Stiff Person Syndrome: From Spotlight to the Science – A New Therapeutic Era

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SPS in the Spotlight

https://news.cuanschutz.edu/medicine/what-does-celine-dions-stiff-person-syndrome-diagnosis-mean

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Stiff Person Syndrome (SPS)

Rare, autoimmune neurological disorder characterized by progressive stiffness and episodic muscle spams, often triggered by noise, touch, or emotional stress

Autoantibodies: GAD65, Glycine Receptor Antibody, Amphiphysin

No FDA-approved therapies for this disease: IVIG often used as first-line therapy (positive control trial)

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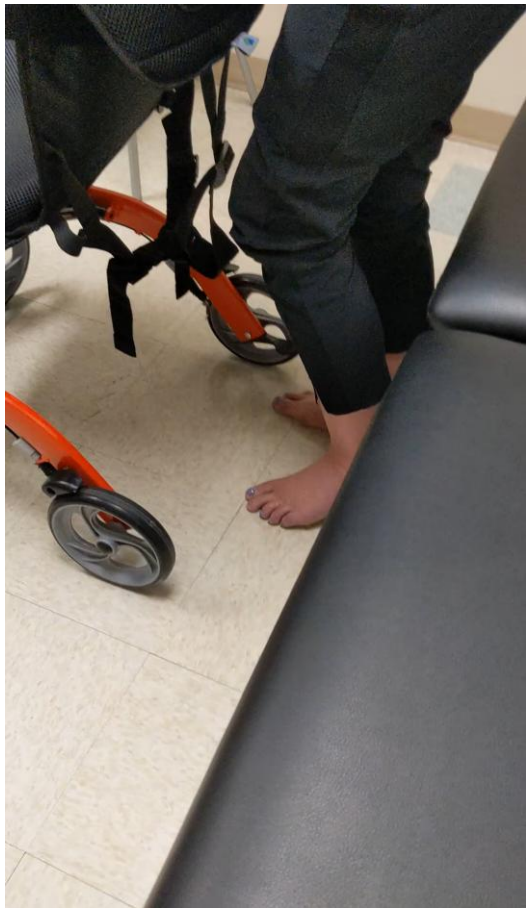
Walking Difficulties are Common in SPS



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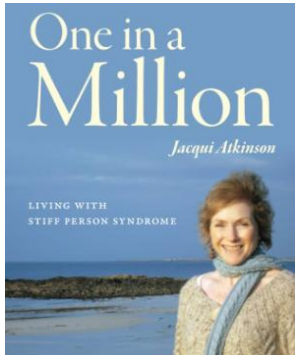
How Common is Stiff Person Syndrome?



One-in-a-million?

- Estimated prevalence of one in 1,250,000 from a Heidelberg, Germany center serving two to three million people, with 20 cases over 10 years (Meinck and Thompson in 2002)
- British Neurological Surveillance Unit identified 119 cases among the UK population over five years (2000-2005)
- US-based study found a point prevalence of 2.06 per million patients in a population of patients evaluated within the VA system (Galli et al, 2018)

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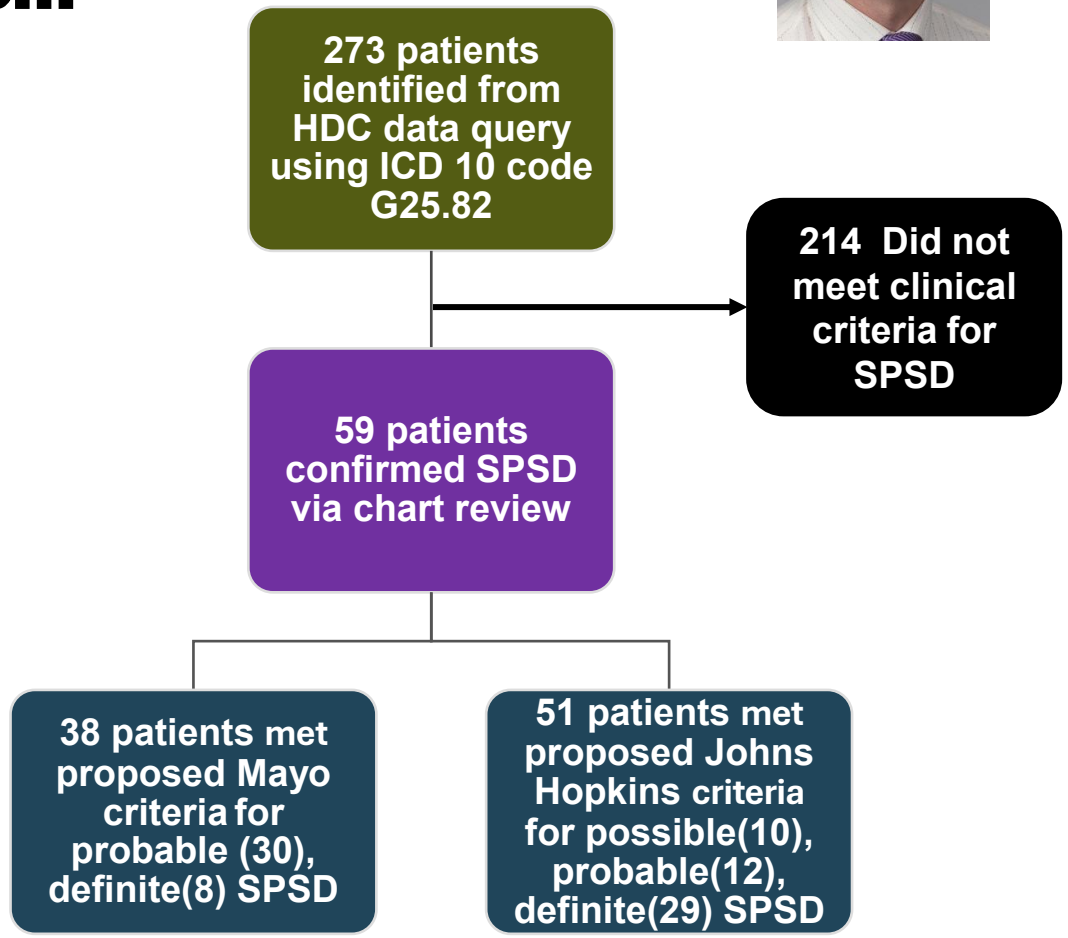
Not one-in-a-million: A Population-Based Study of Prevalence of Patients with Stiff Person Syndrome in a Large Colorado-Based Health System

Objectives:

1. Define the incidence and prevalence of SPSD within the University of Colorado Hospital (UCH) medical system.
2. Apply proposed criteria (Mayo[1] and Hopkins[2]) and examine the agreement between proposed diagnostic criteria.
3. Describe demographics and clinical features of our SPSD cohort



