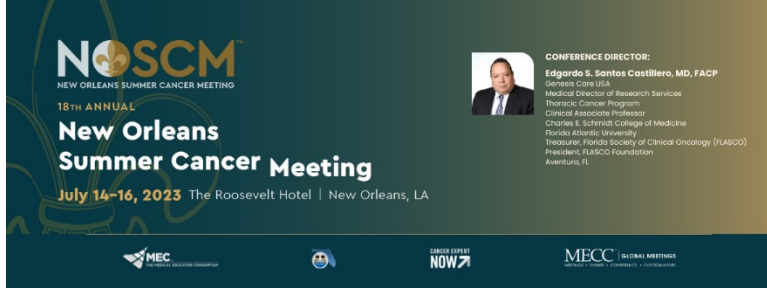



MAYO CLINIC

# Redefining treatment algorithms in B-cell lymphomas: a focus on CAR T-cell therapy

**Mohamed A. Kharfan-Dabaja, MD, MBA, FACP**
**Professor of Medicine**
**Vice-Chair, Hematology**
**Director, Blood and Marrow Transplantation and Cellular Therapies**

**New Orleans, LA**
**July 16, 2023**

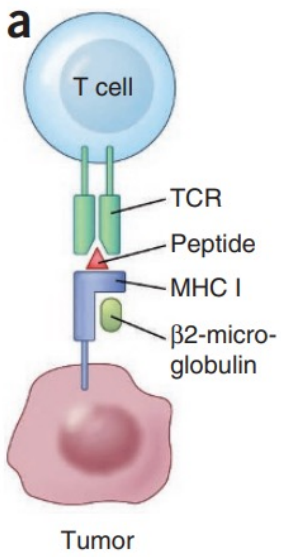
# Outline

- **Diffuse large B-cell lymphoma**
  - 3rd line and beyond (ZUMA 1, JULIET, TRANSCEND NHL 001)
  - 2nd line (ZUMA 7, TRANSFORM)
  - Proposed algorithm
- **Mantle cell lymphoma**
  - ZUMA 2
- **Follicular lymphoma**
  - ZUMA 5
  - ELIANA
- Take home messages

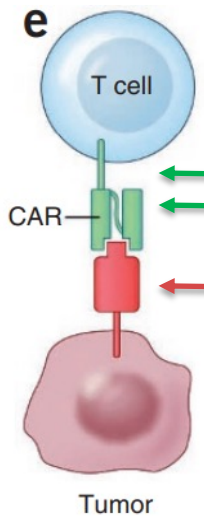
# What is CAR T-cell therapy?

- Stands for Chimeric Antigen Receptor T-cell Therapy
- Immunotherapy that uses engineered T lymphocytes to specifically target the intended cancer cell

**Normal T-cell**




**CAR T-cell**




Signaling domain
Antigen recognition domain
Target antigen

CD19: B-cell lymphoma/ALL
BCMA: Multiple myeloma
FDA approved

CAR T-cell benefits
- Localization
- Cytotoxic killing
- Expansion
- Persistence

*Adapted and modified from Hinrichs CS & Restifo NP. Nat Biotechnol. 2013; 31(11):999-1008*

# Indications for CAR T-cell therapy in lymphomas

| | Large B-cell lymphoma (de novo or transformed) | | Primary mediastinal B cell lymphoma | Mantle cell lymphoma | Follicular lymphoma |
|---|---|---|---|---|---|
| | 2nd line | >2nd line | >2nd line | Relapsed/refractory | >2nd line |
| **Axicabtagene ciloleucel** | Yes | Yes | Yes | - | Yes |
| **Tisagenlecleucel** | No | Yes | Not included in JULIET study | - | Yes |
| **Lisocabtagene maraleucel** | Yes | Yes | Yes | - | Grade 3b included in TRANSCEND NHL 001 study |
| **Brexucabtagene autoleucel** | - | - | - | Yes | - |


*Neelapu SS, et al. N Engl J Med. 2017; 377:2531-44*
*Locke FL, et al. N Engl J Med. 2022;386(7):640-654*
*Schuster SJ, et al. N Engl J Med. 2019; 380:45-56*
*Abramson JS, et al. Lancet. 2020; 396;839-52*
*Kamdar M, et al. Lancet 2022; 399: 2294–308*
*Wang M, et al. NEJM. 2020. 382:1331*

# 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

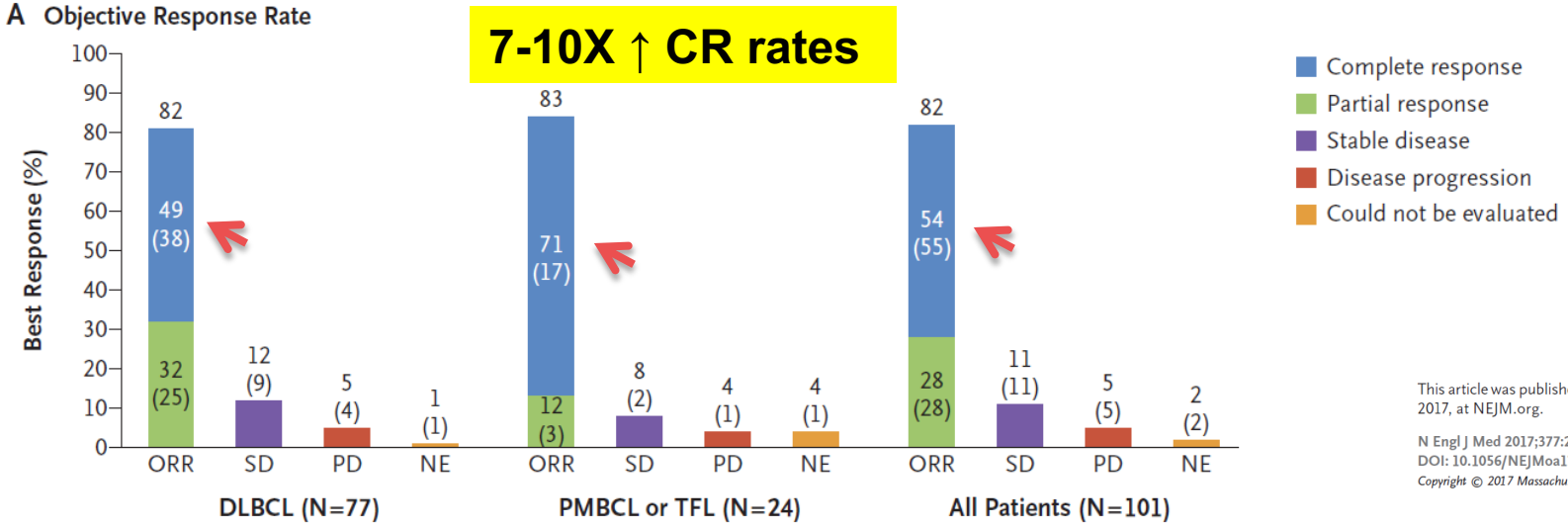
Table 2. Rate of response to chemotherapy after refractory disease

| | 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: 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


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

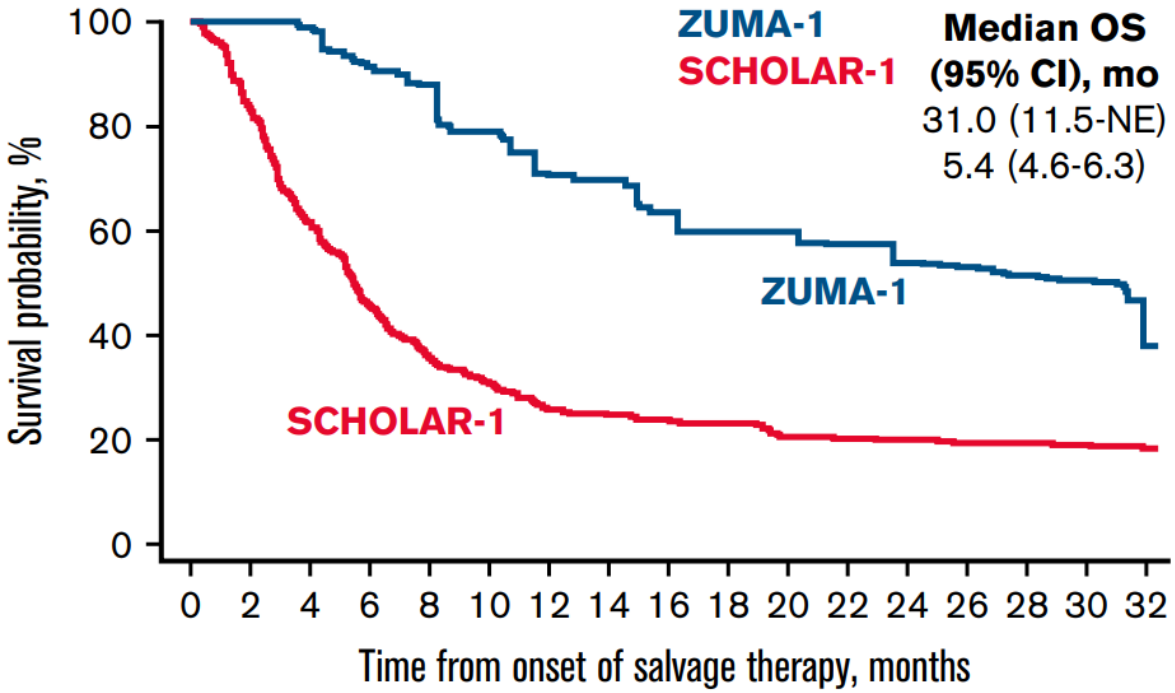
REGULAR ARTICLE

blood advances

# Comparison of 2-year outcomes with CAR T cells (ZUMA-1) vs salvage chemotherapy in refractory large B-cell lymphoma

Sattva S. Neelapu,[1] Frederick L. Locke,[2] Nancy L. Bartlett,[3] Lazaros J. Lekakis,[4] Patrick M. Reagan,[5] David B. Miklos,[6] Caron A. Jacobson,[7] Ira Braunschweig,[8] Olalekan O. Oluwole,[9] Tanya Siddiqi,[10] Yi Lin,[11] Michael Crump,[12] John Kuruvilla,[13] Eric Van Den Neste,[14] Umar Farooq,[15] Lynn Navale,[16] Venita DePuy,[17] Jenny J. Kim,[16] and Christian Gisselbrecht[18]

