CAR-T vs. BiTEs for Autoimmune Diseases
The Case for BiTEs

2025 CELL COAST CONFERENCE

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Relevant Disclosure and Mitigation Report

Under Accreditation Council for Continuing Medical Education (ACCME) guidelines disclosure must be made regarding all financial relationships with ineligible companies within the last 24 months.

Omar A. Castaneda Puglianini, MD

Commercial Interest/Ineligible Company	Nature of Financial Relationship	
	What was received?	For what role?
Legend Biotech USA Inc.	Consultant Fee	Consultant
Bristol Myers Squibb	Consultant Fee	Consultant
Janssen Biotech, Inc.	Consultant Fee	Consultant

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Question for the day

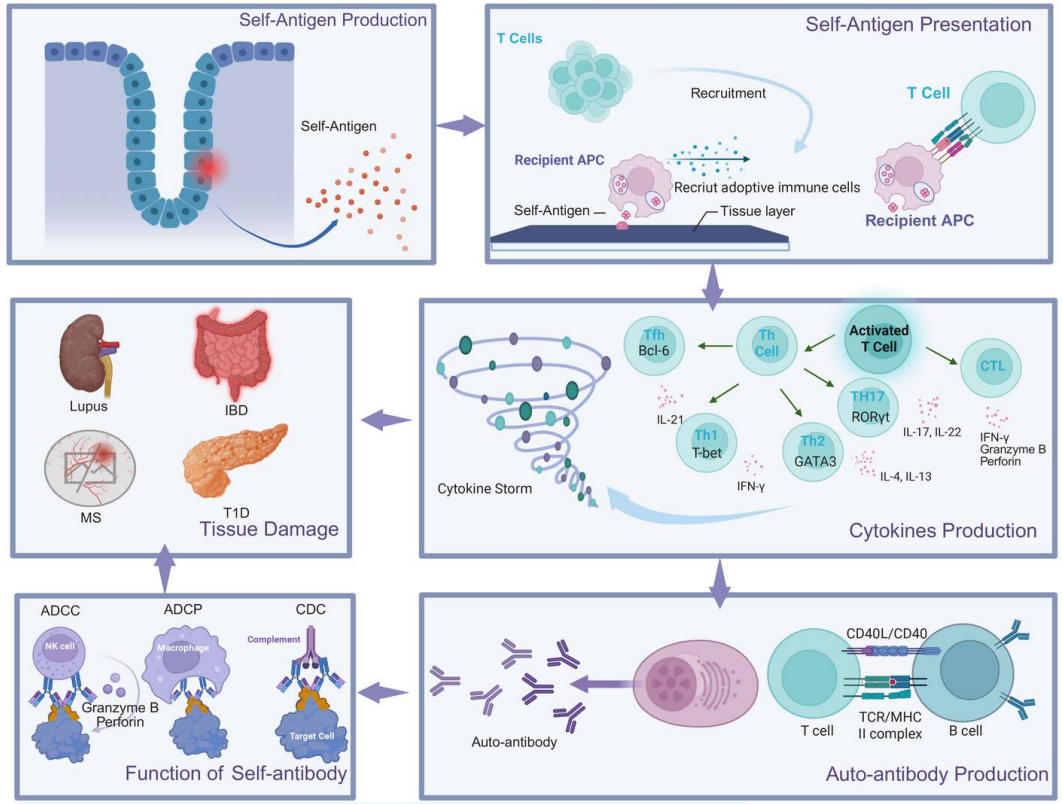
CAR-T or BiTE for Autoimmune Disease?

- ☐ CAR-T
- ☐ BiTE
- ☒ Both

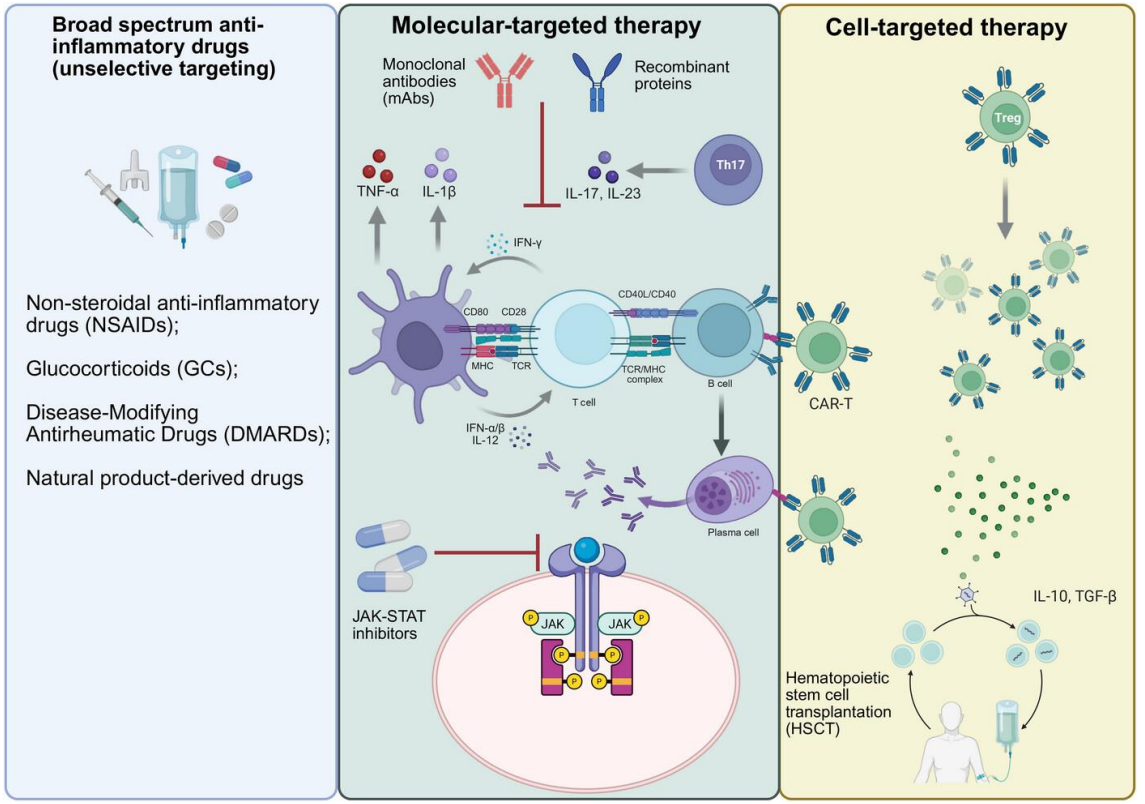
Outline

- Overview Autoimmune Diseases.
- Overview Bispecific T-cell Engagers.
- Clinical Development of Bispecific Therapy in AD.
- Potential Advantages of BiTE Therapy in AD.

