MAYO CLINIC

CAR T cell Therapies in Lymphoid Malignancies: Here to Stay!

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Medical Director, Cancer Research Office (Florida Campus)

NOSCM 2022
June 26, 2022

Outline

- Focus on lymphoma
- CAR-T therapy background on FDA approved products
  - Diffuse large B cell lymphoma (**ZUMA 1, JULIET, TRANSCEND NHL 001**)
  - Mantle cell lymphoma (**ZUMA-2**)
  - Follicular lymphoma (**ZUMA-5, ELARA**)
  - 2nd line studies in large B cell lymphoma **(ZUMA 7)**
- Updates from ASH 2021
  - On above approved indications (when applicable)
  - Allogeneic CAR T cell Therapies (selected studies)
- Take home messages

Immunotherapy

Immunotherapy: a therapeutic revolution

The New York Times

What Is Immunotherapy? The Basics on These Cancer Treatments

By Denise Grady and Andrew Pollack

July 30, 2016

CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships

Hope and hype around cancer immunotherapy

By Jacqueline Howard, CNN
Updated 3:37 PM EDT, Wed September 27, 2017

Immunotherapy cancer treatment a game changer?

BBC Sign in Home News Sport Reel Worklife Travel

NEWS

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Health | Coronavirus

Cancer immunotherapy drug 'less toxic and prolongs life'

By Philippa Roxby
Health reporter, BBC News

23 November 2019

ROYAL MARSDEN HOSPITAL

Derek, from Leicestershire, took part in a trial of pembrolizumab

Large B-cell lymphoma

Diffuse large B-cell lymphoma

- 1st line chemo-immunotherapy yields successful outcomes in two-third of cases[a]

- High-dose therapy and autologous HCT cures ~50% of chemosensitive-relapsed cases[b]

  - But outcomes are dismal for those who receive an auto-HCT with relapsed refractory disease (<15% are cured)[c]

a. Feugier P, et al. J Clin Oncol 23:4117-26, 2005
b. Philip T, et al. N Engl J Med 333:1540-5, 1995
c. Philip T, et al. N Engl J Med 316:1493-8, 1987

Before availability of CAR-T

Table 2. Rate of response to chemotherapy after refractory disease

	MDACC (n = 165)	IA/MC (n = 82)	LY.12 (CCTG) (n = 219)	CORAL (LYSARC) (n = 170)	Pooled* (N = 636)
Patients evaluated for response, n†	165	82	106	170	523
Response rate, % (95% CI)	20	26	26	31	26 (21-31)
CR rate	7	7	2	15	7 (3-15)
PR rate	13	18	25	16	18 (13-23)
Response rate by refractory category, % (95% CI)					
Primary refractory					
RR	—	25	27	10	20 (11-34)
CR rate	—	10	1	2	3 (1-11)
Refractory to second-line or later-line therapy					
RR	20	21	20	40	26 (17-39)
CR rate	7	5	20	18	10 (5-20)
Relapse ≤12 mo post-ASCT					
RR	19	35	—	39	34 (24-45)
CR rate	6	10	—	25	15 (6-31)

Crump M, et al. Blood. 2017; 130 (16): 1800-09

ZUMA-1

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma

S.S. Neelapu, F.L. Locke, N.L. Bartlett, L.J. Lekakis, D.B. Miklos, C.A. Jacobson, I. Braunschweig, O.O. Oluwole, T. Siddiqi, Y. Lin, J.M. Timmerman, P.J. Stiff, J.W. Friedberg, I.W. Flinn, A. Goy, B.T. Hill, M.R. Smith, A. Deol, U. Farooq, P. McSweeney, J. Munoz, I. Avivi, J.E. Castro, J.R. Westin, J.C. Chavez, A. Ghobadi, K.V. Komanduri, R. Levy, E.D. Jacobsen, T.E. Witzig, P. Reagan, A. Bot, J. Rossi, L. Navale, Y. Jiang, J. Aycock, M. Elias, D. Chang, J. Wiezorek, and W.Y. Go

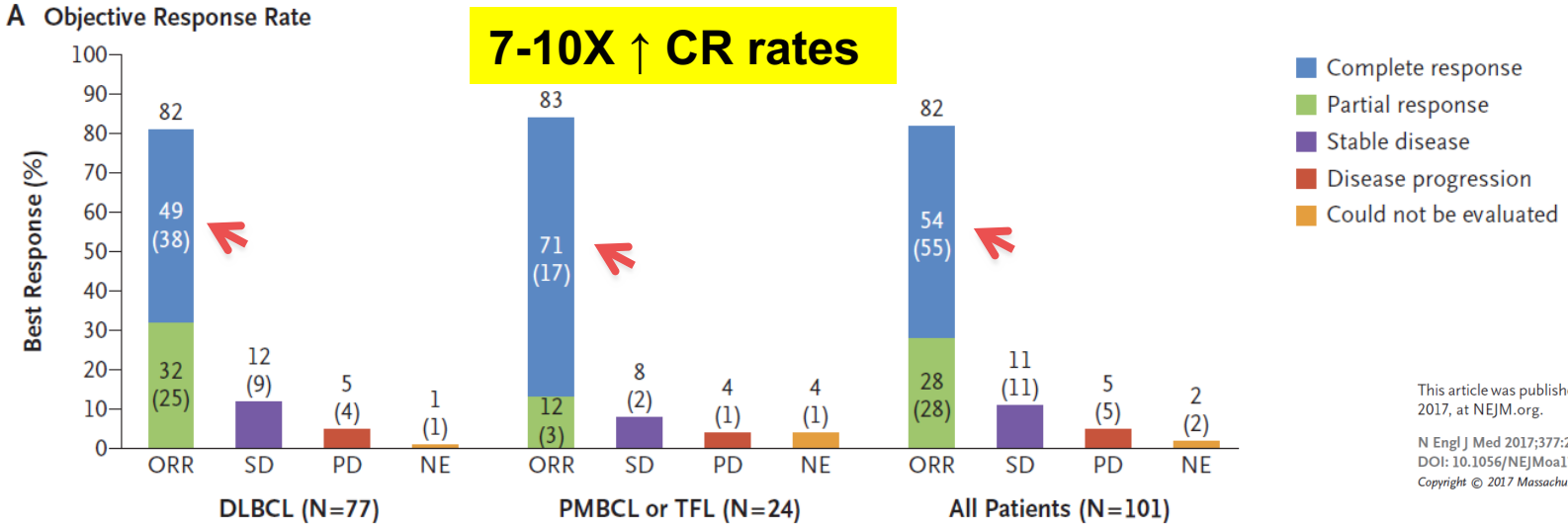
This article was published on December 10, 2017, at NEJM.org.

N Engl J Med 2017;377:2531-44.
DOI: 10.1056/NEJMoa1707447

N=111 patients

ZUMA 1: Axicabtagene ciloleucel

Variables	DLBCL	PMBCL or TFL	All pts
N pts enrolled	81	30	111
N pts treated with axi-cel	77 (95%)	24 (80%)	101 (91%)
Median (range) age, years	58 (25-76)	57 (23-76)	58 (23-76)
Stage III-IV disease	67 (87%)	19 (79%)	86 (85%)
≥ 3 prior lines of therapy	49 (64%)	21 (88%)	70 (69%)
Relapsed after auto-HCT	16 (21%)	5 (21%)	21 (21%)



This article was published on December 10, 2017, at NEJM.org.

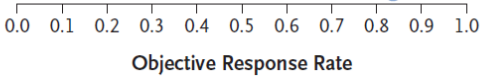
N Engl J Med 2017;377:2531-44.
DOI: 10.1056/NEJMoa1707447

MAYO CLINIC

Neelapu SS, et al. N Engl J Med. 2017; 377:2531-44

B Subgroup Analysis

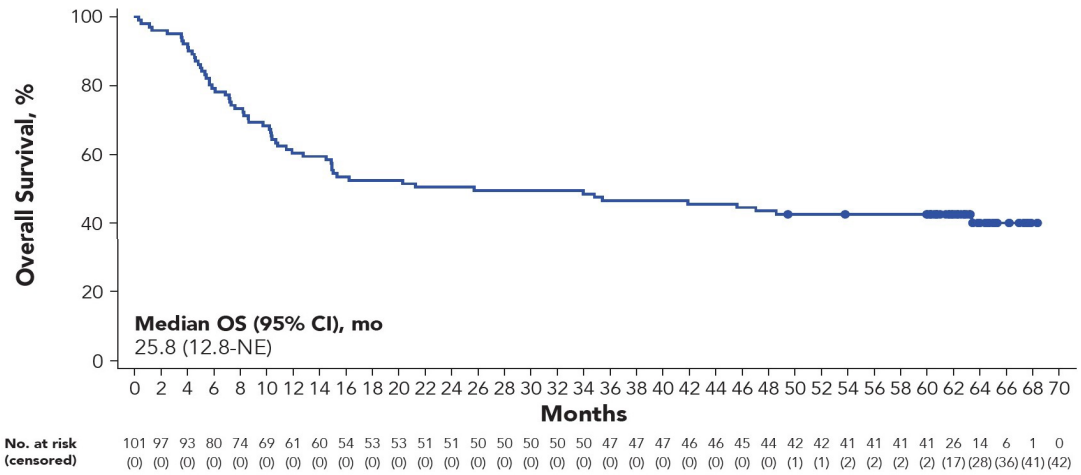
Subgroup	No. of Patients Who Could Be Evaluated	No. of Patients with Event	Objective Response Rate (95% CI)
Overall	101	83	0.82 (0.73–0.89)
Refractory subgroup			
Refractory to ≥second-line therapy	78	65	0.83 (0.73–0.91)
Relapse after ASCT	21	16	0.76 (0.53–0.92)
Age			
<65 yr	77	61	0.79 (0.68–0.88)
≥65 yr	24	22	0.92 (0.73–0.99)
Disease stage			
I or II	15	13	0.87 (0.60–0.98)
III or IV	86	70	0.81 (0.72–0.89)
IPI risk score			
0–2	53	46	0.87 (0.75–0.95)
3 or 4	48	37	0.77 (0.63–0.88)
Extranodal disease			
Yes	70	56	0.80 (0.69–0.89)
No	31	27	0.87 (0.70–0.96)
Bulky disease (≥10 cm)			
Yes	17	12	0.71 (0.44–0.90)
No	84	71	0.85 (0.75–0.91)
Treatment history			
Primary refractory disease	26	23	0.88 (0.70–0.98)
Refractory to two consecutive lines	54	42	0.78 (0.64–0.88)
CD19 status			
Positive	74	63	0.85 (0.75–0.92)
Negative	8	6	0.75 (0.35–0.97)
CD19 histologic score			
≤150	26	22	0.85 (0.65–0.96)
>150	56	47	0.84 (0.72–0.92)
Cell of origin			
Germinal center B-cell–like subtype	49	43	0.88 (0.75–0.95)
Activated B-cell–like subtype	17	13	0.76 (0.50–0.83)
CD4:CD8 ratio			
>1	47	41	0.87 (0.74–0.95)
≤1	52	40	0.77 (0.63–0.87)
Tocilizumab use			
Yes	43	36	0.84 (0.69–0.93)
No	58	47	0.81 (0.69–0.90)
Glucocorticoid use			
Yes	27	21	0.78 (0.58–0.91)
No	74	62	0.84 (0.73–0.91)



