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Clinical Outcomes From the Pooled Safety Analysis of CD19 NEX-T™ (BMS-986353), a Chimeric Antigen Receptor (CAR) T Cell Therapy Manufactured Using a Next-Generation Process, in Severe Refractory Autoimmune Diseases: Results From Phase 1 Breakfree Studies

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Tandem Meetings: Transplantation & Cellular Therapy Meetings of ASTCT® and CIBMTR®
Abstract #1 - Best Abstracts Session
Friday, February 6, 2026 | 8:15 AM MST
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Disclosures

Ran Reshef

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Introduction

CD19 CAR T cell therapies have demonstrated **unprecedented responses** across multiple B cell malignancies, leading to long-term remissions[1]

Given the central role of **autoreactive B cells** in autoimmune diseases, a **single infusion** of CD19 CAR T cell therapy may **reset the immune system**, potentially leading to **long-term, treatment-free disease control**[2]

- Current therapies for autoimmune diseases often fail to achieve adequate disease control or modify disease trajectory[2]

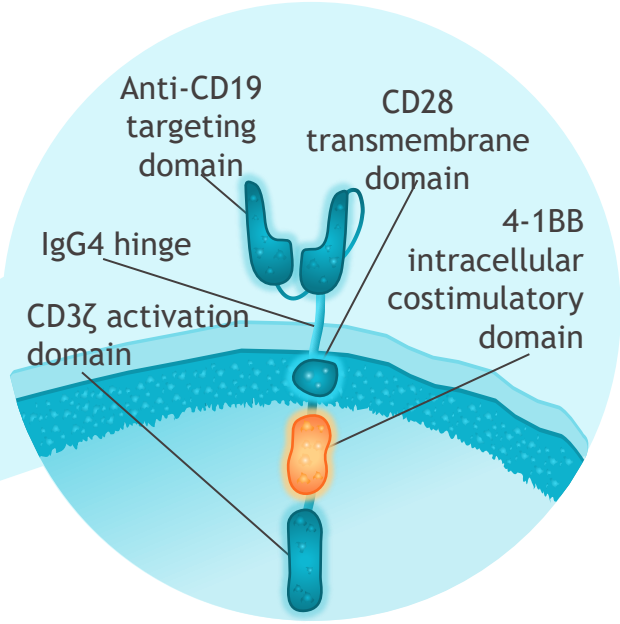
Zola-cel (BMS-986353, formerly CD19 NEX-T™) is an investigational CD19-directed T cell therapy, utilizing the **same CD19-specific CAR construct as liso-cel**,[a] that leverages the next-generation **NEX-T manufacturing process**

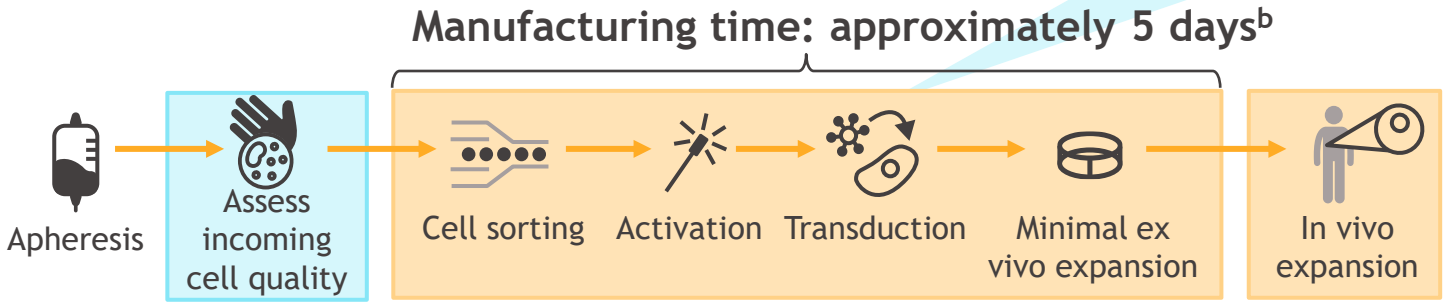
- Zola-cel is currently being evaluated across autoimmune diseases

[a]Liso-cel is only approved to treat certain hematologic malignancies.
CAR, chimeric antigen receptor; liso-cel, lisocabtagene maraleucel; zola-cel, zolacabtagene autoleucel.
1. Anagnostou T, et al. *Lancet Hematol*. 2020;7(11):e816-e826. **2.** Müller F, et al. *N Engl J Med*. 2024;390(8):687–700.

The NEX-T Process Provides a Shorter Manufacturing Time With a High-Quality Product

- **Zola-cel (CD19 NEX-T)** is an investigational **CD19-directed T cell therapy expressing the CAR construct of liso-cel**, which is approved for B cell malignancies[a]
  - The NEX-T process **shortens manufacturing time** while maintaining **cell quality,** allowing **stable transgene integration**, and **optimizing phenotypic attributes**[1]





