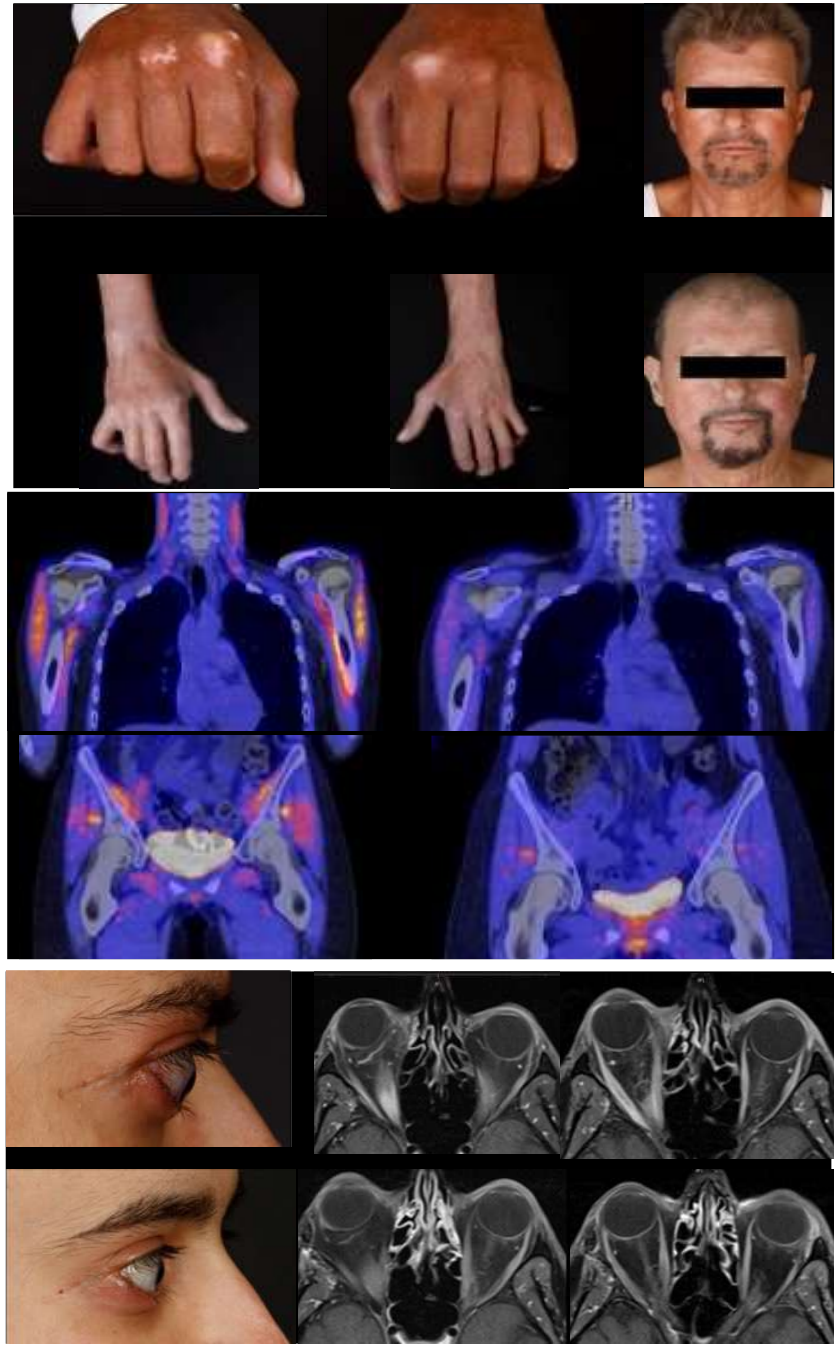


Vancouver 2026

The Future of Rheumatology

Georg Schett

Department of Medicine 3,
Friedrich-Alexander University
Erlangen-Nürnberg

Deutsches Zentrum
Immuntherapie

DZI Deutsches Zentrum Immuntherapie

FAU Friedrich-Alexander-Universität Erlangen-Nürnberg

Rheumatology in the Digital Revolution

Katsushika Hokusai
The great wave of Kanagawa 1830

Digital applications in diagnosis and therapy

mHealth
Mobile health applications

DTx
Digital Therapeutics (DTx)

DIGA
Digitale Gesundheitsapplikationen
(Digital Health Applications)

Europe mhealth apps market 2018-2030 (US$M)

Use of mHealth in chronic diseases

Depression

Psychoeducation, followed by goal setting and gamification strategies. Significant effect in reducing depressive symptoms. Hybrid interventions were found to be the most effective.

Duarte-Díaz A, et al. JMIR Ment Health. 2023 27;10:e46877.

Diabetes

mHealth apps improved the glycemic control by significantly reducing HbA_{1c} values in patients with T1DM and T2DM

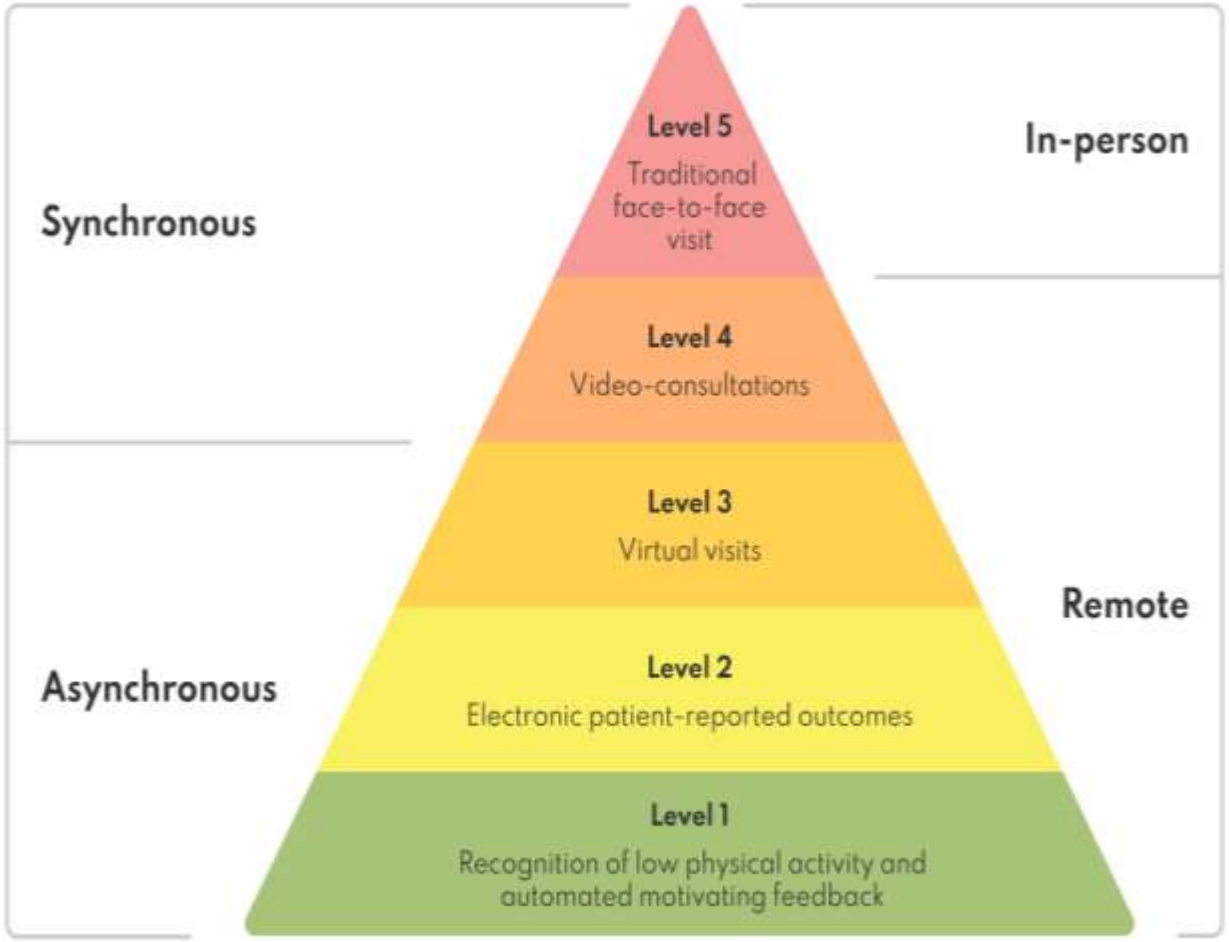
Eberle C, et al.. JMIR Mhealth Uhealth. 2021 15;9(2):e23477.

Asthma

Quality of life significantly improved, number of doctors visits and admission and hospitalization-relevant outcomes significantly declined

Farzandipour M, et al. Appl Clin Inform. 2017;8(4):1068-1081.

Levels of patient monitoring and escalation of care



The higher the level the more *r*essource intensive the approach becomes.

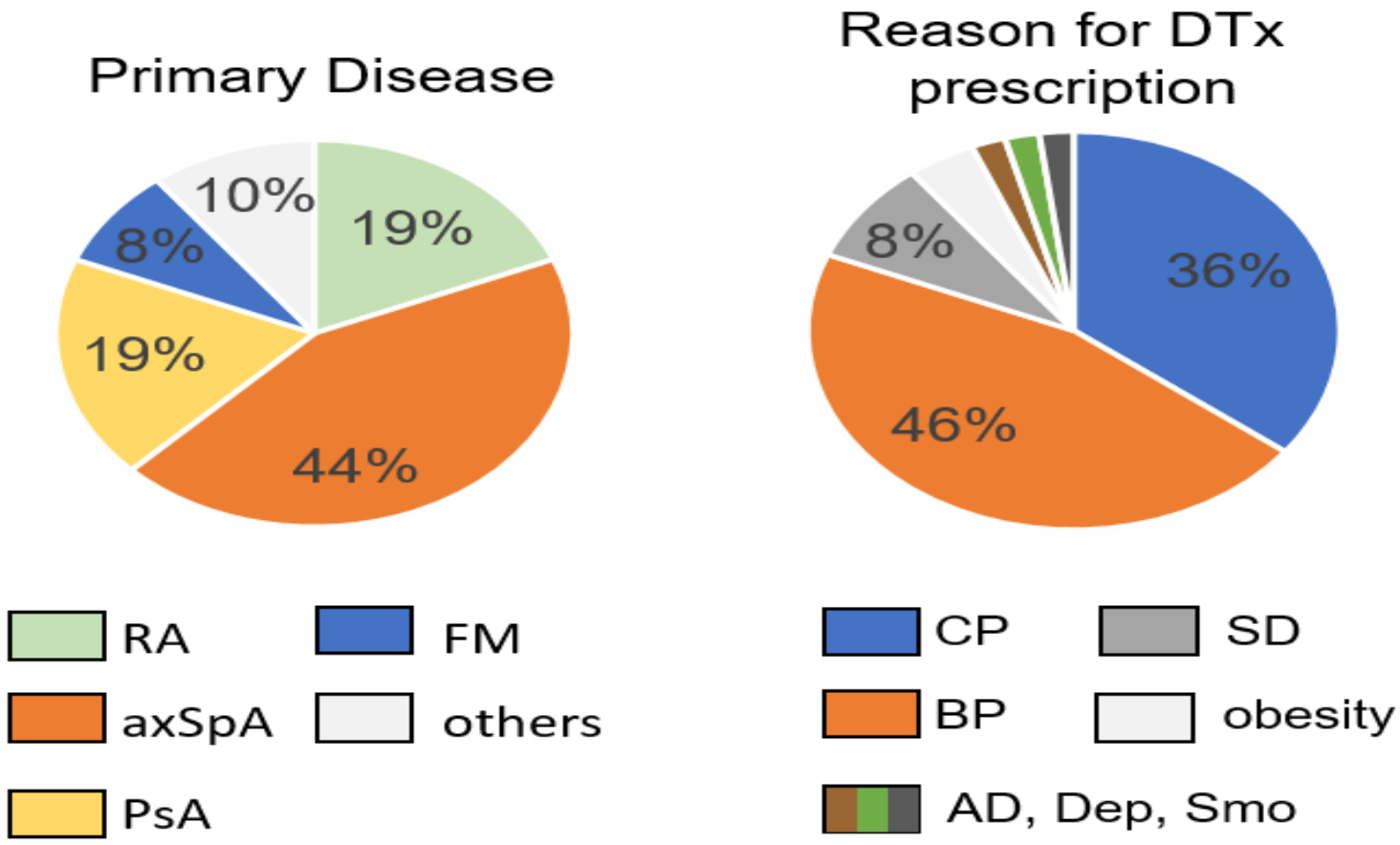
DIGAs are extemely scalable, not time-consuming and inexpensive and can therefore support to reach a broader population despite limited ressources

Aims

- Reduced Costs
- Improved Population Health
- Improved Access to Care
- Enhanced Experience
- Evidence-Based Care

Knitza J et al. Nature Rev Rheumatol. 2024

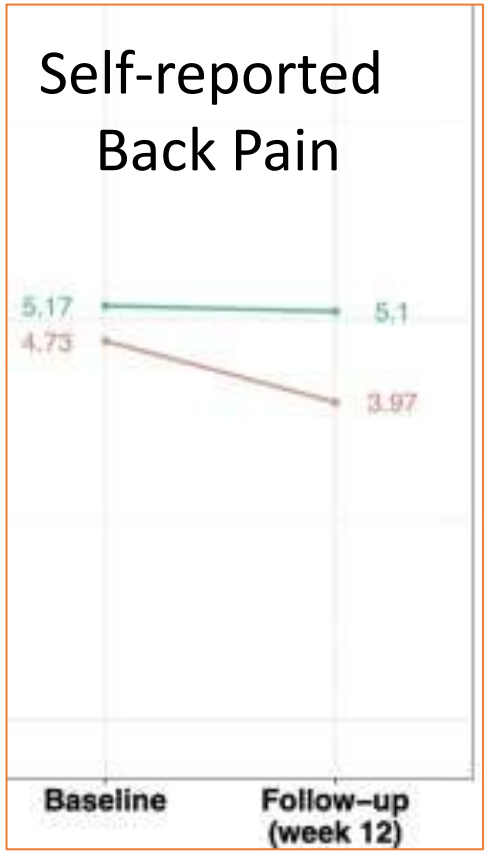
DIGA Prescriptions in Rheumatic Diseases



CP, chronic pain; BP, back pain; AD; anxiety disorder; Dep; depression; Smo, smoking; SD, sleep disorder

Labinsky H, et al Rheumatol Int. 2023;43:713-719.

Impact of DIGA on spinal mobility, physical function, quality of life and pain perception in SpA patients

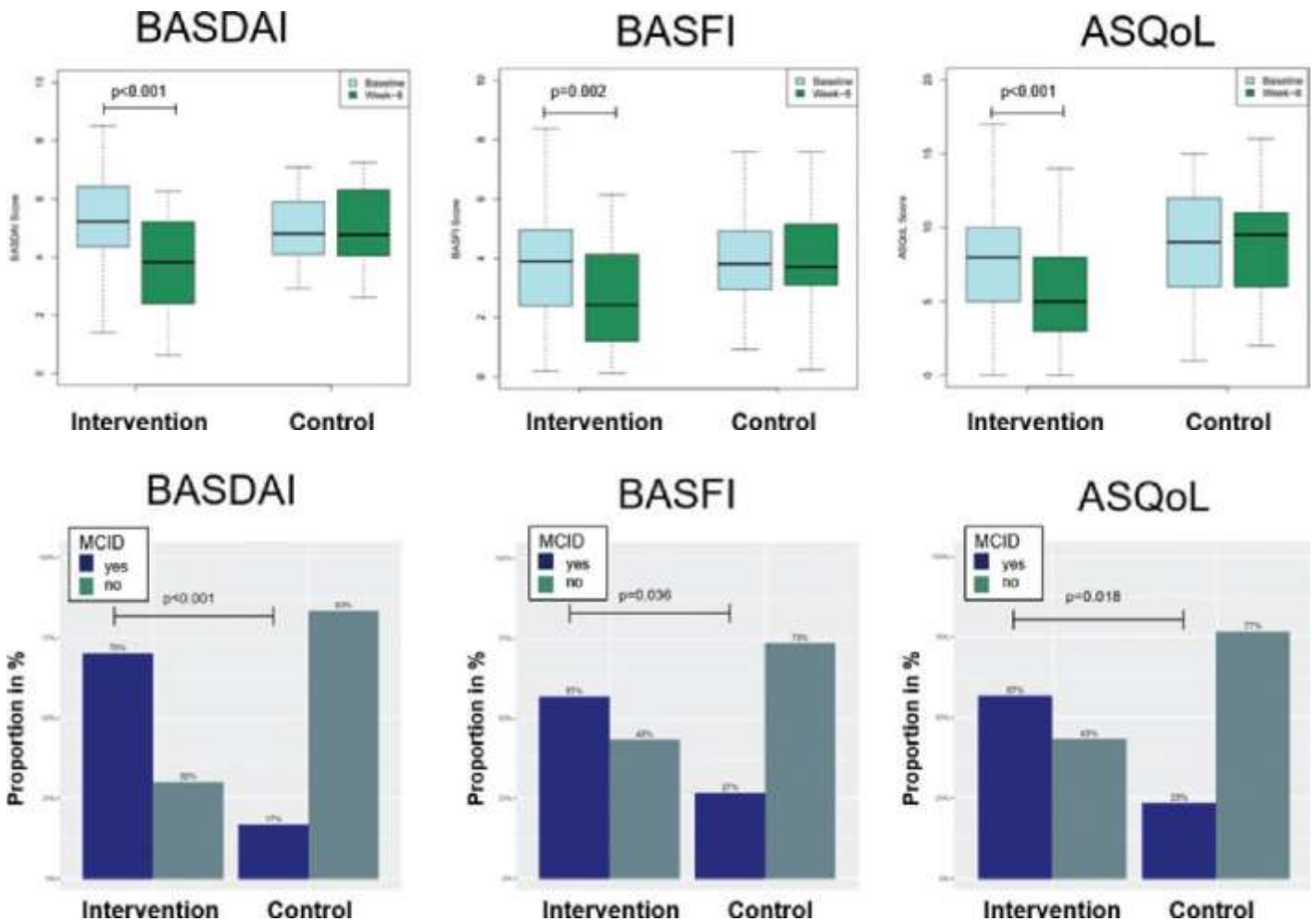


Randomized controlled trial between DIGA and physiotherapy testing the **efficacy of DIGAs** in the treatment of lower back pain in SpA. Compared with the current gold standard, physiotherapy, **DIGA use results in superior outcomes**.

