Kyverna Therapeutics

HARNESSING THE POWER OF CELL THERAPY IN AUTOIMMUNE DISEASE

December 2024

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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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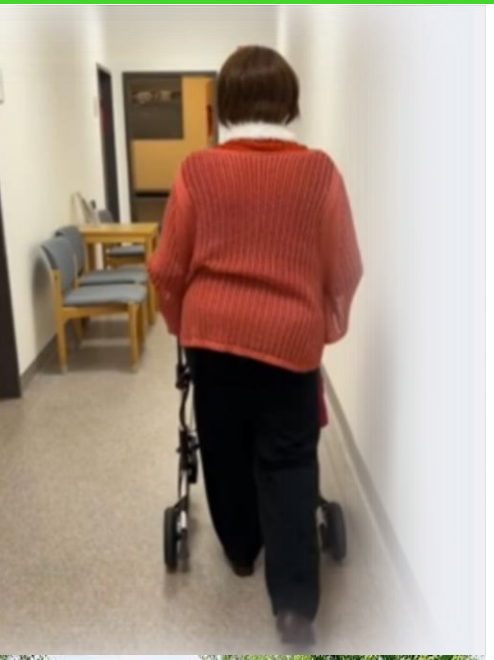

Goal: Durable clinical response and withdrawal of immunosuppressive medications

Before CAR-T		**Aim of CAR T-cell therapy**
Continued disease progression	→	"Once and done"
Refractory to several lines	→	Immune reset
Toxic chronic therapies	→	Free of chronic medications

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Autoimmune Diseases Represent a Large, Under-served Market

Autoimmune diseases prevalence high and increasing (80+ different diseases)

Autoimmune diseases affect 8% of people in the U.S.[1], with prevalence increasing YoY

Autoimmune disease large and growing market

Currently marketed products: >$80B revenue[2]

Current treatments inadequate for patients long-term

Current therapies:
- Low rates of remission
- Serious long-term side effects

B Cell-Driven Diseases	Estimated Number of Diagnosed Patients in US + EU + Japan[3]
Rheumatoid Arthritis	4,700,000
Multiple Sclerosis	1,520,000
Sjogren's Disease	750,000
Systemic Lupus Erythematosus (SLE)	560,000
Systemic Sclerosis	200,000
Lupus Nephritis	160,000
Myasthenia Gravis	160,000
Inflammatory Myositis	120,000
ANCA-Associated Vasculitis	100,000
Neuromyelitis Optica	20,000
Total	**~8.3 Million Patients**

Note: 1. National Institutes of Health (NIH) Autoimmune Diseases Coordinating Committee. Progress in Autoimmune Diseases Research (Publication No. 05–5140). March 2005. 14, Accessed date: October 25, 2022; 2. GlobalData 2021; 3. Published literature through GlobalData market analysis reports and internal data 2022

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Working with Leaders and Trailblazing the Autoimmune CAR-T Field

Autoimmune CAR-T Milestones

BRUDNO[1]
2020
20 patients with B-cell malignancies treated with KYV-101 construct

SCHETT[2]
2021
1st autoimmune disease patient treated (lupus nephritis)

HAGHIKIA[3]
2023
1st neuroinflammatory disease patient treated (KYV-101 in myasthenia gravis)

SCHETT[4]
2024
Single-center case series in rheumatology

2018 — **2024**

Kyverna Founded

Demonstrated Safety & Feasibility with KYV-101 in B-cell Malignancy

1st to Tackle Autoimmune Disease

Partnered with NIH to Deliver KYV-101

Fully Human CD-19

1st Company To Dose Autoimmune Patient

Largest Clinical Experience Using KYV-101

Differentiated with RMAT and FASTRACK Designations

Kyverna Milestones

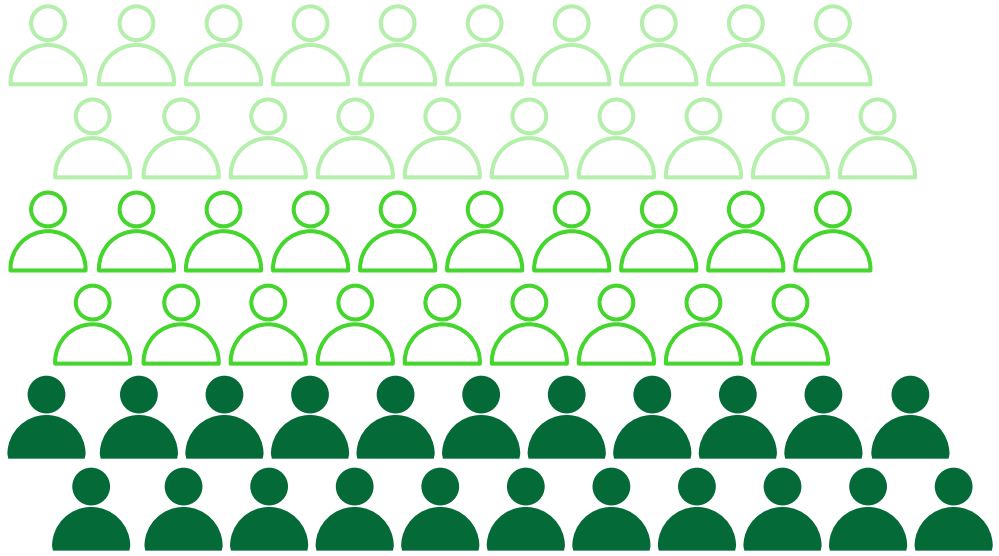
Best Access for Patients with Global Clinical Trial and Manufacturing

1. Brudno JN, et al. *Nat Med*. 2020;26(2):270-280; 2. Mougiakakos D, et al. *N Engl J Med*. 2021;385(6):567-569; 3. Haghikia A, et al. *Lancet Neurol*. 2023;22(12):1104-1105; 4.Muellller F, et al. *N Engl J Med*. 2024;390(7):687-700.

Kyverna's Leading Patient Experience with KYV-101

50+ Autoimmune Patients

Across diverse indications treated with KYV-101



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

As of October 31, 2024.
ANCA, antineutrophil cytoplasmic antibody; CAR, chimeric antigen receptor; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; NMOSD, neuromyelitis optica spectrum disorder.

