A Global Phase 1B Study of JNJ-90014496, A CD19/CD20 Bi-specific Chimeric Antigen Receptor (CAR) T-cell Therapy, in Patients With Relapsed/Refractory Large B-cell Lymphoma

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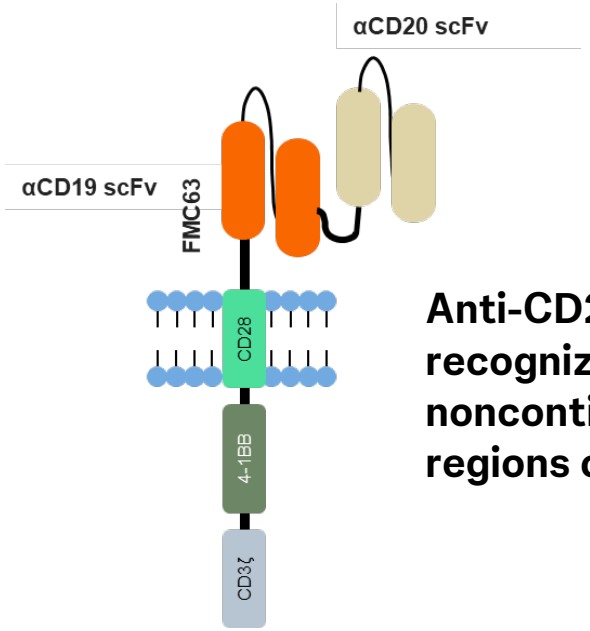
CD19/CD20 Bispecific CAR-T Therapy (JNJ-90014496): Specificity for 2 Validated Targets

- CD19 CAR T-cell therapies have transformed treatment of R/R LBCL, yet most patients do not have long-term remission[1-3]
- Dual targeting may protect against antigen escape as a potential resistance mechanism[4,5]
- C-CAR039: 4-year follow up from first-in-human study in China[6]
  - One Grade 3 CRS; no Grade 3/4 ICANS
  - In LBCL:
    - 86% CR rate (~50% remain in CR)
    - 4-year PFS was 53%
    - 4-year OS was 67%

JNJ'4496 (formerly C-CAR039) targets both CD19 and CD20 antigens



Anti-CD20 scFv recognizing 2 noncontiguous regions on CD20

We report initial results from the Phase 1b study (NCT05421663) evaluating efficacy and safety of JNJ'4496 in R/R CAR T-cell naive patients with LBCL

CD, cluster of differentiation; CR, complete response; CRS, cytokine releasing syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; OS, overall survival; PFS, progression-free survival; scFv, single-chain variable fragment.

1. Shuster SJ, et al. *N Engl J Med* 2019;380(1):45-56. 2. Neelapu SS, et al. N *Engl J Med*; 2017;377(26): 2531-44. 3. Abramson JS, et al. *Lancet* 2020; 396(10254): 839-52. 4. Plaks V, et al. *Blood*. 2021;138(12):1081-5. 5. Yang N, et al. *J Transl Med* 2024;22(1);274. 6. Liang A, et al. EHA 2025. Abstract PS2159.