BASMI	DIGA	PT
BL	1.1	1.5
FU	1.0	1.8
	p=0.05	P=0.01

Blaskowitz PPVA, et al. Arthritis Res Ther. 2024 Dec 3;26(1):208.

Impact of DIGA on pain and quality of life in SpA patients



At week 8, participants in the **DIGA** intervention group presented **significant improvements in BASDAI** while the control group showed no improvement.

Furthermore, significantly **more patients** receiving DIGA reached a minimal clinically important difference (**MCID) improvement** in BASDAI, BASFI and ASQoL than patients of the control group

Strunz PP et al. EULAR 2025; ABS0430

Introduction of DIGAs in Health Care

- In Germany, DIGAs can be **prescribed by physicians for a three-month use** period and are **fully reimbursed** by the insurance companies since October 2020.
- To obtain approval, **safety, functionality, quality, data security and a fundamental benefit must be demonstrated** for the DIGA in a clinical study.

- Patients receive a **written prescription for a DiGA** and have to send it to their insurance company. Patients then receive an activation code to start using the DiGA.

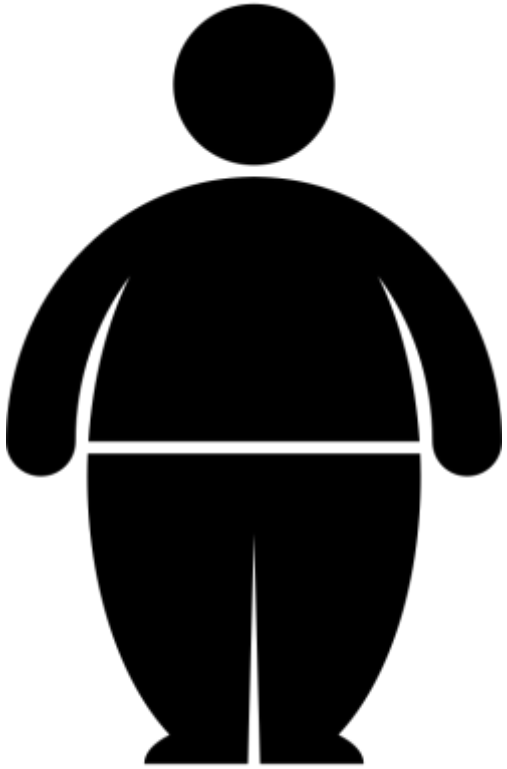
A new view of the story

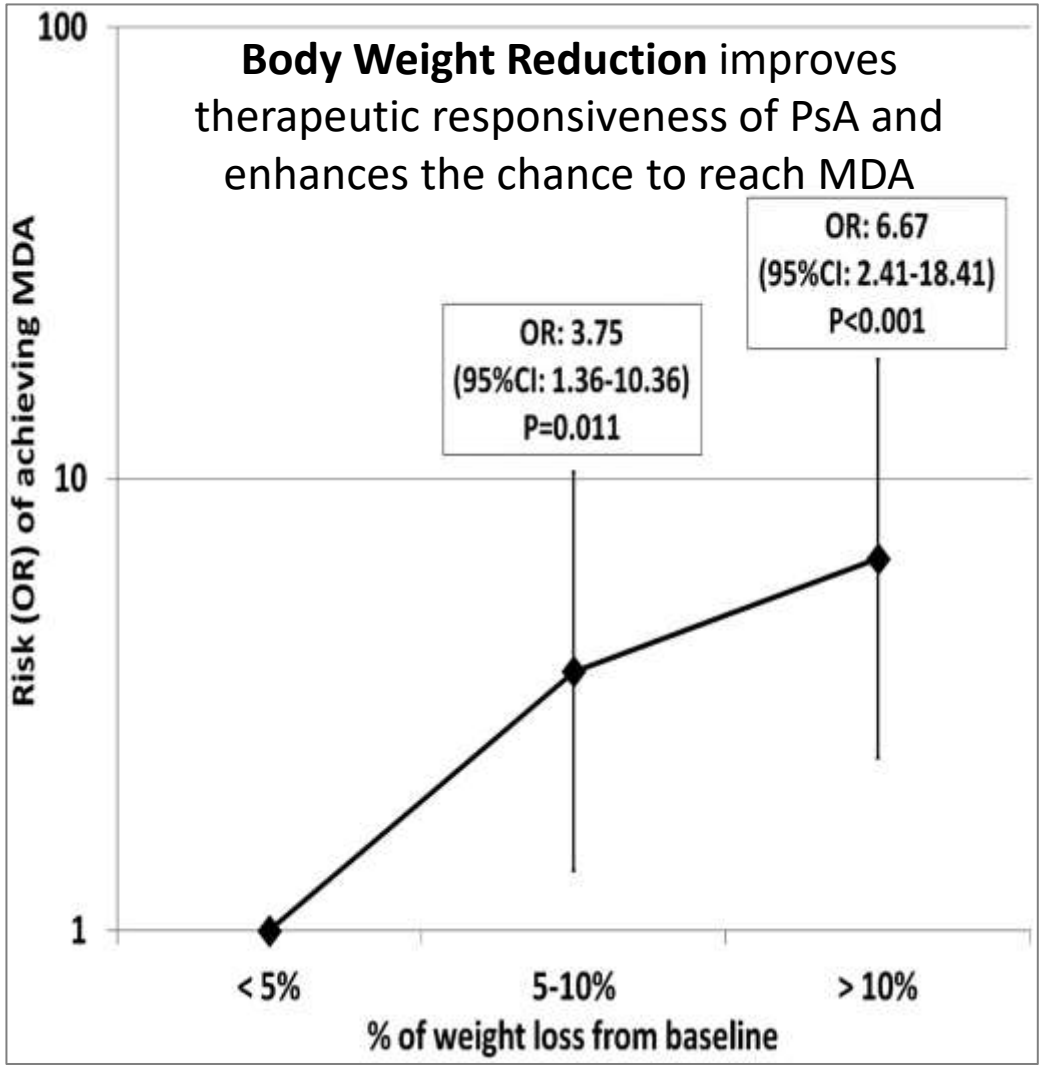
M.C. (Maurits Cornelis) Escher
Sky and Water II 1938

Metabolic impact on psoriatic disease

The **relative risk** for development of psoriasis is **2.7** in subjects with a body mass
index (BMI) of **over 35**.

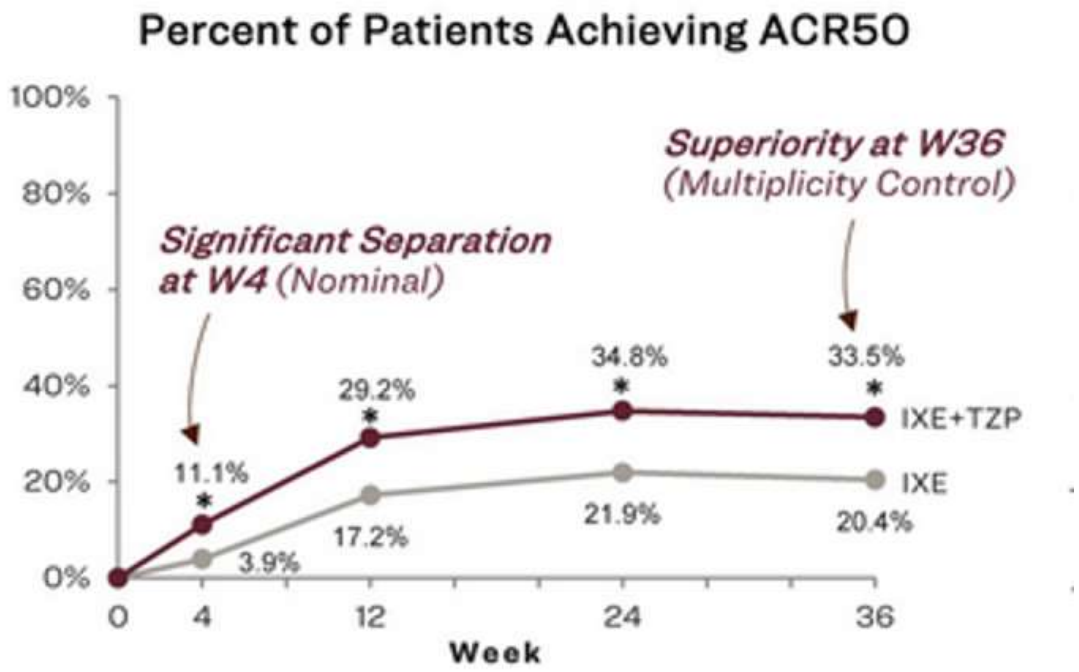
A **1 kg/m2 increase in BMI** isassociated with **4% higher odds of psoriasis.**

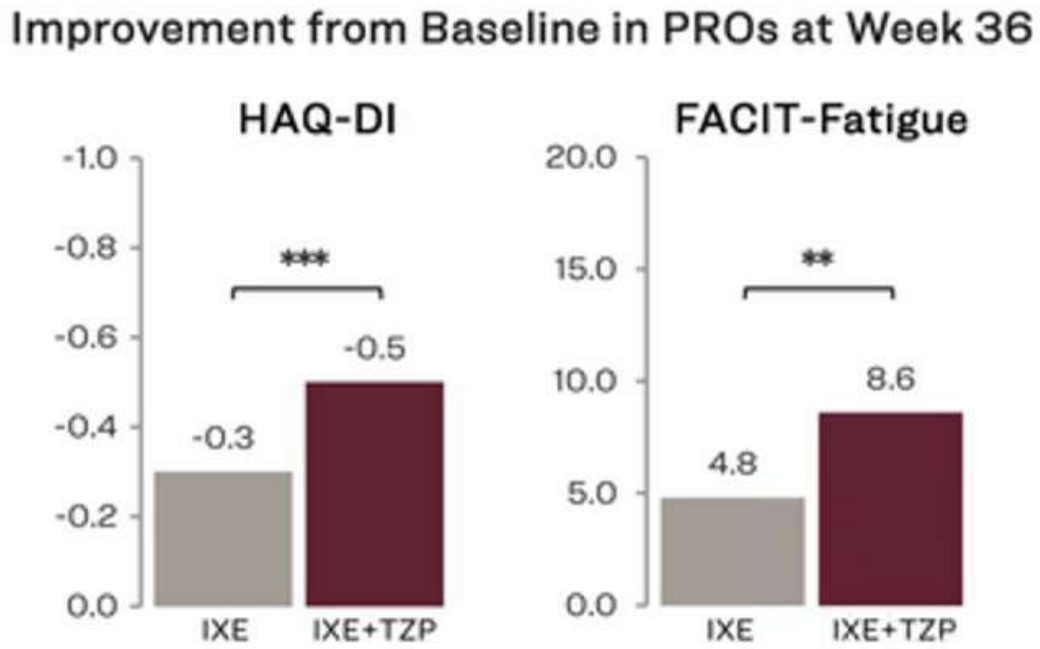




Di Minno MND, Peluso R, Iervolino S*, et al*. *ARD* 2014;**73:**1157-1162

GLP-1 Agonism improves outcomes in PsA





TOGETHER-PsA: randomized trial in patients with active PsA and overweight (BMI ≥27 to <30) with at least one weight-related comorbidity or obesity (BMI ≥30) comparing ixekizumab and ixekizumab plus tirzepatide. The primary end point was simultaneous achievement of 50% improvement in American College of Rheumatology response criteria (ACR50) and ≥10% weight reduction at 36 weeks. 271 participants were randomized (IXE + TZP, n = 138; IXE, n = 133).

Merola JF, et al.Arthritis Rheumatol. 2026 Mar 28.

GLP-1 Agonism improves outcomes in PsA

Retrospective analysis of patients with PsA who initiated GLP-1RAs. PsA disease activity data and cardiometabolic parameters from clinical visits within 1 year before and after GLP-1RA initiation along with demographics and comorbidities were collected.

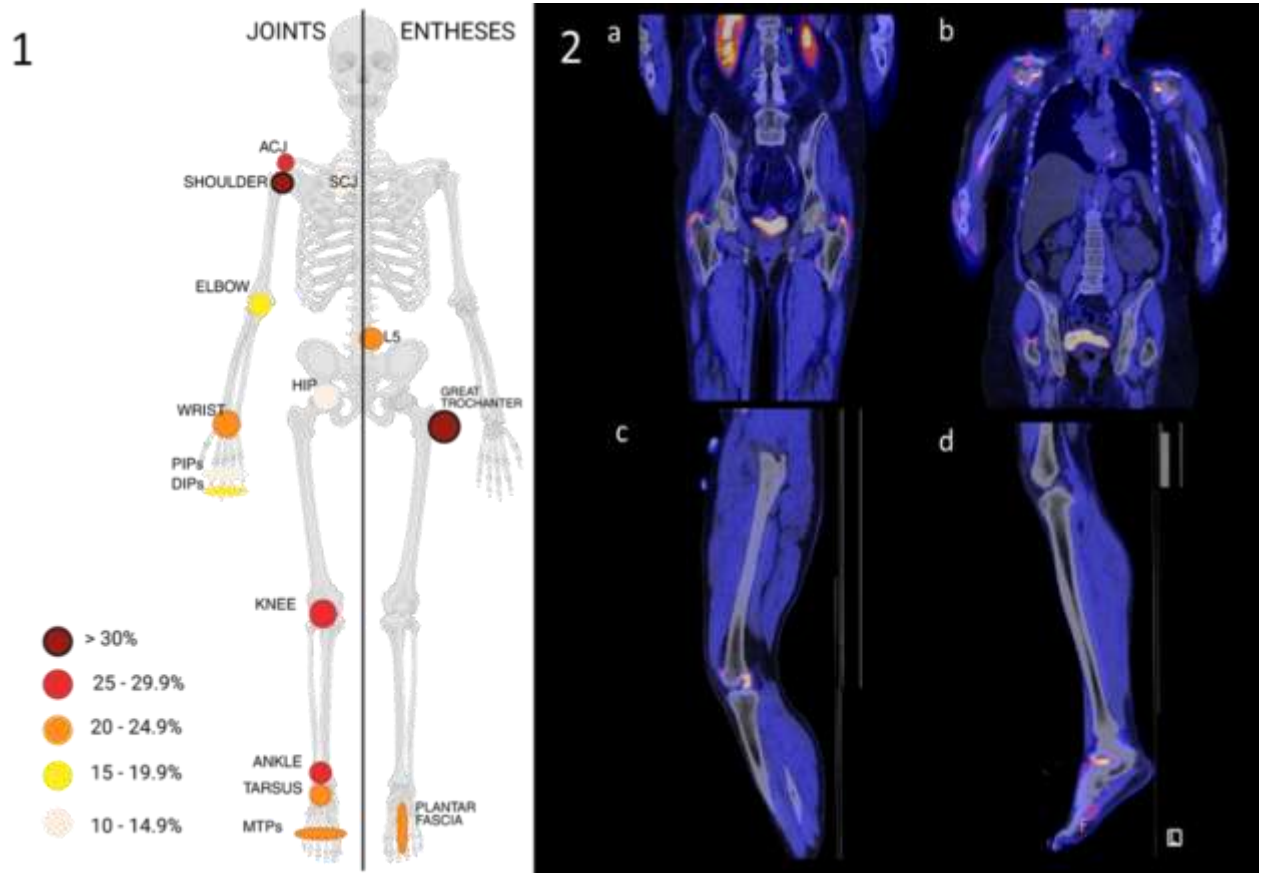
48 patients with a median BMI 34.9 were included.