1764 Long-Term (4- and 5-Year) Overall Survival in ZUMA-1, the Pivotal Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Refractory Large B-Cell Lymphoma (LBCL)

Program: Oral and Poster Abstracts
Session: 704. Cellular Immunotherapies: Clinical: Poster I
Hematology Disease Topics & Pathways:
Biological, Adults, Lymphomas, Non-Hodgkin Lymphoma, B Cell Lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Immune Mechanism, Diseases, Therapies, Lymphoid Malignancies, Biological Processes, Study Population

5-Year Overall Survival



With ≥5 years of F/U:

- **5-year OS rate** was **42.6%** (95% CI, 32.8-51.9) among pts treated with axi-cel

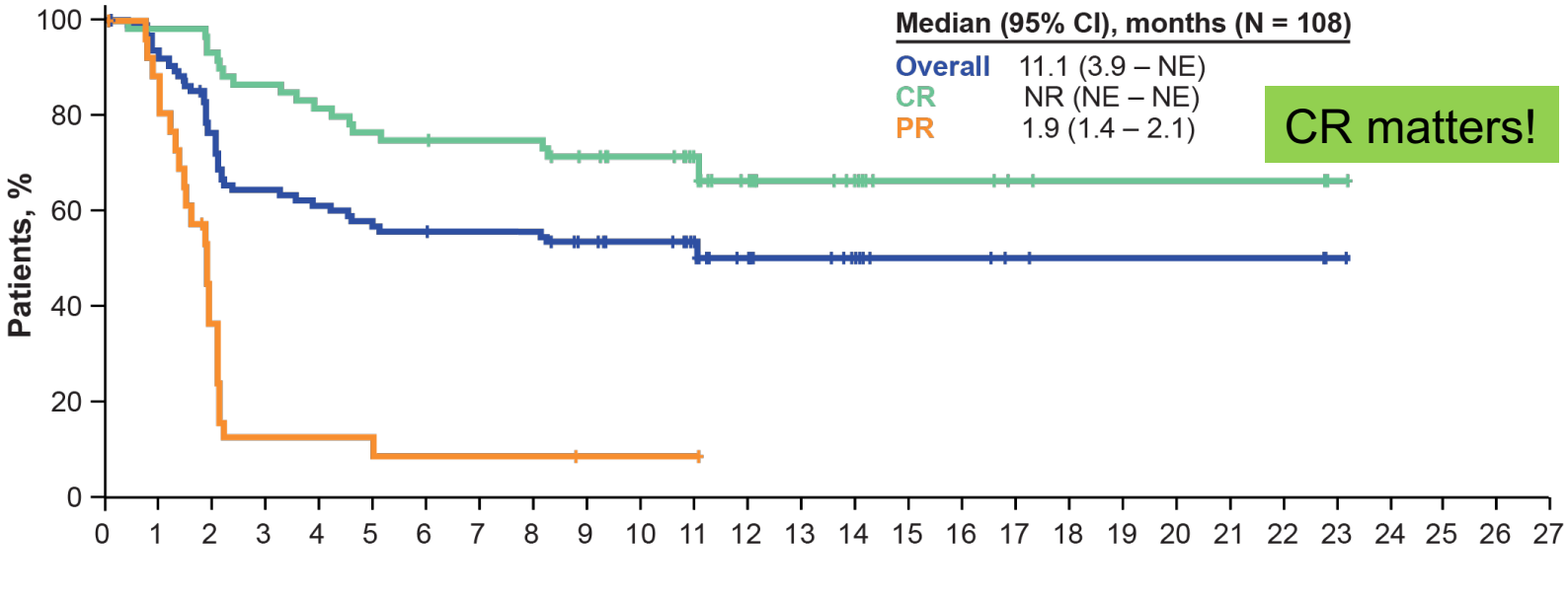
The 5-year OS rate:

- In CR=**64.4%** (95% CI, 50.8-75.1); the median survival time among complete responders was not reached (95% CI, 63.4-NE)
- 37 of 59 CR patients (63%) are still alive at the 5-year data cutoff

- One patient's event time was updated from Month 42 to 39 after data cutoff and is not reflected in this figure
- Axi-cel, axicabtagene ciloleucel; CR, complete response; NE, not estimable; OS, overall survival; PD, progressive disease; PR, partial response

Jacobson C, et al. ASH 2021, Abs 1764

DOR by best objective response (median F/U of 15.4 months)



Patients at Risk

Overall	89	82	67	56	53	49	48	47	47	42	38	31	19	16	12	6	6	4	3	3	3	3	3	1	0
CR	63	61	58	53	50	47	46	45	45	41	37	30	19	16	12	6	6	4	3	3	3	3	3	1	0
PR	26	21	9	3	3	2	2	2	2	1	1	1	0												

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Stephen J. Schuster, M.D., Michael R. Bishop, M.D., Constantine S. Tam, M.D., Edmund K. Waller, M.D., Ph.D., Peter Borchmann, M.D., Joseph P. McGuirk, D.O., Ulrich Jäger, M.D., Samantha Jaglowski, M.D., Charalambos Andreadis, M.D., Jason R. Westin, M.D., Isabelle Fleury, M.D., Veronika Bachanova, M.D., Ph.D., S. Ronan Foley, M.D., P. Joy Ho, M.B., B.S., D.Phil., Stephan Mielke, M.D., John M. Magenau, M.D., Harald Holte, M.D., Ph.D., Serafino Pantano, Ph.D., Lida B. Pacaud, M.D., Rakesh Awasthi, Ph.D., Jufen Chu, Ph.D., Özlem Anak, M.D., Gilles Salles, M.D., Ph.D., and Richard T. Maziarz, M.D., for the JULIET Investigators*

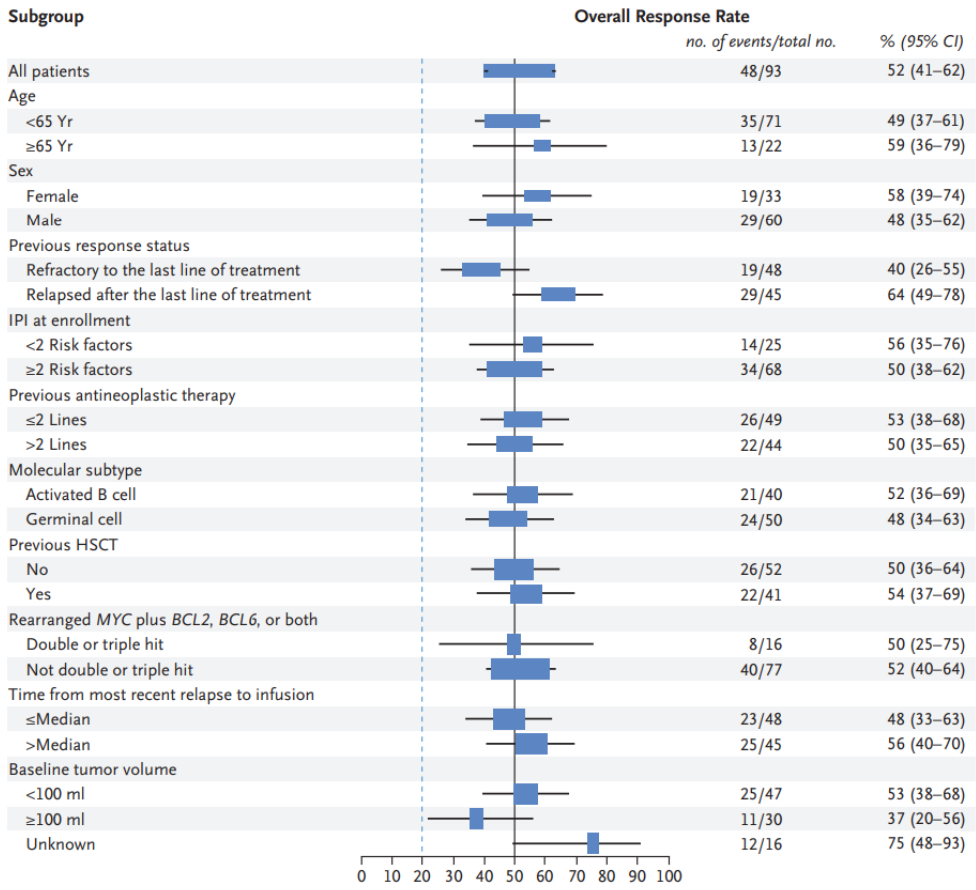
This article was published on December 1, 2018, at NEJM.org.

N Engl J Med 2019;380:45-56.
DOI: 10.1056/NEJMoa1804980

N=111 patients

JULIET: Tisagenlecleucel

Variables	All pts
N pts enrolled	111
Median (range) age, years	56 (22-76)
Stage III-IV disease	84 (76%)
≥ 3 prior lines of therapy	57 (52%)
Relapsed after auto-HCT	54 (49%)



Schuster SJ, et al. N Engl J Med. 2019; 380:45-56

Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): a multicentre, open-label, single-arm, phase 2 study

Stephen J Schuster, Constantine S Tam, Peter Borchmann, Nina Worel, Joseph P McGuirk, Harald Holte, Edmund K Waller, Samantha Jaglowski, Michael R Bishop, Lloyd E Damon, Stephen Ronan Foley, Jason R Westin, Isabelle Fleury, P Joy Ho, Stephan Mielke, Takanori Teshima, Murali Janakiram, Jing-Mei Hsu, Koji Izutsu, Marie José Kersten, Monalisa Ghosh, Nina Wagner-Johnston, Koji Kato, Paolo Corradini, Marcela Martinez-Prieto, Xia Han, Ranjan Tiwari, Gilles Salles, Richard T Maziarz

- At a median follow-up of 40.3 months (IQR 37·8–43·8),
- ORR= 53% by IRC-assessed
- CR= 39%
- The median time to first response= 29 (28-31) days

	All patients (n=115)	Any-grade neurological event (n=23)	Grades 3–4 neurological event (n=13)
No cytokine release syndrome	49 (43%)	4 (17%)	3 (23%)
Grades 1–2 cytokine release syndrome	40 (35%)	6 (26%)	2 (15%)
Grade 3 cytokine release syndrome	17 (15%)	6 (26%)	2 (15%)
Grade 4 cytokine release syndrome	9 (8%)	7 (30%)	6 (46%)
Any-grade cytokine release syndrome	66 (57%)	19 (83%)	10 (77%)

Severe cytokine release syndrome and severe neurological events were defined as the occurrence of grade 3 or 4 events within 8 weeks post-infusion.