Autoimmune Diseases Overview



Pathogenic Events Leading to Chronic Autoimmunity.



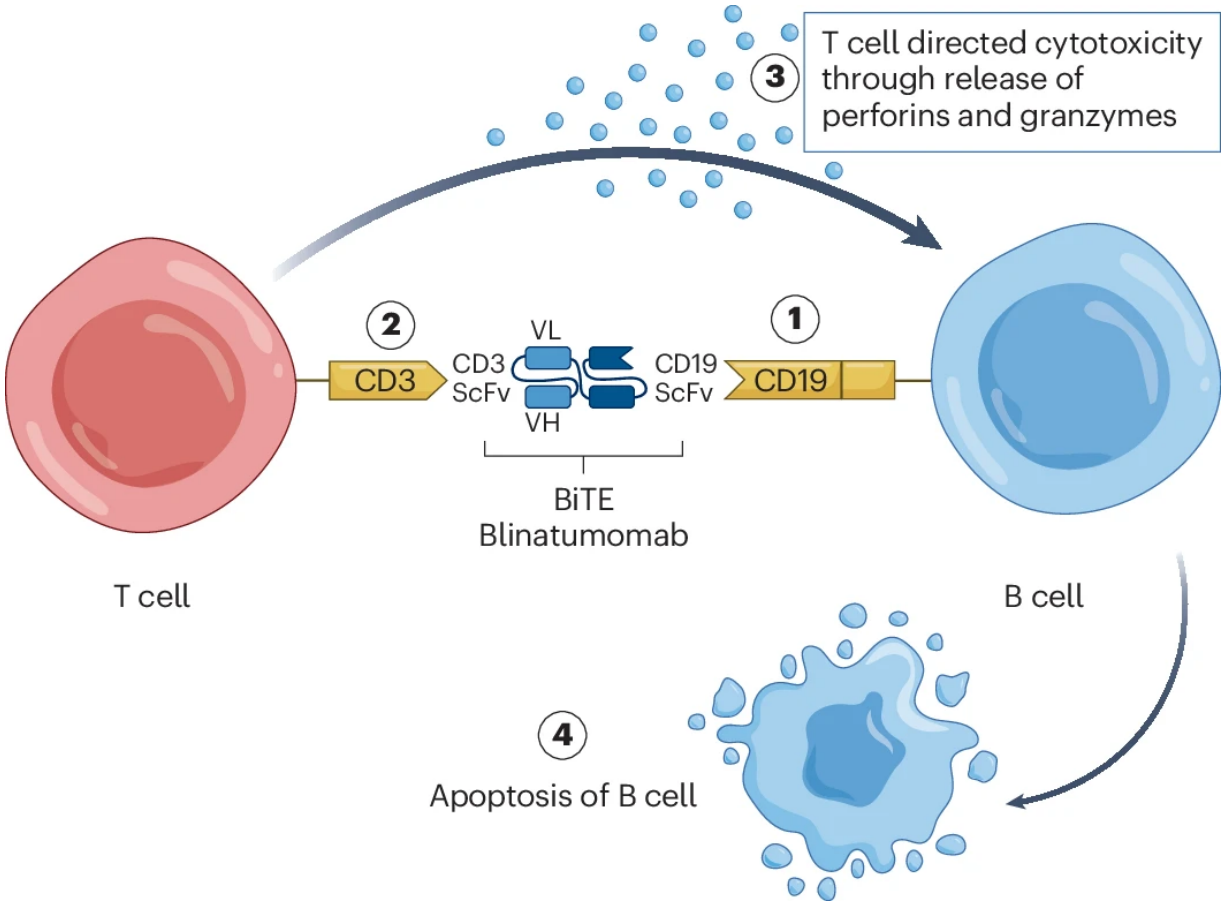
Therapeutic Approach

Autoimmune diseases (AD) comprise a heterogeneous group of systemic conditions that affect the connective tissues of the musculoskeletal system and internal organs. AD are driven by chronic autoimmune responses.

AD typically require continuous or repeated administration of immunosuppressive or biologic disease-modifying drugs. Although generally effective, these therapies can cause both short- and long-term side effects and may fail to control the disease with risk of irreversible tissue damage.

Bispecific T-cell Engagers

- Bispecific antibodies are also referred to as dual specific abs, bifunctional abs, or T-cell engaging ab.
- BiTEs are dual antigen targeting constructs that engage the T cells to the target cell through various target antigens.
- Multiple BiTEs are already FDA approved (only for cancer therapy) and many more are in clinical development.
- Availability is off-the-shelf allowing for immediate treatment