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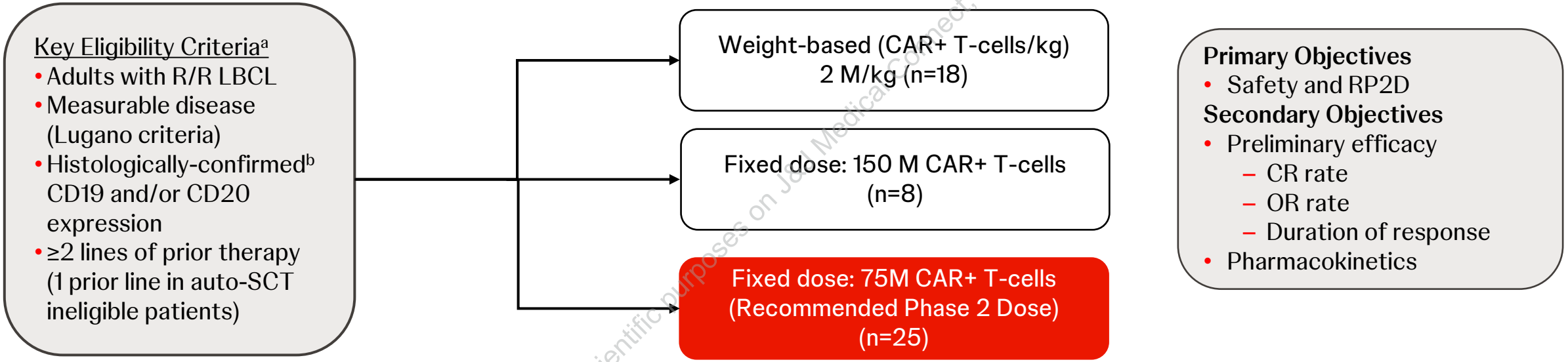
CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): Global Phase 1b Study Design



- Patients were offered bridging therapy at investigator's discretion

NCT05421663 is a global, Phase 1b study enrolling at 31 sites in 8 countries.

Median follow-up time was 8 months at data cutoff (April 21, 2025); database is not locked.
[a]Patients were screened, apheresed, offered bridging therapy (at investigator's discretion); lymphodepletion of cyclophosphamide (300 mg/m^2/d)+ fludarabine (30 mg/m^2) was administered for 3 days. [b]Histologically-confirmed on most recent post-relapse biopsy.
Auto-SCT, autologous stem cell transplant; CR, complete response; M, million; OR, objective response; RP2D, recommended phase 2 dose;.

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CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): Baseline Characteristics in R/R LBCL

Patient characteristics	All Doses (N=51)	RP2D: 75M CAR+ T-cells (n=25)
Age, median (range), years	72.0 (39, 87)	72.0 (40, 87)
Male	35 (69)	19 (76)
DLBCL NOS[a]	37 (73)	18 (72)
ECOG PS 1 or 2	29 (57)	13 (52)
Number of lines of prior therapy, median (range) 1 prior line ≥2 prior lines	1 (1, 3) 31 (61) 20 (39)	2 (1, 3) 12 (48) 13 (52)
Primary refractory disease	29 (57)	14 (56)
Prior bispecific antibodies Anti-CD20[b] Anti-CD19[c]	 5 (10) 2 (4)	 5 (20) 2 (8)
Bulky disease at baseline[d]	13 (26)	8 (33)
IPI score of ≥3,[e,f] n/N (%)	14/49 (29)	6/24 (25)
Ann Arbor (Stage III or IV)[e]	39 (76)	17 (68)
LDH at baseline > ULN	18 (35)	9 (36)
Received bridging therapy	34 (67)	14 (56)

Characteristic reported as n (%) unless noted.
[a]Other types of LBCL include transformed from a lower grade (all doses, n=6; 75M, n=4); high-grade B-cell lymphoma with MYC, BCL2 and/or BCL6 rearrangements (all doses, n=5; 75M, n=2); follicular lymphoma 3b and high-grade B-cell lymphoma not otherwise specified (n=1, each in all doses; none in 75 M group). [b]Includes glofitamab and JNJ-87801493. [c]Includes R07227166 and RO7443904. [d]Bulky disease is defined as disease assessment including at least 1 lesion with longest diameter >7 cm. [e]At screening. [f]No patients had an IPI of 4.
DLBCL, Diffuse Large B-cell Lymphoma; ECOG PS, Eastern Cooperative Oncology Group Performance Status; IPI, International Prognostic Index; LDH, lactose dehydrogenase; NOS, not otherwise specified; ULN, upper limit of normal.