Table 4: **Occurrences of cytokine release syndrome and neurological events**

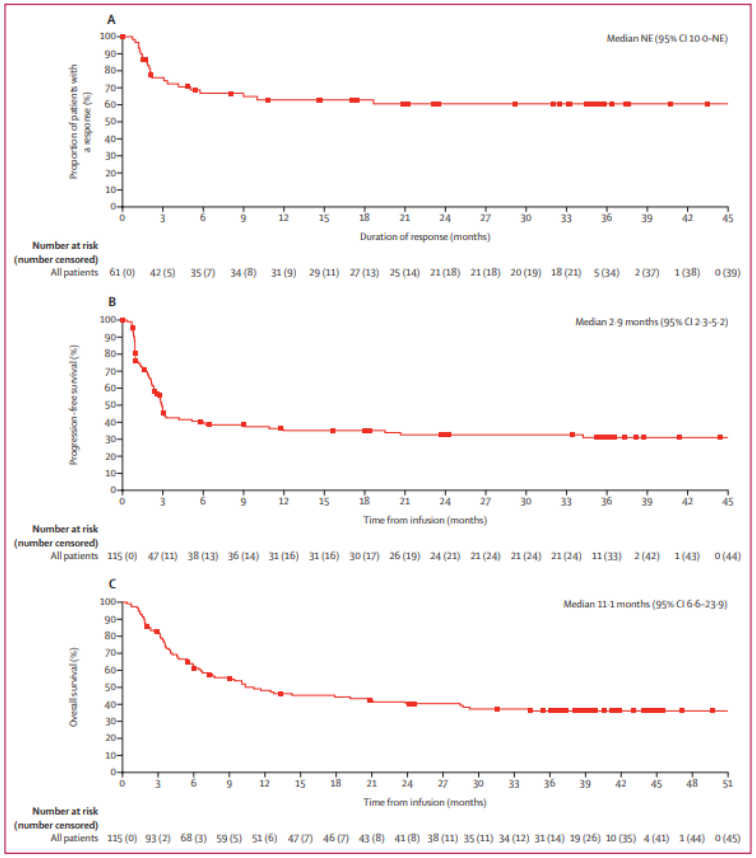
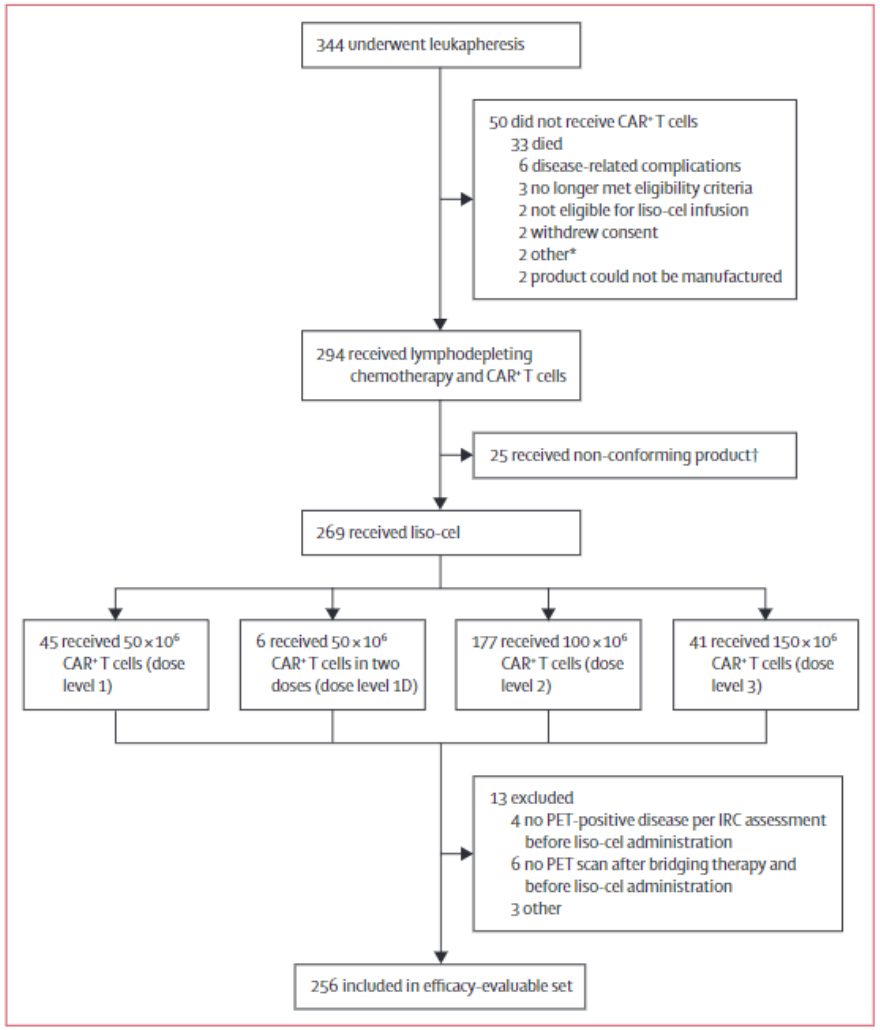


Figure 1: **Kaplan–Meier outcome estimates**
(A) Duration of response. (B) Progression-free survival. (C) Overall survival. NE=not estimable.

Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study

Jeremy S Abramson, M Lia Palomba, Leo I Gordon, Matthew A Lunning, Michael Wang, Jon Arnason, Amitkumar Mehta, Enkhtsetseg Purev, David G Maloney, Charalambos Andreadis, Alison Sehgal, Scott R Solomon, Nilanjan Ghosh, Tina M Albertson, Jacob Garcia, Ana Kostic, Mary Mallaney, Ken Ogasawara, Kathryn Newhall, Yeonhee Kim, Daniel Li, Tanya Siddiqi

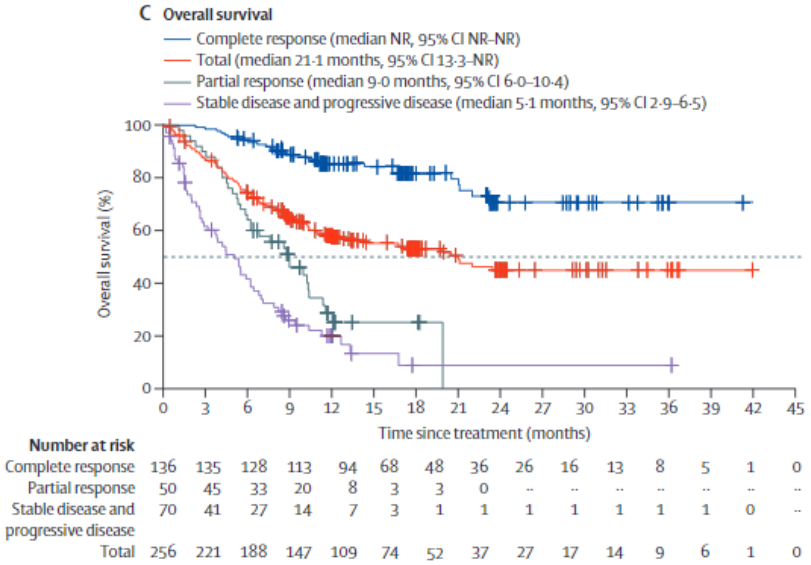


	Patients (n=269)
Gender	
Male	174 (65%)
Female	95 (35%)
Age, years	63 (54–70)
≥65	112 (42%)
≥75	27 (10%)
Diffuse large B-cell lymphoma, not otherwise specified	137 (51%)
Diffuse large B-cell lymphoma transformed from indolent lymphomas	78 (29%)
Transformed from follicular lymphoma	60 (22%)
Transformed from other indolent non-Hodgkin lymphoma subtypes*	18 (7%)
High-grade B-cell lymphoma with gene rearrangments in *MYC* and either *BCL2*, *BCL6*, or both†	36 (13%)
Primary mediastinal B-cell lymphoma	15 (6%)
Follicular lymphoma grade 3B	3 (1%)
ECOG performance status at screening	
0	110 (41%)
1	155 (58%)
2	4 (1%)
Before lymphodepleting chemotherapy	
Sum of product diameter, cm²	22·5 (8·5–57·9)
Sum of product diameter ≥50 cm²‡	73 (28%)
Lactate dehydrogenase, U/L	266·0 (112·0–11 933·0)
Lactate dehydrogenase ≥500 U/L	58 (22%)
Creatinine clearance >30 to <60 mL/min§	51 (19%)
Baseline C-reactive protein, mg/L	27·6 (7·9–81·6)
Left-ventricular ejection fraction ≥40% and <50%¶	13 (5%)
Previous lines of systemic therapy‖	3 (2–4)
1	9 (3%)
2	121 (45%)
3	68 (25%)
≥4	71 (26%)
Chemotherapy refractory**	181 (67%)
Received previous HSCT	94 (35%)
Autologous HSCT	90 (33%)
Allogeneic HSCT	9 (3%)
Never achieved complete response with previous therapy††	119 (44%)
Received bridging therapy	159 (59%)
Secondary CNS lymphoma	7 (3%)

Abramson JS, et al. Lancet. 2020; 396;839-52

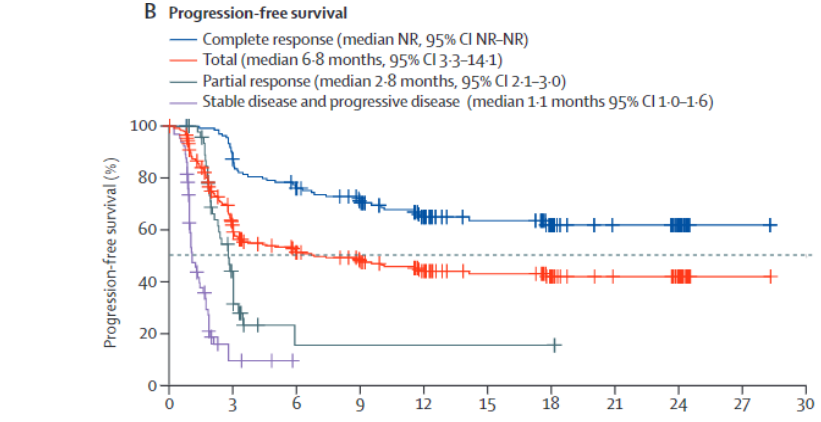
TRANSCEND NHL 001

Overall survival



Number at risk														
Complete response	136	135	128	113	94	68	48	36	26	16	13	8	5	1	0
Partial response	50	45	33	20	8	3	3	0	..	..	..	..	..	..	..
Stable disease and progressive disease	70	41	27	14	7	3	1	1	1	1	1	1	1	0	..
Total	256	221	188	147	109	74	52	37	27	17	14	9	6	1	0

Progression-free survival



Number at risk											
Complete response	136	116	98	85	63	45	31	23	14	1	0
Partial response	50	14	2	2	2	2	2	0	..	..	..
Stable disease and progressive disease	70	3	0	..	..	..	..	..	..	..	..
Total	256	133	100	87	65	47	33	23	14	1	0

Abramson JS, et al. Lancet. 2020; 396;839-52

Mantle cell lymphoma

ZUMA-2

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma

M. Wang, J. Munoz, A. Goy, F.L. Locke, C.A. Jacobson, B.T. Hill, J.M. Timmerman, H. Holmes, S. Jaglowski, I.W. Flinn, P.A. McSweeney, D.B. Miklos, J.M. Pagel, M.-J. Kersten, N. Milpied, H. Fung, M.S. Topp, R. Houot, A. Beitinjaneh, W. Peng, L. Zheng, J.M. Rossi, R.K. Jain, A.V. Rao, and P.M. Reagan

