Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML KONGRESSE

Expert:innen berichten zu Lymphomen & Leukämien

EHA 2025

MAILAND, ITALIEN

12. – 15. Juni 2025

Kompetenznetz Maligne Lymphome

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Prof. Dr. med. Björn Chapuy
Charité Universitätsmedizin Berlin

Diffus großzelliges B-Zell-Lymphom

Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – EHA 2025 Mailand, Italien wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.
Meine persönlichen Disclosures betreffen:

Anstellungsverhältnis, Führungsposition	Anstellung, Charité - Universitätsmedizin Berlin; Vorstandsmitglied, German Lymphoma Alliance
Beratungs-/ Gutachtertätigkeit	AbbVie, BMS, Gilead, Incyte, J&J, Regeneron, Roche, Sobi
Besitz von Geschäftsanteilen, Aktien oder Fonds	-
Patent, Urheberrecht, Verkaufslizenz	Verschiedene Patente zur molekularen Klassifikation des DLBCL, inkl. DLB*class*
Honorare	AbbVie, Art tempi, Astra Zeneca, BMS, Incyte, J&J, Gilead, KML, Regeneron, Roche, Sobi, Ono
Finanzierung wissenschaftlicher Untersuchungen	Prof. Chapuy leitet die akademische R-Pola-Glo Studie, dessen Sponsor das IKF und Geldgeber die Roche Pharma AG ist.
Andere finanzielle Beziehungen	-
Immaterielle Interessenkonflikte	-

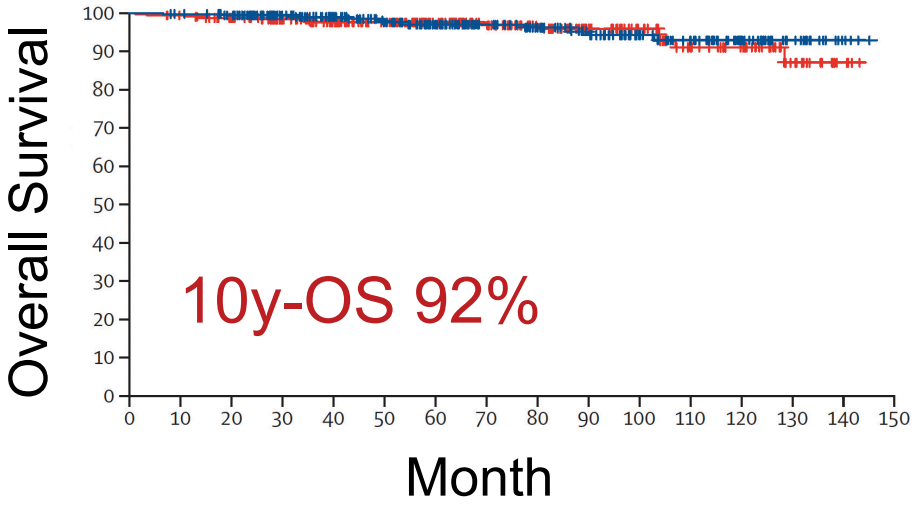
Kapitel 1

Erstlinie

Risk-adapted Firstline Treatment Achieves High Cure Rates

FLYER Trial

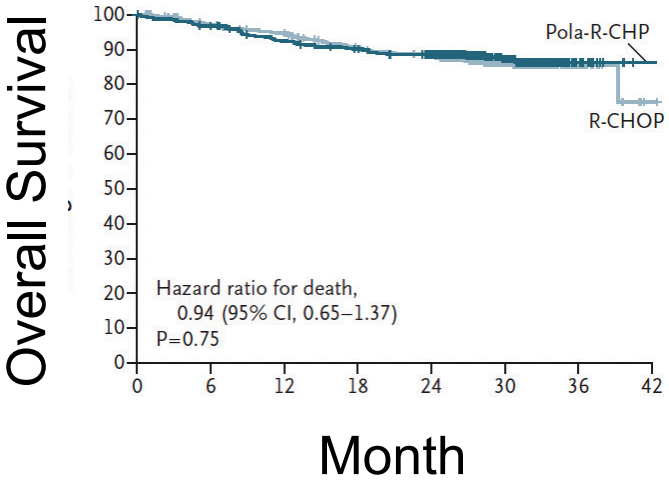
(IPI 0, no bulk,<60y)



Poeschel, Held, Ziepert et al. *Lancet* 2019

Polarix Tiral

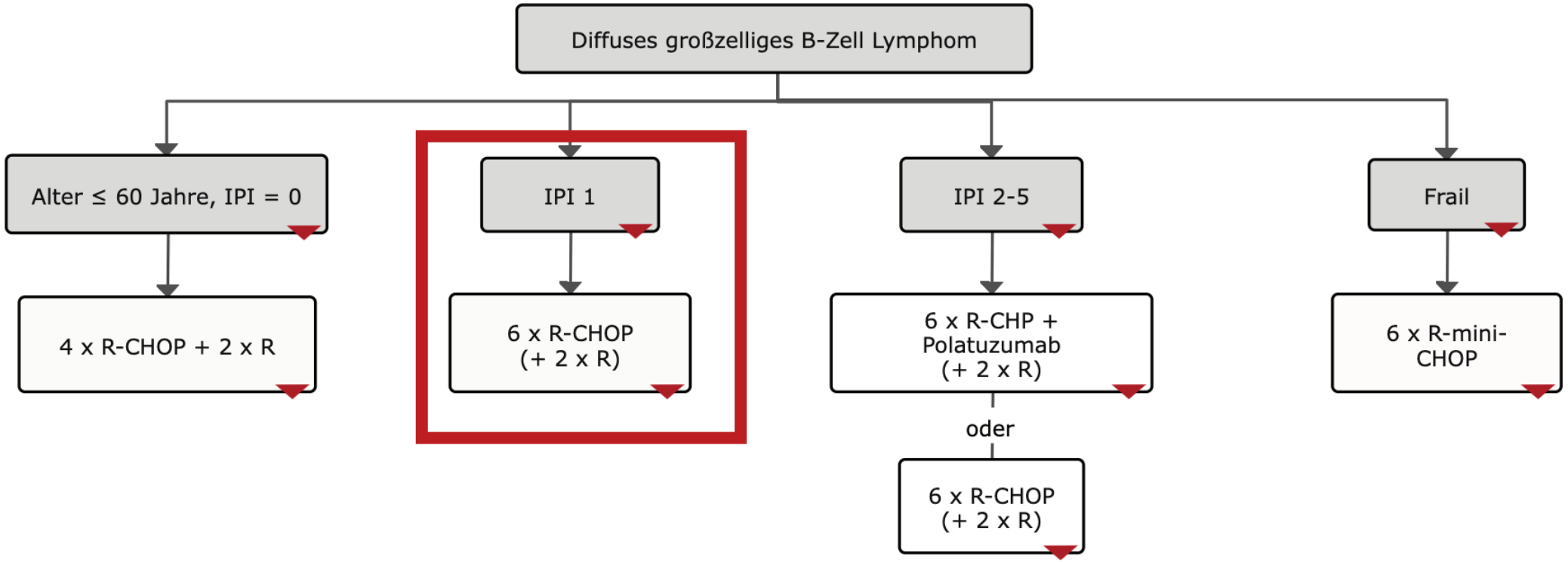
(IPI 2-5, <80y)



Tilly et al *N Engl J Med.* 2021

➔ R-CHOP-like is the established gold standard.

Current Treatment Guidelines for the 1L Treatment of DLBCL



➔ Pola-R-CHP has evolved as the standard of care for patients with IPI 2-5.

➔ IPI 0, no bulk patients are treated with 4xR-CHOP+2R

Onkopedia (2024)

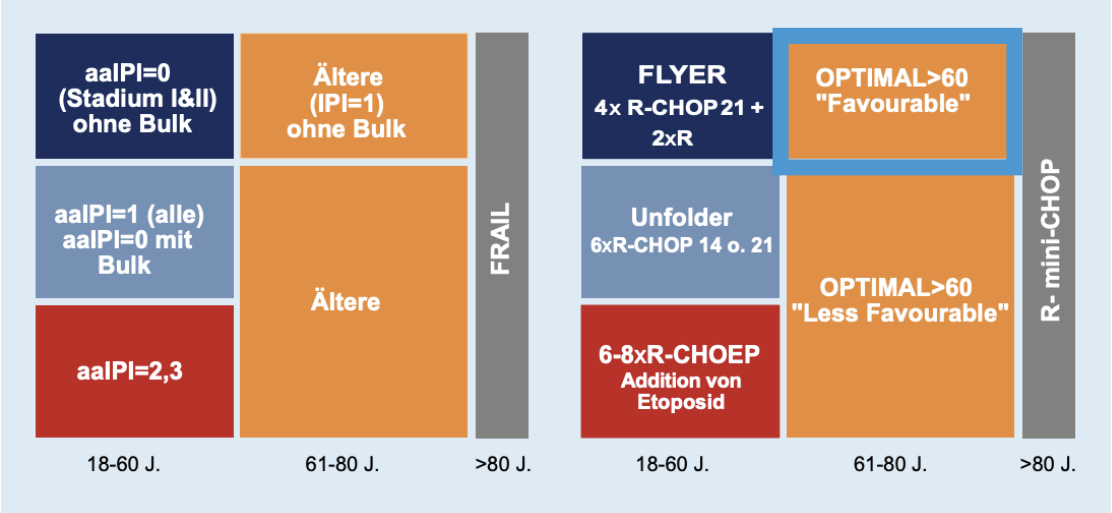
EXCELLENT OUTCOME WITH INTERIM PET ADAPTED TREATMENT REDUCTION IN ELDERLY DLBCL PTS WITH FAVOURABLE PROGNOSIS: RESULTS OF 288 PTS TREATED IN OPTIMAL>60 TRIAL OF THE DSHNHL/GLA