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CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): Safety Profile in R/R LBCL

TEAEs, n (%)	All Doses (N=51)		RP2D (n=25)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Any grade TEAEs	51 (100)	44 (86)	25 (100)	21 (84)
Any Grade TEAEs reported in ≥20% of the all-doses group				
Neutropenia	43 (84)	40 (78)	19 (76)	18 (72)
CRS	41 (80)	2 (4)	22 (88)	0
Thrombocytopenia	24 (47)	10 (20)	11 (44)	3 (12)
Anemia	18 (35)	10 (20)	8 (32)	4 (16)
Fatigue	18 (35)	1 (2)	10 (40)	1 (4)
Diarrhea	15 (29)	1 (2)	9 (36)	1 (4)
Infections[a,b]	14 (27)	3 (6)	5 (20)	1 (4)
Leukopenia	12 (24)	11 (22)	4 (16)	3 (12)
Headache	10 (20)	0	3 (12)	0
Hypokalemia	10 (20)	0	5 (20)	0
Lymphopenia	10 (20)	6 (12)	5 (20)	4 (16)
Nausea	10 (20)	0	4 (16)	0

- Most common TEAEs were cytopenias and CRS
- 7 (28%) patients in the RP2D group reported serious TEAEs
- All 6 deaths on study were due to disease progression (RP2D, n=3)

Treatment-emergent adverse events are defined as adverse events occurring until Day 90 post-administration of study drug or until start of subsequent anti-cancer, whatever comes first.
[a]Grade 3/4 pneumonia (n=2) and peritonitis (n=1) were observed in the All Doses group (1 patient in the 75 M group had Grade 3 peritonitis). [b]Grade 1/2 opportunistic infections (herpes zoster and oral candidiasis) were reported in 2 patients in the 75 M group.
CRS, Cytokine Release Syndrome; RP2D, recommended phase 2 dose; TEAE, treatment-emergent adverse event.

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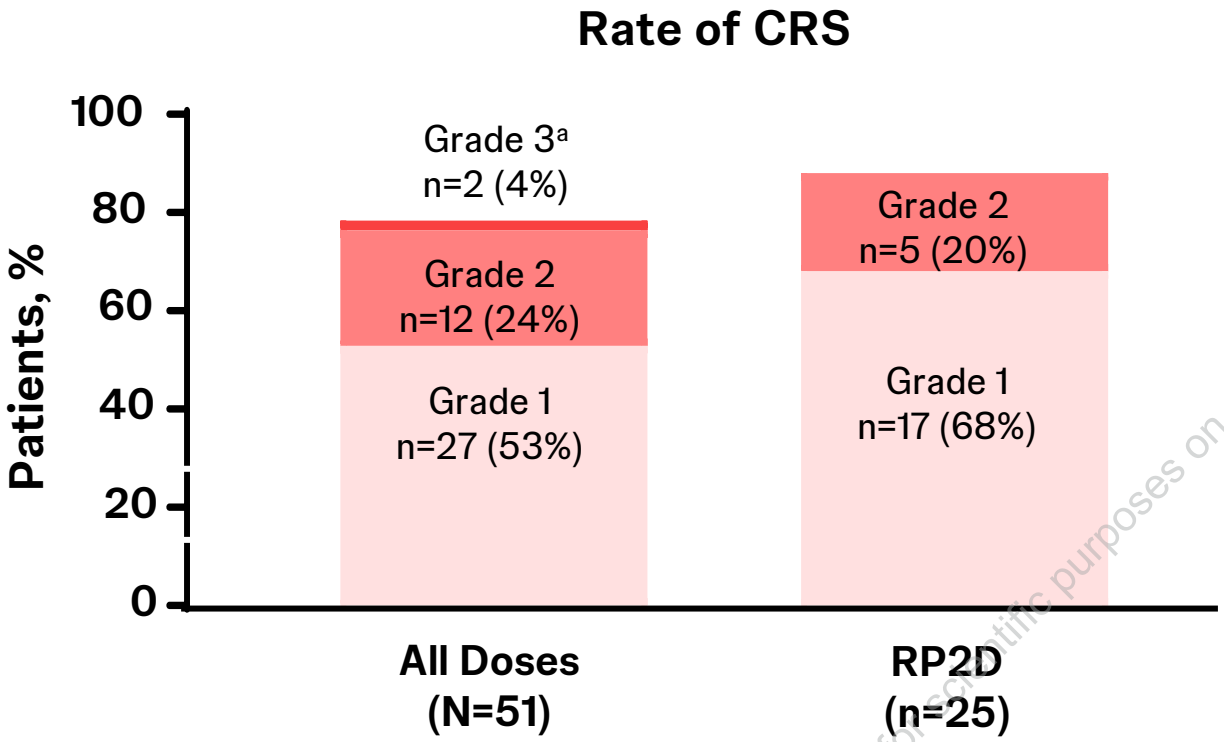
CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): CRS in R/R LBCL Patients