[1]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Department of Blood and Marrow Transplant and Cellular Immunotherapy, Moffitt Cancer Center, Tampa, FL; [3]Siteman Cancer Center, Washington University Medical School, St Louis, MO; [4]Sylvester Comprehensive Care Center, University of Miami Health System, Miami, FL; [5]James P. Wilmot Cancer Institute, University of Rochester School of Medicine, Rochester, NY; [6]Department of Medicine - Blood and Marrow Transplantation, Stanford University School of Medicine, Stanford, CA; [7]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA; [8]Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY; [9]Division of Hematology/Oncology, Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN; [10]Department of Hematology and Hematopoietic Cell Transplantation, City of Hope National Medical Center, Duarte, CA; [11]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN; [12]Canadian Cancer Trials Group, Queen's University, Kingston, ON, Canada; [13]Princess Margaret Cancer Center, Toronto, ON, Canada; [14]Department of Hematology, Cliniques Universitaires UCL Saint-Luc, Brussels, Belgium; [15]Division of Hematology, Oncology, and Blood and Marrow Transplantation, Department of Internal Medicine, University of Iowa, Iowa City, IA; [16]Kite, a Gilead Company, Santa Monica, CA; [17]Bowden Analytics, Raleigh, NC; and [18]Hôpital Saint Louis, Paris, France



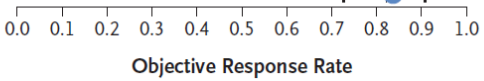

Treatment difference

**HR=0.27 (95%CI=0.00-0.38)**

73% reduction in risk of death

**B** Subgroup Analysis

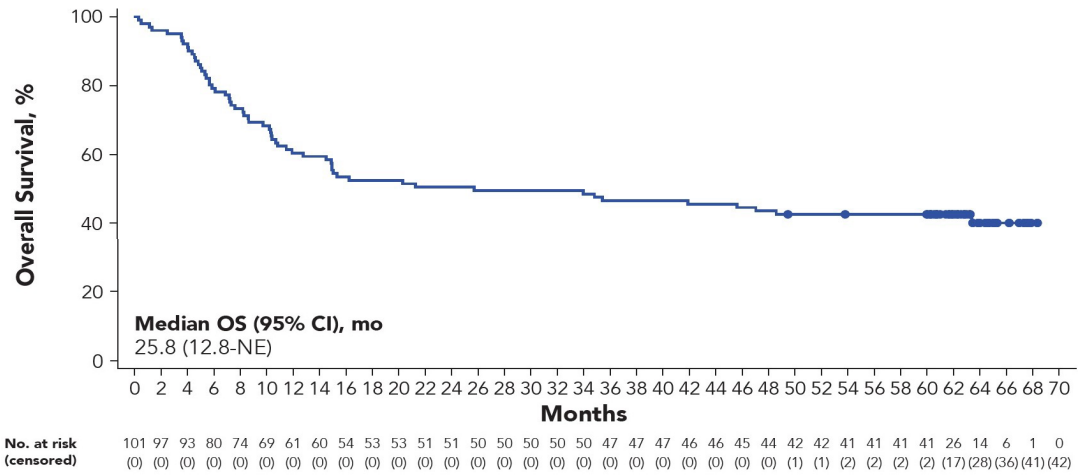
| Subgroup | No. of Patients Who Could Be Evaluated | No. of Patients with Event | Objective Response Rate (95% CI) |
|---|---|---|---|
| Overall | 101 | 83 | 0.82 (0.73–0.89) |
| Refractory subgroup | | | |
| Refractory to ≥second-line therapy | 78 | 65 | 0.83 (0.73–0.91) |
| Relapse after ASCT | 21 | 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:

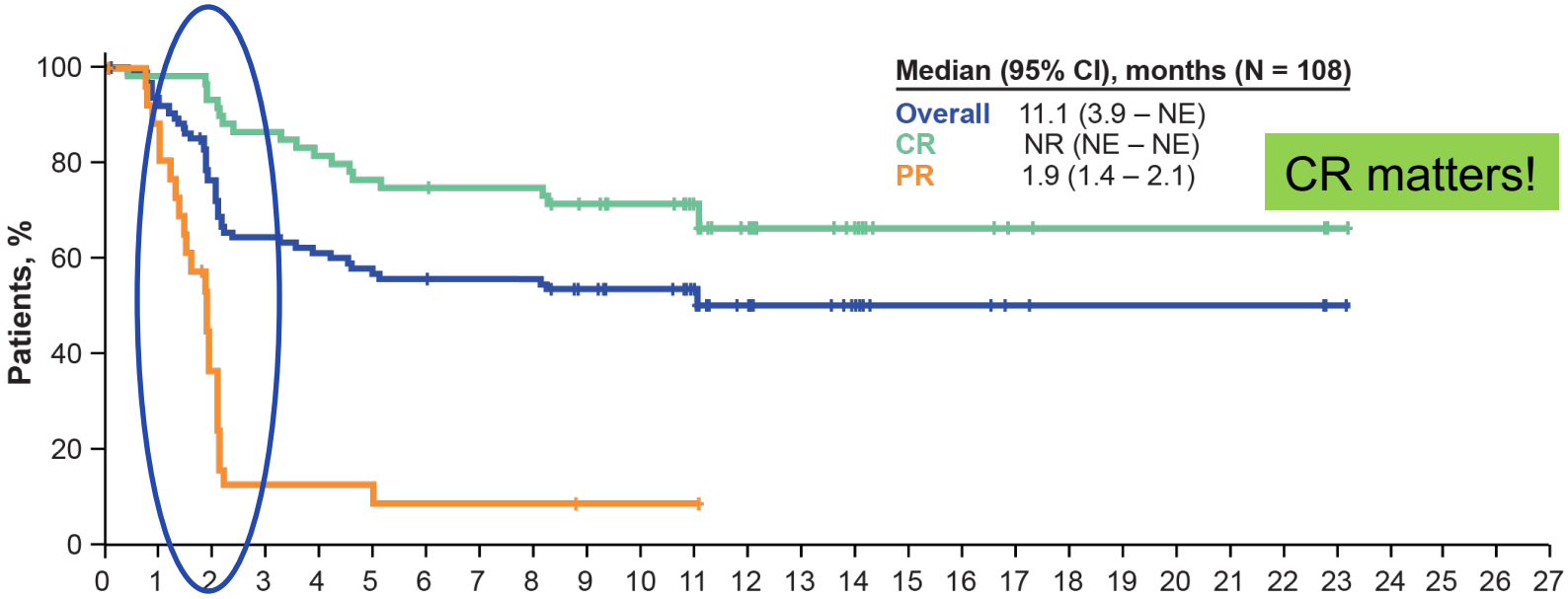
- In CR=**64.4%** (95% CI, 50.8-75.1); the median survival time among complete responders was not reached (95% CI, 63.4-NE)
- 37 of 59 CR patients (63%) are still alive at the 5-year data cutoff

- 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*
*Neelapu SS, et al. Blood. 2023. Online ahead of print*

# 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 | | | | | | | | | | | | |

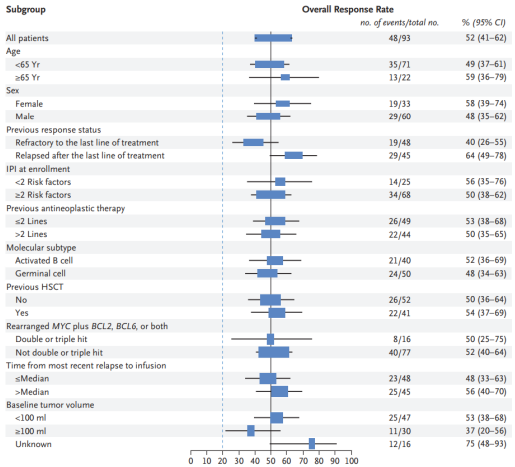
The NEW ENGLAND JOURNAL of MEDICINE

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*

| 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

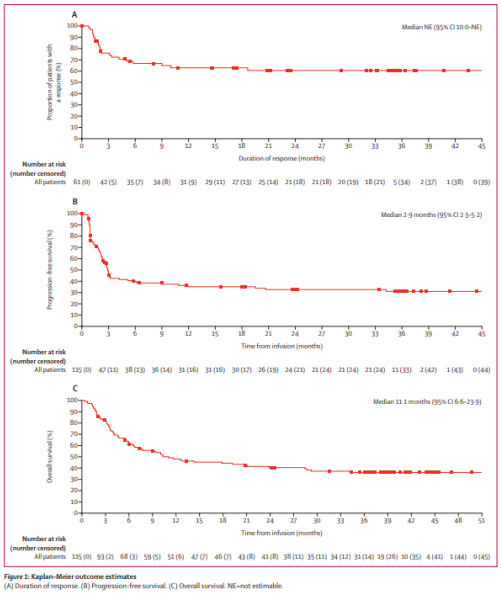



Figure 1: Kaplan–Meier outcome estimates
(A) Duration of response. (B) Progression-free survival. (C) Overall survival. NE=not estimable.