ZUMA-2: Baseline characteristics

Table 1. Baseline Characteristics of All 68 Treated Patients.*

Characteristic	Patients
Median age (range) — yr	65 (38–79)
Intermediate or high risk according to Simplified MIPI — no. (%)†‡	38 (56)
Blastoid or pleomorphic morphologic characteristics of MCL — no. (%)	21 (31)
Ki-67 proliferation index ≥30% — no./total no. (%)‡	40/49 (82)
TP53 mutation — no. (%)	6/36 (17)
Positive CD19 status — no./total no. (%)	47/51 (92)
Median no. of previous therapies (range)§	3 (1–5)
≥3 Previous lines of therapy — no. (%)	55 (81)
Previous autologous stem-cell transplantation — no. (%)	29 (43)
Previous BTK inhibitor therapy — no. (%)§	68 (100)
Ibrutinib	58 (85)
Acalabrutinib	16 (24)
Both	6 (9)
Relapsed or refractory disease — no. (%)	
Relapse after autologous stem-cell transplantation	29 (43)
Refractory to most recent previous therapy	27 (40)
Relapse after most recent previous therapy	12 (18)
Disease that relapsed or was refractory to BTK inhibitor therapy — no. (%)	68 (100)
Refractory to BTK inhibitor therapy	42 (62)
Relapse during BTK inhibitor therapy	18 (26)
Relapse after BTK inhibitor therapy	5 (7)
Could not take BTK inhibitor therapy because of adverse events¶	3 (4)

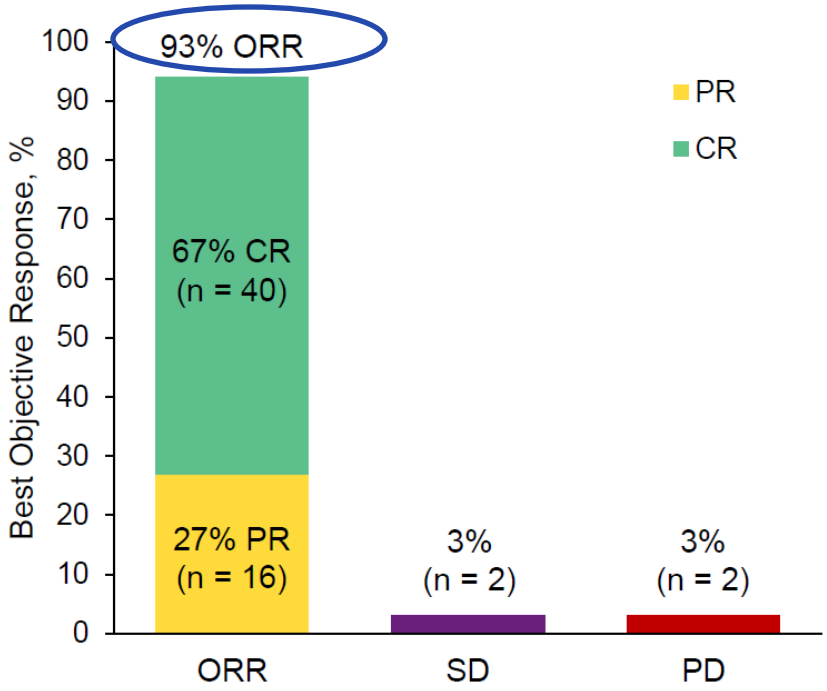
MAYO CLINIC

Wang M, et al. ASH 2019. Abs 754
Wang M, et al. NEJM. 2020. 382:1331

ZUMA-2: ORR

ASH 2019. Abs 754

ORR by IRRC Assessment Was 93% (95% CI, 84 – 98) and CR Rate Was 67% (95% CI, 53 – 78)



	Efficacy-Evaluable N = 60
Median follow-up (range), mo	12.3 (7.0 – 32.3)
Patients with ≥ 24 mo follow-up, n (%)	28 (47)
Median time to response (range), mo	
Initial response	1.0 (0.8 – 3.1)
CR	3.0 (0.9 – 9.3)
Patients converted from PR/SD to CR, n (%)	24 (40)
PR to CR	21 (35)
SD to CR	3 (5)

Investigator-assessed ORR in N = 60 was 88% (CR rate 70%), with 95% and 90% concordance between IRRC- and investigator-assessed ORR and CR rate, respectively. IRRC-assessed ORR in ITT (N = 74) was 85% (CR Rate 59%).
CR, complete response; IRRC, Independent Radiology Review Committee; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

MAYO CLINIC

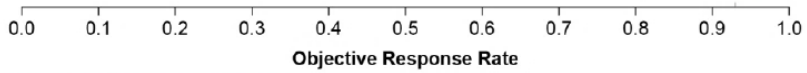
Wang M, et al. ASH 2019. Abs 754
Wang M, et al. NEJM. 2020. 382:1331

ZUMA-2

ASH 2019. Abs 754

ORR Was Consistent Across Key Subgroups

	Evaluable Patients	Responding Patients	ORR (95% CI)
Overall	60	56	0.93 (0.84, 0.98)
Age			
< 65 Years	28	26	0.93 (0.76, 0.99)
≥ 65 Years	32	30	0.94 (0.79, 0.99)
MCL morphology			
Classical MCL	35	32	0.91 (0.77, 0.98)
Pleomorphic	4	4	1.00 (0.40, 1.00)
Blastoid	14	13	0.93 (0.66, 1.00)
Ki-67 index			
< 50%	14	14	1.00 (0.77, 1.00)
≥ 50%	32	30	0.94 (0.79, 0.99)
Disease stage			
I-II	2	2	1.00 (0.16, 1.00)
III-IV	58	54	0.93 (0.83, 0.98)
Simplified MIPI			
Low risk	25	23	0.92 (0.74, 0.99)
Intermediate/high risk	33	31	0.94 (0.80, 0.99)
Steroid use for AE management			
Yes	35	33	0.94 (0.81, 0.99)
No	25	23	0.92 (0.74, 0.99)
Tocilizumab use			
Yes	42	40	0.95 (0.84, 0.99)
No	18	16	0.89 (0.65, 0.99)
Bridging therapy use			
Yes	21	19	0.90 (0.70, 0.99)
No	39	37	0.95 (0.83, 0.99)

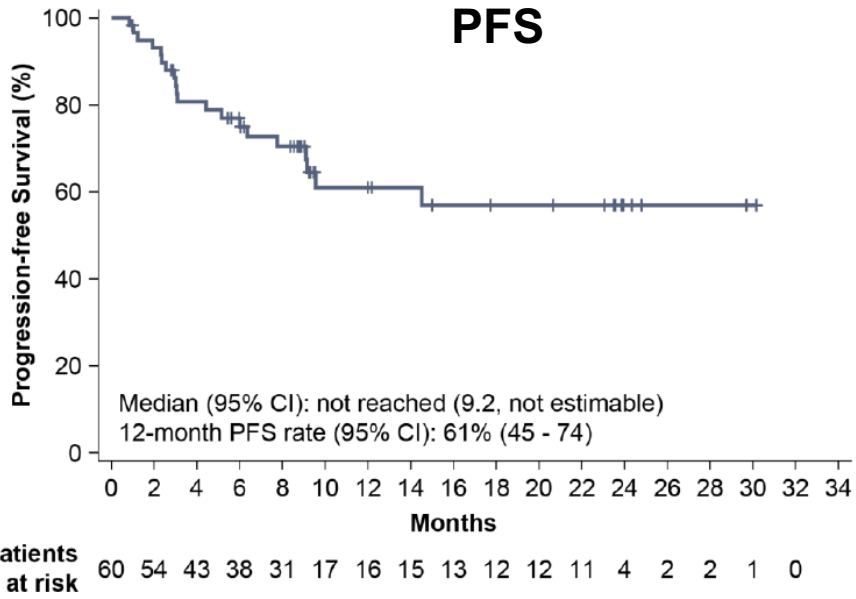


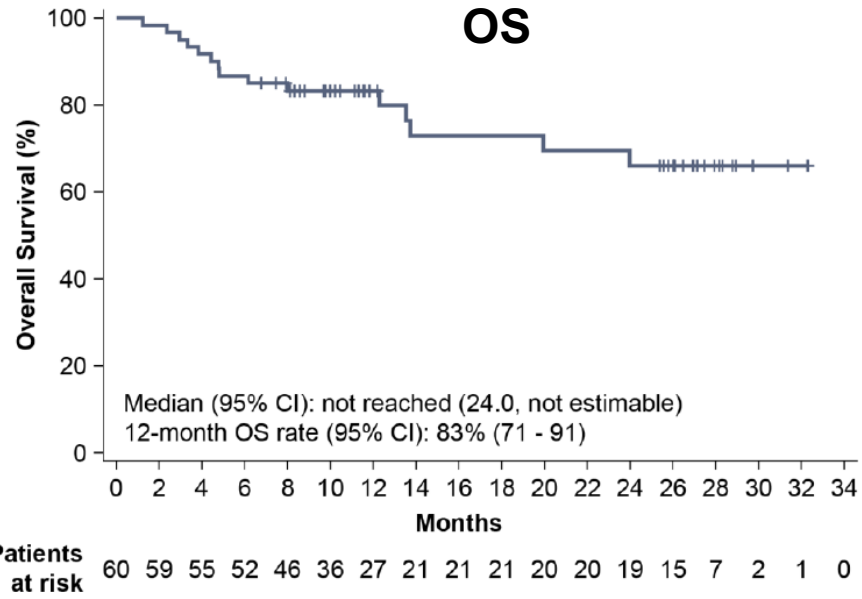
CR, complete response; MCL, mantle cell lymphoma; MIPI, MCL International Prognostic Index; ORR, objective response rate.

ZUMA-2: Survival

ASH 2019. Abs 754

- Median PFS and median OS were not reached after a median follow-up of 12.3 months





OS, overall survival; PFS, progression-free survival.

744 Brexucabtagene Autoleucel for Relapsed/Refractory Mantle Cell Lymphoma: Real World Experience from the US Lymphoma CAR T Consortium

Program: Oral and Poster Abstracts
Type: Oral
Session: 704. Cellular Immunotherapies: Cellular Therapies for Low and High Grade Lymphomas
Hematology Disease Topics & Pathways:
Biological, Lymphomas, Non-Hodgkin Lymphoma, Clinical Research, B Cell Lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, Real World Evidence, Therapies, Lymphoid Malignancies

Monday, December 13, 2021: 4:00 PM

- Retrospective, 14 centers
- Pts who underwent leukapheresis by 6/15/2021 with an intent to manufacture Brexu-cel were included
  - 107 underwent leukapheresis, **93** (87%) completed brexu-cel infusion
  - Median age 67 yrs and 81% male; 32% high-risk simplified MIPI
  - 45% had blastoid or pleomorphic variant

Table 2. Objective response to brexu-cel

	Response at day 30	Response at 3-month
Total evaluable[1]	81	54
Complete response	52 (64%)	34 (63%)
Partial response	18 (22%)	2 (4%)
Stable disease	2 (2%)	1 (2%)
Progressive disease	4 (5%)	9 (17%)
Death[2]	3 (4%)	6 (11%)
Missing[2]	2 (3%)	2 (4%)

CRS= 88% (8% grade ≥3)
ICANS=58% (33% grade ≥3)

Axicabtagene ciloleucel in relapsed or refractory indolent non-Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial

Caron A Jacobson, Julio C Chavez, Alison R Sehgal, Basem M William, Javier Munoz, Gilles Salles, Pashna N Munshi, Carla Casulo, David G Maloney, Sven de Vos, Ran Reshef, Lori A Leslie, Ibrahim Yakoub-Agha, Olalekan O Oluwole, Henry Chi Hang Fung, Joseph Rosenblatt, John M Rossi, Lovely Goyal, Vicki Plaks, Yin Yang, Remus Vezan, Mauro P Avanzi, Sattva S Neelapu

