KYV-101: Unlocking the Potential of CAR-T Cell Therapy in Neuroinflammatory Diseases

Lupus Warrior

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This presentation includes results from named patient activities. Named patient activities are not part of our clinical trials for KYV-101 and data from these trials and activities are reported by the relevant investigators and physicians. Such data are not obtained using a single protocol or designed to be aggregated or reported as study results and may be highly variable. While we do not expect to be able to use the results from these investigator-initiated trials or named patient activities in our applications for marketing approval to the U.S. Food and Drug Administration or other foreign regulatory agencies, we believe that this strategy may provide some competitive advantage as we will be able to acquire additional clinical insights beyond highly focused clinical trials in specific geographies.

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Time	Session Title	Presenter
17:15-17:25	Welcome and Overview of KYV-101	Dominic Borie, MD, PhD Kyverna Therapeutics
17:25-17:40	Potential for KYV-101 in Stiff-Person Syndrome	Ralf Gold, MD Ruhr University Bochum
17:40-17:55	Early Experience With KYV-101 in Myasthenia Gravis	Aiden Haghikia, MD University of Hannover
17:55-18:10	CAR T Cell Therapy in Multiple Sclerosis – Alternative to HSCT?	Nicolaus Kröger, MD University of Hamburg
18:10-18:15	Q&A	

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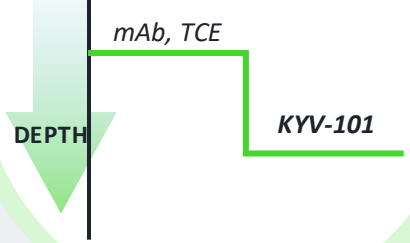
Kyverna's Leadership in Autologous Anti-CD19 CAR T-cell Therapy

A focus on antibody-mediated neuroinflammatory disorders

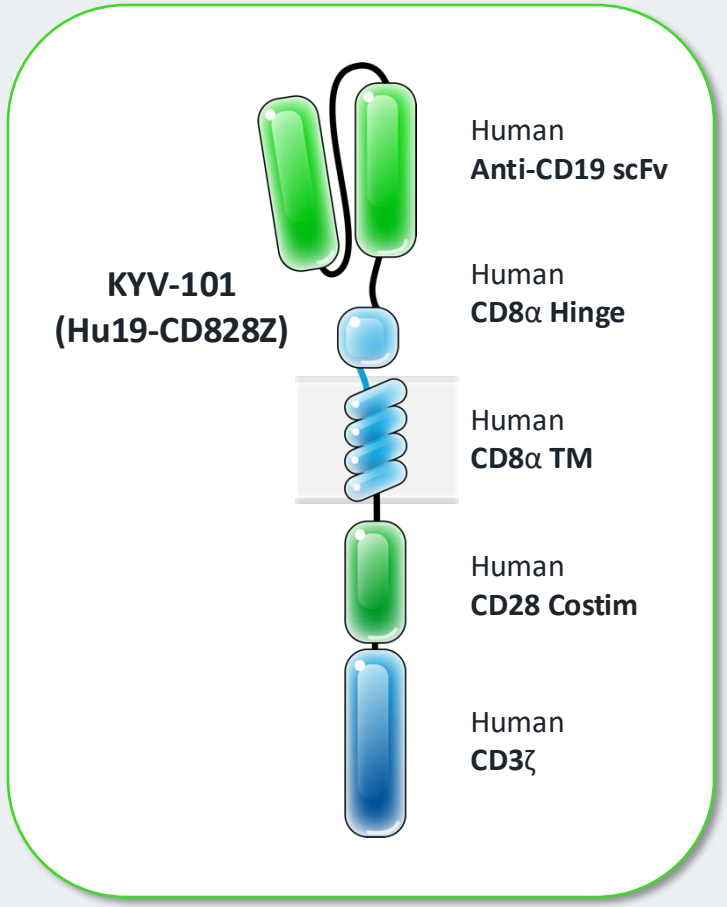
- Stiff-Person Syndrome
- Myasthenia Gravis
- Multiple Sclerosis



A step-change in deep B-cell depletion through KYV-101

- ✓ Clinical efficacy
- ✓ Durability
- ✓ Attractive safety profile

KYV-101, an Autologous, Fully Human, Anti-CD19 CAR T-Cell Therapy



Engineered for improved safety profile

- NIH second-generation innovation[1,2]
  - Fully human single-chain variable fragment
  - CD8α hinge and TM domains

Safety of CAR construct supported by clinical data

- Clinical success with 20 patients in B-cell lymphoma[1]
  - Lower cytokine levels, neurotoxicity and immunogenicity
- Clinical success with 41 patients in autoimmune disease[3]

CAR, chimeric antigen receptor; costim, costimulatory; NIH, National Institutes of Health; scFv, single-chain variable fragment; TM, transmembrane.

1. Brudno JN, et al. *Nat Med*. 2020;26:270-280. 2. Alabanza L, et al. *Mol Ther*. 2017;25(11):2452-2465. 3. Internal data from KYSA-1, KYSA-3, and investigator-reported named patient experience; data cutoff Sept 18, 2024.

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Kyverna: Leading Patient Experience With KYV-101 CAR

Clinical Goal

- Durable clinical response
- Reduction/withdrawal of immunosuppressive medications

Aim of CAR T-cell Therapy

- "One and done"
- Immune reset

Kyverna's experience with KYV-101 CAR

61 Patients

Across diverse indications treated with the KYV-101 CAR construct

15+ Autoimmune Indications

Broad indication experience builds market opportunity with KYV-101

- **Stiff-person syndrome**
- **Myasthenia gravis**
- **Multiple sclerosis**
- **NMOSD**
- **CIDP**
- Rheumatoid arthritis
- Systemic sclerosis
- Lupus nephritis
- ANCA-associated vasculitis
- And others

Data from Kyverna-sponsored clinical trials, investigator-reported named patient, and investigator-initiated trial experience with 14 days of follow-up as of September 18, 2024. KYV-101 CAR refers to both KYV-101 and NIH clinical experience with the underlying CAR used to create KYV-101.

ANCA, antineutrophil cytoplasmic antibody; CAR, chimeric antigen receptor; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; NMOSD, neuromyelitis optica spectrum disorder.

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Our Pipeline of CAR T-cell Therapies for Neuroinflammatory Diseases

2 x FDA RMAT DESIGNATIONS

Technology	Candidates	Target	Indication	Discovery / Validation	Preclinical	Clinical Phase 1	Clinical Phase 2	Clinical Phase 3	Partnership / Commercial Rights	Key Milestone Achieved
Autologous CAR T	KYV-101 Neuro-inflammatory	CD19	**Stiff-person syndrome**	KYSA-8 Phase 2 (US)					kyverna	**RMAT 07/24; ODD 08/24**
			Myasthenia gravis	KYSA-6 Phase 2 (US & EU)					kyverna	**RMAT 08/24; ODD 04/24**
			Multiple sclerosis	KYSA-7 Phase 2 (US & EU)					kyverna	**Fast Track 01/24**
	KYV-101 Rheumatology	CD19	**Lupus nephritis**	KYSA-1 Phase 1/2 (US) KYSA-3 Phase 1/2 (EU)					kyverna	**Fast Track 05/23**
			Systemic sclerosis	KYSA-5 Phase 1/2 (US)					kyverna	
Allogeneic CAR T	KYV-201	CD19	**Multiple indications**						kyverna Intellia THERAPEUTICS	
Other Approaches	Multiple	Multiple	**IBD & other indications**						kyverna	

Note: IBD includes Crohn's disease and ulcerative colitis.
Note: Fast track designation does not assure that we will experience a faster development process, regulatory review or regulatory approval process compared to conventional FDA procedures.
CAR, chimeric antigen receptor; CTA, clinical trial application; FDA, Food and Drug Administration; IND, investigational new drug; ODD, orphan drug designation; RMAT, regenerative medicine advanced therapy.

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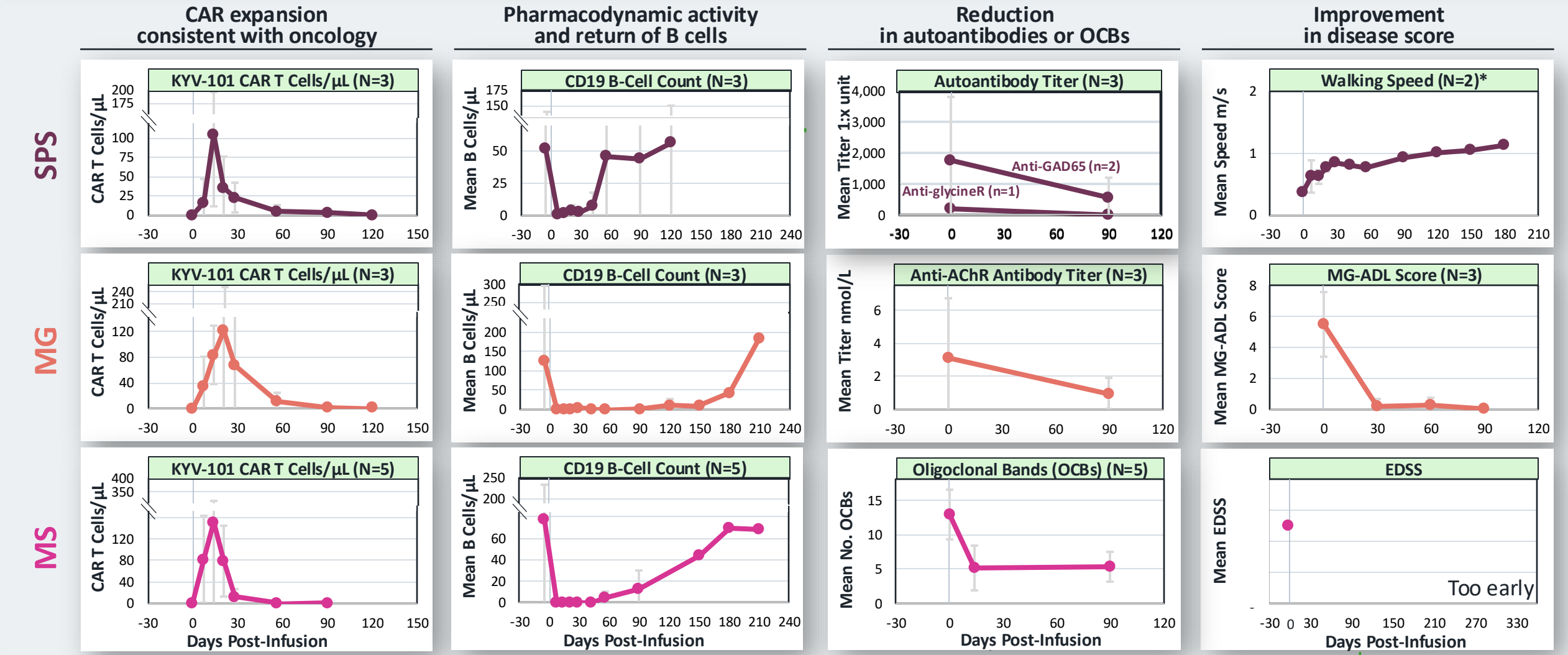
Promising Efficacy Data With KYV-101 in Neuroinflammatory Disease



Note: named patient data; Data on walking speed only available for 2 of 3 patients with SPS.

ADL, activities of daily living; CAR, chimeric antigen receptor; MG, myasthenia gravis; MS, multiple sclerosis; OCB, oligoclonal band; SPS, stiff-person syndrome.

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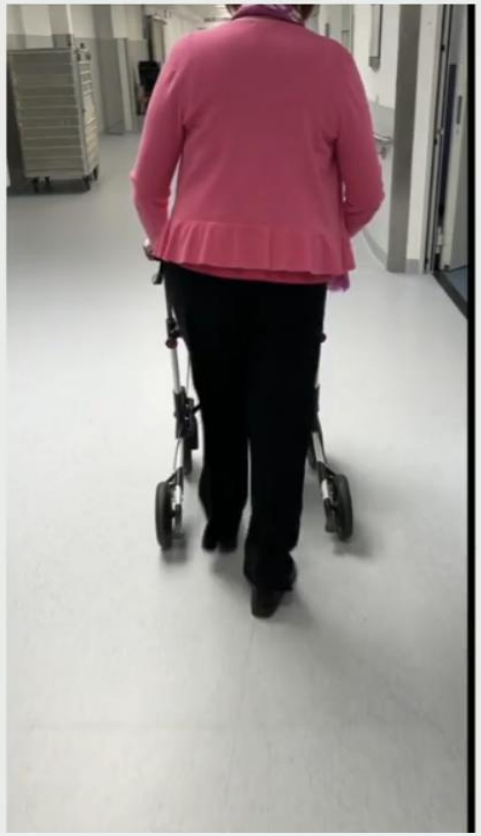
KYV-101 in SPS Shows Promising Efficacy

Bedbound, Unable to Bend Legs

Preinfusion

Able to Walk and Turn With Aids



4-6 Months Post

Able to Walk Unaided Without Fear of Falling

8 Months Post

PNAS BRIEF REPORT | IMMUNOLOGY AND INFLAMMATION OPEN ACCESS

Successful use of anti-CD19 CAR T cells in severe treatment-refractory stiff-person syndrome

Simon Faissner[a,2,1], Jeremias Motte[a,1], Melissa Sgodzai[a,1], Christian Geis[b], Aiden Haghikia[c], Dimitrios Mougiakakos[d], Dominic Borie[e], Roland Schroers[f,2], and Ralf Gold[a,2]

Edited by Lawrence Steinman, Stanford University, Stanford, CA; received February 22, 2024; accepted May 10, 2024

June 17, 2024 | 121 (26) e2403227121 | https://doi.org/10.1073/pnas.2403227121

At 1 year after KYV-101:

- Reduced stiffness
- Improved mobility
- Stable gait
- Better walking speed
- 90% reduction in anti-GAD antibody

Note: named patient data; GAD, glutamic acid decarboxylase; SPS, stiff-person syndrome.

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Immune Reset Leading to Durable Treatment Response

Schett Experience

First CAR T SLE patient at >3 years[1-3]

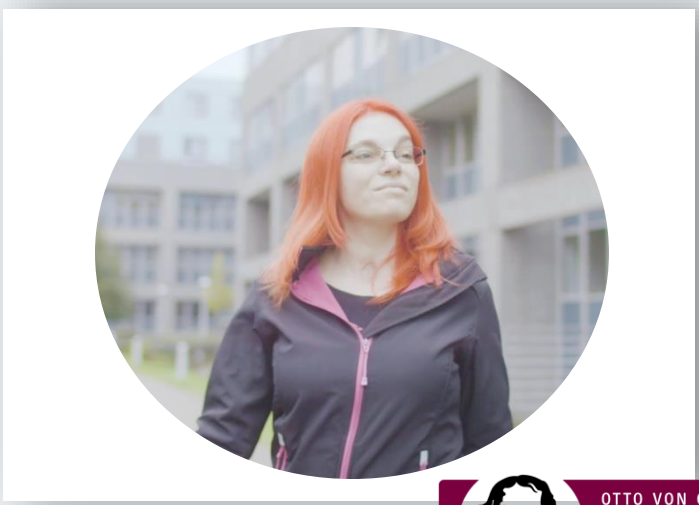
- Disease free
- No serious adverse events
- Off immunosuppressants and glucocorticoids
- B cells repopulated as of day 148

FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG

Kyverna Experience

First KYV-101 MG patient at 15 months[4,5]

- Disease free
- No serious adverse events
- Off immunosuppressants and glucocorticoids
- B cells repopulated as of day 132



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Second KYV-101 MG patient at 12 months[5]

- Disease free
- No serious adverse events
- Off immunosuppressants and glucocorticoids
- B cells repopulation pending as of month 10

RUB

Note: named patient data; CAR, chimeric antigen receptor; MG; myasthenia gravis; SLE, systemic lupus erythematosus.

