POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

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Milano
Teatro Dal Verme
2-3-4 Febbraio 2023

CAR-T
Linfomi Aggressivi

Dr. Massimo Martino
Centro Unico Regionale Trapianti Cellule Staninali e Terapie Cellulari
GOM BMM, Reggio Calabria

DICHIARAZIONE

Massimo Martino

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **- NIENTE DA DICHIARARE**
- Consulenza ad aziende con interessi commerciali in campo sanitario - **NIENTE DA DICHIARARE**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **- NIENTE DA DICHIARARE**
- Partecipazione ad Advisory Board **– Novartis, Kite, BMS, MEDAC, Takeda, Jansenn-Cilag, Italfarmaco, GSK, Gentili, Astellas**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **- NIENTE DA DICHIARARE**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **- NIENTE DA DICHIARARE**
- Altro - **- NIENTE DA DICHIARARE**

655 Lisocabtagene Maraleucel (liso-cel) Versus Standard of Care (SOC) with Salvage Chemotherapy Followed By Autologous Stem Cell Transplantation (ASCT) As Second-Line (2L) Treatment in Patients with Relapsed or Refractory Large B-Cell Lymphoma (LBCL): Primary Analysis of the Randomized, Phase 3 Transform Study

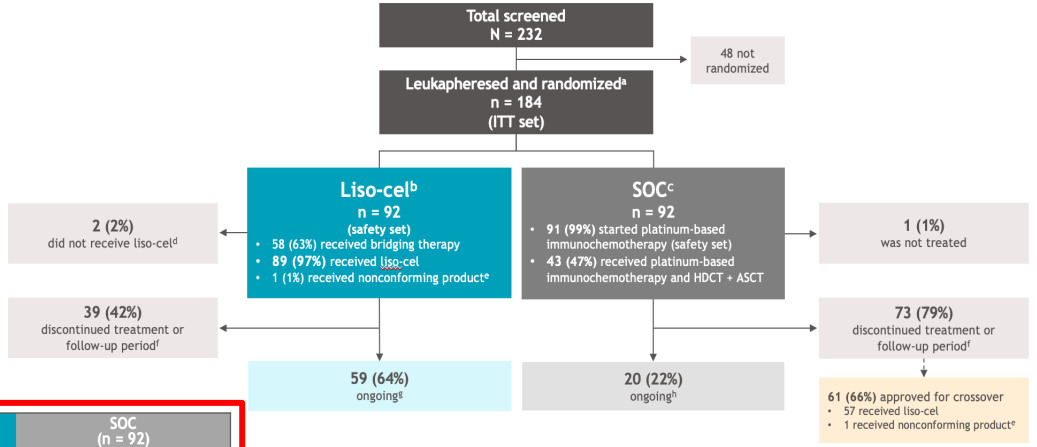
Massachusetts General Hospital Cancer Center.

Program: Oral and Poster Abstracts
Type: Oral
Session: 705. Cellular Immunotherapies: Results from CD19-Directed CAR T in treating Aggressive B-cell Lymphomas
Hematology Disease Topics & Pathways:
Research, clinical trials, Biological therapies, adult, Lymphomas, non-Hodgkin lymphoma, Clinical Research, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, aggressive lymphoma, Therapies, Lymphoid Malignancies, Study Population, Human

Sunday, December 11, 2022: 4:30 PM

Jeremy S. Abramson, MD[1], *Scott R. Solomon, MD*[2], *Jon E. Arnason, MD*[3], *Patrick B. Johnston, MD, PhD*[4], *Bertram Glass, MD*[5*], *Veronika Bachanova, MD, PhD*[6], *Sami Ibrahimi, MD*[7], *Stephan Mielke, MD*[8], *Pim Mutsaers, MD*[9*], *Francisco Hernandez-Ilizaliturri, MD*[10], *Koji Izutsu*[11*], *Franck Morschhauser, MD, PhD*[12*], *Matthew A. Lunning, DO, FACP*[13], *Alessandro Crotta, MD*[14*], *Sandrine Montheard, MS*[14*], *Alessandro Previtali, MSc*[14*] *and Manali Kamdar, MD, MBBS*[15*]

- Lisocabtagene maraleucel (liso-cel) is an autologous, CD19-directed, 4-1BB chimeric antigen receptor (CAR) T cell product administered at equal target doses of $CD8^+$ and $CD4^+$ CAR^+ T cell
- Interim analysis of the TRANSFORM study performed at a median follow-up of 6.2 months, demonstrated superior efficacy of liso-cel compared with SOC as second-line treatment for patients with primary refractory or early relapsed LBCL

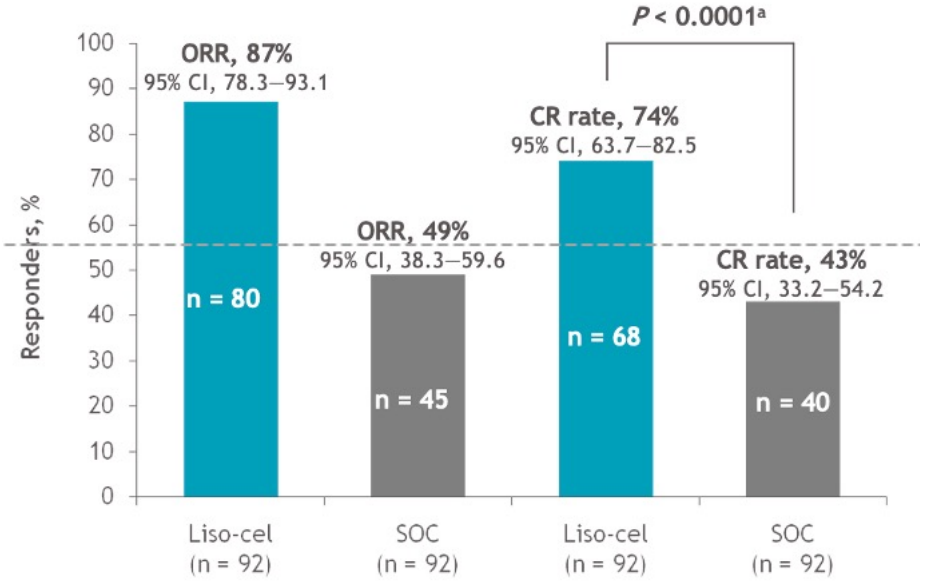


	Liso-cel (n = 92)	SOC (n = 92)
Male, n (%)	44 (48)	61 (66)
Age, years		
Median (range)	60 (20–74)	58 (26–75)
≥ 65, n (%)	36 (39)	25 (27)
LBCL subtypes,[a] n (%)		
DLBCL NOS	53 (58)	50 (54)
HGBCL with rearrangements in *MYC* and *BCL2*, *BCL6*, or both[b]	22 (24)	21 (23)
PMBCL	8 (9)	9 (10)
DLBCL transformed from any indolent lymphoma	7 (8)	8 (9)
THRBCL	1 (1)	4 (4)
FL3B	1 (1)	0
LBCL subtype based on cell of origin, n (%)		
GCB	45 (49)	40 (43)
ABC, non-GCB	21 (23)	29 (32)
ECOG PS, n (%)		
0	48 (52)	57 (62)
1	44 (48)	35 (38)
LDH ≥ 500 units/L, n (%)	10 (11)	11 (12)
sAAIPI, n (%)		
0 or 1	56 (61)	55 (60)
2 or 3	36 (39)	37 (40)
Prior response status, n (%)		
Refractory[c]	67 (73)	70 (76)
Relapsed[d]	25 (27)	22 (24)

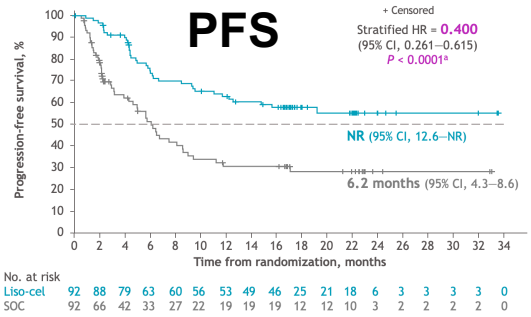
Results of the event-driven primary analysis of TRANSFORM are reported here, with a median follow-up from randomization of 17.5 months

Abramson JS, et al. ASH 2022

TRANSFORM: Outcomes

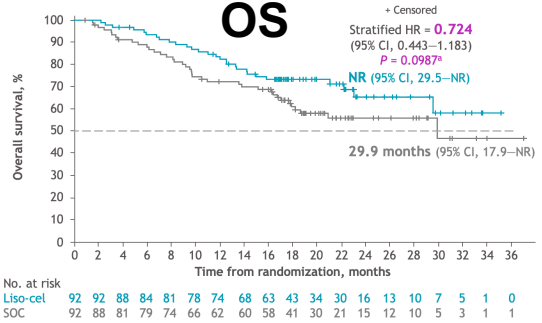


Abramson JS, et al. ASH 2022



18-month PFS rate	
Liso-cel	SOC
58.2% (95% CI, 47.7–68.7)	28.8% (95% CI, 17.7–40.0)

Median follow-up: 17.5 months



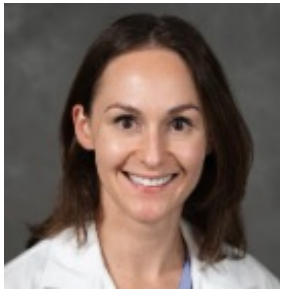
18-month OS rate	
Liso-cel	SOC
73.1% (95% CI, 63.9–82.3)	60.6% (95% CI, 50.2–71.1)

Median follow-up: 17.5 months

- Patients in SOC arm who crossed over to receive liso-cel continue to be followed for OS in the SOC arm

154 Double Hit/Double Expressor Lymphomas: A Multicenter Analysis of Survival Outcomes with CD19-Directed CAR T-Cell Therapy

Program: Oral and Poster Abstracts
Type: Oral
Session: 627. Aggressive Lymphomas: Clinical and Epidemiological: Treatment of CNS Lymphoma, Neurologic Toxicities, and Relapsed/Refractory DLBCL
Hematology Disease Topics & Pathways:
Research, Biological therapies, adult, Lymphomas, non-Hodgkin lymphoma, Clinical Research, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, real-world evidence, aggressive lymphoma, Therapies, Lymphoid Malignancies, Study Population, Human



