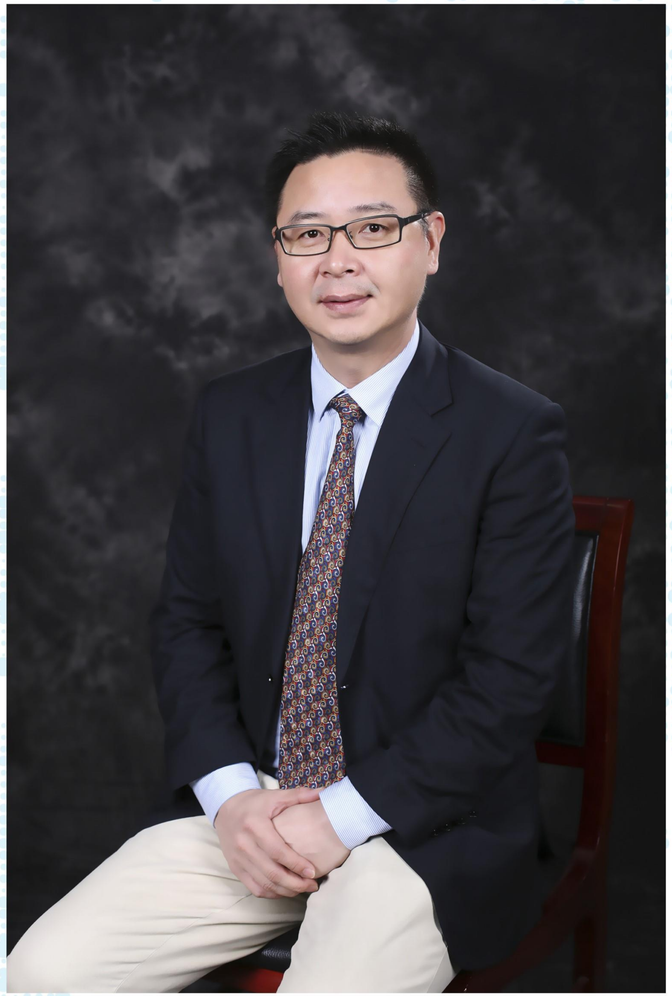
2021 ASCO ANNUAL MEETING

SAFETY AND EFFICACY OF A NOVEL ANTI-CD20/CD19 BI-SPECIFIC CAR T-CELL THERAPY (C-CAR039) IN RELAPSED OR REFRACTORY (R/R) B-CELL NON-HODGKIN LYMPHOMA (B-NHL)