Patients	All Doses (N=51)	RP2D (n=25)
Patients with CRS	41 (80)	22 (88)
Time to onset, median (range), d	3 (1, 6)	3 (2, 5)
Duration,[b] median (range), d	5 (1, 13)	6 (1, 12)
Supportive measures for CRS,[c] n (%)		
Tocilizumab	39 (76)	21 (84)
Corticosteroids	20 (39)	10 (40)
Oxygen	6 (12)	1 (4)
Vasopressor	2 (4)	0
Anakinra	1 (2)	0

- At RP2D, no Grade 3/4 CRS events; most were Grade 1
- No prophylactic tocilizumab or steroids

[a]Two Grade 3 CRS were observed at the 150 M dose: one CRS event resolved within 61h; the second CRS event improved to Grade 2 within 24 hours. [b]In case of multiple CRS events, the duration or time to recovery was calculated as the sum of the duration/time to recovery of the individual events. [c]Patients may have received more than one supportive therapy. Treatments, such as analgesics/anti-inflammatory agents, anti-infectives, and intravenous fluids were also administered.
CRS, cytokine-releasing syndrome; RP2D, recommended phase 2 dose.

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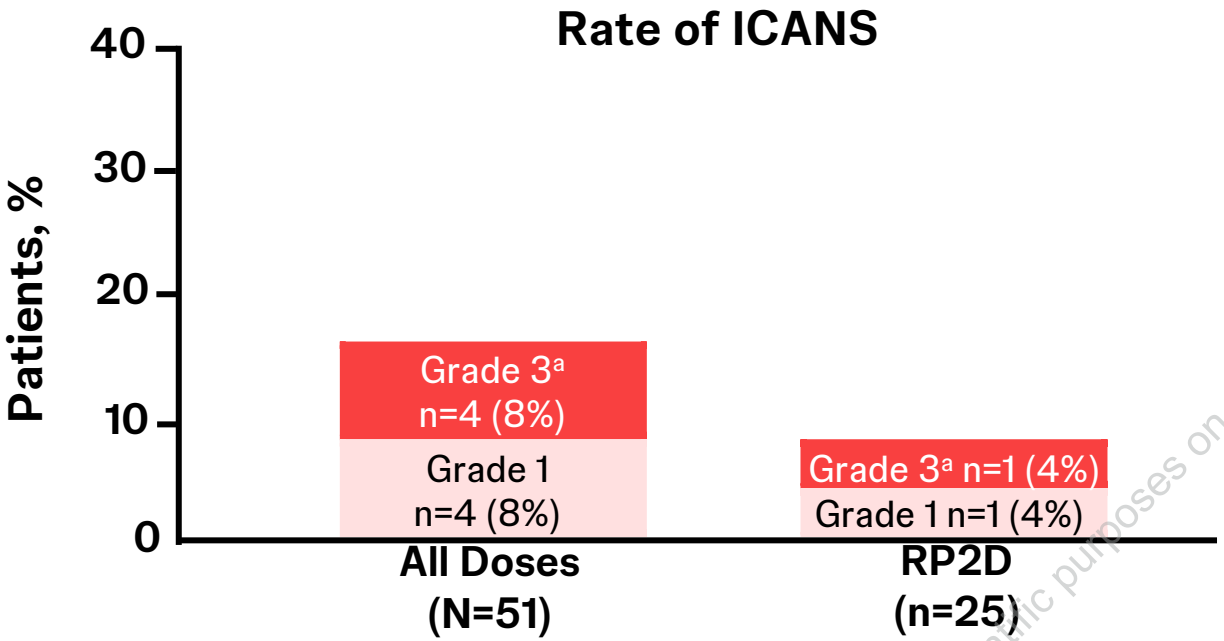
CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): ICANS in R/R LBCL



