ALGORITMI TERAPEUTICI NEL 2026

Linfomi aggressivi

Prof. Marco Ladetto, MD
AOU SS Antonio e Biagio e Cesare Arrigo, Alessandria
Università degli Studi del Piemonte Orientale

UPO UNIVERSITÀ DEL PIEMONTE ORIENTALE

FONDAZIONE ITALIANA LINFOMI

AOU AL Azienda Ospedaliero-Universitaria di ALESSANDRIA

Disclosures

I declare in the last five years the following relationships in terms of consultancy, participation to advisory boards, invitation to scientific meetings, institutional research support and contracts with: AbbVie, Amgen, ADC Therapeutics, Sobi, BeOne, BMS, Eusapharma, GSK, Gentili, Gilead/Kite, Novartis, Incyte, Janssen, Jazz, Lilly, Regeneron, Roche, Ellipses, MSD, Genmab, Astrazeneca

AGENDA

- Mantle Cell Lymphoma
- Large B-Cell Lymphoma

- Mantle Cell Lymphoma

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Treatment of Older Patients with Mantle-Cell Lymphoma

H.C. Kluin-Nelemans, E. Hoster, O. Hermine, J. Walewski, M. Trneny, C.H. Geisler, S. Stilgenbauer, C. Thieblemont, U. Vehling-Kaiser, J.K. Doorduijn, B. Coiffier, R. Forstpointner, et al.

N Engl J Med 2012; 367:520-531

June,2012

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rituximab after Autologous Stem-Cell Transplantation in Mantle-Cell Lymphoma

Steven Le Gouill, M.D., Ph.D., Catherine Thieblemont, M.D., Ph.D., Lucie Oberic, M.D., Anne Moreau, M.D., Krimo Bouabdallah, M.D., Caroline Dartigeas, M.D., Gandhi Damaj, M.D., Ph.D., Thomas Gastinne, M.D., Vincent Ribrag, M.D., Ph.D., Pierre Feugier, M.D., Ph.D., Olivier Casasnovas, M.D., Hacène Zerazhi, M.D., et al., for the LYSA Group*

N Engl J Med 2017; 377:1250-1260

September, 2017

The NEW ENGLAND JOURNAL of MEDICINE

Ibrutinib plus Bendamustine and Rituximab in Untreated Mantle-Cell Lymphoma

Michael L. Wang, M.D., Wojciech Jurczak, M.D., Ph.D., Mats Jerkeman, M.D., Ph.D., Judith Trotman, F.R.A.C.P., Pier L. Zinzani, M.D., Ph.D., David Belada, M.D., Ph.D., Carola Boccomini, M.D., Ian W. Flinn, M.D., Ph.D., Prayush Giri, F.R.A.C.P., Andre Goy, M.D., Paul A. Hamlin, M.D., Olivier Hermine, M.D., Ph.D., et al., for the SHINE Investigators*

June 30, 2022
N Engl J Med 2022; 386:2482-2494
DOI: 10.1056/NEJMoa2201817

January, 2022

June,2016

Addition of high-dose cytarabine to immunochemotherapy before autologous stem-cell transplantation in patients aged 65 years or younger with mantle cell lymphoma (MCL Younger): a randomised, open-label, phase 3 trial of the European Mantle Cell Lymphoma Network

Olivier Hermine*, Eva Hoster*, Jan Walewski, André Bosly, Stephan Stilgenbauer, Catherine Thieblemont, Michal Szymczyk, Reda Bouabdallah, Michael Kneba, Michael Hallek, Gilles Salles, Pierre Feugier, Vincent Ribrag, Josef Birkmann, Roswitha Forstpointner, Corinne Haioun, Matthias Hänel, René Olivier Casasnovas, Jürgen Finke, Norma Peter, Kamal Bouabdallah, Catherine Sébban, Thomas Fischer, Ulrich Dührsen, Bernd Metzner, Georg Mauchmeyer, Lothar Kanz, Christian Schmidt, Richard Delarue, Nicole Brousse, Wolfram Klapper, Elizabeth Macintyre, Marie-Hélène Delfau-Larue, Christiane Pott, Wolfgang Hiddemann, Michael Unterhalt, Martin Dreyling, on behalf of the European Mantle Cell Lymphoma Network

The Lancet. VOLUME 388, ISSUE 10044, P565-575, AUGUST 06, 2016

January, 2020

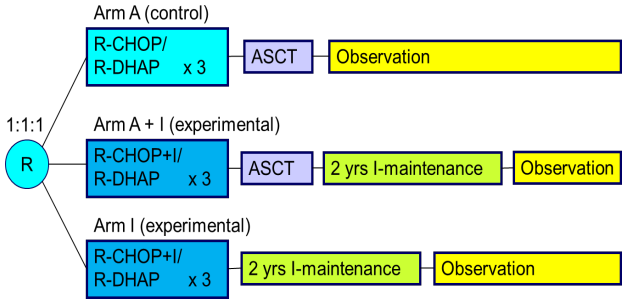
Lenalidomide maintenance after autologous haematopoietic stem-cell transplantation in mantle cell lymphoma: results of a Fondazione Italiana Linfomi (FIL) multicentre, randomised, phase 3 trial

Marco Ladetto*, Sergio Cortelazzo†, Simone Ferrero, Andrea Evangelista, Michael Mian, Rita Tavarozzi, Manuela Zanni, Federica Cavallo, Alice Di Rocco, Vittorio Stefoni, Chiara Pagani, Alessandro Re, Annalisa Chiappella, Monica Balzarotti, Vittorio R Zilioli, Maria Gomes da Silva, Luca Arcaini, Anna L Molinari, Filippo Ballerini, Andrés J M Ferreri, Benedetta Puccini, Fabio Benedetti, Piero M Stefani, Franco Narni, Ivana Casaroli, Caterina Stelitano, Giovannino Ciccone, Umberto Vitolo, Maurizio Martelli

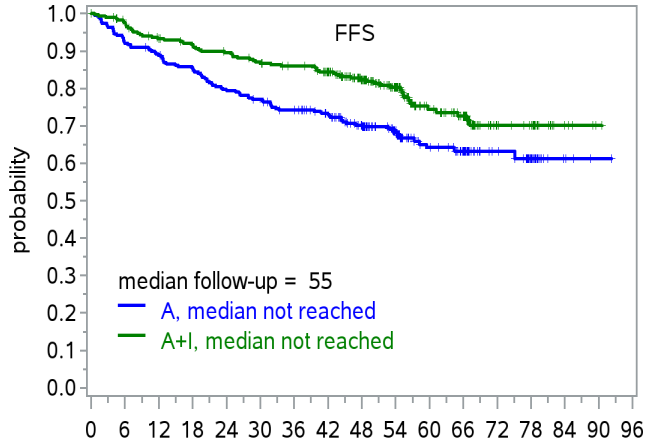
The Lancet Haematology.VOLUME 8, ISSUE 1, E34-E44, JANUARY 01, 2021

RANDOMIZED POPULATION

FFS/OS FROM RANDOMIZATION (ITT ANALYSIS)



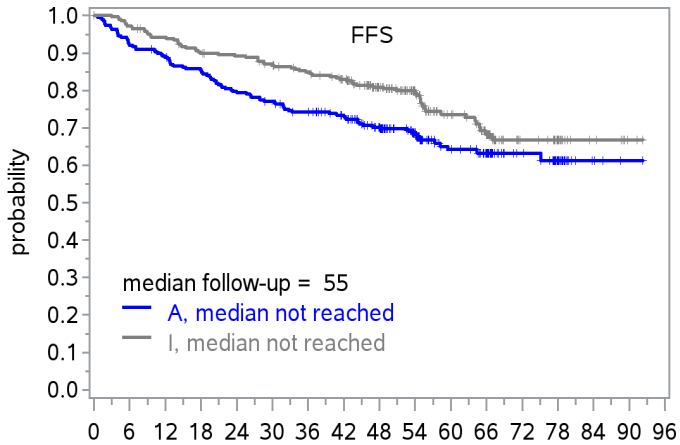
FFS Superiority of A+I vs. A



Numbers At Risk

A	288	255	245	235	219	211	200	187	158	121	74	57	32	20	4	1	0
A+I	292	274	259	252	245	236	230	217	180	141	89	70	28	24	6	2	0

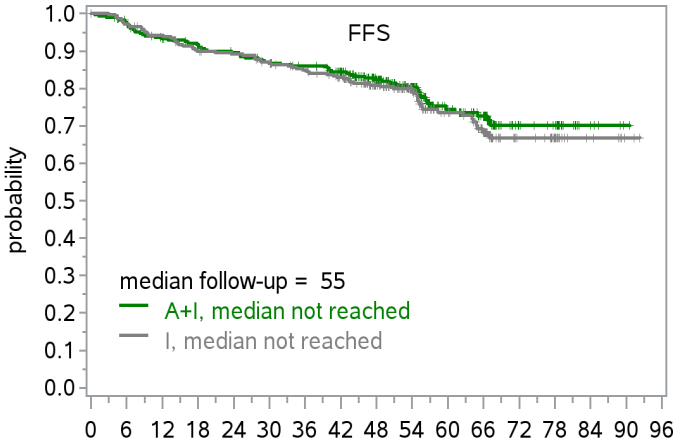
FFS Superiority of A vs. I



Numbers At Risk

A	288	255	245	235	219	211	200	187	158	121	74	57	32	20	4	1	0
I	290	273	263	250	246	237	228	213	167	129	89	67	31	20	7	2	0

FFS Superiority of A+I vs. I

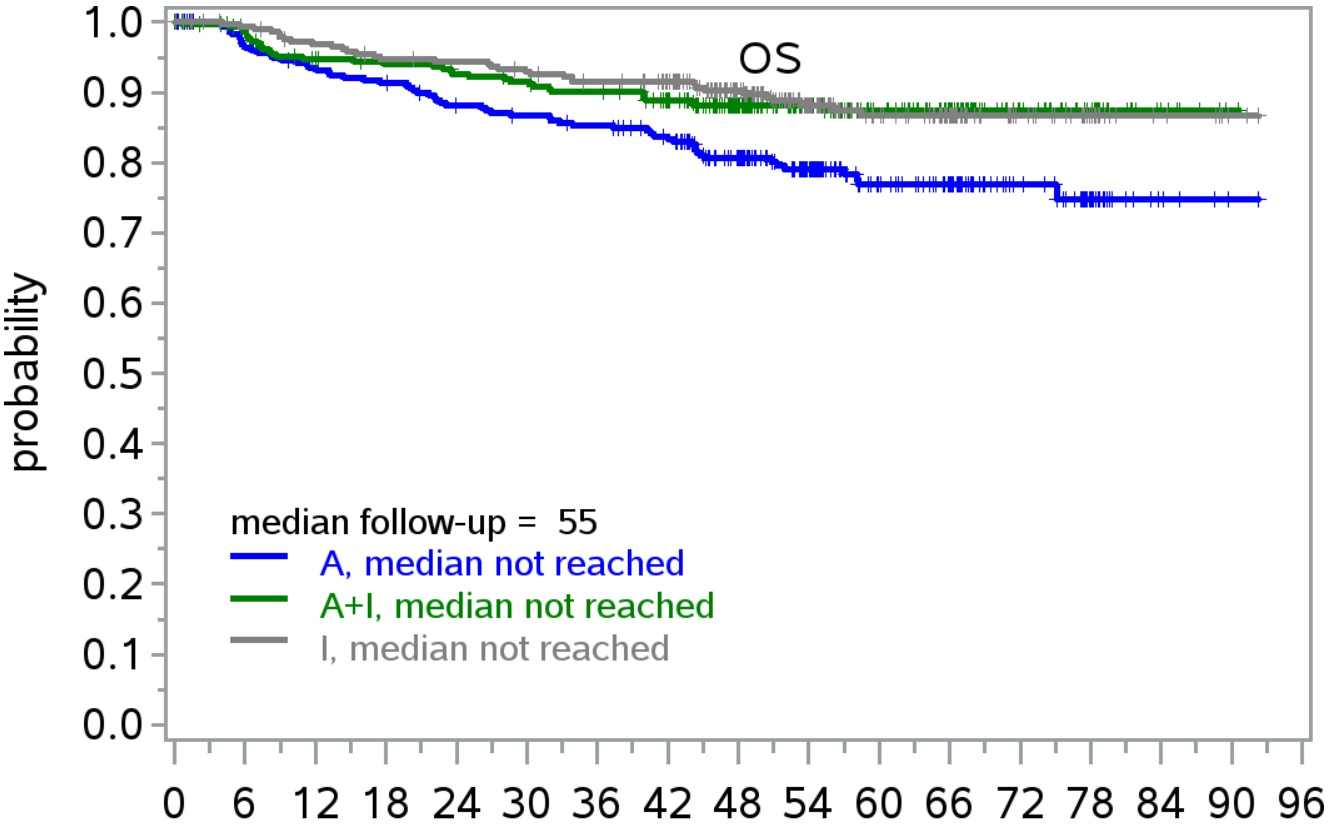


Numbers At Risk

A+I	292	274	259	252	245	236	230	217	180	141	89	70	28	24	6	2	0
I	290	273	263	250	246	237	228	213	167	129	89	67	31	20	7	2	0