Table 2: Longitudinal Changes in Cardio-Metabolic and PsA Outcomes in Patients Initiated on GLP-1

Outcome	Median Change (IQR)	P Value	N
Cardiometabolic			
Total cholesterol (mg/dL)	-8.9 (-17.4, 7.7)	0.10	28
Triglycerides (mg/dL)	-13.5 (-27.5, -5)	0.02	28
High density lipoprotein (mg/dL)	3 (-3.4, 6.5)	0.13	28
Low density lipoprotein (mg/dL)	1 (-16.9, 6.5)	0.49	28
Creatinine (mg/dL)	-0.02 (-0.08, 0.04)	0.27	41
Alanine aminotransferase (U/L)	-2.5 (-6, 1)	0.24	42
Systolic blood pressure (mmHg)	0 (-4, 5)	0.88	42
Diastolic blood pressure (mmHg)	1 (-9, 10)	0.68	42
Psoriatic arthritis activity			
DAPSA*	-3.52 (-8.62, 2.77)	0.11	21
CRP (mg/L)	-1.1 (-2, -0.2)	0.002	31
Tender Joint Count	0 (-1, 0)	0.29	45
Swollen Joint Count	0 (0, 0)	0.03	45
Pain Score^	-1.0 (-1.75, 0)	0.01	25
Patient Global Score	-0.5 (-1.67, 0)	0.08	23
HAQ-DI	-0.05 (-0.25, 0.08)	0.27	18
FACIT-Fatigue	+2.75 (-3, 7.5)	0.14	18
EuroQol-5D	+0.01 (0, 0.14)	0.14	18
Psoriasis body surface area (%)	+0.01 (0, 1)	0.56	45

Haberman RH, et al. Arthritis Rheumatol. 2026 Apr 6.

Tissue pathology in the musculoskeletal structures related to BMI in patients with psoriatic disease

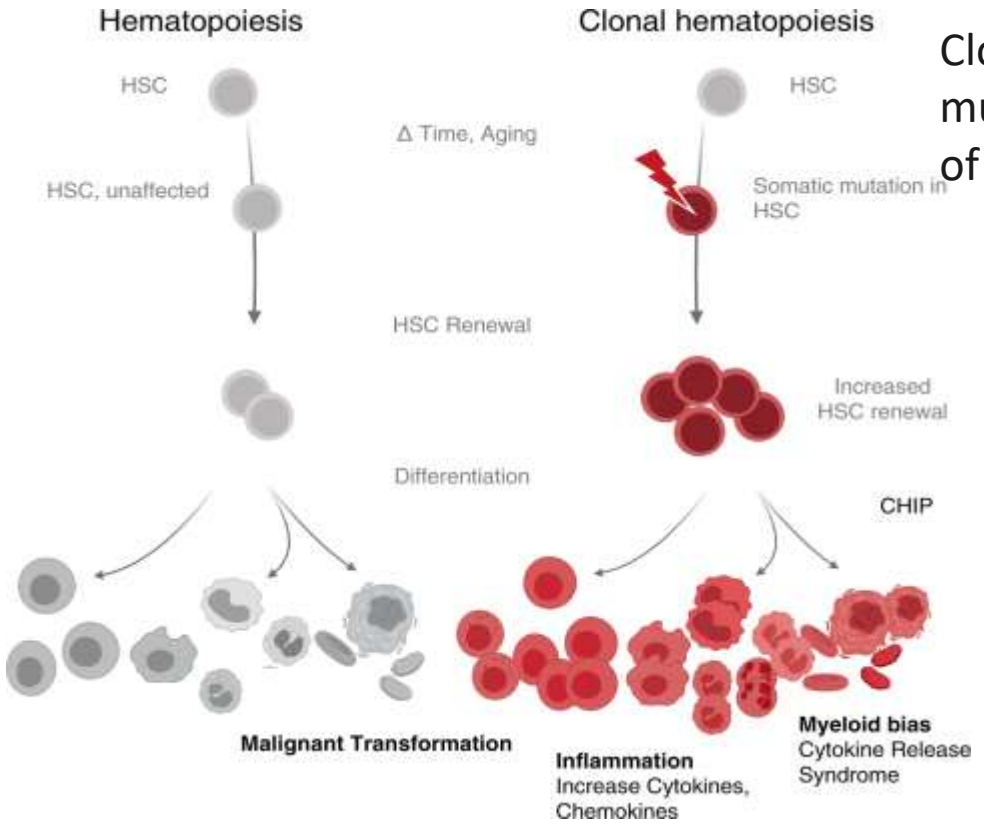


Stromal cell activation in the joints and entheses of patients with psoriasis as measured by fibroblast-specific tracer accumulation (FAP)

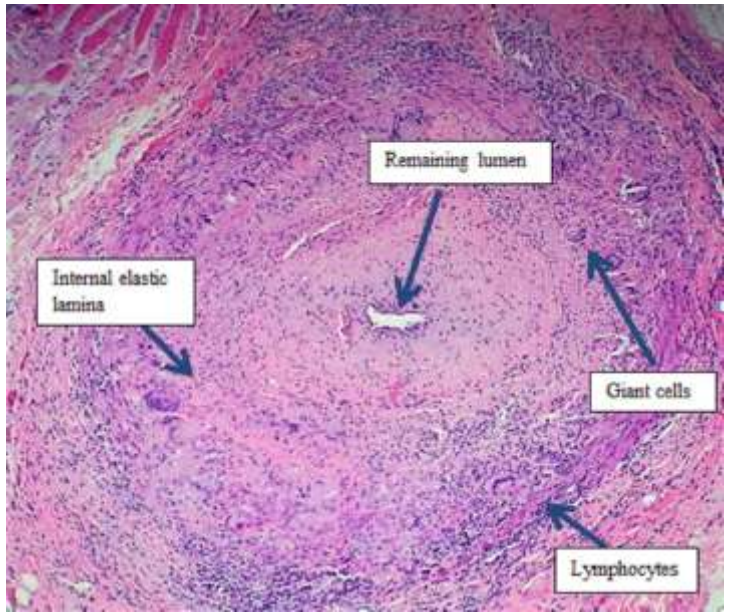
FAPI-positive psoriasis patients have significantly **higher BMI**. FAP uptake most frequent in large joints and **mechanically stressed sites** and was more likely in the presence of low-grade synovial hyperplasia and entheseal Power Doppler.

Corte G, et al. RMD Open. 2026;12:e006567.

Inflammaging as new explanation of elderly onset rheumatic disease

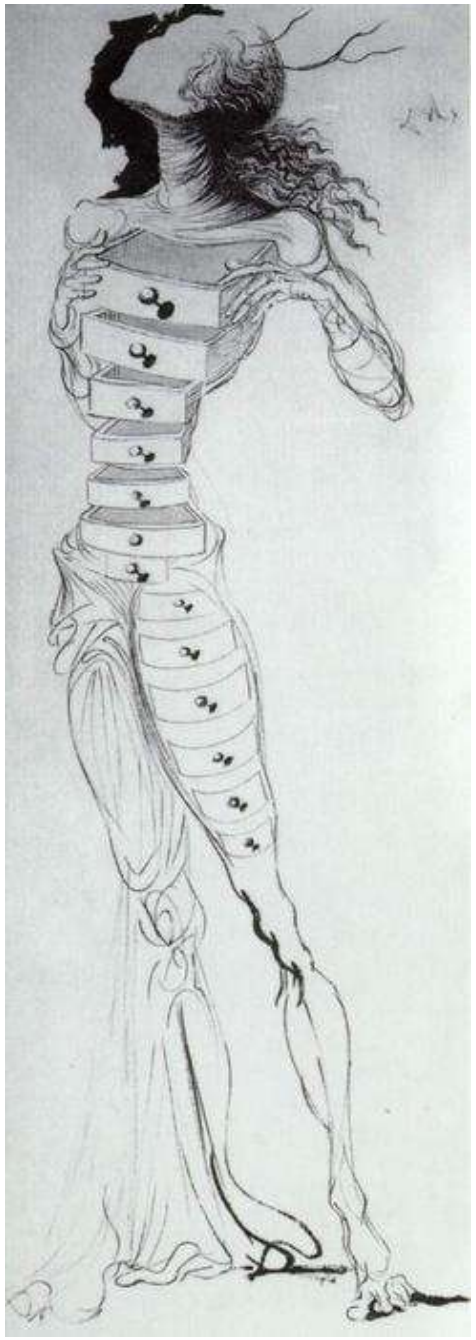


Clonal populations of blood cells with somatically acquired mutations occur in fewer than 5% of those before the age of 50 but in 20% of individuals over 70 (inflamaging)



Clonal hematopoiesis is a key driver of inflammation in aging that significantly increases the risk and severity of **Giant Cell Arteritis**

Robinette W, et al. : TET2 Mutations are Associated with Giant Cell Arteritis. Arthritis Rheumatol 2023



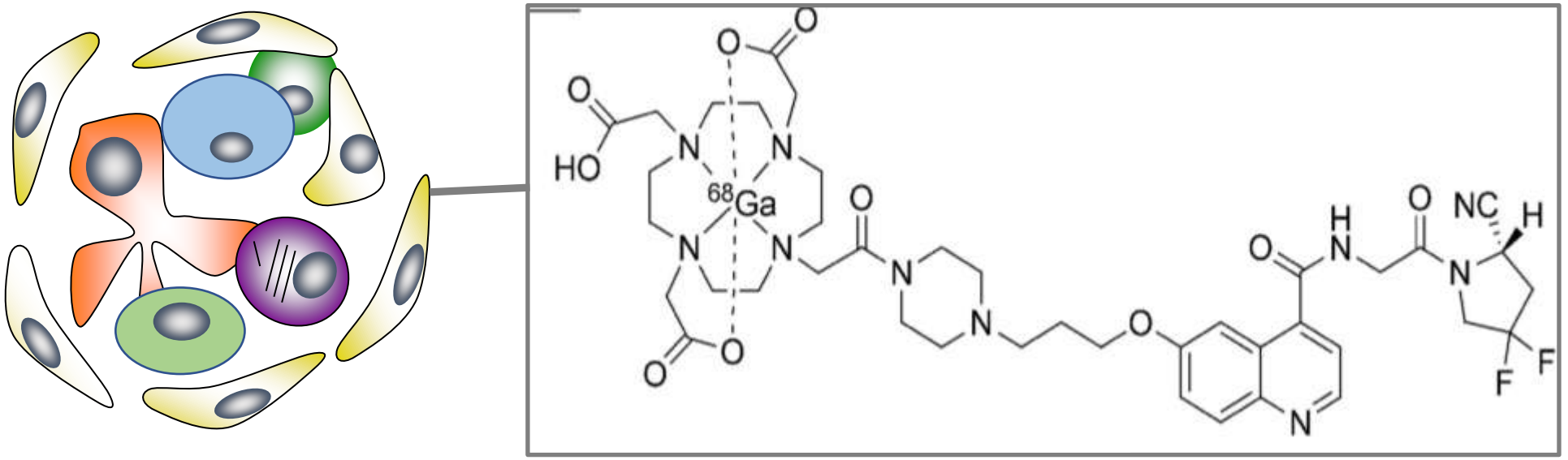
Looking Inside

Can we non-invasively measure molecular mechanisms in rheumatic diseases in humans in vivo?

Figure
with drawers

Salvador Dali 1934

Diving into “tectonic” tissue responses using PET tracers binding to FAP

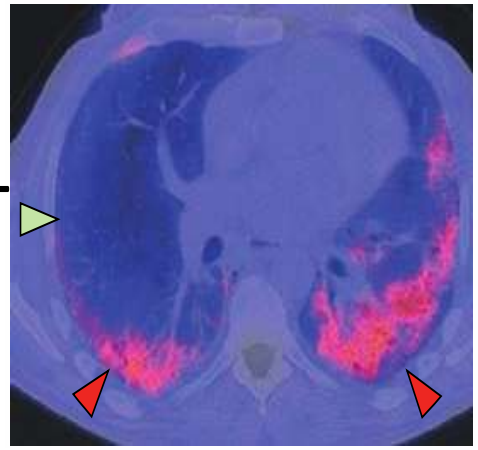


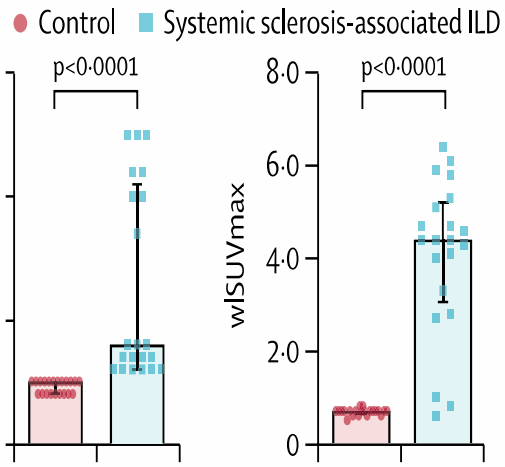
Gallium-labeled small molecule inhibitor of fibroblast activation protein (FAP) as theranostic marker[1,2]

1. Lindner T, et al. J Nucl Med. 2018;59(9):1415-1422; 2. Toms J, et al. J Nucl Med. 2020;61(12):1806-1813.

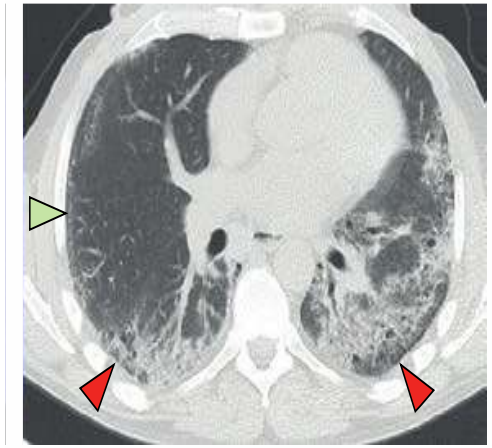
Depiction of the fibrotic process in SSc and association with disease activity

