



Memorial Sloan Kettering
Cancer Center™



Patients not eligible for CAR-T therapy: do they exist and if so, how to treatment them?

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Disclosures for Andrew D. Zelenetz, MD, PhD

Research Support/P.I.	Genentech/Roche, Gilead, BeiGene, Abbvie, Pharmacyclics/Janssen
Employee	None
Consultant	BMS/Celgene/JUNO, Genentech/Roche, Gilead/Kite; BeiGene; Pharmacyclics, Jansen, Amgen, Astra-Zeneca, Novartis, MEI Pharma
Major Stockholder	None
Speakers Bureau	None
Scientific Advisory Board	Lymphoma Research Foundation
Stockholder	None (not including potential holding of a 401K mutual fund)



Standard of Care axicabtagene ciloleucel versus ZUMA1

ZUMA1

- ECOG performance status of 0 or 1
- Absolute neutrophil count $\geq 1,000/\mu\text{L}$
- Platelet count $\geq 75,000/\mu\text{L}$
- Adequate renal, hepatic, and cardiac function defined as:
 - Serum creatinine ≤ 1.5 mg/dL
 - Serum ALT/AST ≤ 2.5 ULN
 - Total bilirubin ≤ 1.5 mg/dl (save for Gilbert's syndrome)
 - Cardiac ejection fraction $\geq 50\%$ with no pericardial effusion
- No prior alloBMT

SOC Axicabtagene ciloleucel

- Pt with ZUMA1 exclusion: 129 (43%)
 - 1 criterion 76 (58.9%)
 - ≥ 2 criteria 51 (41.1%)
- Specific criteria
 - ECOG PS > 1 58 (19%)
 - PLTS $< 75,000$ 34 (11.4)
 - DVT/PE within 6 months 31 (10.4%)
 - History of CNS disease 21 (7%)
 - CrCl < 60 21 (7%)
 - Prior CPI 17 (5.7%)
 - LVEF $< 50\%$ 10 (3.4%)
 - Pleural effusion 10 (3.4%)
 - Bilirubin > 1.5 7 (2.4%)

Standard of Care axicabtagene ciloleucel versus ZUMA1

ZUMA1

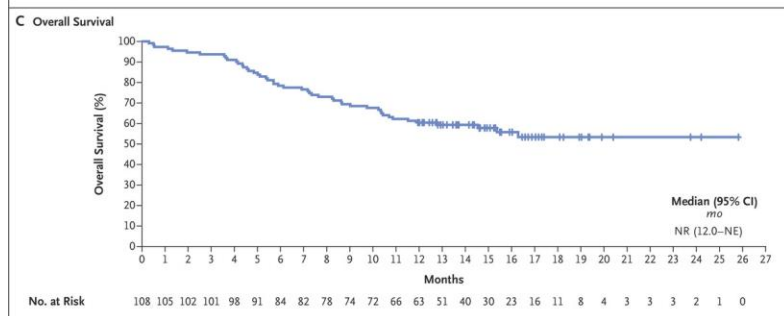
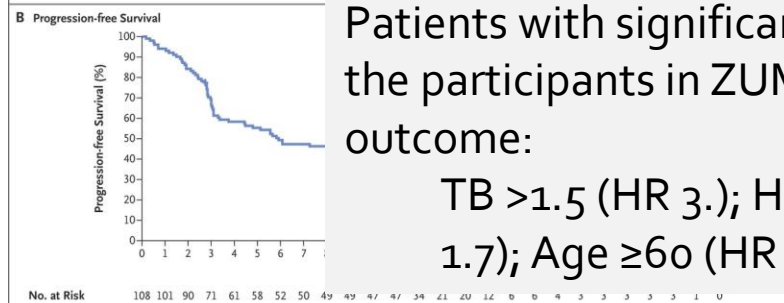
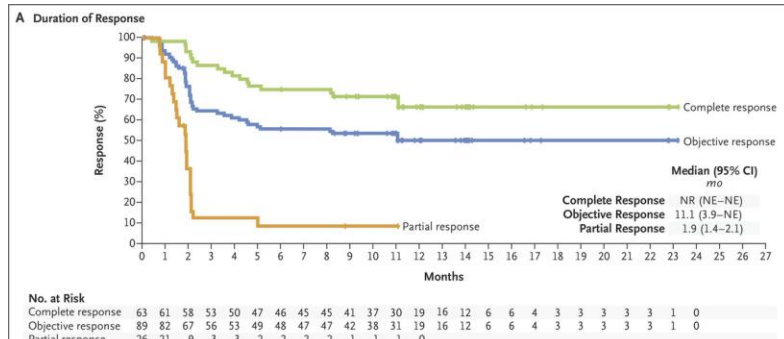
- CRS 94 (93%)
 - Gr 1 37%
 - Gr 2 44%
 - Gr 3 9%
 - Gr 4 3%
 - Gr 5 1%
- ICANS 65 (64%)
 - Gr 1-2 28%
 - Gr 3-4 28%
 - Gr 5 0

SOC Axicabtagene ciloleucel

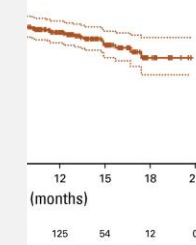
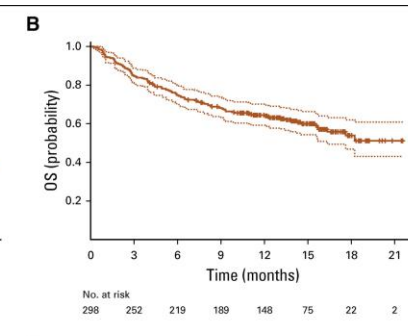
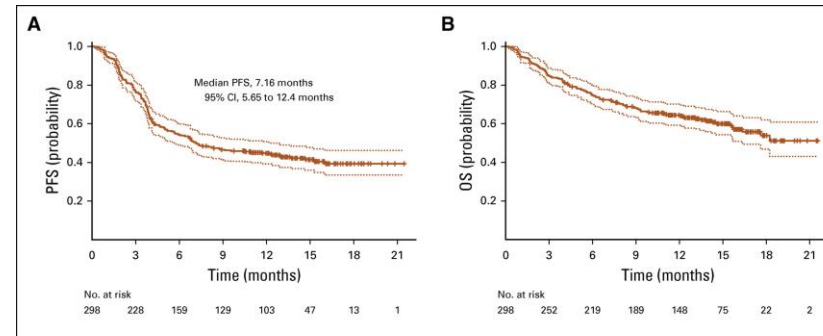
- CRS 251 (91.2%)
 - Gr 1 94 (34.2%)
 - Gr 2 138 (50.2%)
 - Gr 3 12 (4.4%)
 - Gr 4 5 (2.2%)
 - Gr 5 1 (0.4%)
- ICANS 189 (68.7%)
 - Gr 1-2 114 (37.8%)
 - Gr 3-4 84 (30.6%)
 - Gr 5 1

