Preliminary Safety and Efficacy Results From a First-in-Human Phase 1 Clinical Study of ALLO-329, a Dual Anti-CD19/Anti-CD70 Allogeneic CAR T-Cell Therapy for Autoimmune Disease

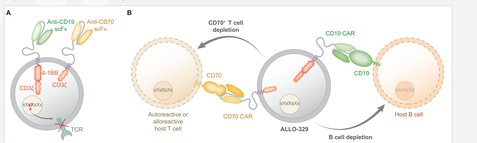
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INTRODUCTION

- Autologous chimeric antigen receptor (CAR) T-cell therapy has shown promising early efficacy in autoimmune disease; however, barriers to access include patient-specific product manufacturing and safety risks from both conventional chemotherapy-based lymphodepletion (LD) and CAR T-cell therapy–related toxicity in patients with chronic autoimmune disease
- Off-the-shelf allogeneic CAR T-cell therapies offer immediate availability but require a strategy to prevent rapid rejection by the patient's immune system
- ALLO-329 is an off-the-shelf, dual CD19/CD70 allogeneic CAR T-cell therapy designed specifically for autoimmune disease, with a goal of depleting CD19+ B cells and plasmablasts, as well as CD70+ T and other immune cells[1] (**Figure 1**)
- Patient T cells that react against allogeneic CAR T cells will upregulate expression of CD70, marking them for destruction by ALLO-329 and providing a proliferative stimulus to ALLO-329
  - Preclinical studies have shown that this anti-rejection mechanism may reduce or eliminate the need for chemotherapy-based LD[1]
- RESOLUTION (NCT07085104) is an ongoing, phase 1, first-in-human study evaluating ALLO-329 at escalating cell doses with and without LD in adults with systemic sclerosis (SSc/scleroderma), idiopathic inflammatory myopathies (IIM/myositis), or systemic lupus erythematosus (SLE/lupus)
- The study is designed to characterize the safety, tolerability, and preliminary efficacy of ALLO-329, to determine the role of LD in clinical and translational outcomes, and to inform further development, including the optimal phase 2 strategy
- This report is focused on safety and B-cell dynamics from all enrolled and treated patients and efficacy in the 10 patients with skin-predominant SSc. Four patients with IIMs, 2 with SLE and 2 with non–skin-predominant SSc were also treated and will be the focus of a future presentation

Figure 1. ALLO-329: Allogeneic CD19/CD70 Dual CAR T Cells (A) and Mechanism of Action (B)

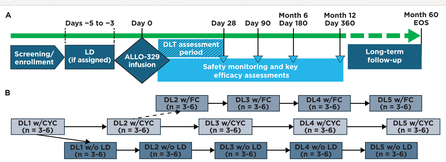


CAR, chimeric antigen receptor; CD, cluster of differentiation; scFv, single-chain variable fragment; TCR, T-cell receptor.

METHODS

- The study design of RESOLUTION is shown in **Figure 2**
  - Key eligibility criteria include adults aged ≥18 to <70 years with active SLE, IIMs, or SSc, despite standard-of-care therapy, including ≥1 immunosuppressive agent for ≥3 months
  - Eligible patients enter the dose-escalation portion of the study, which uses a modified 3+3 design with 5 ALLO-329 cell dose levels (DLs; 20M, 40M, 80M, 160M, or 320M) ± LD. At the time of the data cutoff, patients had enrolled into the DL1, DL2, and DL3 cohorts
  - All patients discontinue immunosuppressive medications prior to initiation of LD or, for no-LD cohorts, prior to ALLO-329 infusion
  - All patients receive ALLO-329 via intravenous infusion on Day 0; patients assigned to LD receive either cyclophosphamide (CYC) on Day −3 or fludarabine on Days −5, −4, and −3, combined with a single dose of CYC (FC) on Day −3
  - An independent safety review team monitors safety and applies prespecified dose-limiting toxicity (DLT) criteria
  - Patients are followed for 60 months post-treatment
- The primary endpoint is the incidence of DLTs and other safety parameters; secondary endpoints include drug-free remission and duration, and efficacy according to disease-specific criteria
  - In SSc patients, the extent of skin involvement is measured using the modified Rodnan skin score (mRSS)
  - Patient-reported disability is measured with the Health Assessment Questionnaire Disability Index (HAQ-DI) and the Patient Global Assessment of Disease Status (PtGA)

Figure 2. RESOLUTION Study Design (A) and Dose Escalation and Expansion Plan (B)



CYC, cyclophosphamide; DL, dose level; DLT, dose-limiting toxicity; EOS, end of study; FC, fludarabine and cyclophosphamide; LD, lymphodepletion; w/, with; w/o, without.
DLs in RESOLUTION are 20M (DL1), 40M (DL2), 80M (DL3), 160M (DL4), and 320M (DL5) ALLO-329 cells.