Saturday, December 10, 2022: 12:45 PM

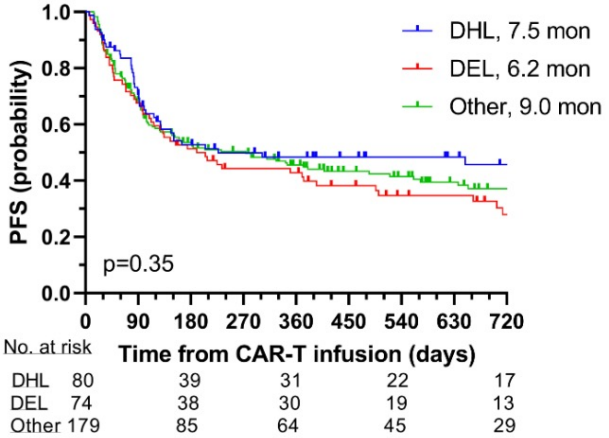
Joanna Zurko, MD[1], *Geoffrey Shouse, PhD, DO*[2], *Pallawi Torka, MD*[3], *Tamara K. Moyo, MD, PhD*[4*], *Jason T. Romancik, MD*[5], *Imran A. Nizamuddin, MD*[6], *Kaitlin Annunzio, DO*[7], *Jieqi Liu, MD*[8*], *Stefan K. Barta, MD*[9], *Robert Ferdman, MD*[3*], *Rahul Bhansali, MD*[10*], *Jonathon B. Cohen, MD, MS*[11], *Sayan Mullick Chowdhury, DO, PhD*[12*], *Nirav N. Shah, MD*[13], *Elyse I. Harris, MD*[14], *Vaishalee P. Kenkre, MD*[1], *McKenzie Sorrell, DO*[15], *Brian T. Hess, MD*[15], *Deborah M. Stephens, DO*[16], *Lindsey A. Fitzgerald, MD*[17], *Thomas A. Ollila, MD*[18], *Ishan Roy*[19*], *Shuo Ma, MD*[20], *Jane N. Winter, MD*[21], *Barbara Pro, MD*[22], *Jonathan Moreira, MD*[23], *Leo I. Gordon, MD*[23], *Alexey V Danilov, MD*[24], *Andrew M. Evens, DO, MBA, MMSc*[25], *Narendranath Epperla, MD, MS*[26] *and Reem Karmali, MD, MSc*[27]

Medical College of Wisconsin, Milwaukee, WI, United States

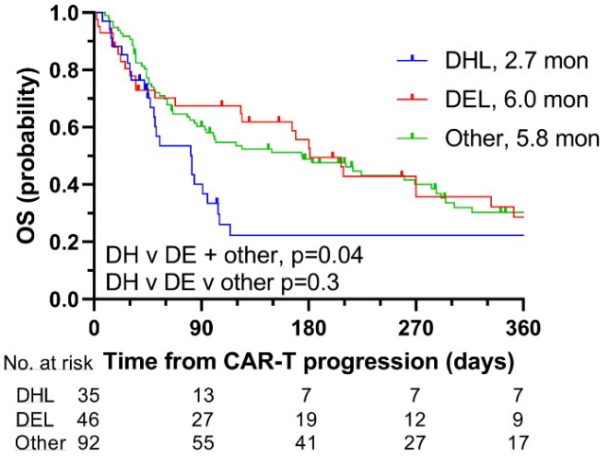
Double hit lymphoma (DHL)
Double expressor lymphoma (DEL; overexpression of *MYC* and *BCL2* on IHC)

- 333 Adult pts with R/R aggressive B-NHL
- 80 with DHL, 74 with DEL and 179 other pts
- 64% received axi-cel, 26% tisa-cel and 10% liso-cel

PFS, all CAR-T patients



OS, after CAR-T progression



Joanna Zurko, et al. ASH 2022

166 Axicabtagene Ciloleucel As Second-Line Therapy for Large B-Cell Lymphoma in Transplant-Ineligible Patients: Primary Analysis of Alycante, a Phase 2 Lysa Study

Program: Oral and Poster Abstracts
Type: Oral
Session: 704. Cellular Immunotherapies: Early Phase and Investigational Therapies: Lymphoma
Hematology Disease Topics & Pathways:
Biological therapies, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Therapies

Saturday, December 10, 2022: 12:45 PM

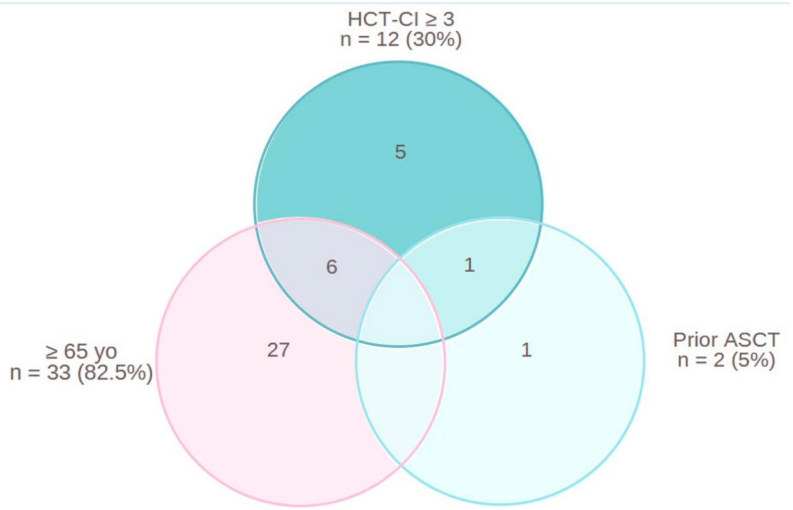
Roch Houot[1*], *Emmanuel Bachy, MD, PhD*[2*], *Guillaume Cartron, MD, PhD*[3*], *François-Xavier Gros*[4*], *Franck Morschhauser, MD, PhD*[5*], *Lucie Oberic, MD*[6*], *Thomas Gastinne, MD*[7*], *Pierre Feugier, MD*[8*], *Remy Dulery*[9*], *Catherine Thieblemont, MD, PhD*[10], *Magalie Joris, MD*[11*], *Francisco Llamas-Gutierrez*[12*], *Emmanuel Itti, MD, PhD*[13*], *Cedric Menard*[14*], *Yassine Al-Tabaa*[15*], *Clement Bailly*[16*], *Marie-Helene Delfau*[17*], *Camille Laurent, MD, PhD*[18*] *and Francois Lemonnier*[19*]

Rennes University Hospital, Rennes, France

Rationale

- Axicabtagene ciloleucel (axi-cel; Yescarta®) demonstrated superior efficacy compared to standard of care in 2nd line R/R large B-cell lymphoma (LBCL) in patients considered eligible for ASCT (ZUMA-7).[1]
- However, Axi-cel has not been evaluated in 2nd line R/R LBCL in patients who are not eligible for ASCT. These patients, notably when they are refractory or experience early relapse, have a particularly poor prognosis with current treatments.[2]
- Importantly, patients who are not eligible to ASCT may still remain eligible to CAR T-cell therapy.[3]
- **Hypothesis :** Axi-cel may be superior to SOC in 2nd line R/R LBCL patients who are refractory or relapse early and who are deemed ineligible for HDCT/ASCT.

Causes of ASCT-ineligibility



1. Locke et al, NEJM 2022. 2. Cazelles et al, Leukemia & Lymphoma 2021. 3. Vic et al, EJC 2022

Houot et al. ASH 2022 Abstract 166

Patients and Disease Characteristics

Axi-cel treated patients	N=40
Sex male, n (%)	28 (70.0)
Age (years), median (min-max)	68 (49 - 81)
Age, n (%)	
≥ 65 years	33 (82.5)
≥ 70 years	18 (45.0)
Prior autologous transplant, n (%)	2 (5.0)
HCT-CI[1] ≥ 3, n (%)	12 (30.0)
ECOG PS 0-1 at inclusion, n (%)	40 (100.0)
IPI, n (%)	
0-1	3 (7.5)
>=2	37 (92.5)
Ann Arbor stage, n (%)	
I-II	9 (22.5)
III-IV	31 (77.5)
LDH ≥ ULN at baseline, n (%)	7 (17.5)
CRP > 20 mg/L at infusion, n (%)	15 (37.5)

Axi-cel treated patients	N=40
Relapsed or refractory, n (%)	
Refractory	21 (52.5)
Relapsed ≤ 12 months	19 (47.5)*
Histology (central review), n (%)	
DLBCL	33 (82.5)
HGBL (DH/TH + NOS)	4 + 1 (12.5)
Indolent B-NHL transformed into aggressive B-NHL	1 (2.5)
Follicular lymphoma, grade 1,2*	1 (2.5)
Bridging therapy, n (%)	37 (92.5)
Corticosteroids	0 (0)
R-GEMOX	37 (92.5)
Response to bridging therapy, n (%)	
Complete Metabolic Response	4 (10.0)
Partial Metabolic Response	8 (20.0)
No Metabolic response/stable disease	12 (30.0)
Progressive Metabolic Disease	15 (37.5)
Not evaluated	1 (2.5)
Median time between diagnosis and R/R, Mo (Q1;Q3)	8 (5 ; 12)
Median time between inclusion and infusion, days (Q1;Q3)	42 (38 ; 49)

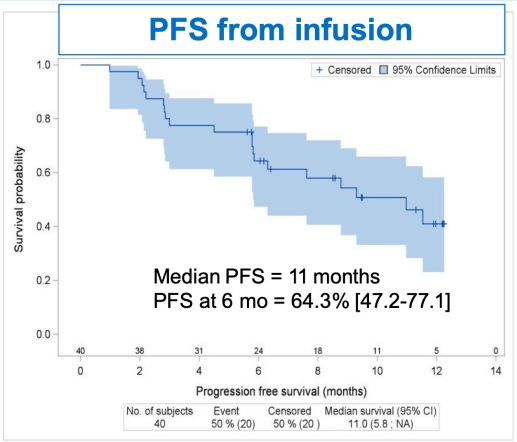
1. Sorror ML, et al. *Blood*. 2005;106:2912-2919.

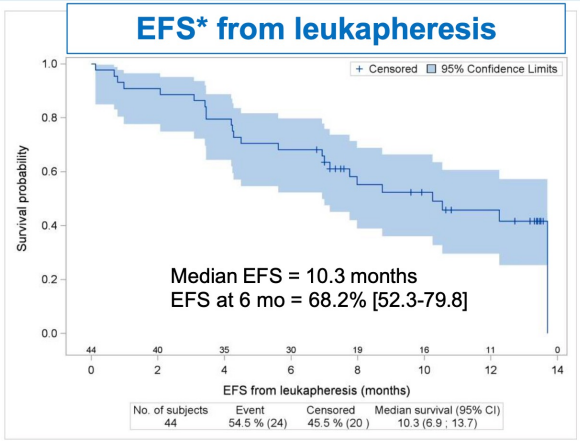
Houot et al. ASH 2022 Abstract 166

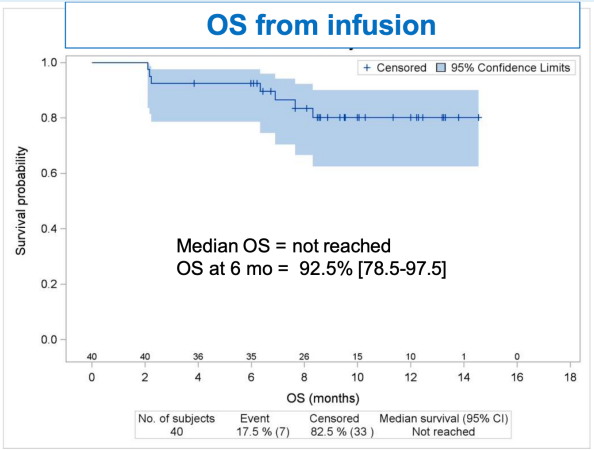
	Patients treated with Axi-cel (n = 40)
CRS, n (%)	**36 (90.0)**
Grade 1-2	32 (80.0)
Grade 3-4	4 (10.0)
Median (Q1;Q3) time to onset, days	2 (1;4)
Median (Q1;Q3) duration, days	3.5 (1;7)
ICANS, n (%)	**22 (55.0)**
Grade 1-2	14 (35.0)
Grade 3-4	8 (20.0)
Median (Q1;Q3) time to onset, days	6 (5;7)
Median (Q1;Q3) duration, days	3 (1;7)
Tocilizumab use, n (%)	31 (77.5)
Corticosteroid use, n (%)	27 (67.5)
ICU transfer, n (%)	12 (30.0)
Prolonged grade ≥3 cytopenia*, n (%)	15 (37.5)
Infections n (%)	
Grade ≥3	12 (30.0)
Grade = 5	5 (12.5)