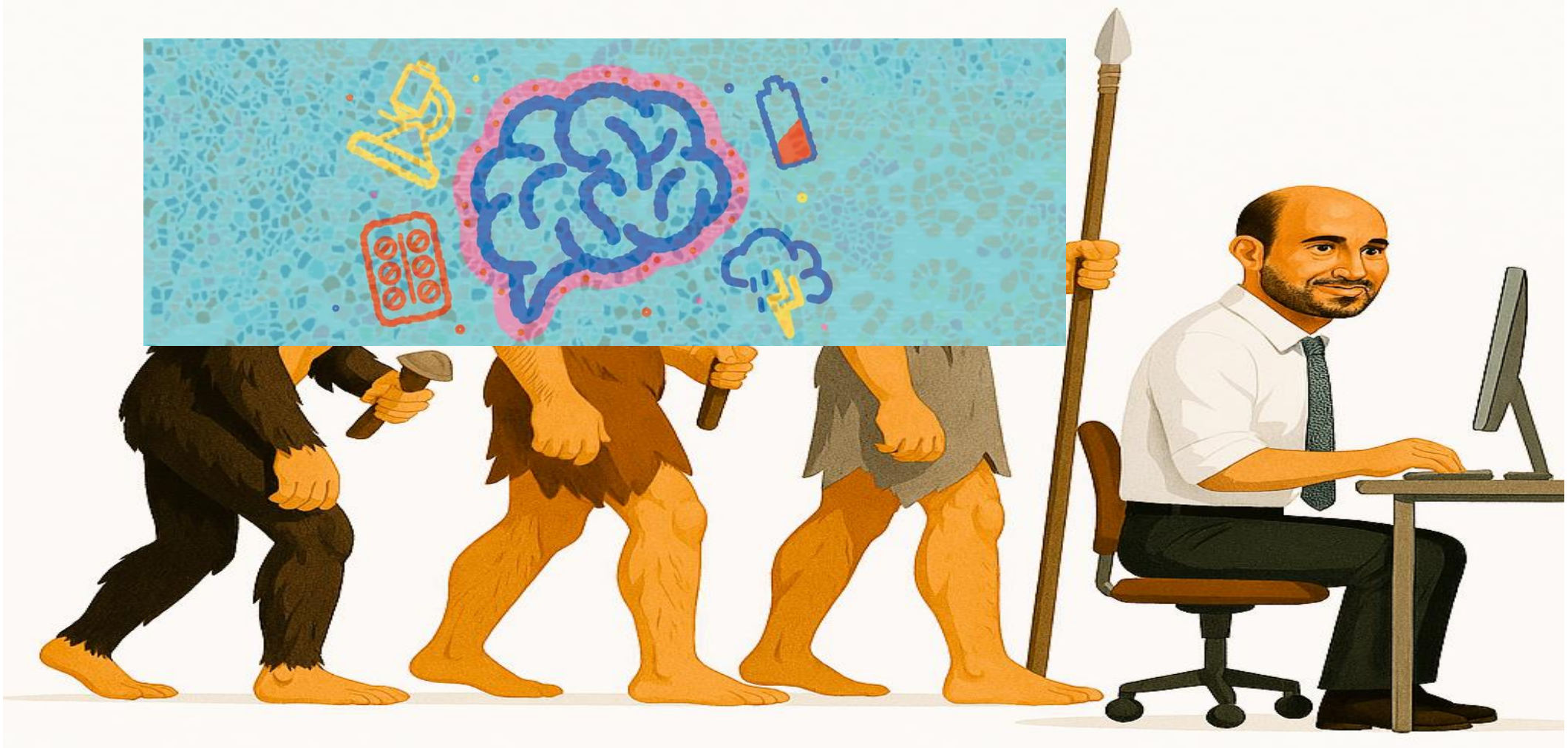


Bispecific T cell engagers (BiTEs) kill B cells by engaging T cells.

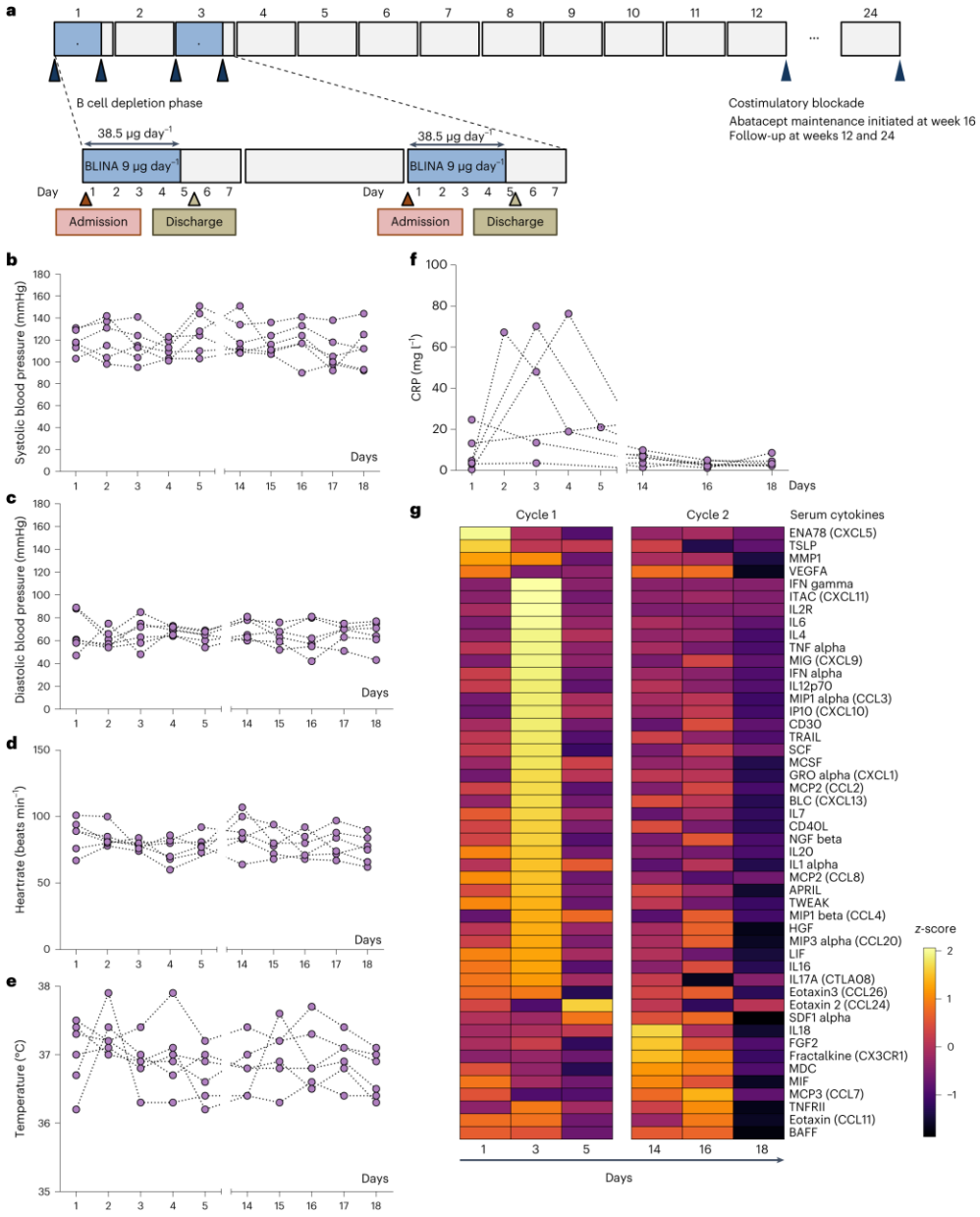
Clin Cancer Res. 2020;26:1541

Nat Med **30**, 1533–1534 (2024)