Viola Pöschel

Author(s): Viola Pöschel, Bettina Altmann, Gerhard Held, Andreas Neubauer, Jörg Thomas Bittenbring, Andreas Viardot, Mathias Hänel, Rolf Mahlberg, Stefan Wirths, Martin Dreyling, Tobias Gaska, Ulrich Langenkamp, Ulrich Keller, Alexander Kiani, Kai Hübel, Justin Hasenkamp, Heinz-Gert Höffkes, Ahmet H. Elmaagacli, Thomas Illmer, Andreas Rank, Peter Staib, Kai Wille, Lothar Müller, Holger Hebart, Frank Griesinger, Bertram Glass, Maike Nickelsen, Norbert Schmitz, Lorenz TRÜMPER, Markus Löffler, Alexander Hasse, Vadim Lesan, Onur Cetin, Niels Murawski, Moritz Bewarder, Dominic Kaddu-Mulindwa, Igor Age Kos, Konstantinos Christofyllakis, Günther Schneider, Christian Berdel, Dirk Hellwig, Marita Ziepert, Lorenz Thurner

(Abstract release date: 05/14/25) EHA Library. Pöschel V. 06/15/2025; 4159326; S249

Phase III OPTIMAL>60 Trial – Favorable Cohort



Treiber, et al. Der Onkologe · Suppl 1 · 2021

Aims:

i) Reduction of PNP by substituting conventional by liposomal vincristine,

ii) Reduction of chemotherapy to 4 cy in FDG-PET-4 negative (neg) pat.

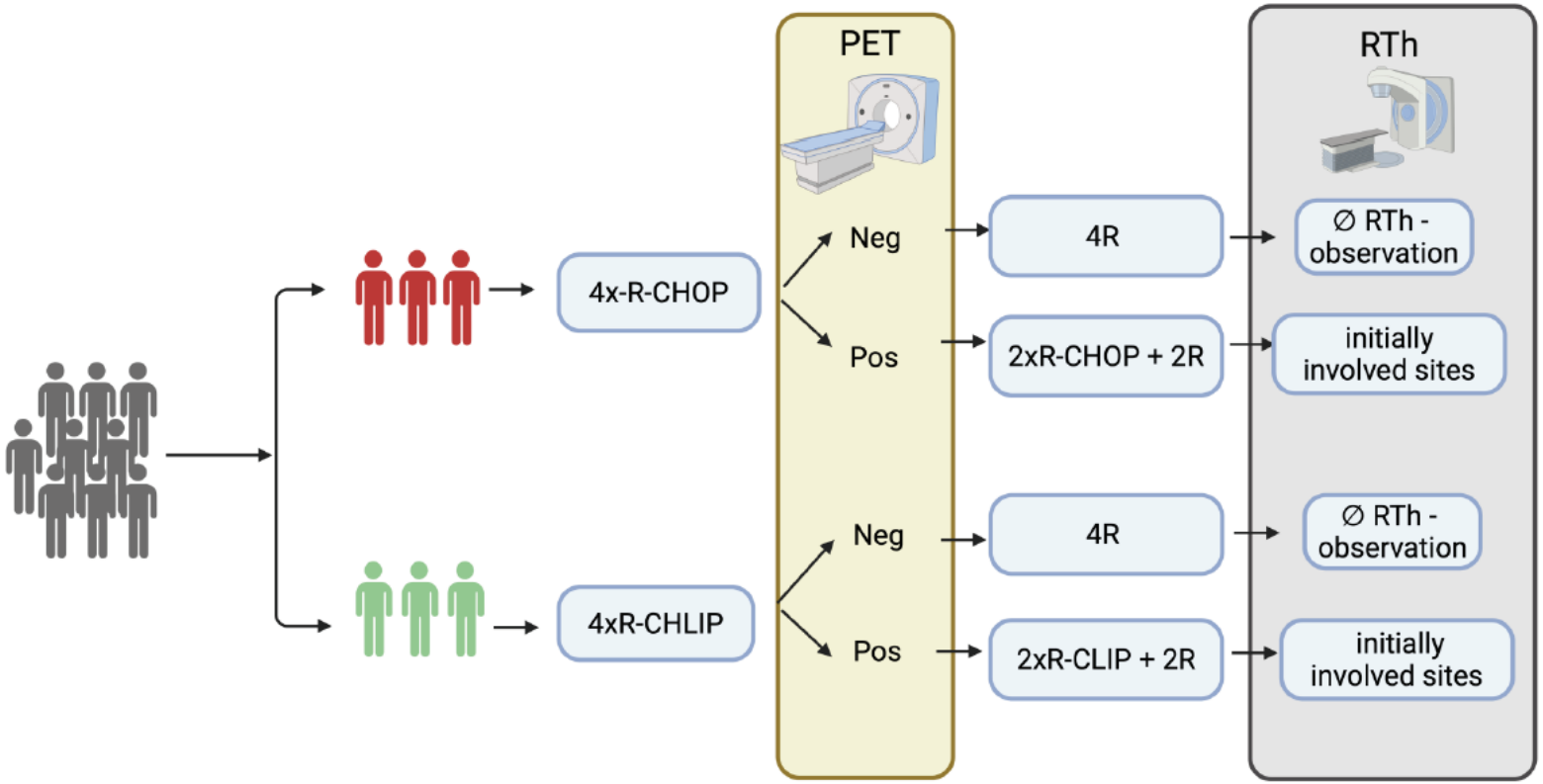
Cohort:

- From 11/2011 to 05/2020, 288 pts were randomized into the favorable cohort (IPI1, no bulk).
- Median age was 70y.

Pöschel et al. EHA 06/15/2025; 4159326; S249

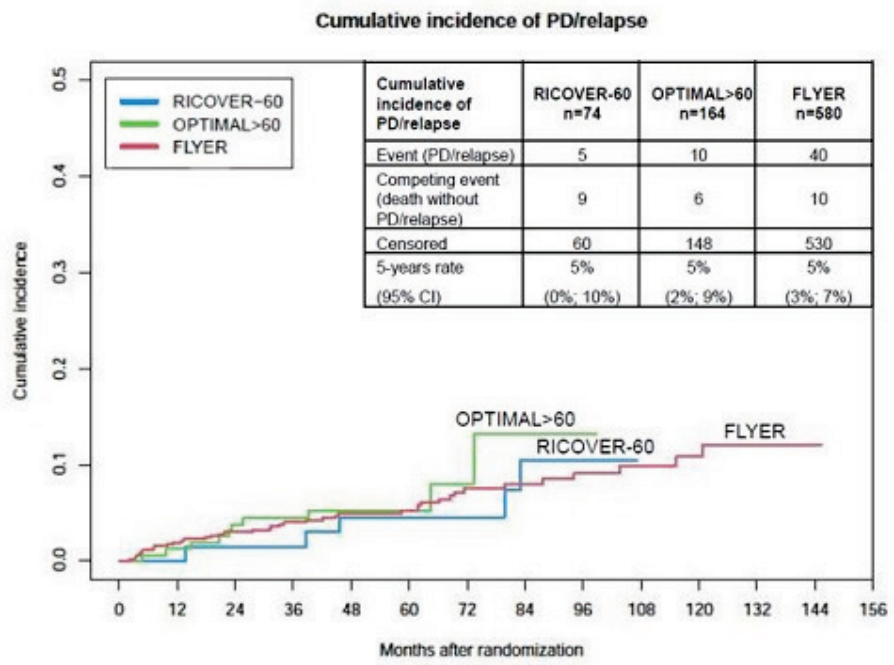
Phase III OPTIMAL>60 Trial – Design

- **Aggressive B-cell lymphoma**
- **61-80 years, Stage I/II, IPI = 1 (age), no bulk (max. diameter < 7.5 cm)**



Pöschel et al. EHA 06/15/2025; 4159326; S249

Phase III OPTIMAL>60 Trial – Favorable Cohort - Results



- **3-y PFS was 91%** and **3-y OS was excellent with 95%**; no significant difference regarding type of VCR (p=0.421).
- **51 PET-4 pos** pts received 6 cy and **193 PET-4 neg pts** received 4 cy per protocol; **3-y PFS: 92% in both cohorts.**
- Incidence of PD/relapse for PET-4-adapted treatment within OPTIMAL>60 was comparable to younger patients with fav DLBCL treated within the FLYER

  ➔**non-inferiority of 6xR-CHOP and 4xR-CHOP+2R**.