Standard of Care axicabtagene ciloleucel versus ZUMA1

ZUMA1

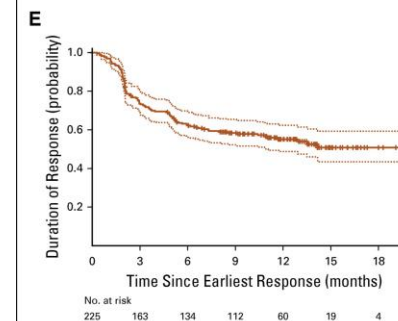


SOC Axicabtagene ciloleucel



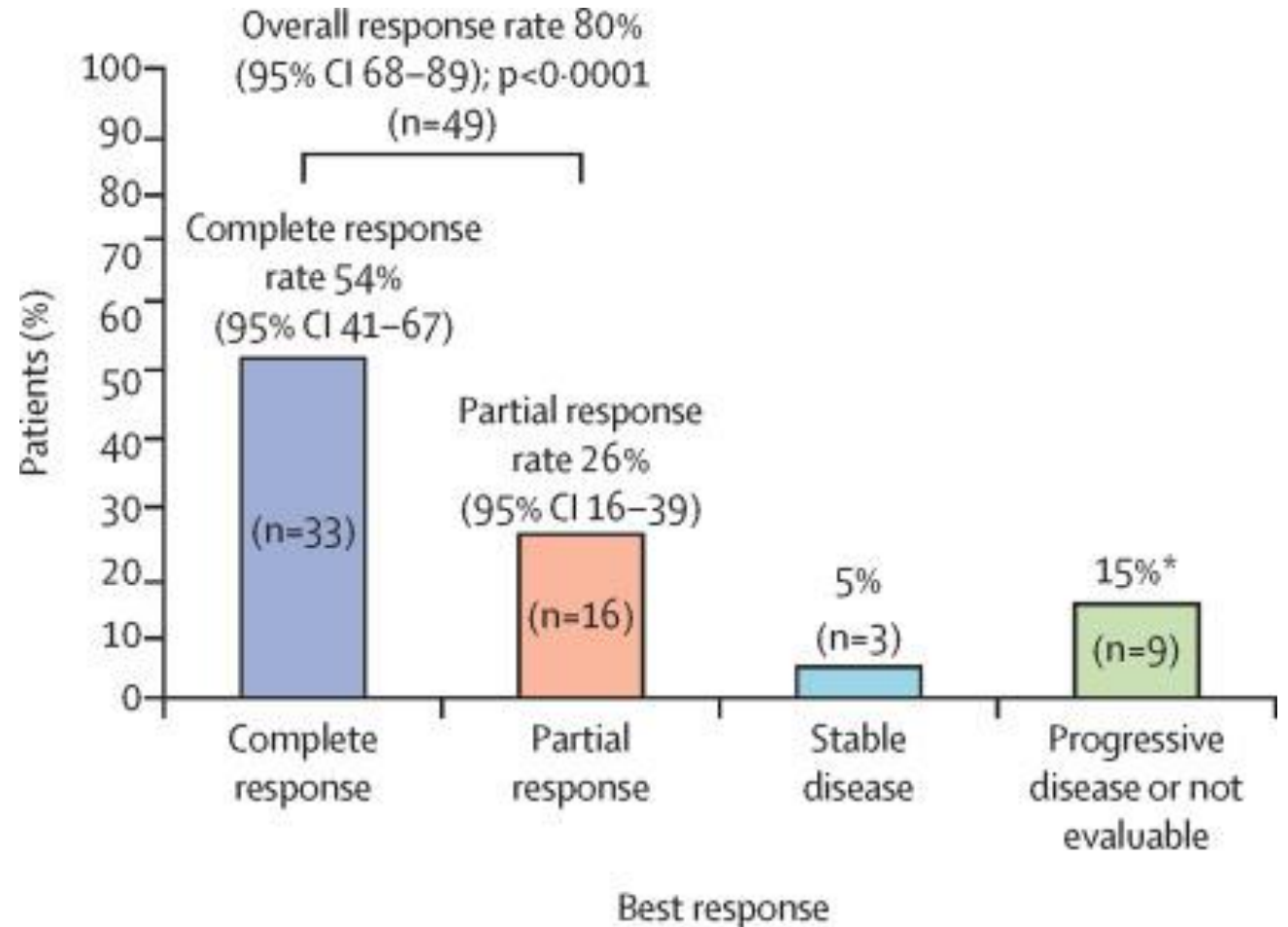
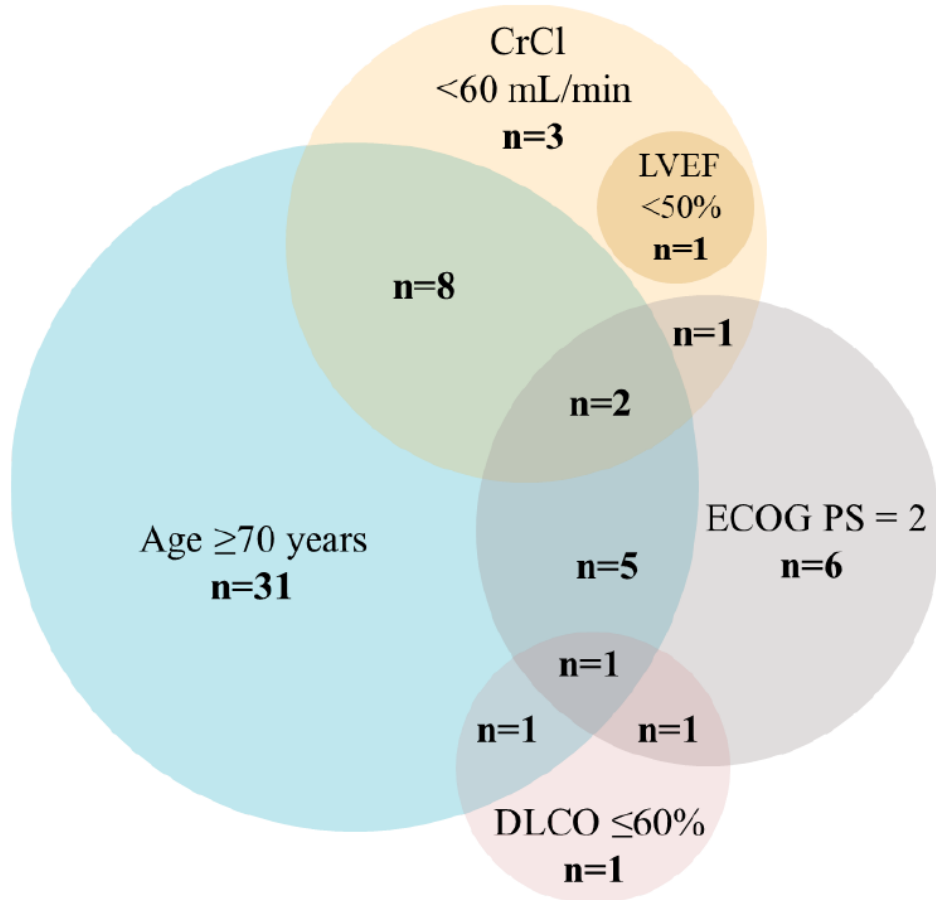
Patients with significant co-morbidities had efficacy and safety similar to the participants in ZUMA1; however, factors were found to have impact outcome:

TB >1.5 (HR 3.); High LDH (HR 1.9); Male Sex (HR 1.8); PS 2-4 (HR 1.7); Age ≥60 (HR 1.6)

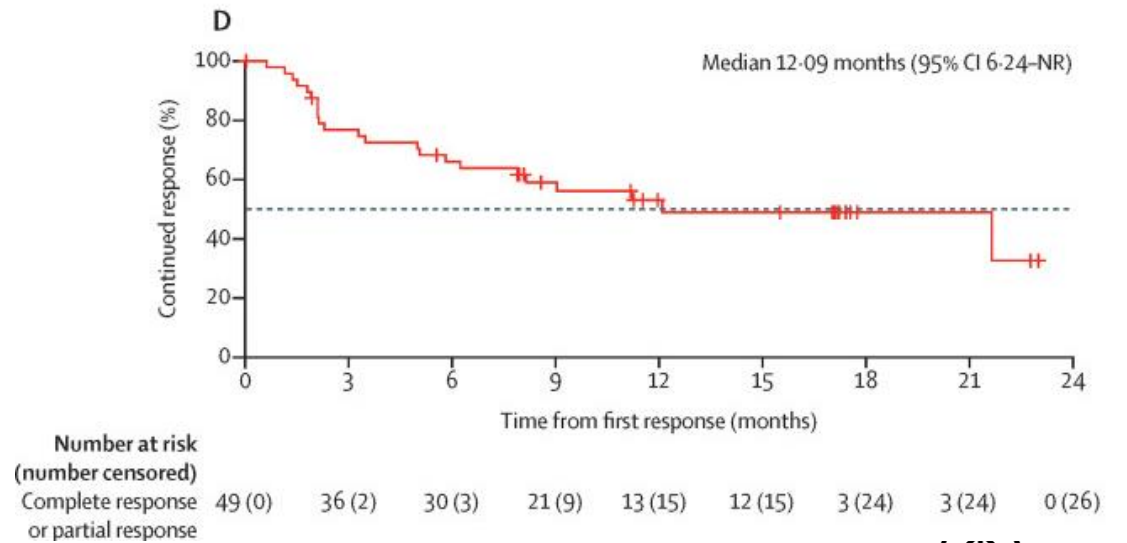
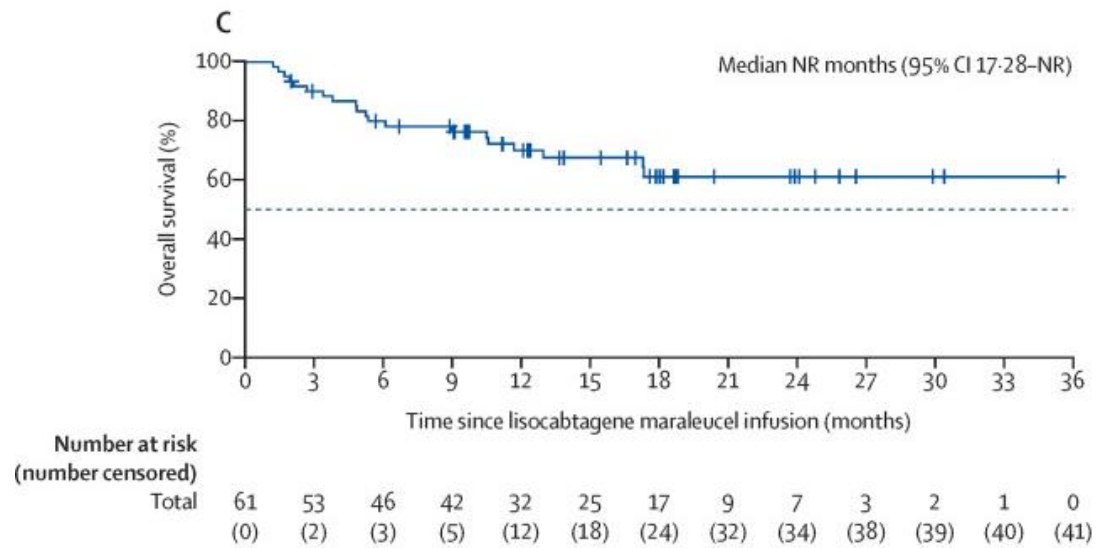
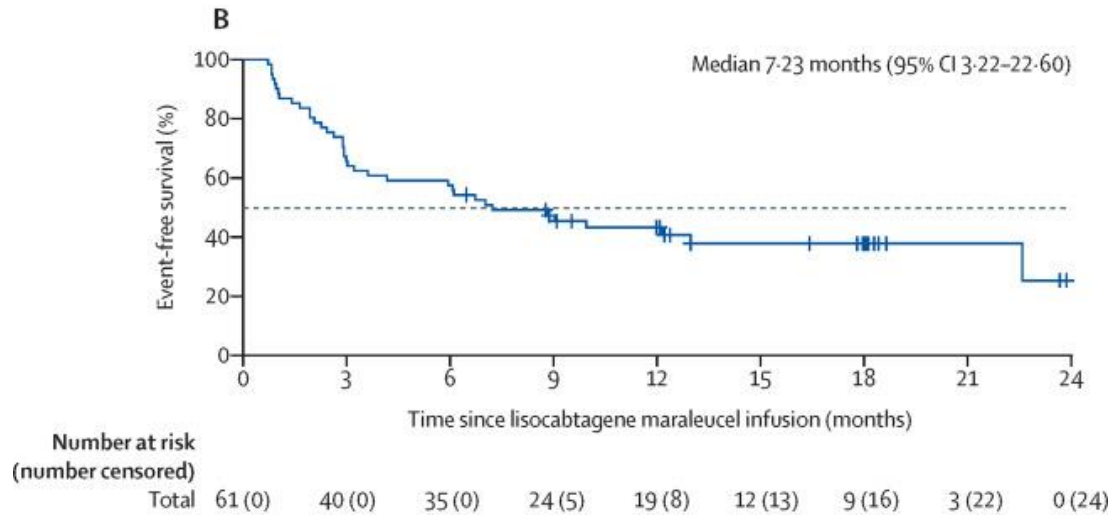
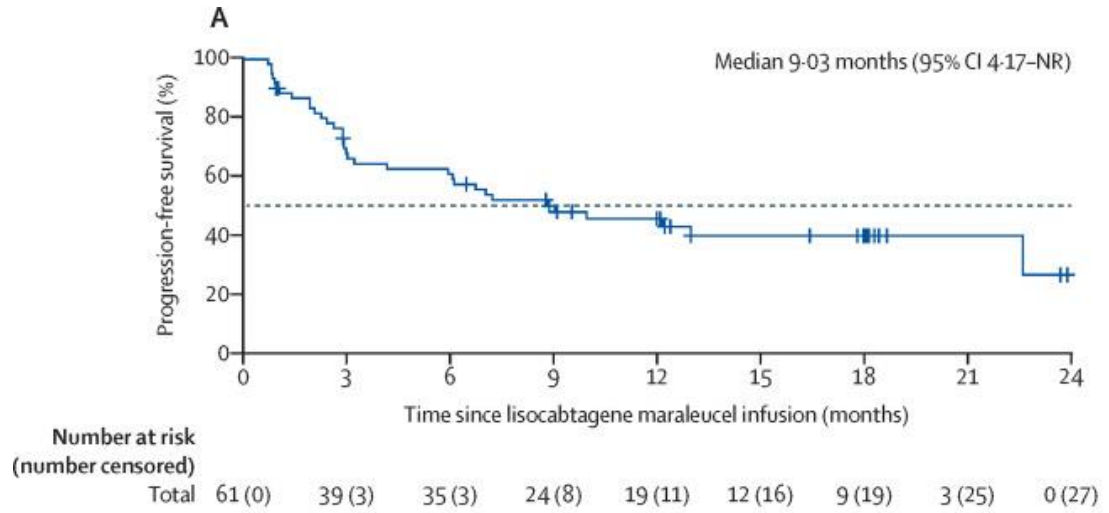


