Lymphome

Y. Ko

Patiententag – 16. August 2023

JOHANNITER
Competence Center

Lymphome 2000 2023

Cyclophosphamid/
Ifosfamid

Cytarabin

Bendamustin

MTX

Doxorubicin/
Mitoxantron

Pixantrone

Cisplatin/
Carboplatin

Vincristin/
Vindesin

Gemcitabin

Etoposid

Prednisolon/
Dexamethason

Targets

Proteasom Bortezomib

iMiD Lenalidomid

PI3CA Copanlisib, Idelalisib

BTK Zanubrutinib, Ibrutinib, Aclabrutinib

Bcl-2 Venetoclax

CD20 Obinutuzumab, Rituximab, Ofatumumab

CD19 Tafasitamab

ADC Brentuximab-Vedotin (CD30), Polatuzumab-Vedotin (CD19), Longcastixumab-Tesirine (CD19)

Immunmodulation

CART Axicaptagen-Ciloleucel (CD19/DLBCL)
Tisagenlecleucel (CD19/DLBCL/ALL/FL)
Brexucaptagen Autoleucel (CD19/MCL/ALL)
Lisocaptagene Maraleucel (CD19/DLBCL/FL)

BiTES Mosunetuzumab (CD3-CD20/FL)
Glofitamab (CD3-CD20/DLBCL)

wie geht es weiter ?

ADC (Antibody Drug Conjugate)