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June, 7 2021

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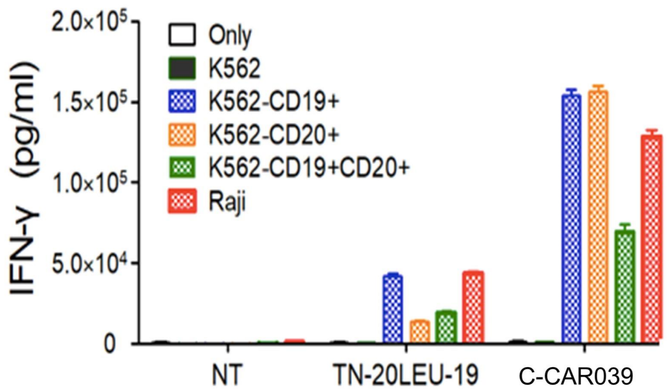
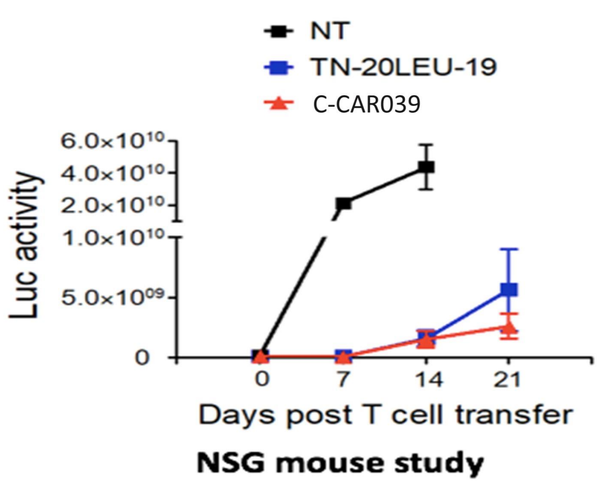
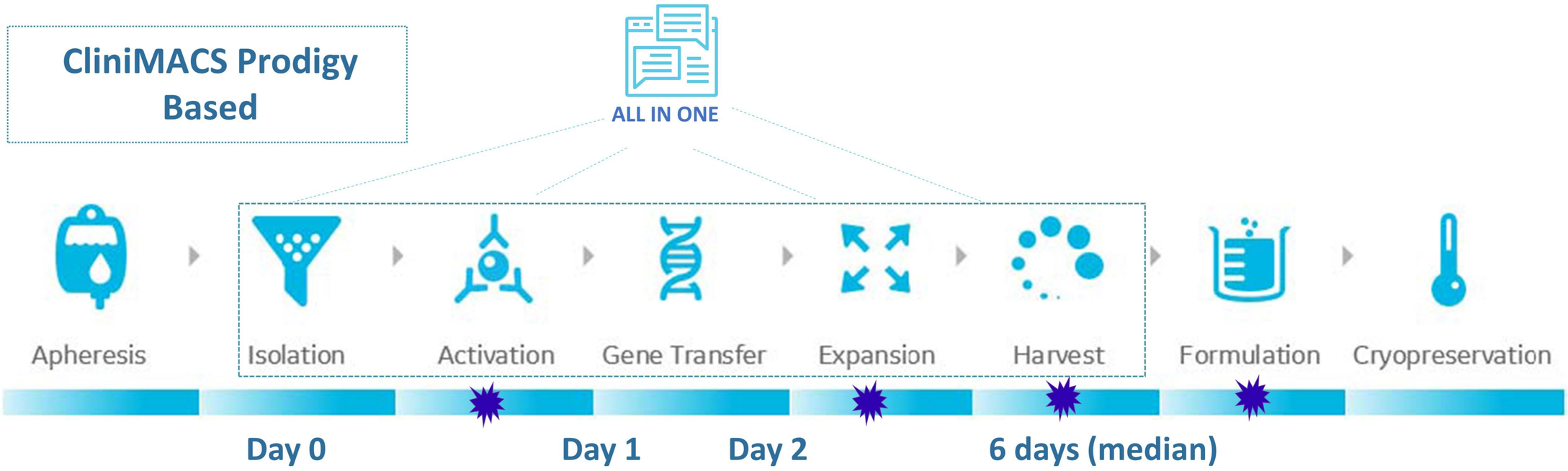
C-CAR039 Shows Superior Anti-tumor Activity vs. anti-CD20/CD19 Bi-specific CAR-T with Leu16-FMC63 *in vitro* and *in vivo*





- C-CAR039 is a novel 2nd generation 4-1BB bi-specific chimeric antigen receptor T (CAR-T) targeting both CD19 and CD20 antigens
- C-CAR039 shows *in vitro* anti-tumor activity against both single positive and double-positive CD20/CD19 expressing tumors
- C-CAR039 shows superior anti-tumor activity both *in vitro* and *in vivo* to the CD20/CD19 bispecific CAR-T with the tandem linked scFvs of Leu16 and FMC63

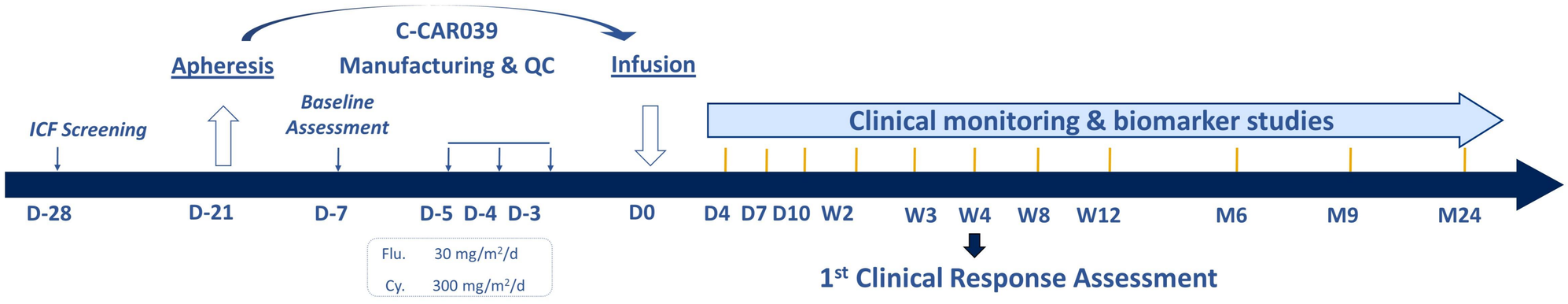
C-CAR039 Manufacture Process



- Serum-free
- Functionally Closed, Highly Automated System
- Improved Process

Study Design

- A phase 1, open-label, dose escalation and expansion study conducted at four sites in China

