

SAFETY AND EFFICACY OF A NOVEL ANTI-CD20 CHIMERIC ANTIGEN RECEPTOR (CAR)-T CELL THERAPY IN RELAPSED/REFRACTORY (R/R) B-CELL NON-HODGKIN LYMPHOMA (B-NHL) PATIENTS AFTER FAILING CD19 CAR-T THERAPY

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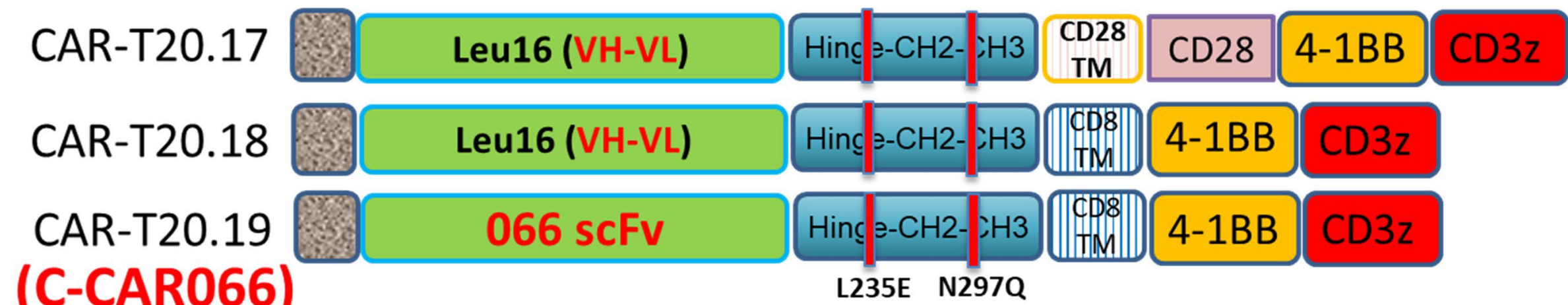