	Patients with follicular lymphoma (n=124)	Patients with marginal zone lymphoma (n=24)	All patients (N=148)
Age, years			
Median	60 (53–67)	65 (61–72)	61 (53–68)
≥65	38 (31%)	13 (54%)	51 (34%)
Sex			
Female	51 (41%)	13 (54%)	64 (43%)
Male	73 (59%)	11 (46%)	84 (57%)
Race			
Asian	2 (2%)	0	2 (1%)
Black or African American	4 (3%)	1 (4%)	5 (3%)
White	115 (93%)	22 (92%)	137 (93%)
Other or missing	3 (3%)	1 (4%)	4 (3%)
Ethnicity			
Hispanic or Latino	6 (5%)	2 (8%)	8 (5%)
Not Hispanic or Latino	118 (95%)	21 (88%)	139 (94%)
Missing	0	1 (4%)	1 (1%)
Follicular lymphoma histological category			
Grade 1	33 (27%)	NA	NA
Grade 2	61 (49%)	NA	NA
Grade 3a	30 (24%)	NA	NA
Marginal zone lymphoma histological category			
Nodal	NA	7 (29%)	NA
Extranodal	NA	17 (71%)	NA
ECOG performance status			
0	78 (63%)	14 (58%)	92 (62%)
1	46 (37%)	10 (42%)	56 (38%)
Disease stage			
Stage I–II	18 (15%)	2 (8%)	20 (14%)
Stage III	45 (36%)	3 (13%)	48 (32%)
Stage IV	61 (49%)	19 (79%)	80 (54%)
Follicular Lymphoma International Prognostic Index			
Low risk (0–1)	22 (18%)	NA	NA
Intermediate risk (2)	48 (39%)	NA	NA
High risk (≥3)	54 (44%)	NA	NA
High tumour bulk (GELF criteria)*	64 (52%)	10 (42%)	74 (50%)
Sum of product diameters, mm²	2790 (1443–4936)	1720 (861–3348)	2723 (1391–4219)

(Table 1 continues in next column)

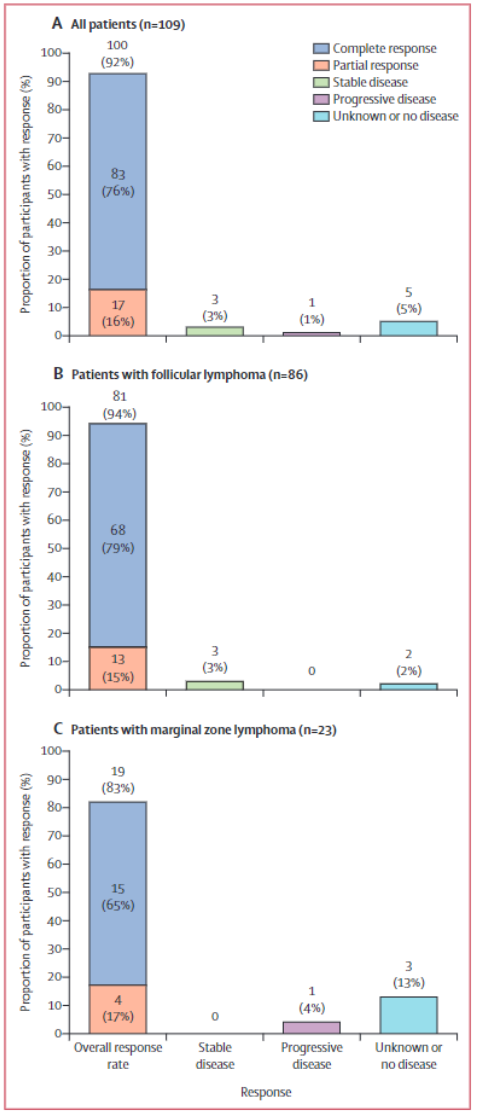
	Patients with follicular lymphoma (n=124)	Patients with marginal zone lymphoma (n=24)	All patients (N=148)
(Continued from previous column)			
Previous lines of therapy			
Median†	3 (2–4)	3 (2–5)	3 (2–4)
≥3 previous lines of therapy	78 (63%)	16 (67%)	94 (64%)
Previous PI3K inhibitor	34 (27%)	9 (38%)	43 (29%)
Previous autologous stem-cell transplantation	30 (24%)	3 (13%)	33 (22%)
Previous anti-CD20 mAb and alkylating agent	123 (99%)	23 (96%)	146 (99%)
Previous anti-CD20 mAb single agent	39 (31%)	10 (42%)	49 (33%)
Previous alkylating single agent	16 (13%)	6 (25%)	22 (15%)
Previous lenalidomide	38 (31%)	8 (33%)	46 (31%)
Relapsed or refractory subgroup‡			
Refractory to last previous therapy	84 (68%)	18 (75%)	102 (69%)
POD24 from initiating first anti-CD20 mAb-containing therapy§	68 (55%)	13 (57%)	81 (55%)
Positive CD19 status¶	93/103 (90%)	15/16 (94%)	108/119 (91%)
Lymphoma present in bone marrow‖	33 (27%)	11 (46%)	44 (30%)

1ry endpoint: ORR by IRRC

Median F/U=17.5 months

Median PFS= Not reached for FL; 12 months for MZL

Median OS= Not reached for FL and MZL



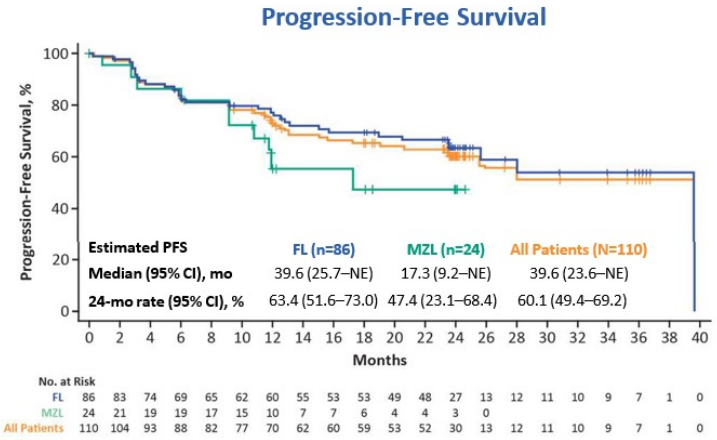
Jacobson CA, et al. Lancet Oncol. 2022 Jan;23(1):91-103

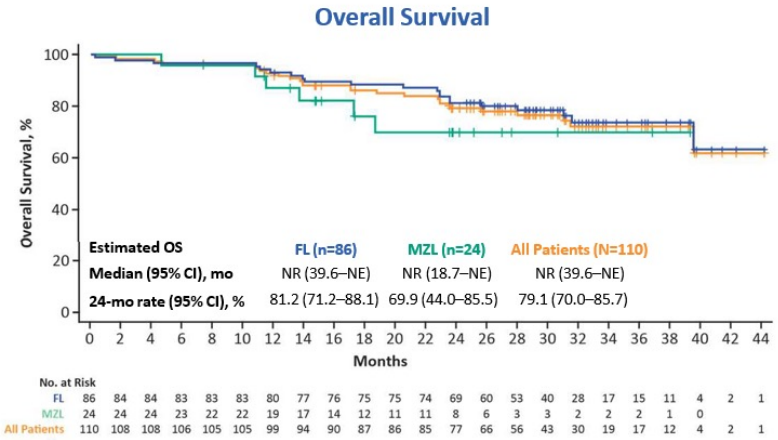
93 Long-Term Follow-up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL)

Program: Oral and Poster Abstracts
Type: Oral
Session: 704. Cellular Immunotherapies: Cellular Therapies for Lymphomas
Hematology Disease Topics & Pathways:
Clinical Trials, Biological, Adults, Lymphomas, Non-Hodgkin Lymphoma, Clinical Research, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Clinically Relevant, Diseases, Indolent Lymphoma, Therapies, Lymphoid Malignancies, Study Population

- With long-term F/U in ZUMA-5, axi-cel showed continued benefit in pts with iNHL
- In FL, high response rates translated to durability, with a median DOR of **38.6 months** and 57% of eligible pts in ongoing response at data cutoff
- In MZL, outcomes improved with longer F/U, with median DOR and OS not reached

PFS and OS





- Median OS was not yet reached in efficacy-eligible patients with FL or MZL
- Among patients with FL, 3 deaths occurred after Month 24[a]; no disease progression events occurred after Month 24

[a] Of the 3 deaths, 2 were from COVID-19 and 1 was from sepsis.
FL, follicular lymphoma; MZL, marginal zone lymphoma; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

Neelapu SS, et al. ASH 2021; Abs 93

93 Long-Term Follow-up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL)

Program: Oral and Poster Abstracts
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Session: 704. Cellular Immunotherapies: Cellular Therapies for Lymphomas
Hematology Disease Topics & Pathways:
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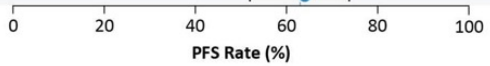
PFS Rate at 24 Months in Key FL Subgroups

		No. of Patients	No. of Patients At Risk	PFS Rate (95% CI)
Overall		86	27	63 (52–73)
Age, years	<65	55	17	65 (50–76)
	≥65	31	10	61 (41–77)
Sex	Male	48	13	59 (43–72)
	Female	38	14	69 (51–82)
ECOG performance status	0	51	17	67 (52–79)
	1	35	10	56 (36–72)
High tumor burden (GELF criteria)	Yes	42	10	55 (37–69)
	No	44	17	71 (55–83)
Relapse/refractory subgroup	Relapsed	23	8	73 (49–87)
	Refractory	63	19	60 (46–72)
Number of prior lines of therapy	2	26	11	73 (51–86)
	3	20	3	45 (22–66)
	≥4	40	13	66 (48–79)
Prior stem cell transplantation	Yes	21	7	85 (61–95)
	No	65	20	56 (42–68)
Prior lenalidomide	Yes	27	6	58 (36–75)
	No	59	21	66 (51–77)
Prior PI3K inhibitor	Yes	28	9	56 (35–73)
	No	58	18	67 (53–78)
Prior BTK inhibitor	Yes	6	2	50 (11–80)
	No	80	25	64 (52–74)



- Long-term PFS rates in patients with FL were generally consistent among key subgroups

BTK, Bruton tyrosine kinase; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; FL, follicular lymphoma GELF, Groupe d'Etude des Lymphomes Folliculaires; PI3K, phosphoinositide 3-kinase; PFS, progression-free survival.

nature medicine

ARTICLES

https://doi.org/10.1038/s41591-021-01622-0

Check for updates

Tisagenlecleucel in adult relapsed or refractory follicular lymphoma: the phase 2 ELARA trial

