



KML-Expert:innen berichten  
**17<sup>th</sup> ICML 2023 LUGANO**

# Lymphom Kompetenz KOMPAKT



**KML KONGRESSE**

Expert:innen berichten zu  
Lymphomen & Leukämien



**Prof. Dr. med. Björn Chapuy**  
Charité - Universitätsmedizin Berlin

# Diffus großzelliges B-Zell-Lymphom (DLBCL)

# Offenlegung potentieller Interessenskonflikte

LymphomKompetenz KOMPAKT – ICML2023 wird in Kooperation mit fünf unterstützenden Firmen durchgeführt.

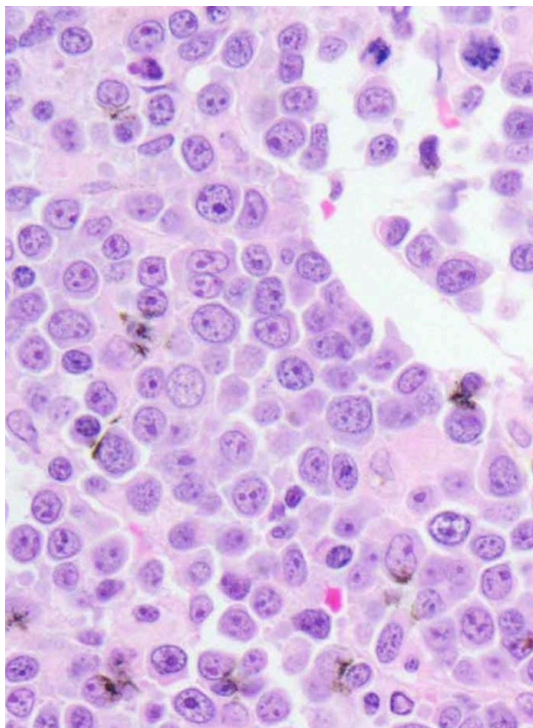
Meine persönlichen Disclosures betreffen:

<b>Anstellungsverhältnis, Führungsposition</b>	
<b>Beratungs-/ Gutachtertätigkeit</b>	Regeneron, BMS, Roche, ADC, Sobi, Incyte, Abbvie
<b>Besitz von Geschäftsanteilen, Aktien oder Fonds</b>	-
<b>Patent, Urheberrecht, Verkaufslizenz</b>	I hold several patents on molecular subtyping of large B-cell lymphoma
<b>Honorare</b>	BMS, Astra Zeneca, Gilead, Roche, Sandoz, Incyte, Abbvie, Sobi, Ono
<b>Finanzierung wissenschaftlicher Untersuchungen</b>	Gilead Oncology Award Winner 2021 (with S. Dietrich)
<b>Andere finanzielle Beziehungen</b>	-
<b>Immaterielle Interessenkonflikte</b>	-

# Kapitel 1

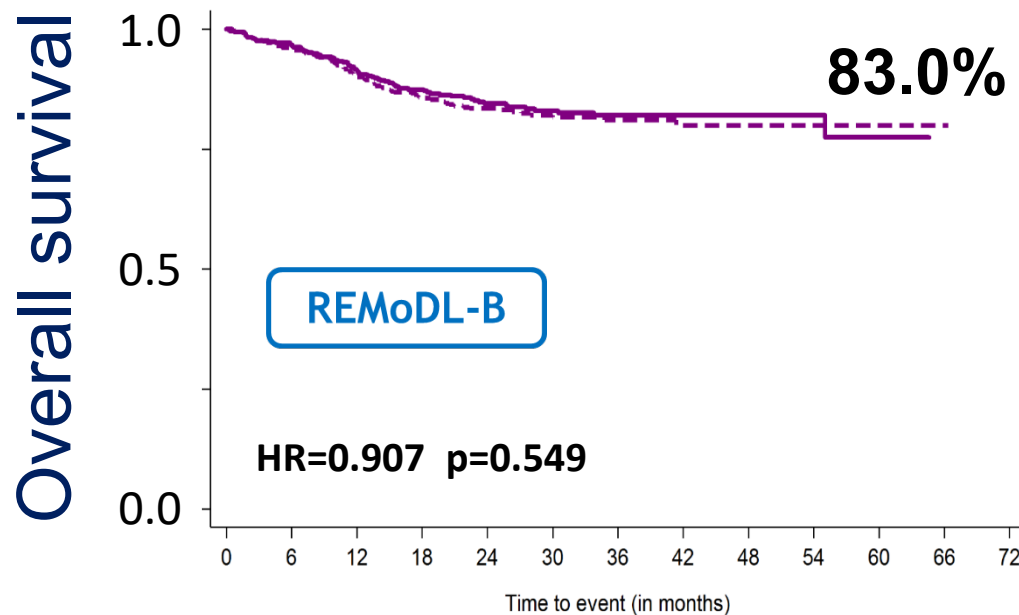
## DLBCL - Erstlinientherapie

# DLBCL



<https://imagebank.hematology.org/image/1811>

# R-CHOP



R-CHOP	459	429	399	336	269	173	127	69	36	16	4	1	0
RB-CHOP	459	424	394	322	257	182	131	82	51	20	6	0	0

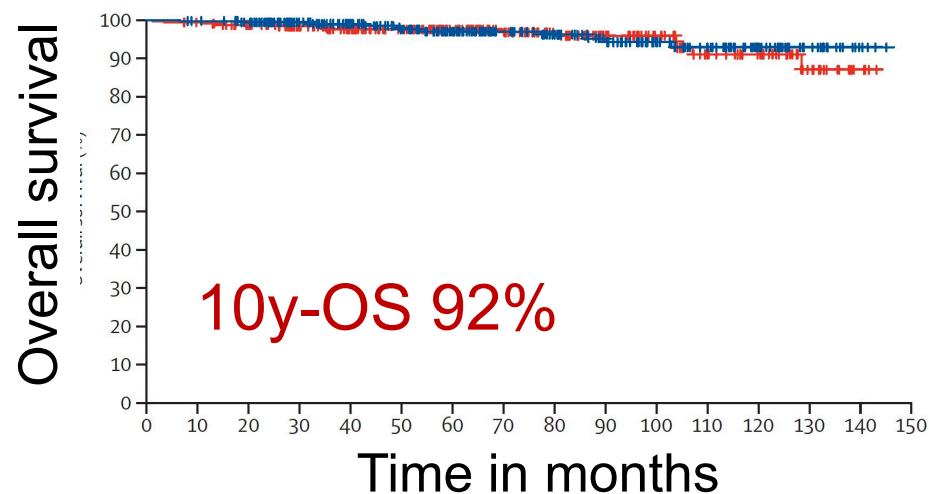


Davies ICML 2017

→ R-CHOP-like ist der etablierte Goldstandard für die DLBCL in der Erstlinie.

## FLYER Trial

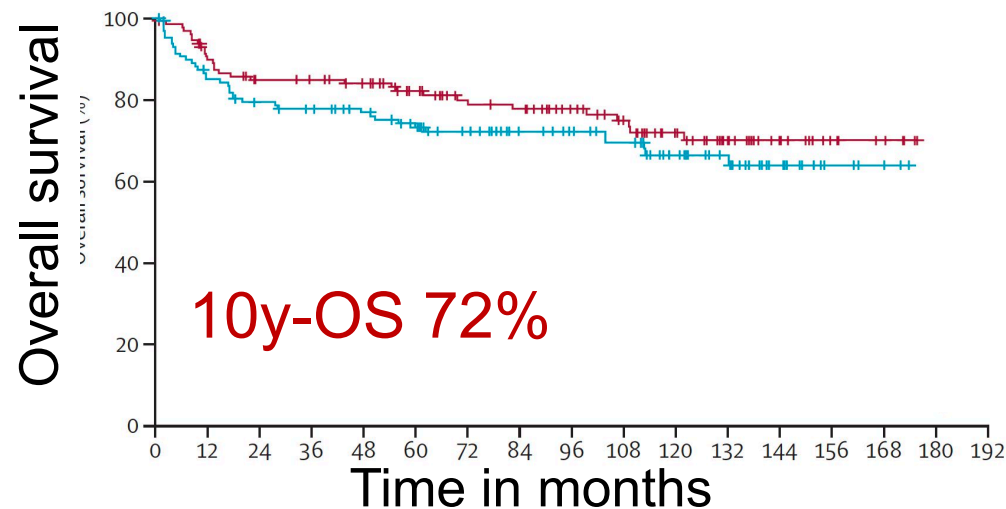
(IPI 0, no bulk, <60y)



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

## Mega-CHOEP Trial

(IPI 2/3, <60y)



Fronzek, Ziepert et al. *Lancet Haem* 2021

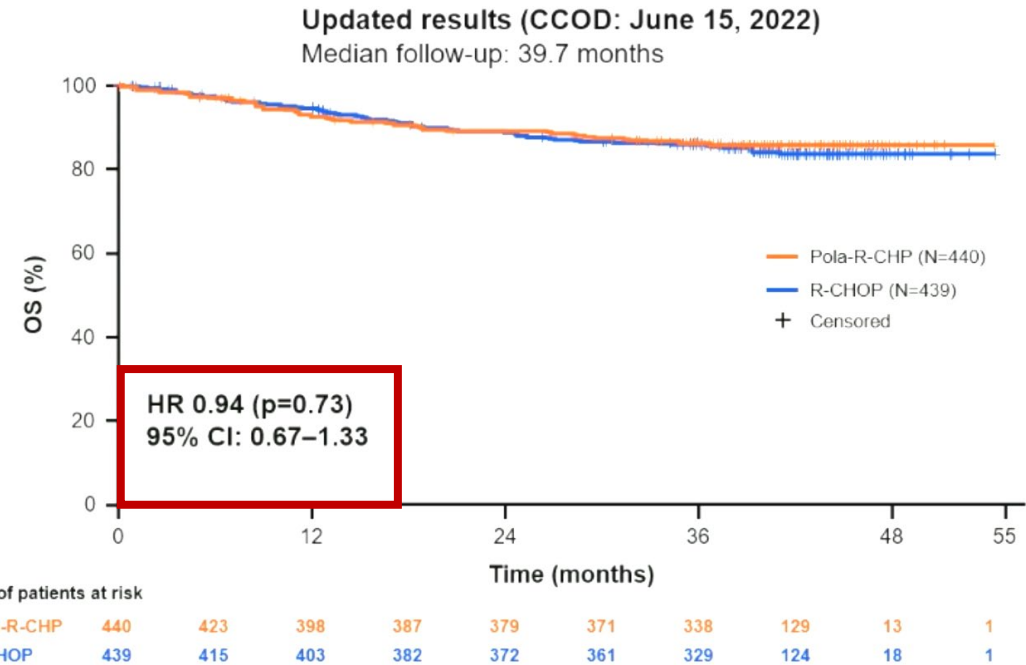
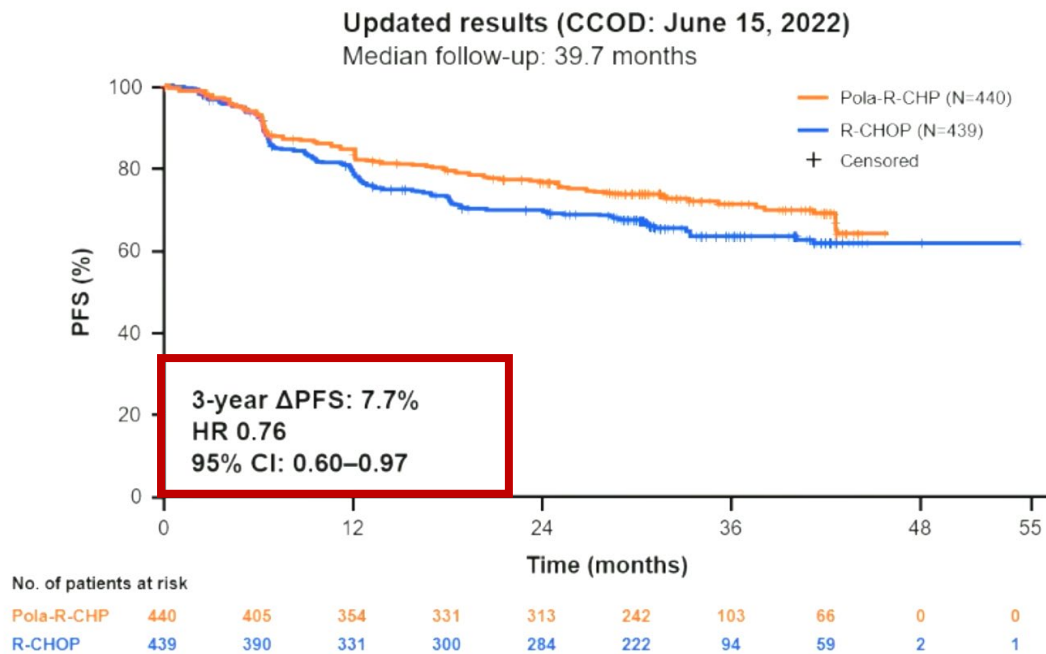
➔ Hohe Heilungsraten bei risikoadaptierter Therapie limitieren weitere empirische Therapieoptimierung.



