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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TRAVERSE: First-in-Human Trial of Allogeneic Anti-CD70 CAR T Candidate for RCC

- 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

TRAVERSE: Study Design and Objectives

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

<table>
<thead>
<tr>
<th>Conditioning Regimen</th>
<th>FCA</th>
<th>FC</th>
</tr>
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<tbody>
<tr>
<td>Fludarabine (F)</td>
<td>30 mg / m² daily x 3</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide (C)</td>
<td>300* mg / m² daily x 3</td>
<td></td>
</tr>
<tr>
<td>ALLO-647 (A)</td>
<td>10 mg daily x 3</td>
<td>-</td>
</tr>
</tbody>
</table>

*Optional to increase cyclophosphamide to 500mg / m²

<table>
<thead>
<tr>
<th>Dose Regimen</th>
<th>DL1</th>
<th>DL2</th>
<th>DL3</th>
<th>DL4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell Dose (CAR+ T cells)</td>
<td>40 x 10⁶</td>
<td>80 x 10⁶</td>
<td>120 x 10⁶</td>
<td>240 x 10⁶</td>
</tr>
</tbody>
</table>

Treatment Schema

- Establishment of 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

Enrollment in dose escalation is ongoing
TRAVERSE: Patient Demographics and Disposition

- All patients had advanced or metastatic ccRCC and prior therapy ICI and TKI

- 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)
ALLO-316: 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\(^a\)) 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**

### Patients who received ALLO-316 (n=19)

<table>
<thead>
<tr>
<th>TEAEs of Interest(^b)</th>
<th>All Grades</th>
<th>Grade 3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion-Related Reaction</td>
<td>1 (5)</td>
<td>0</td>
</tr>
<tr>
<td>CRS</td>
<td>11 (58)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>ICANS</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>GvHD</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neurotoxicity(^c)</td>
<td>13 (68)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Infection(^d)</td>
<td>8 (42)</td>
<td>4 (21)</td>
</tr>
<tr>
<td>Prolonged Grade 3+ Cytopenia(^e)</td>
<td>N/A</td>
<td>3 (16)</td>
</tr>
</tbody>
</table>

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\(^a\) DLT initially reported as elevated AST/elevated ALT.

\(^b\) 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.

\(^c\) 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.

\(^d\) 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.

\(^e\) Prolonged Cytopenia at Day 28, includes Grade 3 or above neutropenia, thrombocytopenia, anaemia or pancytopenia which is present at Study Day 28.

Data Extract: March 23, 2023
ALLO-316: 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
  - DCR = 100%
  - Median progression-free survival of 5.0 months
  - Higher Baseline tumor CD70 IHC H-Score correlated with greater tumor reduction

<table>
<thead>
<tr>
<th>Response Rates</th>
<th>All Patients (n=18(^c))</th>
<th>CD70+ Patients (n=10(^c))</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR(^a), n (%)</td>
<td>3 (17)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>DCR, n (%)</td>
<td>16 (89)</td>
<td>10 (100)</td>
</tr>
</tbody>
</table>

\(^a\) 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
\(^b\) H-Score is the weighted CD70 expression on a scale of 0–300; H-score = CD70 intensity x % positivity
\(^c\) Of 19 patients dosed with ALLO-316, 18 had at least 1 tumor assessment

Data Extract: March 23, 2023
ALLO-316: Anti-Tumor Activity in CD70+ RCC

Data Extract: March 23, 2023

CD70 Negative or Unknown (N=8)

- 5% Reduction
- 30% Reduction

CD70 Positive (N=10)

- PD
- SD
- PR

* Confirmed PRs
ALLO-316: 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.

Data Extract: March 23, 2023
TRAVERSE Case Study 1: Deepening Response After Lowest Tested Cell Dose

- 68-year-old man with metastatic RCC to the lungs, refractory to multiple ICIs (ipilimumab, nivolumab, and pembrolizumab) and axitinib

- Treated with FCA and ALLO-316 40M CAR+ cells

- Responded with initial partial response at Month 1 that continued to deepen until Month 8, demonstrating durability of response to low dose ALLO-316
TRAVERSE Case Study 2: Primary Tumor Shrinkage in Patient With Stable Disease

- 70-year-old male with RCC metastatic to adrenal and bone, refractory to axitinib and pembrolizumab
- Treated with FCA and 80M CAR+ cells
- Best Overall Response of Stable Disease with 45% decrease in size of primary left kidney tumor
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.
ALLO-316 Eliminates CD70+ Host T Cells, Preventing Allorejection and Supporting Persistence

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.
Summary: Preliminary Safety and Efficacy of ALLO-316 in Advanced RCC

Off-the-shelf CAR T with encouraging anti-tumor activity and no 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
Thank You!

To our patients, their families and caregivers, &

our clinical trial investigators and sites

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