1. Mougiakakos D, et al. *N Engl J Med*. 2021;385:567-569. 2. Taubmann J, et al. EULAR 2023, Abstract OP0141. *Ann Rheum Dis*. 2023;82:93-94. 3. World exclusive: CAR-T cell therapy successfully used against autoimmune disease. https://www.fau.eu/2021/08/11/news/research/world-exclusive-car-t-cell-therapy-successfully-used-against-autoimmune-disease/. 4. Haghikia A, et al. *Lancet Neurol*. 2023;22:1104-5. 5. Unpublished data.

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KYV-101 CAR Safety Data

Source	Indication	N	CRS Grade 1/2	CRS Grade 3/4	ICANS Grade 1	ICANS Grade 2-4
KYV-101 experience	Neuroimmunology	22	15	0	3	0
KYV-101 experience	Rheumatology	17	16	0	1	0
KYV-101 experience	Other Autoimmune	2	2	0	0	0
KYV-101 experience	**All Autoimmune**	**41**	**33**	**0**	**4**	**0**

Differentiated safety profile with a CAR with fully human scFv and CD28 costimulatory domain

Internal data from Kyverna-sponsored clinical trials, investigator-reported named patient, and investigator-initiated trial experience with 14 days of follow-up as of September 18, 2024. These observations are derived from separate clinical settings, including information from case reports. Future clinical trials may not confirm the clinical safety observations discussed in these case reports and studies.
CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; scFv, single chain variable fragment.

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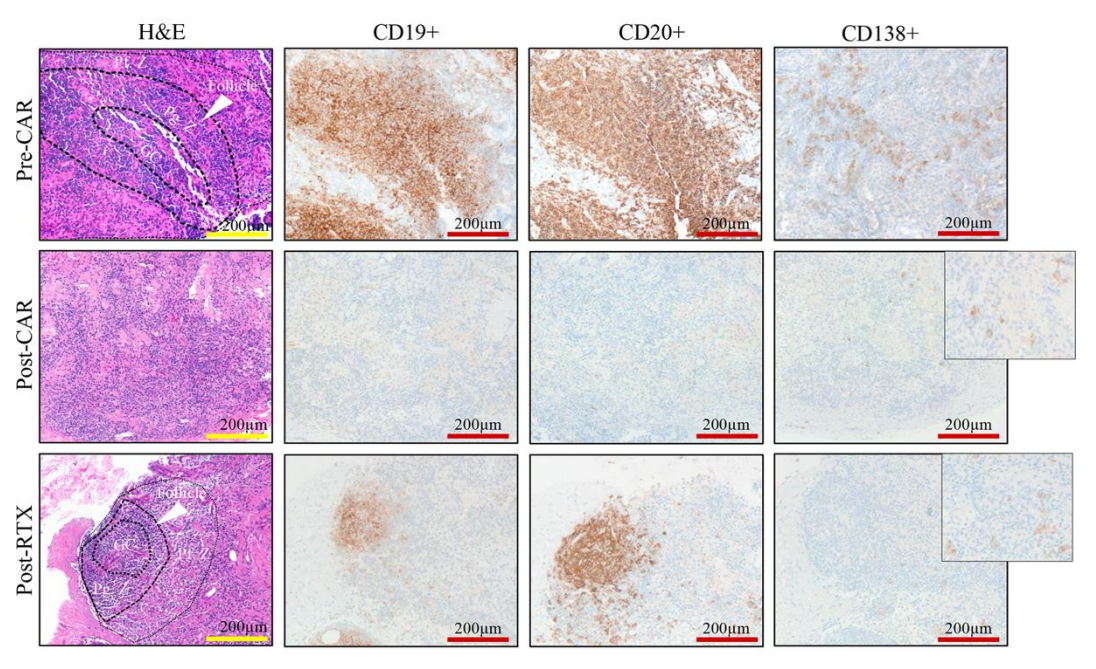
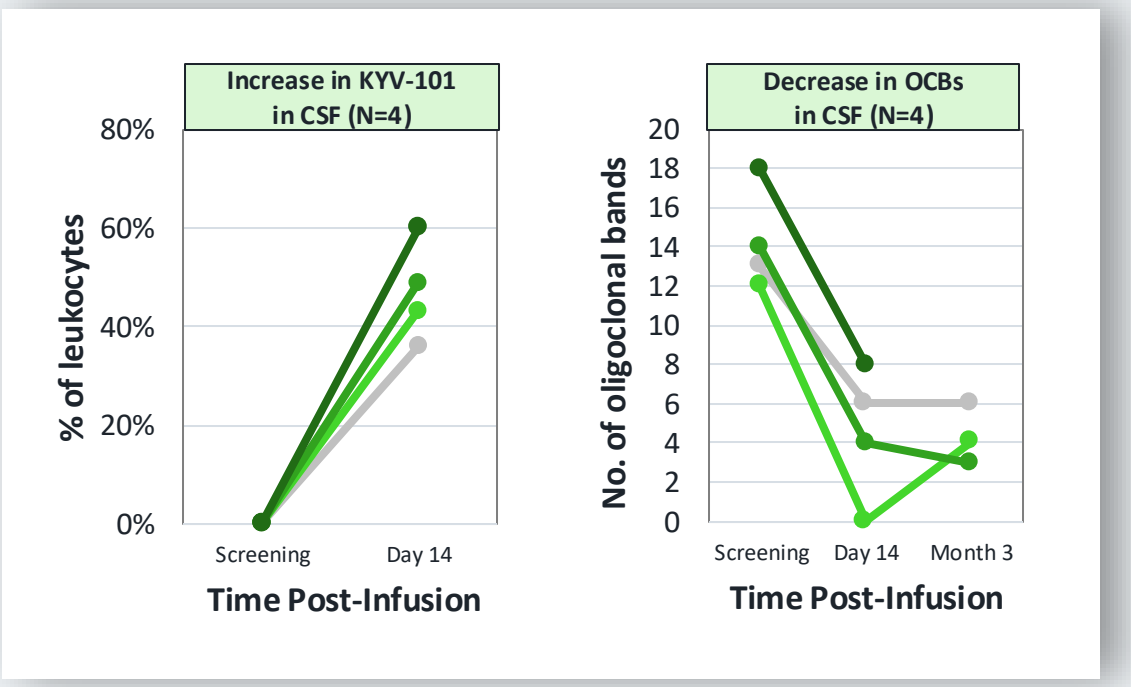
KYV-101 May Define the Gold Standard in Tissue-Based B-Cell Depletion

Anti-CD19 CAR T completely depletes B cells in lymph nodes



Tur C, et al. *Ann Rheum Dis*. 2024;0:1–8.

KYV-101 expands in CSF and suppresses oligoclonal bands



Fischbach et al. Med. 2024;5:1-9 and unpublished data.

KYV-101 can achieve deep tissue penetration leading to immune reset with an appropriate safety profile

Note: named patient data; BBB, blood-brain barrier; CNS, central nervous system; CSF, cerebrospinal fluid; OCB, oligoclonal band.

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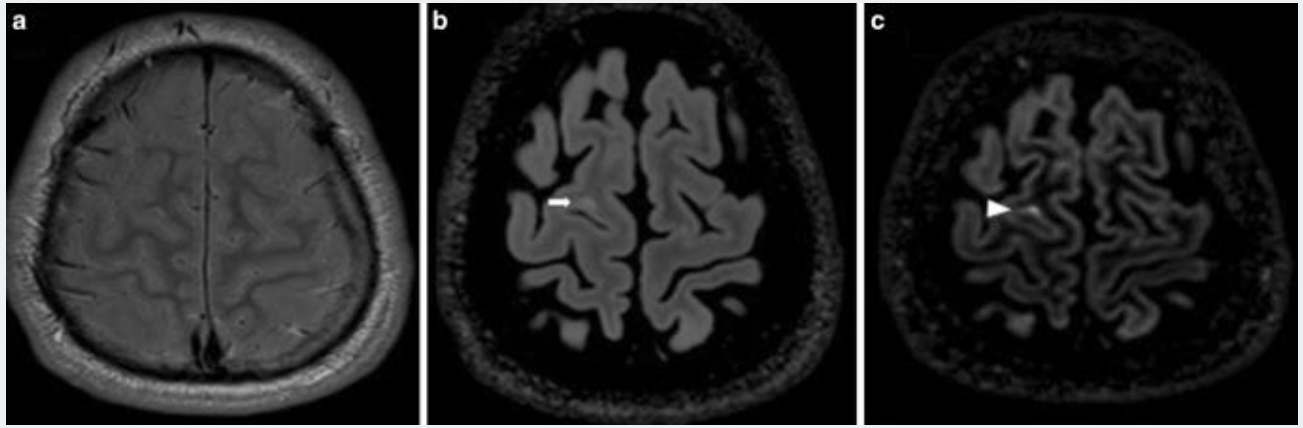
Considerations for Multiple Sclerosis Patient Selection

	KYV-101	Antibody Therapy
Decreases OCBs	✓	–
Penetrates CNS	✓	–
Balanced safety profile	✓	✓
Activity in PMS & RRMS	✓ (early)	+/–

Cortical/juxtacortical lesions in a PPMS patient

PD-weighted image | FLAIR image | DIR image



Siger M. *Neuroradiol*. 2022;32:625-641.

CNS, central nervous system; DIR, Double inversion recovery; FLAIR, fluid attenuated inversion recovery; OCB, oligoclonal band; PD, proton-density; PMS, progressive multiple sclerosis; PPMS, primary progressive multiple sclerosis; RRMS, relapsing remitting multiple sclerosis.

KYV-101 Published Case Reports Lead the Clinical and Scientific Advancement of the Field

CAR T in Autoimmunity Review Article


nature reviews immunology

Chimeric antigen receptor T cell therapy for autoimmune disease

James B. Chung[1], Jennifer N. Brudno[2], Dominic Borie[1] & James N. Kochenderfer[2]

Multiple Sclerosis


Med

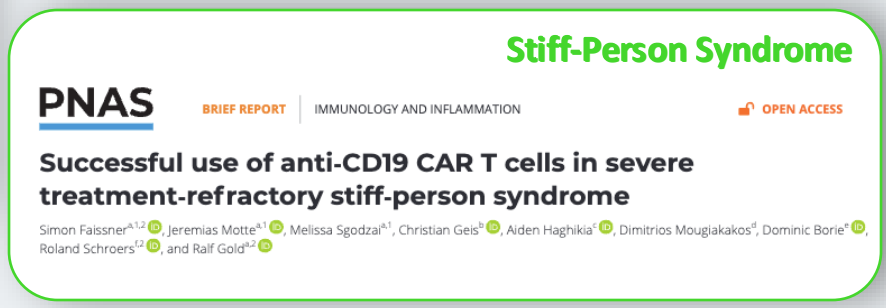
CellPress OPEN ACCESS

Case Report

CD19-targeted chimeric antigen receptor T cell therapy in two patients with multiple sclerosis

Felix Fischbach,[1,6] Johanna Richter,[2,6] Lena Kristina Pfeffer,[1,6] Boris Fehse,[2] Susanna Carolina Berger,[2] Stefanie Reinhardt,[1] Jens Kuhle,[3] Anita Badbaran,[2] Kristin Rathje,[2] Nico Gagelmann,[2] Dominic Borie,[4] Johan Seibel,[5] Francis Ayuk,[2] Manuel A. Friese,[1] Christoph Heesen,[1,*] and Nicolaus Kröger[2,7,*]

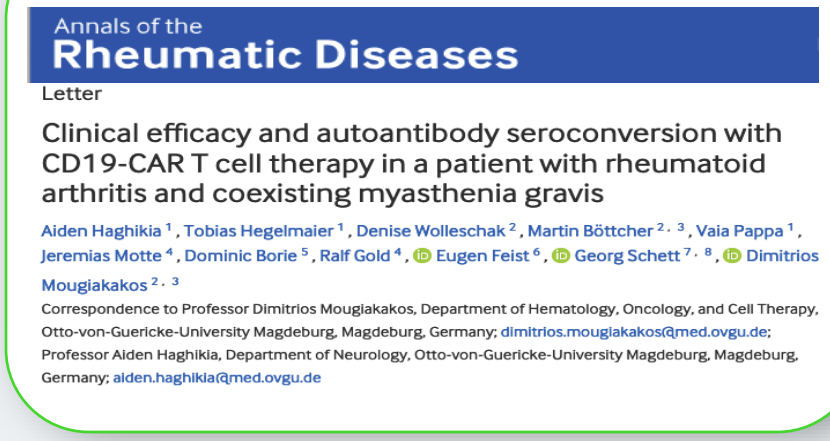
Stiff-Person Syndrome


PNAS BRIEF REPORT | IMMUNOLOGY AND INFLAMMATION OPEN ACCESS

Successful use of anti-CD19 CAR T cells in severe treatment-refractory stiff-person syndrome

Simon Faissner[a,1,2], Jeremias Motte[a,1], Melissa Sgodzai[a,1], Christian Geis[b], Aiden Haghikia[c], Dimitrios Mougiakakos[d], Dominic Borie[e], Roland Schroers[f,2], and Ralf Gold[a,2]

Rheumatoid Arthritis & Myasthenia Gravis


Annals of the Rheumatic Diseases

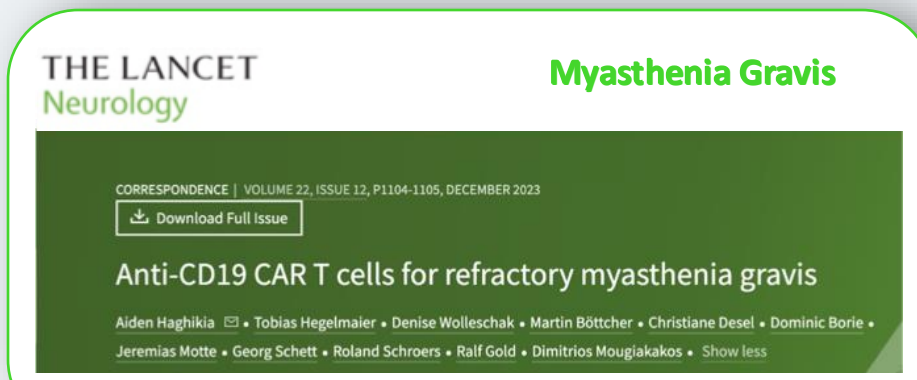
Letter

Clinical efficacy and autoantibody seroconversion with CD19-CAR T cell therapy in a patient with rheumatoid arthritis and coexisting myasthenia gravis

Aiden Haghikia [1], Tobias Hegelmaier [1], Denise Wolleschak [2], Martin Böttcher [2, 3], Vaia Pappa [1], Jeremias Motte [4], Dominic Borie [5], Ralf Gold [4], Eugen Feist [6], Georg Schett [7, 8], Dimitrios Mougiakakos [2, 3]

Correspondence to Professor Dimitrios Mougiakakos, Department of Hematology, Oncology, and Cell Therapy, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany; dimitrios.mougiakakos@med.ovgu.de; Professor Aiden Haghikia, Department of Neurology, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany; aiden.haghikia@med.ovgu.de

Myasthenia Gravis


THE LANCET Neurology

CORRESPONDENCE | VOLUME 22, ISSUE 12, P1104-1105, DECEMBER 2023

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Anti-CD19 CAR T cells for refractory myasthenia gravis

