2025 ASCO ANNUAL MEETING

ALLO-316 in Advanced Clear Cell Renal Cell Carcinoma: Updated Results From the Phase 1 TRAVERSE Study

Samer A. Srour[1]; Jad Chahoud[2]; Alexandra Drakaki[3]; Brendan D. Curti[4]; Geoffrey T. Gibney[5]; Sumanta Pal[6]; Lily Tang[7]; Sara Charmsaz[7]; Joy Atwell[7]; Paul B. Robbins[7]; Chelsea Williams[7]; Srinivas Ghatta[7]; Christopher J. Severyn[7]; John Le Gall[7]; Nizar M. Tannir[8]; Ritesh R. Kotecha[9]

[1]Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Moffitt Cancer Center, Tampa, FL, USA; [3]UCLA Health, Los Angeles, CA, USA; [4]Providence Cancer Institute, Franz Clinic, Portland, OR, USA; [5]Georgetown University Hospital, Washington, DC, USA; [6]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [7]Allogene Therapeutics, San Francisco, CA, USA; [8]Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [9]Memorial Sloan Kettering Cancer Center, New York, NY, USA

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Key Takeaway Points

A confirmed ORR of 31% was observed after a single dose of ALLO-316, an allogeneic CD70 CAR T product, in patients with heavily-pretreated advanced or metastatic ccRCC, with multiple ongoing responses, including one extending beyond a year after treatment

Safety profile was manageable and consistent with standard lymphodepletion and an active CAR T cell therapy

ALLO-316 delays allorejection by depleting patient CD70^{+} cells, driving robust and sustained CAR T-cell expansion

Results underscore the transformative potential of allogeneic CAR T in solid tumors and validate further development of ALLO-316 in RCC and other CD70^{+} malignancies

CAR, chimeric antigen receptor; ccRCC, clear cell renal cell carcinoma; ORR, objective response rate.

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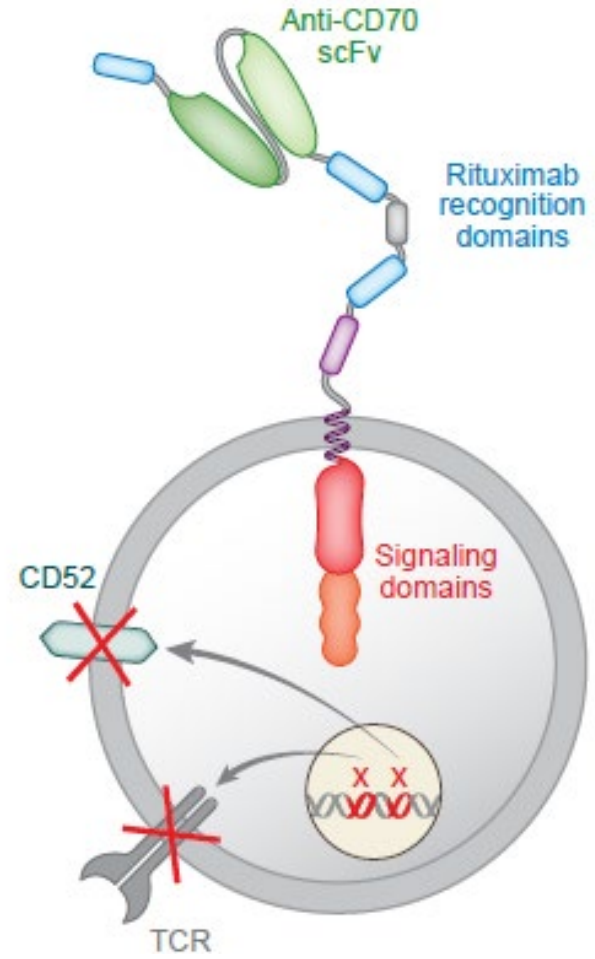
Background

- CAR T therapy has revolutionized treatment of hematologic malignancies, but progress has been slow in solid tumors[1]
- ALLO-316 is an off-the-shelf, HLA-unmatched allogeneic CD70 CAR T product designed to target both CD70$^+$ tumors and alloreactive host T cells
- Phase 1a data from the TRAVERSE study of ALLO-316 in patients with ccRCC showed manageable safety with promising antitumor activity[2]
- Results from 20 heavily pretreated, refractory patients in the phase 1b part of the study treated with standard lymphodepletion and 80M CD70 CAR T cells are reported



1. Albelda SM *Nat Rev Clin Oncol.* 2024;21:47-66. 2. Srour SA et al, *J Immunother Cancer,* 2024;12(Suppl 2):A1–A1683.
CAR, chimeric antigen receptor; ccRCC, clear cell renal cell carcinoma; HLA, human leukocyte antigen; ScFv, single-chain variable fragment; TCR, T cell receptor.