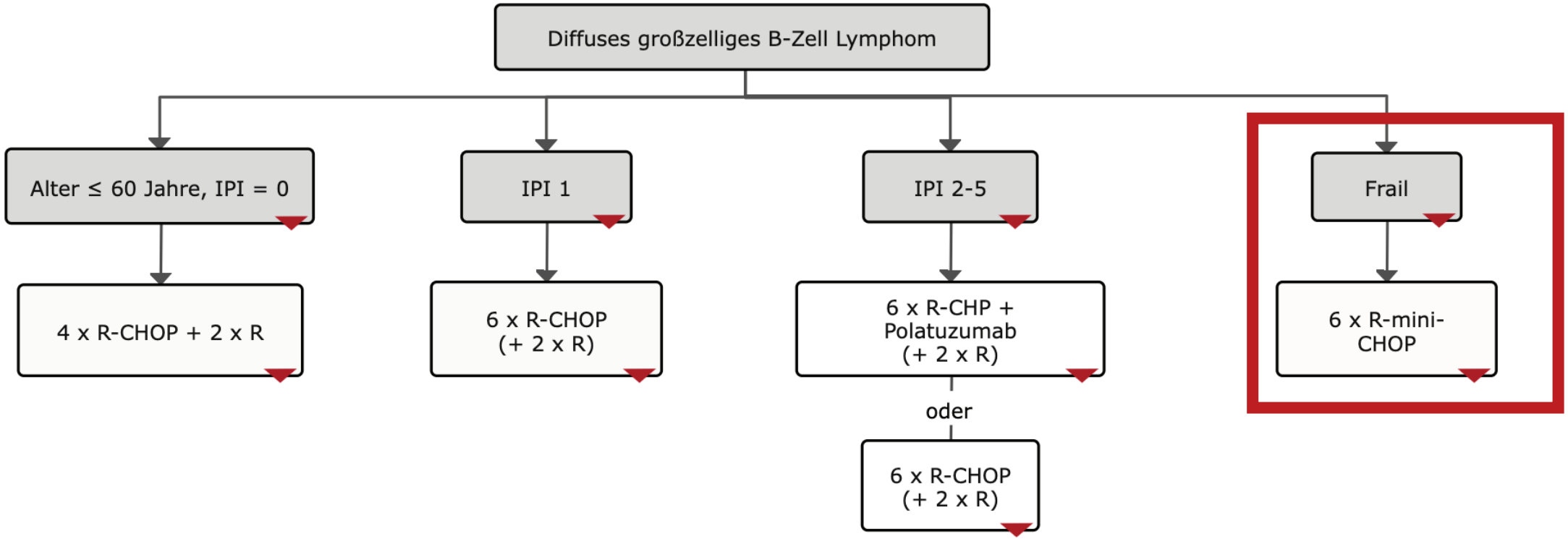
Pöschel et al. EHA 06/15/2025; 4159326; S249

OPTIMAL>60, favorable

Conclusion

PET-4 adapted treatment with R-CHOP is save and results in reduced treatment exposure in 2/3 of elderly pts with fav DLBCL.

Current Treatment Guidelines for the 1L Treatment of DLBCL



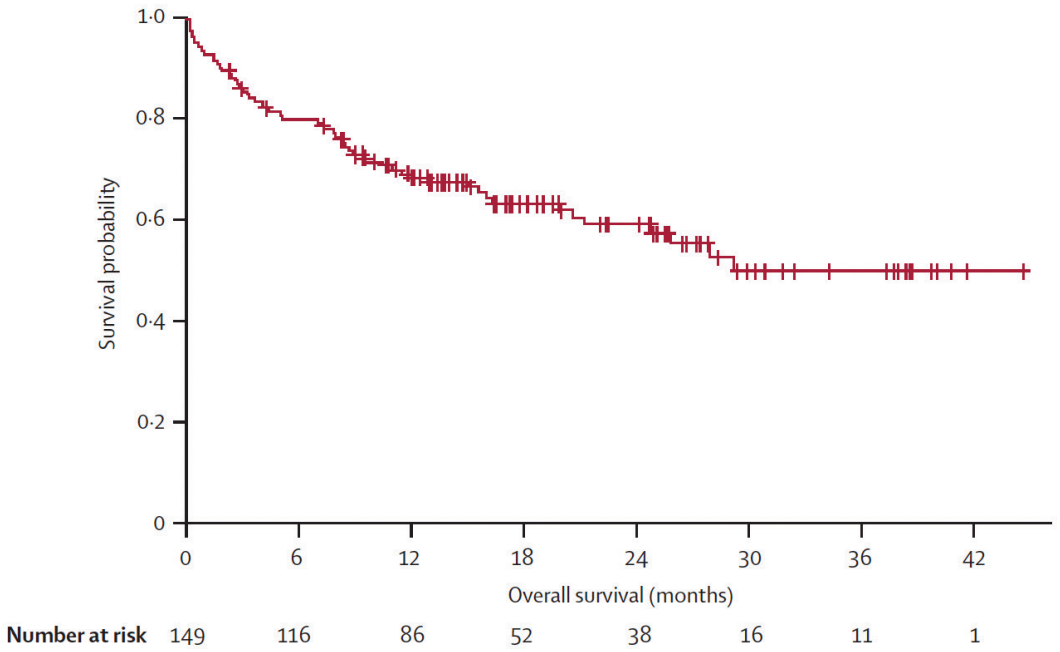
➔ Pola-R-CHP has evolved as the standard of care for patients with IPI 2-5.

➔ IPI 0, no bulk patients are treated with 4xR-CHOP+2R

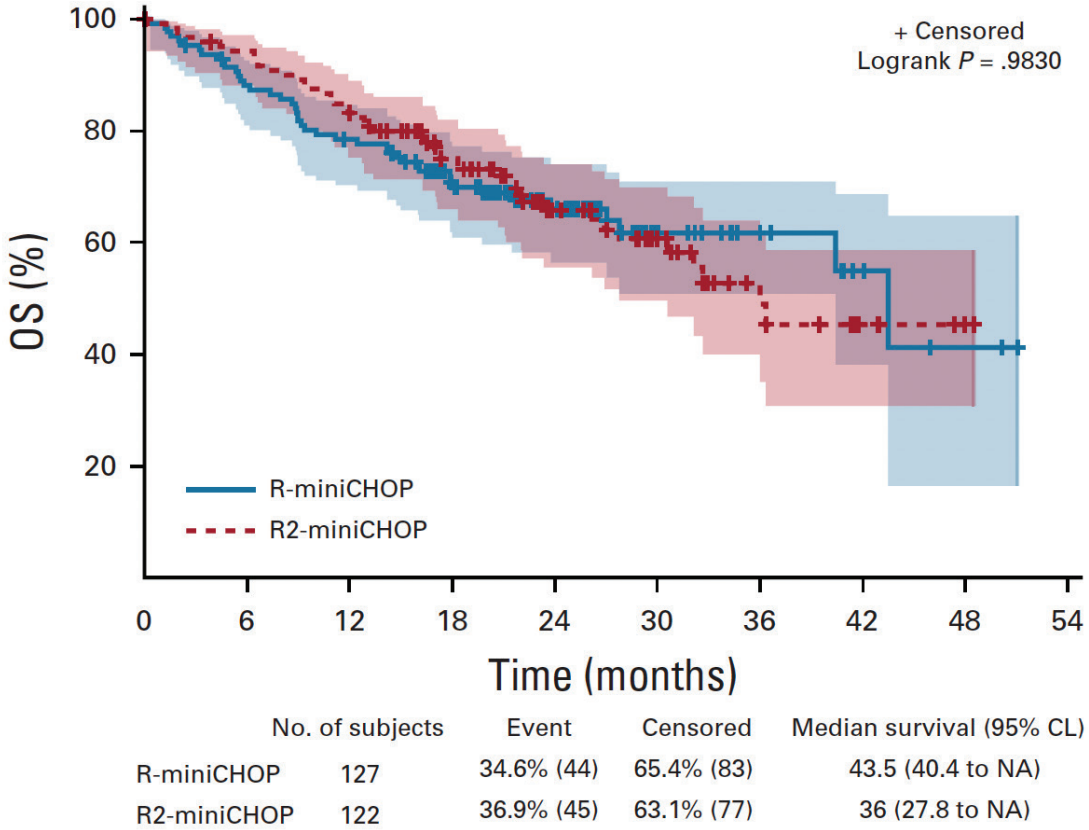
Onkopedia (2024)

R-mini-CHOP is the Standard-of-Care for Elderly/Frail Patients

R-mini-CHOP



R²-mini-CHOP



	No. of subjects	Event	Censored	Median survival (95% CL)
R-miniCHOP	127	34.6% (44)	65.4% (83)	43.5 (40.4 to NA)
R2-miniCHOP	122	36.9% (45)	63.1% (77)	36 (27.8 to NA)

➔ R-miniCHOP is established gold standard since decades.