Dreyling M, et al. ASH 2024

TRIANGLE: Overall survival



Numbers At Risk

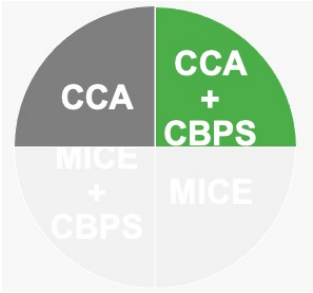
A	288	270	260	255	243	238	233	222	186	145	92	73	41	23	5	1
A+I	292	281	267	262	257	253	248	235	201	160	107	83	39	26	8	2
I	290	282	273	266	264	259	253	243	194	147	101	78	41	21	7	2

- 4-year OS:
  - A: 81%
    (MCL Younger exp.: 80%)
  - A+I: 88%
  - I: 90%

- two-sided test, (α = 5%):
  - A vs. I: p=0.0019, HR: 0.565
  - A vs. A+I: p=0.0036, HR I: 0.587
  - A+I vs. I: ongoing

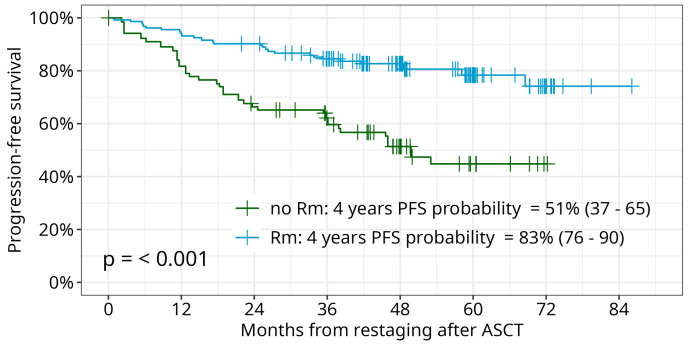
Dreyling M, et al. ASH 2024

WHAT DO WE KNOW ABOUT RITUXIMAB MAINTENANCE (Rm) IMPACT ON SURVIVAL?



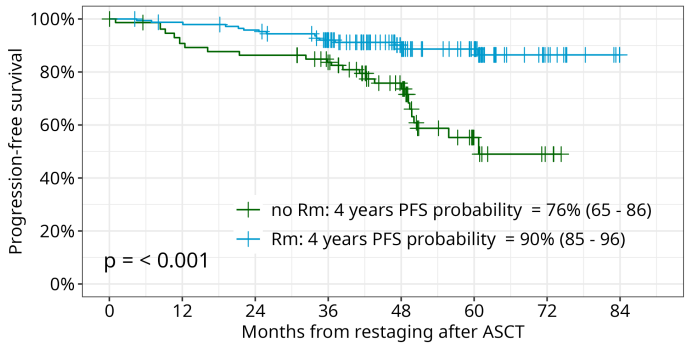
- **R maintenance was added following national guidelines in all 3 trial arms**

Arm A: PFS



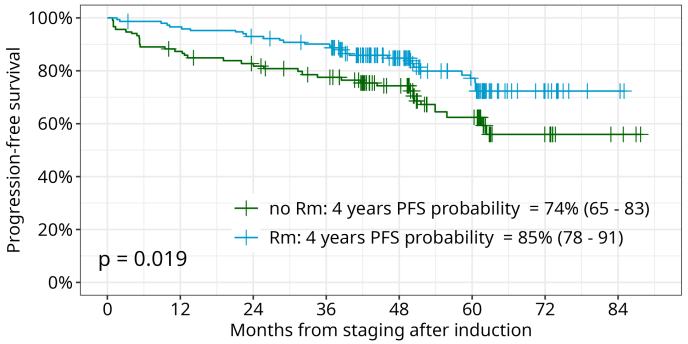
noRm group								
At risk	76.5	66.8	52.2	41	23.8	12.9	2.6	0
Event	0	8.5	21.9	26.2	31.8	33.4	33.4	33.4
Rm group								
At risk	156.8	145.9	140	122.7	86	49.5	16.1	1.7
Event	0	10.9	15.8	24.6	26.9	28.5	30	30

Arm A+I: PFS



noRm group								
At risk	85.3	75.1	71.6	63.8	41	12.9	6	0
Event	0	8.1	11.5	13.5	19.5	28.7	29.7	29.7
Rm group								
At risk	151.8	146.9	142.1	125.8	85.7	63	24.5	0
Event	0	3.1	6.9	12.8	14.6	15.5	16.6	16.6

Arm I: PFS



noRm group								
At risk	116.7	100.7	92.5	82.6	59.8	38.2	19.3	6
Event	0	14.1	20.2	26.2	29.2	35.8	37.7	37.7
Rm group								
At risk	157.2	148.3	141.5	135.3	87.3	57.9	23	3.9
Event	0	7	12.8	16.9	22.8	28.7	30.6	30.6

Blood (2024) 144 (Supplement 1): 237.

MCL Treatment: The Horizon for Older MCL

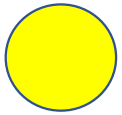
Trials of relevance for an elderly population

- SHINE trial: BR + ibrutinib until PD
- ECHO: BR + acalabrutinib until PD
- ENRICH: Ibrutinib-R vs. BR/R-CHOP
- AVR: acalabrutinib-venetoclax-R
- ALR: acalabrutinib-lenalidomide-R
- BOVEN: zanubrutinib-obinu-venetoclax
- GloVe: Glofitamab-obinu-lenalidomide
- VR-BAC: venetoclax consolidation after R-BAC

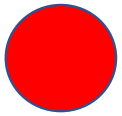
- MANGROVE: Zanubrutinib-R vs. BR

- VIRAL: VR+ibrutinib vs V+R-benda+ibrutinib

PUBLISHED RESULTS



PENDING RESULTS



ONGOING TRIAL

ELSEVIER

Blood 146 (2025) 885–886

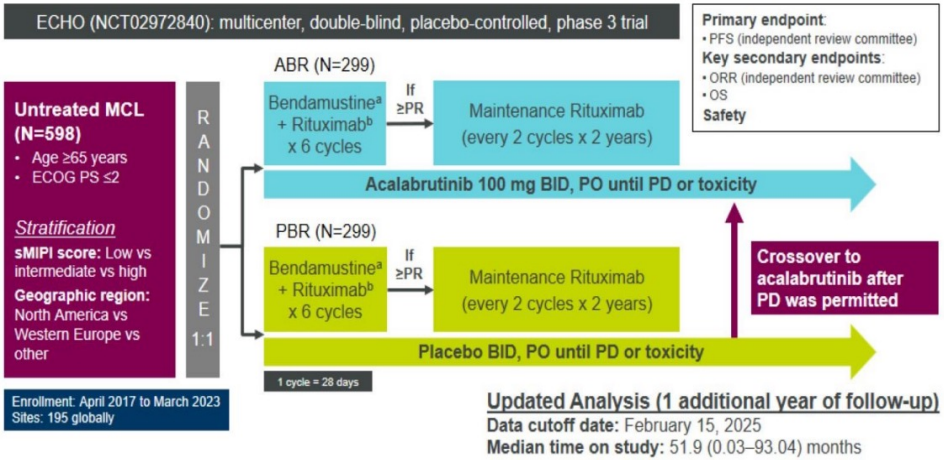
The 67th ASH Annual Meeting Abstracts

ORAL

623. MANTLE CELL, FOLLICULAR, WALDENSTROM'S, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

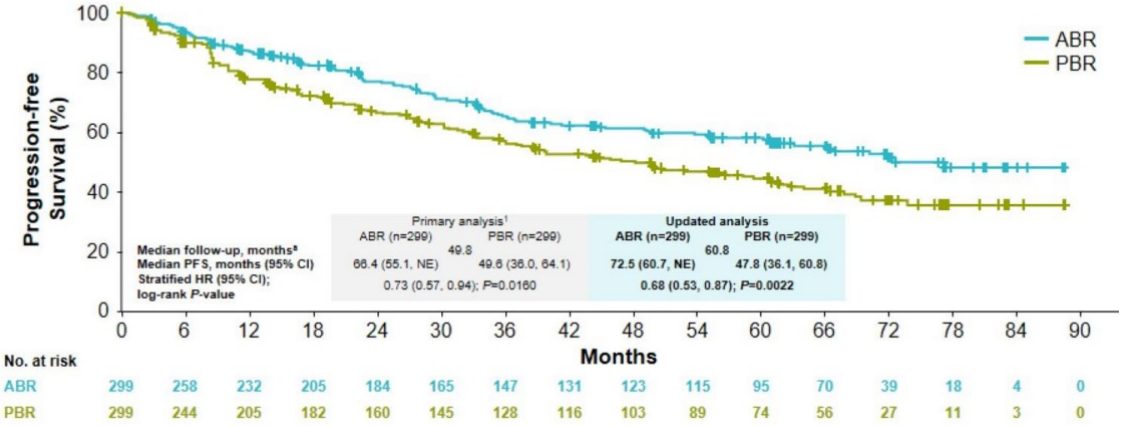
Time to third-line treatment after bendamustine-rituximab with or without acalabrutinib in patients with previously untreated mantle cell lymphoma: Updated analysis of the phase 3 ECHO trial after 50 months of follow-up

Michael Wang[1], Jonas Paludo[2], João Samuel de Holanda Farias[3], Diego Villa[4], Cecily Forsyth[5], Ellie John[6], Menglu Che[7], Harneet Arora[7], Craig Delury[8], Victoria Otero[8], Yuqin Song[9]

