



## Debate 1

CD19 CAR T vs. CD19+BCMA CAR T

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# DISCLOSURES

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## **LUPUS RESEARCH ALLIANCE**

Scientific Advisory Board, Member

Lupus Clinical Investigators Network (LuCIN), Vice Chair

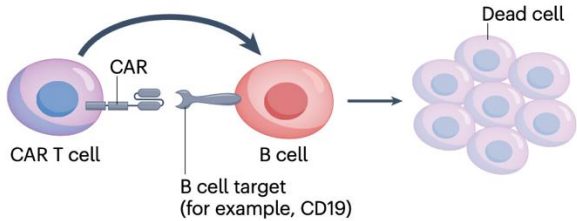
LuCIN Cell Therapy Advisory Group, Chair

## **INDUSTRY**

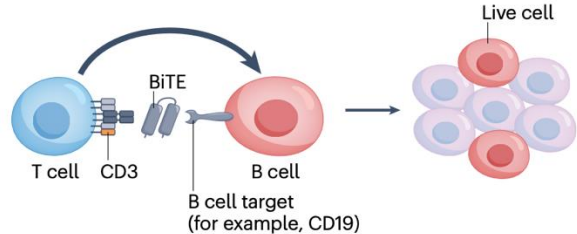
Consultant: Kyverna, Cabaletta, NKarta, Novartis, GSK, CRISPR, CLADE, Abbvie, Cullinan, Merk