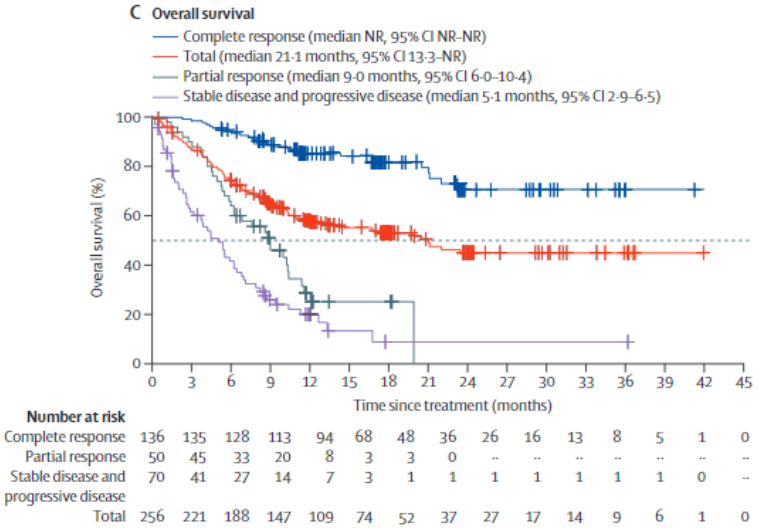
- At a median follow-up of 40.3 months (IQR 37·8–43·8)
- ORR= 53% by IRC-assessed
- CR= 39%
- The median time to first response= 29 (28-31) days

*Schuster SJ, et al. Lancet Oncol. 2021; 22:1403-15*

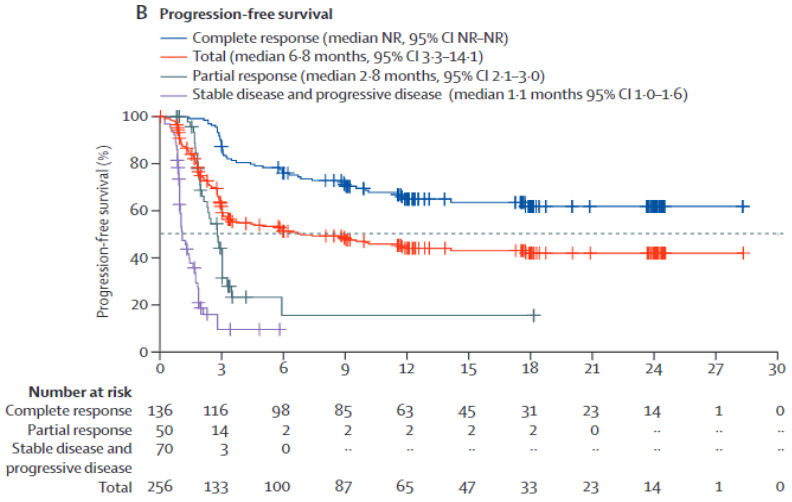
# Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study

*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*

## Overall survival




## Progression-free survival




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

# Moving CAR T-cell therapy to 2nd line

- **3 randomized studies:**
  - **ZUMA-7:** Axi-cel vs. SOC (Axi-cel better)
  - **TRANSFORM:** Liso-cel vs. SOC (Liso-cel better)
  - **BELINDA:** Tisagenlecleucel vs. SOC (no difference)

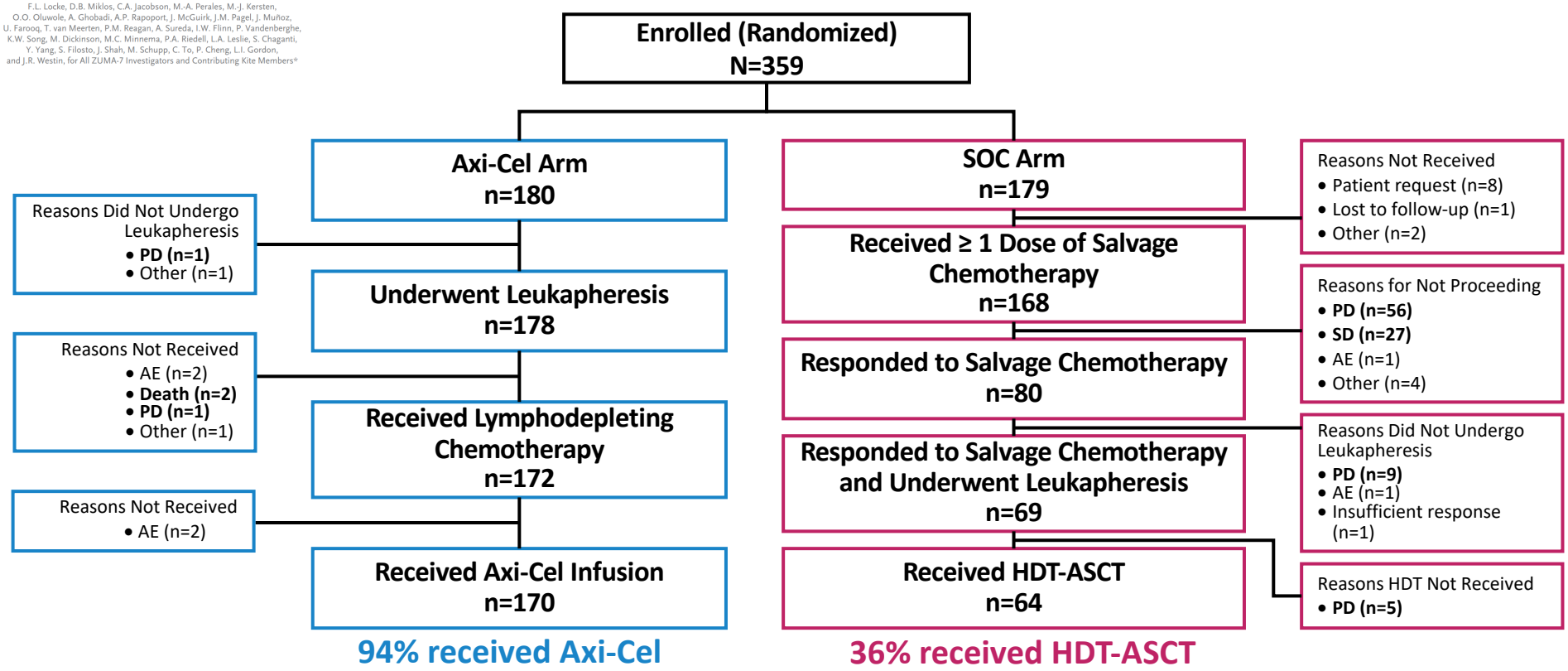
# Patient Disposition: Nearly 3× as Many Axi-Cel Patients Received Definitive Therapy Versus SOC Patients

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

F.L. Locke, D.B. Miklos, C.A. Jacobson, M.-A. Perales, M.-J. Kersten, O.O. Oluwole, A. Ghobadi, A.P. Rapoport, J. McGuirk, J.M. Pagel, J. Muñoz, U. Farooq, T. van Meerten, P.M. Reagan, A. Sureda, I.W. Flinn, P. Vandenberghe, K.W. Song, M. Dickinson, M.C. Minnema, P.A. Riedell, L.A. Leslie, S. Chaganti, Y. Yang, S. Filosto, J. Shah, M. Schupp, C. To, P. Cheng, L.I. Gordon, and J.R. Westin, for All ZUMA-7 Investigators and Contributing Kite Members*

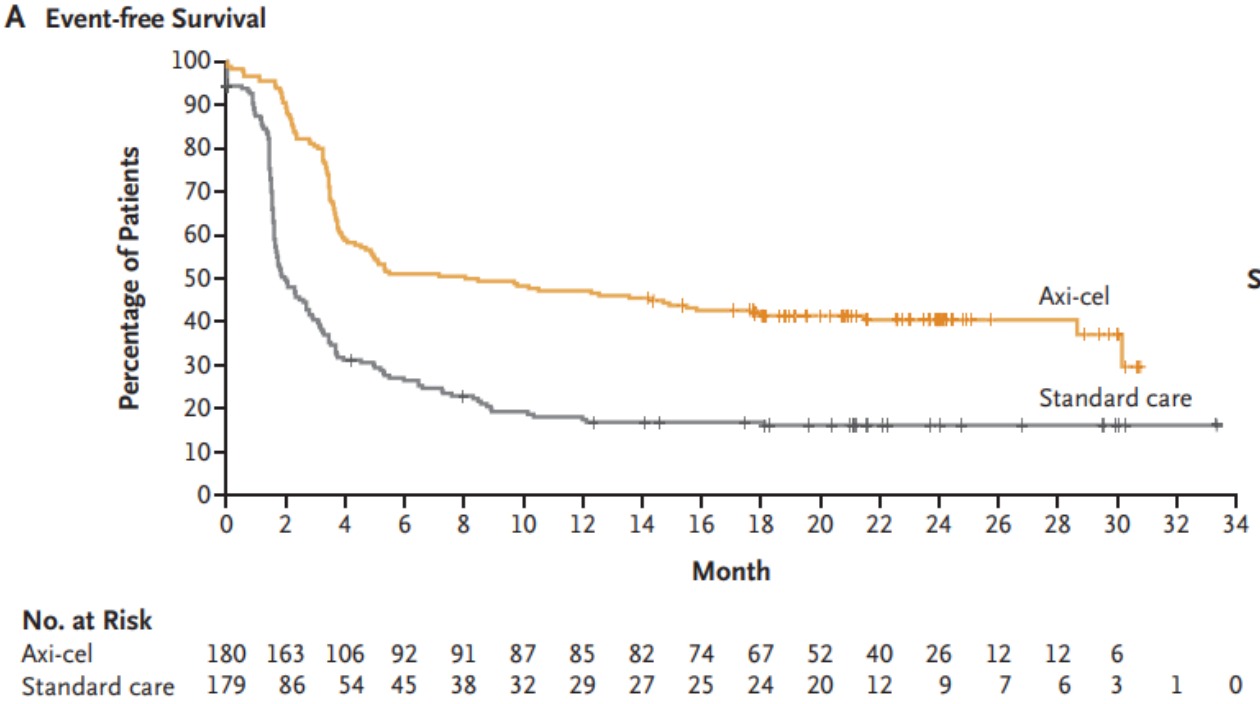



ASH Plenary presentation: courtesy Dr. Frederick Locke

*Locke FL, et al. N Engl J Med. 2022;386(7):640-654*

# Primary endpoint: event-free survival

## EFS




| | No. of Patients | Median Event-free Survival (95% CI) |
|---|---|---|
| | | *mo* |
| **Axi-cel** | 180 | 8.3 (4.5–15.8) |
| **Standard Care** | 179 | 2.0 (1.6–2.8) |