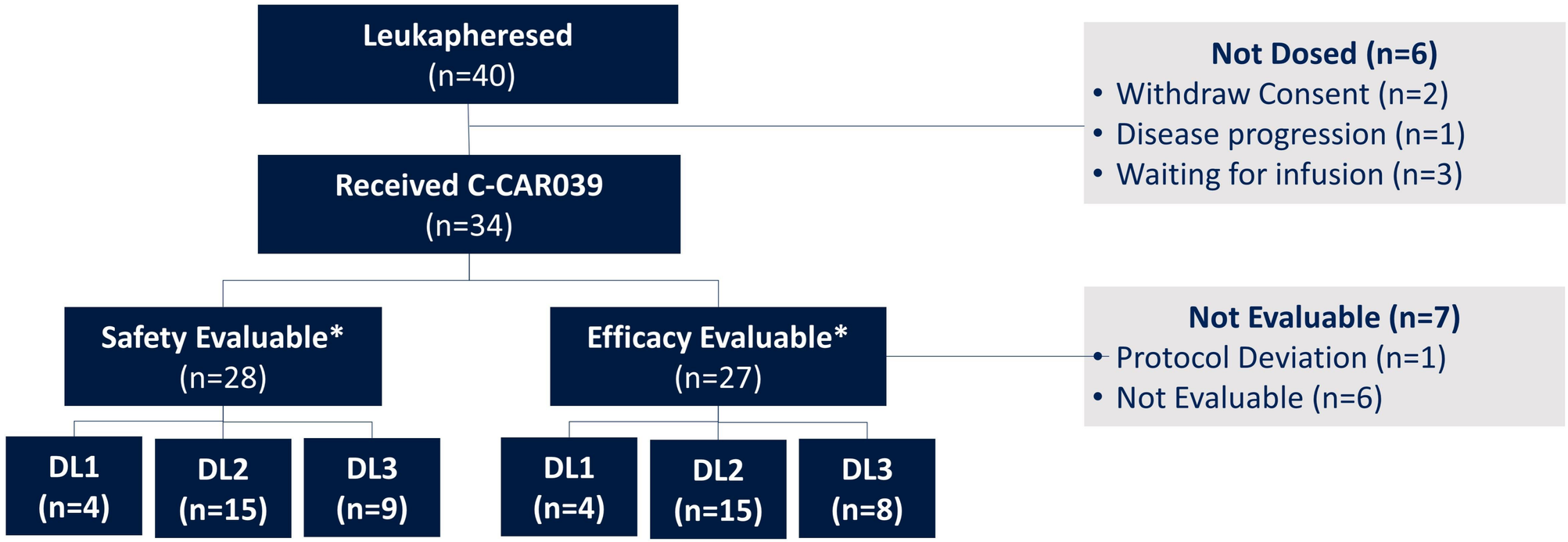


DL1: 1.0×10^6/Kg → DL2: 2.5×10^6/Kg → DL3: 5.0×10^6/Kg [Range: ± 20% of the target dose]

Initiate expansion cohorts to determine RP2D

- **Key Eligibility Criteria:**
  - 18-75 years of age
  - r/r B-NHL including DLBCL, FL, MCL
  - Either CD19 or CD20 positive disease
  - No active CNS involvement
  - Received anti-CD20 monoclonal antibodies
- **Safety Assessment:**
  - Incidence and severity of treatment-emergent adverse events (CTCAE V5.0 and ASTCT)
- **Efficacy Assessment:**
  - ORR (CR+PR); DOR; PFS; OS (Lugano 2014)