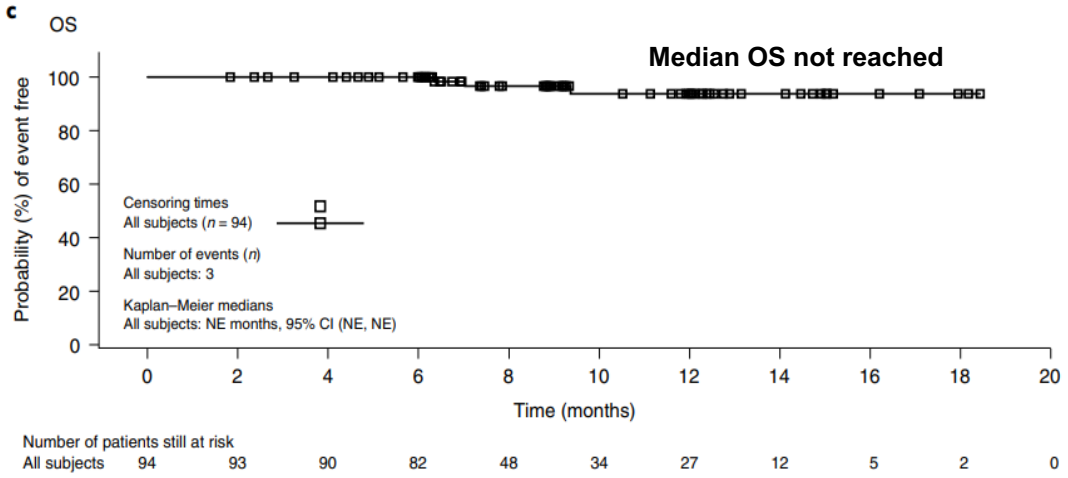
Nathan Hale Fowler[1,2]✉, Michael Dickinson[3], Martin Dreyling[4], Joaquin Martinez-Lopez[5], Arne Kolstad[6], Jason Butler[7], Monalisa Ghosh[8], Leslie Popplewell[9], Julio C. Chavez[10], Emmanuel Bachy[11], Koji Kato[12], Hideo Harigae[13], Marie José Kersten[14], Charalambos Andreadis[15], Peter A. Riedell[16], P. Joy Ho[17], José Antonio Pérez-Simón[18], Andy I. Chen[19], Loretta J. Nastoupil[1], Bastian von Tresckow[20,21], Andrés José María Ferreri[22], Takanori Teshima[23], Piers E. M. Patten[24,25], Joseph P. McGuirk[26], Andreas L. Petzer[27], Fritz Offner[28], Andreas Viardot[29], Pier Luigi Zinzani[30,31], Ram Malladi[32], Aiesha Zia[33], Rakesh Awasthi[34], Aisha Masood[35], Oezlem Anak[33], Stephen J. Schuster[36,38] and Catherine Thieblemont[37,38]

Table 2 | Best overall response in the EAS and per-protocol population[a]

Parameter	Per-protocol set, $n = 85$		EAS, $n = 94$	
	Local assessment	IRC assessment	Local assessment	IRC assessment
Best overall response, *n* (%)				
CR	64 (75.3); 95% CI, 64.7–84.0	62 (72.9); 95% CI, 62.2–82.0	68 (72.3); 95% CI, 62.2–81.1	65 (69.1); 95% CI, 58.5–78.3
PR	14 (16.5)	12 (14.1)	17 (18.1)	16 (17.0)
SD	2 (2.4)	3 (3.5)	3 (3.2)	3 (3.2)
PD	5 (5.9)	8 (9.4)	6 (6.4)	9 (9.6)
UNK				1 (1.1)
Overall response rate (CR + PR), *n* (%)	78 (91.8); 95% CI, 83.8–96.6	74 (87.1); 95% CI, 78.0–93.4	85 (90.4); 95% CI, 82.6–95.5	81 (86.2); 95% CI, 77.5–92.4

[a]The per-protocol set is a subset of patients in the primary analysis efficacy set with no major protocol deviations. UNK, unknown.

N=97
Median prior therapies of 4 (2-13)
FLIPI high >3=59.8%
Median F/U 9.9 months



Events, n (%)	Infused patients N=97
CRS	47 (48.5)
Grade 1 or 2	47 (48.5)
Grade ≥3	0
In patients with CRS (n=47)	
Tocilizumab use during CRS	16 (34.0)
1 dose	8 (17.0)
2 doses	5 (10.6)
3 doses	3 (6.4)
Corticosteroids	3 (6.4)
Median time to onset, days (IQR)	4.0 (2–7)
Admitted to ICU, n (%)	4 (8.5)
Median total duration of ICU stay during CRS, days (range)	4.0 (2.5–5)
Patients with resolved events, n (%)	47 (100)

Extended Data Fig. 1 | Cytokine release syndrome within 8 weeks of tisagenlecleucel infusion. CRS=cytokine release syndrome; ICU=intensive care unit; IQR=interquartile range. Column titles are bolded for clarity.

Events, n (%)	Treated patients N=97 All Grades	Grade ≥3
Number of patients with at least one event	36 (37.1)	3 (3.1)
Headache	23 (23.7)	1 (1.0)
Dizziness	6 (6.2)	0
Encephalopathy	2 (2.1)	0
Immune effector cell-associated neurotoxicity syndrome	4 (4.1)	1 (1.0)
Paraesthesia	2 (2.1)	0
Tremor	2 (2.1)	0
Dyskinesia	1 (1.0)	0
Dysgeusia	1 (1.0)	0
Migraine	1 (1.0)	0
Peripheral sensory neuropathy	1 (1.0)	0
Syncope	1 (1.0)	1 (1.0)

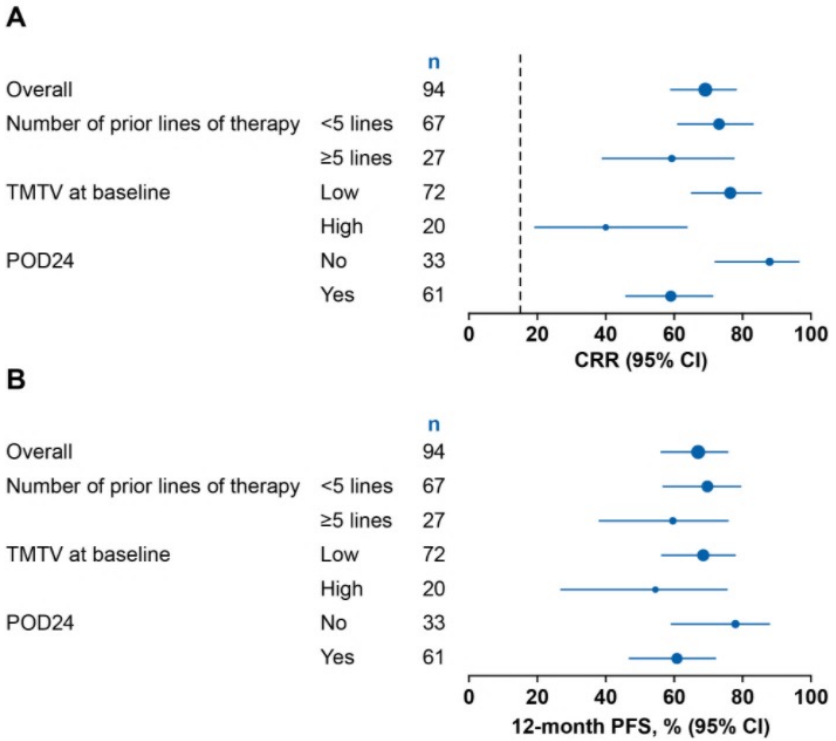
Extended Data Fig. 3 | Neurological events within 8 weeks of tisagenlecleucel infusion. [a]G4 ICANS: Onset D10, recovered - Related to tisagenlecleucel. Patient presenting with tremors, then seizures, with concomitant HHV6 positivity on CSF. The event fully recovered after high-dose MPD and GCV. CSF=cerebrospinal fluid; GCV=ganciclovir; ICANS=immune effector cell-associated neurotoxicity syndrome; HHV6, Human Herpesvirus 6; MPD=methylprednisolone. Column titles are bolded for clarity.

131 Efficacy of Tisagenlecleucel in Adult Patients (Pts) with High-Risk Relapsed/Refractory Follicular Lymphoma (r/r FL): Subgroup Analysis of the Phase II Elara Study

Program: Oral and Poster Abstracts
Type: Oral
Session: 623. Mantle Cell, Follicular, and Other B-Cell Lymphomas: Clinical and Epidemiological: Evolution of Immunotherapeutic Regimens in B-cell Lymphomas
Hematology Disease Topics & Pathways:
Biological, Clinical Trials, Adults, Lymphomas, B Cell Lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Clinical Research, Clinically Relevant, Diseases, Therapies, Lymphoid Malignancies, Study Population

Saturday, December 11, 2021: 1:00 PM

Catherine Thieblemont, MD, PhD[1], *Michael Dickinson, MBBS*[2], *Joaquin Martinez-Lopez, MD, PhD*[3,v], *Arne Kolstad, MD, PhD*[4,v], *Jason P Butler, MBBS, MMedSc*[5], *Monalisa Ghosh, MD*[6], *Leslie L. Popplewell, MD, FACP*[7], *Julio C. Chavez, MD, MS*[8,v], *Emmanuel Bachy, MD, PhD*[9,v], *Koji Kato, MD, PhD*[10], *Hideo Harigae, MD, PhD*[11], *Marie Jose Kersten, MD, PhD*[12], *Charalambos Andreadis, MD, MSCE*[13,v], *Peter A. Riedell, MD*[14], *P. Joy Ho, MBBS*[15,v], *Jose Pérez-Simón, MD*[16], *Andy Chen, MD, PhD*[17], *Loretta Nastoupil, MD*[18], *Bastian Von Tresckow, MD*[19,v], *Andres JM Ferreri, MD*[20], *Takanori Teshima*[21], *Piers EM Patten, MB, ChB, FRCP, FRCPath, PhD*[22], *Joseph P. McGuirk, DO*[23], *Andreas Petzer, MD*[24,v], *Fritz Offner, MD, PhD*[25], *Andreas Viardot, MD*[26], *Pier Luigi Zinzani, MD, PhD*[27], *Ram Malladi, MD*[28,v], *Aiesha Zia*[29,v], *C Lobetti Bodoni, MD, PhD*[29,v], *Aisha Masood, MD*[30], *Stephen J. Schuster, MD*[31], *Nathan H. Fowler, MD*[18] *and Martin H. Dreyling, MD, PhD*[32]



- With 17-mos median F/U, tisagenlecleucel yielded high ORR and CRR and durable response and promising 12-mo PFS in R/R FL and 2+ prior therapies
- Safety consistent with known tisagenlecleucel profile
- **POD24** and **high TMTV** were independently associated with PFS
- Tisagenlecleucel induces high rates of durable response, including in high-risk subgroups, who have poor prognosis with non-CAR-T cell therapies

POD24: Progression of disease within 2 years
TMTV: Total metabolic tumor volume (high defined as >510 cm^3)

Allogeneic CAR T cell therapy

ALPHA study

- Allogeneic (off the shelf) CAR T-cell therapy addresses several logistical challenges
  - Readily available
  - Uniform product quality
- **ALPHA**: phase 1, open-label, multicenter dose escalation study in R/R large B-cell or FL and ≥2 prior lines Rx
  - Lymphodepletion with Flu-CY
- 98% (46/47) of pts enrolled were treated in the single-dose (n=39) and consolidation cohort (n=7)
  - Median time from enrollment to LD was **5 days**
  - No dose-limiting toxicities (DLTs) or GVHD observed
  - **ORR and CR rates were 75% and 50%, respectively**
    - **DLBCL**: ORR=61.5%; CR=46.2%
    - **FL**:ORR=82.6%; CR=52.2%
  - Grade 1-2 CRS=21.7%; Grade 3=2.2%