# CD19-CAR-T Cell Therapy – Plenty of depletion

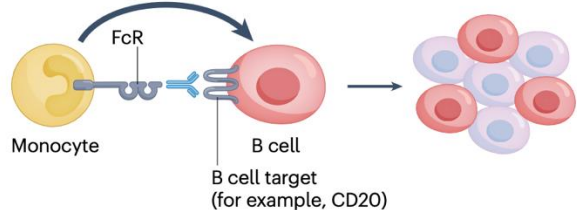
### CAR T cell-mediated killing



### Bi-specific T cell engager mediated killing

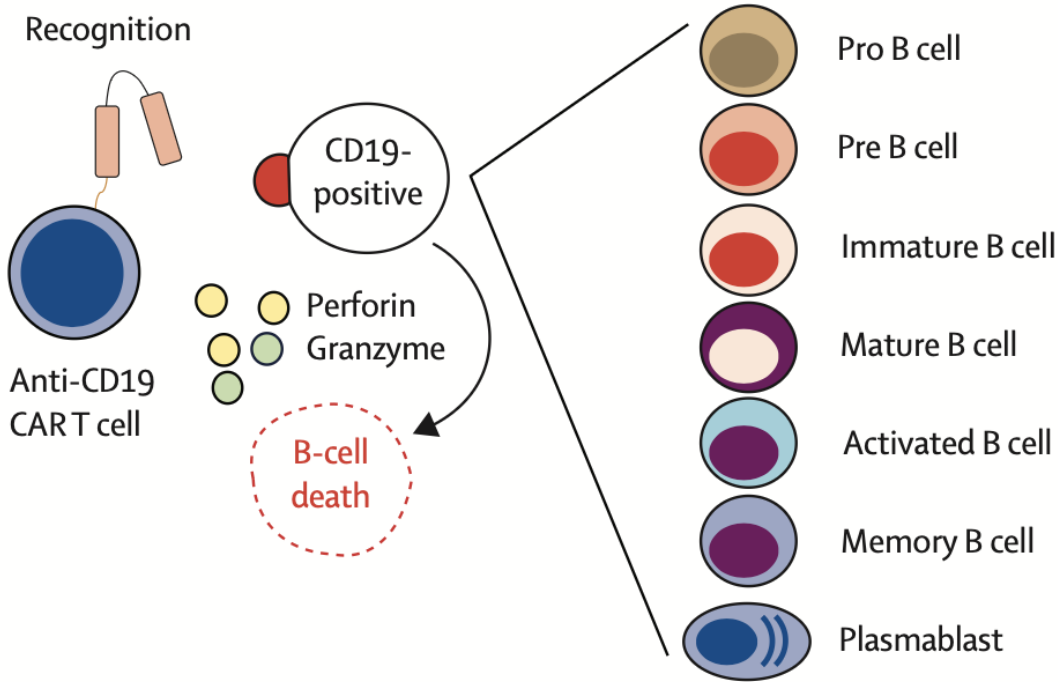


### Antibody-mediated killing



Residual B cells

### Recognition



# CD19-CAR-T Cell Therapy – A Data Driven point

## Clinical points

- Multiple Cohorts, some  $\geq 2$  years FUP
- >50 patients treated with publicly available results
- Excellent tolerability
- Unprecedented Efficacy
- Rare relapse
- Preservation of long term humoral immunity

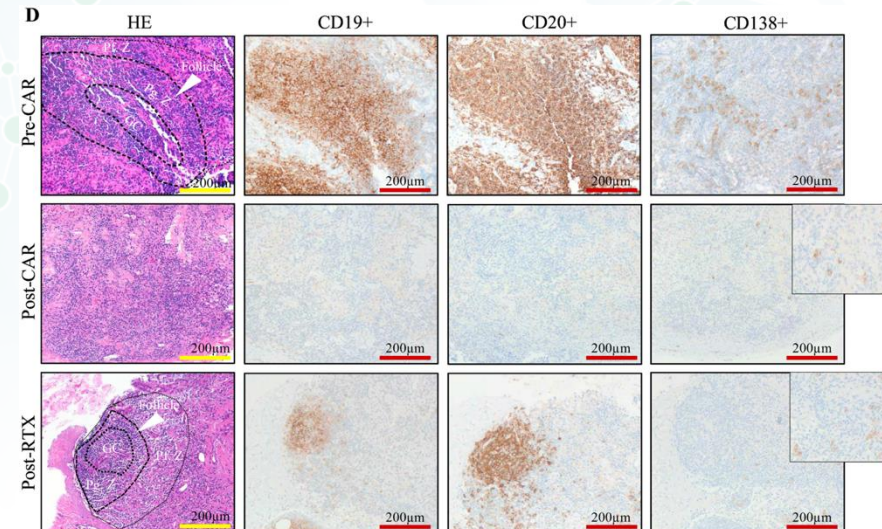
## Mechanistic Points

- Tissue CD19+ B cell depletion
- Deep CD19+ B cells reset to naïve status
- Type I IFN signature reset

A Short-Term Efficacy of CD19 CAR T-Cell Therapy in Autoimmune Disease

Patient No.	1	2	3	4	5	6	7	8
Disease	SLE							
DORIS Remission	+	+	+	+	+	+	+	+*
LLDAS	+	+	+	+	+	+	+	+*
SLEDAI-2K Score	0	0	0	0	0	0	0	0
ACR-EULAR Major Clinical Response	N/A							
Normalization of CK Level	N/A							
Change in EUSTAR-AI Score	N/A							
Change in mRSS	N/A							
Glucocorticoid-free State	+	+	+	+	+	+	+	+*
No Immunosuppressive Drugs	+	+	+	+	+	+	+	+*

N Engl J Med 2024; 390:687-700



Tur et al. *Ann Rheum Dis* 2024

# CD19-CAR-T Cell Therapy Allows potential rescue with BCMA-CAR T

nature medicine



Brief Communication

<https://doi.org/10.1038/s41591-025-03718-3>

## BCMA CAR T cells in a patient with relapsing idiopathic inflammatory myositis after initial and repeat therapy with CD19 CAR T cells