Patient Disposition



- As of April 20, 2021, 40 patients had been leukapheresed in four clinical centers, 34 patients were infused
- The median manufacturing time was 6 days (range, 5 to 11 days)
- The median vein to vein time was 19 days (range, 12 to 67 days)
- 28 patients have at least 1 month data. Only 27 patients were evaluable for efficacy since 1 patient does not have measurable disease at baseline

*Includes all treated patients who have ≥ 1 month of follow up

Demographic and Baseline Characteristics

Characteristics	N=28
Median age, yrs (range) • Age ≥ 65, n (%)	55.5 (28-71) 8 (28.6)
Male, n (%)	19 (67.9)
NHL Subtype, n (%) • DLBCL,NOS • PMBCL • tFL • FL	 25 (89.3) 1 (3.6) 1 (3.6) 1 (3.6)
ECOG PS, n (%) • 0 • 1	 18 (64.3) 10 (35.7)
IPI score 3/4, n (%)	7 (25.0)
Ann Anbor stage III / IV, n (%)	21 (75.0)

Characteristics	N=28
Double-expressor lymphoma, n (%)	8 (28.6)
Median number of prior lines of therapy, n (range) • 1, n (%) • 2, n (%) • 3, n (%) • 4, n (%) • 5, n (%)	3 (1-5) 1 (3.6) 10 (35.7) 4 (14.3) 7 (25.0) 6 (21.4)
Prior ASCT, n (%)	5 (17.9)
Prior BTK inhibitor, n (%)	8 (28.6)
Prior Lenalidomide, n (%)	9 (32.1)
Never Achieved CR to prior therapies, n (%)	8 (28.6)
Received bridging therapy, n (%)	5 (17.9)

Most Common Adverse Events

AE*, n (%)	All Grades (n=28)	Grade ≥3 (n=28)
Hematologic		
Leukopenia	28 (100)	25 (89.3)
Neutropenia	28 (100)	25 (89.3)
Anemia	28 (100)	9 (32.1)
Lymphopenia	27 (96.4)	27 (96.4)
Thrombocytopenia	18 (64.3)	7 (25.0)
CRS	26 (92.9)	1 (3.6)
Infection	15 (53.6)	1 (3.6)
Gastrointestinal		
Constipation	13 (46.4)	0 (0)
Other		
Hypertriglyceridemia	21 (75.0)	1 (3.6)
Hypoalbuminemia	18 (64.3)	0 (0)
Hypogammaglobulinemia	15 (53.6)	0 (0)
Lactate dehydrogenase increased	15 (53.6)	0 (0)
Hypokalemia	14 (50.0)	1 (3.6)
Alanine aminotransferase increased	13 (46.4)	2 (7.1)
Hyperuricemia	10 (35.7)	0 (0)
Hyperglycemia	10 (35.7)	0 (0)
Aspartate aminotransferase increased	10 (35.7)	2 (7.1)

- 100% of patients experienced at least 1 AE of any grade
- Cytopenias were common, mostly related to Cy/Flu lymphodepletion and are reversible
- 92.9% of patients experienced CRS. Most were grade 1 or 2. Only 1 patient experienced grade 3 CRS. All CRS are reversible
- Infections were common (53.6%). Only 1 patient experienced grade 3 infection

*Events reported in 35% or more patients; CRS, Cytokine Release Syndrome

Cytokine Release Syndrome

CRS	All (N=28)	1.0X10^6/kg (N=4)	2.5x10^6/kg (N=15)	5.0x10^6/kg (N=9)
CRS*, n(%)				
Any grade	26 (92.9)	4 (100)	14 (93.3)	8 (88.9)
Grade ≥ 3	1 (3.6)	0 (0)	1 (6.7)	0 (0)
Most common symptoms of any grade, n/n (%)				
Pyrexia	26/26 (100)	4/4 (100)	14/14 (100)	8/8 (100)
Hypotension	6/26 (23.1)	1/4 (25.0)	4/14 (28.6)	1/8 (12.5)
Hypoxemia	0 (0)	0 (0)	0 (0)	0 (0)
CRS Management, n(%)				
Tocilizumab alone	4 (14.3)	0 (0)	2 (13.3)	2 (22.2)
Corticosteroids alone	1 (3.6)	0 (0)	1 (6.7)	0 (0)
Tocilizumab and Corticosteroids	1 (3.6)	0 (0)	1 (6.7)	0 (0)
Median days to onset, d (range)	2.5 (0-10)	7 (2-10)	3.5 (1-10)	1 (0-9)
Median days to resolution, d (range)	4 (1-25)	2.5 (1-7)	4.5 (1-25)	4 (1-7)

- Only 1 grade 3 CRS. CRS in higher dose groups showed shorter time to onset and longer resolution time.