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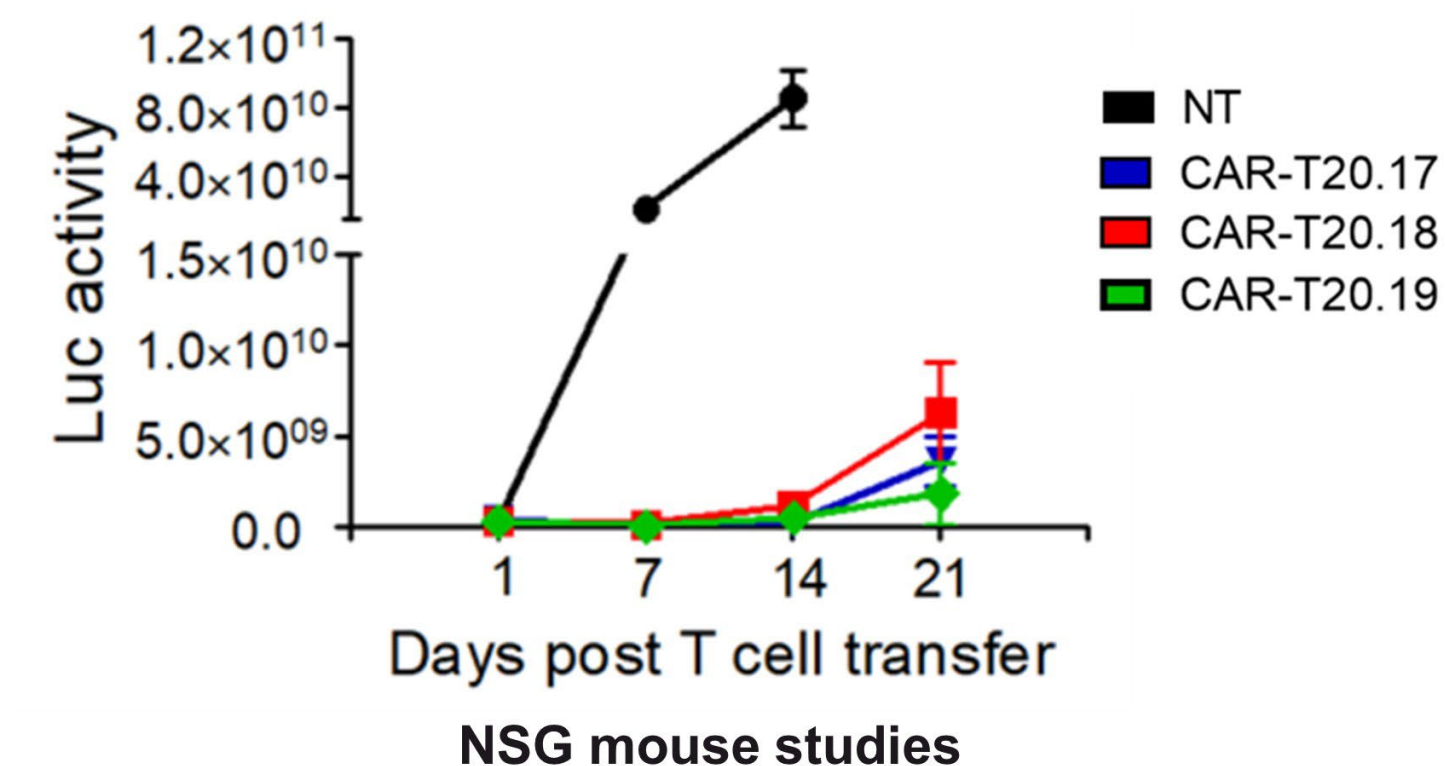
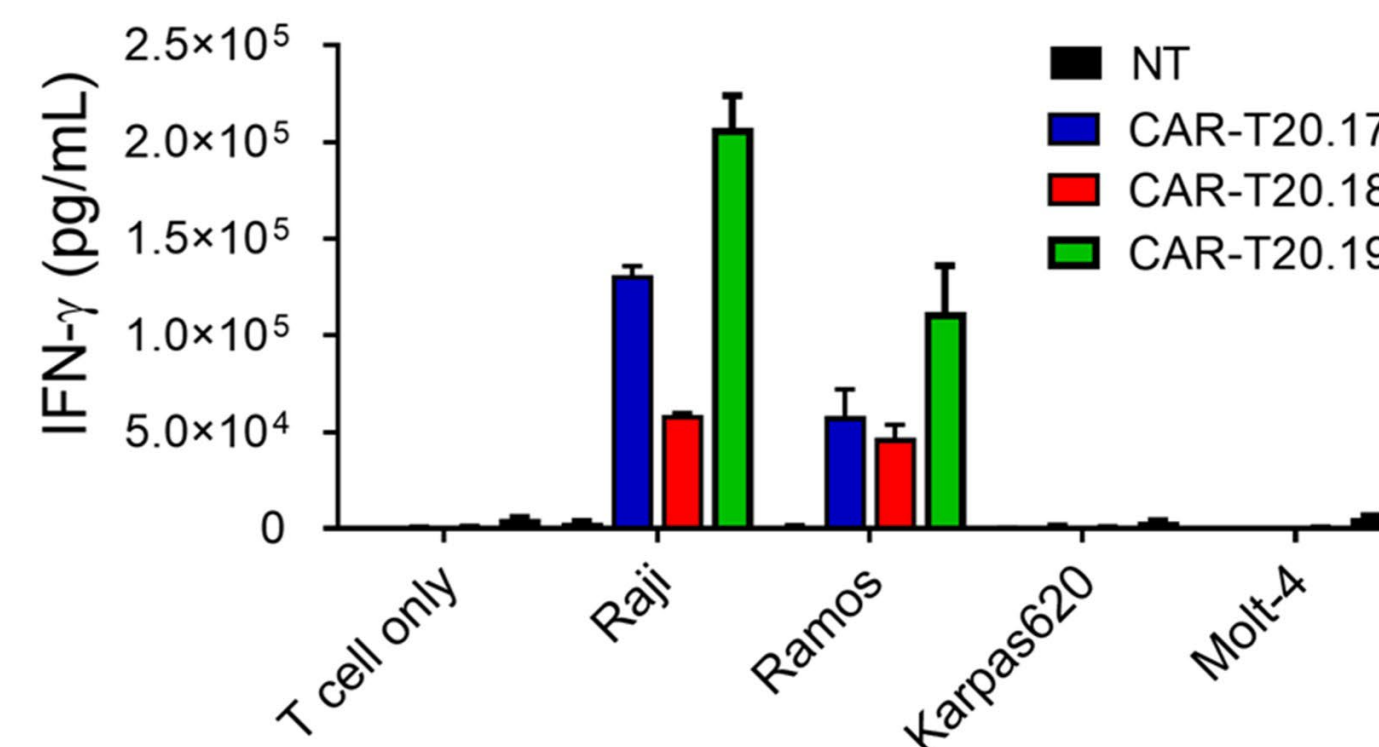
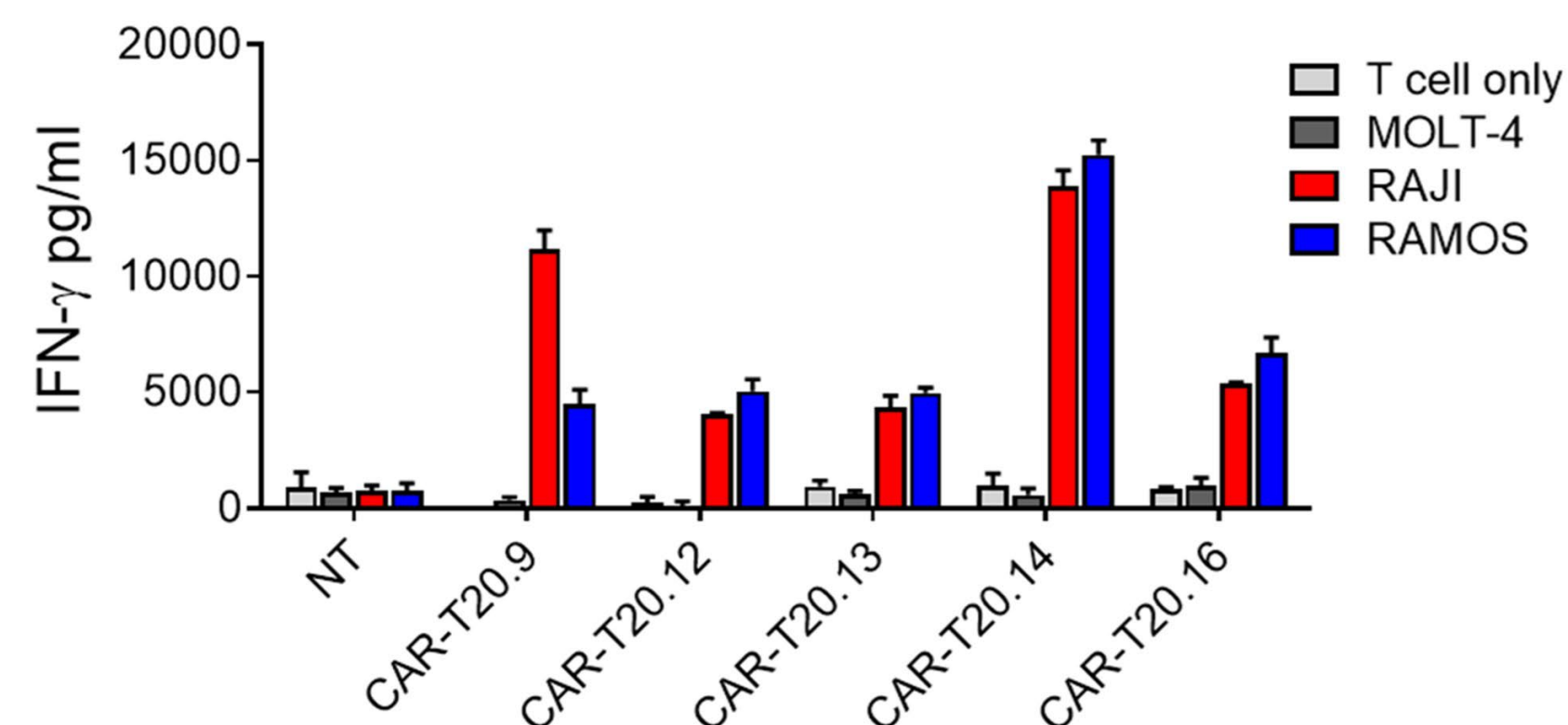
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Background of C-CAR066 (anti-CD20 CAR-T)