Response according to Lugano classification*	Response at 3 months from infusion	Best response
Overall response rate, n (%)	30 (75.0)	37 (92.5)
Complete Metabolic Response, n (%)	28 (70.0)	32 (80.0)
Partial Metabolic Response, n (%)	2 (5.0)	5 (12.5)
No Metabolic Response/stable disease, n	0	0
Progressive Metabolic Disease, n (%)	6 (15.0)	2 (5)
Death before assessment, n (%)	4 (10.0)	1 (2.5)

- The CMR at 3 months post-infusion (primary endpoint) in the 40 patients of the efficacy analysis set was 70% (95% CI, 53.5-83.4)
- 24 patients (60%) remain in CMR at 6 months





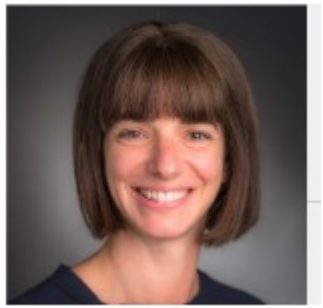


Median (range) on-study follow-up at time of analysis : 10 months [2.1-14.6]**

Houot et al. ASH 2022 Abstract 166

440 A Pilot Study of Axicabtagene Ciloleucel (axi-cel) for the Treatment of Relapsed/Refractory Primary and Secondary Central Nervous System Lymphoma (CNSL)

Program: Oral and Poster Abstracts
Type: Oral
Session: 626. Aggressive Lymphomas: Prospective Therapeutic Trials: Immune Based and Targeted Therapies in Relapsed/Refractory Large B-Cell Lymphoma
Hematology Disease Topics & Pathways:
Biological therapies, Lymphomas, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, aggressive lymphoma, Therapies, Lymphoid Malignancies



Sunday, December 11, 2022: 9:45 AM

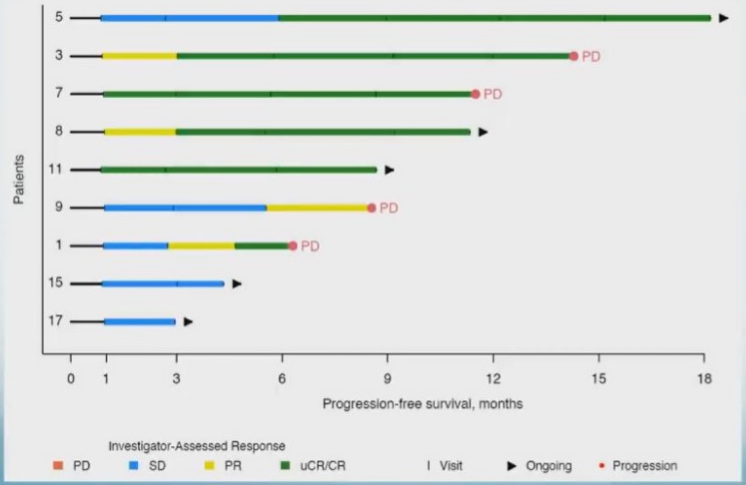
Caron A. Jacobson, MD[1], *Caroline Falvey*[1*], *Riemke Bouvier*[1*], *Sarah Hogan*[1*], *Elizabeth Kendricken, BSN, RN*[1*], *Julia Jones*[1*], *Elizabeth Grimm*[1*], *Robert A. Redd, MS*[2*], *Eudocia Q Lee*[1*], *Luis Gonzalez Castro*[1*], *Ugonma Chukwueke*[1*], *Jose McFaline Figueroa*[1*], *Austin I. Kim, MD*[3], *Alexandra Torres*[1*], *Linda Ramsdell*[1*], *Leslie S. Kean, MD, PhD*[4], *Ulrike Gerdemann, MD*[5], *Alexandre Albanese*[6*], *Paula Keskula*[5*], *David Meredith*[7*], *Lynette Sholl*[7*], *Soumya Poddar, PhD*[8*], *Madison Davis*[9*], *Daquin Mao*[9*], *Simone Filosto, PhD*[8*], *Mike Mattie, PhD*[8*], *Philippe Armand, MD PhD*[10] *and Lakshmi Nayak, MD*[11]

Dana-Farber Cancer Institute, Boston, MA, United States

Table 1. Patient Characteristics

Characteristic		N (%)
Gender		
	Male Female	4 (44) 5 (56)
Age (years)	Median (Range)	60 (33-74)
Primary v Secondary CNSL	Primary Secondary	6 (67) 3 (33)
Cell of Origin	GCB Non-GCB Unknown	1 (11) 5 (56) 3 (33)
DHL/THL	Yes No Unknown	0 (0) 6 (67) 3 (33)
Double Expresor	Yes No Unknown	3 (33) 4 (44) 2 (22)
Tumor Location	Parenchymal only Leptomeningeal only Both Ocular CSF cytology positive	8 (89) 0 (0) 1 (11) 1 (11) 2 (22)
Number or prior systemic therapies	Median (Range)	2 (1-6)
Disease status to last line of therapy	Relapsed Refractory	4 (44) 5 (56)
Time from CNSL diagnosis to enrollment	Days (range)	281 (121-8666)
Time from last therapy to enrollment	Days (range)	57 (16-392)

Results: Efficacy



Median f/u: 11.3m (3.0-19.0m)

Best ORR: 78%
- uCR/CR: 67%
- PR: 11%

6m ORR: 78%

Time to best response (median): 3m

Adverse Events of Interest

	CRS	ICANS
Any grade, n (%)	8 (89)	4 (44)
Grade 3+, n (%)	0 (0)	3 (33)
Median time to onset (range)	2 days (1-6)	3.5 days (1-6)
Median duration (range)	4 days (1-8)	5.5 days (4-22)
Toci administered, n (%)	7 (78%)	0 (0)
Median number of doses (range)	1 (1-3)	n/a
Dex administered, n (%)	6 (67%)	3 (33%)
Median number of doses (range)	2 (1-10)	10 (9-26)

	1m	3m
Prolonged grade 3+ cytopenias	3/9 (33%)	0/9 (0%)
Neutropenia	3/9 (33%)	0/9 (0%)
Thrombocytopenia	1/9 (11%)	0/9 (0%)
Anemia	0/0 (0%)	0/9 (0%)

- There were no TLTs
- There was one SAE: staphylococcus meningitis related to an Ommaya infection requiring explant
- No patients experienced grade 4 ICANS
- There have been two deaths due to PD

4199 Assessment of Durable Responses after Brexucabtagene Autoleucel (KTE-X19) in the ZUMA-2 Study in Relapsed/Refractory Mantle Cell Lymphoma (R/R MCL)

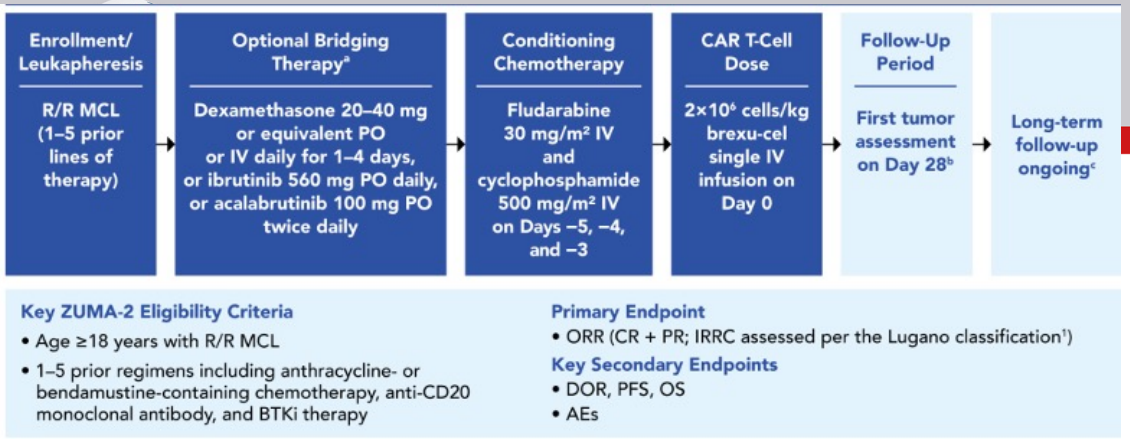
Program: Oral and Poster Abstracts
Session: 623. Mantle Cell, Follicular, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: Poster III
Hematology Disease Topics & Pathways:
Research, clinical trials, Biological therapies, Lymphomas, Clinical Research, Chimeric Antigen Receptor (CAR)-T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

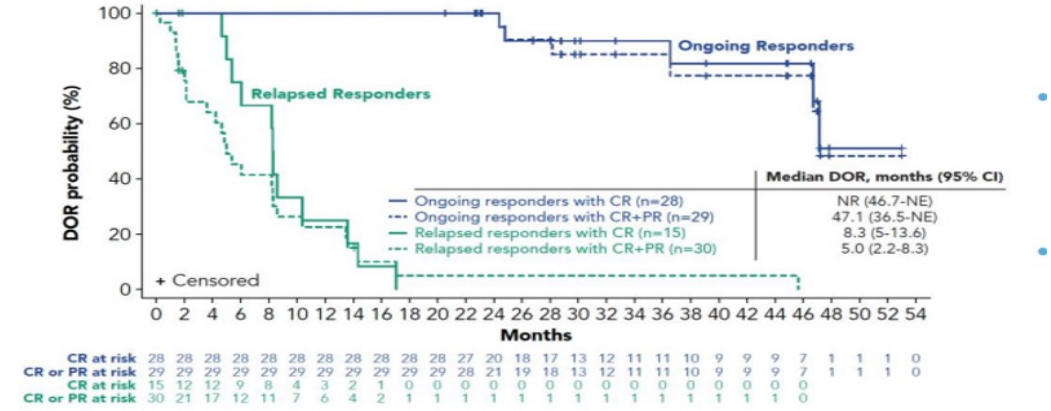
Monday, December 12, 2022, 6:00 PM-8:00 PM

Phoenix, Arizona

Javier Munoz, MD, MS, MBA[1], *Patrick M. Reagan, MD*[2], *Andre H. Goy, MD, MS*[3*], *David B. Miklos, MD, PhD*[4], *Dan Zheng, PhD*[5*], *Xiang Fang, PhD*[5*], *Rhine R. Shen, PhD*[5*], *Rubina Siddiqi, PhD, MBA*[5*], *Ioana Kloos, MD, FRCPC*[5*], *Marie José Kersten, MD, PhD*[6] *and Michael Wang, MD*[7]

