CAR-T cell therapy in autoimmune diseases

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LINKÖPING UNIVERSITY

BMS is investigating multiple assets targeting distinct pathways involved in lupus pathology

CD19 NEX-T™ CAR T

CD19+ B cell depletion

Phase 1: Study of CC-97540, CD19-targeted NEX-T™ CAR T Cells in Participants with Severe, Refractory Autoimmune Diseases (SLE, IIM, SSc)

Deucravacitinib

TYK2 inhibition

Phase 3: Two Studies to Assess Effectiveness and Safety of Deucravacitinib (BMS-986165) Compared with Placebo in Participants with Active Systemic Lupus Erythematosus (SLE) (POETYK SLE-1 and POETYK SLE-2)

Afimetoran

TLR7/8 inhibition

Phase 2: A Study Evaluating the Efficacy and Safety of Afimetoran (BMS-986526) Compared With Placebo in Participants With Active Systemic Lupus Erythematosus (SLE)

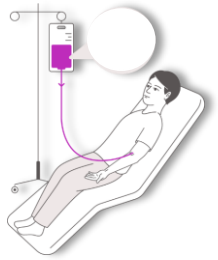
IL-2/CD25

IL-2 mediated Treg induction

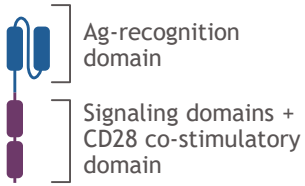
Phase 1b: Randomized, Double-Blind, Placebo-Controlled, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BMS-986326 in Adult Participants with Discoid Lupus Erythematosus, Subacute Cutaneous Lupus Erythematosus, or Systemic Lupus Erythematosus

CAR, chimeric antigen receptor; CD, cluster of differentiation; IL, interleukin; IIM, idiopathic inflammatory myopathy; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; TLR, toll-like receptor; Treg, regulatory T cell; TYK, tyrosine kinase.

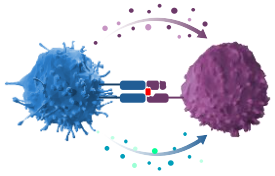
CAR T cell therapy is continuously evolving



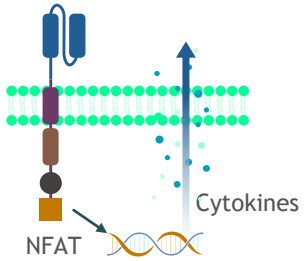
1988 — TILs used to treat metastatic cancer[1]



1998 — 2nd generation of CAR T cells (CD28 incorporation)[1]



2006 — TCR therapy used in metastatic melanoma trial[1]



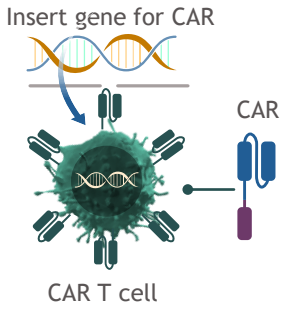
2012 — 4th generation of CAR T cells (encodes cytokines)[1]

CD19 CAR T-Cell Therapy in Autoimmune Disease — A Case Series with Follow-up

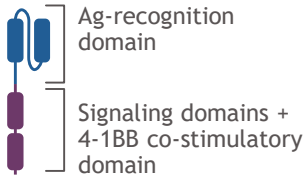
2021 — FDA approval of first CAR T cell therapy for myeloma[1]

2024

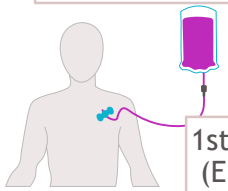
1993 — 1st generation of CAR T cells[1]



1998 — 2nd generation of CAR T cells (4-1BB incorporation)[1]

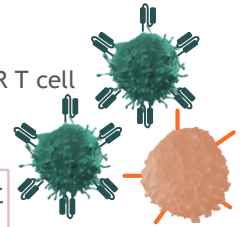


2004 — 1st trial patient treated with CD19 CAR T cells and 3rd generation of CAR T cells arise[1]

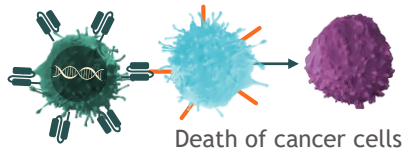


2010 — 1st pediatric patient (Emily Whitehead)[2]

2017 — FDA approval of CD19 CAR T cell therapy for lymphoma and leukemia[1]



2023 — Mutated c-KIT added to CAR T cells used in solid tumor trial[1]



Adapted from *Int J Mol Sci*.[1]

Ag, antigen; CAR, chimeric antigen receptor; CD, cluster of differentiation; c-KIT, tyrosine-protein kinase Kit; NFAT, nuclear factor of activated T cell; TCR, T cell receptor; TIL, tumor-infiltrating lymphocyte.

1. Uscanga-Palomeque AC et al. *Int J Mol Sci*. 2023;24:15688. 2. Bouzianas D, Bouziana S. *Hum Vaccin Immunother*. 2024;20:2321678.

CAR T cell therapy may provide long-term disease control in hematologic diseases

The first pediatric patient (Emily Whitehead) treated with CAR T cell therapy for **relapsed/refractory acute lymphoblastic leukemia** remains in remission > 10 years later

This case involved a non-BMS investigational CAR T cell therapy.

Image source: *Emily Whitehead Foundation. Accessed October 2024. https://emilywhiteheadfoundation.org/news/celebrating-10-years-cancer-free/*

CAR, chimeric antigen receptor.

Bouzianas D, Bouziana S. *Hum Vaccin Immunother* 2024;20:2321678.

Approved CAR T cell therapies in hematology provide learnings to investigate safety, efficacy, and manufacturing in rheumatology

34000+

Patients treated with CAR T cell therapies[1]

6

Approved indications[2-7]

- Large B-cell lymphoma
- Follicular lymphoma
- Multiple myeloma
- Mantle cell lymphoma
- Acute lymphoblastic leukemia
- Chronic lymphoblastic leukemia

6

Approved cell therapies[2-7]

Goals:

- Investigation of safety and efficacy[8]
- Optimization of CAR T cell manufacturing[8]
- Expansion of access to CAR T cell therapy[8]

CAR, chimeric antigen receptor.

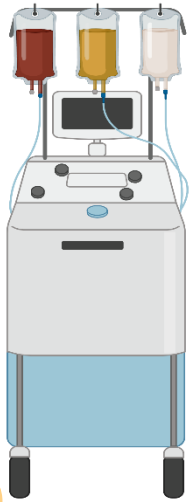
1. Levine BL et al. *Nat Med*. 2024;30:338–341. 2. ABECMA. Package insert. Celgene Corporation; 2024. 3. BREYANZI. Package insert. Juno Therapeutics Inc; 2024. 4. YESCARTA. Package insert. Kite Pharma, Inc; 2024. 5. TECARTUS. Package insert. Kite Pharma, Inc; 2024. 6. CARVYKTI. Package insert. Janssen Biotech, Inc; 2024. 7. KYMRIAH. Package insert. Novartis Pharmaceuticals Corporation; 2024. 8. D'Agostino M and Raje N. *Leukemia*. 2020;34:21–34.

Patient journey through the CAR T cell therapy process

Patient selection → Patient consent & education → Patient screening → Leukapheresis and cell transport → CAR T manufacturing → Lymphodepletion → CAR T infusion & patient monitoring → Post-hospital discharge monitoring → Long-term monitoring

1 Patient identification

- Appropriate patients will be identified at qualified treatment sites[1]

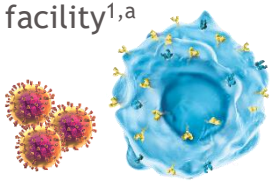


2 Leukapheresis

- Patient will undergo apheresis to collect white blood cells through a catheter[1]
- Collected product will be sent to the manufacturer for production[1]

3 Manufacturing

- CAR T cell product is created at a manufacturing facility[1,a]



4 Prep

- Shortly before CAR T cell administration, the patient is prepared for treatment with lymphodepletion[1]

5 Treat

- The CAR T cell product is delivered to the treatment site and administered[1]

6 Monitor

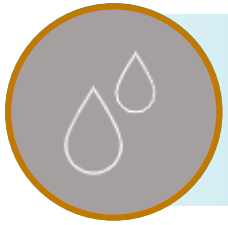
- The patient is monitored closely by HCPs for at least 4 weeks[1]
- Adverse events are promptly managed[1]
- Lifelong periodic monitoring[1]

[a]There are different CAR T platforms available that differ in their construct components.[2]

CAR, chimeric antigen receptor; HCP, healthcare provider.

1. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23:27–34. 2. Maus MV, Levine BL. *Oncologist*. 2016;21:608–617.

