

Clinical Impact of C-CAR168, a Novel Anti-CD20/BCMA Composite Autologous CAR-T Therapy, in Refractory Lupus Nephritis

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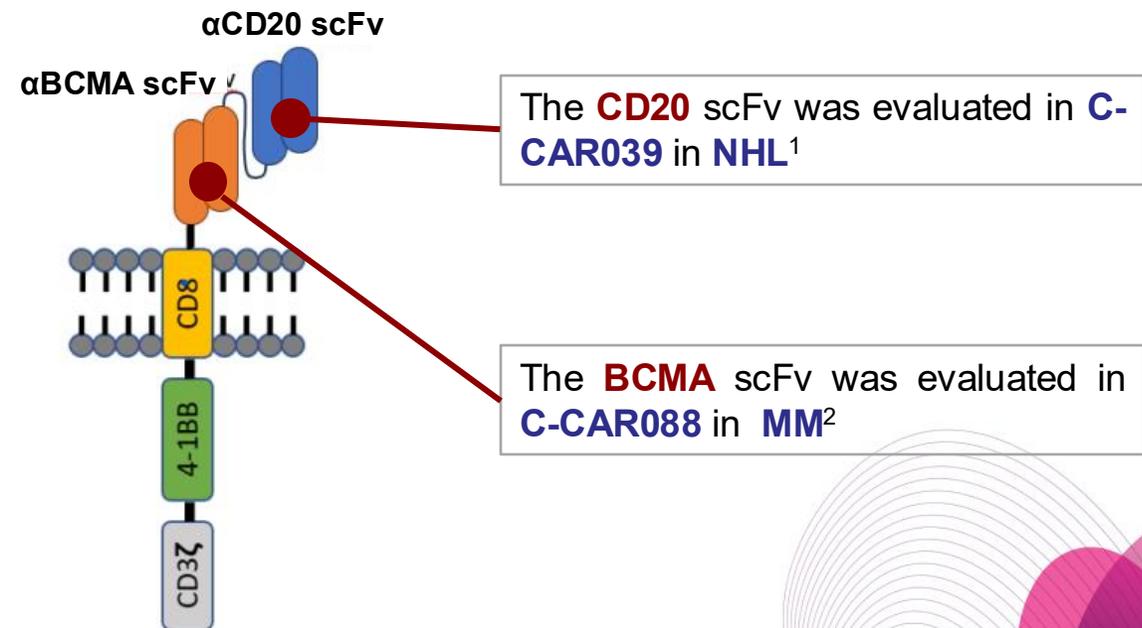
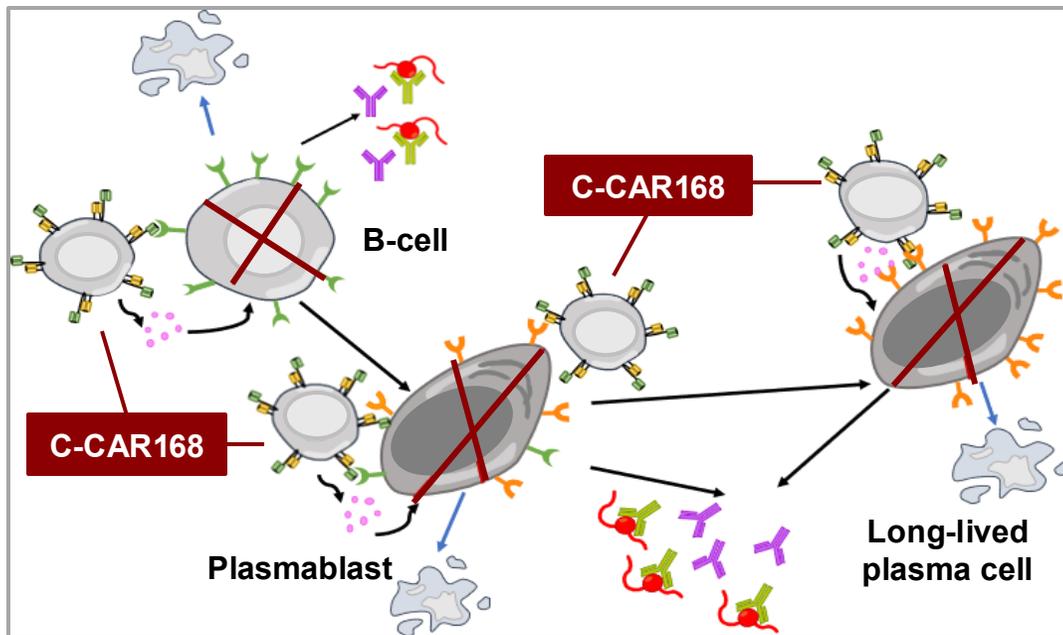
Abstract ID: #730

Presented at 16th International Congress on Systemic Lupus Erythematosus (LUPUS 2025), Toronto, Canada, May 21-24, 2025

- I consult for several pharmaceutical companies including AbelZeta on SLE programs.

C-CAR168: A 2nd Generation Bispecific CAR-T Targeting CD20 and BCMA

- **B cells and plasma cells** drive autoimmunity via both antibody-dependent and -independent mechanisms;
- Targeting antibody-secreting cells shows broad efficacy across autoimmune diseases;
- Our strategy is to target both **CD20** and **BCMA** that depletes B cells, plasmablasts, short- and long-lived plasma cells, as well as CD20dim T cells.