Peyrade et al Lancet Oncol 2011
Oberic et al JCO 2021

FRONTLINE PHASE II RITUXIMAB-POLATUZUMAB-GLOFITMAB (R-POLA-GLO) TRIAL DEMONSTRATES A MANAGEABLE SAFETY PROFILE AND HIGH RESPONSE RATES IN ELDERLY AND MEDICAL UNFIT PATIENTS WITH AGGRESSIVE LYMPHOMA

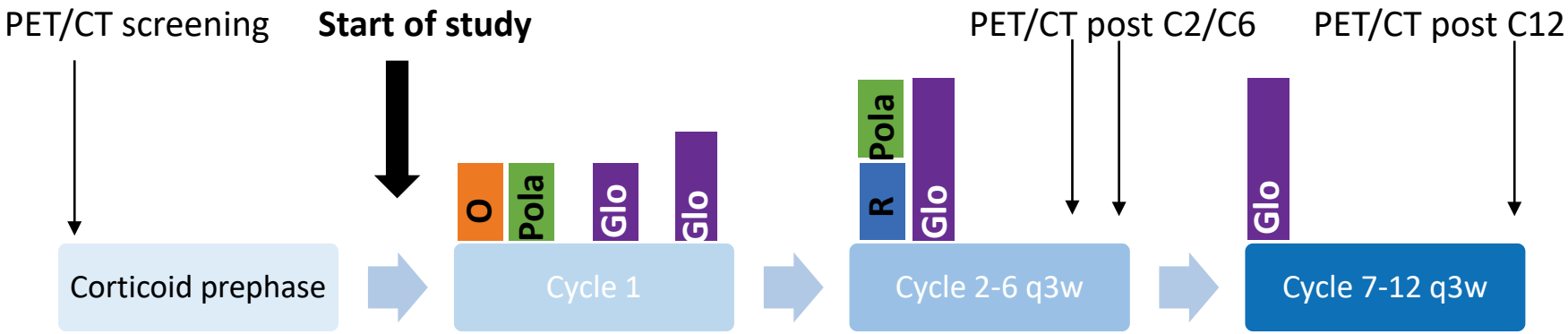
Thomas Melchardt

Author(s): Thomas Melchardt *, Rebecca Wurm-Kuczera *, Petra Pichler, Angela Huster, Andrea Kerkhoff, Michael Panny, Roland Schroers, Anna Ossami Saidy, Fabian Müller, Frederik Damm, Manuel Orlinger, Philipp Staber, Carsten Schwaenen, Ralph Michael, Luisa Wohn, Clemens A. Schmitt, Martin Hoffmann, Mathias Hänel, Johannes Duell, Simone Heyn, Stephanie Mayer, Thomas Weber, Peter Reimer, Natalia Magdalena Rotter, Ulf Schnetzke, Bastian von Tresckow, Gabriel Kammerer, Julia Rasvina, Barbara Lehner, Thomas Mika, David Böckle, Corinna Leng, Anna Lena Illert, Bettina Altmann, Birte Friedrich, Ella Willenbacher, Dimitrios Mougiakakos, Christiane Pott, Salah-Eddin Al-Batran, Andreas Rosenwald, Dirk Hellwig, Sascha Dietrich, Bertram Glass, Georg Lenz, Ulrich Keller, Marita Ziepert, Richard Greil, Björn Chapuy

(Abstract release date: 05/14/25) EHA Library. Melchardt T. 06/15/2025; 4159325; S248

R-Pola-Glo

Study Design



Debulking

Prednisone/
Dexamethsone

Step-up cycle

Obinutuzumab
Polatuzumab
Glofitamab

Target dose

Rituximab
Polatuzumab
Glofitamab

Consolidation

Glofitamab

- *Supportive treatment:*
  antibacterial & antiviral prophylaxis & growth factor support.
- *Cycle 1-6:* Mandatory as inpatient in the initial cohort of 80 pts.

Melchardt T. EHA2025; 4159325; S248

Indication

- Aggressive large B-cell lymphoma
- Previously untreated pts > 60 years
- Not eligible for full dose R-CHOP-like therapy at discretion of the treating physician

Study Design

- One arm, multicentric Phase II
- Germany/Austria
- **Initial cohort: 80 pts**
- **extension cohort:** 45 pts; **total:** 125 pts
- 30 centers in Germany/Austria

Endpoints

- Primary: 1y PFS rate
- Secondary:
  - Efficacy
  - Feasibility and Toxicities
  - Exploratory
  - Feasibility of outpatient care. (extension cohort)

Patient Characteristics

Baseline Characteristic (N=80)	
Median Age **Age > 85**	80 (66-92) 19%
ECOG >1	28%
Elevated LDH	63%
IPI 3 **IPI 4-5**	33% 33%

Simplified Geriatric Assessment (sGA)

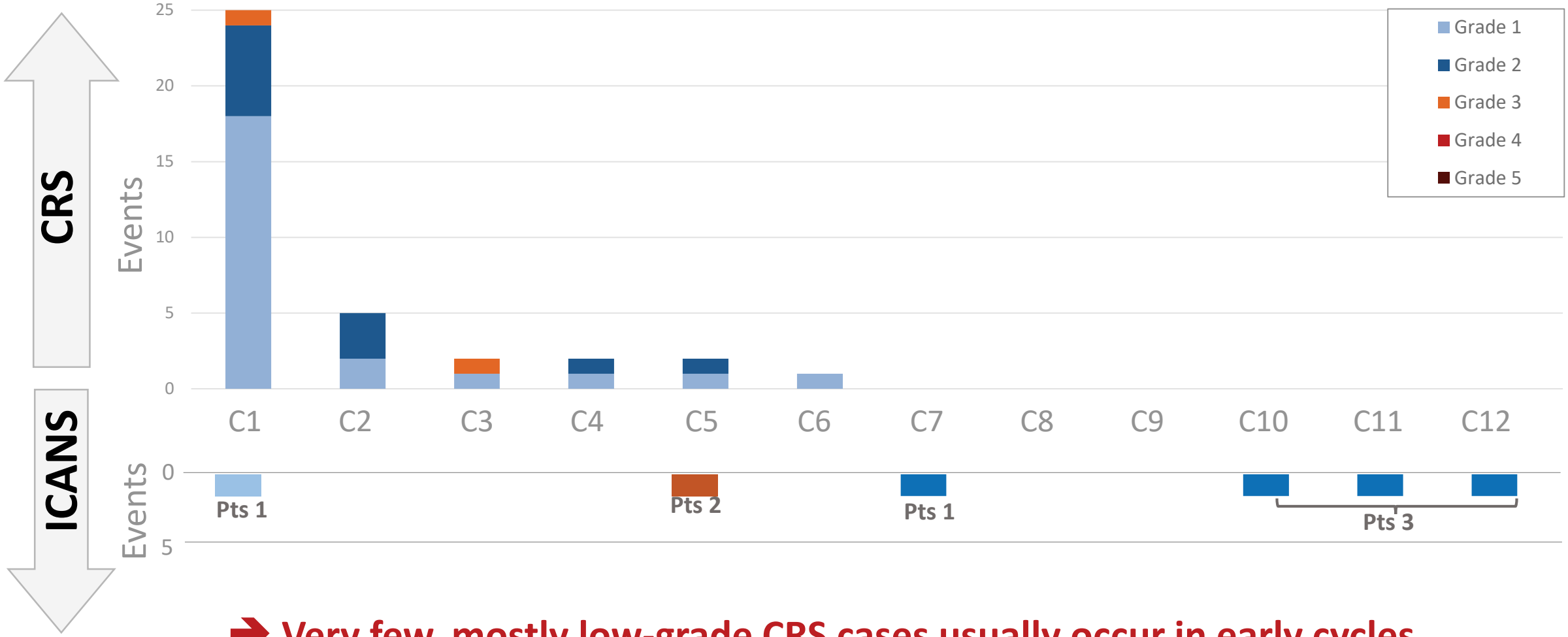
	FIT	UNFIT		FRAIL
ADL	**≥5***	**< 5***	**6***	**<6***
	and	*and/or*	*and*	*and/or*
IADL	**≥6***	**<6***	**8***	**<8***
	and	*and/or*	*and*	*and/or*
CIRS-G	**0 score =3-4** *and* **≤8 score =2**	**≥1 score =3-4** *and/or* **> 8 score =2**	**0 score =3-4** *and* **<5 score =2**	**≥1 score =3-4** *and/or* **≥5 score =2**
	and	*and*	*and*	*and*
Age	**<80**	**<80**	**≥80**	**≥80**
R-Pola-Glo (n=79)	**6 (7.5 %)**	**28 (35.0 %)**	**15 (18.8 %)**	**30 (37.5 %)**