B-cell–targeted therapies in hematology and rheumatology



Hematology

- Rituximab[1]
- Obinutuzumab[2]
- CAR T cell therapy[3]

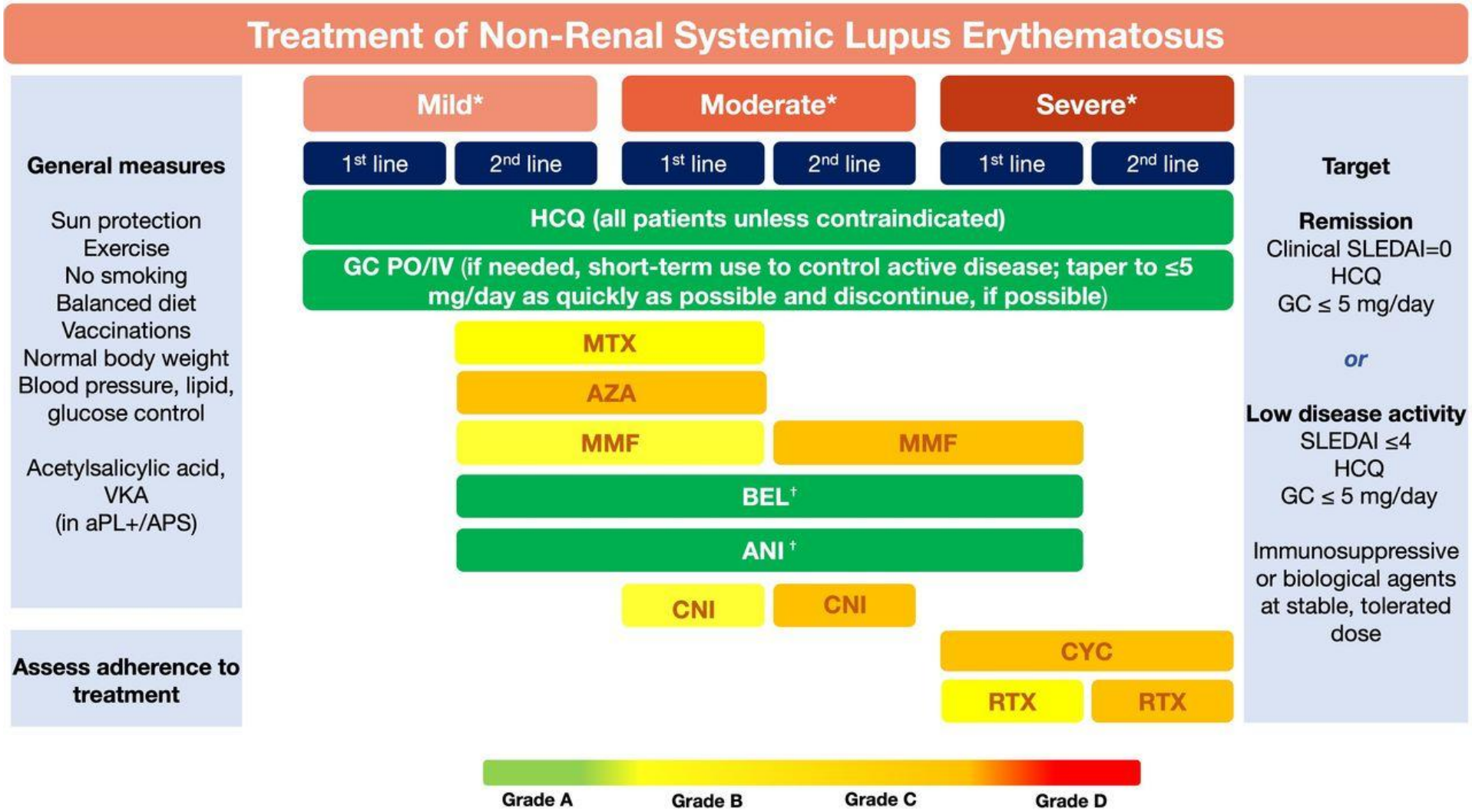
Rheumatology (SLE)

- Rituximab (off-label use)[4]
- Obinutuzumab (Lupus nephritis)[5]
- CAR T cell therapy (not yet approved)[3]

CAR, chimeric antigen receptor; LN, lupus nephritis; sBLA, supplemental biologics license application; SLE, systemic lupus erythematosus.

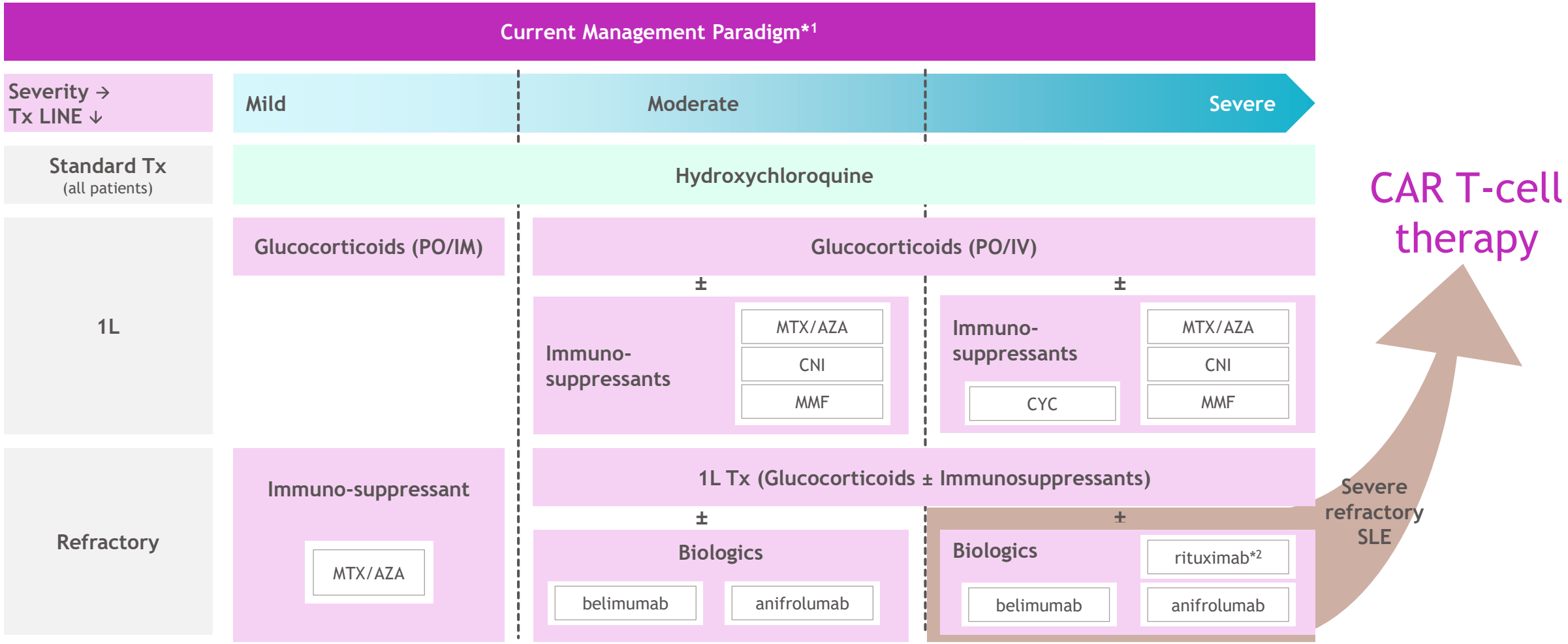
1. RITUXAN® (rituximab). Package insert. Genentech Inc; 2021; 2. GAZYVA® (obinutuzumab). Package insert. Genentech Inc; 2022; 3. Kuipers MT, Kersten MJ. *Lupus Sci Med* 2025;12:e001157; 4. Saegusa K, et al. *Int J Mol Sci* 2025;26:929; 5. FDA Accepts Obinutuzumab (Gazyva/Gazyvaro) sBLA for Lupus Nephritis. https://www.hcplive.com/view/fda-accepts-obinutuzumab-gazyva-gazyvaro-sbla-lupus-nephritis. Accessed March 2025.

Up-dated EULAR guidelines (2023)



Fanouriakis A, et al. Ann Rheum Dis 2024;83(1):15-29

Potential CAR T-cell therapy eligible patient population

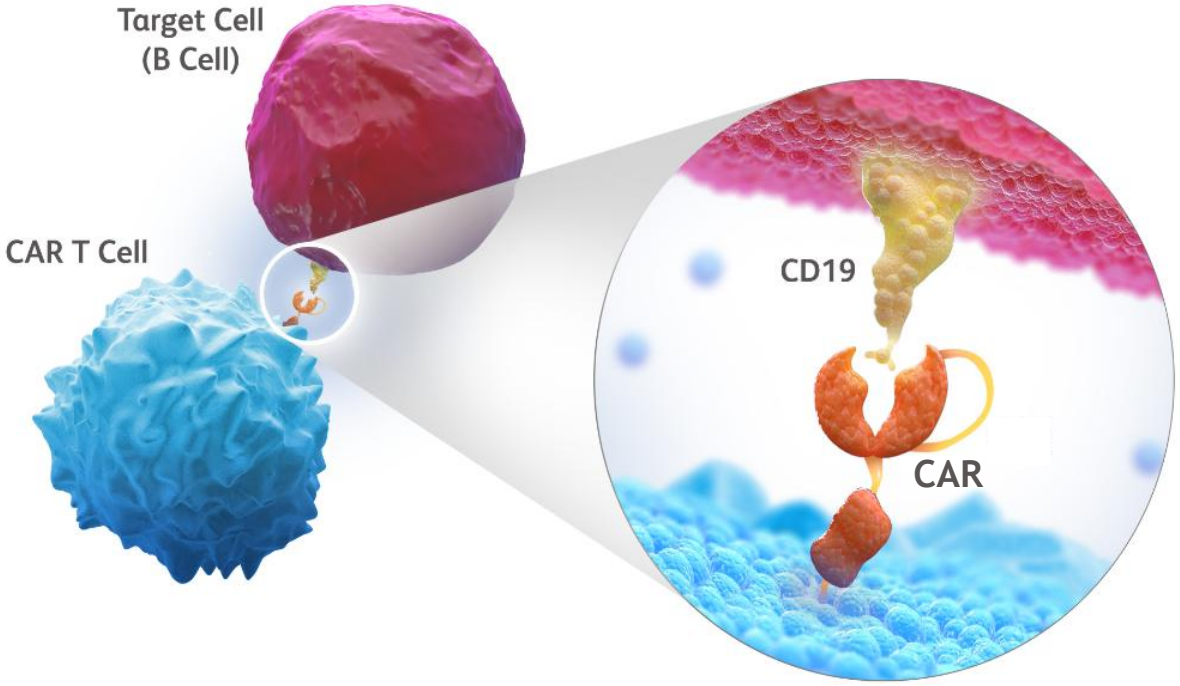


*1 Modified after 2019 EULAR guidelines on the treatment of non-renal SLE (Fanouriakis A et al. *Ann Rheum Dis*. 2019;78:736-745.)