PILOT: Lisocabtagene for patients not intended for transplant

Transplant not intended reasons



PILOT: Lisocabtagene for patients not intended for transplant



PILOT: Lisocabtagene for patients not intended for transplant

Grade	1-2	3	4	5
Haematological events				
Anaemia	12 (20%)	7 (11%)	0	0
Thrombocytopenia	5 (8%)	4 (7%)	8 (13%)	0
Neutropenia	2 (3%)	8 (13%)	21 (34%)	0
Leukopenia	1 (2%)	3 (5%)	10 (16%)	0
Lymphopenia	0	3 (5%)	5 (8%)	0
Hypofibrinogenaemia	0	1 (2%)	0	0
Febrile neutropenia	0	0	1 (2%)	0

Grade	1-2	3	4	5
Non-haematological events				
Fatigue	24 (39%)	0	0	0
Cytokine release syndrome	22 (36%)	1 (2%)	0	0
Nausea	14 (23%)	1 (2%)	0	0
Hypomagnesaemia	10 (16%)	1 (2%)	0	0
Hypotension	10 (16%)	1 (2%)	0	0
Diarrhoea	10 (16%)	0	0	0
Tremor	10 (16%)	0	0	0
Hypokalaemia	9 (15%)	2 (3%)	0	0
Peripheral oedema	9 (15%)	0	0	0
Constipation	8 (13%)	0	0	0
Cough	8 (13%)	0	0	0
Dizziness	8 (13%)	0	0	0
Insomnia	8 (13%)	0	0	0

Grade	1-2	3	4	5
Confusional state	7 (11%)	2 (3%)	0	0
Decreased appetite	7 (11%)	1 (2%)	0	0
All rash	7 (11%)	0	0	0
Dyspnoea	6 (10%)	1 (2%)	0	0
Headache	6 (10%)	1 (2%)	0	0
Hypertension	3 (5%)	3 (5%)	0	0
Hyponatraemia	2 (3%)	3 (5%)	0	0
Hypophosphataemia	2 (3%)	3 (5%)	0	0
Decreased neutrophil count	1 (2%)	3 (5%)	1 (2%)	0
Decreased lymphocyte count	0	2 (3%)	1 (2%)	0

PILOT: Lisocabtagene for patients not intended for transplant

	N
Cytokine release syndrome, neurological events, or both	30 (49%)
Cytokine release syndrome	
Any grade	23 (38%)
Grade 1	11 (18%)
Grade 2	11 (18%)
Grade 3	1 (2%)
Grade 4 or 5	0
Time to onset [*] , days	4 (3–7)
Time to resolution [†] , days	4 (2–5)
Tocilizumab, corticosteroids, or both for cytokine release syndrome [‡]	16 (26%)
Tocilizumab only	6 (10%)
Tocilizumab and corticosteroids	10 (16%)
Corticosteroids only	0
Number of tocilizumab doses	1 (1–1)
One	15 (25%)
Two	1 (2%)
Three or more	0
Other drugs used for treatment of cytokine release syndrome [§]	0

Neurological events	
Any grade	19 (31%)
Grade 1	11 (18%)
Grade 2	5 (8%)
Grade 3	3 (5%)
Grade 4 or 5	0
Time to onset [*] , days	7 (5–12)
Time to resolution [†] , days	6 (3–11)
Tocilizumab, corticosteroids, or both for neurological events [‡]	8 (13%)
Tocilizumab only	0
Tocilizumab and corticosteroids	0
Corticosteroids only	8 (13%)
Other drugs used for treatment of neurological events [§]	0
Grade ≥3 prolonged cytopenias at day 28 after infusion [¶]	18 (30%)
Grade ≥3 infections	4 (7%)
Hypogammaglobulinaemia ^{**}	5 (8%)

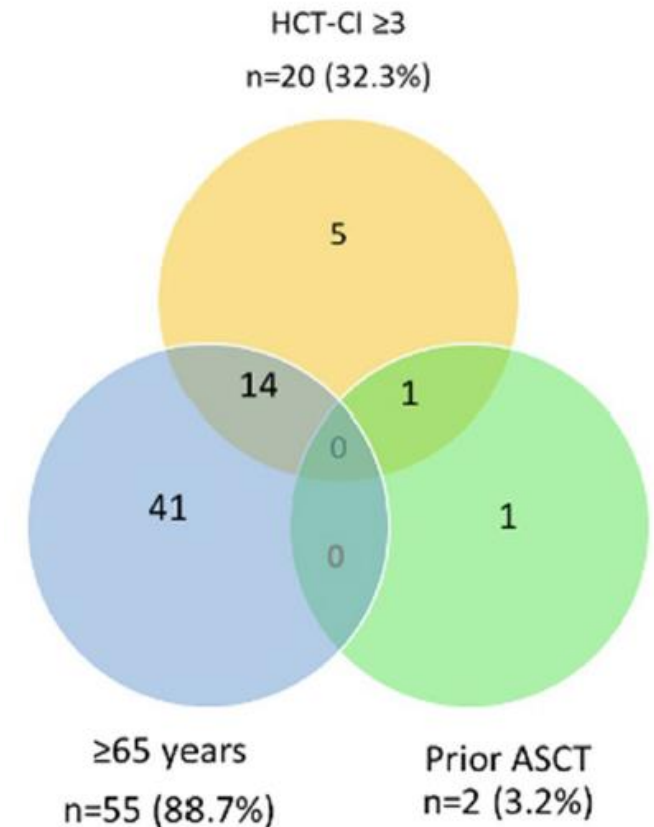
ALYCANATE: Axicabtagene ciloleucel for transplant ineligible patients

CAR-T-eligible

- Eligible by the CAR-T physician AND all the following criteria:
 - ECOG 0-2
 - Adequate vascular access for leukapheresis
 - ANC ≥ 1 G/L
 - Platelets ≥ 75 G/L
 - Absolute lymphocyte count ≥ 0.1 G/L
 - Creatinine clearance ≥ 40 mL/min
 - ALT/AST $\leq 2.5 \times$ ULN
 - Total bilirubin ≤ 26 μ mol/L
 - Cardiac ejection fraction $\geq 45\%$
 - Baseline oxygen saturation $\geq 92\%$ on room air

General eligibility criteria for autologous hematopoietic cell transplantation

Disease-related indication
Performance status: Karnofsky performance status ≥ 70 or ECOG performance status ≤ 2
Renal function: Serum creatinine < 2 mg/dL (177 micromol/L), unless autologous HCT is for myeloma
Cardiac function: Left ventricular ejection fraction (LVEF) ≥ 40 percent, no uncontrolled coronary artery disease or uncontrolled arrhythmias, and NYHA class I or class II
Pulmonary function: Corrected DLCO ≥ 50 percent
Liver function: No frank cirrhosis of the liver
Adequate psychosocial and financial support
No evidence of myelodysplasia on bone marrow examination