Signal Transduction and Targeted Therapy

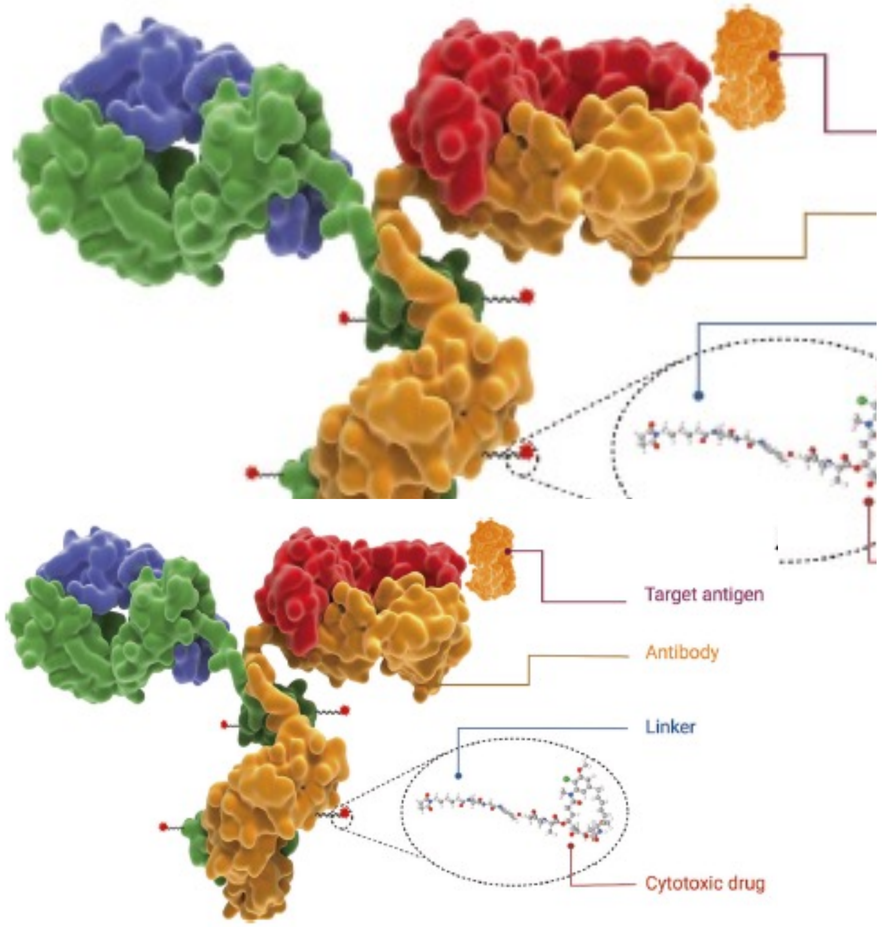
www.nature.com/sigtrans

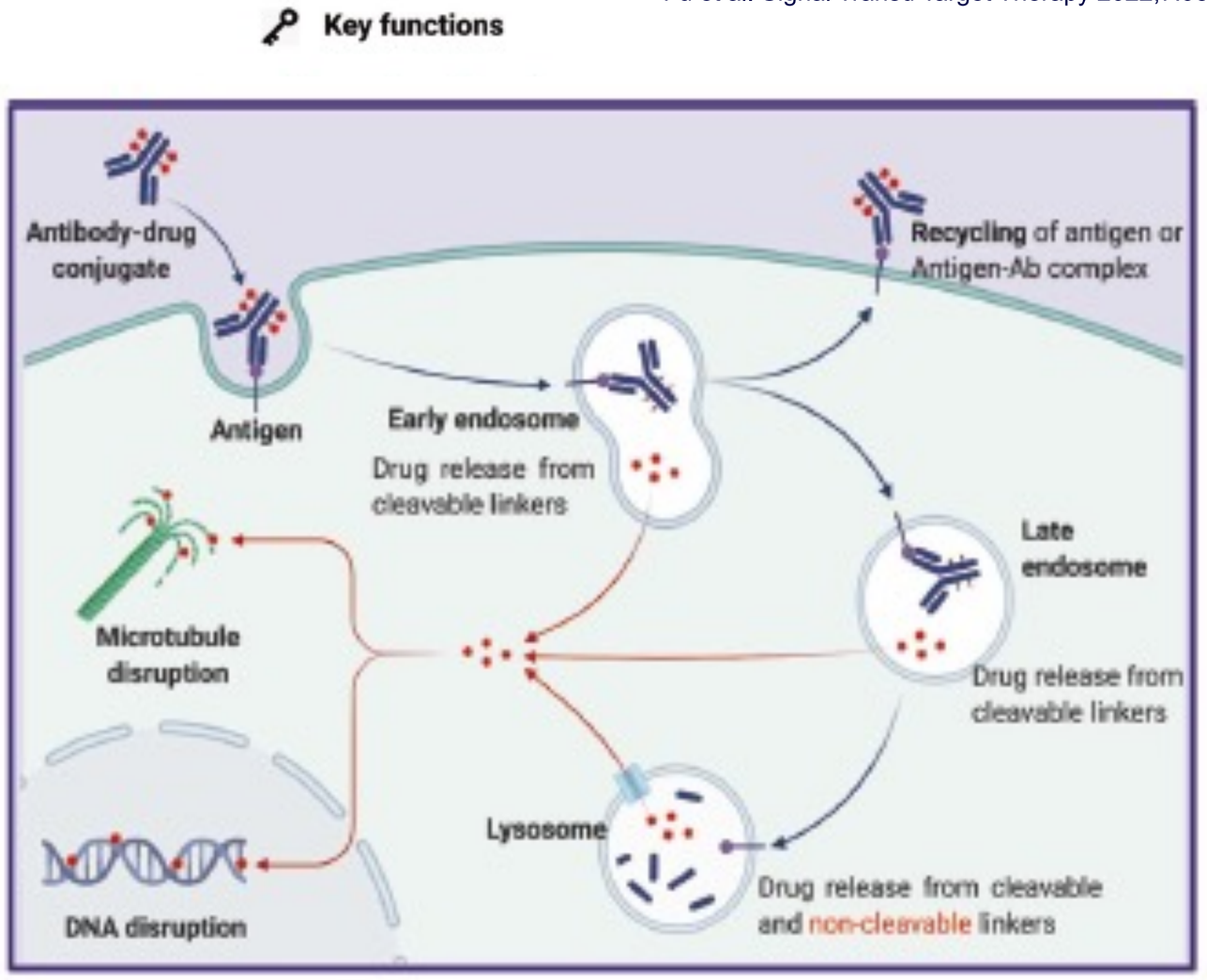
REVIEW ARTICLE OPEN

Antibody drug conjugate: the "biological missile" for targeted cancer therapy

Zhiwen Fu[1,2], Shijun Li[1,2], Sifei Han[3,4], Chen Shi[1,2]✉ and Yu Zhang[1,2]✉