Key Inclusion Criteria

SLE

- Diagnosed with SLE for ≥ 6 months, with renal biopsy proven LN
- Had failed ≥ 2 immunosuppressants (IS) or biologic agents
- SLEDAI-2K ≥ 7 , AND clinical SLEDAI-2K ≥ 6
- UTP $\geq 1\text{g}/24\text{h}$ or UPCR $\geq 1.0\text{g}/\text{g}$
- ANA $\geq 1:80$, OR a positive anti-dsDNA, OR a positive anti-Sm

Other CTD

- IMNM
- SSc

Neurology

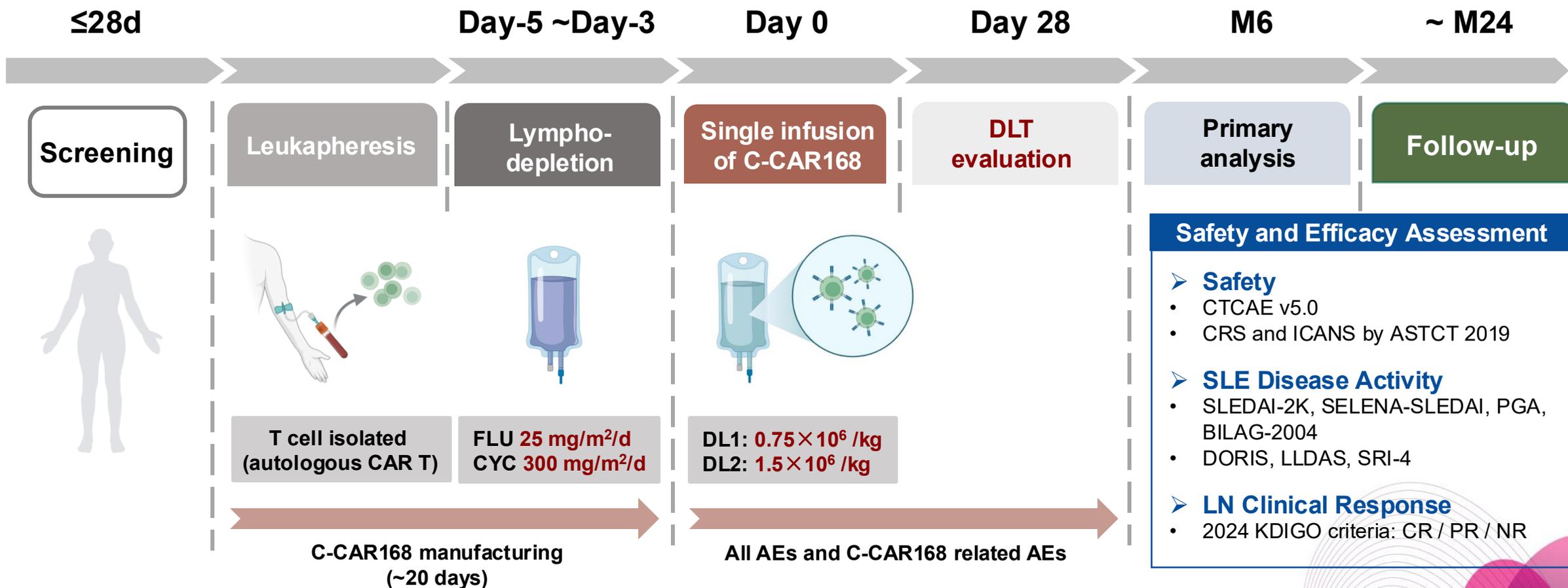
- MS
- NMOSD
- MG

Key Exclusion Criteria

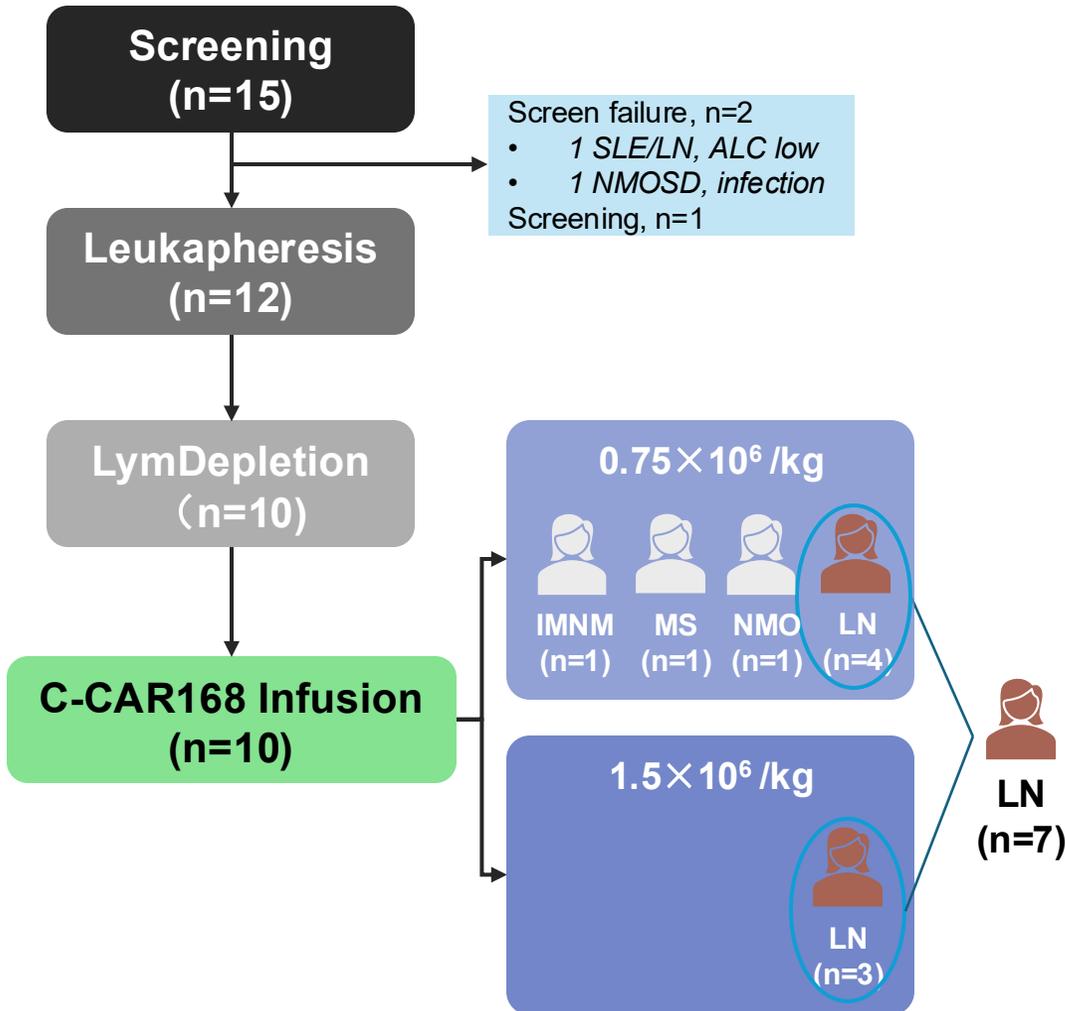
- Active infection
- Impaired organ function