*CRS, Cytokine Release Syndrome, graded by ASTCT; AE, Adverse Events

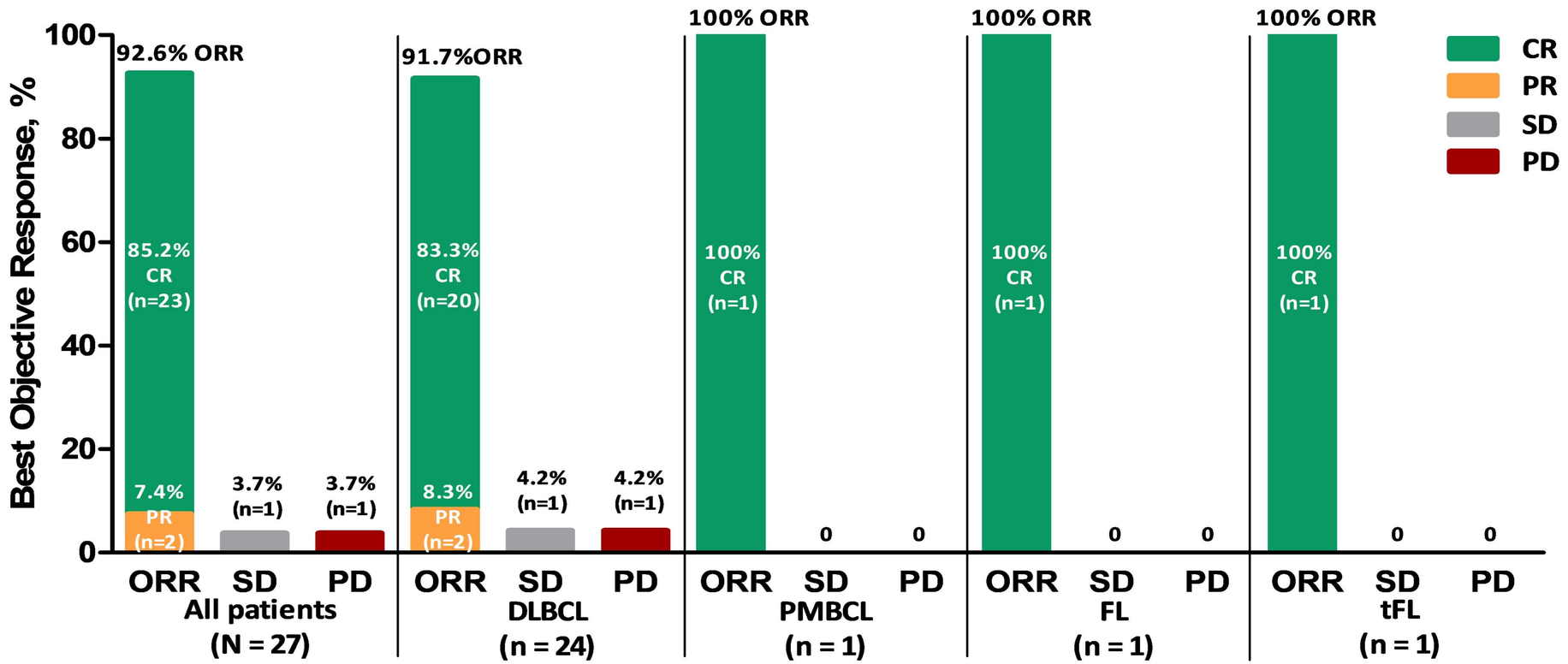
Neurologic Events

ICANS	All (N=28)	1.0X10^6/kg (N=4)	2.5x10^6/kg (N=15)	5.0x10^6/kg (N=9)
Neurologic events*, n(%)				
Any grade	2 (7.1)	0 (0)	0 (0)	2 (22.2)
Grade ≥ 3	0 (0)	0 (0)	0 (0)	0 (0)
Most common symptoms of any grade, n/n(%)				
Tremor	2/2 (100)	0 (0)	0 (0)	2/2 (100)
Confusion	0 (0)	0 (0)	0 (0)	0 (0)
ICANS management, n(%)				
Corticosteroids	1 (3.6)	NA	NA	1 (11.1)
Tocilizumab	0 (0)	NA	NA	0 (0)
Median days to onset, d (range)	16 (4-28)	NA	NA	16 (4-28)
Median days to resolution, d (range)	31.5 (11-52)	NA	NA	31.5 (11-52)