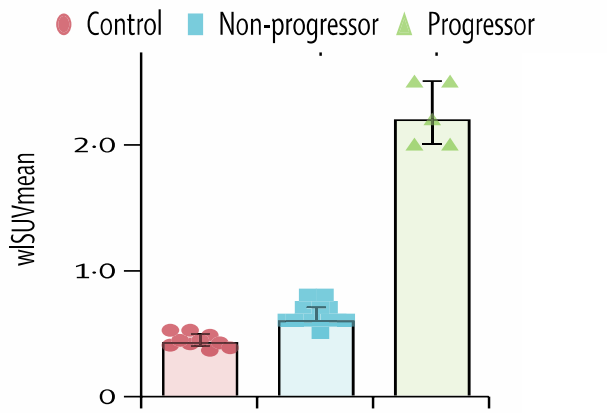
FAPI-PET





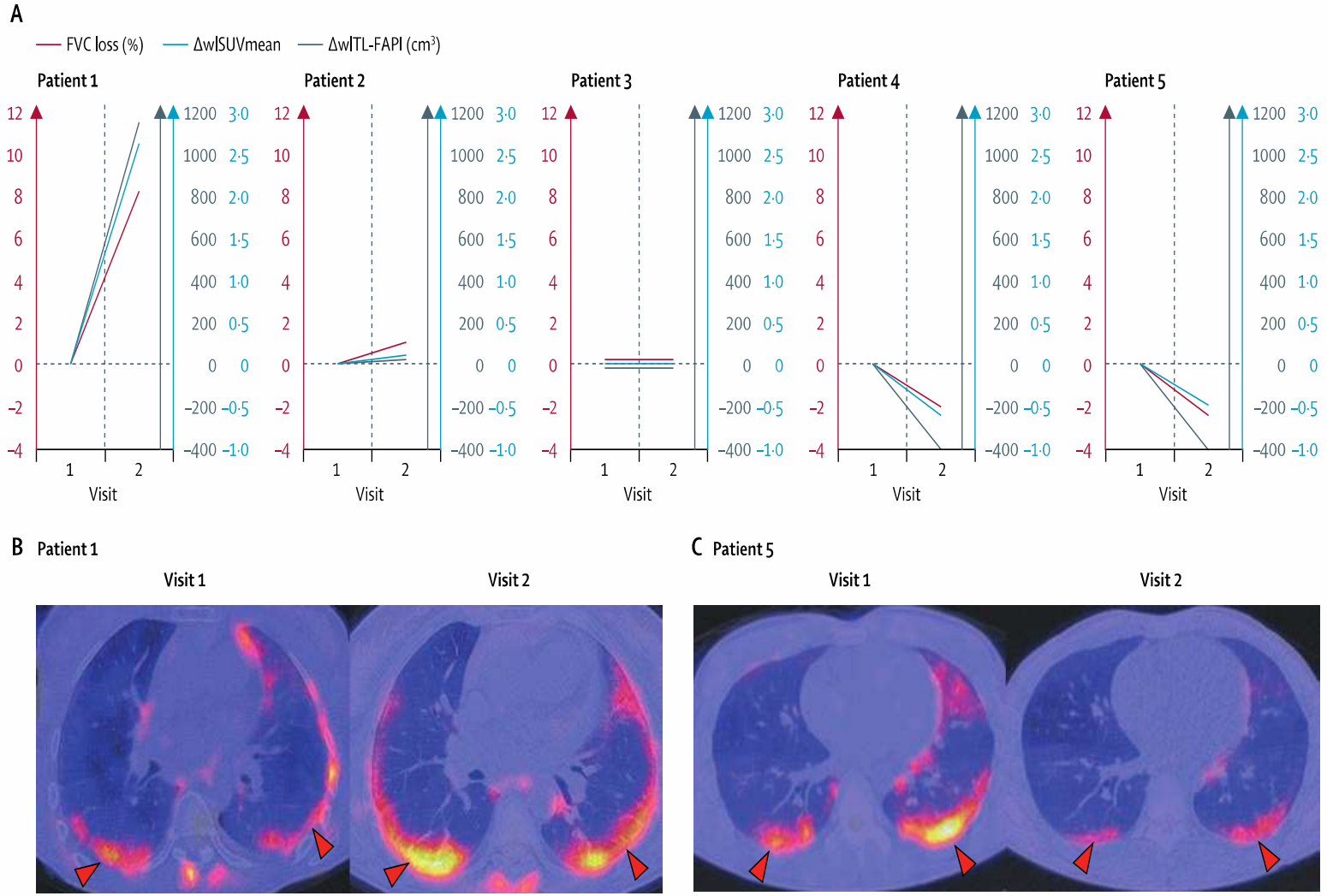
HR-CT





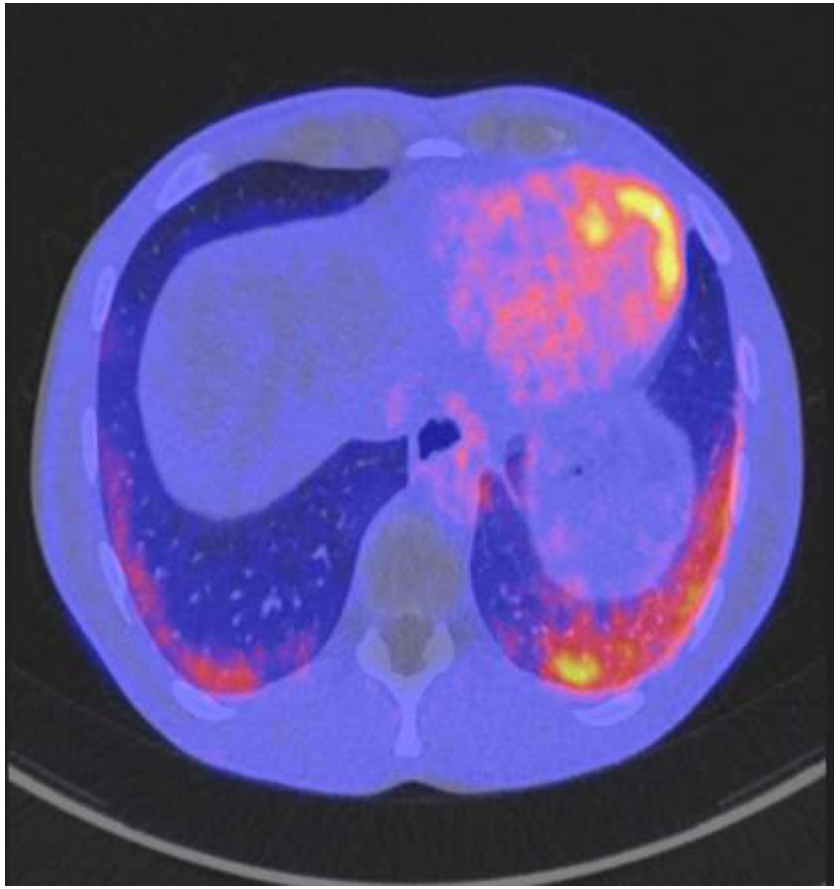
Bergmann C et al., Lancet Rheumatol 2021;3: March 1

Response to anti-fibrotic treatment with nintedanib

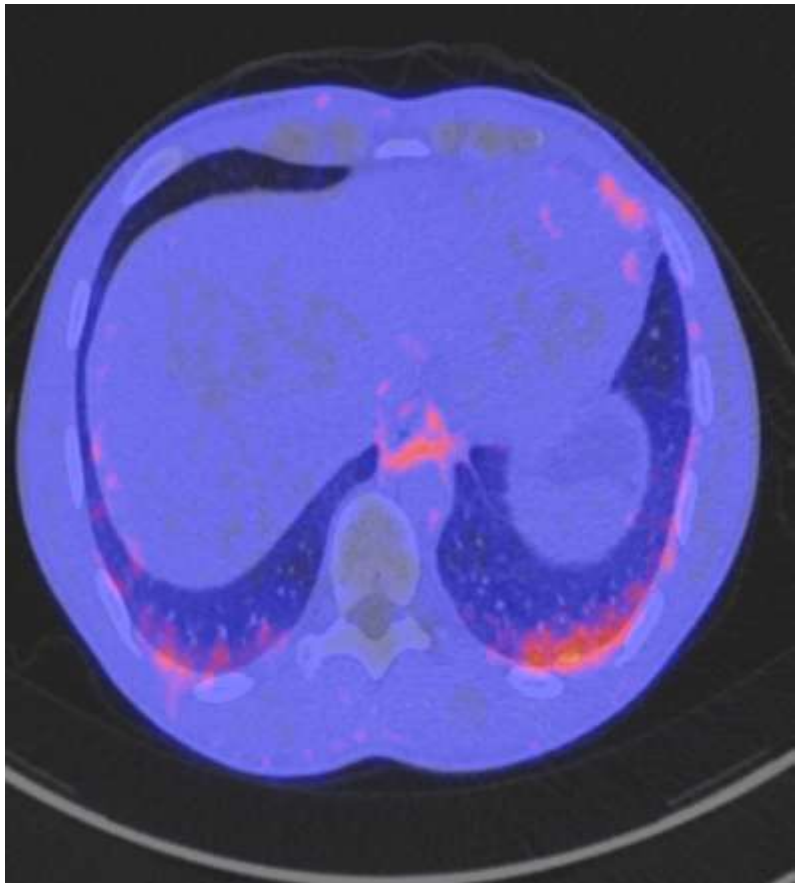


Bergmann C et al., Lancet Rheumatol 2021;3: March 1

Combined heart and lung involvement in SSc with regression of fibroblast activation after CD19-CAR T-cells



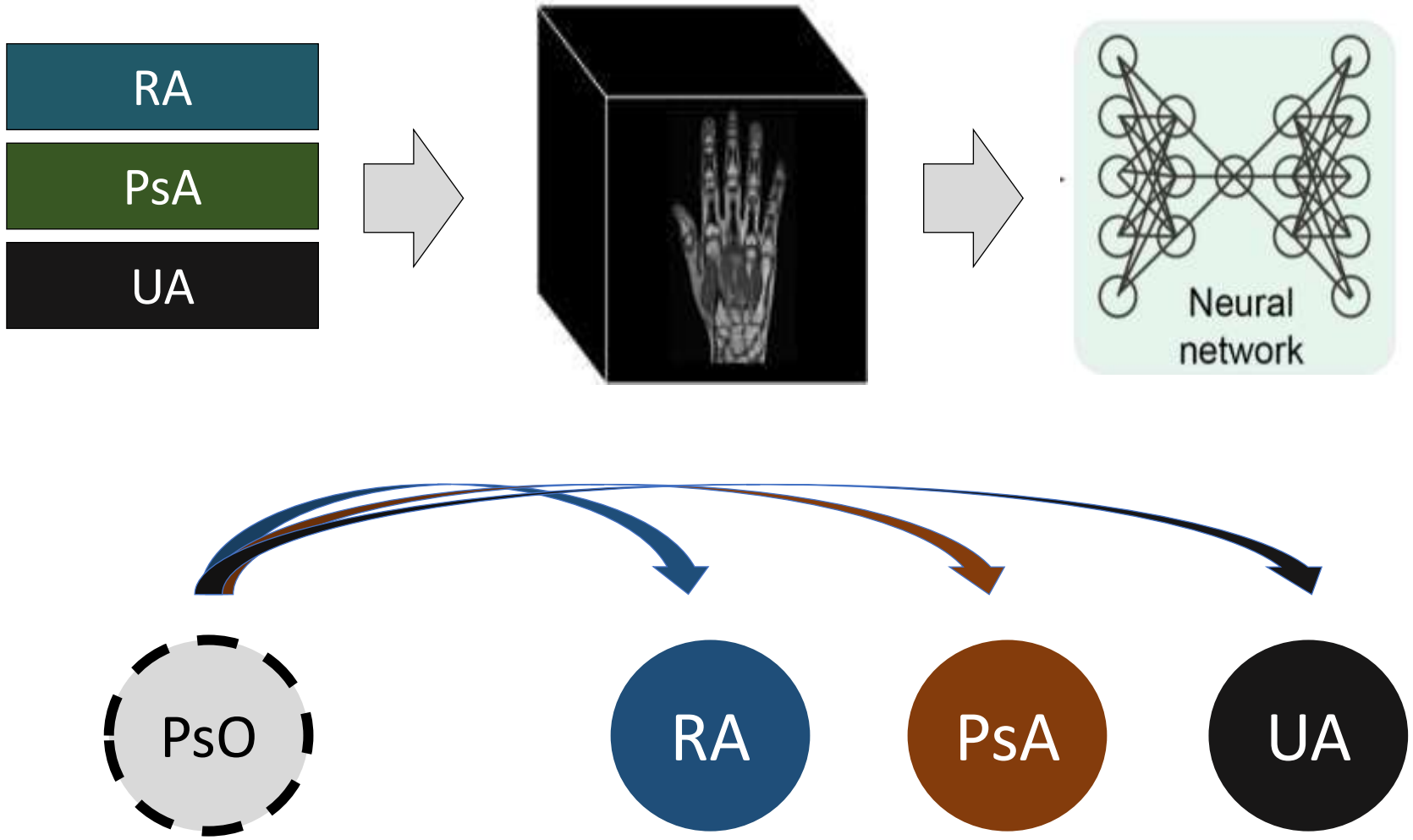
Baseline (before
CAR T cell therapy)



4 months after
CAR T cell therapy

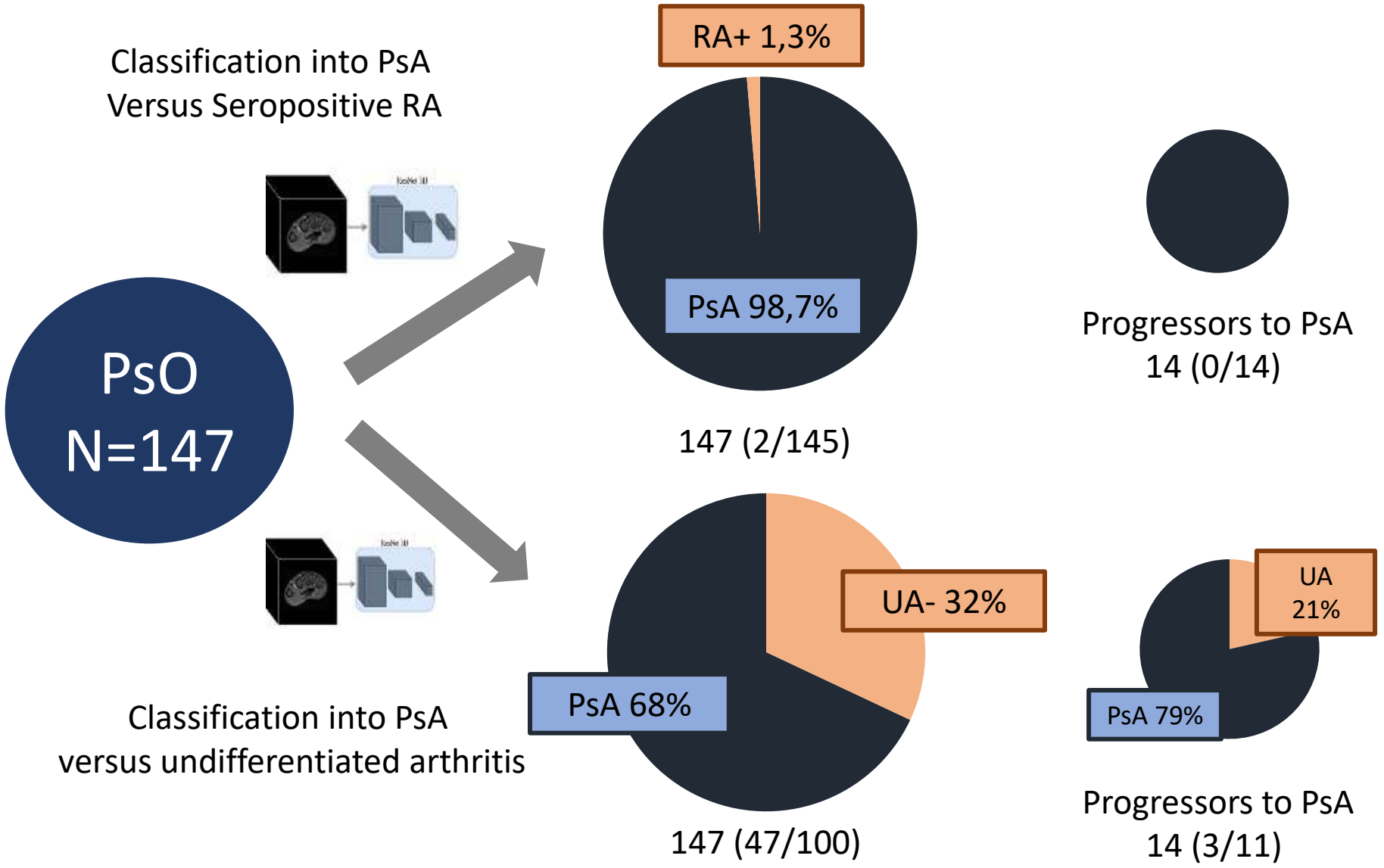
Bergmann C et al., Ann Rheum Dis 2023 in press and unpublished observations

AI- based classification of PsO patients with subclinical disease



Folle L et al. Rheumatology, 2022; 61: 4945–4951,

AI- based classification of PsO patients with subclinical disease



Folle L et al. Rheumatology, 2022; 61: 4945–4951,

New Perspectives

Can we cure autoimmune diseases?