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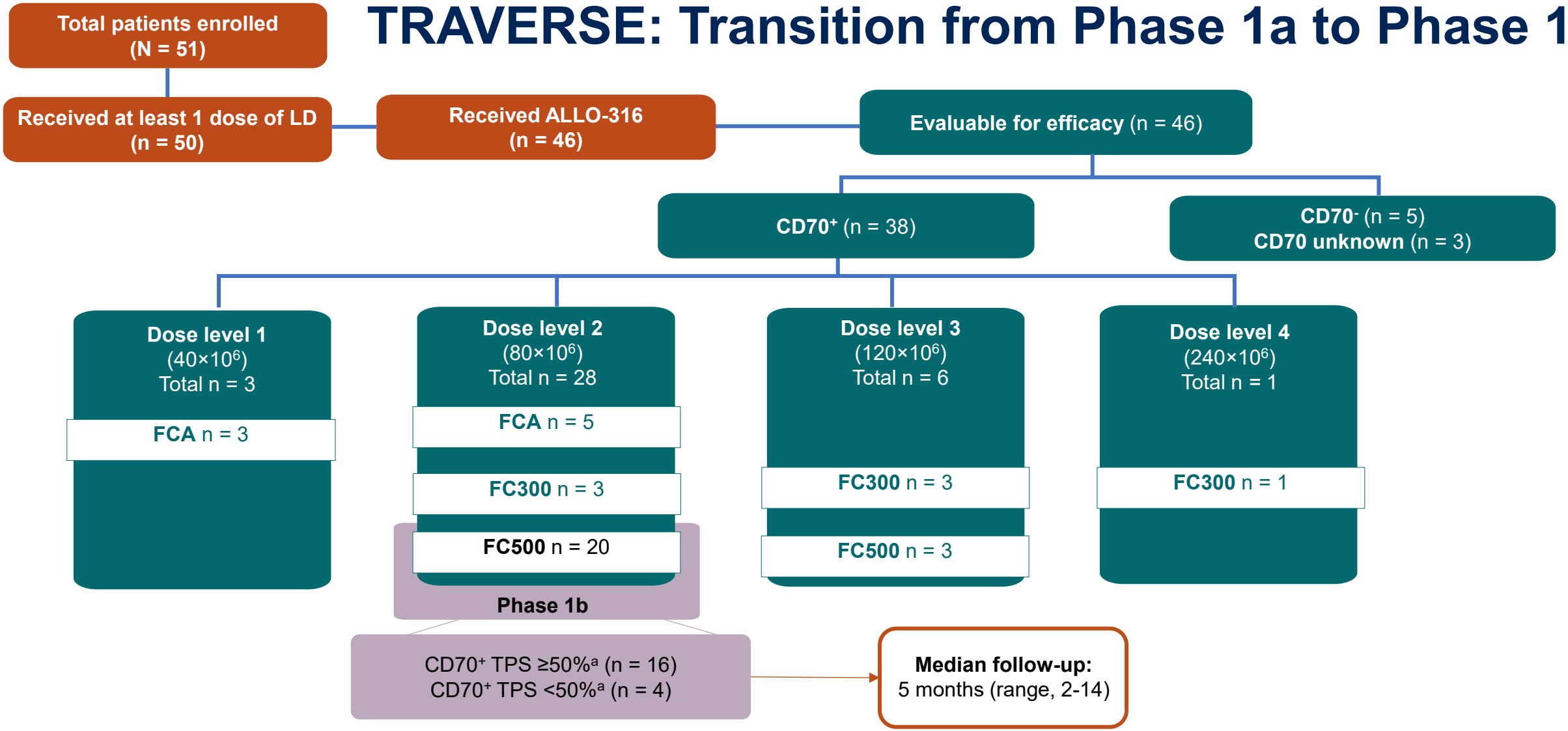
TRAVERSE: Transition from Phase 1a to Phase 1b



FCA, fludarabine, cyclophosphamide, and ALLO-647 (an anti-CD52 monoclonal antibody)
FC300, fludarabine 30 mg/m^2 and cyclophosphamide 300 mg/m^2
FC500, fludarabine 30 mg/m^2 and cyclophosphamide 500 mg/m^2

[a]IHC-based CD70 expression.
LD, lymphodepletion; TPS, Tumor Proportion Score.

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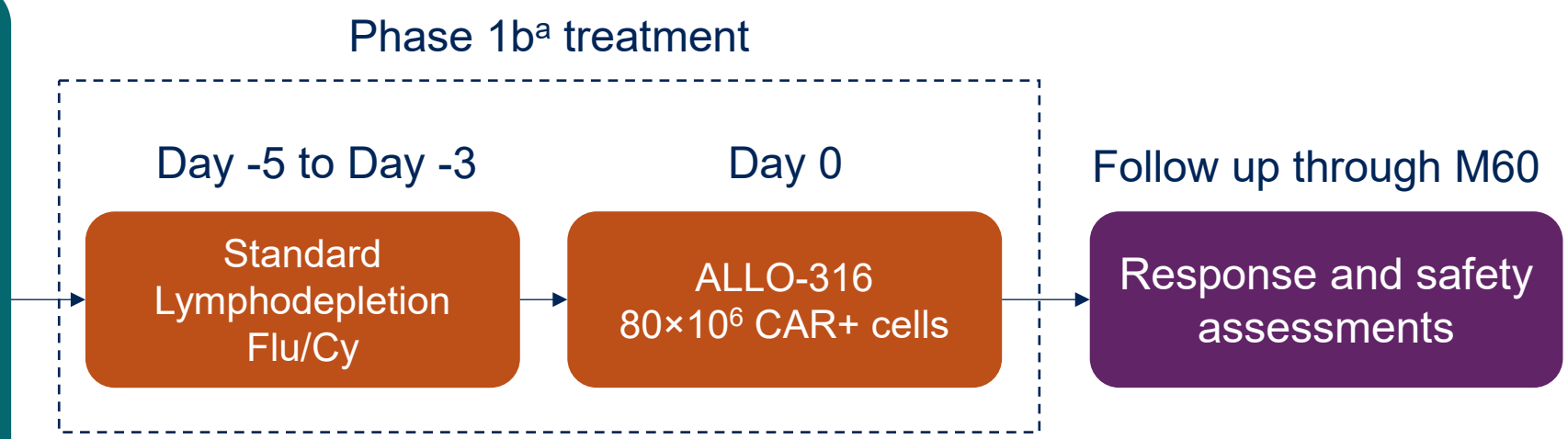
TRAVERSE Phase 1b Study Design (NCT04696731)