- Only 2 patients had grade 1 ICANS, all in 5.0x10^6 CAR-T cell/kg dosing group

ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome, graded by ASTCT; AE, Adverse Events; NA, not applicable

Best Overall Response



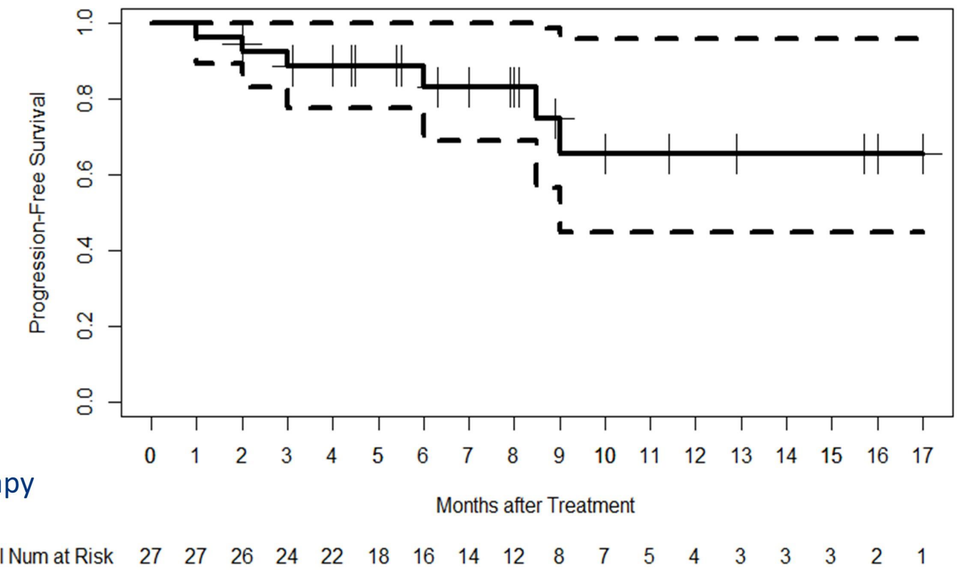
- 92.6% ORR and CR rate was 85.2% in all patients
- 91.7% ORR and CR rate was 83.3% in DLBCL patients
- The median time to first response was 1 month (range, 0.9-1.6)
- The median time to CR was 1 month (range, 0.9-6.0)

Response was assessed by investigators

Duration of Response and Progression-Free Survival

Responses over time

Kaplan Meyer estimation of PFS

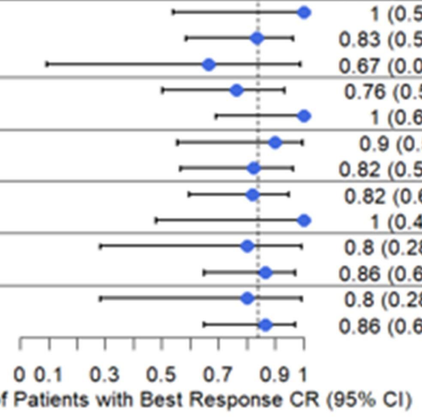


- Pt. No 10 had no significant CAR expansion and no clinical response
- Pt. No 23 experienced second malignancy and dropped out
- 4 patients relapsed at 3, 6, 8 and 9 months respectively after achieving CR

- Median follow-up was 7 months (range,1.9-17.2)
- Six-month PFS rate: 83.2% (95% CI, 69.1 to100.0)
- Median DOR has not been reached