No. 6
(Violet Green And Red)

Mark Rothko 1951

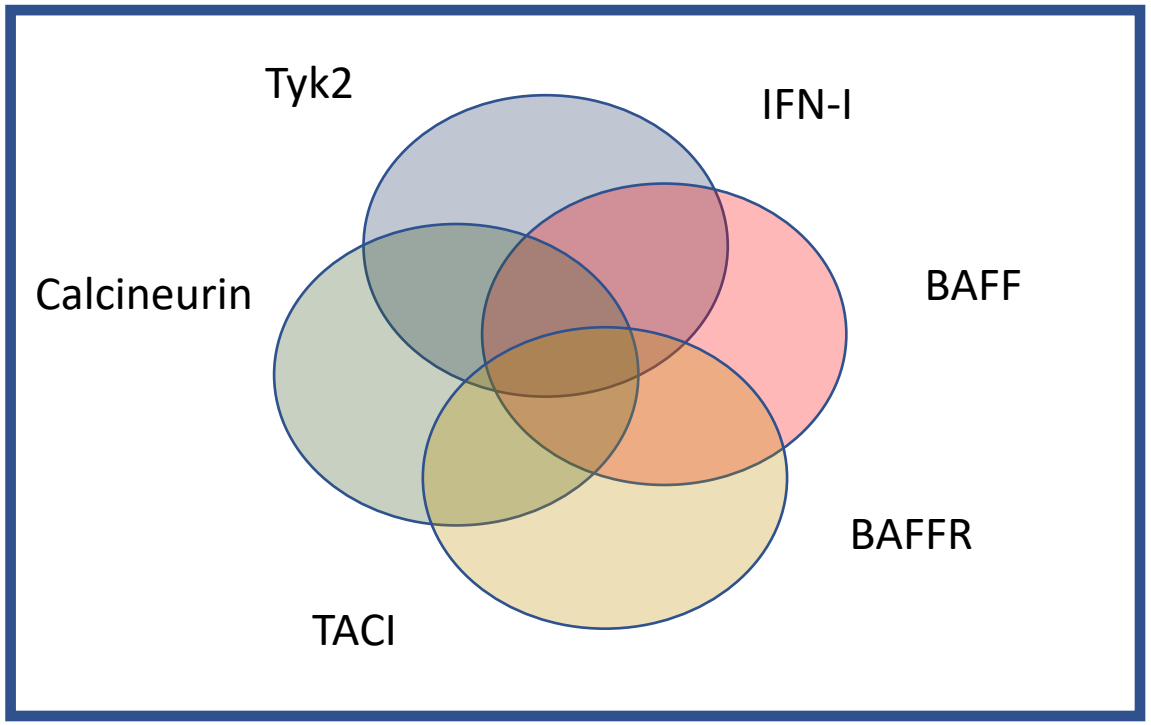
From Remission to Cure

	Remission	Cure
Disease State	Presence of Disease	Absence of Disease
Mechanism	Suppression of Symptoms	Elimination of Causing Factor
Subclinical Disease Signs	Detectable	Absent
Course	Relapse possible	No Relapse
Prognosis	Progression possible	No progression possible
Follow-Ups	Indicated	Not Indicated
Management	Continuation of Treatment	Stop of Treatment

Schett G et al. Nat Rev Rheumatol. 2021 Mar;17(3):135-144

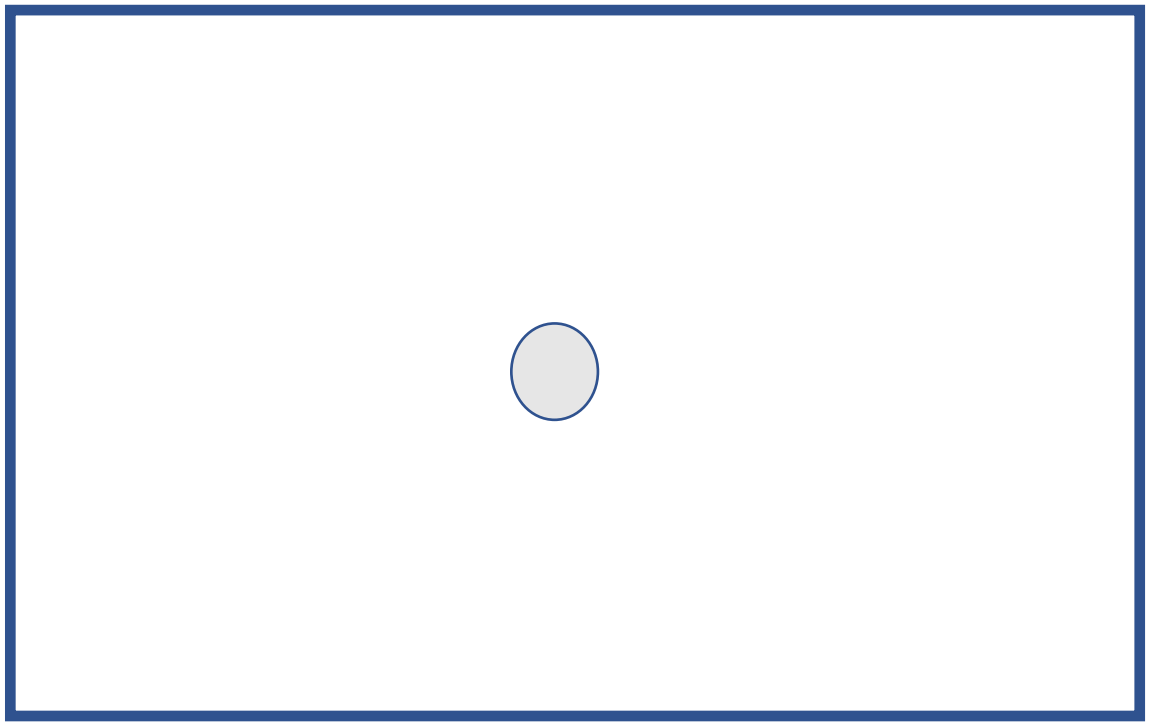
New concept of drug development in rheumatology

Immunosuppressive/-modulatory



Example SLE: Growing number of drugs that show a similar efficacy and safety profile with increasing competition but no transformational consequences

Resetting/Curative



Development of resetting and curative treatments requires different approaches; e.g. stopping drugs; severe and resistant populations first; platform trials

Rheuma-Pearl 3

Can we achive cure?

Emily Whitehead
>10 years cancer-free

Vu-Thi Thu Tao
>5 years lupus-free

Long-Term Absence of Disease

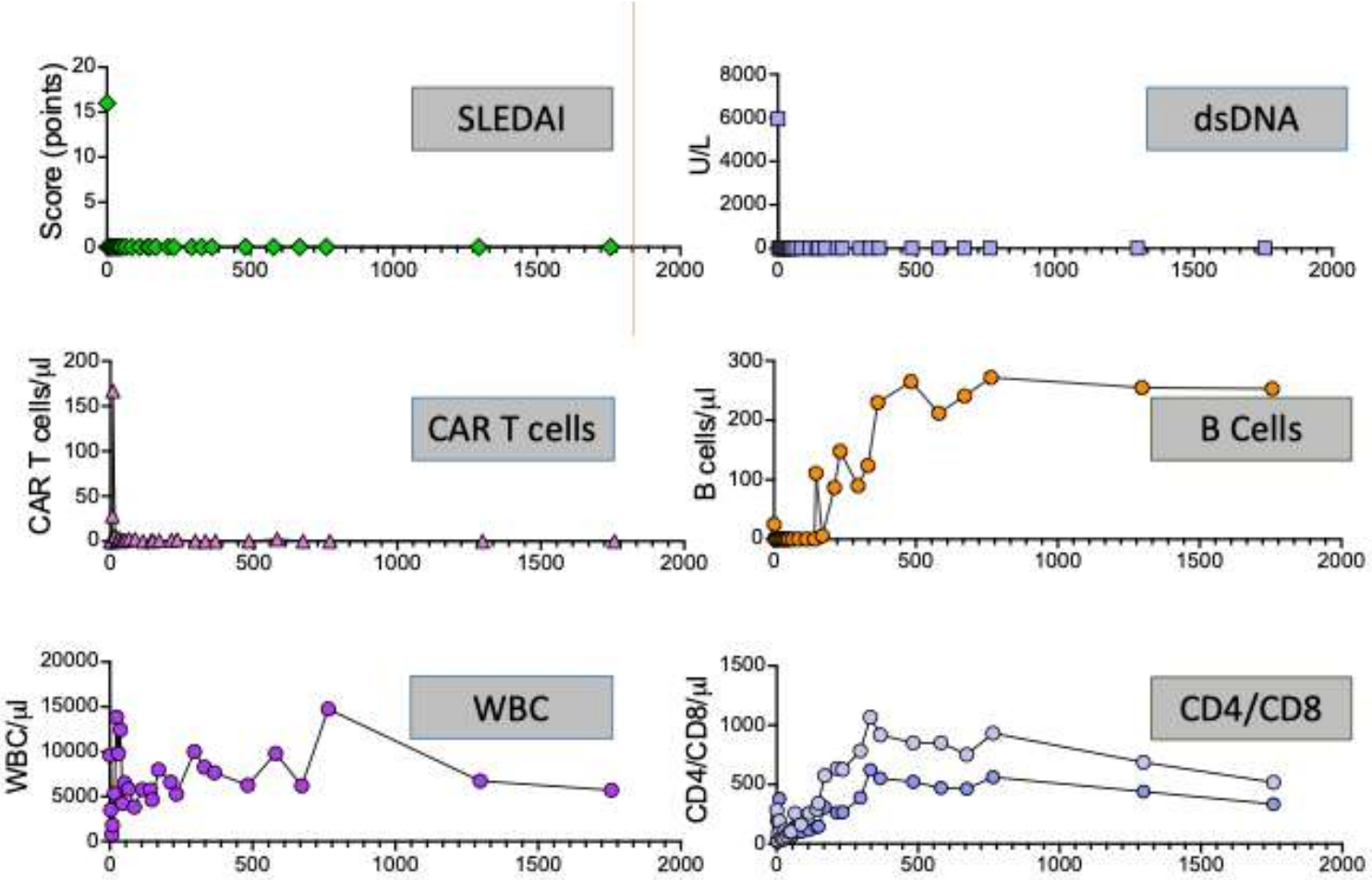
<u>5 years healthy</u>

No Symptoms

No Treatment

No Signs of Autoimmunity

Normal Life

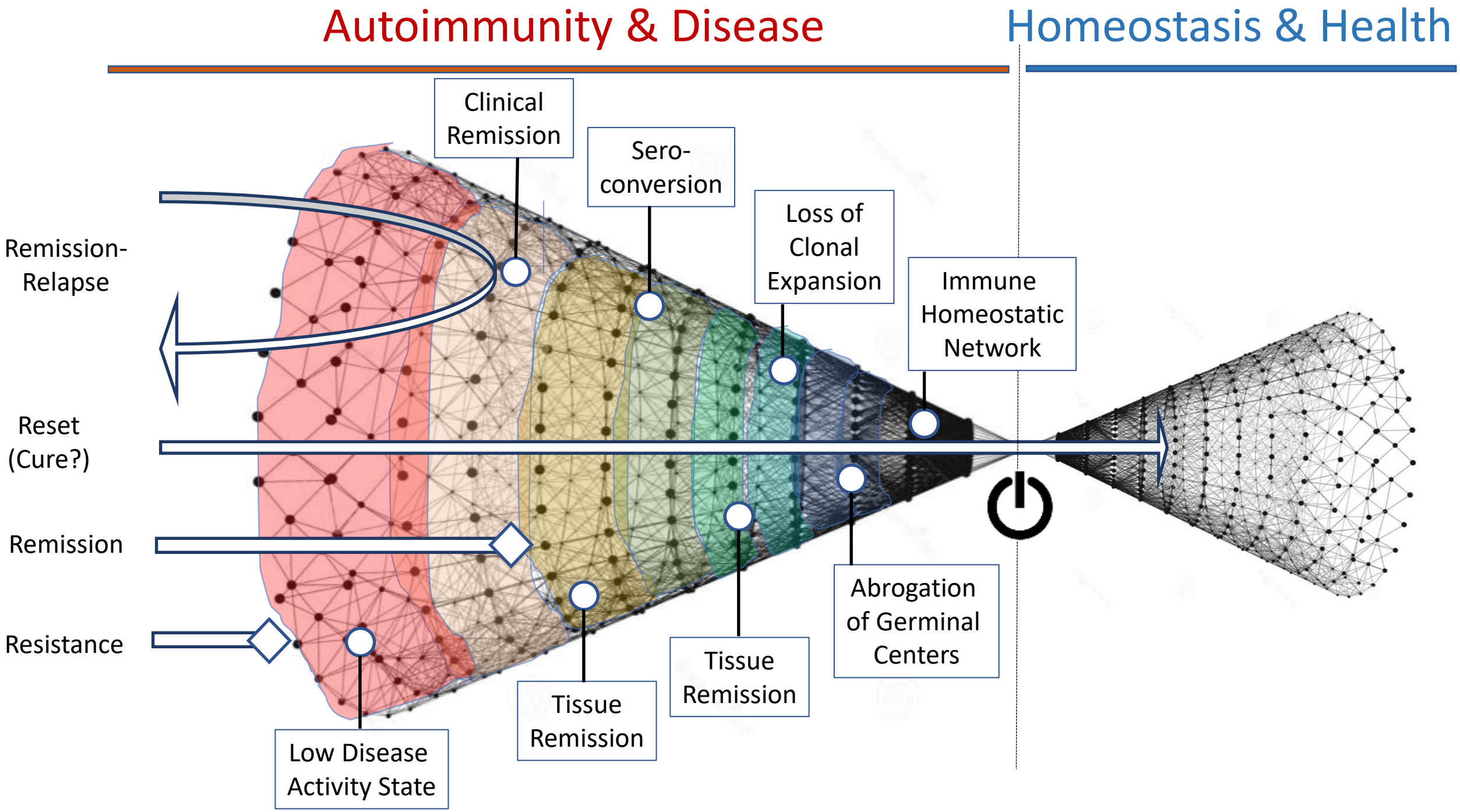


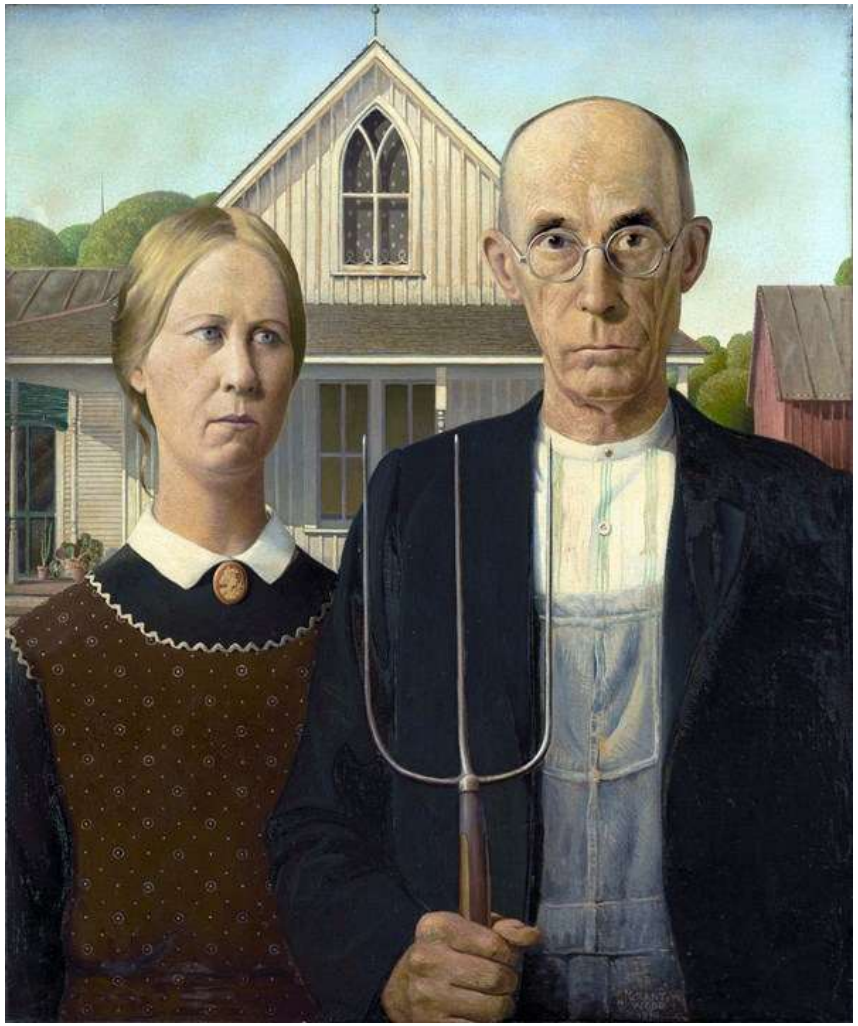
Magic 5-years for the Definition of Cure of Cancer: National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) Program

Stable absence of disease under „stress“

	SLE Patient #3	SLE Patient #9
CY Pre-Exposure	CY 1g	CY 3g
Time after CAR T	42 months	17 months
CY Pre-Exposure	CY 1g	CY 3g
Drug-Free State	Yes	Yes
Relapse of SLE	No	No
B-cells at conception	334/microliter	0/microliter
Gestation	40 weeks	39 weeks
Birth	Yes	Yes
Newborn Weight	3280g	2980g
Newborn B cells	152/microliter	239/microliter

In contrast to cancer, patients are exposed to less chemotherapy and fertility remains intact. Premenopausal women are the main target population in SLE.