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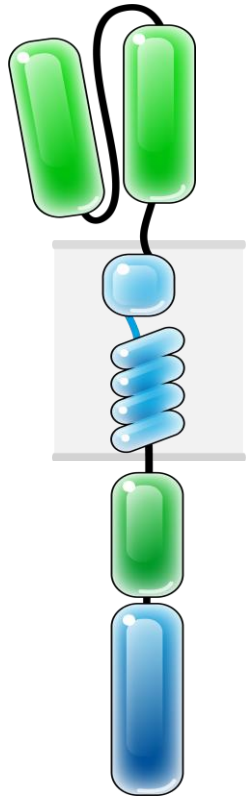
KYV-101: Uniquely Designed to Impact the Unmet Need in Autoimmune Disease

KYV-101 Design

KYV-101 (Hu19-CD828Z)



Human **Anti-CD19 scFv**

Human **CD8α Hinge**

Human **CD8α TM**

Human **CD28 Costim**

Human **CD3ζ**

Designed for **POTENCY**

- The only construct with **highly potent CD28**
- **Maximal B-cell depletion** and **immune reset** ability

Potential for **TRANSFORMATIVE EFFICACY**

- Largest clinical experience across **15+ indications**
- Potential **life-changing efficacy** in refractory patients
- "One and Done" **impacting chronic disease**

Engineered for **SAFETY**

- Unique CAR **designed to minimize toxicity**
- **Fully human** single-chain variable fragment
- CD8α hinge and TM domains

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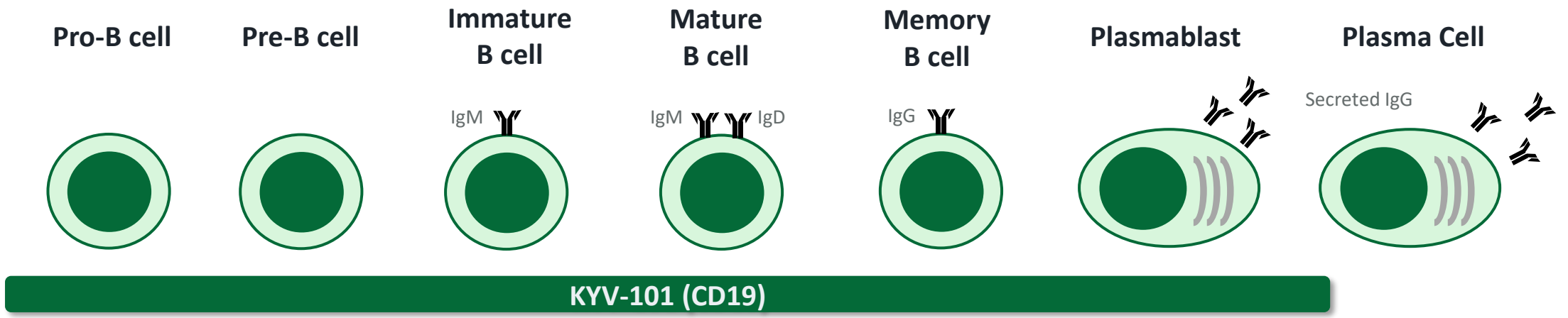
Differentiated Broad Impact of KYV-101: The Value of CD19



Maximizing the depth of B cell cleanout is how we reset the disease

CD19-targeted depletion eliminates the broadest range of B-cell subsets showing promising efficacy while preserving humoral immunity

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Leading Pipeline Recognized for Addressing Clinical Unmet Need

Actively enrolling studies in the US and Europe

Technology	Candidates	Target	Indication	Discovery / Validation	Preclinical	Clinical Phase 1	Clinical Phase 2	Clinical Phase 3	Regulatory Milestone
Autologous CAR T	KYV-101 Rheumatology	CD19	Lupus nephritis	KYSA-1, KYSA-3	Phase 1/2				Fast Track
			Systemic sclerosis	KYSA-5	Phase 1/2				ODD
	KYV-101 Neurology	CD19	Myasthenia gravis	KYSA-6	Phase 2				ODD, RMAT
			Multiple sclerosis	KYSA-7	Phase 2				Fast Track
			Stiff person syndrome	KYSA-8	Phase 2				ODD, RMAT
Allogeneic CAR T	KYV-201	CD19	Multiple						

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; FDA, Food and Drug Administration; ODD, orphan drug designation; RMAT, regenerative medicine advanced therapy.

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KYV-101 in Neuroinflammatory Diseases

Presented Case Reports – Company Symposium at ECTRIMS 2024

KYV-101 Shows Promising Efficacy in Stiff-Person Syndrome

Bedbound, Unable to Bend Legs

Pre-infusion

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.