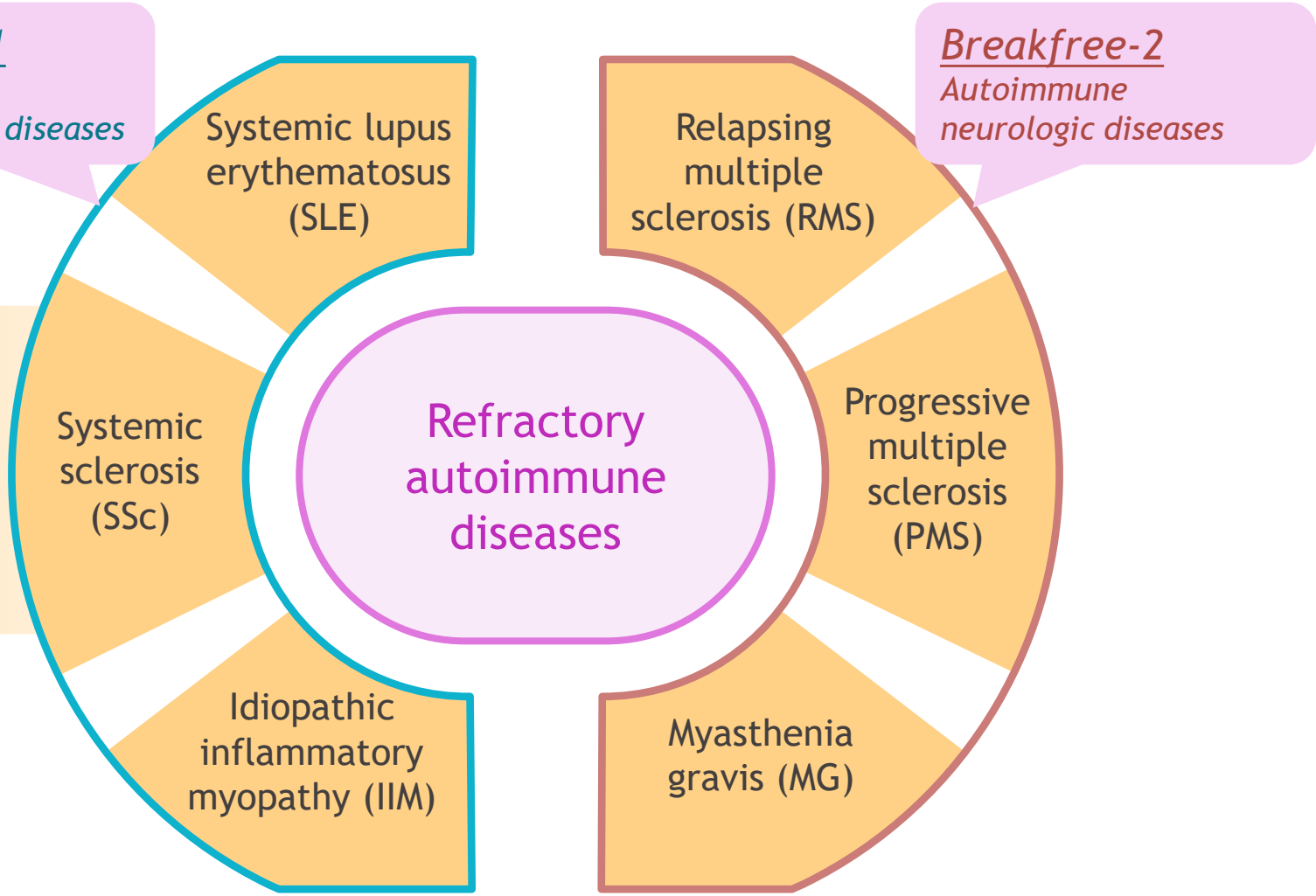
Key considerations

- Process informed by extensive CAR T cell manufacturing experience in products for hematologic indications (>15,000 patients)
- Rapid manufacturing time followed by QC/QA testing and release
- Robust and scalable manufacturing

[a]Liso-cel is only approved to treat certain hematologic malignancies.
[b]Individual manufacturing times may vary.
CAR, chimeric antigen receptor; IgG, immunoglobulin G; liso-cel, lisocabtagene maraleucel; QA, quality assurance; QC, quality control; zola-cel, zolacabtagene autoleucel.
1. Costa L, et al. *Blood*. 2022;140(suppl 1):1360-1362.

Objective

Evaluate the **pooled safety** and **preliminary efficacy** of zola-cel in severe, refractory autoimmune diseases from the **phase 1 Breakfree-1 and Breakfree-2 studies**



zola-cel, zolacabtagene autoleucel.

Breakfree-1 & Breakfree-2 Study Design

Patients with active autoimmune disease refractory to treatment:

Breakfree-1 (NCT05869955)

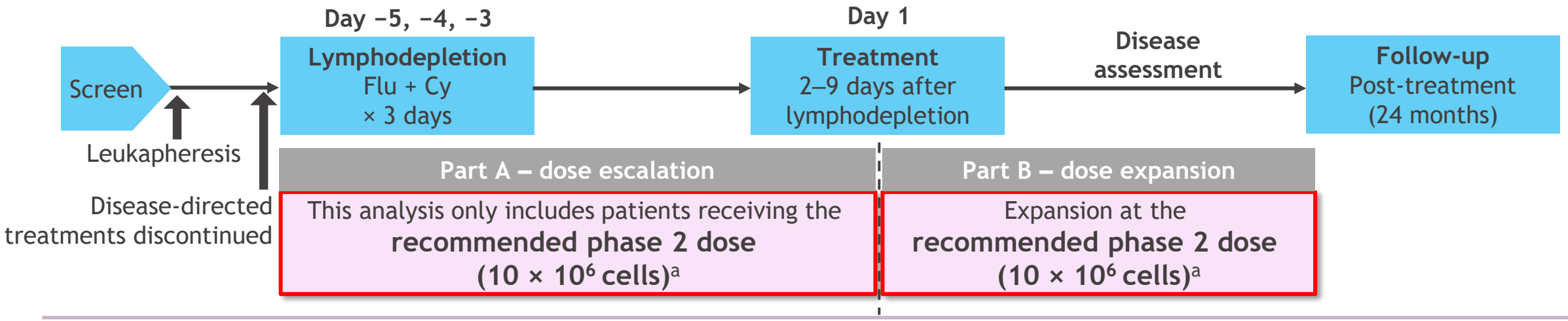
SLE | IIM | SSc

\+

Breakfree-2 (NCT06220201)

RMS | PMS | MG

Phase 1 study design



1° Primary endpoint Evaluate the **safety and tolerability** of zola-cel and determine **the recommended phase 2 dose**

2° Secondary endpoint Evaluate the **preliminary efficacy** and **pharmacokinetics** of zola-cel

[a]As of the pooled data cutoff date of August 20, 2025.

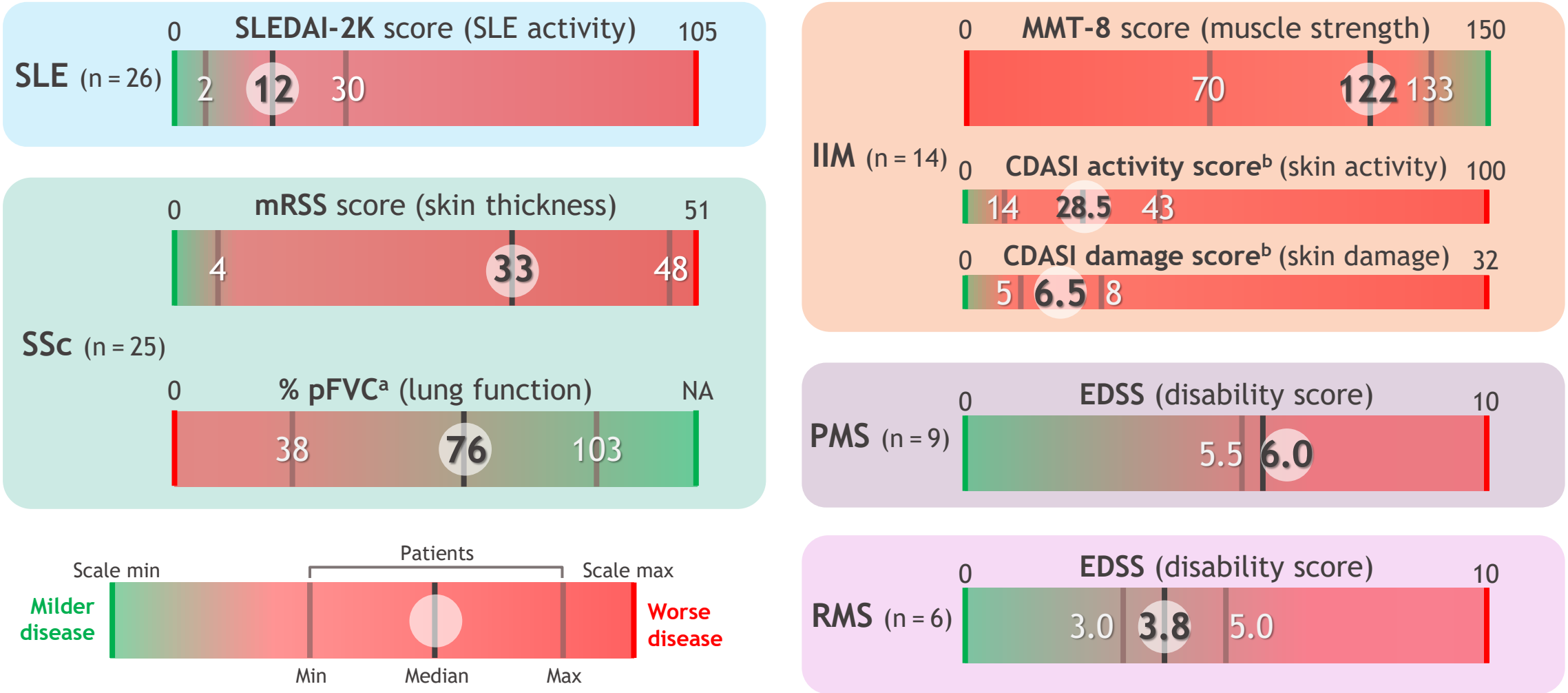
Cy, cyclophosphamide; Flu, fludarabine; IIM, idiopathic inflammatory myopathy; MG, myasthenia gravis; PMS, progressive multiple sclerosis; RA, rheumatoid arthritis; RMS, relapsing-remitting multiple sclerosis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; zola-cel, zolacabtagene autoleucel.

