CAR-T in Autoimmune Diseases

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Disclosures

I have autoimmune alopecia
(skin in the game?)

Site PI: : Breakfree-SLE Phase 2 trial (CC-97540 (BMS-986353)
Sponsor: BMS

Site PI: anitocabtagene autoleucel (formerly CART-ddBCMA) in patients with Generalized Myasthenia Gravis.
Sponsor: ARCELLX

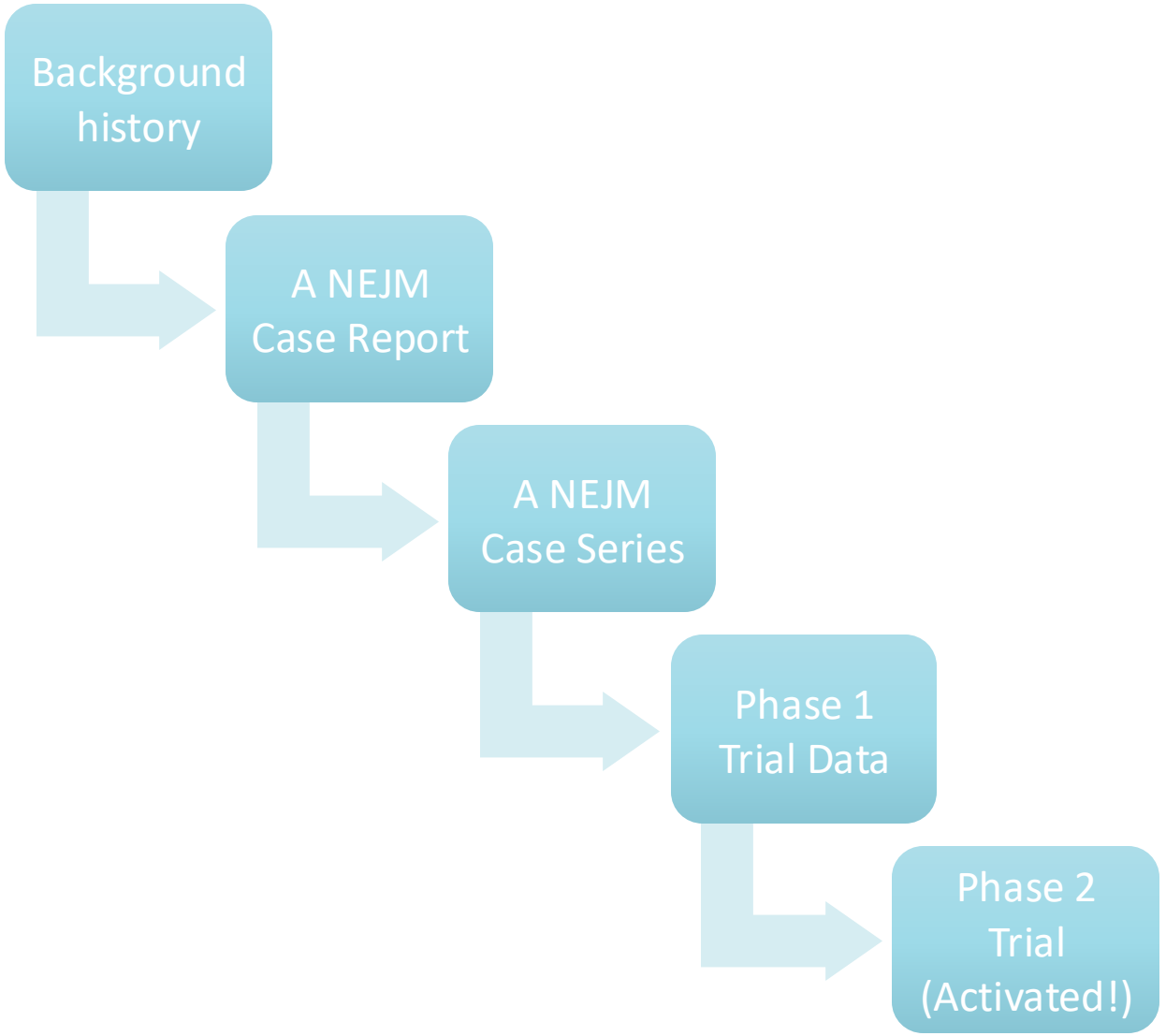
Site PI: open-label study of AZD0120 in autoimmune diseases
Sponsor: Astrazeneca

Views and opinions expressed here are solely those of the presenter and do not necessarily reflect the views and opinions of BMS, ARCELLX, AZ