Fu et al. Signal Transd Target Therapy 2022;7:93





Diffus großzelliges B-Zell-Lymphom (DLBCL)
Polatuzumab-Vedotin

1993

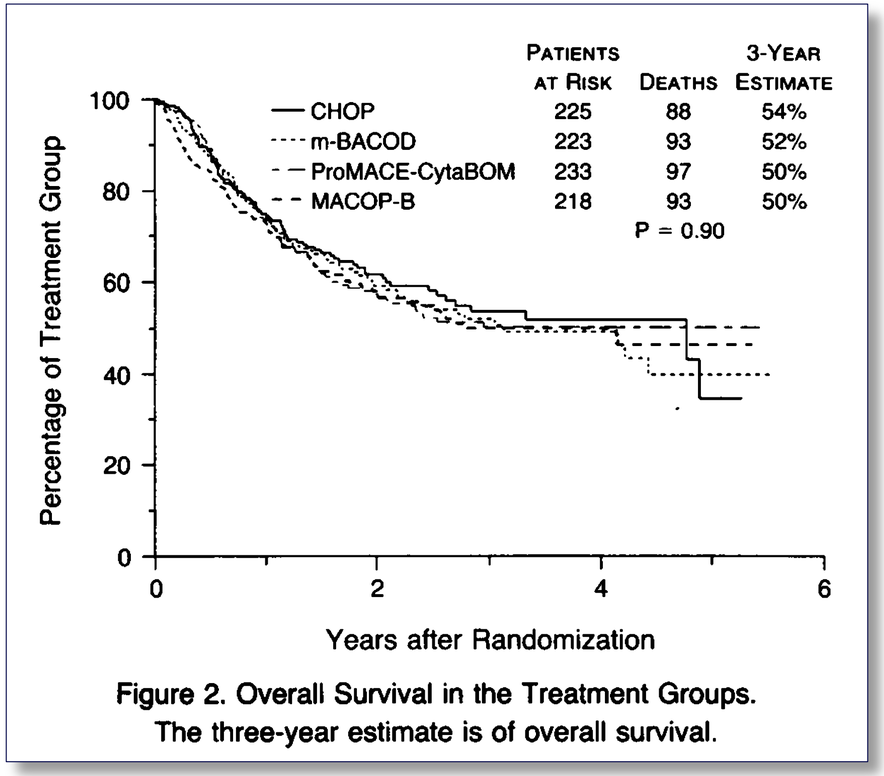


Figure 2. Overall Survival in the Treatment Groups. The three-year estimate is of overall survival.