91.3%

➔ **Patient profile aligns with the expected real-world profile of medical unfit/frail DLBCL patients with high treatment complexity.**

Melchardt T. EHA2025; 4159325; S248

Safety – ICANS and CRS Over Time by Cycle

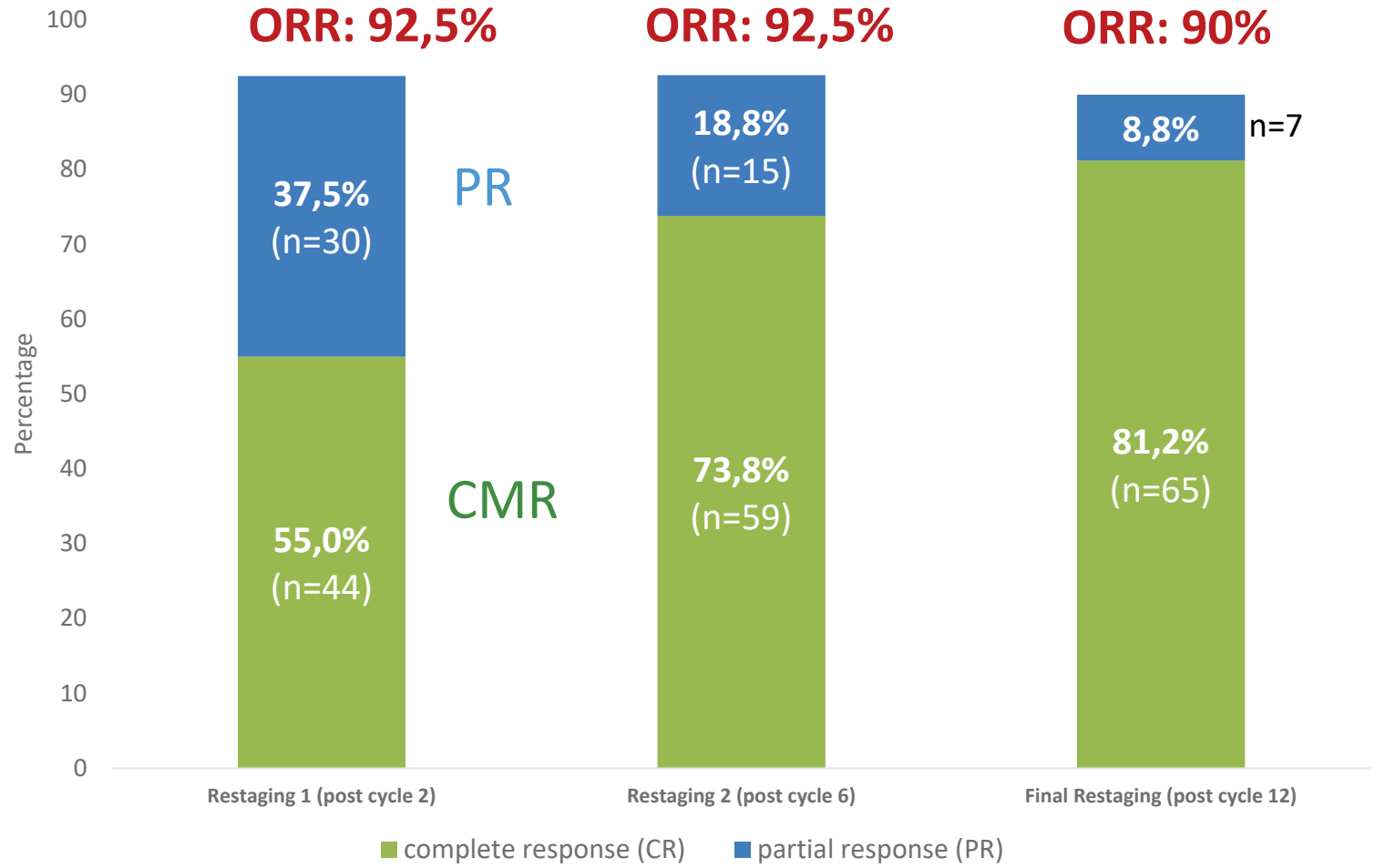


➔ **Very few, mostly low-grade CRS cases usually occur in early cycles.**

➔ **ICANS are infrequent events**

Melchardt T. EHA2025; 4159325; S248

Response Over Time – Initial Cohort (n=80)



➔ **R-Pola-Glo has an overall response rate (ORR) of 90% with a 81.3% complete metabolic response rate (CMR) at end of treatment.**

Melchardt T. EHA2025; 4159325; S248

Conclusion

Chemotherapy-light R-Pola-Glo shows outstanding response rates and a manageable safety profile, supporting further clinical evaluation as a first-line treatment option for elderly, frail, or medically unfit patients with aggressive lymphoma.

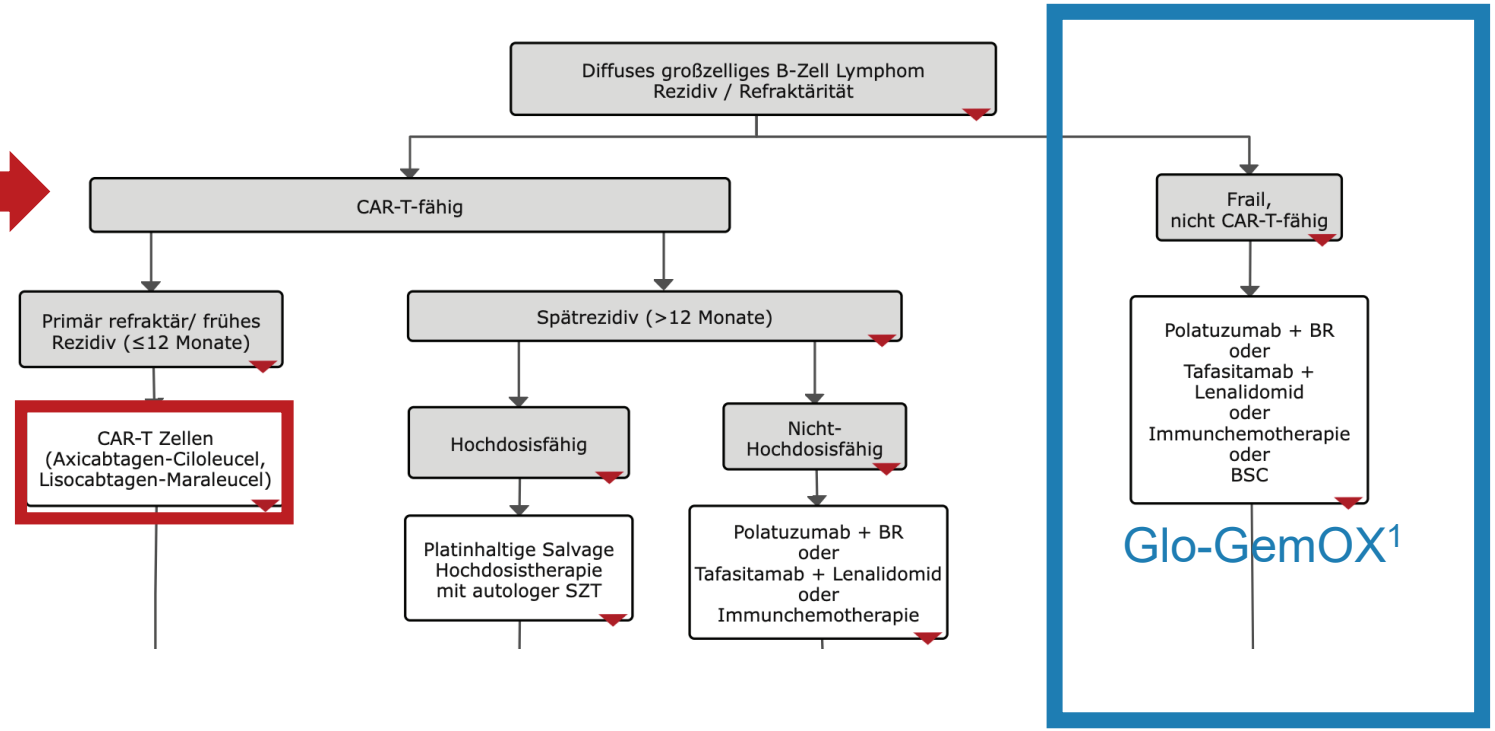
Kapitel 2

Zweitlinie

Current Treatment Guidelines for the 1st Relapse of DLBCL in Germany

CAR-T-eligibility

CAR-T



➔ CAR T-cells are SOC in an early relapse of DLBCL.

➔ Non-transplant erigible segment is dynamically expanding.

