated liposarcoma.



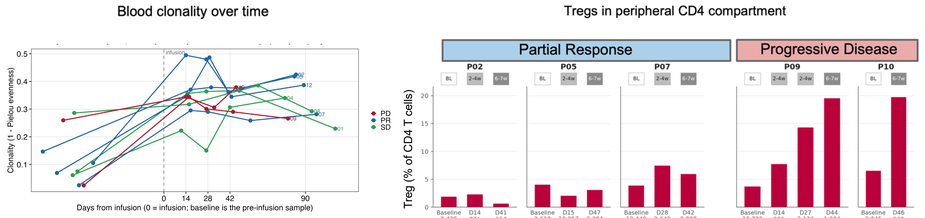
Blue = PR, green = SD, red = PD; * out-of-spec product. Left: target-lesion change over time. Right: time on study (top) and best change from baseline (bottom).

Representative responses (CT)



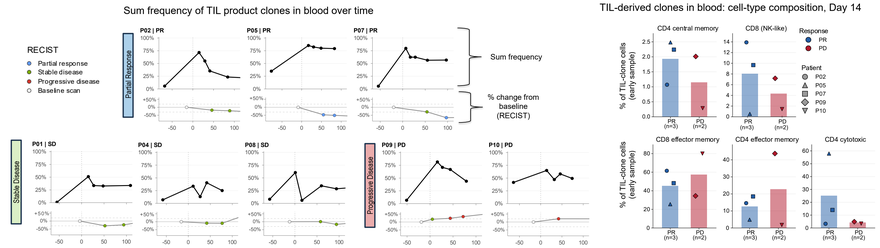
Correlative studies

1 Blood clonality rises after infusion; Tregs increase in PD



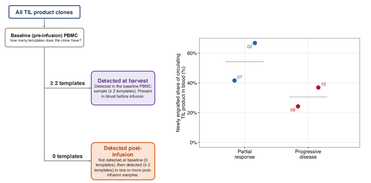
Left: blood TCR clonality (1 − Pielou), downsampled within patient; day 0 = infusion. Right: Tregs as % of CD4 T cells by scRNAseq (cells per sample below bars).

2 TIL product clones persist in blood; PRs show more CD4 cytotoxic signal

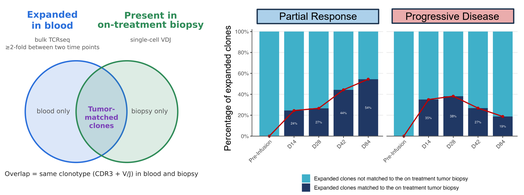


Left: summed frequency of TIL product clones in blood (top) with RECIST change (bottom). Right: phenotype of TIL clones in blood at day 14 (scRNAseq + V(D)J); PR n = 3, PD n = 2.

3 PRs have more TIL clones detected only after infusion



4 Tumor-matched clones take up more of the expanded niche in PRs



3) Left: TIL product clones classified by detection in blood (bulk TCRseq): detected at harvest (≥2 templates at baseline) or detected only after infusion (0 at baseline, ≥2 templates afterward). Right: Share of day-14 blood TIL clones detected only after infusion, by response (PR n = 3, PD n = 2); line = median.

Conclusions

- **Feasible and tolerable:** 11/13 patients infused; toxicity as expected for lymphodepletion and IL-2.
- **Durable responses:** ORR 5/9 with in-spec product and 5/11 overall; ***4/5 PRs ongoing***.
- **Exploratory signals:** in PRs, more TIL clones only detected after infusion, persistent tumor-matched clones, and CD4 cytotoxic TIL clones; in PD, rising Tregs.
- **Next:** SARATOGA (IOV-SAR-201), a multicenter phase II study sponsored by Iovance, is now open.

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