Autoimmunity & Disease
Homeostasis & Health
Clinical Remission
Sero-conversion
Loss of Clonal Expansion
Immune Homeostatic Network
Remission-Relapse
Reset (Cure?)
Remission
Resistance
Abrogation of Germinal Centers
Tissue Remission
Tissue Remission
Low Disease Activity State



Grant Wood
American Gothic 1930

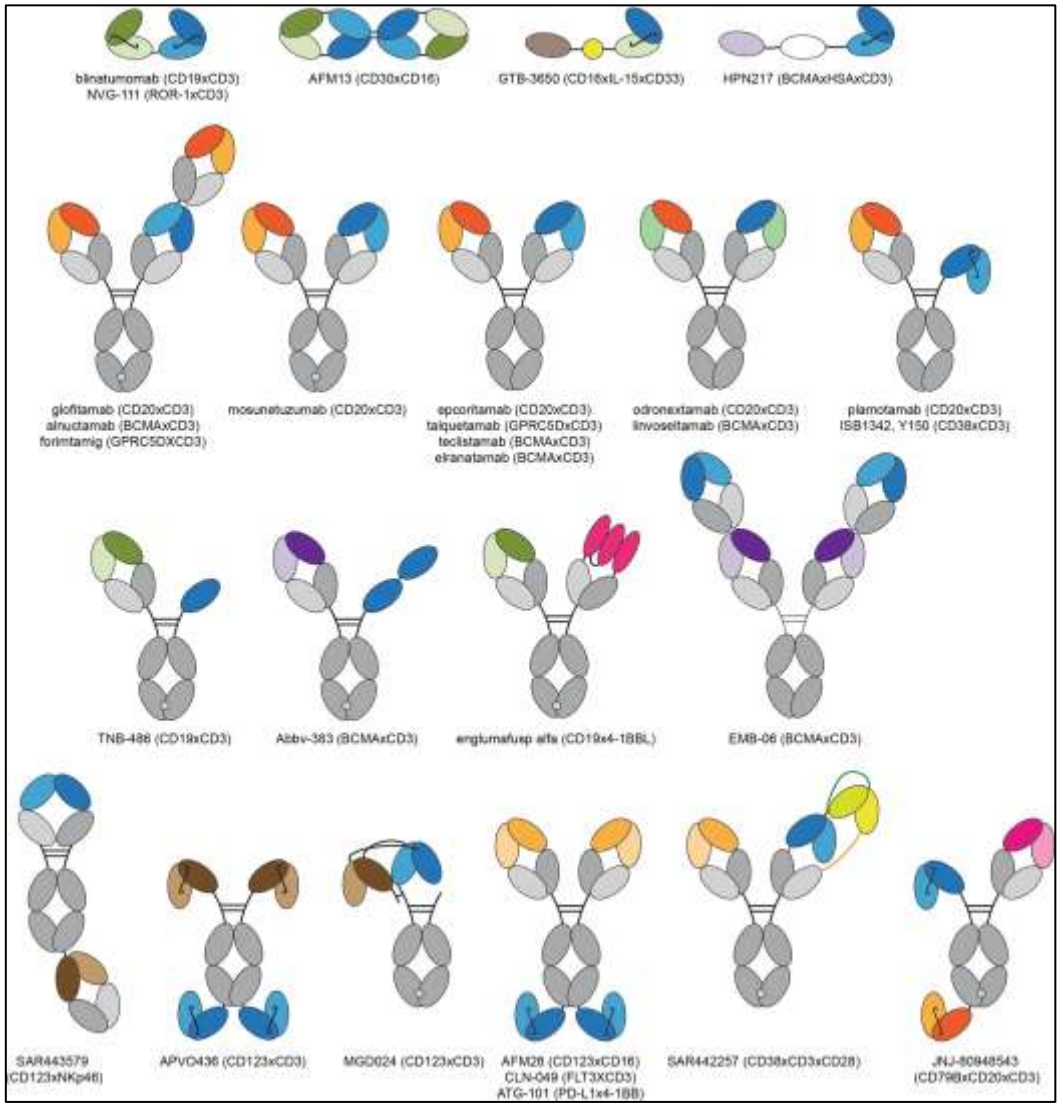
Determines in fighting disease:

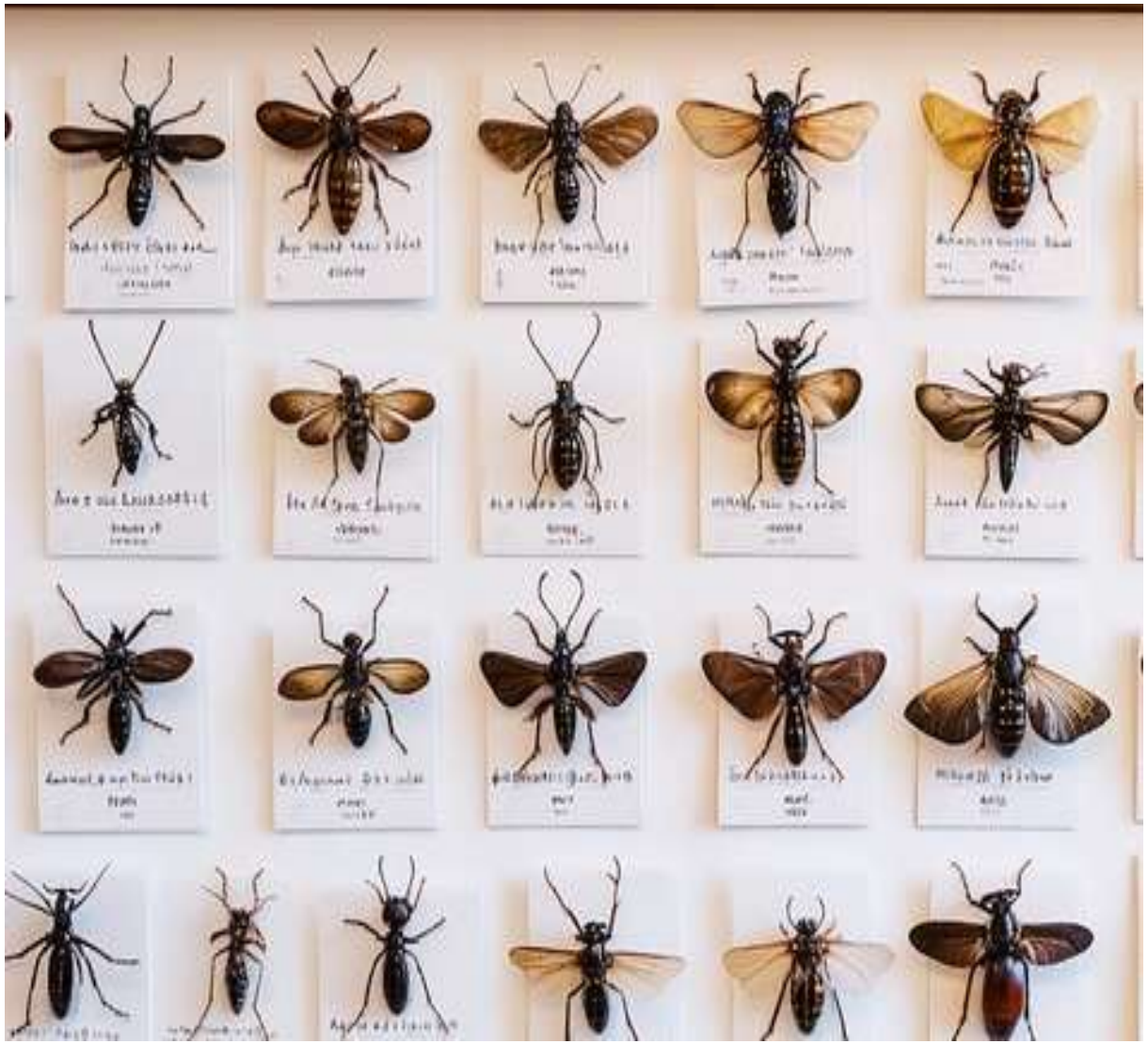
New treatment approaches based on advanced molecular technologies

Advantages and limitations of autologous CAR T cell therapy

Pros	Advantage	Cons	Potential Solution
One shot treatment with no further immuno-suppression	• Infection Risk • Organ Toxicity • Cancer Risk • Family Planning	Complex and Expensive Procedure	Off the shelf approaches Outpatient treatment
Penetration into all tissues	Extinction of B-cells in tissues allowing an “immune reset”	Necessity of Lymphodepletion	Reduction of Dose
Fast B-cell repopulation	Short vaccination-refractory state	Effect of repeated exposure to ATMP uncertain	Switch to other ATMP

Protein engineering creating a ”zoo” of T-cell engagers

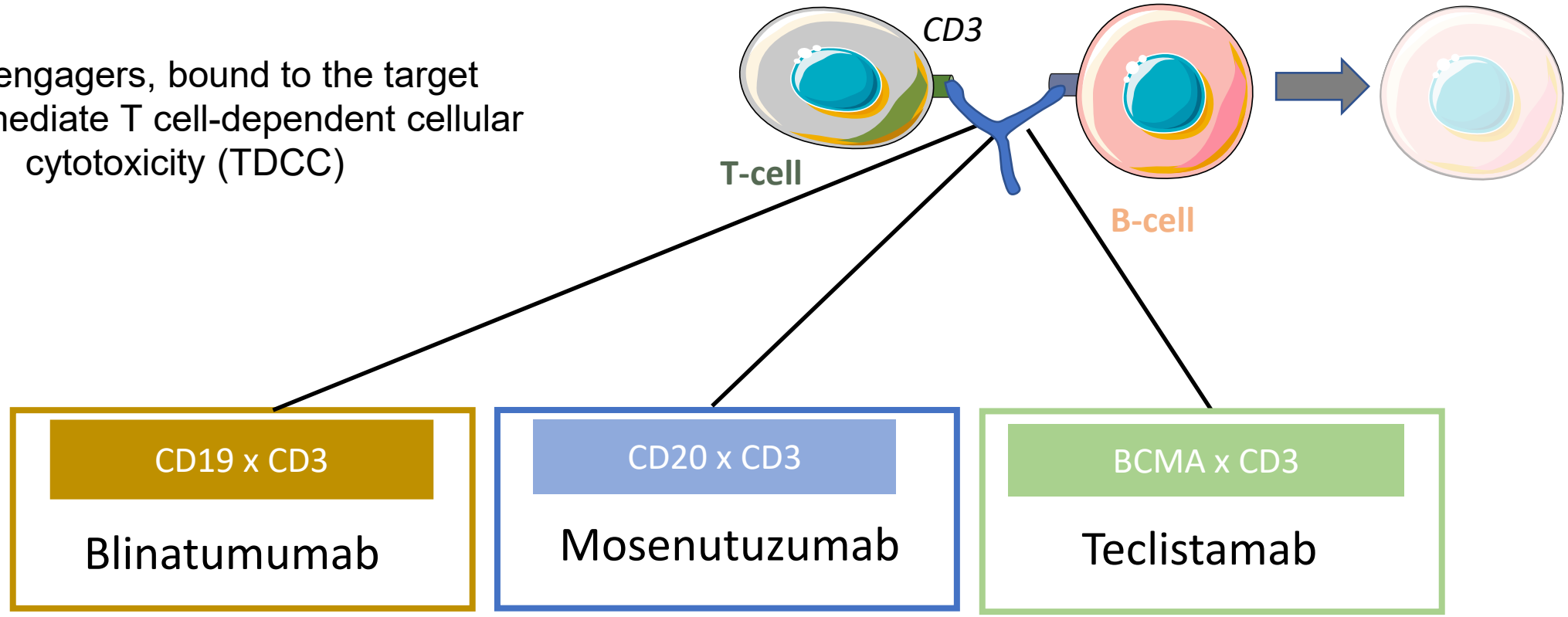




Can we achive CAR-like effects with protein-based drugs?

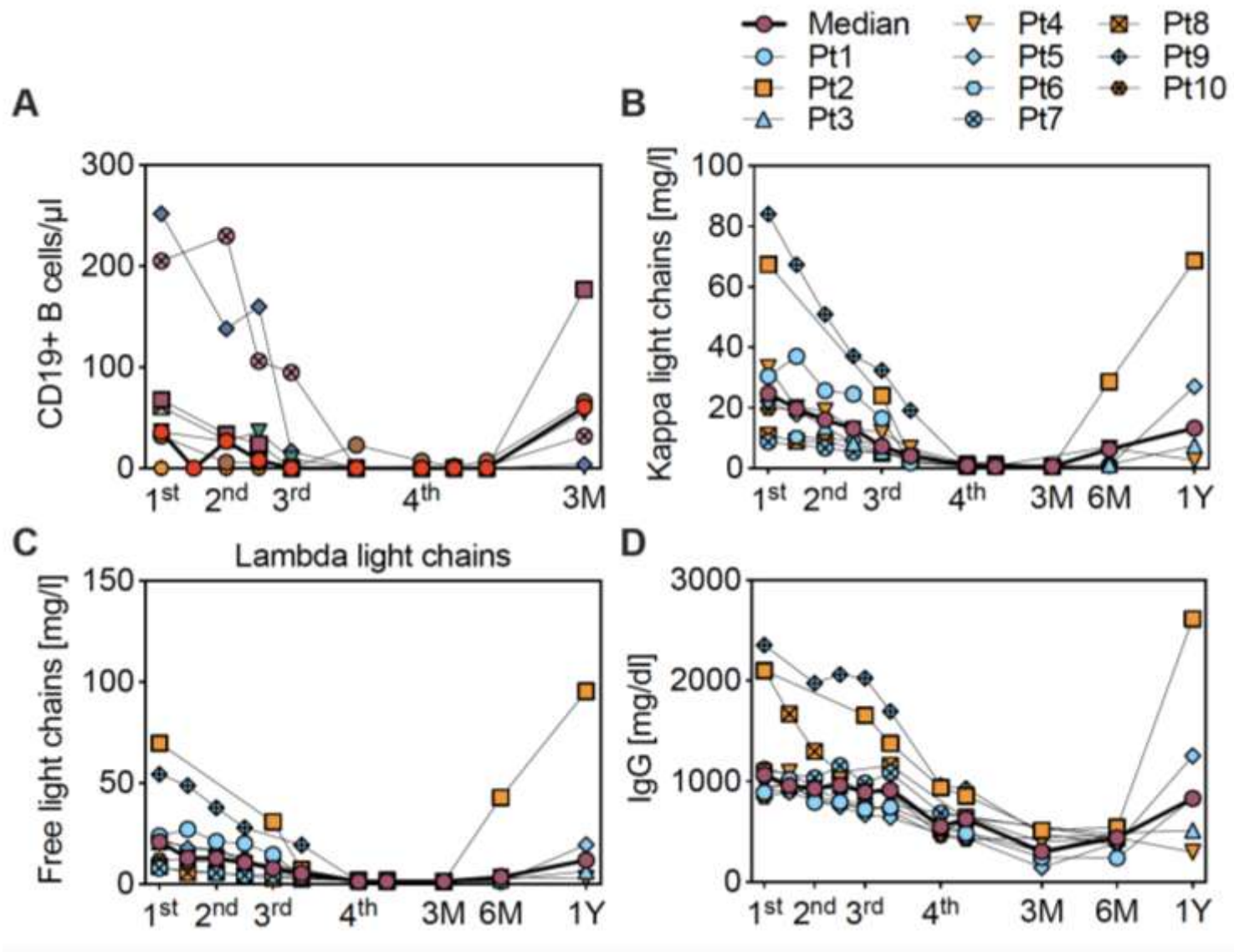
Principle of T-cell engagers and clinical examples

T-cell engagers, bound to the target antigen mediate T cell-dependent cellular cytotoxicity (TDCC)



BCMA x CD3 engager therapy in patients with autoimmune disease

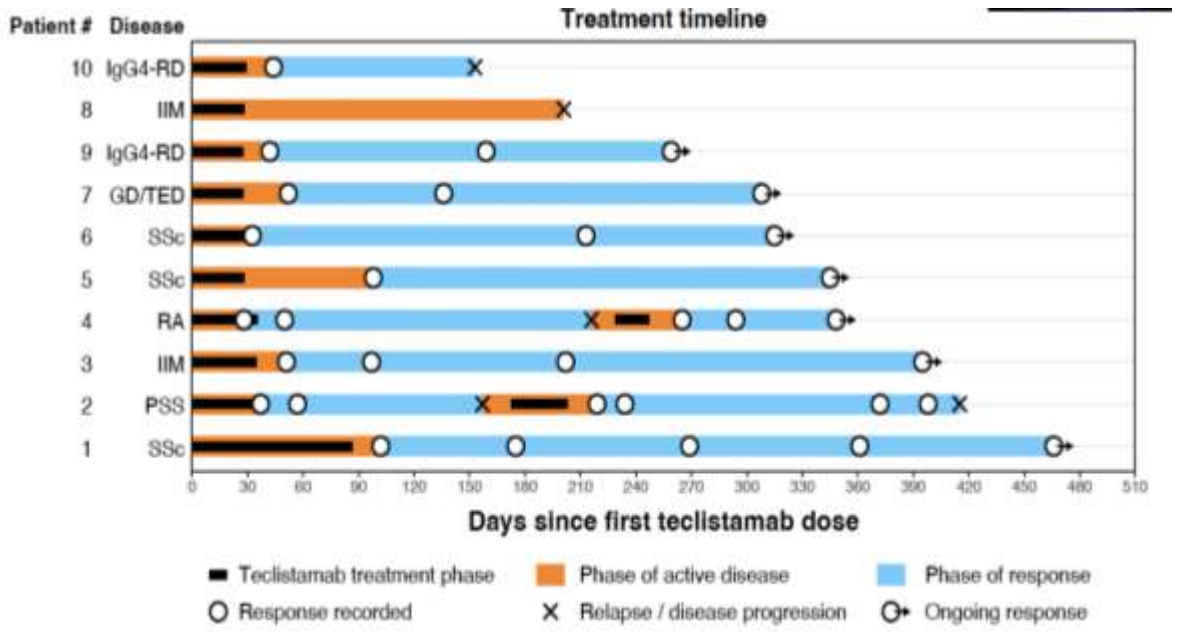
Dynamic B-cell depletion (despite BCMA target!) and decrease of free light chain levels and immunoglobulins in AID patients treated with teclistamab