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

OTTO VON GUERICKE UNIVERSITÄT MAGDEBURG

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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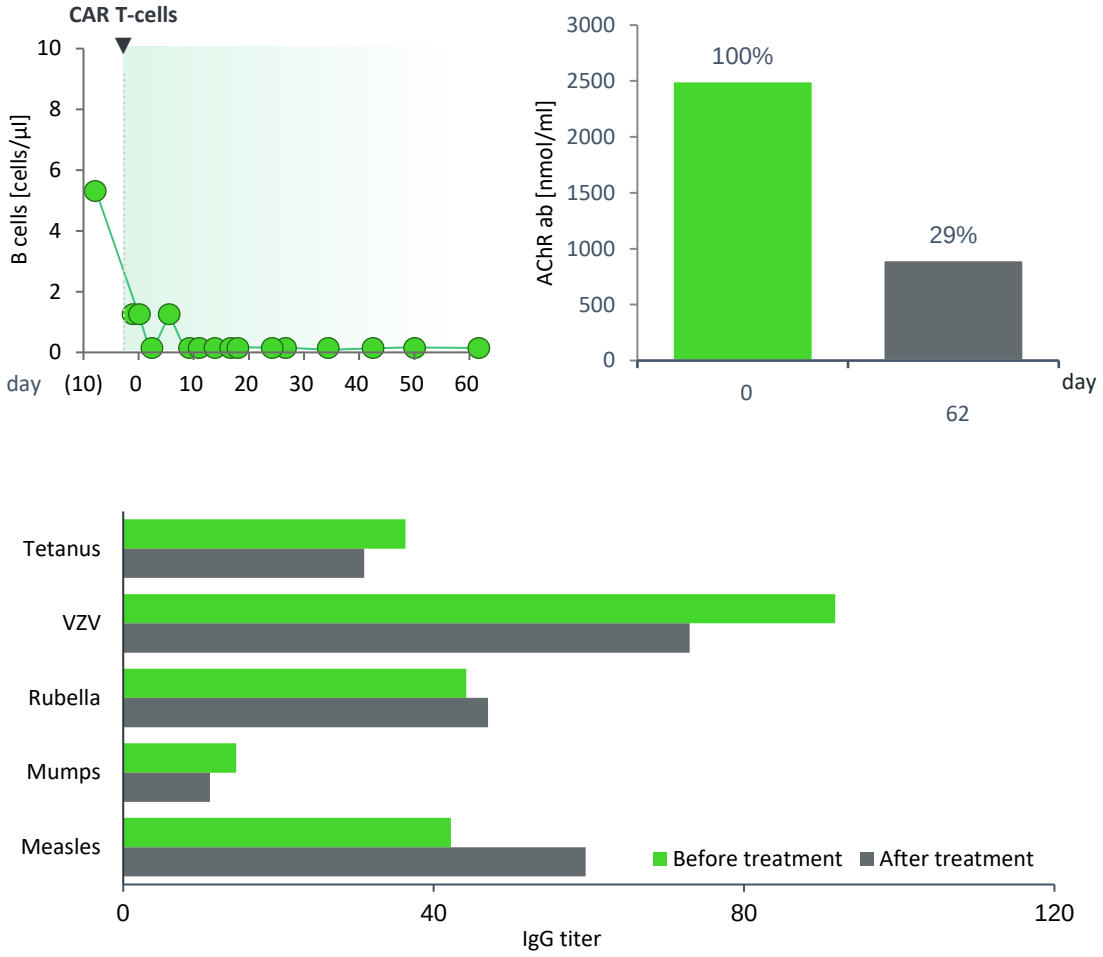
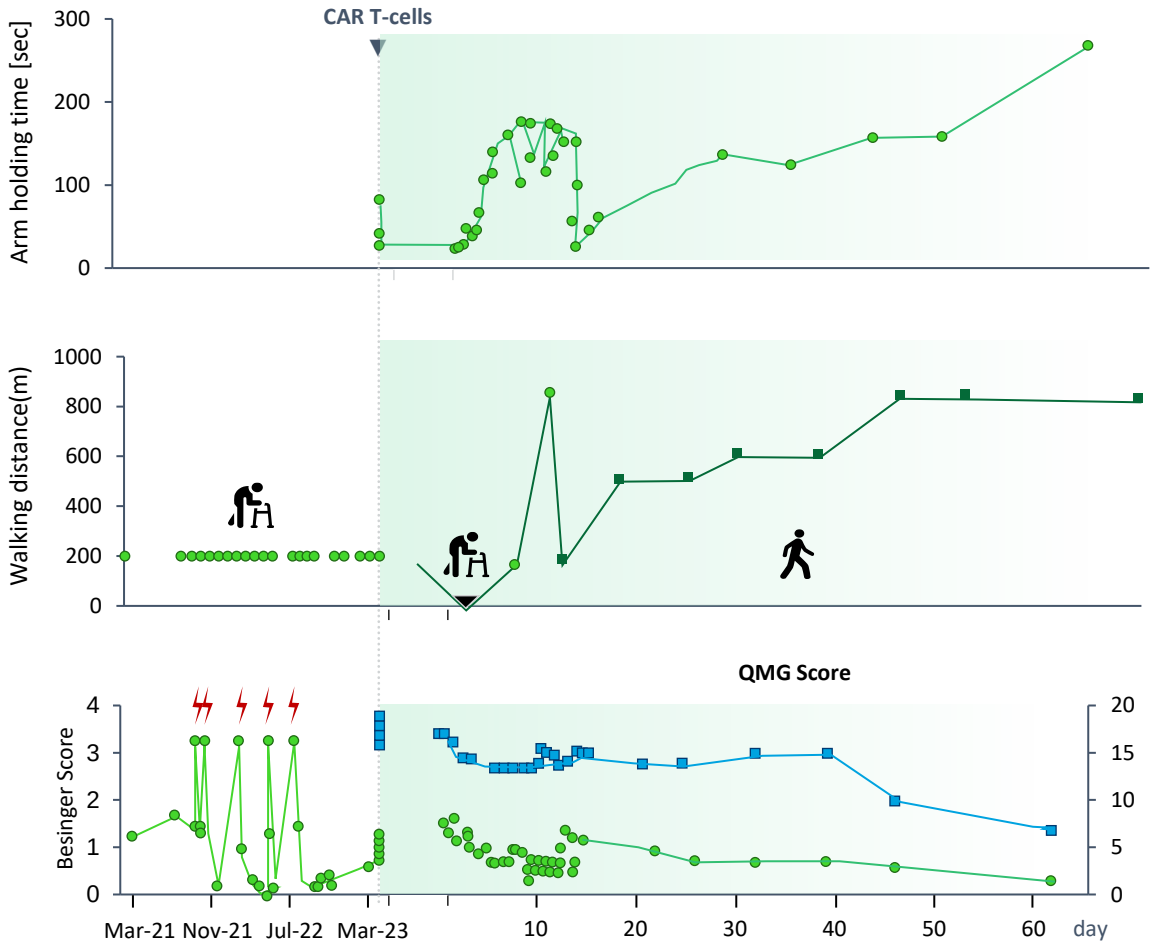
Published Case Reports – Lancet Neurology

Within 60 Days Of Infusion, Observed Improved Symptoms and Mobility in Myasthenia Gravis

Observed dramatic reduction in AChR-ab serum levels, while maintaining antibody titers



After 5 ICU admissions in 18 months, improvement in QMG score and mobility observed



Haghikia A, et al. Anti-CD19 CAR T cells for refractory myasthenia gravis. The Lancet: Neurology 2023. 22(12):1104-1105

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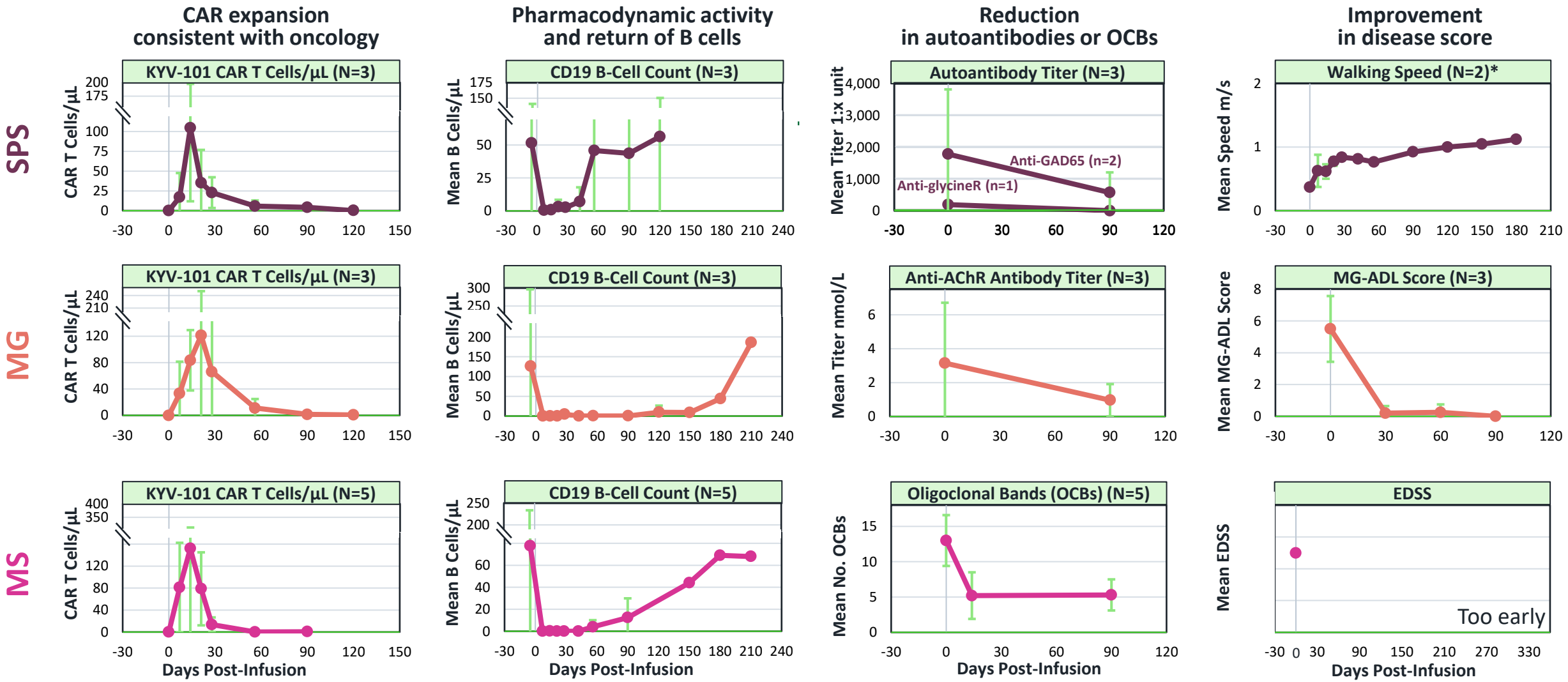
Presented Case Reports – Company Symposium at ECTRIMS 2024