Clinical Development of Bispecific Therapy in AD



BiTE Therapy for Multidrug Resistant/Refractory RA

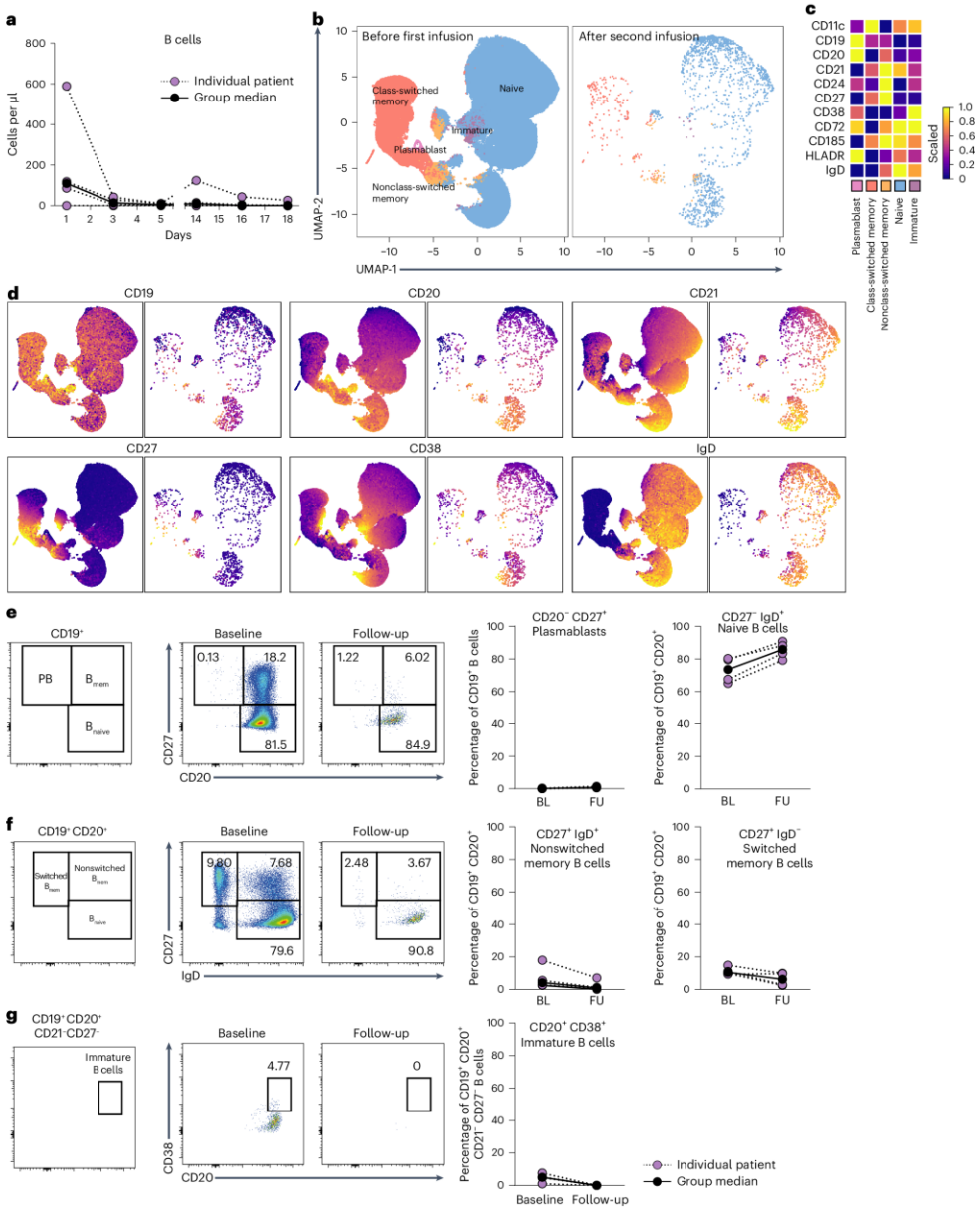


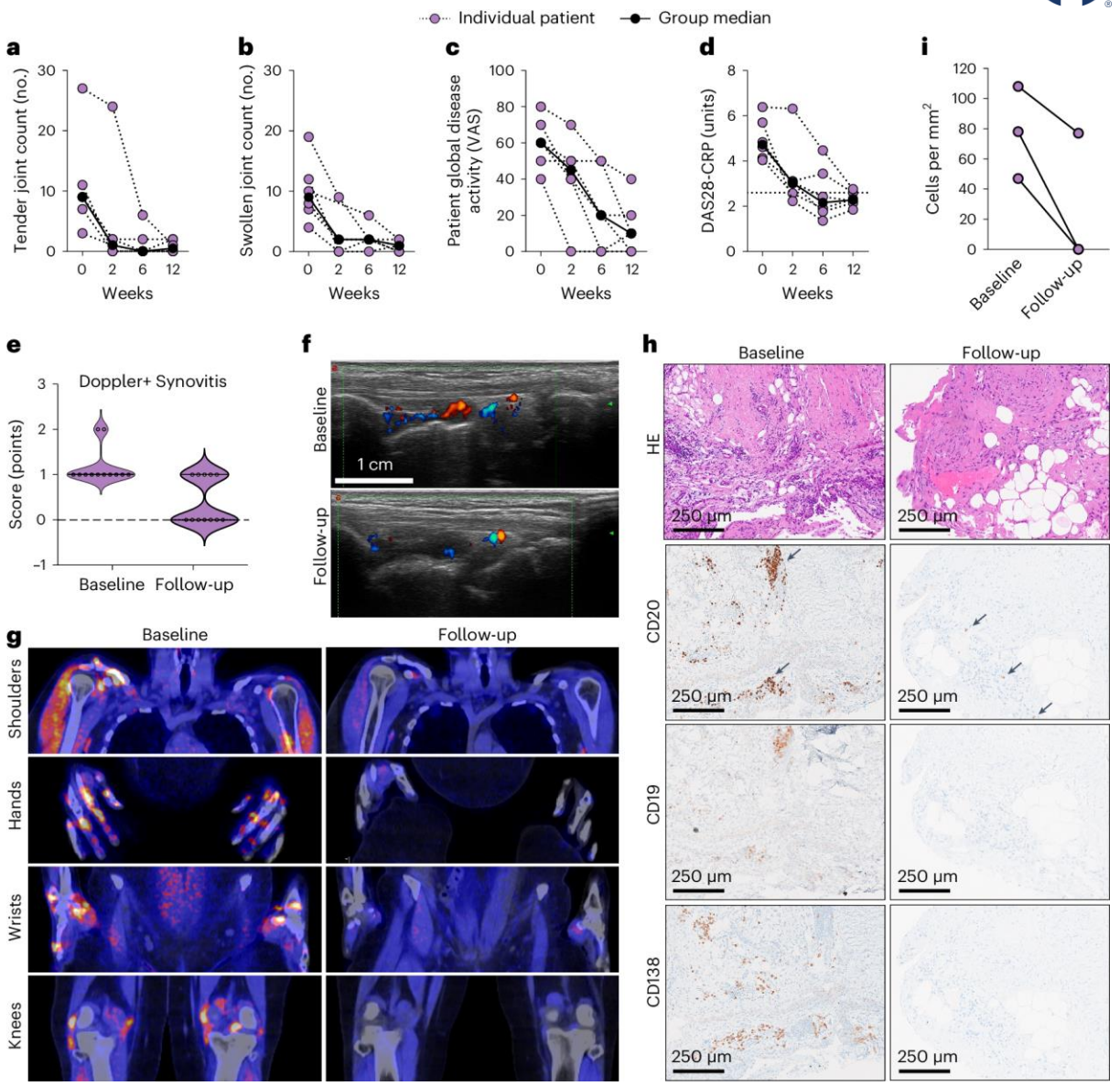
Treatment schedule and tolerability of Blinatumomab in RA.

Patient no.	1	2	3	4	5	6
Inflammation						
Subfebrile state	Week 1 of 3	Week 1 of 3	0	0	Week 1	Week 1
Chills	Week 1 of 3	0	0	0	0	0
Fever	0	0	0	0	0	0
Elevated CRP	Week 1	Week 1	0	Week 1	0	Week 1
Worsening of RA	0	0	0	0	0	0
Neurotoxicity						
Headache, malaise, confusion	0	0	0	0	0	0
Infections						
Urinary tract Infection	0	0	0	Week 1	0	0
Herpes simplex	0	Week 3	0	0	0	0
SARS-CoV-2	0	Week 12	0	0	0	0
Opportunistic	0	0	0	0	0	0
Myelotoxicity						
Neutropenia	0	0	0	0	0	0
Thrombocytopenia	0	0	0	0	0	0
Liver enzymes	0	0	0	0	0	0
Hypogammaglobulinemia	0	0	0	0	0	Week 3
Others						
Nausea	Week 3 of 5	0	0	0	0	0
Tachycardia	Week 2	0	0	Week 9	0	0
Headache	0	0	0	Week 1	0	0

Nat Med **30**, 1593–1601 (2024)