# Die Polarix Studie – Pola-R-CHP vs. R-CHOP

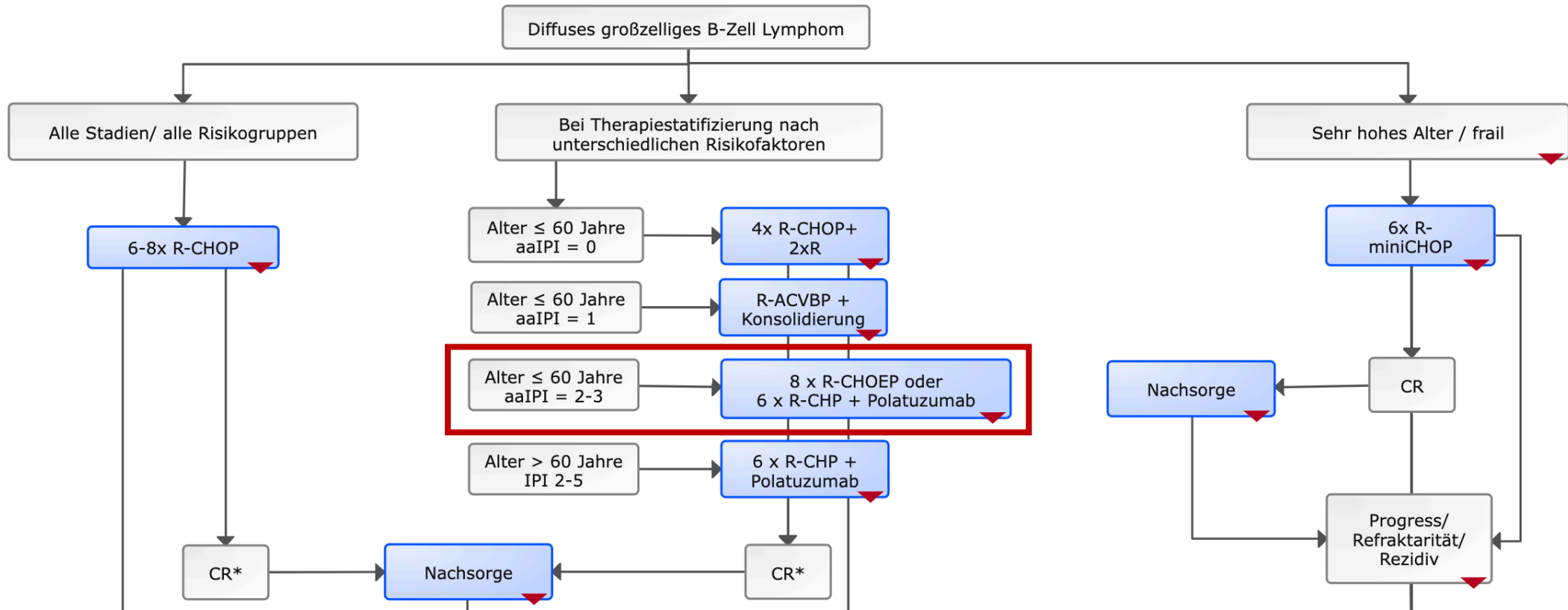
## Progression free survival

## Overall survival



➔ Pola-R-CHP stellt gegenüber R-CHOP eine effizientere Therapie bei fast gleicher Toxizität dar und erweitert damit das Spektrum der zugelassenen R-CHOP-like Therapien in der Erstlinie

# Erstlinien Therapie des DLBCL



→ R-CHOP-like ist der etablierte Goldstandard für die DLBCL in der Erstlinie.



P308

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# Pola-R-CHP vs R-CHOEP in young patients with high-risk diffuse large B-cell lymphoma

Georg Lenz,<sup>1\*</sup> Hervé Tilly,<sup>2</sup> Marita Ziepert,<sup>3</sup> Bettina Altmann,<sup>3</sup> Veronica Craine,<sup>4</sup> Mark Yan,<sup>4</sup> Charles Herbaux,<sup>5</sup> Fabian Frontzek,<sup>1</sup> Maïke Nickelsen,<sup>6</sup> Jamie Hirata,<sup>7</sup> Deniz Sahin,<sup>8</sup> Calvin Lee,<sup>7</sup> Franck Morschhauser,<sup>9</sup> Norbert Schmitz<sup>1</sup>

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<sup>1</sup>Medical Department A, University Hospital Münster, Münster, Germany; <sup>2</sup>Centre Henri-Becquerel and University of Rouen, Rouen, France; <sup>3</sup>Institute for Medical Informatics, Statistics and Epidemiology, Medical Faculty, Leipzig University, Leipzig, Germany; <sup>4</sup>Hoffmann-La Roche Ltd, Mississauga, ON, Canada; <sup>5</sup>University of Montpellier, Montpellier, France; <sup>6</sup>Onkologie Lerchenfeld, Hamburg, Germany; <sup>7</sup>Genentech, Inc., South San Francisco, CA, USA; <sup>8</sup>F. Hoffmann-La Roche Ltd, Basel, Switzerland; <sup>9</sup>University of Lille, Centre Hospitalier Universitaire, Lille, France

# Pola-R-CHP vs R-CHOEP in jungen Patienten mit hochrisiko DLBCL

Table 1. Baseline demographics and clinical characteristics<sup>c</sup>

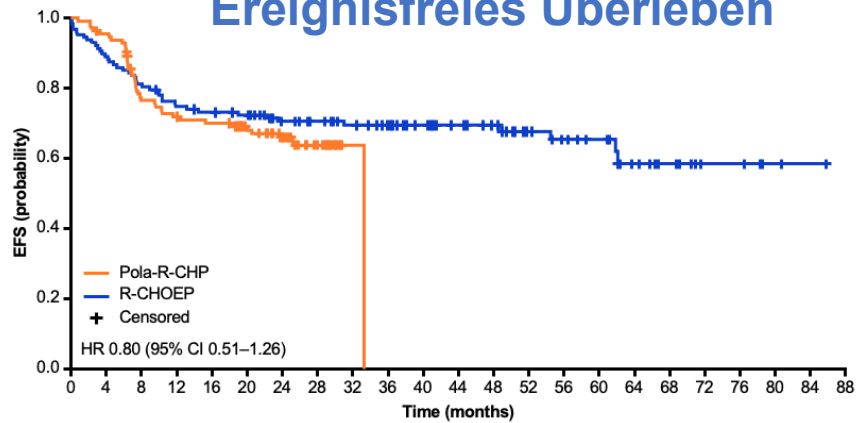
	Pola-R-CHP (n=113)	R-CHOEP (n=127)
Median age (range), years	52 (19–60)	50 (18–60)
Sex, n (%)		
Male	68 (60.2)	79 (62.2)
Female	45 (39.8)	48 (37.8)
aalPI score, n (%)		
2	99 (87.6)	92 (72.4)
3	14 (12.4)	35 (27.6)
Elevated LDH level, n (%)	100 (88.5)	124 (97.6)
ECOG PS,* n (%)		
0–1	92 (81.4)	85 (66.9)
>1	21 (18.6)	42 (33.1)
Ann Arbor stage,* n (%)		
I–II	3 (2.6)	4 (3.1)
III–IV	110 (97.4)	123 (96.9)
Extranodal sites >1,* n (%)	61 (54.0)	55 (43.3)
Bone marrow involvement, n (%)	26 (23.0)	16 (12.6)
Bulky disease (≥7.5 cm), n (%)	60 (53.1)	75 (59.1)
Tumor expression, <sup>†</sup> n (%)		
BCL2 positive	48/96 (50.0)	26/36 (72.2)
MYC positive	63/98 (64.3)	8/38 (21.1)
Tumor gene rearrangements, n (%)		
BCL2	17/95 (17.9)	9/52 (17.3)
BCL6	2/8 (25.0)	18/51 (35.3)
MYC	8/90 (8.9)	4/47 (8.5)
DEL status, n (%)		
DEL	37 (32.7)	5 (3.9)
non-DEL	61 (54.0)	32 (25.2)
Unknown	15 (13.3)	90 (70.9)
Double-/triple-hit lymphoma, n (%)		
Negative	86 (76.1)	43 (33.9)
Positive	4 (3.5)	4 (3.1)
Unknown	23 (20.4)	80 (63.0)

\*Related to aalPI score. <sup>†</sup>By immunohistochemistry.  
aalPI, age-adjusted International Prognostic Index; DEL, double-expressor lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase.

- Patients included in the analysis were **≤60 years** with an **aalPI score of 2–3**.
- **Treatments:**
  - 6 x Pola-R-CHP + 2 R q3w, oder
  - 8 X CHOEP q2w + 6 R.

