

4th Cuneo City ImmunoTherapy Conference (CCITC)

Immunotherapy in Hematological Malignancies **2024**



CUNEO
October 10-12, 2024
Spazio Incontri Fondazione CRC

CAR-T cell therapy in Autoimmune diseases

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Organized by Prof. Massimo Massaia, SC Ematologia AO S.Croce e Carle, Cuneo - Italy and
Centro Interdipartimentale di Biotecnologie Molecolari "Guido Tarone" (MBC), Torino - Italy

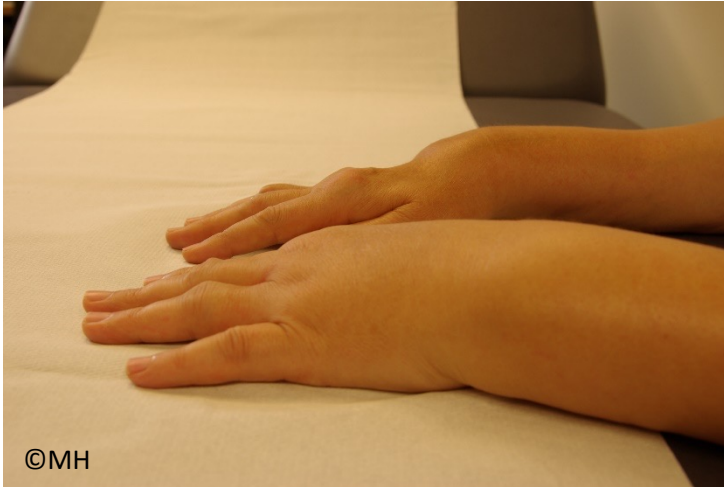
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Disclosures

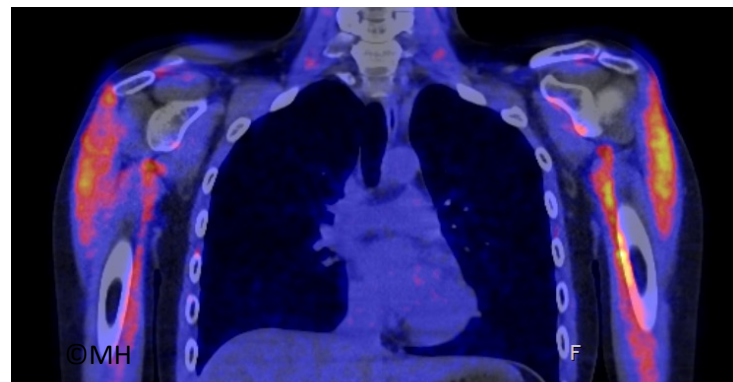
Honoraria and travel grants from:
Lilly, BMS, Kyverna, UCB, Sanofi, AlfaSigma

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When you think about rheumatology...



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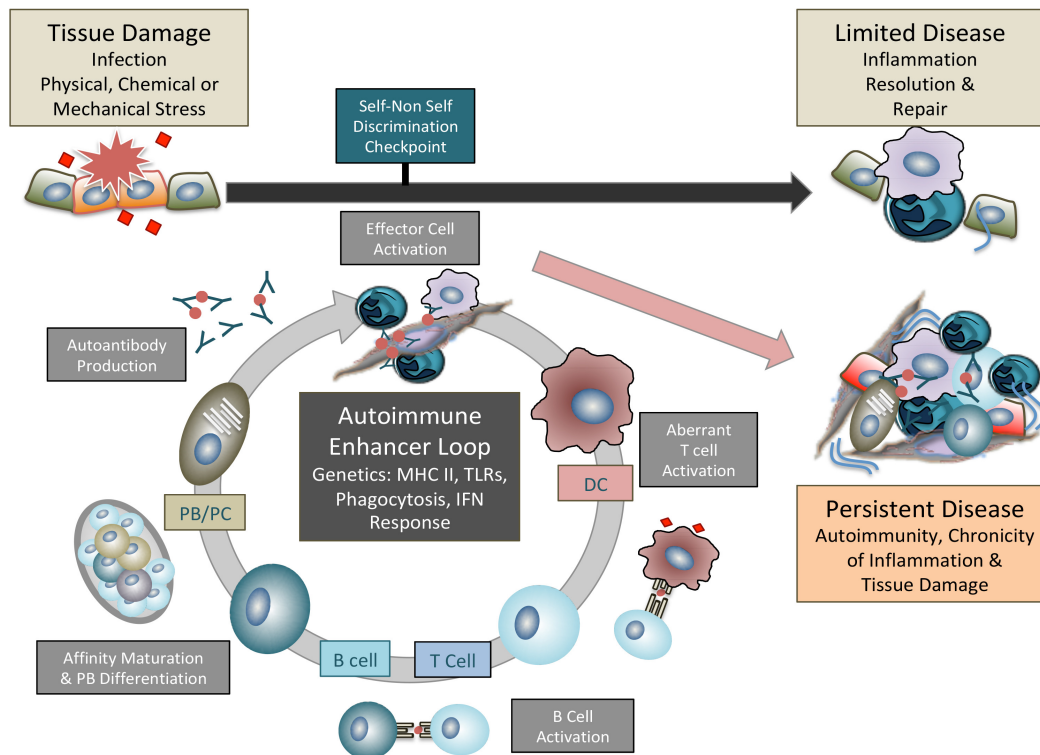


