Anti-CD20/BCMA Bispecific CAR-T Cell Therapy Promotes Immune Reset and Sustained Drug Free Remission in Refractory Autoimmune Diseases

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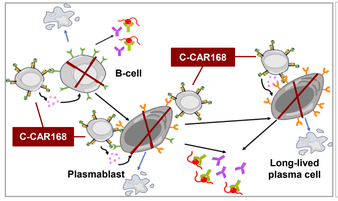
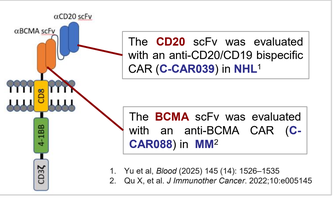
Background

Refractory autoimmune diseases characterized by progressive organ damage represent a significant unmet medical need. C-CAR168 is an autologous bispecific CAR-T therapy targeting both CD20 and BCMA, designed to simultaneously eliminate autoantibody-producing plasma cells and their B-cell precursors, aiming to induce a complete "immune reset". This first-in-human Phase I clinical trial (NCT06249438) is evaluating C-CAR168 in patients with treatment-refractory autoimmune diseases. Here, we present the safety outcomes and early efficacy data from the refractory lupus nephritis (LN) and progressive multiple sclerosis (MS) cohorts.





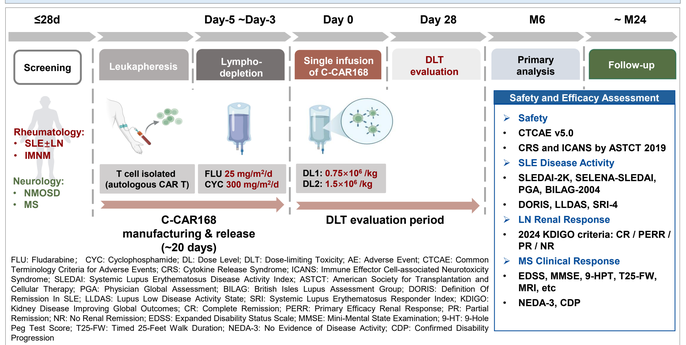
The **CD20** scFv was evaluated with an anti-CD20/CD19 bispecific CAR (**C-CAR039**) in **NHL**[1]

The **BCMA** scFv was evaluated with an anti-BCMA CAR (**C-CAR088**) in **MM**[2]

1. Yu et al, *Blood* (2025) 145 (14): 1526–1535
2. Qu X, et al. *J Immunother Cancer*. 2022;10:e005145

Method

This Phase I, open-label study enrolled patients with refractory systemic lupus erythematosus (SLE), with or without LN, immune mediated necrotizing myositis (IMNM), neuromyelitis optica spectrum disorder (NMOSD), and MS, who had failed ≥2 standard immunosuppressive therapies. After lymphodepletion, patients received a single infusion of C-CAR168 at either 0.75×10⁶ or 1.5×10⁶ CAR-T cells/kg.



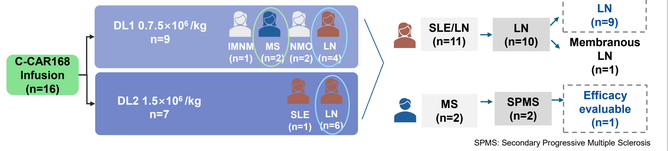
FLU: Fludarabine; CYC: Cyclophosphamide; DL: Dose Level; DLT: Dose-limiting Toxicity; AE: Adverse Event; CTCAE: Common Terminology Criteria for Adverse Events; CRS: Cytokine Release Syndrome; ICANS: Immune Effector Cell-associated Neurotoxicity Syndrome; SLEDAI: Systemic Lupus Erythematosus Disease Activity 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; PERR: Primary Efficacy Renal Response; PR: Partial Remission; NR: No Renal Remission; EDSS: Expanded Disability Status Scale; MMSE: Mini-Mental State Examination; 9-HT: 9-Hole Peg Test Score; T25-FW: Timed 25-Feet Walk Duration; NEDA-3: No Evidence of Disease Activity; CDP: Confirmed Disability Progression

Safety and Efficacy Assessment

- **Safety**
  - CTCAE v5.0
  - CRS and ICANS by ASTCT 2019
- **SLE Disease Activity**
  - SLEDAI-2K, SELENA-SLEDAI, PGA, BILAG-2004
  - DORIS, LLDAS, SRI-4
- **LN Renal Response**
  - 2024 KDIGO criteria: CR / PERR / PR / NR
- **MS Clinical Response**
  - EDSS, MMSE, 9-HPT, T25-FW, MRI, etc
  - NEDA-3, CDP