# Pola-R-CHP und R-CHOEP haben vergleichbare Effektivität in jungen Patienten mit Hochrisiko-DLBCL (aaIPI 2–3)

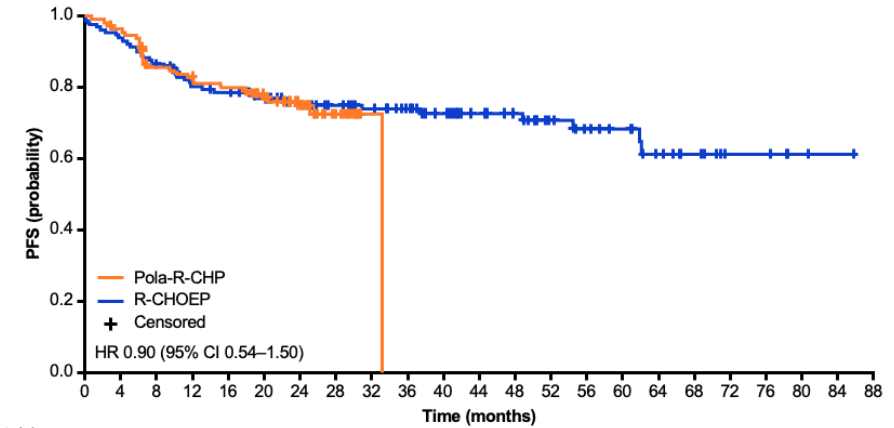
## Ereignisfreies Überleben



Number at risk

Time (months)	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88
Pola-R-CHP	113	107	83	77	75	67	56	24	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
R-CHOEP	127	113	103	93	90	87	76	72	64	58	50	44	39	32	26	23	14	10	5	5	2	1	0

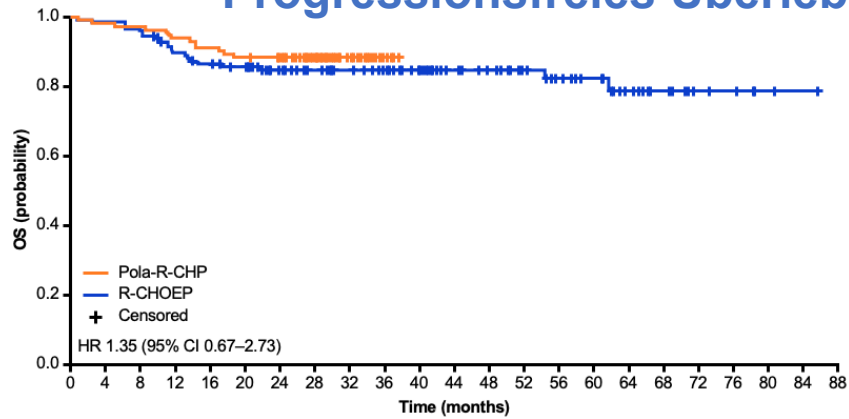
## Gesamtüberleben



Number at risk

Time (months)	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88
Pola-R-CHP	113	108	91	87	84	75	61	24	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
R-CHOEP	127	119	110	98	95	90	79	75	67	61	52	45	39	32	26	23	14	10	5	5	2	1	0

## Progressionsfreies Überleben



Number at risk

Time (months)	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76	80	84	88
Pola-R-CHP	113	111	108	103	100	97	92	51	22	4	0	0	0	0	0	0	0	0	0	0	0	0	0
R-CHOEP	127	125	122	110	105	101	90	84	77	71	62	52	46	38	30	26	17	11	6	5	2	1	0

## Landmark Analyse nach 2 Jahren

% (95% CI)	Pola-R-CHP (n=113)	R-CHOEP (n=127)
<b>EFS</b>	65.9 (56.9–74.8)	70.5 (62.5–78.5)
<b>PFS</b>	74.8 (66.5–83.0)	74.9 (67.3–82.6)
<b>OS</b>	88.3 (82.3–94.3)	84.6 (78.3–91.0)

CI, confidence interval; EFS, event-free survival; PFS, progression-free survival; OS, overall survival.

# Pola-R-CHP hat ein besseres Sicherheitsprofil als R-CHOEP

n (%)	Pola-R-CHP (n=113)	R-CHOEP (n=127)
<b>Grade ≥3 AEs</b>		
Leukopenia	6 (5.3)	45 (35.4)
Infection†	17 (15.0)	38 (29.9)
Nausea	2 (1.8)	1 (0.8)
Vomiting	0	2 (1.6)
Diarrhea	2 (1.8)	4 (3.2)
Constipation	0	4 (3.2)
<b>Grade ≥3 AESIs</b>		
Thrombocytopenia	2 (1.8)	25 (19.7)
Anemia	11 (9.7)	51 (40.2)
Cardiotoxicity	0	1 (0.8)
Sensory neuropathy	0	10 (7.9)

\*AEs classified according to NCI CTCAE, version 4.0. †By system organ class.  
AE, adverse event; AESI, adverse event of special interest.

- Patienten mit **R-CHOEP** hatten mehr:
  - Zytopenien
  - Infektionen
  - sensorische PNP
  - Todesfälle (2 vs.4)

# Zusammenfassung

- Beide Therapieregime führen zu sehr guten Überlebensraten von  $> 85\%$ .
- R-CHOEP hat im Vergleich zu Pola-R-CHP signifikant mehr Zytopenien, Infektionen und sensorische PNP.
- Die Autoren folgern, dass Pola-R-CHP das bevorzugte Therapieregime für junge Patienten ( $<60\text{J}$ ) mit aaIPI 2–3 sein sollte.
- R-CHOEP kann als Alternative fungieren, wo Pola-R-CHP nicht verfügbar ist.



# Kapitel 2

## DLBCL - Zweitlinientherapie

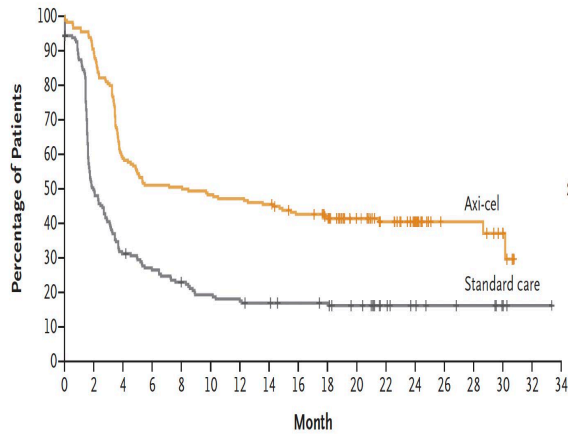


# CAR T-cells vs. SOC in 2L LBCL

**Axi-cel (ZUMA-7)**  
NCT 03391466

CAR T

SOC



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

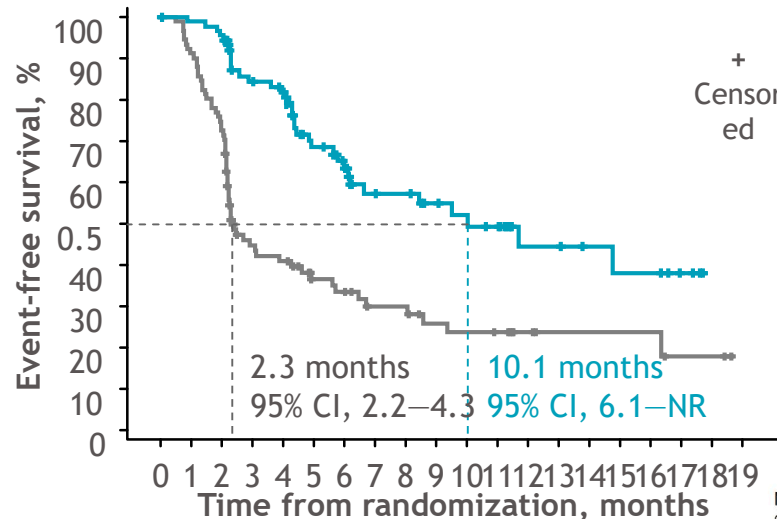
F.L. Locke, D.B. Milosavljevic, C. J. Johnson, M. A. Ghera, M. A. Krsten, O.O. Oluwole, A. Ghobadi, A.P. Rapoport, J. McGuirk, J.M. Pagel, J. Muñoz, U. Farooq, T. van Meerten, P.M. Reagan, A. Sureda, I.W. Flinn, P. Vandenberghe, K.W. Song, M. Dickinson, M.C. Minnema, P.A. Riedell, L.A. Leslie, S. Chaganti,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

**positive**

**Liso-cel (TRANSFORM)**  
NCT 03575351

CAR T

SOC



Articles

## Lisocabtagene maraleucel versus standard of care with salvage chemotherapy for relapsed or refractory large B-cell lymphoma (TRANSFORM): results from an interim analysis of an open-label, randomised, phase 3 trial

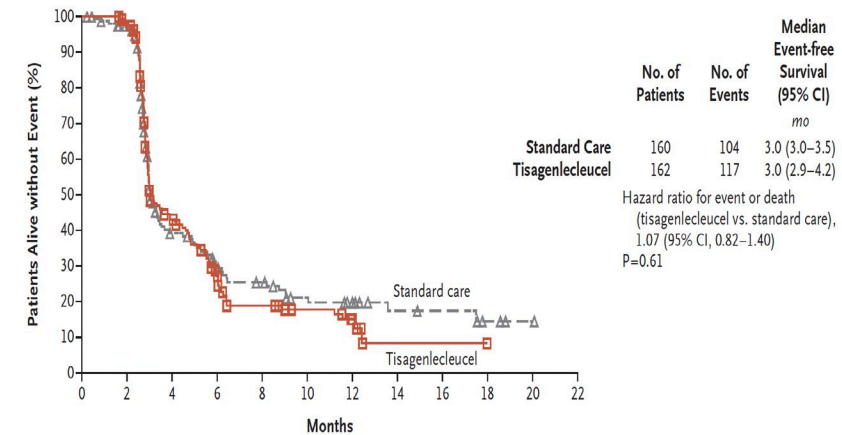
Manali Kamdar, Scott R Solomon, Jon Arnason, Patrick B Johnston, Bertram Glass, Veronika Bachanova, Sami Ibrahim, Stephan Mielke, Pim Mutsaers, Francisco Hernandez-Ilizaliturri, Koji Izutsu, Franck Morschhauser, Matthew Lunning, David G Maloney, Alessandro Crotta, Sandrine Montheard, Alessandro Previtali,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

**positive**

**Tisa-cel (BELINDA)**  
NCT 03570892

CAR T

SOC



ORIGINAL ARTICLE

## Second-Line Tisagenlecleucel or Standard Care in Aggressive B-Cell Lymphoma

M.R. Bishop, M. Dickinson, D. Purtill, P. Barba, A. Santoro, N. Hamad, K. Kato, A. Sureda, R. Coombs, C. Thibault, M. Fisher, J. Thomas, M. J. Flinn, W. Rabitsch, Y.-L. Joo, G. G. Kostelny, M. Minnema, M. J. Flinn, H.-L. Chan, J. Martinez-Lopez, A. M. Munier, K. I. Maizumi, J. P. McGuirk, E. Bachy, S. Le Gouill, M. Dreyling, H. Hangaee, D. Bond, C. Andreadis, P. McSweeney, M. Kharfan-Dabaja, S. Newsome, E. Degtyarev, R. Awasthi, C. del Corral, G. Andreola, A. Masood, S.J. Schuster, U. Jäger, P. Borchmann, and J.R. Westin

**negative**

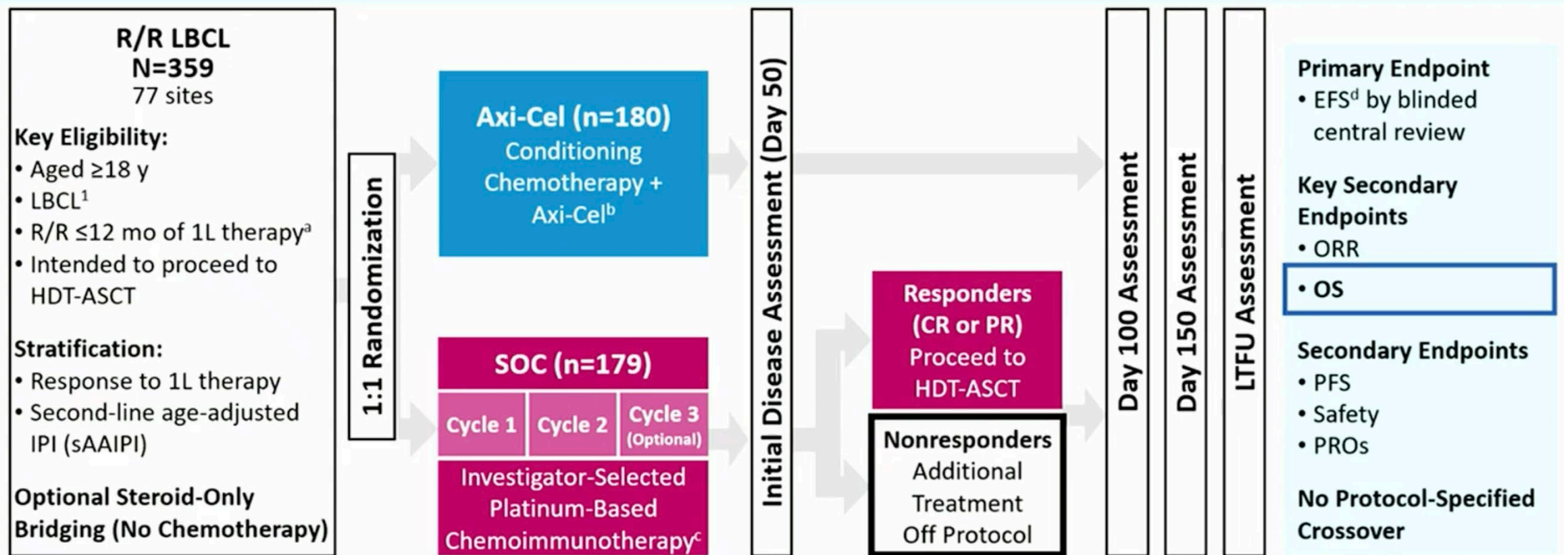
# Primary Overall Survival Analysis of the Phase 3 Randomized ZUMA-7 Study of Axicabtagene Ciloleucel Versus Standard of Care in Relapsed/Refractory Large B-Cell Lymphoma