This presentation may include information about unapproved products

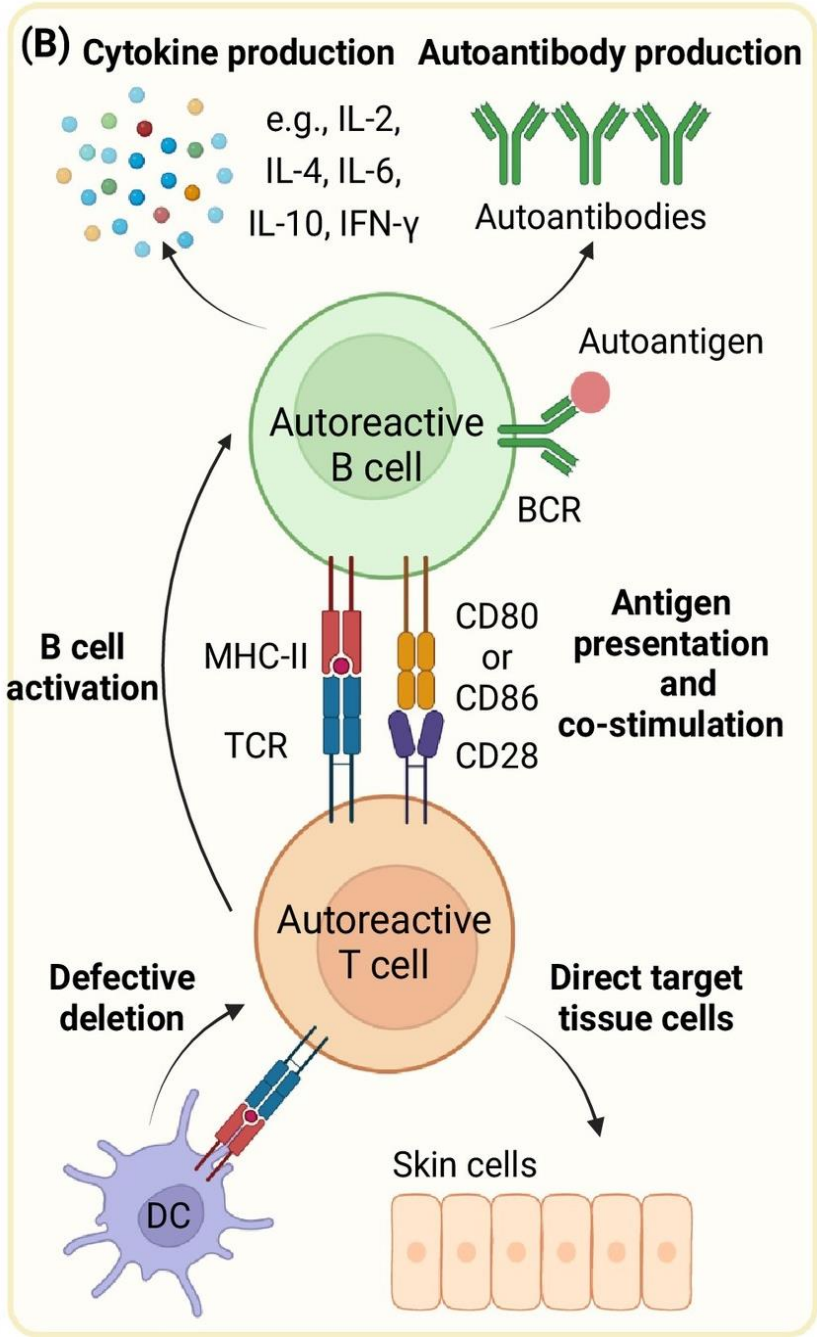
BMS-Speaker's Bureau

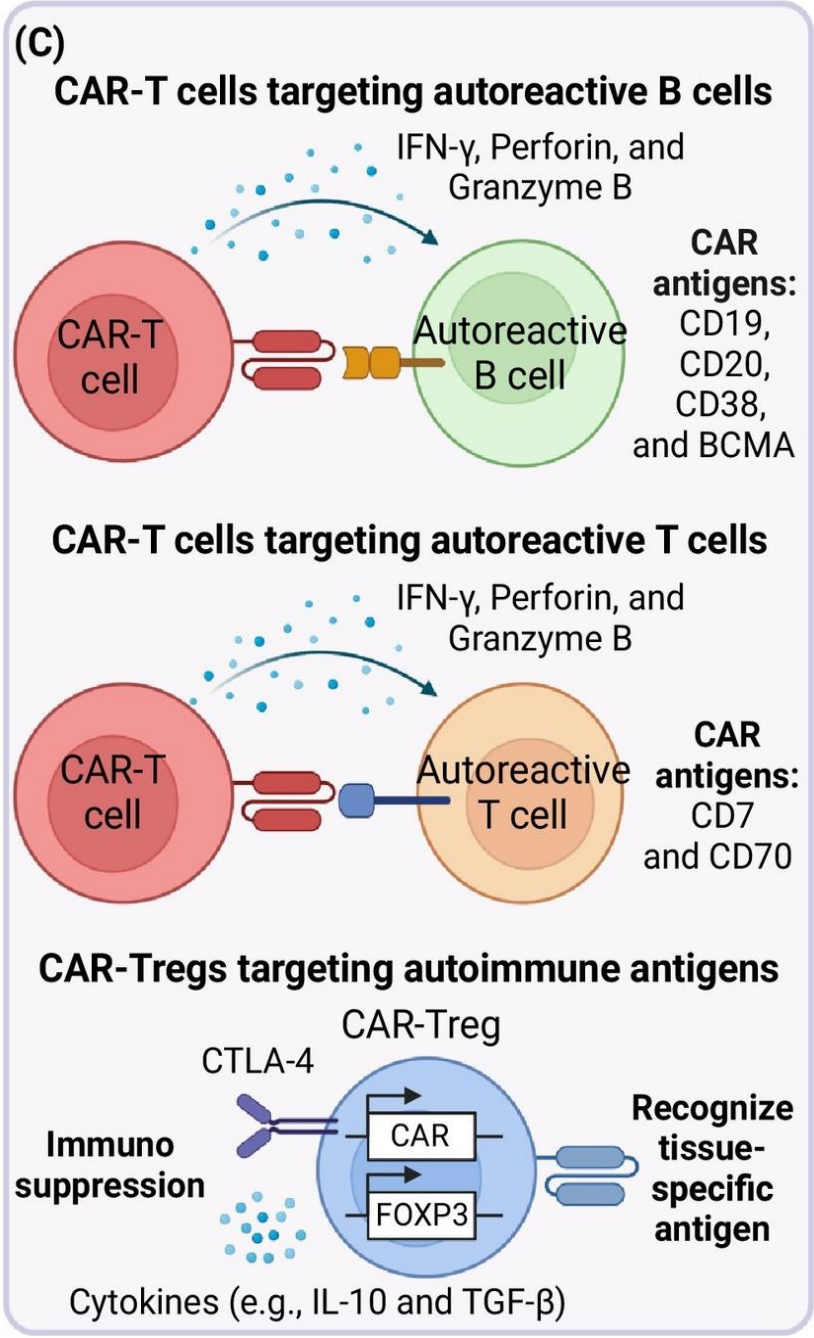
From Science to a Clinical Trial



Background

- Autoimmune disorders driven by autoreactive B and T cells.
- Indefinite Monoclonal antibody therapy results in incomplete control
- CAR-T cell therapy mitigates autoimmune diseases by targeting specific markers on B cells (CD19, CD20, CD38, BCMA) and T cells (CD7, CD70).