Aiden Haghikia • Tobias Hegelmaier • Denise Wolleschak • Martin Böttcher • Christiane Desel • Dominic Borie • Jeremias Motte • Georg Schett • Roland Schroers • Ralf Gold • Dimitrios Mougiakakos • Show less

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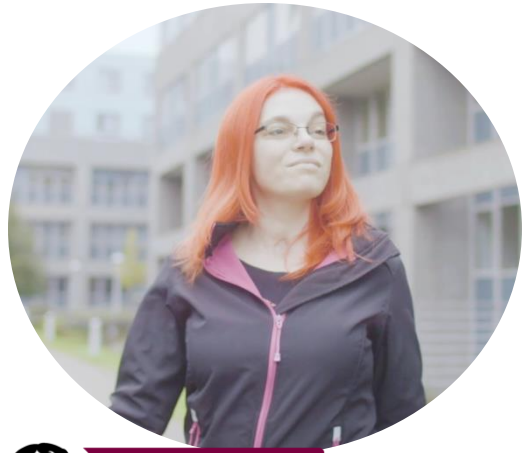
Stiff-Person Syndrome

RUB

Myasthenia Gravis



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Multiple Sclerosis

UKE HAMBURG

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Potential for KYV-101 in Stiff-Person Syndrome

Ralf Gold, MD
Ruhr University Bochum

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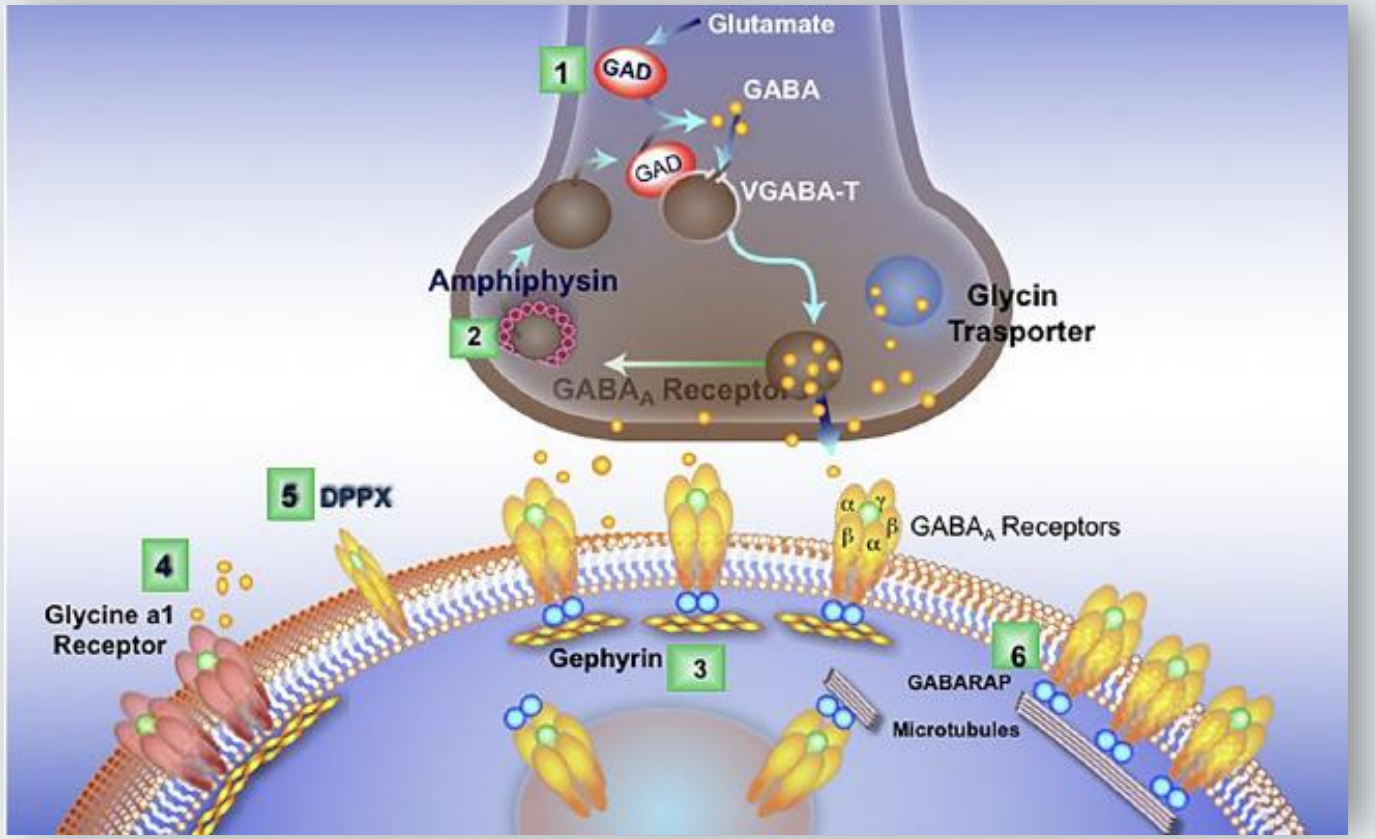
Stiff-Person Syndrome Is Highly Disabling Due to Falls and Lack of Mobility

Pathophysiology

- Progressive rigidity and muscle spasms[1]
- GABAergic inhibitory pathways and synaptic signaling targeted[2]
- Classical SPS characterized by GAD autoantibodies[1]



Dalakas M. *Neurotherapeutics*. 2022. https://doi.org/10.1007/s13311-022-01188-w.

Standard of Care

Symptomatic Control

Physical Therapy

Immunotherapy
Limited response (~30%) to off label IVIG and rituximab

CNS, central nervous system; DPPX, dipeptidyl peptidase-like protein; GABA, gamma aminobutyric acid; GABARAP, gamma-aminobutyric acid receptor-associated protein; GAD, glutamic acid decarboxylase; SPS, stiff-person syndrome.

1. Baizabal-Carvallo. *J Neurol Neurosurg Psychiatry*. 2015;86:840-848. 2. Dalakas. *Neurotherapeutics*. 2022;19:687-690.

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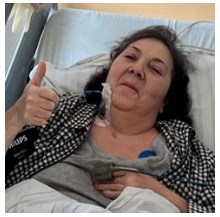
KYV-101 Emerging Clinical Experience in 3 Patients With Stiff-Person Syndrome

Patient		Diagnosis	Disease Duration	Age	Disease Description	Prior Lines of Treatment
1		SPS	9 years	69 years	Severe disability, bed bound, severe leg pain due to spasms	**4**
2		SPS+MG	14 years	61 years	Progressive leg spasticity of legs, impaired mobility; multiple prolonged ICU admissions requiring intubation and tracheostomy	**8**
3		SPS+PERM	3 years	21 years	Impaired mobility SPS: Painful spastic tetraparesis and spasms PERM: psychiatric symptoms and ocular movement disorders	**8**

Note: named patient experience; CIPD, chronic inflammatory demyelinating polyradiculoneuropathy; ICU, intensive care unit; MG, myasthenia gravis; PERM, progressive encephalomyelitis with rigidity and myoclonus; SPS, stiff-person syndrome.

KYV-101 Shows Promising Efficacy in Stiff-Person Syndrome

Bedbound, Unable to Bend Legs

Preinfusion

Able to Walk and Turn With Aids

4-6 Months Post

Able to Walk Unaided without Fear of Falling

8 Months Post

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Edited by Lawrence Steinman, Stanford University, Stanford, CA; received February 22, 2024; accepted May 10, 2024

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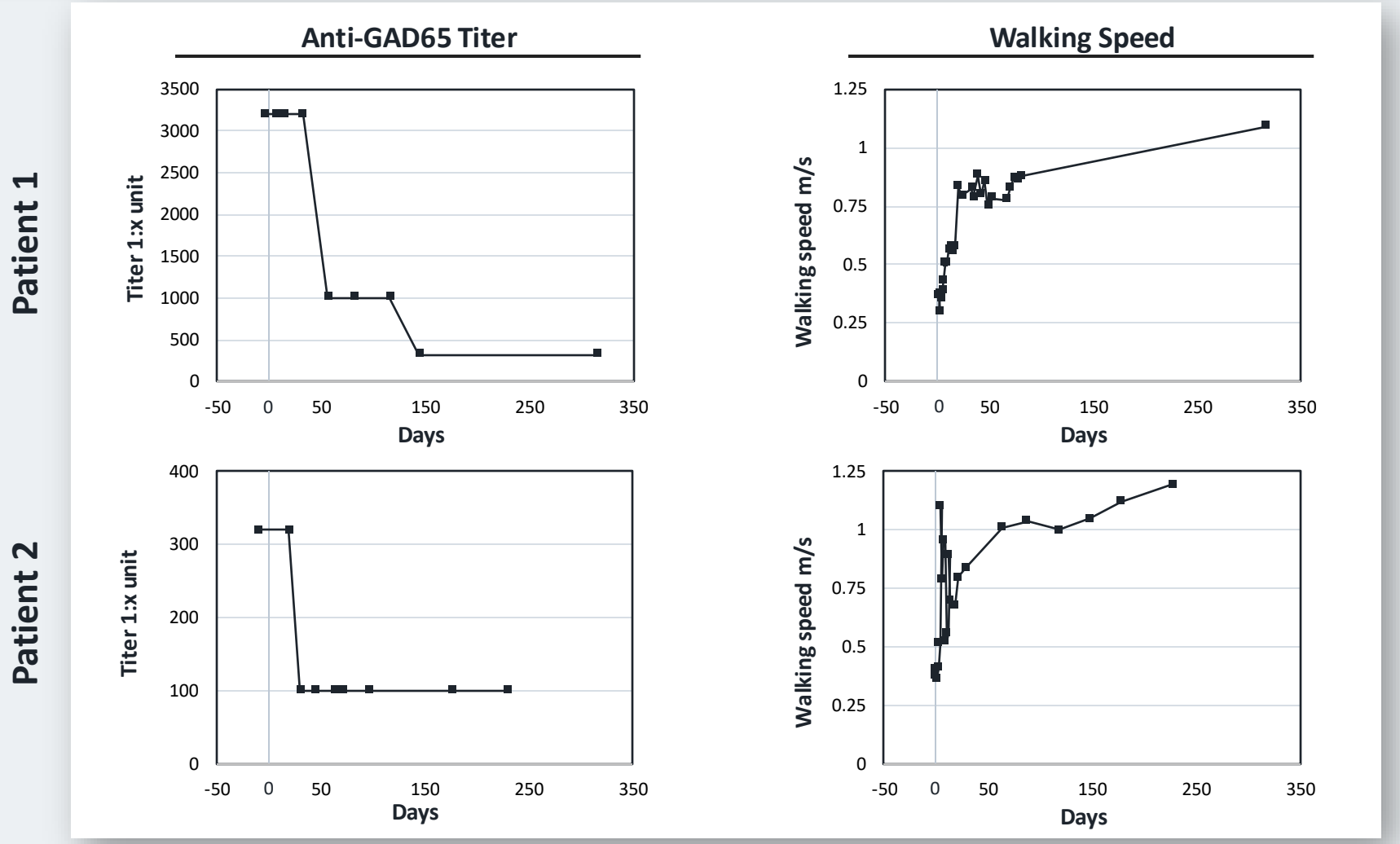
At 1 year after KYV-101:

- Reduced stiffness
- Improved mobility
- Stable gait
- Better walking speed
- 90% reduction in anti-GAD antibody

GAD, glutamic acid decarboxylase.

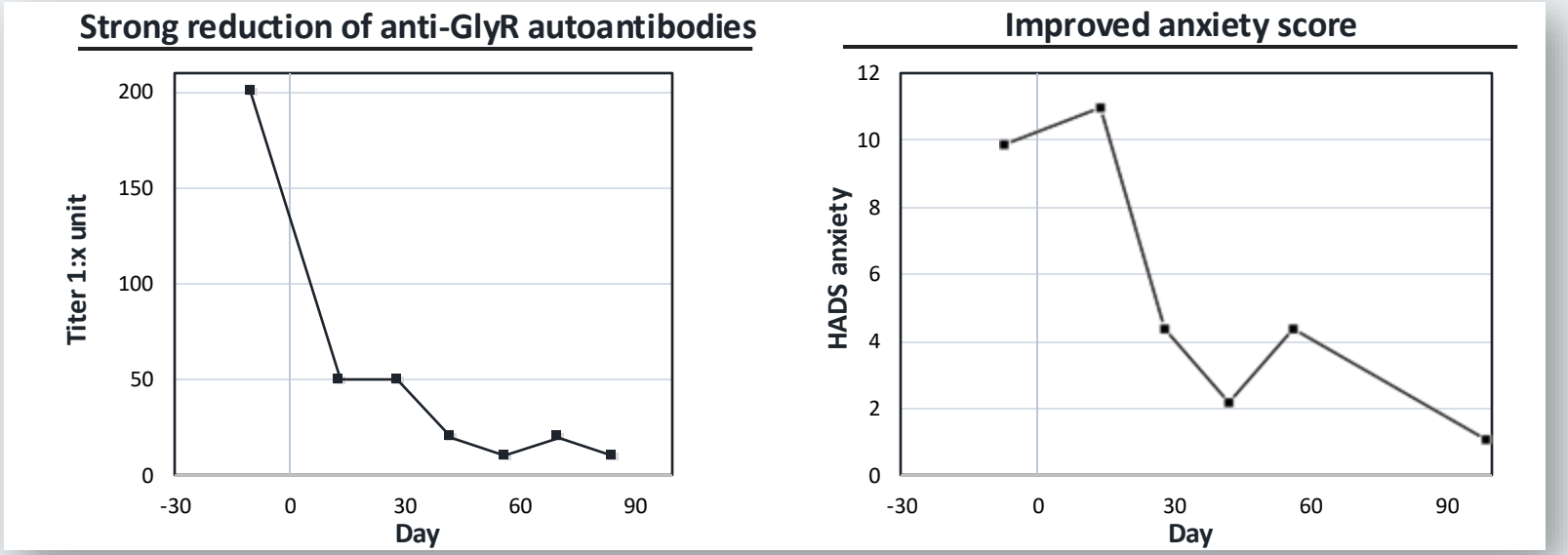
In Anti-GAD65 SPS, KYV-101 Improves Autoantibodies and Clinical Outcomes Over Time



Note: named patient data; GAD, glutamic acid decarboxylase.

In SPS + PERM, KYV-101 Reduces Autoantibodies and Psychogenic Disease Component

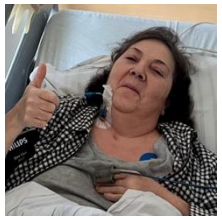
Patient 3



PERM to be excluded from KYSA-8

Note: named patient data; GlyR, glycine receptor; HADS, hospital anxiety and depression score; PERM, progressive encephalomyelitis with rigidity and myoclonus.
Data courtesy of Pr Dr Christian Geis, Dr Jonathan Wickel, and Dr Ulf Schnetzke (Jena University Hospital); and Carmen Villmann (Würzburg).