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Check for updates

Fabian Müller <sup>1,2,6</sup>, Andreas Wirsching <sup>2,3,6</sup>, Melanie Hagen <sup>2,3</sup>, Simon Völkl <sup>1,2</sup>, Carlo Tur <sup>2,3</sup>, Maria Gabriella Raimondo <sup>2,3</sup>, Jule Taubmann <sup>2,3</sup>, Laura Bucci <sup>2,3</sup>, Liang Zhang <sup>2,3</sup>, Sascha Kretschmann <sup>1,2</sup>, Michael Aigner <sup>1,2</sup>, Markus Eckstein <sup>4</sup>, Silvia Spörl <sup>1,2</sup>, Soraya Kharboutli <sup>1,2</sup>, Sebastian Böltz <sup>2,3</sup>, Armin Atzinger <sup>5</sup>, Luis Munoz <sup>2,3</sup>, Georg Schett <sup>2,3,6</sup>, Andreas Mackensen <sup>1,2,6</sup> & Ricardo Grieshaber-Bouyer <sup>2,3,6</sup>

If you believe the power of numbers...

	<b>CD19 CAR T</b>	<b>CD19/BCMA CAR T</b>
<b>lupus OR scleroderma OR dermatomyositis OR Sjogren OR ANCA OR multiple sclerosis OR myasthenia gravis</b>	<b>46</b>	<b>22</b>

Clinicaltrial.gov



# BCMA-CD19

## COMBINED CAR-T THERAPY

Jennifer Barnas, MD, PhD

Assistant Professor

University of Rochester Medical Center

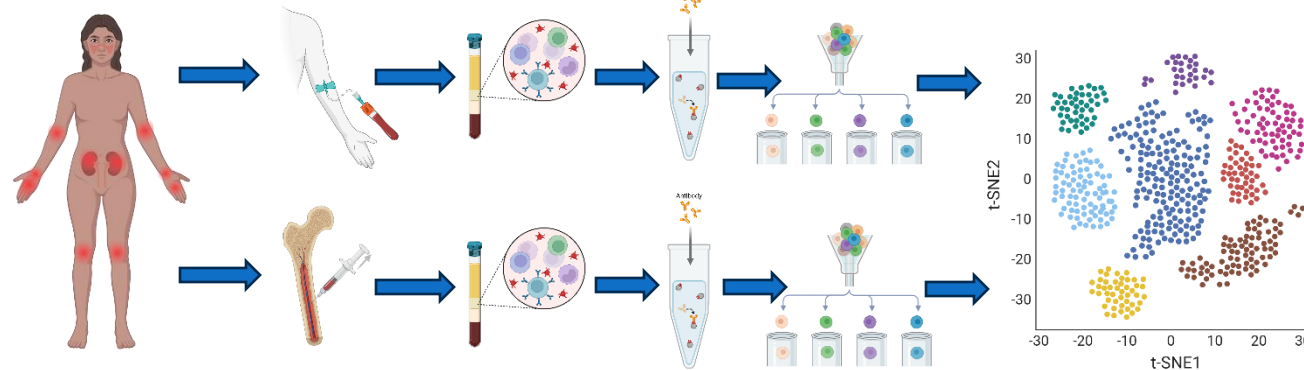
Rochester, New York, United States

# DISCLOSURES

- Nothing to Disclose

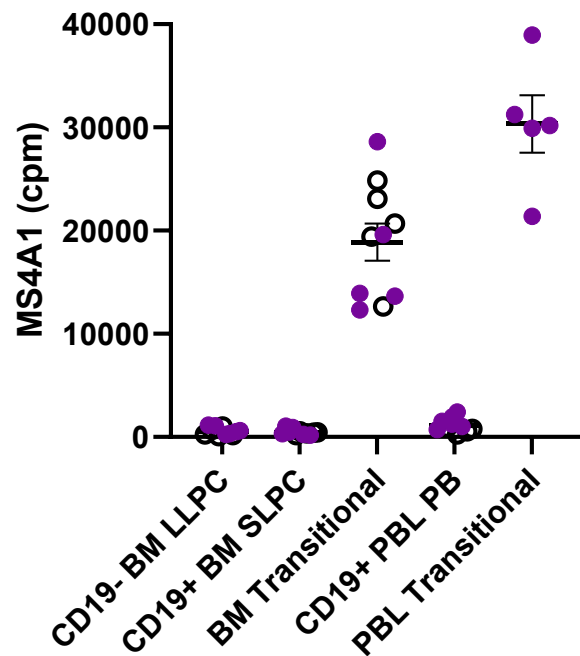
# CD19 CAR-T FOR AUTOIMMUNITY: WE HAVE A PROBLEM