Jason R. Westin, MD, MS, FACP<sup>1</sup>; Olalekan O. Oluwole, MBBS, MPH<sup>2</sup>; Marie José Kersten MD, PhD<sup>3</sup>; David B. Miklos, MD, PhD<sup>4</sup>; Miguel-Angel Perales, MD<sup>5</sup>; Armin Ghobadi, MD<sup>6</sup>; Aaron P. Rapoport, MD<sup>7</sup>; Anna Sureda, MD, PhD<sup>8</sup>; Caron A. Jacobson, MD<sup>9</sup>; Umar Farooq, MD<sup>10</sup>; Tom van Meerten, MD, PhD<sup>11</sup>; Matthew L. Ulrickson, MD<sup>12</sup>; Mahmoud Elsayy, MD, MSc<sup>13</sup>; Lori A. Leslie, MD<sup>14</sup>; Sridhar Chaganti, MD<sup>15</sup>; Michael Dickinson, MBBS, D Med Sci, FRACP, FRCPA<sup>16</sup>; Yin Yang, MD<sup>17</sup>; Marco Schupp, MD<sup>17</sup>; Christina To, MD<sup>17</sup>; and Frederick L. Locke, MD<sup>18</sup>

<sup>1</sup>The University of Texas MD Anderson Cancer Center, Houston, TX, USA; <sup>2</sup>Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; <sup>3</sup>Amsterdam UMC, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, The Netherlands; <sup>4</sup>Stanford University School of Medicine, Stanford, CA, USA; <sup>5</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA; <sup>6</sup>Washington University School of Medicine, St Louis, MO, USA; <sup>7</sup>The Marlene and Stewart Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD, USA; <sup>8</sup>Servei d'Hematologia Clínica, Institut Català d'Oncologia-Hospitalet, Institut de Recerca Biomèdica de Bellvitge (IDIBELL), Universitat de Barcelona, Barcelona, Spain; <sup>9</sup>Dana-Farber Cancer Institute, Boston, MA, USA; <sup>10</sup>University of Iowa, Iowa City, IA, USA; <sup>11</sup>University Medical Center Groningen, Groningen, The Netherlands; <sup>12</sup>Banner MD Anderson Cancer Center, Gilbert, AZ, USA; <sup>13</sup>Division of Hematology and Hematologic Oncology, Department of Medicine, Dalhousie University and QEII Health Sciences Center, Halifax, Nova Scotia, Canada; <sup>14</sup>John Theurer Cancer Center, Hackensack, NJ, USA; <sup>15</sup>Centre for Clinical Haematology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; <sup>16</sup>Peter MacCallum Cancer Centre, Royal Melbourne Hospital and the University of Melbourne, Melbourne, Victoria, Australia; <sup>17</sup>Kite, a Gilead Company, Santa Monica, CA, USA; and <sup>18</sup>Moffitt Cancer Center, Tampa, FL, USA



# Design der ZUMA-7 Studie und Endpunkte



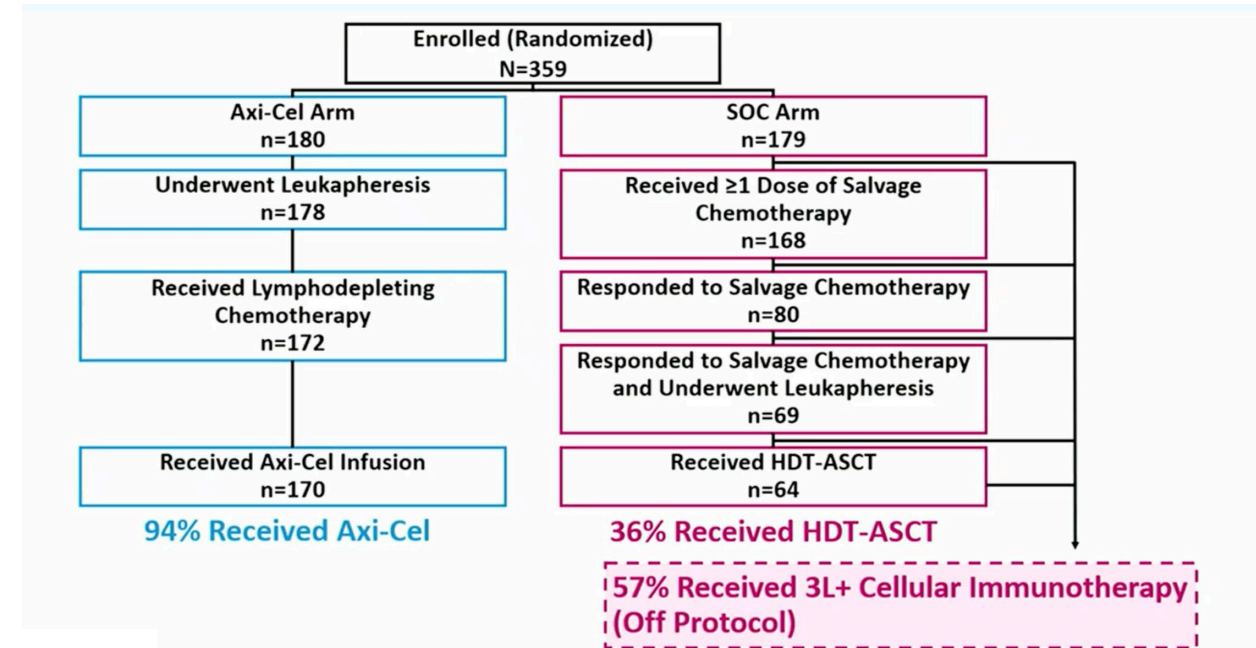
<sup>a</sup> Refractory disease was defined as no complete response to 1L therapy; relapsed disease was defined as complete response followed by biopsy-proven disease relapse  $\leq 12$  months from completion of 1L therapy. <sup>b</sup> Axi-cel patients underwent leukapheresis followed by conditioning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

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

1L, first line; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; EFS, event-free survival; HDT-ASCT, high-dose therapy with autologous stem cell transplantation; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; LTFU, long-term follow-up; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; PRO, patient-reported outcome; R/R, relapsed/refractory; SOC, standard of care.

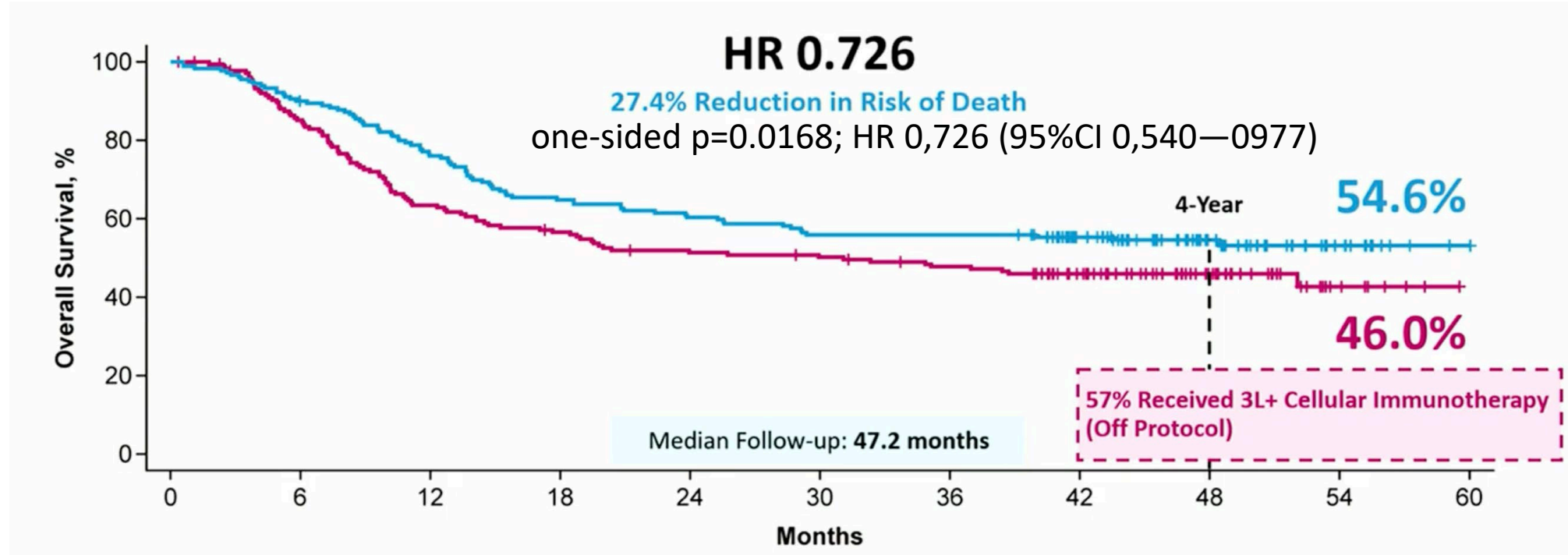
# Patienten Charakteristik

Characteristic	Axi-Cel n=180	SOC n=179	Overall N=359
<b>Median age (range), years</b>	58 (21-80)	60 (26-81)	59 (21-81)
≥65 years, n (%)	51 (28)	58 (32)	109 (30)
<b>Disease stage III-IV, n (%)</b>	139 (77)	146 (82)	285 (79)
<b>sAAPI of 2-3<sup>a</sup>, n (%)</b>	82 (46)	79 (44)	161 (45)
<b>Response to 1L therapy<sup>a</sup>, n (%)</b>			
Primary refractory	133 (74)	131 (73)	264 (74)
Relapse ≤12 mo of 1L therapy	47 (26)	48 (27)	95 (26)
<b>Prognostic marker per central laboratory, n (%)</b>			
HGBL (including double-hit lymphomas)	32 (18) <sup>b</sup>	25 (14)	57 (16) <sup>b</sup>
Double expressor lymphoma	57 (32)	62 (35)	119 (33)
MYC rearrangement	15 (8)	7 (4)	22 (6)
<b>Elevated LDH level<sup>c</sup></b>	101 (56)	94 (53)	195 (54)