Stratified hazard ratio for event or death, 0.40 (95% CI, 0.31–0.51)
P<0.001

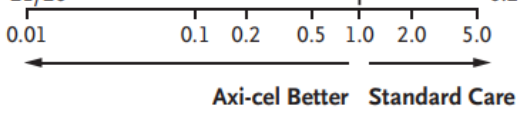


*Locke FL, et al. N Engl J Med. 2022;386(7):640-654*

# ZUMA-7 subgroup analysis

**B Subgroup Analysis**

| Subgroup | Axi-cel | Standard Care | Hazard Ratio for Event or Death (95% CI) |
|---|---|---|---|
| | *no. of patients with event/total no.* | | |
| Overall | 108/180 | 144/179 | 0.40 (0.31–0.51) |
| Age | | | |
| <65 yr | 81/129 | 96/121 | 0.49 (0.36–0.67) |
| ≥65 yr | 27/51 | 48/58 | 0.28 (0.16–0.46) |
| Response to first-line therapy at randomization | | | |
| Primary refractory disease | 85/133 | 106/131 | 0.43 (0.32–0.57) |
| Relapse ≤12 mo after initiation or completion of first-line therapy | 23/47 | 38/48 | 0.34 (0.20–0.58) |
| Second-line age-adjusted IPI | | | |
| 0 or 1 | 54/98 | 73/100 | 0.41 (0.28–0.58) |
| 2 or 3 | 54/82 | 71/79 | 0.39 (0.27–0.56) |
| Prognostic marker according to central laboratory | | | |
| HGBL, double- or triple-hit | 15/31 | 21/25 | 0.28 (0.14–0.59) |
| Double-expressor lymphoma | 35/57 | 50/62 | 0.42 (0.27–0.67) |
| Molecular subgroup according to central laboratory | | | |
| Germinal center B-cell–like | 64/109 | 80/99 | 0.41 (0.29–0.57) |
| Activated B-cell–like | 11/16 | 9/9 | 0.18 (0.05–0.72) |
| Unclassified | 8/17 | 12/14 | — |
| Disease type according to investigator | | | |
| DLBCL, not otherwise specified | 68/110 | 97/116 | 0.37 (0.27–0.52) |
| Large-cell transformation from follicular lymphoma | 10/19 | 24/27 | 0.35 (0.16–0.77) |
| HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both | 23/43 | 18/27 | 0.47 (0.24–0.90) |
| Disease type according to central laboratory | | | |
| DLBCL | 79/126 | 95/120 | 0.44 (0.32–0.60) |
| HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both | 15/31 | 21/26 | 0.28 (0.14–0.59) |




*Locke FL, et al. N Engl J Med. 2022;386(7):640-654*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma

J.R. Westin, O.O. Oluwole, M.J. Kersten, D.B. Miklos, M.-A. Perales, A. Ghobadi, A.P. Rapoport, A. Sureda, C.A. Jacobson, U. Farooq, T. van Meerten, M. Ulrickson, M. Elsawy, L.A. Leslie, S. Chaganti, M. Dickinson, K. Dorritie, P.M. Reagan, J. McGuirk, K.W. Song, P.A. Riedell, M.C. Minnema, Y. Yang, S. Vardhanabhuti, S. Filosto, P. Cheng, S.A. Shahani, M. Schupp, C. To, and F.L. Locke, for the ZUMA-7 Investigators and Kite Members*

The NEW ENGLAND JOURNAL of MEDICINE

**ZUMA 7 update**

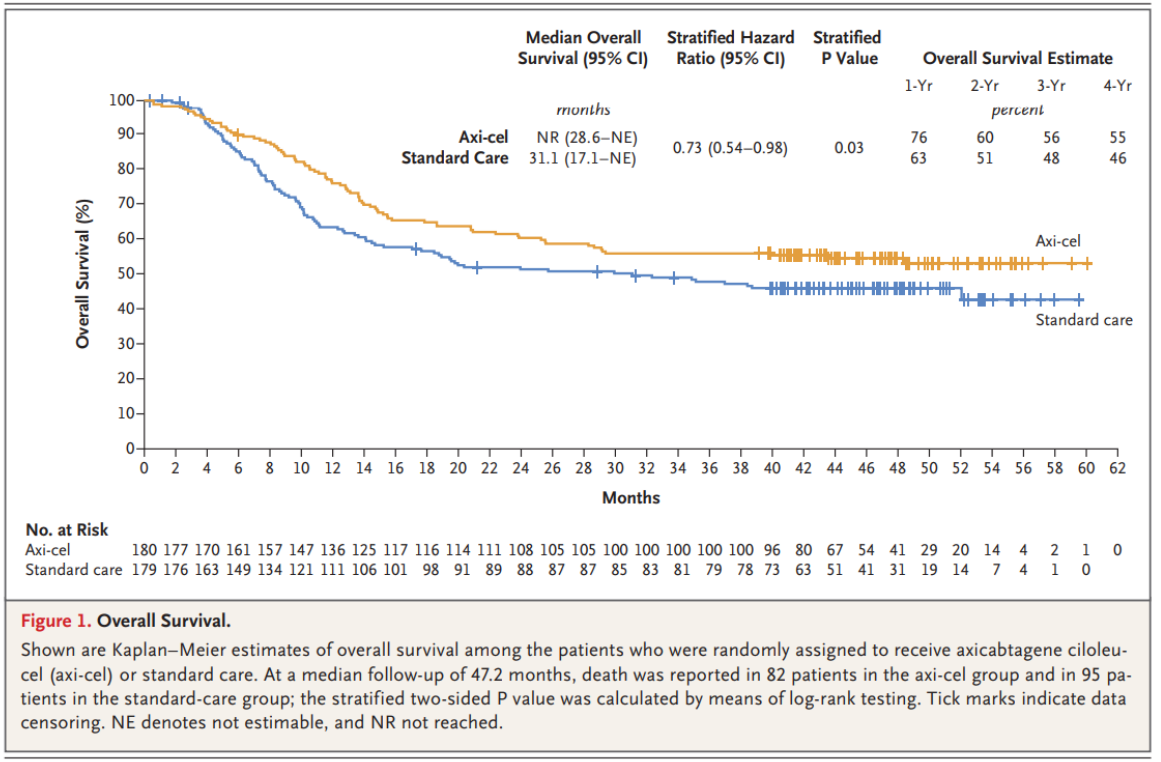


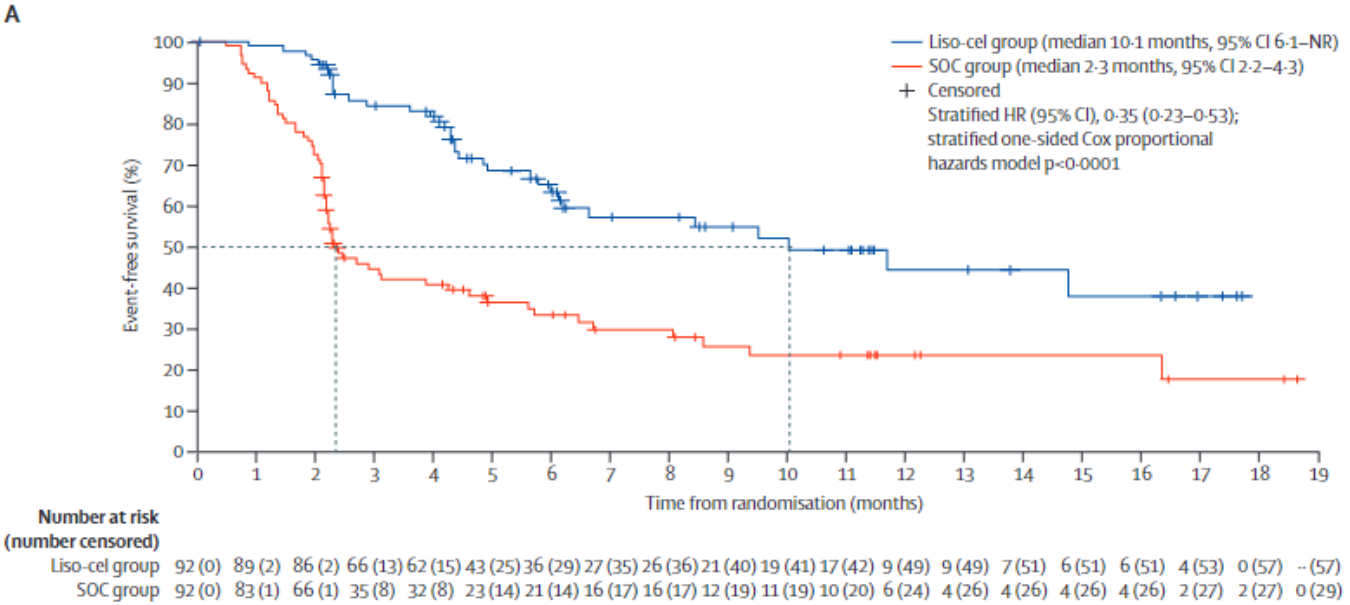

**Figure 1. Overall Survival.**

Shown are Kaplan–Meier estimates of overall survival among the patients who were randomly assigned to receive axicabtagene ciloleucel (axi-cel) or standard care. At a median follow-up of 47.2 months, death was reported in 82 patients in the axi-cel group and in 95 patients in the standard-care group; the stratified two-sided P value was calculated by means of log-rank testing. Tick marks indicate data censoring. NE denotes not estimable, and NR not reached.