Key Eligibility Criteria

- Aged ≥18 years with advanced or metastatic ccRCC
- Disease progression after PD-1 axis and VEGF targeted therapies
- CD70 positive by IHC on archival or fresh tumor tissue
- ECOG 0-1
- Adequate pulmonary, cardiac, renal, hepatic, and hematologic function



Phase 1b Endpoints

- Primary
  - TEAEs
- Secondary
  - ORR, CRR, DOR, TTR, PFS, OS, CAR T expansion kinetics

[a]Phase 1a evaluated escalating doses of both ALLO-316 and various lymphodepletion regimens in a 3+3 design.

CAR, chimeric antigen receptor; ccRCC, clear cell renal cell carcinoma; CRR, complete response rate; DOR, duration of response; ECOG, Eastern Cooperative Oncology Group; Flu/Cy, fludarabine 30 mg/m^2 and cyclophosphamide 500 mg/m^2 daily for 3 days; IHC, immunohistochemistry; M, month; ORR, objective response rate; OS, overall survival; PD-1, programmed cell death protein 1; PFS, progression-free survival; TEAE, treatment-emergent adverse events; TTR, time to response; VEGF, vascular endothelial growth factor.

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All Patients Had Multiple Treatment-Refractory Advanced or Metastatic ccRCC

Phase 1b patients received a median of 4 prior lines of therapy: 59% had received 3+ prior TKIs, 41% had received belzutifan, and 32% were quadruple class refractory to inhibition of the CTLA-4, PD-(L)1, TKI, and HIF-2α pathways

Demographics and Disease Characteristics	Phase 1b n = 22[a]	All patients N = 50
Age, median (range), years	56 (35-67)	60 (35-70)
Male sex, n (%)	20 (91)	44 (88)
ECOG PS 0, n (%)	10 (45)	27 (54)
Disease stage IV, n (%)	22 (100)	50 (100)
Prior nephrectomy, n (%)	22 (100)	45 (90)
IMDC risk at screening, n (%)		
Favorable	8 (36)	19 (38)
Intermediate	14 (64)	27 (54)
Poor	0	3 (6)
Not available	0	1 (2)
Treatment timing	**Phase 1b n = 22[a]**	**All patients N = 50**
Time from enrollment to treatment, median (range), days	4 (1-15)	4 (1-15)

Prior Treatment	Phase 1b n = 22[a]	All patients N = 50
Lines of prior therapy, median (range)	4 (1-11)	4 (1-11)
Prior therapies, n (%)		
Anti-PD-(L)1 therapy	22 (100)	50 (100)
Anti-CTLA-4 therapy	12 (55)	31 (62)
Cabozantinib	18 (82)	39 (78)
≥2 TKIs	18 (82)	32 (64)
≥3 TKIs	13 (59)	17 (34)
mTOR inhibitor	15 (68)	20 (40)
Belzutifan	9 (41)	10 (20)
Received CTLA-4 inhibitor, PD-(L)1 inhibitor, TKI, and HIF-2α inhibitor	7 (32)	8 (16)

[a]Includes 2 patients who received LD but did not receive ALLO-316.

ccRCC, clear cell renal cell carcinoma; CTLA-4, cytotoxic T-lymphocyte associated protein 4; ECOG, Eastern Cooperative Oncology Group; HIF-2α , hypoxia-inducible factor 2α; IMDC, International Metastatic RCC Database Consortium; LD, lymphodepletion; PD-1, programmed cell death protein 1; TKI, tyrosine kinase inhibitor. Data cutoff: 02-May-2025

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Adverse Event Profile Consistent With Lymphodepletion and an Active CAR T Therapy

TEAEs ≥20% incidence in Phase 1b, n (%)	Phase 1b n = 22[a]		All patients N = 50	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Neutropenia	15 (68)	15 (68)	30 (60)	28 (56)
WBC decreased	15 (68)	15 (68)	28 (56)	26 (52)
Anemia	13 (59)	9 (41)	26 (52)	17 (34)
Thrombocytopenia	12 (55)	6 (27)	23 (46)	13 (26)
Nausea	8 (36)	0	25 (50)	0
ALT increased	7 (32)	2 (9)	16 (32)	7 (14)
Peripheral edema	7 (32)	0	17 (34)	0
Pyrexia	7 (32)	0	19 (38)	1 (2)
Arthralgia	6 (27)	0	13 (26)	0
AST increased	6 (27)	2 (9)	15 (30)	7 (14)
Fatigue	5 (23)	0	26 (52)	1 (2)
Headache	5 (23)	0	16 (32)	0