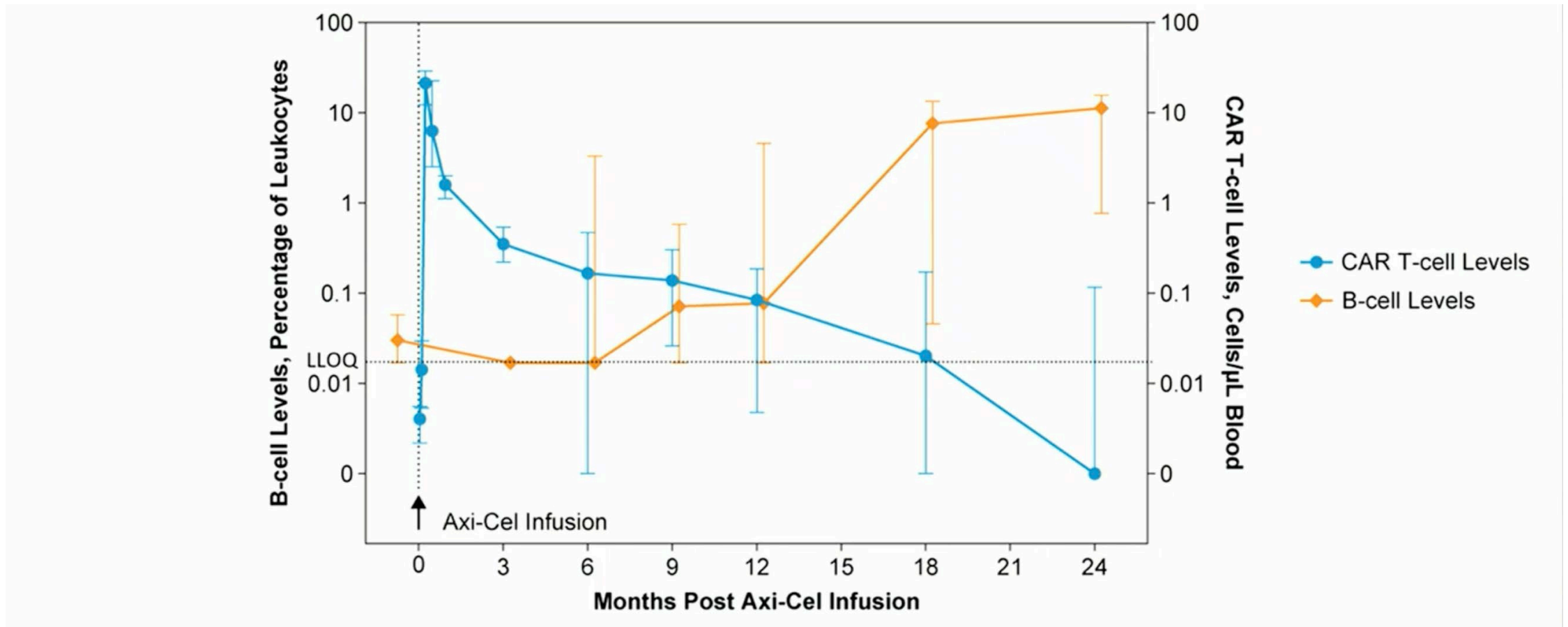
- 2,6 x mehr Patienten konnten CAR-T Therapie im Vergleich zu SOC bekommen
- 57% bekamen CAR-T Therapie off label in 3. Therapielinie

# Axi-cel steigert gegenüber dem SOC signifikant das Gesamtüberleben



- 27,4% reduziertes Risiko zu sterben gegenüber SOC, trotz cross-over bei 57% der Pat. außerhalb der Studie
- Kein neues Sicherheitssignal

# CAR-T Persistenz und B-Zell Recovery



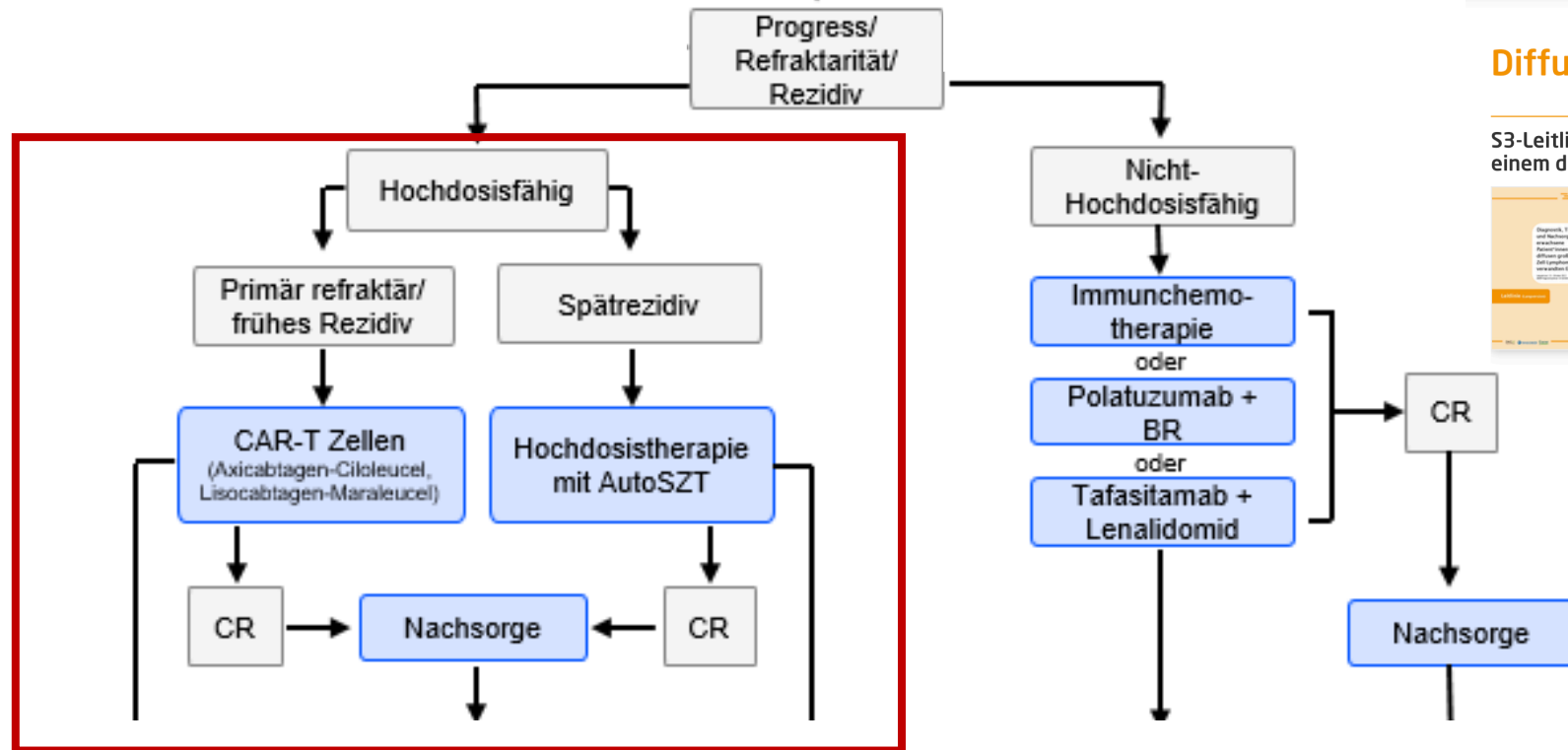
Westin ICML 2023



# Zusammenfassung

- 27,4% reduziertes Risiko zu sterben gegenüber SOC, trotz cross-over bei 57% der Pat. außerhalb der Studie
  - Mit Nachbeobachtung von 47,2 Monaten entspricht Plateau wohl „Heilung“
  - Kein neues Sicherheitssignal
  - Effizient in alle Subgruppen
- ➔ 1. Studie seit 30 Jahren, die klar signifikanten Gesamtüberlebens Vorteil in 2L DLBCL zeigt.

# Therapiealgorithmus des rezidierten/refraktären DLBCL



## Diffuses großzelliges B-Zell-Lymphom (DLBCL)

S3-Leitlinie Diagnostik, Therapie und Nachsorge für erwachsene Patient\*innen mit einem diffusen großzelligem B-Zell-Lymphom und verwandten Entitäten

