CAR T Cells in Autoimmune Disorders - an Update

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Disclosures

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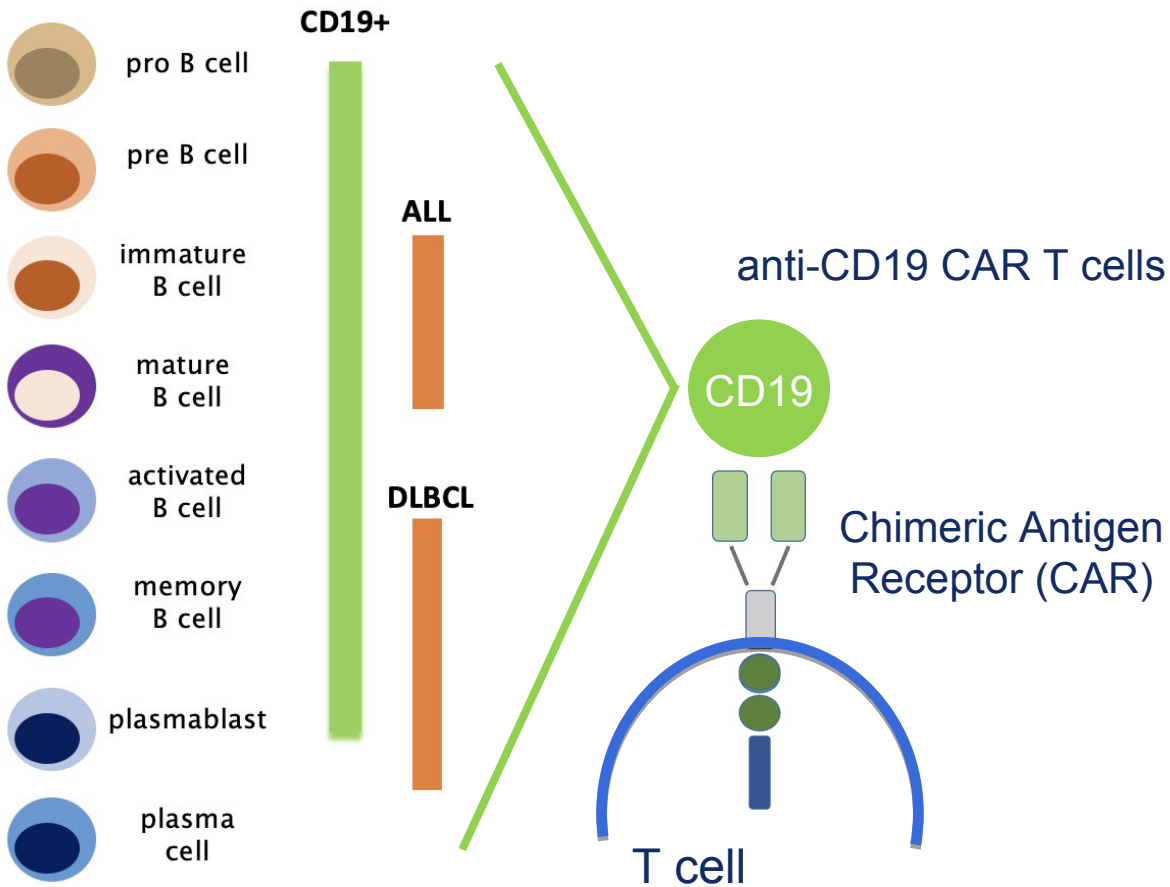
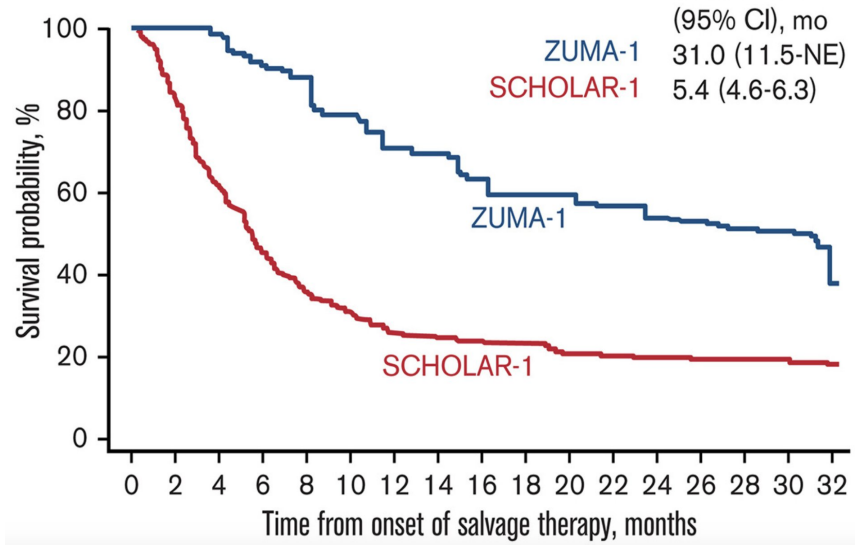
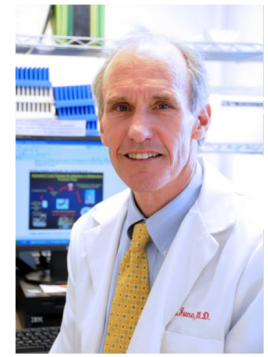
The CAR T cell concept

Transformative potential for the treatment of B cell-derived malignancies







C. June, MD

- effective
  e.g. r/r large B cell lymphoma (LBCL) following 1+ previous therapies
- TRM ca. 5%
  cytokine release syndrome
  neurotoxicity
  hematotoxicity
  infections
  secondary malignancies

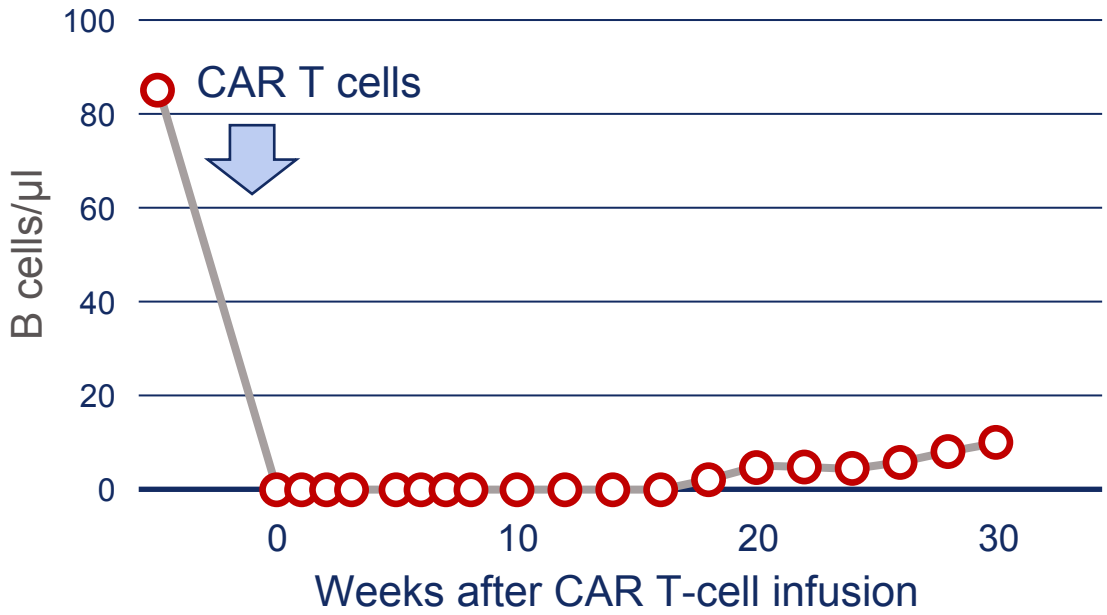
ALL, acute lymphatic laukemia; DLBCL, diffuse large B cell lymphoma; OS, overall survival

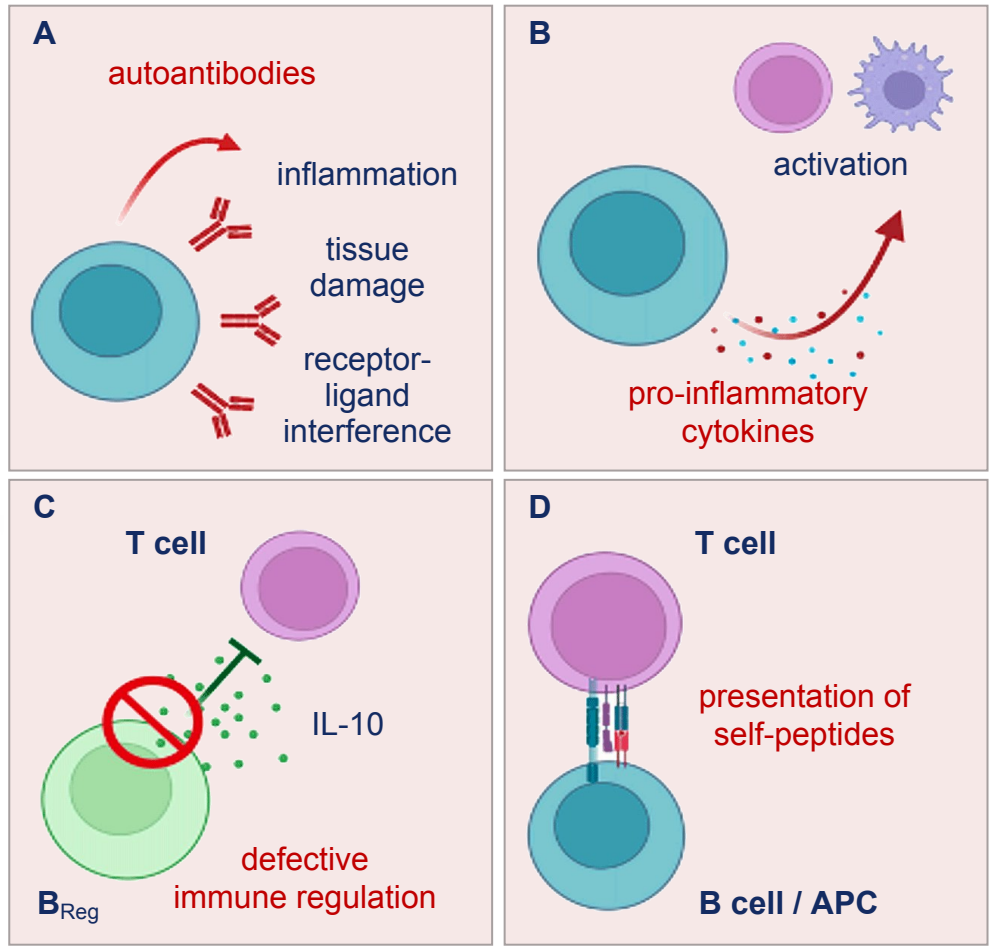
Ref: Crump M et al., Blood 2017, Locke FL et al., Lancet Oncol 2019

The Therapeutic Principle (in Cancer)

Lessons learnt from the treatment of cancer patients

Anti-CD19 CAR T cells lead to deep B cell depletion (on target, off tumor)



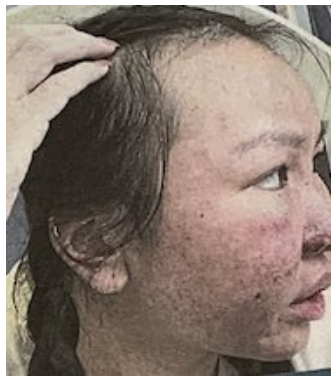


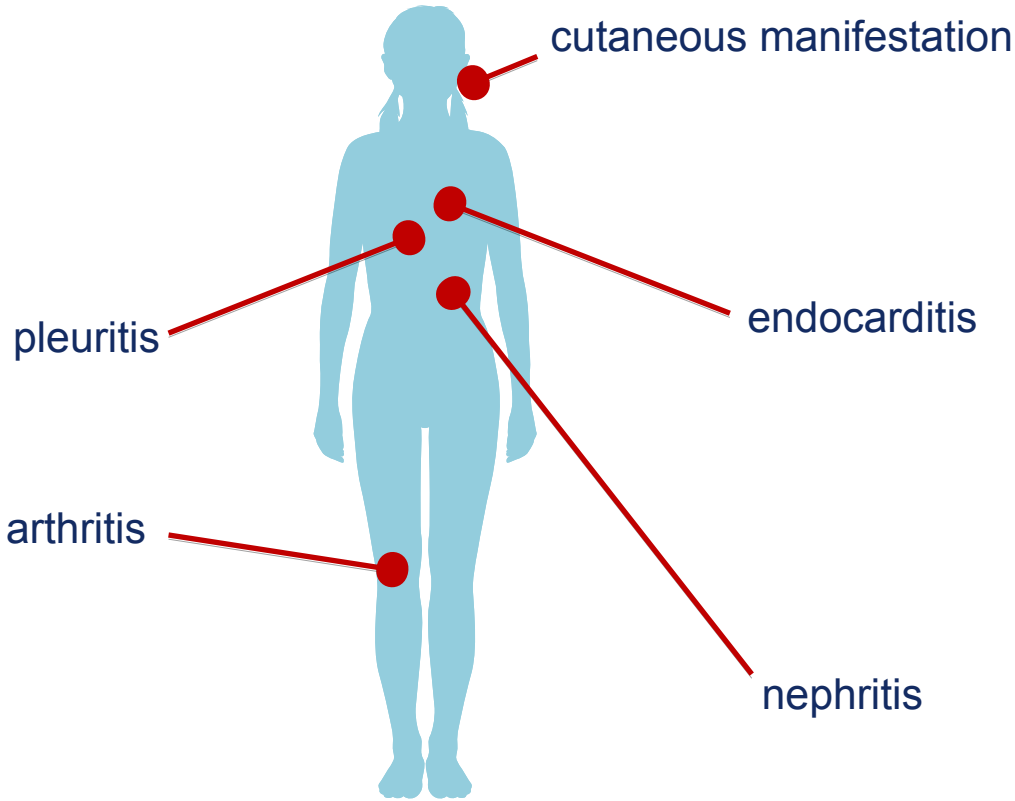
B cells play a central role in many autoimmune diseases