Subgroup Analysis of Patients with Best Response of CR

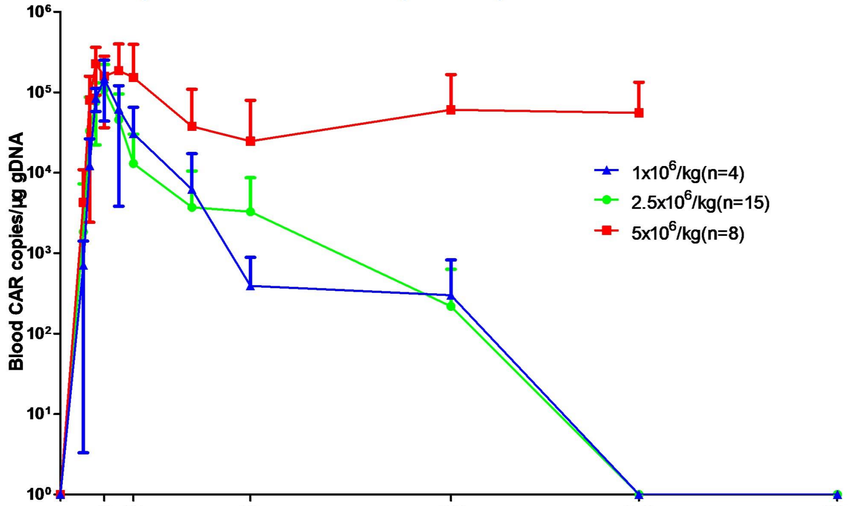
Subgroup	Condition	Total Number	Number with CR	Mean (95% CI)
All patients		27	23	0.85 (0.66 - 0.96)
Dose level	DL1	4	4	1 (0.4 - 1)
	DL2	15	13	0.87 (0.6 - 0.98)
	DL3	8	6	0.75 (0.35 - 0.97)
Disease type	DLBCL	24	20	0.83 (0.63 - 0.95)
	PMBCL	1	1	1 (0.03 - 1)
	TFL	1	1	1 (0.03 - 1)
	FL	1	1	1 (0.03 - 1)
Cell of origin of cancer	Germinal center B-cell type	5	5	1 (0.48 - 1)
	Non–germinal center B-cell type	20	16	0.8 (0.56 - 0.94)
	UK	1	1	1 (0.03 - 1)
Age	≥65	8	6	0.75 (0.35 - 0.97)
	<65	19	17	0.89 (0.67 - 0.99)
Sex	Male	19	16	0.84 (0.6 - 0.97)
	Female	8	7	0.88 (0.47 - 1)
Stage	I or II	6	6	1 (0.54 - 1)
	III or IV	21	17	0.81 (0.58 - 0.95)
IPI	<2	10	9	0.9 (0.55 - 1)
	≥2	17	14	0.82 (0.57 - 0.96)
Double expressors	Y	6	6	1 (0.54 - 1)
	N	18	15	0.83 (0.59 - 0.96)
	UK	3	2	0.67 (0.09 - 0.99)
Extranodal disease	Y	17	13	0.76 (0.5 - 0.93)
	N	10	10	1 (0.69 - 1)
Prior lines	<3	10	9	0.9 (0.55 - 1)
	≥3	17	14	0.82 (0.57 - 0.96)
Previous response status	Refractory to the last line of treatment	22	18	0.82 (0.6 - 0.95)
	Relapsed after the last line of treatment	5	5	1 (0.48 - 1)
Previous ASCT	Y	5	4	0.8 (0.28 - 0.99)
	N	22	19	0.86 (0.65 - 0.97)
Bridging	Y	5	4	0.8 (0.28 - 0.99)
	N	22	19	0.86 (0.65 - 0.97)



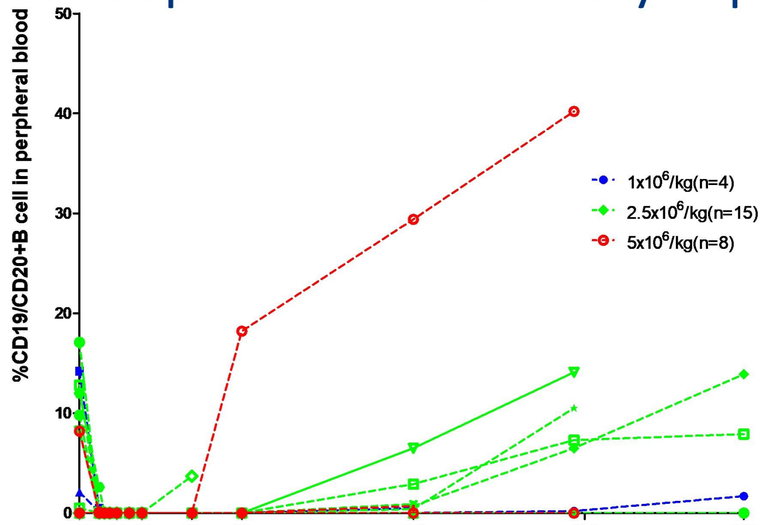
- CR rate was consistent among key subgroups