SLE: Systemic Lupus Erythematosus; LN: Lupus nephritis; SSc: Systemic Sclerosis; IMNM: Immune-Mediated Necrotizing Myopathy; NMOSD: Neuromyelitis Optica Spectrum Disorders; MS: Multiple Sclerosis; MG: Myasthenia Gravis; IS: Immunosuppressants; BA: Biologic agents

Study Design



FLU: Fludarabine; CYC: Cyclophosphamide; DL: Dose level; DLT: Dose-limiting toxicity; AE: Adverse event; CTCAE: Common Terminology Criteria for Adverse Events; CRS: Cytokine Release Syndrome; ICANS: Immune effector Cell-Associated Neurotoxicity Syndrome; SLEDAI: Systemic lupus erythematosus disease activity index; ASTCT: American Society for Transplantation and Cellular Therapy; PGA: physician global assessment; BILAG: British Isles Lupus Assessment Group; DORIS: Definition Of Remission In SLE; LLDAS: Lupus Low Disease Activity State; SRI: Systemic Lupus Erythematosus Responder Index; KDIGO: Kidney Disease Improving Global Outcomes; CR: complete remission; PR: partial remission; NR: no renal remission



Characteristics of Patients with Refractory LN

| Demographics | Clinical assessment |
|--|--|
| <ul style="list-style-type: none"> • Age (yr): 30 (26-41) • Female, n(%): 6 (85.7) • SLE duration (yr): 9 (5-14) • LN duration (yr): 5 (2-9) | <ul style="list-style-type: none"> • SLEDAI-2K: 12 (8-24) • PGA: 1.5 (1.1-2.4) • 24h UP (g/24h): 3.71 (1.23-8.16) • UPCR (g/g): 2.64 (1.64-10.84) • Low complement, n (%): 6 (85.7) |
| LN ISN/RPS, n (%) | Previous treatment |
| <ul style="list-style-type: none"> • III+V: 2 (28.6) • IV+V: 3 (42.9) • III/IV+V: 1 (14.3) • V: 1 (14.3) | <ul style="list-style-type: none"> • No. of IS/biologics, n (range): 4 (3-8) |

C-CAR168 is Well Tolerated in Terms of Low-grade CRS, no ICANS, no Severe Infection

| | 0.75 × 10 ⁶ /kg (n=4) | 1.5 × 10 ⁶ /kg (n=3) | Total (n=7) |
|---|-------------------------------------|------------------------------------|----------------|
| Treatment emergent SAE | 0 | 1* | 1 |
| C-CAR168-related SAE | 0 | 0 | 0 |
| CRS | | | |
| Any Grade | 1 | 3 | 4 |
| Grade 1 | 1 | 2 | 3 |
| Grade 2 | 0 | 1 | 1 |
| Grade ≥ 3 | 0 | 0 | 0 |
| Median to onset, day | 2 | 2 | 2 |
| Median duration, days | 8 | 8 | 8 |
| Tocilizumab use | 0 | 2 | 2 |
| Dexamethasone use | 0 | 2 | 2 |
| ICANS | 0 | 0 | 0 |
| DLT | 0 | 0 | 0 |
| Grade ≥ 3 Infection | 0 | 0 | 0 |
| Long-term hematological toxicities | 0 | 0 | 0 |

*: Pt C009 experienced G4 thrombocytopenia at M2 caused by disease flare. The patient was fully recovered with GC, TPO, transfusion treatment

Robust SLE and LN Responses to C-CAR168 6 Months Post Treatment

- 4 patients completed M6 efficacy evaluation, **all achieved SRI-4**
- Pt C004/C007 have not yet reached the M6 evaluation timepoint
- Pt C009 flared at M3 and withdrew from the study thereafter
- All patients discontinued IS/biologics after lymphodepletion
- Most patients reached steroids free after C-CAR168 infusion

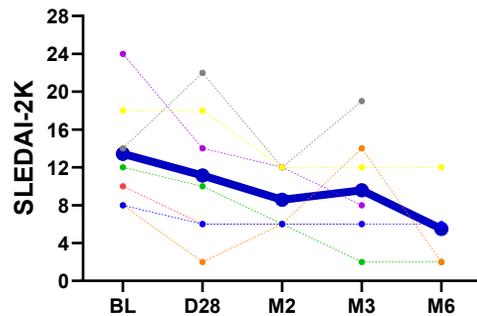
| DL | Pt No | SLE response at M6 | | | LN response at M6 | |
|--------------------------------|-------|--------------------|-------|-------|-------------------|----|
| | | DORIS | LLDAS | SRI-4 | CR | PR |
| 0.75×10^6 cells/kg | C001 | | | √ | | √ |
| | C002 | √ | √ | √ | √ | |
| | C003 | √ | √ | √ | √ | |
| 1.5×10^6 cells/kg | C006 | | | √ | | |
| | C009 | / | / | / | / | / |