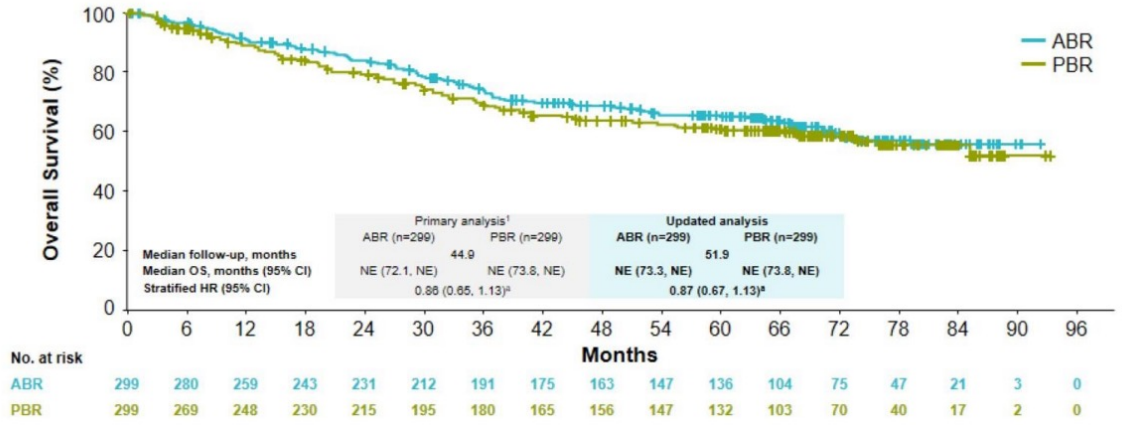


Need for Subsequent Anticancer Therapy Was 3-fold Higher With PBR

At 60.8 Months of Follow-up, PFS Further Improved With ABR vs PBR

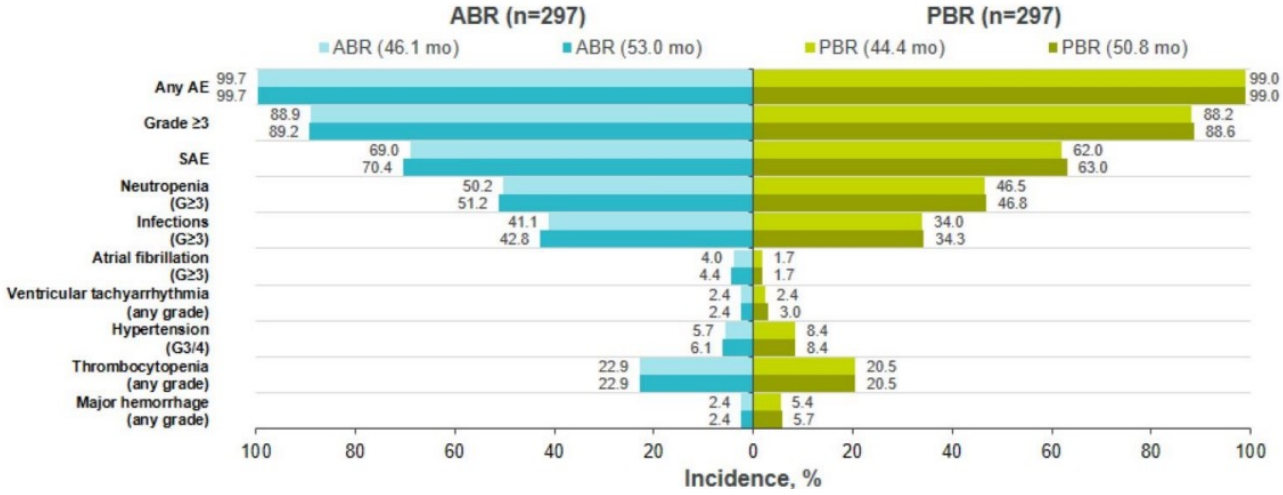


OS Results Were Consistent With the Previous Analysis

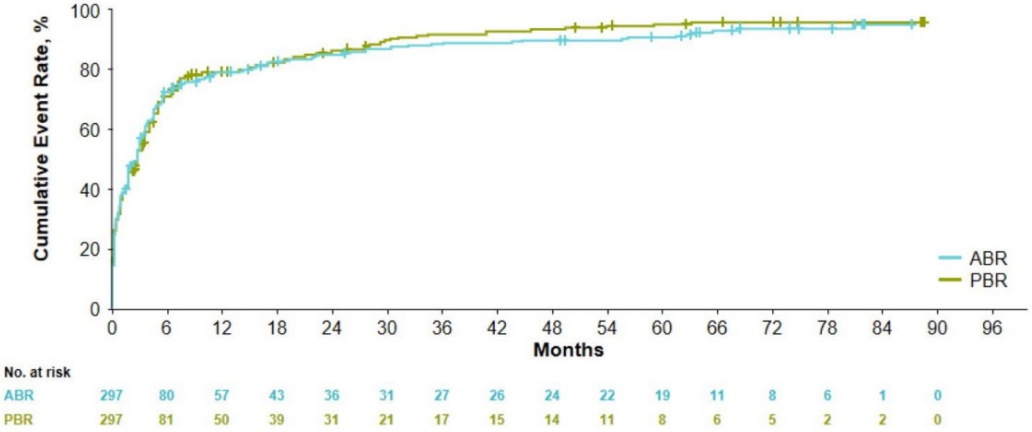


Wang et al. Blood (2025) 146 (Supplement 1): 885

Safety Profile Remains Favorable and Similar Between Arms With Longer Follow-up, With No New Signals Despite Continuous Acalabrutinib Therapy in ABR Arm

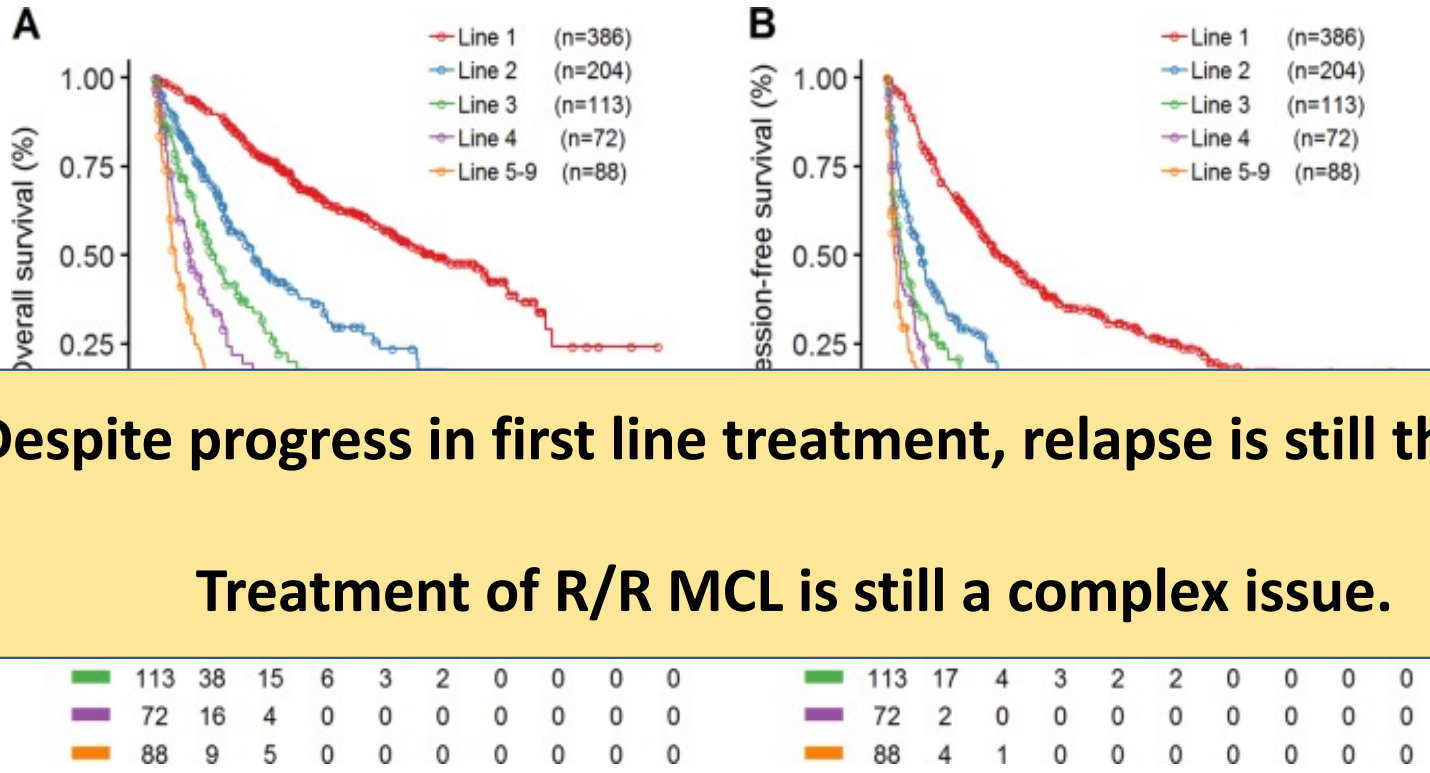


Cumulative Event Rate of Grade ≥3 Adverse Events Was Comparable Between Treatment Arms



Wang et al. Blood (2025) 146 (Supplement 1): 885

Patterns of survival in patients with recurrent mantle cell lymphoma in the modern era: progressive shortening in response duration and survival after each relapse.



Despite progress in first line treatment, relapse is still the rule.

Treatment of R/R MCL is still a complex issue.

Kumar et al. Blood Cancer Journal volume 9, Article number: 50 (2019).

Ibrutinib plus venetoclax in relapsed or refractory mantle cell lymphoma (SYMPATICO): a multicentre, randomised, double-blind, placebo-controlled, phase 3 study

Michael Wang, Wojciech Jurczak, Marek Trneny, David Belada, Tomasz Wrobel, Nilanjan Ghosh, Mary-Margaret Keating, Tom van Meerten, Ruben Fernandez Alvarez, Gottfried von Keudell, Catherine Thieblemont, Frederic Peyrade, Marc Andre, Marc Hoffmann, Edith Szafer-Glusman, Jennifer Lin, James P Dean, Jutta K Neuenburg, Constantine S Tam

SYMPATICO Study Design

- SYMPATICO (NCT03112174) is multinational, randomized, double-blind, placebo-controlled, phase 3 study

SYMPATICO (N=267)
- Age ≥18 years
- R/R MCL
- 1–5 prior therapies for MCL
- ≥1 prior rituximab/ anti-CD20-containing regimen
- ECOG PS 0–2

Randomized 1:1

Ibrutinib + venetoclax (n=134)
Ibrutinib 560 mg once daily + venetoclax 5-week ramp-up to 400 mg once daily for 24 months

Ibrutinib + placebo (n=133)
Ibrutinib 560 mg once daily + placebo once daily for 24 months

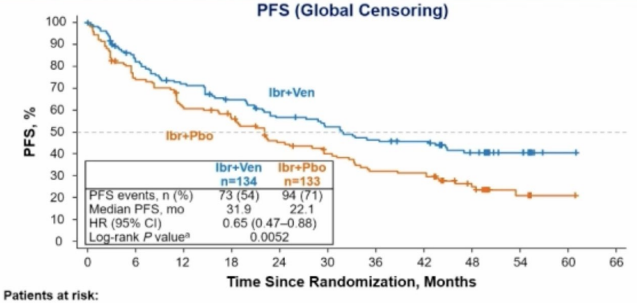
Single-agent ibrutinib 560 mg once daily until PD or unacceptable toxicity

Stratification: ECOG PS, prior lines of therapy, TLS risk[a]

- **Primary endpoint:**
  - PFS by investigator assessment using Lugano criteria
- **Secondary endpoints (tested hierarchically in the following order):**
  - CR rate by investigator assessment
  - TTNT[b]
  - OS (interim analysis)
  - ORR by investigator assessment

CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; PFS, progression-free survival; ORR, overall response rate; OS, overall survival; TLS, tumor lysis syndrome; TTNT, time to next treatment.
[a]Increased TLS risk was defined as at least 1 lesion >10 cm, or at least 1 lesion >5 cm with circulating lymphocytes >25,000 cells/mm³, and/or creatinine clearance <60 mL/min. [b]For hierarchical testing per US FDA censoring, TTNT was tested after OS.

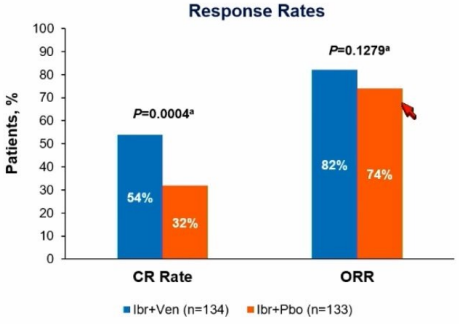
Primary Endpoint: Investigator-Assessed PFS Was Significantly Improved With Ibrutinib + Venetoclax Versus Ibrutinib + Placebo

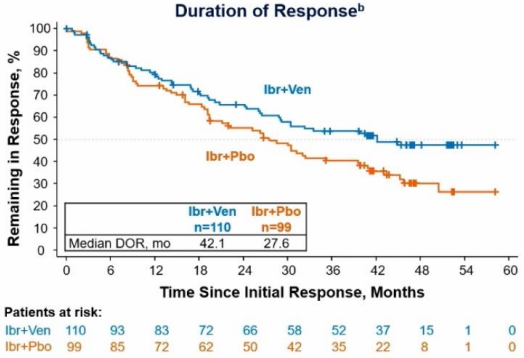


Median PFS, mo	Global Censoring[b]				US FDA Censoring[c]			
	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]	Ibr+Ven n=134	Ibr+Pbo n=133	HR (95% CI)	Log-rank *P* value[a]
Investigator assessment	31.9	22.1	0.65 (0.47–0.88)	0.0052	42.6	22.1	0.60 (0.44–0.83)	0.0021
IRC assessment	31.8	20.9	0.67 (0.49–0.91)	0.0108	43.5	22.1	0.63 (0.45–0.87)	0.0057

HR, hazard ratio; Ibr, ibrutinib; Pbo, placebo; Ven, venetoclax.
[a]*P* values were determined by stratified log-rank test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]). [b]Censoring at last non-PD assessment for patients without PD or death. [c]Patients were censored at last non-PD assessment before start of subsequent anticancer therapy or missing ≥2 consecutive visits prior to a PFS event, whichever occurred first.

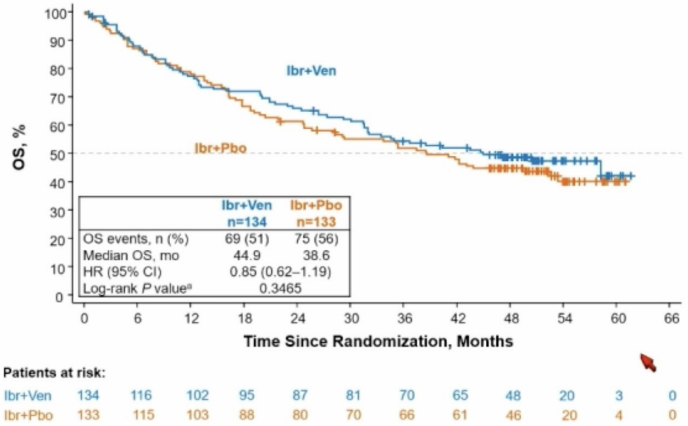
CR Rate Was Significantly Improved With Ibrutinib + Venetoclax





DOR, duration of response.
[a]*P* values were determined by stratified Cochran-Mantel-Haenszel test (stratification factors: prior lines of therapy [1–2 vs ≥3] and TLS risk category [low vs increased risk]). [b]Global censoring (censoring at last non-PD assessment for patients without PD or death).