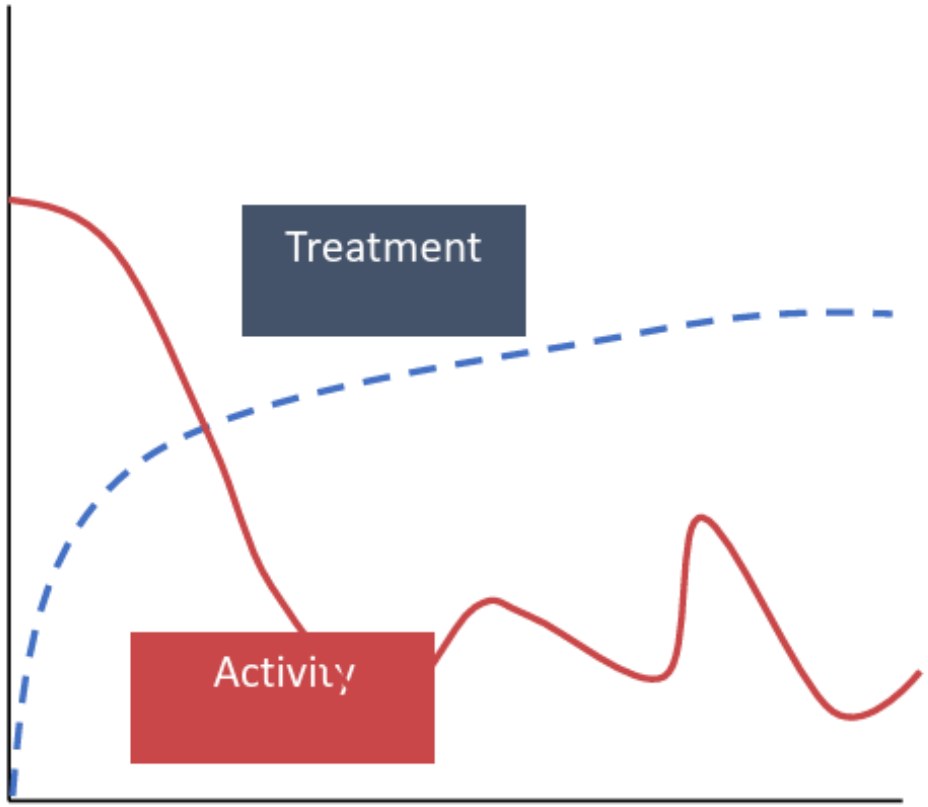




Li YR, et al. Frontiers in CAR-T cell therapy for autoimmune diseases. Trends Pharmacol Sci. 2024 Sep

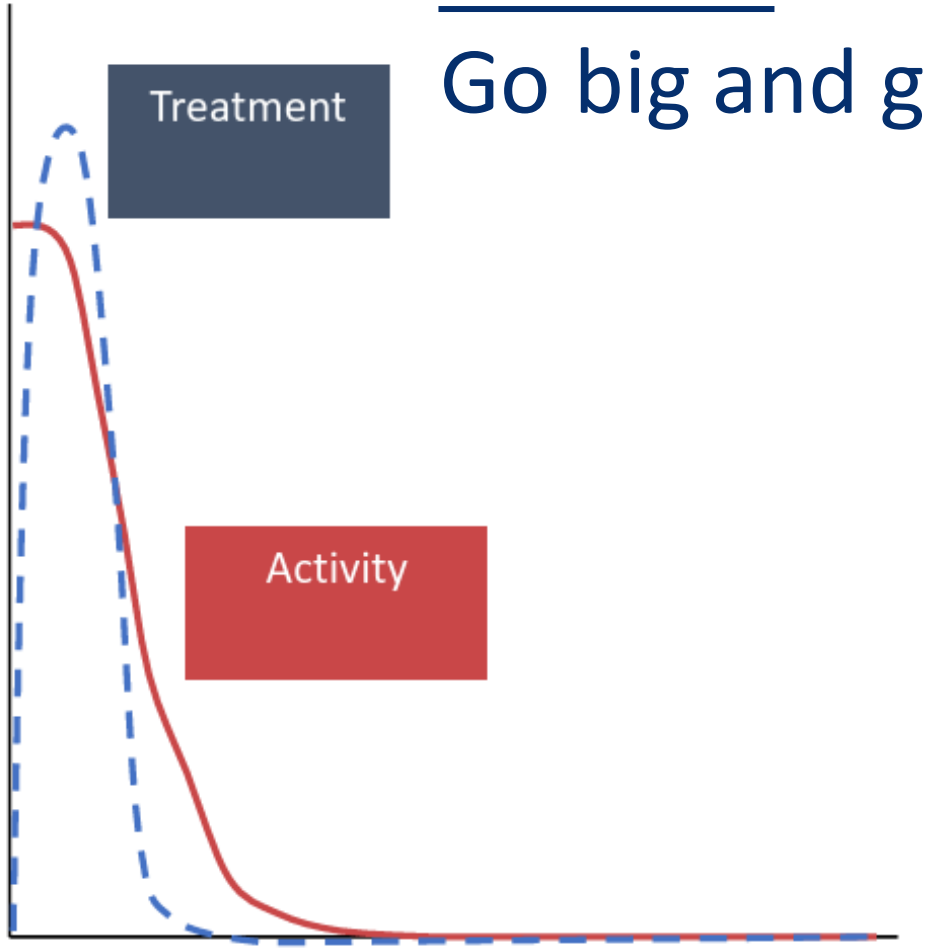
Traditional Medicine:

Go low and go Slow

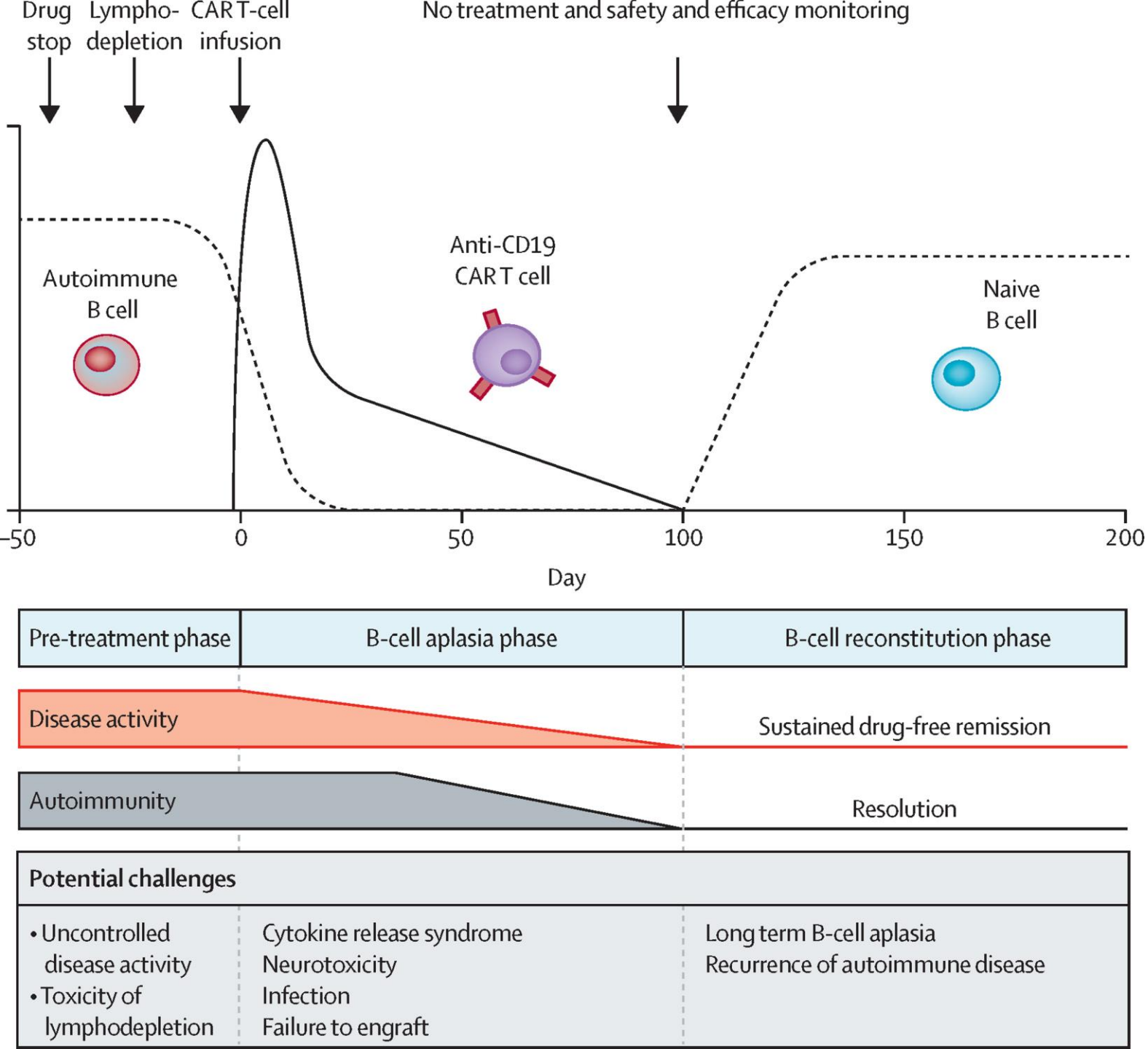


BMTI-CI:

Go big and go home



Life-long suppression → cure?



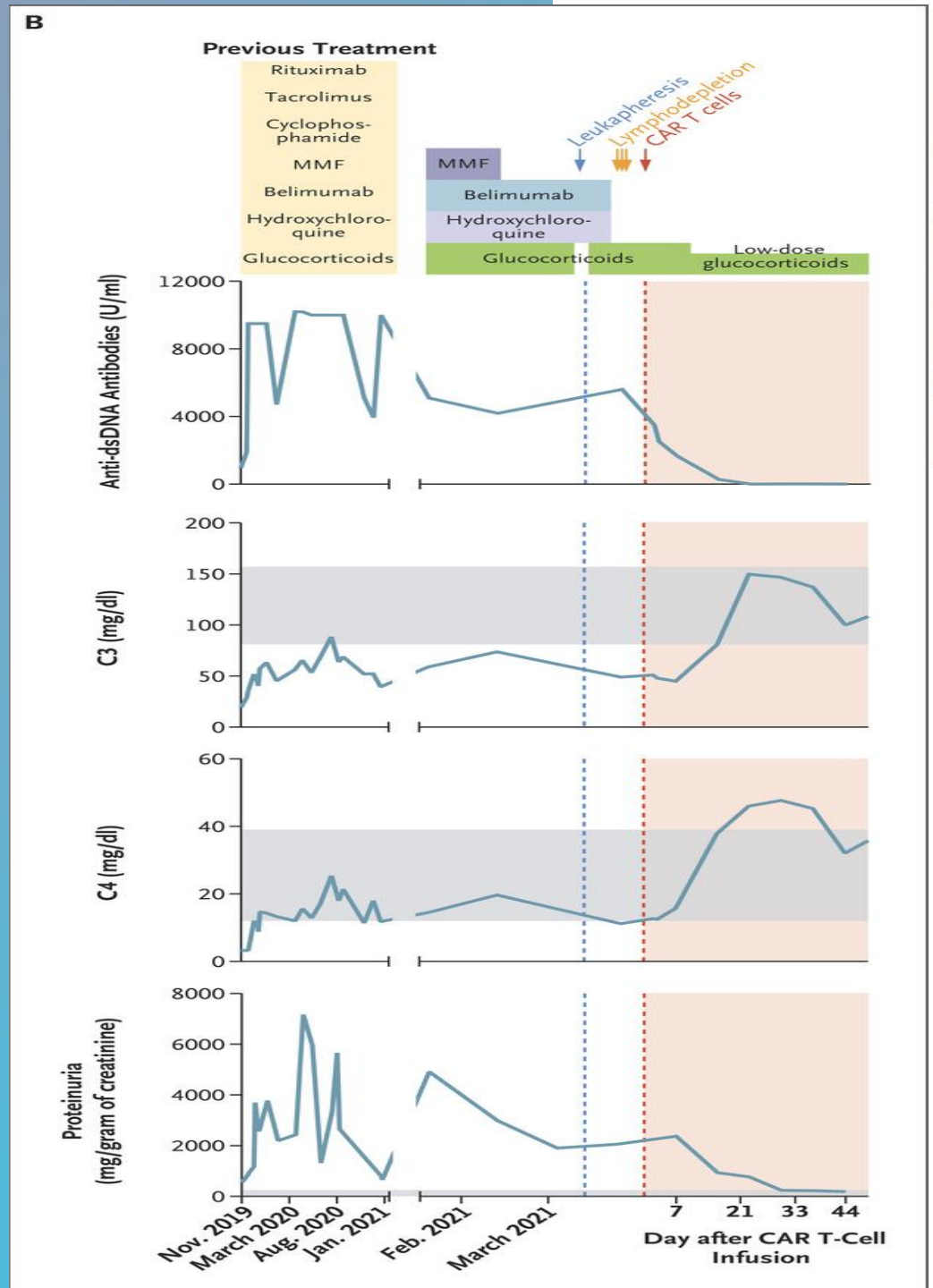
- First, we need to stop immunosuppressive therapy prior to leukapheresis
- After lymphodepleting chemotherapy and CAR T-cell infusion/expansion, patients experience B-cell aplasia, corresponding with decrease in disease activity and autoimmunity
- Finally with naïve B-cell recurrence and reconstitution, patients may enter a phase of (indefinite?) drug-free remission.