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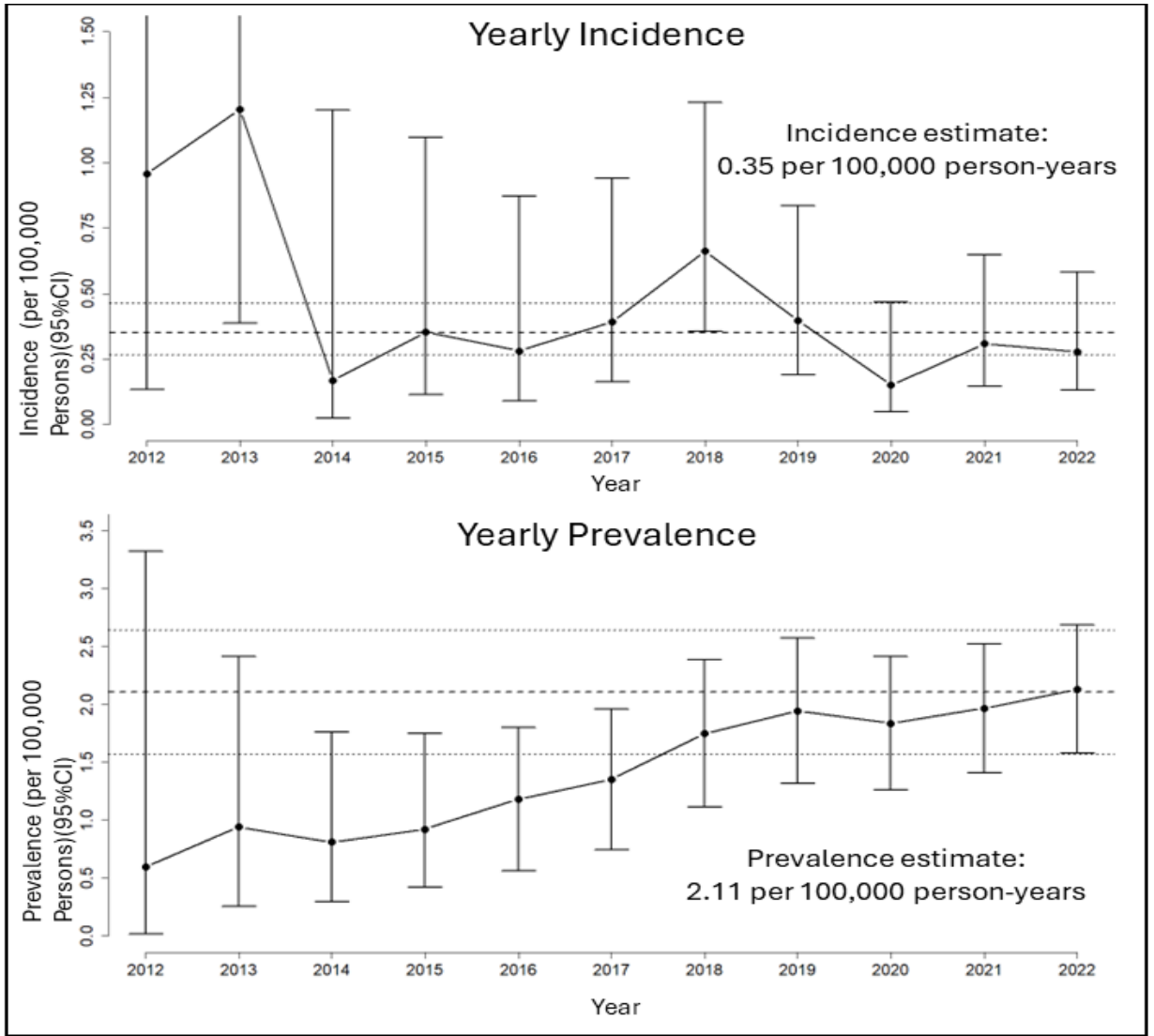
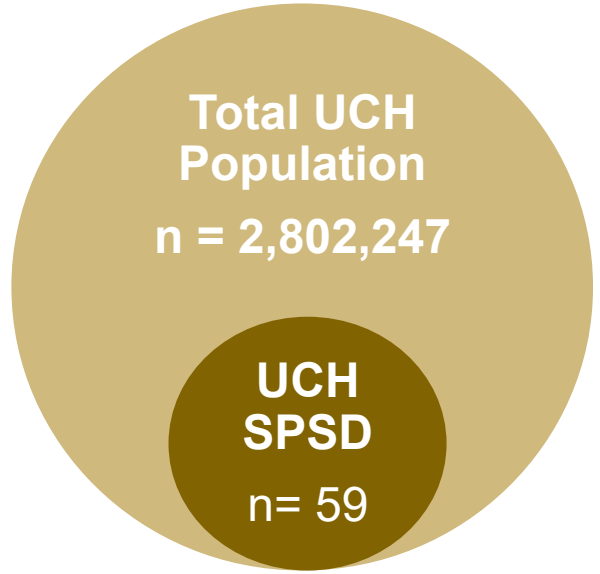
Crane PD, Sillau S, Dreher R, Fix R, Winters P, Van Coevering R, Engebretson E, Valdez B, Matthews E, Nair KV, Carlson AM, Piquet AL. Population-Based Study of the Epidemiology of Stiff Person Syndrome in a Large Colorado-Based Health System. Neurology. 2024 Dec 24;103(12).

Prevalence of Patients with Stiff Person Syndrome in a Large Colorado-Based Health System