OS Was Numerically Improved At This Interim Analysis



Michael Wang, et al. Ibrutinib Combined with Venetoclax in Patients with Relapsed/Refractory Mantle Cell Lymphoma: Primary Analysis Results from the Randomized Phase 3 Sympatico Study. *Blood, Volume 142, Supplement 2, 2023, Page LBA-2*

OPEN ACCESS | RAPID COMMUNICATIONS | May 16, 2023

Pirtobrutinib in Covalent Bruton Tyrosine Kinase Inhibitor Pretreated Mantle-Cell Lymphoma

Authors: Michael L. Wang, MD, Wojciech Jurczak, MD, PhD, Pier Luigi Zinzani, MD, PhD, Toby A. Eyre, MD, MBChB, DipMedEd, MRCP, FRCPath, Chan Y. Cheah, MD, Chaitra S. Ujjani, MD, Youngil Koh, MD, ... SHOW ALL ..., and Nirav N. Shah, MD | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 41, Number 24 • https://doi.org/10.1200/JCO.23.00562

TABLE 2. Efficacy of Pirtobrutinib in Patients With cBTKi Pre-treat and cBTKi-Naïve MCL

Response	cBTKi Pretreated MCL (n = 90)	cBTKi-Naïve MCL (n = 14)
Overall response rate, % (95% CI)	57.8 (46.9 to 68.1)	85.7 (57.2 to 98
Best overall response, No. (%)		
Complete response	18 (20.0)	5 (35.7)
Partial response	34 (37.8)	7 (50)
Stable disease	14 (15.6)	0
Progressive disease	15 (16.7)	1 (7.1)
Not evaluable[a]	9 (10.0)	1 (7.1)
DOR		
Patients with a response, No.	52	12
Patients with censored data, No. (%)	33 (63.5)	12 (100)
DOR, months, median (95% CI)	21.6 (7.5 to NR)	NR (NR to NR)
Median follow-up, months	11.9	7.1
PFS		
Patients with censored data, No. (%)	45 (50.0)	13 (92.9)
PFS, months, median (95% CI)	7.4 (5.3 to 12.5)	NR (NR to NR)
Median follow-up, months	9.2	8.6
OS		
Patients with censored data, No. (%)	60 (66.7)	13 (92.9)
OS, months, median (95% CI)	NR (14.8 to NR)	NR (NR to NR)
Median follow-up, months	16.6	9.4

NOTE. Overall response and best response were determined accord to the 2014 Lugano criteria[20] and on the basis of independent rev committee assessment.
Abbreviations: cBTKi, covalent Bruton tyrosine kinase inhibitor; DC duration of response; MCL, mantle-cell lymphoma; NR, not reached; overall survival; PFS, progression-free survival.
[a]Patients without postbaseline disease assessment were not

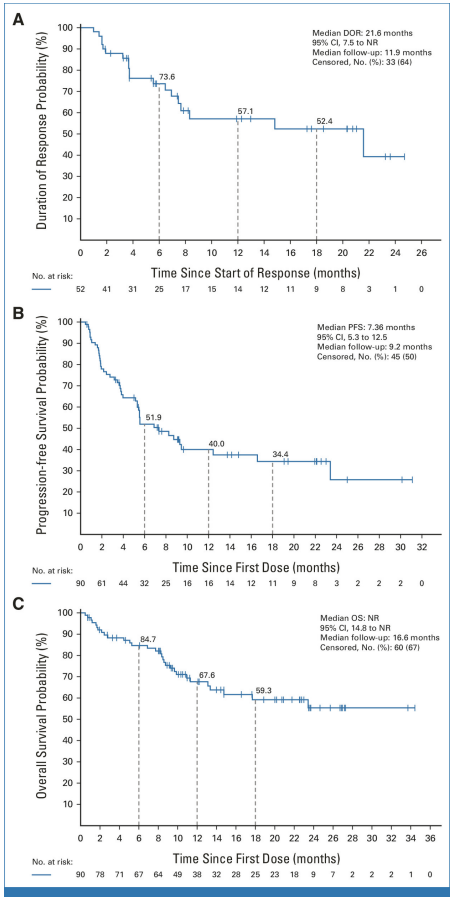


TABLE 3. Adverse Events in At Least 10% of All Patients With MCL

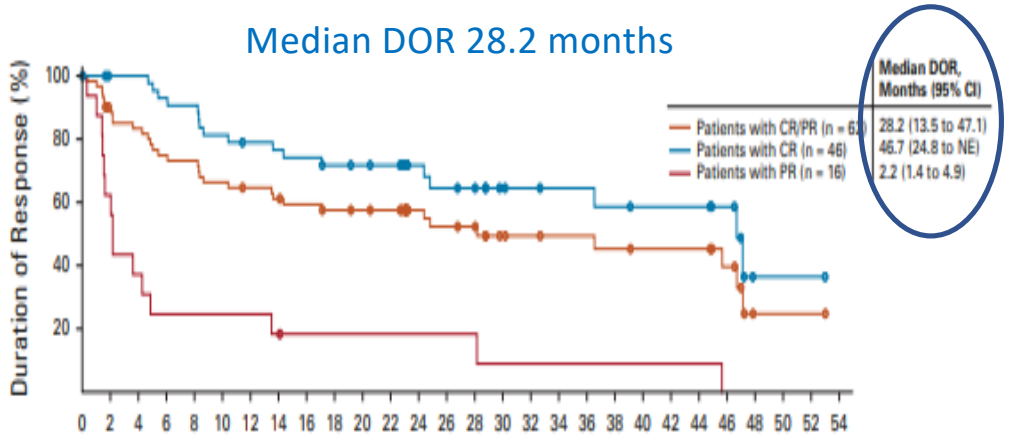
	MCL Safety Population (n = 164)			
	TEAE, (≥10%), No. (%)		TRAE, No. (%)	
Adverse Event	Any Grade	Grade ≥3	Any Grade	Grade
Fatigue	49 (29.9)	4 (2.4)	34 (20.7)	4 (2.4
Diarrhea	35 (21.3)	0	20 (12.2)	0
Dyspnea	27 (16.5)	3 (1.8)	15 (9.1)	1 (0.6
Contusion	24 (14.6)	0	16 (9.8)	0
Anemia	21 (12.8)	8 (4.9)	10 (6.1)	4 (2.4
Back pain	21 (12.8)	2 (1.2)	2 (1.2)	0
Cough	20 (12.2)	0	10 (6.1)	0
Pyrexia	19 (11.6)	0	6 (3.7)	0
Constipation	18 (11.0)	0	3 (1.8)	0
Nausea	18 (11.0)	0	7 (4.3)	0
Pneumonia	17 (10.4)	14 (8.5)	5 (3.0)	4 (2.4
Myalgia	17 (10.4)	0	14 (8.5)	0
Adverse event of special interest[a]				
Infections	59 (36.0)	28 (17.1)	24 (14.0)	5 (3.0
Bleeding	45 (27.4)	6 (3.7)	26 (15.9)	1 (0.6
Thrombocytopenia	24 (14.6)	11 (6.7)	2 (1.2)	0
Neutropenia[b]	23 (14.0)	22 (13.4)	15 (9.1)	14 (8.5
Bruising[c]	27 (16.5)	0	19 (11.6)	0 (0.0
Hemorrhage	25 (15.2)	6 (3.7)	11 (6.7)	1 (0.6
Atrial fibrillation/atrial flutter[d]	6 (3.7)	2 (1.2)	1 (0.6)	0 (0.0

NOTE. There were 11 grade 5 adverse events, none of which were considered treatment-related (two respiratory failure and one each of pneumo COVID-19 pneumonia, multiple organ dysfunction syndrome, cardiac arrest, hemorrhage, malignant pleural effusion, mucormycosis, streptococ infection, and sudden death).
Abbreviations: cBTKi, covalent Bruton tyrosine kinase inhibitor; MCL, mantle cell lymphoma; TEAE, treatment-emergent adverse event; TRA treatment-related adverse event.
[a]Adverse events of special interest are those that were previously associated with cBTKi and are all composite terms.
[b]Combines neutrophil count decreased, neutropenia, febrile neutropenia, and neutropenic sepsis.
[c]Bruising includes contusion, petechia, ecchymosis, and increased tendency to bruise.

CAR-T cells therapy: KTE-X19 – ZUMA 2 trial long term FU

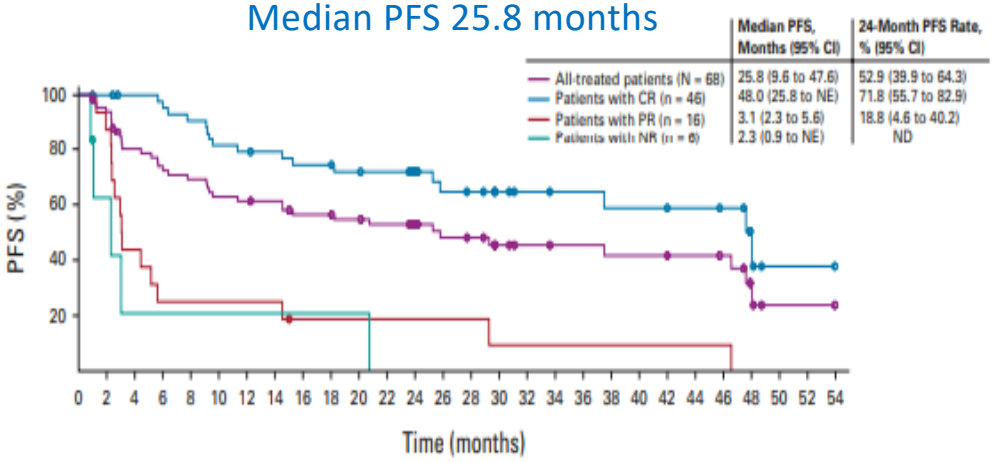
A

Median DOR 28.2 months



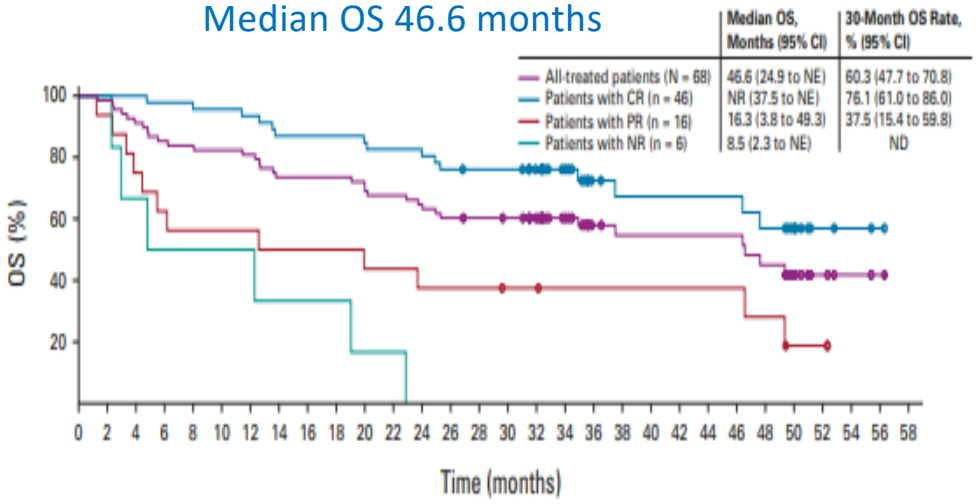
B

Median PFS 25.8 months



C

Median OS 46.6 months



Best ORR/CR: 92%/68%

Wang et al. JCO,2022 Jun 4;JCO2102370.

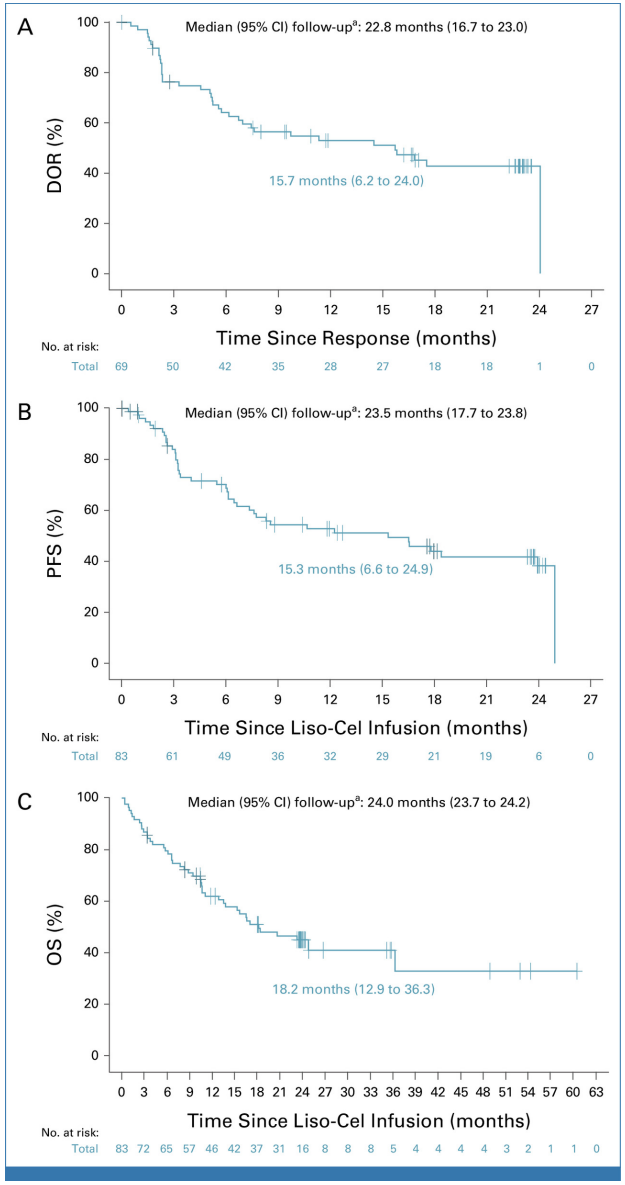
FREE ACCESS | ORIGINAL REPORTS | December 10, 2023