Patients	All Doses (N=51)	RP2D (n=25)
Patients with ICANS	8 (16)	2 (8)
Time to onset, days, median (range)	3 (3, 12)	3 (3, 3)
Duration,[c] days, median (range)	17 (1, 89)	22 (17, 26)
With concurrent CRS	7 (14)	2 (8)
Supportive measures for ICANS,[d] n (%)		
Corticosteroids	8 (16)	2 (8)
Anakinra	5 (10)	2 (8)
Levetiracetam	3 (6)	2 (8)
Tocilizumab	2 (4)	0

- At all doses, ICANS resolved without sequelae
- At RP2D
  - Few ICANS observed
  - One Grade 3 ICANS event improved to Grade 1 at 40 hours with treatment (CNS lymphoma[b])
- No prophylactic tocilizumab or steroids

[a]All Grade 3 ICANS had a duration of ≤2 days. [b]CNS lymphoma at study entry. [c]In case of multiple ICANS events, the duration/time to recovery was calculated as the sum of the duration/time to recovery of the individual events.
[d]Patients may have received more than one supportive therapy. Treatments, such as intravenous fluids, antihistamines, pain medications and antipsychotics, were also administered.
CRS, cytokine-releasing syndrome; ICANS, immune-effector Cell-Associated Neurotoxicity Syndrome; RP2D, recommended phase 2 dose.

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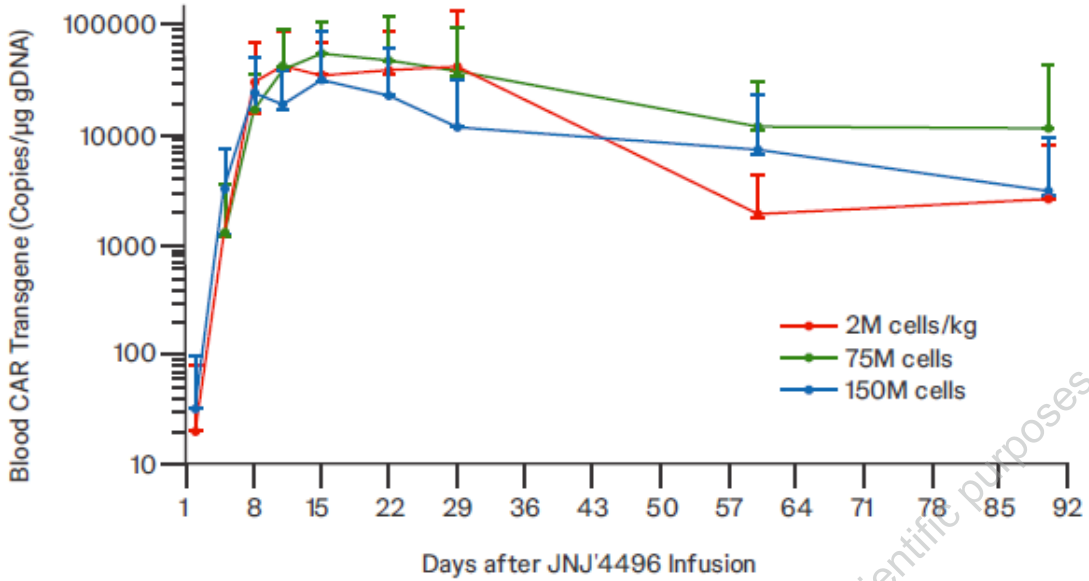
CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): Pharmacokinetics