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Autoimmune loops trigger persistent inflammation




Schett et al.2023

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Potential targets for B-cell derived AID

B-cell lineage differentiation

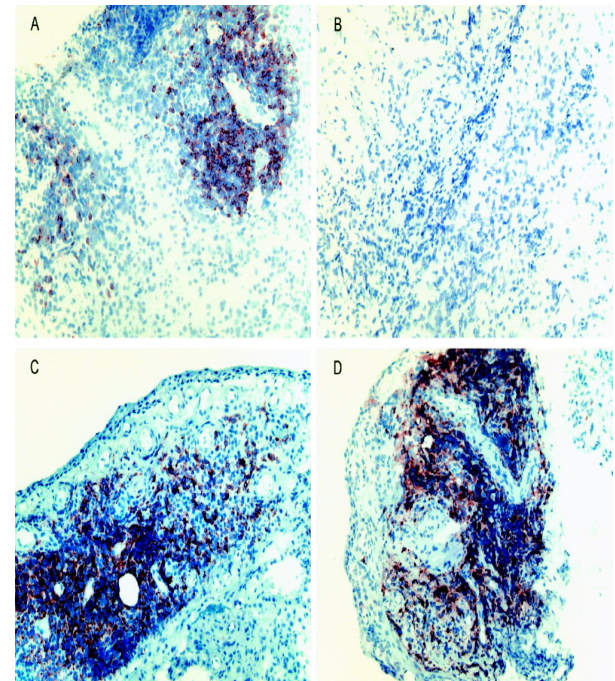
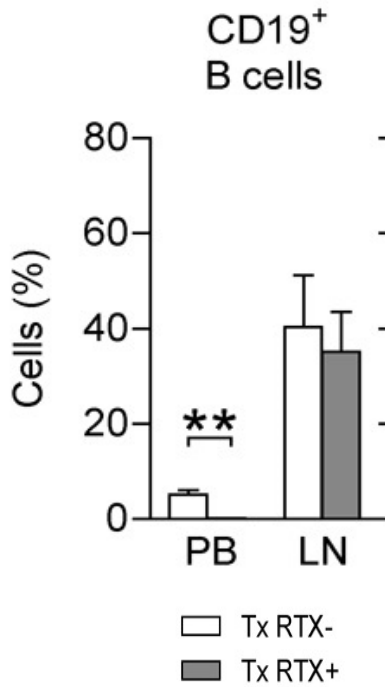
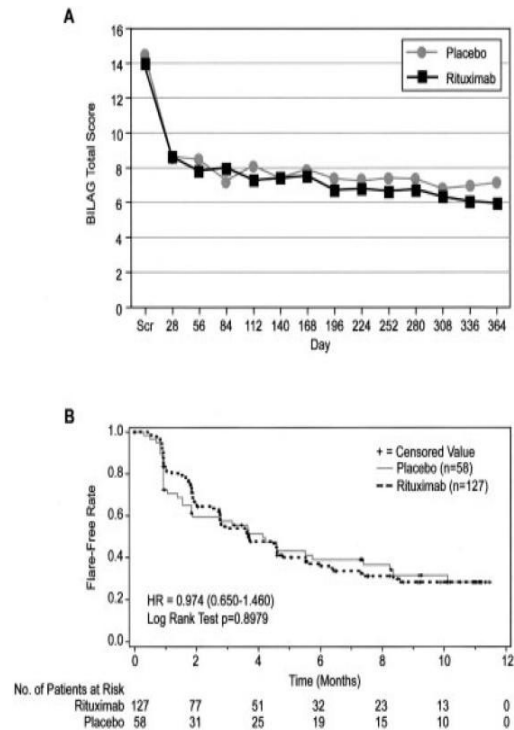


