TRAVERSE: A Phase 1 Multicenter Study Evaluating the Safety and Efficacy of ALLO-316 in Patients With Advanced or Metastatic Clear Cell Renal Cell Carcinoma (ccRCC)

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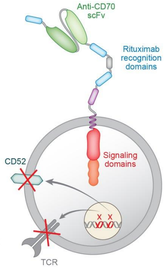
Background

- Relapsed and refractory RCC represents high unmet need
  - Large patient population with poor survival outcomes[1-3]
  - Limited effective therapeutic options after failure of immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs)
- CD70 is a promising target for CAR T therapy[4]
  - Expressed in up to 80% of RCC; expressed in other hematologic and solid tumors
  - Restricted expression in normal tissue
- ALLO-316: a novel off-the-shelf CAR T candidate targeting CD70
  - HLA-unmatched T cell product engineered to express anti-CD70 CAR
  - Double knock-out (TCR and CD52) to reduce GvHD risk and facilitate conditioning with fludarabine, cyclophosphamide, and ALLO-647, an anti-CD52 antibody
  - CD70 CAR designed to avoid fratricide, thereby avoiding disrupting CD70 in CAR T cells
  - Includes CD20 mimotope-based intra-CAR off switch, enabling effective CAR T elimination with rituximab



Study Design and Objectives

- Phase 1 multicenter, dose-escalation study, exploring **two conditioning regimens** and **4 cell dose levels** (DLs)

Table 1. Dosing & Administration with Selected Conditioning Regimens

Conditioning Regimen	FCA	FC
Fludarabine (F)	30 mg / m^2 / day x 3 days	
Cyclophosphamide (C)	300 mg / m^2 / day x 3 days*	
ALLO-647 (A)	30 mg	–

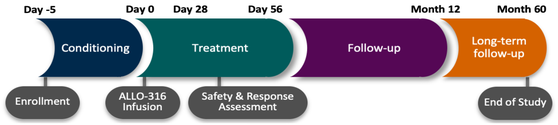
* Optional to increase cyclophosphamide to 500mg/m^2

Table 2. Selected Escalating Cell DLs

Dose Regimen†	DL1	DL2	DL3	DL4
Cell Dose (CAR+ T cells)	40 x 10^6	80 x 10^6	120 x 10^6	240 x 10^6

† Enrollment in dose escalation is ongoing.

Figure 1. Treatment Schema



Key Objectives

- Establish safety and tolerability of ALLO-316
- Determine the recommended cell dose and conditioning regimen
- Evaluate antitumor activity of ALLO-316 in subjects with varying levels of CD70 expression
- Investigate ALLO-316 kinetics with different conditioning regimens

Patient Demographics and Disposition

- All patients had advanced or metastatic ccRCC and prior therapy with ICIs and TKIs
- **Median time from enrollment to initiation of conditioning:** 5 days (range: 1-15)
- 95% of enrolled patients (n=19) received ALLO-316
  - DL1 (40 x 10^6): 9 patients
  - DL2 (80 x 10^6): 8 patients
  - DL3 (120 x 10^6): 2 patients
- Median follow-up time: 7.8 months (range: 0.4, 18.1)

Table 3. Demographic Data at Baseline

	Patients who received ALLO-316‡ (n=19)
Age, median (range), yrs	62 (50, 70)
Gender: Male / Female, %	84 / 16
ECOG PS: 0 / 1, %	63 / 37
Disease Stage IV, %	100
Previous Nephrectomy, %	79
Tumor Burden at Baseline	
≥50 mm, %	79
≥100 mm, %	42
Time Since Original Diagnosis, median (range), months	42.7 (12.1, 216.3)
Lines of Prior Therapy, median (range)	3 (1, 8)
Failed >1 ICI / AI, %	73.7 / 52.6

‡ Of 20 patients enrolled, the Safety Analysis Set includes 19 patients who underwent conditioning and received ALLO-316; this dataset excludes one patient who received one dose of conditioning but did not receive ALLO-316 because the subject tested positive for COVID-19