Onkopedia (2024)

[1] *Abramson et al Lancet 2024*

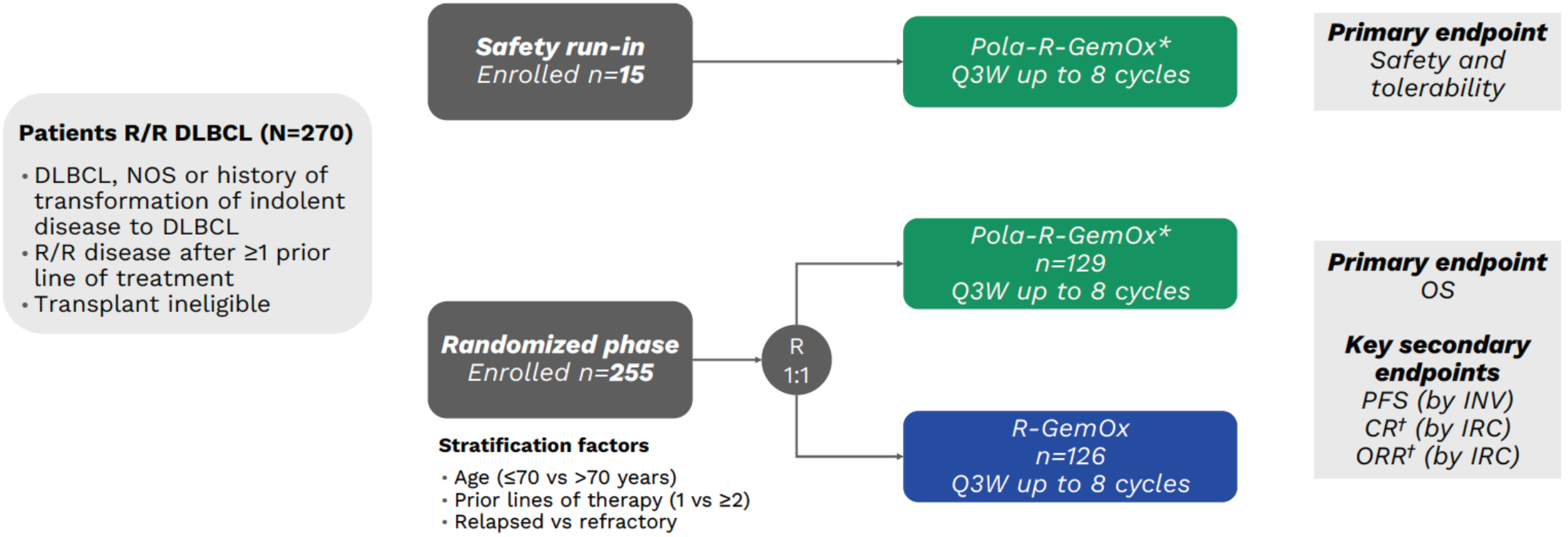
POLATUZUMAB VEDOTIN, RITUXIMAB, GEMCITABINE AND OXALIPLATIN (POLA-R-GEMOX) FOR RELAPSED/REFRACTORY (R/R) DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): RESULTS FROM THE RANDOMIZED PHASE III POLARGO TRIAL

Matthew Matasar

Author(s): Matthew Matasar, Zhi-Ming Li, T.P Vassilakopoulos, Juan Manuel Sancho Cia, Andreas Viardot, Andrew McMillan, Mehmet Sinan Dal, JULIANA PEREIRA, Jin Seok Kim, lugui qiu, Connie Batlevi, Rania Ibrahim, Juana HERNANDEZ, Bruce Mccall, Yanwen Jiang, Mark Yan, Will Harris, Lisa Musick, Corinne Haioun

(Abstract release date: 06/13/25) EHA Library. Matasar M. 06/14/2025; 4159178; S101

Phase III POLARGO: Pola-R-GemOx vs R-GemOx



Matasar M. 06/14/2025; 4159178; S101

Phase III POLARGO: Safety

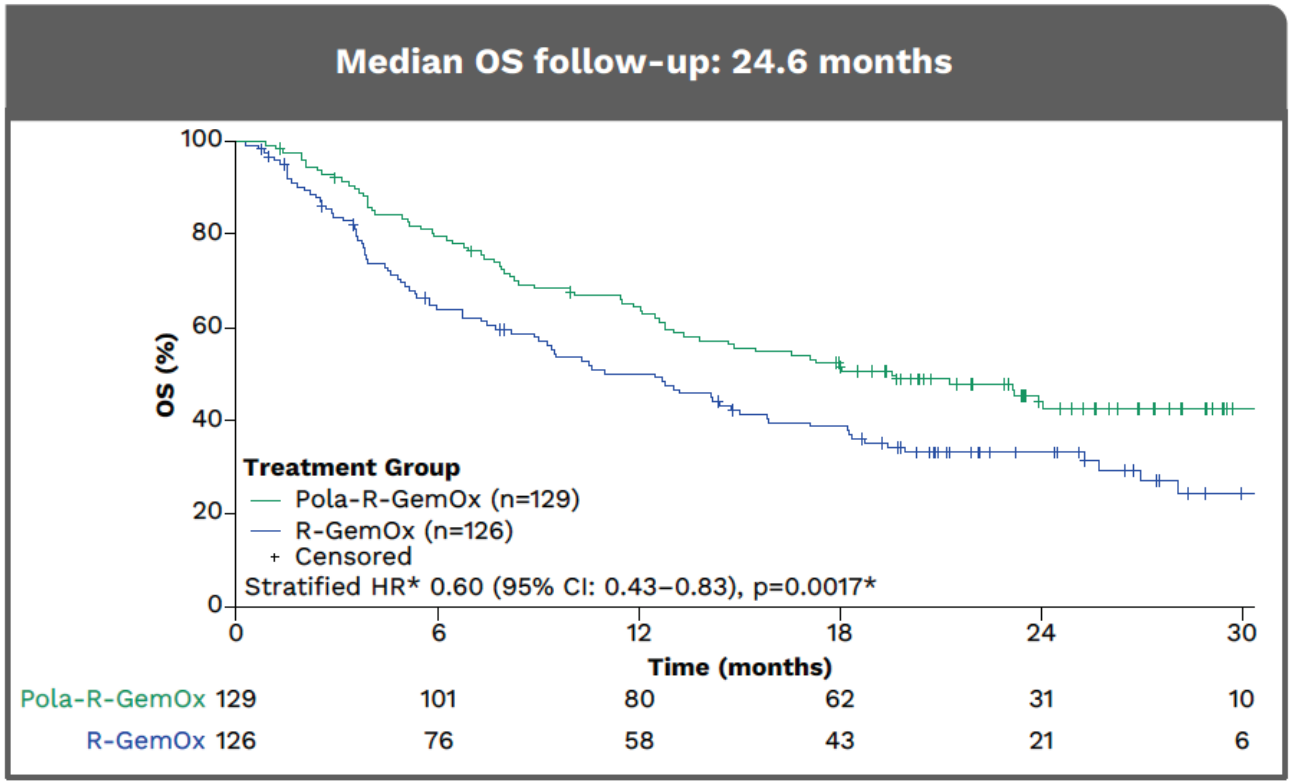
n (%), unless otherwise stated	Pola-R-GemOx (n=128)	R-GemOx (n=125)
Number of cycles,* median (range)	7.5 (1-8)	4 (1–8)
Treatment duration (months),† median (range)	4.8 (0–7.6)	2.1 (0–6.2)
Any AEs Treatment-related Grade 3/4 AE as highest grade	125 (97.7) 118 (92.2) 73 (57.0)	117 (93.6) 103 (82.4) 73 (58.4)
Serious AEs Treatment-related	49 (38.3) 36 (28.1)	39 (31.2) 28 (22.4)
Grade 5 (fatal) AEs Treatment-related	15 (11.7) 4 (3.1)	5 (4.0) 3 (2.4)
AEs leading to any study drug discontinuation	30 (23.4)	10 (8.0)
AE leading to any dose reduction	31 (24.2)	14 (11.2)

n (%)	Pola-R-GemOx (n=128)	R-GemOx (n=125)
Peripheral neuropathy Grade 1 Grade 2 Grade 3	73 (57.0) 48 (37.5) 20 (15.6) 5 (3.9)	36 (28.8) 29 (23.2) 7 (5.6) 0
Thrombocytopenia‡ Grade ≥3	68 (53.1) 44 (34.4)	51 (40.8) 33 (26.4)
Neutropenia‡ Grade ≥3	53 (41.4) 43 (33.6)	52 (41.6) 38 (30.4)
Febrile neutropenia Grade ≥ 3	3 (2.3) 3 (2.3)	3 (2.4) 3 (2.4)
Anemia Grade ≥ 3	48 (37.5) 17 (13.3)	35 (28.0) 19 (15.2)
Hepatic toxicity Grade ≥ 3	41 (32.0) 11 (8.6)	25 (20.0) 2 (1.6)
Infections and Infestations (SOC) Grade ≥ 3	53 (41.4) 28 (21.9)	39 (31.2) 12 (9.6)
Patients with ≥1 AE of COVID-19 (SMQ)	26 (20.3)	17 (13.6)

➔ Safety profile of Pola-R-GemOx consistent with the known risk of the individual study drugs, including infections and PNP.