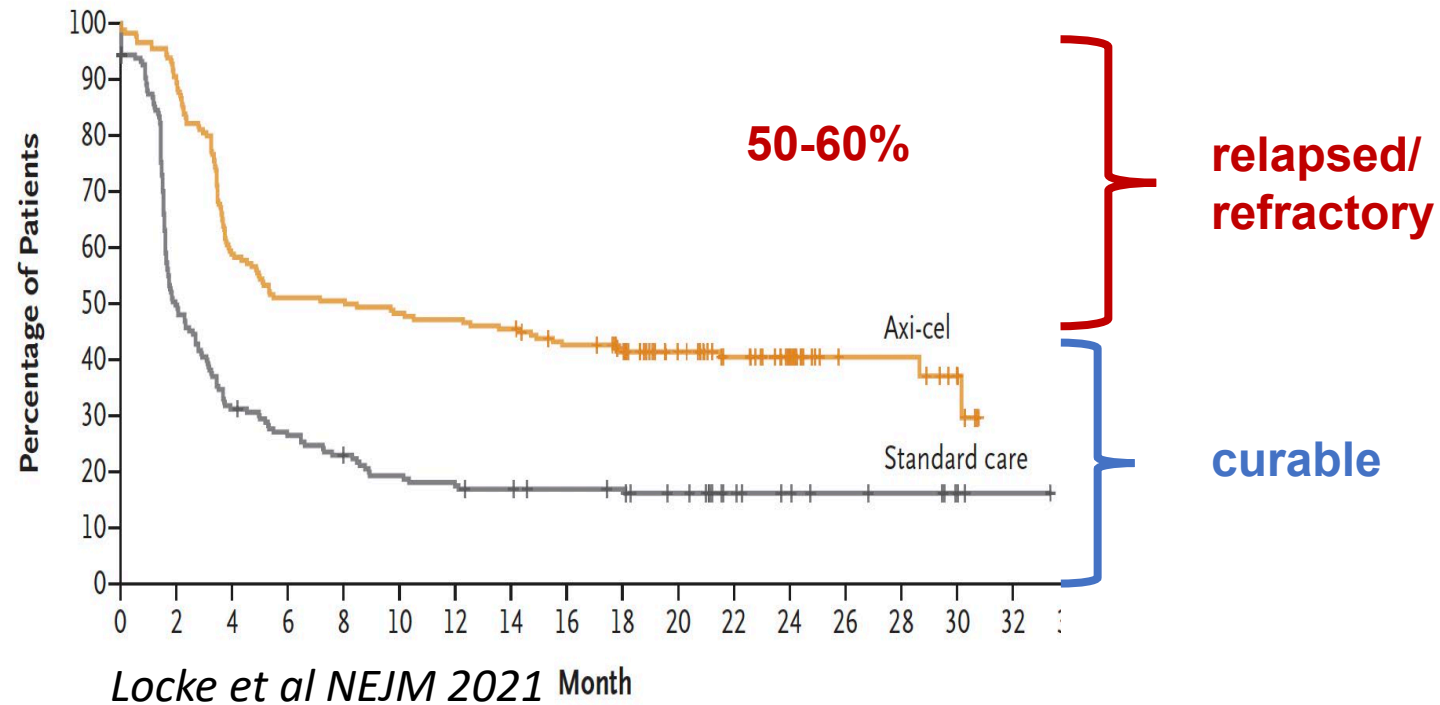


[LL\\_DLBC\\_Langversion\\_1.0.pdf](#)  
5 MB

### Unterscheidung **Früh-** vs. **Spätrezidiv**

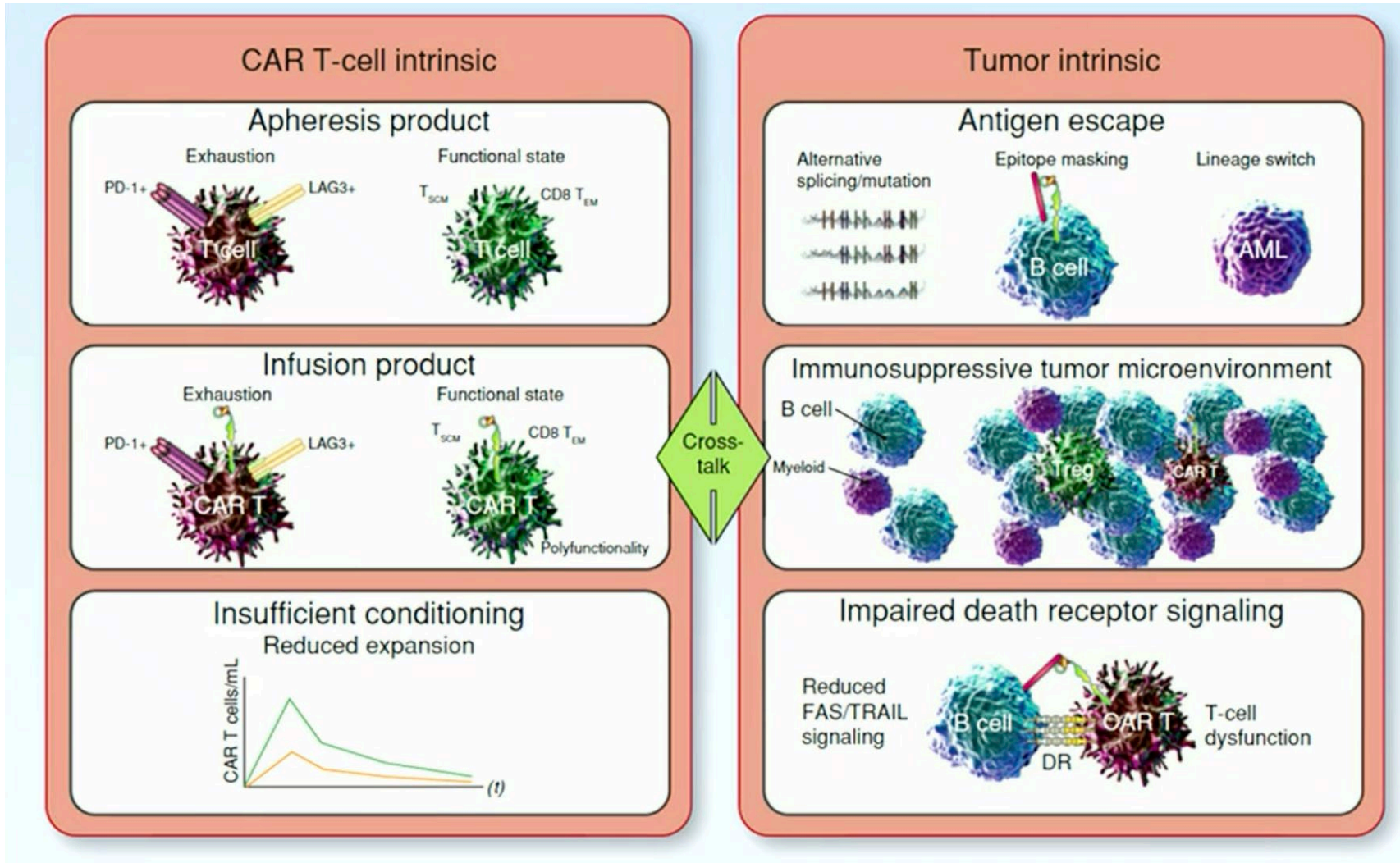
- *Früh*: CAR-T
- *Spät*: Platin-basierte Chemo/autoPBSCT

# Das Problem

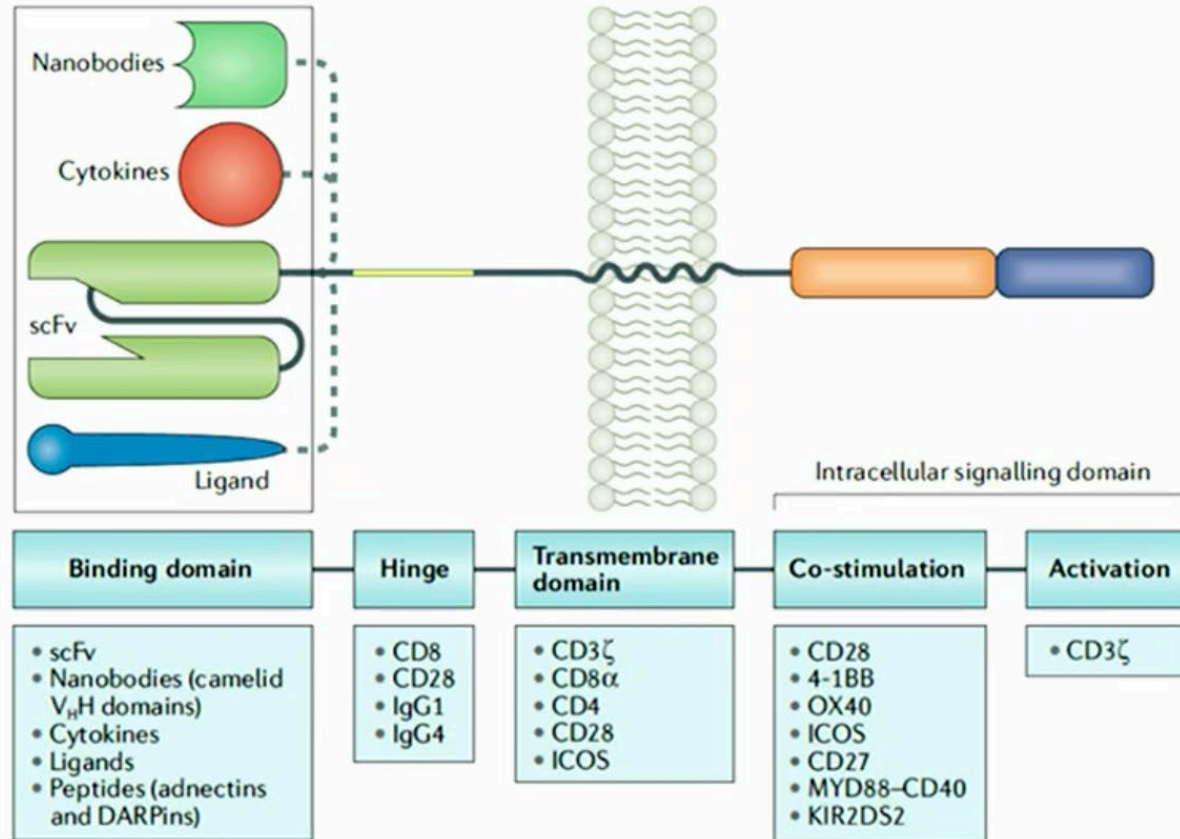


→ Mehrheit der Patienten rezidiert, dann mit sehr schlechter Prognose

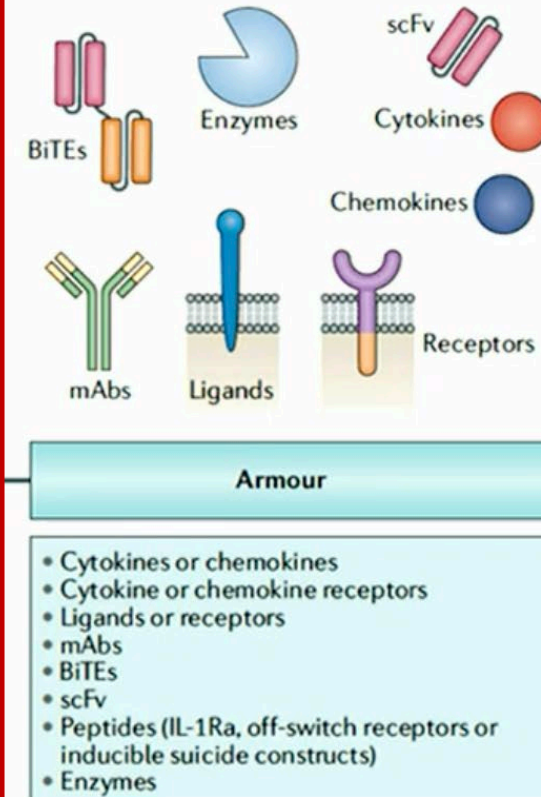
# Mechanismen der Resistenz



# Strategien zur Verbesserung des CAR-T Produkt



## 4. Generation CAR-T “Bewaffnete CAR-T”



Rafiq et al Nat Rec Clin Oncol 2020



# Fourth generation huCART19-IL18 produces durable responses in lymphoma patients previously relapsed/refractory to anti-CD19 CAR T-cell therapy

J. Svoboda, D.L. Landsburg, E.A. Chong, S.K. Barta, S.D. Nasta, M. Ruella, E.O. Hexner, A. Marshall, R. Leskowitz, M. Four, J. Shea, A. Cervini, M.M. Davis, G. Please, D. Hasenmayer, J.R. Amortegui, W. Hwang, N. Frey, D.L. Siegel, J. Fraietta, B. Levine, D.L. Porter, S.J. Schuster, and C.H. June  
University of Pennsylvania, Philadelphia, U.S.A.



17-ICML  
June 14, 2023  
Lugano, Switzerland



# First-in-human Studie mit huCART19-IL18 in CD19+ NHL

## huCART19-IL18

### CONSTRUCT DESIGN



### Patients

Median prior Rx (range)	8 (4-14)
B cell lymphoma	7 large cell (5 DLBCL, 1 TCHRBCL, 1 HGBL) 4 follicular 2 mantle cell
Previous CAR T	12 out of 13 patients

### RELATED ADVERSE EVENTS OF SPECIAL INTEREST

	CRS	NEURO
Any grade	7 (58%)	2 (17%)
Grade 1	4 (33%)	1 (8%)
Grade 2	2 (17%)	1 (8%)
Grade 3	1 (8%)	0

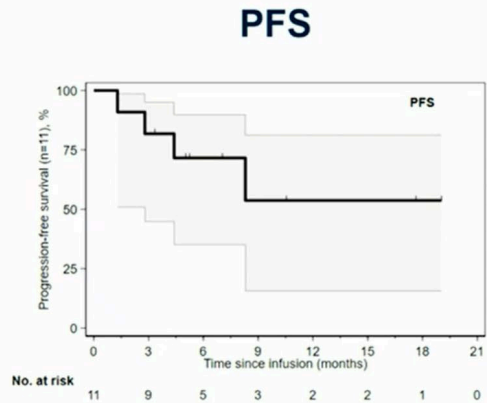
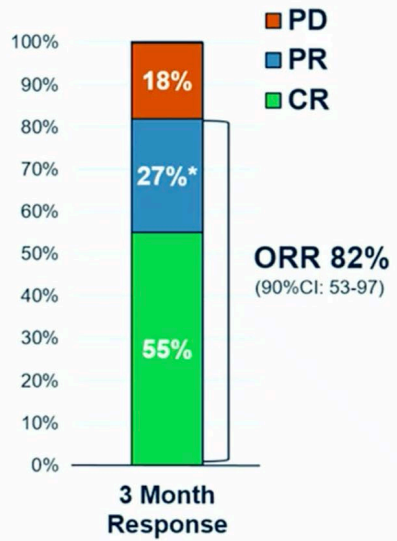
### RELATED NON-HEMATOLOGIC ADVERSE EVENTS ≥ GRADE 3

Infections	2 (17%)
Hypotension	2 (17%)
Hypoxia	2 (17%)
Pulmonary edema*	1 (8%)