Schett, George et al. The Lancet. Nov 2023.

CD19-CAR-T for SLE

Mougiakakos, et al.

August 4, 2021



20 yo woman with:

- active lupus nephritis (World Health Organization class IIIA, indicating focal proliferative disease with active lesions)
- nephrotic syndrome
- Pericarditis
- Pleurisy
- Rash
- Arthritis
- history of Libman–Sacks endocarditis

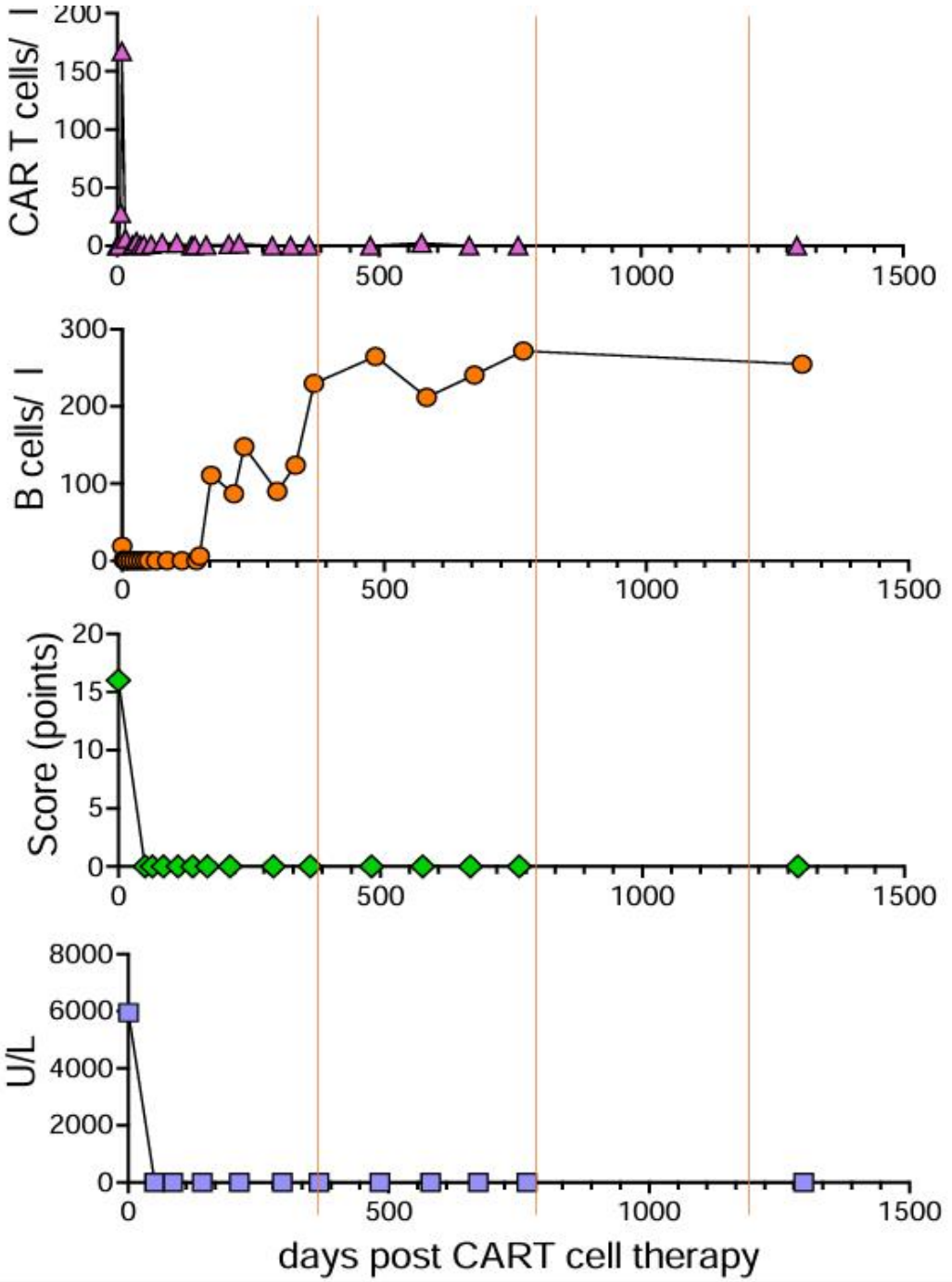
3 years healthy
No Treatment, No Signs of Autoimmunity
Normal Life