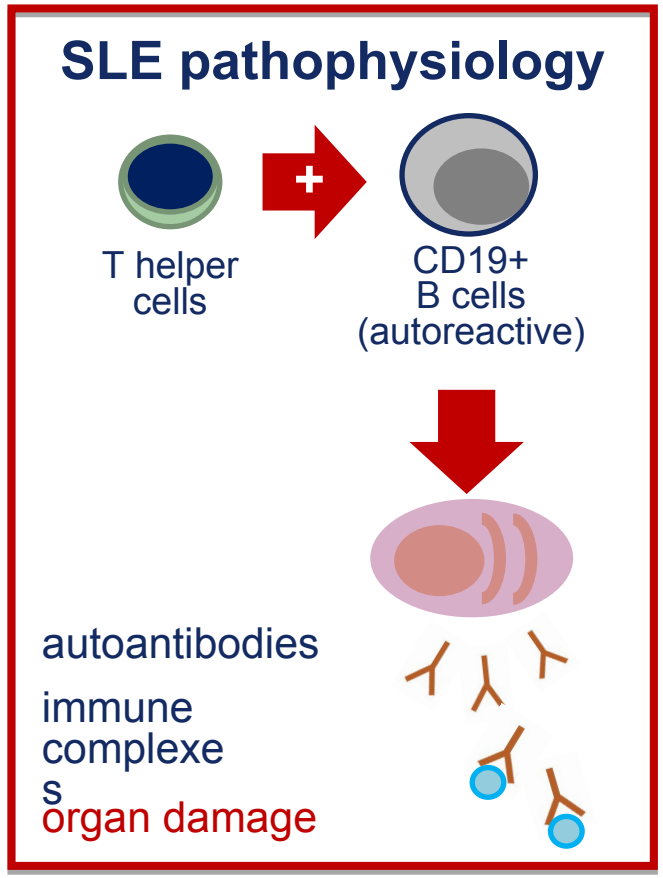
Is it possible to derive a therapeutic principle from a side effect?

Ref: Mougiakakos D et al., Blood 2025

Our/the first patient with systemic lupus erythematosus (SLE)







20-year old patient

systemic lupus erythematosus (SLE)

therapy at presentation: hydroxychloroquin, MMF, steroids, belimumab

previous therapy: high dose steroids, rituximab, tacrolimus, cyclophosphamide

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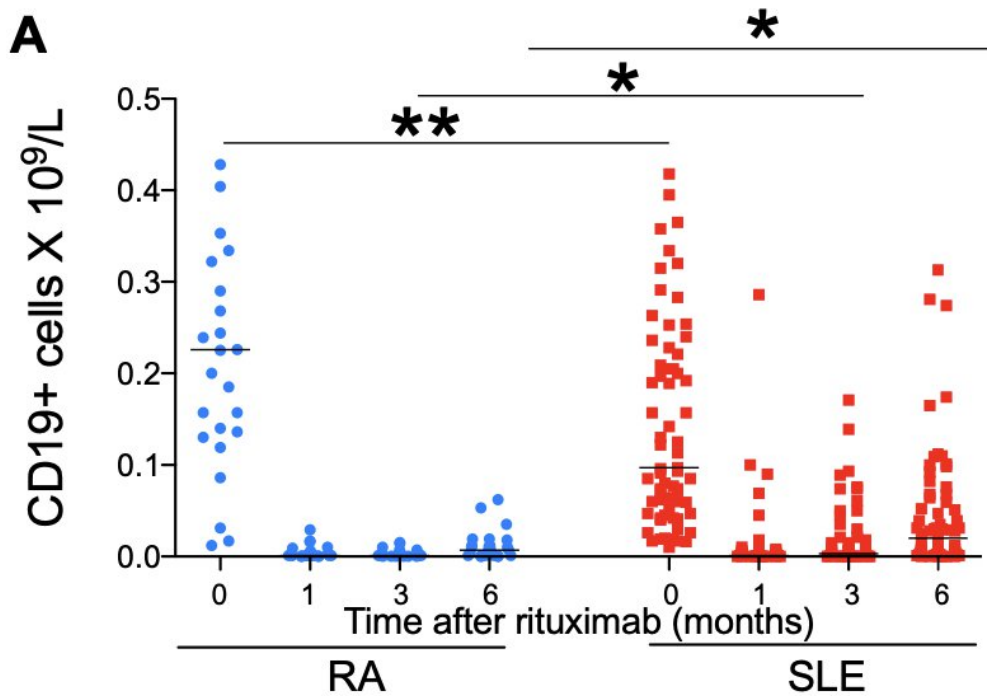
Ref: Mougiakakos D et al., NEJM 2021

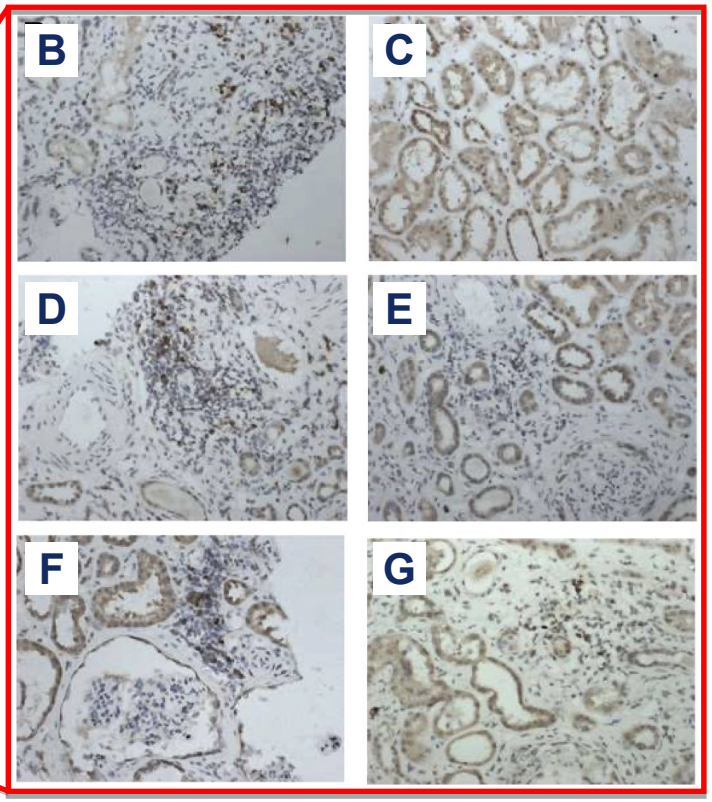
Clinical studies in SLE (and rheumatoid arthritis/RA)

Incomplete antibody-mediated depletion of B cells in tissue

- discrepancy between circulating and tissue-resident B cells



peripheral blood



kidneys

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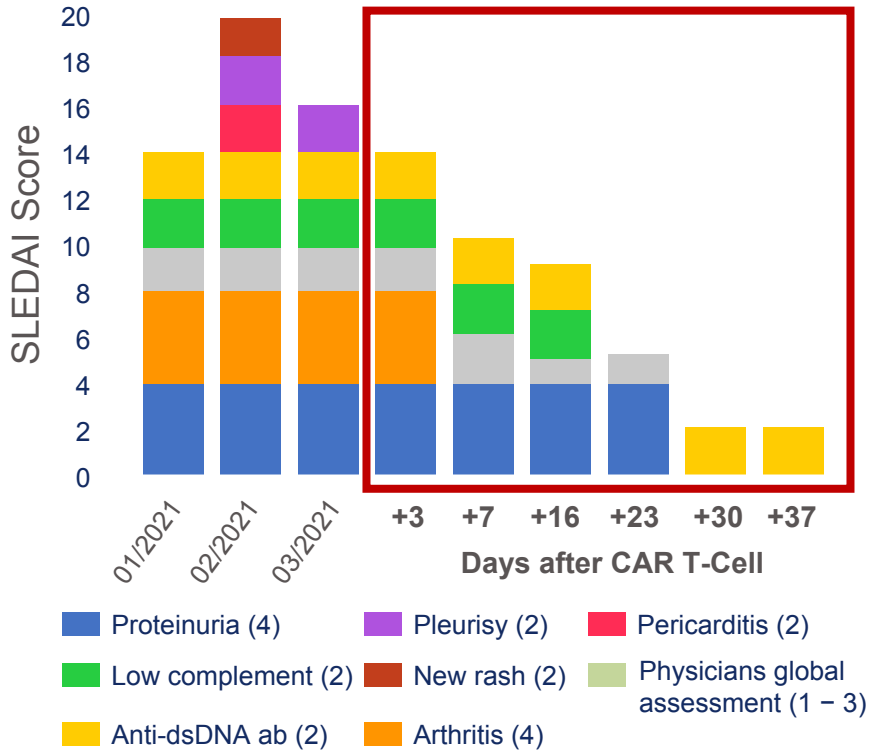
Ref: Venkat RR et al., Rheumatology 2022

Course of laboratory chemical parameters after infusion of CAR T cells

Sustained therapeutic success without severe toxicity



>5 years after treatment:

- no medication
- SLEDAI score = 0
- C3, C4 and anti-dsDNA antibody levels normalized
- CAR T-cells not detectable
- B-cell reconstitution

anti-CD19 CAR T-cells in 8 SLE patients 100% remission without any signs of severe toxicity