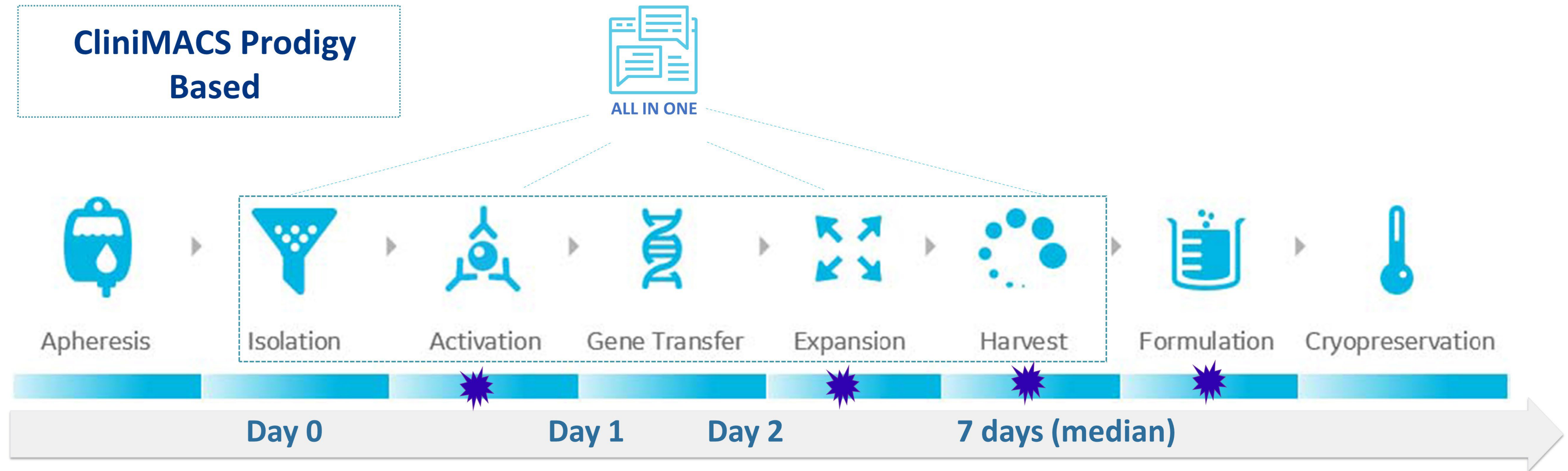
L235E/N297Q mutations in the hinge to abolish the binding of FcγRI/II and minimize the non-specific background.



- 066 scFv showed higher *in vitro* reactivity than other anti-CD20 scFvs including Leu16, Obinutuzumab, and Rituximab

- C-CAR066 (20.19) showed higher *in vitro* and *in vivo anti-tumor* activity than CAR-Ts with Leu16 (2nd and 3rd generation)

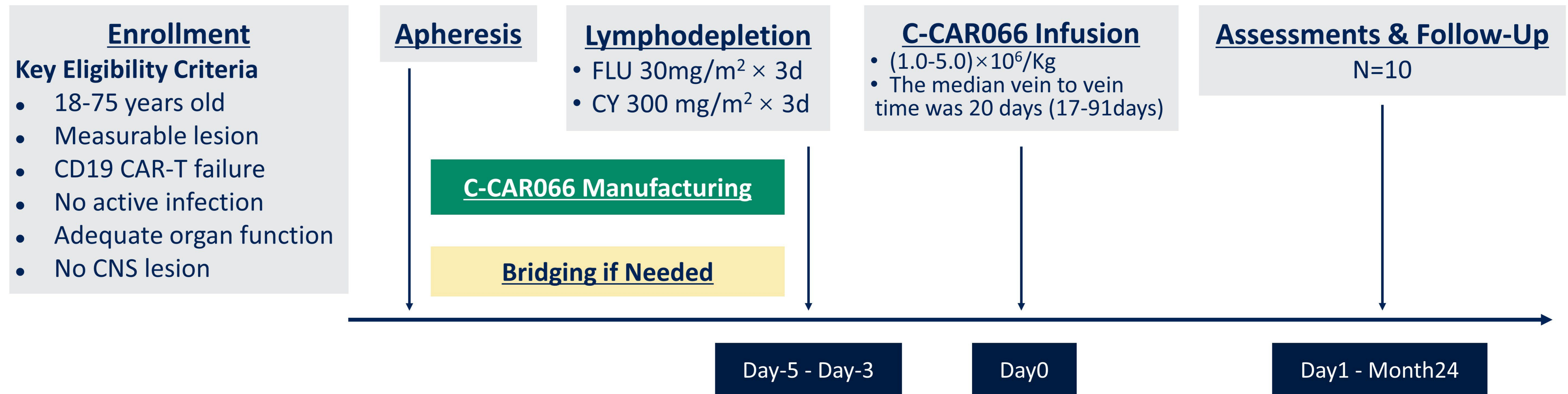
C-CAR066 Manufacture Process



- Serum-free
- Functionally closed, highly automated system
- ✦ Improved process

C-CAR066 Clinical Study Design and Objectives

A phase 1, first in human, open-label study targeting r/r B-NHL patients after failing CD19 CAR-T therapy conducted at 2 sites in China