CAR T

B Cells

SLEDAI

dsDNA

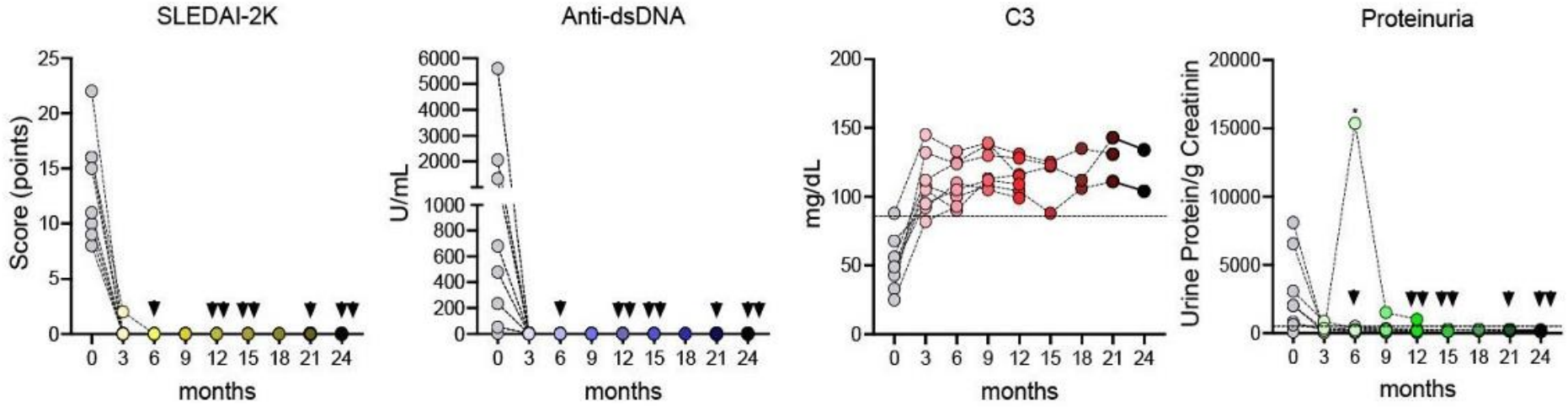


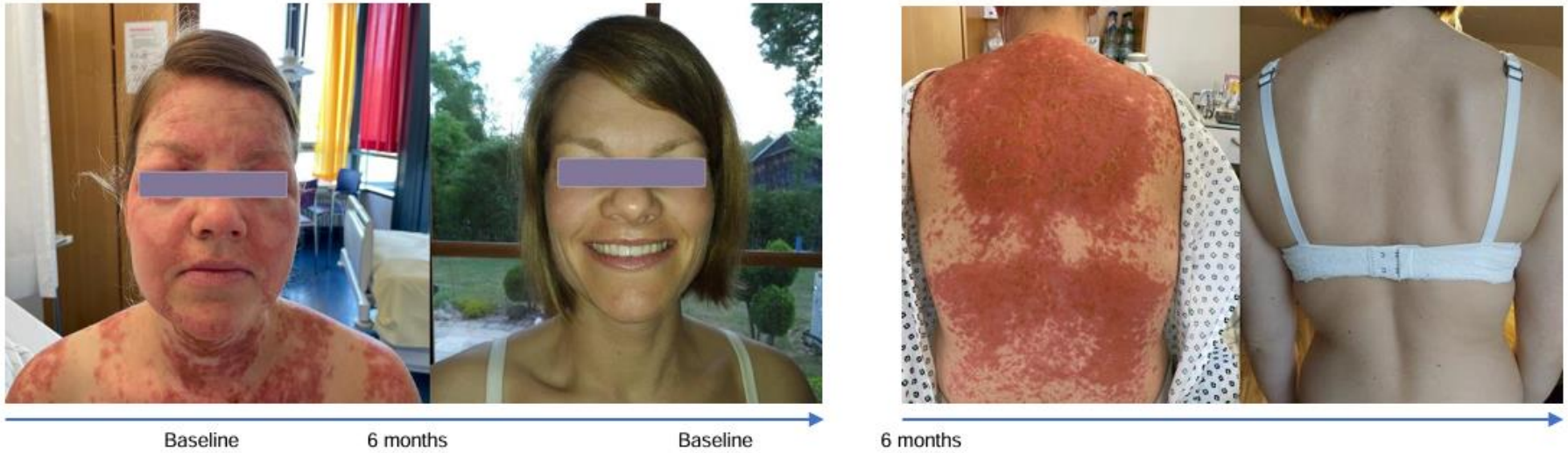
15 patient case series

systemic lupus erythematosus (SLE)
idiopathic inflammatory myositis (IIM)
systemic sclerosis (SSc)

- Median follow-up = 15 months (4-29)
- Mean duration of B-cell aplasia: 112+/- 47 days
- Grade 1 cytokine release syndrome occurred in 10 patients. One patient each had grade 2 cytokine release syndrome, grade 1 immune effector cell–associated neurotoxicity syndrome, and pneumonia that resulted in hospitalization.
- seroconversion of antibodies against dsDNA, single-stranded DNA, secondary necrotic cells, nucleosomes, and Smith protein
- vaccination-related antibodies were not eliminated (implying CD19-negative plasma cells were not depleted)

Muller et al, NEJM Feb 21, 2024.





- All the patients with SLE had DORIS remission
- All the patients with idiopathic inflammatory myositis had an ACR–EULAR major clinical response
- All the patients with systemic sclerosis had a decrease in the score on the EUSTAR activity index.
- Immunosuppressive therapy was completely stopped in all the patients.

Muller et al, NEJM Feb 21, 2024.