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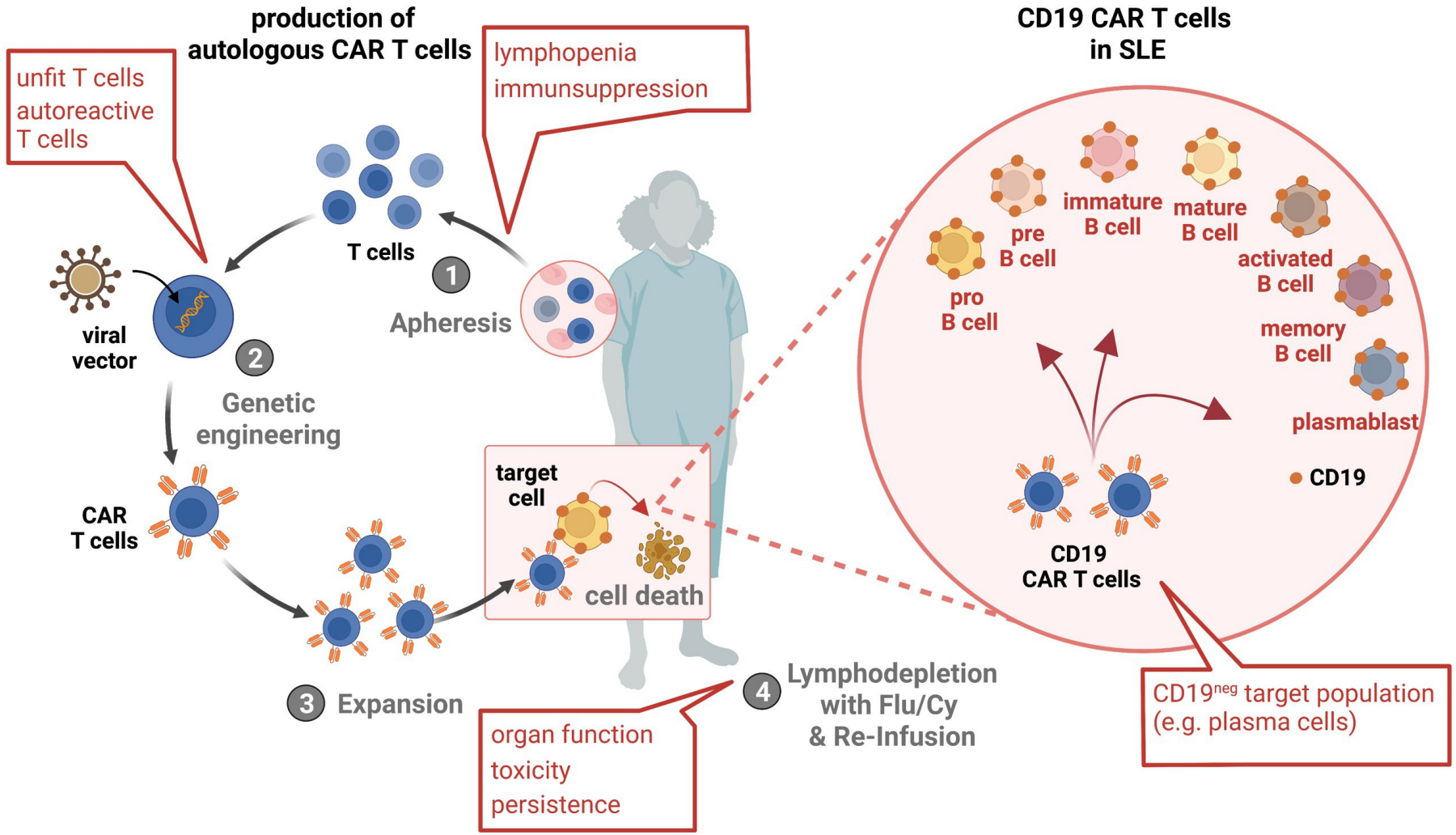
Ref: Mougiakakos D et al., NEJM 2021,
Mackensen A et al., Nat Med 2022,
Müller F et al., NEJM 2024

The therapeutic principle of anti-CD19 CAR T cells in autoimmune diseases



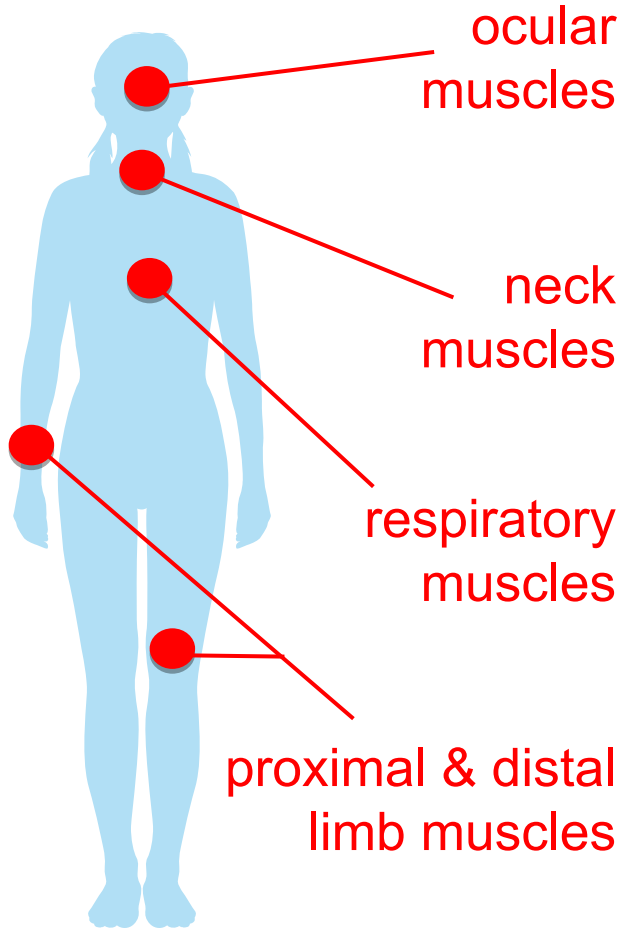
Ref: Schett G et al., Lancet 2023

Can This Principle Work For Neuroimmunological Diseases?

Our (first) patient

Refractory severe myasthenia gravis (MG) with recurrent myasthenic crises

34 years old



- active (refractory) disease
- current medication: bortezomib, steroids, and AchE-I
- previous treatment: HD steroids, azathioprine, rituximab MMF, plasma separation, thymectomy

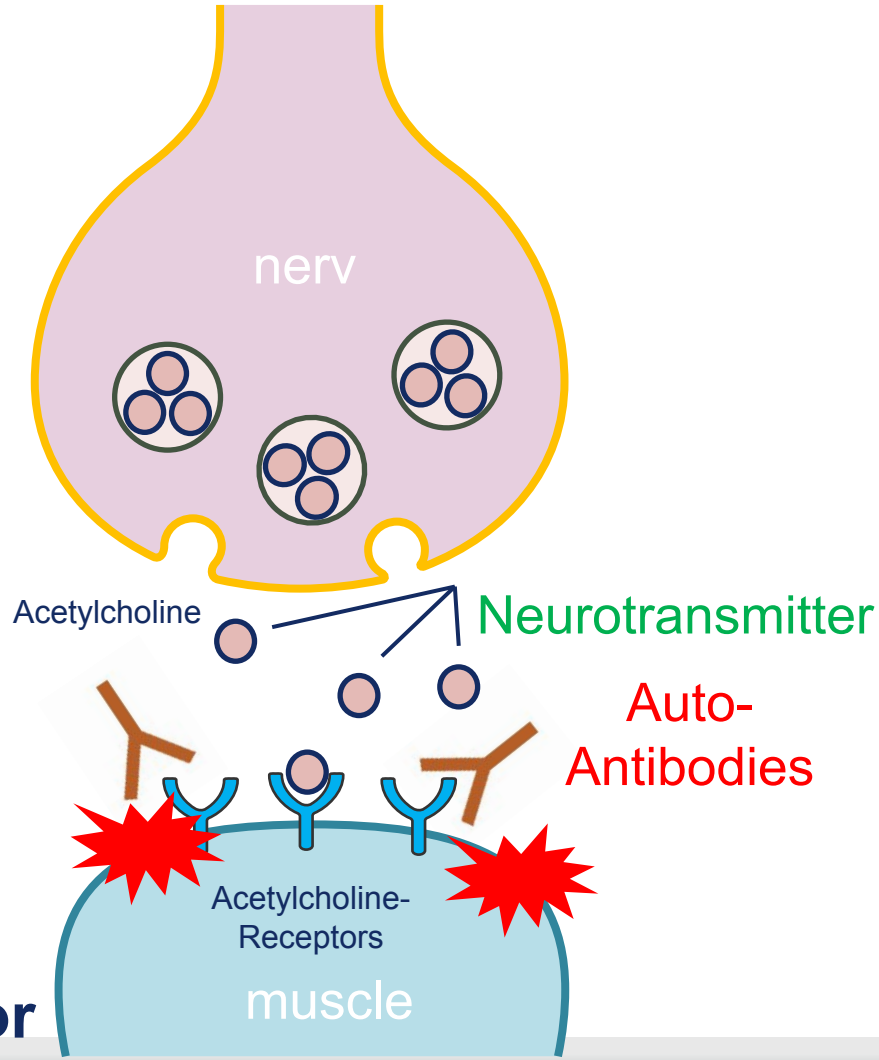
Patient with severe, therapy refractory myasthenia gravis

Ref: Haghikia et al, Lancet Neurology 2023

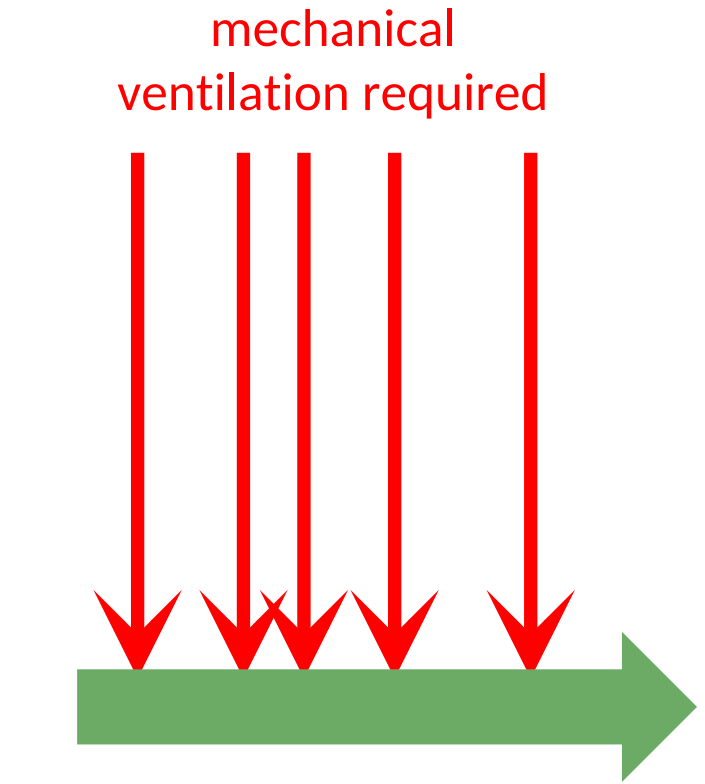
Myasthenia gravis

Prototypical B cell-mediated autoimmune disorder

in 80% of the cases presence of **autoantibodies** against the **acetylcholine-receptor**



Disturbed Muscle Innervation



Life-threatening
despite 8 pre-treatments

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Ref: Haghikia et al, Lancet Neurology 2023

Clinical efficacy

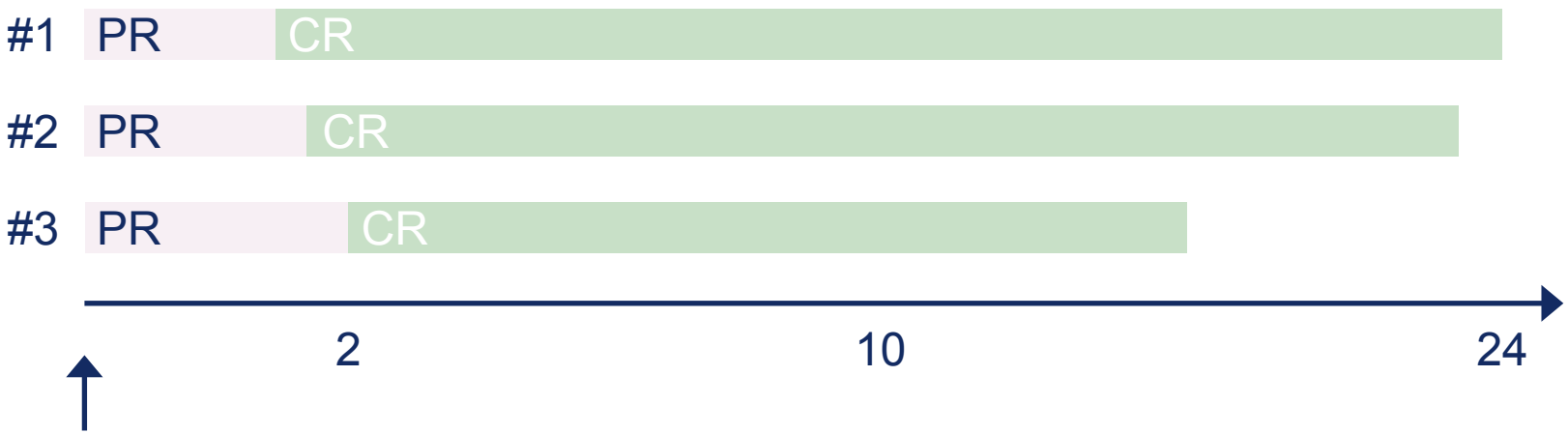
before infusion

two weeks after infusion

➢ clinical remission despite presence of AchR-antibodies

Ref: Haghikia et al, Lancet Neurology 2023

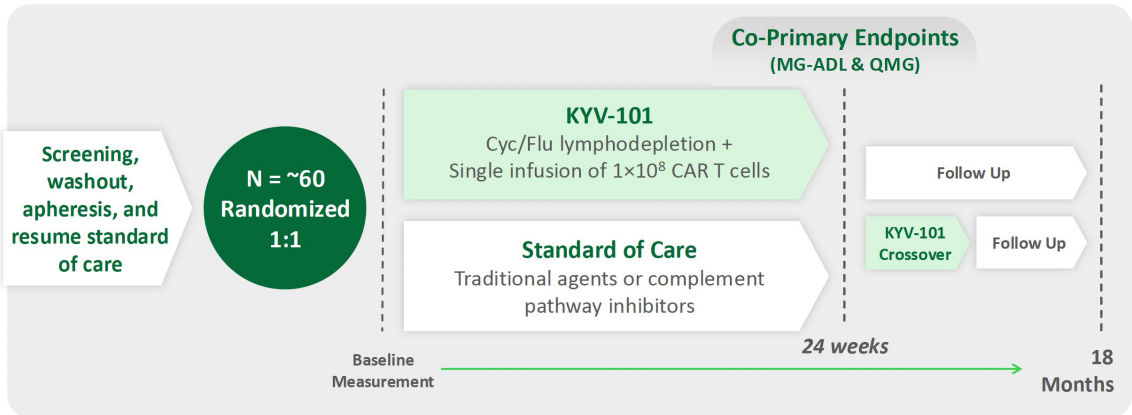
…and long lasting



3 patients with autoantibody positive severe and refractory myasthenia gravis

CR, complete remission = disease and therapy free

KYSA-6, Phase 3 trial for patients with refractory Myasthenia Gravis



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Ref: Haghikia A et al., Lancet Neurology 2023, Annals Rheumatic Diseases 2024, Motte J et al., Neuron 2024, Hegelmaier T et al., under review

What Have We Learnt So Far?