## LONG-LIVED PLASMA CELLS DOWNREGULATE CD20 AND CD19

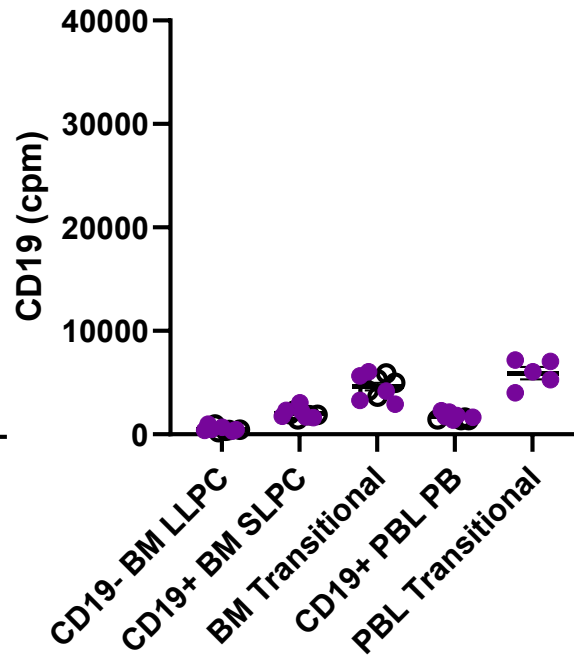


PLASMA CELLS MAKE  
AUTOANTIBODIES

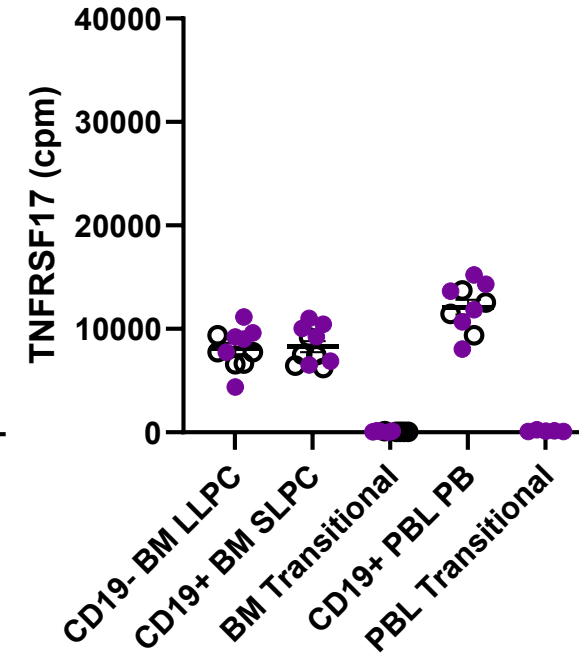
CD20 RNA



CD19 RNA



BCMA RNA



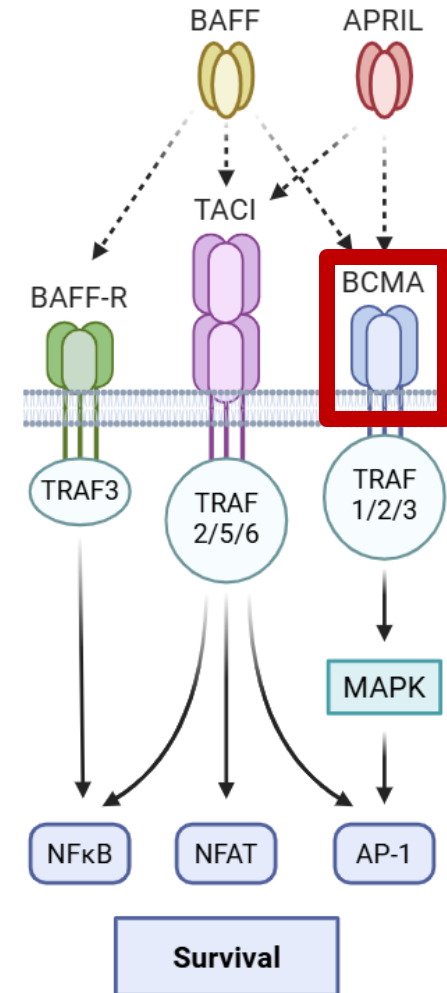
● SLE  
○ Healthy Donor

BM = bone marrow  
PBL = peripheral blood  
mononuclear cells

Barnas, unpublished data  
Bulk RNA-sequencing  
GEO GSE278120