Patient Demographics and Baseline Characteristics[a]

	Breakfree-1			Breakfree-2			
	SLE (n = 26)	SSc (n = 25)	IIM (n = 14)	PMS (n = 9)	RMS (n = 6)	MG (n = 3)	Overall (N = 83)
Age, median (range), y	33 (18–53)	50 (29–65)	45 (24–74)	51 (34–57)	36 (27–50)	49 (37–53)	44 (18–74)
Sex, female, n (%)	21 (80.8)	21 (84.0)	10 (71.4)	3 (33.3)	5 (83.3)	2 (66.7)	62 (74.7)
Race, n (%)							
White	14 (53.8)	22 (88.0)	6 (42.9)	8 (88.9)	4 (66.7)	3 (100)	57 (68.7)
Black or African American	5 (19.2)	0	2 (14.3)	0	0	0	7 (8.4)
Asian	2 (7.7)	0	2 (14.3)	0	0	0	4 (4.8)
Multiple	1 (3.8)	0	1 (7.1)	1 (11.1)	0	0	3 (3.6)
Unknown/not reported	4 (15.4)	3 (12.0)	3 (21.4)	0	2 (33.3)	0	12 (14.5)
Number of prior failed disease-directed treatments, median	7	3	6	2	2	6	-
Time from diagnosis to infusion, median (range), y	9.2 (1.0–37.5)	1.7 (0.4–4.4)	3.5 (0.8–14.2)	5.6 (2.6–15.4)	9.0 (2.4–16.3)	12.3 (6.7–26.5)	-
Median (range) follow-up, d	142 (24–644)	80 (16–430)	86 (9–381)	63 (2–106)	61.5 (21–190)	22 (4–52)	92 (2–644)

[a]Based on the safety-evaluable population who received the RP2D as of the pooled data cutoff date of August 20, 2025.
IIM, idiopathic inflammatory myopathy; MG, myasthenia gravis; PMS, progressive multiple sclerosis; RMS, relapsing multiple sclerosis; RP2D, recommended phase 2 dose; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

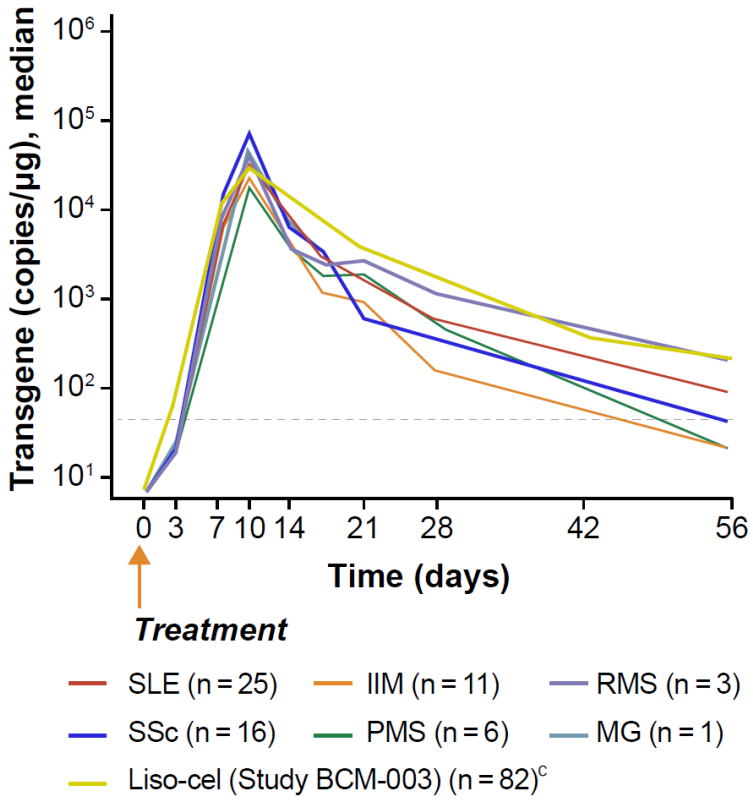
Patients Had High Baseline Disease Activity Across Indications