CAR T cell-mediated deep B cell depletion as a biology-driven therapeutic strategy…

rheumatology

Mougiakakos et al., NEJM

2021

first patient
with non-malignant disease

neurology

2023

first patient
with myasthenia

Haghikia et al.,
Lancet Neurology

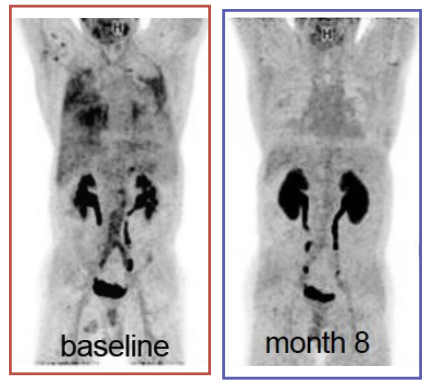
benign hematology

Trautmann et al.,
Lancet

2025

first patient
benign hematology

gastroenterology



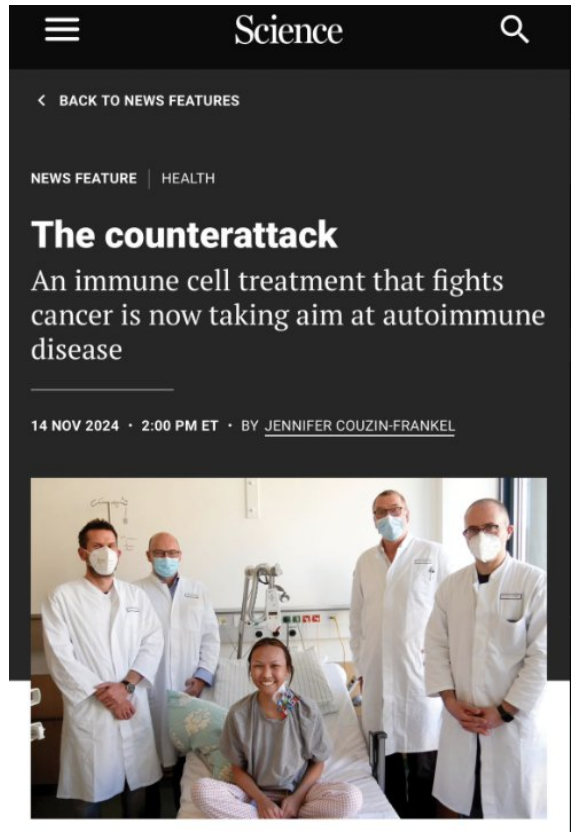
patient with hepato-
biliary involvement
of IgG4 related disease

Keitel et al.,
Journal of Hepatology

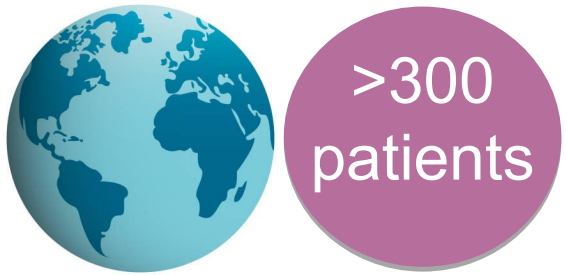
>300
patients

first patient with
autoantibody-
mediated encephalitis

Hegelmaier et al., Med



… with evident therapeutic potential



Search Details: Viewing 1-10 out of **180** studies for: Autoimmune Diseases | CAR T cells

Condition/disease

Autoimmune Diseases

Other terms

Intervention/treatment

CAR T cells

ITP encephalitis NMOSD rheumatoid arthritis myasthenia hemophilia SLE myositis SPS

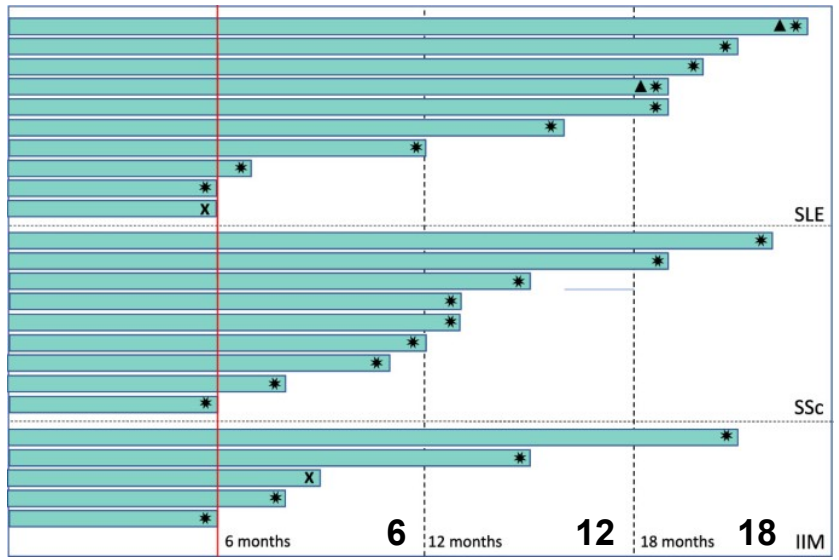
B cell-mediated autoimmune disorders

Case Reports

Case Series

Clinical Trials

CASTLE trial: drug free remission



systemic lupus erythematosus (SLE) n=10

systemic sclerosis (SSc) n=9

idiopathic inflammatory myopathies (IIM) n=5

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Ref: Müller F et al., Nature Med. 2026

New patient populations and randomized trials

hit early, hit hard?

nature medicine

Article

https://doi.org/10.1038/s41591-025-04191-8

Anti-CD19 CAR T cells for pediatric patients with treatment-refractory autoimmune diseases

systemic lupus erythematosus (SLE)
n=4
systemic sclerosis (SSc)
n=1
juvenile dermatomyositis (JDM)
n=3

100% treatment free remission [ø16.5 m follow up]

important **benchmarking** against alternative **B cell-depleting strategies**

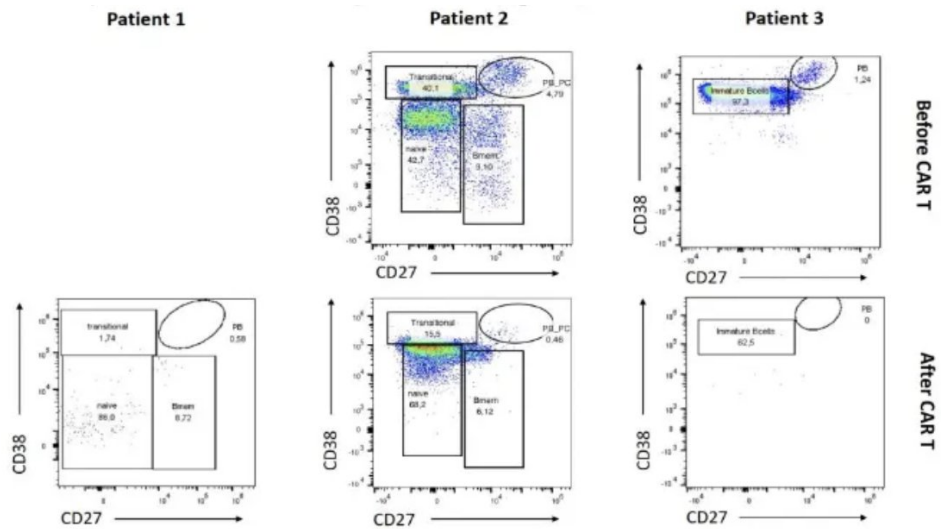
Comparison of B-cell Depletion by Rituximab and Anti-CD 19 CAR-T Therapy in Patients With Rheumatoid Arthritis (COMPARE)

ClinicalTrials.gov ID NCT06475495

Sponsor Charite University, Berlin, Germany

Information provided by David Simon, Charite University, Berlin, Germany (Responsible Party)

Last Update Posted 2024-06-26



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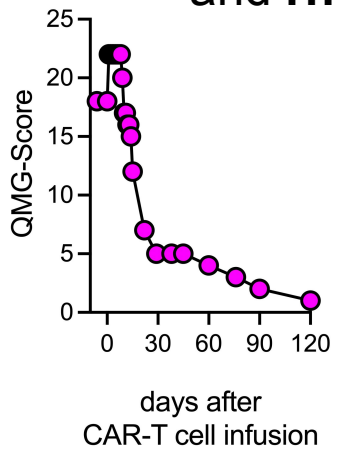
Ref: Becilli M et al., Nature Med 2026,
Minopoulou I et al., EULAR meeting

Resistance and relapse(s) occur

One size might not fit all & inflammation ≠ degeneration

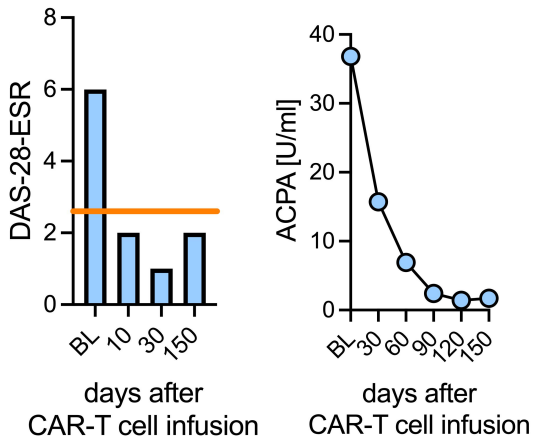
Concomitant **myasthenia gravis** (MG) and **rheumatoid arthritis** (RA)

MG

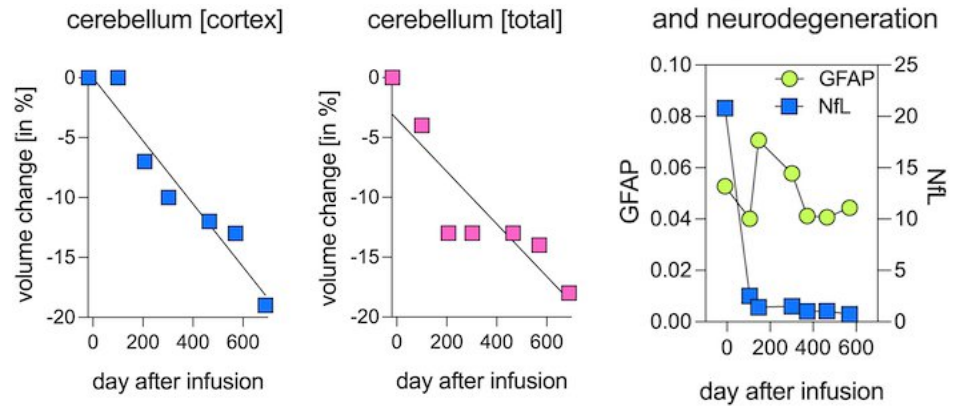


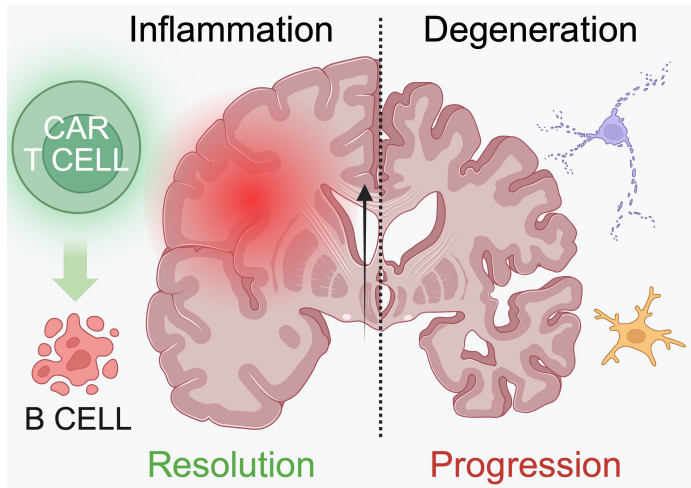
treatment free remission (24 month follow up)