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RESULTS

Enrollment Status

- Enrollment in RESOLUTION began in November 2025 and is ongoing
- As of the data cutoff of September 21, 2026, 18 patients had received 1 dose of ALLO-329 and completed the 28-day DLT period across 15 sites
- Demographic and disease characteristics for the 10 patients with skin-predominant SSc are shown in **Table 1**

Table 1. Demographic and Disease Characteristics for Patients With Skin-Predominant SSc

Pt. #	DL/LD	Age/Sex	Antibody	Duration of Disease, mos	Prior treatment	Disease Manifestations
1	20M/CYC	48/F	POL3	20	MMF	Contractures, GERD
2	40M/CYC	55/F	POL3	29	HCQ, MMF	Contractures
3	40M/CYC	58/F	Centromere	84	MTX, HCQ, MMF, AZA, myfortic	GI
4	40M/CYC	38/F	SCL70	34	MTX, MMF, RTX, tocilizumab	GI, ILD, contractures, TFR
5	20M/no LD	30/F	SCL70	68	IVIG, MMF	ILD, DU, GI
6	40M/FC	62/M	SCL70	27	LEF, MMF	Arthritis, DU, ILD
7	40M/no LD	40/M	SCL70	15	RTX, MMF	DU, ILD, contractures, esophageal dysmotility
8	40M/no LD	34/F	SCL70	27	AZA, MMF, IVIG	DU, contractures, GI
9	80M/CYC	36/F	SCL70	23	MTX, MMF, tocilizumab	Contractures, GI, GAVE
10	40M/FC	39/F	U1-RNP	71	AZA, SSZ, certolizumab, RTX, MTX, HCQ, tocilizumab	Contractures, DU, TFR, arthritis

AZA, azathioprine; CYC, cyclophosphamide; DL, dose level; DU, digital ulcer; F, female; FC, fludarabine and cyclophosphamide; GAVE, gastric antral vascular ectasia; GERD, gastroesophageal reflux disease; GI, gastrointestinal; HCQ, hydroxychloroquine; ILD, interstitial lung disease; IVIG, intravenous immunoglobulin; LD, lymphodepletion; LEF, leflunomide; M, male; MMF, mycophenolate mofetil; MTX, methotrexate; Pt, patient; RTX, rituximab; SSc, systemic sclerosis; SSZ, sulfasalazine; TFR, tendon friction rub; U1-RNP, U1 ribonucleoprotein.

Safety

- A summary of safety data for all patients who received ALLO-329 and completed the 28-day DLT period is shown in **Table 2**
- No DLTs, immune effector cell–associated hemophagocytic syndrome (IEC-HS), immune effector cell–associated neurotoxicity syndrome (ICANS), or graft-verus-host disease (GvHD) occurred in any patients
- Four patients (22%) experienced cytokine release syndrome (3 with Grade 1, and 1 with Grade 2)
- All patients experienced at least 1 TEAE; 83% had Grade 1 or Grade 2 TEAEs only
- No patients in the no-LD cohorts experienced any TEAEs greater than Grade 2