Objectives

- **Primary** Incidence and severity of TEAEs (CTCAE V5.0 and ASTCT)
- **Secondary** ORR, DOR, PFS, OS (Lugano 2014)
- **Exploratory** CAR-T expansion and persistence

cut-off date: April 30, 2021

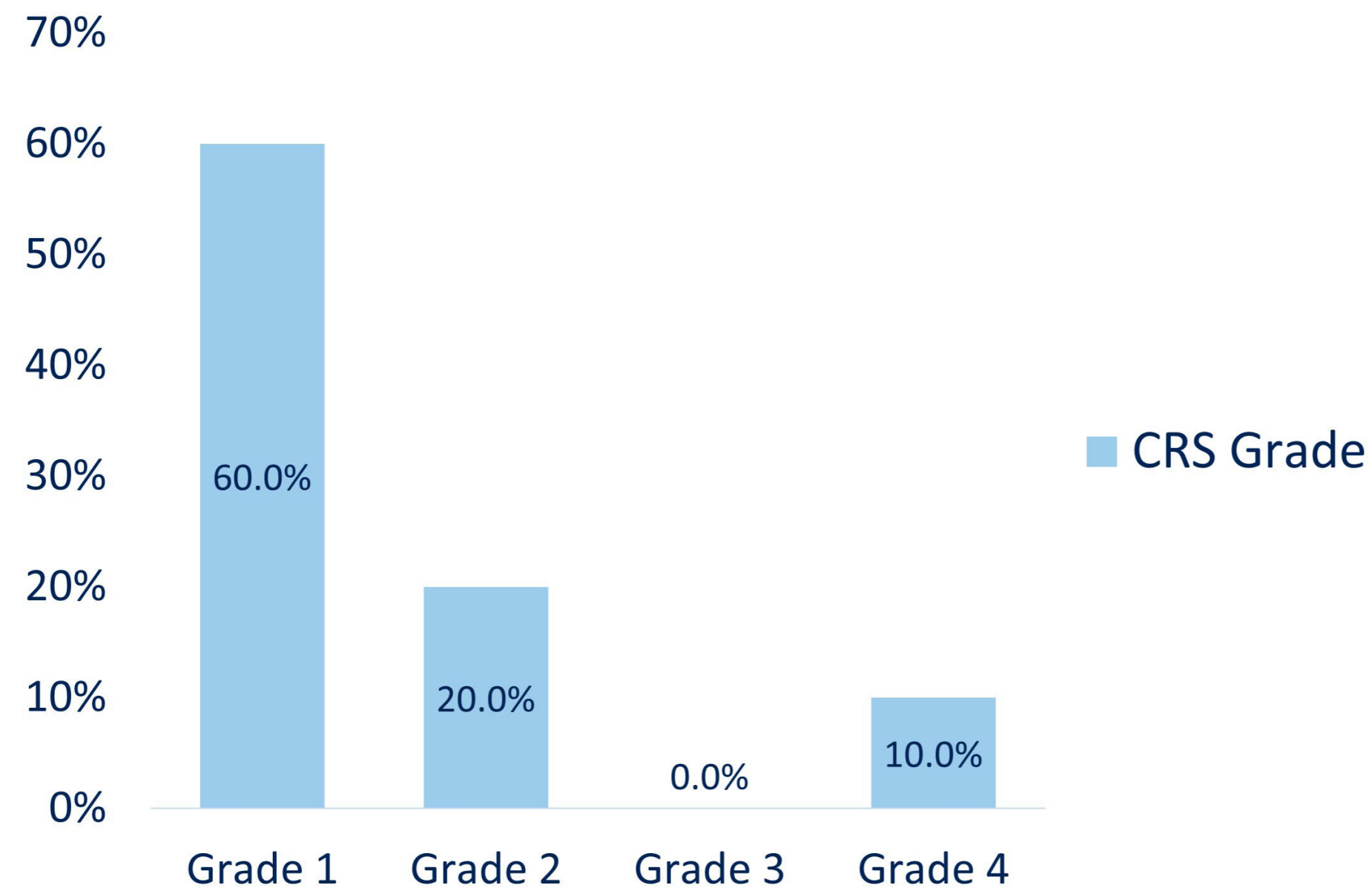
Demographic and Baseline Characteristics

Characteristics	N=10
Median age, yrs (range)	55.5 (41-67)
• Age ≥ 65, n (%)	2 (20.0)
Male, n (%)	5 (50.0)
NHL Subtype, n (%)	
• DLBCL,NOS	8 (80.0)
• tFL	2 (20.0)
ECOG PS, n (%)	
• 0	1 (10.0)
• 1	9 (90.0)
IPI score 3-5, n (%)	6 (60.0)
Ann Arbor stage III / IV, n (%)	9 (90.0)
Double-expressor lymphoma, n (%)	4 (40.0)