2002

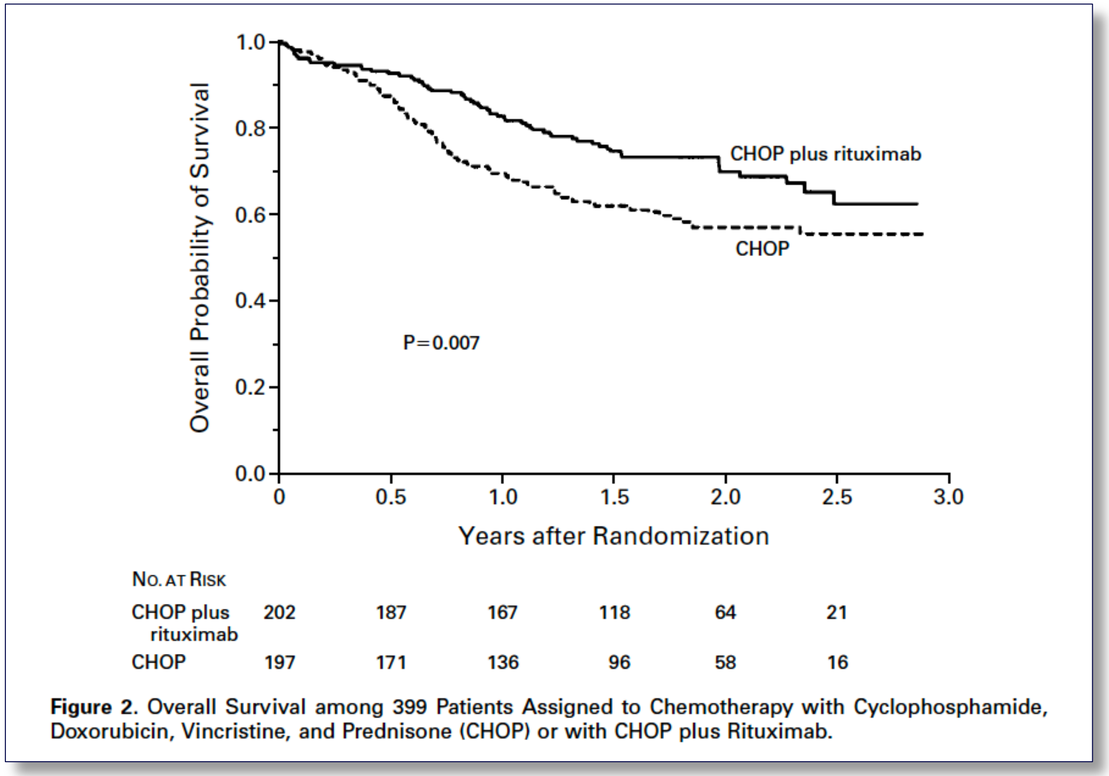
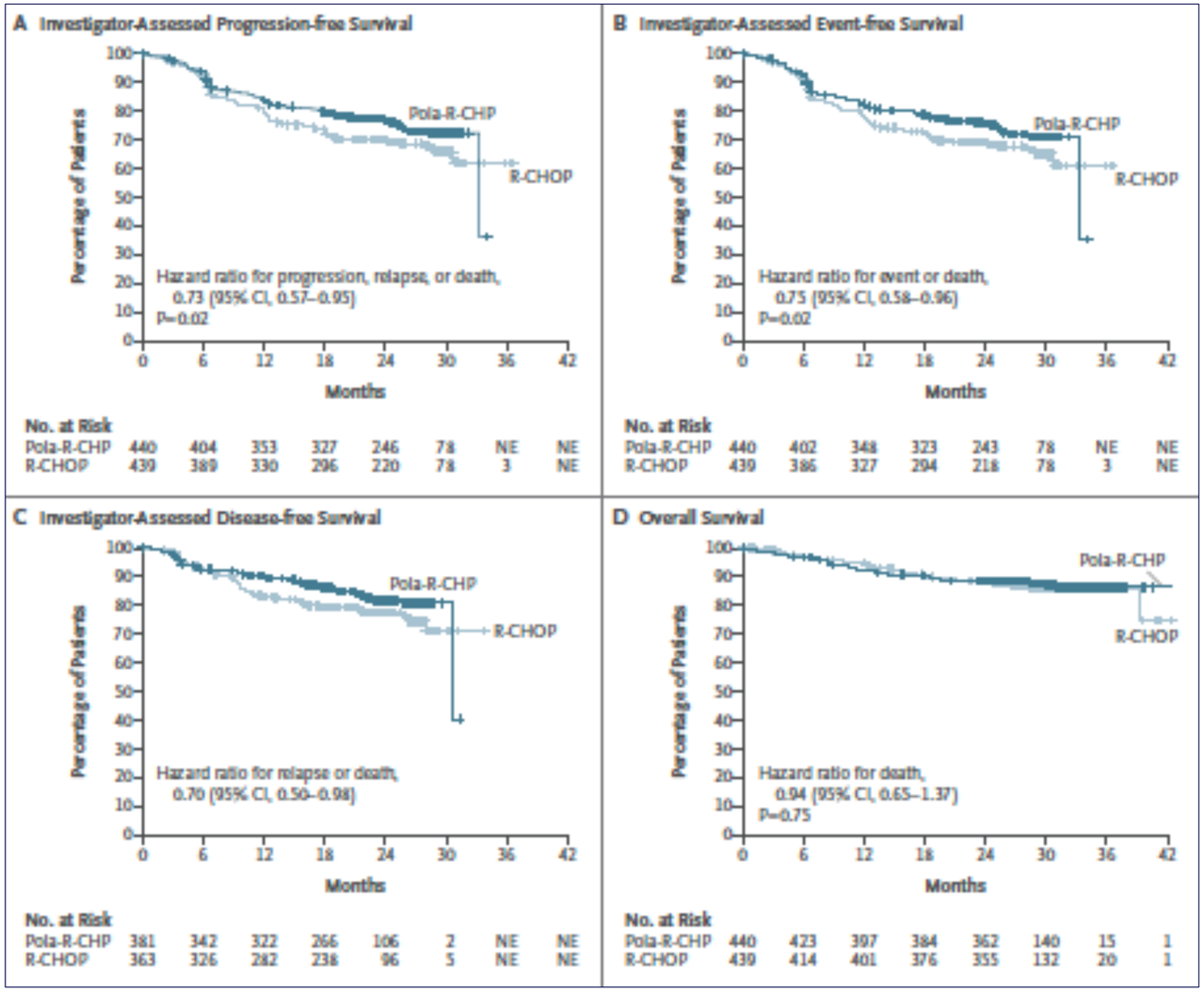