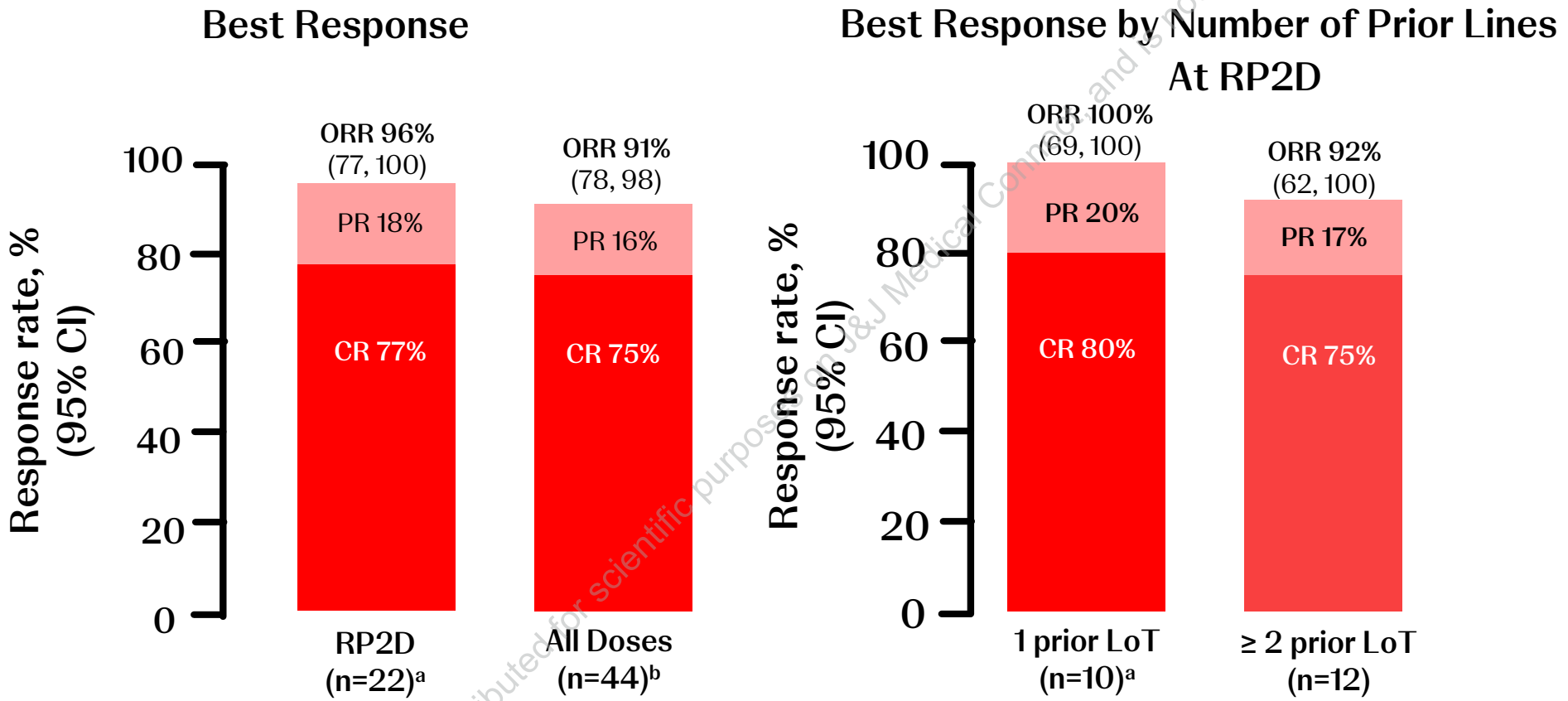


Pharmacokinetic Parameter, Unit	2 M/kg (n=18)	150 M (n=8)[a]	75 M (n=22)
$C_{max,}$ copies/µg g DNA	83390 (106%)	52152 (102%)	80300 (102%)
$AUC_{0\text{-}29d,}$ day × copies/µg g DNA	862954 (91%)	515465 (122%)	962526 (102%)
$t_{max,}$ median (min, max), days	12 (7, 28)	12 (7, 21)	14 (7, 28)