Safety and Tolerability

- **Toxicity**
  - The safety profile is overall comparable to what is seen with autologous CAR T
  - One DLT event (Gr 3 type 2 autoimmune hepatitis§) in DL2 FCA
  - Manageable low-grade CRS
  - No ICANS or GVHD
  - Two Gr 3 neurotoxicity (syncope and fatigue)
  - One patient had Gr 5 respiratory failure in the setting of COVID-19 infection deemed unrelated to study treatment
  - Infections now managed with enhanced prophylaxis
- **Dose exploration continuing**

Table 4. Treatment-Emergent Adverse Events of Interest¶

	Patients who received ALLO-316 (n=19)	
	All Grades n (%)	Grade 3+ n (%)
CRS	11 (58)	1 (5)
Infusion-Related Reaction	1 (5)	0
Neurotoxicity#	13 (68)	2 (11)
ICANS	0	0
GvHD	0	0
Infection‖	9 (47)	5 (26)
Prolonged Grade 3+ Cytopenia**	N/A	3 (16)

§ DLT initially reported as elevated AST/elevated ALT. ¶ Number of patients with AE occurring from the start of study drug up to subsequent anti-cancer therapy. For patients reporting more than one AE within a preferred term, only one AE with the maximum grade is reported. # Neurotoxicity including ICANS: includes preferred terms (PT) from the Allogene MedDRA Query (AMQ) for Neurologic toxicities including ICANs, a broad search basket of over 200 PTs selected to identify the medical concept. The majority of neurotoxicities are fatigue and headache. ‖ The 4 Gr 3+ infections comprised 2 bacterial (PICC line infection and UTI), 1 fungal (bronchopulmonary aspergillosis) and 1 viral (Gr 5 respiratory failure in setting of COVID-19). At the time of data cut, one additional Gr 3 fungal sinusitis had not yet been recoded as disease progression. ** Prolonged Cytopenia at Day 28, includes Grade 3 or above neutropenia, thrombocytopenia, anaemia or pancytopenia which is present at Study Day 28.

Anti-Tumor Activity in CD70+ RCC

- **Patients evaluable for efficacy (n=18):**
  - ORR = 17%, DCR = 89%
- **Patients with CD70+ RCC (n=10):**
  - 3/10 (30%) achieved PR (2 confirmed)
  - DCR = 100%
  - Median progression-free survival of 5.0 months
  - Higher baseline tumor CD70 IHC H-Score‡‡ correlated with greater tumor reduction

Table 5. Response Rates in Evaluable Patients (mITT)††

	All Patients (n=18§§)	CD70+ Patients (n=10§§)
ORR††, n (%)	3 (17)	3 (30)
DCR, n (%)	16 (89)	10 (100)

†† Modified intention-to-treat (mITT) analysis (n=18); DOR values for the 2 confirmed PRs per RECIST 1.1 were 2.9 and 7.0 months; median follow-up time of 8 months; DCR includes initial assessment of SD. ‡‡ H-Score is the weighted CD70 expression on a scale of 0-300; H-score = CD70 intensity x % positivity. §§ Of 19 patients dosed with ALLO-316, 18 had at least 1 tumor assessment.

Figure 2. H-Score Correlation With Tumor Reduction

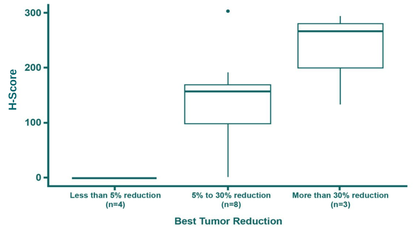


Figure 3. Best Overall Response in Evaluable Patients (mITT)