C-CAR168 Alleviates Disease Activity and Reduces Proteinuria

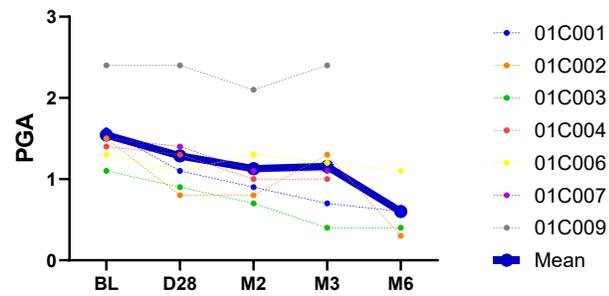
- 6 patients were under follow up and showed downward trend in SLEDAI score, PGA and proteinuria, of whom 3 maintained with low dose steroids, 3 were steroids free;
- C002 and C003 reached LN-CR
- C009 flared at M3

Disease Activity

SLEDAI-2K

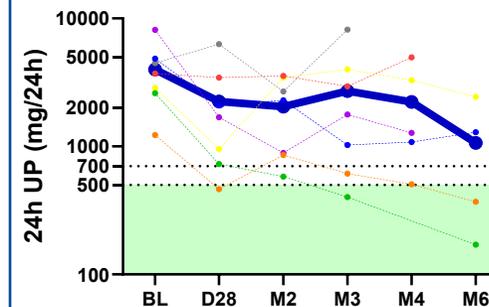


PGA

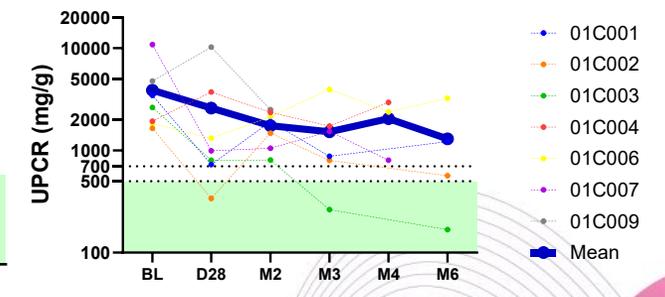


Proteinuria

24h Proteinuria



UPCR

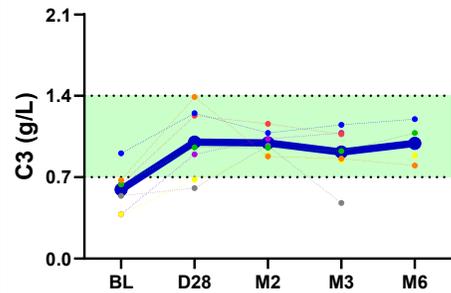


C-CAR168 Results in Complement Recovery, Autoantibody Reduction, and Renal Function Stabilization

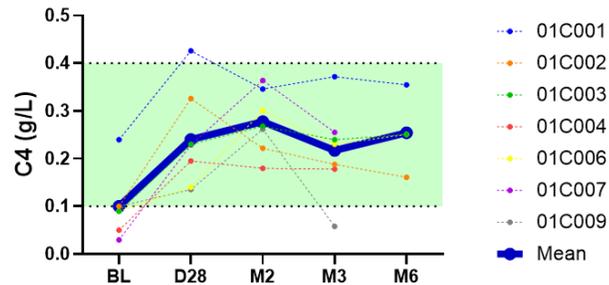
- Early recovery of complement levels was observed in all patients, with 6/7 achieving normal levels during follow-up
- All patients showed stable renal function, with no deterioration in eGFR
- A downward trend in anti-dsDNA level was observed in most patients

Complement Levels

C3

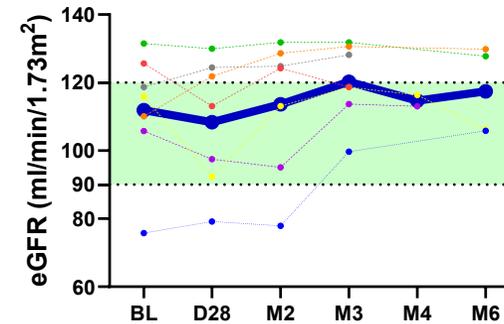


C4



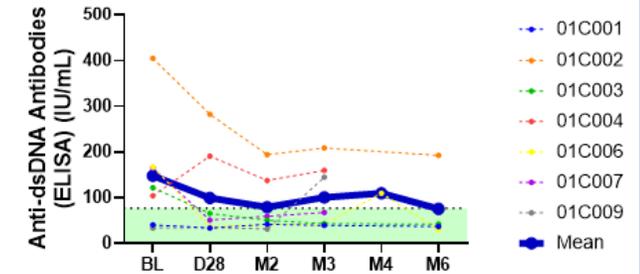
Renal Function

eGFR-EPI Cr



Autoantibody Level

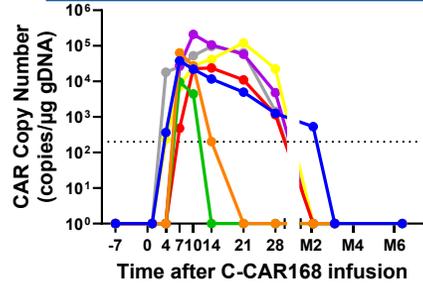
Anti-dsDNA



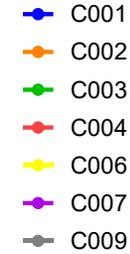
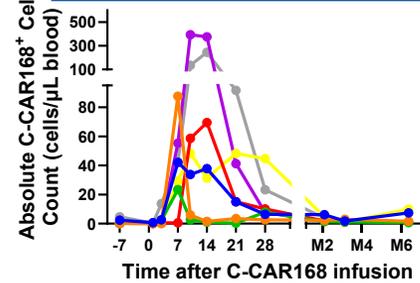
Pharmacokinetics and Pharmacodynamics of C-CAR168 in LN