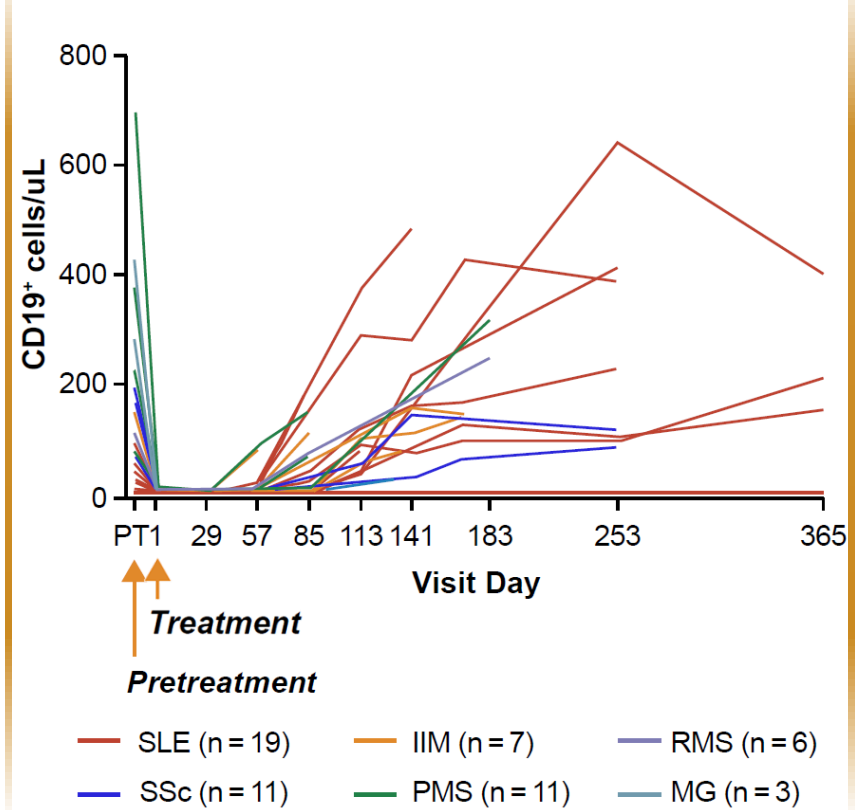
Based on the safety-evaluable population as of the pooled data cutoff date of August 20, 2025.
[a]In patients with SSc-ILD (n = 15). [b]In patients with dermatomyositis (n = 3).
CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; EDSS, Expanded Disability Status Scale; IIM, idiopathic inflammatory myopathy; ILD, interstitial lung disease; MMT-8, Manual Muscle Test-8; mRSS, modified Rodnan skin score; NA, not applicable; pFVC, predicted forced vital capacity; PMS, progressive multiple sclerosis; RMS, relapsing multiple sclerosis; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SSc, systemic sclerosis.

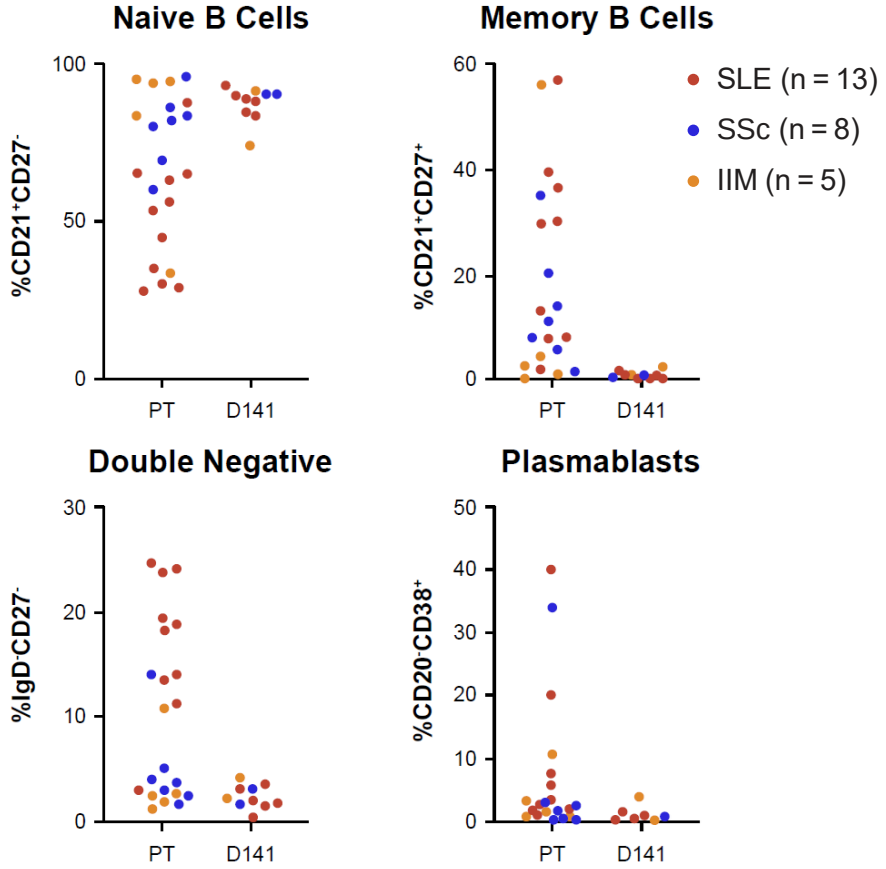
All Patients Achieved Robust CAR T Cell Expansion and Complete Peripheral B Cell Depletion[a] After Zola-cel Infusion

Transgene PK profile of zola-cel[b] (10 × 10^6 cells)



Peripheral B cell concentration and phenotype after zola-cel (10 × 10^6 cells)





Median (range) time to B cell repopulation was 113 (57–NR) days, and **repopulated B cells were predominantly naive** with a **decrease in memory B cells and double-negative B cells**

Available PK data are shown as of the PK data cutoff date of September 12, 2025. All available PD data are shown for patients with ≥1 month of follow-up.
[a]Complete B cell depletion defined as 0 CD19+ cells/µL. [b]Dashed horizontal line represents the limit of detection for the assay (40 copies/µg).[c]Liso-cel was assessed in a hematological study.
CAR, chimeric antigen receptor; IIM, idiopathic inflammatory myopathy; MG, myasthenia gravis; NR, not reached; PD, pharmacodynamic; PK, pharmacokinetic; PMS, progressive multiple sclerosis; PT, pretreatment; RMS, relapsing multiple sclerosis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

CRS and ICANS Events Were Brief, Transient, and Reversible

CRS and ICANS (up to 90 days post-infusion)	Total (N = 83)	
	CRS	ICANS
Any grade, n (%)	48 (57.8)	10 (12.0)
Grade 1	40 (48.2)	6 (7.2)
Grade 2	7 (8.4)	1 (1.2)
Grade 3	1 (1.2)	3 (3.6)
Grade ≥4	0	0
Time to onset, median (range), d	7.5 (2—11)	9.0 (7—12)
Duration[a], median (range), d	3.0 (1—11)	3.0 (1—10)
CRS and ICANS treatment, n (%)		
Tocilizumab	25 (30.1)[b]	1 (1.2)
Corticosteroids	8 (9.6)[c]	10 (12.0)[d]
Anakinra	0	3 (3.6)

- Up to 90 days post-infusion, most CRS and ICANS events were **grade 1** and **resolved in a median of 3 days**
  - One grade 3 CRS (SLE) was treated with tocilizumab and corticosteroids and resolved within 1 day
  - Three grade 3 ICANS events (SSc, n = 2; IIM, n = 1) were **transient** and resolved completely with standard treatment (corticosteroids, anakinra) within 3–5 days

All patients received zola-cel at a dose level of 10×10^6 CAR+ T cells.
[a]Multiple events occurring within 7 days of each other were considered as 1 episode. [b]Includes tocilizumab and tocilizumab-aazg. [c]Includes dexamethasone. [d]Includes dexamethasone and methylprednisolone sodium succinate.
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IIM, idiopathic inflammatory myopathy; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; zola-cel, zolacabtagene autoleucel.