Patient allocation

As of September 10, 2025, a total of 16 patients had been treated with a median follow-up of 177 days:

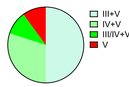


SPMS: Secondary Progressive Multiple Sclerosis

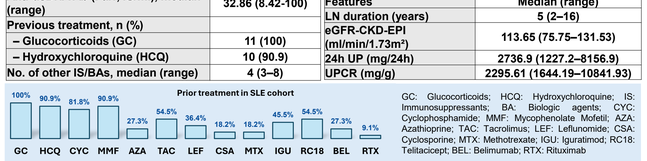
Demographics, disease profile in SLE cohort (n=11)

Age (years), median (range)	32 (26–42)
Female, n (%)	10 (90.9)
SLE duration (years), median (range)	9 (3–16)
SLEDAI-2K, median (range)	12 (8–24)
PGA, median (range)	1.5 (1.0–2.4)
Low complement, n (%)	8 (72.7)
Anti-dsDNA Ab (Farr, IU/ml), median (range)	32.86 (8.42-100)
Previous treatment, n (%)	
– Glucocorticoids (GC)	11 (100)
– Hydroxychloroquine (HCQ)	10 (90.9)
No. of other IS/BAs, median (range)	4 (3–8)

LN parameters and characteristics n=10



Features	Median (range)
LN duration (years)	5 (2–16)
eGFR-CKD-EPI (ml/min/1.73m²)	113.65 (75.75–131.53)
24h UP (mg/24h)	2736.9 (1227.2–8156.9)
UPCR (mg/g)	2295.61 (1644.19–10841.93)

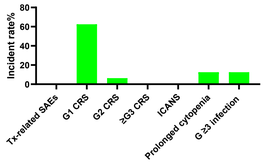


GC: Glucocorticoids; HCQ: Hydroxychloroquine; IS: Immunosuppressants; BA: Biologic agents; CYC: Cyclophosphamide; MMF: Mycophenolate Mofetil; AZA: Azathioprine; TAC: Tacrolimus; LEF: Leflunomide; CSA: Cyclosporine; MTX: Methotrexate; IGU: Iguratimod; RC18: Telitacicept; BEL: Belimumab; RTX: Rituximab

Safety profile of all patients

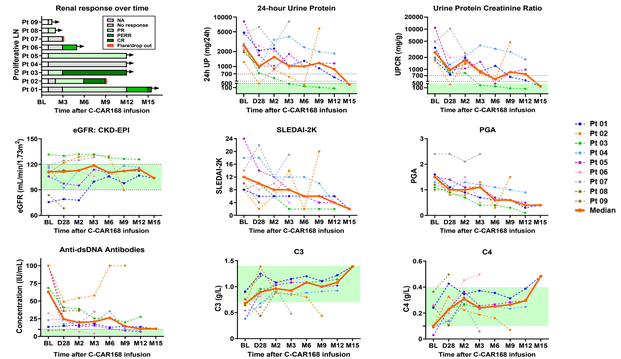
C-CAR168 was well tolerated.

- Grade 1-2 CRS occurred in 11/16 patients (68.8%) and resolved with supportive care.
- No ICANS or DLTs were observed.
- Grade ≥3 AEs were primarily hematologic and transient.
- Prolonged cytopenia and Grade 3 treatment-emergent infections each occurred in 2 patients (12.5%) and were successfully managed with standard therapies.