Pharmacokinetics

CAR Copy Number

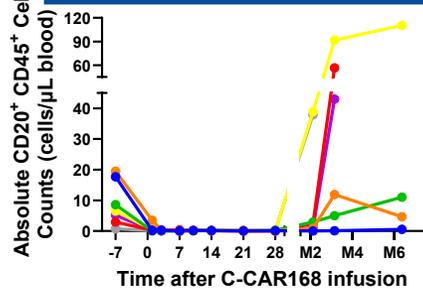


CAR-T Cell Counts

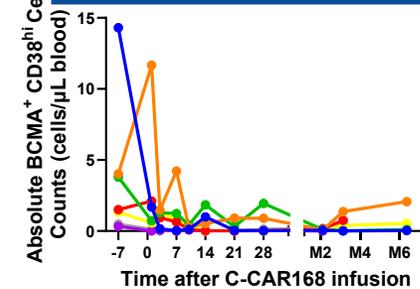


Pharmacodynamics

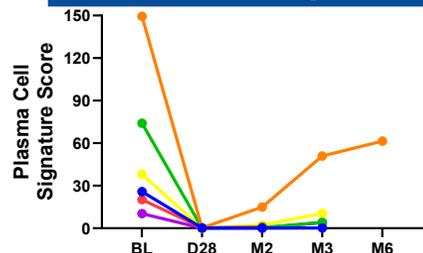
CD20⁺ B Cell Counts



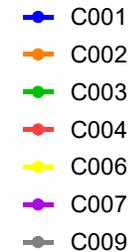
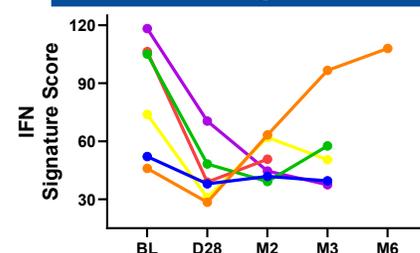
BCMA⁺CD38^{hi} Cell Counts



Plasma Cell Signature



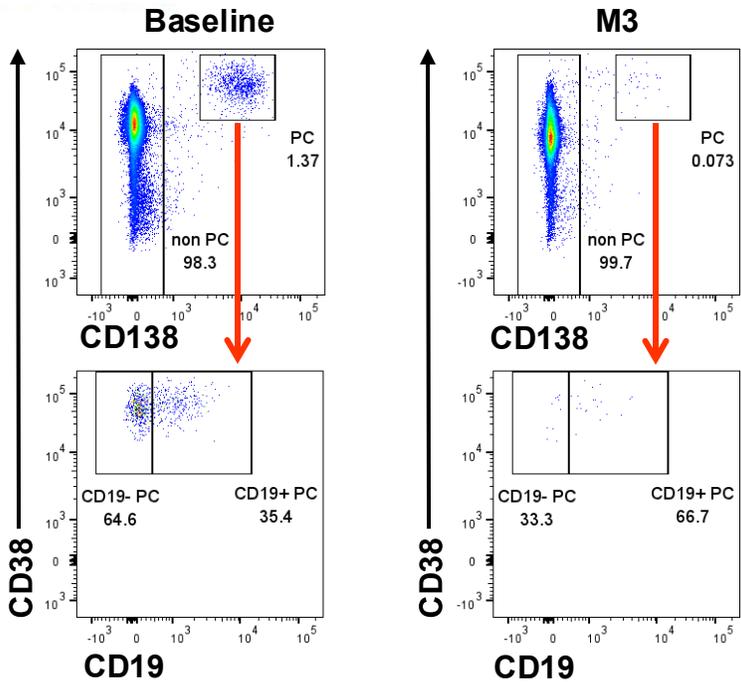
IFN Signature



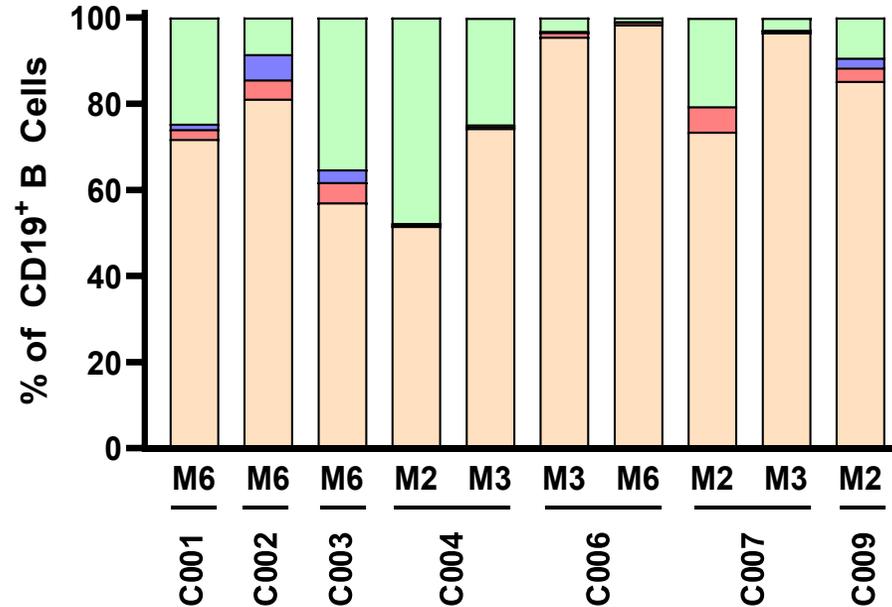
- Rapid C-CAR168 expansion was observed in the peripheral blood in all patients (median T_{max} : 11 days (range: 7 to 21 days))
- CAR-T cells persisted for 1 to 3 months in 5 patients. Two patients in DL1 group (Pt 02 and Pt 03) had shorter persistence
- Rapid and profound depletion of circulating B cells and plasma cells were observed
- Gene signature analysis further supported deep depletion of plasma cells and alleviation of type I IFN pathway activity