Promising PK, Biomarker and Efficacy Data for KYV-101 in Neuroinflammatory Diseases



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 Rheumatologic Diseases

Leading the Way to Life Changing Impacts for Patients

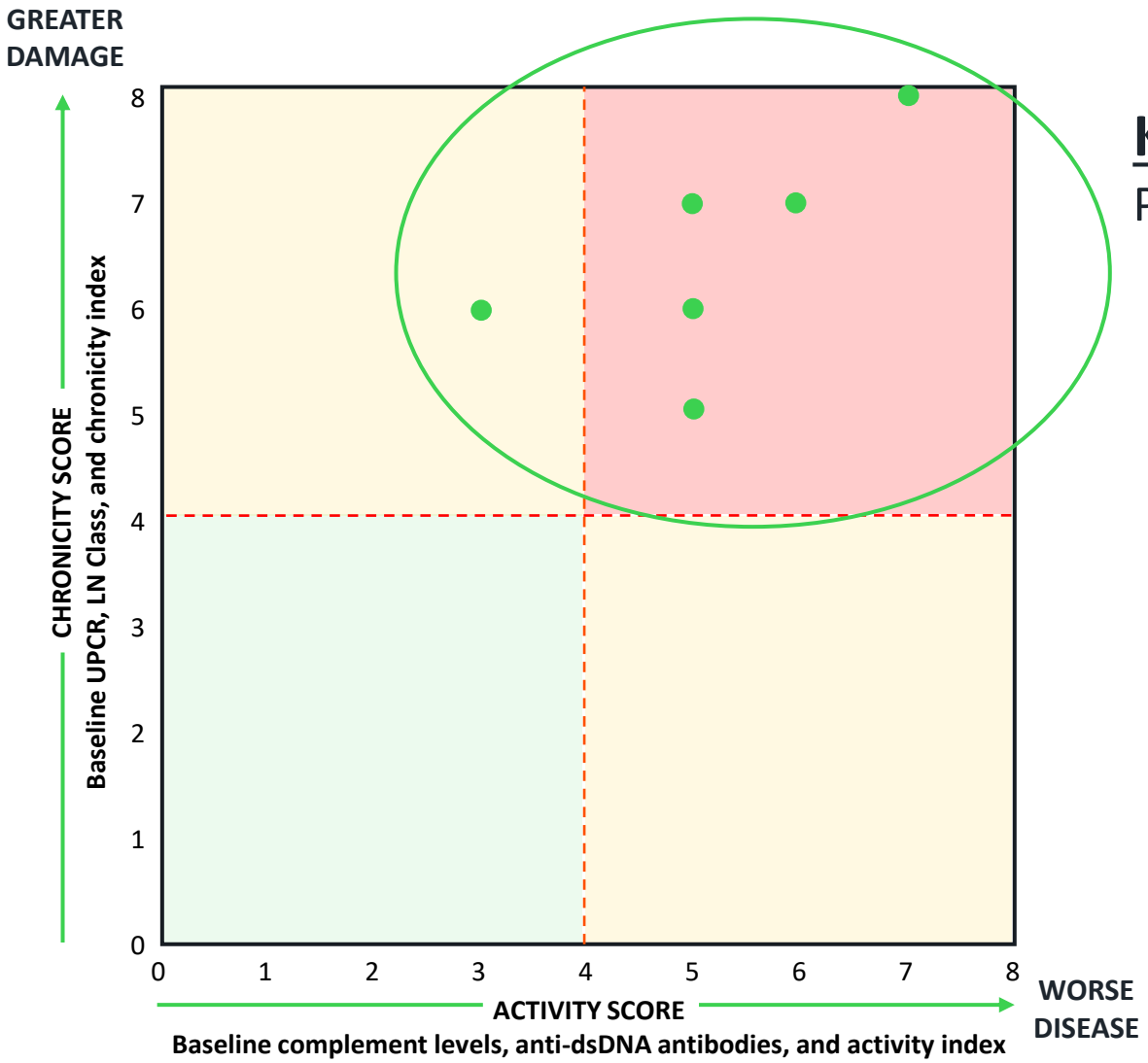
Before KYV-101

- Severe Disease
- Rash
- SLEDAI score 27

After KYV-101

- Disease Free
- No immunosuppressants
- No glucocorticoids

KYV-101 Refractory LN Patients Have High Disease Activity and Kidney Damage



KYV-101 100M Target Dose

Patient Baseline Characteristics

- Refractory LN patients experience uncontrolled inflammation and accumulated kidney damage
- KYV-101 patients have particularly high baseline disease activity and kidney damage
  - Activity: Low complement, high levels of anti-dsDNA antibodies, and high activity indices by biopsy
  - Chronicity: High levels of proteinuria, Class II-V histology, and high chronicity indices by biopsy

Patients from Kyverna-sponsored clinical trials, investigator-reported named patient, and investigator-initiated trial experience as of October 31, 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.

LN, lupus nephritis; UPCR, urine protein creatinine ratio.

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KYV-101: Treatment of Heavily Pretreated LN Patients

Demographic summary of patients receiving 1×10^8 CAR T-cells

Patient Characteristic	*N=6*
Age (Range)	29 – 55 years
Sex (Female : Male)	4:2
Prior Lines Of Therapy	3 – 7
SLEDAI-2K	8 – 27
Histologic Class of Nephritis (WHO)	II – V
UPCR (Range)	1.4 – 8.0

4 of 6 patients with ≥6 months follow up included in efficacy analysis

2 of 6 patients with <2 months follow up not in efficacy analysis (too short follow-up to assess efficacy)

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LN, lupus nephritis; UPCR, urine protein-creatinine ratio.