# Lisocabtagene maraleucel versus standard of care with salvage chemotherapy followed by autologous stem cell transplantation as second-line treatment in patients with relapsed or refractory large B-cell lymphoma (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial

*Manali Kamdar, Scott R Solomon, Jon Arnason, Patrick B Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahimi, Stephan Mielke, Pim Mutsaers, Francisco Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew Lunning, David G Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali, Lara Stepan, Ken Ogasawara, Timothy Mack*, Jeremy S Abramson, for the TRANSFORM Investigators†*

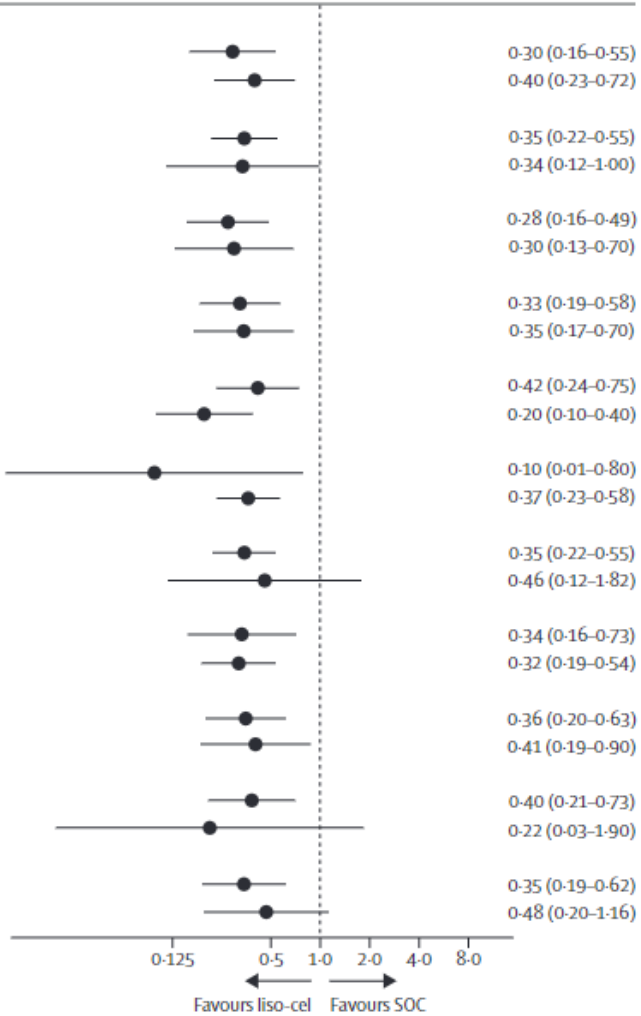
## EFS



# TRANSFORM: subgroup analysis

B

| | Liso-cel group Events/patients (%) | SOC group Events/patients (%) | Stratified HR (95% CI) |
|---|---|---|---|
| **sAAIPI** | | | |
| 0 or 1 | 16/56 (29%) | 32/55 (58%) | 0·30 (0·16–0·55) |
| 2 or 3 | 19/36 (53%) | 31/37 (84%) | 0·40 (0·23–0·72) |
| **Previous response status** | | | |
| Refractory | 30/67 (45%) | 52/68 (76%) | 0·35 (0·22–0·55) |
| Relapse to last previous therapy | 5/25 (20%) | 11/24 (46%) | 0·34 (0·12–1·00) |
| **Age group, years** | | | |
| <65 | 17/56 (30%) | 46/67 (69%) | 0·28 (0·16–0·49) |
| ≥65 to <75 | 18/36 (50%) | 15/23 (65%) | 0·30 (0·13–0·70) |
| **Sex** | | | |
| Male | 19/44 (43%) | 44/61 (72%) | 0·33 (0·19–0·58) |
| Female | 16/48 (33%) | 19/31 (61%) | 0·35 (0·17–0·70) |
| **ECOG performance status (at screening)** | | | |
| 0 | 18/48 (38%) | 36/57 (63%) | 0·42 (0·24–0·75) |
| 1 | 17/44 (39%) | 27/35 (77%) | 0·20 (0·10–0·40) |
| **SPD, cm²** | | | |
| >50 | 3/10 (30%) | 9/10 (90%) | 0·10 (0·01–0·80) |
| ≤50 | 29/77 (38%) | 53/76 (70%) | 0·37 (0·23–0·58) |
| **Lactate dehydrogenase, units per L** | | | |
| <500 | 30/79 (38%) | 53/81 (65%) | 0·35 (0·22–0·55) |
| ≥500 | 4/10 (40%) | 10/11 (91%) | 0·46 (0·12–1·82) |
| **Previous chemotherapy response status** | | | |
| Chemo refractory (progressive or stable disease) | 15/25 (60%) | 16/18 (89%) | 0·34 (0·16–0·73) |
| Chemo sensitive (partial or complete response) | 20/67 (30%) | 47/74 (64%) | 0·32 (0·19–0·54) |
| **NHL type** | | | |
| DLBCL | 21/60 (35%) | 36/57 (63%) | 0·36 (0·20–0·63) |
| HGBCL | 14/22 (64%) | 19/21 (90%) | 0·41 (0·19–0·90) |
| **DLBCL subtype** | | | |
| DLBCL NOS de novo | 19/53 (36%) | 30/49 (61%) | 0·40 (0·21–0·73) |
| DLBCL transformed from indolent NHL | 2/7 (29%) | 6/8 (75%) | 0·22 (0·03–1·90) |
| **DLBCL subtype based on cell of origin** | | | |
| GCB | 21/45 (47%) | 29/40 (73%) | 0·35 (0·19–0·62) |
| ABC, non-GCB | 7/21 (33%) | 22/29 (76%) | 0·48 (0·20–1·16) |




*Kamdar M, et al. Lancet 2022; 399: 2294–308*

# 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

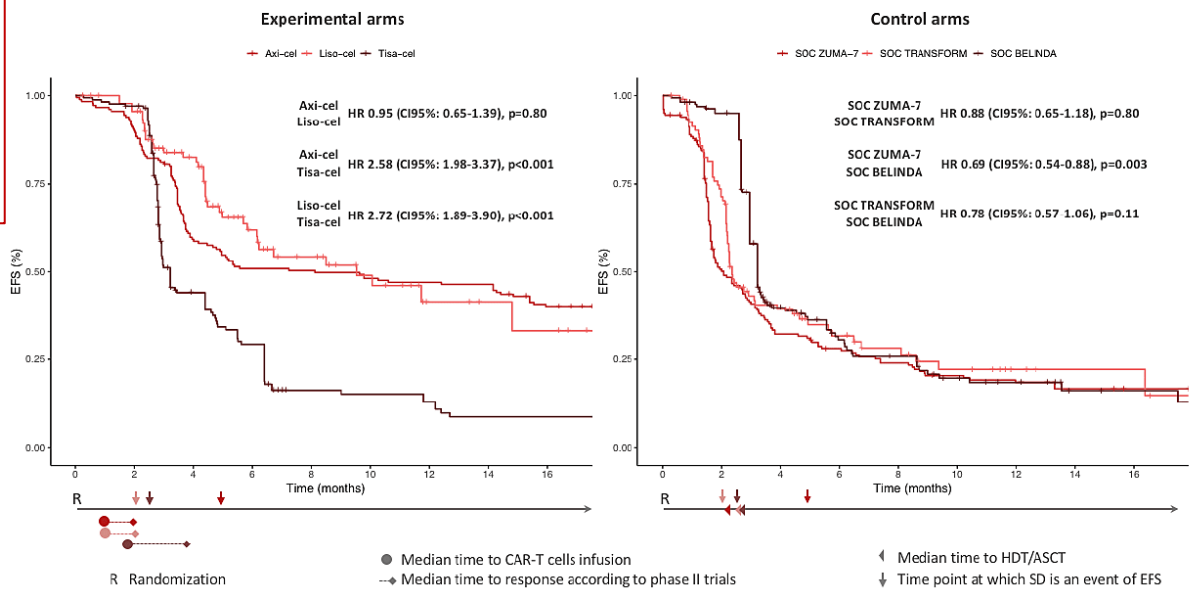
LETTER TO THE EDITOR

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

Côme Bommier, Jérôme Lambert, Catherine Thieblemont

First published: 08 April 2022 | https://doi.org/10.1002/hon.3001

## Reconstructed EFS curves




*Bommier C, et al. Hematol Oncol. 2022 Dec;40:1090-1093*

# CIBMTR analysis: CAR-T vs. auto-HCT in chemosensitive disease (PR)

blood Regular Article

LYMPHOID NEOPLASIA

## Autologous transplant vs chimeric antigen receptor T-cell therapy for relapsed DLBCL in partial remission

Mazyar Shadman,[1,2] Marcelo Pasquini,[3] Kwang Woo Ahn,[3,4] Yue Chen,[3] Cameron J. Turtle,[1,2] Peiman Hematti,[5] Jonathon B. Cohen,[6] Farhad Khimani,[7] Siddhartha Ganguly,[8] Reid W. Merryman,[9] Jean A. Yared,[10] Frederick L. Locke,[7] Nausheen Ahmed,[8] Pashna N. Munshi,[11] Amer Beitinjaneh,[12] Patrick M. Reagan,[13] Alex F. Herrera,[14] Craig S. Sauter,[15,16] Mohamed A. Kharfan-Dabaja,[17] and Mehdi Hamadani[3,18]

- Patients in partial response (PR)
  - CAR T=145
  - Auto-HCT=266
- Median age, years
  - CAR T= 60 (24-91) yrs
  - Auto-HCT=58 (18-80), p=0.07
- Median lines of prior therapies
  - CAR T= 3 (2-11)
  - Auto-HCT=2 (1-6), **p<0.001**