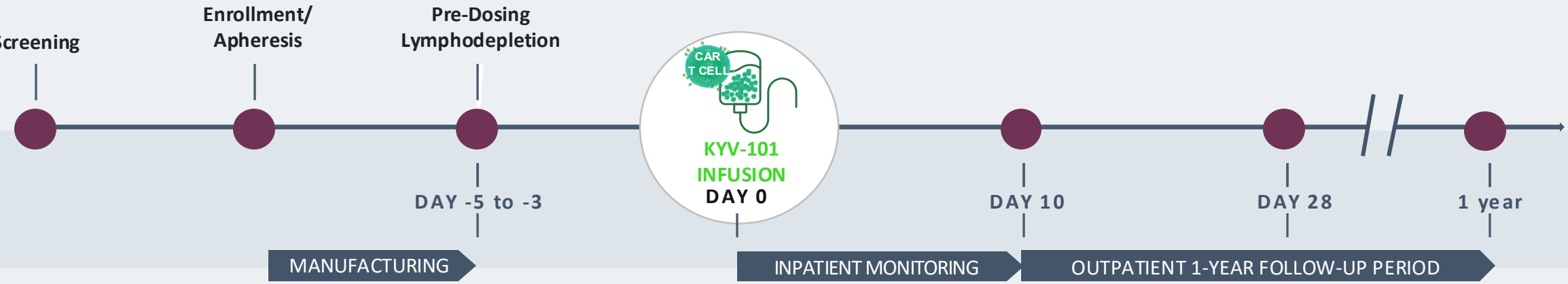
Safety Profile Consistent With Overall KYV-101 Experience

Patient		Diagnosis	Duration	Age	CRS Grade (1-4)*	ICANS Grade (1-4)
1		SPS	9 years	69 years	2	None
2		SPS+MG	14 years	61 years	1	None
3		SPS+PERM	3 years	21 years	1	None

- No ICANs with transient and easily manageable CRS

*Grade 1-2 CRS is mild to moderate.
Note: named patient data; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; MG, myasthenia gravis; PERM, progressive encephalomyelitis with rigidity and myoclonus; SPS, stiff-person syndrome.

A Phase 2, Open-Label, Single-Arm, Multicenter Study of KYV-101 in Refractory Stiff-Person Syndrome (N=25)



Primary

- Change in the T25-FW at 16 weeks
- Incidence and severity of AEs

Secondary

- Change in Modified Ranking Scale at 16 weeks
- Change in the distribution-of-stiffness index scores at 16 weeks
- Change in anti-GAD65 and anti-glycine receptor antibodies

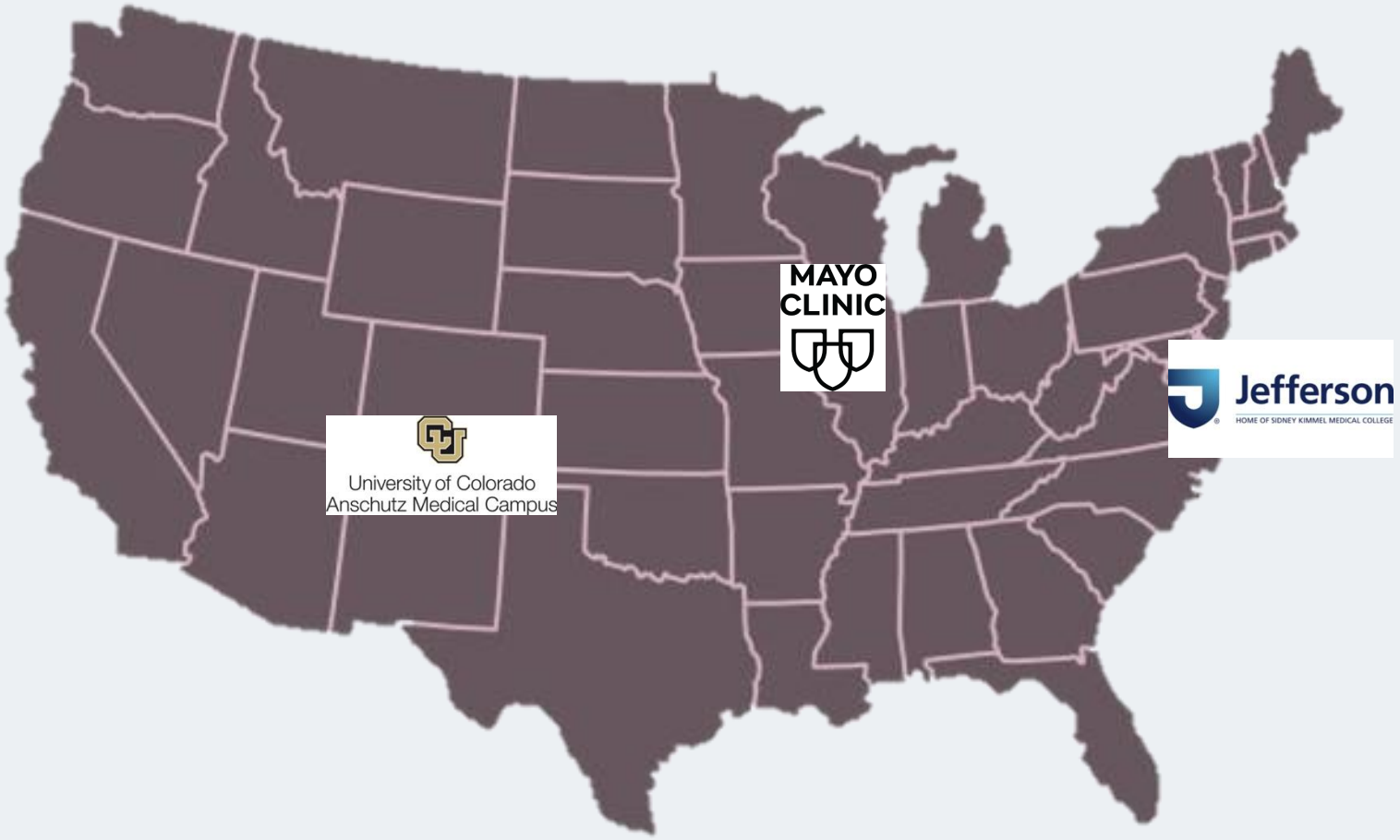
AE, adverse event; CAR, chimeric antigen receptor; GAD, glutamic acid decarboxylase; SF-36, 36-Item Short Form Health Survey; T25FW, timed 25-foot walk.

Eligible Patients Must Have Treatment Refractory Stiff-Person Syndrome

Key Inclusion Criteria	Key Exclusion Criteria
⊹ 18 to 75 years of age	⊹ Bedridden for more than 3 months
⊹ Diagnosis of SPS	⊹ History of allogeneic or autologous stem cell transplant
⊹ Active symptoms with inadequate response to at least one immunomodulatory therapy	⊹ PERM[a]
⊹ Stiffness index ≥2	

[a]Planned protocol amendment.
PERM, progressive encephalomyelitis with rigidity and myoclonus; SPS, stiff-person syndrome.

First-in-Class KYV-101: Partnering With Leaders in the Field



- FDA RMAT Designation
- 3 sites
- Actively enrolling

FDA, Food and Drug Administration; RMAT, regenerative medicine advanced therapy.

Early Experience With KYV-101 in Myasthenia Gravis

Aiden Haghikia, MD
University of Hannover

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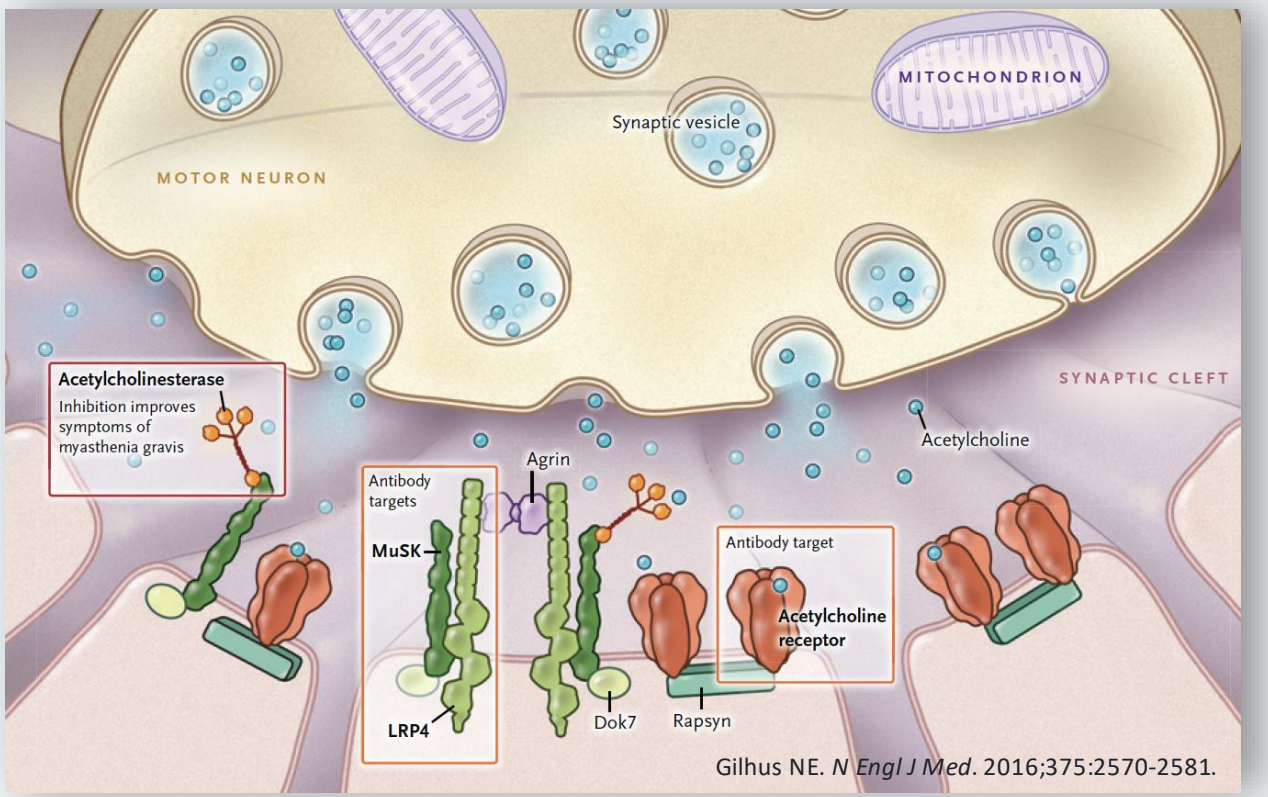
Myasthenia Gravis Is Associated With Increased Disability and Mortality

- Autoantibodies bind to ACh receptors, or related molecules, causing muscle weakness[1-4]
- Associated with increased mortality risk[1-4]
- Treatments remove/block autoantibodies or prevent postsynaptic receptor destruction
- Up to 15% of patients are disabled[3,5]



Gilhus NE. *N Engl J Med*. 2016;375:2570-2581.

There is a need for new therapeutic paradigms for MG that can stop the progression of disability[3]

ACh, acetylcholine; MG, myasthenia gravis.

1. Myasthenia Gravis. Accessed January 29, 2024. https://www.ninds.nih.gov/health-information/disorders/myasthenia-gravis. 2. Dalakas MC, *Nat Rev Neurol*. 2019;15(2):113-124. 3. DeHart-McCoyle M, et al. *BMJ Med*. 2023;2(1):e000241. 4. Dresser L, et al. *J Clin Med*. 2021;10(11). 5. Narayanaswami P, et al. *Neurology*. 2021;96(3):114-122.

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KYV-101 Emerging Clinical Experience in 3 Patients With Myasthenia Gravis

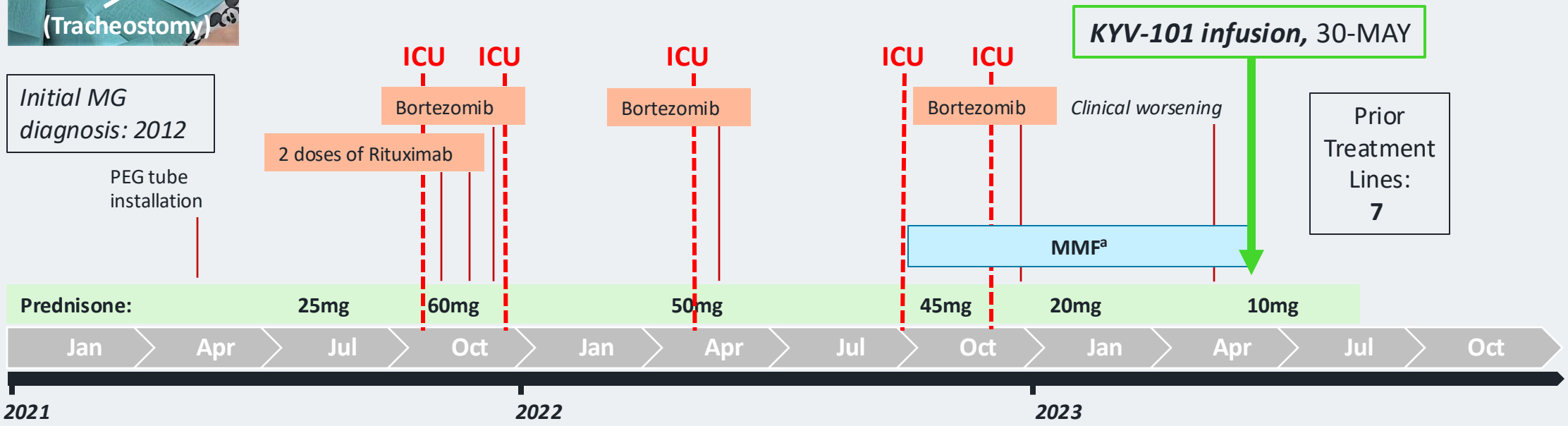
Patient		Diagnosis	Disease Duration	Age	Disease Description	Prior Lines of Treatment	CD20 Failure
1		Seropositive MG	11 years	33 years	5 myasthenic crises in 2 years requiring ICU care and tracheostomy	7	✓
2		Seropositive MG	1 year	75 years	Rapid onset of severe disease; inability to swallow; PEG feeding tube due to aspiration pneumonia	2	✓
3		Seropositive MG	10 years	36 years	Exhausted available therapies	5	✓

Note: named patient experience; ICU, intensive care unit; MG, myasthenia gravis; PEG, percutaneous endoscopic gastrostomy.

Patient 1: Severe Refractory Anti-AChR Seropositive Myasthenia Gravis

Kyverna Patient 1: 33 year-old mother of 4, disability pension, initial MG diagnosis 2012

- **Five myasthenic crises in the last two years, requiring ICU care and tracheostomy**
- Refractory to rituximab, bortezomib
- Chronic treatment with Cellcept (MMF) and steroids
- May 2023: rising clinical score (need to use a walker); rising AChR titers
- Physicians moved to consider CD19 CAR T "healing attempt"



[a]MMF interrupted briefly for apheresis.

MG, myasthenia gravis; PEG, percutaneous endoscopic gastrostomy; ICU, intensive care unit; MMF, mycophenolate mofetil; AChR, acetylcholine-receptor.