Lisocabtagene Maraleucel in Relapsed/Refractory Mantle Cell Lymphoma: Primary Analysis of the Mantle Cell Lymphoma Cohort From TRANSCEND NHL 001, a Phase I Multicenter Seamless Design Study

Authors: Michael Wang, MD, Tanya Siddiqi, MD, MBBS, Leo I. Gordon, MD, Manali Kamdar, MD, MBBS, Matthew Lunning, DO, Alexandre V. Hirayama, MD, Jeremy S. Abramson, MD, MMSc, ... SHOW ALL ... , and M. Lia Palomba, MD AUTHORS INFO & AFFILIATIONS

J Clin Oncol **42**, 1146-1157(2024) • Volume 42, Number 10 • DOI: 10.1200/JCO.23.02214

Best ORR/CR: 87%/75%



Pivotal trials of CARTs labelled for R/R MCL

Toxicity	ZUMA-2 (KTE-X19)	TRANSCEND (Liso-cel)
Neurotox ≥ G3	**31%**	**9%**
CRS ≥ G3	**15%**	**1%**
Late ICAHT ≥ G2	**≥16%**	**24%**
Severe infection	**32%**	**15%**
ICU admission	**n.a.**	**7%**
Non-relapse mortality	**7.4%**	**18%**

Wang et al. JCO,2022 Jun 4;JCO2102370.
Wang et al. J Clin Oncol. 2024;42:1146–57

OPEN ACCESS | ORIGINAL REPORTS | October 04, 2024

Glofitamab in Relapsed/Refractory Mantle Cell Lymphoma: Results From a Phase I/II Study

Authors: Tycel Jovelle Phillips, MD, Carmelo Carlo-Stella, MD, Franck Morschhauser, MD, PhD, Emmanuel Bachy, MD, PhD, Michael Crump, MD, FRCPC, Marek Trněný, MD, Nancy L. Bartlett, MD, ... SHOW ALL ... , and Michael Dickinson, MBBS, DMedSc | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 43, Number 3 • https://doi.org/10.1200/JCO.23.02470

TABLE 1. Baseline Characteristics in the Overall Populations and in Patients With and Without Previous BTKi Treatment

Characteristic	Previous BTKi (n = 31)	No Previous BTKi (n = 29)	All Patients (N = 60)
Age, years, median (range)	70.0 (41-84)	72.0 (52-86)	72.0 (41-86)
Male sex, No. (%)	23 (74.2)	21 (72.4)	44 (73.3)
ECOG PS, No. (%)			
0	14 (45.2)	14 (48.3)	28 (46.7)
1	17 (54.8)	15 (51.7)	32 (53.3)
Ann Arbor stage at study entry, No. (%)			
I	1 (3.2)	2 (6.9)	3 (5.0)
II	2 (6.5)	3 (10.3)	5 (8.3)
III	5 (16.1)	6 (20.7)	11 (18.3)
IV	23 (74.2)	18 (62.1)	41 (68.3)
MCL IPI score ≥6, No. (%)	7 (22.6)	8 (27.6)	15 (25.0)
Extranodal disease present, No. (%)	20 (64.5)	19 (65.5)	39 (65.0)
Bulky disease, cm, No. (%)			
>6	7 (22.6)	6 (20.7)	13 (21.7)
>10	2 (6.5)	3 (10.3)	5 (8.3)
Time since last previous therapy to first study treatment, months, median (range)	1.3 (0.1-53.2)	7.4 (1.1-132.5)	2.4 (0.1-132.5)
Time since last anti-CD20 therapy to first study treatment, months, median (range)	15.1 (0.7-159.0)	25.1 (1.4-132.5)	16.3 (0.7-159.0)
No. of previous lines of therapy, median (range)	3.0 (1-5)	2.0 (1-4)	2.0 (1-5)
Previous therapy for lymphoma, No. (%)			
CAR T-cell therapy	1 (3.2)	1 (3.4)	2 (3.3)
ASCT	7 (22.6)	9 (31.0)	16 (26.7)
Refractory status, No. (%)			
Any previous therapy	30 (96.8)	20 (69.0)	50 (83.3)
First-line therapy	17 (54.8)	14 (48.3)	31 (51.7)
Last previous therapy	27 (87.1)	17 (58.6)	44 (73.3)
Progress or relapse ≤24 months after first-line treatment start, No. (%)	17 (54.8)	14 (48.3)	31 (51.7)

TABLE 2. Efficacy in the Overall Population (efficacy-evaluable population), and in Patients With and Without Previous BTKi Treatment

	Glofitamab SUD		All Patients		
Efficacy (INV-assessed)	1,000 mg Gpt Cohort (n = 16)	2,000 mg Gpt Cohort (n = 44)	Previous BTKi (n = 31)	No Previous BTKi (n = 29)	All Patients (N = 60)
Complete response rate					
No. (%)	11 (68.8)	36 (81.8)	22 (71.0)	25 (86.2)	47 (78.3)
95% CI	41.3 to 89.0	67.3 to 91.8	52.0 to 85.8	68.3 to 96.1	65.8 to 87.9
Partial response rate					
No. (%)	1 (6.3)	3 (6.8)	1 (3.2)	3 (10.3)	4 (6.7)
95% CI	0.2 to 30.2	1.4 to 18.7	0.1 to 16.7	2.2 to 27.4	1.9 to 16.2
Overall response rate					
No. (%)	12 (75.0)	39 (88.6)	23 (74.2)	28 (96.6)	51 (85.0)
95% CI	47.6 to 92.7	75.4 to 96.2	55.4 to 88.1	82.2 to 99.9	73.4 to 92.9

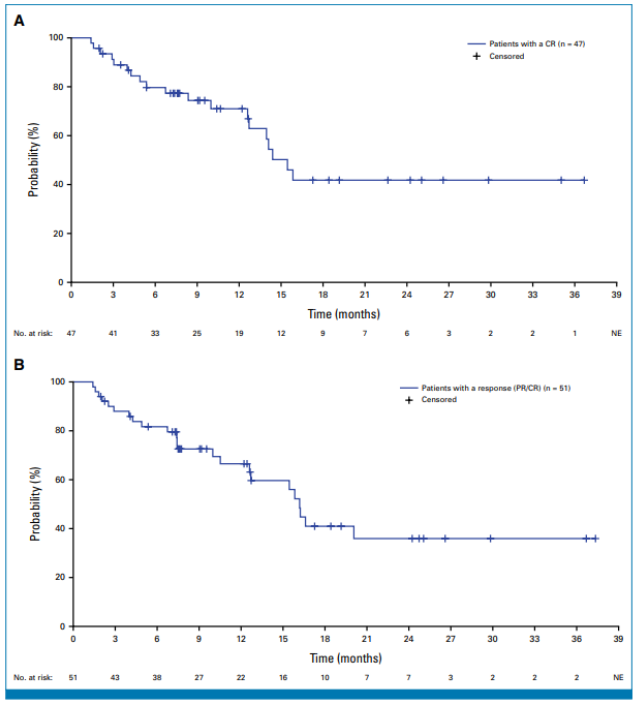
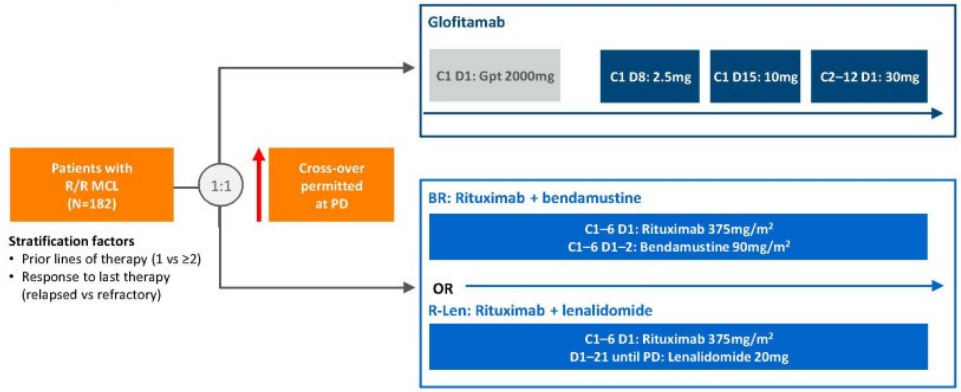


FIG 2. (A) Duration of CR, (B) duration of response, and (C) time on treatment. CR, complete response; CT, computed tomography; NE, not estimable; PD, progressive disease; PR, partial response. (continued on following page)

GLOBRYTE: A Phase III, Open-Label, Multicenter, Randomized Trial Evaluating Glofitamab Monotherapy in Patients with Relapsed or Refractory Mantle Cell Lymphoma

Figure. Study schema



B, bendamustine; C, cycle; D, day; Gpt, obinutuzumab pretreatment; Len, lenalidomide; MCL, mantle cell lymphoma; PD, progressive disease; R/R, relapsed/refractory; R, rituximab. Relapsed disease is defined as disease progression after the last regimen; refractory disease is defined as failure to achieve a partial response or complete response to the last regimen.

MD01-01_I01_PFIL06

FONDAZIONE ITALIANA LINFOMI

Clinical Protocol

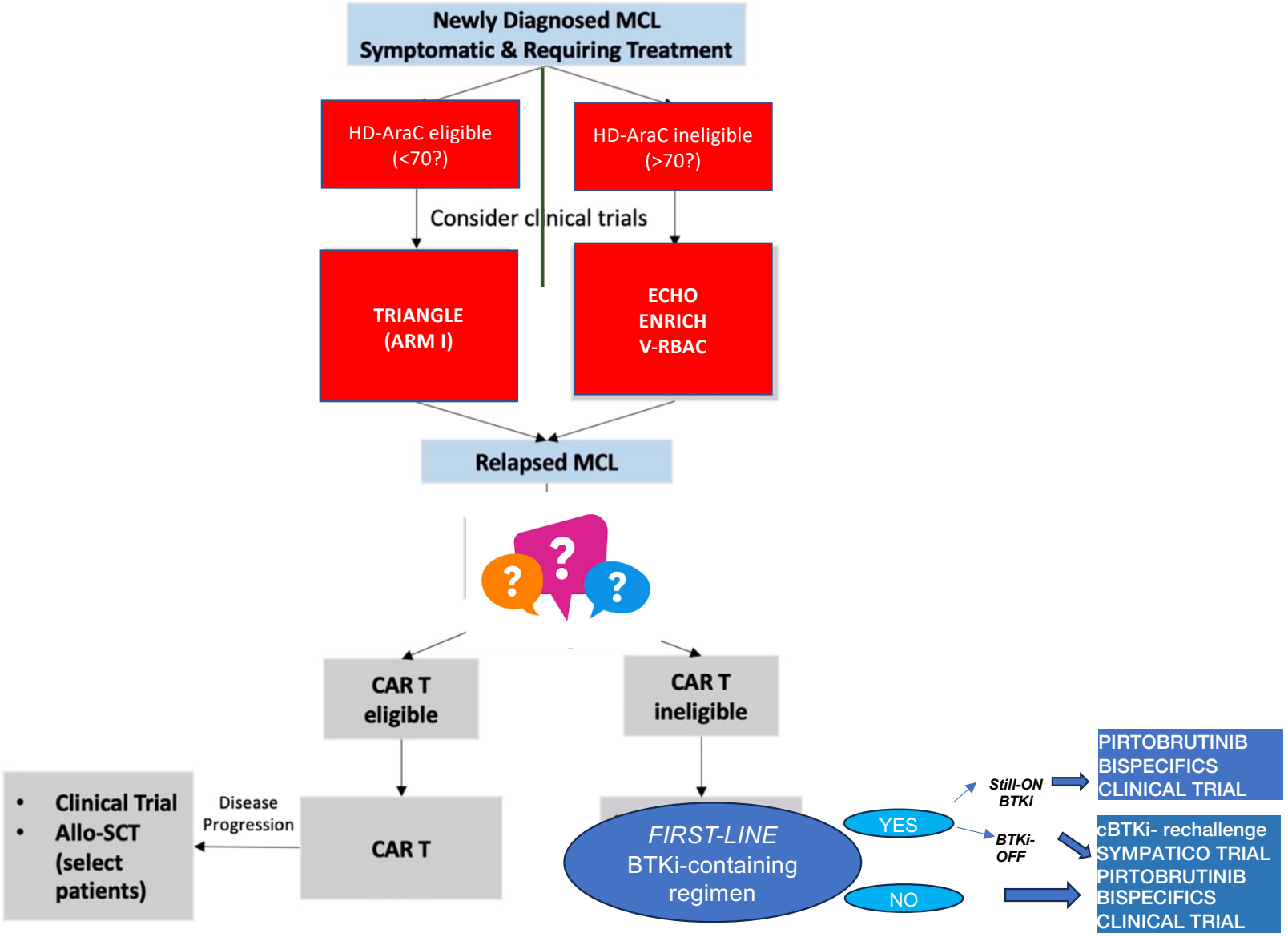
Title

A phase II, multicenter study of GlOfitamab in patients with mantle cell Lymphoma and inaDequate response or relapse following CAR T-cell therapy