# A PLASMA CELL TARGET: B-CELL MATURATION ANTIGEN (BCMA)

- Membrane bound surface receptor expressed on B cell lineage, especially plasmablast, plasma cells, and activated CD38+ memory B cells
- Also shed in the blood as soluble BCMA
- Binds B cell survival factors: BAFF & APRIL
- Combined CAR-T against BCMA & CD19 results in sustained remission in SLE

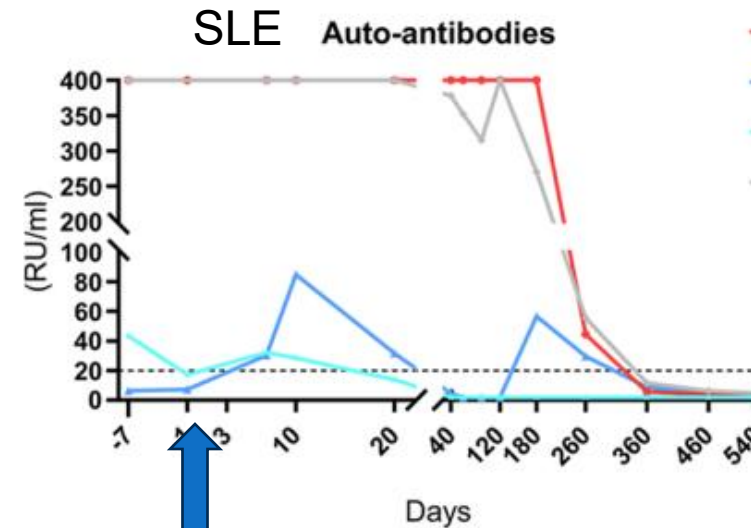
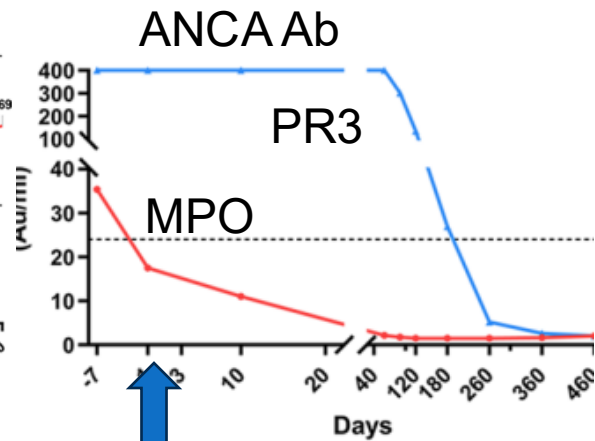
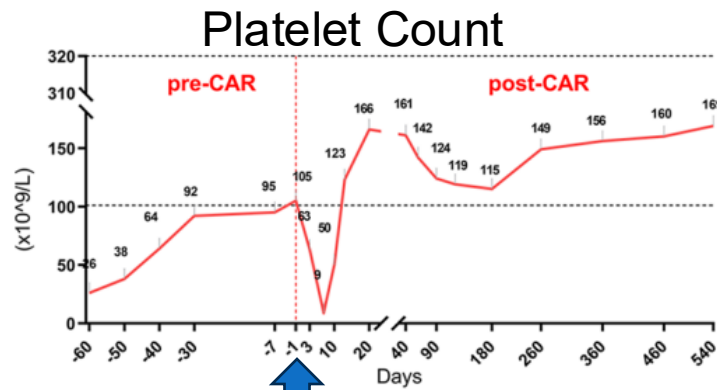