[1]*Banner MD Anderson Cancer Center, Gilbert, AZ*
[2]*University of Rochester School of Medicine, Rochester, NY*
[3]*John Theurer Cancer Center, Hackensack, NJ*
[4]*Division of BMT and Cellular Therapy, Stanford University, Stanford, CA*
[5]*Kite, a Gilead Company, Santa Monica, CA*
[6]*on behalf of HOVON/LLPC, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands*
[7]*University of Texas MD Anderson Cancer Center, Houston, TX*





Duration of Response for Ongoing and Relapsed Responders in ZUMA-2

The median (95% CI) DOR in ongoing responders with CR (n=28) was not reached (46.7-not estimable [NE]) and was 8.3 months (5.0-13.6) in relapsed responders with CR (n=15)

After 35.6 months of median follow-up, brexu-cel continues to demonstrate durable responses with 47% of responders still in ongoing response at 24 months postinfusion in ZUMA-2

Ongoing responders tended to have lower ECOG PS scores, lower tumor burden, and less frequent use of prior platinum therapy or bridging therapy compared with relapsed responders, suggesting the potential for greater benefit with brexu-cel in earlier courses of disease

Munoz et al. ASH 2022 Abstract 4199

656 Real-World Outcomes for Patients with Relapsed or Refractory (R/R) Aggressive B-Cell Non-Hodgkin's Lymphoma (aBNHL) Treated with Commercial Tisagenlecleucel: Subgroup Analyses from the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry

Program: Oral and Poster Abstracts
Type: Oral
Session: 705. Cellular Immunotherapies: Results from CD19-Directed CAR T in treating Aggressive B-cell Lymphomas
Hematology Disease Topics & Pathways:
Research, Biological therapies, adult, Lymphomas, non-Hodgkin lymphoma, Clinical Research, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, real-world evidence, Therapies, registries, Lymphoid Malignancies, Adverse Events, Study Population, Human

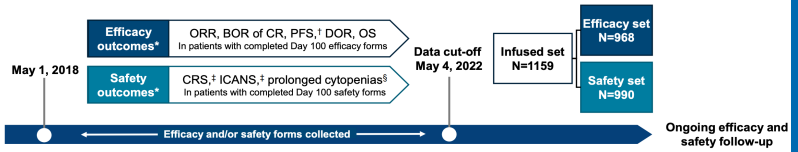
Sunday, December 11, 2022: 4:45 PM

Daniel J. Landsburg, MD[1], *Matthew Frigault, MD, MS*[2], *Michael Heim*[3*], *Stephen Ronan Foley, MD, FRCPC*[4], *Brian T. Hill, MD, PhD*[5], *Christine M. Ho, MD*[6], *Caron A. Jacobson, MD*[7], *Samantha Jaglowski, MD, MPH*[8], *Frederick L. Locke, MD*[9], *Ron Ram, MD*[10*], *Peter A. Riedell, MD*[11*], *Gunjan L. Shah, MD*[12*], *Leslie L. Popplewell, MD, FACP, MPH*[13], *Ranjan Tiwari*[14*], *Stephen Lim, MD*[15*], *Marta Majdan, DPhil*[15*], *Aisha Masood, MD*[15], *Marcelo C Pasquini, MD, MS*[3] *and Cameron J. Turtle, MBBS, PhD*[16,17]

Hospital of the University of Pennsylvania

Study design

- Non-interventional, prospective, longitudinal study using CIBMTR cellular therapy registry data
- Patients were treated in the USA, Canada and Israel
- At data cut-off, 1159 patients had received tisagenlecleucel (infused set)



*Center-reported; †Defined as time from first tisagenlecleucel infusion to first documented disease progression or death due to any cause; ‡ASTCT grading criteria; §Patients with longer than 30 days of follow-up and who failed to recover neutrophil/platelet levels at Day 30 (never recovered or recovered after Day 30)
ASTCT, American Society for Transplantation and Cellular Therapy; BOR, best overall response; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell-associated neurotoxicity syndrome; ORR, overall response rate; OS, overall survival; PFS, progression-free survival

Oral presentation at the 2022 ASH Annual Meeting & Exposition, held December 10–13, 2022

Baseline demographics and disease characteristics

Infused set (N=1159)	n (%)
Age ≥65 years	668 (57.6)
Comorbidities (any)*	511 (44.1)
Pulmonary	305 (26.3)
Renal	36 (3.1)
Cardiac	186 (16.0)
Hepatic	121 (10.4)
ECOG performance status	
0–1	967 (83.4)
≥2	55 (4.7)
Unknown	137 (11.8)
Disease status at infusion	
Active disease	1071 (92.4)
Morphologic CR	78 (6.7)
Unknown	10 (0.9)
≥3 prior therapies	707 (61.0)

Infused set (N=1159)	n (%)
Prior HSCT	288 (24.8)
LDH prior to infusion†	
Normal	498 (43.0)
Elevated	508 (43.8)
Unknown	153 (13.2)
LDC regimen	
Fludarabine-based	979 (84.5)
Bendamustine	159 (13.7)
Other	13 (1.1)
Unknown	8 (0.7)
Disease histology	
DLBCL (*de novo*)	713 (61.5)
DLBCL (with transformation)‡	230 (19.8)
HGBCL	169 (14.6)
Other§	47 (4.1)

*Includes comorbidities at a severity level that would have made patients ineligible for the JULIET trial. Patients may have more than one comorbidity; †LDH was taken as the last known value prior to LDC, or prior to infusion for patients who did not receive LDC; ‡May include transformation from FL, CLL and other histologies; §Including PMBCL and FL
CLL, chronic lymphocytic leukemia; CR, complete remission; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; HSCT, hematopoietic stem cell transplant; LDC, lymphodepleting chemotherapy; LDH, lactate dehydrogenase; PMBCL, primary mediastinal large B-cell lymphoma

Oral presentation at the 2022 ASH Annual Meeting & Exposition, held December 10–13, 2022

Daniel J. Landsburg, et al. ASH 2022

Safety outcomes

Safety set (N=990)	n (%)
CRS*	576 (58.2)
Grade ≥3	59 (6.0)
CRS grade on receipt of tocilizumab†	
Grade 1	134 (42.5)
Grade 2	122 (38.7)
Grade ≥3	56 (17.8)
Grade unknown	3 (1.0)
ICANS*	223 (22.5)
Grade ≥3	73 (7.4)
Prolonged cytopenia‡	
Neutropenia	66 (6.7)
Thrombocytopenia	132 (13.3)

Efficacy outcomes

Efficacy set (N=968)	% (95% CI)
ORR	59.5 (56.3–62.6)
BOR of CR	44.5 (41.4–47.7)
Month 24 PFS	28.4 (24.7–32.1)
Month 24 DOR*	52.6 (46.9–58.0)
Month 24 OS	43.6 (39.1–48.0)

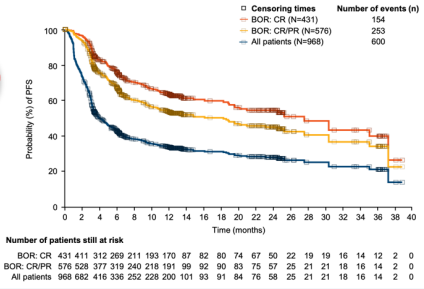
Progression-free survival

In patients who achieved CR

Month 6	Month 12	Month 24
76.2% (71.7–80.1)	**63.7%** (58.3–68.5)	**54.7%** (48.2–60.8)

Overall population

Month 6	Month 12	Month 24
43.2% (40.0–46.5)	**34.1%** (30.8–37.4)	**28.4%** (24.7–32.1)



PFS defined as time from first tisagenlecleucel infusion to first documented disease progression or death due to any cause. With censoring at post-infusion HSCT. Time is relative to tisagenlecleucel infusion (1 month = 30.4 days)
BOR, best overall response; CR, complete response; HSCT, hematopoietic stem cell transplant; PFS, progression-free survival; PR, partial response

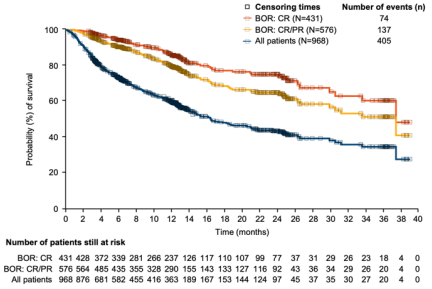
Overall survival

In patients who achieved CR

Month 6	Month 12	Month 24
94.2% (91.4–96.1)	**85.9%** (81.6–89.2)	**75.2%** (68.8–80.5)

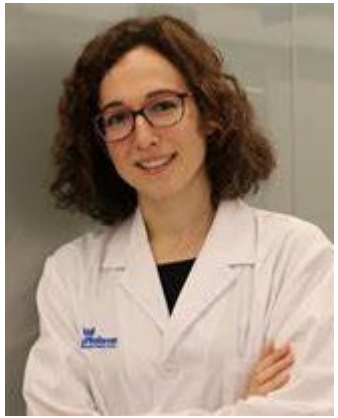
Overall population

Month 6	Month 12	Month 24
73.2% (70.2–76.0)	**59.7%** (56.1–63.0)	**43.6%** (39.1–48.0)



Without censoring at post-infusion HSCT. Time is relative to tisagenlecleucel infusion (1 month = 30.4 days)
BOR, best overall response; CR, complete response; HSCT, hematopoietic stem cell transplant; PR, partial response

658 Recent Bendamustine Treatment before Apheresis Has a Negative Impact on Outcomes in Patients with Large B-Cell Lymphoma Receiving Chimeric Antigen Receptor T-Cell Therapy



Barcelona, Spain

Program: Oral and Poster Abstracts
Type: Oral
Session: 705. Cellular Immunotherapies: Results from CD19-Directed CAR T in treating Aggressive B-cell Lymphomas
Hematology Disease Topics & Pathways:
Research, Biological therapies, Lymphomas, Clinical Research, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, real-world evidence, Therapies, Lymphoid Malignancies

Sunday, December 11, 2022: 5:15 PM

Gloria Iacoboni, MD[1*], *ANA Africa Martin Lopez*[2*], *Katarzyna Aleksandra Jalowiec*[3*], *Mi Kwon, MD, PhD*[4*], *Kai Rejeski, MD*[5], *Víctor Navarro Garcés*[6*], *Paula Amat, MD PhD*[7*], *Juan Luis Reguera, MD*[8*], *Laura Gallur, MD*[1*], *Sara Gutierrez-Herrero*[9*], *Claire Roddie*[3*], *Gillen Oarbeascoa*[10*], *Ana Benzaquén, MD*[7*], *Cecilia Carpio, MD*[1*], *Lucía López Corral, MD*[2*], *Rafael Hernani, MD*[7*], *Mariana Bastos-Oreiro, MD, PhD*[10*], *Marion Subklewe, MD*[11], *Maeve O'Reilly*[3*], *Lourdes Martín*[9*] *and Pere Barba, MD*[1*]

Figure 1.- CAR T-cell composition at peak expansion after infusion according to previous bendamustine exposure.