(GOLD)

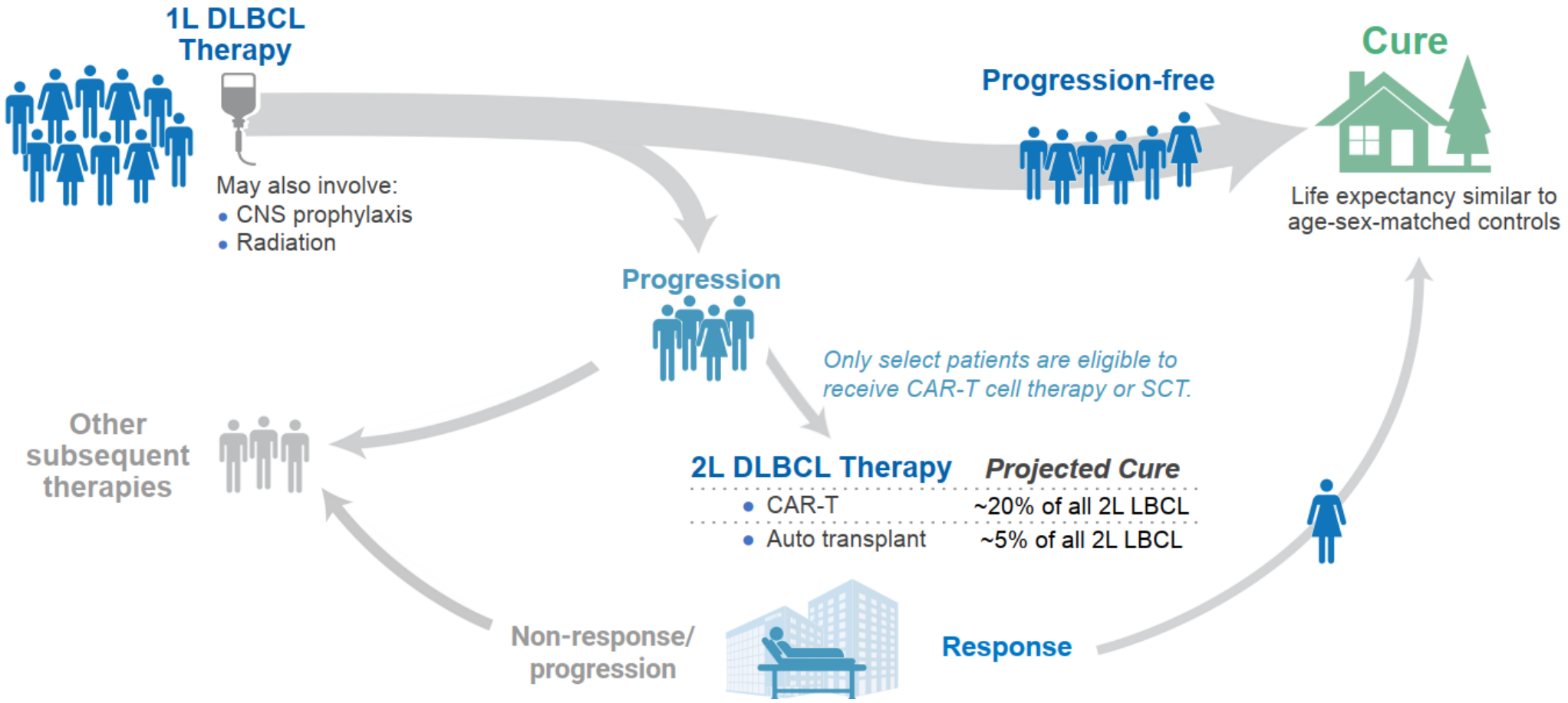
BTKi ERA

Personal Opinion



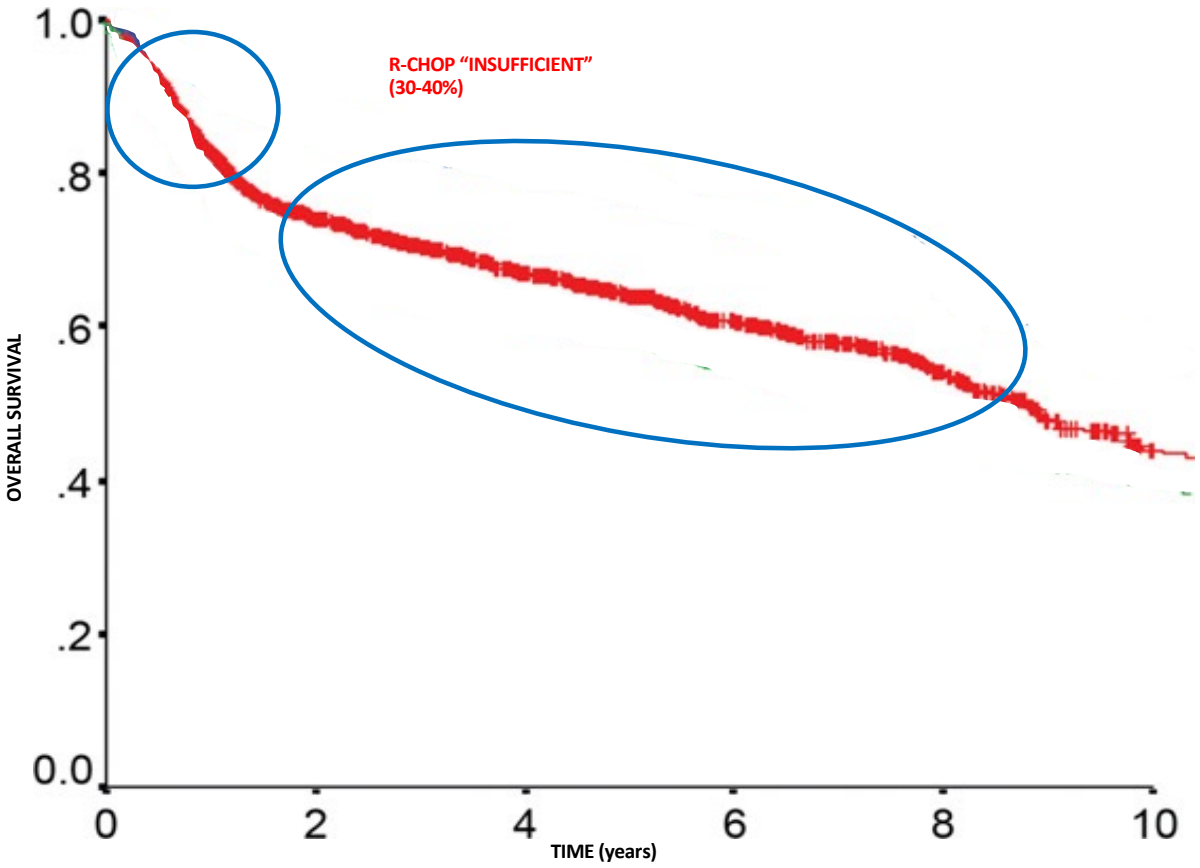
- **Large B-Cell Lymphoma**

DLBCL Patient Journey : Likelihood of cure is highest with treatment in 1L setting



Westin J and Sehn LH. Blood 2022;139 (18): 2737–2746.

R-CHOP has been the SoC for patients with previously untreated DLBCL for the past 20 years



BC Cancer Agency Database, Sehn, Hematology 2012

R-CHOP is insufficient in 35% of DLBCL:

- High-Risk "Clinical" (IPI 3-5)
- High-Risk "Biological"

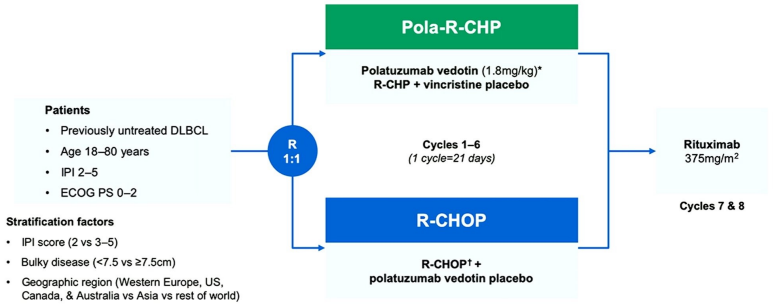
OPEN ACCESS | CLINICAL TRIAL UPDATES | September 24, 2025

Five-Year Outcomes of the POLARIX Study Comparing Pola-R-CHP and R-CHOP in Patients With Diffuse Large B-Cell Lymphoma

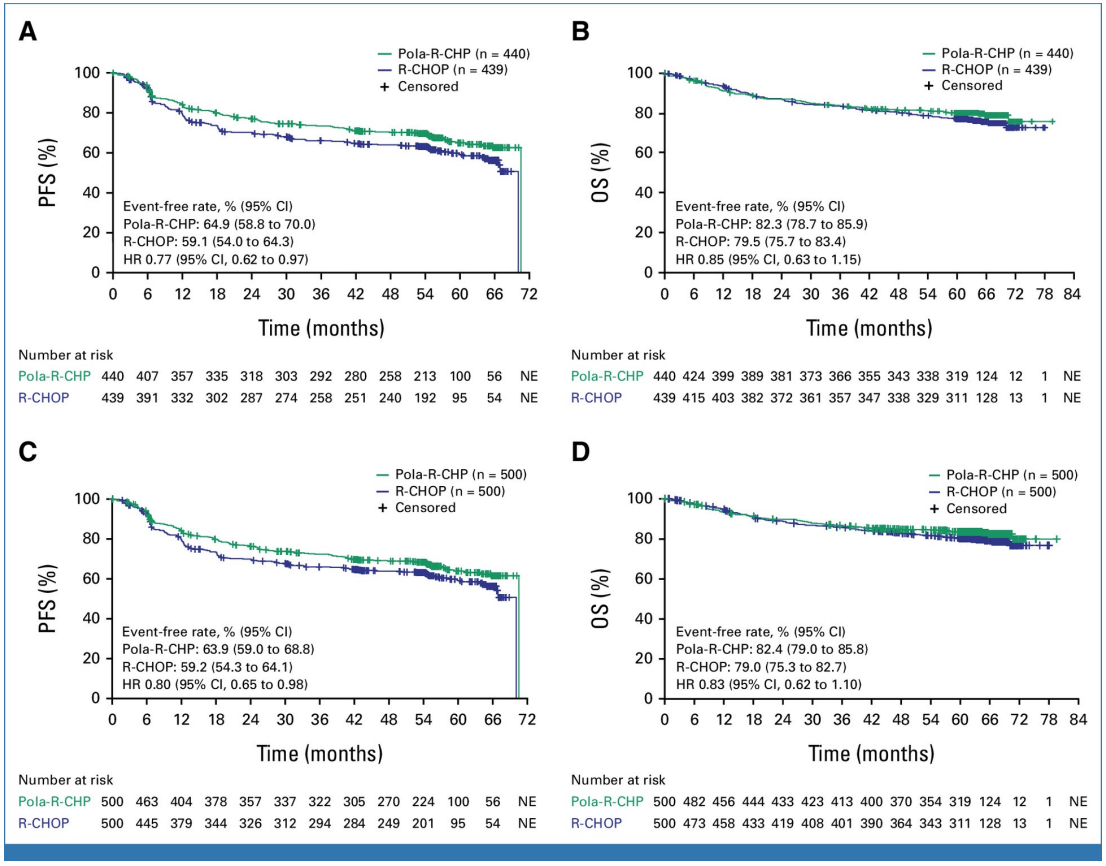
Authors: Franck Morschhauser, MD, PhD, Gilles Salles, MD, PhD, Laurie H. Sehn, MD, MPH, Alex F. Herrera, MD, Jonathan W. Friedberg, MD, Marek Trněný, MD, Georg Lenz, MD, ... SHOW ALL ..., and Christopher R. Flowers, MD | AUTHORS INFO & AFFILIATIONS