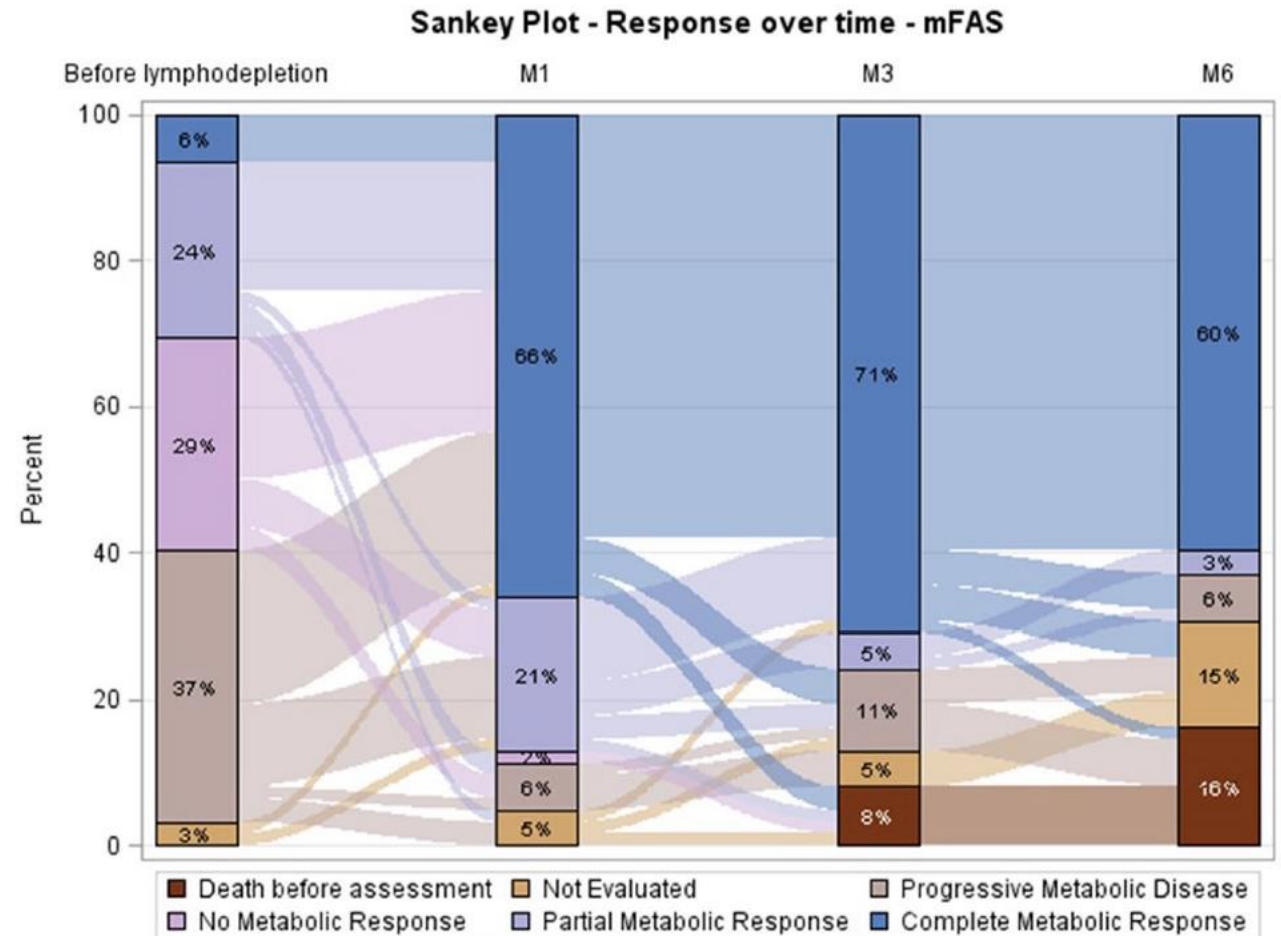


Physiologic age \neq chronological age; however, 88.7% of patients in the trial were TE because of age > 65 .

ALYCANATE: Axicabtagene ciloleucel for transplant ineligible patients

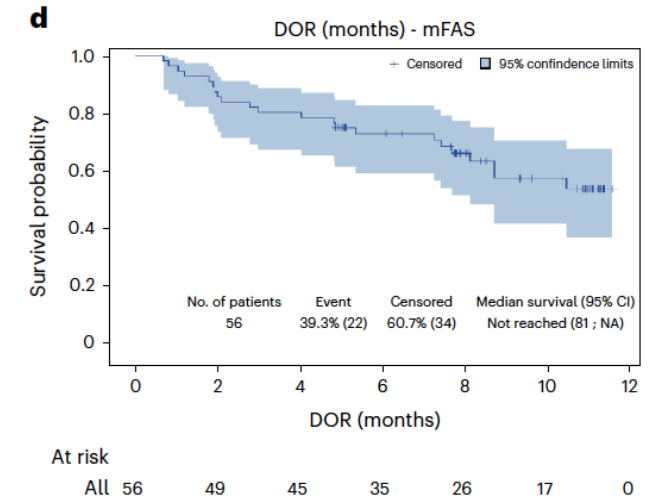
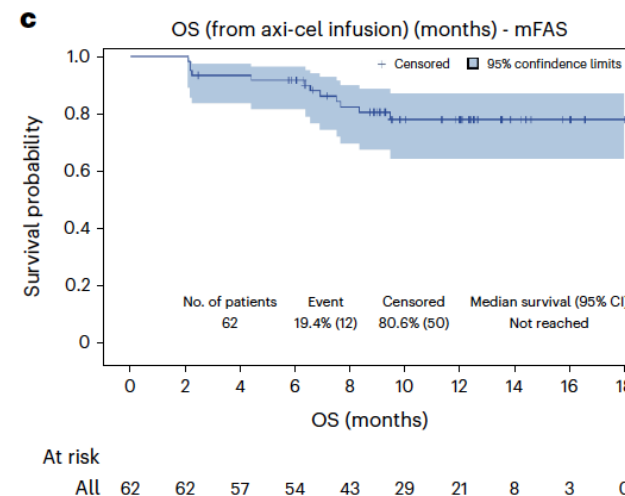
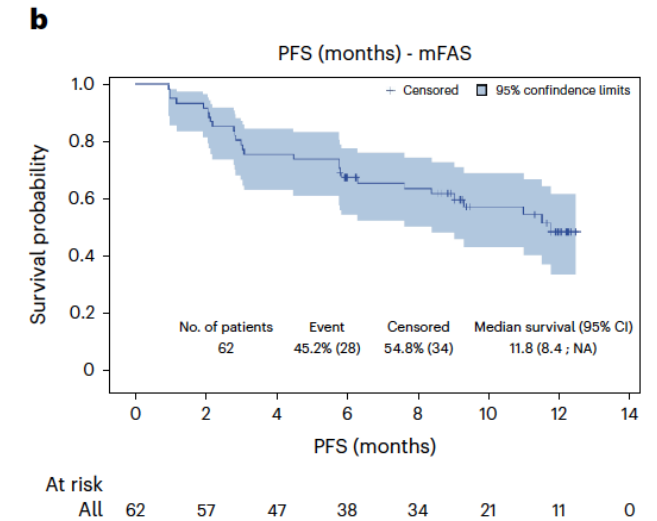
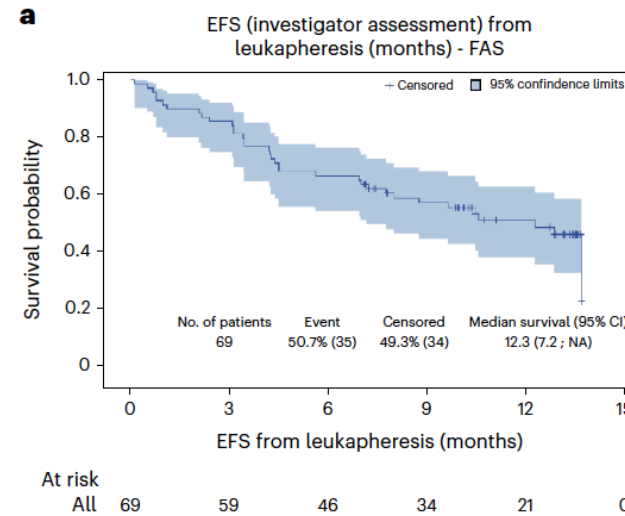
Response	Investigator-assessed (%)	Assessed by a central review panel (%)
Response at 3 months		
Objective response	47 (75.8)	43 (69.4)
Complete response	44 (71.0)	41 (66.1)
Partial response	3 (4.8)	2 (3.2)
Stable disease	0	1 (1.6)
Progressive disease	7 (11.3)	9 (14.5)
Not evaluated	8 ^a (12.9)	9 (14.5)
Best response		
Objective response	56 (90.3)	57 (91.9)
Complete response	49 (79.0)	51 (82.3)
Partial response	7 (11.3)	6 (9.7)
Stable disease	3 (4.8)	1 (1.6)
Progressive disease	3 (4.8)	4 (6.5)
Not evaluated	0	0

All data are expressed as n (%). ^aFive patients died before reaching the evaluation at 3 months (three due to adverse effects and two due to lymphoma) and three patients relapsed before reaching the evaluation at 3 months.



ALYCANATE: Axicabtagene ciloleucel for transplant ineligible patients

- Median follow-up: 12.0 months
- Median EFS: 12.3 months (95% CI, 7.2–NR)
- EFS at 12 months: 51.2% (95% CI, 38.2–62.8%)
- Median PFS: 11.8 months (95% CI, 8.4–NR)
- Estimated PFS at 12 months: 48.8% (95% CI, 34.0–62.0%)
- Median OS: Not reached
- Estimated OS at 12 months: 78.3% (95% CI, 64.7–87.1%)
- Median DOR was not reached



ALYCANATE: Axicabtagene ciloleucel for transplant ineligible patients

	Patients who received axi-cel (N=62)
CRS, n (%)	
Any	58 (93.5)
Grade 1-2	53 (85.5)
Grade 3-4	5 (8.1)
Median time to onset (Q1-Q3), days	1.5 (1.0-3.0)
Median duration (Q1-Q3), days	5.0 (4.0-9.0)
ICANS, n (%)	
Any	32 (51.6)
Grade 1-2	23 (37.1)
Grade 3-4	9 (14.5)
Median time to onset (Q1-Q3), days	6.0 (5.0-8.0)
Median duration (Q1-Q3), days	5.0 (3.0-8.0)
Grade ≥ 3 prolonged cytopenia^a, n (%)	23 (37.1)
Grade ≥3 prolonged neutropenia	15 (24.2)
Grade ≥3 prolonged anemia	14 (22.6)
Grade ≥3 prolonged thrombocytopenia	14 (22.6)
Use of tocilizumab to manage CAR-T cell toxicities, n (%)	48 (77.4)
Use of corticosteroids to manage CAR-T cell toxicities, n (%)	40 (64.5)
ICU transfer due to CAR-T cell toxicities, n (%)	16 (25.8)
Infections, n (%)	
Any	33 (53.2)
Grade 3-4	11 (17.7)
Grade 5	6 (9.7)
Nonrelapse mortality, n (%)	6 (9.7)

Age	Sex	Cause of death	Time of death (days post-infusion)	CRS (maximum grade)	ICANS (maximum grade)	Neutropenia at day 30 (grade)	Tocilizumab total dose	Corticosteroid total dose (equivalent DXM)	Specific infection prophylaxis	Status at death
74	Male	Pulmonary mucormycosis	63	4	4	3	1,720 mg	910 mg	Posaconazole	CMR
72	Male	Sepsis with multi-organ failure secondary to mesenteric infarction	65	1	1	0	800 mg	10 mg	None	PMR
72	Male	Perineal infection	67	1	3	0	960 mg	710 mg	None	Not assessed
66	Male	Bronchopulmonary aspergillosis	107	1	2	0	700 mg	730 mg	None	PMD
70	Male	COVID-19	192	2	0	4	550 mg	20 mg	COVID-19 vaccine before CAR T-cells	CMR
73	Male	COVID-19	232	2	0	3	1,776 mg	320 mg	COVID-19 vaccine before CAR T-cells	CMR

12 patients died

- 5 of whom from lymphoma and 1 of unknown reason
- Nonrelapse mortality was recorded in six patients (9.7%).