C-CAR168 Eliminates Long-Lived Plasma Cells in Bone Marrow and Induces Immune Reset

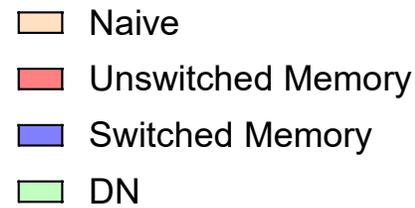
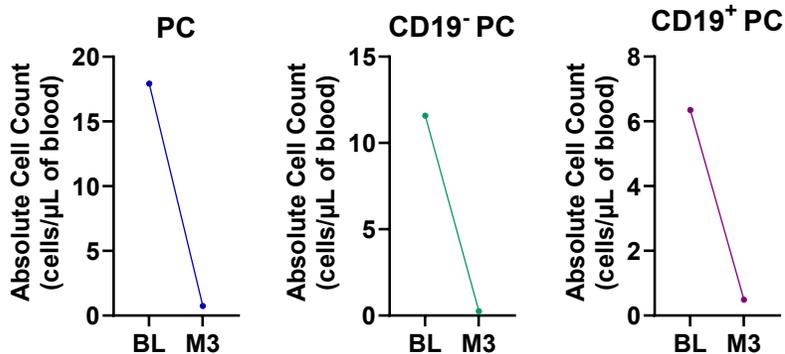
BM PCs of Pt C009



Phenotype of Recovered B Cells



- Analysis of a bone marrow biopsy (Pt C009) indicated that both CD19⁺ PCs and CD19⁻ long-lived PCs were eliminated by C-CAR168
- Analysis of peripheral blood samples demonstrated that most recovered B cells were naïve cells, implying immune reset

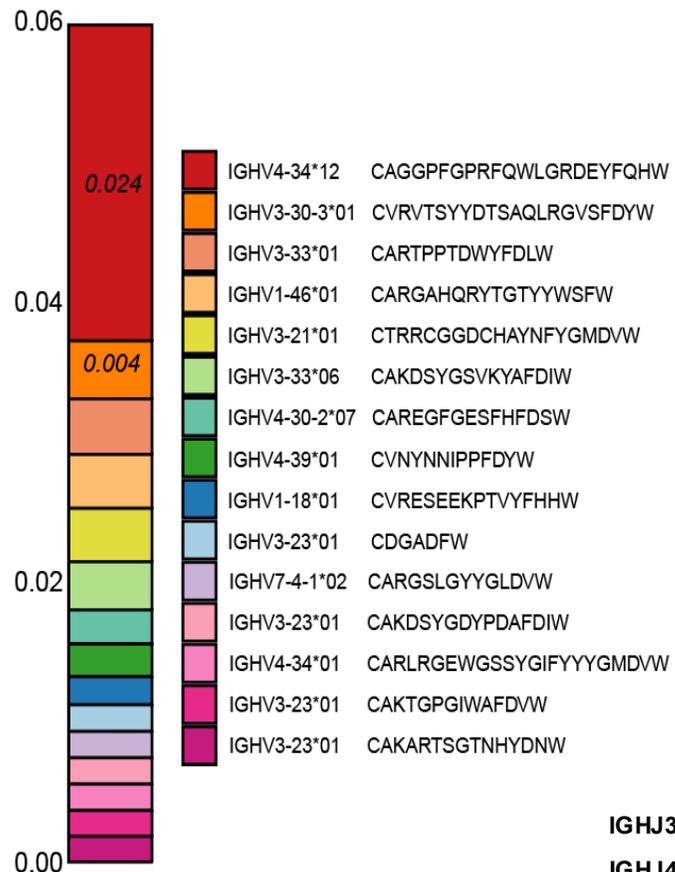


(Data is available for 7 patients of indicated follow up)