Tumour cells antigen	Pro B cell	Prä B cell	Imm B B cell	Mature B cell	Memory B cell	Plasma blast	Plasma cell	Target
CD19	Red	Red	Red	Red	Red	Red	Light Blue	B cell
CD20	Light Blue	Orange	Orange	Orange	Orange	Light Blue	Light Blue	B cell
CD22	Light Blue	Light Orange	Light Orange	Light Orange	Light Orange	Light Blue	Light Blue	B cell
BCMA	Light Blue	Light Blue	Light Blue	Light Blue	Purple	Purple	Purple	PC
CD38	Light Blue	Light Blue	Light Blue	Light Blue	Purple	Purple	Purple	PC
CD138	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Blue	Light Purple	PC

Schett et al.2023

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Rituximab: hype or hope?



Merrill JT, et al. 2010

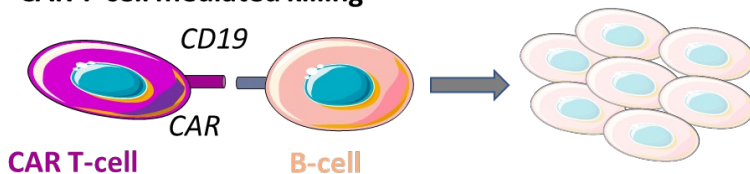
Kamburova EG et al. 2013

Vos K et al. 2007

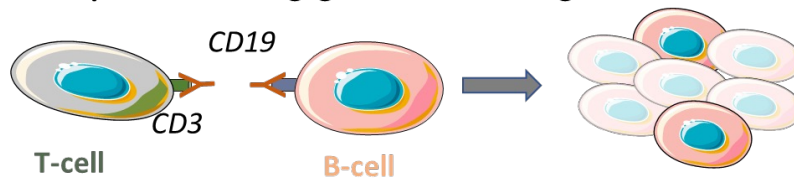
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CD19 as new target for deep B cell depletion

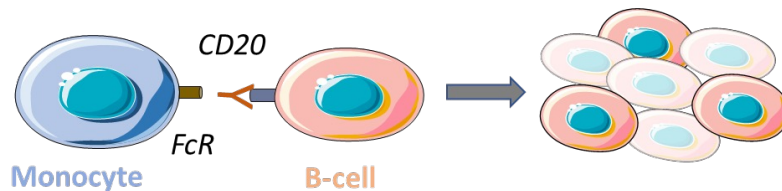
CAR T-cell mediated killing



Bi-specific T cell engager mediated killing



Antibody-mediated killing



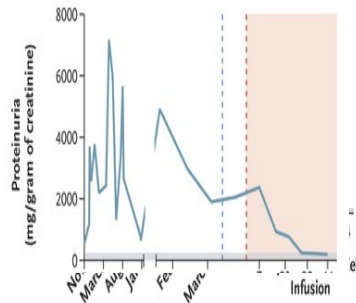
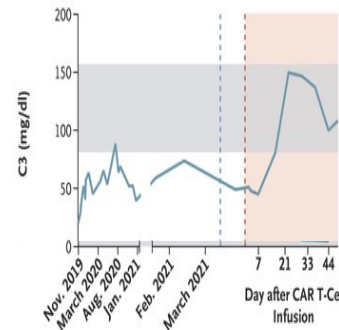
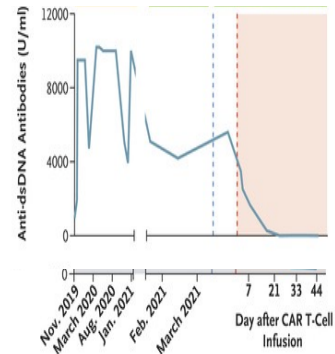
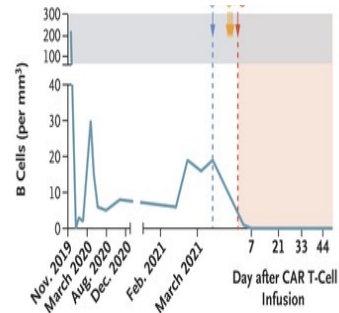
Schett et al.2023