AEs of Special Interest, n (%)	Phase 1b n = 22[a]		All patients N = 50	
	All Grades	Grade ≥3	All Grades	Grade ≥3
CRS	15 (68)	0	31 (62)	1 (2)
Infection	10 (45)	8 (36)	29 (58)	18 (36)
IEC-HS	8 (36)	2 (9)[b]	12 (24)	3 (6)
ICANS	4 (18)	0	4 (8)	0
GVHD	0	0	0	0

- Any-grade TEAEs occurred in 100% of Phase 1b patients, including:
  - Majority of grade ≥3 TEAEs were hematologic events
  - No treatment related grade 5 AEs

[a]Includes 2 patients who received LD but did not receive ALLO-316. [b]One patient experienced G4 IEC-HS based on GI bleeding with subsequent improvement and 1 patient experienced G3 IEC-HS based on hypotension managed without pressors with subsequent improvement. There were no grade 5 events of IEC-HS.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; GVHD, graft versus host disease; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; LD, lymphodepletion; TEAE, treatment-emergent adverse event; WBC, white blood cell. Data cutoff: 02-May-2025

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Confirmed Responses in Patients With High Tumor CD70 Expression

	CD70+[a] patients Phase 1b n = 20	All CD70+[a] patients n = 38
ORR (confirmed CR or PR per RECIST v1.1), n/N (%)	5/20 (25)	8/38 (21)
CD70+ TPS ≥50%	5/16 (31)	8/31 (26)
CD70+ TPS <50%	0/4 (0)	0/7 (0)

[a]IHC-based CD70 expression.
CR, complete response; IHC, immunohistochemistry; PR, partial response; ORR, objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; TPS, tumor proportion score.
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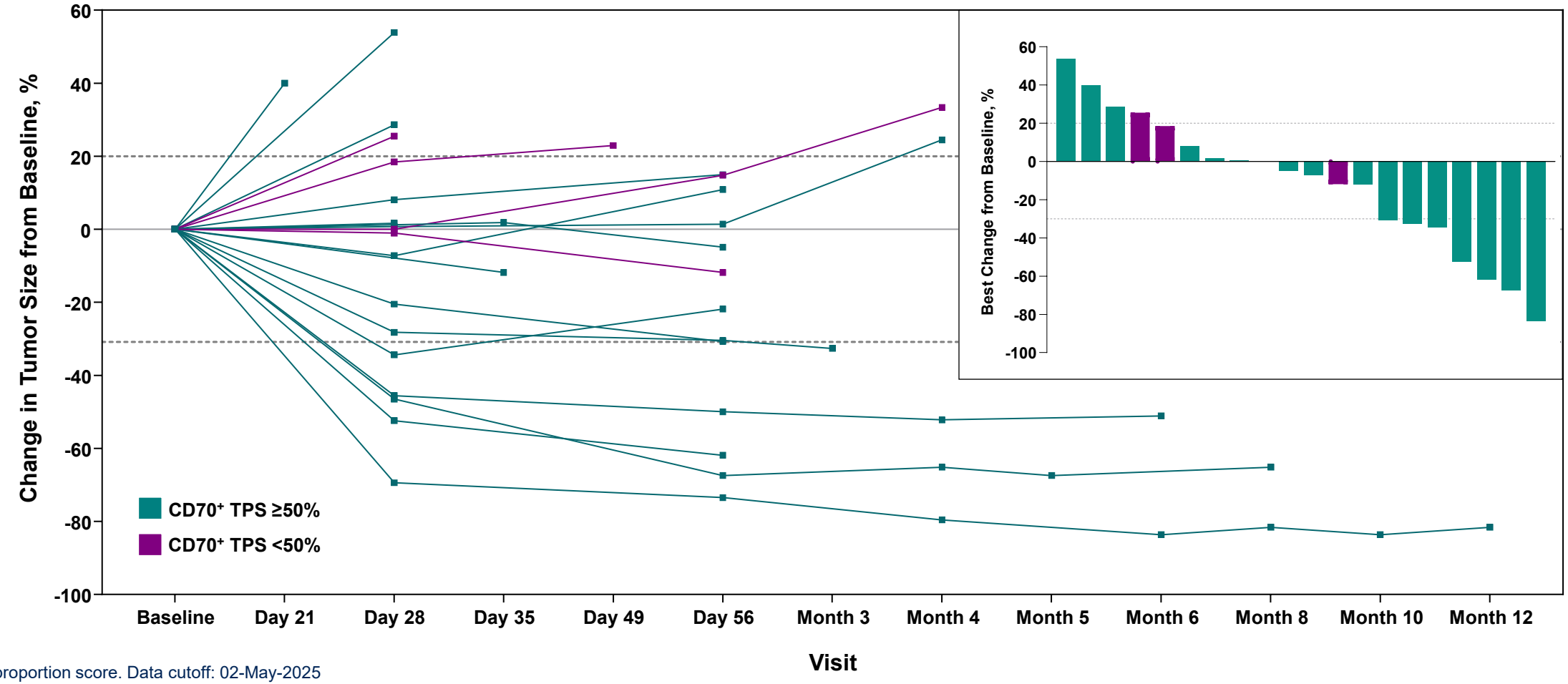
Tumor Responses Occur Early and Are Sustained Following a Single Infusion of ALLO-316