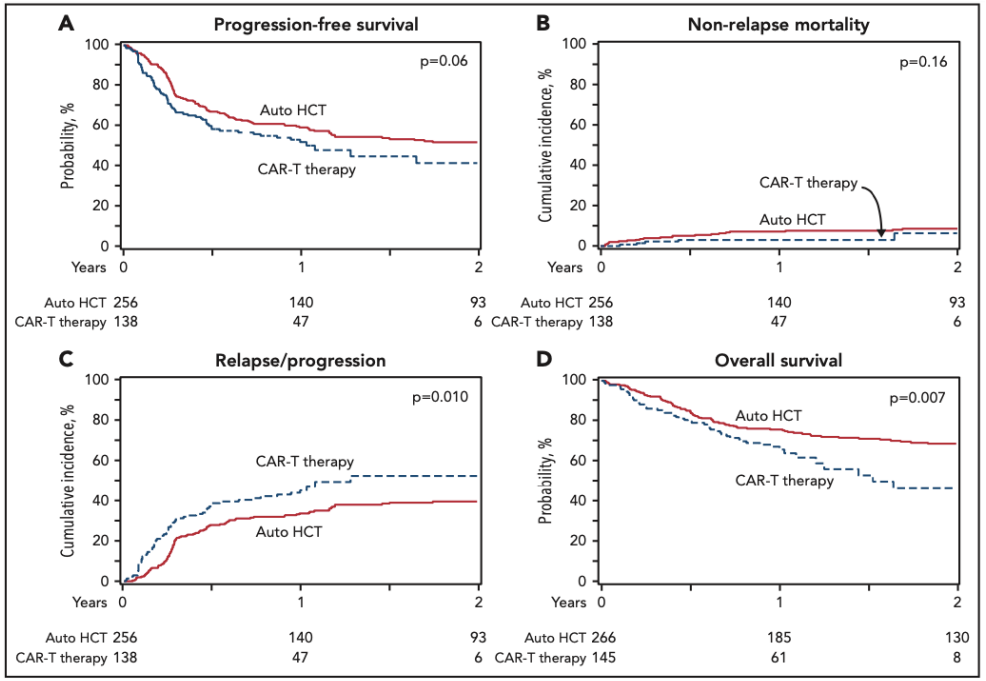
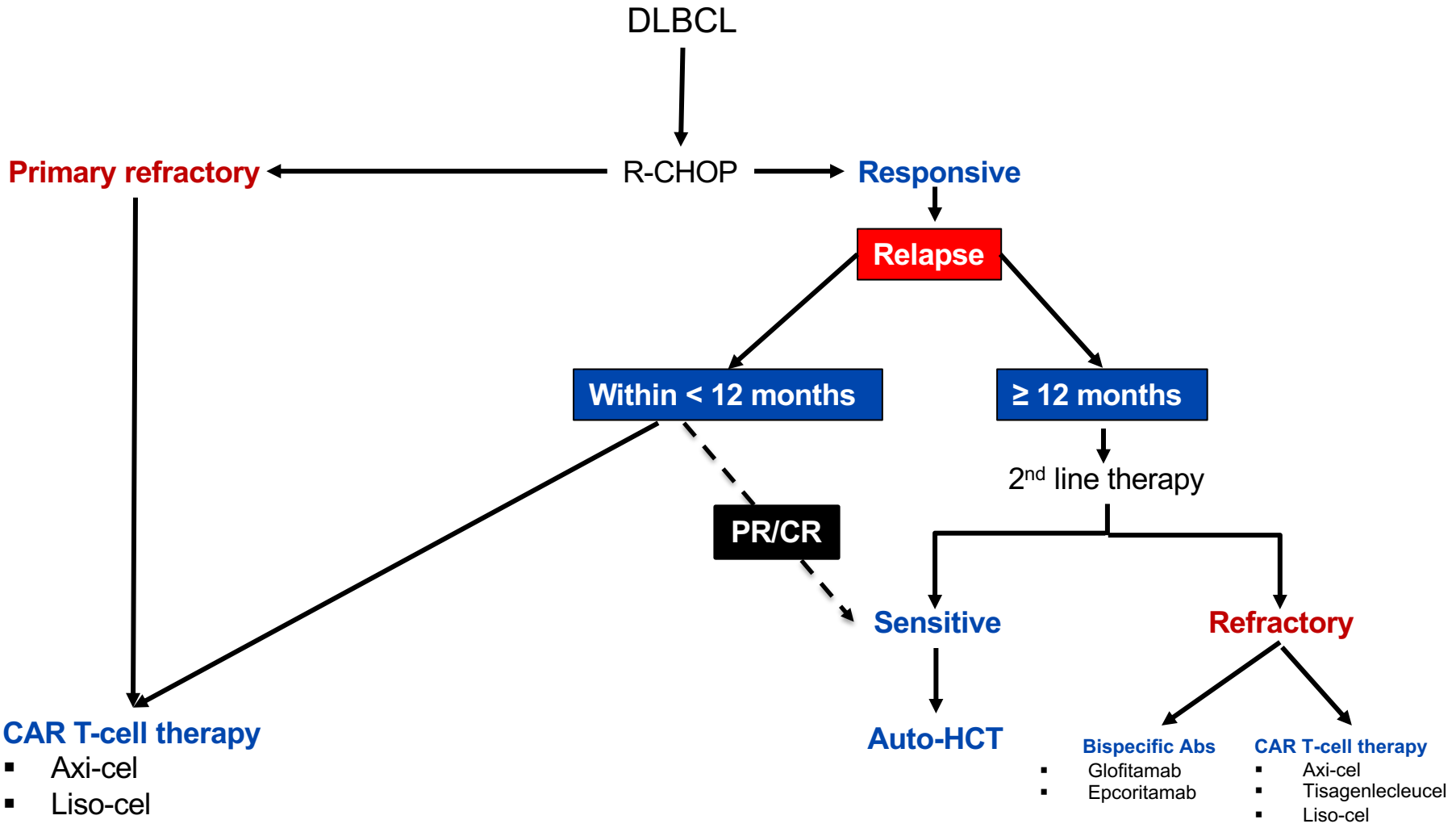



**Figure 1. Auto-HCT vs CAR-T in patients with DLBCL in PR (all patients).** (A) Progression-free survival. (B) Nonrelapse mortality. (C) Progression/relapse. (D) Overall survival.

# Proposed treatment algorithm in DLBCL



# ZUMA-2: Baseline characteristics

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

**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

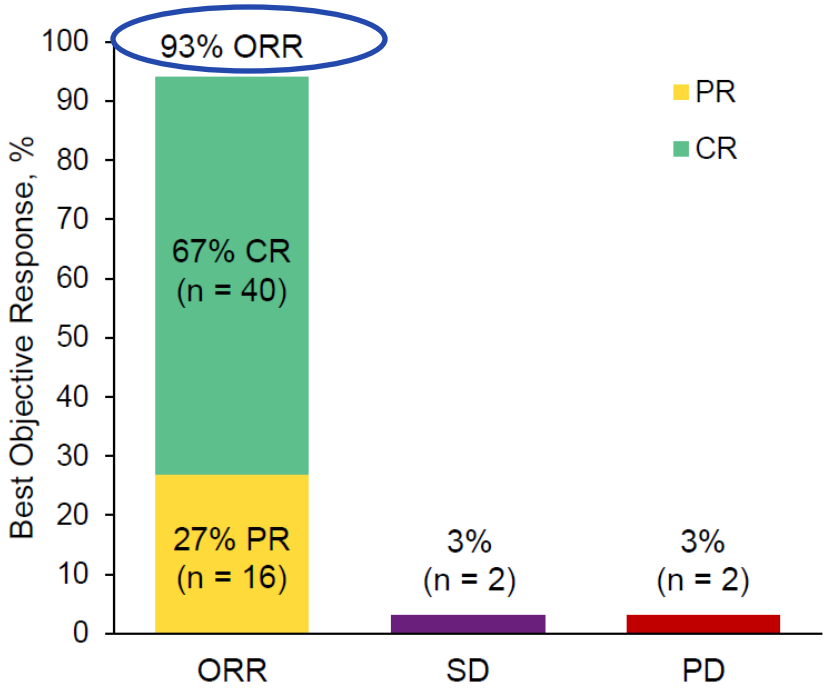
*Wang M, et al. ASH 2019. Abs 754*
*Wang M, et al. NEJM. 2020. 382:1331*

# 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.



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

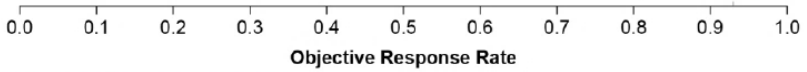
 

# ZUMA-2

*ASH 2019. Abs 754*

## ORR Was Consistent Across Key Subgroups

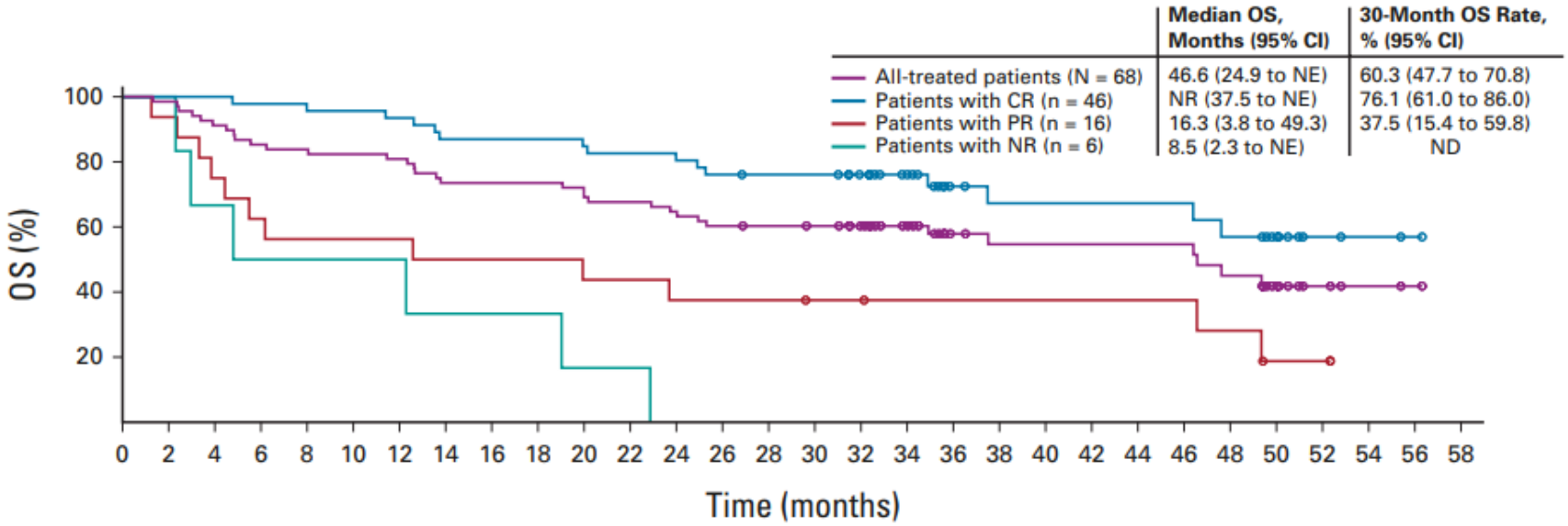
| | Evaluable Patients | Responding Patients | ORR (95% CI) |
|---|---|---|---|
| **Overall** | 60 | 56 | 0.93 (0.84, 0.98) |
| **Age** | | | |
| < 65 Years | 28 | 26 | 0.93 (0.76, 0.99) |
| ≥ 65 Years | 32 | 30 | 0.94 (0.79, 0.99) |
| **MCL morphology** | | | |
| Classical MCL | 35 | 32 | 0.91 (0.77, 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.