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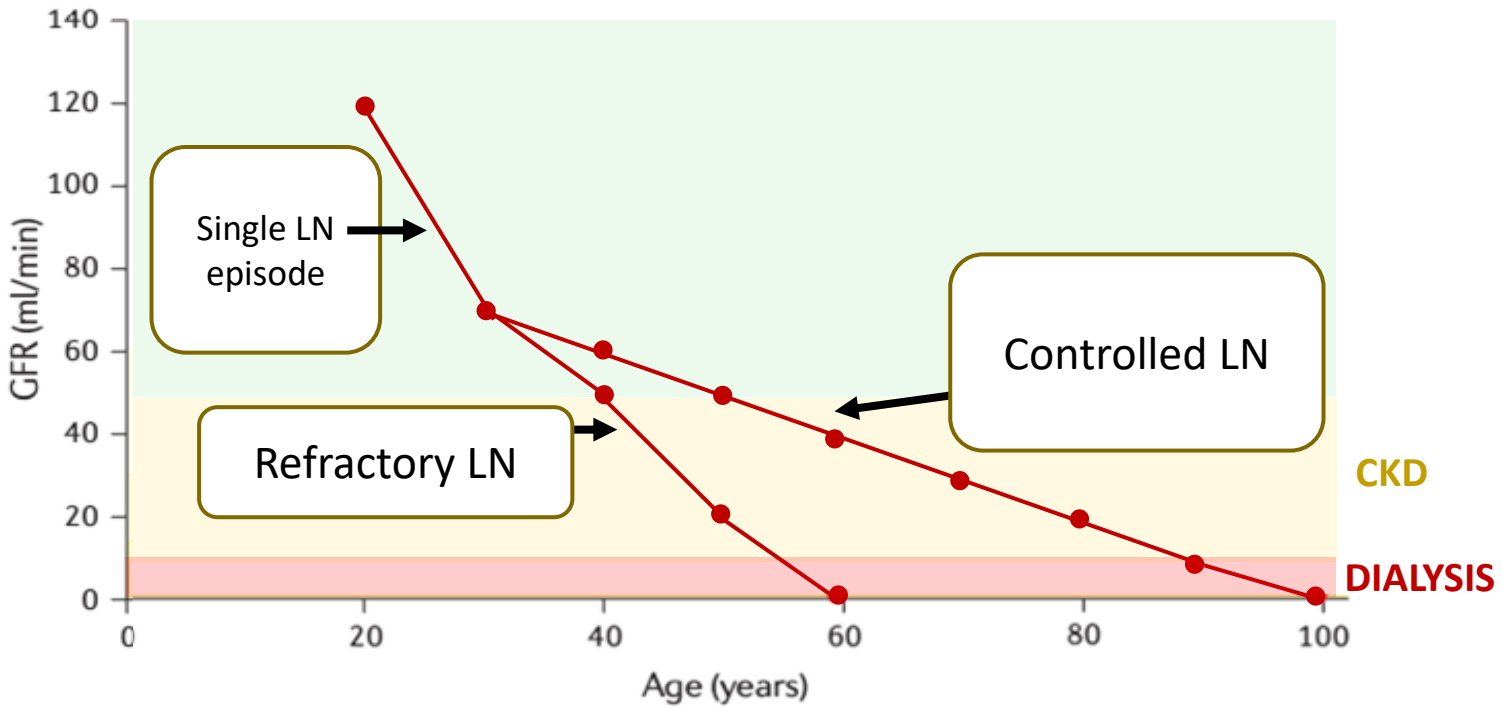
Steep Loss of Kidney Function in Refractory Lupus Nephritis

Loss of Kidney Function in LN Over Time[1]



- Despite therapy, patients progress with eGFR decline and loss of Kidney Function
- Single episodes can impact the slope of decline significantly
- Risk of Dialysis, Kidney Transplantation and Death increase, as eGFR declines

30% with progressive eGFR loss despite treatment[2]

Anders H-J, et al. *Nat Rev Disease Primers*. 2020;6(1):7; Weeding E, et al. *Lupus Sci Med*. 2022;9(1):e000684.

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KYV-101: Potential to Redefine Success in Lupus Nephritis

1. Preservation of Kidney Function

- Stabilization of eGFR
- Decreasing Proteinuria
- Avoiding Dialysis

2. Improvement in SLE

- Decrease in SLEDAI
- Decrease in anti-dsDNA
- Normalization of complement

3. Reduction or Elimination of Therapy

- No immunosuppressants
- No or physiological glucocorticoids

After a single infusion of KYV-101 (1×10^8 CAR T cells), none of the patients require active treatment for LN

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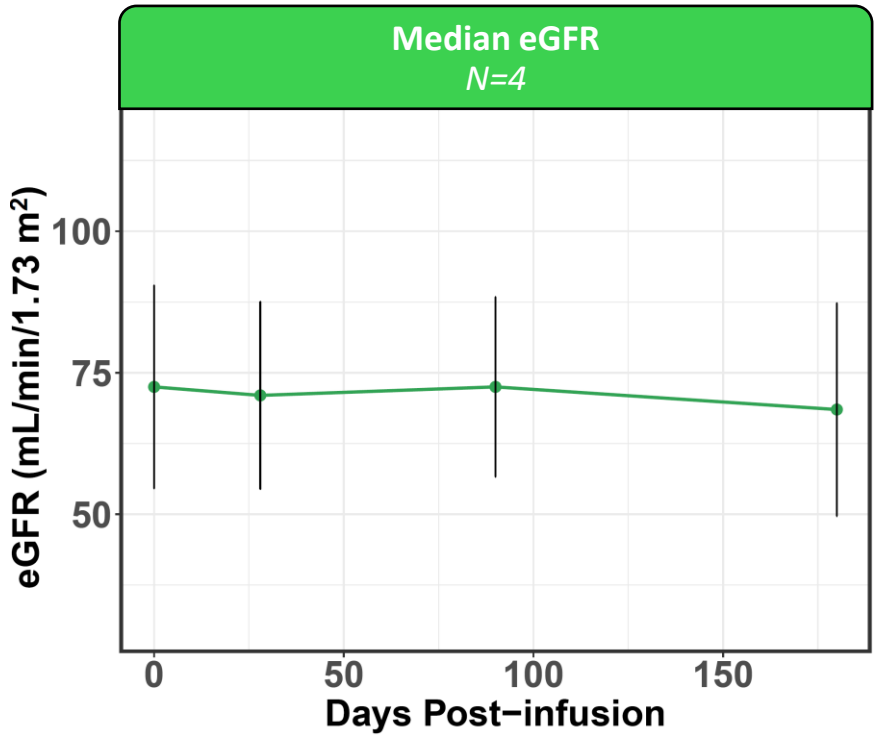
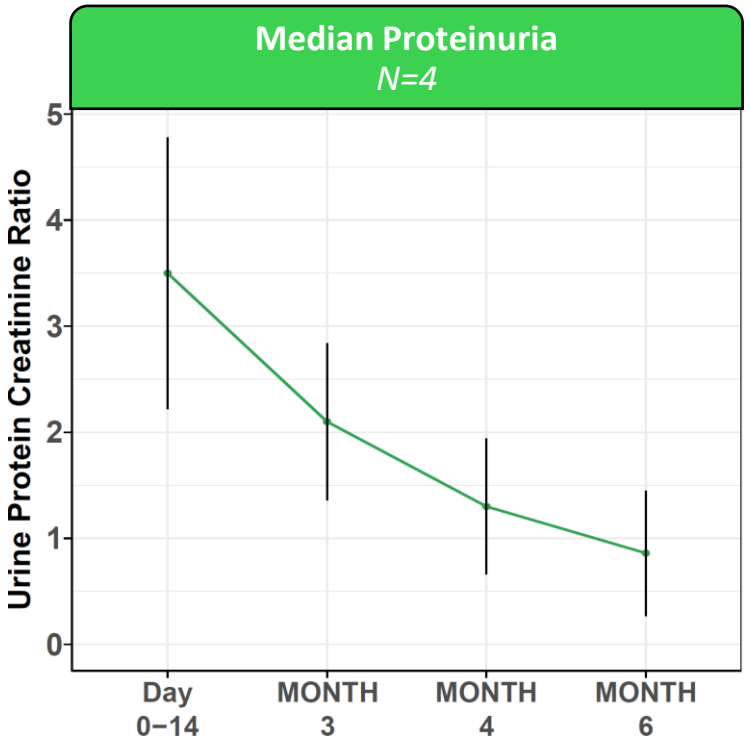
Pillar 1: KYV-101 Potential for Preservation of Kidney Function