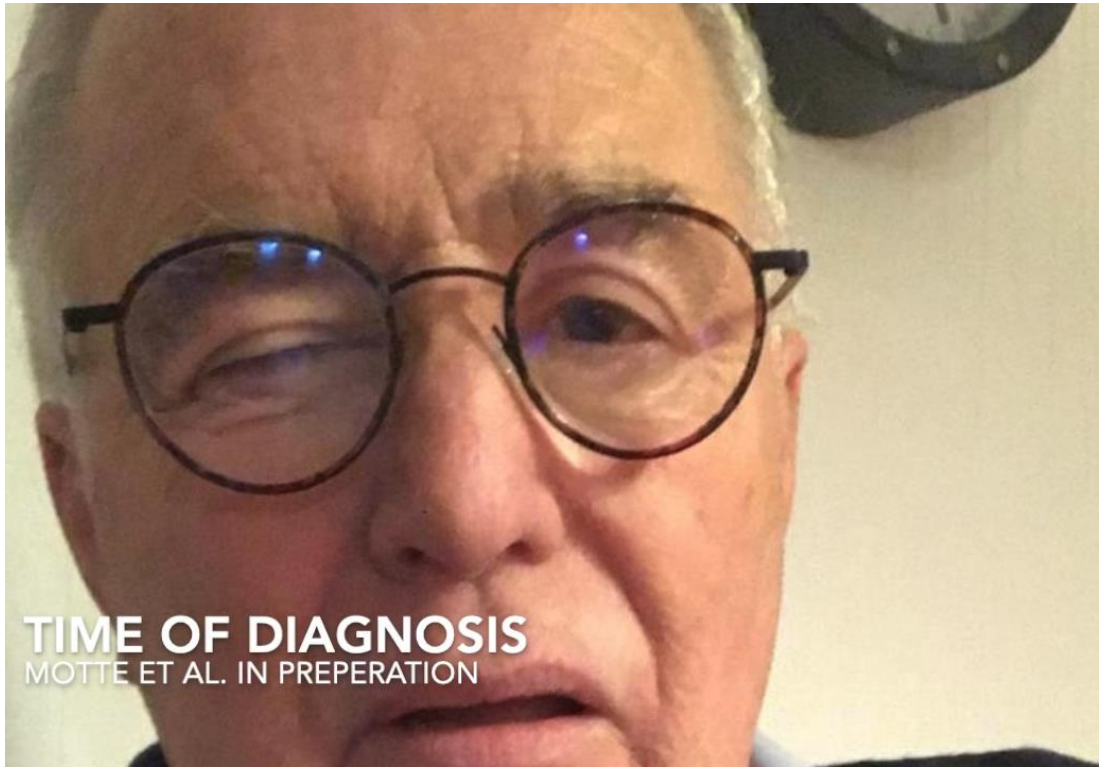
Patient 1: KYV-101 Shows Promising Efficacy in Myasthenia Gravis

6 Days Post-CAR T-Cell Therapy

13 Days Post-CAR T-Cell Therapy

Patient 2: KYV-101 Shows Promising Efficacy in Myasthenia Gravis

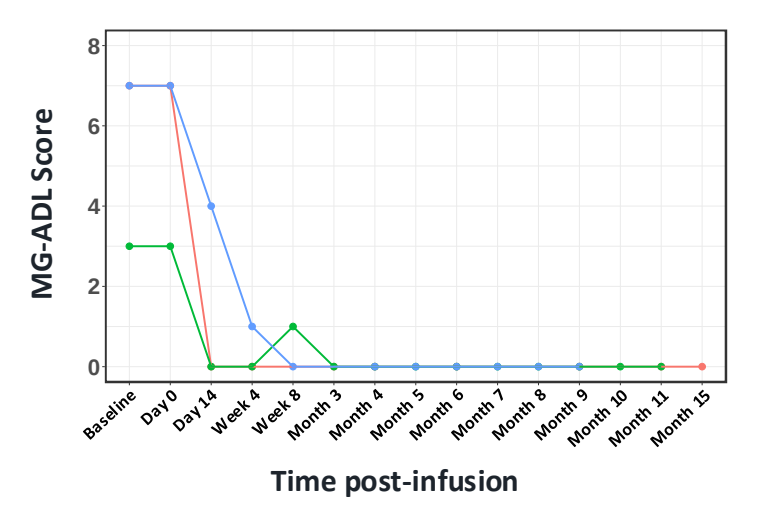
Time of Diagnosis



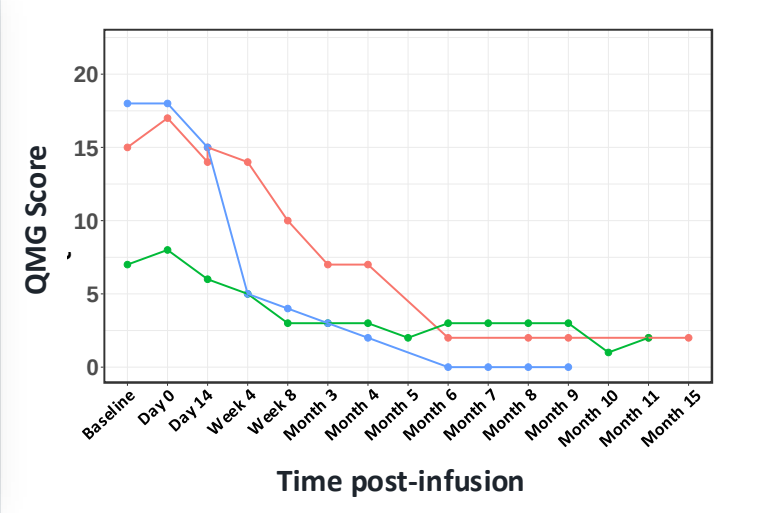
6 Months Post CAR T-cell Therapy

KYV-101 Enables Prompt and Sustained Myasthenia Gravis Disease Control

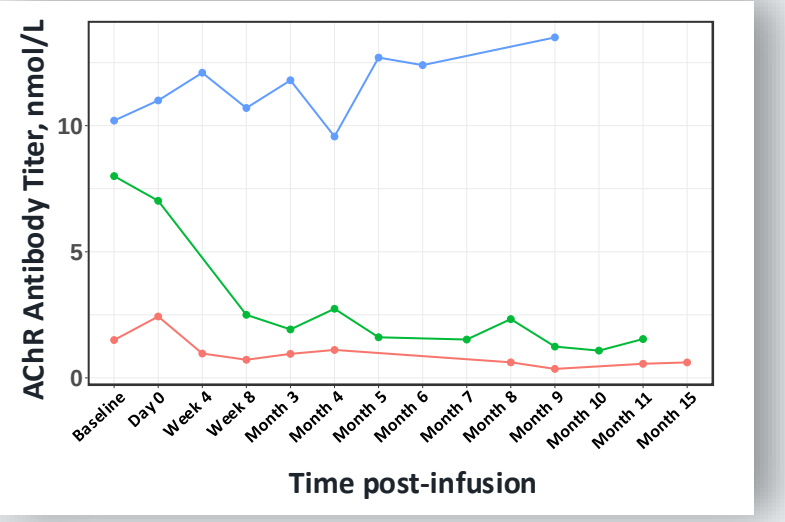
MG-ADL (n=3)



QMG (n=3)



Anti-AChR Antibody Titer (n=3)



Patient 1 Patient 2 Patient 3

- All 3 patients are off immunosuppressive therapy

Note: named patient data; AChR, acetylcholine receptor; ADL, activities of daily living; ICU, intensive care unit; MG, myasthenia gravis; MMF, mycophenolate mofetil; PEG, percutaneous endoscopic gastrostomy; QMG; Quantitative Myasthenia Gravis.

Safety Profile Consistent With Overall KYV-101 Experience

Patient		Diagnosis	Disease Duration	Age	CRS Grade (1-4)*	ICANS Grade (1-4)
1		Seropositive MG	11 years	33 years	None	None
2		Seropositive MG	1 year	75 years	2	None
3		Seropositive MG	10 years	36 years	None	None

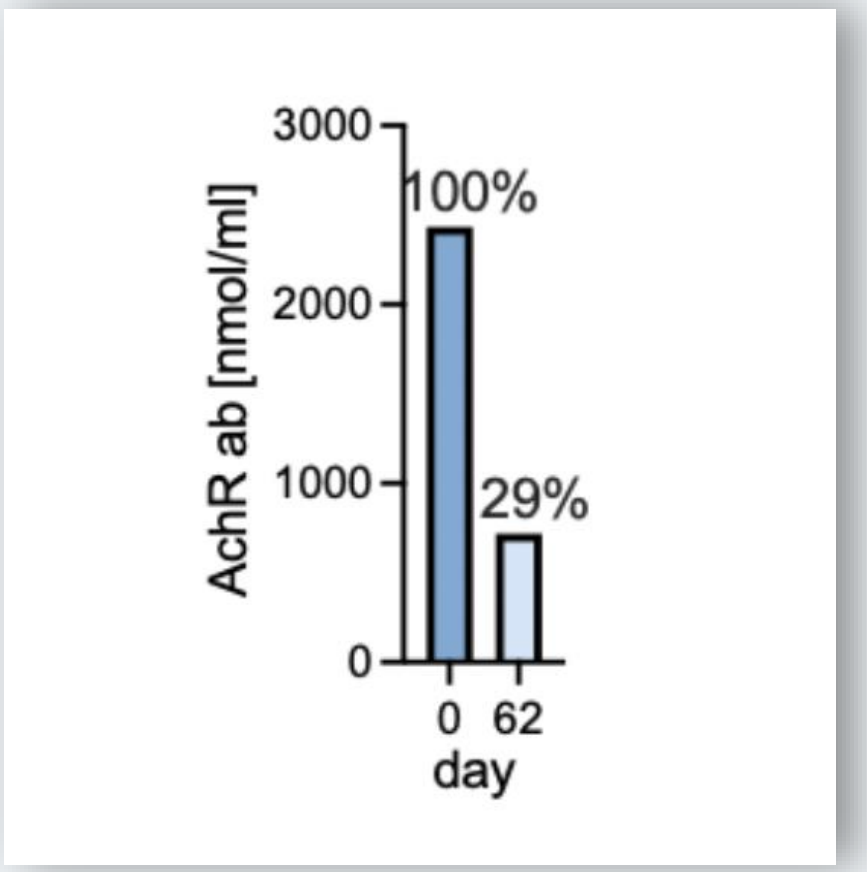
- No ICANs with transient and easily manageable CRS

*Grade 1-2 CRS is mild to moderate.
Note: named patient data; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; MG, myasthenia gravis.

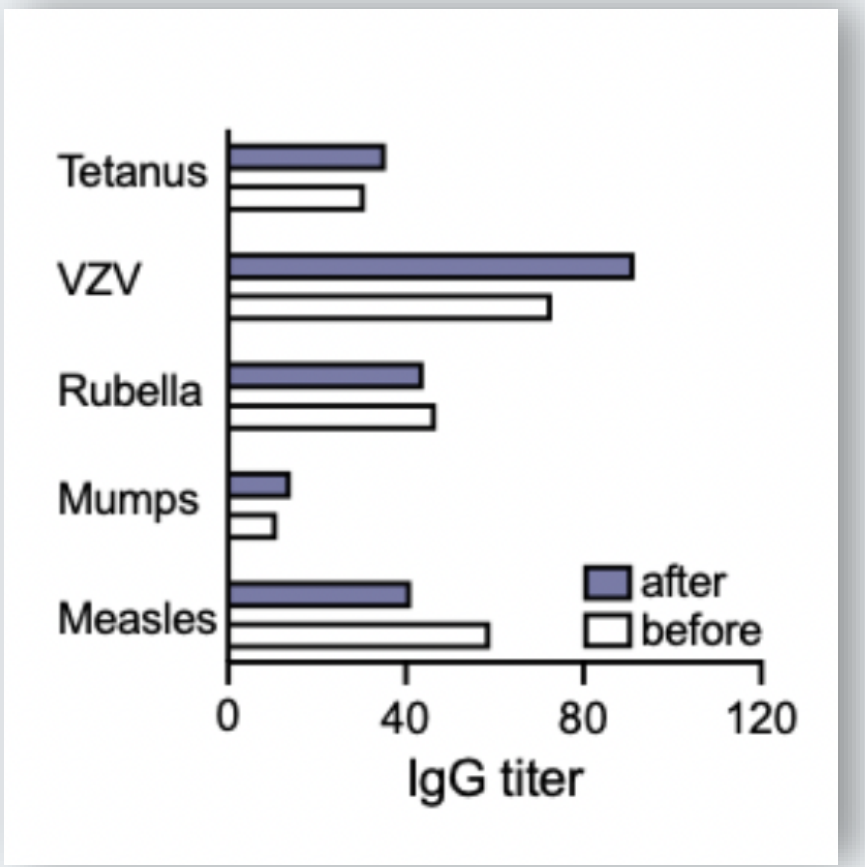
KYV-101 Reduction of Autoantibodies With Preservation of Humoral Immunity

Patient 1

Reduction of pathogenic autoantibodies



Maintenance of humoral protection

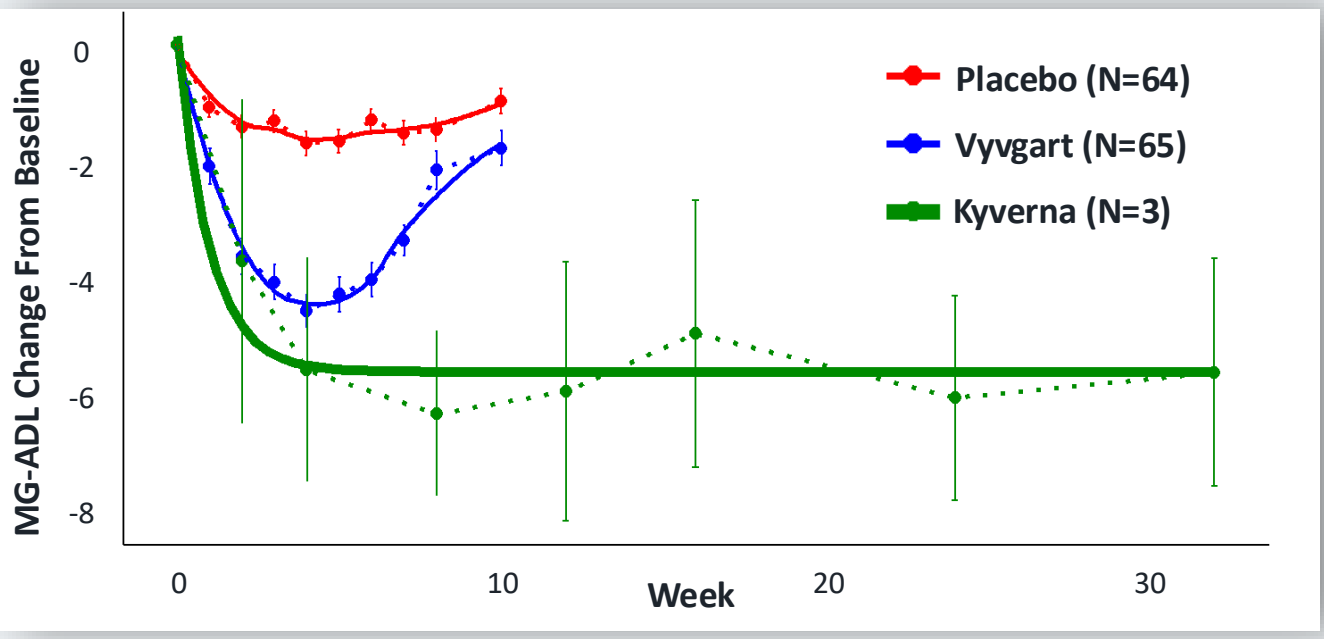


Note: named patient data; ab, antibody; AChR, acetylcholine receptor; IgG, immunoglobulin G; VZV, varicella zoster virus.

Haghikia A, et al. *Lancet Neurol*. 2023; 22: 1104–05.

KYV-101 Promises Durable Treatment Response in Myasthenia Gravis

Comparison of Single Dose Vyvgart to Single Dose KYV-101 Emerging Data*



FcRn Blocker	Chronic administration	Background immunosuppressants
KYV-101 case reports	Single infusion	None

*These limited observations are derived from separate clinical settings, and with respect to the KYV-101 data are based on information from named patient case reports rather than clinical trials. They do not represent head-to-head comparisons of KYV-101 to Vyvgart or placebo. Future clinical trials may not confirm the observations in these case reports. Patients treated on a named patient basis should not be viewed as representative of how the product candidate will perform in our clinical trials and may not be able to be used to establish safety or efficacy for purposes of obtaining regulatory approval.