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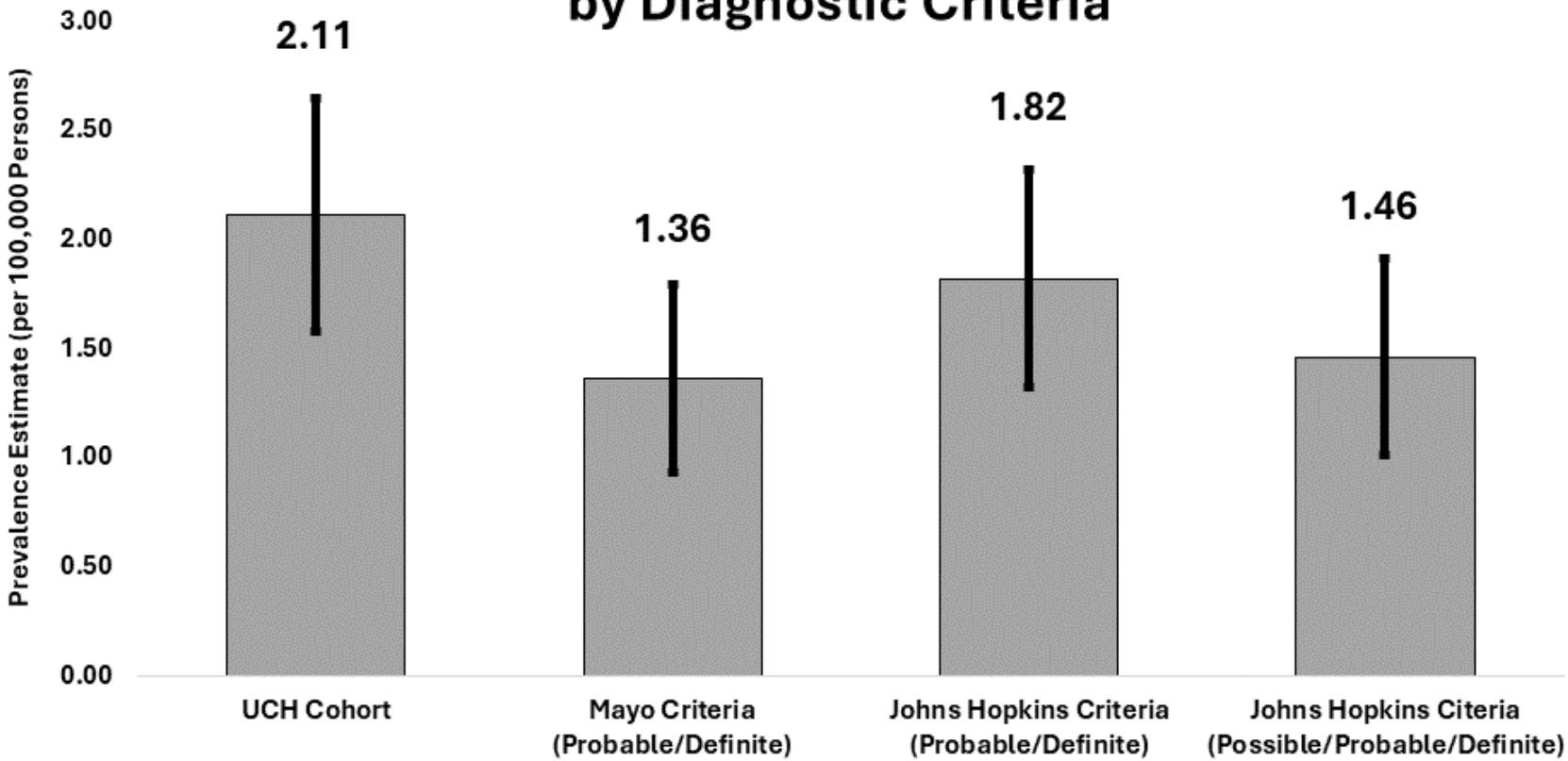
Prevalence Estimate (per 100,000 Persons) by Diagnostic Criteria



Diagnostic Designation	Time Range	Population Sample Size	Positive Patients	Prevalence Estimate (per 100,000 Persons)	95% Confidence Interval
UCH Cohort	2012-2022	2801674	59	2.11	1.57 - 2.64
Mayo Criteria (Probable/Definite)	2012-2022	2801674	38	1.36	0.93 - 1.79
Johns Hopkins Criteria (Probable/Definite)	2012-2022	2801674	41	1.46	1.02 – 1.91
Johns Hopkins Criteria (Possible/Probable/Definite)	2012-2022	2801674	51	1.82	1.32 – 2.32

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2-Pronged Treatment Approach

Symptomatic Therapies

- Benzodiazepines (GABA agonists)
- Anti-spasticity agents (baclofen)
- Anti-epileptics (gabapentin)
- Botulinum Toxin
- Supportive therapies: Physical therapy, hydrotherapy, psychological support (anxiety and phobias are common)

Immune Therapies

- Steroids
- Plasmapheresis
- IVIG (POSITIVE controlled trial)
- Rituximab (NEGATIVE controlled trial)
- Autologous hematopoietic stem cell transplant (aHSCT) - Research only
- Chimeric Antigen Receptor (CAR) T-cell therapy – Phase 2 clinical trial

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Miv-cel (Mivocabtagene Autoleucel; KYV-101) CD19 CAR T-Cell Therapy Shows Efficacy and Safety in Stiff Person Syndrome in a Pivotal, Multicenter, Phase 2 Study (KYSA-8)

Amanda L. Piquet, MD; Anastasia Zekeridou, MD, PhD; Usama Gergis, MD, MBA; Jonathan Gutman, MD; Saad S. Kenderian, MD; Mallory Lowe, MD; Sadie Eggmann, BS; Andrew McKeon, MD, PhD; Sean J. Pittock, MD, PhD; Goran Rakocevic, MD; Jessica J. Yi, MD; Scott D. Newsome, DO; Justin Chou, PhD; Tom Van Blarcom, PhD; Xue Han, MS, MPH; John Sun, PhD; Shouvonik Sengupta, PhD; Ryan Tooker, PhD; Aditi Mehta, DO; Dena Grayson, MD, PhD; Naji Gehchan, MD, MBA; Marinos C. Dalakas, MD, PhD

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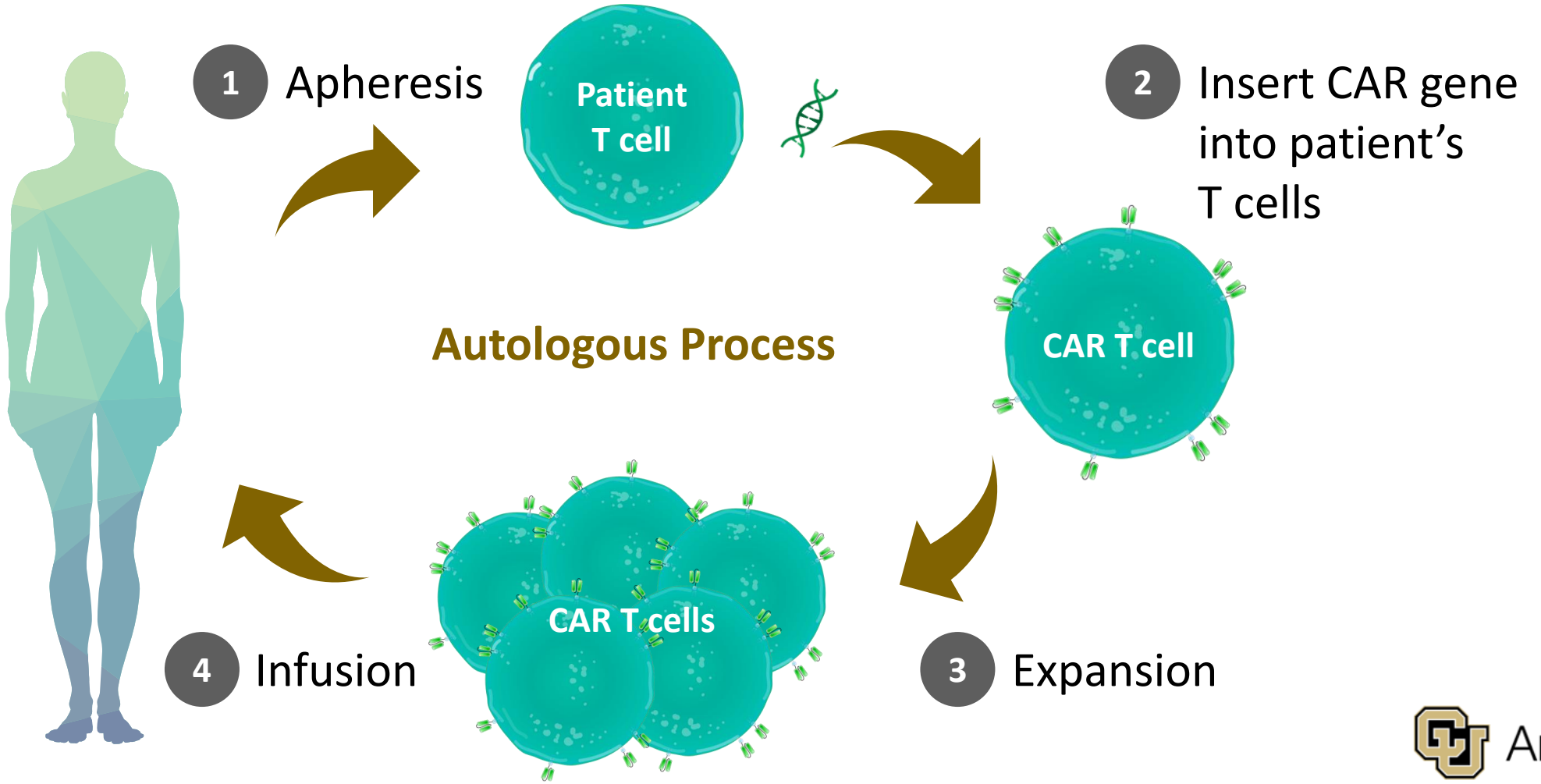
Abstract ID: 5919
Presented at the 2026 American Academy of Neurology Annual Meeting
April 21, 2026, Chicago, IL