Table 2. Summary of Treatment-Emergent Adverse Events

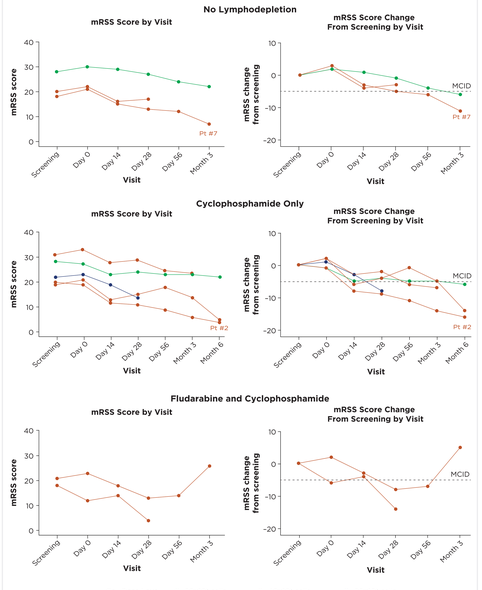
Cohort	20M/40M no LD (n=6)	20M/40M/80M + CYC (n=9)	40M + FC (n=3)	Total (N=18)
TEAEs, n (%)				
Any grade; Grade ≥3	6 (100.0); 0	9 (100.0); 3 (33.3)	3 (100.0); 0	18 (100.0); 3 (16.7)
TESAEs, n (%)				
Any grade; Grade ≥3	1 (16.7); 0	4 (44.4); 1 (11.1)	1 (33.3); 0	6 (33.3); 1 (5.6)
TEAEs of special interest, n (%)				
CRS, any grade; Grade ≥3	1 (16.7); 0	2 (22.2); 0	1 (33.3); 0	4 (22.2); 0
ICANS, any grade; Grade ≥3	0; 0	0; 0	0; 0	0; 0
IEC-HS, any grade; Grade ≥3	0; 0	0; 0	0; 0	0; 0
Infections, any grade; Grade ≥3	0; 0	2 (22.2); 0	1 (33.3); 0	3 (16.7); 0
GvHD, any grade; Grade ≥3	0; 0	0; 0	0; 0	0; 0
Prolonged Grade ≥3 cytopenia[a]	0	1 (11.1)	0	1 (5.6)
DLTs, n (%)	0	0	0	0

CRS, cytokine release syndrome; CYC, cyclophosphamide; DLT, dose-limiting toxicity; FC, fludarabine and cyclophosphamide; GvHD, graft-versus-host disease; ICANS, immune effector cell–associated neurotoxicity syndrome; IEC-HS, immune effector cell–associated hemophagocytic syndrome; LD, lymphodepletion; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.
[a]A prolonged cytopenia was defined as a Grade ≥3 anemia, neutropenia, or thrombocytopenia present on the day of or 30 days following the ALLO-329 infusion.

Clinical Efficacy in Patients With Skin-Predominant SSc

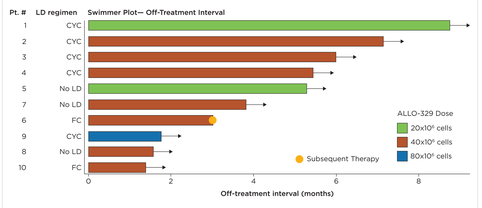
- Changes in total mRSS scores over time among patients with skin-predominant SSc are shown in **Figure 3**
  - Baseline mRSS scores reflected severe to extensive skin involvement
  - Improvements in total mRSS scores were observed as early as Day 14 after ALLO-329 infusion across all 3 LD regimens and all 3 DLs, with the greatest reductions observed at DL2 (40M) and DL3 (80M)
  - Clinical improvement deepened over time, with 8 patients achieving and maintaining the 5-point minimal clinically important difference (MCID) in mRSS score
  - Four patients achieved mRSS scores <10 between Day 28 and Month 6, indicating marked reductions in skin thickening
- A swimmer plot depicting the treatment-free interval for patients with skin-predominant SSc is shown in **Figure 4**

Figure 3. mRSS Score and Change in mRSS Score From Screening by Visit Following ALLO-329 Infusion in Patients With Skin-Predominant SSc, by LD Regimen and Cell DL



DL, dose level; LD, lymphodepletion; MCID, minimal clinically important difference; mRSS, modified Rodnan skin score; Pt, patient; SSc, systemic sclerosis.
Two SSc patients, 1 who received 20M cells with no LD and 1 who received 40M cells with no LD, were excluded because their screening mRSS scores were <10 (lung-predominant disease).
SSc disease activity assessments include measurement of skin involvement using the mRSS, with scores 0 to 9 indicating mild involvement, 10 to 19 indicating moderate involvement, 20 to 30 indicating severe involvement, and >30 indicating extensive involvement.

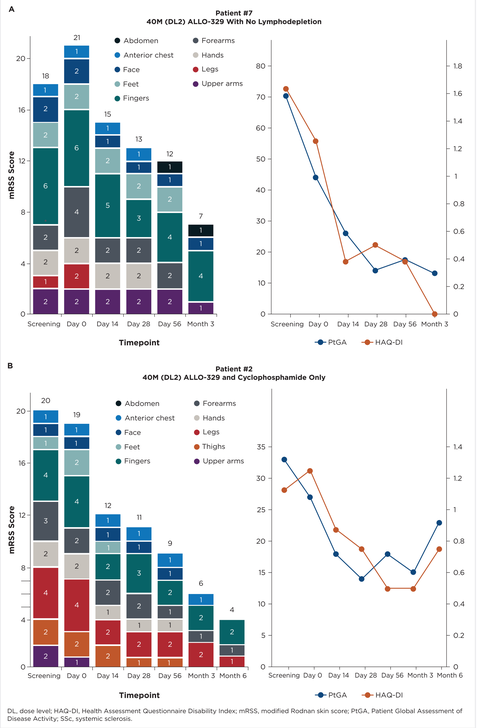
Figure 4. Treatment-Free Interval Following ALLO-329 Infusion in Patients With Skin-Predominant SSc



CYC, cyclophosphamide; FC, fludarabine and cyclophosphamide; LD, lymphodepletion; Pt, patient; SSc, systemic sclerosis.