Outcome of CAR T-cell similar in Age ≥ 70 versus <70

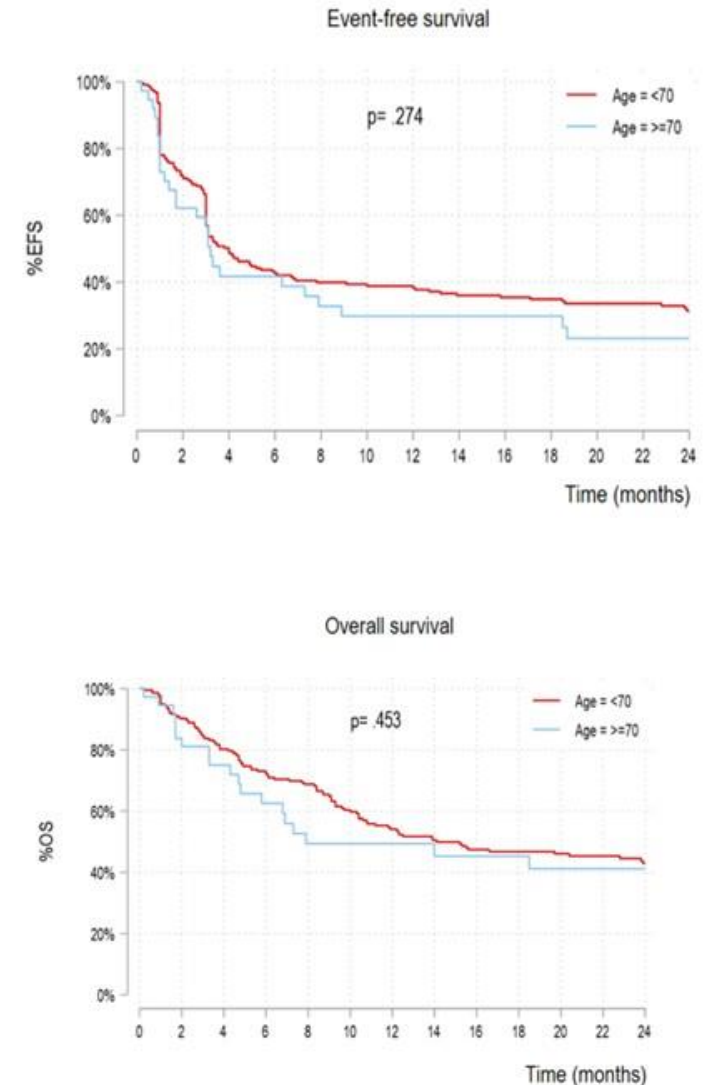
- No major difference in patient characteristics based on age cutoff of 70
- Mixed CD19-directed CAR T-cell products
- Comparing age ≥ 70 to <70 , CRS 88% vs. 80% and ICANS 31% vs. 29%, $p=0.843$ were similar
 - Grade 3-4 events for CRS (11% vs. 6.5%, $p=0.277$) and ICANS (18% vs. 10%, $p=0.146$) were also similar
 - Median duration of CRS (4 and 5 days, $p=0.150$), ICANS (4 and 5 days, $p=0.540$)
 - Hospitalization length (20 days for both groups, $p=0.995$)
- Age did not impact outcome in a multivariable analysis

Table 1. Characteristics of the full patient population.

	<70y n=253	≥ 70 y N=54	p
Sex, male, n (%)	157 (62)	29 (54)	0.254
Age, median (range)	56 (23-69)	73 (70-79)	0.000
Product, n (%)			
Axi-cel	129 (51)	23 (43)	0.263
Tisa-cel	124 (49)	31 (57)	
Infused patients, n (%)	216 (85)	45 (83)	0.703
Production failure, n (%)	14 (5.5)	3 (5.6)	0.995
Bridging therapy, n (%)	204 (81)	47 (89)	0.197
HCT-CI, n (%)			0.047
0-2	201 (80)	36 (67)	
3 or more	48 (19)	17 (31)	
Not available	1 (1)	1 (2)	
ECOG at apheresis, n (%)			0.054
0-1	239 (95)	48 (89)	
2-3	14 (5)	5 (9)	
Histology, n (%)			0.846
DLBCL, NOS	174 (69)	40 (74)	
DH/TH HGBCL	39 (15)	6 (11)	
Transformed FL	36 (14)	7 (13)	
Transformed from other indolent	4 (2)	1 (2)	
Disease stage at apheresis, n (%)			0.085
I-II	58 (23)	15 (28)	
III-IV	195 (77)	39 (72)	
R-IPI score at apheresis, n (%)			0.345
0-2	123 (48)	20 (37)	
3-5	118 (47)	32 (69)	
NA	12 (5)	2 (4)	
Bulky disease at apheresis, n (%)	66 (26)	9 (17)	0.341
Disease status at apheresis, n (%)			0.069
Progressive disease	227 (90)	49 (91)	
Stable disease	20 (8)	1 (2)	
Partial response	5 (2)	4 (7)	
Complete response	1 (0)	0 (0)	
Primary refractory, n (%)	151 (60)	27 (50)	0.191
Previous lines, median (range)	2.7 (2-7)	2.5 (2-6)	0.190
Prior ASCT, n (%)	76 (30)	12 (22)	0.240
Prior Allo-SCT, n (%)	3 (1)	0 (0)	0.421

HCT-CI, hematopoietic cell transplant comorbidity index. ECOG, eastern cooperative group performance status. DLBCL, diffuse large B-cell lymphoma. DH/TH HGBCL, double/triple hit high-grade B-cell lymphoma. R-IPI, revised international prognosis index. ASCT, autologous hematopoietic stem cell transplant. Allo-SCT, allogeneic hematopoietic stem cell transplant.

Figure 1. Event-free and overall survival (infused population).



Impact of age on outcome with CAR T-cell therapy.

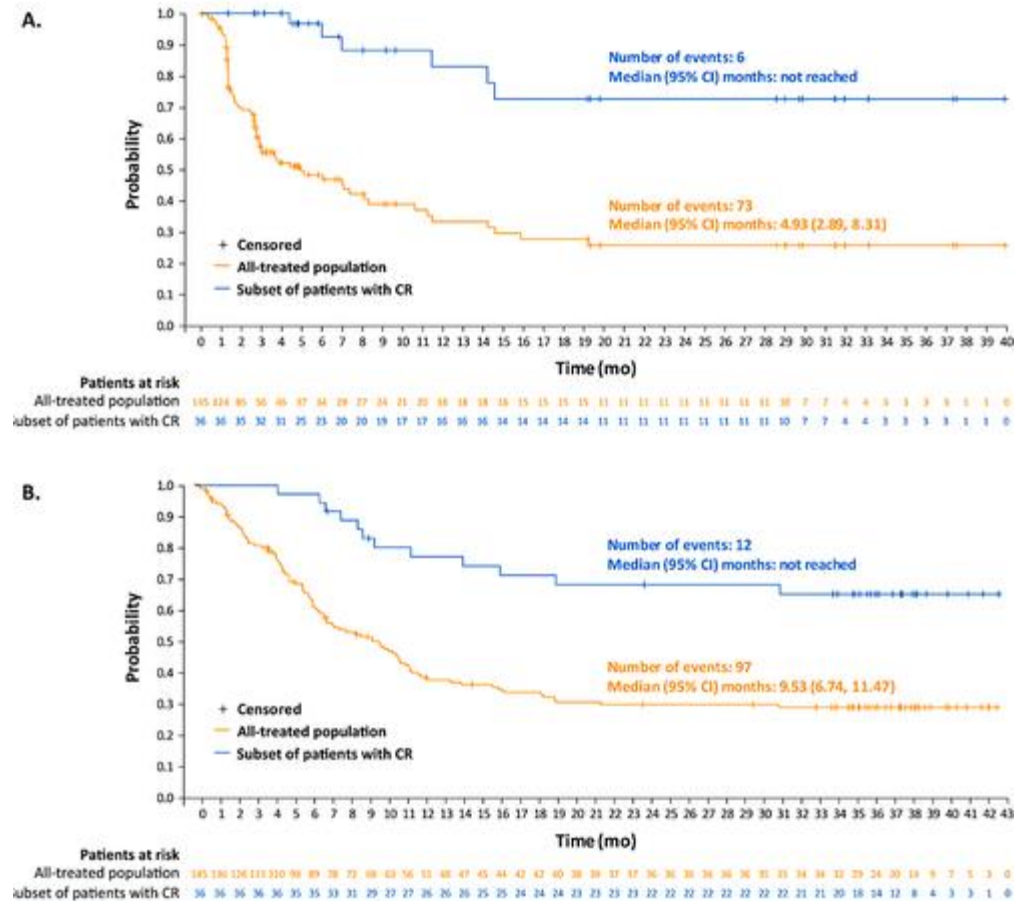
	ALYCANTE N=62	ZUMA-7 N=180	ZUMA-1 N= 27	PILOT N=61	Ram, et al. N=41	Real life N= 551
Product	Axi-cel	Axi-cel	Axi-cel	Liso-cel	Tisa-cel (80%)	All commercial
Criteria	Non ASCT eligible	ASCT eligible	Age >65	Non ASCT eligible	Age >70	Age >65
Median age	70 (49-81)	58 (21-80)	69 (65-76)	74 (53-84)	76	72 (65-90)
>70 years	33 (53.2)	51 (28) (>65)	NA	48 (79)	41 (100)	349 (63.3)
Indication	Second line	Second line	Third or later	Second line	Third or later	Second or later
Relapse >12 mo	3 (5)	0	NA	15 (25)	NA	NA
Bridging therapy	52 (83.9)	65 (36) steroids	Not permitted	32 (52)	34 (83)	262 (47.5)
ORR	56 (90.3)	150 (83)	22 (92)	49 (80)	26 (63)	NA
CR	49 (79)	117 (65)	18 (75)	33 (54)	19 (46)	NA
Median PFS	11.8 (8.4-NE)	14.7 (5.4-42.7)	13.2 (3.1-NE)	9.03 (4.17-NE)	3.6 (1.6-5.6)	7.2 (EFS)
Median OS	Not reached	Not reached	NA	Not reached	Not reached	17.1
Grade ≥3 AEs	59 (95.2)	155 (91)	27 (100)	NA	NA	NA
Grade ≥3 CRS	5 (8.1)	11 (6)	2 (7)	1 (2)	4 (9.8)	NA
Grade ≥3 ICANS	9 (14.5)	36 (21)	12 (44)	3 (5)	1(2.5)	NA