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First SLE-patient was treated in 2021



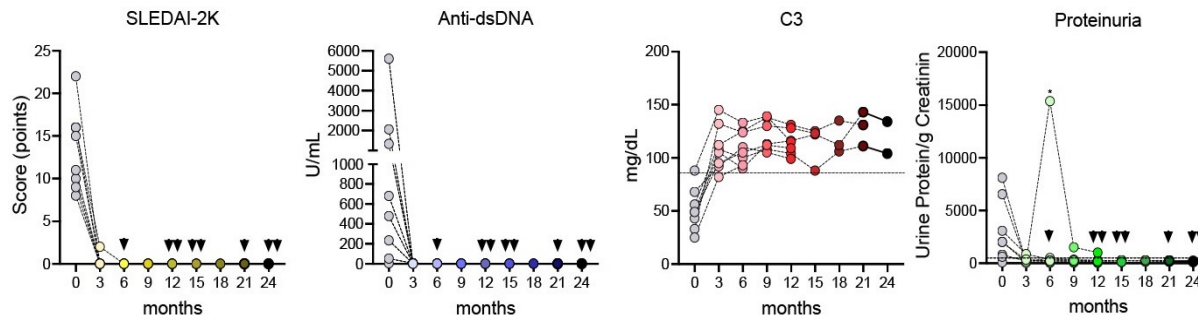
Mougiakakos D et al., N Engl J Med 2021; 385: 567-569.



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Case series of 15 patients

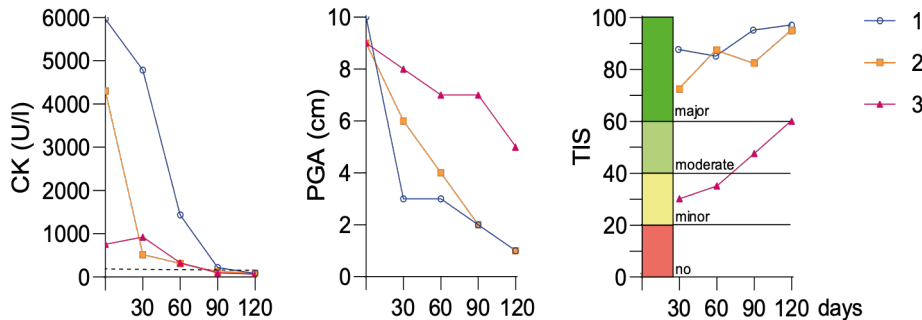
Patient #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
Disease	SLE	SLE	SLE	SLE	SLE	SLE	SLE	SLE	SLE	IIM	IIM	IIM	SSc	SSc	SSc	SSc
Follow-Up (months)	40	35	31	31	29	26	22	17	26	21	14	23	19	18	14	
Drug-Free Remission/No Progression	+	+	+	+	+	+	+	+	+	15mo	+	+	+	+	+	
Glucocorticoid-free state	+	+	+	+	+	+	+	+	+	15mo	+	+	+	+	+	
No Immunosuppressive Drugs	+	+	+	+	+	+	+	+	+	15mo	+	+	+	+	+	



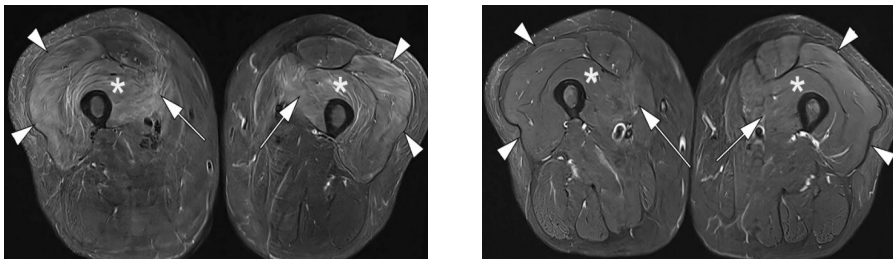
All patients were treated with Miltenyi MB19.1

Müller F, Taubmann J et al. N Engl J Med. 2024 Feb

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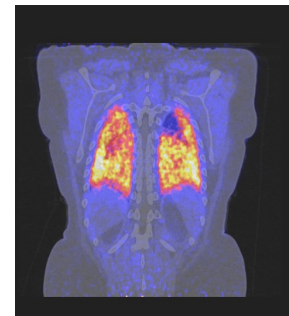