RA



seropositive relapse at 15 months





Patient with anti-DAGLA AE

GFAP, glial fibrillary acidic protein
NfL, neurofilament light chain

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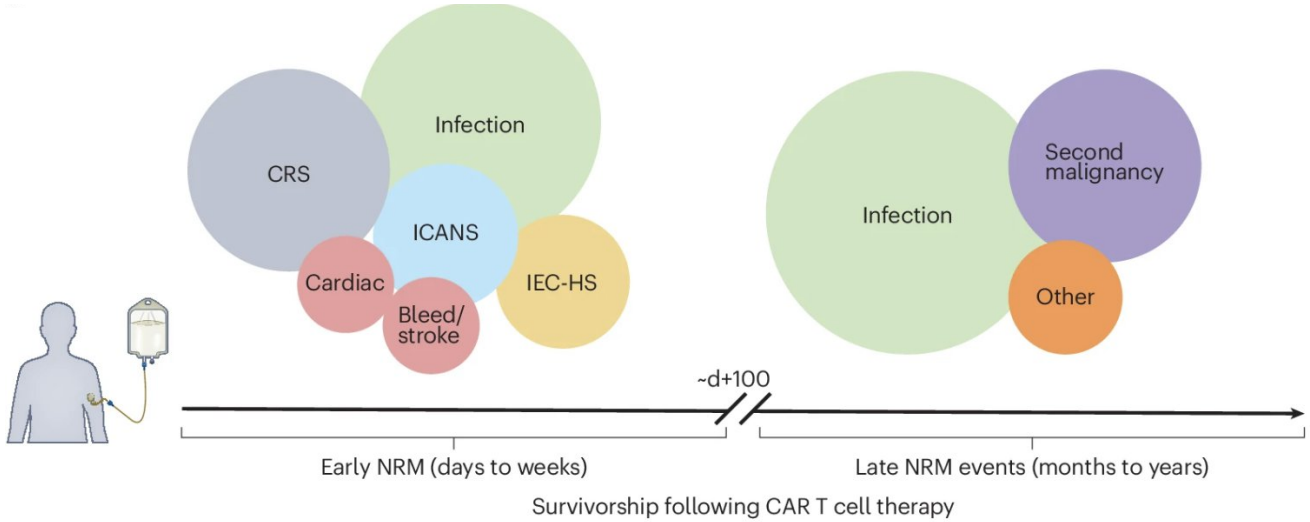
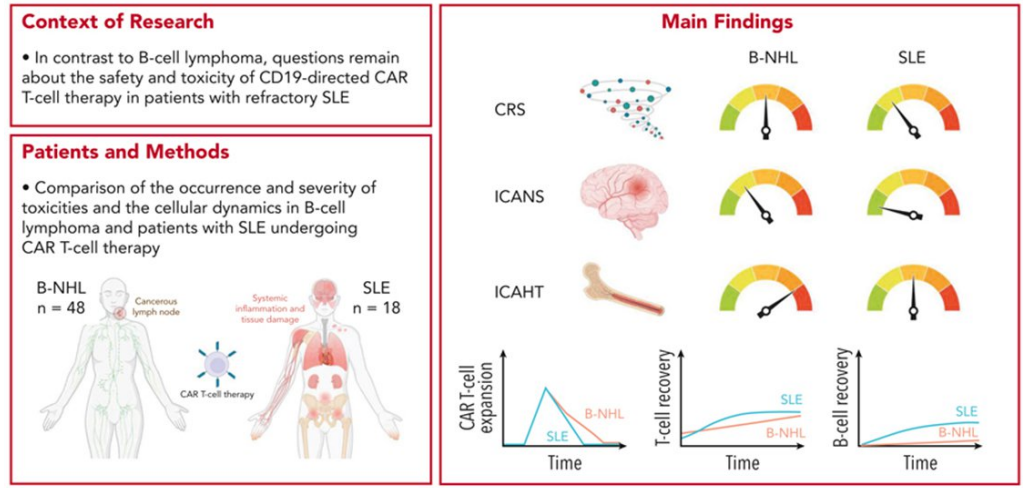
Ref: Mougiakakos D et al, ACTN 2026,
Haghikia A et al., ARD 2024,
unpublished data

Favorable safety profile as compared to their use in malignancies



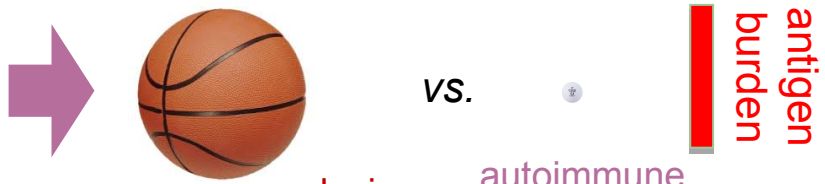


CAR T cell-associated toxicities
Treatment-related mortality ca. 5% (in malignant diseases)
Infections are the most common cause for non-relapse mortality

CAR T cell-associated toxicities: yes
Grade of toxicities: lower
Incidence of toxicities: lower
TRM: 0%

anti-CD19
4-1BB

proposed explanation



In B cell-derived malignancies high tumor (=antigenic) burden prior CAR T cell infusion is associated with higher risk for (severe) toxicity

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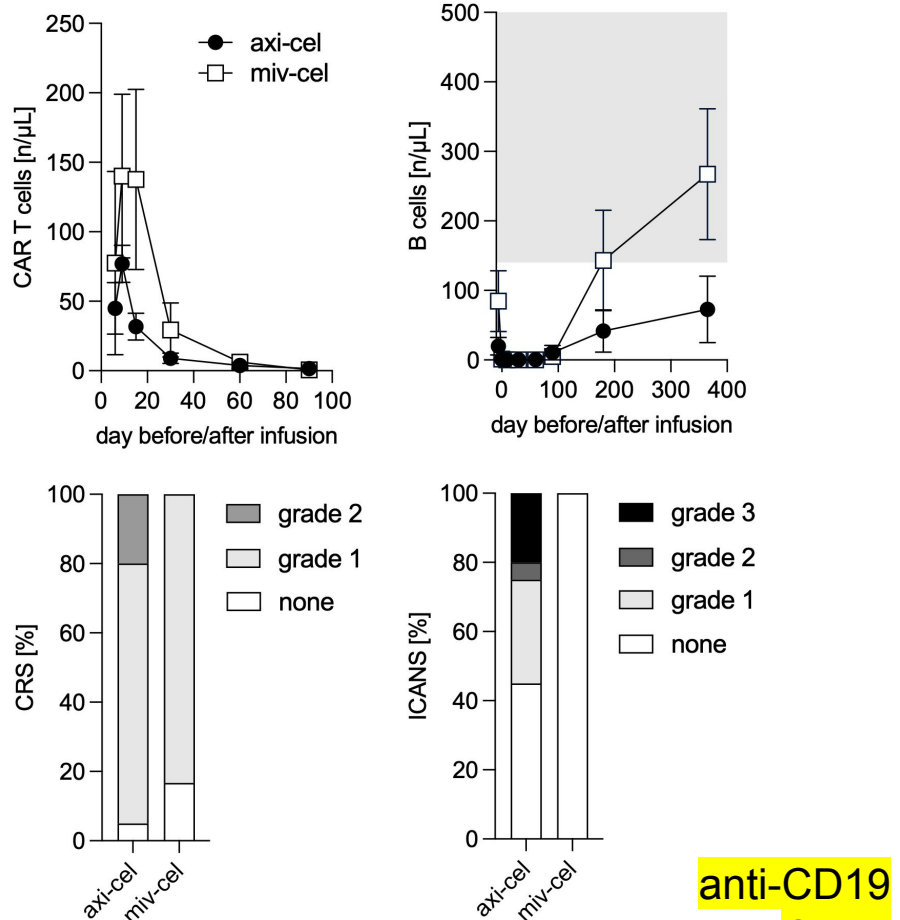
Ref: Rejeski K et al., Nature Med. 2025,
Müller F et al., Blood 2025

Favorable safety profile but…



anti-CD19
CD28

B-NHL = B non-Hodgkin lymphoma
AD = autoimmune disease

Contents lists available at ScienceDirect

EULAR Rheumatology Open

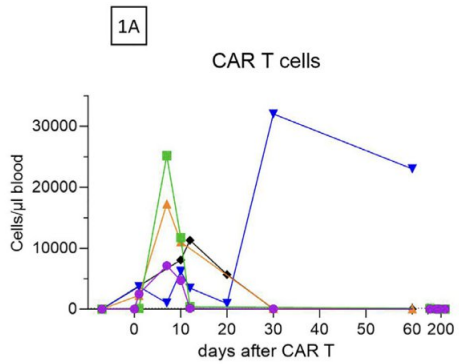
journal homepage: https://www.sciencedirect.com/journal/eular-rheumatology-open

CD19-targeting CAR T cell therapy in five patients with systemic sclerosis unsuitable for autologous stem cell transplantation

Ann-Christin Pecher, Luca Hensen, Rebekka Schairer, Reinhild Klein, Wolfgang Bethge, Claudia Lengerke, Jörg Henes*

Department for Internal Medicine II (Haematology, Oncology, Rheumatology and Clinical Immunology), University Hospital Tuebingen, Tuebingen, Germany

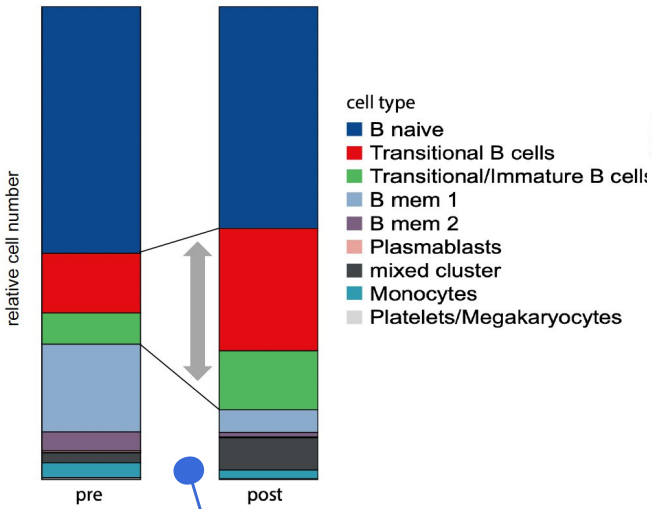
- pt. with terminal renal insufficiency
- HSV and CMV reactivation
- secondary CAR T cell expansion
- severe HLH
- fatal course (day +74)
- TET2 loss of function mutation



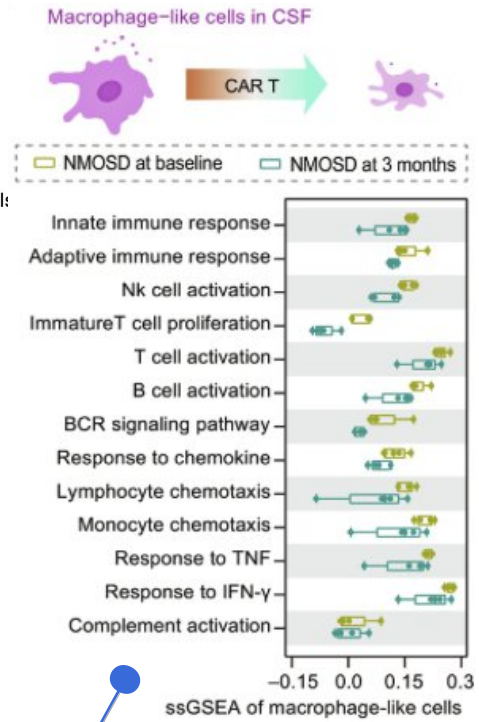
…not without risk

Ref: Berisha M et al., under review,
Pecher AC et al., EULAR Rheum Open 2025

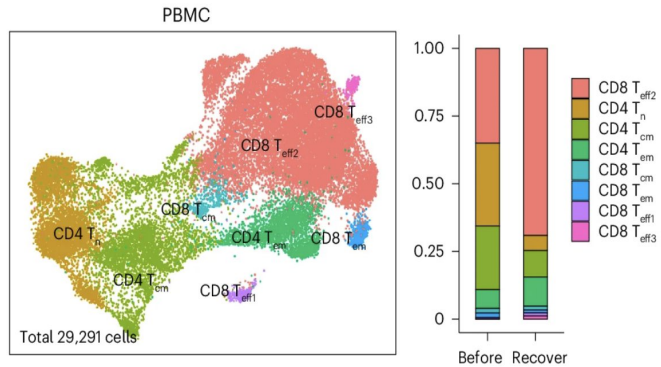
Evidence of an immune reset?