Autologous CAR T Cells Are a Personalized Therapy



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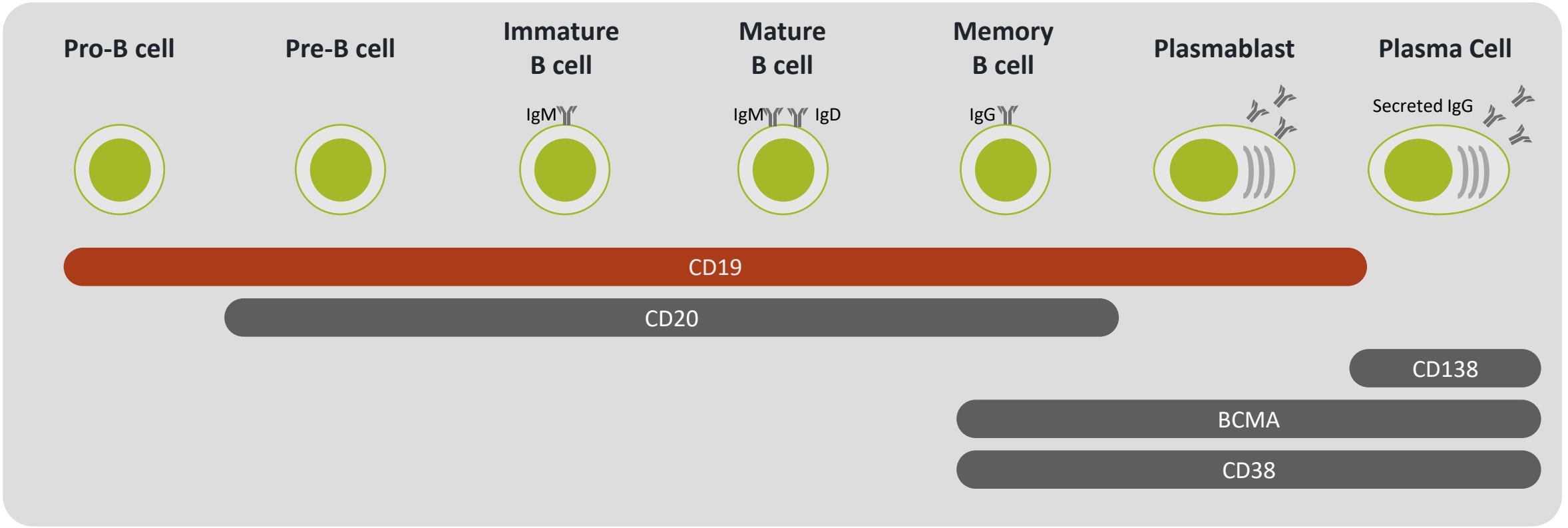
CD19 Is the Optimal Target for B-Cell Mediated Autoimmune Diseases



**CD19-targeted depletion of B cells eliminates the broadest range of B cell subsets while sparing long-lived plasma cells,
the reservoir of established humoral immunity, and avoids off target effects in the CNS[2,3]**

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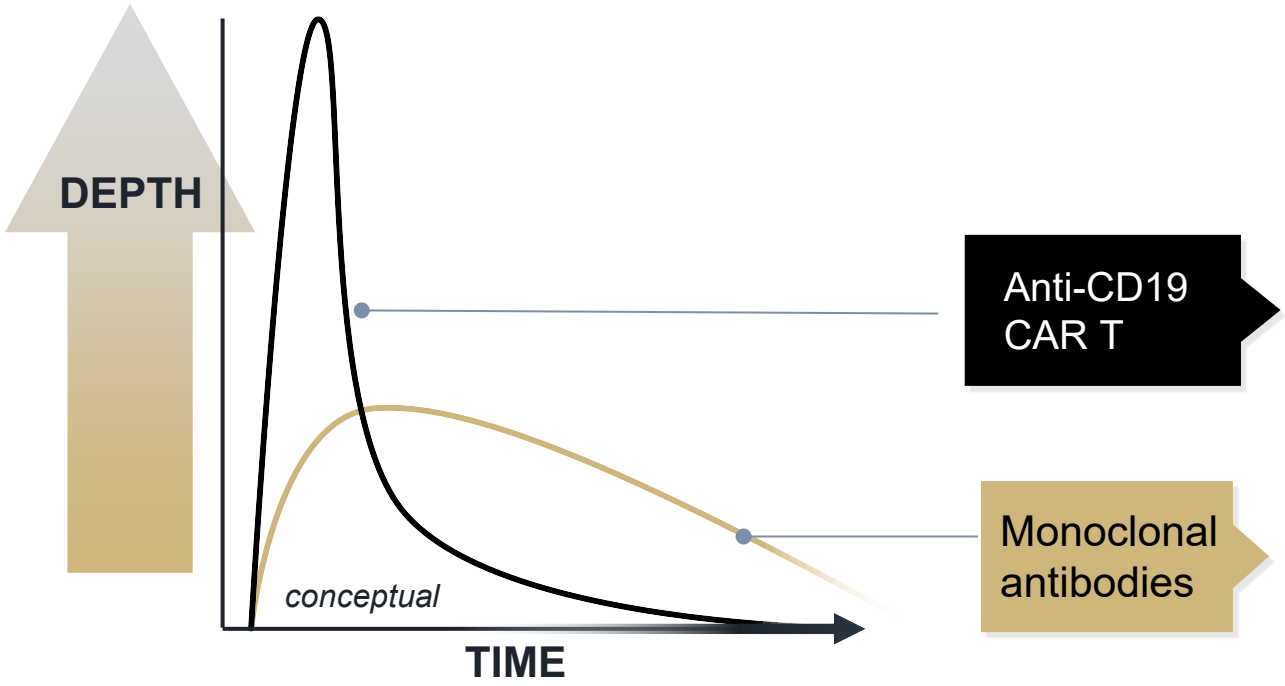
BCMA, B-cell maturation antigen; CD, cluster of differentiation; CNS, central nervous system; IgG, immunoglobulin G; IgM, immunoglobulin M.