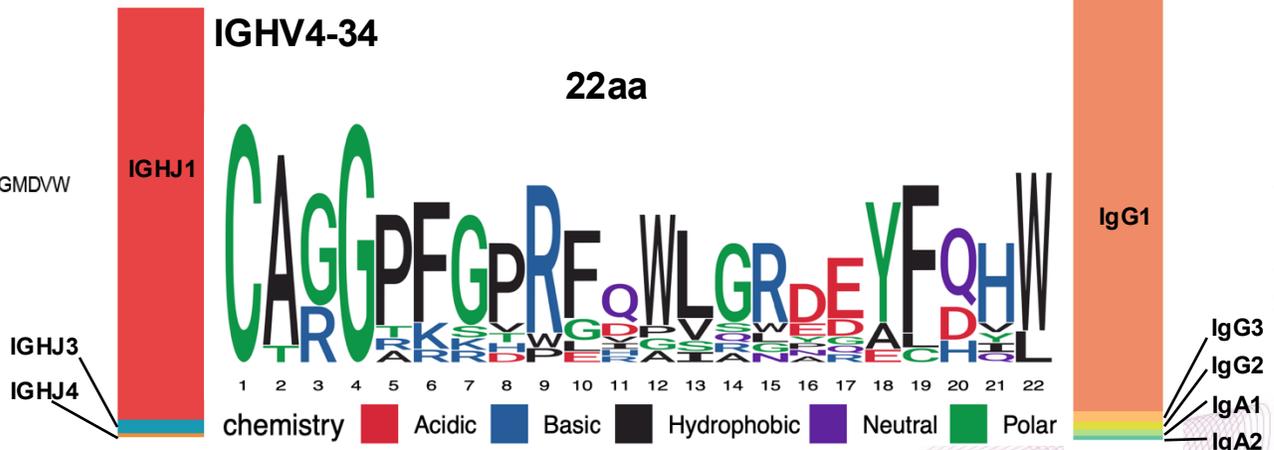
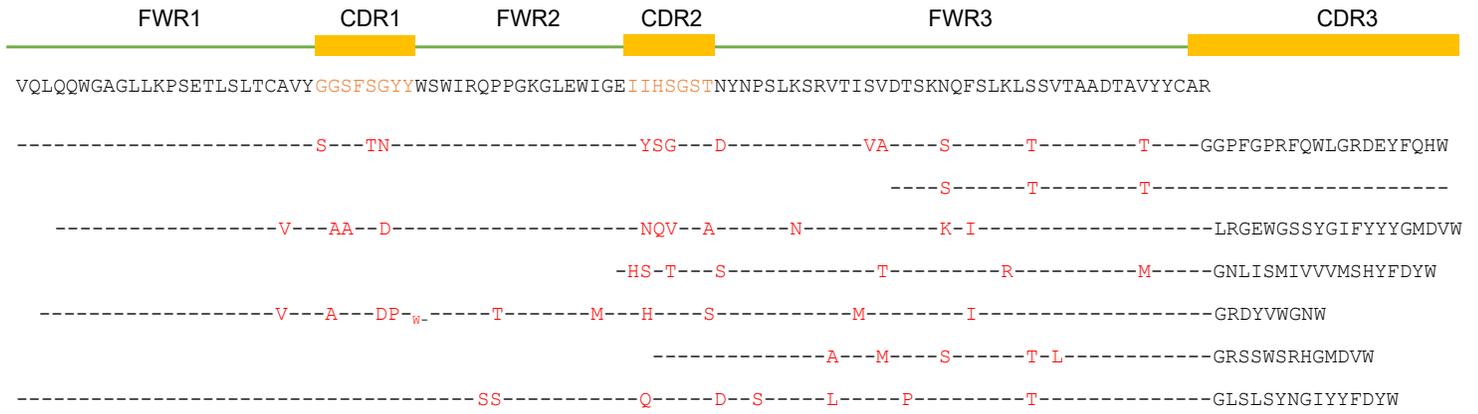
C-CAR168 Eliminates Dominant B Cell Clone and Reshapes the BCR Repertoire

IGHV4-34 is predominantly used in Pt C001 at baseline and be effectively eliminated after treatment

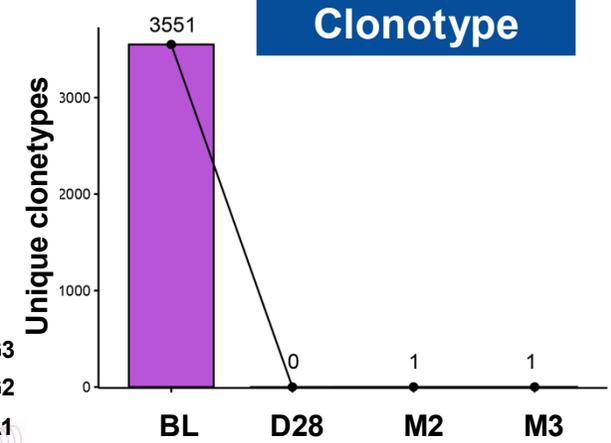
Top15 clone at baseline



Amino acid mutations in the large IGHV4-34+ clonotypes at baseline



Clonotype



CASE Study of C-CAR168 in a Secondary Progressive MS Patient

Patient information

31-year-old male

MS history: Initially diagnosed with relapsing-remitting multiple sclerosis (RRMS) in 2014, diagnosed with secondary progressive multiple sclerosis (SPMS) in 2024

Recent relapses: Two relapses in the past 12 months, evidenced by MRI deterioration and exhibited mild intellectual impairment

Prior treatment: GC, Betaferon (Recombinant human interferon beta-1b), Teriflunomide, AZA (Azathioprine)

MRI at the base line: approximately 20-50 lesions in the brain and brainstem, diffuse cervical and thoracic spinal cord lesions

C-CAR168 treatment

0.75×10^6 cells/kg and was IS/steroid free after infusion

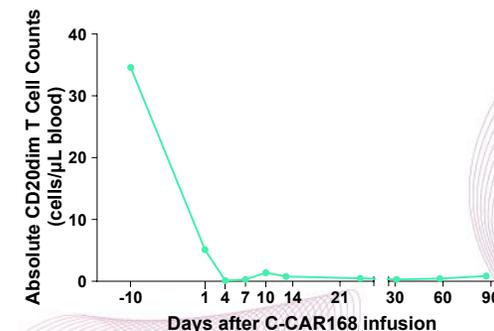
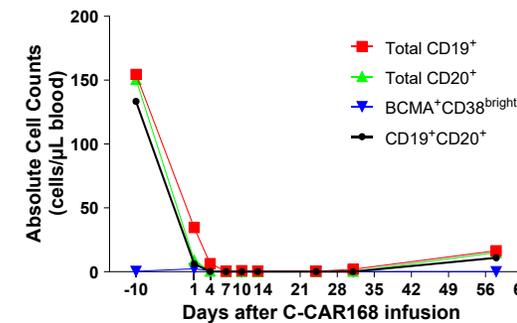
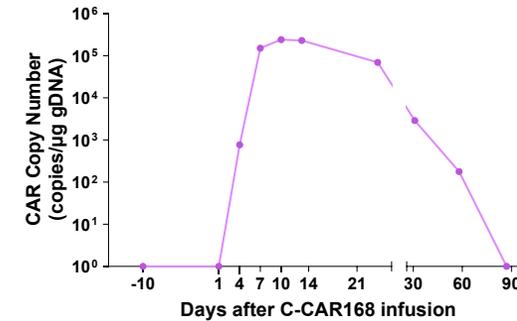
Safety