# Mantle cell lymphoma: ZUMA-2 study 3-year update (OS)

C



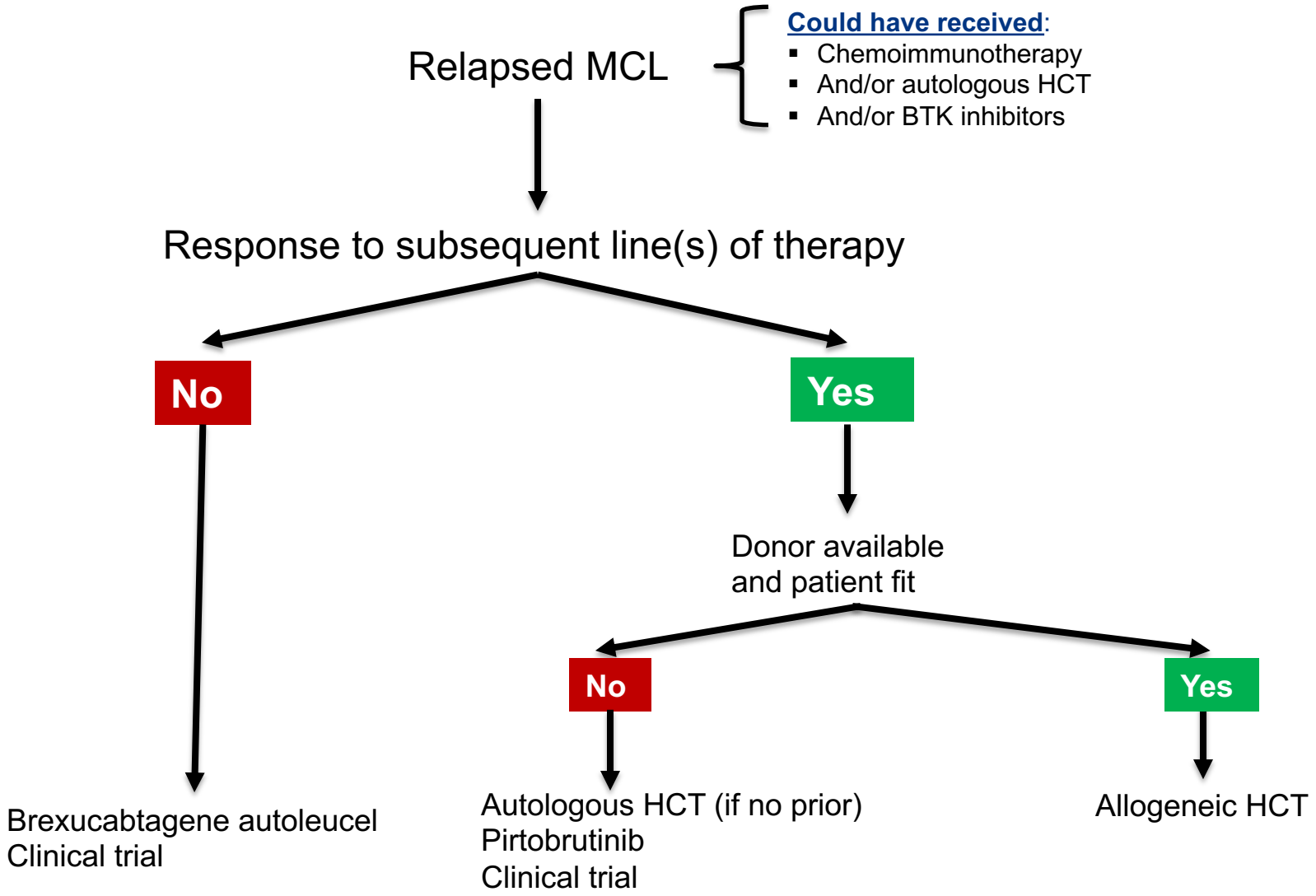

No. at risk:

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All-treated patients | 68 | 67 | 62 | 58 | 56 | 56 | 55 | 50 | 50 | 50 | 47 | 46 | 43 | 41 | 40 | 39 | 35 | 28 | 19 | 17 | 17 | 17 | 17 | 17 | 14 | 9 | 4 | 2 | 1 | 0 |
| Patients with CR | 46 | 46 | 46 | 45 | 44 | 44 | 43 | 40 | 40 | 40 | 39 | 38 | 37 | 35 | 34 | 34 | 30 | 24 | 15 | 13 | 13 | 13 | 13 | 13 | 11 | 8 | 3 | 2 | 1 | 0 |
| Patients with PR | 16 | 15 | 12 | 10 | 9 | 9 | 9 | 8 | 8 | 8 | 7 | 7 | 6 | 6 | 6 | 5 | 5 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 3 | 1 | 1 | 0 | 0 | 0 |
| Patients with NR | 6 | 6 | 4 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |



*Wang M, et al. J Clin Oncol. 2023;41(3):555-567*

# Proposed algorithm for relapsed MCL



# Follicular lymphoma

- ~5% of all hematologic neoplasms
- Marked heterogeneity, several morphological variants and specific subtypes
- Usually indolent, with a median overall survival of >15 years
- Yet, remains incurable
- ~20% progress or relapse within 2 years of treatment initiation → dismal prognosis (POD24)



Carbone A, et al. Nat Rev Dis Primers. 2019; 5(1):83

# 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)

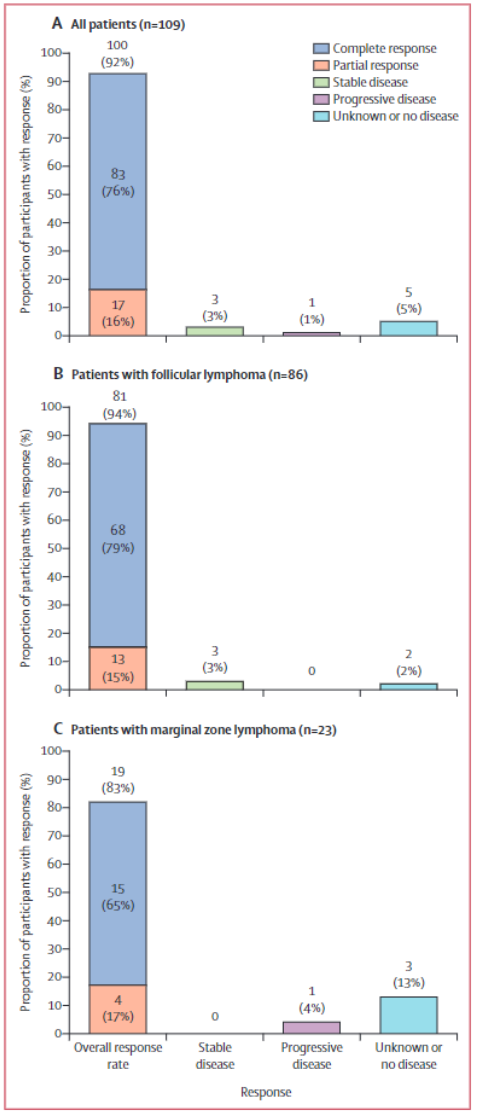
| | Patients with follicular lymphoma (n=124) | Patients with marginal zone lymphoma (n=24) | All patients (N=148) |
|---|---|---|---|
| (Continued from previous column) | | | |
| Previous lines of therapy | | | |
| Median† | 3 (2–4) | 3 (2–5) | 3 (2–4) |
| ≥3 previous lines of therapy | 78 (63%) | 16 (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**



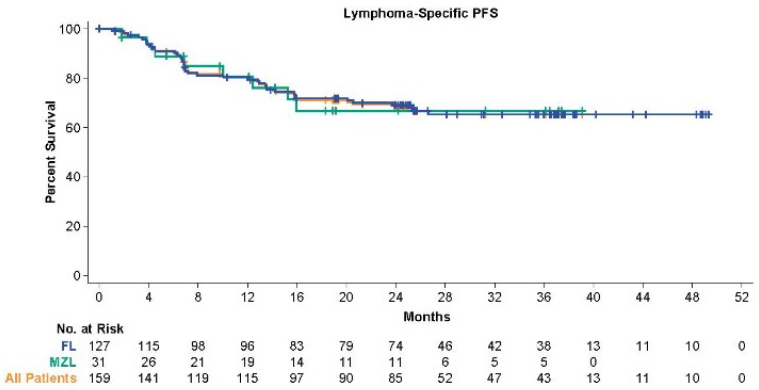
## 4660 3-Year Follow-up Analysis of ZUMA-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL)