*2 or Obinutuzumab | *Abbreviations*: AZA=Azathioprine; BEL=Belimumab; CNI=Calcineurin Inhibitor; CYC=Cyclophosphamide; HCQ=Hydroxychloroquine; IM=Intramuscular; IV=Intravenous; MMF=Mycophenolate Mofetil; MTX=Methotrexate; PO=Orally; pts.=Patients Tx=Therapy

What is CAR T cell therapy?

Autologous **CAR T cell therapy** reprograms T cells to express a CAR that binds to a specific antigen on target cells, leading to **T cell activation, expansion, and cytotoxicity**[1]



Gene transfer technology is used to express CARs on T cells[2]

CAR T cell therapy targets cells that express the target antigen, eg **CD19** on B lineage cells, which is highly specific and **ubiquitously expressed from pro-B cells to plasmablasts**[2,3]

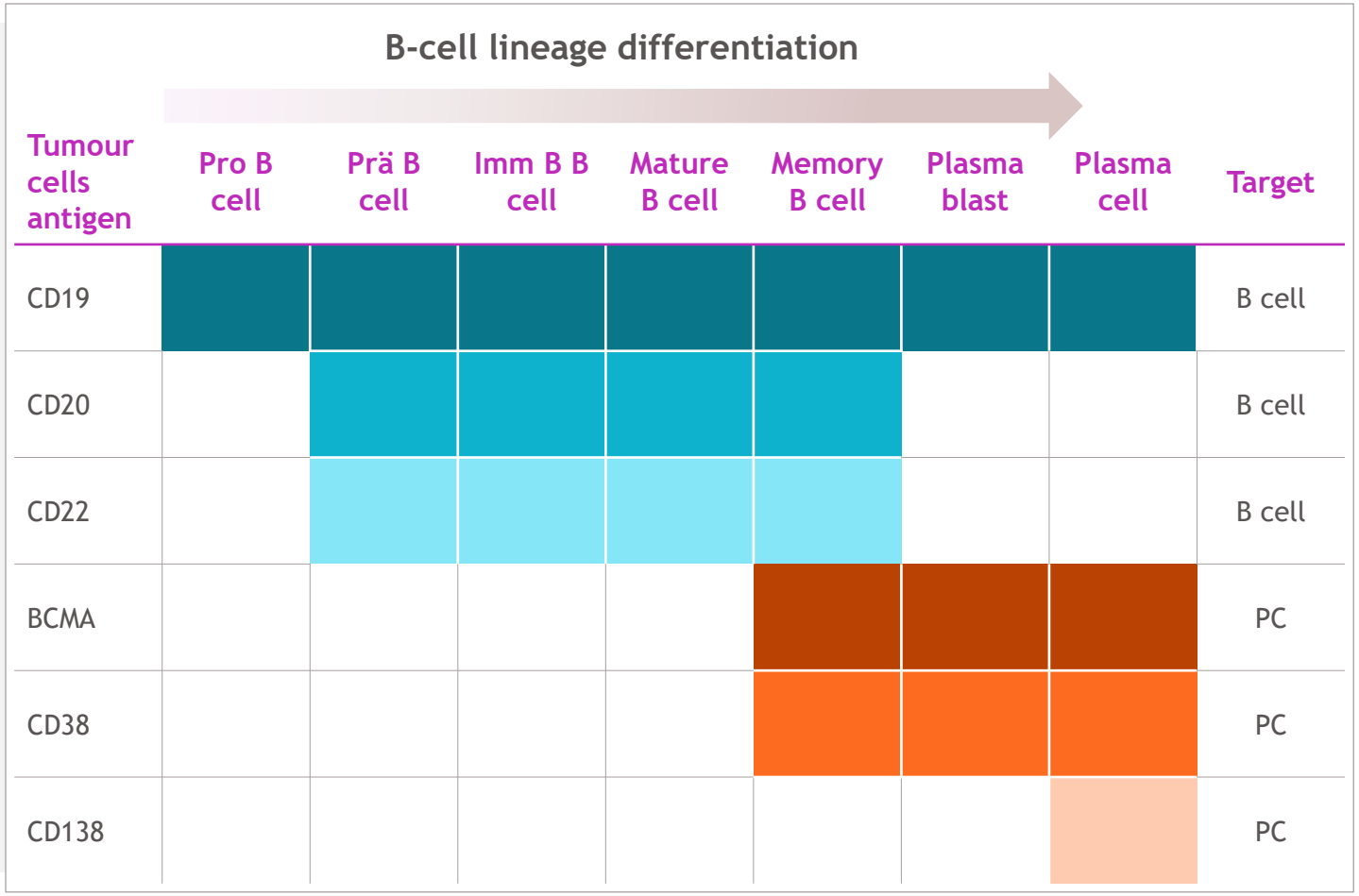
CAR, chimeric antigen receptor; CD, cluster of differentiation.

1. Leukemia & Lymphoma Society. Accessed October 30, 2023. https://www.lls.org/sites/default/files/2023-10/FSHP1_CART_Factsheet_June2022_rev.pdf. 2. Oluwole OO, Davila ML. *J Leukoc Biol*. 2016;100:1265–1272.
3. Kanatas P et al. *Can J Neurol Sci*. 2022;1–10.

CD19 CAR T-cell therapy may reset the immune system by deeply depleting B cells[1]

CAR T cells can be tailored to target specific markers of elevated autoimmune activity such as CD19 on B cells[1]

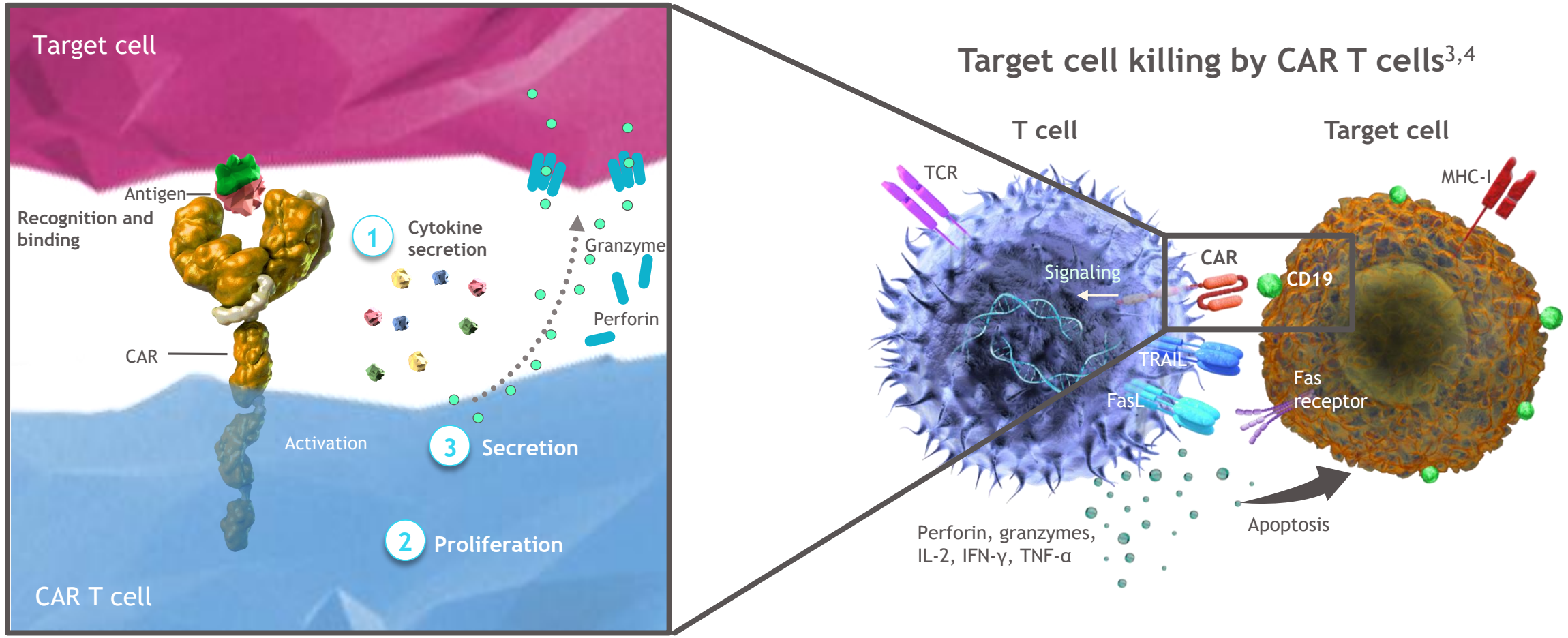
CD19 is expressed ubiquitously and selectively on B cells and plasmablasts, so CD19-targeted treatments lead to deeply deplete B cells[1-3]



CAR, chimeric antigen receptor; CD, cluster of differentiation.

1. Schett G et al. *Lancet*. 2023;402:2034-2044. 2. Kanatas P et al. *Canadian Journal of Neurological Sciences*. 2023; 50:355-364. 3. Taubmann J et al. *Arthritis Rheumatol*. 2023. doi:10.1002/art.42784.