Grade 1 CRS and totally recovered without tocilizumab and dexamethasone treatment

No ICANS, no SAE, no infection \geq G3

PK/PD profile

Robust CAR-T expansion, complete depletion of B cells, plasma cells and CD20dim T cell in blood



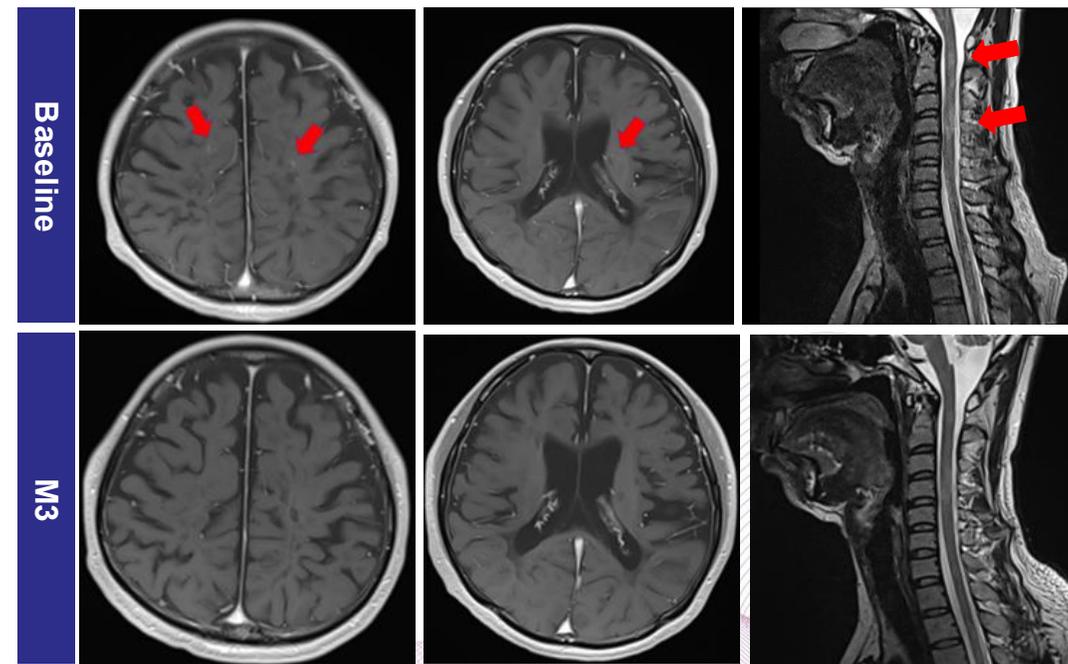
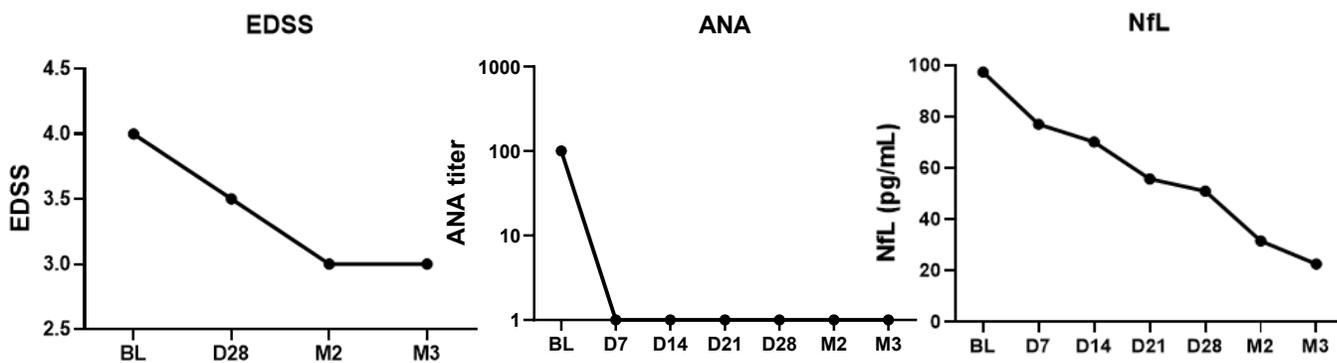
C-CAR168 Showed Early Promising Efficacy in a Secondary Progressive MS Patient

Improved test scores in 9-Hole Peg Test (9-HPT), the timed 25-foot walk (T25-FW) and Mini-Mental State Examination (MMSE)

- Reduction in periventricular/paraventricular enhancing lesions on T1-weighted imaging
- No new T1-enhancing lesions, no new T2-enlarging/new lesions found by M3

| | 9-HPT (s) | | | T25-FW (s) | | | | MMSE |
|-----|-----------|-------|-------|------------|-----------------|-----------------|-----|------|
| | R | L | Ave | devices | 1 st | 2 nd | Ave | / |
| BL | 35.38 | 37.13 | 36.26 | N | 7.9 | 7.2 | 7.6 | 24 |
| D28 | 31.25 | 34.27 | 32.76 | N | 6.1 | 6.2 | 6.2 | 25 |
| M2 | 32.25 | 34.11 | 33.18 | N | 5.8 | 7.6 | 6.7 | 26 |
| M3 | 29.55 | 32.15 | 30.85 | N | 5.5 | 6.1 | 5.8 | 24 |

Improved EDSS scores and decrease of ANA and NFL levels



- C-CAR168 shows promising efficacy in highly refractory LN, with reduction in proteinuria, preserved renal function, and improvement in laboratory and extra-renal features of LN, including enabling withdrawal of IS
- Robust PK/PD profile, excellent safety, and efficacy signals in a SPMS patient
- Continued IIT in China will enroll more patients with LN and/or SLE, progressive MS, and indications such as NMOSD, SSc to explore and confirm the clinical utility of C-CAR168 in a variety of autoimmune and neurological diseases

Thank You!