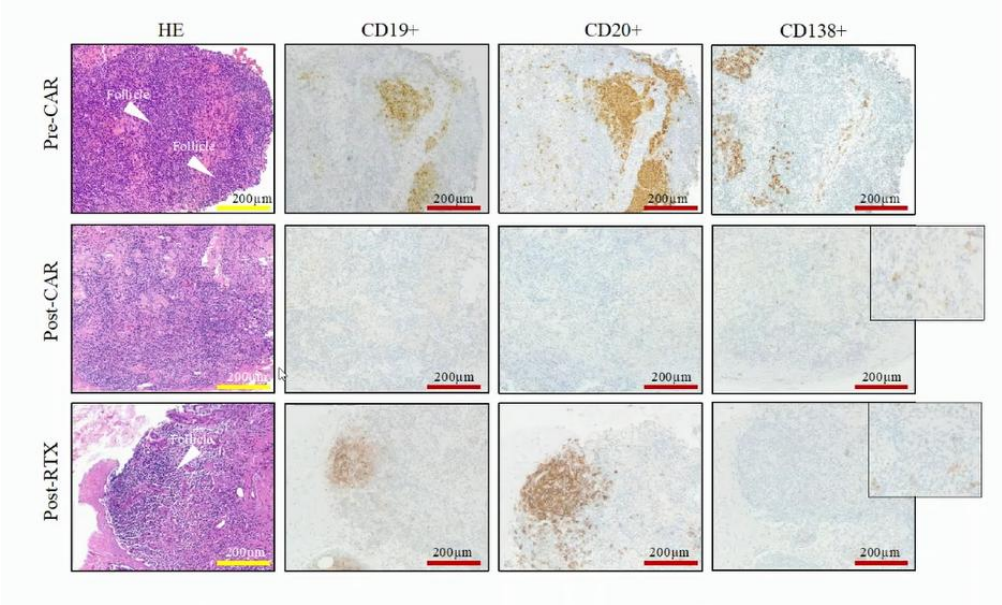
1. Lejeune et al. *Front Immunol.* 2020;11:762. 2. Bhoj VG, et al. *Blood*. 2016;128(3):360-370. 3. Li Y-R, et al. *Trends Pharm Sci*. 2024;45(9):839-857.

Potential for Greater Depth of Depletion to Drive Immune Reset

Depth of B-Cell Depletion



Complete depletion of B cells in the lymph nodes after a CD19 CAR T-cell therapy



Tur C, Eckstein M, Velden J, Rauber S, Bergmann C, Auth J, Bucci L, Corte G, Hagen M, Wirsching A, Grieshaber-Bouyer R, Reis P, Kittan N, Wacker J, Rius Rigau A, Ramming A, D'Agostino MA, Hartmann A, Müller F, Mackensen A, Bozec A, Schett G, Raimondo MG. CD19-CAR T-cell therapy induces deep tissue depletion of B cells. Ann Rheum Dis. 2024 Sep 11:ard-2024-226142. doi: 10.1136/ard-2024-226142

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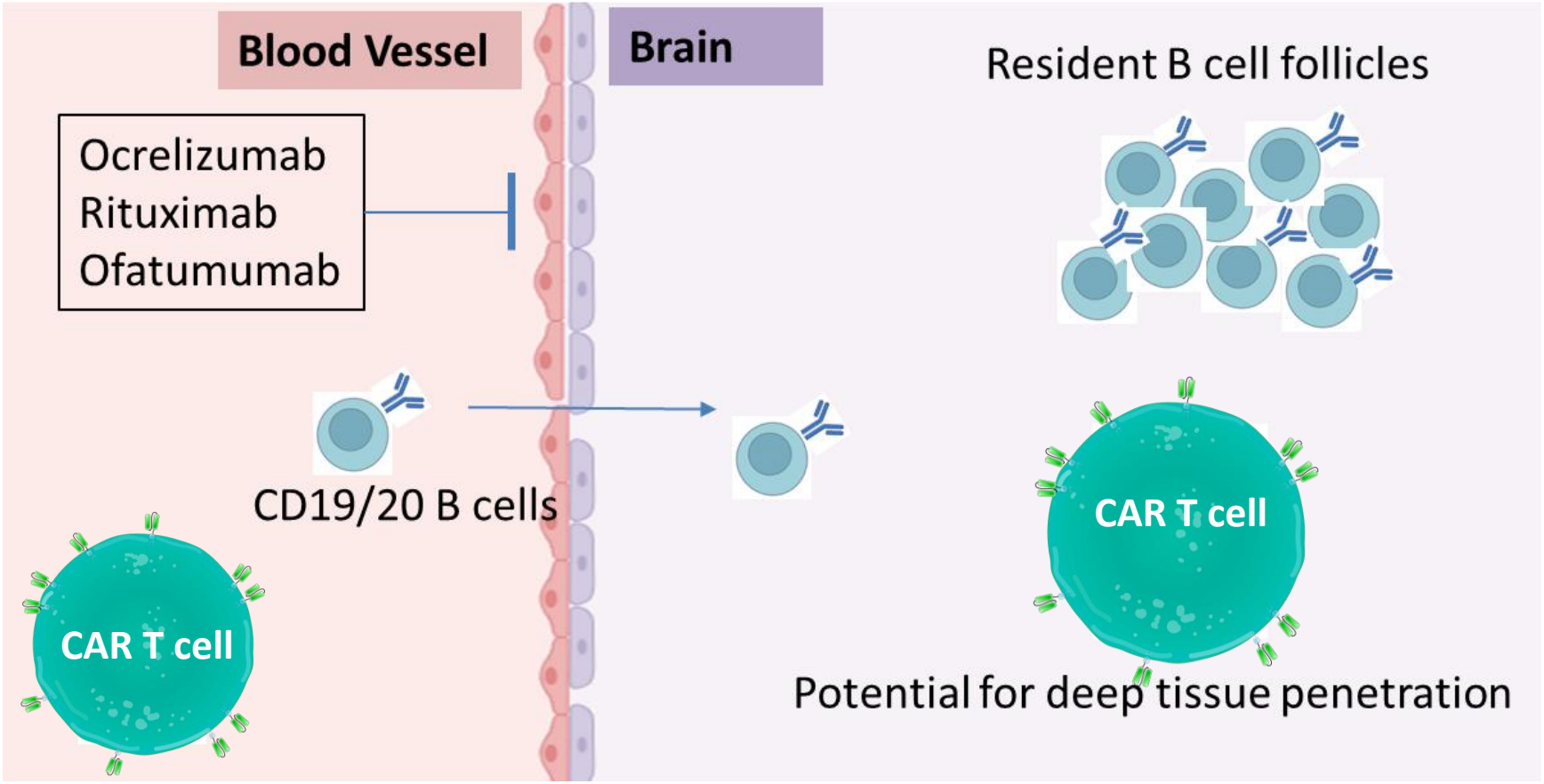
Potential for Depletion of Resident B cells in the CNS