Characteristics	N=10
Median number of prior lines of therapy, n (range)	5 (2-6)
• 2, n (%)	1 (10.0)
• 4, n (%)	3 (30.0)
• 5, n (%)	4 (40.0)
• 6, n (%)	2 (20.0)
Prior ASCT, n (%)	2 (20.0)
Prior BTK inhibitor, n (%)	2 (20.0)
Prior Lenalidomide, n (%)	6 (60.0)
Best response to prior CAR-T therapy, n (%)	
• CR	2 (20.0)
• PR	8 (80.0)
Duration of response of prior CAR-T therapy, m (range)	2.1 (0.7-12.6)
Received bridging therapy, n (%)	4 (40.0)

Safety Profile of C-CAR066

- 8/10 patients had grade 1-2 CRS
- 1/10 patient had grade 4 CRS*
- No ICANS events
- Cytopenias mostly related to Cy/Flu lymphodepletion which were reversible



*The patient presented with high fever, hypotension and hypoxia on day 6 and resolved on day 10. Treated with Tocilizumab and steroids, and with non-invasive ventilation support. Not admitted to the ICU.

AEs, n (%)	All Grades (n=10)	Grade ≥3 (n=10)
CRS	9 (90.0)	1 (10.0)
ICANS	0 (0)	0 (0)
Neutropenia	10 (100)	8 (80.0)
Anemia	10 (100)	5 (50.0)
Thrombocytopenia	7 (70.0)	3 (30.0)
Infection	7 (70.0)	1 (10.0)

CRS	N=10
CRS , n (%)	9 (90.0)
• Median days to onset, d (range)	2 (1-9)
• Median days to resolution, d (range)	4 (2-17)
• Treated with Tocilizumab alone, n (%)	0 (0)
• Treated with steroids alone, n (%)	0 (0)
• Treated with Tocilizumab and steroids, n (%)	1 (10.0)

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Best Overall Response

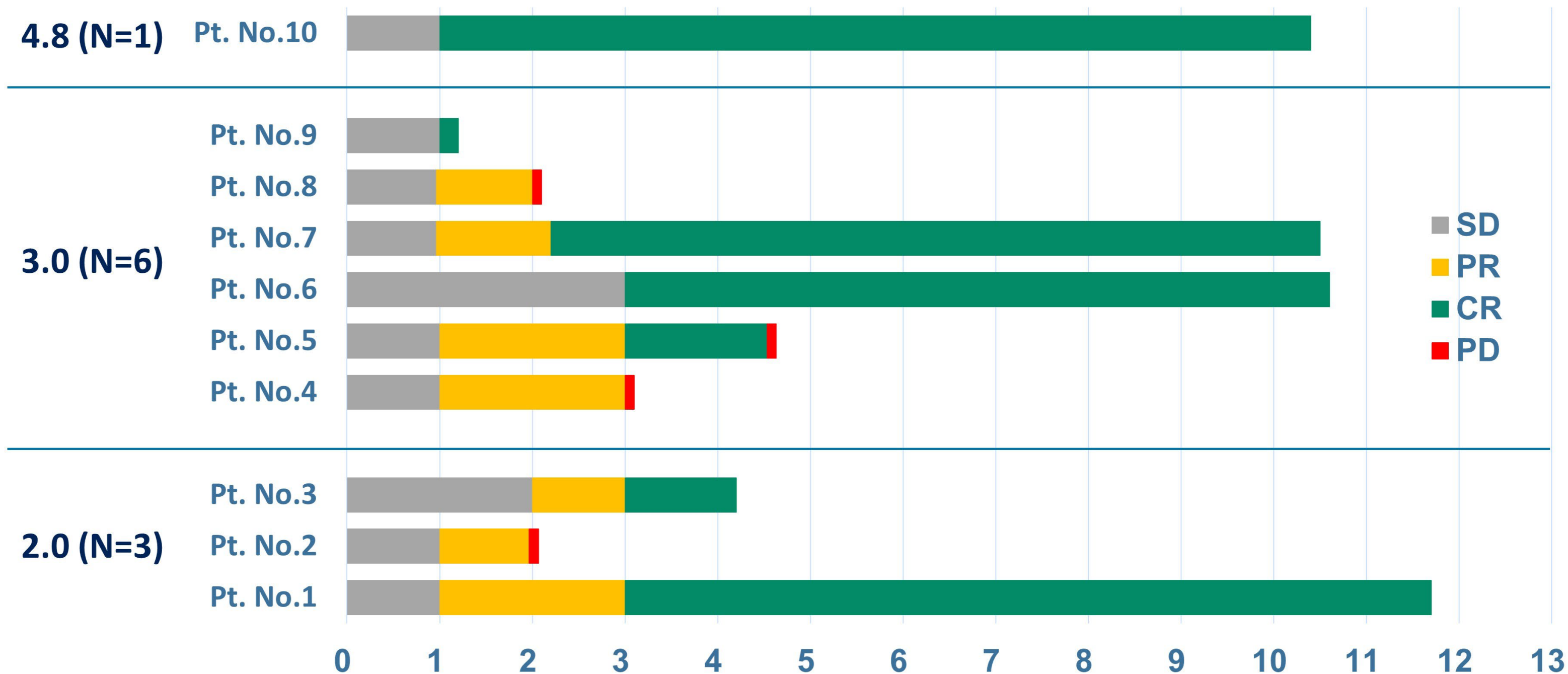
Response*	N=10
ORR, n (%)	10 (100)
• CR rate	7 (70.0)
• PR rate	3 (30.0)
Median time to response, m (range)	1.0 (0.9-2.7)
Median duration of response, m (range)	NR (1.0-NR)
Median time to CR, m (range)	2.7 (0.9-2.9)
Median duration of CR, m (range)	NR (1.5-NR)
Median follow-up, m (range)	4.2 (1.2-11.7)