Among CD70+ TPS ≥50% patients, 44% (7/16) had >30% reduction in diameter of baseline target lesions



TPS, tumor proportion score. Data cutoff: 02-May-2025

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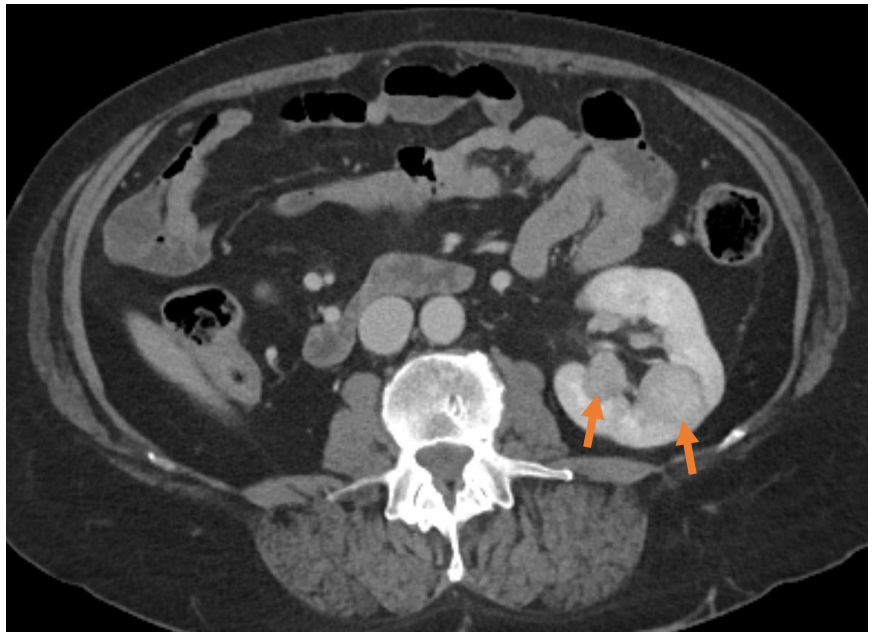
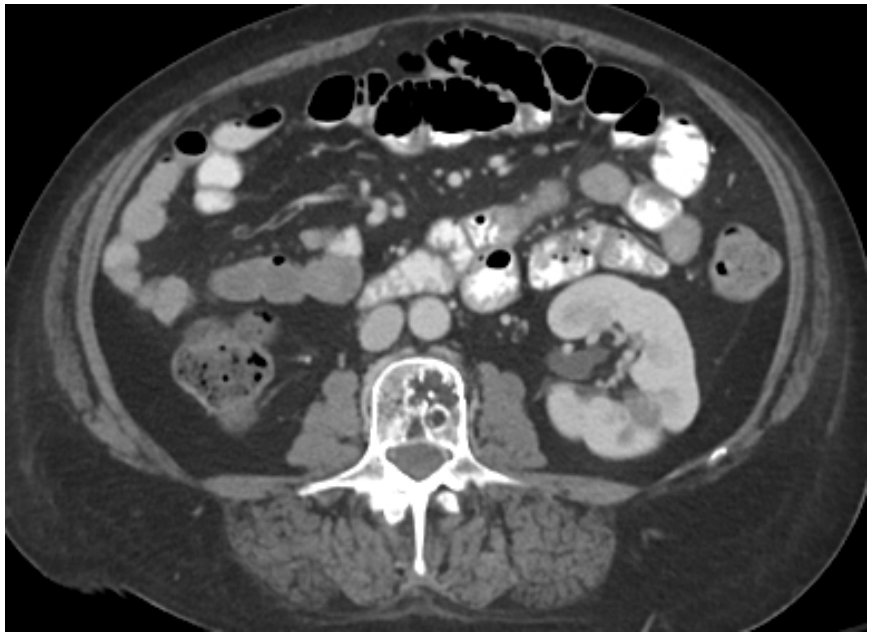
Regression of Contralateral Kidney Metastasis Following a Single Dose of ALLO-316