# NOT ALL AUTOANTIBODIES ARE CREATED EQUALLY

- Case report of SLE overlap patient with ANCA antibodies, lupus nephritis, Sjogren's and immune-mediated thrombocytopenia
- Lymphodepletion with cyclophosphamide 300 mg/m<sup>2</sup>/day normalized anti-MPO
- Anti-platelet & anti-Smith respond rapidly to BCMA-CD19 CAR-T
- Anti-PR3, Anti-U1-snRNP, anti-SSA and ANA antibodies eliminated more slowly with CAR-T BCMA-CD19

Remission for 1.5 years with no autoantibodies

Patient had grade 1 cytokine release storm



- Anti U1-snRNP antibodies
- Anti SSA/Ro52 antibodies
- Anti Sm antibodies
- Anti nuclear antibodies

BCMA-CD19  
CAR T

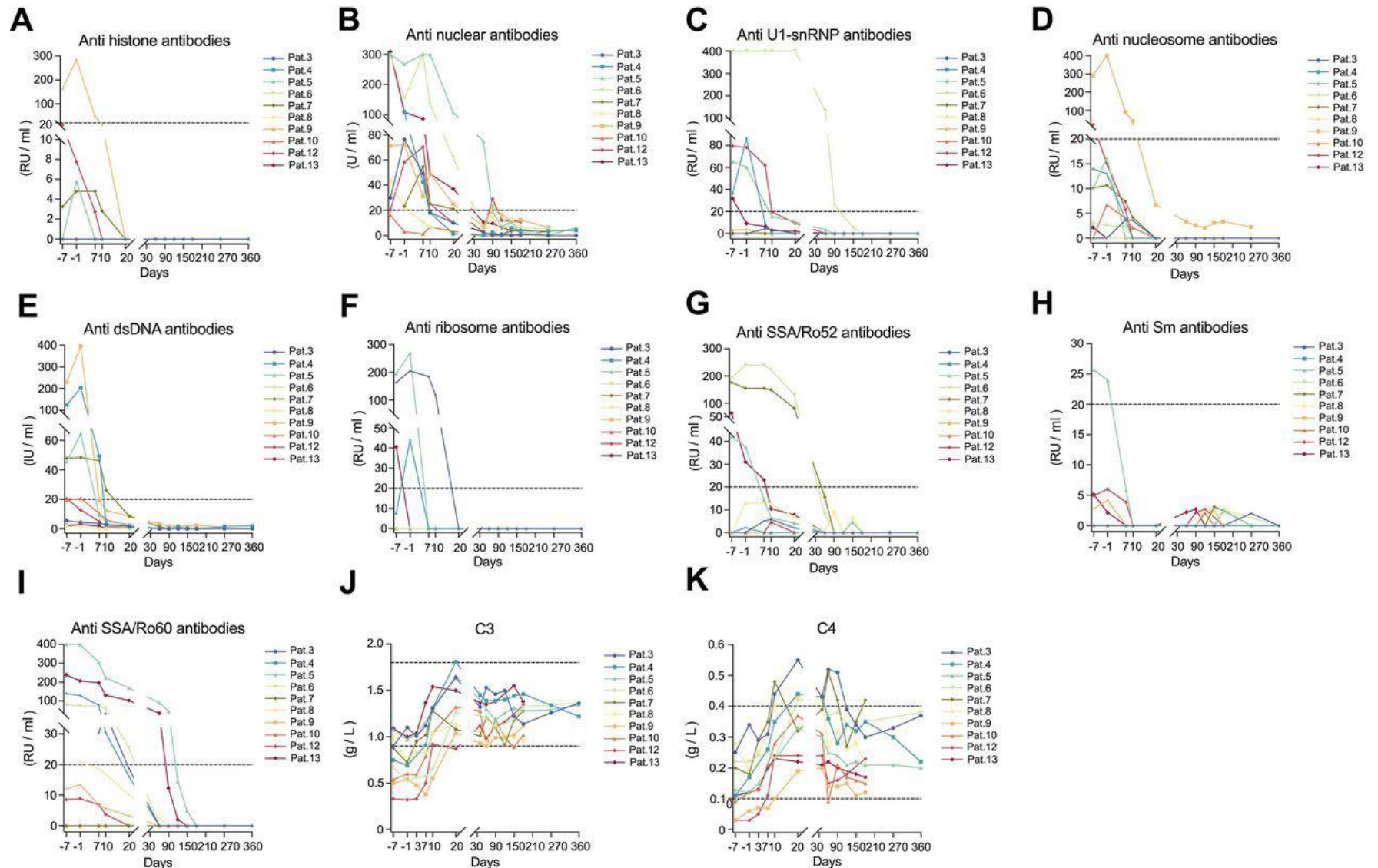
Wang W, et al. *Ann Rheum Dis* 2024; 83:1304–1314.