BiTE Therapy for Multidrug Resistant/Refractory RA

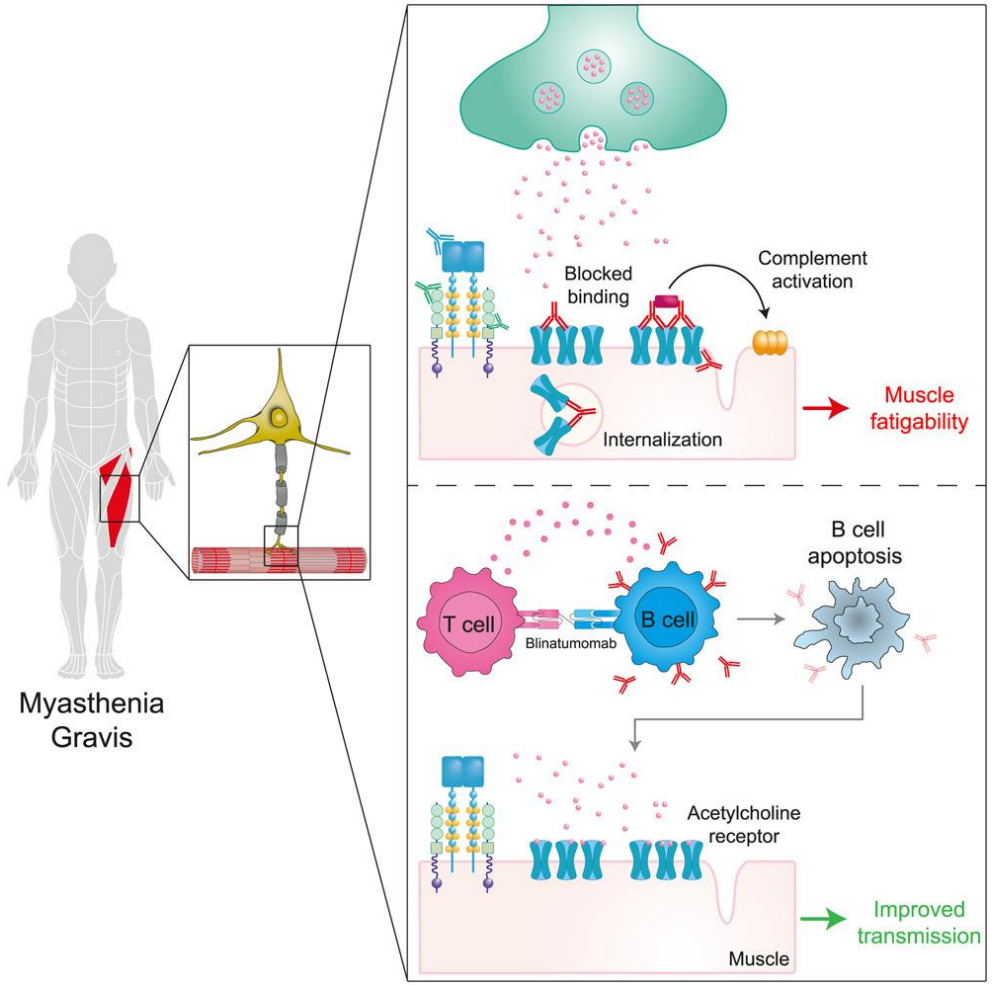


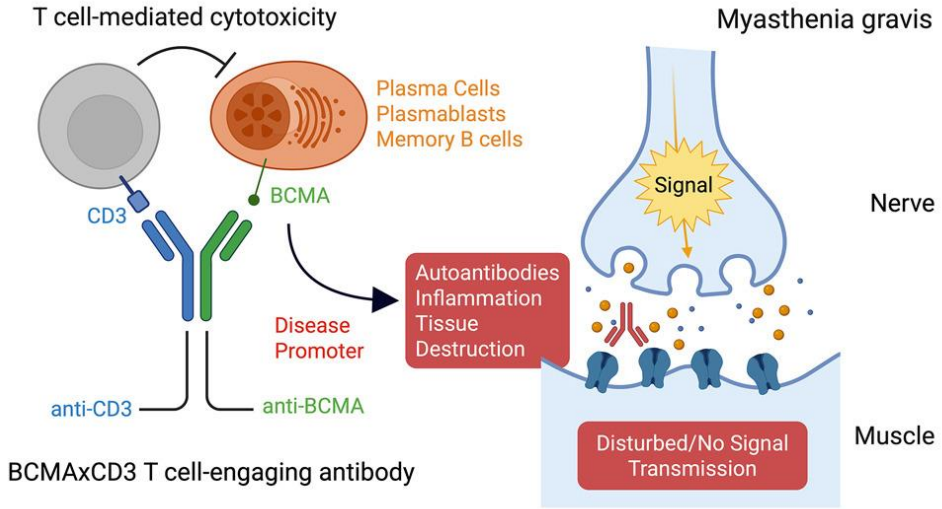


Deep remodeling in the B cell compartment → Clinical Efficacy

Nat Med **30**, 1593–1601 (2024)