Adapted from Howard JF, et al. *Lancet Neurol*. 2021;20:526-536 and unpublished data.

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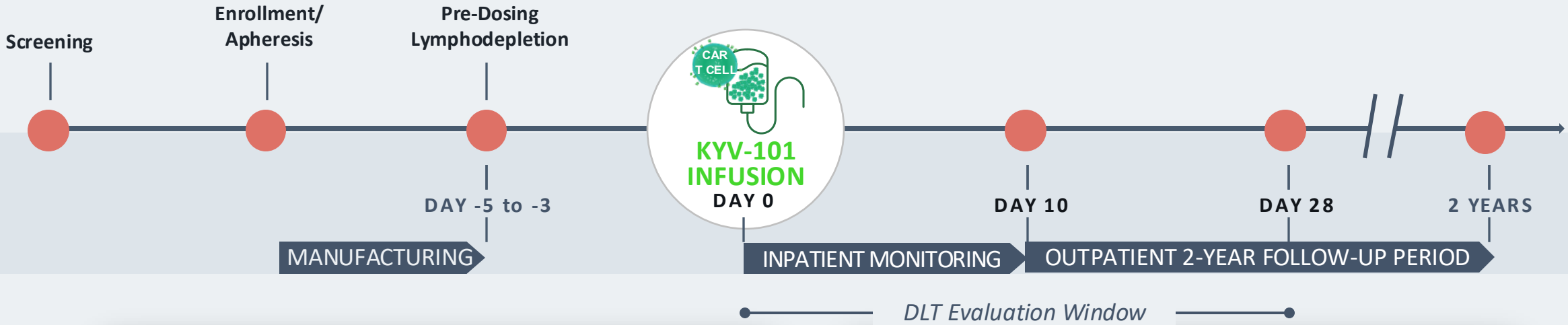
A Phase 2, Open-Label, Multicenter Study of KYV-101 in Refractory Generalized Myasthenia Gravis (N=20)



Primary

- MG-ADL at 24 weeks
- Incidence and severity of AEs

Secondary

- QMG and MGC scores at 12, 24, and 52 weeks
- Change in anti-AChR, anti-MuSK, and anti-LRP4 antibodies

NCT06193889

AE, adverse event; AChR, acetylcholine receptor; CAR, chimeric antigen receptor; DLT, dose-limiting toxicity; LRP4, low density lipoprotein receptor-related protein 4; MG-ADL, myasthenia gravis activities of daily living; MGC, Myasthenia Gravis Composite; MuSK, muscle-specific kinase; PD, pharmacodynamics; PK, pharmacokinetics; QMG, quantitative myasthenia gravis.

KYSA-6

Eligible Patients Must Have Generalized Seropositive Myasthenia Gravis

Key Inclusion Criteria	Key Exclusion Criteria
⊹ 18 to 75 years of age with a diagnosis of generalized MG; Class III-IV per MGFA criteria ⊹ Presence of autoantibodies to AChR, MuSK, or LRP4 ⊹ MG-ADL total score of ≥6 ⊹ Failed treatment with immunosuppressive/ immunomodulatory therapies	⊹ Prior treatment with cellular immunotherapy (CAR T) or gene therapy product ⊹ History of allogeneic or autologous stem cell transplant or organ transplant

Visit ePoster P1628:
Design of KYSA-6, a Phase 2, Open-Label, Multicenter Study of KYV-101, a Novel Fully Human Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy in Refractory Generalized Myasthenia Gravis

AChR, acetylcholine receptor; CAR, chimeric antigen receptor; HIV, human immunodeficiency virus; IVIg, intravenous immunoglobulin; LRP4, low density lipoprotein receptor-related protein 4; MG, myasthenia gravis; MG-ADL, myasthenia gravis activities of daily living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific kinase.

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CAR T-Cell Therapy in Multiple Sclerosis – Alternative to HSCT?

Nicolaus Kröger, MD
University of Hamburg

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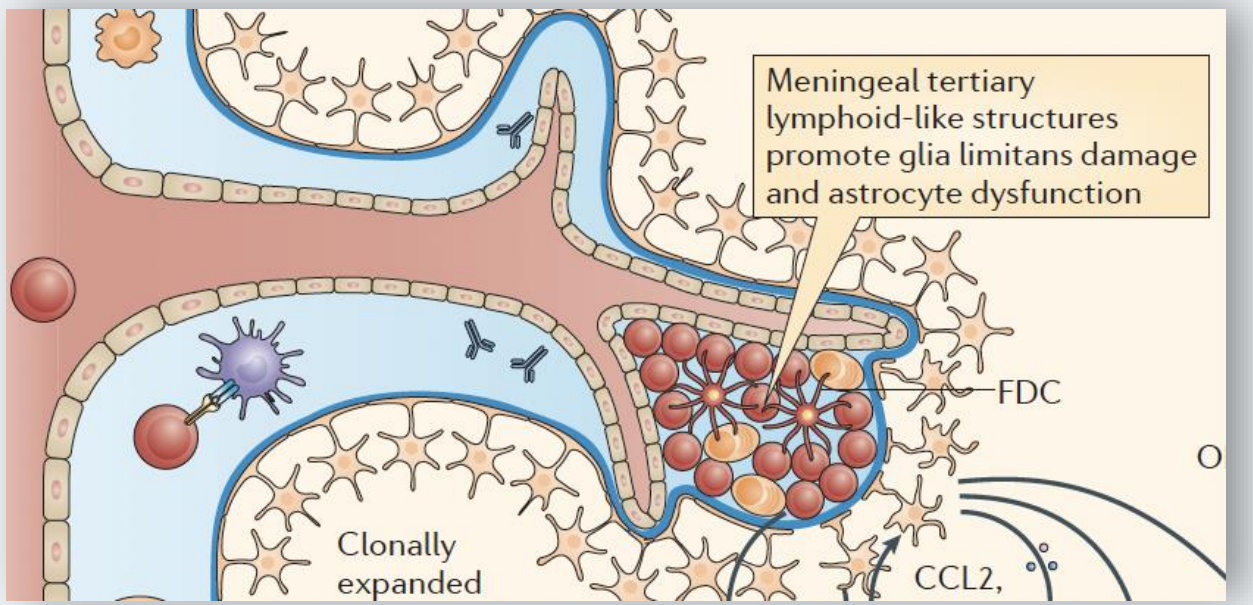
B Cells Play a Central Role in Neuroinflammatory Diseases

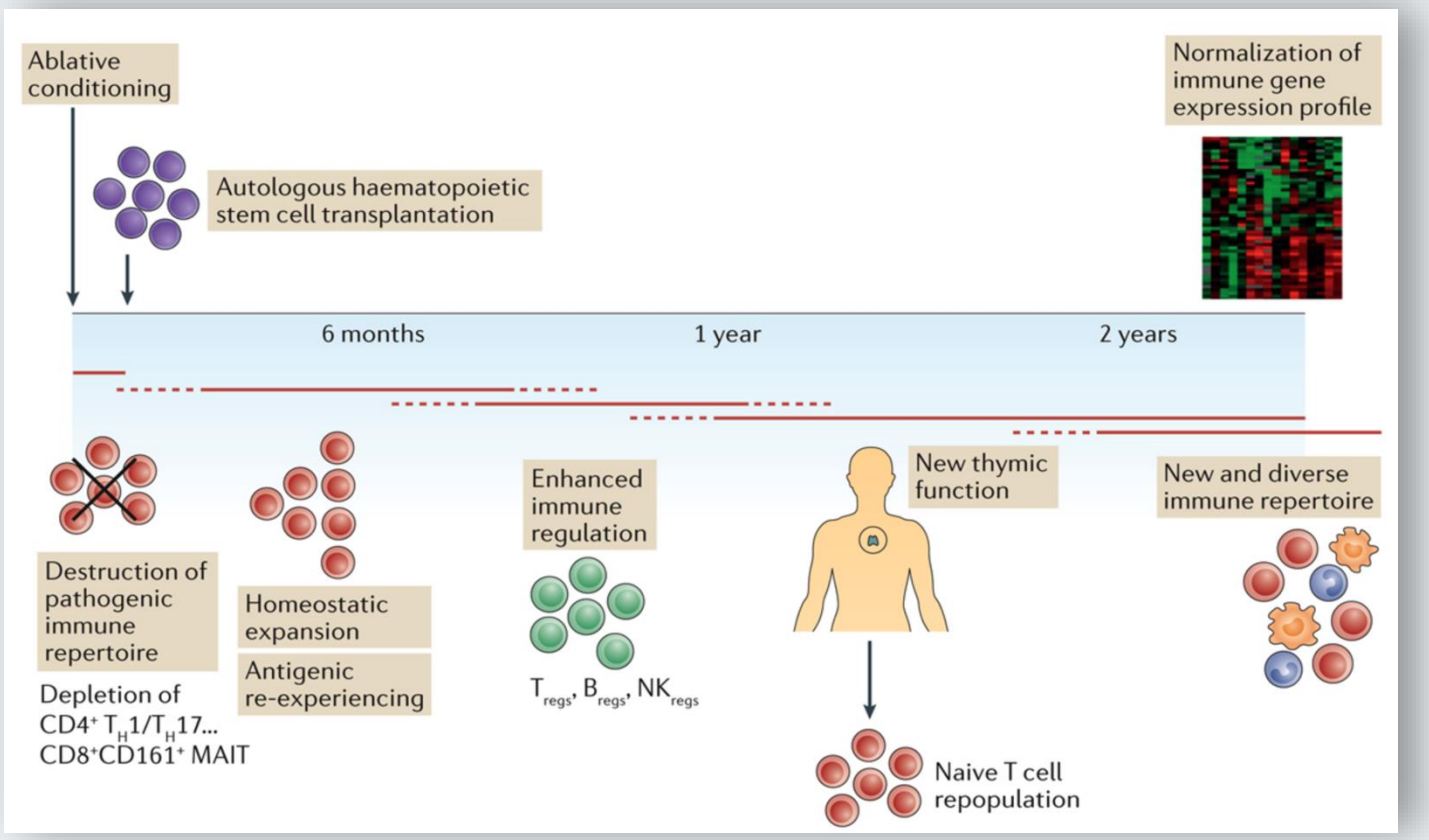
- Role of B cells supported by approval of B-cell depleting monoclonal antibodies[1]
- Growing recognition of local B cell contribution to CNS inflammation[2,3]
- **B cell-rich tertiary lymphoid structures** in the meninges of MS patients[3-5] contribute to meningeal inflammation and neuronal damage
- **Monoclonal antibodies cannot cross the blood-brain barrier** and are unable to target CNS B cells



Dendrou, et al. *Nat Rev Immunol*. 2015;15:545-558.

1. Hauser SL, et al. *N Engl J Med*. 2008;358:676. 2. Mendez et al. *Nat Immunol*. 2018;19:696-707. 3. Dendrou, et al. *Nat Rev Immunol*. 2015;15:545-558. 4. Midstdoerffer and Peters. *Frontiers Immunol*. 2016;7:451. 5. Zhan. et al. *Immunology*. 2021;00:1-17.

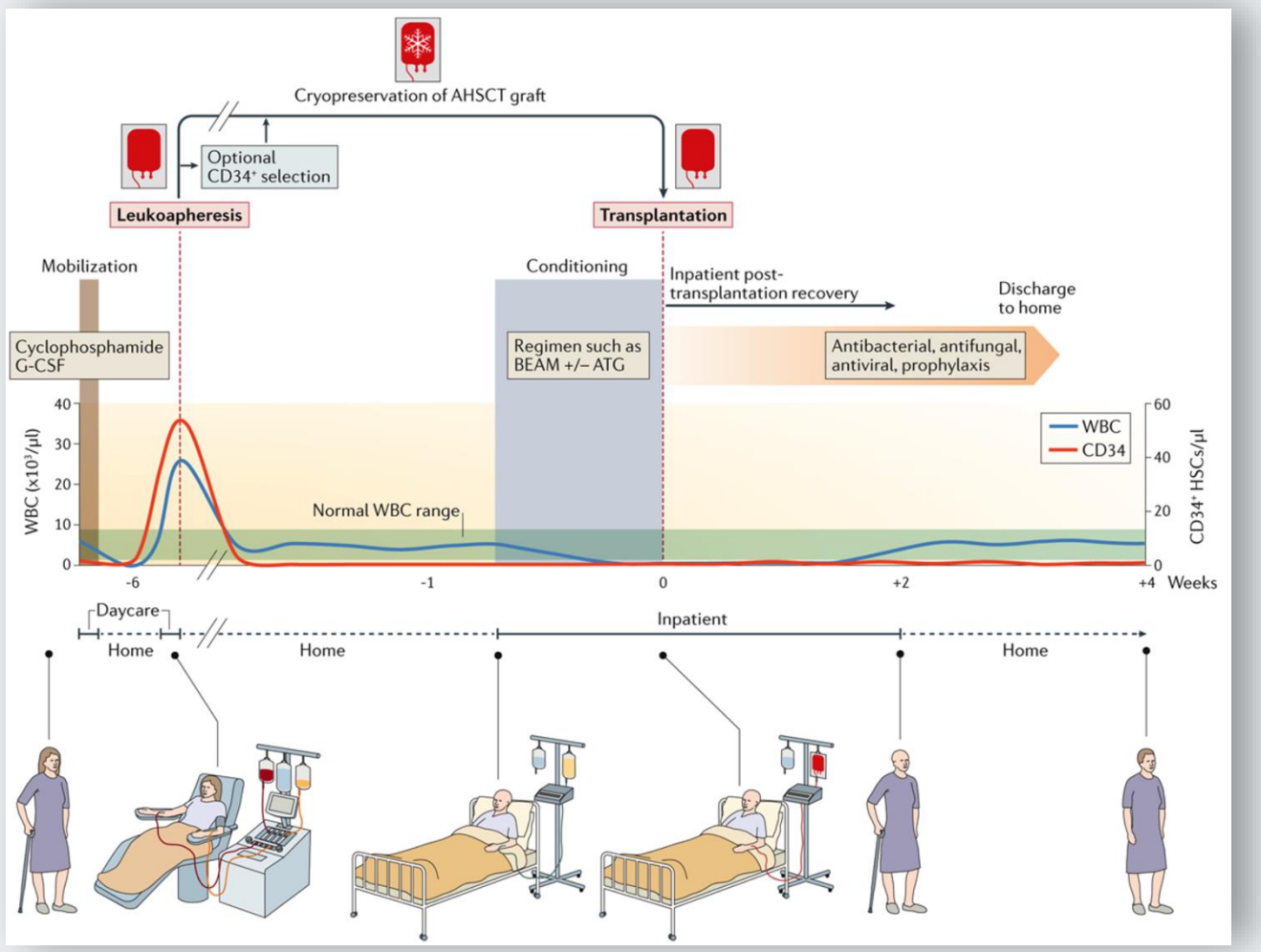
Autologous Hematopoietic Stem Cell Transplantation in MS: Proposed Mechanism



Replacing the entire hematopoietic lineage to reset the immune repertoire including B cells

MS, multiple sclerosis.
Muraro PA, et al. *Nat Rev Neurol*. 2017;13(7):391-405.