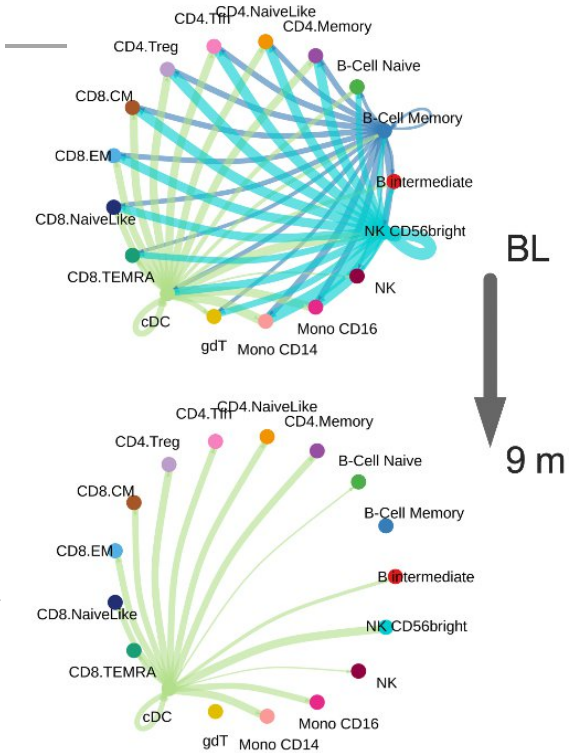
Expansion of immature and transitional B cells in SLE (and other entities)



Macrophage repolarization in the CSF of NMOSD patients



Alterations in the T cell compartment of SLE patients (and other disease groups)



Changes in the cell-to-cell communication in systemic IgG4-related disease

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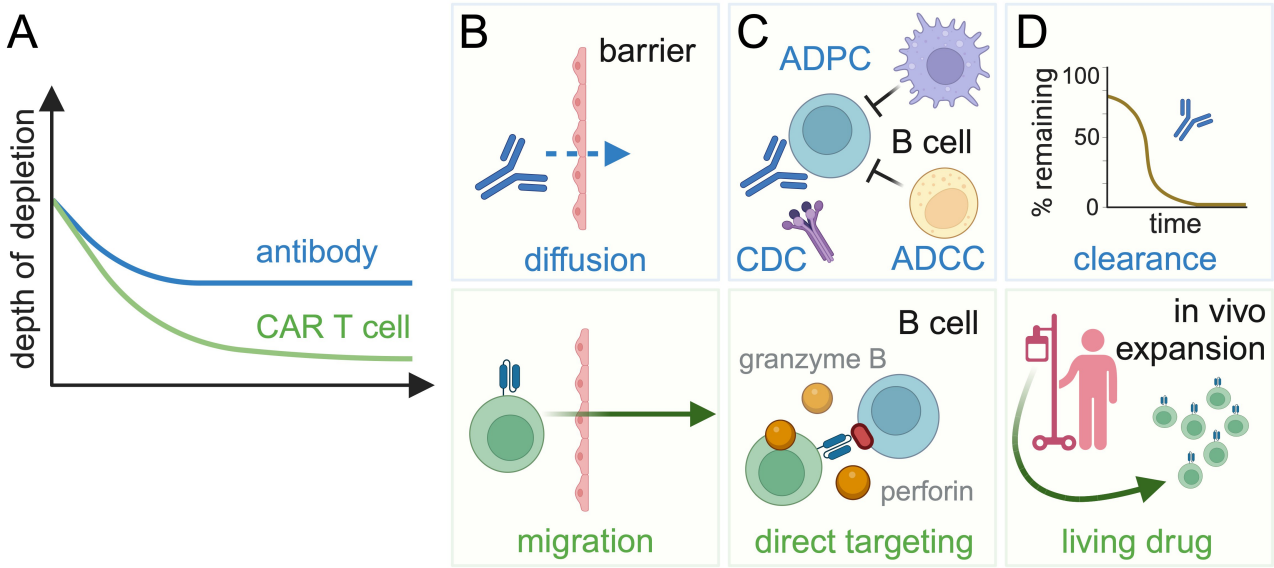
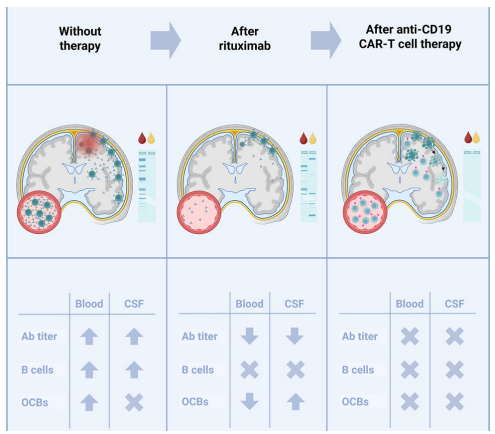
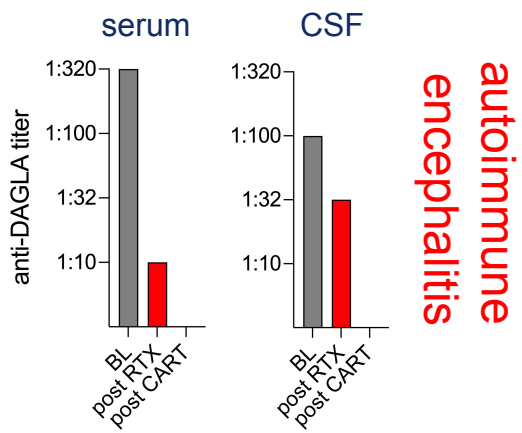
Ref: Wilhelm A et al., JCI 2024,
Qin C et al., Science Immunology 2024,
Feng J et al., Nature Medicine 2025, Keitel V et al., J Hepatology 2026

The depth of B-cell depletion and tissue accessibility matter

CAR T cells‘ unique biological properties

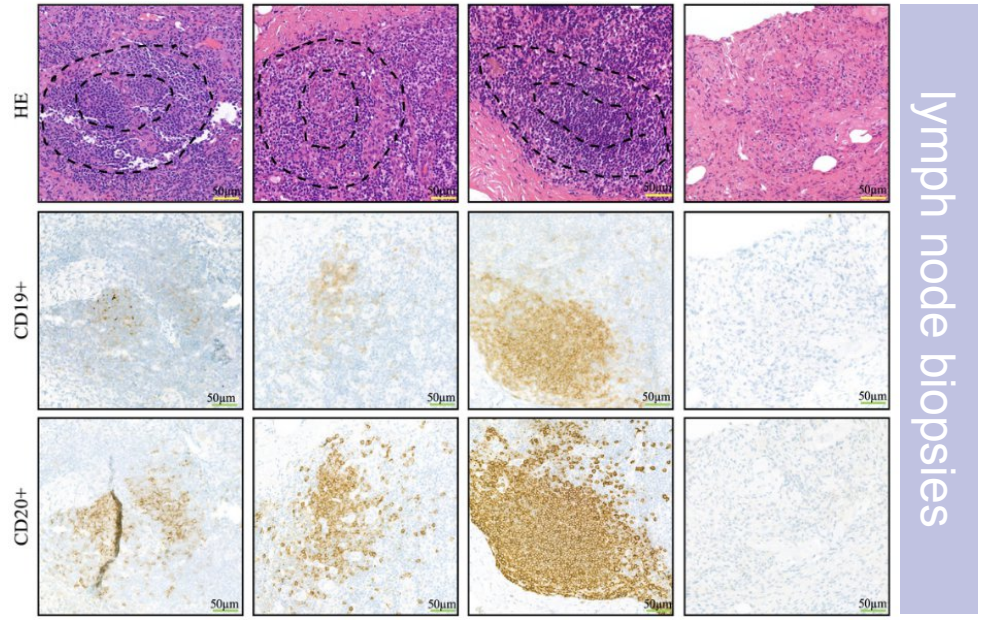






autoimmune encephalitis

Obinutuzumab Blinatumomab Rituximab anti-CD19 CART



lymph node biopsies

rheumatologic diseases

multiple scleroris

Excellent CAR-T Expansion in Blood and CSF								
	1		2		3		4	
	Total Counts (cells)	Fold Increase	Total Counts (cells)	Fold Increase	Total Counts (cells)	Fold Increase	Total Counts (cells)	Fold Increase
Peak CAR-T in Circulation (Blood)	475 M	14.5	254 M	7.7	1.3 B	40	124 M	1.24
CAR-T in CSF on D+14	300 K		3.78 M		1.65 M		1.33 M	

BL, baseline; RTX, rituximab; CART, CAR T cells; CSF, cerebrospinal fluid

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MAGDEBURGER ZENTRUM FÜR ZELL- UND IMMUNTHERAPIE

Ref: Dunn J et al., AAN 2025, Hegelmeier T et al., Med 2025, Tur C et al., Ann Rheum Dis 2025, Mougiakakos D et al., Blood 2025

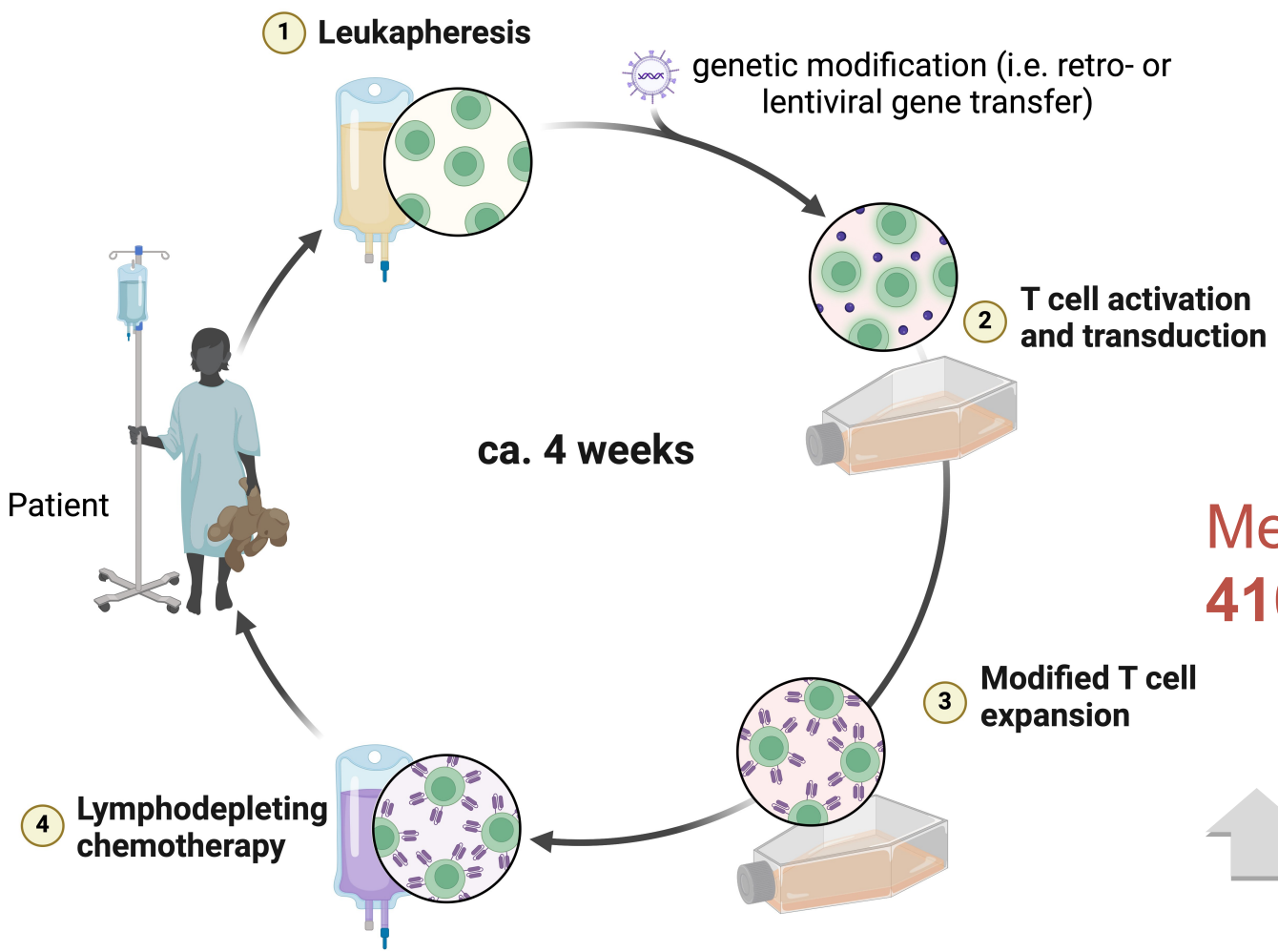
What Can/Should We Improve?