Neelapu SS, ASH 2021; Abs 3878

Moving CAR T-cell therapy to 2nd line

- 3 randomized studies
  - **ZUMA-7:** Axi-cel vs. SOC
  - **TRANSFORM:** Liso-cel vs. SOC
  - **BELINDA:** Tisagenlecleucel vs. SOC

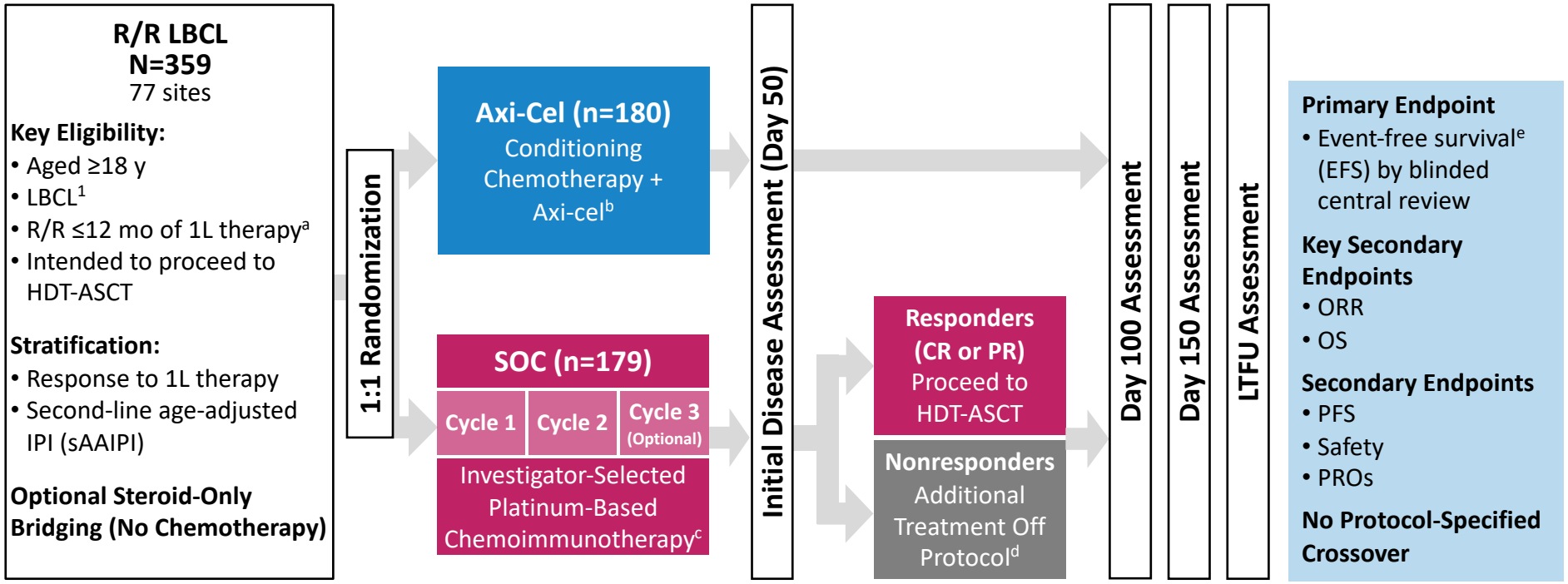
Primary Analysis of ZUMA-7: a Phase 3 Randomized Trial of Axicabtagene Ciloleucel versus Standard-of-Care Therapy in Patients with Relapsed/Refractory Large B-Cell Lymphoma

Frederick L. Locke, MD[1]; David B. Miklos, MD, PhD[2]; Caron A. Jacobson, MD, MMSc[3]; Miguel-Angel Perales, MD[4]; Marie José Kersten MD, PhD[5]; Olalekan O. Oluwole, MBBS, MPH[6]; Armin Ghobadi, MD[7]; Aaron P. Rapoport, MD[8]; Joseph P. McGuirk, DO[9]; John M. Pagel, MD, PhD[10]; Javier Muñoz, MD, MS, MBA, FACP[11]; Umar Farooq, MD[12]; Tom van Meerten, MD, PhD[13]; Patrick M. Reagan, MD[14]; Anna Sureda, MD, PhD[15]; Ian W. Flinn, MD, PhD[16]; Peter Vandenberghe, MD, PhD[17]; Kevin W. Song, MD, FRCPC[18]; Michael Dickinson, MBBS, D Med Sci, FRACP, FRCPA[19]; Monique C. Minnema, MD, PhD[20]; Peter A. Riedell, MD[21]; Lori A. Leslie, MD[22]; Sridhar Chaganti, MD[23]; Yin Yang, MS, MD[24]; Simone Filosto, PhD[24]; Marco Schupp, MD[24]; Christina To, MD[24]; Paul Cheng, MD, PhD[24]; Leo I. Gordon, MD[25]; and Jason R. Westin, MD, MS, FACP[26], on behalf of all ZUMA-7 investigators and contributing Kite members

[1]Moffitt Cancer Center, Tampa, FL, USA; [2]Stanford University School of Medicine, Stanford, CA, USA; [3]Dana-Farber Cancer Institute, Boston, MA, USA; [4]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [5]Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, on behalf of HOVON/LLPC; [6]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [7]Washington University School of Medicine, St Louis, MO, USA; [8]The Marlene and Stewart Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD, USA; [9]University of Kansas Cancer Center, Kansas City, KS, USA; [10]Swedish Cancer Institute, Seattle, WA, USA; [11]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [12]University of Iowa, Iowa City, IA, USA; [13]University Medical Center Groningen, Groningen, Netherlands, on behalf of HOVON/LLPC; [14]University of Rochester School of Medicine, Rochester, NY, USA; [15]Hematology Department, Institut Català d'Oncologia-Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain; [16]Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; [17]University Hospitals Leuven, Leuven, Belgium; [18]Division of Hematology, University of British Columbia and Leukemia/BMT Program of BC, Vancouver General Hospital, Vancouver, BC, Canada; [19]Peter MacCallum Cancer Centre, Royal Melbourne Hospital and the University of Melbourne, Melbourne, Victoria, Australia; [20]UMC, University of Utrecht, The Netherlands, on behalf of HOVON/LLPC; [21]The University of Chicago Medical Center, Chicago, IL, USA; [22]John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ, USA; [23]Centre for Clinical Haematology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [24]Kite, a Gilead Company, Santa Monica, CA, USA; [25]Northwestern University Feinberg School of Medicine and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL, USA; and [26]The University of Texas MD Anderson Cancer Center, Houston, TX, USA

ASH Plenary presentation: courtesy Dr. Frederick Locke

ZUMA-7 Study Schema and Endpoints: Axi-Cel Versus SOC as Second-Line Therapy in Patients With R/R LBCL

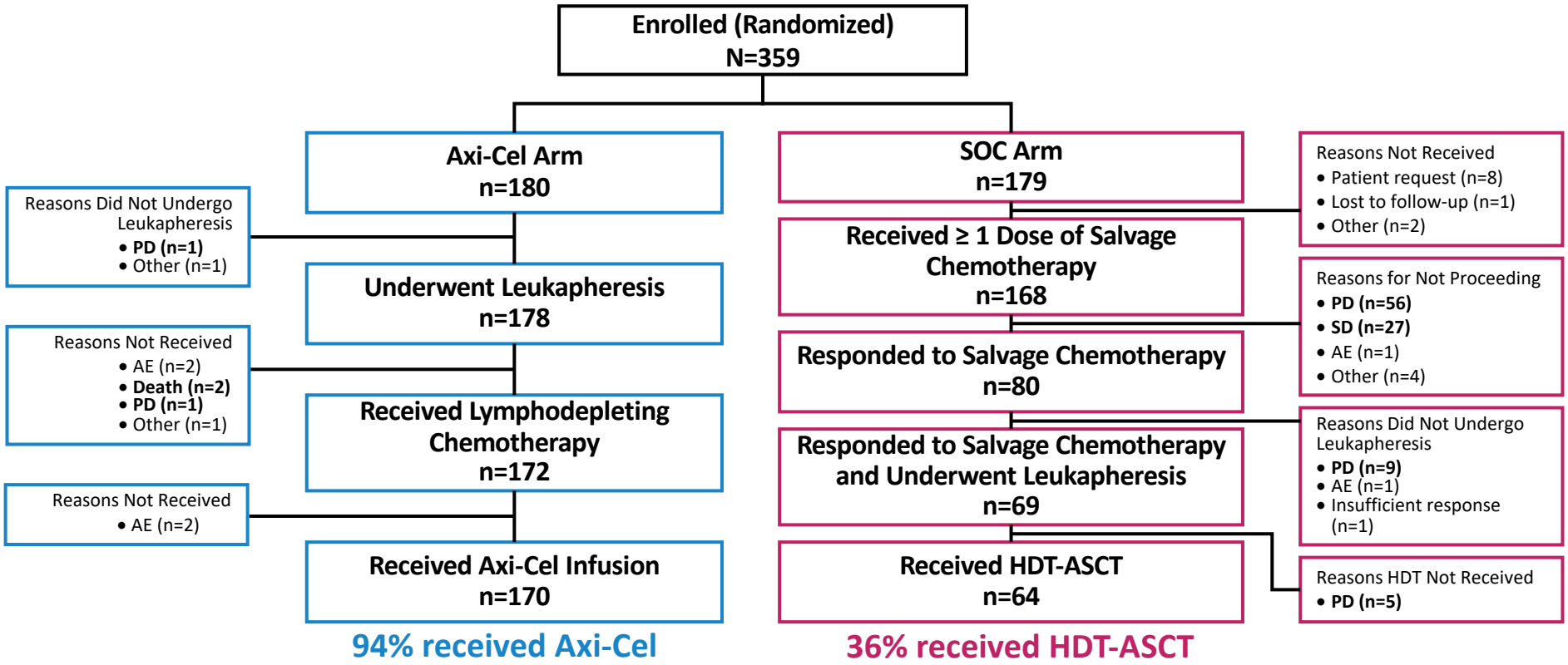


[a] Refractory disease was defined as no CR to 1L therapy; relapsed disease was defined as CR followed by biopsy-proven disease relapse ≤12 months from completion of 1L therapy. [b] Axi-cel patients underwent leukapheresis followed by conditioning chemotherapy with cyclophosphamide (500 mg/m^2/day) and fludarabine (30 mg/m^2/day) 5, 4, and 3 days before receiving a single axi-cel infusion (target intravenous dose, 2×10^6 CAR T cells/kg). [c] Protocol-defined SOC regimens included R-GDP, R-DHAP, R-ICE, or R-ESHAP. [d] 56% of patients received subsequent cellular immunotherapy. [e] EFS was defined as time from randomization to the earliest date of disease progression per Lugano Classification,[2] commencement of new lymphoma therapy, or death from any cause.