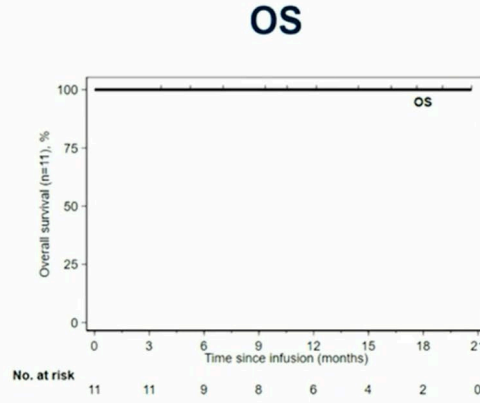
*Svoboda et al ICML 2023*

*Salles et al ICML 2023*

# Effektivität

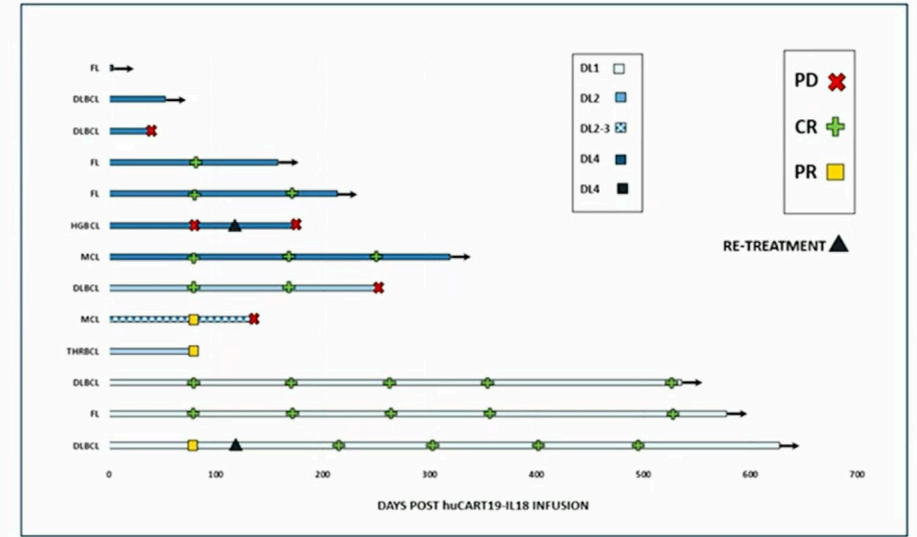


**12-month PFS: 54% (95%CI: 15-81)**



**12-month OS: 100%**

Median follow-up: 12 months (3-20)



**RESPONSES ARE DURABLE: Median DOR not reached (6.6-NR)**

# Zusammenfassung

- 4.Generation (“bewaffnete”) CAR T-Zell Therapie ist möglich und weist ein vertretbares Sicherheitsprofil und eine gute Expansion auf
- Es kommt zu anhaltendem Ansprechen von zuvor rrDLBCL nach anti-CD19 CAR-T Therapien
- 3 Folgekohorten rekrutieren derzeit (NHL, CLL, ALL)
- Biomarkeranalysen laufen, die auch den Einfluss des vorherigen Produktes untersuchen.

# Kapitel 3

## PMBL - Erstlinientherapie





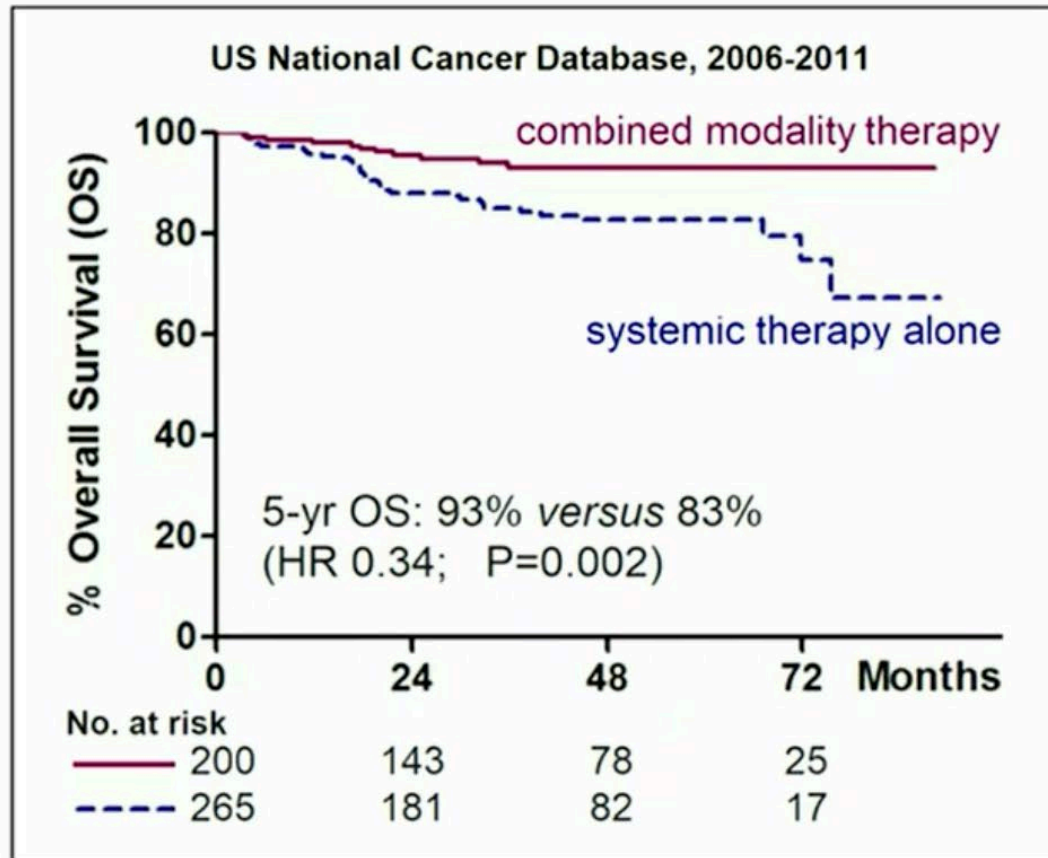
## **A randomised trial of observation versus radiotherapy in primary mediastinal B-cell lymphoma patients with complete metabolic response after standard immunochemotherapy (NCT01599559)**

A.J. Davies, E. Zucca, L. Ceriani, I. Kryachok, G. Ciccone, B. Botto, M. Balzarotti, A. Tucci, C. Rusconi, S.V. Usai, E. Pennese, L. Arcaini, A. Dabrowska-Iwanicka, A. J. M. Ferreri, F. Merli, W. Zhao, D. Hodgson, L. Rigacci, C. Cellini, C. Stelitano, F. Zaja, A. Guarini, C. Ionescu, M. Spina, A. Fossà, K. Cwynarski, G. Mikhaeel, M. Jerkeman, A. Janikova, A. Hüttmann, M. Gomes Silva, D. Stevens, S. Barrington, B. Malkowski, U. Metser, A. Versari, S. Chauvie, U. Ricardi, O. Bagni, A. Di Rocco, M. Gospodarowicz, F. Cavalli, P. W. Johnson and M. Martelli

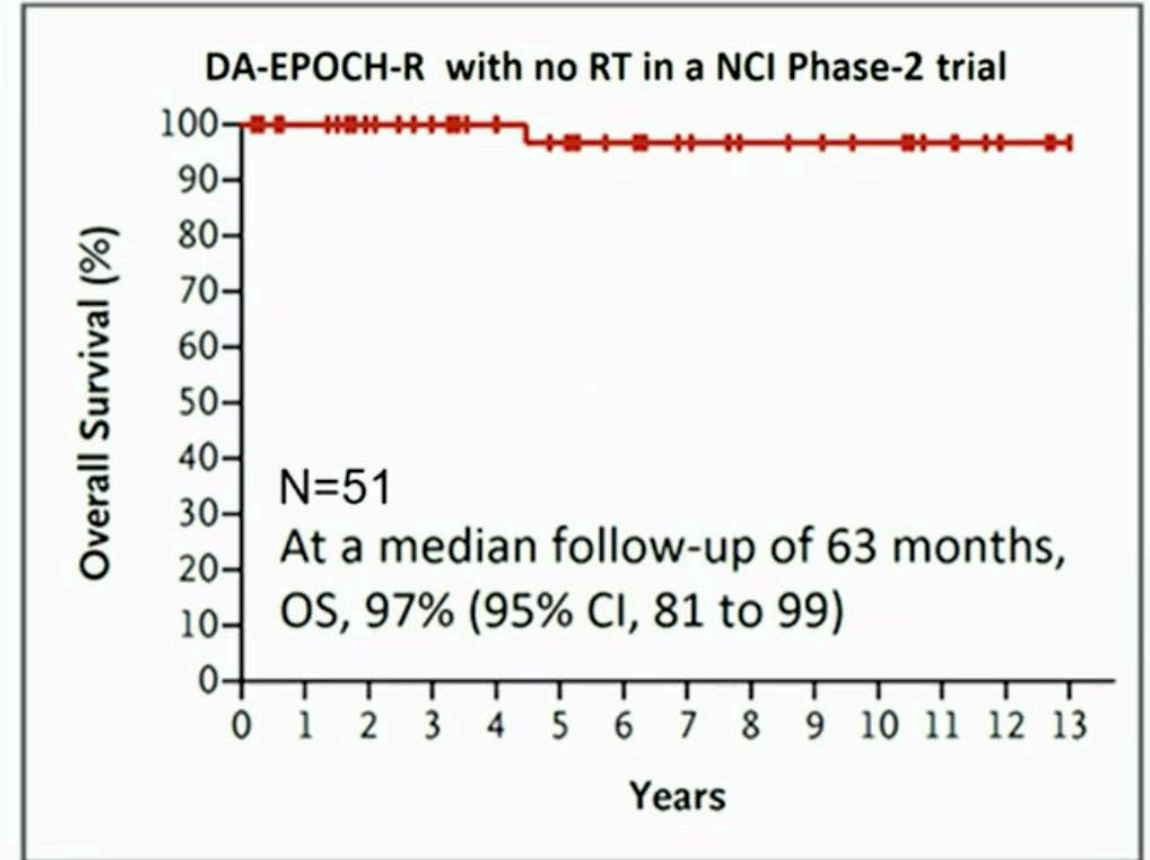
*On behalf of the International Extranodal Lymphoma Study Group (IELSG)*