- **ORR rate was 100% and CR rate was 70%**
- **The median time to first response was 1 month (range, 0.9-2.7)**
- **The median time to CR was 2.7 months (range, 0.9-2.9)**

*Assessed by investigators
NR: not reached

Patient Responses Over Time

Dosage($\times 10^6$ CAR-T cell/kg)

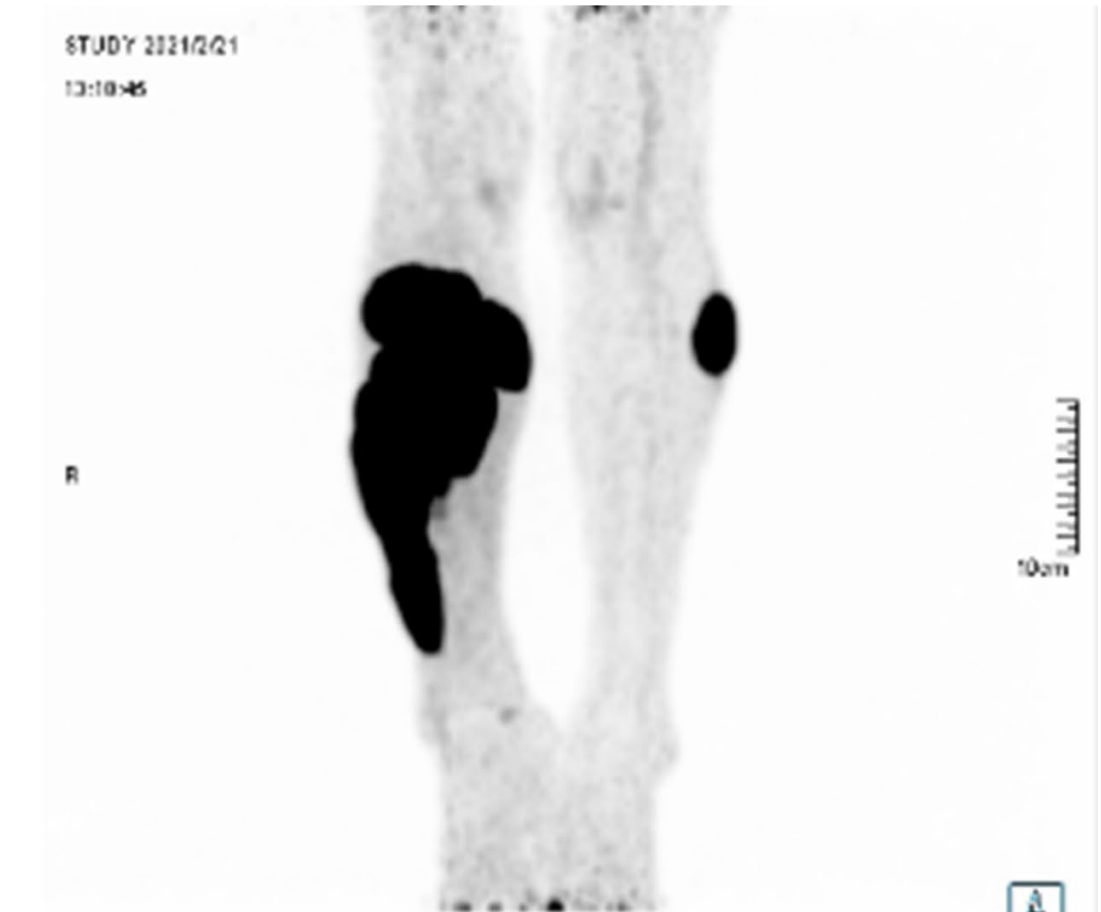


- Median follow-up was 4.2 months (range, 1.2-11.7)
- Median DOR has not been reached
- 4 patients remain CR after 10 months

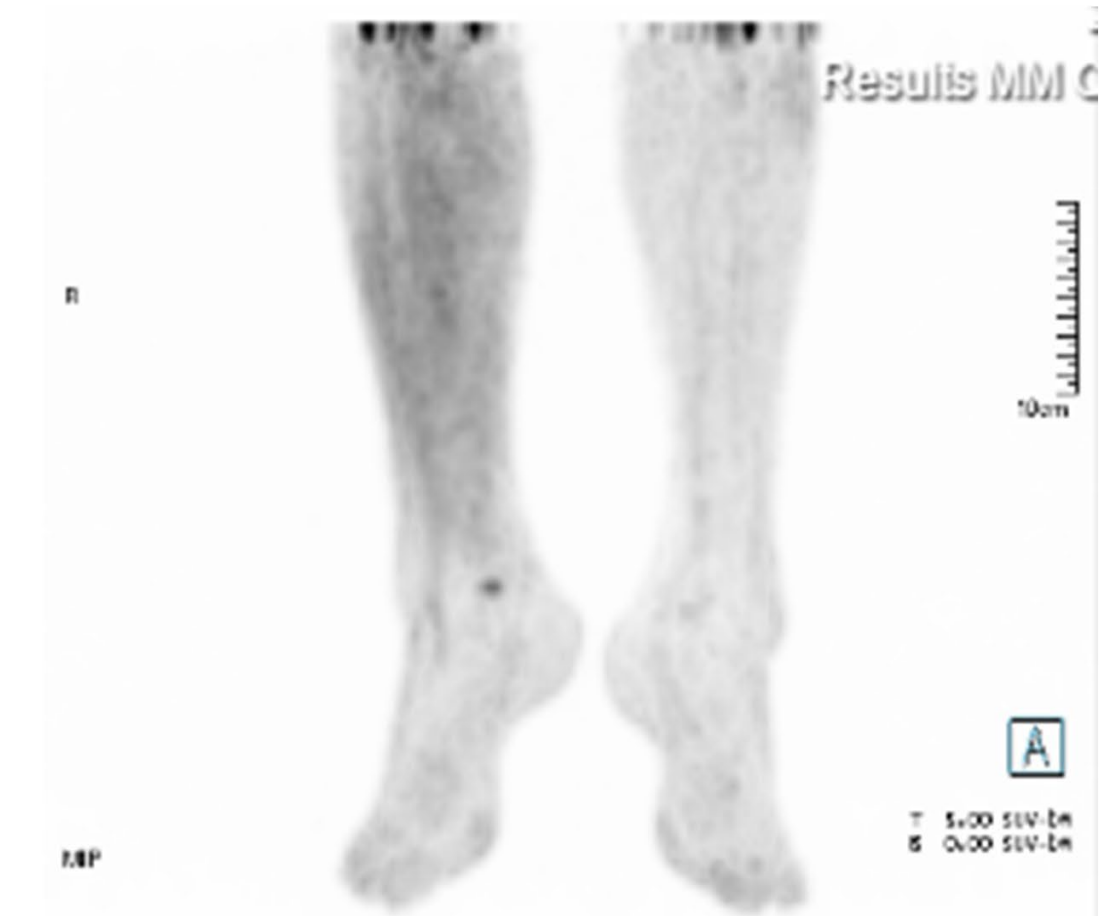
A Case Study: CR at 4w with Bulky Disease