C-CAR039 PK/PD Profile

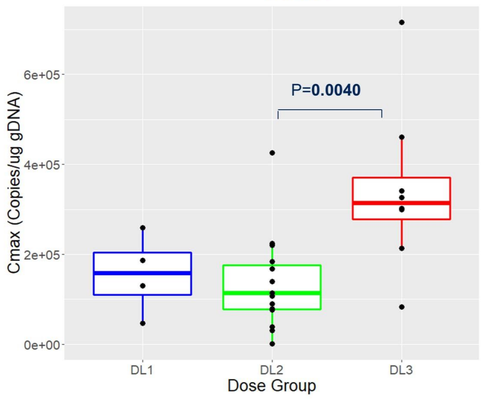
CAR-T expansion in peripheral blood over time



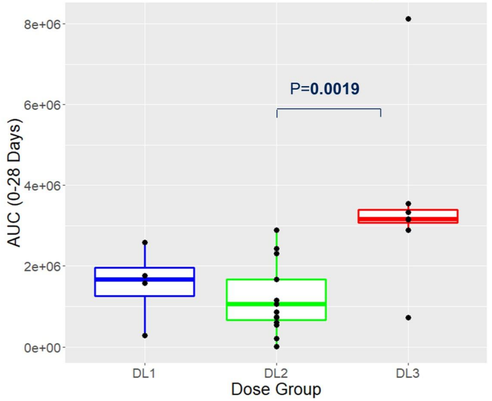
B cell depletion and recovery in peripheral blood



C_{max}



$AUC_{0\text{-}28day}$



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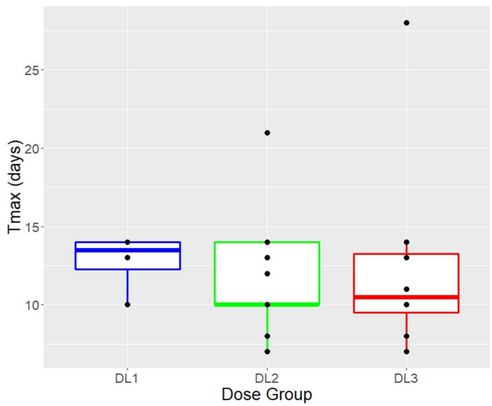
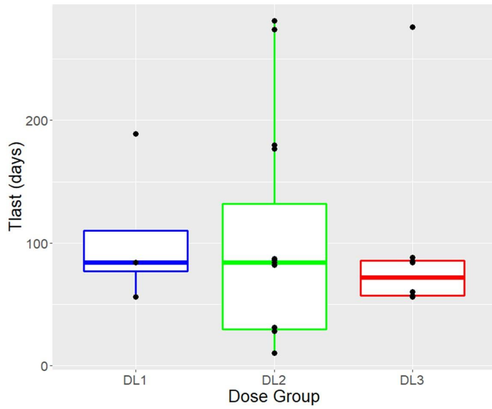


T_{last}



Conclusions

Of 28 patients evaluable for safety, 26 (92.9%) experienced CRS, and only 1 (3.6%) was grade 3

- 4 (14.3%) patients received tocilizumab alone, 1 (3.6%) patient received corticosteroids alone, and 1 (3.6%) patient received both tocilizumab and corticosteroids
- Higher dose groups showed shorter time for CRS onset and longer resolution time

2 (7.1%) patients experienced a grade 1 ICANS, both in highest dose group

- 1 (3.6%) patient received corticosteroids

Of 27 patients evaluable for efficacy, C-CAR039 treatment resulted in an ORR of 92.6% and a CR rate of 85.2% in r/r NHL predominantly DLBCL patients

- Median time to response and to CR were both 1.0 month
- With median follow-up of 7.0 months, the median DOR has not yet been reached

C-CAR039 proliferation and expansion in the peripheral blood correlated with B cell depletion

C-CAR039 has demonstrated a favorable safety profile and highly promising efficacy in patients with r/r B-NHL