Blinatumomab and Teclistamab for Refractory Myasthenic Syndromes

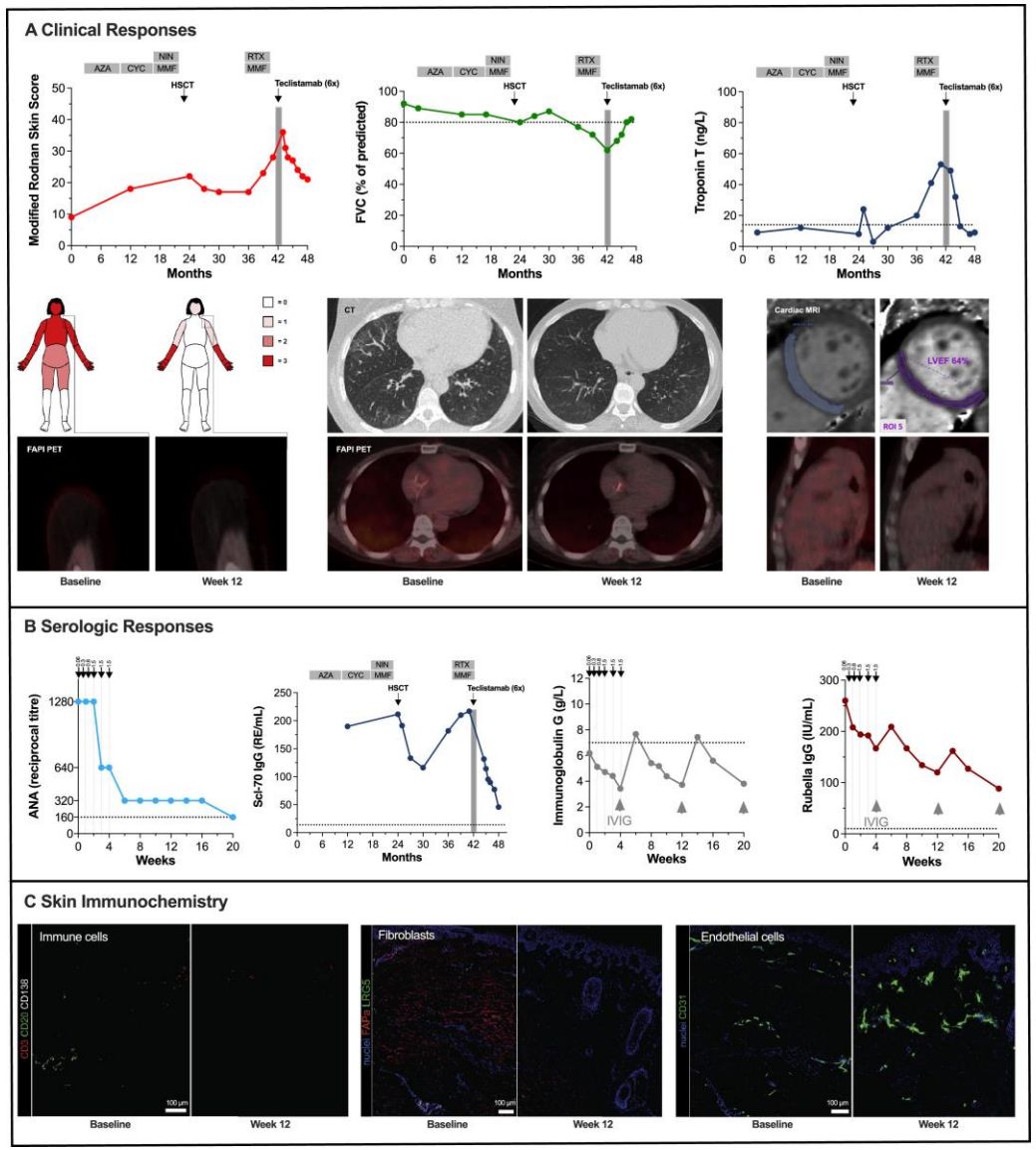


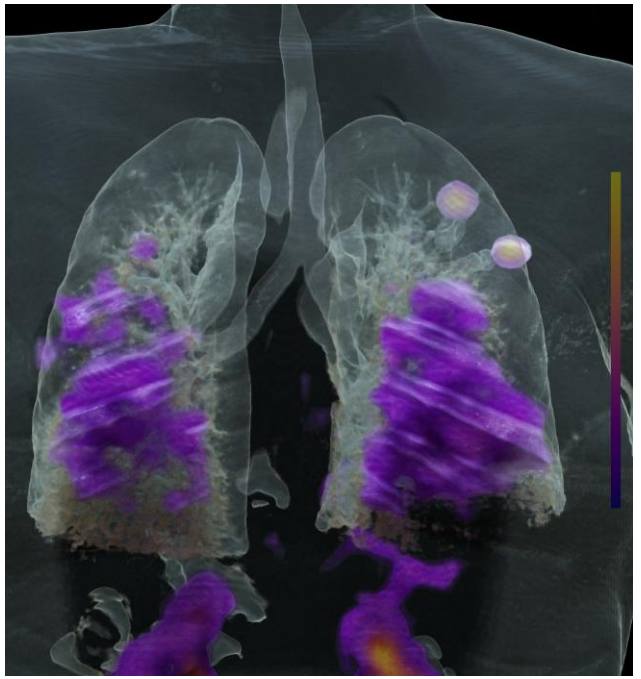


Potential of short-term treatment with CD19- & BCMA-targeting T cell engagers in autoimmune neurological disorders such as refractory MG.

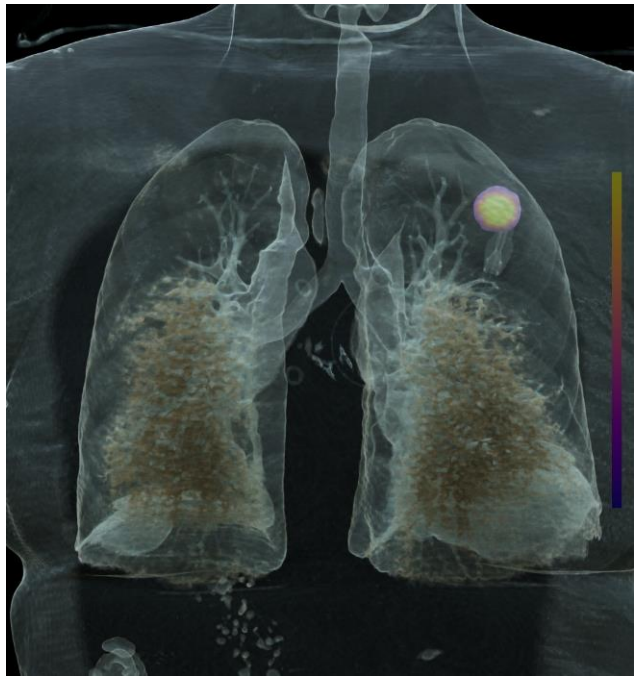
Mol Ther. 2025 Sep 3;33(9):4135-4142. Mol Ther. 2025 Sep 3;33(9):4130-4134