Autologous HSCT Is a Clinically Aggressive Approach to Immune System Reset



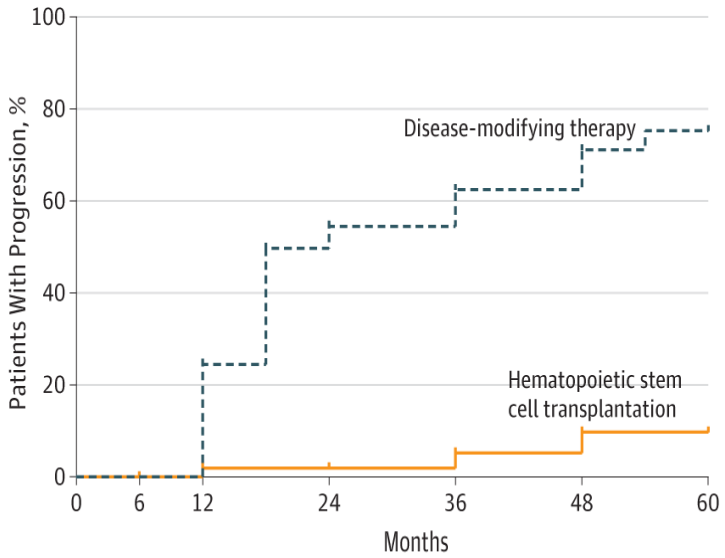
Muraro PA, et al. *Nat Rev Neurol*. 2017;13(7):391-405.

AD, autoimmune disorder; AHSCT, autologous hematopoietic stem cell transplantation; BEAM, bis-chloroethylnitrosourea [BCNU], etoposide, cytosine arabinoside [ARA-C], and melphalan; G-CSF, granulocyte-colony stimulating factor; HSC, hematopoietic stem cell; IDD, insulin-dependent diabetes mellitus; MS, multiple sclerosis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; WBC, white blood cell.

Comparison of Autologous HSCT Versus Disease-Modifying Therapy

MIST Study
(randomized Phase 3)
- 100 patients with RRMS
- **EDSS change by group:**
  - HSCT: -1.02 points
  - DMT: +0.67 points

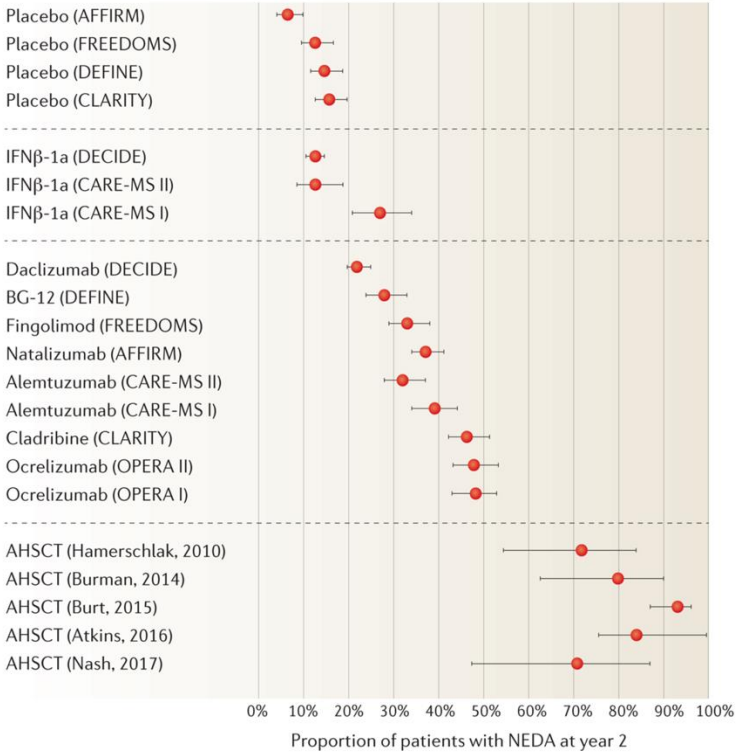
Time to Disease Progression



No. at risk							
Hematopoietic stem cell transplantation	52	52	51	51	50	49	48
Disease-modifying therapy	54	54	43	30	26	24	23

Burt RK, et al. *JAMA*. 2019;321(2):165–174.

Proportion of patients for whom NEDA was achieved at 2 years with DMT and AHSCT



Muraro PA, et al. *Nat Rev Neurol.* 2017;13(7):391-405.

For some patients, autologous HSCT may be associated with an appropriate risk-benefit

AHSCT, autologous hematopoietic stem cell transplantation; DMT, disease-modifying therapy; EDSS, expanded disability status scale; IFNβ-1α, interferon beta 1-alpha; MIST, Multiple Sclerosis International Stem Cell Transplant; MS, multiple sclerosis; NEDA, no evidence of disease activity; RRMS, relapsing remitting multiple sclerosis.

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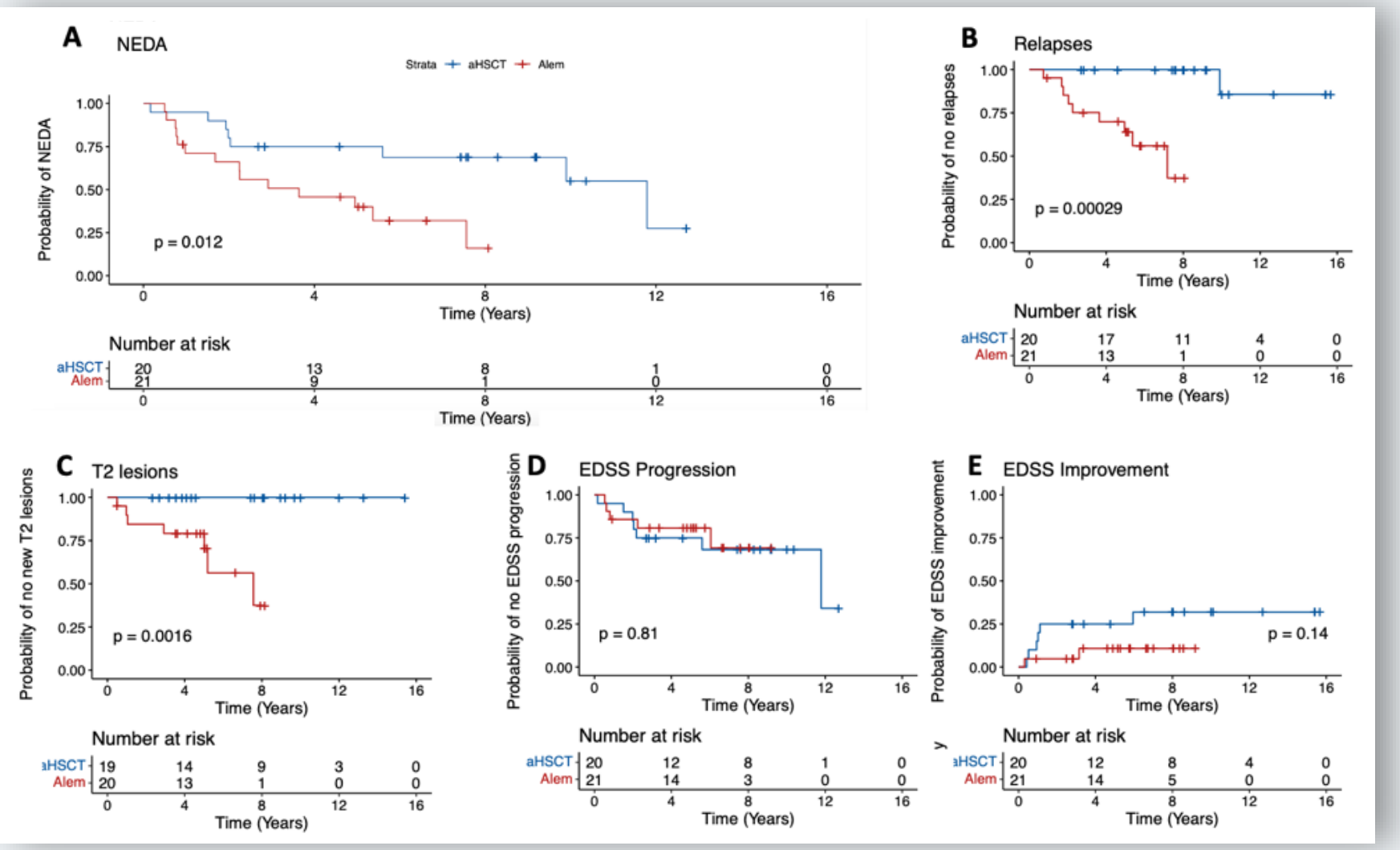
Autologous Hematopoietic Stem Cell Transplantation for MS: Hamburg Experience



Survival:
NEDA-3 and EDSS-Improvement

aHSCT:
- NEDA-3 after 5 years:
  75.0% (95% CI 58.2 - 96.6)
- NEDA-3 after 10 years:
  55.0% (95%CI 32.2 - 93.8)

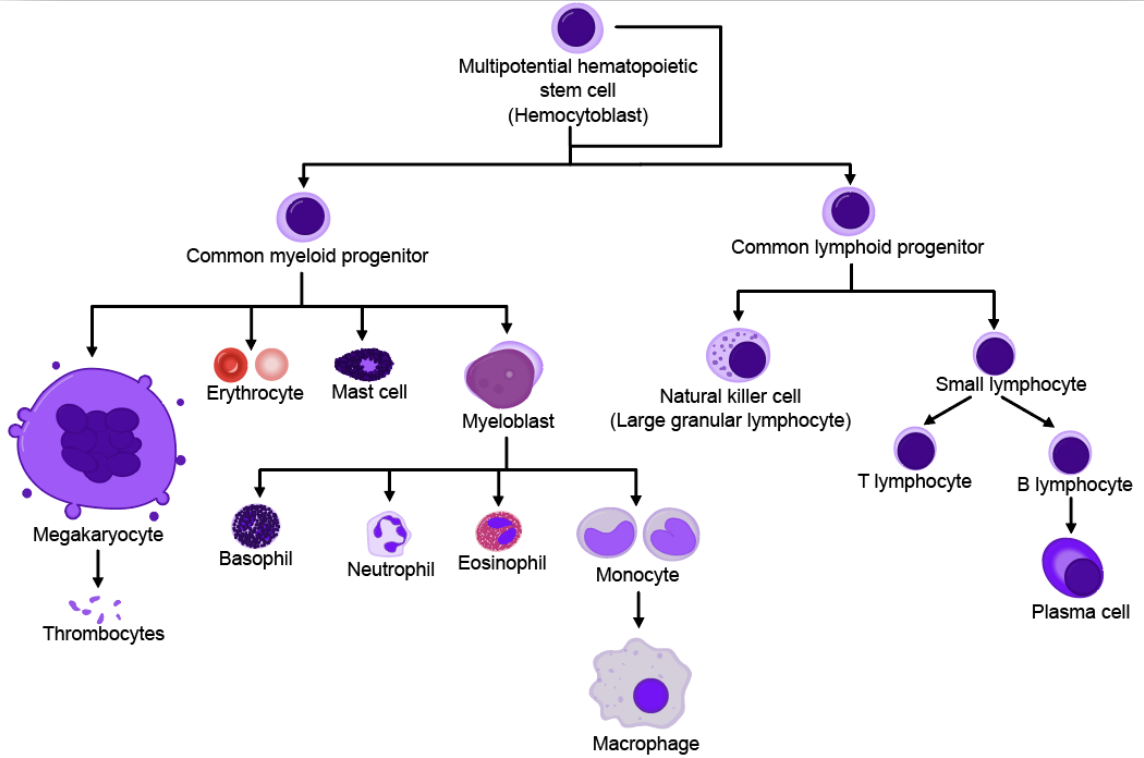
Alemtuzumab:
- NEDA-3 after 5 years:
  40.0% (95%CI 23.2 - 69.0)

aHSCT, autologous hematopoietic stem cell transplantation; EDSS, expanded disability status scale; MIST, Multiple Sclerosis International Stem Cell Transplant; NEDA, no evidence of disease activity.
Braun B, et al. *Mult Scler Relat Disord*. 2024:82:105414.

43

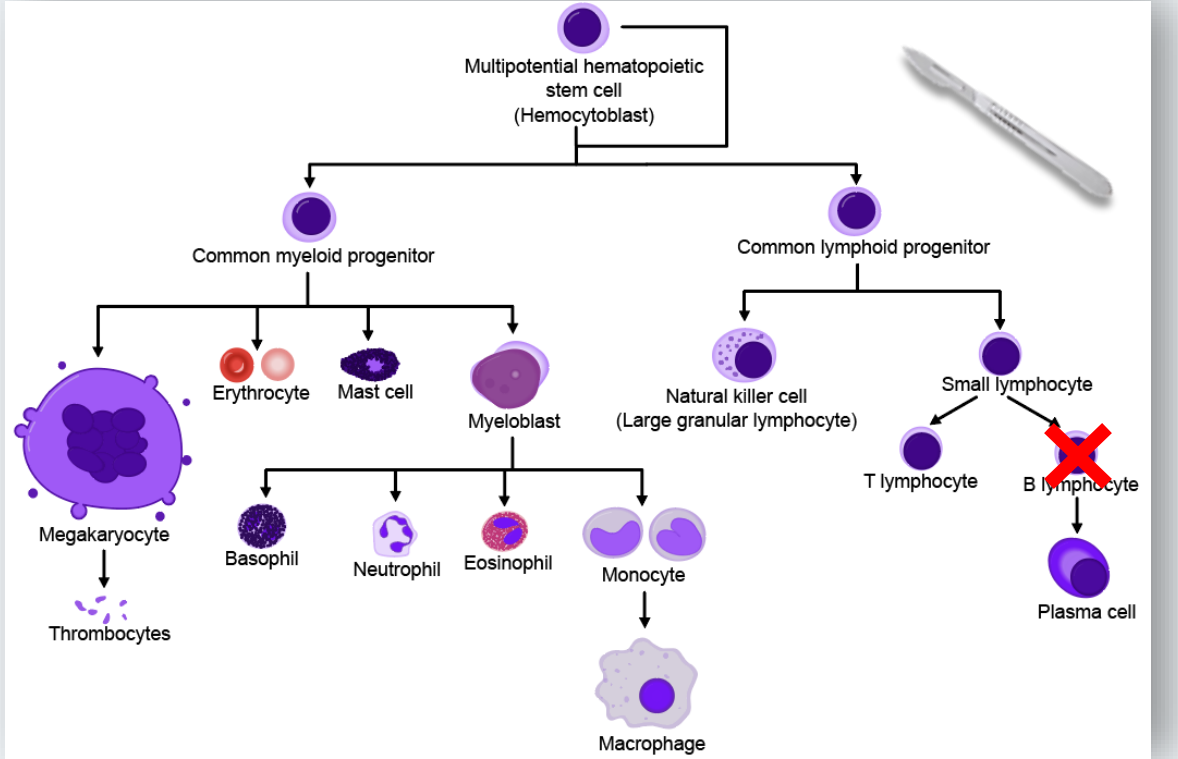
Evolution of Immune Reset From HSCT to CAR T