- At RP2D (75 M), CAR expansion and persistence were comparable to those observed at higher doses
- At RP2D median t_{max} was noted to occur slightly later at 14 days post-infusion
- Efficacy was comparable across doses, which was supported by a consistent dose-response relationship for CR rate

Reported as mean (% coefficient of variance) unless otherwise noted.
JNJ'4496 showed concordant cellular kinetic profiles by CAR transgene and CAR+ T-cell levels
PK sample cutoff date was Feb 28, 2025, with n=18 for 2 M T-cells/kg, n=8 at 150 M T-cell level, and n=22 for 75 M T-cell level.
[a]n=7 for $AUC_{0\text{-}29d}$.
$AUC_{0\text{-}29d}$, Area under the curve from day 0 to day 29; CR, complete response; C_{max}, maximum concentration; M, million; t_{max}, time at maximum observed concentration.; RP2D, recommended phase 2 dose.

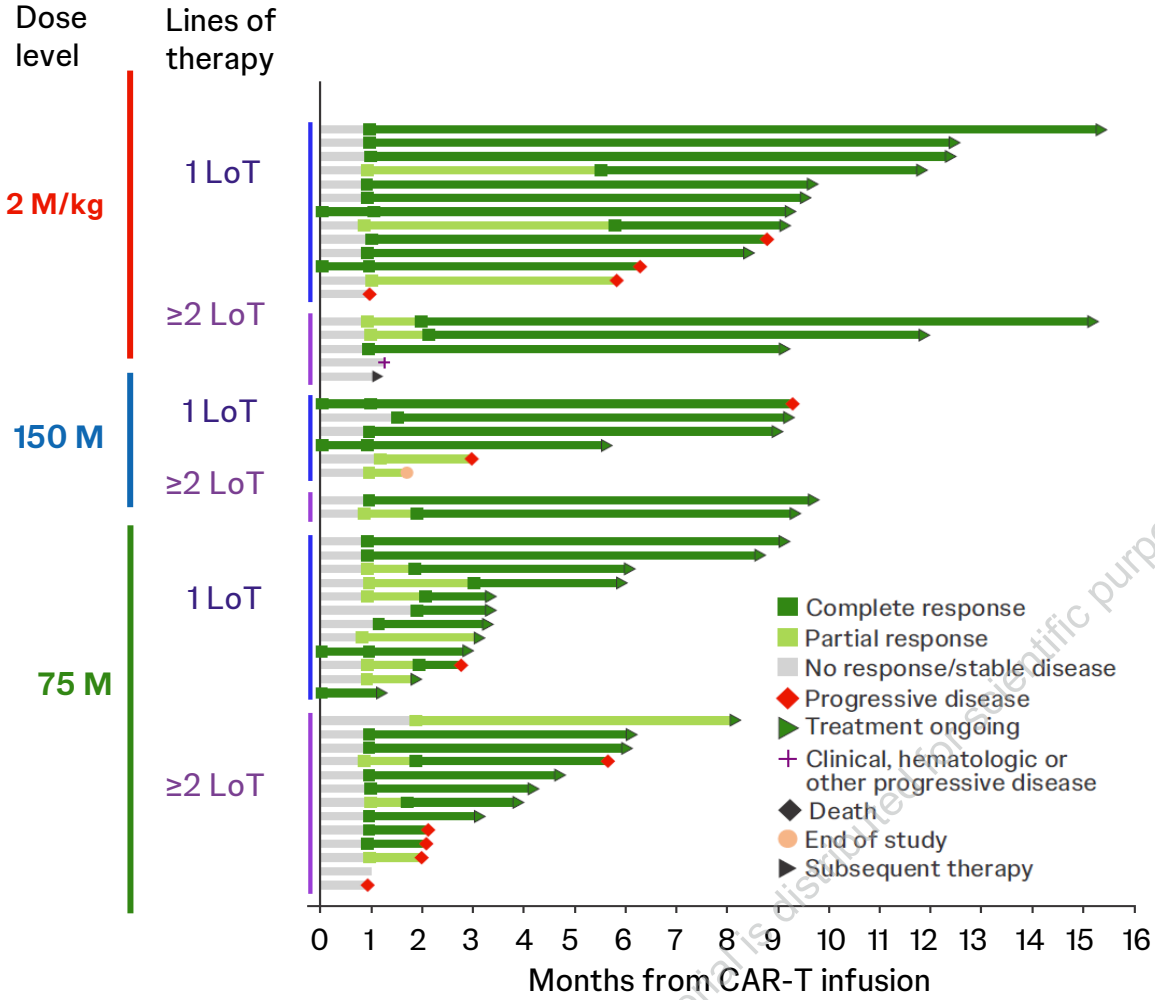
CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): High Complete Response Rate in R/R LBCL