CAR T cell mechanism of action involves recognition, binding, and activation of the CAR[1,2]



CAR, chimeric antigen receptor; CD, cluster of differentiation; FasL, Fas ligand; IFN, interferon; IL-2, interleukin-2; MHC, major histocompatibility complex; TCR, T-cell receptor; TRAIL, tumor necrosis factor-related apoptosis inducing ligand; TNF, tumor necrosis factor.

1. June CH, Sadelain M. *N Engl J Med*. 2018;379:64-73. 2. Dotti G et al. *Immunol Rev*. 2014;257:107-126. 3. Cartellieri M et al. *J Biomed Biotechnol*. 2010;2010:956304. 4. Schett G et al. *Lancet*. 2023;402:2034-2044.

ACR Convergence 2024
November 14–19, 2024; Washington, District of Columbia, USA
Presentation and Abstract Number 1753

A phase 1, multicenter, open-label study (Breakfree-1) to establish the preliminary tolerability, efficacy, pharmacokinetics, and pharmaco-dynamics of BMS-986353 (CC-97540), a CD19-directed CAR T cell therapy manufactured using a next-generation process for severe, refractory autoimmune diseases

Georg Schett,[1] Emily Littlejohn,[2] Neil Kramer,[3] Amit Saxena,[4] Philip Mease,[5] Margrit Wiesendanger,[6] Fabian Müller,[7] Ran Reshef,[8] Paolo Caimi,[9] Mohamad Cherry,[10] Jingmei Hsu,[4] Krish Patel,[11] Jacques Azzi,[6] Susana Barriga Falcon,[12] Thomas Ly,[13] Ken Ogasawara,[12] Sharmila Das,[12] Jerill Thorpe,[14] Michael A. Maldonado,[12] Giuseppina Stifano,[12] Ashley Koegel,[12] Anca Askanase[15]

[1]Friedrich Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany; [2]Cleveland Clinic Rheumatology, Cleveland, OH, USA; [3]Overlook Medical Center, Summit, NJ, and Atlantic Medical Group, Atlantic Health System, Morristown, NJ, USA; [4]NYU Grossman School of Medicine, New York, NY, USA; [5]Providence Swedish Medical Center and University of Washington, Seattle, WA, USA; [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [7]University Hospital of Erlangen, Department of Internal Medicine 5 – Hematology and Oncology, Erlangen, Germany; [8]Columbia University Irving Medical Center, New York, NY, USA; [9]Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, USA; [10]Atlantic Health System, Morristown, NJ, USA; [11]Center for Blood Disorders and Cellular Therapy, Swedish Cancer Institute, Seattle, WA, USA; [12]Bristol Myers Squibb, Princeton, NJ, USA; [13]Bristol Myers Squibb, San Diego, CA, USA; [14]Bristol Myers Squibb, Seattle, WA, USA; [15]Columbia University Irving Medical Center, New York, NY, USA

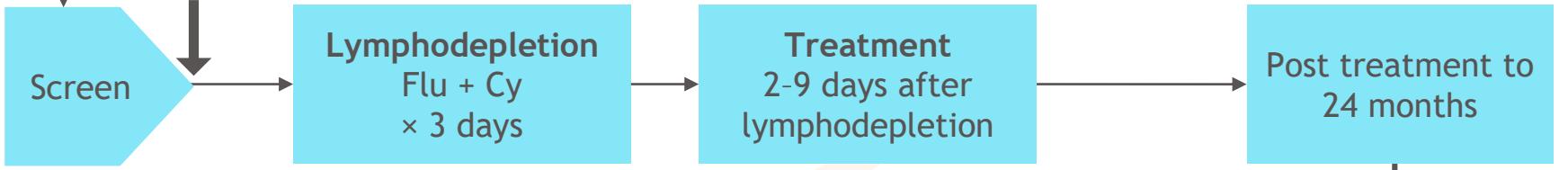
ACR, American College of Rheumatology; CAR, chimeric antigen receptor; CD, cluster of differentiation.

Breakfree-1 study design (Ph1 clinical trial)

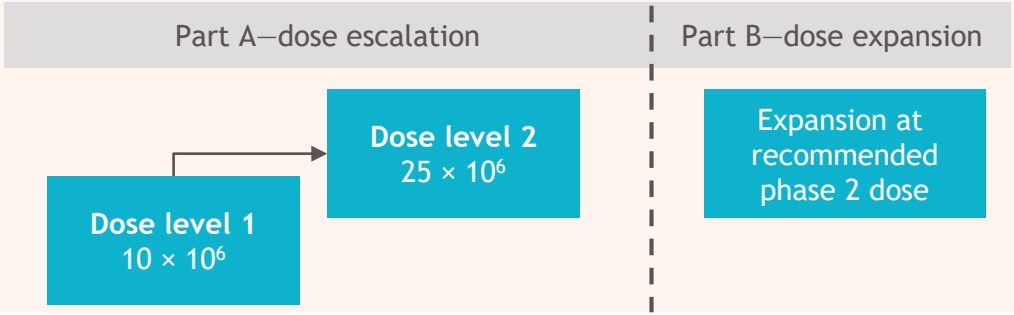
Key inclusion criteria

Cohort	Active disease	Inadequate treatment responses
SLE (n = 11)	≥ 1 major organ system with a recent **BILAG A score**	Glucocorticoids and **2 other immunosuppressants**
SSc (n = 3)	**Progressive diffuse cutaneous involvement OR ILD[a]**	1 **immunosuppressant**
IIM (n = 1)	**Severe muscle OR skin involvement**	Glucocorticoids and **2 other immunosuppressants**

Overall study design



Dosing scheme



Endpoints

Primary endpoints: safety/tolerability and recommended phase 2 dose in each indication

Secondary endpoints: preliminary efficacy and pharmacokinetics in each indication

[a]Progressive ILD as defined by Raghu G, et al. *Am J Respir Crit Care Med* 2022;205:e18-e47.

BILAG, British Isles Lupus Assessment Group; Cy, cyclophosphamide; Flu, fludarabine; IIM, idiopathic inflammatory myopathy; ILD, interstitial lung disease; SLE, systemic lupus erythematosus; SSc, systemic sclerosis.

Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14-19, 2024; Washington, DC; Presentation 1753.

Patient baseline characteristics

	SLE (n = 11)	SSc (n = 3)	IIM (n = 1)
Median age (range), years	29.0 (18-49)	47.0 (43-55)	30.0 (30-30)
Female sex, n (%)	10 (90.9)	3 (100.0)	1 (100.0)
Median time from disease diagnosis to BMS-986353 infusion (range), years	7.3 (1.1-17.0)	1.2 (0.4-1.3)	3.6 (3.6-3.6)
Median number of prior therapies (range)	7.0 (3-10)	2.0 (2-5)	4.0 (4-4)
Median Physician's Global Assessment (range)[a]	2.0 (1.0-2.7)	6.5 (6.0-7.0)[b]	3.4 (3.4-3.4)
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)		
Median total mRSS (range)[d]	—	34.0 (14-42)	—
Median total MMT-8 (range)[e]	—	—	91.0 (91.0-91.0)

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

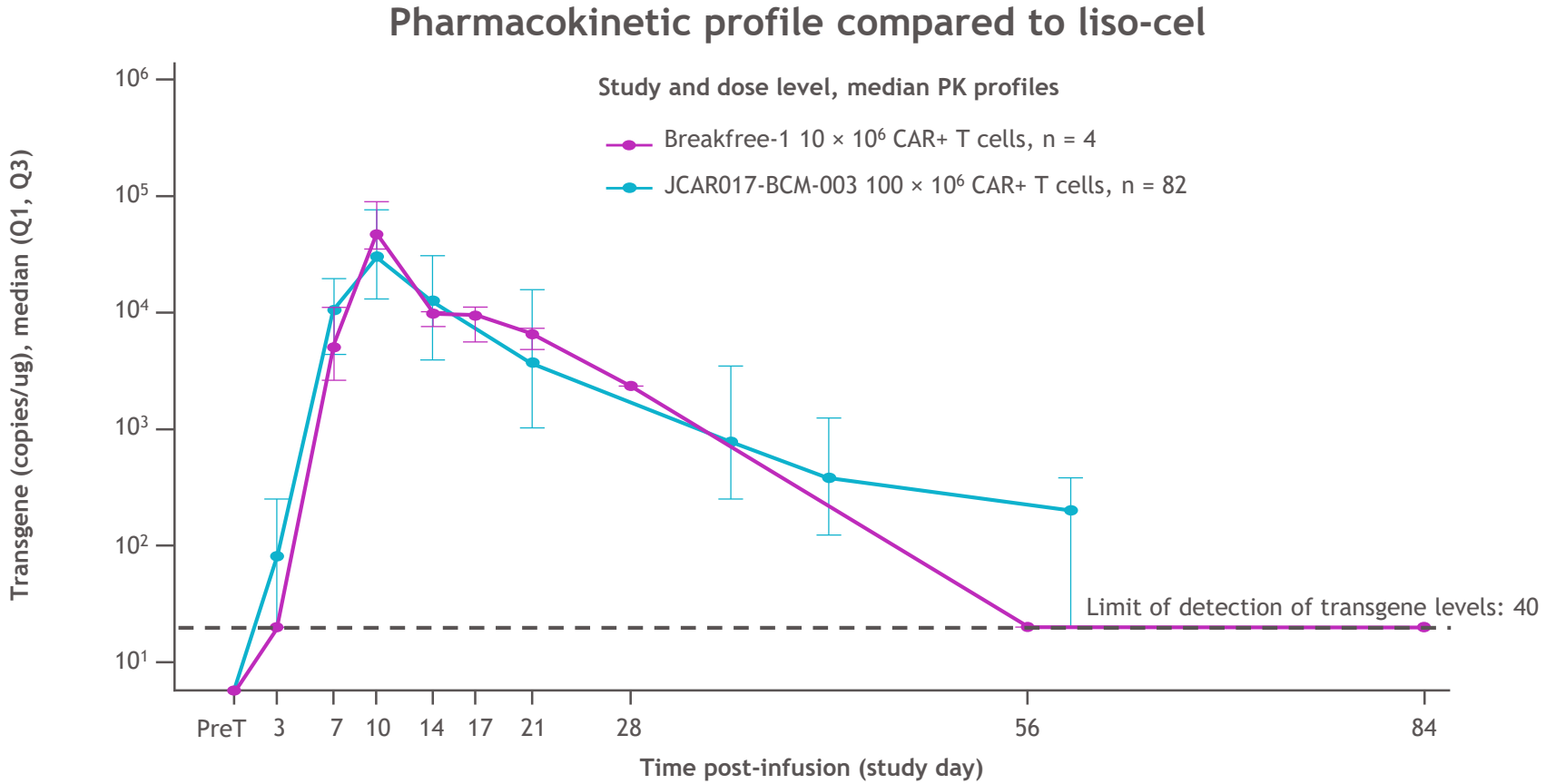
Safety evaluable patients (n = 15) are those treated with BMS-986353; efficacy evaluable patients (n = 7) are those who received ≥ 1 SLE efficacy assessment.
[a]Score scale: 1-10; [b]n = 2; [c]Score scale: 0-105; [d]Score scale: 0-51; [e]Score scale: 0-150.
BILAG, British Isles Lupus Assessment Group; IIM, idiopathic inflammatory myopathy; MMT-8, Manual Muscle Testing 8; mRSS, modified Rodnan skin score; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SSc, systemic sclerosis.
Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14-19, 2024; Washington, DC; Presentation 1753.