Loncastuximab Tesirine: Update Results of LOTIS-2

- Study: LOTIS-2 was a multicenter, open-label, single-arm phase 2 study of Lonca monotherapy in pts with R/R DLBCL after ≥ 2 prior systemic therapies.
 - Lonca was administered every 3 weeks (150 $\mu\text{g}/\text{kg}$ for 2 cycles; 75 $\mu\text{g}/\text{kg}$ thereafter).
 - Primary efficacy endpoint was overall response rate (Lugano 2014 criteria).
 - Secondary endpoints included DOR; CR rate; and relapse-free, progression-free (PFS; measured from start of therapy), and overall survival (OS).
- As of final data cutoff (15 September 2022; median follow-up: 7.8 mo [range: 0.3, 42.6]), 70 (48%) of 145 pts achieved response and 36 (25%) pts achieved CR
- Among all pts, the mDOR was 13.4 mo (95% CI: 6.9, -), mPFS 4.9 mo (2.9, 8.3), and mOS 9.5 mo (6.7, 11.5). Among pts with CR, mDOR, mPFS, and mOS were NR

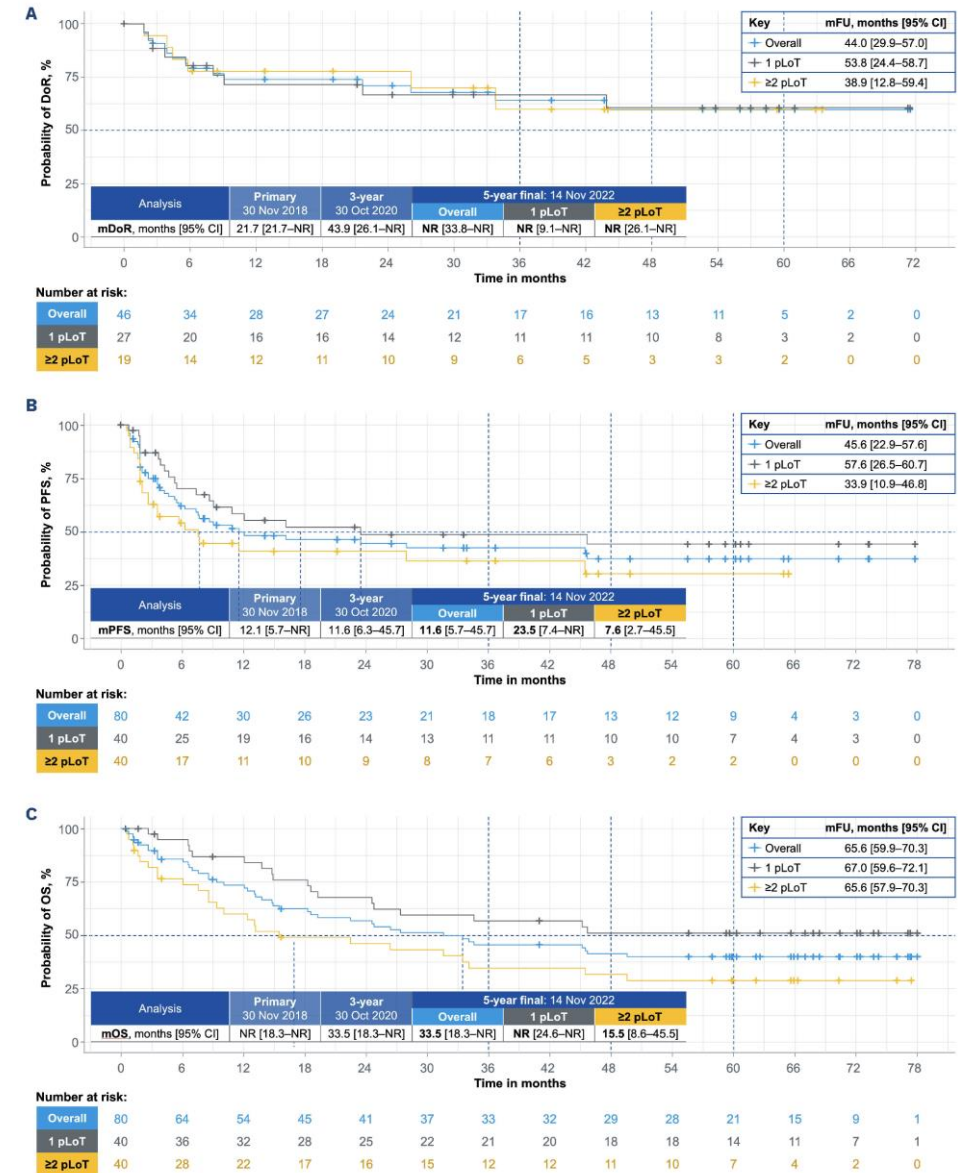
Figure 1. Kaplan–Meier curves of (A) progression-free survival and (B) overall survival in the all-treated population and the subset of patients with a complete response (CR)



L-MIND: Final 5 year Efficacy

Characteristics	Primary analysis	3-year follow-up	Final 5-year data	5-year data for patients with 1 prior line of therapy, N=40	5-year data for patients with ≥2 prior lines of therapy, N=40
Data cut-off date	Nov 30, 2018	Oct 30, 2020	Nov 14, 2022	Nov 14, 2022	Nov 14, 2022
Best ORR, N (%) [95% CI]	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	46 (57.5) [45.9-68.5]	27 (67.5) [50.9-81.4]	19 (47.5) [31.5-63.9]
CR rate, N (%) [95% CI]	34 (42.5) [32.0-54.0]	32 (40.0) [29.2-51.6]	33 (41.3) [30.4-52.8]	21 (52.5) [36.1-68.5]	12 (30.0) [16.6-46.5]
PR rate, N (%) [95% CI]	14 (17.5) [10.0-28.0]	14 (17.5) [9.9-27.6]	13 (16.3) [8.9-26.2]	6 (15.0) [5.7-29.8]	7 (17.5) [7.3-32.8]
Median DoR in months [95% CI]	21.7 [21.7-NR]	43.9 [26.1-NR]	NR [33.8-NR]	NR [9.1-NR]	NR [26.1-NR]
Median PFS in months [95% CI]	12.1 [5.7-NR]	11.6 [6.3-45.7]	11.6 [5.7-45.7]	23.5 [7.4-NR]	7.6 [2.7-45.5]
Median OS in months [95% CI]	NR [18.3-NR]	33.5 [18.3-NR]	33.5 [18.3-NR]	NR [24.6-NR]	15.5 [8.6-45.5]

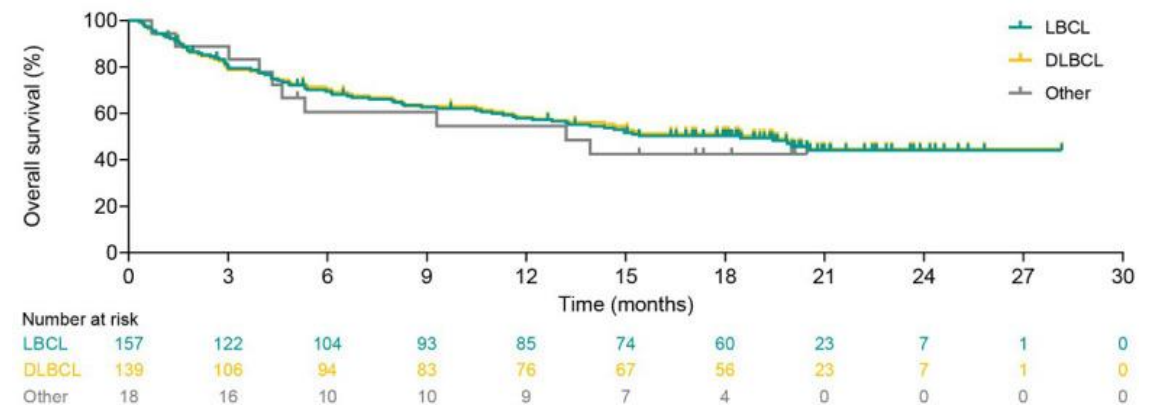
ORR: objective response rate; 95% CI: 95% confidence interval; CR: complete response; PR: partial response; DoR: duration of response; NR: not reached; PFS: progression-free survival; OS: overall survival.