Resolution of muscle inflammation in MRI

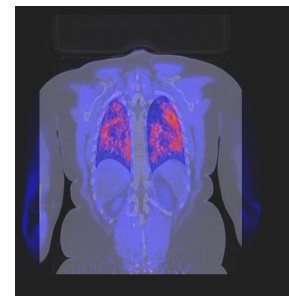


Baseline

3 months



Baseline



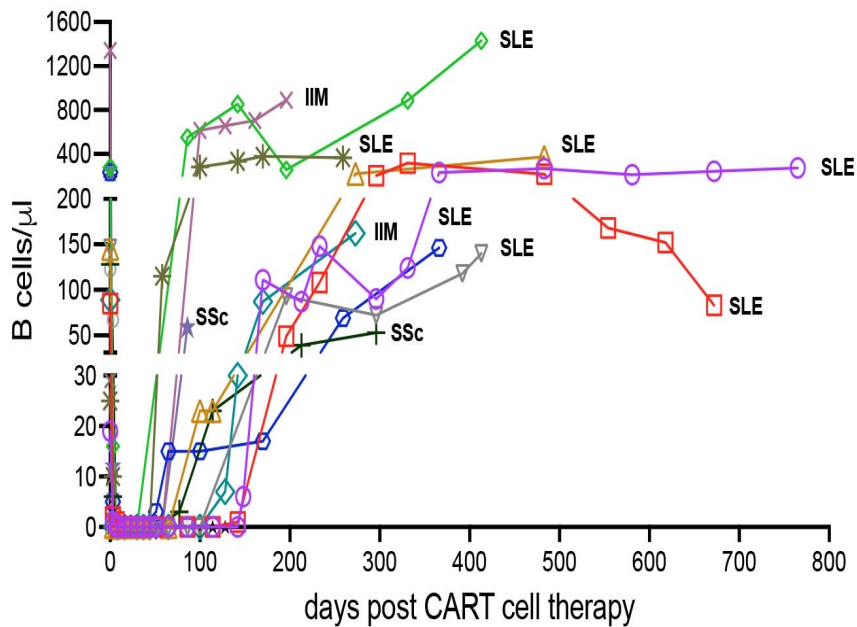
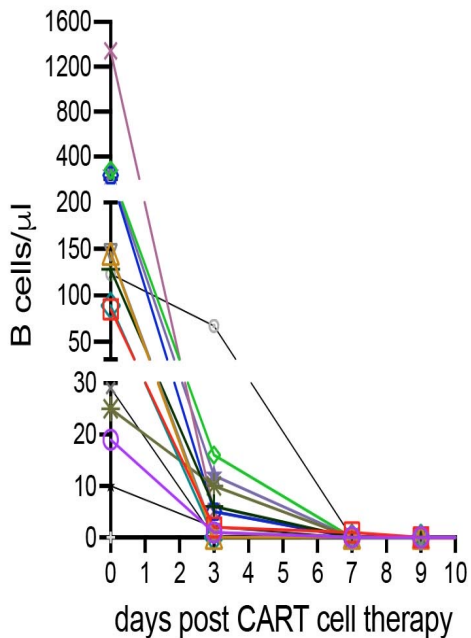
3 months