Prior medications

	SLE (n = 11)
Median number of prior therapies, n (range)	7.0 (3–10)
Biologics, n (%)	
Anifrolumab	4 (36.4)
Belimumab	8 (72.7)
Obinutuzumab	1 (9.1)
Rituximab	6 (54.5)
Other immunosuppressants, n (%)	
Azathioprine	5 (45.5)
Cyclosporin	1 (9.1)
Cyclophosphamide	3 (27.3)
Hydroxychloroquine	9 (81.8)
Methotrexate	2 (18.2)
Mycophenolate[a]	11 (100)
Tacrolimus	2 (18.2)
Voclosporin	1 (9.1)

[a]Includes mycophenolate mofetil (n = 6), mycophenolate sodium (n = 3), and mycophenolic acid (n = 2).
SLE, systemic lupus erythematosus.
Bristol Myers Squibb. Data on file. 2025.

Robust CAR T cell expansion in all evaluable patients with SLE after BMS-986353 infusion



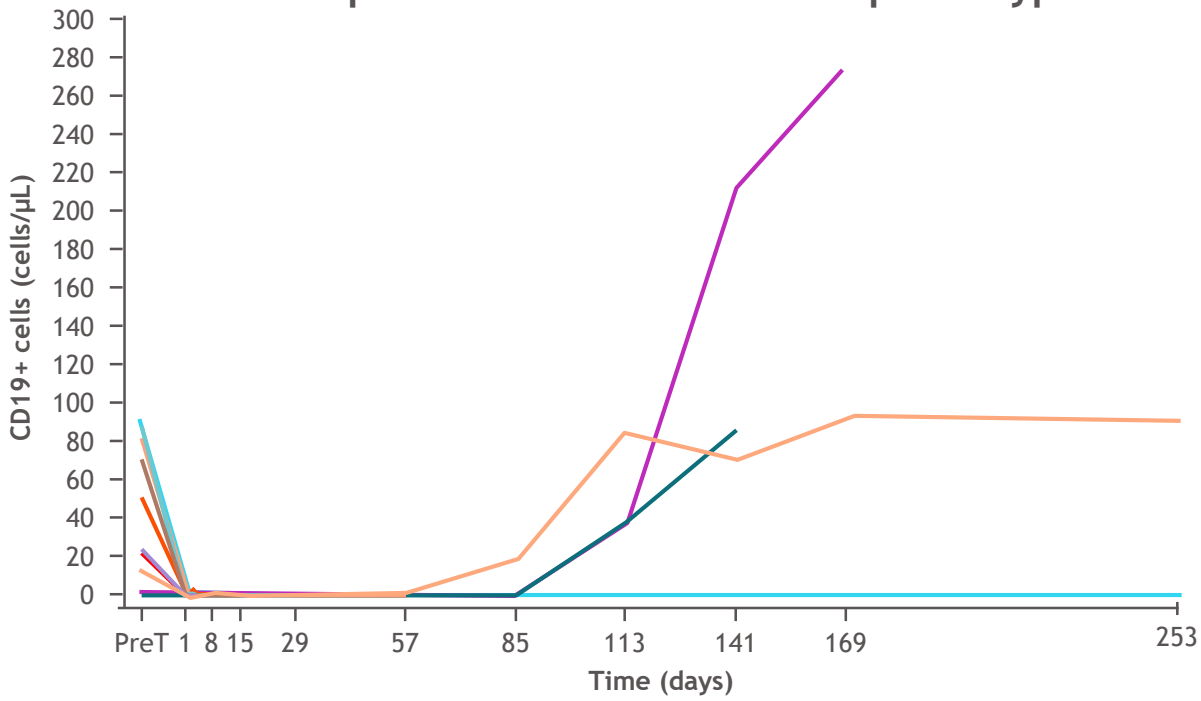
Robust CD19 NEX-T® cell expansion at 10 × 10^6 (dose level 1) CAR+ T cells in patients with SLE is comparable to that at 10-fold higher dose of liso-cel (approved dose, 100 × 10^6 CAR+ T cells) in patients with non-Hodgkin lymphoma

CAR, chimeric antigen receptor; CD, cluster of differentiation; liso-cel, lisocabtagene maraleucel; PK, pharmacokinetic; PreT, pretreatment; SLE, systemic lupus erythematosus.

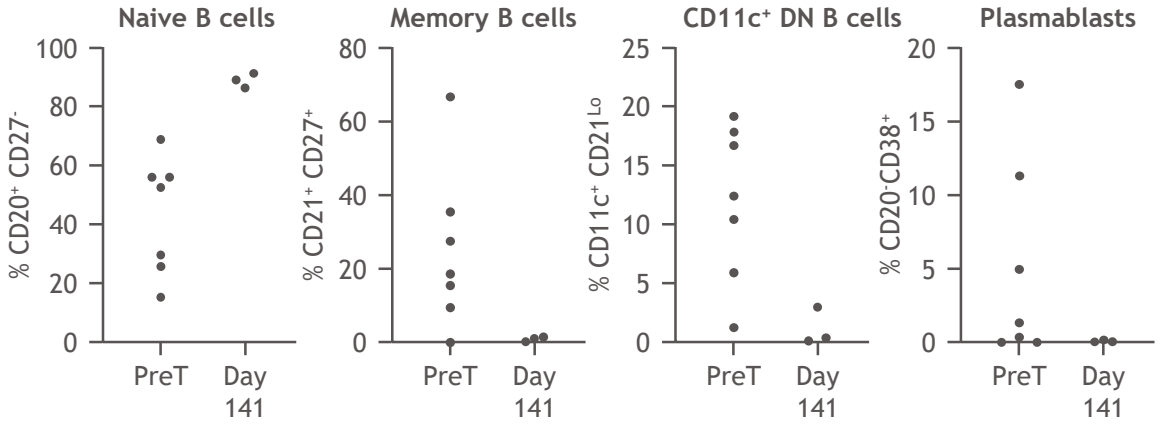
Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14-19, 2024; Washington, DC; Presentation 1753.

Complete peripheral B-cell depletion in all evaluable patients with SLE after BMS-986353 infusion

Peripheral B-cell kinetics and phenotypes[a]



SLE B-cell phenotyping



- In all patients, B cells were undetectable in the periphery by day 8 post–BMS-986353 infusion
- In patients with > 3 months of follow-up, B cells returned at a median (range) of 113 days (not reached at 85 days)
- In patients with SLE, repopulating B cells were mainly naive B cells, with very few memory B cells, CD11c+ DN B cells or plasmablasts

[a]Each line represents a patient with SLE.
CD, cluster of differentiation; DN, double negative; PreT, pretreatment; SLE, systemic lupus erythematosus.
Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14–19, 2024; Washington, DC; Presentation 1753.