EPCORE NHL-1: Longer Follow Up

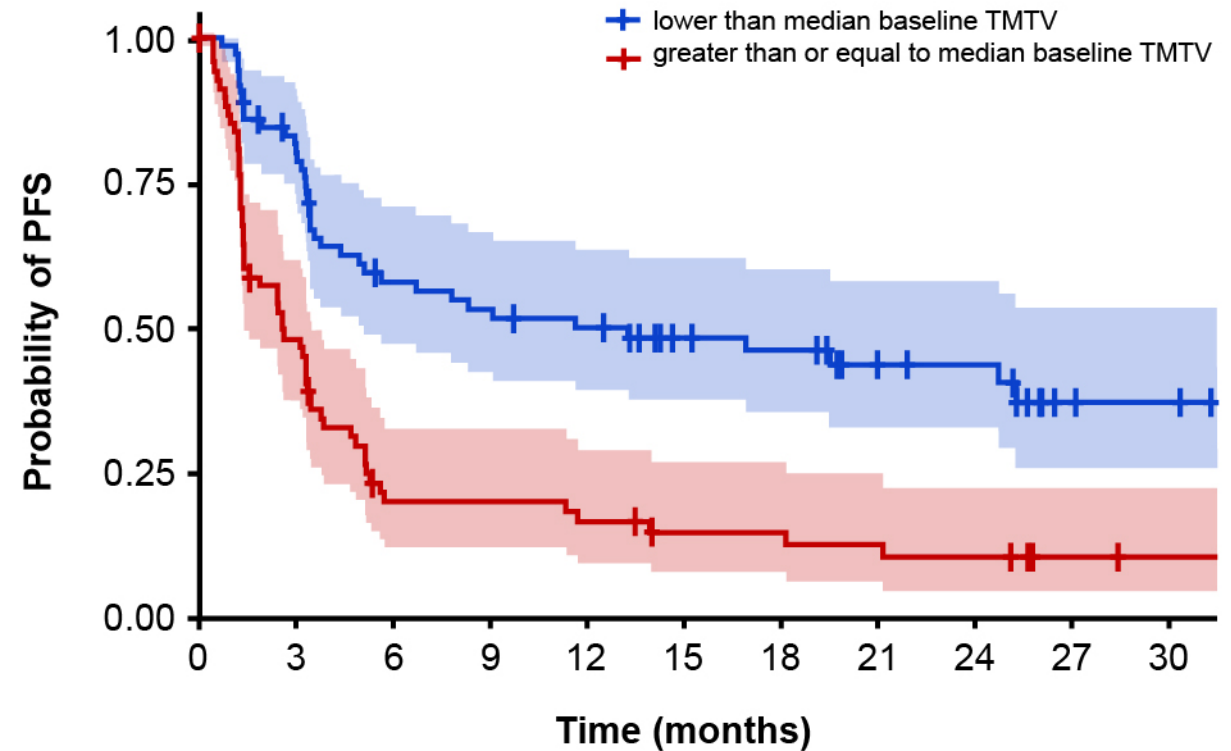
- **Methods:** Patients with R/R CD20+ LBCL received subcutaneous epcoritamab (step-up priming and intermediate doses followed by 48-mg full doses) in 28-d cycles: QW, cycles 1–3; Q2W, cycles 4–9; Q4W, cycles ≥10 until PD or unacceptable toxicity.
- 157 patients (median age, 64 y) with LBCL (including DLBCL [n=139; 12/88 double/triple-hit by FISH], HGBCL [n=9], PMBCL [n=4], and FL grade 3B [n=5]), 36 remain on treatment.
 - Median of 1.6 y from initial diagnosis to first dose and a median of 3 (range, 2–11) prior lines of treatment
 - 61% of patients had primary refractory disease
 - 39% had prior CAR T
 - Median follow-up was 20 mo (range, 0.3+ to 28.2).
 - Patients received a mean of 9.1 cycles.
- LBCL overall response and CR rates were 63.1% and 39.5%, respectively, and were consistent for DLBCL (61.9% and 39.6%).
 - Median duration of CR was 20.8 mo.
 - Median time to CR was 2.7 mo
 - 8 patients converted from partial response to CR at ≥36 wk
- Median overall survival was 18.5 mo (95% CI, 11.7–not reached [NR]) for patients with LBCL and 19.4 mo (95% CI, 11.7–NR) for patients with DLBCL

Figure. Overall survival



Glofitamab Monotherapy for R/R DLBCL, Extended Followup

- Regimen: Obinutuzumab pretreatment (1000mg) on Day (D) 1 of Cycle (C) 1. Intravenous glofitamab was then given as step-up doses during C1 (2.5mg on D8; 10mg on D15), followed by the target dose (30mg) on D1 of C2–12 (21-day cycles; total of 8.3 months)
- N=154
- ORR 52%, CR 40%
- Median duration of CR 29.6 months
- Prior CAR T-cell (N = 52): CR 37%
- Baseline TMTV (N = 144): median 128.7 (0-3820)
- High TMTV associated with increased risk of \geq grade 2 CRS (by quartile: 2.8%, 11.1%, 16.7%, 38.9%)
- Glofitamab monotherapy is less effective in patients with high baseline TMTV



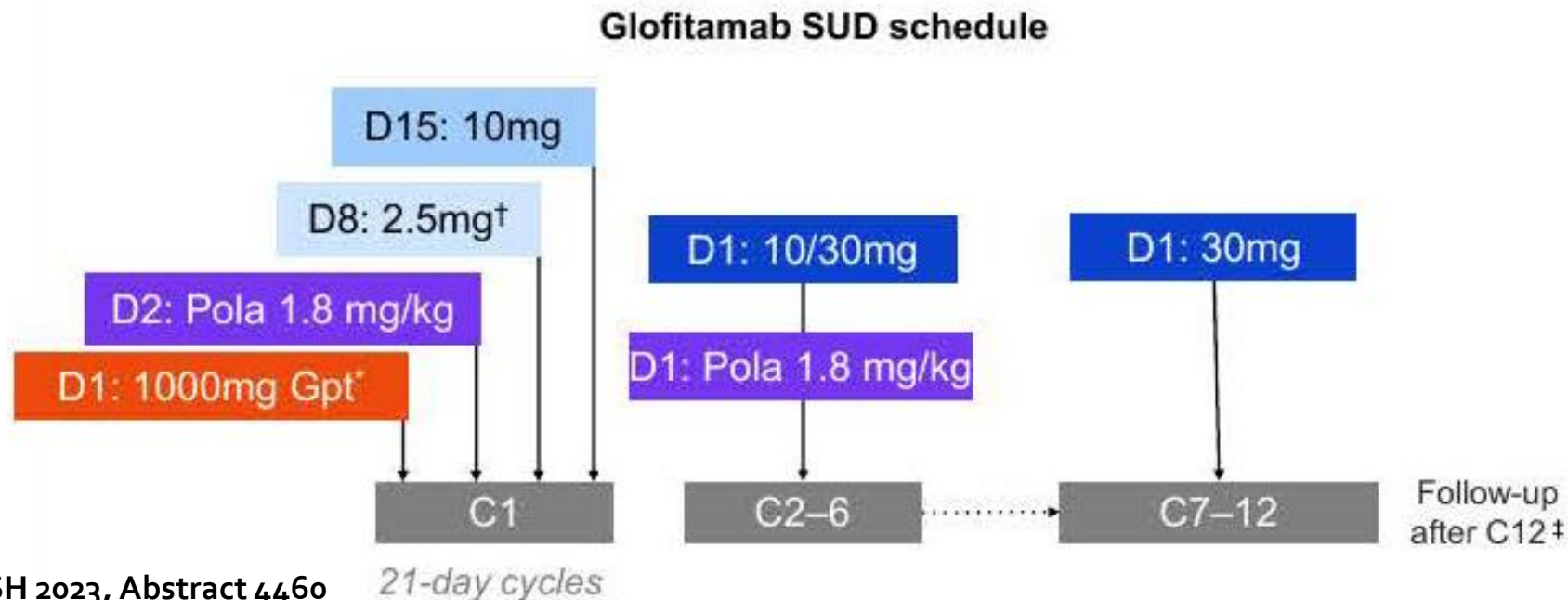
No. of pts at risk

—	72	56	37	34	31	23	21	15	14	5	4
—	72	32	12	12	10	7	7	6	5	2	1

Glofit-Pola: Study design

Methods:

- Patients with R/R DLBCL and ≥ 1 prior therapy received 1000mg obinutuzumab pre-treatment 7 days prior to the first glofitamab dose
- Polatuzumab vedotin 1.8mg/kg was given on C1D2 and D1 in C2-6 (21-day cycles)
- Intravenous glofitamab was administered with step-up dosing (SUD) during C1 (D8, 2.5mg; D15, 10mg) followed by the target dose {30mg) on D1 of C2-12 (21-day cycles)
- The primary endpoint was to establish the recommended Phase II dose of glofitamab when combined with polatuzumab vedotin (identified as 30mg from Part I of the study).