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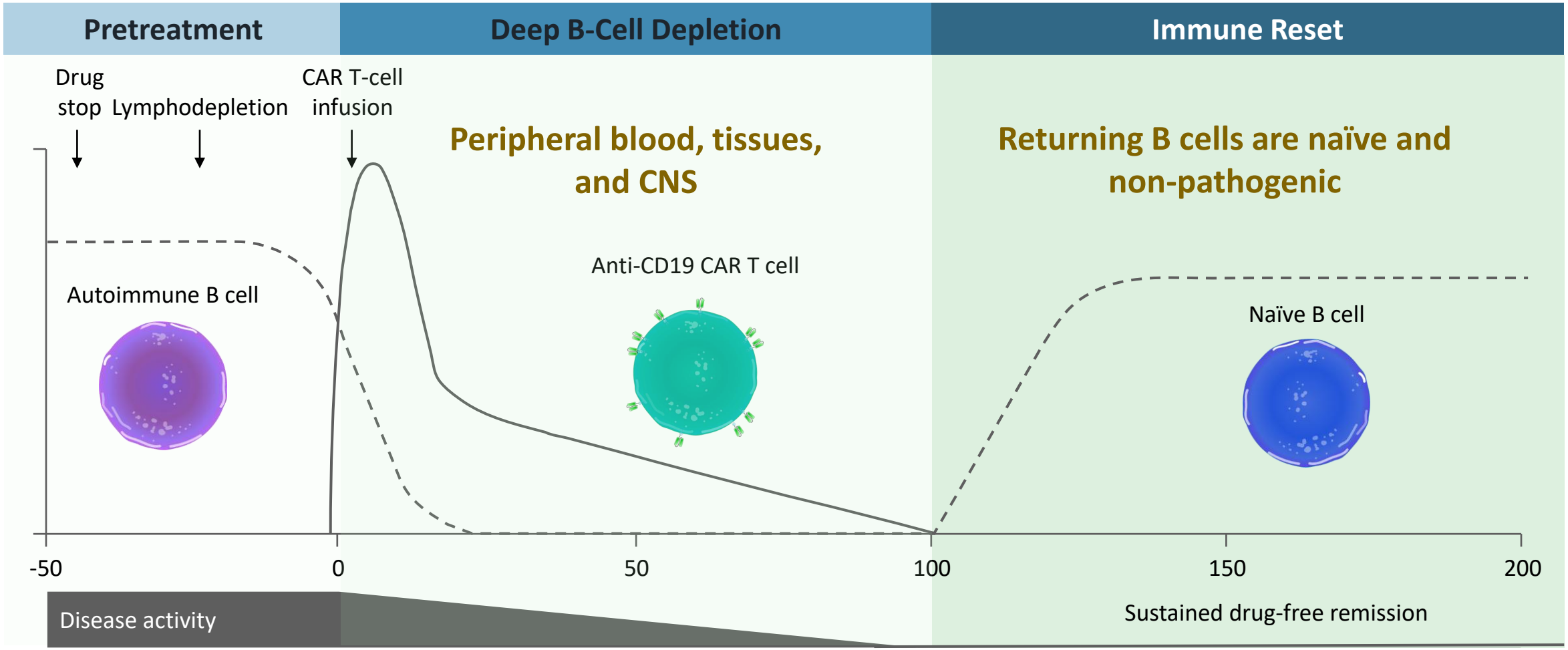
Deep and Transient B-Cell Depletion With CAR T-Cell Therapy Triggers Immune Reset to Provide Potential for Sustained Drug-Free Remission



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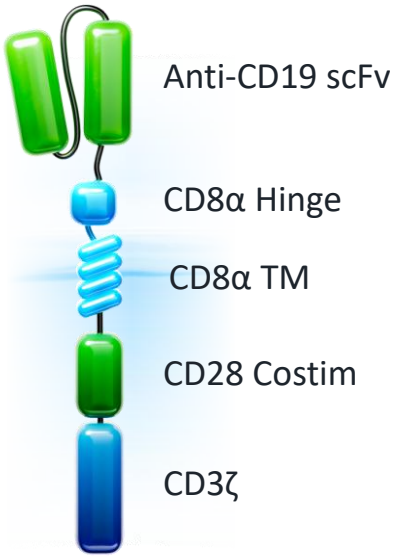
KYSA-8: Registrational, Phase 2 Single-Arm, Open-Label, Multicenter Study of Miv-cel in Stiff Person Syndrome (SPS)

Unique design of fully human miv-cel CAR construct[1,2]



N = 26

- Age 18 to 75 years
- Diagnosed with SPS
- Seropositivity for high-titer GAD65 or GlyR antibodies historically or at screening
- Inadequate response to ≥1 immunomodulatory therapy (including IVIg, rituximab, and/or plasmapheresis)
- Distribution-of-stiffness index ≥2

Miv-cel

Low-dose Cy/Flu lymphodepletion

+

Single infusion of 1×10^8 CAR T cells

Primary endpoints

- Change from baseline in T25FW at 16 weeks
- Safety

Secondary endpoints:

change from baseline at 16 weeks

- Modified Rankin scale (mRS)
- Distribution-of-stiffness index (DSI)
- Hauser ambulation index (HAI)
- Heightened sensitivity scale (HSS)

12-month follow up

SPS immunotherapies are discontinued prior to lymphodepletion

Patients were representative of a real-world SPS population with inadequate response to prior treatment

Primary analysis with data cutoff November 26, 2025 and a median follow-up of 6.5 months (range, 4.4–12.2)

NCT06588491

CAR, chimeric antigen receptor; Cy/Flu, cyclophosphamide/fludarabine; GAD65, glutamic acid decarboxylase 65; GlyR, glycine receptor; IVIg, intravenous immunoglobulin; SPS, stiff person syndrome; T25FW, timed 25-foot walk; TM, transmembrane; scFv, single-chain variable fragment.