Autologous HCST



Hemato-lymphopoietic reset

Anti-19 CAR T-cell Therapy



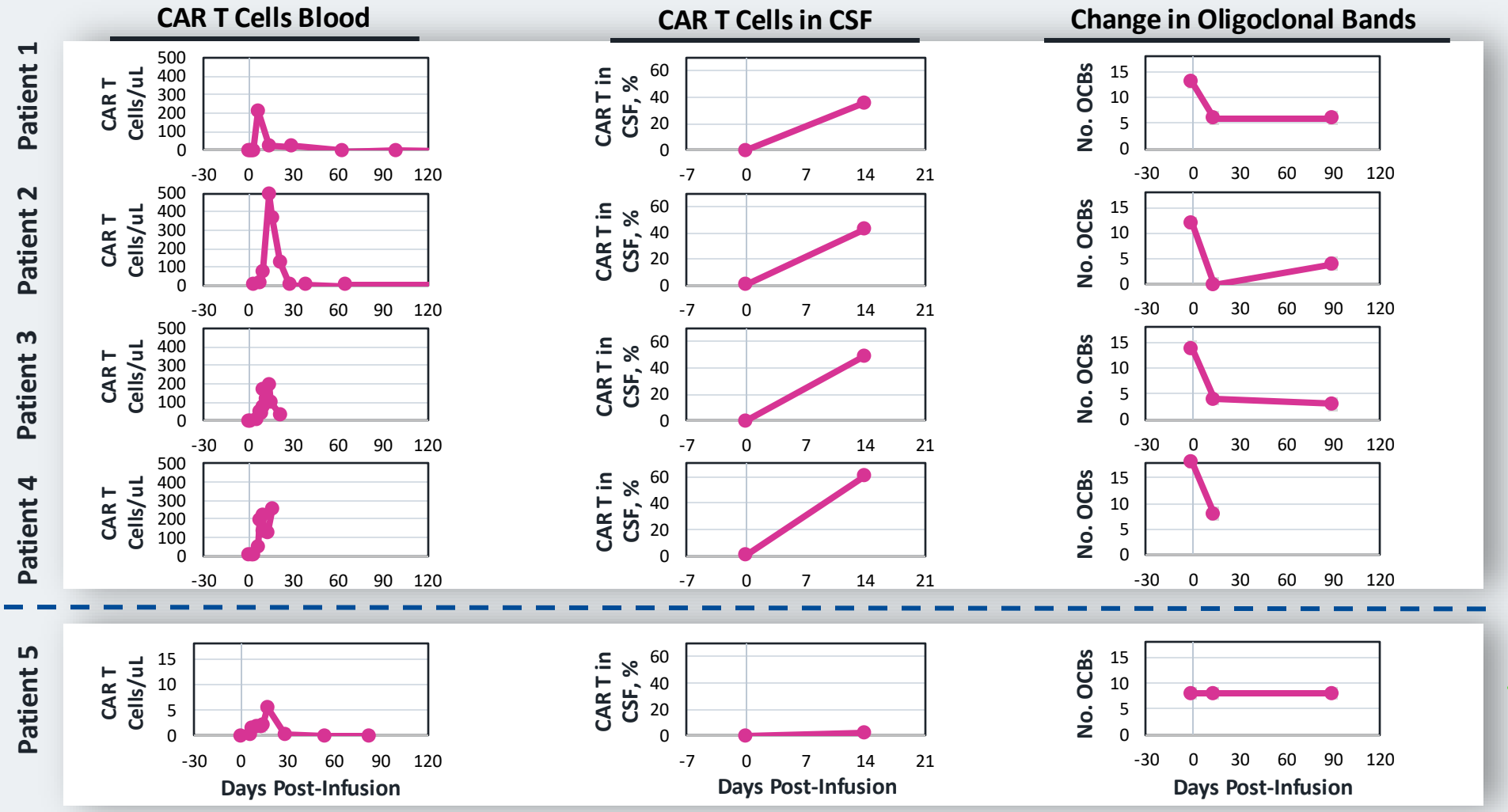
Lineage specific B-cell reset

KYV-101 Emerging Clinical Experience in 5 Patients With Multiple Sclerosis

Patient	Diagnosis	Duration	Age	EDSS at Baseline (0-10)	Prior Treatment	CD20 Failure	KYV-101 Dose
1 	SPMS	24 years	47 years	4.5	Ocrelizumab (600 mg)	✓	1×10^8 anti-CD19 CAR T cells
2 	RRMS	3 years	36 years	2	Ozanimod (0.92 mg/d), Ofatumumab (20 mg/4 wk)	✓	1×10^8 anti-CD19 CAR T cells
3 	RRMS	1 year	29 years	2	Methyl-prednisolone (1000 mg/d), Ofatumumab (20 mg)	✓	1×10^8 anti-CD19 CAR T cells
4 	RRMS	5 years	27 Years	3.5	Glatiramer acetate (20 mg/d), Ofatumumab (20 mg/4 wk), Natalizumab (300mg/4 wk)	✓	1×10^8 anti-CD19 CAR T cells
5 	PPMS	5 years	36 years	7	Ocrelizumab (600 mg)	✓	1×10^8 anti-CD19 CAR T cells

Note: named patient data; CAR, chimeric antigen receptor; PPMS, primary progressive multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

Expansion of CAR T Cells With Penetration of CNS: Impact on Oligoclonal Bands



Lack of expansion in 1 of 41 AI patients similar to <5% in oncology setting

Note: named patient data; AI, autoimmune; CAR, chimeric antigen receptor; CSF, cerebrospinal fluid; OCB, oligoclonal bands.

1. Fischbach F, et al. Med. 2024;22:S2666-6340(24)00114-4. 2. Unpublished data.

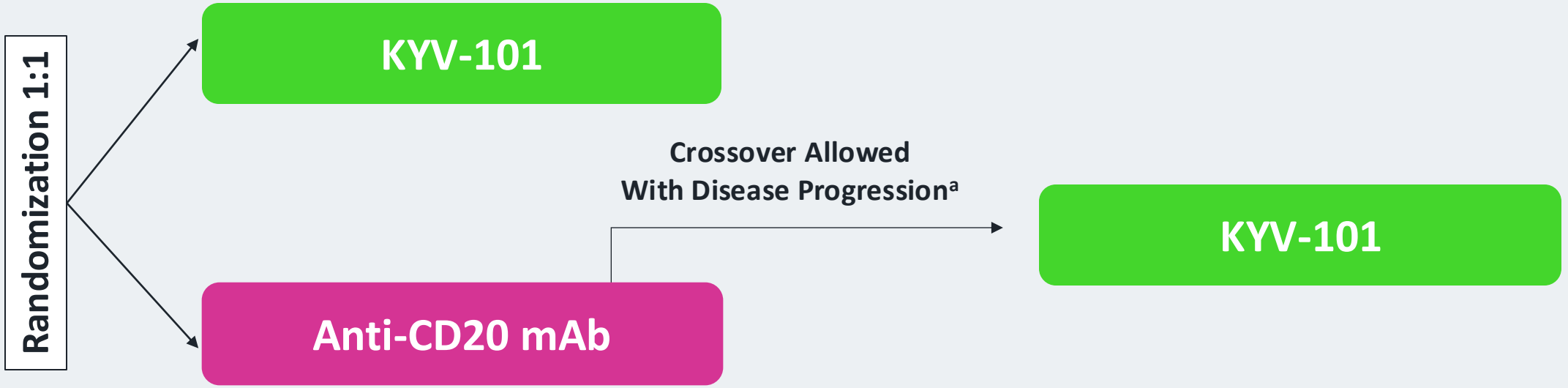
Safety Profile Consistent With Overall KYV-101 Experience

Patient	Diagnosis	Duration	Age	CRS Grade (1-4)*	ICANS Grade (1-4)
1 	SPMS	24 years	47 years	1	None
2 	RRMS	3 years	36 years	1	None
3 	RRMS	1 year	29 years	1	None
4 	RRMS	5 years	27 Years	1	None
5 	PPMS	5 years	36 years	None	None

- CNS expansion is not associated with ICANs; transient and easily manageable CRS

*Grade 1-2 CRS is mild to moderate.
Note: named patient data; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; PPMS, primary progressive multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis.

A Phase 2, Open-Label, Randomized, Multicenter Study of KYV-101 in Refractory Primary and Secondary Progressive Multiple Sclerosis (N=120)

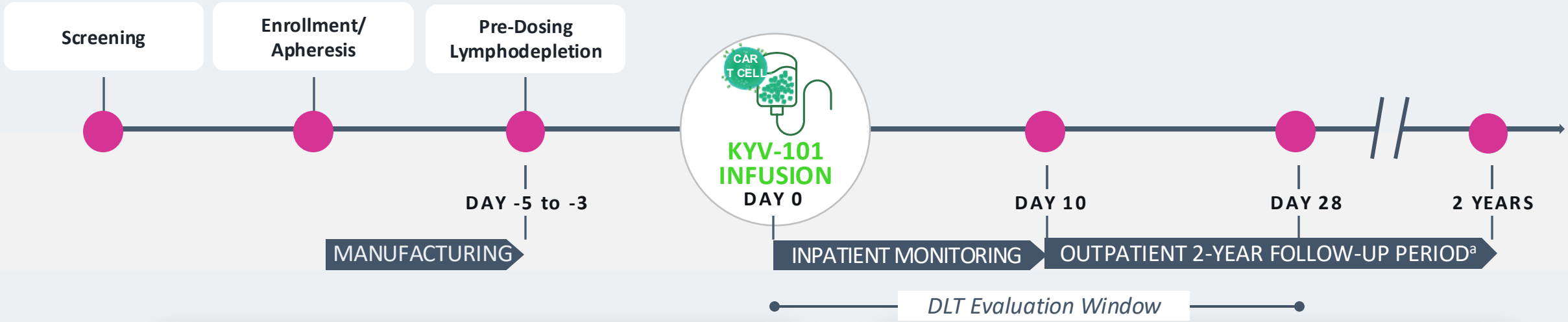


NCT06451159

[a]Patients on anti-CD20 mAb who progress according to protocol will be allowed to crossover to KVY-101.
mAB, monoclonal antibody.

KYSA-7

A Phase 2, Open-Label, Randomized, Multicenter Study of KYV-101 in Refractory Primary and Secondary Progressive Multiple Sclerosis



Primary

- CDP measured by EDSS at 12 weeks

Secondary

- Incidence and severity of AEs
- Changes in oligoclonal bands[a]
- Composite CDP[b]
- ARR in active SPMS
- Changes in brain MRI

NCT06451159

[a]For the CSF consenting patients. Defined as disability progression measured by EDSS, or ≥20% timed 25-foot walk test increase, or ≥20% 9-hole peg test increase, confirmed after ≥12 weeks.
AE, adverse event; ARR, annualized relapse rate; CDP, confirmed disability progression; CSF, cerebrospinal fluid; DLT, dose-limiting toxicity; EDSS, expanded disability status scale; MRI, magnetic resonance imaging; SPMS, secondary progressive multiple sclerosis.

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KYSA-7

Eligible Patients Must Have Primary Progressive or Secondary Progressive MS

Key Inclusion Criteria	Key Exclusion Criteria
⊹ 18 to 60 years of age ⊹ Diagnosis PPMS or SPMS ⊹ EDSS of 3.0 to 5.5 ⊹ Inadequate response to anti-CD20 monoclonal antibody	⊹ Monophasic disease, radiologically isolated syndrome, clinically isolated syndrome, progressive solitary sclerosis or relapsing-remitting disease ⊹ History of NMOSD or MOGAD ⊹ Prior treatment with cellular immunotherapy (CAR T) or gene therapy product directed at any target ⊹ History of allogeneic or autologous stem cell transplant

Visit ePoster P1594 :
Design of KYSA-7, A Phase 2, Open-Label, Randomized, Multicenter Study of KYV-101, an Autologous Fully Human Anti-CD19 Chimeric Antigen Receptor (CAR) T-Cell Therapy, in Treatment Refractory Primary and Secondary Progressive Multiple Sclerosis

CAR, chimeric antigen receptor; CNS, central nervous system; EDSS, expanded disability status scale; MOGAD, MOG antibody associated disease; MS, multiple sclerosis; NMOSD, neuromyelitis optica spectrum disorder; PPMS, primary progressive multiple sclerosis; PML, progressive multifocal leukoencephalopathy; SPMS, secondary progressive multiple sclerosis.

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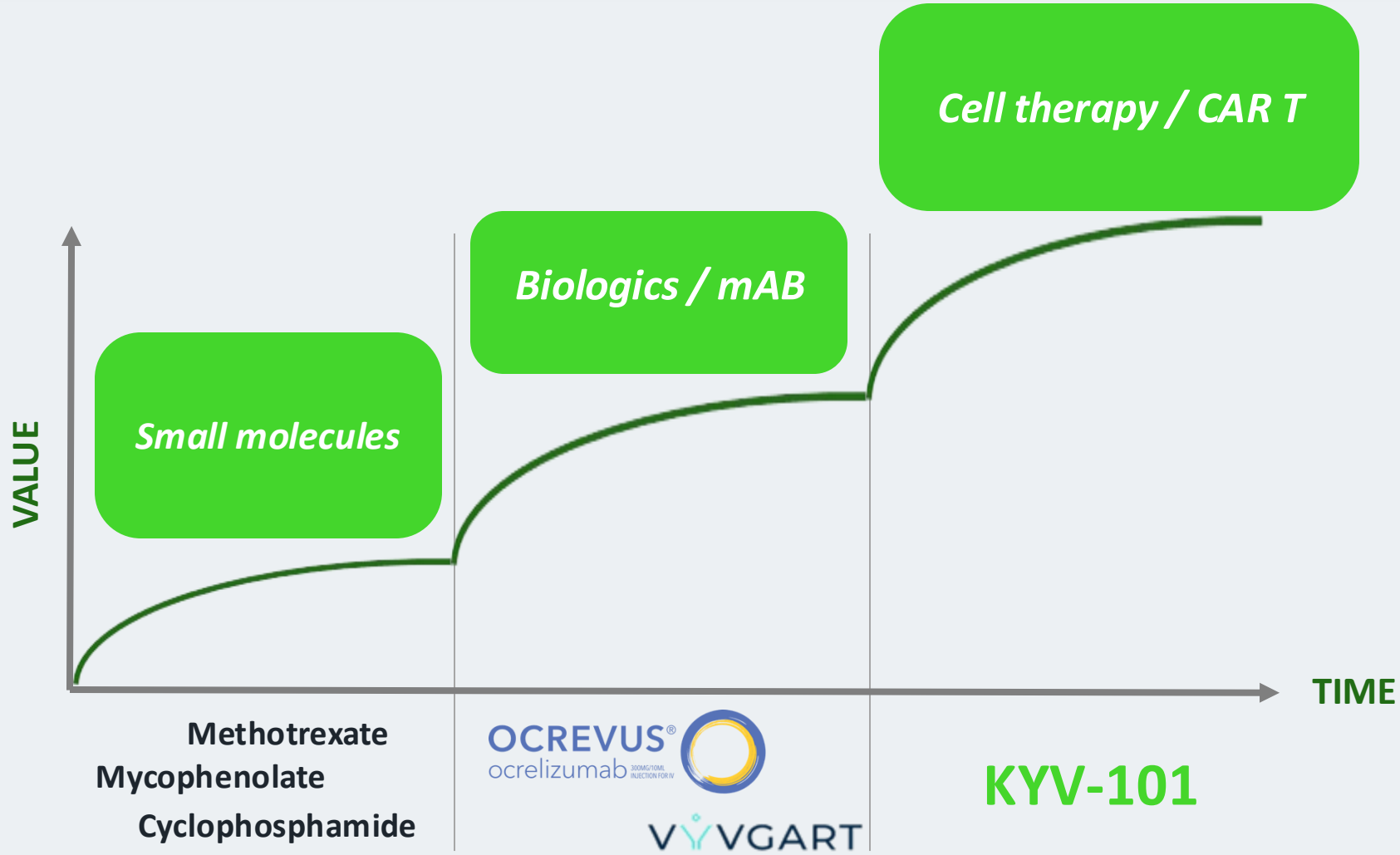
Cell Therapy Is Shifting the Paradigm in Neuroinflammatory Diseases



CAR, chimeric antigen receptor, mAB, monoclonal antibodies.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Acknowledgments – Creating the Kyverna Village

Patients and Their Families
for their courage and trust

Kyverna Employees for their
hard work and dedication

Care Givers and Collaborators for their partnership