SUCCESSFUL GENERATION OF TUMOR-INFILTRATING LYMPHOCYTE (TIL) PRODUCT FROM RENAL CELL CARCINOMA (RCC) TUMORS FOR ADOPTIVE CELL THERAPY

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Background Patients with RCC may achieve remission with immune-checkpoint inhibitors (ICI); however, most patients will progress. Adoptive cell therapy with autologous TIL allows for expansion of T-cells from tumor tissue leading to a polyclonal T-cell product with a diverse T-cell receptor repertoire capable of recognizing an array of tumor antigens. TIL therapy with centrally manufactured lifileucel demonstrated a 36% overall response rate in patients with ICI-refractory melanoma.¹ We present our preclinical experience of TIL production in RCC.

Methods This study was approved by the DF/HCC Institutional Review Board. Fresh tumor samples (≥ 1.5 -cm) were harvested from consented patients undergoing resection for RCC. TIL were manufactured using pre-rapid expansion (1/10th scale) and rapid expansion (1/100th scale) protocol for 22 days. Characterization (total viable cells [TVC], % viability, identity, and potency) was performed on the final TIL product. TIL purity, differentiation, memory, activation, and exhaustion status were characterized using multi-color flow cytometry.

Results Baseline characteristics of 11 recruited patients are shown in table 1. Clear cell was the most common histology (73%). Two patients had previously treated metastatic disease with samples harvested from the lung and adrenal gland; one patient had prior cryoablation with adjacent local recurrence. The remainder were treatment-naïve primary nephrectomy samples. Eight products (73%) showed acceptable TIL product attributes (table 2). Median (range) TVC, viability, and identity (CD45+CD3+%) for the final TIL product were 74×10^9 (18×10^9 – 133×10^9), 95% (86%–97%), and 98% (94%–99%), respectively. Median (range) percentage of CD4+ cells was 69% (21%–97%) and CD8+ cells was 27% (2%–72%). The non-T-cell population, including B cells, monocytes, and NK cells, was <7%. The final TIL product was functional, and responded to polyclonal bead stimulation; the median (range) IFN γ and granzyme B were 8834 (3319–12,957) pg/mL and 34,329 (15,565–65,521) pg/mL, respectively. Acceptable TIL product was generated from both metastatic lesions and primary tumor samples. Of the 3 tumor samples that did not demonstrate acceptable TIL product attributes, one (ID 1) was from a patient treated with a CXCR4 inhibitor <1 month before resection, another (ID 4) was from a patient previously treated with ocrelizumab (CD20-directed cytolytic antibody) for multiple sclerosis, and the final (ID 8) was harvested from the cryoablated tumor nodule rather than the adjacent recurrent tumor.

Conclusions These feasibility data suggest that TIL can be successfully expanded ex vivo from RCC samples (including pre-treated and metastatic tumors) and support potential clinical investigation of TIL in patients with RCC.

Abstract 176 Table 1 Baseline demographics and tumor characteristics

N = 11	
Age, years, median (IQR)	59 (52-68)
Sex, n (%)	
Male	10 (91)
Race, n (%)	
White	9 (82)
Histology, n (%)	
Clear cell	8 (73)
Papillary	2 (18)
Chromophobe	1 (9)
Tumor site, n (%)	
Kidney	9 (82)
Adrenal	1 (9)
Lung	1 (9)

Abstract 176 Table 2 Summary of product attributes. 1, No CD3 + subset. 2, Product not available to test

Tumor ID	Histology	Tumor	Acceptance Criteria	TVC ($\times 10^9$)	Viability (%)	CD45 ⁺ CD3 ⁺ (%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD41 ⁺ CD8 ⁺
1	Clear cell	Lung	Not met	1	64	0		-1	
2	Clear cell	Primary	Met	77	97	99	48	34	1
3	Clear cell	Primary	Met	96	95	96	21	72	0
4	Clear cell	Primary	Not met	2	67	0		-1	
5	Clear cell	Primary	Met	71	91	99	77	18	4
6	Papillary	Primary	Met	63	95	98	58	29	2
7	Papillary	Primary	Met	81	94	99	97	2	49
8	Clear cell	Primary	Not met	1	92	75		-2	
9	Chromophobe	Primary	Met	27	91	94	72	25	3
10	Clear cell	Primary	Met	113	95	99	65	29	2
11	Clear cell	Adrenal	Met	18	86	94	80	18	4

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Ethics Approval This study was approved by the DF/HCC Institutional Review Board protocol # 06-105.

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