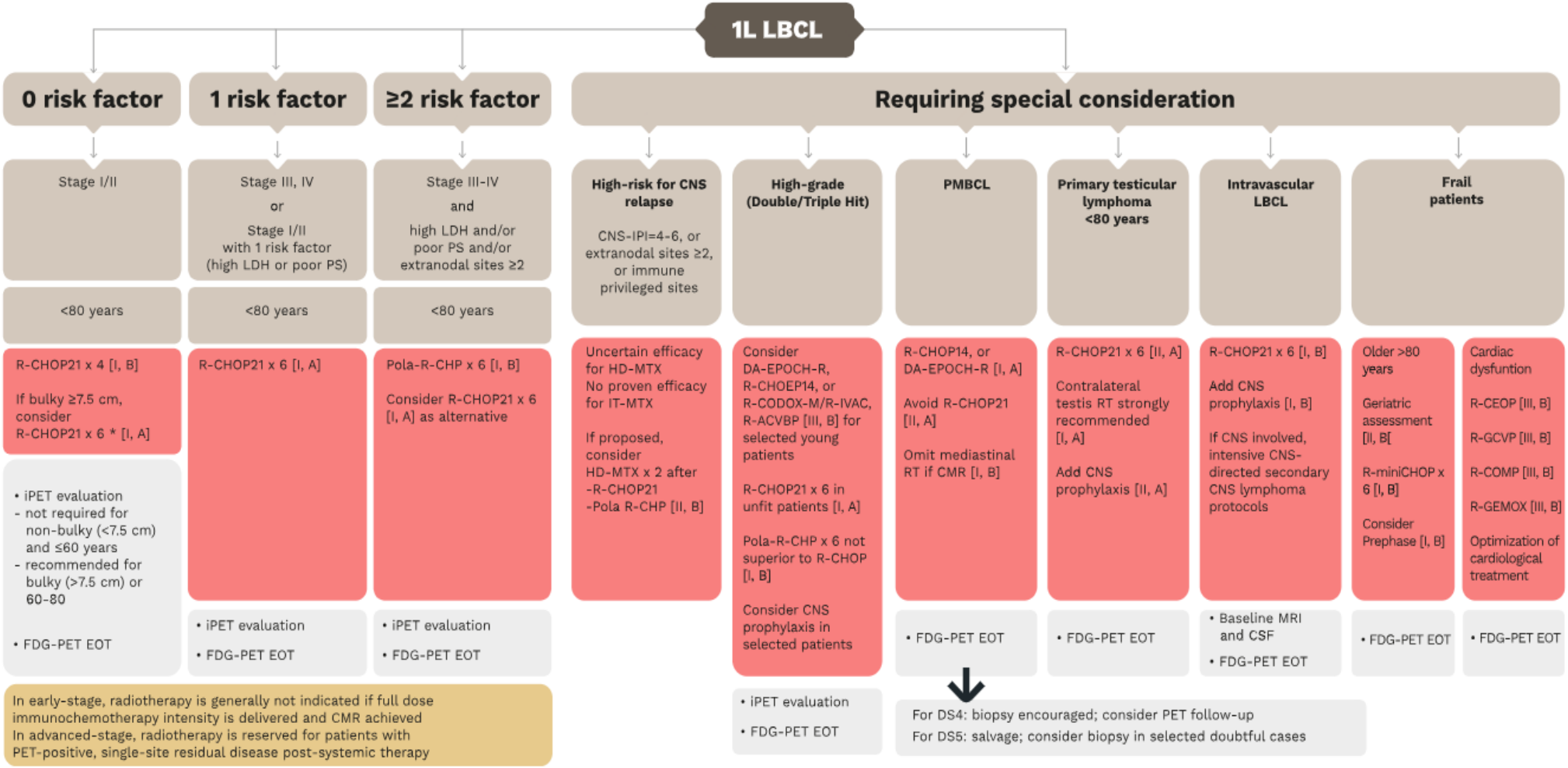
J Clin Oncol **43**, 3698-3705(2025) • Volume 43, Number 35 • DOI: 10.1200/JCO-25-00925

POLARIX: A randomized double-blinded study



*IV on Day 1; †R-CHOP: IV rituximab 375mg/m², cyclophosphamide 750mg/m², doxorubicin 50mg/m², and vincristine 1.4mg/m² (max. 2mg) on Day 1, plus oral prednisone 100mg once daily on Days 1–5. ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International prognostic index; IV, intravenous; R, randomized.



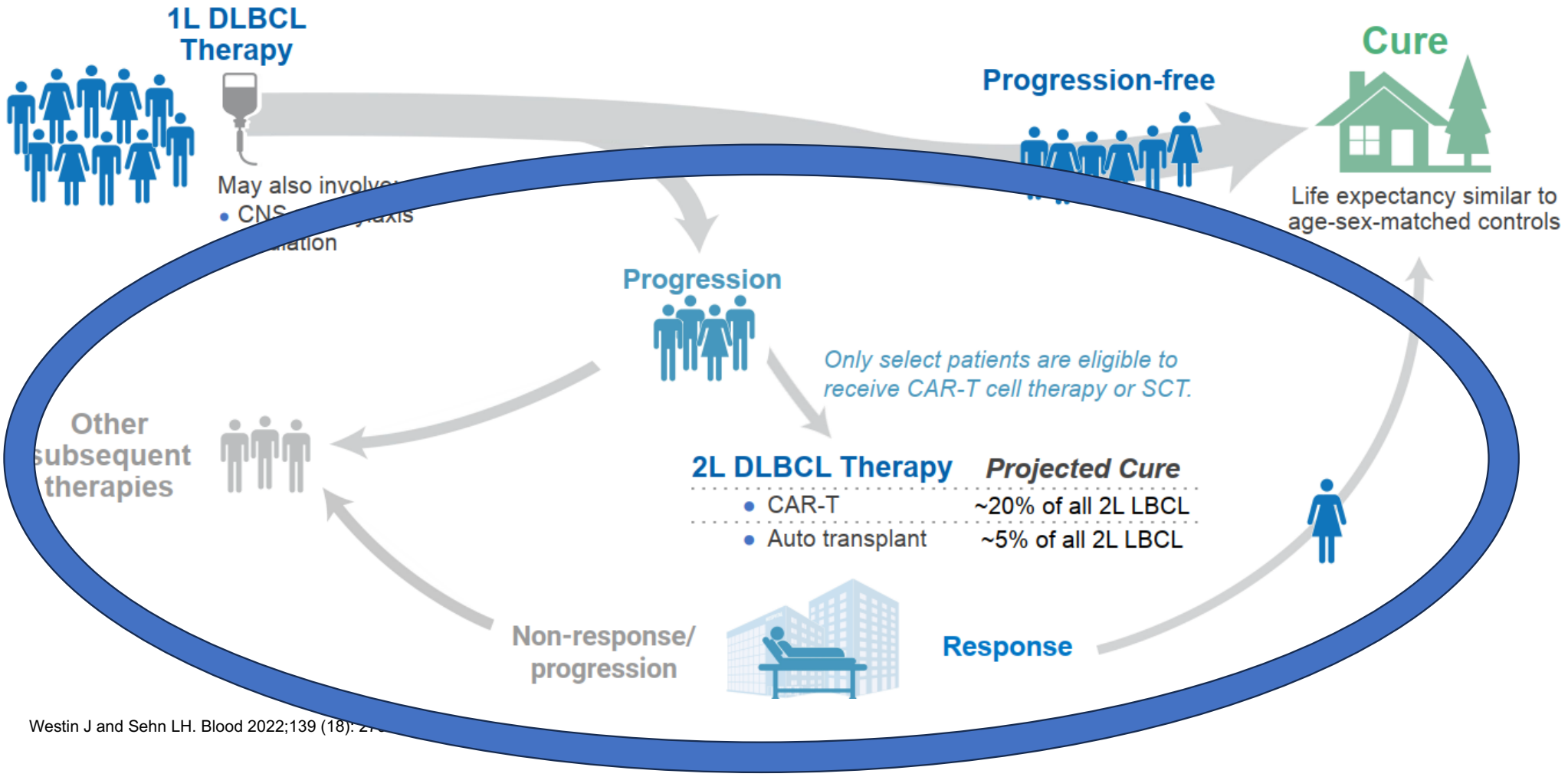


Catherine Thieblemont et al. Large B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up. Volume9, Issue9. September 2025. e70207

ONGOING CLINICAL TRIALS IN 1L DLBCL

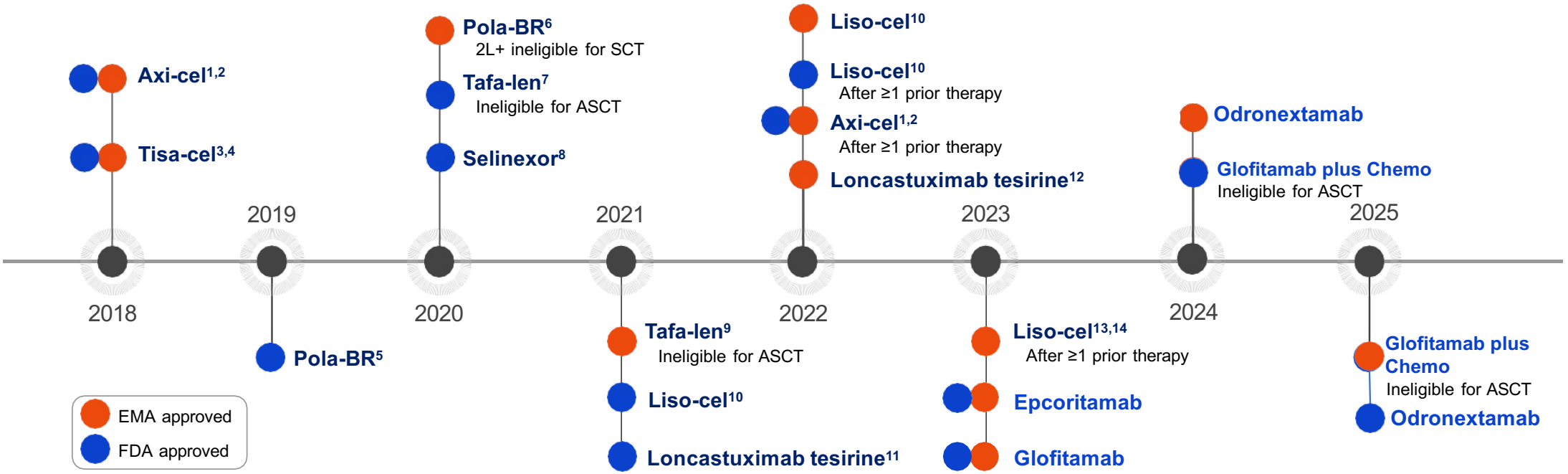
TRIAL	AGENTS	HIGH-RISK	LOW-RISK
POLARIX	*R-CHOP+POLATUZUMAB*	X IPI 2-5	-
waveLINE-010 study	*R-CHOP+ZILOVERTAMAB*	X IPI 2-5	X IPI 1
ESCALADE	*R-CHOP+ACALABRUTINIB*	X IPI 2-5	X IPI 1
BELIEVE-01	*R-CHOP+ORELABRUTINIB*	X IPI 2-5	
GOLSEEK-1	*R-CHOP+GOLCADOMIDE*	X IPI 2-5	X IPI 1
DEB STUDY	*R-CHOP+TUCIDINOSTAT*	X IPI 2-5	X IPI 1
GUIDANCE-002	*R-CHOP+X*	X IPI 2-5	-
FRONT-MIND	*R-CHOP+TAFA/LENA*	X IPI 3-5	-
EPCORE DLBCL-02	*R-CHOP+EPCORITAMAB*	X IPI 2-5	-
SKY-GLO	*R-POLA-CHP-GLOFITAMAB*	X IPI 2-5	-
OLYMPIA-3	*O-CHOP*	X IPI 2-5	-
ZUMA-23	*CAR-T*	X IPI 4-5, DH/TH	-

DLBCL Patient Journey : Likelihood of cure is highest with treatment in 1L setting



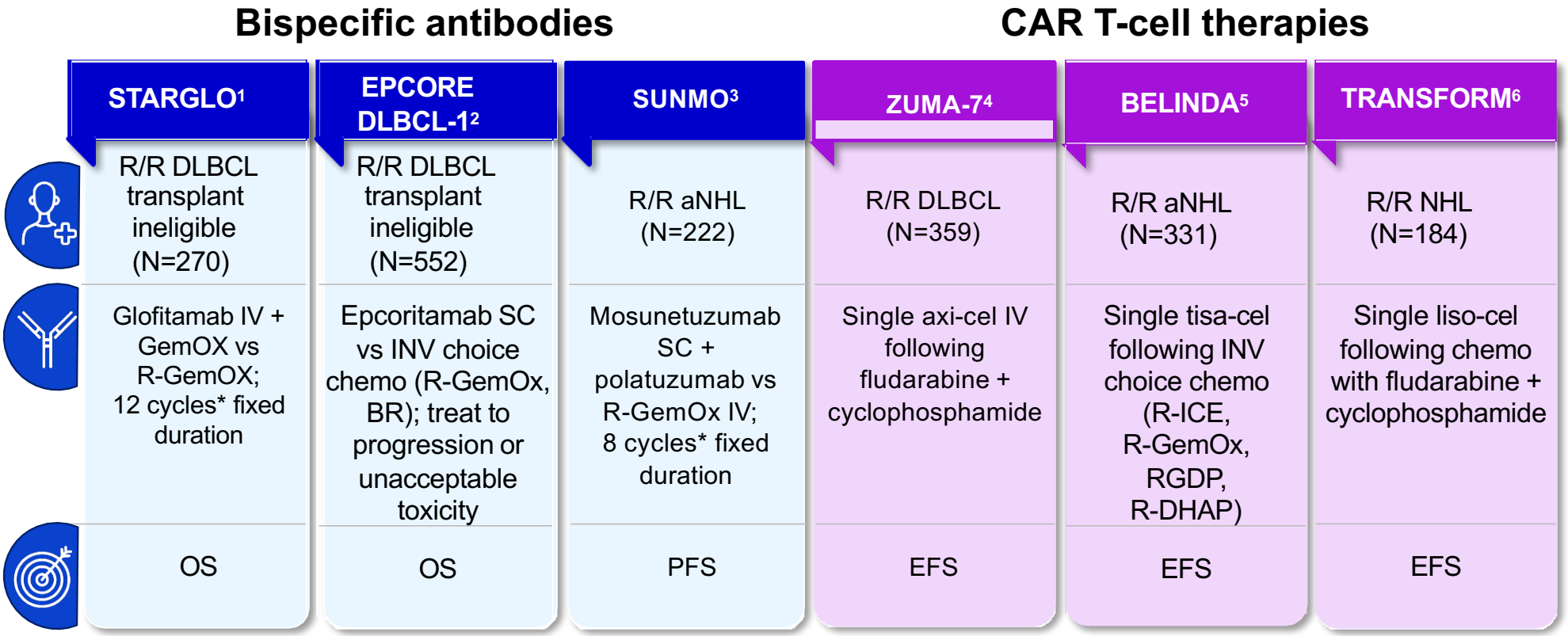
Westin J and Sehn LH. Blood 2022;139 (18):