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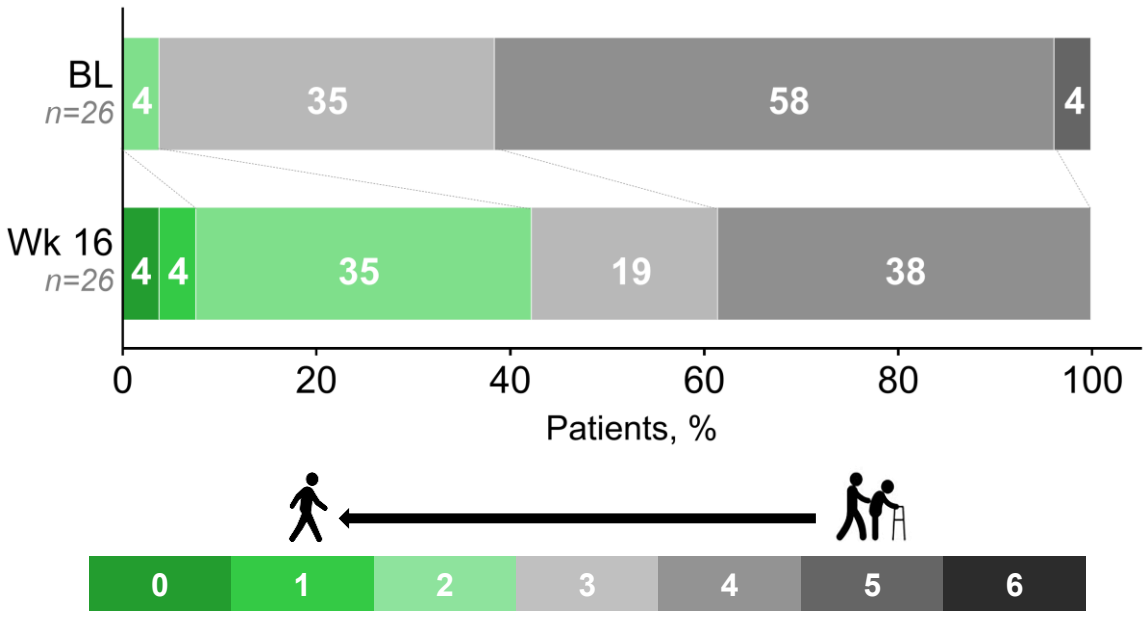
Patient Before Miv-cel (KYV-101)

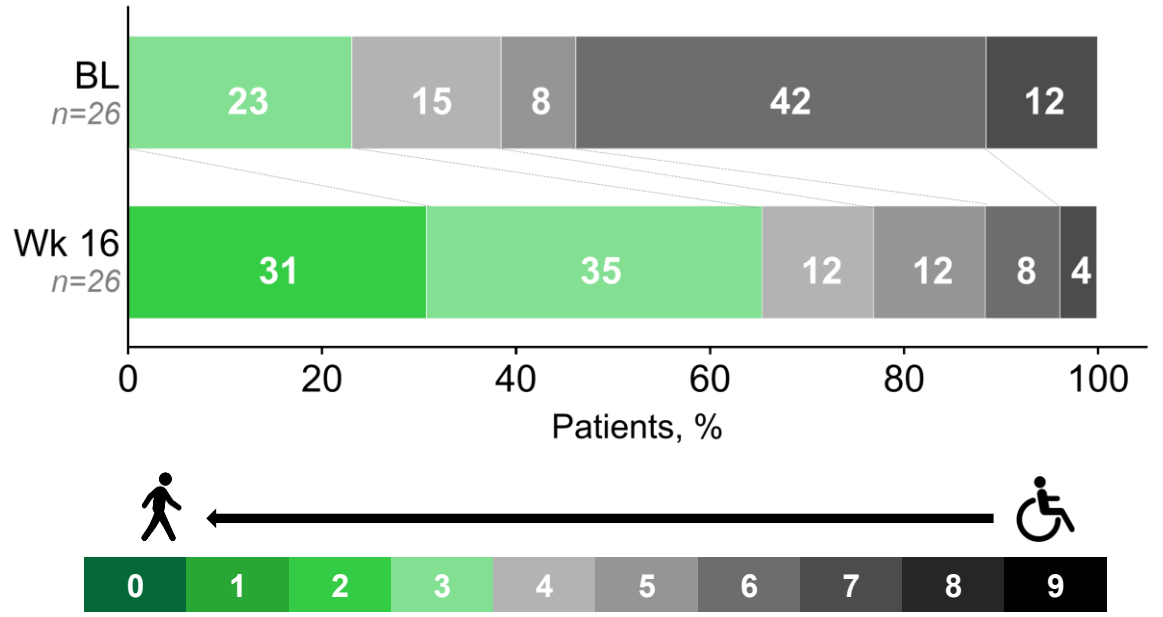
Miv-cel (mivocabtagene autoleucel, KYV-101) is an investigational therapy.

Secondary Endpoints Met: Miv-cel Achieved Significant (*P* < .0001) Improvements in Disability, Mobility, Stiffness, and Hypersensitivity

Modified Rankin Scale



Hauser Ambulation Index



- mRS and HAI, as well as the SPS-specific measures DSI and HSS, showed significant (P < .0001) mean improvements of -0.8 (SD, 0.86), -1.6 (1.13), -1.5 (1.75) and -3.2 (2.01), respectively
- 96% of patients (25/26) had improvement in ≥1 primary or secondary efficacy endpoint

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Data cutoff: 26Nov2025. Percentages may total more than 100% due to rounding.
BL, baseline; DSI, distribution-of-stiffness index; HAI, Hauser ambulation scale; HSS, heightened sensitivity scale; mRS, modified Rankin scale; SPS, stiff person syndrome; wk, week

Miv-cel Showed a Consistent, Well-Tolerated, and Manageable Safety Profile

Treatment-Related Adverse Events, n (%)	N=26
CRS (any Grade)	24 (92)
Grade 1	10 (38)
Grade 2	14 (54)
ICANS (any Grade)	3 (12)
Grade 1	3 (12)
Grade 3/4 neutropenia	4 (15)
Any treatment-related serious AE	3 (12)

- No high-grade CRS or ICANS
- Most common treatment-related AEs were CRS (92%), fatigue (54%), diarrhea (38%), and headache (31%)
- 4 patients had Grade 3/4 neutropenia, an expected AE with lymphodepletion and CAR T-cell therapies
  - All events were manageable with treatment including G-CSF, fully resolved in 3 patients (median duration of 85 days), and was ongoing in 1 patient
  - No serious infections associated with neutropenia
- Serious treatment-related AEs occurred in 3 patients; all fully resolved without sequalae

Data cutofcf: 26Nov2025
CRS and ICANS graded using ASTCT criteria; other AEs graded using CTCAE criteria.
AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; CAR, chimeric antigen receptor; CTCAE, Common Terminology Criteria for Adverse Events; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

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Miv-cel Demonstrates the Potential to Deliver Durable, Drug-Free, Disease-Free Remission, Reverse Disability, and Change the SPS Treatment Paradigm

In this landmark, pivotal, multicenter phase 2 study of 26 patients with SPS, a single dose of miv-cel resulted in:

- Significant, robust, rapid improvements in mobility, disability, stiffness, and hypersensitivity
- 100% free of immunomodulatory or immunosuppressive therapies for SPS as of last follow-up
- A consistent, well-tolerated, and manageable safety profile, with the potential for outpatient administration
- Sustained clinical benefit following deep B-cell depletion and broad immune reset

Miv-cel addresses high, unmet need in this progressive disease; Data supports SPS BLA submission for miv-cel