- Changes in mRSS scores across individual body sites after at least 3 months of treatment in 2 individual patients are shown in **Figure 5**
  - The first patient was a 40-year-old male with anti-SCL70 diffuse cutaneous SSc, with rapidly progressive disease along with interstitial lung disease, joint contractures, digital ulcers, and esophageal dysmotility despite methotrexate and mycophenolate mofetil, who received 40M (DL2) ALLO-329 with no LD (**Figure 5A**)
  - The second patient was a 55-year-old female with anti-POL3 diffuse cutaneous SSc with progressive skin thickening and joint contractures refractory to hydroxychloroquine and mycophenolate mofetil, who received 40M (DL2) ALLO-329 and CYC (**Figure 5B**)

Figure 5. Change in mRSS Scores After Treatment With ALLO-329 in 2 Patients With Diffuse SSc

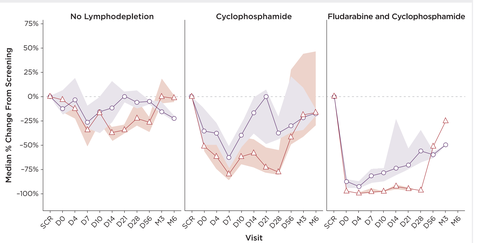


DL, dose level; HAQ-DI, Health Assessment Questionnaire Disability Index; mRSS, modified Rodnan skin score; PtGA, Patient Global Assessment of Disease Activity; SSc, systemic sclerosis.

B Cell and Total Lymphocyte Kinetics

- B-cell–specific suppression was observed across LD regimens, including in patients who received no lymphodepletion
- The extent of B-cell suppression appeared to correlate with LD intensity (**Figure 6**)
- Restoration of pre-treatment B-cell and absolute lymphocyte counts occurred most rapidly in patients who did not receive LD

Figure 6. Change in B-Cell and Absolute Lymphocyte Count Over Time by Lymphodepletion Group



CD, cluster of differentiation; D, day; IQR, interquartile range; M, month; SCR, screening.
Lines are median participant level percentage change; ribbons are IQR; Screening = 0%.
Percentage change was calculated separately for each participant and measure. A valid positive SCR value was required for the corresponding measure.

CONCLUSIONS

- Accrual in RESOLUTION was rapid, with 18 patients enrolled over approximately 10 months in this novel, first-in-human trial of ALLO-329, a dual CD19/CD70 allogeneic CAR T-cell therapy designed specifically for autoimmune disease
- ALLO-329 with and without LD demonstrated a favorable safety profile in 18 patients with autoimmune disease with no DLTs, no IEC-HS, ICANS, or GvHD, and only low-grade cytokine release syndrome
- Diffuse cutaneous SSc carries high morbidity and mortality, yet no therapy has been shown to reliably halt or reverse disease progression; current treatment options are largely immunosuppressive, chronic, and organ-directed and do not address underlying immune-mediated pathology
- Preliminary efficacy was observed in 10 patients with skin-predominant SSc, with early and durable improvements in mRSS scores observed in the majority of patients following ALLO-329 treatment, including those who received ALLO-329 without LD
- Nine of 10 patients with SSc remained off background immunosuppressives at the time of data cutoff
- Preliminary evidence of B-cell suppression was observed in all cohorts, including in patients who received only ALLO-329. Durable clinical improvement occurred despite absence of complete B-cell depletion, suggesting peripheral B-cell aplasia may not be necessary to achieve immune reset. Additional correlative investigation is ongoing to identify key immunological determinants of clinical response to ALLO-329
- Enrollment and dose escalation in DL3, DL4, and DL5 cohorts is ongoing. Cohort expansion, identification of a recommended phase 2 regimen, and exploration of ALLO-329 in additional autoimmune indications are future goals for the program

Reference

1. Zhang K, et al. *Nat Commun*. 2026;17(1):5055.

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