Bucci L et al. N Engl J Med 2025

Clinical responses to BCMAxCD3 TCE teclistamab in patients with treatment-resistant autoimmune disease

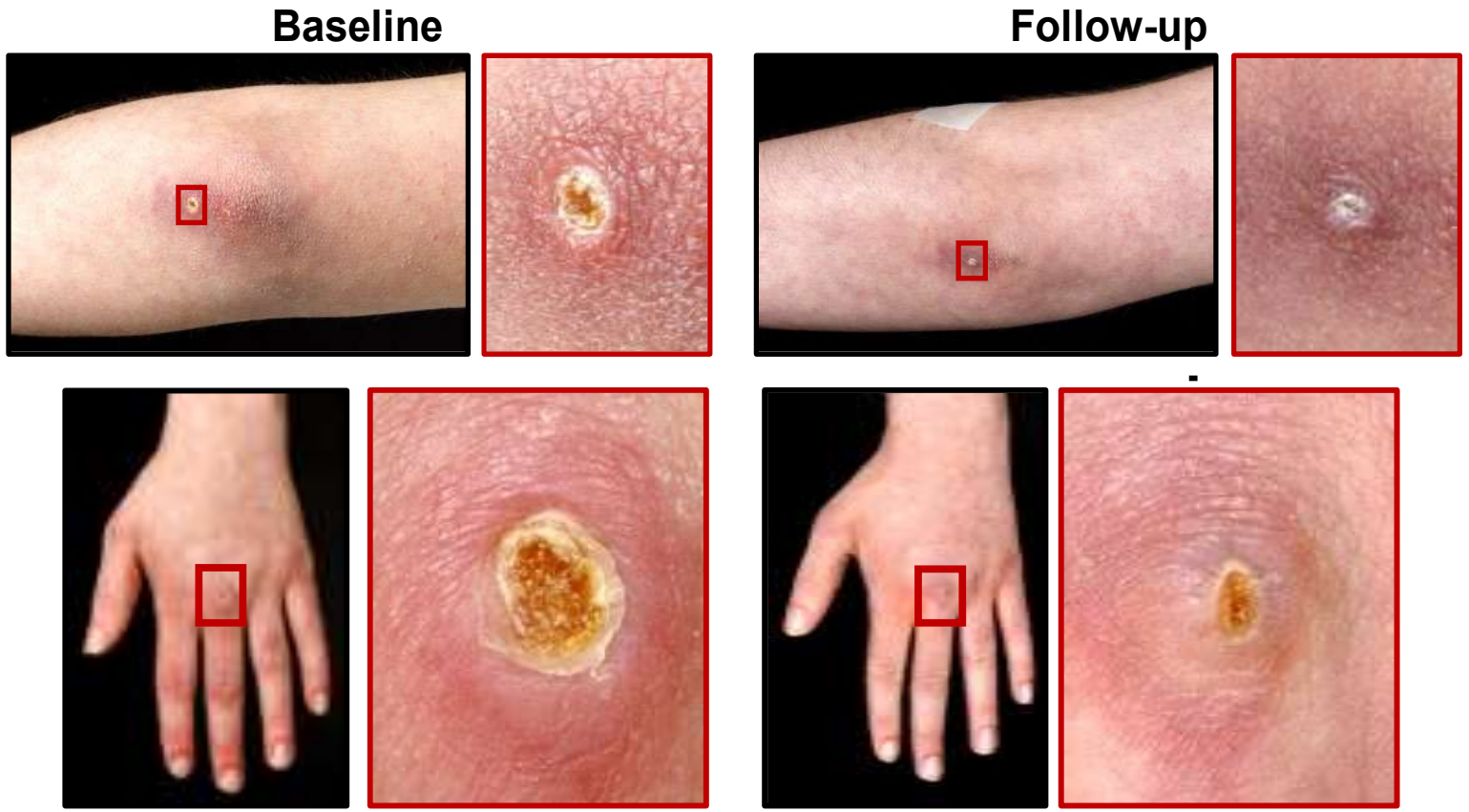
Disease	Outcome	BL	3mo
SSc (N= 3)	mRSS (3)	34	16
PSS (N= 1)	ESSDAI (1)	35	15
RA (N= 1)	DAS28 (1)	5.6	2.1
IIM (N= 2)	CDASI (2)	22	5
Graves´Disease (N= 1)	Orbitopathy	+	-
IgG4-RD (N= 2)	Clinical manifestations	+	-
All (N= 10)	DF Remission	n.a.	8
All (N= 10)	Relapse (N)	n.a.	2



Teclistamab was administered as subcutaneous injection using the standard step-up dose (d1: 0.06 mg/Kg; d3: 0.3 mg/Kg; d5: 1.5 mg/Kg). A maintenance dose of 1.5 mg/Kg was administered after 4 weeks.

Bucci L et al. N Engl J Med 2025

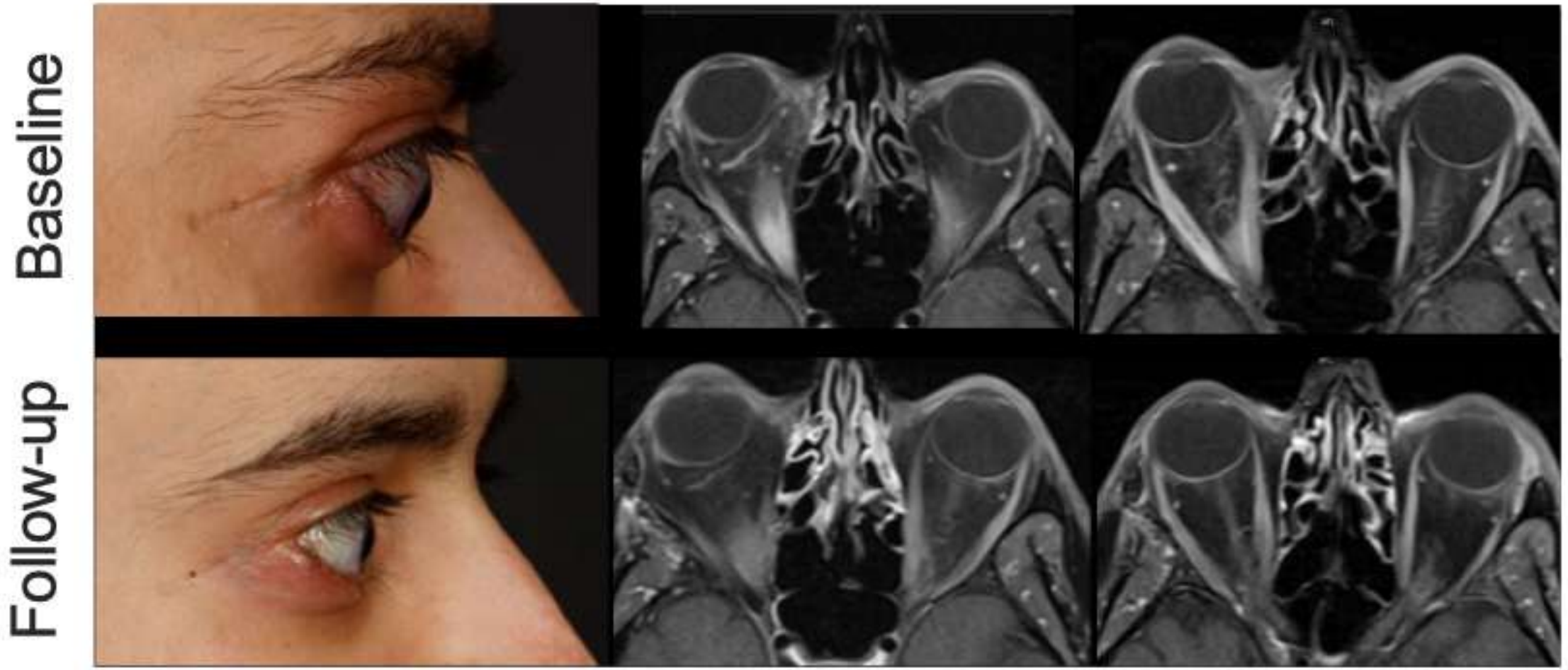
Skin response in the SSc patient treated with BCMA x CD3 engager



Calcification associated skin ulders in the PM-Scl + SSc patient and their reponse to teclistamab treatment

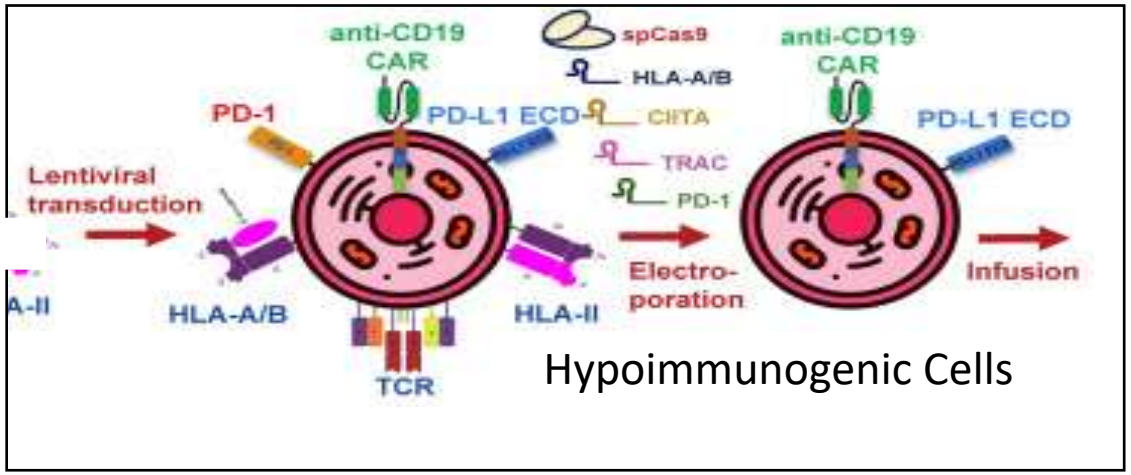
Hagen M, et al.N Engl J Med. 2024;391:867-869;; Bucci L et al. N Engl J Med 2025

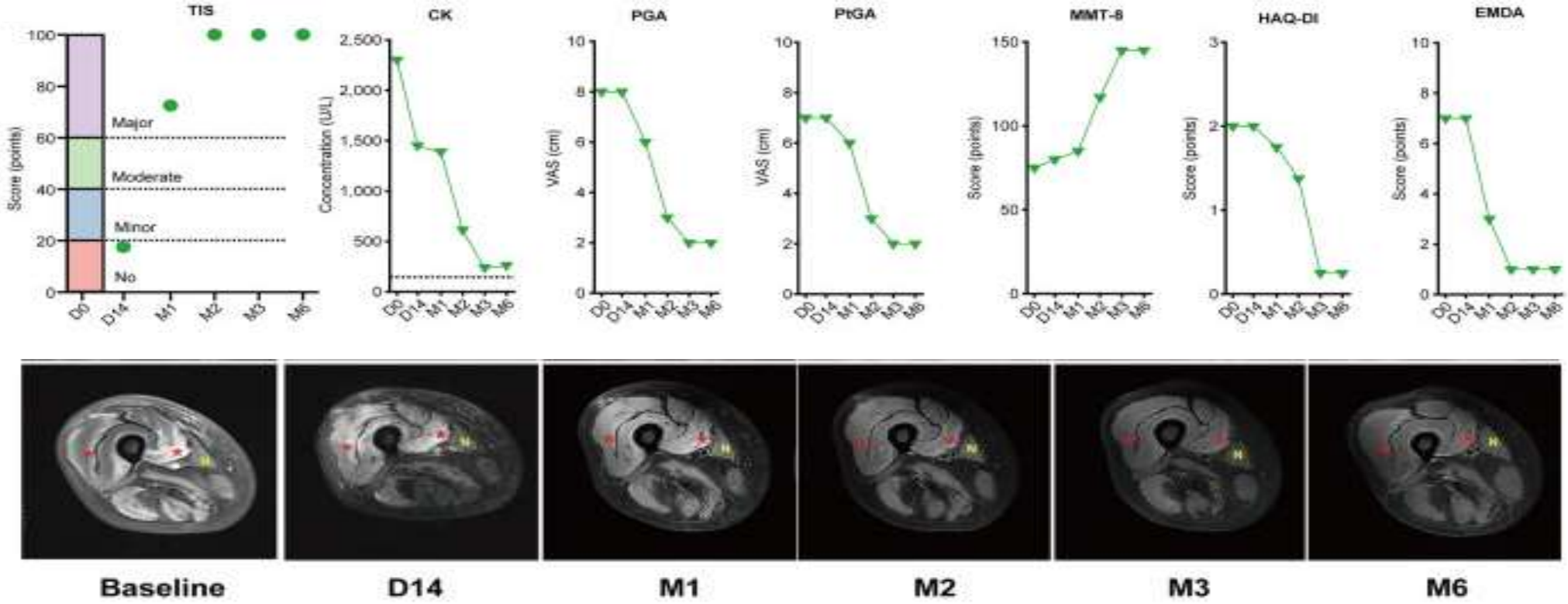
Improvement of endocrine ophtalmopathy upon BCMA x CD3 engager



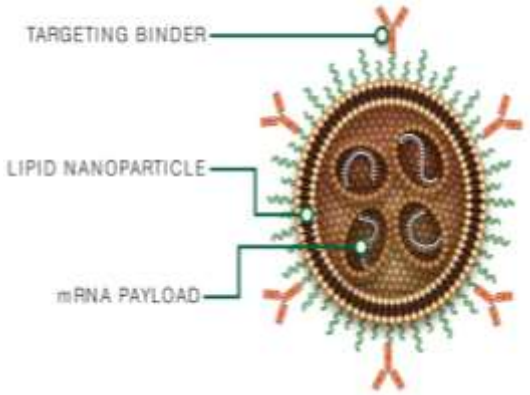
Bucci L et al. N Engl J Med 2025

Allogeneic CD19 CAR T-cells in a patient with severe myositis

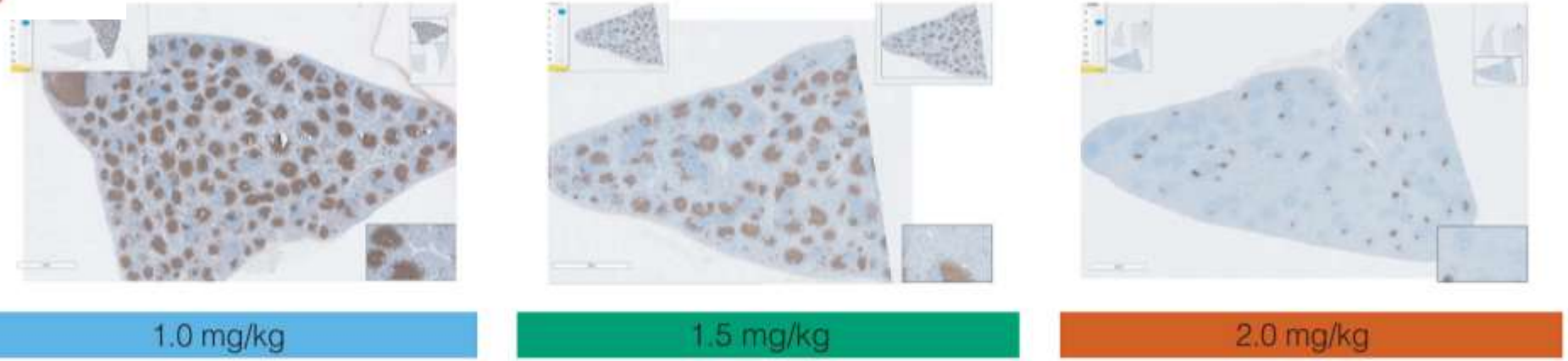


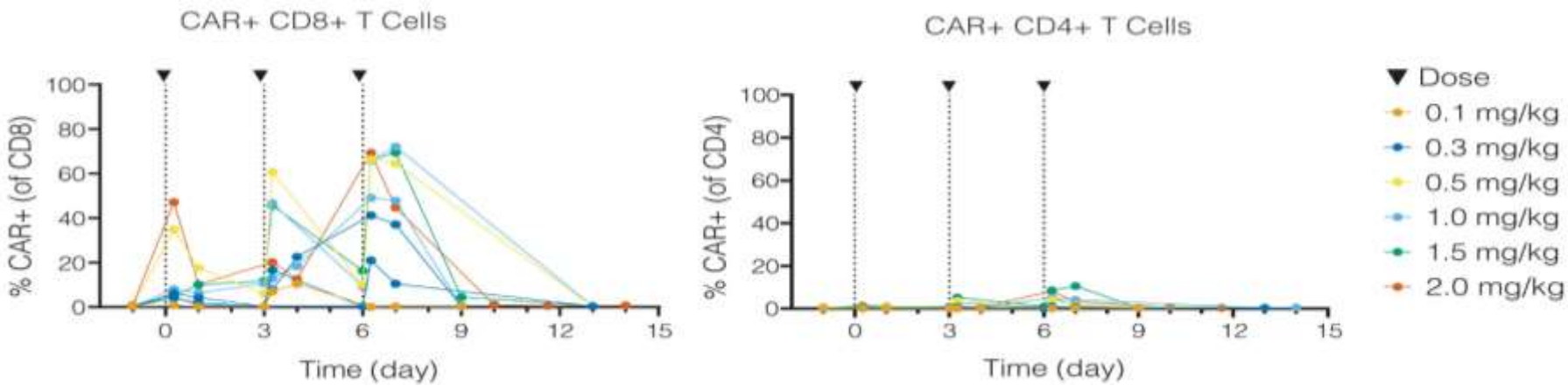


Wang X et al., Cell 2024;187:4890-4904.e9.