Stable and Durable Kidney Function



Clinically Meaningful Decline in Proteinuria



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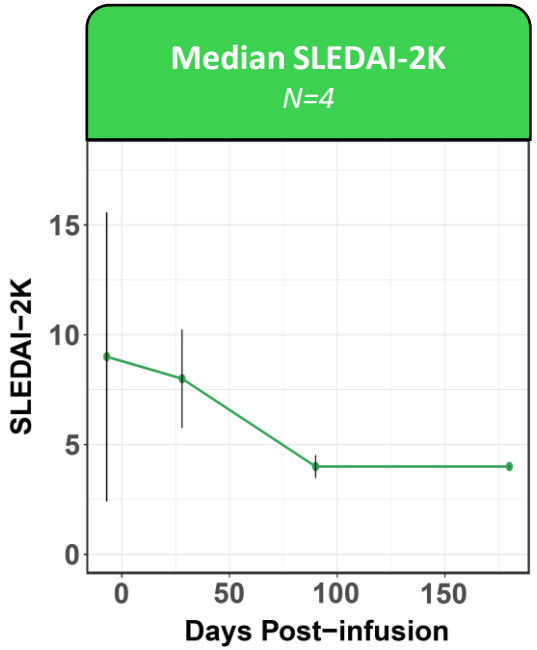
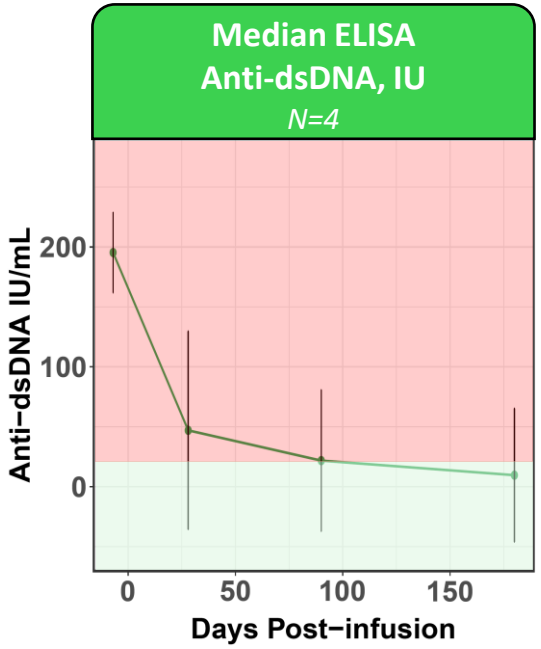
Pillar 2: KYV-101 Potential for Improvement of SLE