The Safety Profile of Zola-cel in Autoimmune Diseases Is Manageable

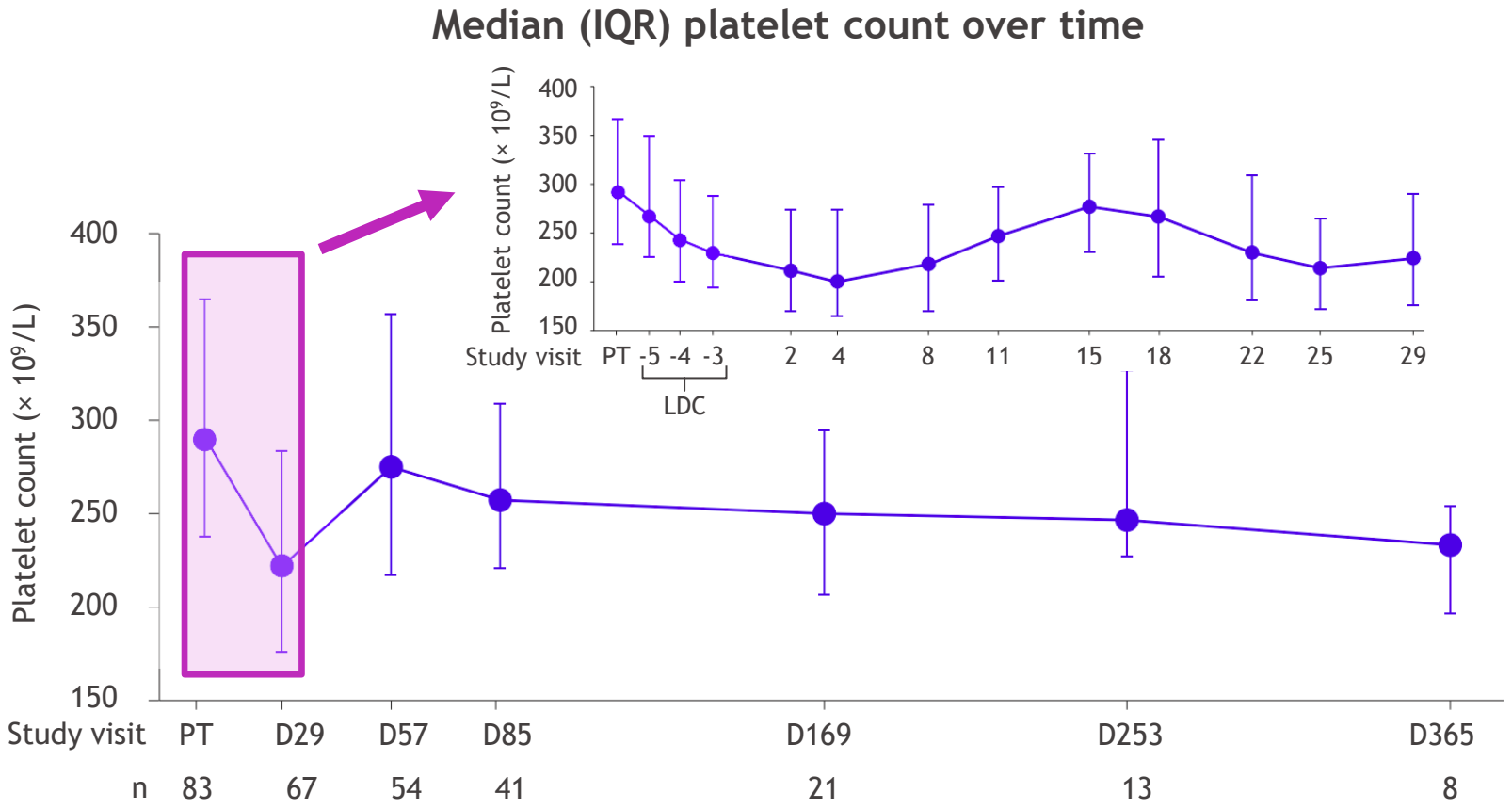
TEAEs, n (%)	Total (N = 83)	
	Any grade	Grade 3/4
Patients with any TEAE	80 (96.4)	51 (61.4)
TEAEs of interest[a]		
Hematologic TEAEs	44 (53.0)	36 (43.4)
Hypogammaglobulinemia	1 (1.2)	0
Grade 3/4 infections	–	5 (6.0)
Hemophagocytic lymphohistiocytosis (IEC-HS)	1 (1.2)	0
Prolonged cytopenia[b]	0	0

- Up to 90 days post-infusion, most TEAEs of interest were **brief**, **manageable**, and **completely reversible** with **no clinical sequelae**
- All infections **resolved completely** after treatment
- **No prolonged grade 4 cytopenias**[b] were observed in 83 treated patients across autoimmune diseases
- **No CAR-related malignancies** were observed

All patients received zola-cel at a dose level of 10×10^6 CAR+ T cells. Median (range) follow-up was 92 (2–644) days.
[a]Excluding CRS and ICANS. [b]Grade ≥4 lasting for 28 days (Breakfree-1) or 42 days (Breakfree-2) post-infusion.
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IEC-HS, immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome; TEAE, treatment-emergent adverse event; zola-cel, zolacabtagene autoleucel.

Low Rates of High-Grade Cytopenias Were Reported Post Infusion

	Total (N = 83)
Any cytopenia, n (%)	41 (49.4)
Grade 3	13 (15.7)
Grade 4	18 (21.7)
Thrombocytopenia, n (%)	
Grade 3	0 (0.0)
Grade 4	1 (1.2)
Neutropenia, n (%)	
Grade 3	10 (12.0)
Grade 4	18 (21.7)
Anemia, n (%)	
Grade 3	10 (12.0)
Grade 4	0