Figure 2. Overall Survival among 399 Patients Assigned to Chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) or with CHOP plus Rituximab.

2022

?

Diffus großzelliges B-Zell-Lymphom (DLBCL)
Polatuzumab-Vedotin



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma

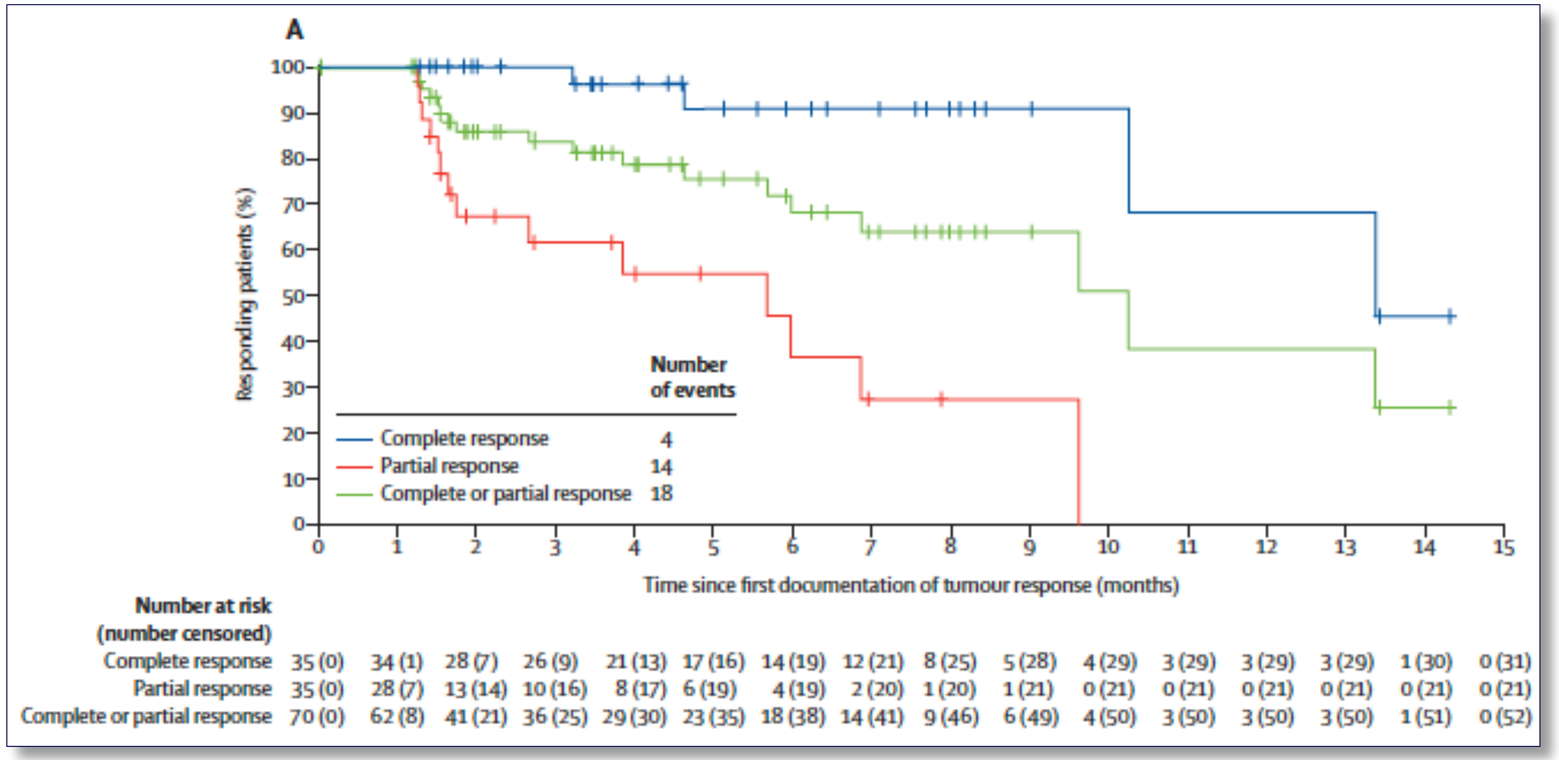
H. Tilly, F. Morschhauser, L.H. Sehn, J.W. Friedberg, M. Trněný, J.P. Sharman, C. Herbaux, J.M. Burke, M. Matasar, S. Rai, K. Izutsu, N. Mehta-Shah, L. Oberic, A. Chauchet, W. Jurczak, Y. Song, R. Greil, L. Mykhalska, J.M. Bergua-Burgués, M.C. Cheung, A. Pinto, H.-J. Shin, G. Hapgood, E. Munhoz, P. Abrisqueta, J.-P. Gau, J. Hirata, Y. Jiang, M. Yan, C. Lee, C.R. Flowers, and G. Salles

- Alter 18-80 Jahre
- 1. Linie
- ECOG 0-2
- IPI 2-5
- MYC, bcl-2/6 unabhängig

Tilly et al. NEJM 2022;386:351-63

DLBCL Rezidiv/Refraktär

Loncastuximab tesirine



Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial

Paolo F Caimi, Weiyun Ai, Juan Pablo Alderuccio, Kirit M Ardeshna, Mehdi Hamadani, Brian Hess, Brad S Kahl, John Radford, Melhem Solh, Anastasios Stathis, Pier Luigi Zinzani, Karin Havenith, Jay Feingold, Shui He, Yajuan Qin, David Ungar, Xiaoyan Zhang, Carmelo Carlo-Stella

	As-treated population (n=145)
Overall response rate (complete or partial response)	70 (48·3% [39·9–56·7])
Complete response rate	35 (24·1% [17·4–31·9])
Complete response	35 (24%)
Partial response	35 (24%)
Stable disease	22 (15%)
Progressive disease	30 (21%)
Not evaluable*	23 (16%)

Data are n (% [95% CI]) or n (%). Response was assessed by central independent review. A best overall response of stable disease could only be achieved after the patient was on the study for a minimum of 35 days following the first dose of loncastuximab tesirine. Any disease assessment indicating stable disease before this timepoint was considered not evaluable for response if no assessment after this timepoint was available. *Patients without any scan available to the independent reviewer or patients whose scan was determined to be not evaluable by the independent reviewer.