Baseline



After 1 month



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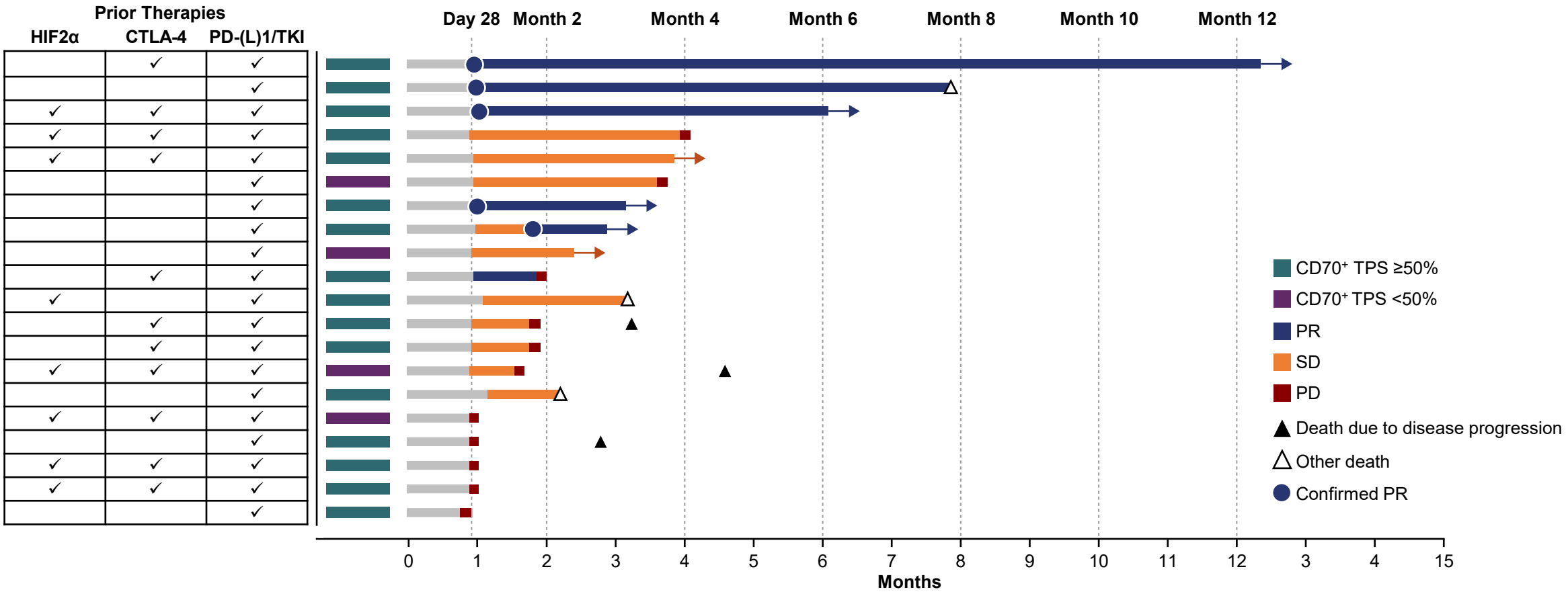
High Response Rate and Ongoing Remissions

Out of 5 confirmed responders, 4 have an ongoing response; 1 has reached the 1 year mark post–ALLO-316



CTLA-4, cytotoxic T-lymphocyte associated protein 4; HIF-2α , hypoxia-inducible factor 2α; PD, progressive