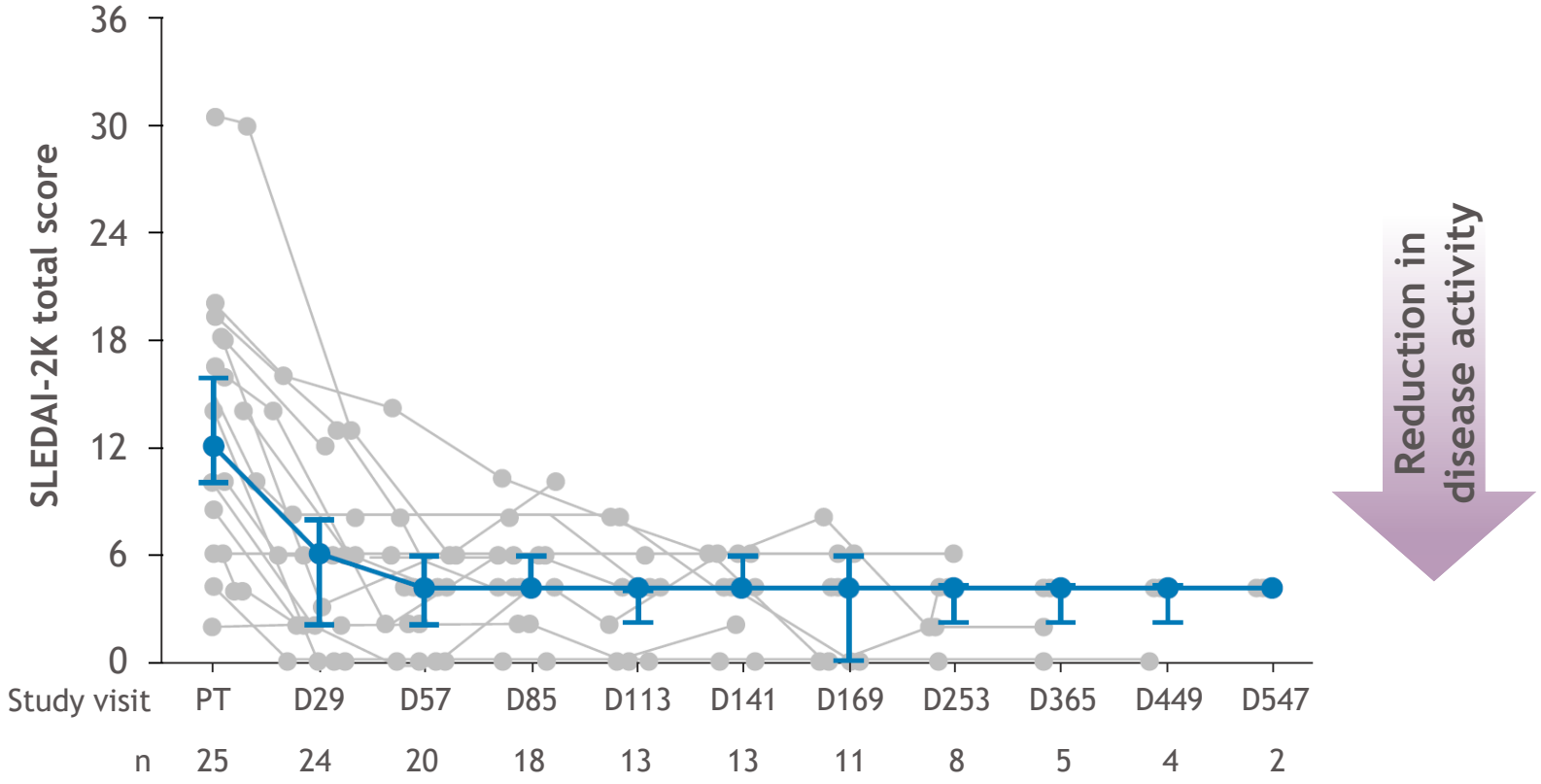


Grade 3 or 4 cytopenias were **not** reported in **62.7%** of patients

All patients received zola-cel at a dose level of 10 × 10^6 CAR+ T cells.
CAR, chimeric antigen receptor; D, day; IQR, interquartile range; LDC, lymphodepleting chemotherapy; PT pretreatment; zola-cel, zolacabtagene autoleucel.