Program: Oral and Poster Abstracts
Session: 705. Cellular Immunotherapies: Late Phase and Commercially Available Therapies: Poster III
Hematology Disease Topics & Pathways:
Research, clinical trials, Biological therapies, adult, Lymphomas, non-Hodgkin lymphoma, Clinical Research, Chimeric Antigen Receptor (CAR)-T Cell Therapies, B Cell lymphoma, Diseases, indolent lymphoma, Therapies, Lymphoid Malignancies, Study Population, Human

Monday, December 12, 2022, 6:00 PM-8:00 PM

***Sattva S. Neelapu, MD***[1], *Julio Chavez*[2], *Alison R. Sehgal, MD*[3], *Narendranath Epperla, MD, MS*[4,5], *Matthew Ulrickson, MD*[6], *Emanuel Bachy, MD, PhD*[7*], *Pashna N. Munshi, MD*[8*], *Carla Casulo, MD*[9], *David G. Maloney, MD, PhD*[10], *Sven de Vos, MD, PhD*[11], *Ran Reshef, MD, MSc*[12], *Lori A. Leslie, MD*[13*], *Olalekan O. Oluwole, MBBS*[14], *Ibrahim Yakoub-Agha, MD, PhD*[15], *Rashmi Khanal, MD*[16*], *Joseph D. Rosenblatt, MD*[17], *Jiali Yan, MS*[18*], *Qinghua Song, PhD*[18*], *Weixin Peng, MS*[18*], *Christine Lui, MS*[18*], *Jacob Wulff, DrPH*[19*], *Rhine R. Shen, PhD*[18*], *Soumya Poddar, PhD*[18*], *Harry Miao, MD, PhD*[18*], *Sara Beygi, MD*[18*] *and Caron A. Jacobson, MD*[20]

- Updated outcomes from ZUMA-5 after >3 years median follow-up
- 159 pts enrolled (127 FL; 31 MZL) and 152 treated with axi-cel (124 FL; 28 MZL)
- **Median F/U 40.5 months** (range, 8.3-57.4; FL: 41.7, MZL: 31.8)
- Median progression-free survival= 40.2 months (FL: 40.2, MZL: NR)
- **Median overall survival (OS)= Not reached; 3-year OS rate=75%**




*Neelapu SS, et al. Am Soc Hematol 2022 (Abs 4660)*

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]

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

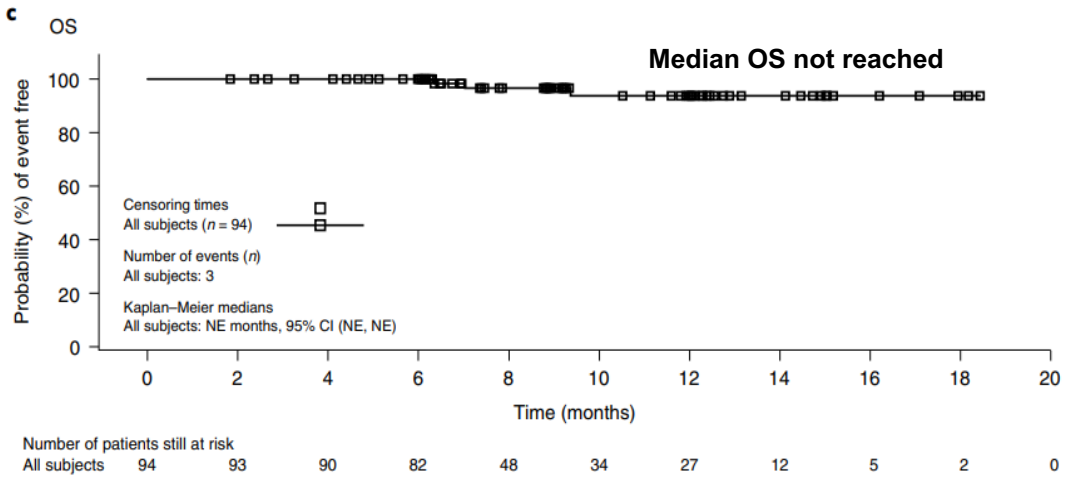



**Table 2 | Best overall response in the EAS and per-protocol population[a]**

| 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.

| 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.

| | Treated patients N=97 | |
|---|---|---|
| Events, n (%) | 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.

## 608 Long-Term Clinical Outcomes and Correlative Efficacy Analyses in Patients (Pts) with Relapsed/Refractory Follicular Lymphoma (r/r FL) Treated with Tisagenlecleucel in the Elara Trial

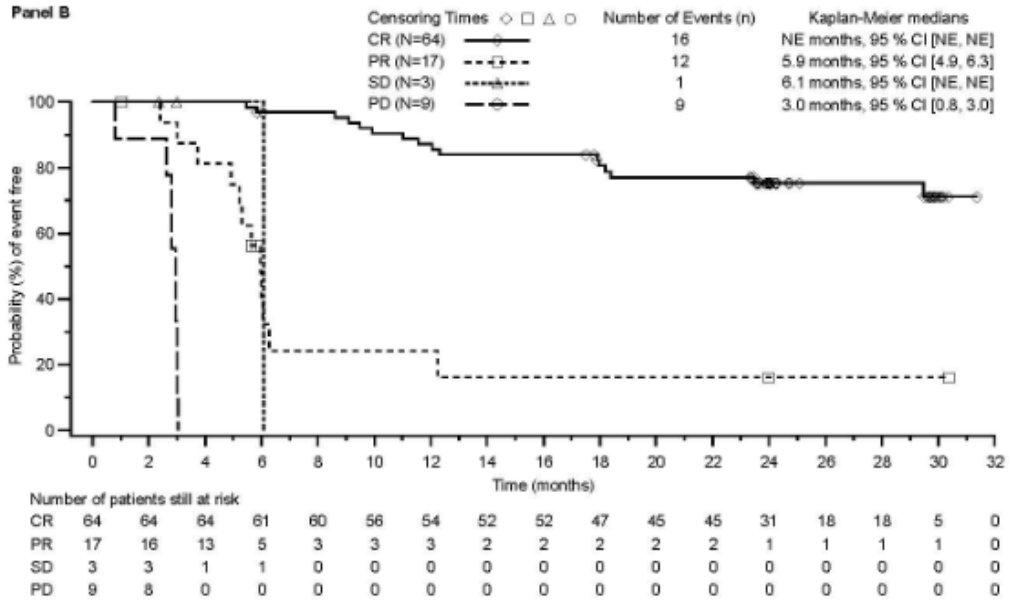
Program: Oral and Poster Abstracts
Type: Oral
Session: 623. Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological IV
Hematology Disease Topics & Pathways:
Research, clinical trials, Biological therapies, Lymphomas, non-Hodgkin lymphoma, Clinical Research, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, Therapies, Lymphoid Malignancies

Sunday, December 11, 2022: 4:45 PM

***Martin Dreyling, MD***[1], *Michael Dickinson, MD*[2], *Joaquin Martinez Lopez*[3*], *Arne Kolstad, MD, PhD*[4*], *Jason P Butler, MBBS, MMedSc*[5], *Monalisa Ghosh, MD*[6], *Leslie L. Popplewell, MD, FACP, MPH*[7], *Julio Chavez*[8], *Emmanuel Bachy, MD, PhD*[9*], *Koji Kato, MD, PhD*[10*], *Hideo Harigae, MD, PhD*[11], *Marie Jose Kersten, MD, PhD*[12,13], *Charalambos Andreadis, MD, MSCE*[14*], *Peter A. Riedell, MD*[15*], *Phoebe Joy Ho, MBBS(Syd) DPhil(Oxon) FRACP FRCPA FFSc(RCPA)*[16*], *Jose A. Perez-Simon, MD, PhD*[17], *Andy Chen, MD, PhD*[18], *Loretta J. Nastoupil, MD*[19], *Bastian von Tresckow, MD*[20], *Andrés J M Ferreri, MD*[21], *Takanori Teshima, M.D., Ph.D.*[22], *Piers E.M. Patten*[23,24*], *Joseph P. McGuirk, DO*[25], *Andreas Petzer, MD*[26], *Fritz Offner, MD, PhD*[27], *Andreas Viardot, MD*[28], *Pier Luigi Zinzani, MD, PhD*[29,30], *Ram Malladi, MD*[31*], *Ines Paule*[32*], *Aiesha Zia*[32*], *Rakesh Awasthi, PhD*[33*], *Xia Han, MS*[34*], *Davide Germano*[32*], *Darragh O'Donovan, PhD*[35*], *Roberto Ramos, MD*[34*], *Aisha Masood, MD*[34], *Catherine Thieblemont, MD, PhD*[36], *Nathan H. Fowler, MD*[37] *and Stephen J. Schuster, MD*[38*]

- 94 pts evaluable for efficacy
- Median F/U= 28.9 months
- Complete response rate=68%
- Overall response rate= 86.2%
- Median PFS= Not reached
- Estimated 2-year PFS=**57.4%**
- Estimated 2-year OS=**87.7%**

## PFS by best overall response




*Dreyling M, et al. Am Soc Hematol 2022 (Abs 608)*

# Take home messages

- CAR-T revolutionized Rx of B-cell DLBCL, MCL, and FL. Here to stay!
- In relapsed/refractory DLBCL, 5-year OS ≥ 42.6% (axi-cel)
  - For patients in CR, 5-year OS=64.4% (axi-cel)
- Axicabtagene ciloleucel and lisocabtagene maraleucel also approved in the 2nd line setting in patients with LBCL
  - Axi-cel showed OS advantage (vs. SOC)
  - Data for liso-cel on OS (not reported yet)
- Impressive survival in MCL and FL
  - In MCL, 30-month OS=60.3% (all pts); OS=76.1% (CR cases)
  - In FL
    - Axi-cel: 3-year OS=75%
    - Tisagenlecleucel: 2-year OS=87.7%

# Thank you