- **67-year-old male with double-expressor DLBCL**
 - Diagnosed on May 2019
 - 4 prior lines of therapy, including CD19 CAR-T treatment
 - Right and left calves lesions
 - Bulky disease, **25.9*6.3*10.1 cm** in the right leg at baseline
- **Prior CD19 CAR-T treatment**
 - Best response: PR
 - Duration of Response: 1.2 months
- **C-CAR066 treatment**
 - $3.0 \times 10^6/\text{kg}$ dosage
 - Grade 2 CRS: Onset on day 2, resolved on day 11
 - No neurotoxicity
 - Achieved CR by Day 27
- **Longer follow-up is needed**

Pre-treatment

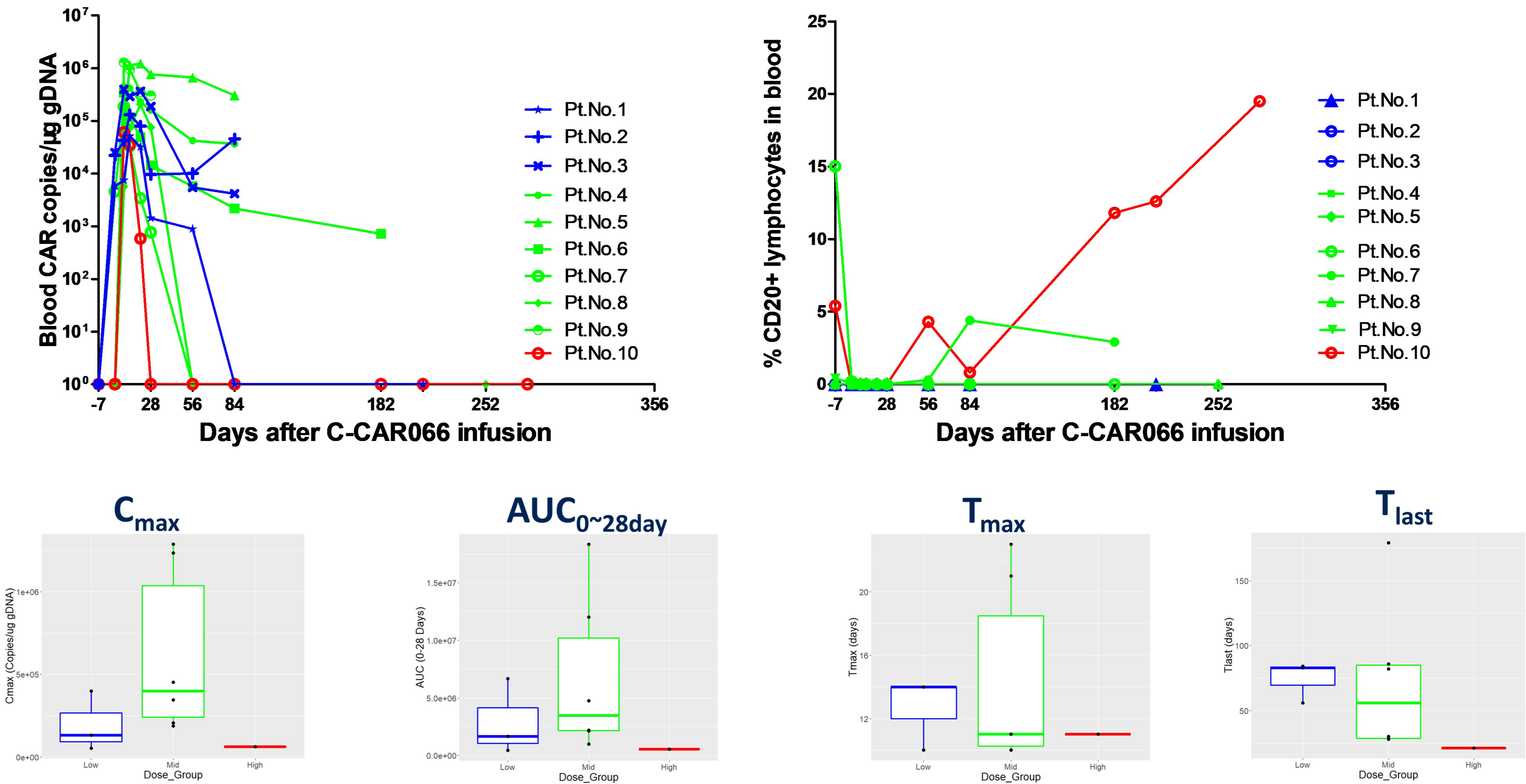


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C-CAR066 PK/PD Profiles

The changes of C-CAR066 CAR copies and CD20+ B cell level in the peripheral blood over time