disease; PD-(L)1, programmed cell death protein/ligand 1; PR, partial response; SD, stable disease; TKI, tyrosine kinase inhibitor; TPS, tumor proportion score. Data cutoff: 02-May-2025

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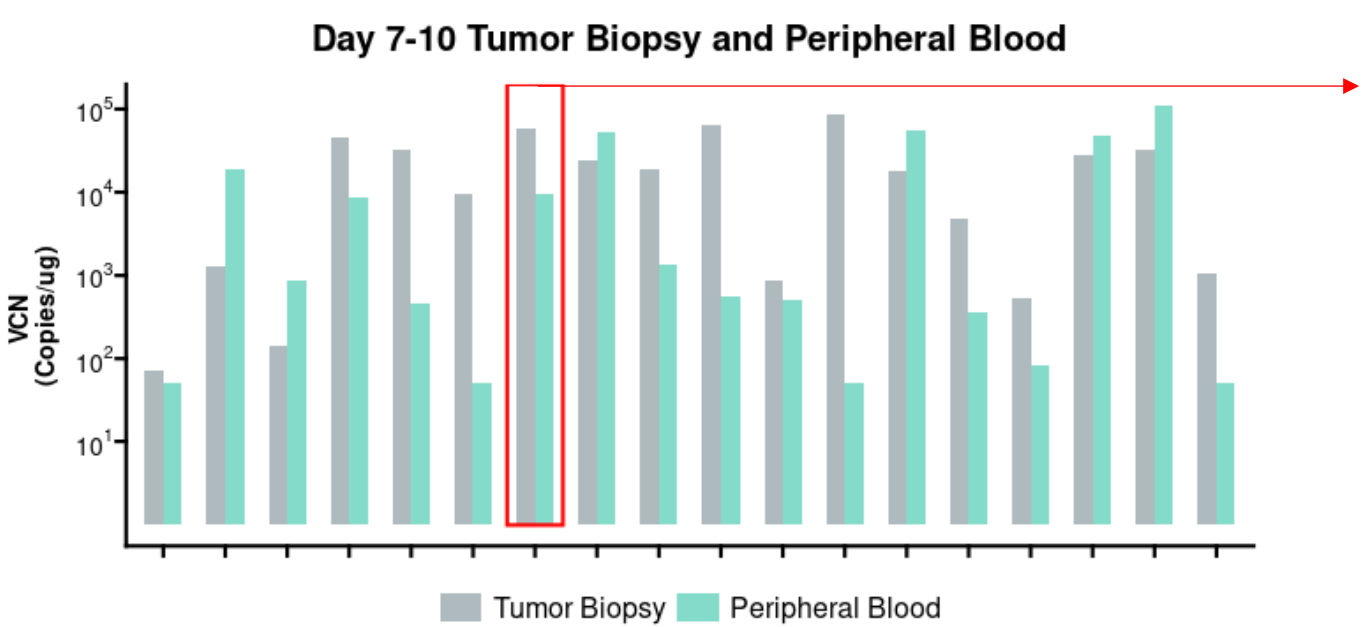
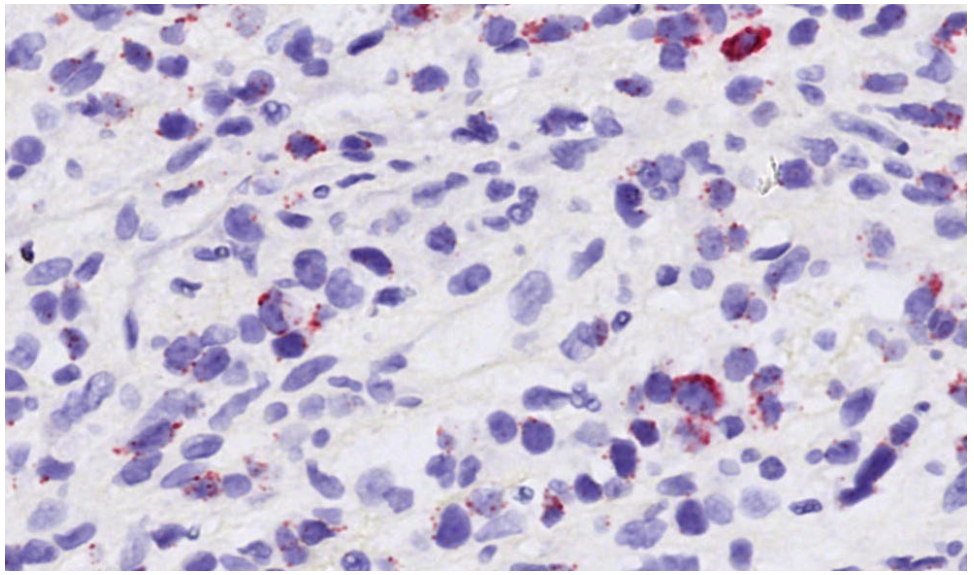
Marked Tumor Infiltration by ALLO-316 Seen in Paired Tumor/Blood Samples