Matasar M. 06/14/2025; 4159178; S101

Phase III POLARGO: Primary Endpoint



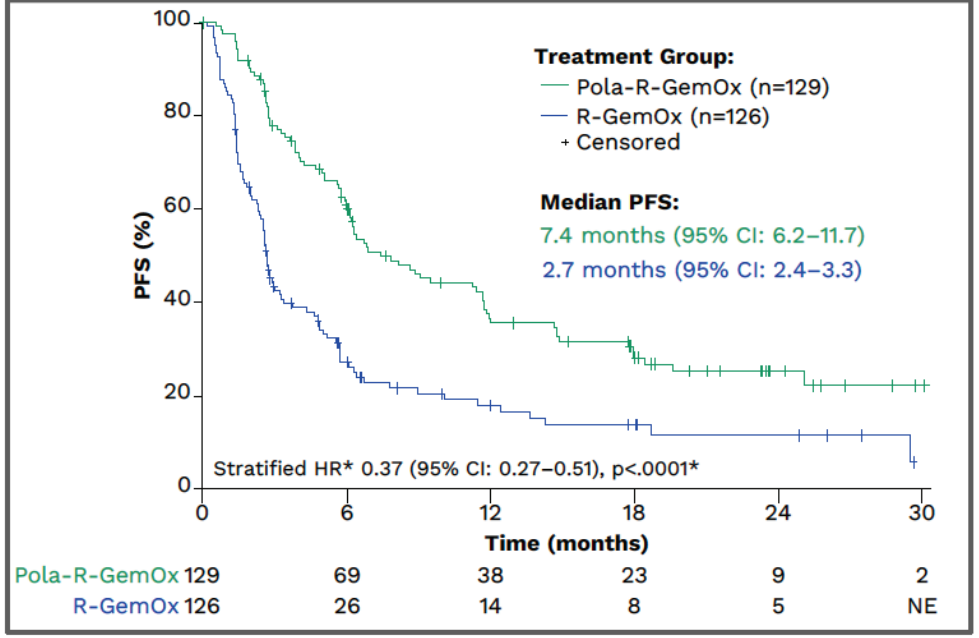
- **40% reduction in relative risk of death with Pola-R-GemOx** compared with R-GemOx
- **Median OS was 19.5 months** with Pola-R-GemOx (vs 12.5 months with R-GemOx)
- 24-month event-free rate was 44.0% with Pola-R-GemOx (vs 33.2% with R-GemOx)

➔ Significant overall survival benefit of Pola-GemOx vs. R-GemOX

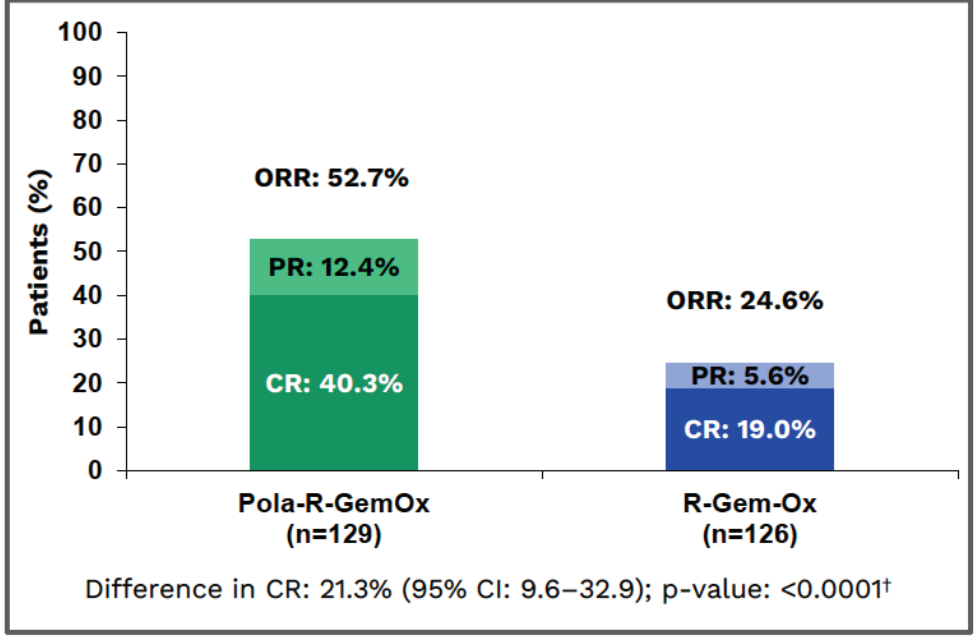
Matasar M. 06/14/2025; 4159178; S101

Phase III POLARGO: Key Secondary Endpoints

Statistically significant **PFS benefit** with Pola-R-GemOx versus R-GemOx



Significantly higher response rates with Pola-R-GemOx versus R-GemOx



- **Median PFS: 7.4 months** with Pola-R-GemOx versus 2.7 months with R-GemOx
- **CR rate doubled** with Pola-R-GemOx (40.3%) versus R-GemOx (19.0%)

POLARGO

Conclusion

Pola-R-GemOx significantly improves overall survival, including a 40% reduction in the relative risk of death compared to R-GemOX, resulting in another combination regimen available for patients with transplant-ineligible rrDLBCL.

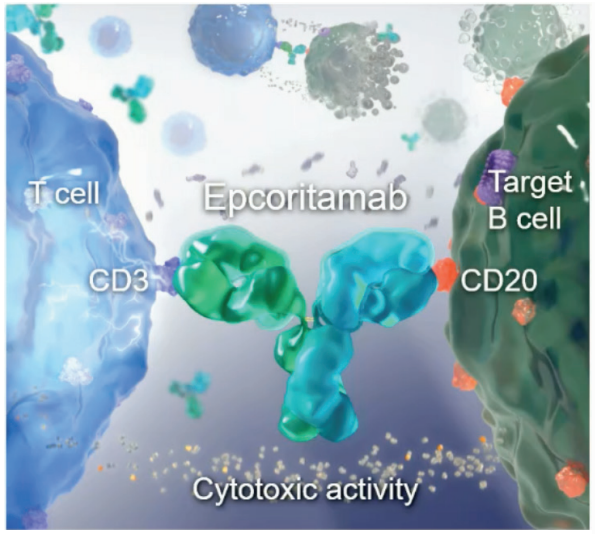
Kapitel 3

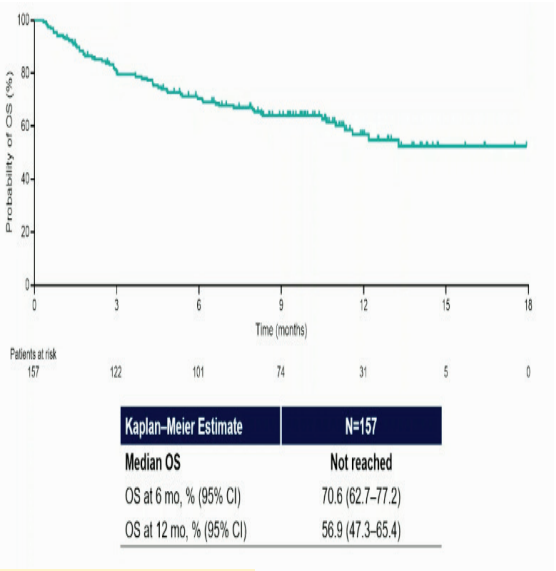
Drittlinie

Two CD20xCD3 Bispecific Antibodies

Epcoritamab

(anti-CD20/CD3)





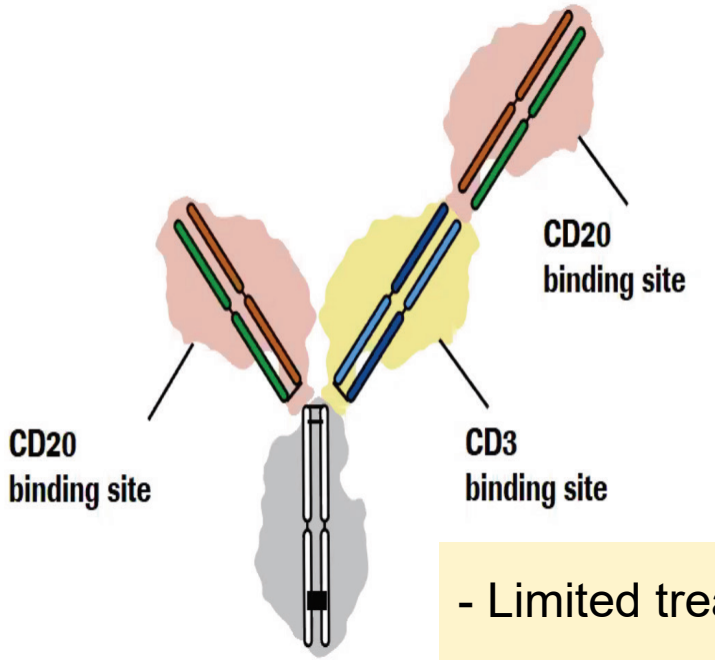
Kaplan-Meier Estimate	N=157
Median OS	Not reached
OS at 6 mo, % (95% CI)	70.6 (62.7–77.2)
OS at 12 mo, % (95% CI)	56.9 (47.3–65.4)