Phase 1: CC-97540 in Participants With Severe, Refractory Autoimmune Diseases (Breakfree-1)

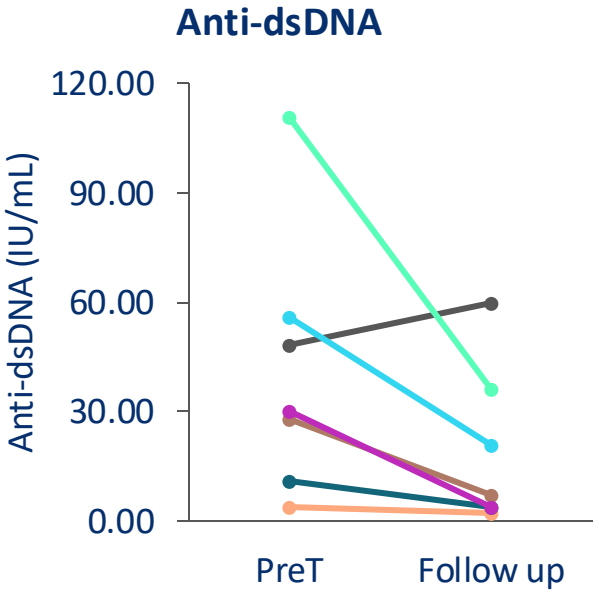
Schett et al. AACR 2024

	SLE (n = 11)
Median age (range), years	29.0 (18-49)
Female sex, n (%)	10 (90.9)
Median time from disease diagnosis to BMS-986353 infusion (range), years	7.3 (1.1-17.0)
Median number of prior therapies (range)	7.0 (3-10)
Median Physician's Global Assessment (range)[a]	2.0 (1.0-2.7)
Median total SLEDAI-2K score (range)[c]	14.0 (0.0-18.0)
BILAG category A, n (%)	
Renal	9 (81.8)
Cardiorespiratory	2 (18.2)

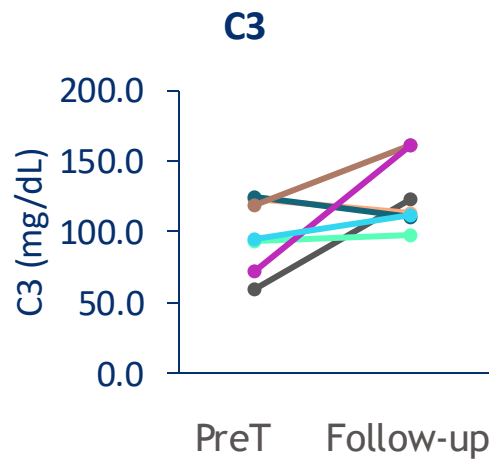
- At a data cut-off of September 26, 2024, the median follow-up (range) was 65.0 (3-316) days
- No patients discontinued study at data cut-off

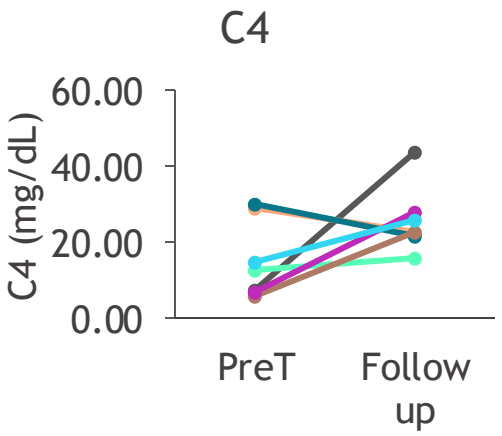
Phase 1: CC-97540 in Participants With Severe, Refractory Autoimmune Diseases (Breakfree-1)