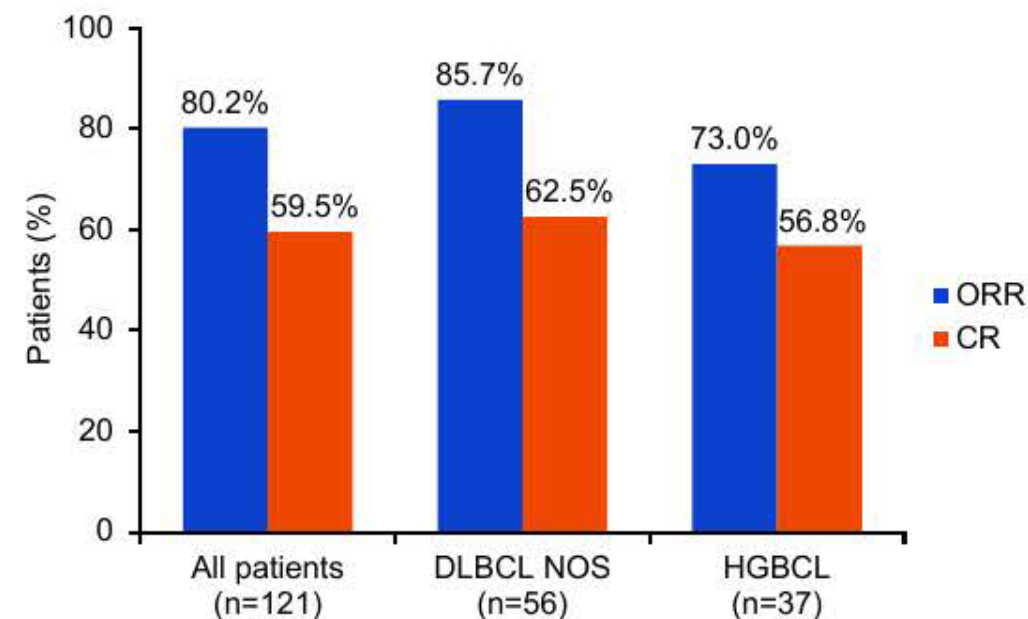


Glofit-Pola: Efficacy

- Median follow-up was 20.4 months (95% confidence interval [CI]: 17.5-23.2)
- The overall investigator (INV)-assessed objective response rate (ORR) was 80.2% and CR rate was 59.5% (Table 2). In patients with HGBCL (n=37), ORR was 73.0% and CR rate was 56.8% (Figure 2).

n (%)	All patients (n=121)*	Prior CAR-T (n=27)	DLBCL NOS (n=56)	HGBCL (n=37)	trFL (n=26)	PMBCL (n=2)
Objective response	97 (80.2)	21 (77.8)	48 (85.7)	27 (73.0)	20 (76.9)	2 (100)
Complete response	72 (59.5)	13 (48.1)	35 (62.5)	21 (56.8)	14 (53.8)	2 (100)
Partial response	25 (20.7)	8 (29.6)	13 (23.2)	6 (16.2)	6 (23.1)	0
Stable disease	5 (4.1)	1 (3.7)	1 (1.8)	2 (5.4)	2 (7.7)	0
Progressive disease	16 (13.2)	4 (14.8)	6 (10.7)	7 (18.9)	3 (11.5)	0
Not determined†	3 (2.5)	1 (3.7)	1 (1.8)	1 (2.7)	1 (3.8)	0

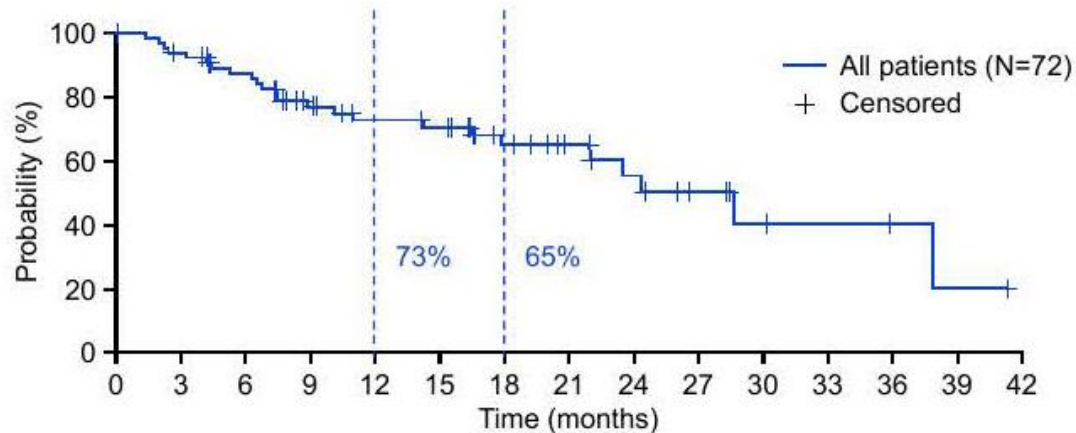
*121/125 efficacy-evaluable population: patients who had been on the study long enough to have at least one response assessment. †Missing or not done.



Glofit-Pola: Duration of CR and PFS

- In 72 patients with a CR and median CR follow-up of 16.6 months (range: 0-41), median duration of CR (DoCR) was 28.6 months (95% CI: 21.9-not estimable [NE]) for all histologies, 21.9 months (95% CI: 10.1-NE) for DLBCL and NE for HGBCL.
- The estimated 12- and 18-month DoCR was 72.9% and 65.1%, respectively
- With a median follow-up of 20.4 months, median progression-free survival (PFS) was 10.4 months (95% CI: 7.0-23.5)
- The 12-month PFS rate was 47.4% (95% CI: 37.9-57.0).

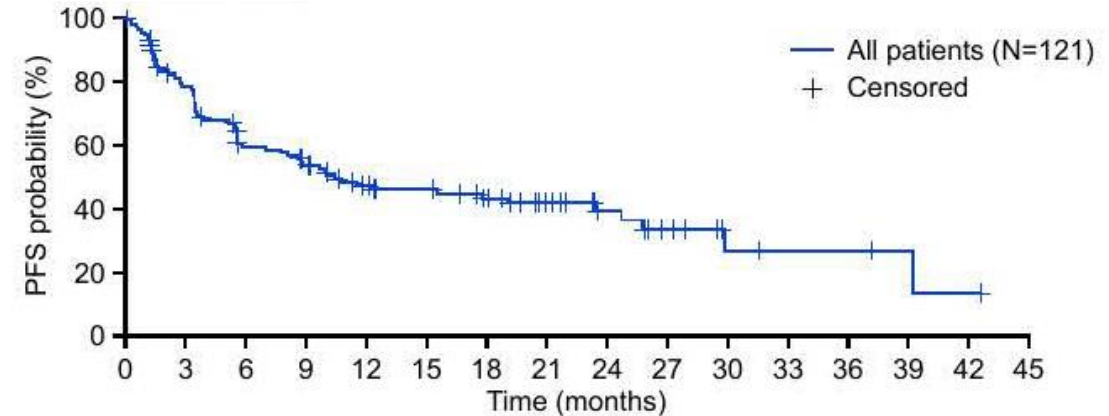
DoCR



No. at risk:

72 62 52 40 34 32 22 16 11 7 4 3 2 1 NE

PFS



No. at risk:

121 90 62 53 41 37 31 22 14 9 4 3 3 2 1 NE

Median PFS by histology was 10.4 months (95% CI: 7.7-25.7) for DLBCL, 9.9 months (95% CI: 3.4-NE) for HGBCL, and 9.6 months (95% CI: 5.1-NE) for trFL

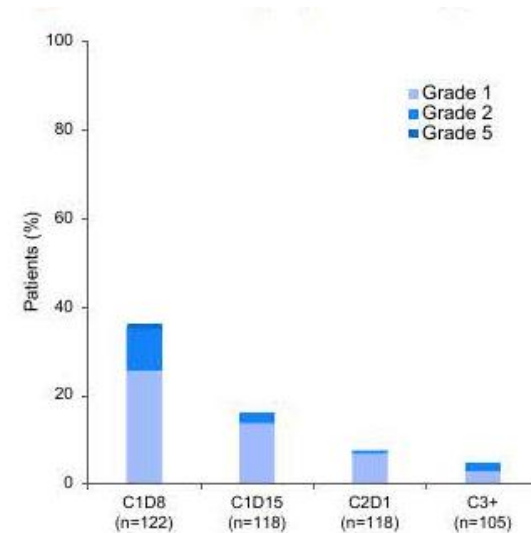
Glofit-Pola: Safety

- The safety profile was consistent with that of the individual drugs (Table 3).
- Grade 5 (fatal) adverse events (AEs) included COVID-19 (n=3); COVID-19 pneumonia (n=2), general deterioration (n=1), CRS (n=1), and second malignancies (n=2).
- Glofitamab-related AEs potentially consistent with immune effector cell-associated neurotoxicity syndrome (ICANS) occurred in four patients and were all Grade 1-2.

n (%) of patients with ≥1 AE	N=125
Any AEs	124 (99.2)
Grade 3–4 AEs	75 (60.0)
Grade 5 AEs	9 (7.2)
Serious AEs	75 (60.0)
AEs leading to treatment discontinuation	13 (10.4)
Glofitamab discontinuation	10 (8.0)
Polatuzumab vedotin discontinuation	8 (6.4)

- CRS was mostly Grade 1-2; time of onset was predictable, and the majority of events occurred during C1 and were well managed
- Tocilizumab was the most common CRS management strategy (n=18); intensive care unit admission rates were low (n=2).

n=122*	
CRS, n (%)	
Any grade	56 (45.9)
Grade 1	36 (29.5)
Grade 2	19 (15.6)
Grade 5†	1 (0.8)
Serious AE (any grade)	37 (30.3)
Median time to CRS onset after glofitamab dose, hours (range)	
2.5mg	16.2 (5.4–42.1)
10mg	35.9 (8.9–129.5)
30mg	36.2 (18.5–55.9)



*122/125 patients who received ≥1 dose of glofitamab.

†Patient (aged 73, with advanced HGBCL and multiple CRS risk factors) developed Grade 3 CRS (with a background of urosepsis and herpetic stomatitis) and declined further intensive management for CRS, resulting in fatal outcome.

Summary

- CAR T-cell can be administered to older patients with co-morbidities
 - The efficacy is similar to younger patients
 - Safety and tolerability appear to be similar to younger patients
 - Tisagenlecleucel and lisocabtagene maracleucel are better tolerated in older adults
- Are there patient ineligible for CAR T-cell that could tolerate other therapy?
 - This has not been formally evaluated
 - Alternative CD19-directed therapy including loncastuximab tesirine and tafasitamab-lenalidomide have activity but these regimens have their own toxicity and are not necessarily better tolerate in “CAR T-cell” ineligible patient
 - Bispecific antibodies are can be use but have not specifically been studied in “unfit” patients
- **If a patient is truly not a candidate for CAR T-cell therapy, then treatment will need to be individualized for that patient to address the issue(s) that prevent the use of potentially curative therapy**