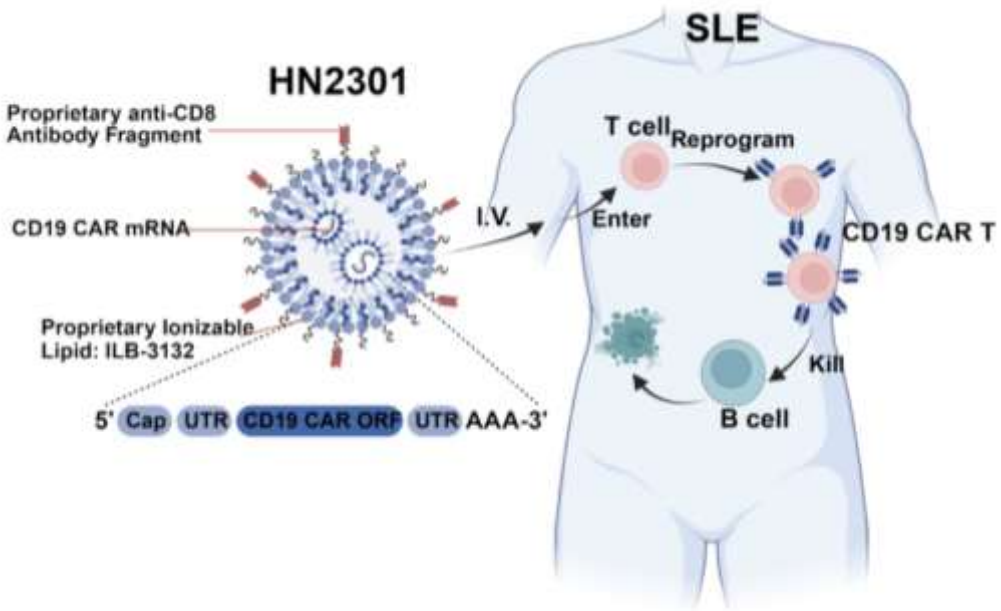
In Vivo CAR approach with a targeted LNP and mRNA payload

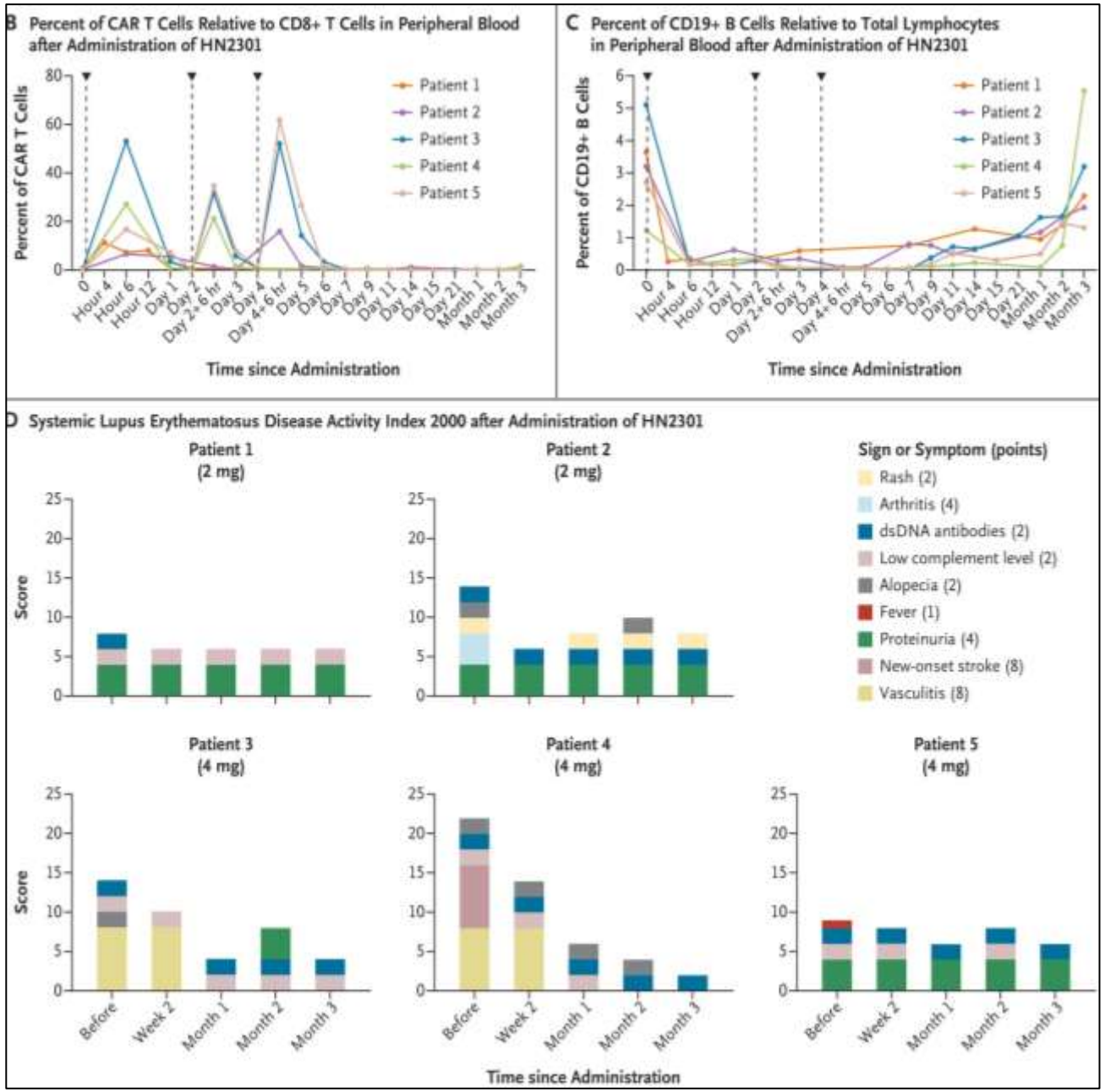




Hunter TL, et al. Science. 2025 Jun 19;388(6753):1311-1317.

In Vivo CAR T-cell therapie with targeted lipid nanoparticles in SLE

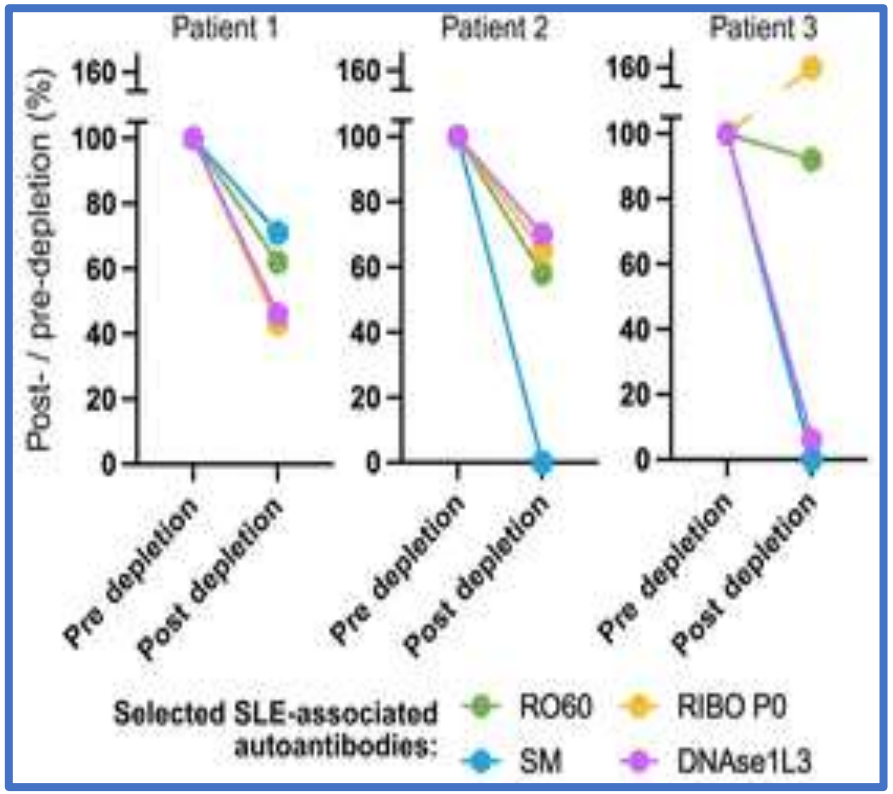




Wang Q,et el. In Vivo CD19 CAR T-Cell Therapy for Refractory Systemic Lupus Erythematosus. N Engl J Med 2025; DOI: 10.1056/NEJMc2509522

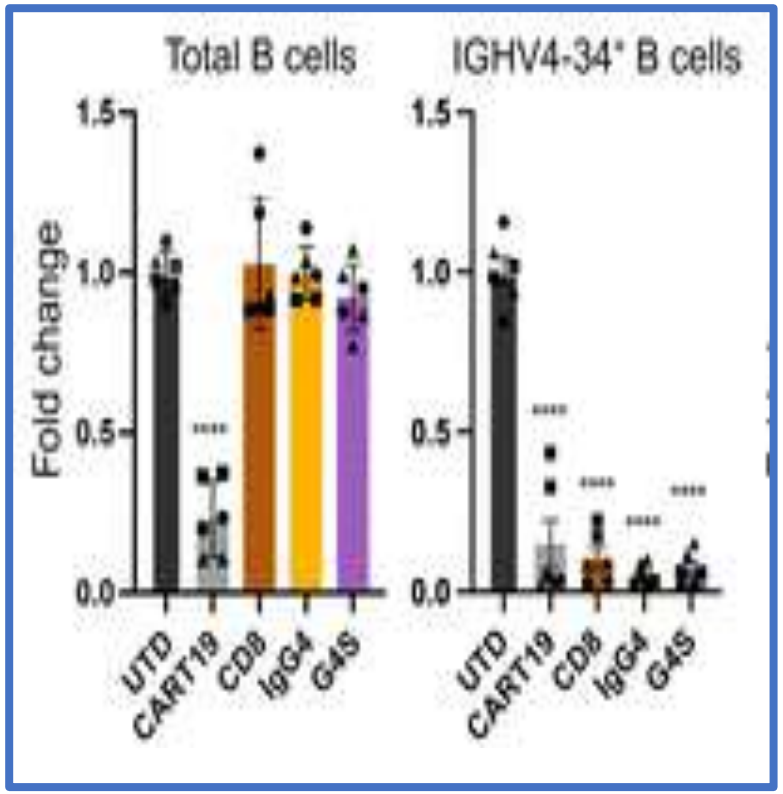
Selective depletion of pathogenic B cells

Targeting specific BCR that are associated with SLE by CAR T cells



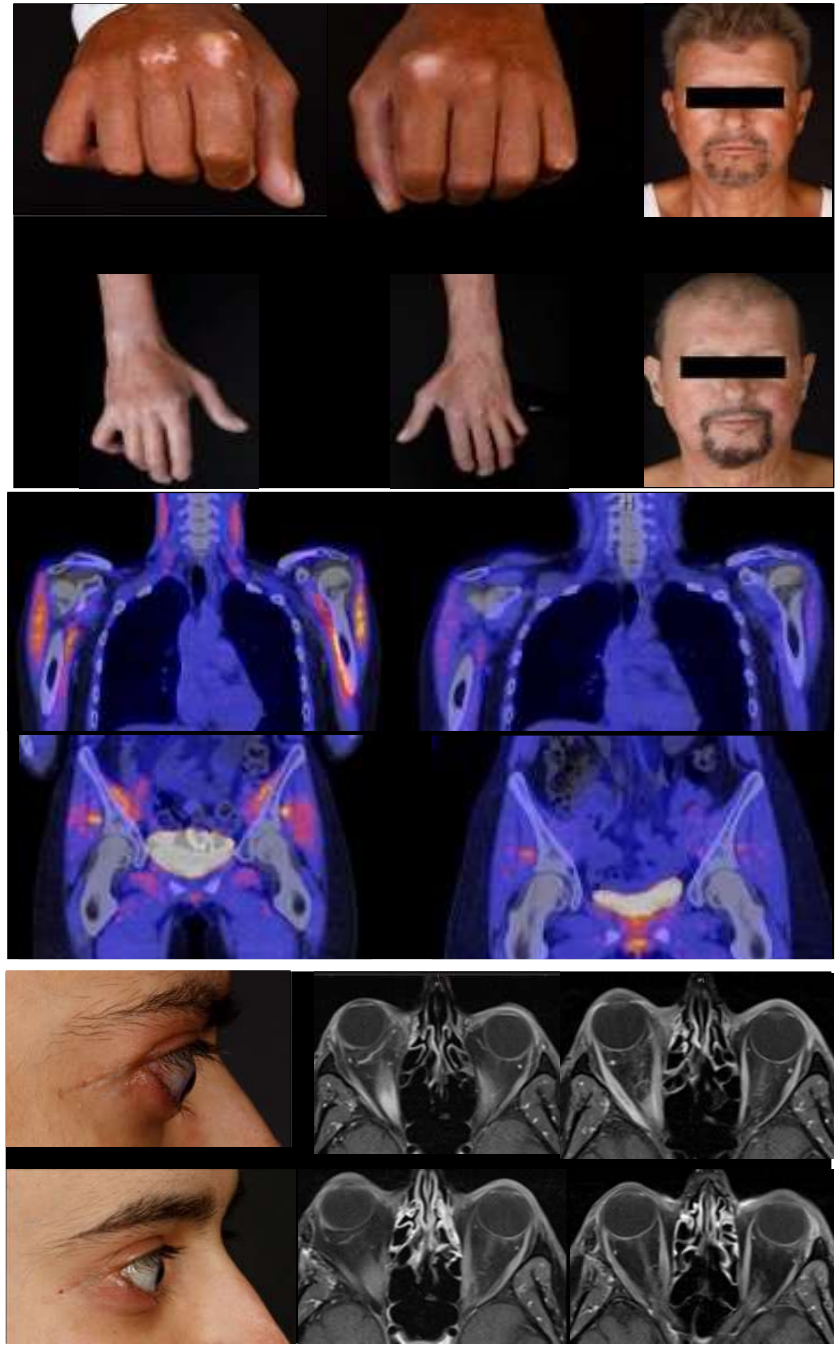
Depletion of IGHV4-34 antibodies leads to decrease in autoantibodies (in vitro)

IGHV4-34 antibodies deposit in SLE kidneys



IGHV4-34 directed CAR deplete IGHV4-34 expressing B-cells (in vitro)

Cohen IJ, et al. Sci Translat Med 2026; : 18,:eadr9382.



Vancouver 2026

The Future of Rheumatology

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DZI Deutsches Zentrum Immuntherapie

FAU Friedrich-Alexander-Universität Erlangen-Nürnberg