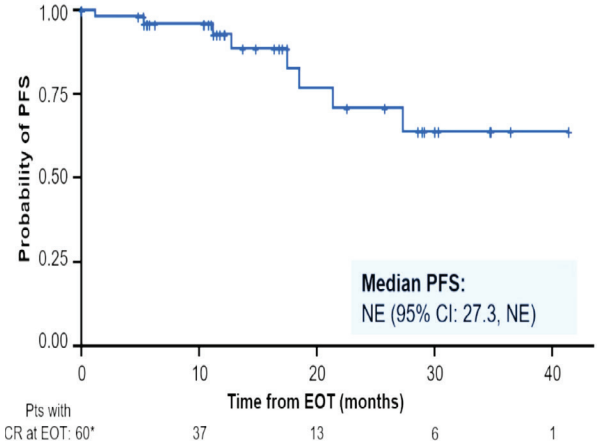
- Continous treatment
- s.c. appplication

Hutchings M et al., Lancet 2021
Thieblemont C, J Clin Oncol. 2023

Glofitamab

(anti-CD20/CD3-TCB)





- Limited treatment (usually 12 cycles)
- i.v. application

Sun LL, Sci Transl Med 2015
Dickinson et al NEJM 2022

SUSTAINED REMISSION IN RELAPSED OR REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA WITH EPCORITAMAB MONOTHERAPY: EPCORE NHL-1 3-Y RESULTS AND NOVEL SUBGROUP ANALYSES IN PATIENTS WITH COMPLETE RESPONSE AT 2 Y

Chan Y. Cheah

Author(s): Chan Y Cheah, Yasmin H Karimi, Julie M Vose, Michael Roost Clausen, David Cunningham, Umar Farooq, Tatyana Feldman, Herve Ghesquieres, Wojciech Jurczak, Kim M Linton, Tycel Phillips, Won Seog Kim, Pegah Jafarinasabian, Andrew J Steele, David Soong, Milan Geybels, Barbara D'Angelo Månsson, Christian W Eskelund, Mohammad Atiya, Martin Hutchings, Catherine Thieblemont

(Abstract release date: 05/22/25) EHA Library.
Cheah C. 06/13/2025; 4160326; PF920

EPCORE NHL-1: 3-Year Response Data for Patients With CR at 2 Years

Aim:

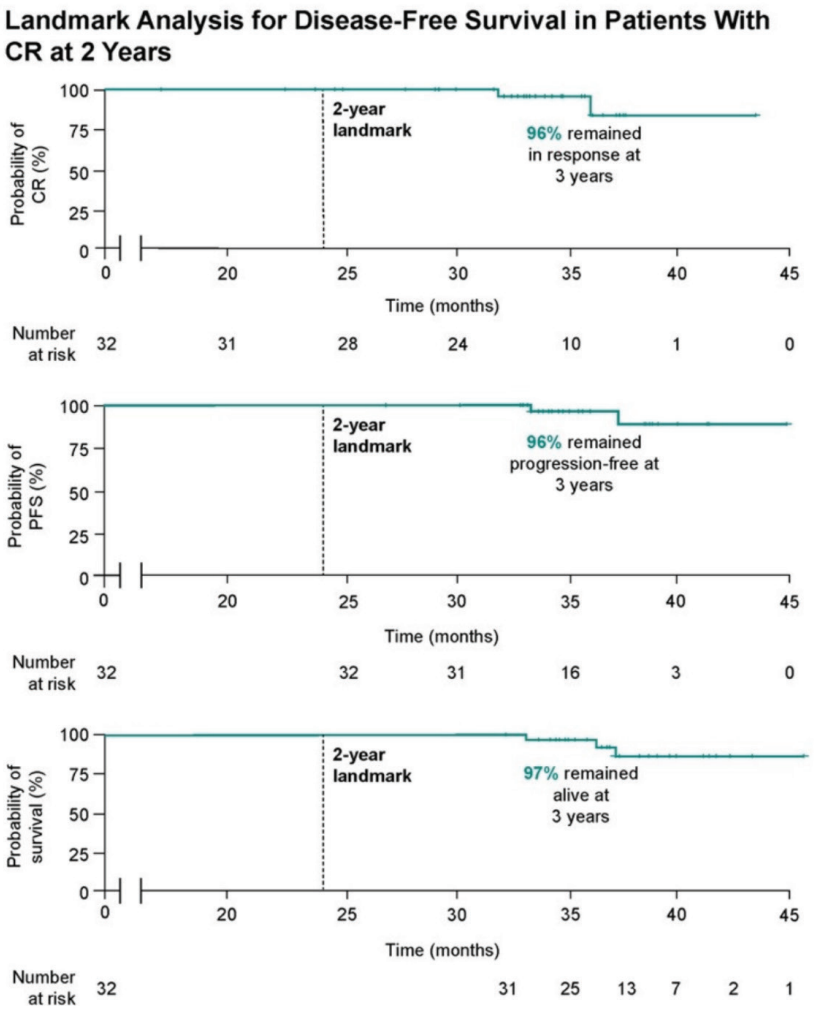
To report the 3-y follow-up results from NHL-1, and outcomes from a post hoc analysis of patients remaining in CR at 2 y after starting treatment (tx).

Patient Characteristics and Prior Treatments

	Dose-expansion cohort (N=157)	Patients with CR at 2 years (n=32)
Mean age, years (SD)	62 (14)	63 (14)
Male sex at birth, n (%)	94 (60)	15 (47)
Race, n (%)[a]		
White	78 (50)	19 (59)
Asian	30 (19)	4 (13)
Other	6 (4)	1 (3)
Disease type, n (%)		
DLBCL	139 (89)[b]	28 (88)
FL[c]	5 (3)	1 (3)
HGBCL	9 (6)	2 (6)
PMBCL	4 (3)	1 (3)
IPI score, n (%)[d]		
0–2	55 (35)	10 (31)
≥3	83 (53)	18 (56)
Median prior LOTs, n (range)	3 (2–11)	3 (2–8)
Primary refractory disease, n (%)[e,f]	95 (61)	13 (41)
Refractory to ≥2 consecutive prior LOTs, n (%)	118 (75)	21 (66)
Prior CAR T cell therapy, n (%)	61 (39)	12 (38)
Refractory to prior CAR T cell therapy, n (%)[g]	46 (29)	8 (25)
Bulky disease >7 cm, n (%)	49 (31)	6 (19)
LDH levels, serum or plasma (U/L)	338	294
Ferritin levels, serum or plasma (µg/L)	406	383

- The safety profile in the overall pt population (N=157) was consistent with previous reports.
- Median age of pts in CR at 2 y was 63 y, 81% had Ann Arbor stage III/IV disease, 38% had received prior CAR-T tx, and 66% were refractory to ≥2 prior LOT.

EPCORE NHL-1: 3-Year Response Data for Patients With CR at 2 Years



Survival at 3 years among 32 pts in CR at 2 y

PFS: 96% / OS 97%

EPCORE NHL-1

Conclusion

➔ At the 3-y follow-up, epcoritamab demonstrated long-term disease remission and the potential for cure in some pts with 3L+ R/R LBCL.

➔ The long-term safety profile was consistent with the established safety profile of epcoritamab.

Zusammenfassung | Take-Home-Messages

- **Erstlinie**
  - PET4-adjustierte Reduktion der Chemotherapie zu 4x R-CHOP für IPI1 (Alter, kein bulk) analog OPTIMAL>60-favorable wird nach Vollpublikation wahrscheinlich den Therapiestandard verändern.
  - Chemotherapie-arme Kombination von Rituximab, Polatuzumab und Glofitamab (R-Pola-Glo) kombiniert sehr gute Verträglichkeit mit herausragendem Ansprechen. Phase III ausstehend.
- **Zweitlinie**
  - Polatuzumab in Kombination zu GemOx erzeugt einen Gesamtüberlebensvorteil gegenüber R-GemOX und etabliert damit eine weitere Kombinationstherapie für Transplant nicht-eligible Patienten.
- **Drittlinie**
  - Maturierende Daten zu bispezifischen Antikörpern, hier Epcoritamab, erzeugen anhaltende Langzeitremissionen und produzieren keine neuen Sicherheitssignale.

Alle Kurzpräsentationen sind online unter

www.lymphome.de/eha2025

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