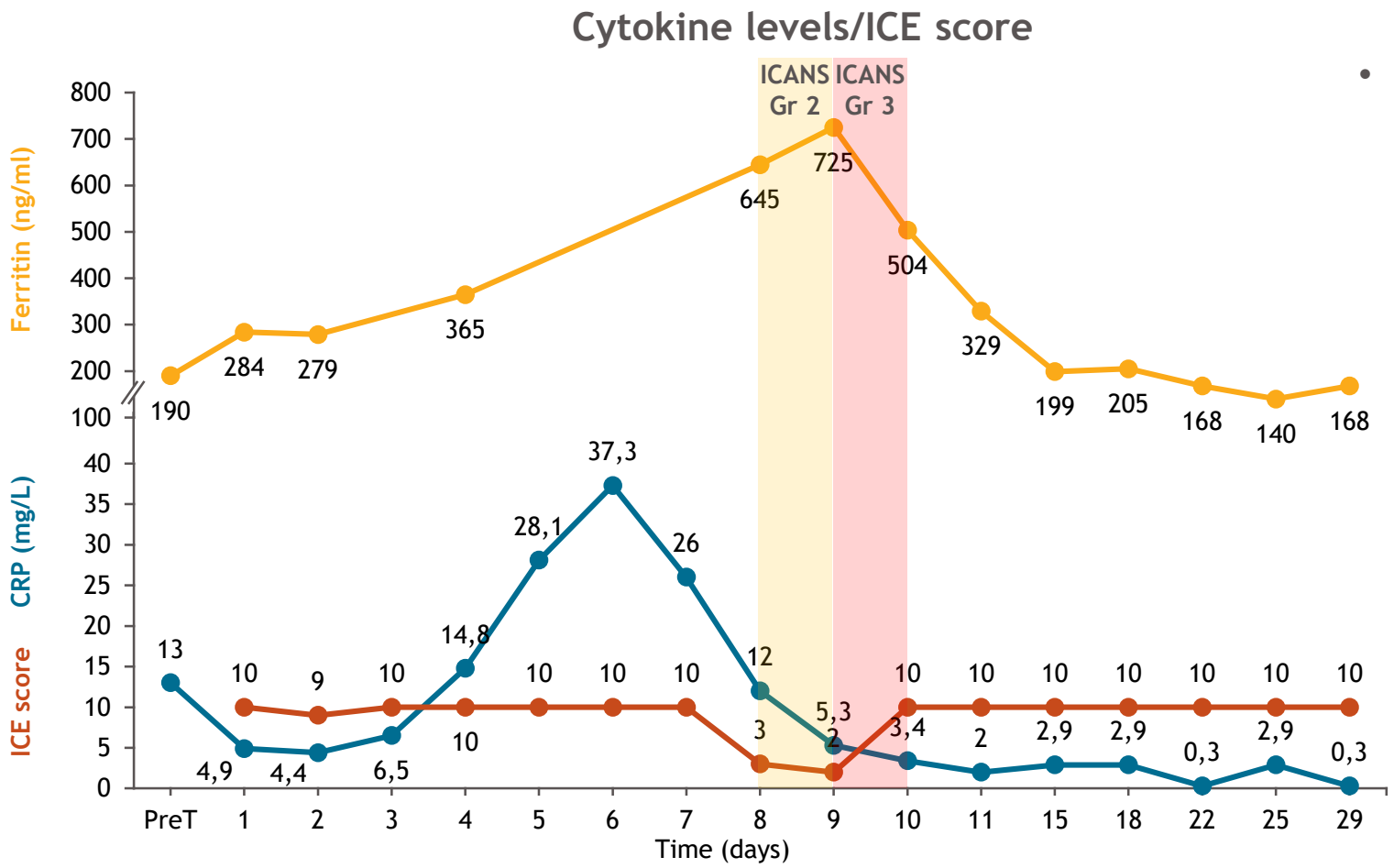
Safety: all TEAEs of interest were transient and reversible

TEAEs, n (%)	Overall (n = 15)	
	Any grade	Grade 3/4
Any TEAE	15 (100)	11 (73.3)
Hematologic[a]	11 (73.3)	8 (53.3)
Neutropenia	10 (66.6)	7 (46.7)
Anemia	5 (33.3)	1 (6.7)
Thrombocytopenia	3 (20.0)	0
TEAEs of interest		
Prolonged cytopenias (> 28 days)	0	0
Infections	3 (20.0)	0

CRS and ICANS	SLE (n = 11)		Overall (n = 15)	
	CRS	ICANS	CRS	ICANS
Max grade, n (%)	6 (54.5)	1 (9.1)	8 (53.3)	2 (13.3)
Grade 1	5 (45.5)	0	6 (40.0)	1 (6.7)
Grade 2	1 (9.1)	0	2 (13.3)	0
Grade 3	0	1 (9.1)	0	1 (6.7)
Grade 4/5	0	0	0	0
Median onset (range), days	7.0 (2-11)	8.0 (8-8)	7.5 (2-11)	9.0 (8-10)
Median duration[b] **(range), days**	2.0 (1-5)	3.0 (3-3)	2.0 (1-5)	3.0 (3-3)
Common treatments,[c] **n (%)**				
Tocilizumab	3 (27.3)	0	5 (33.3)	0
Glucocorticoids	2 (18.2)	1 (9.1)	2 (13.3)	1 (6.7)
Anakinra	0	1 (9.1)	0	1 (6.7)

Data cutoff: September 26, 2024; median follow-up (range): 65.0 (3-316) days. Common Terminology Criteria for Adverse Events, Version 5.0 are used for AE grading except for CRS, which is graded based on Lee DW et al. *Blood*. 2014;124:188-195, and for tumor lysis syndrome, which is graded based on the Cairo-Bishop Criteria.
[a]Neutrophil count decrease and lymphocyte count decrease are included in the overall hematologic TEAEs and are distinct terms from neutropenia and lymphopenia; [b]Multiple events occurring within 7 days from each other are considered as one episode; [c]Data on common treatment were validated after data cutoff.
AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; SLE, systemic lupus erythematosus; TEAE, treatment-emergent AE.
Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14-19, 2024; Washington, DC; Presentation 1753.

ICANS grade 3 patient resolved completely



- 25-year-old female patient diagnosed with SLE in June 2023
- Prior therapies included methylprednisolone, MMF, HCQ, tacrolimus, belimumab, anifrolumab, and colchicine

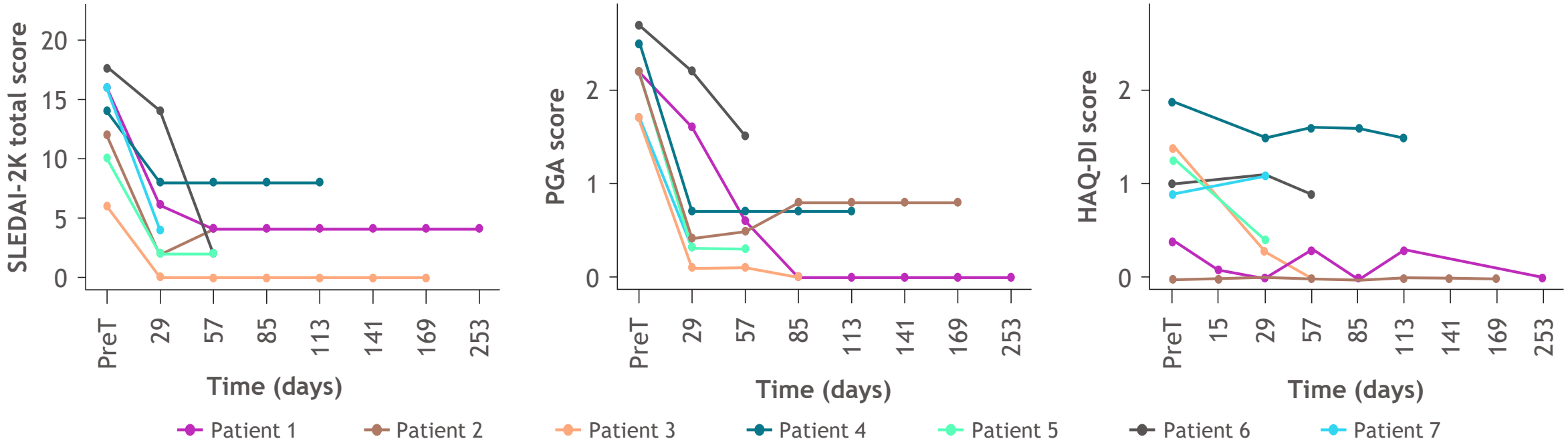
Grade 3 ICANS occurred on days 8–10 after a grade 1 CRS (days 6–8, treated with tocilizumab)

- Symptoms: “waxing and waning mental status” and “decreased level of consciousness”
- Transient and resolved completely on day 10 after cessation of confounding medications (including oxycodone for pleuritic pain) and the prompt treatment with dexamethasone and anakinra

Ferritin level was measured in ng/mL (range, 5–204). CRP level was measured in mg/L (range, 0–5).
CRP, C-reactive protein (mg/L); CRS, cytokine release syndrome; Gr, grade; HCQ, hydroxychloroquine; ICANS, immune effector cell-associated neurotoxicity syndrome; ICE, immune effector cell encephalopathy; MMF, mycophenolate mofetil; PreT, pretreatment; SLE, systemic lupus erythematosus.
Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14–19, 2024; Washington, DC; Presentation 1753.

Efficacy: clinical response in patients with SLE

Clinical responses in SLE with follow-up of at least 1 month after BMS-986353 infusion (n = 7)



Median SLEDAI score reduction of 10 points

Median PGA score reduction of 82%

Median HAQ-DI score reduction of 60%

All patients with SLE remain off all therapies including glucocorticoids
No evidence of new disease activity in patients with SLE at up to 11 months of follow-up

HAQ-DI, health assessment questionnaire disability index; PGA, physician global assessment; PreT, pretreatment; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000.