# Die Rolle der Strahlentherapie in PMBL ist ungeklärt



Jackson MW et al. *Am J Hematol* 2016; 91:476

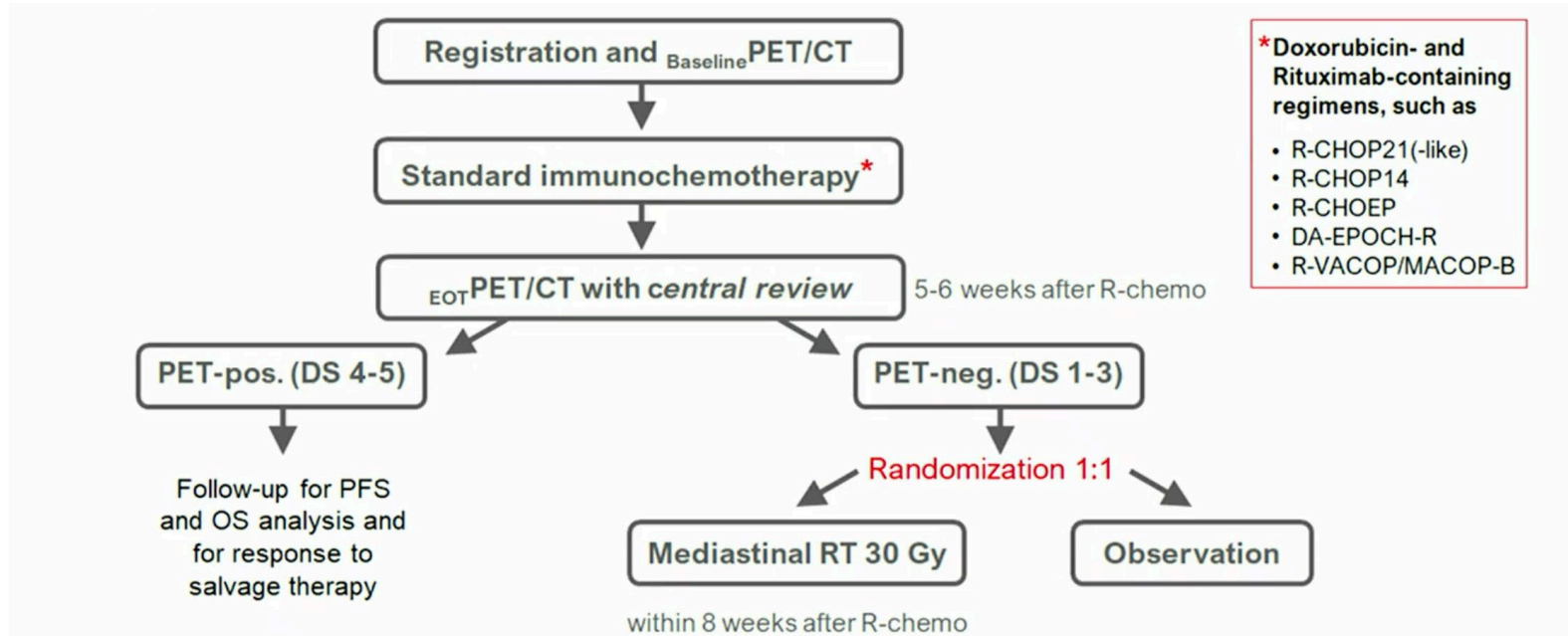


Dunleavy K et al. *N Engl J Med* 2013; 368:1408

Davies et al *ICML 2023*



# Randomisierte nicht-inferiority Studie



## Ziel

Testen, ob die mediastinale Bestrahlung bei Patienten mit CR nach konventioneller Chemo vermeidbar ist

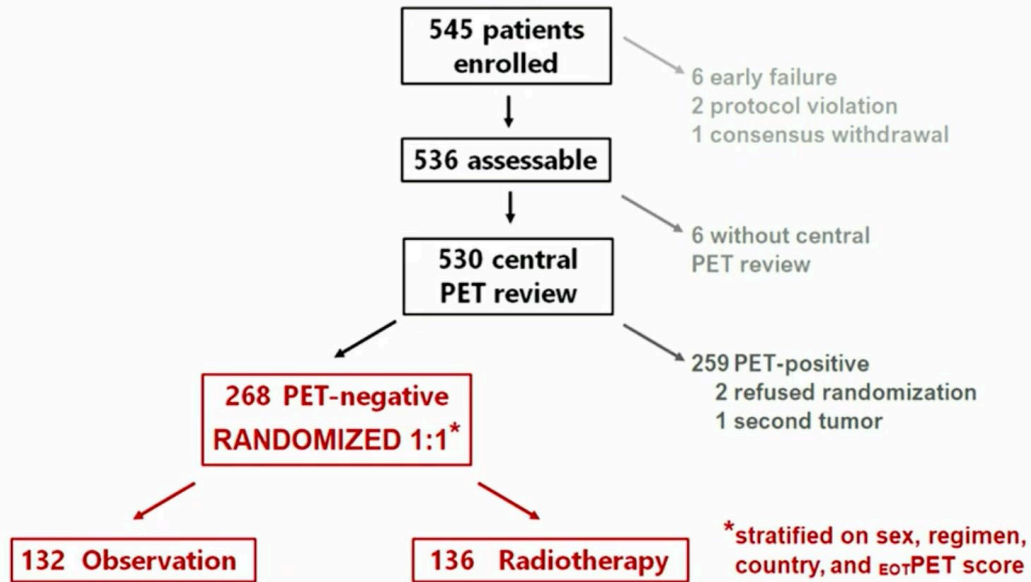
## Primärer/Sekundärer Endpunkt

30 Monate PFS / 5 Jahre OS

Davies et al ICML 2023

# Patienten Demographie und Verteilung

## Patient flow



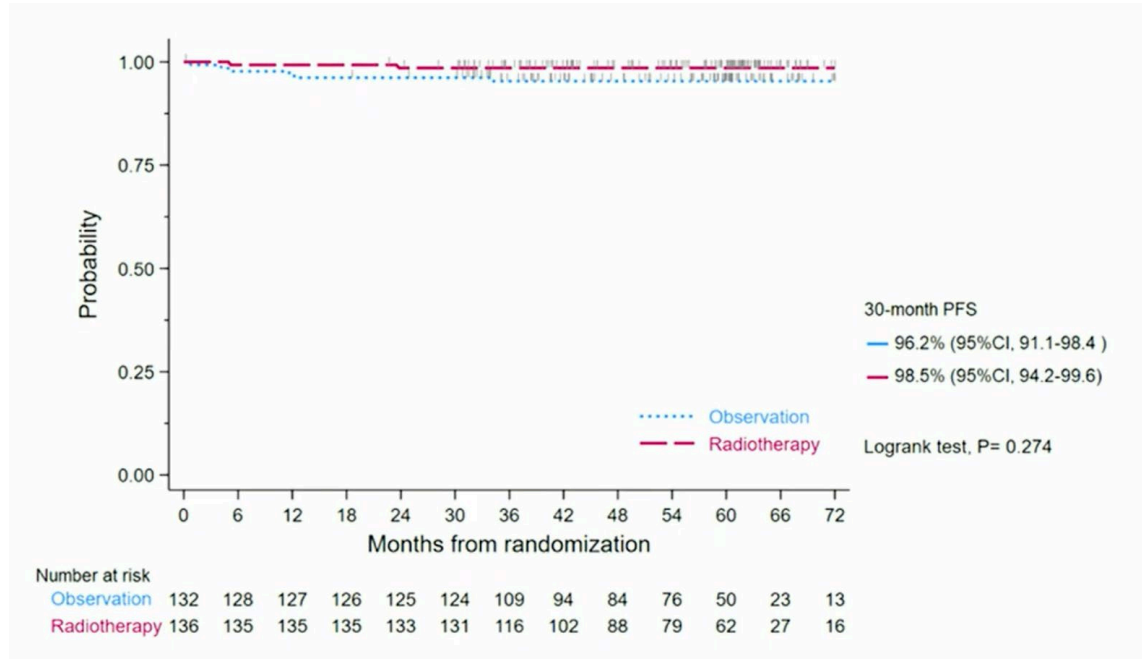
## Baseline demographic and clinical features

Feature		Radiotherapy	Observation
Number of patients		136	132
Median age, years (IQR)		35.5 (29-46.5)	35.5 (29-46.5)
Sex, N (%)	Female	88 (65)	83 (63)
	Male	48 (35)	49 (37)
EGOG PS, N (%)	0	74 (54)	69 (52)
	1	50 (37)	54 (41)
	≥2	12 (9)	9 (7)
Bulky disease, N (%)	>10 cm	89 (65)	79 (60)
Elevated LDH, N (%)	>UNL	91 (67)	88 (67)
R-IPI score, N (%)	Low risk	30 (22)	31 (23)
	Intermediate risk	98 (72)	96 (73)
	High risk	8 (6)	5 (4)

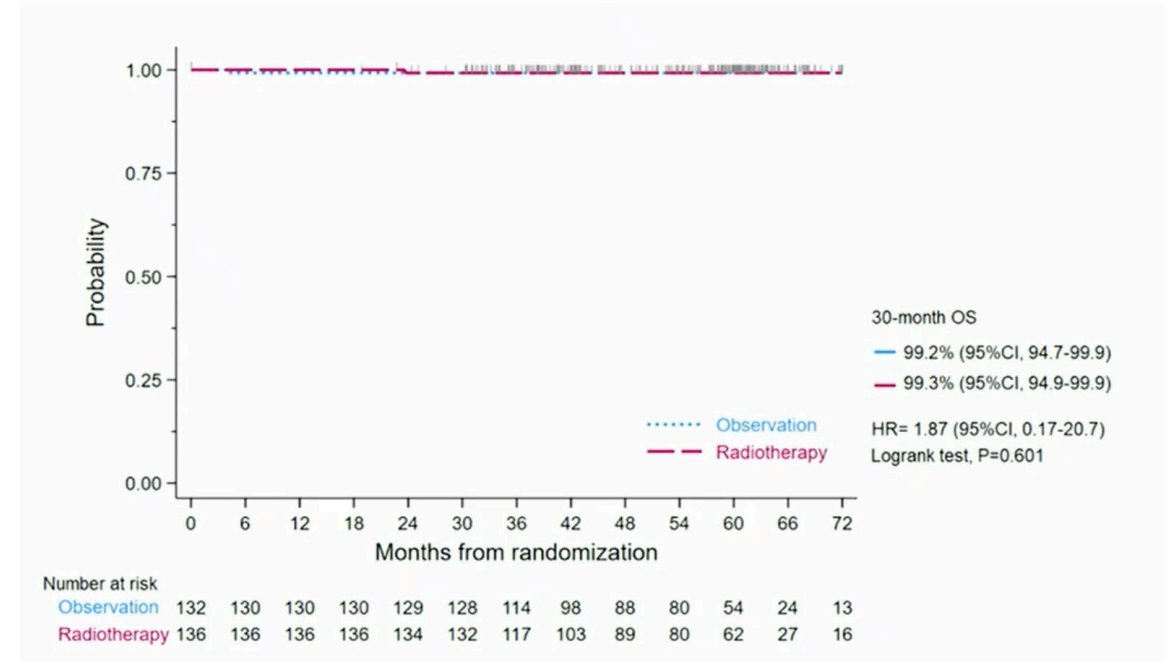
Davies et al ICML 2023

# Überleben

## Progresionsfreies Überleben



## Gesamtüberleben



Davies et al ICML 2023

# Unverwünschte NW/Spättoxizität

Event	Grade*	Arm	Time from randomisation	Outcome	PMBCL status at last visit
Left ventricular systolic dysfunction*	3	RT	during chemotherapy	resolved	continuous CR
Acute heart failure**	4		18 months	resolved	
Hypertension**	3	RT	8 months	resolved	continuous CR
Metastatic melanoma	4	RT	22 months	death from concurrent sepsis	continuous CR
Glioblastoma	3	RT	>55 months	death	continuous CR
Acute myeloid leukemia	4	RT	15 months	CR after allotrasplant	continuous CR

\* according to CTCAE v5.0

\*\* occurred in the same patient



# Zusammenfassung

- IELSG37 ist die größte randomisierte Studie im PMBCL
- Mediastinale Bestrahlung kann sicher für Patienten vermieden werden, wenn durch die Erstlinien Immuntherapie eine CMR erreicht wurde
- Längere Nachbeobachtung nötig um Spättoxizitäten zu beurteilen, aber bisher 3 schwere kardiologische Ereignisse und 3 sekundäre Tumoren in der Strahlentherapiekohorte.

*Davies et al ICML 2023*

Die Kurzpräsentationen sind online unter

**[www.lymphome.de/icml2023](http://www.lymphome.de/icml2023)**

Für den Inhalt verantwortlich:

Prof. Dr. med. Björn Chapuy

Charité - Universitätsmedizin Berlin

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