Patients With SLE Demonstrated Rapid Improvements in Disease Activity

Median (IQR) SLEDAI-2K total score over time in patients with SLE

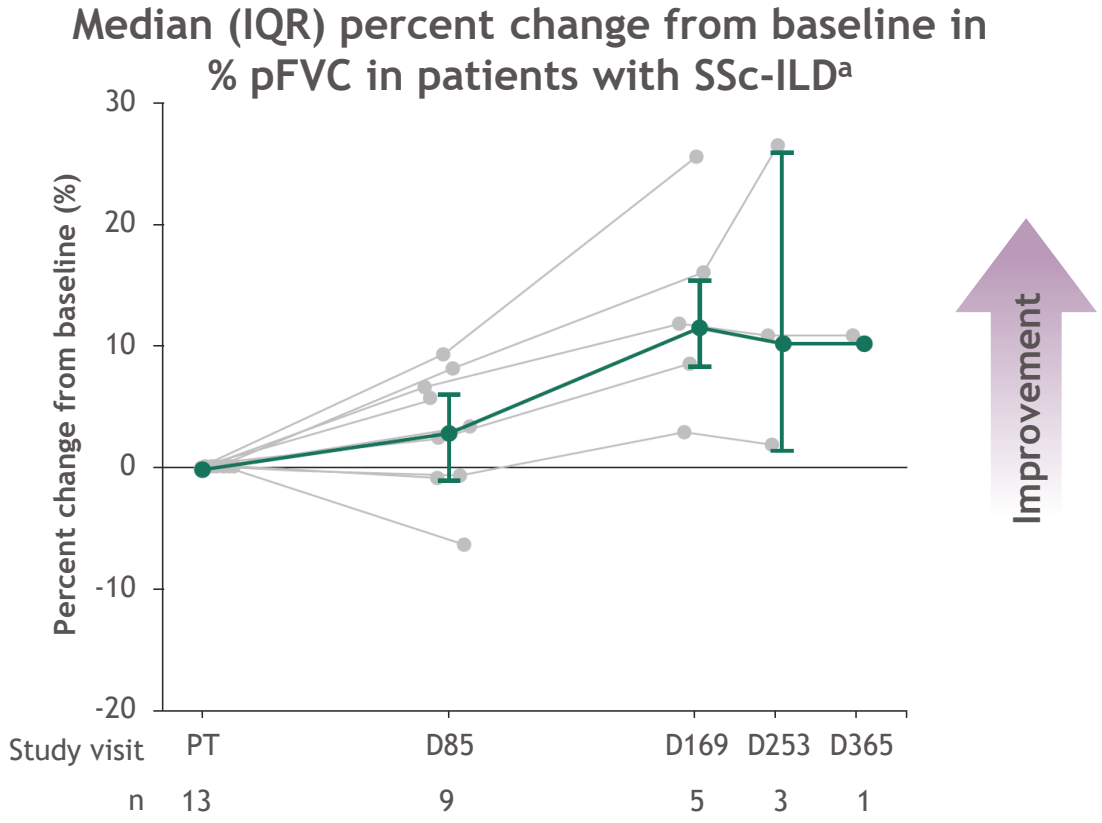


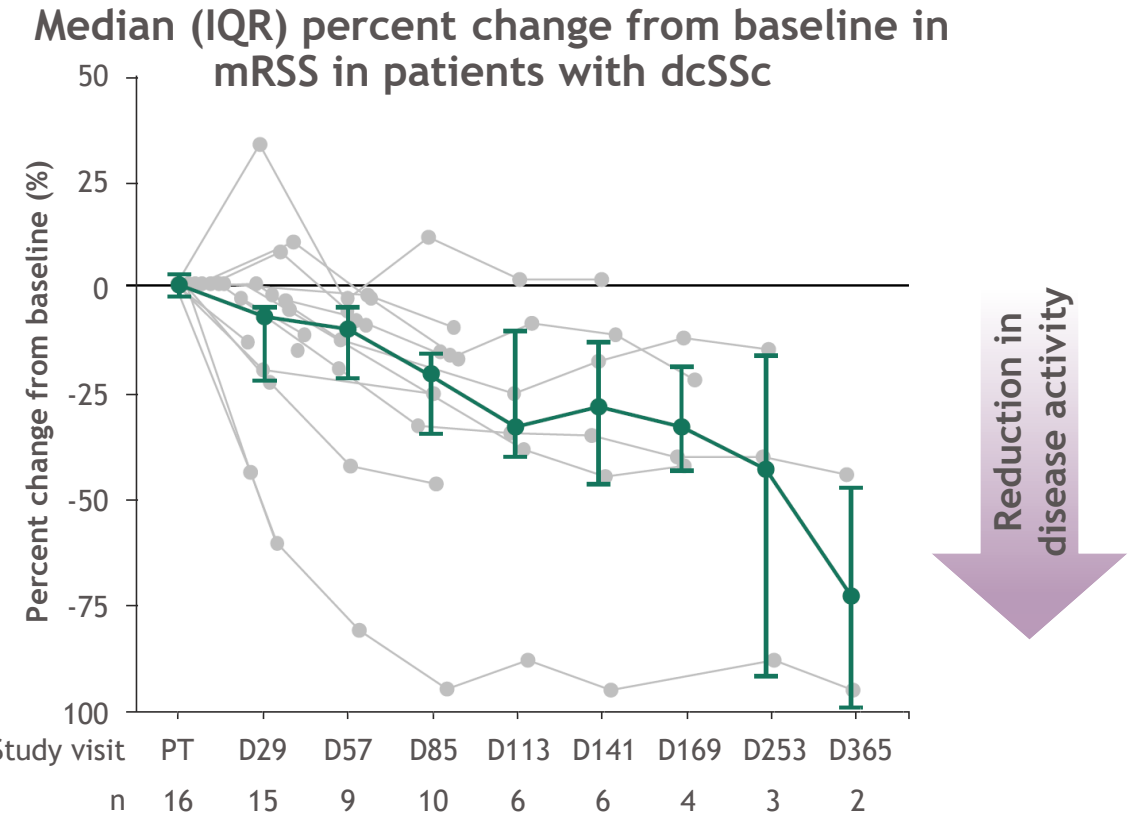
All efficacy-evaluable patients with SLE, except 1, had **resolution of clinical symptoms**

- *Patients had a median (range) 10 (0–18) point reduction in SLEDAI-2K score at 6 months (n = 11)*

Baseline median (range) SLEDAI-2K score was 12 (2–30).
D, day; IQR, interquartile range; PT, pretreatment; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

Patients With SSc Demonstrated Improvements in Lung Function and Skin Thickness





Improvement in lung function in patients with SSc-ILD

- *Median (range) improvement from baseline in % pFVC was 11.6% (2.8%–25.5%) at 6 months (n = 5)*

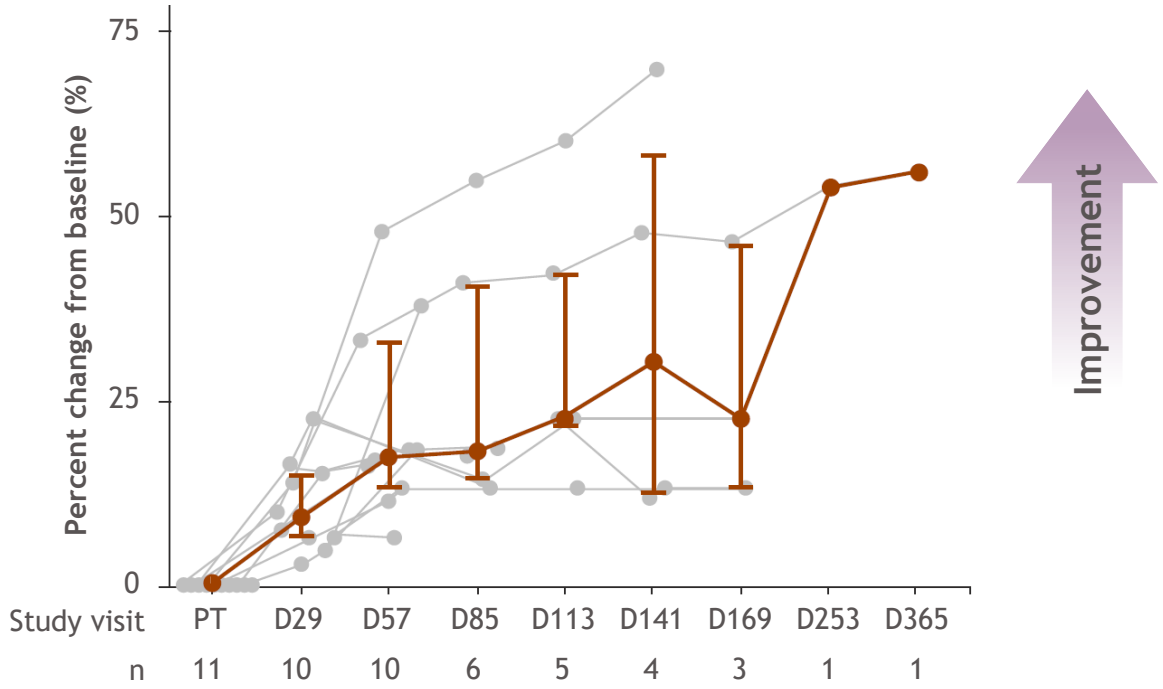
Improvement in skin thickness in patients with dcSSC

- *Median (range) change from baseline in mRSS was –33.3 (–45.5 to –13.9) at 6 months (n = 4)*

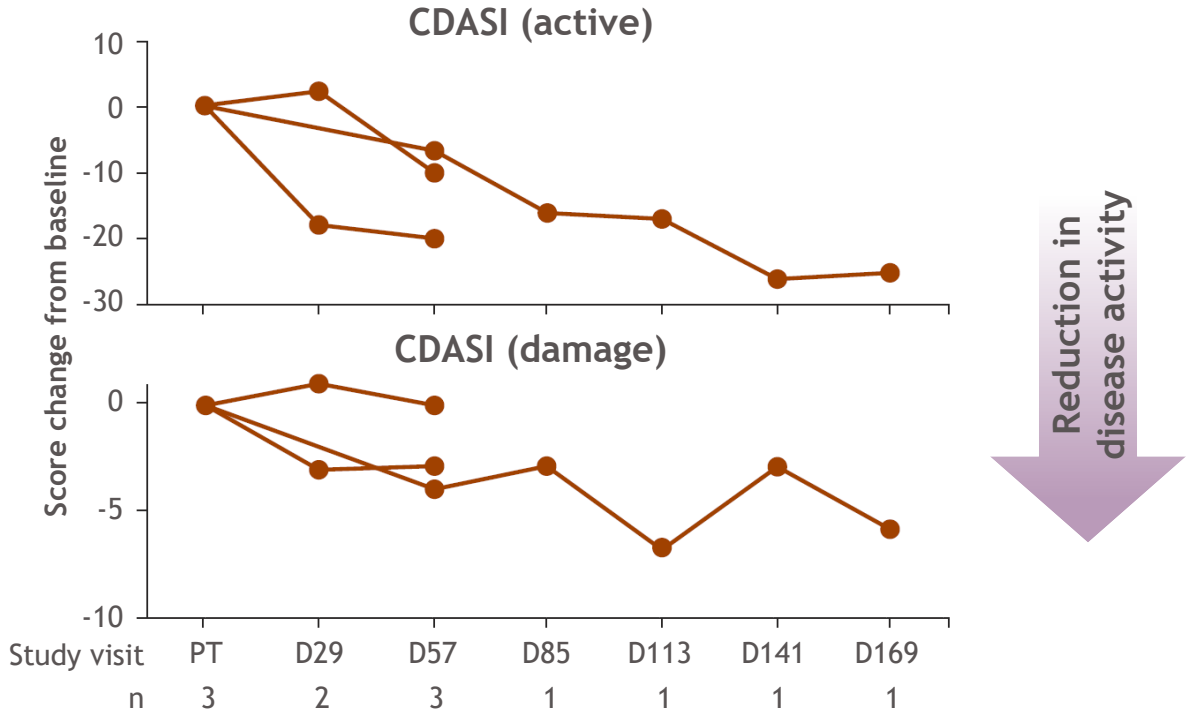
Baseline median (range) pFVC% was 76 (38–103). Baseline median (range) mRSS score was 33 (4–48).
[a]In patients with ≥3 months of follow-up.
D, day; dcSSC, diffuse cutaneous systemic sclerosis; ILD, interstitial lung disease; IQR, interquartile range; mRSS, modified Rodnan skin score; pFVC, predicted forced vital capacity; PT, pretreatment; SSc, systemic sclerosis.