The evolving range of available treatments for R/R DLBCL after ≥2 prior therapies



EMA, European Medicines Agency; FDA, United States Food and Drug Administration;

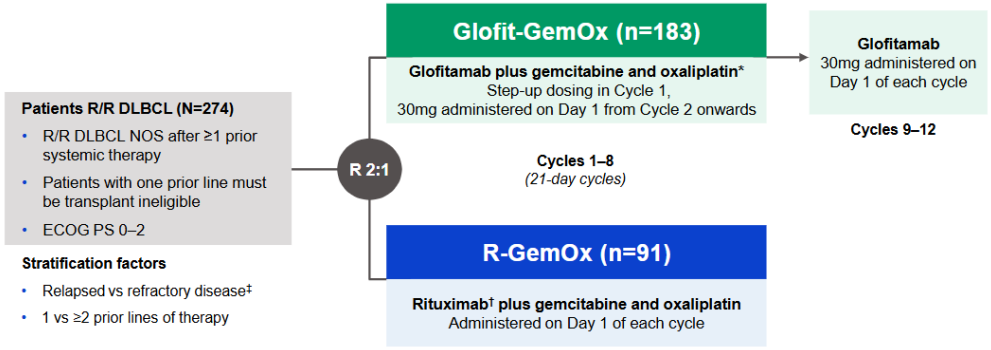
Bispecific antibody and CAR T-cell therapy Phase III studies in 2L+ DLBCL



*21-day cycles.
aNHL, aggressive non-Hodgkin lymphoma; chemo, chemotherapy; GemOx, gemcitabine, oxaliplatin; RGDP, rituximab, gemcitabine, dexamethasone, cisplatin; R-DHAP, rituximab, dexamethasone, cytarabine, cisplatin; R-GemOx, rituximab, gemcitabine, oxaliplatin; R-ICE, rituximab, ifosfamide, carboplatin, etoposide phosphate; vs, versus.

1. NCT04408638. Available at: https://clinicaltrials.gov; 2. NCT04628494. Available at: https://clinicaltrials.gov;
3. NCT05171647. Available at: https://clinicaltrials.gov; 4. NCT03391466. Available at: https://clinicaltrials.gov;
5. NCT03570892. Available at: https://clinicaltrials.gov; 6. NCT03575351. Available at: https://clinicaltrials.gov.

STARGLO

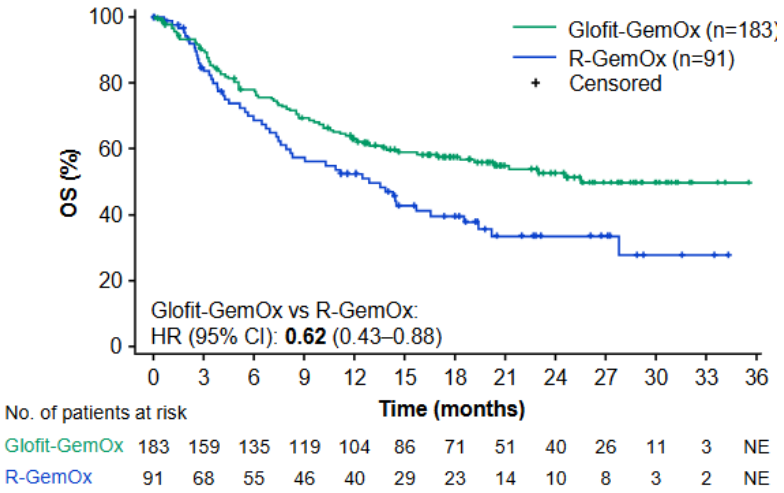


Baseline characteristics

n (%), unless otherwise stated		R-GemOx (n=91)	Glofit-GemOx (n=183)
Age, years	Median (range) ≥65 years	68.0 (20–84) 56 (61.5)	68.0 (22–88) 116 (63.4)
Sex	Male	53 (58.2)	105 (57.4)
Race	Asian Black or African American White Unknown	51 (56.0) 1 (1.1) 33 (36.3) 6 (6.6)	86 (47.0) 2 (1.1) 82 (44.8) 13 (7.1)
ECOG PS	0 1 2	44 (50.0) 36 (40.9) 8 (9.1)	72 (40.0) 89 (49.4) 19 (10.6)
Ann Arbor stage	I–II III–IV	20 (22.0) 70 (76.9)	60 (32.8) 123 (67.2)
Number of prior lines of therapy	1 ≥2	57 (62.6) 34 (37.4)	115 (62.8) 68 (37.2)
Primary refractory	Yes	47 (51.6)	106 (57.9)
R/R to last prior therapy	Relapsed / refractory	37 (40.7) / 54 (59.3)	71 (38.8) / 112 (61.2)
Bulky disease (≥10cm)	Present	14 (15.4)	23 (12.6)
Cell of origin at initial diagnosis	GCB Non-GCB (including ABC) Unknown	29 (31.9) 50 (54.9) 12 (13.2)	60 (32.8) 103 (56.3) 20 (10.9)
Prior CAR T-cell therapy	Received	8 (8.8)	13 (7.1)

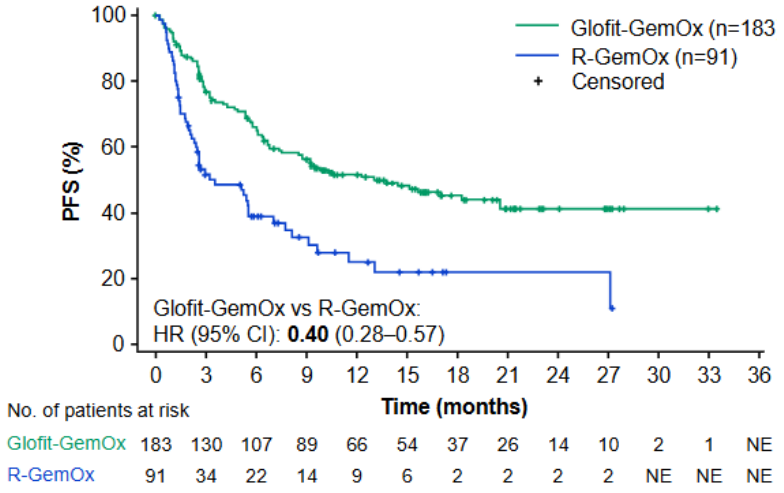
Abramson JS, et al. Glofitamab plus gemcitabine and oxaliplatin (GemOx) versus rituximab-GemOx for relapsed or refractory diffuse large B-cell lymphoma (STARGLO): a global phase 3, randomised, open-label trial. Lancet. 2024 Nov 16;404(10466):1940-1954.

Updated analysis

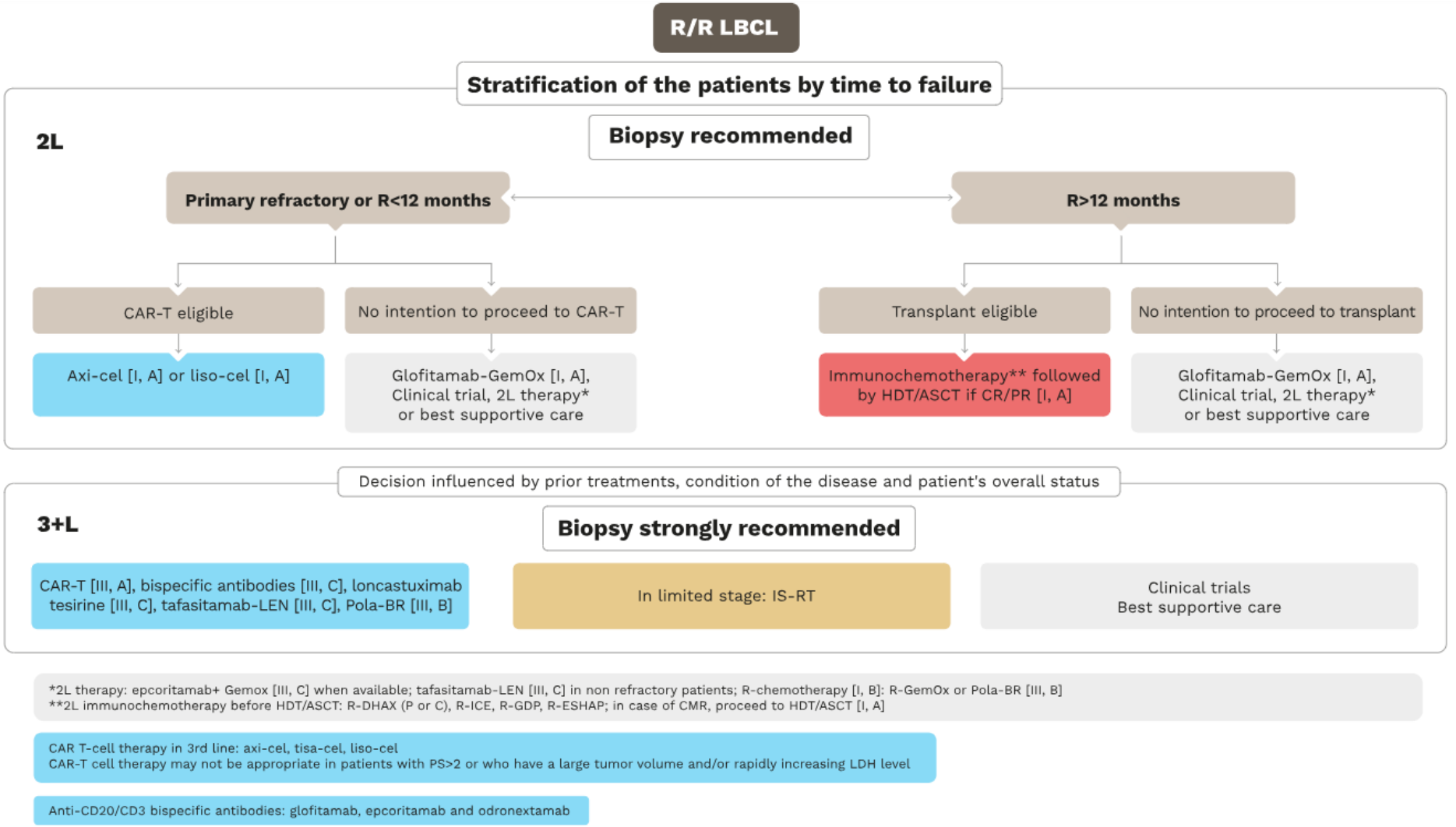


No. of patients at risk													
Glofit-GemOx	183	159	135	119	104	86	71	51	40	26	11	3	NE
R-GemOx	91	68	55	46	40	29	23	14	10	8	3	2	NE

Updated analysis



No. of patients at risk													
Glofit-GemOx	183	130	107	89	66	54	37	26	14	10	2	1	NE
R-GemOx	91	34	22	14	9	6	2	2	2	2	NE	NE	NE



Catherine Thieblemont et al. Large B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up. Volume9, Issue9. September 2025. e70207

- The treatment landscape of MCL and DLBCL is rapidly evolving, driven by early use of targeted agents and novel immunotherapies.
- In MCL, the shift of BTK inhibitors to the frontline setting makes management of R/R disease a critical unmet need.
- In DLBCL, bispecific antibodies and CAR T-cell therapies are redefining treatment paradigms and enabling more personalized, targeted approaches.
- Ongoing clinical trials continue to expand therapeutic options, improving outcomes even in high-risk and heavily pretreated populations.
- Despite major advances, challenges remain in treatment access, cost, and long-term monitoring of efficacy and durability of response.

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Thank You

For Your Attention