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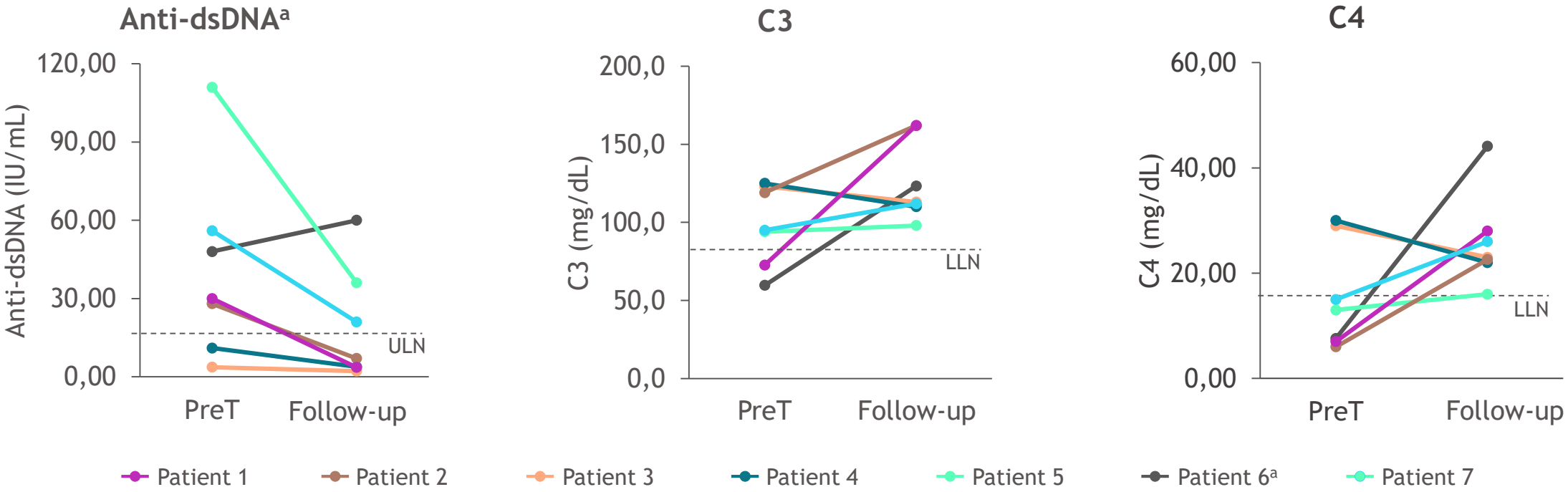
Effects of BMS-986353 on autoantibody and complements



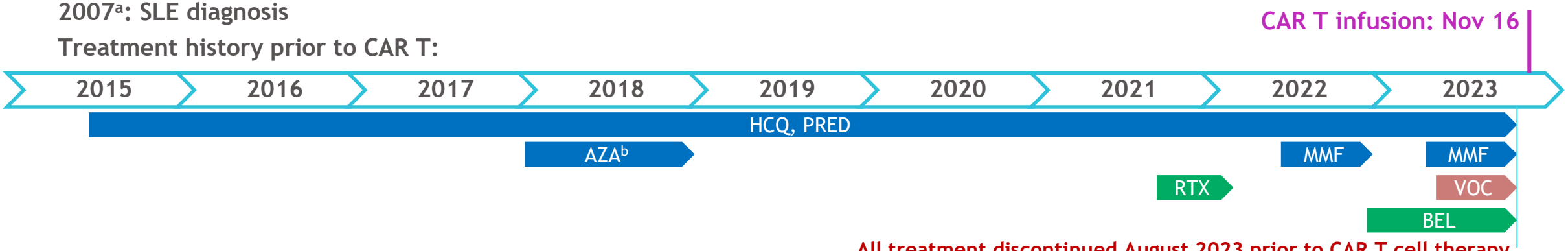
- **Anti-dsDNA antibodies decreased over time and were negative by day 85 (month 3)[a]**
- **C3 and C4 reached normal range by day 29**

Follow-up value used the measurement at most recent follow-up. Patient 1, 253 days; Patient 2, 253 days; Patient 3, 169 days; Patient 4, 113 days; Patient 5, 57 days; Patient 6, 57 days; Patient 7, 29 days.
[a]Anti-dsDNA: local from 276.00 IU at pre-treatment to 41.00 IU.
C, complement factor; ds, double-stranded; LLN, lower limit of normal; PreT, pretreatment; ULN, upper limit of normal.
Schett G, et al. Oral presentation at the ACR Convergence 2024 meeting; November 14-19, 2024; Washington, DC; Presentation 1753.

Example: Female, 30 yrs, 17-year history of SLE and LN

2007[a]: SLE diagnosis

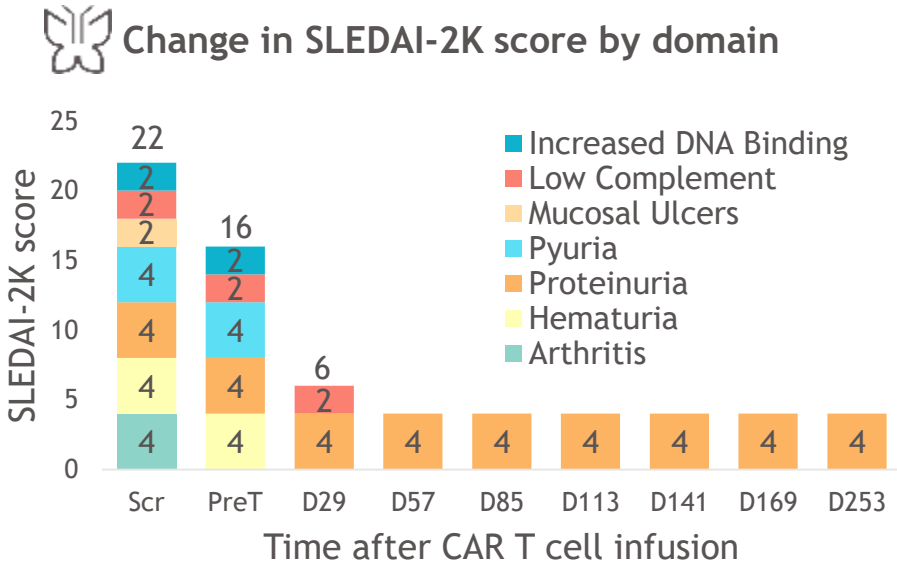
Treatment history prior to CAR T:



All treatment discontinued August 2023 prior to CAR T cell therapy

Presentation at screening

Body system	BILAG	Comments
Renal	A	At screening: deteriorating proteinuria (UPCR = 545 mg/mmol) and active sediment (hematuria, pyuria) Renal biopsy (18-May-23) Lupus nephritis class IIIC/V Chronicity: 05/12 (moderate) Activity: 12/24 (moderate to severe)
Musculoskeletal	B	Moderate arthritis/tendonitis/tenosynovitis
Mucocutaneous	C	Mucosal ulcers
Hematologic	D	Previous involvement Isolated Coombs test-positive
Autoantibodies at screening: **ANA, anti-chromatin, anti-dsDNA, anti-Smith** SLE-related medical history: hemolytic anemia (Coombs+)		

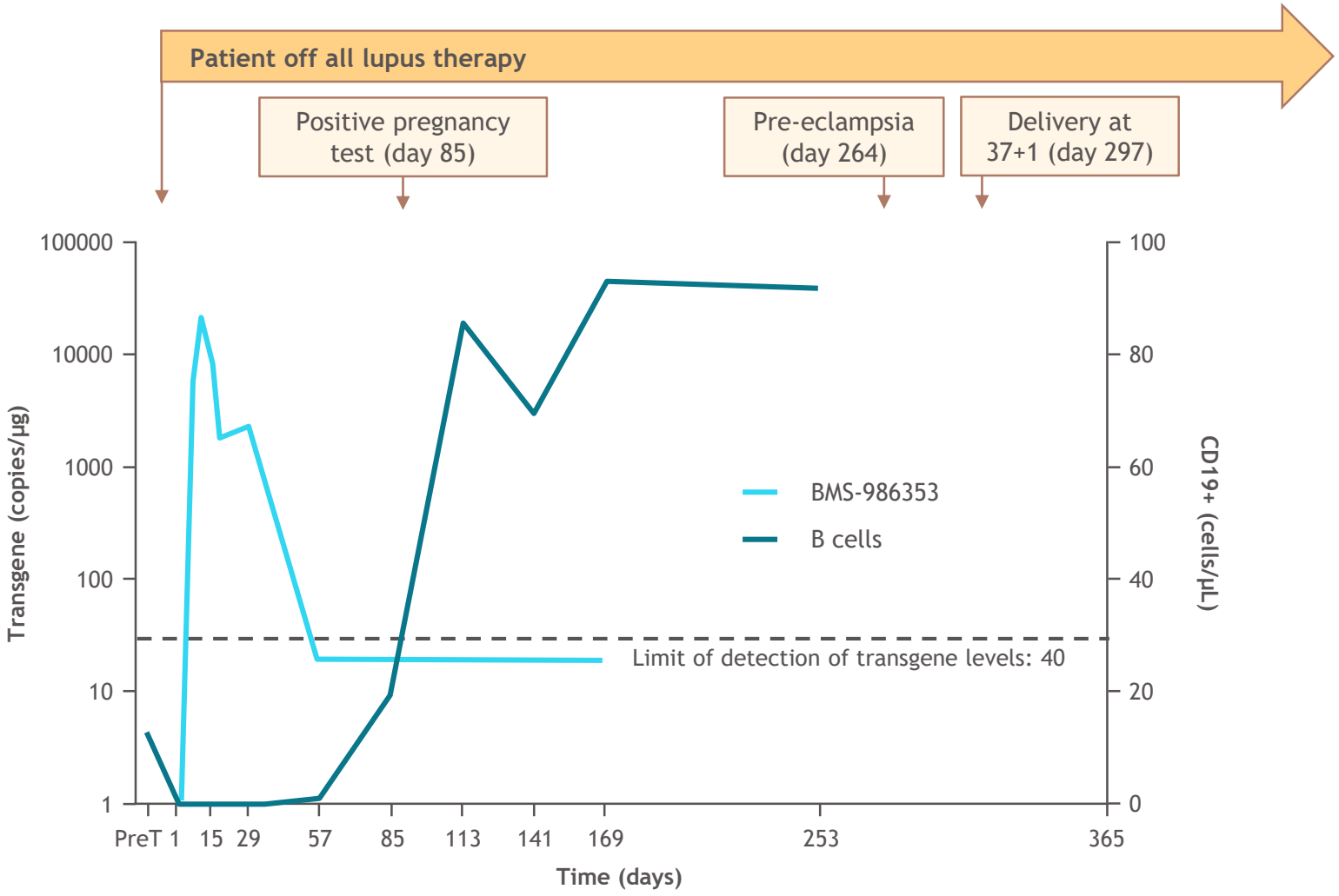


[a]Date of diagnosis unknown. [b]Start date unknown.