Key areas for optimization

compromised immune cells

faster availability

less/no chemotherapy



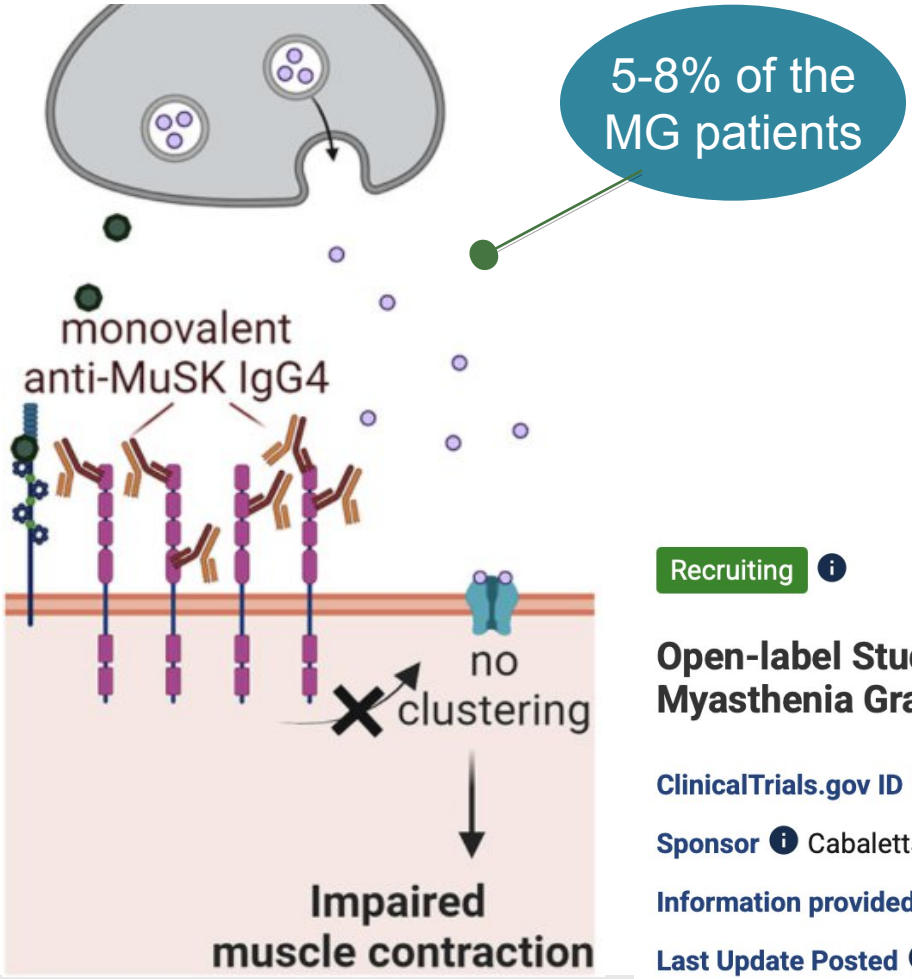
no insertional mutagenesis

better access

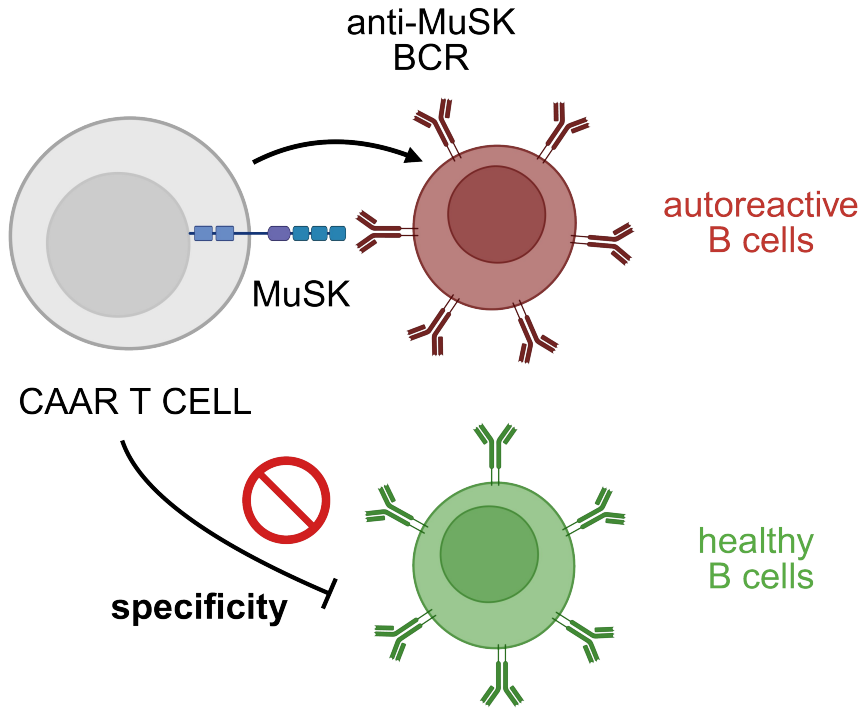
Median drug cost
410.000 $

Adapted from biorender.com

Trading the hammer for a scalpel: selective targeting in autoimmune disease with CAAR-T Therapy



Chimeric Auto-Antibody Receptor T Cells [4-1BB co-stimulation & CD3z chain]



Recruiting

Open-label Study to Evaluate the Safety of Various Dosing Regimens of MuSK-CAART for MuSK Myasthenia Gravis

ClinicalTrials.gov ID NCT05451212

Sponsor Cabaletta Bio

Information provided by Cabaletta Bio (Responsible Party)

Last Update Posted 2024-10-29

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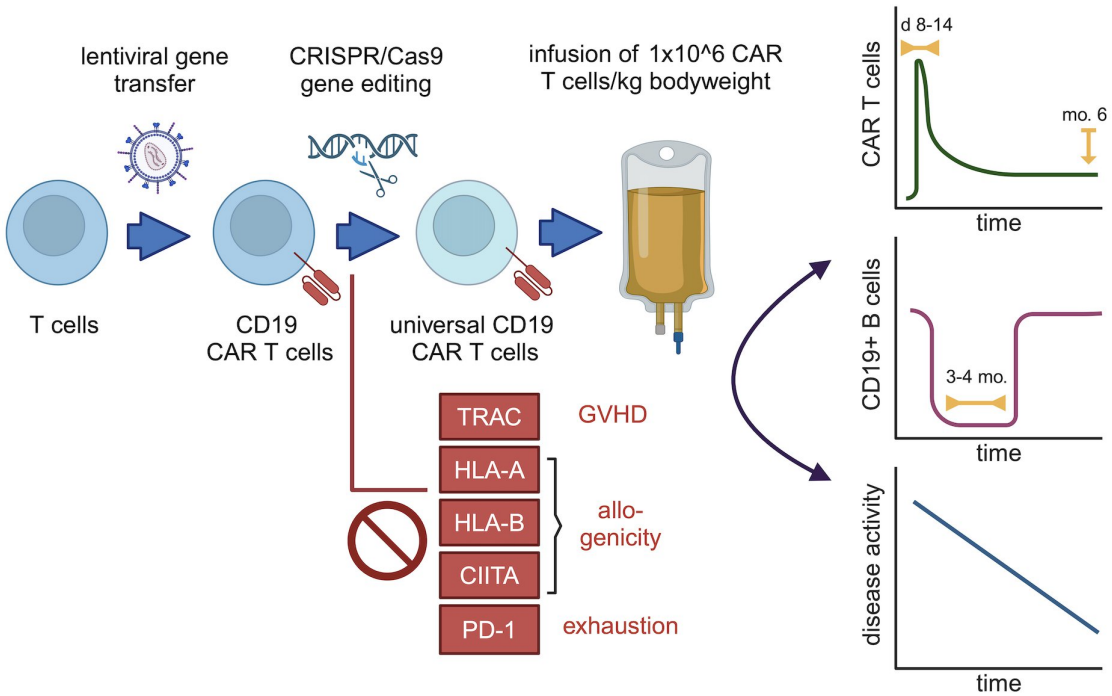
Ref: Adapted from biorender.com, Lim JL et al., iScience 2025, Oh S et al., Nature Biotechnology 2023

Allogeneic solutions gaining momentum



Letter to the Editor | Open access | Published: 08 May 2025

Allogeneic anti-CD19 CAR-T cells induce remission in refractory systemic lupus erythematosus

Chunmei Yang, Chuanyin Sun, Binghe Tan, Chao Hu, Liyan Wan, Chris Wang, Xiujuan Shi, Juliang Qin, Na Zhang, Biao Zheng, Mingyao Liu ✉, Jin Lin ✉, Bing Du ✉ & Hongyan Tong ✉

Cell Research **35**, 607–609 (2025) | Cite this article

Cell

CellPress

Volume 188, Issue 16, 7 August 2025, Pages 4225-4238.e12

Short article

An iPSC-derived CD19/BCMA CAR-NK therapy in a patient with systemic sclerosis

Xiaobing Wang [1 16], Yi Zhang [1 16], Yi Jin [2 16], Lie Dai [3 16], Yanan Yue [4], Jiapan Hu [4], Xin Liu [1], Kun Pang [5], Songying Ye [1], Yue Chen [6], Wenjing Ye [7], Xiaofei Shi [8], Xin Ma [8], Lehang Guo [9], Yanfang Liu [10], Na Ta [10], Xiaofang Zhu [11], Li Lin [1], Jiazheng Wang [1], Ran Yan [1]... Huji Xu [1 14 15 17] ✉

ARTICLE · Volume 187, Issue 18, P4890-4904.E9, September 05, 2024

Open Archive

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Allogeneic CD19-targeted CAR-T therapy in patients with severe myositis and systemic sclerosis

Xiaobing Wang [1,2,22] · Xin Wu [1,2,22] · Binghe Tan [3,4,22] · Liang Zhu [5,22] · Yi Zhang [1] · Li Lin [1,2] · Yi Xiao [6] · An Sun [6] · Xinyi Wan [6] · Shiyuan Liu [6] · Yanfang Liu [2,7] · Na Ta [7] · Hang Zhang [8] · Jialin Song [8] · Ting Li [1] · Ling Zhou [1] · Jian Yin [1] · Lingying Ye [1] · Hongjuan Lu [1] · Jinwei Hong [9] · Hui Cheng [9] · Ping Wang [9] · Weiqing Li [10] · Jianfeng Chen [3] · Jin Zhang [11] · Jing Luo [12] · Miaozhen Huang [12] · Lehang Guo [13] · Xiaoming Pan [14] · Yi Jin [15] · Wenjing Ye [16] · Lie Dai [17] · Jian Zhu [18] · Lingyun Sun [19] · Biao Zheng [4] · Dali Li [3,4] · Yanran He [20] · Mingyao Liu [3,4] ✉ · Huaxiang Wu [5] ✉ · Bing Du [3,4] ✉ · Huji Xu [1,2,12,21,23] ✉ Show less