Wang et al. Validation of BCMA-CD19 Compound CAR-T Therapy in SLE Overlap Syndrome: Over 1.5-Year Follow-Up. *Stem Cell Rev Rep*. 2025 Jun 23

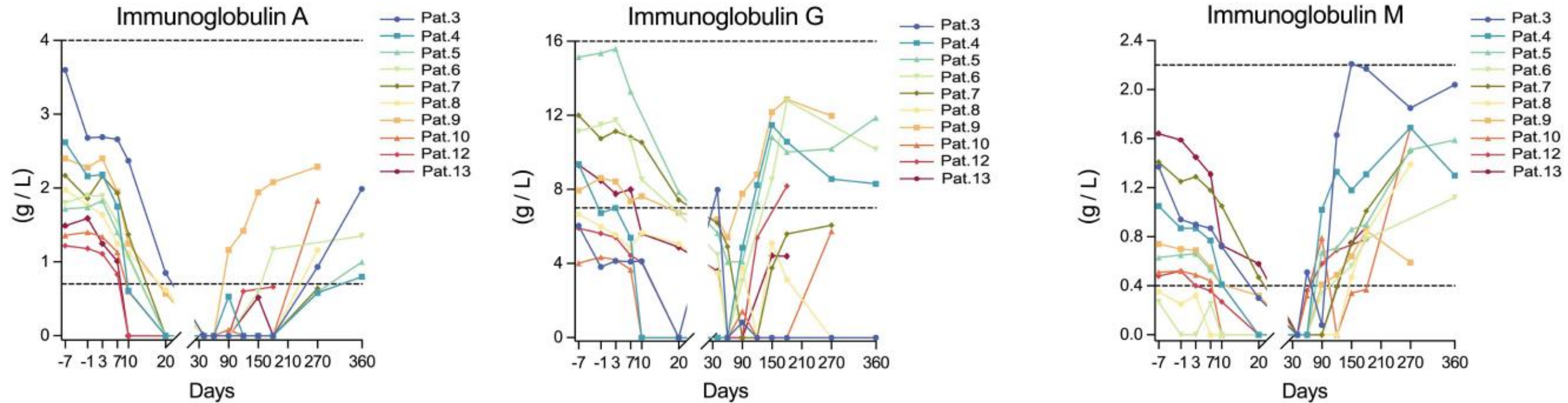


# BCMA-CD19 cCAR-T FOR SLE NEPHRITIS WORKS: AUTOANTIBODIES ALL GO DOWN

- Phase 1 open-label clinical trial in China
- 13 patients, first 2 also had lymphoma



# BUT OTHER ANTIBODIES ALSO GO DOWN....



- Vaccine titers are also falling
- B cell aplasia or hypogammaglobulinemia may necessitate immunoglobulin replacement

# BCMA-CD19 cCAR-T THERAPY CONCLUSIONS

- Offers both B cell and plasma cell targeting
- Allows for elimination of difficult to target autoantibodies from long-lived plasma cells
- Cytokine release storm adverse events have been mild
- Concerns for reduced titers against infectious diseases
- Greater concern immunoglobulin replacement might be needed