Lung Remodeling in FAPI-PET/CT

Müller F, Taubmann J et al. N Engl J Med. 2024 Feb

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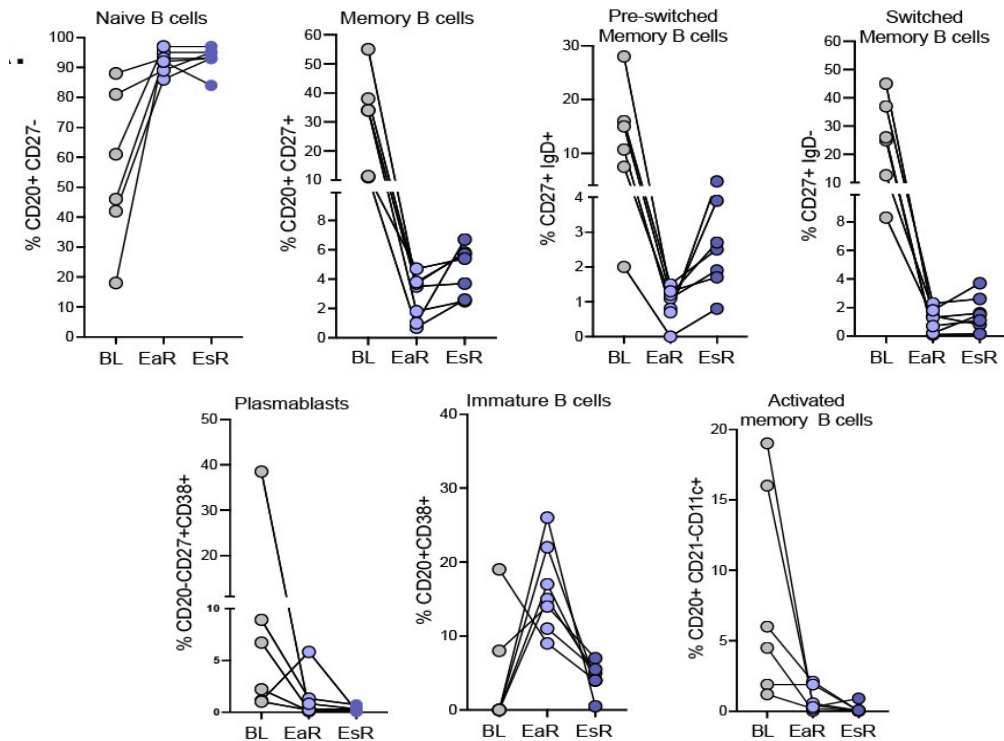
Course of B cells after CD19 CAR-T cell therapy



Müller F, Taubmann J et al. N Engl J Med. 2024 Feb

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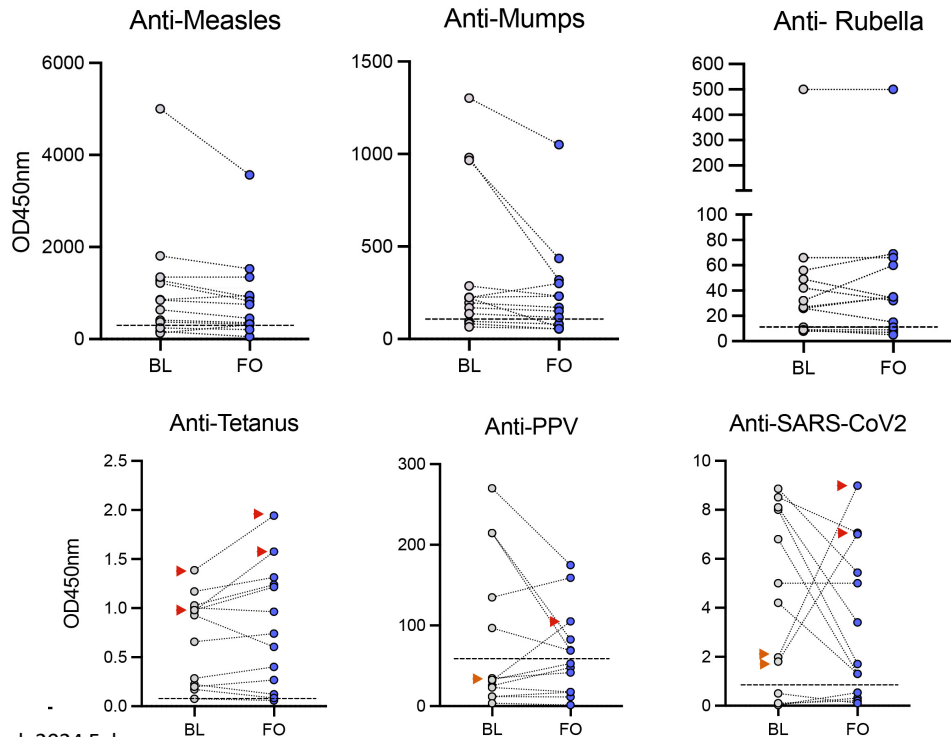
Analysis of memory B cells and plasmablasts in early and established reconstitution of B cells