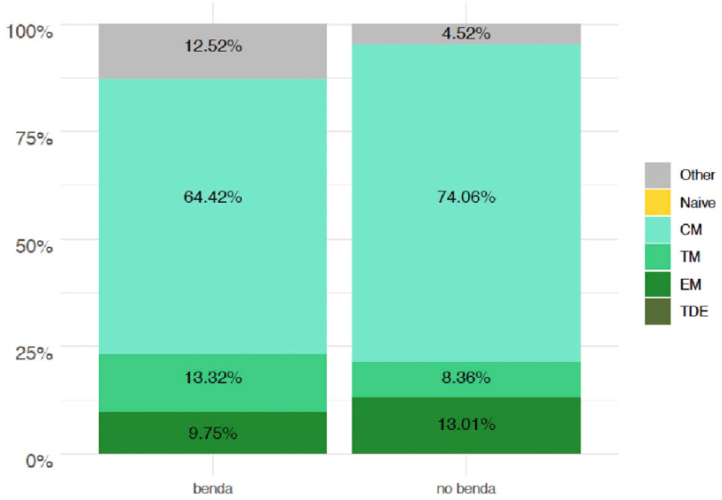


Figure 2.- Best response achieved after CAR T-cell therapy depending on the use and timing of previous bendamustine.

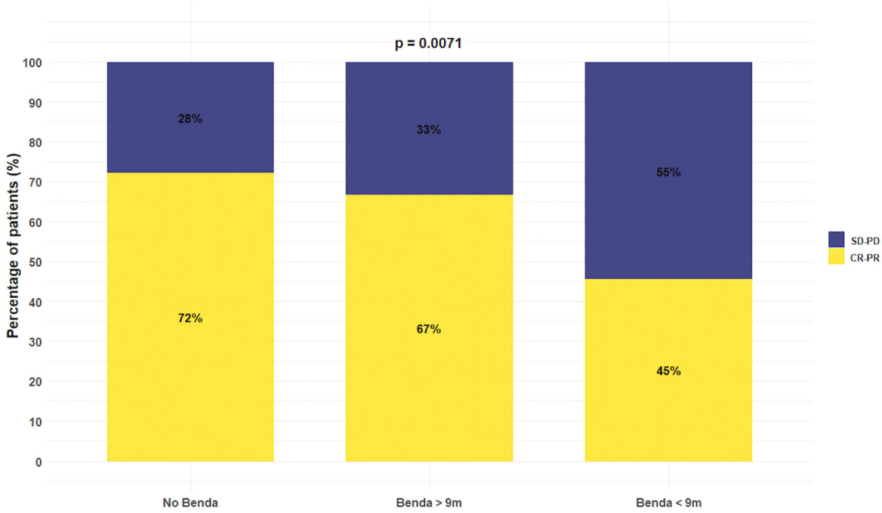


Figure abbreviations: CM central memory, TM transitional memory, EM, effector memory, TDE terminal effector, CR complete response, PR partial response, SD stable disease, PD progressive disease

Gloria Iacoboni, et al. ASH 2022

705. Cellular Immunotherapies: Late Phase and Commercially Available Therapies: Poster I

Symposia: Cellular Immunotherapies: Late Phase and Commercially Available Therapies Program: Oral and Poster Abstracts
Type: Poster

Saturday, December 10, 2022: 5:30 PM-7:30 PM
Hall D (Ernest N. Morial Convention Center)

Phoenix, Arizona

2022

Real-World Bridging Therapy (BT) of Patients with Relapsed or Refractory (r/r) Large B-Cell Lymphoma (LBCL) Treated with Chimeric Antigen Receptor (CAR) T-Cell Therapy: A Systematic Literature Review (SLR) and Meta-Analysis

Javier Muñoz, MD, MS, MBA, FACP[1*], *Zhen-Huan Hu, MPH*[2*], *Steve Kanters, PhD, MSc*[3*], *Eve H Limbrick-Oldfield*[3*], *Harry Miao, MD, PhD*[2*], *Clare Spooner, MBBS, BSc*[2*], *Hairong Xu, MD, PhD*[2*] *and Robin Sanderson, PhD, FRCPath*[4]

[1]*Banner MD Anderson Cancer Center, Gilbert, AZ*
[2]*Kite, a Gilead Company, Santa Monica, CA*
[3]*RainCity Analytics, Vancouver, BC, Canada*
[4]*King's College Hospital, London, United Kingdom*

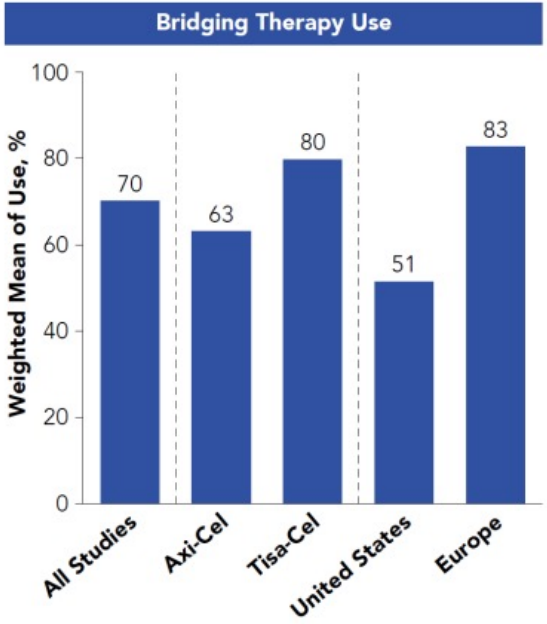
Baseline Characteristics of Axi-Cel and Tisa-Cel Recipients

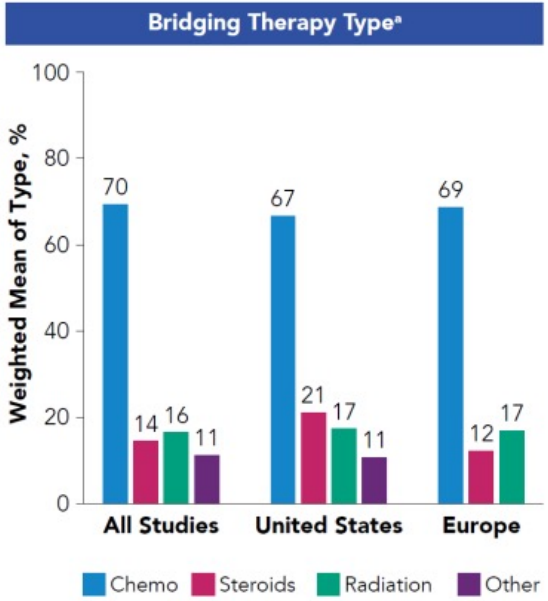
- Use of bridging therapy, defined as anticancer therapy given between leukapheresis and lymphodepletion, has varied in clinical studies of chimeric antigen receptor (CAR) T-cell therapy in patients with relapsed/refractory (R/R) large B-cell lymphoma (LBCL)[1-3]
  - In the pivotal ZUMA-1 study of axicabtagene ciloleucel (axi-cel), use of bridging therapy was not allowed[1]
  - In the JULIET trial for tisagenlecleucel (tisa-cel), bridging therapy was allowed and given to 92% of the patients before infusion[2]
  - In the TRANSCEND trial for lisocabtagene maraleucel (liso-cel), systemic and/or radiation therapy as bridging therapy was allowed and given to 59% of the patients[3]
- Across all product types, bridging therapy is used in real-world settings among patients with R/R LBCL treated with CAR T-cell therapy
  - Use of bridging therapy is at the discretion of treating physicians

	Axi-Cel		Tisa-Cel		
	N Studies	Estimate (95% CI)	N Studies	Estimate (95% CI)	*P* Value[a]
Median age, y	**25**	**59.5 (58.3-60.6)**	**6**	**62.6 (60.6-64.6)**	**<.01**
Male sex	23	65% (62-67)	6	64% (60-67)	.61
DLBCL	19	73% (67-78)	6	78% (66-86)	.41
PMBCL	**16**	**6% (5-8)**	**4**	**1% (0-3)**	**<.01**
tFL	17	18% (14-22)	6	15% (10-22)	.42
Double-/triple-hit	11	18% (15-21)	2	15% (11-21)	.39
Stage III or IV	16	77% (73-80)	5	75% (71-78)	.43
IPI ≥3	**11**	**51% (47-54)**	**3**	**41% (33-49)**	**.03**
ECOG PS ≥2	17	10% (7-14)	7	11% (5-21)	.79
Bulky disease	**10**	**24% (21-27)**	**5**	**16% (13-21)**	**<.01**
Refractory disease	8	47% (31-64)	4	57% (31-80)	.50
Median prior lines	14	3.2 (2.8-3.7)	2	3.0 (2.0-5.0)	.80
No. of prior lines ≥4	13	66% (57-74)	4	66% (47-81)	1.00
Prior ASCT	16	29% (23-35)	5	27% (20-35)	.67
Mean vein-to-vein time, d	**8**	**31.1**	**3**	**47.8**	**N/A[b]**

Munoz et al. ASH 2022 Abstract 2022

Patterns of Bridging Therapy Overall, By Product and By Regions





- On average, 63% of axi-cel patients received bridging therapy compared with 80% of tisa-cel patients
- Use of bridging therapy was more common in Europe (83%) than in the United States (51%)
- Among patients who received bridging therapy, the most common type was chemotherapy/ chemoimmunotherapy (70% overall; 62% for axi-cel; 88% for tisa-cel), followed by steroids in the United States (21%), or radiation therapy in Europe (17%)

Munoz et al. ASH 2022 Abstract 2022

264 The CAR-Hematotox Score Identifies Patients at High Risk for Hematological Toxicity, Infections and Poor Clinical Outcomes Following Brexucabtagene Autoleucel in Relapsed/Refractory Mantle Cell Lymphoma

Program: Oral and Poster Abstracts
Type: Oral
Session: 705. Cellular Immunotherapies: Novel Predictors of Response or Toxicity to Cellular Therapies
Hematology Disease Topics & Pathways:
Biological therapies, adult, Lymphomas, non-Hodgkin lymphoma, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, Therapies, Lymphoid Malignancies, Adverse Events, Study Population, Human

Saturday, December 10, 2022: 3:15 PM

Kai Rejeski, MD[1], *Yucai Wang, MD, PhD*[2], *Omar Albanyan, MD*[3], *Javier L Munoz, MD, MBA*[4*], *Pierre Sesques, MD*[5*], *Gloria Iacoboni, MD*[6*], *Lucía López Corral, MD PhD*[7*], *Razan Mohty, MD*[3], *Martin Dreyling, MD*[1], *Frederick L. Locke, MD*[3], *Pere Barba, MD, PhD*[6*], *Emmanuel Bachy, MD, PhD*[5*], *Yi Lin, MD, PhD*[8], *Marion Subklewe, MD*[9] *and Michael D. Jain, MD, PhD*[10]

Munich, Germany

- The CAR-HEMATOTOX represents an easy-to-apply score that helps to identify patients at high risk for severe infections and poor clinical outcomes prior to lymphodepletion. Post-CAR-T infection risk is driven by prolonged neutropenia and steroid use, but reduced by fluoroquinolone prophylaxis in high-risk patients.