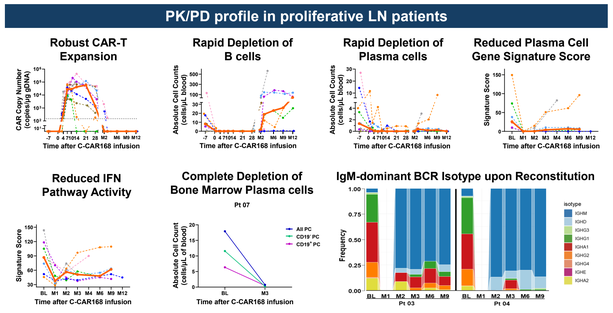


Robust efficacy in refractory proliferative LN patients

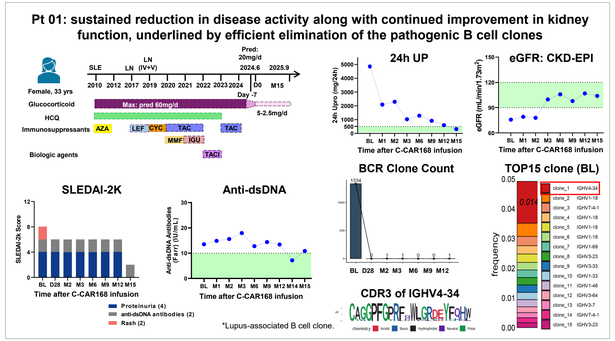
- All patients discontinued IS/biologics, with no or low corticosteroids ≤10 mg/day.
- 77.8%renal response , including 3 CR, 1 PERR and 3 PR.
- Improvement in proteinuria was rapid, continued to improve with longer follow-up.



PK/PD profile in proliferative LN patients

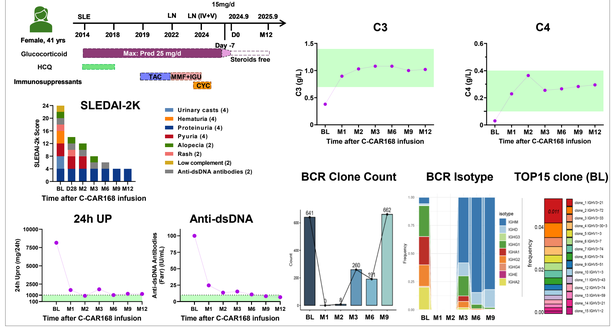


Pt 01: sustained reduction in disease activity along with continued improvement in kidney function, underlined by efficient elimination of the pathogenic B cell clones

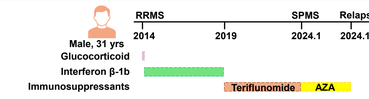


*Lupus-associated B cell clone.

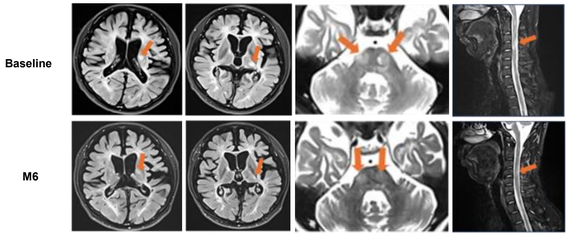
Pt 05: severe kidney involvement at baseline; achieved deep (>90% by M2) and sustained reduction in proteinuria , along with B cell clonal clearance and durable immune reset

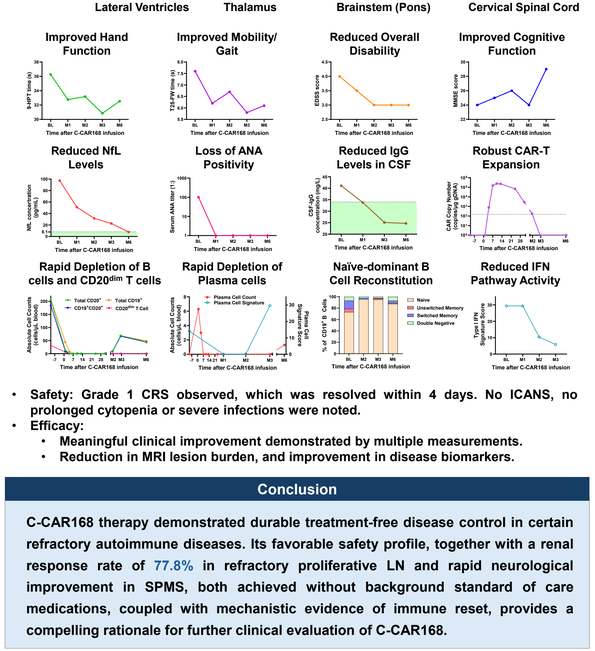


First SPMS Patient Shows Meaningful Clinical and Radiographic Improvement



T2-weighted Imaging Showing Radiologic Response





- **Safety:** Grade 1 CRS observed, which was resolved within 4 days. No ICANS, no prolonged cytopenia or severe infections were noted.
- **Efficacy:**
  - Meaningful clinical improvement demonstrated by multiple measurements.
  - Reduction in MRI lesion burden, and improvement in disease biomarkers.

Conclusion

C-CAR168 therapy demonstrated durable treatment-free disease control in certain refractory autoimmune diseases. Its favorable safety profile, together with a renal response rate of 77.8% in refractory proliferative LN and rapid neurological improvement in SPMS, both achieved without background standard of care medications, coupled with mechanistic evidence of immune reset, provides a compelling rationale for further clinical evaluation of C-CAR168.