Müller F, Taubmann J et al. N Engl J Med. 2024 Feb

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Vaccination titers

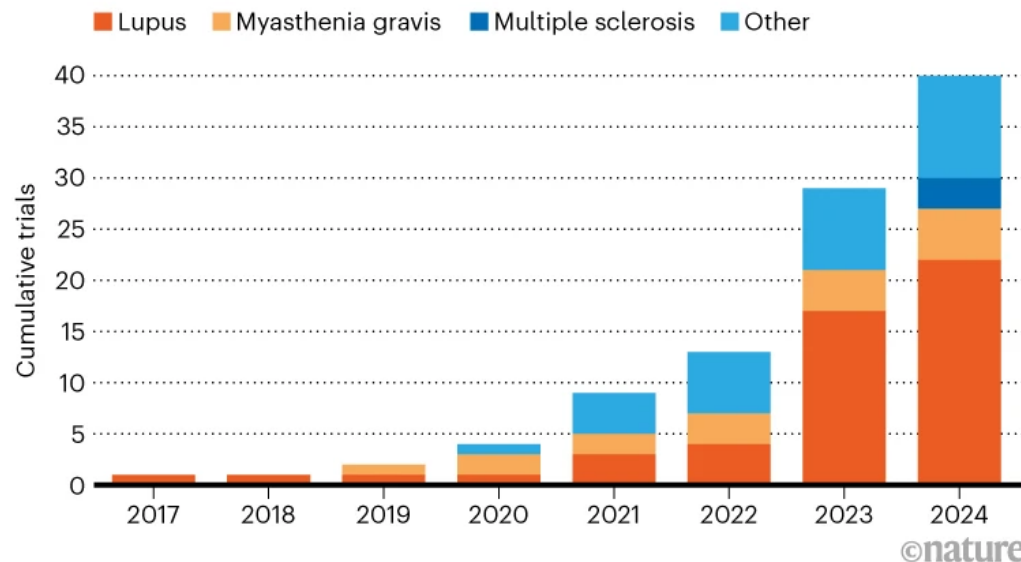


Müller F, Taubmann J et al. N Engl J Med. 2024 Feb

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ENLISTING IMMUNE CELLS TO TREAT AUTOIMMUNE DISEASE

The number of clinical trials of CAR T cells — engineered immune cells — used to treat autoimmune disorders has grown rapidly over the past seven years. Testing of CAR-T therapy for the autoimmune disorder lupus accounts for the bulk of the trials.



Mullard A. 2024

Search Results

Viewing 1-10 out of 93 studies

Showing results for: **Autoimmune Diseases** | CAR-T cells

Clinical trials.gov, 10.10.2024

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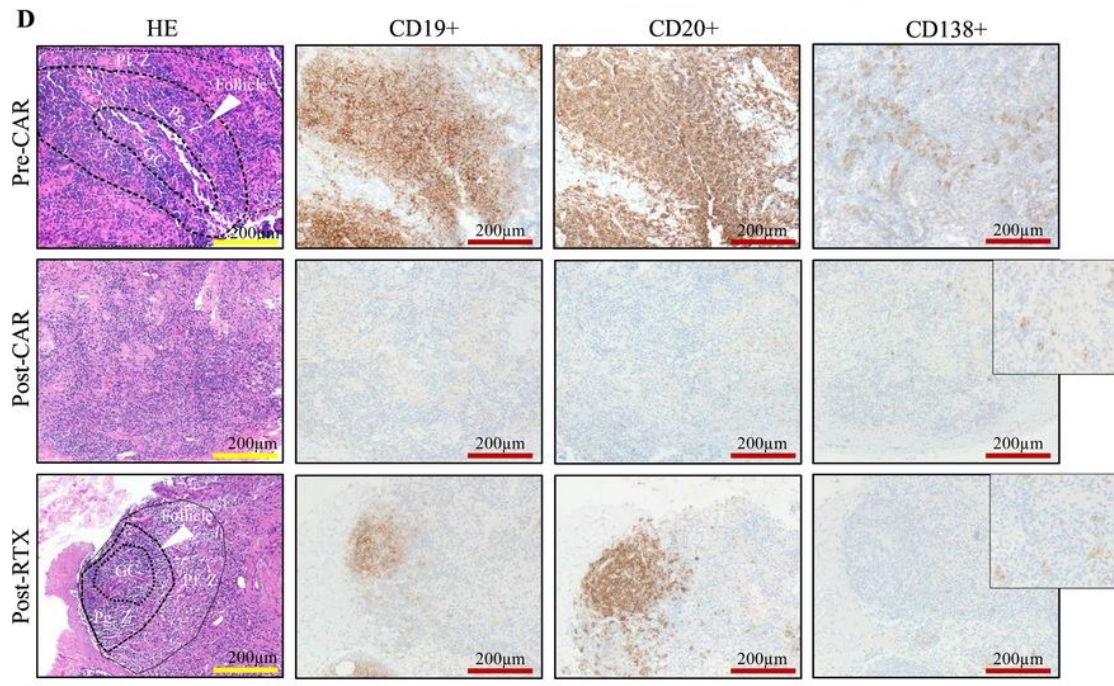
Recent Data