CAR Vector Copy Number (VCN) by PCR



CAR T cell chromogenic RNA *in situ* hybridization

- Homing and infiltration of ALLO-316 CAR T cells into tumor was demonstrated by two independent methods: VCN (PCR) and chromogenic RNA *in situ* hybridization assay using a probe against CAR transcripts
- The high VCN levels observed in the tumor samples demonstrated the extensive infiltration of ALLO-316

CAR, chimeric antigen receptor; PCR, polymerase chain reaction; RNA, ribonucleic acid. Data cutoff: 02-May-2025

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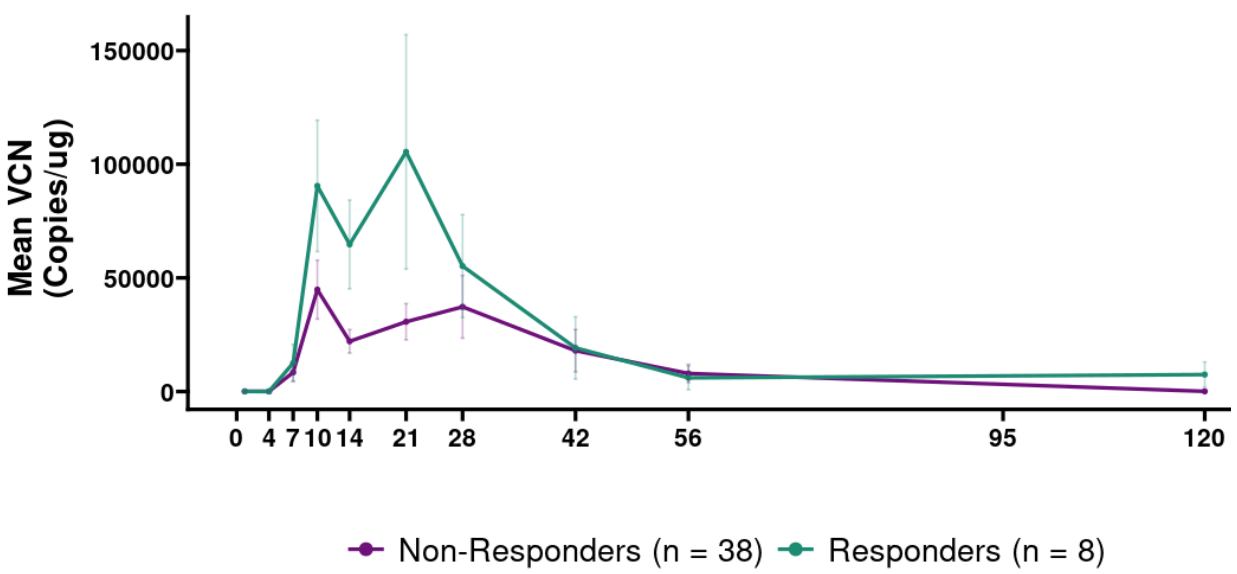
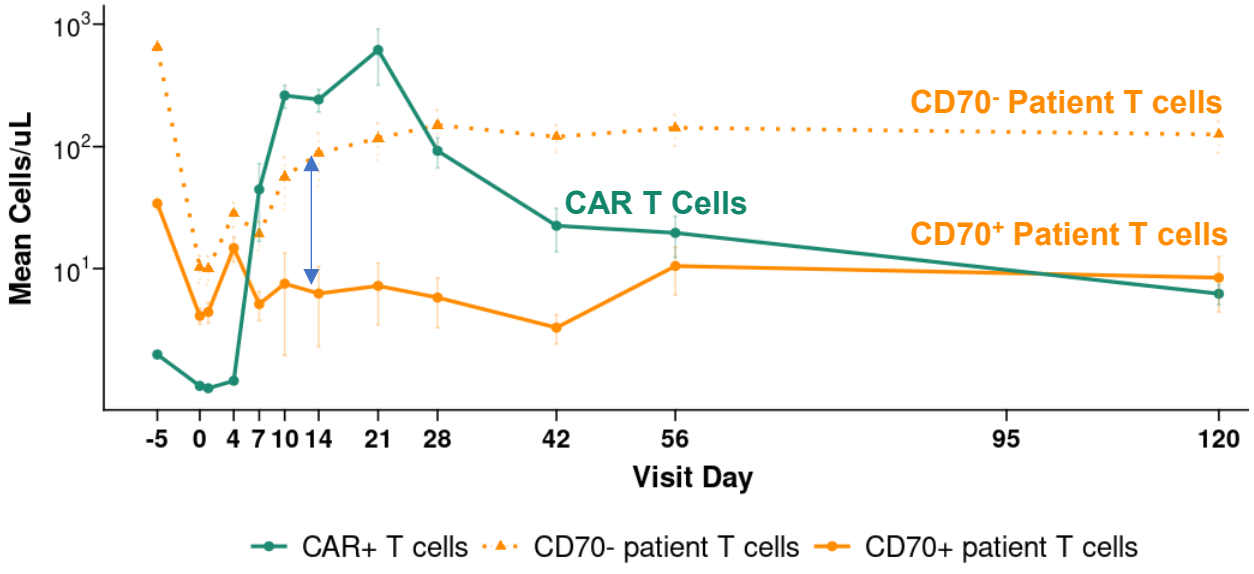
Responders Had Robust Expansion and Persistence of CAR T Cells

CD70⁻ patient T cells quickly rebounded while CD70⁺ patient T cells remained low until ALLO-316 CAR T contraction (Dagger® Effect)

VCN Over Time by Best Overall Response



CD70⁺ Host T Cells are eliminated by ALLO-316



CAR, chimeric antigen receptor; VCN, vector copy number. Data cutoff: 02-May-2025

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Conclusions

- Patients with advanced or metastatic ccRCC have limited options following development of disease resistant to checkpoint blockers, TKIs and HIF-2α inhibitors
- A single dose of ALLO-316 demonstrated a 31% confirmed ORR in patients with heavily-pretreated advanced or metastatic ccRCC. 4 of 5 responses are ongoing, including one extending beyond a year after treatment, representing a potential breakthrough for CAR T therapy in solid tumors
- Safety profile was manageable and consistent with standard Flu/Cy lymphodepletion and an active CAR T therapy. Improvements in the diagnosis of IEC-HS enabled early intervention and effective management
- ALLO-316 delays allorejection by depleting patient $CD70^+$ cells, driving robust and sustained CAR T-cell expansion. This Dagger® effect may be incorporated into other allogeneic CAR T products to enable CAR T expansion and improve responses with reduced intensity of lymphodepletion.
- Results underscore the transformative potential of allogeneic CAR T in solid tumors and validate further development of ALLO-316 in RCC and other $CD70^+$ malignancies

CAR, chimeric antigen receptor; ccRCC, clear cell renal cell carcinoma; Flu/Cy, fludarabine 30 mg/m^2 and cyclophosphamide 500 mg/m^2 daily for 3 days; HIF-2α , hypoxia-inducible factor 2α; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; ORR, objective response rate; TKI, tyrosine kinase inhibitor. Data cutoff: 02-May-2025

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- AlloCAR T™ and Dagger® are trademarks of Allogene Therapeutics, Inc.
- This research was in part made possible by an award from the California Institute of Regenerative Medicine (CLIN2-15343)
- ALLO-316 utilizes Cellectis technology and is licensed exclusively from Cellectis. Allogene holds global development and commercial rights.

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Lay Summary

What did this research tell us?

- A one-time treatment with healthy donor-derived CD70 CAR T cells, ALLO-316, had a treatable side effect profile and showed that approximately 1 in 3 patients with high CD70 in the tumor had a response to therapy. Responses could be long lived, with 1 patient being off therapy and in ongoing response for 1 year after treatment

Who does this research impact?

- Adult patients with advanced kidney cancer that is still growing despite standard treatments

What does this mean for patients right now?

- This study suggests treatment with ALLO-316 may benefit patients with advanced $CD70^{+}$ cancer
- More studies are needed to confirm these results

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