Patients With IIM Demonstrated Improvements in Muscle Strength and Skin Disease

Median (IQR) percent change from baseline in MMT-8 score in patients with IIM



Change from baseline in CDASI score in patients with dermatomyositis



Improvement in muscle strength in patients with IIM

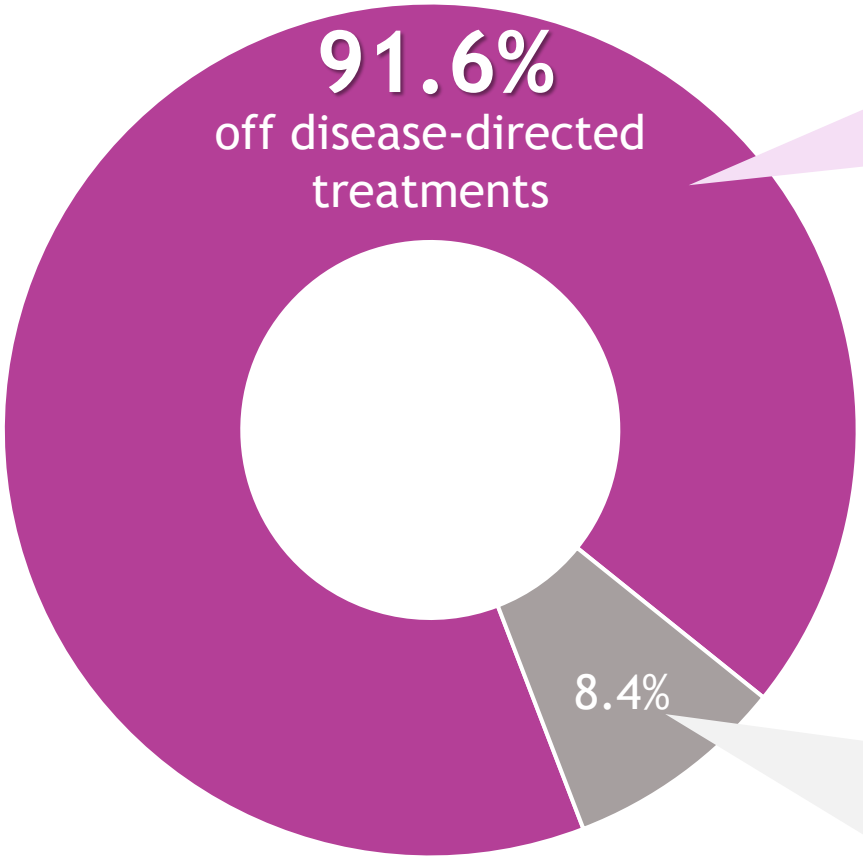
- *Median (range) % improvement from baseline in MMT-8 was 22.0% (12.8%–46.2%) at 6 months (n = 3)*

Improvement in skin disease in patients with dermatomyositis

- *Median (range) change from baseline in CDASI active and damage scores were –10 (–20 to –7) and –3 (–4 to 0) points at Day 57 (n = 3)*

Baseline median (range) MMT-8 score was 122 (70-133). Baseline median (range) CDASI active and damage scores were 28 (14-43) and 6.5 (5-8), respectively.
CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; D, day; IIM, idiopathic inflammatory myopathy; MMT-8, Manual Muscle Test-8; PT, pretreatment; SD, standard deviation.

91.6% of Patients Across Indications Remained Off Disease-Directed Treatments at Last Follow-Up, up to ~18 Months



76 out of 83 (91.6%) patients remained off disease-directed treatments at last follow-up, up to ~18 months after a single, one-time infusion of zola-cel

Patients remaining on disease-directed treatments

SLE	n = 2 (empirical tacrolimus >1 year post-infusion for persistent proteinuria)
SSc	n = 1 (nintedanib after a lung infection in a patient with low baseline lung volume reserve)
IIM	n = 2 (IVIG empirically for CK elevation [n = 1]; prednisone 20 mg [n = 1])
MS	n = 1 (mitoxantrone)
MG	n = 1 (IVIG)

CK, creatinine kinase; IIM, idiopathic inflammatory myopathy; IVIG, intravenous immunoglobulin; MG, myasthenia gravis; MS, multiple sclerosis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; zola-cel, zolacabtagene autoleucel.

Author's Conclusions

- **In a pooled dataset from two phase 1 trials, one-time infusion of zola-cel (CD19 NEX-T) demonstrated a manageable safety profile and meaningful clinical improvements in patients with severe refractory autoimmune diseases**
- Most TEAEs of interest were brief, manageable, and completely reversible with no clinical sequelae
- CRS and ICANS events were mainly grade 1 and resolved quickly, and prolonged cytopenias were not observed
- Among patients with refractory autoimmune disease and multiple prior treatment failures, zola-cel showed preliminary efficacy with reductions in disease activity across SLE, SSc, and IIM, and 91.6% of patients remained off disease-directed therapies up to ~18 months
- CAR T cell expansion, complete B cell depletion, and subsequent re-emergence of naive B cells, accompanied by treatment-free disease control, indicate potential for immune reset with a one-time infusion of zola-cel
- The phase 2 Breakfree-SLE (NCT07015983) and phase 3 Breakfree-SSc (NCT07335562) trials of zola-cel are enrolling

CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IIM, idiopathic inflammatory myopathy; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; TEAE, treatment-emergent adverse event; zola-cel, zolacabtagene autoleucel.