	SLE	SSc	IIM	Total
Demographic characteristics				
Numbers	18	7	5	30
Age, years (mean)	27	41	50	34
Females, N (%)	14	3	4	21 (70)
Follow-up Time (months)	6	3,4	1,8	4,7
CAR T-/B-cell Dynamics				
CAR-T-cell presence, days (median, range)	37 [16;100]	51 [16;77]	37 [23;100]	47 [16;100]
B-cell aplasia, days (median, range)	93 [58;128]	86 [30;196]	86 [77;170]	86 [30;196]
Safety				
CRS 1°, n (%)	11	4	2	17 (56,7)
CRS 2°, n (%)	1	1	1	3 (10)
CRS 3/4°, n (%)	0	0	0	0 (0)
ICANS (any grade), n (%)	0	0	0	0 (0)
ICAHT (any grade), n (%)	0	0	0	0 (0)
Late Neutropenia, n(%)	3	0	1	4 (13,3)
Pneumonia, n (%)	2	1	1	4 (16)
Efficacy				
>6 months follow-up, n	15	6	4	25
DORIS Remission, n	15	n.a.	n.a.	n.a.
No progression of SSc	n.a.	6	n.a.	n.a.
2016 ACR/EULAR Major response (%)	n.a.	n.a.	4	n.a.
Relapse of Disease	0	0	1	0

Hagen et al. ACR 2024

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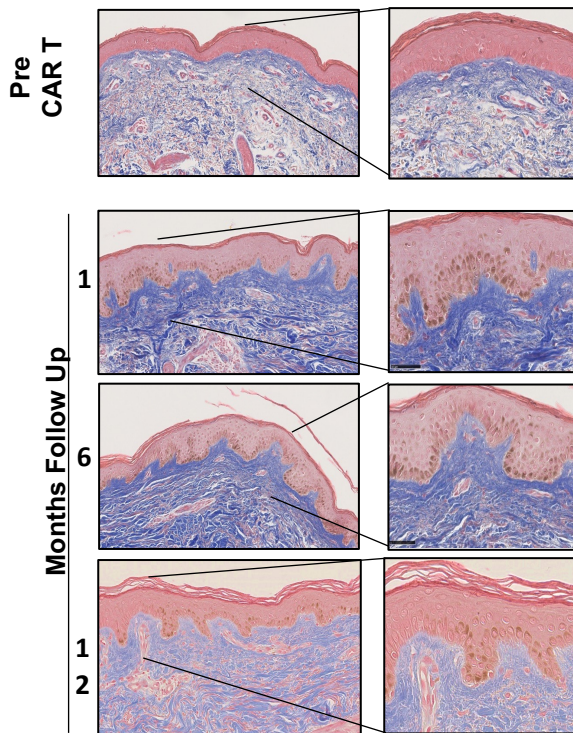
CD19 CAR-T cells induce deep tissue depletion in AID



Tur et al. 2024

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Skin structure changes in SSc



Bergmann et al. 2023
Follow-up in press Lancet

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What is left to do?

Safety

CRS/ICAN

ICAHT

Infections

Immuno-phenomenons

B-cell burden

Lymphodepletion

Efficacy

Patient profile

Flare

Vector

Target

Allo vs autologous

Biomarkers

T cell engager

vs

CAR

Education patients

Education colleagues

Costs

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Preview

nature medicine

Article

<https://doi.org/10.1038/s41591-024-01038-8>

Bispecific T cell engager therapy for refractory rheumatoid arthritis

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Published online: 26 April 2024

 Check for updates

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CORRESPONDENCE



BCMA-Targeted T-Cell–Engager Therapy for Autoimmune Disease

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DOI: 10.1056/NEJMc2408786 | [VOL. 391 NO. 9](#)

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Inflammation Research
Erlangen

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