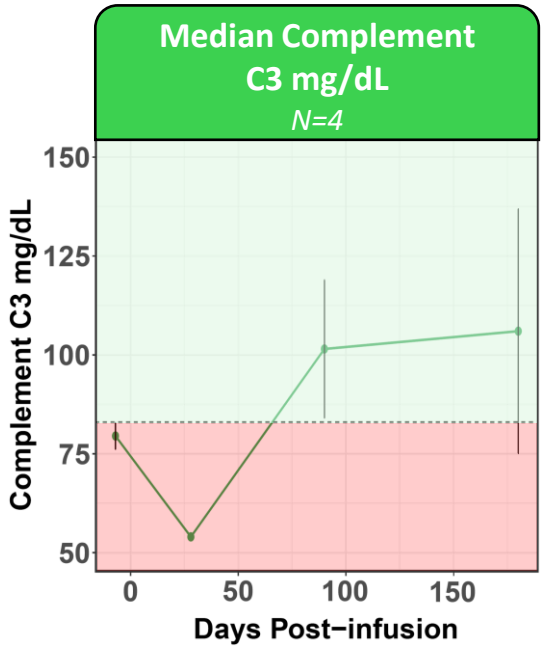
Reduction in SLEDAI Score

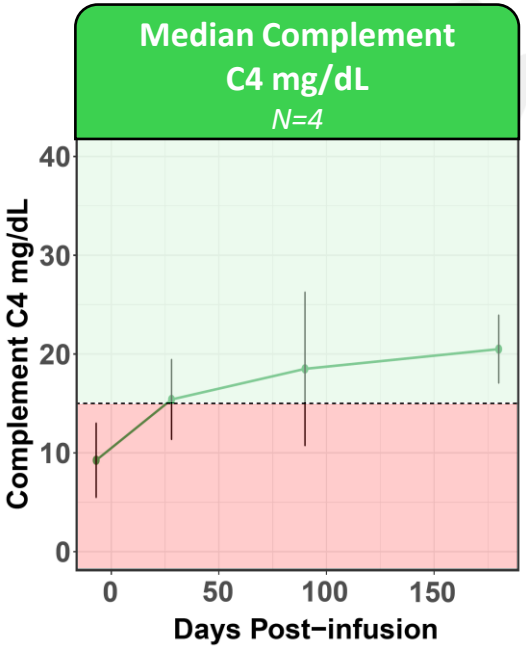


Reduction in Autoantibodies



Normalization of Complement





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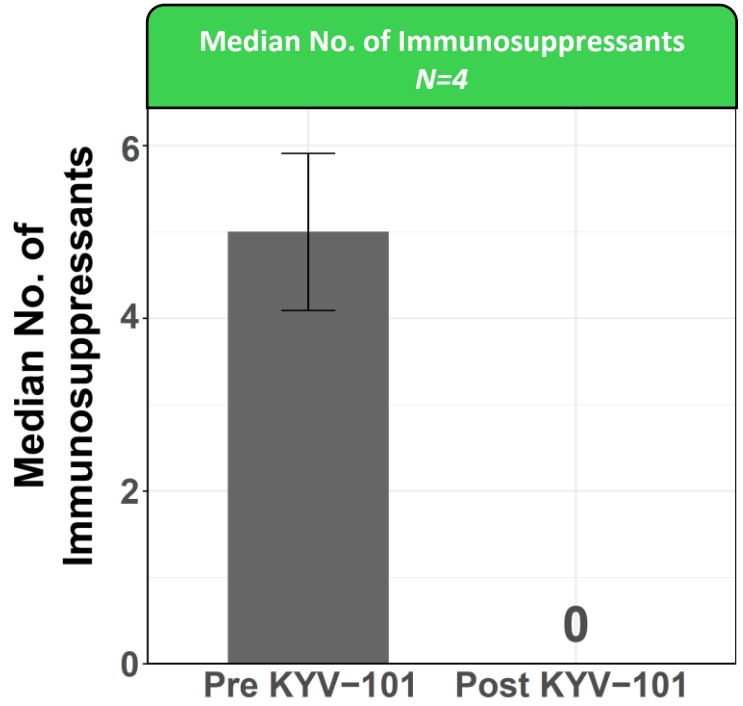
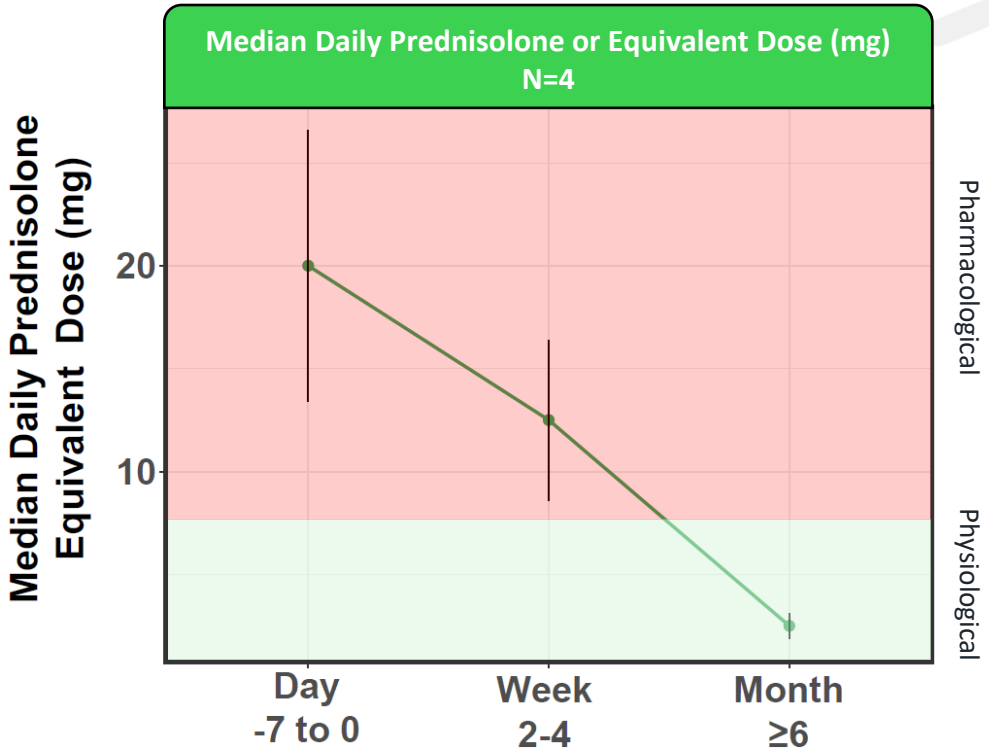
Pillar 3: KYV-101 Potential to Eliminate Immunosuppressants

Eliminating Immunosuppressants



Reducing Glucocorticoids to Physiological Levels



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KYV-101: Potential for Immune System Reset in Lupus Nephritis

UNMET NEED

LN is a severe condition with **high risk to develop kidney failure**

PROMISE OF KYV-101

KYV-101 achieves potential for significant progress in the treatment of LN via:

- Preserving kidney function
- Improving SLE activity
- Eliminating immunosuppression
- Predictable and robust safety profile

NEXT STEPS

KYSA-1 and KYSA-3 continuing to enroll and treat patients in order to bring a **new, transformative treatment option** to patients with LN

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KYV-101
Combined Experience

KYV-101: Potential for Predictable, Well Tolerated, and Robust Safety Profile in First 50 Patients Across Different Autoimmune Diseases

KYV-101 All 15+ AID indications

RHEUMATOLOGY

- Rheumatoid arthritis
- Systemic sclerosis
- Lupus nephritis
- ANCA-associated vasculitis
- Anti-Synthetase Syndrome
- And others

NEUROLOGY

- Stiff-person syndrome
- Myasthenia gravis
- Multiple sclerosis
- NMOSD
- CIDP
- And others

Indication Category	CRS	ICANS
	Grade 3/4	Grade 2–4
Neuroimmunology	0	0
Rheumatology	0	0
Other Autoimmune	0	0

No grade 3/4 CRS and **no grade 2-4 ICANS** observed across **50+ patients dosed**

Observed CRS and ICANS events were transient, low-grade, and manageable

Patients from Kyverna-sponsored clinical trials, investigator-reported named patient, and investigator-initiated trial experience as of October 31, 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.

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

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

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]

Myasthenia Gravis & LEMS

Neuron

Treatment of concomitant myasthenia gravis and Lambert-Eaton myasthenic syndrome with autologous CD19-targeted CAR T cells

Highlights

- Anti-CD19 CAR T cell therapy led to clinical recovery in two cases of MG and LEMS
- Patients regained full mobility, with ongoing recovery 4- and 6-months post infusion
- Deep B cell depletion and normalization of pathogenic autoantibodies was observed
- Application of anti-CD19 CAR T cells was safe, with manageable side effects

Authors

Jeremias Motte, Melissa Sgodzai, Christiane Schneider-Gold, ..., Dimitrios Mougiakakos, Roland Schroers, Ralf Gold

Correspondence

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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

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]

LEMS, Lambert-Eaton myasthenic syndrome.

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KYV-201 and Ingenui-T

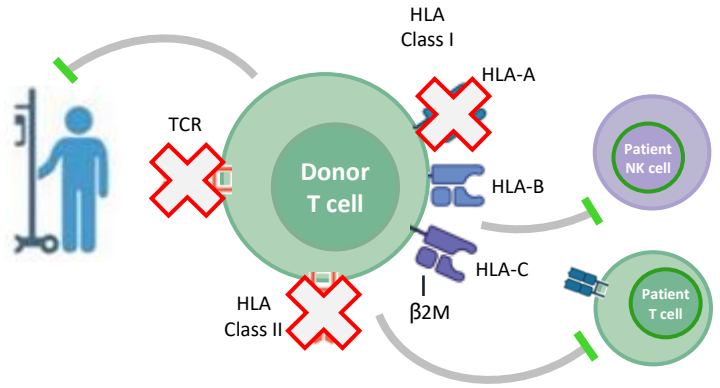
Allogeneic KYV-201 Protection from T Cells Supports Potential for Longer-term Persistence