- The score integrates parameters associated with pre-CAR-T hematopoietic reserve (e.g. ANC, hemoglobin, platelet count) and inflammation (e.g. CRP, ferritin). Whether the HT score is of prognostic utility in relapsed/refractory mantle cell lymphoma (R/R MCL) remains unstudied.

Platelet Count	> 175,000 /µl
Absolute Neutrophil Count (ANC)	< 1,200 /µl
Hemoglobin	> 9.0 g/dl
C-reactive protein (CRP)	> 3.0 mg/dl
Ferritin	< 650 ng/ml
CAR-HEMATOTOX score	2

Patient belongs to CAR-HEMATOTOX *high* risk group.

Hematological Toxicity	
Median duration of neutropenia (days 0-60)	12 days (95% CI: 10-16 days)
Severe neutropenia (ANC <500/µl)	99%
Profound neutropenia (ANC <100/µl)	89%
Severe, protracted neutropenia (ANC <500/µl, ≥7 days)	88%
Profound, protracted neutropenia (ANC <100/µl, ≥7 days)	47%
Prolonged neutropenia (ANC <1000/µl after day 21)	81%
Severe thrombocytopenia (PLT count <50 G/l)	87%
Severe anemia (Hb <8 g/dl or requiring pRBC)	96%

Infectious Complications (Day 0-90)	
Infection Rate, Any-Grade	56%
Infection Rate, Severe (Grade ≥3)	40%
Infection Rate, Any-Grade Bacterial	38%
Infection Rate, Severe (Grade ≥3) Bacterial	27%

Clinical Outcomes	
Median Progression-Free Survival	3.4 months (95% CI: 3.0 - 5.2 mo)
Median Overall Survival	9.1 months (95% CI: 7.4 - 17.6 mo)

Possible Next Steps
Consider antibacterial (e.g. fluoroquinolone) and antifungal prophylaxis
Consider early G-CSF growth factor support

German Lymphoma Alliance (german-lymphoma-alliance.de)

Rejeski et al. Blood (2021) 138 (24): 2499-2513.

705. Cellular Immunotherapies: Late Phase and Commercially Available Therapies: Poster II

Symposia: Cellular Immunotherapies: Late Phase and Commercially Available Therapies Program: Oral and Poster Abstracts
Type: Poster

Sunday, December 11, 2022: 6:00 PM-8:00 PM
Hall D (Ernest N. Morial Convention Center)

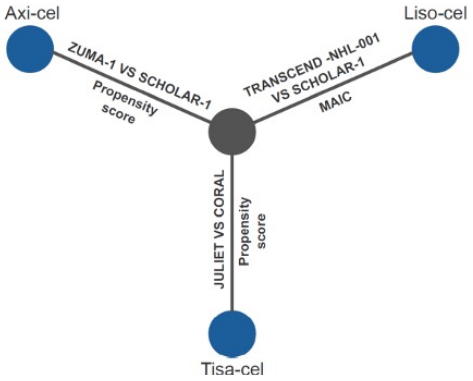
MOFFITT CANCER CENTER

3346 Network Meta-Analysis (NMA) of Chimeric Antigen Receptor (CAR) T-Cell Therapy for the Treatment of Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL) after 2 Prior Treatments Using Published Comparative Studies

Frederick L. Locke, MD[1], *Sattva S. Neelapu, MD*[2], *Markqayne D. Ray, PharmD, MBA*[3*], *Eve H Limbrick-Oldfield*[4*], *Sally W Wade, MPH*[5*], *Steve Kanters, PhD, MSc*[4*], *Anik R. Patel, PhD*[3*] *and Olalekan O. Oluwole, MBBS*[6]

[1]*H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*
[2]*Department of Lymphoma and Myeloma, M.D. Anderson Cancer Center, Houston, TX*
[3]*Kite, A Gilead Company, Santa Monica, CA*
[4]*RainCity Analytics, Vancouver, BC, Canada*
[5]*Wade Outcomes Research and Consulting, Salt Lake City, UT*
[6]*Vanderbilt University Medical Center, Nashville, TN*

Network of Evidence



- The three studies were a comparison of a CAR-T therapy to a historical SoC. One study was available for each of the approved CAR-T treatments.
- This allowed the creation of a connected network, with SoC as the common comparator.

Study Characteristics of Included Publications

CAR-T	Sample size*	Method	Variables included in adjustment
Axi-cel	Axi: 80 SoC: 340	Propensity scoring	Age, sex, NHL subtype, relapse post auto SCT, refractory to ≥2 lines of therapy, primary refractory, number prior lines
Liso-cel	Liso: 248 SoC: 636	MAIC	Age, sex, NHL subtype, prior auto SCTs, disease stage, IPI score, refractory to last therapy
Tisa-cel	Tisa: 111 SoC: 145	Propensity scoring	Age at diagnosis, disease stage, extranodal site involvement, r/r status (last line, all lines), time to 2nd line after diagnosis, prior auto SCT, number of relapses

Locke et al. ASH 2022 Abstract 3346

Network Meta-analysis Results

	OS (HR, 95% CrI)	ORR (OR, 95% CrI)	CR (OR, 95% CrI)
Compared to historical SoC:			
Axi-cel vs SoC	0.27 (0.00, 0.38)*	9.32 (5.11, 18.08)*	8.57 (4.96, 15.05)*
Liso-cel vs SoC	0.50 (0.40, 0.60)*	7.05 (4.71, 10.74)*	12.90 (8.17, 20.73)*
Tisa-cel vs SoC	0.57 (0.44, 0.73)*	1.66 (1.05, 2.65)*	--
Between CAR-T comparison:			
Axi-cel vs tisa-cel	0.47 (0.26, 0.88)*	5.62 (2.64, 12.42)*	--
Axi-cel vs liso-cel	0.54 (0.37, 0.79)*	1.32 (0.64, 2.87)	0.67 (0.32, 1.37)
Liso-cel vs tisa-cel	0.87 (0.42, 1.78)	4.24 (2.28, 7.91)*	--

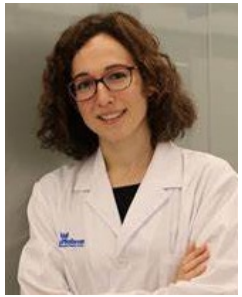
- As expected, all three CAR-T therapies resulted in significantly improved outcomes across OS, ORR and CR when compared to SoC.
- Axi-cel demonstrated significantly longer OS compared to both liso-cel (HR: 0.54) and tisa-cel (HR: 0.47). There was no difference between liso-cel and tisa-cel for OS.
- Axi-cel (OR: 5.62) and liso-cel (OR: 4.24) had significantly higher probability of objective response compared to tisa-cel, but there was no significant difference between axi-cel and liso-cel.
- Complete response was not reported for tisa-cel vs. SoC, so comparisons were limited.

Locke et al. ASH 2022 Abstract 3346

155 Salvage Treatment with Novel Agents Is Preferable to Standard Chemotherapy in Patients with Large B-Cell Lymphoma Progressing after Chimeric Antigen Receptor T-Cell Therapy

Program: Oral and Poster Abstracts
Type: Oral
Session: 627. Aggressive Lymphomas: Clinical and Epidemiological: Treatment of CNS Lymphoma, Neurologic Toxicities, and Relapsed/Refractory DLBCL
Hematology Disease Topics & Pathways:
Research, Lymphomas, Clinical Research, Combination therapy, Diseases, real-world evidence, aggressive lymphoma, Therapies, Lymphoid Malignancies

Saturday, December 10, 2022: 1:00 PM



Barcelona, Spain

Gloria Iacoboni, MD[1*], *Josu Iraola-Truchuelo*[2*], *Alberto Mussetti*[3*], *Paula Fernández-Caldas*[4*], *Víctor Navarro Garcés*[5*], *ANA Africa Martin Lopez*[6*], *Javier Delgado*[7*], *Ariadna Pérez Martínez*[8*], *Manuel Guerreiro, MD*[9*], *Ana Carolina Carolina Caballero Gonzalez, MD*[10*], *Nuria Martínez-Cibrián*[11*], *Hugo Daniel Luzardo Henriquez*[12*], *Jose M. Sanchez, MD*[13*], *Juan-Manuel Sancho, MD, PhD*[14*], *Pere Barba, MD*[1*], *Mi Kwon, MD, PhD*[15*], *Lucía López Corral, MD*[6*], *Rafael Hernani, MD*[8*], *Juan Luis Reguera, MD*[7*], *Anna Sureda*[3], *Alejandro Martín García-Sancho, MD, PhD*[6*], *Mariana Bastos-Oreiro, MD, PhD*[4*] *and Pau Abrisqueta, MD, PhD*[1*]

A retrospective, multicenter study including 217 patients with R/R LBCL infused at 12 sites with commercially available CAR T-cell products until June 2022 who had a confirmed progression

Gloria Iacoboni, ASH 2022

Table 1.- Baseline characteristics of patients who progressed after CAR T-cell treatment