- At all doses and at RP2D, high CR rates were observed irrespective of number of lines of prior therapy

Best response was assessed by investigators, based on LUGANO Criteria, using disease evaluations at any point in between the time of JNJ'4496 infusion until progressive disease or start of subsequent anti-lymphoma therapy, whichever occurred first.
[a]Three patients were not included in the efficacy analysis (2 patients achieved CR to bridging therapy and 1 patient was ongoing without any disease evaluations). [b]Seven patients were not included in the efficacy analysis (6 patients achieved CR to bridging therapy and 1 patient was ongoing without any disease evaluations).
CR, complete response; LoT, lines of therapy; ORR, objective response rate; PR, partial response; RP2D, recommended phase 2 dose.

CD19/CD20 Bispecific CAR-T Therapy (JNJ'4496): Response Profile for R/R LBCL



At all doses (median follow up, 8 mo):

- Median time to CR: 1 (range 1-6) month
- Duration of response ≥3 months: 87% (95% CI: 71, 94)
- 10 responses deepened from PR to CR

At RP2D (median follow up, 4 mo):

- Median time to CR: 1 (range 1-3) month
- Duration of response ≥3 months: 79% (95% CI: 54, 92)
- 5 responses deepened from PR to CR

Time from CAR-T infusion until first response assessment is shown as stable disease. Participants with complete response after bridging are shown as having complete response from CAR-T infusion until the last post-infusion response evaluation prior to progressive disease or start of subsequent anticancer therapy. Response profile segments for CR, PR,, no response/stable disease are drawn until death, progressive disease, start of subsequent therapy, end of study or last contact, whichever occurred first. Subsequent events are not shown.
CR, complete response; PR, partial response; RP2D, recommended phase 2 dose.

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Conclusions

- **Safety, efficacy, and pharmacokinetic profile support 75M CAR+ T-cells as RP2D of the CD19/CD20 CAR-T Therapy, JNJ'4496, in a broad population of patients with R/R LBCL**
- **At the RP2D**
  - No Grade 3/4 CRS to date; 1 Grade 3 ICANS lasting 40 hours in a patient with CNS lymphoma
  - No prophylactic treatment for CRS or ICANS
  - 100% ORR and 80% CR rate in patients who received 1 prior LoT; 75% CR rate in patients who received ≥2 prior LoT
- Findings are consistent with results shown for C-CAR039,[4] and compare favorably to historical data with approved anti-CD19 CAR T-cell therapies[1-3]

These findings support further development of JNJ'4496 in R/R LBCL

CR, complete response; CRS, cytokine-releasing syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; LoT, line of therapy; RP2D, recommended phase 2 dose.

1. Shuster SJ, et al. *N Engl J Med* 2019;380(1):45-56. 2. Neelapu SS, et al. N *Engl J Med*; 2017;377(26): 2531-44. 3. Abramson JS, et al. *Lancet* 2020; 396(10254): 839-52. 4. Liang A, et al. EHA 2025. Abstract #PS2159.

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Acknowledgments

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Please see the Poster Presentation on Long-term Follow up of C-CAR039 in Patients with R/R B-NHL. Liang A, et al. June 14, 2025 (Abstract #PS2159)

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