1. Swerdlow SH, et al. *Blood.* 2016;127:2375-2390. 2. Cheson BD, et al. *J Clin Oncol.* 2014;32:3059-3068.

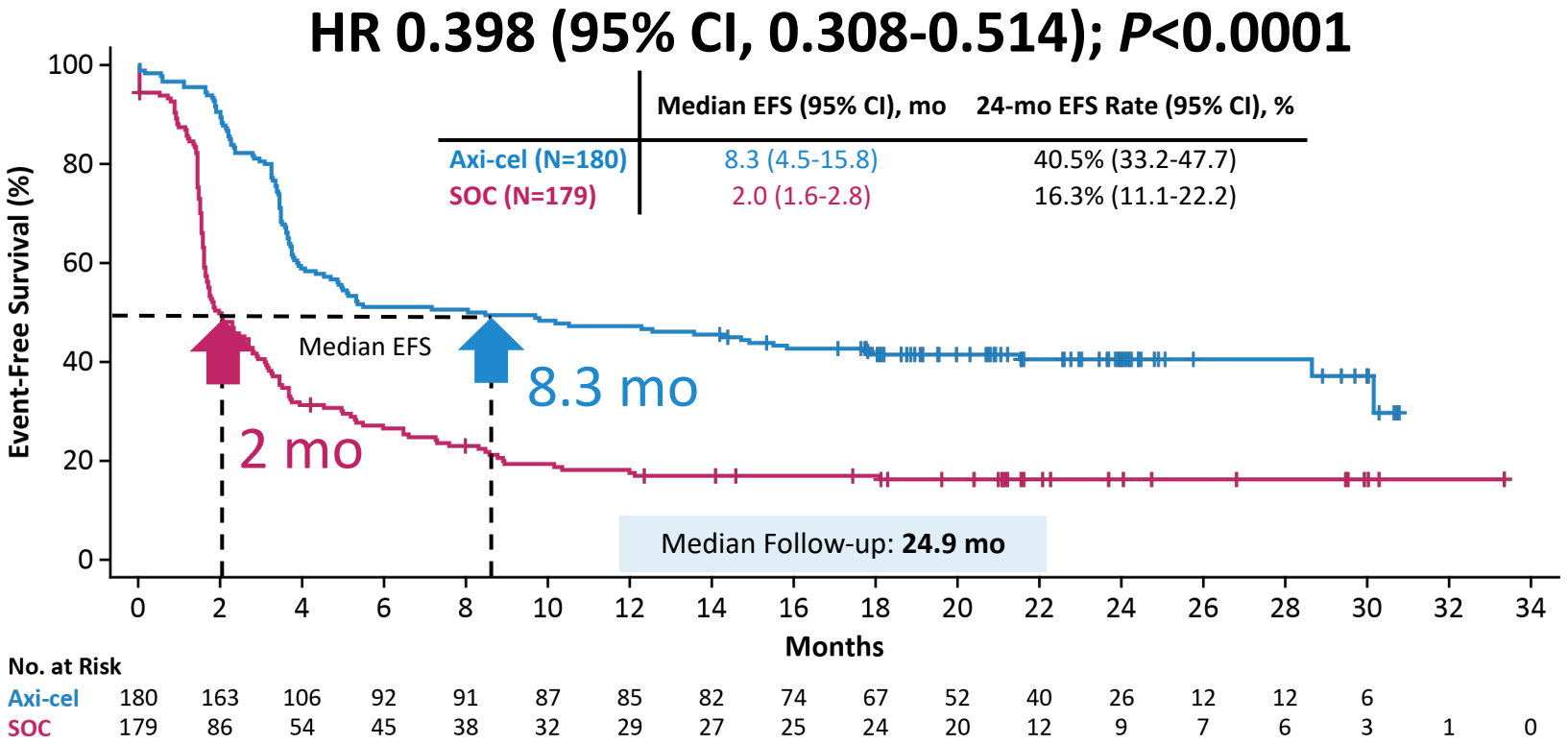
ASH Plenary presentation: courtesy Dr. Frederick Locke

Patient Disposition: Nearly 3× as Many Axi-Cel Patients Received Definitive Therapy Versus SOC Patients



ASH Plenary presentation: courtesy Dr. Frederick Locke

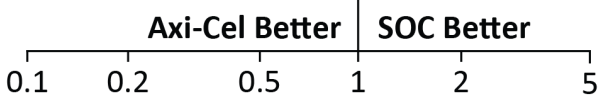
Primary EFS Endpoint: Axi-Cel Is Superior to SOC



ASH Plenary presentation: courtesy Dr. Frederick Locke

EFS Improvements With Axi-Cel Versus SOC Were Consistent Among Key Patient Subgroups

	Axi-Cel EFS Event/N	SOC EFS Event/N	HR (95% CI)
Overall	108/180	144/179	0.398 (0.308-0.514)
Age, years			
<65	81/129	96/121	0.490 (0.361-0.666)
≥65	27/51	48/58	0.276 (0.164-0.465)
Response to 1L therapy at randomization			
Primary refractory	85/133	106/131	0.426 (0.319-0.570)
Relapse ≤12 months of 1L therapy	23/47	38/48	0.342 (0.202-0.579)
sAAIPI			
0-1	54/98	73/100	0.407 (0.285-0.582)
2-3	54/82	71/79	0.388 (0.269-0.561)
Prognostic marker per central laboratory			
HGBL-double/triple hit	15/31	21/25	0.285 (0.137-0.593)
Double expressor lymphoma	35/57	50/62	0.424 (0.268-0.671)



ASH Plenary presentation: courtesy Dr. Frederick Locke

Characteristics of patients enrolled second line CAR T cell therapy trials

	ZUMA-7 N=180	TRANSFORM N=184	BELINDA N=322
CAR T product	Axicabtagene Ciloleucel	Lisocabtagene Maraleucel	Tisagenlecleucel
Signaling domain	CD28 	4-1BB 	4-1BB 
Median age, years (range)	58 (21–80)	58 (26-75)	59.5 (19–79)
Patients >65 years, %	30%	NR	31.10%
Patients who received TT			
CAR T arm, %	94%	97%	96%
SOC arm, %	**36%**	**46%**	**32%**
HGBCL/double/triple hit, (CART/SOC), %	17/15%	23/24%	19.8/11.9%
ABC subtype, (CAR T/SOC), %	9/5%	N/A	32/26.2%
Stage III/IV, %	79%	N/A	64%
Primary refractory	74%	73%	66%
Relapse within 12 months of first-line treatment	26%	27%	34%
Progressive disease at time of CAR T cell	1%	N/A	**26%**
Bridging therapy allowed	**No**	Yes	Optional
Bridging options	**Glucocorticoid only**	**RDHAP, RICE, and RGDP x1 cycle**	**RDHAP, RICE, RGemOx, and RGDP**
%	**36%**	**63%**	**83%**
Median time from leukapheresis to CAR T cell infusion, days	29	31	**54**
Crossover	**Not allowed** **Patients who did not respond to SOC received CAR T**	**Allowed**	**Allowed**
Primary endpoints	EFS	EFS	EFS
EFS, start time point	Randomization	Randomization	Randomization
EFS definition	1) Disease progression 2) Death from any cause 3) New therapy started 4) SD as best response within 150 days from randomization	1) Disease progression 2) Death from any cause 3) New therapy started 4) Not achieving CR/PR by 9-weeks	1) SD or PD at or after week 12 2) Death (any time)

Summary of responses and adverse events in ZUMA-7, TRANSFORM, and BELINDA trials

	ZUMA-7					TRANSFORM N=184					BELINDA N=322				
	CAR T arm (N=180)	SOC arm (N=179)	HR	95% CI	P-value	CAR T arm (N=92)	SOC arm (N=92)	HR	95% CI	P-value	CAR T arm (N=162)	SOC arm (N=160)	HR	95% CI	P-value
Median follow up, months	25					6.2					10				
ORR	83%	50%			<0.001	86%	48%			<0.0001	**46%**	42%			
CR rate	65%	32%				66%	39%			<0.0001	**28%**	28%			
mEFS, months	8.3	2	0.4	0.31-0.51	<0.001	10.1	2.3	0.349		<0.0001	**3**	**3**	**1.07**	**0.82-1.40**	**0.61**
2-year OS, %	61%	52%				N/A					Not reached				
mOS, months	NR	32.1	0.73	0.53-1.01	0.054	NR	16.4	0.509	0.258-1.004	P=0.0257	NR	NR			
CRS, any grade	92%					49%					61.30%				
CRS, grade 3-4	6%					1 patient					5.20%				
NE, any grade	60%	20%				12%					10.30%				
NE, grade 3-4	21%	1%				4%					1.90%				

Hematological ONCOLOGY

LETTER TO THE EDITOR

Comparing apples and oranges: The ZUMA-7, TRANSFORM and BELINDA trials

Côme Bommier, Jérôme Lambert, Catherine Thieblemont

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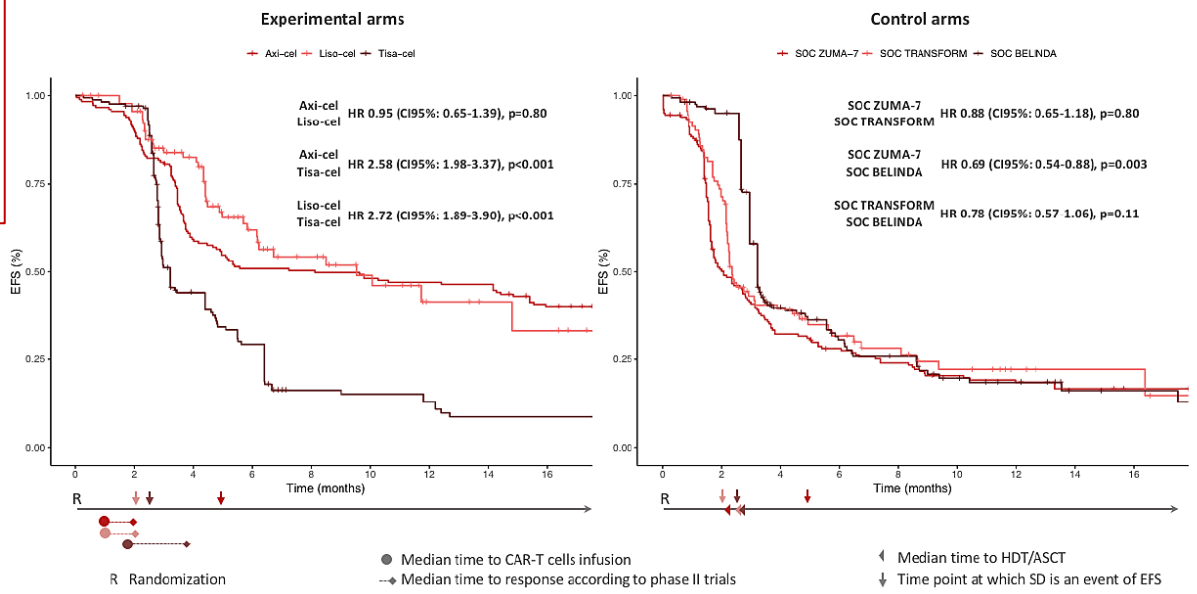
Reconstructed EFS curves



Bommier C, et al. Hematol Oncol. 2022 online ahead of print

Take home messages

- CAR-T definitely revolutionized Rx of DLBCL, MCL, and FL. Here to stay!

- In relapsed/refractory DLBCL, 5-year OS ≥ 40%
  - For patients in CR, 5-year OS=64.4%
- Now approved in 2nd line: axi-cel

- Responses remain sustained in MCL and FL, but longer F/U is needed

- Allogeneic CAR T cells showing promise
  - Advantage: no waiting time. Would it lower the cost?

Thank you