Differentiated allogeneic platform based 3 genetic deletions

TCR KO + HLA-A KO + pan HLA Class II

Genetic deletion of the TCR avoids GvHD
TRAC KO

Partial genetic deletion of HLA inhibits NK cells
HLA-A-KO



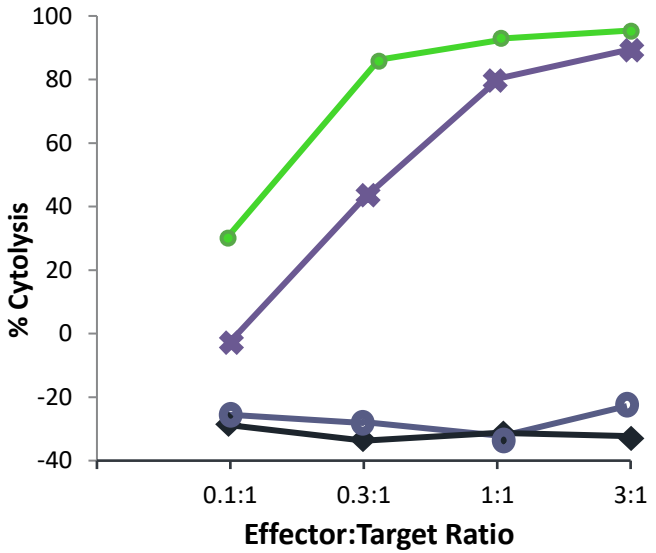
Intellia THERAPEUTICS

Match remaining HLA Class I alleles between donor and patient
HLA-B and HLA-C matching

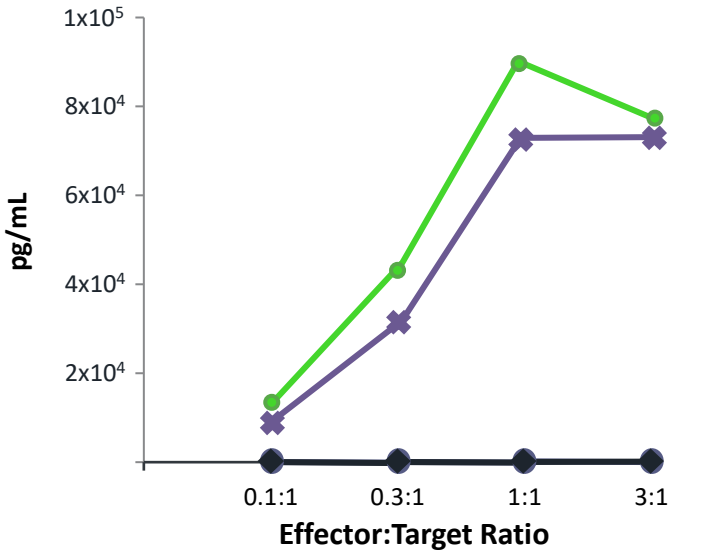
KYV-201 demonstrates robust CAR-mediated activity against CD19+ cells

Similar to HLA Class I deficient b2M KO[1]

Dose-Dependent Cytotoxicity



Dose-Dependent IFNγ Secretion



24h incubation with NALMS target cells
Representative of 3 donors
WT = Mock (unedited), untransducted
KO only = HLA-A / CIITA / TRAC KO
CAR only = CAR LV
KYV-201 = HLA-A / CIITA / TRAC KO + CAR LV

WT
CAR only
KO only
KYV-201

Note: Internal data. β2M, beta2-macroglobulin; HLA, human leukocyte antigen; IFNγ, interferon gamma; KO, knockout, LV, lenti vector; NK, natural killer, TRAC, T-cell receptor α constant; WT, wild type.

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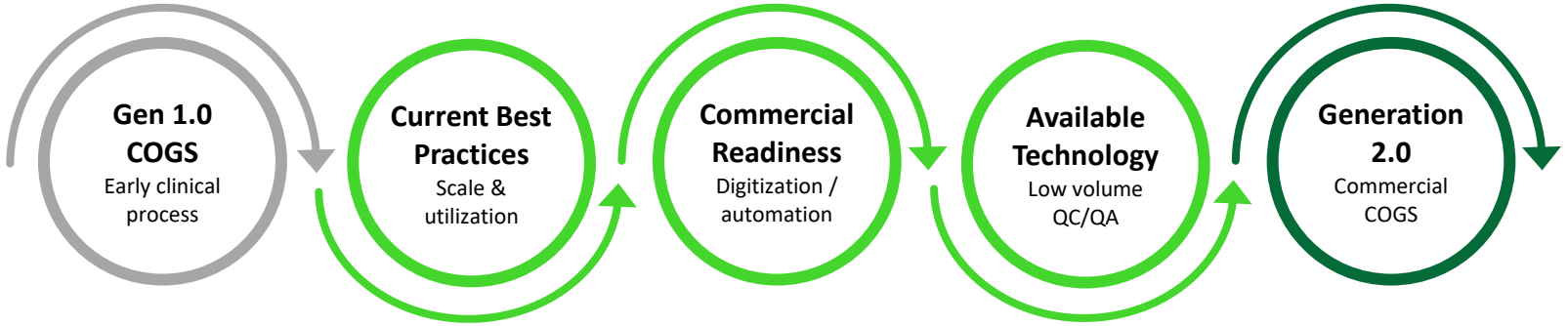
Kyverna's Ingenui-T Process Leverages Industry Leaders to Target Pharma-like COGS

Evolution of the Autologous Process: KYV-101 Gen 1.0 to Ingenui-T



Capturing unrealized value Gen 1.0 – Gen 2.0: Ingenui-T concept work packages

1	Cell isolation	kyverna. internal
2	Modernized cell process	elevatebio
3	Low volume fill for highly active dose	elevatebio
4	Low volume analytics w/ safety tests	TBD
5	Digitization	TBD

Key Component	Kyverna's Approach	COGS	Supply Chain	Speed
Manufacturing and supply chain partnerships	**ElevateBio's BaseCamp** for process development and cell product manufacturing **Oxford Biomedica** supply agreement, enabling use of **LentiVector**	✓	✓	
Pharma-like COGS	Foundation of **industry-best practices** ElevateBio and other processes to **streamline COGS**	✓	✓	✓

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Corporate

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Strong Financial Position Provides Runway to Multiple Potential Value Inflection Catalysts

Successful IPO in February 2024 – secures Kyverna's leadership position in autoimmunity

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Proven Leadership Team with Significant CAR T and Autoimmune Experience

Leadership Team

Warner Biddle
Chief Executive Officer

Karen Walker
Chief Technology Officer

Dominic Borie, MD, PhD
President, Research and Development

Ryan Jones, MBA
Chief Financial Officer

Dan Maziasz
Chief Business Officer

Cara Bauer
Chief Human Resources Officer

Tom Van Blarcom, PhD
Senior Vice President and Head of Research

Tracy Rossin
Senior Vice President, Corporate Affairs, Communications and Investor Relations

Sunetra Biswas, PhD
Vice President, Program Lead

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Mert Aktar
Independent Director

Ian Clark
Chairperson and Director

Warner Biddle
Chief Executive Officer

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Kyverna's Near-term Events in the Coming Quarters

Key Meeting	✓ ECTRIMS Copenhagen	✓ ACR Washington DC	JPMorgan Conference San Francisco
Date	September 2024	November 2024	January 2025
What to Expect	Discussion of neurological case reports	Continuation of rheumatological dataset	Long-term plan and upcoming catalysts in rheum & neuro
	Symposium at 5:15pm CET Wednesday Sep 18, 2024	**Symposium at 5:45pm EST Monday Nov 18, 2024**	

ACR, American College of Rheumatology; ECTRIMS, European Committee for Treatment and Research in Multiple Sclerosis.

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