Schett et al. AACR 2024

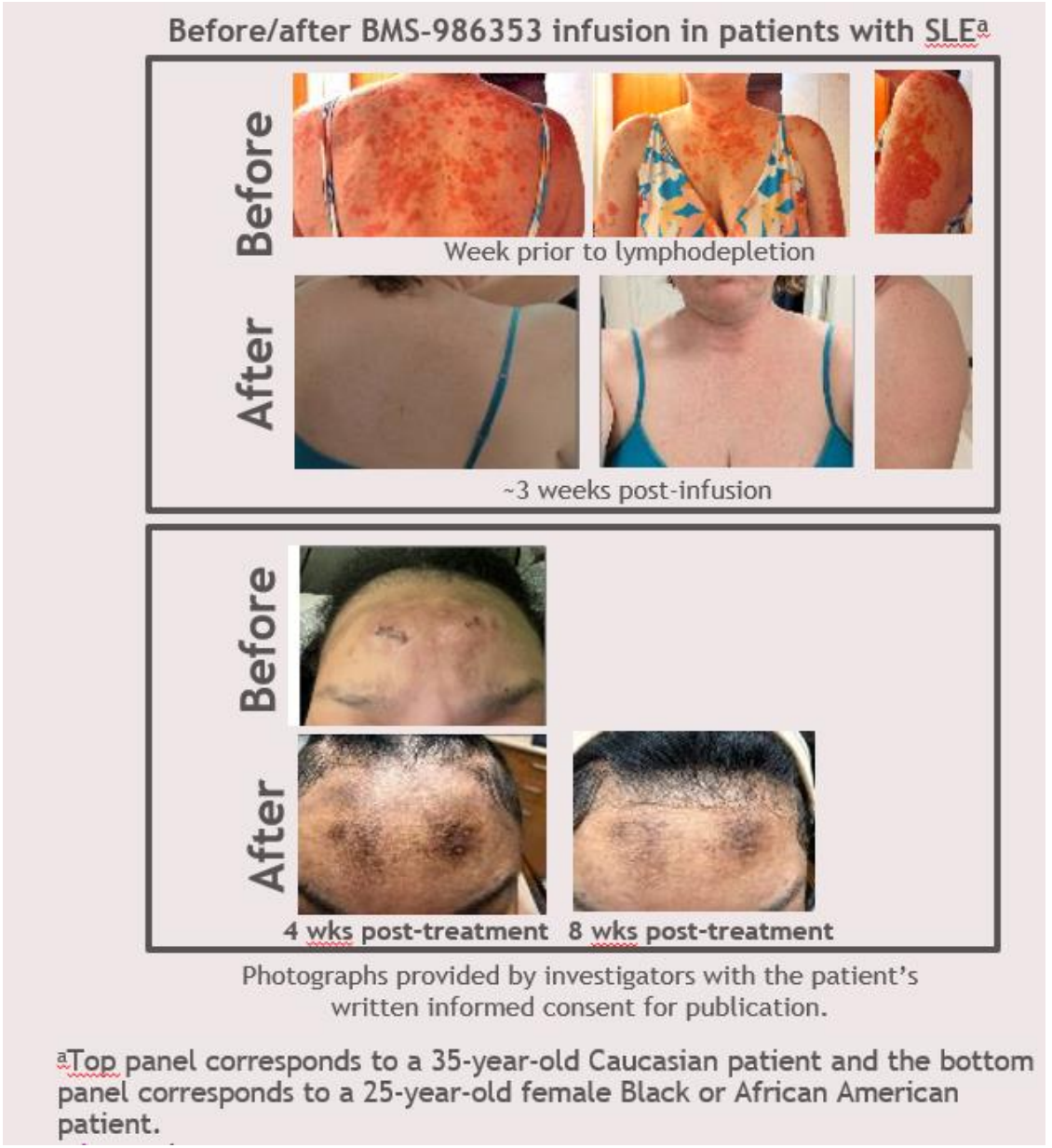


Anti-dsDNA antibodies decreased overtime and became negative by day 85 (month 3).





C3 and C4 reached the normal range by day 29



Phase 1: CC-97540 in Participants With Severe, Refractory Autoimmune Diseases (Breakfree-1)

Schett et al. AACR 2024

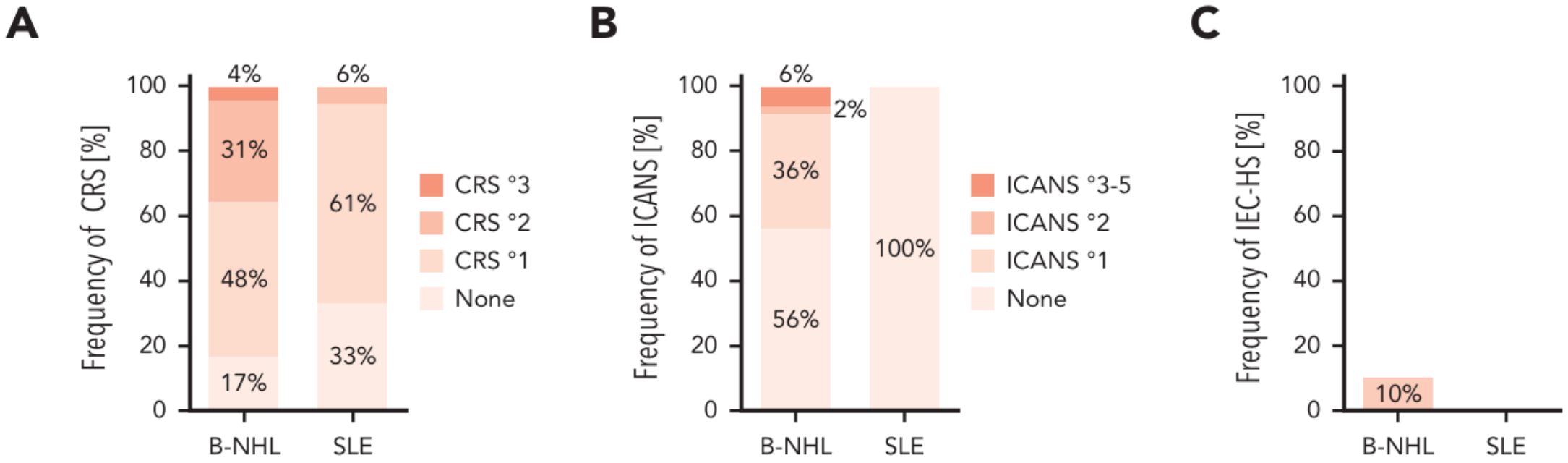
CRS and ICANS	SLE (n = 11)	
	CRS	ICANS
Max grade, n (%)	6 (54.5)	1 (9.1)
Grade 1	5 (45.5)	0
Grade 2	1 (9.1)	0
Grade 3	0	1 (9.1)
Grade 4/5	0	0
Median onset (range), days	7.0 (2–11)	8.0 (8–8)
Median duration[b] (range), days	2.0 (1–5)	3.0 (3–3)
Common treatments[c] n (%)		
Tocilizumab	3 (27.3)	0
Glucocorticoids	2 (18.2)	1 (9.1)
Anakinra	0	1 (9.1)

- All TEAEs of interest were transient and reversible
- CRS grade 2 occurred in one patient with a median duration of 2 days
- ICANS grade 3 occurred in one patient with a median duration of 3.0 days

Comparison of Safety Profiles of CAR-T cell Therapy in SLE vs. B-cell Lymphoma

Despite similar CAR T-cell dynamics, SLE pts experienced less severe adverse events after CAR T-cell therapy than those with B-NHL.

In patients with SLE, the adaptive immunity reconstituted faster after CAR T-cell therapy than in patients with B-NHL.



Muller F et al. Blood 2025.

CD19-CAR T cell therapy for AD is evolving along with innovations in CAR-T cell technology

	Arcellyx	BMS	Caribou	Novartis	KYVERNA	Autolus Therapeutics	Allogene	Genentech/ Roche	Astrazeneca
Product	anitocabtagene autoleucel (anito-cel)	lisocabtagene maraleucel (NEX-T platform)	CB-010	rapcabtagene autoleucel	KYV-101	obecabtagene autoleucel (obe-cel)	ALLO-329	P-CD19CD20-ALLO1	AZD0120
Phase	1, escalation + expansion	2	1	2	2	2	1	1	1
Target	BCMA/auto	CD19/auto	CD19/allo (CRISPR)	CD19/auto	CD19/auto	CD19/auto	CD19/CD70	CD19/CD20	CD19/CD20
Target disease	MG	SLE Lupus nephritis	SLE	GPA, MPA [lupus nephritis]	MS	MS	SLE, Lupus nephritis IIM SSc	SLE Lupus nephritis	SLE IIM RA MS SSc

Questions?

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