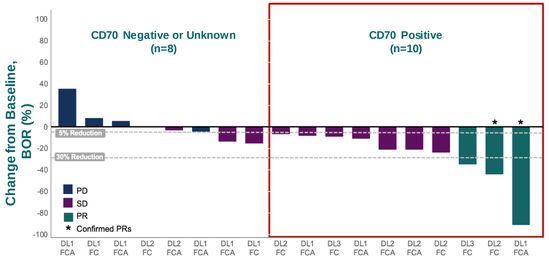
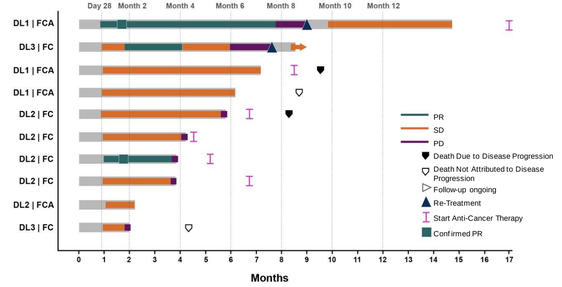


Figure 4. Durable Disease Control in CD70+ RCC



*Deepening response from D28 (27% reduction from baseline) to D56 (35% reduction from baseline). Unconfirmed response at M4 with 17% increase from nadir. PD at M6. Follow-up ongoing post re-treatment.

CAR T Cell Expansion, Persistence and Tumor Trafficking

- High CAR T cell expansion was observed following both conditioning regimens and at relatively low cell doses; in peripheral blood, median peak expansion was 35,000 copies/µg
- High VCN observed in 3 of 4 available tumor aspirates; demonstrates the ability of ALLO-316 to infiltrate the tumor environment

Figure 5. ALLO-316 Expansion After Single-Dose

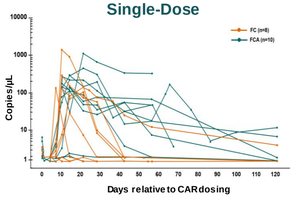
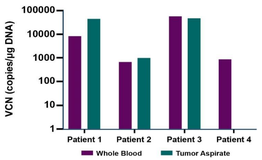


Figure 6. ALLO-316 Detected in 3 of 4 Available Tumor Aspirates



- Following ALLO-316 infusion, alloreactive host T cells upregulate CD70 by Day 4
- ALLO-316 expands by Day 10 and eliminates CD70+ host T cells while CD70- host T cells are spared
- Host CD70+ T cells recover as ALLO-316 contracts

Figure 7. Host T CD70+ and CAR T Cell Counts

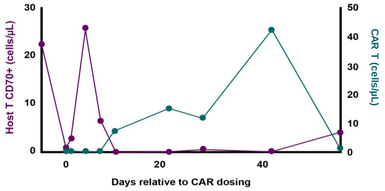
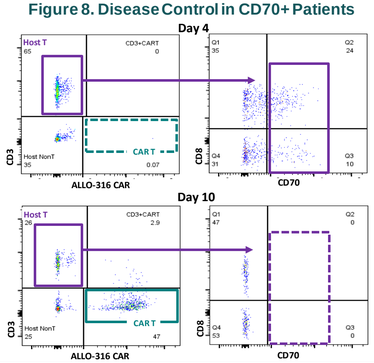


Figure 8. Disease Control in CD70+ Patients



Conclusions

Off-the-shelf CAR T with encouraging anti-tumor activity and no new or unexpected safety signals

- Treatment initiated with a median of 5 days from enrollment
- Safety profile consistent with autologous CAR T
- Anti-tumor activity in relapsed/refractory advanced CD70+ metastatic RCC
  - 100% disease control and 30% objective response rates in a heavily pretreated population with few therapeutic options
- ALLO-316 depleted alloreactive CD70+ host T cells ("Dagger™ effect"), leading to marked expansion and persistence of allogeneic CAR T cells, even at low cell doses
- Dose escalation ongoing in CD70+ RCC; expansion cohorts planned by the end of 2023 with potential inclusion of additional CD70+ tumors

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1. Rao A, et al. *Ann Transl Med*. 2018;6(9):165. 2. Hsieh JJ, et al. *Nat Rev Dis Primers*. 2017;3:17009. 3. Huang JJ, Hsieh JJ. *Kidney Cancer*. 2020;4:121-129. 4. Ruf M, et al. *Clin Cancer Res*. 2015;21(4):889-898.

Data Extract: March 23, 2023