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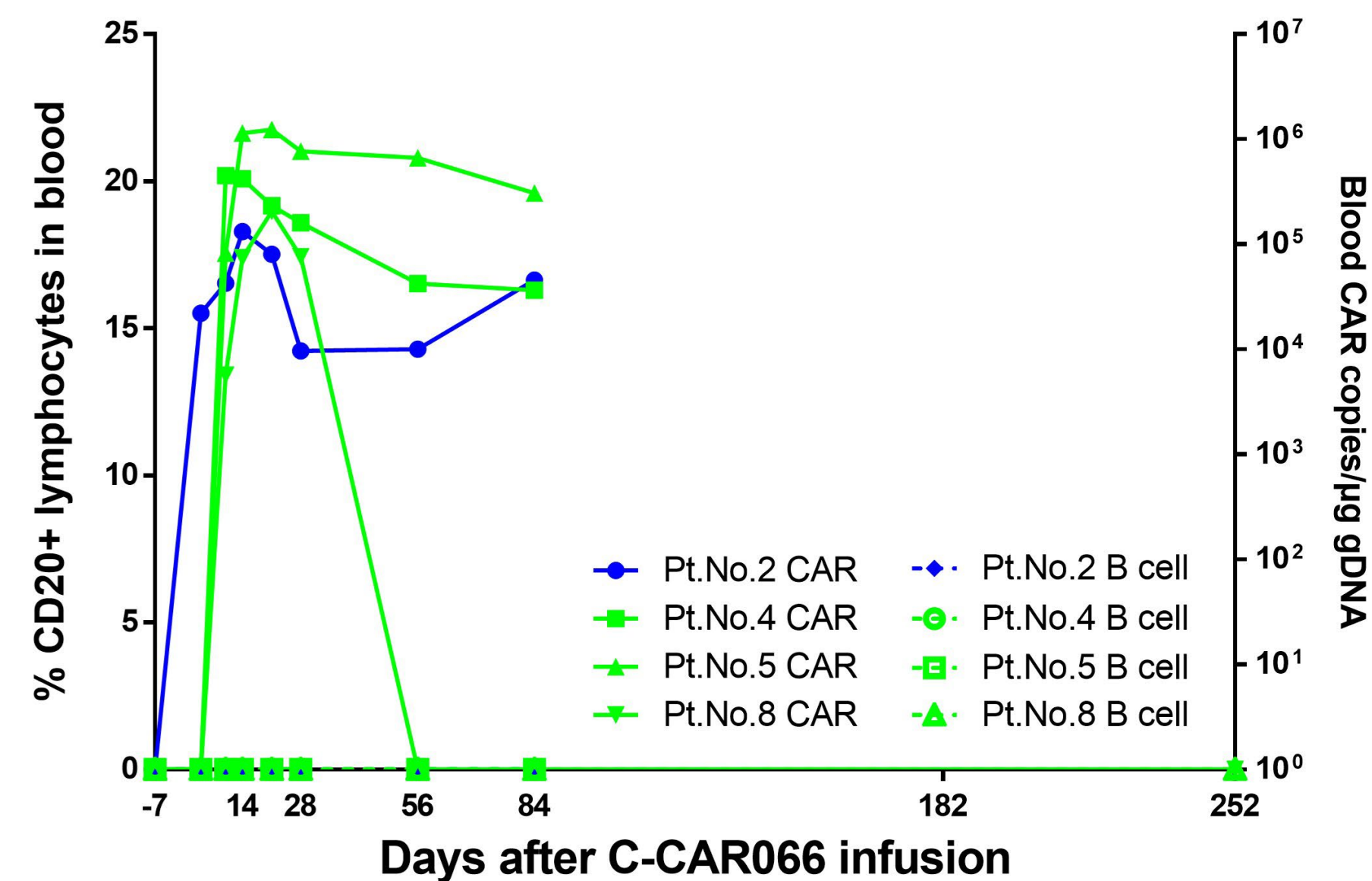


CD19/CD20 Expression and PK/PD in C-CAR066 Relapsed Patients

CD19/CD20 expression tested in tumor tissues by IHC

Patient	Before C-CAR066 Treatment	Relapsed after C-CAR066 Treatment
Pt. No 2	CD19(+) CD20(+)	CD19(+) CD20(+)
Pt. No 4	CD19(dim) CD20(+)	CD19(-) CD20(-)
Pt. No 5	CD19(+) CD20(+)	CD19(-) CD20(-)
Pt. No 8	CD19(UK) CD20(+)	CD19(+) CD20(+)

CAR-T expansion and B cell depletion in peripheral blood



Conclusions

- **This is a First in Human study of CD20 CAR-T (C-CAR066) in r/r B-NHL patients after failing CD19 CAR-T treatment**
- **Of the 10 patients, 9 (90%) experienced \leq grade 2 CRS, 1 patient experienced grade 4 CRS**
 - 1 (10%) patient received tocilizumab and corticosteroids
- **No patients experienced ICANS**
- **C-CAR066 demonstrated an ORR of 100%, CR rate of 70%, PR rate of 30%**
 - Median time to response and to CR were 1.0 and 2.7 months, respectively
 - With a median follow-up of 4.2 months, the median duration of response was not yet reached
- **The expansion in the peripheral blood of C-CAR066 correlated with B cell depletion**
- **C-CAR066 has shown a favorable safety profile and very promising clinical benefit in patients with r/r DLBCL following failure of CD19 CAR-T therapy**