CD3-BCMA BiTE in Relapsed Systemic Sclerosis after ASCT





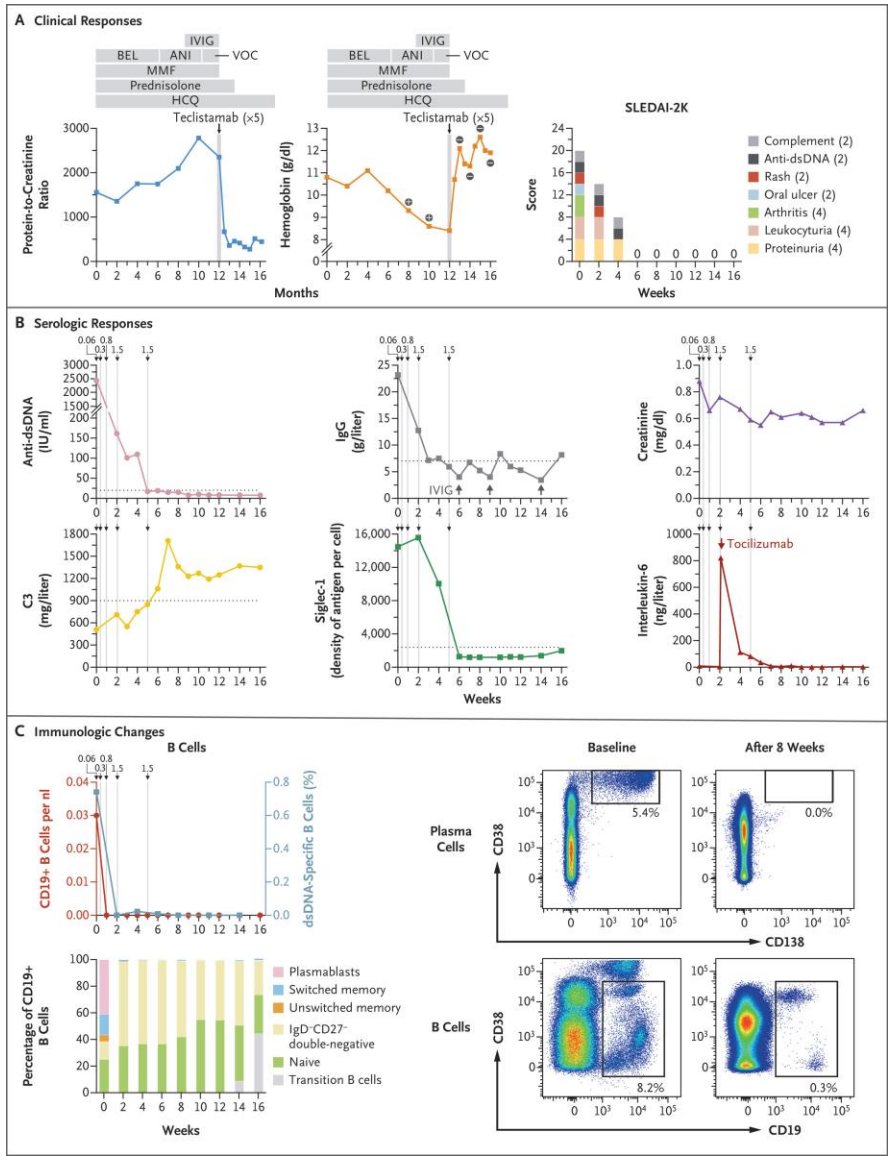
Baseline



Week 12

Ann Rheum Dis. 2025 Apr;84(4):653-656

Teclistamab in Autoimmune Diseases



Teclistamab-Induced Remission in Refractory

A Baseline Characteristics of Patients

Variable	Patient 1	Patient 2	Patient 3	Patient 4
Disease	Systemic sclerosis	Primary Sjögren's syndrome	Idiopathic inflammatory myositis	Rheumatoid arthritis
Age — yr	60	57	24	52
Sex	Female	Female	Female	Female
Disease duration — mo	108	20	29	336
Arthritis	No	Yes	Yes	Yes
Myositis	No	Yes	Yes	No
Skin manifestation	Yes	Yes	Yes	No
Interstitial lung disease	Yes	Yes	Yes	Yes
Small-vessel vasculitis	No	Yes	Yes	No
Antinuclear antibodies — titer	1:3200	1:10,000	1:100	<1:40
Specific autoantibodies	PM-Scl	Ro, La, PL-7	MDA5	CCP2, MCV
Teclistamab dose — mg	3.3/16.0/ 81.9/75.0	3.3/16.0/ 82.0/82.0	3.3/16.0/ 80.0/79.5	3.8/19.0/ 94.2/94.2
Length of follow-up after first dose — wk	22	18	12	12

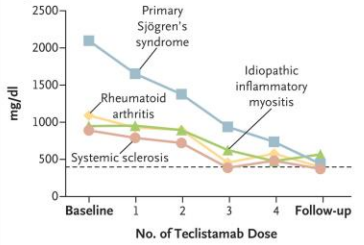
B Schematic Treatment Protocol

Day 1 Teclistamab, 0.06 mg/kg → Day 3 Teclistamab, 0.3 mg/kg → Day 5 Teclistamab, 1.5 mg/kg → 1× Maintenance Teclistamab, 1.5 mg/kg

C Safety Analysis Results

	Patient 1 (systemic sclerosis)	Patient 2 (primary Sjögren's syndrome)	Patient 3 (idiopathic inflammatory myositis)	Patient 4 (rheumatoid arthritis)
CRS grade	1	2	0	0
ICANS grade	0	0	0	0
Myelotoxicity grade	0	0	0	0
Hypogammaglobulinemia (IgG, <4 g/liter)	No	No	Yes	No
Infections	GI	CUT	None	HSV, URTI

D IgG Levels in Serum



E Changes in Serum Autoantibodies at Latest Follow-up

	Autoantibody	Baseline	Follow-up
Patient 1 (systemic sclerosis)	ANA — titer	1:3200	1:100
	PM-Scl-75 — RU (normal <15)	30	1
	PM-Scl-100 — RU (normal <15)	35	3
Patient 2 (primary Sjögren's syndrome)	ANA — titer	1:10,000	1:3200
	SS-A/Ro-52 — U/ml (normal <25)	129.7	55.3
	SS-A/Ro-60 — U/ml (normal <25)	189.5	131.3
	SS-B/La — U/ml (normal <25)	222.5	165.2
	PL-7 — RU (normal <15)	122	91
Patient 3 (idiopathic inflammatory myositis)	ANA — U/ml (normal <25)	1:100	1:100
	MDA5 — RU (normal <15)	38	18
Patient 4 (rheumatoid arthritis)	RF — U/ml (normal <25)	507.2	18.4
	CCP2 — U/ml (normal <25)	2.7	0.9
	MCV — U/ml (normal <25)	82.9	3.0

F Clinical Efficacy Analysis

	Patient 1 (systemic sclerosis)		Patient 2 (primary Sjögren's syndrome)		Patient 3 (idiopathic inflammatory myositis)		Patient 4 (rheumatoid arthritis)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Visual analogue scale (patient global) — mm	90	50	50	10	50	20	60	40
Modified Rodnan skin score — units	39	24	N/A	N/A	N/A	N/A	N/A	N/A
ESSDAI (Sjögren's syndrome activity) — units	N/A	N/A	34	15	N/A	N/A	N/A	N/A
CDASI (skin inflammation) — units	N/A	N/A	N/A	N/A	22	6	N/A	N/A
MMT-8 (diffusion capacity of lung) — units	N/A	N/A	N/A	N/A	138	150	N/A	N/A
DAS28–CRP (arthritis) — units	N/A	N/A	N/A	N/A	3.6	1.6	5.6	1.9
Health assessment questionnaire — units	2.5	2.1	1.3	1.1	1.8	1.0	3.0	1.6
DLCOSB (single-breath diffusion capacity of lung for carbon monoxide) — percent of predicted	34	33	23	27	44	57	76	72

Teclistamab-Induced Remission in Refractory

N Engl J Med 2024;391:864-866. N Engl J Med 2024;391:867-869

Potential BiTEs Advantages

- Less expensive and time consuming than CAR-T.
- Readily available – “Off the Shelf”.
- No need to account for manufacturing process or conditioning regimens.
- Lower toxicity profile specially for patients with comorbidities.
- Likely less expensive as needs lower doses/short courses.
- Therapy can be given fully outpatient and no need for prolonged observation periods close to the treatment center.
- BiTE therapy could be implemented in the community easily compared to CAR-T.
- Easier to manage and potentially more controllable in case of over-suppression of the immune system or off-target effects.
- Adaptability in chronic AD where repeated treatment may be necessary.

THANK YOU