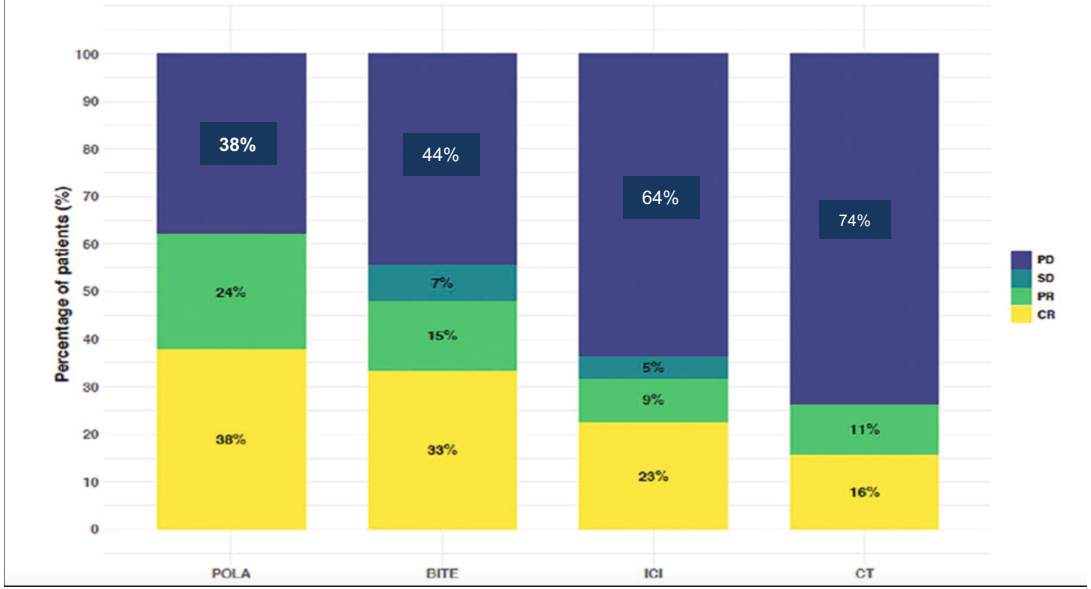
Variables	Full population n=217	No Treatment n=79	Treatment n=138
Patient and lymphoma characteristics			
Male gender, n (%)	143 (66)	50 (63)	93 (67)
Age, median years (IQR)	56 (45-64)	61 (51-68)	52 (43-62)
Histology, n (%)			
- DLBCL	147 (68)	52 (68)	95 (69)
- HGBCL	35 (16)	13 (17)	22 (16)
- PMBCL	10 (5)	2 (3)	8 (6)
- THRLBCL	11 (5)	7 (9)	4 (3)
- tFL	12 (6)	3 (4)	9 (7)
> 3 prior lines, n (%)	40 (19)	19 (25)	21 (16)
Previous SCT, n (%)	54 (25)	16 (20)	38 (28)
Primary refractory*, n (%)	138 (64)	47 (60)	91 (66)
Refractory to last therapy**, n (%)	185 (86)	67 (86)	118 (87)
Stage III-IV, n (%)***	176 (83)	67 (86)	109 (81)
IPI score 3-5, n (%)***	116 (57)	49 (67)	67 (51)
LDH > 2xULN, n (%)***	56 (26)	26 (33)	30 (22)
ECOG >1, n (%)***	16 (8)	10 (13)	6 (4)
CAR-T related characteristics			
CAR costimulatory domain, n (%)			
- CD28	84 (39)	25 (32)	59 (43)
- 4-1BB	132 (61)	54 (68)	78 (57)
Best response after CAR-T			
- CR/PR	106 (49)	28 (35)	78 (57)
- SD/PD	111 (51)	51 (65)	60 (43)
CRS, n (%)			
- Any grade	163 (75)	62 (78)	101 (73)
- Grade ≥3	13 (6)	9 (11)	4 (3)
ICANS, n (%)			
- Any grade	57 (26)	27 (34)	30 (22)
- Grade 3-4	22 (10)	12 (15)	10 (7)
Time from infusion to progression			
- < 2 months	96 (45)	46 (60)	50 (36)
- 2-6 months	95 (44)	28 (36)	67 (49)
- > 6 months	23 (11)	3 (4)	20 (15)

138 (64%) patients received treatment

- POLA (+ R + Benda), (N=31)
- BITE (N=27) in monotherapy or combination,
- Standard chemotherapy (CT) (N=27)
- Checkpoint inhibitors (ICI) (N=23)

Gloria Iacoboni, ASH 2022

Figure 1.- Best response achieved after first-line salvage treatment in LBCL patients progressing after CAR T-cells.



Fondazione IRCCS
Istituto Nazionale dei Tumori
via Venezian, 1 20133 Milano

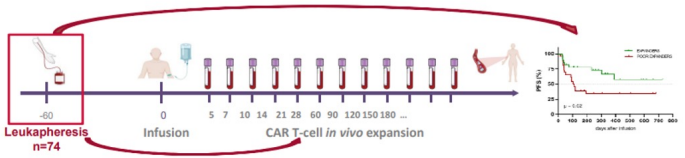
260 A 7-Gene Signature in Unmanipulated Leukaphereses Correlates with *in-Vivo* CAR T-Cell Expansion and Survival of Lymphoma Patients Receiving Tisagenlecleucel or Axicabtagene Ciloleucel Therapy

Program: Oral and Poster Abstracts
Type: Oral
Session: 705. Cellular Immunotherapies: Novel Predictors of Response or Toxicity to Cellular Therapies
Hematology Disease Topics & Pathways:
Research, Biological therapies, Translational Research, Lymphomas, B Cell lymphoma, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Diseases, cell expansion, Therapies, Lymphoid Malignancies, Technology and Procedures, profiling

Saturday, December 10, 2022: 2:15 PM

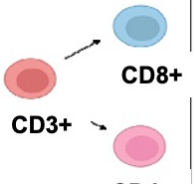
Cristiana Carniti[1*], *Nicole Caldarelli*[1,2*], *Francesca Nanetti*[1*], *Martina Magni*[1*], *Emma Esposito*[3*], *Tommaso Torelli*[4*], *Luca Agnelli*[4*], *Silvia Brich*[5*], *Chiara Monfrini*[1*], *Eugenio Fardella*[6*], *Paolo Longoni*[7*], *Daniele Lorenzini*[5*], *Martina Pennisi*[1*], *Annalisa Chiappella*[1*] *and Paolo Corradini*[1,8]

Do T-cell features at LK influence the outcome?



Patient characteristics do not affect T-cell composition at LK (assessed by flow cytometry)

- Age (median 56 years, range 24-73)
- Sex (62% males)
- Histologies
- Normalised LDH (UNL in 34%)
- Number of prior treatments (75% >2)
- High dose chemotherapy pre ASCT (27%)
- Prior Checkpoint inhibitors (in 15%)
- CAR T-cell product (54% Axi; 46% Tisa)



T naïve [T_N (CD45RO−/CD197+/CD62L+)]

T stem cell memory [T_{SCM}(CD45RO-/CD197+/CD62L+/CD95+)]

T central memory [T_{CM}(CD45RO+/CD197+)]

T effector [T_E(CD45RO-/CD197-)]

T naïve [T_N (CD45RO−/CD197+/CD62L+)]

→ *age and sex do not affect the T-cell composition at leukapheresis nor do the type and N° of prior treatment patients received*

Carniti C, ASH 2022 Oral Presentation

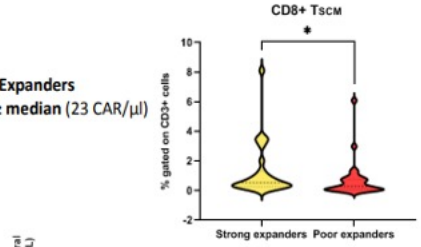
- **Median concentration of CAR T cells at day 10 (C_{10}=26 cells/ul) after infusion was used to dichotomize pts into "expanders" (EX, n=28) and "poor-expanders" (PEX, n=27)**

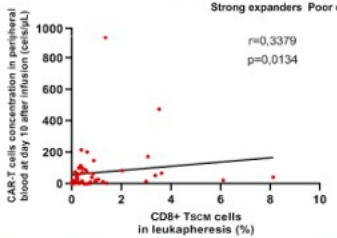
- **EX had significantly higher levels of CD3+ and CD8+T_{SCM} cells than PEX**

T stem cell memory= T_{SCM}

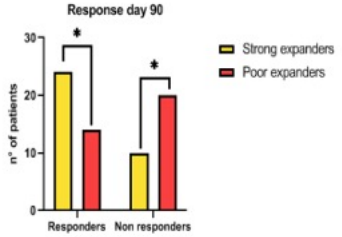
Does T-cell differentiation at LK affects expansion?

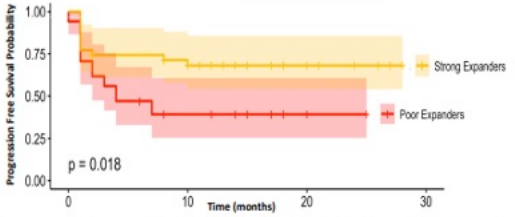
Strong Expanders
→ **C_{10} ≥ median** (23 CAR/µl)





Response
→ **CR + PR by day 90** after CAR T



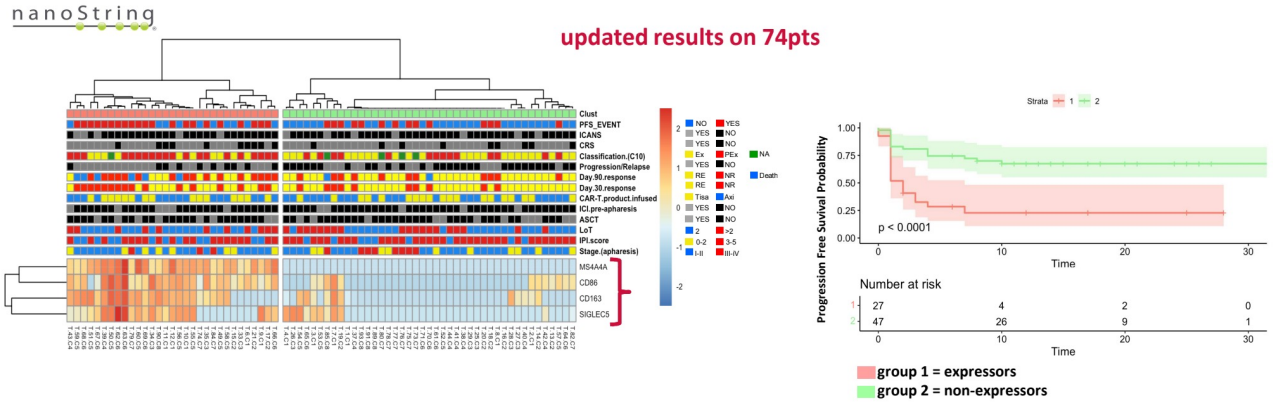


→ ***A less-differentiated state of CD8 T cells at leukapheresis is associated to in vivo CAR T-cell expansion and thus response and survival***

Carniti C, ASH 2022 Oral Presentation

A 4-gene signature in LK correlates with survival

Gene model (including *PSAT1*, *BATF3*, *SIGLEC5*, *CD86*, *MS4A4A*, *HLA-DQA1* and *MS4A1*) capable of distinguishing EX and PEX and segregating pts with different survival probabilities



→ ***a 4-gene model segregates pts with different progression free survival***

The predictive power of the 4-gene model was confirmed by leave-one-out cross validation, gaining >93% overall accuracy (with only 5/74 misclassified samples)

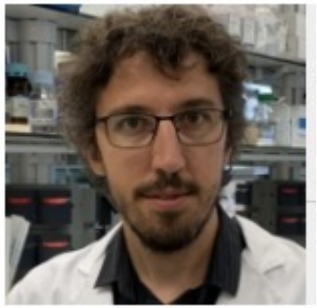
The 4-gene signature supports the idea that specific subsets of T suppressive monocytes at LK might be detrimental for CAR T production but might also reflect the immunosuppressive status of the tumor microenvironment in lymphoma patients receiving CAR T cells

Carniti C, ASH 2022 Oral Presentation

439 YTB323 (Rapcabtagene Autoleucel) Demonstrates Durable Efficacy and a Manageable Safety Profile in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Phase I Study Update

Program: Oral and Poster Abstracts
Type: Oral
Session: 626. Aggressive Lymphomas: Prospective Therapeutic Trials: Immune Based and Targeted Therapies in Relapsed/Refractory Large B-Cell Lymphoma
Hematology Disease Topics & Pathways:
Research, clinical trials, Biological therapies, adult, Clinical Research, Chimeric Antigen Receptor (CAR)-T Cell Therapies, Therapies, Adverse Events, Study Population, Human