ANA, antinuclear antibody; AZA, azathioprine; BEL, belimumab; BILAG, British Isles Lupus Assessment Group; CAR, chimeric antigen receptor; ds, double-stranded; HCQ, hydroxychloroquine; MMF, mycophenolate mofetil; PRED, prednisone; PreT, pretreatment; RTX, rituximab; Scr, screening; SLE, systemic lupus erythematosus; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index-2000; UPCR, urine protein-to-creatinine ratio; VOC, voclosporin.

Bristol Myers Squibb. Data on file. 2025.

One patient became pregnant shortly after BMS-986353 infusion



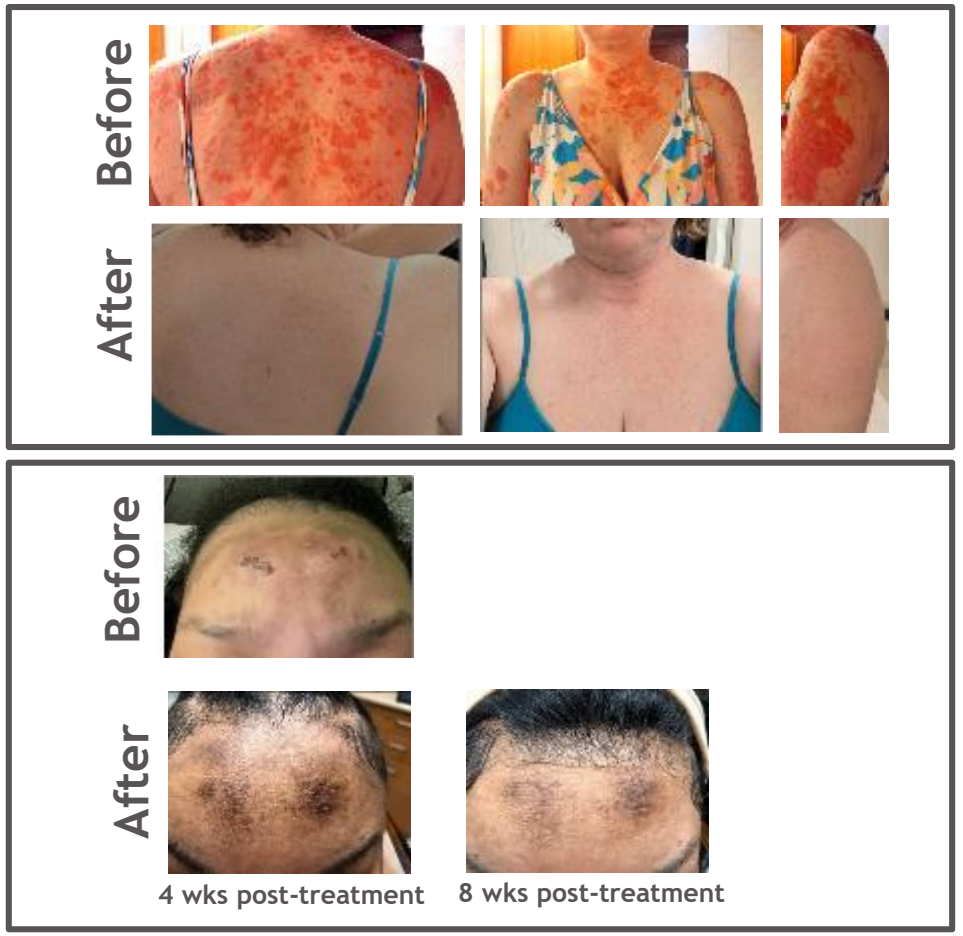
- Patient weaned off all lupus-directed medications prior to BMS-986353 infusion
- Uncomplicated vaginal delivery at 37+1 weeks, following induction due to pre-eclampsia
- Newborn male was born with normal CD19+ B cell and CD3+ T cell numbers
  - Small for gestational age (attributed to pre-eclampsia)
- Patient remains off all lupus-directed medications without evidence of new disease activity

Bristol Myers Squibb. Data on file. 2025.

Summary

Promising preliminary safety results of BMS-986353 in patients with severe, refractory SLE, SSc and IIM, and efficacy in SLE from ongoing phase 1 study

- Safety data for the first 15 treated patients (SLE, SSc, IIM) show a good safety profile with no unexpected AEs
- Complete B-cell depletion and robust CAR T cell expansion comparable to hematology-established liso-cel treatment at the approved dose
- Efficacy data for the first 7 treated patients with SLE
  - Regression of disease activity and autoantibodies
  - Immunosuppression-free without evidence of new disease activity at up to 11 months of follow-up
- Re-emerging B cells were mainly naive and their reappearance was not associated with lupus flare
- Dose escalation is ongoing to determine recommended phase 2 dose of BMS-986353 with optimal safety and efficacy profiles



Photographs provided by investigators with the patient's written informed consent for publication.

[a]Top panel corresponds to a 35-year-old Caucasian patient; the "before" pictures were taken during the week prior to lymphodepletion and "after" pictures were taken ~3 weeks post-infusion; bottom panel corresponds to a 25-year-old female Black or African American patient.
AE, adverse event; CAR, chimeric antigen receptor; IIM, idiopathic inflammatory myositis; liso-cel, lisocabtagene maraleucel; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; wk, week.
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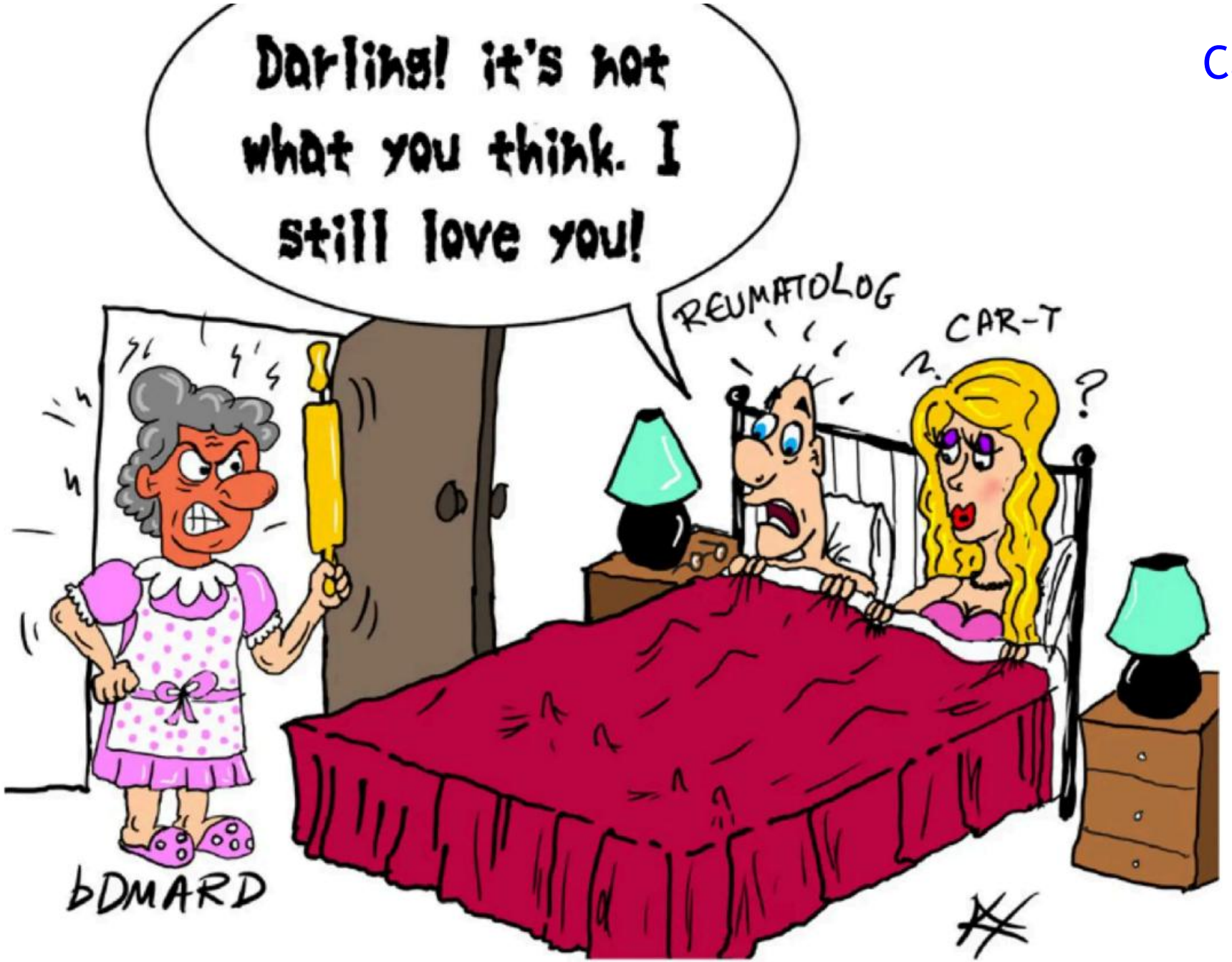

Cartoon by Aikaterini Chatzidionysiou, Karolinska Institute

Questions?