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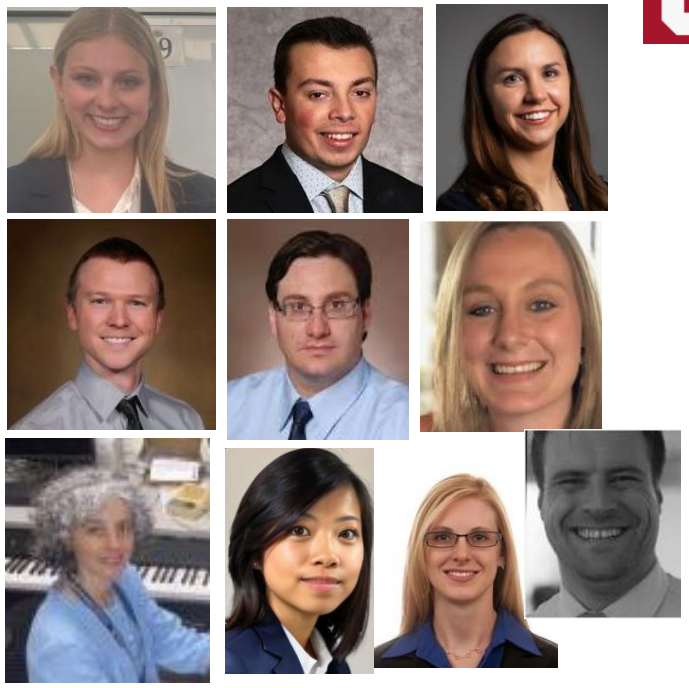
BLA, biologics license application; SPS, stiff person syndrome.

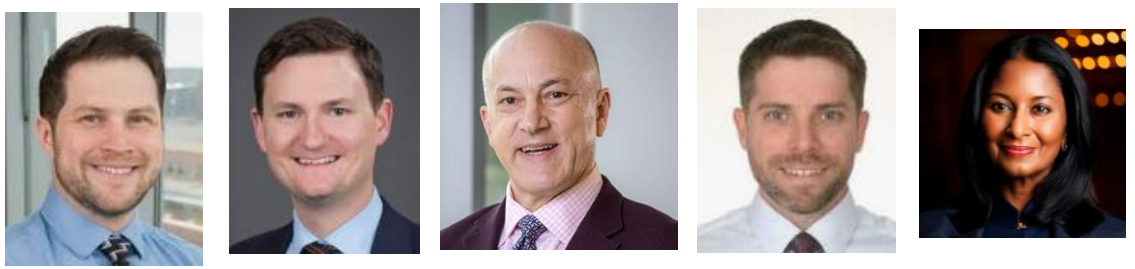
Thank you to all my collaborators in Autoimmune Neurology!

Past and Current Fellows

Clinical Research Team



Collaborators throughout the Neurology Department and CU Anschutz Medical Campus



Rocky Mountain MS Center Tissue Bank and Neuropathology

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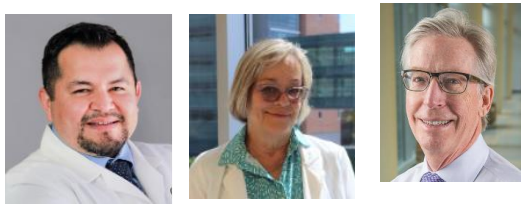
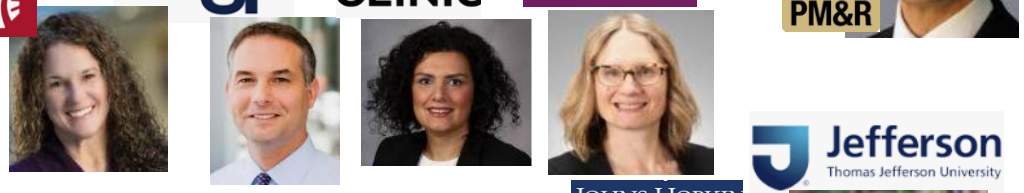


Collaborations Across Institutions

UCSF · MAYO CLINIC · UPMC · Jefferson Thomas Jefferson University · JOHNS HOPKINS UNIVERSITY



Department of Hematology at CU with CAR T studies

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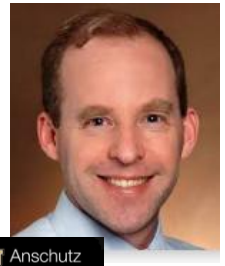
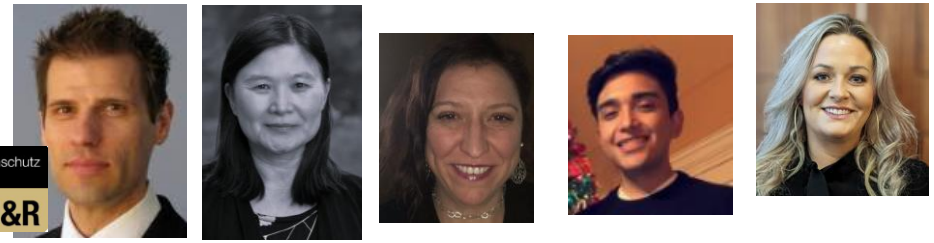


Hematopoietic Stem Cell Transplant studies

CBCI COLORADO BLOOD CANCER INSTITUTE



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Institution, Philanthropy and Industry Support

uchealth

Celine Dion Foundation

Rocky Mountain MS Center – the answers begin here –

The Stiff Person Syndrome Research Foundation

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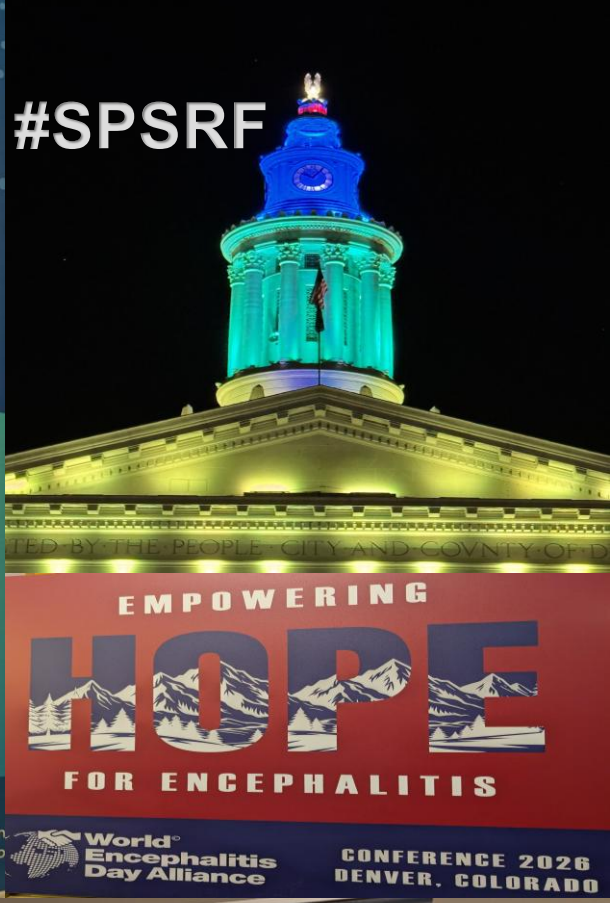
kyverna

Patients

Questions?


STIFF PERSON
SYMPOSIUM
Collaborate.
Innovate.
Cure.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