Sunday, December 11, 2022: 9:30 AM



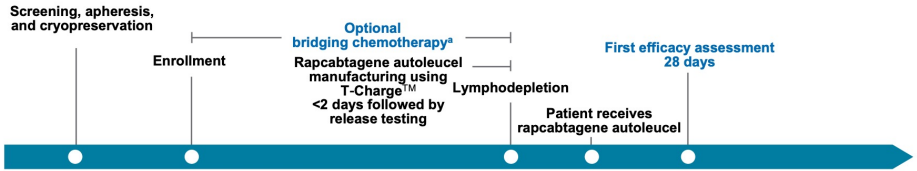
Pere Barba, MD[1*], *Mi Kwon, MD, PhD*[2*], *Javier Briones, MD, PhD*[3*], *Ulrich Jaeger, MD*[4], *Emmanuel Bachy, MD, PhD*[5*], *Didier Blaise, MD, PhD*[6], *Nicolas Boissel, MD, PhD*[7], *Koji Kato, MD, PhD*[8*], *Nirav N. Shah, MD*[9], *Matthew Frigault, MD, MS*[10], *Peter A. Riedell, MD*[11*], *Leyla O. Shune, MD*[12], *Takanori Teshima, M.D., Ph.D.*[13], *Fabio Ciceri, MD*[14*], *David Pearson, PhD*[15*], *Elena J Orlando, PhD*[16*], *Lan Yi, PhD*[17*], *Jaclyn Davis, MD*[18], *Aisha Masood, MD*[17], *Ian W. Flinn, MD PhD*[19] *and Michael Dickinson, MD*[20]

Vall d'Hebron University Hospital, Barcelona, Spain

- Rapcabtagene autoleucel (YTB323) is an autologous CD19-directed CAR-T cell therapy rapidly manufactured (<2 days) using the next-generation T-Charge™ platform that preserves T-cell stemness
- **This presentation focuses on the r/r DLBCL cohort (N=47) with 13 months' median follow-up (data cutoff September 15, 2022) in the Phase I, first-in-human trial[3] of rapcabtagene autoleucel**

CAR, chimeric antigen receptor; CD, cluster of differentiation; DLBCL, diffuse large B-cell lymphoma; r/r, relapsed or refractory.
1. Friedberg JW. *Hematology Am Soc Hematol Educ Program*. 2011;2011:498-505; 2. Crump M, et al. Blood. 2017;130(16):1800-1808;
3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03960840. Accessed October 26, 2022.

Study Design: DLBCL Treatment Arm



Key eligibility criteria	Study treatment	End points
• ≥18 years of age • Measurable disease at enrollment • ECOG PS 0-1 • Relapsed/refractory disease[b]	• Lymphodepleting chemotherapy: fludarabine (30 mg/m² IV daily ×3 days) + cyclophosphamide (500 mg/m² IV daily ×3 days) • Rapcabtagene autoleucel dose levels (single IV dose): – DL1, 2.5×10⁶ CAR+ cells – DL2, 12.5×10⁶ CAR+ cells – DL3, 25×10⁶ CAR+ cells – DL4, 40×10⁶ CAR+ cells	**Primary:** Incidence of DLTs[c] and safety to determine a recommended dose **Secondary:** Cellular kinetics, ORR, DOR, OS

CAR, chimeric antigen receptor; DL, dose level; DLBCL, diffuse large B-cell lymphoma; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HSCT, hematopoietic stem cell transplant; IV, intravenous; ORR, overall response rate; OS, overall survival.
[a]Optional bridging therapies were investigator's decision. [b]Relapsed/refractory disease is defined as patients who have failed 2 or more lines of chemotherapy and either progressed (or relapsed) after autologous HSCT or were ineligible for or did not consent to the procedure. [c]Within 28 days of receiving rapcabtagene autoleucel.

Presented at the 2022 ASH Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA, USA, and Virtual

Patient and Disease Baseline Characteristics

Baseline Variable	Rapcabtagene Autoleucel Infused (N=47)
Median age (range), y	65 (35-79)
IPI score, n (%)	
<3	25 (53.2)
≥3	20 (42.6)
Unknown	2 (4.3)
Rearrangements in *MYC/BCL2/BCL6* genes, n (%)	
Double/triple hits	16 (34.0)
Negative	14 (29.8)
Unknown	17 (36.2)
Relapsed/refractory disease status, n (%)	
Refractory to all prior lines	10 (21.3)
Refractory to last line of therapy only	16 (34.0)
Relapsed after last line of therapy	21 (44.7)
Histology, n (%)	
DLBCL	45 (95.7)
Transformed lymphoma/other	2 (4.3)
Elevated LDH (>ULN),[a] n (%)	26 (55.3)
Prior HSCT, n (%)	14 (29.8)
No. prior lines of therapy, n (%)	
2	34 (72.3)
≥3	13 (27.7)
Time since most recent relapse/progression to rapcabtagene autoleucel infusion, median (range), mo	2.8 (1.4-11.1)
Received bridging therapy,[b] n (%)	32 (68.1)

Rapcabtagene Autoleucel: Best Overall Response

	Rapcabtagene Autoleucel Dose Levels			
	DL1 2.5×10⁶ (N=4)	DL2 12.5×10⁶ (N=30)	DL3 25×10⁶ (N=7)	DL4 40×10⁶ (N=6)
	n (%)	n (%)	n (%)	n (%)
Best overall response				
CR	3 (75)	**22 (73)**	5 (71)	4 (67)
CR excluding patients with CR before infusion[a]	1/2 (50)	**19/27 (70)**	5/7 (71)	4/6 (67)
PR	0	**3 (10)**	0	0
Overall response rate[b] [95% CI][c]	3 (75) [19.4-99.4]	**25 (83) [65.3-94.4]**	5 (71) [29.0-96.3]	4 (67) [22.3-95.7]

- Median follow-up (infusion to cutoff date) across the 4 dose levels was 13 months (4.4-34.3 months)

CR, complete response; DL, dose level; PR, partial response.
Patients infused at least 28 days before cutoff.
[a]Excludes patients who were in CR prior to receiving rapcabtagene autoleucel due to either a late effect of prior therapies or bridging chemotherapy.
[b]Overall response rate = CR + PR.
[c]95% CIs are exact Clopper-Pearson CIs.

5

Presented at the 2022 ASH Annual Meeting and Exposition; December 10-13, 2022; New Orleans, LA, USA, and Virtual

YTB323

Abstract # 439 - Oral
December 11, 2022 | 9:30 AM CT

YTB323 (Rapcabtagene Autoleucel) Demonstrates Durable Efficacy and a Manageable Safety Profile in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma (R/R DLBCL): Phase I Study Update

CRS Was Low Grade and Resolved Within a Median of 6 Days from Onset at DL2

	Treated Patients (N=47)			
	DL1 2.5×10⁶ (N=4)	DL2 12.5×10⁶ (N=30)	DL3 25×10⁶ (N=7)	DL4 40×10⁶ (N=6)
CRS,[a] n (%)	1 (25)	**11 (37)**	2 (29)	2 (33)
Grade 1/2	1 (25)	**9 (30)**	2 (29)	2 (33)
Grade 3/4	0	**2 (7)**	0	0
Time to onset, days	9	**8 (1-17)[b]**	7, 36	2, 9
Time from onset to resolution, days	5	**6 (2-25)[b]**	5, 10	5, 7
Admitted to ICU for CRS, n/N (%)	0	**3/11 (27)**	0	0
Management of CRS, n/N (%[c])				
Tocilizumab	0	**8/11 (73)**	1/2 (50)	0
Corticosteroids	0	**4/11 (36)**	0	0
Vasopressors	0	**2/11 (18)**	0	0

ICANS Was Manageable

	Treated Patients (N=47)			
	DL1 2.5×10⁶ (N=4)	DL2 12.5×10⁶ (N=30)	DL3 25×10⁶ (N=7)	DL4 40×10⁶ (N=6)
ICANS,[a] n (%)	0	**3 (10)**	0	2 (33)
Grade 1/2	0	**1 (3)**	0	2 (33)
Grade 3/4	0	**2 (7)**	0	0
Time to onset, days	–	**16 (10-28)[b]**	–	6, 28
Time from onset to resolution, days	–	**16 (11-24)[b]**	–	1, 25
Management of ICANS, n/N (%[c])				
Dexamethasone	–	**2/3 (67)**	–	1/2 (50)
Methylprednisolone	–	**1/3 (33)**	–	0
Anakinra	–	**1/3 (33)**	–	0

4198 Results from a Phase 1/2 Study of Tandem, Bispecific Anti-CD20/Anti-CD19 (LV20.19) CAR T-Cells for Mantle Cell Lymphoma

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

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

Nirav N. Shah, MD[1], *Fateeha Furqan, MD*[2], *Aniko Szabo, PhD*[3*], *Jessica Neumann*[2*], *Parameswaran Hari, MD, MRCP*[4], *Dina Schneider*[5*], *Bryon Johnson, PhD*[1], *Mehdi Hamadani, MD*[1] *and Timothy S. Fenske, MD*[2]

[1]*Department of Hematology & Oncology, Medical College of Wisconsin, Milwaukee, WI*
[2]*Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee, WI*
[3]*Division of Biostatistics, Institute of Health & Equity, Medical College of Wisconsin, Milwaukee, WI*
[4]*Medical College of Wisconsin, Milwaukee, WI*
[5]*A Miltenyi Biotec Company, Lentigen Technology Inc., Gaithersburg, MD*

Table 1: Clinical characteristics of patients receiving LV20.19 CAR T-cells

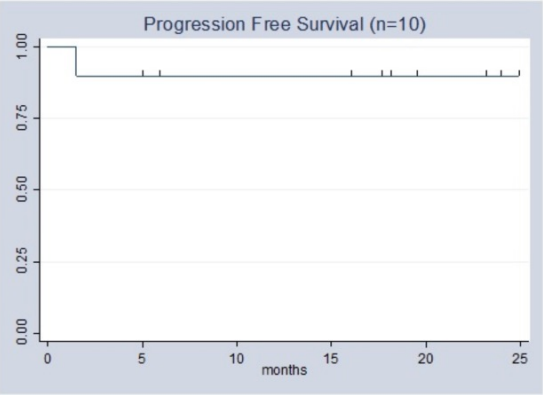
	MCL patients (n=10)
Median Age, years	62 (50-74)
Male % (n)	90% (9)
Prior auto-HCT % (n)	30% (3)
Prior allo-HCT % (n)	20% (2)
Median LDH (Day 0)	220 (152-393)
BTKi exposed % (n)	100% (10)
BTKi progressed % (n)	80% (8)
Non-covalent BTKi progressed % (n)	40% (4)
Median Prior Lines (including transplant)	4 (3-8)
MIPI at Diagnosis (n=9) Low Intermediate High	 4 patients 3 patients 2 patients
Complex Cytogenetics	3 patients
p53 aberrations (not uniformly assessed)	2 patients with p53 deletion 1 patient with p53 somatic mutation

Abbreviations: MCL: mantle cell lymphoma, LDH=Lactate Dehydrogenase, BTKi=bruton kinase inhibitor, MIPI=mantle cell international prognostic index

LV20.19 CAR T-cells were manufactured onsite in the CliniMACS Prodigy device

8 of 10 patients received 8-day manufactured CAR-T cells whereas two pts received a 12-day product in the Phase 1 cohort.
Manufacturing was successful in 100% of patients
All patients received a fresh (non-cryopreserved) product

Figure 1



Nirav N. Shah et al. ASH 2022