- fit/competent immune cells
- faster availability
- better access

Modern bioengineering enables third-party cell therapies

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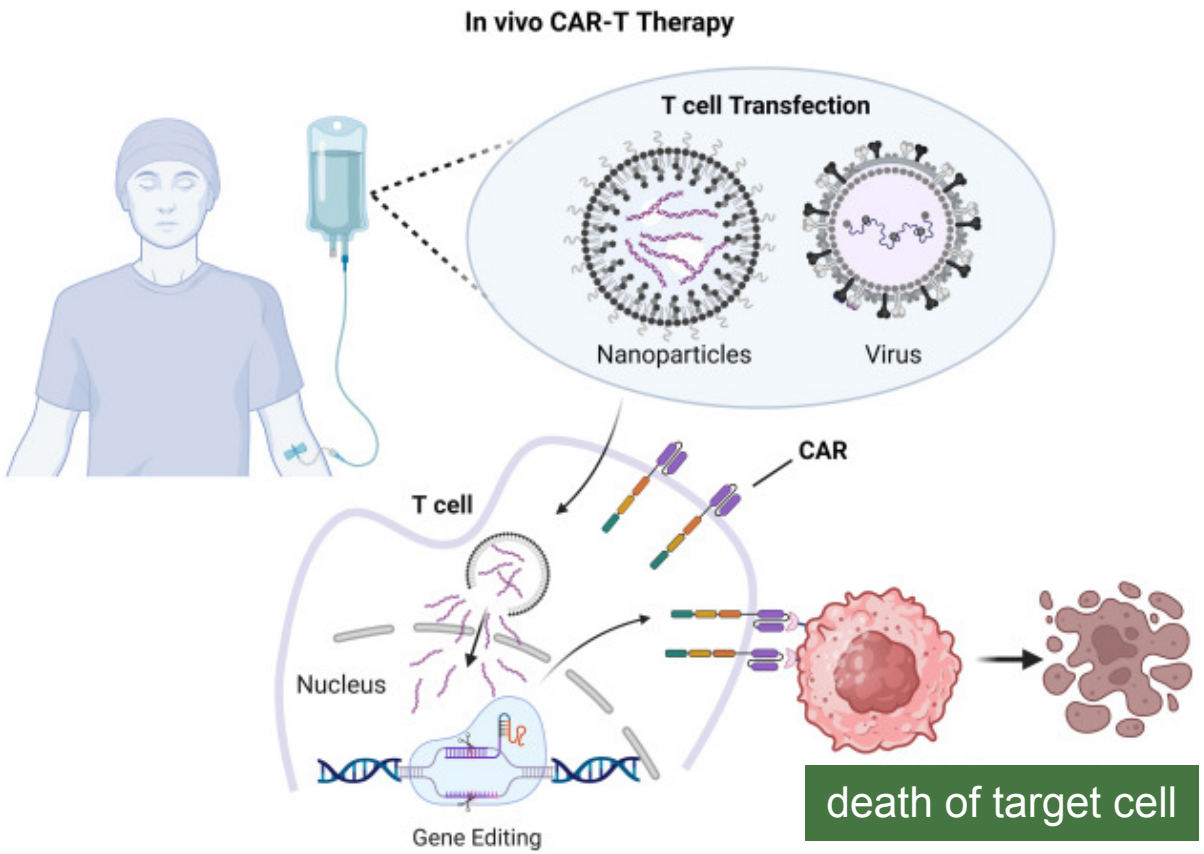
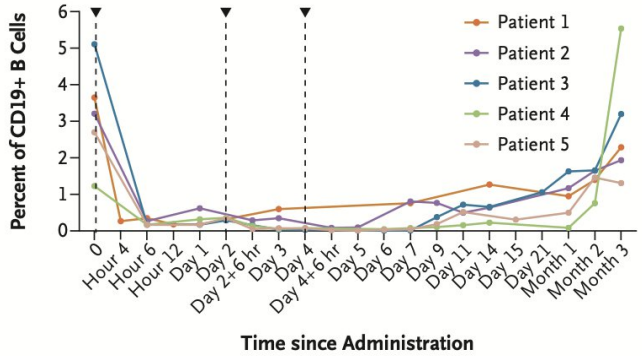
Ref: Yan C et al., Cell Research 2025, Wang X et al., Cell 2025, Mougiakakos D et al., STTT 2024, Wang X et al., Cell 2024

The next big „in vivo“ step



death of target cell

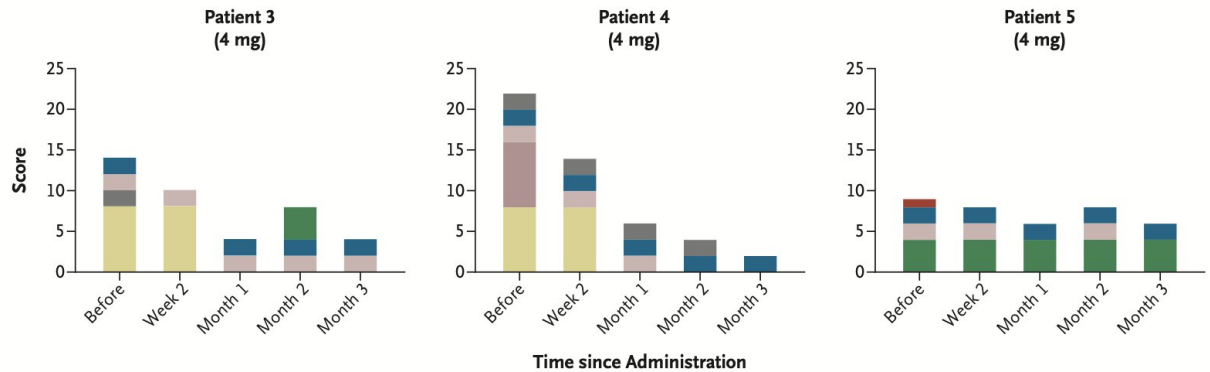
Patients with SLE treated with in vivo anti-CD19 CAR T cells



no chemo-therapy

faster availability

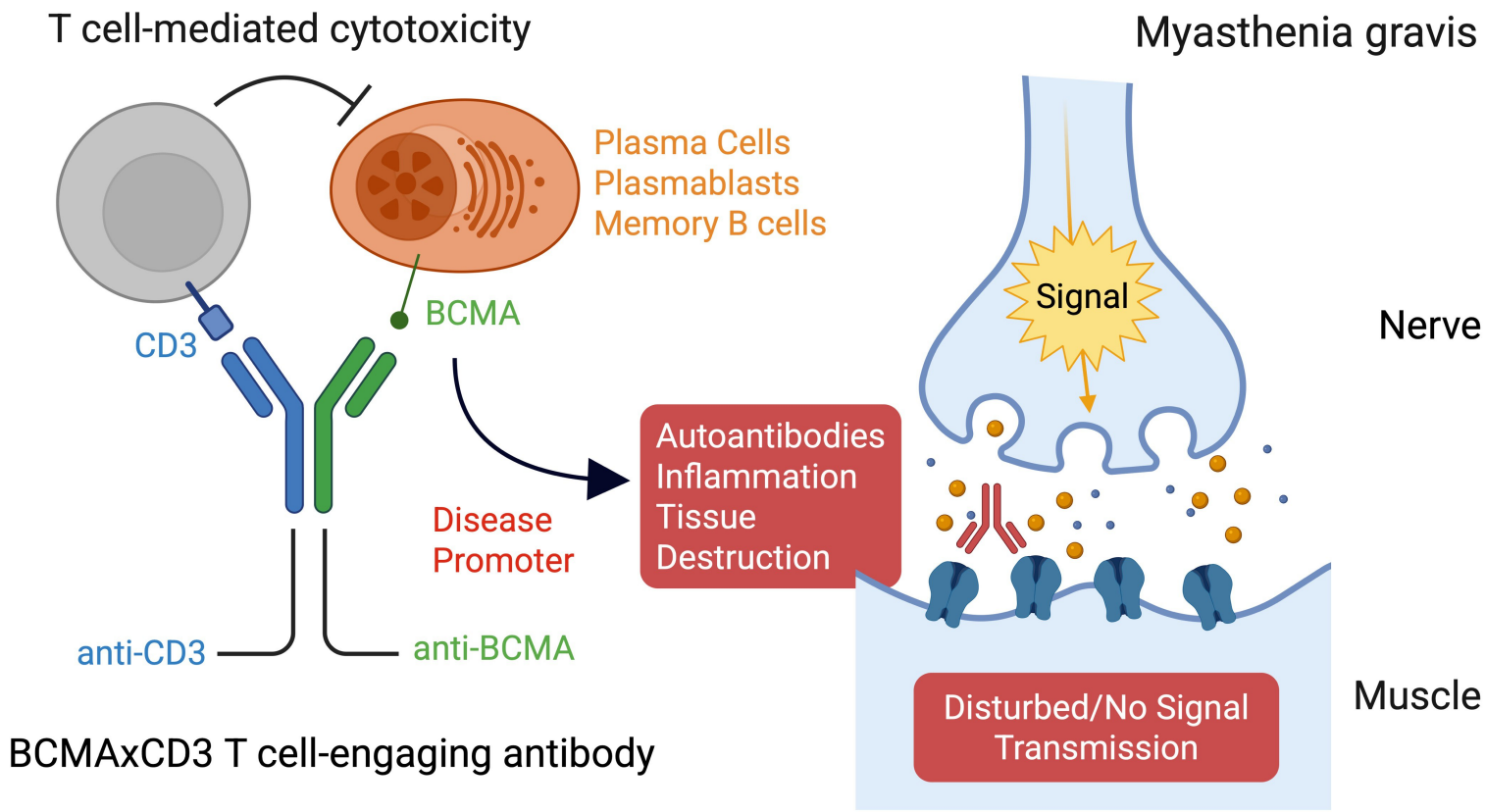
better access

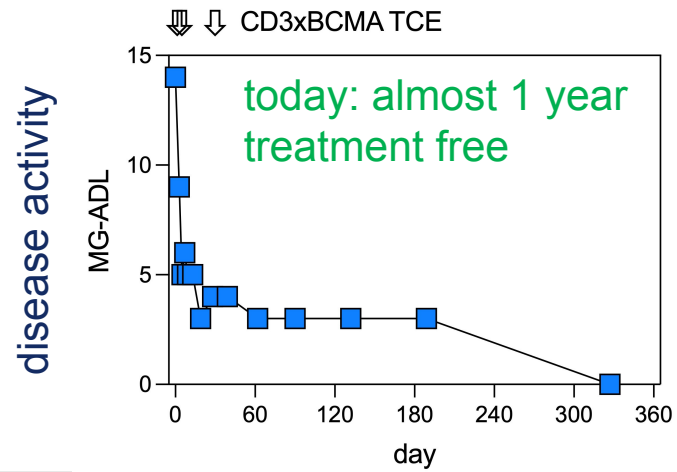


feasible, no dose limiting toxicity

Ref: Wang Q et al., NEJM 2025

Redirecting polyclonal T cells against specific antigens without genetic engineering





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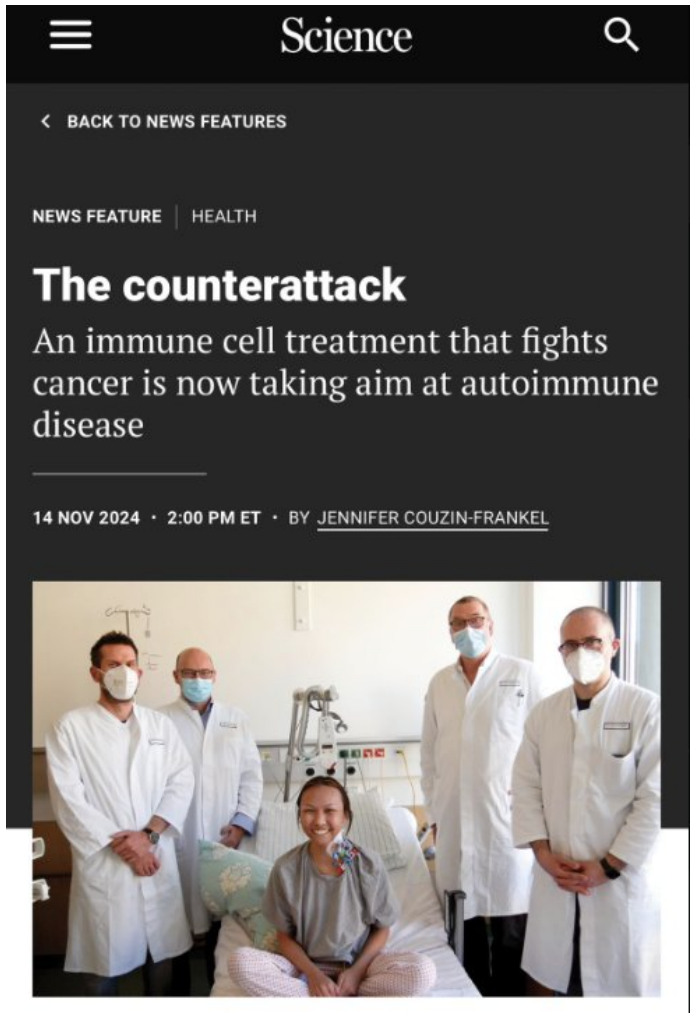
Ref: Schreiber S et al., Molecular Therapy 2025,
Ruck T et al., Molecular Therapy 2025

Conclusion and Outlook



- CAR T cell therapy is well established in hemato-oncology
- data regarding its use in autoimmune diseases shows:

  feasibility and **good tolerability** ✓

  B cell **reconstitution** without relapse ✓

  temporary but **deep depletion** of B cells could induce an **immunological restart** ✓
- results of first registration-enabling trials expected in 2026-2027
- most extensive experience to date among T cell-based therapies for autoimmunity
- **dual-track strategy**: use of established CAR T cell concepts and development of innovative next-gen platforms in parallel

Ref: Couzin-Frankel J. Science 2024

SAVE THE DATE!

Immune RESET 2026

17–18 September 2026

University Hospital Magdeburg, Germany

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Thank You

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