Table 2: **Best overall responses and overall response rate**

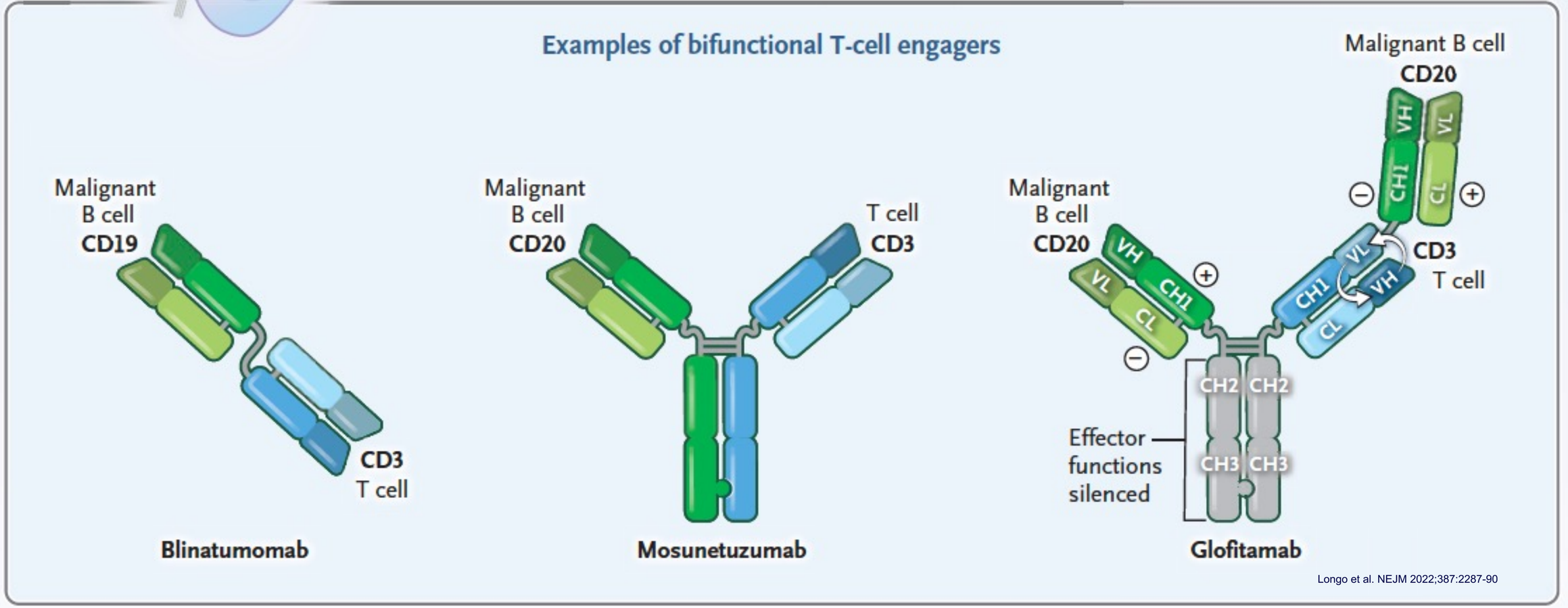
Toxizität:

- Hämatotoxizität
- Hepatotoxizität
- SAE 39%
- Todesfälle 6% Therapie-bedingt

Caimi et al. Lancet Oncol 2021;22:790-800

BiTE (Bispecific T-cell Engagers)

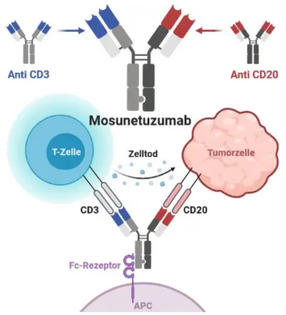
Bispezifische Antikörper



Longo et al. NEJM 2022;387:2287-90

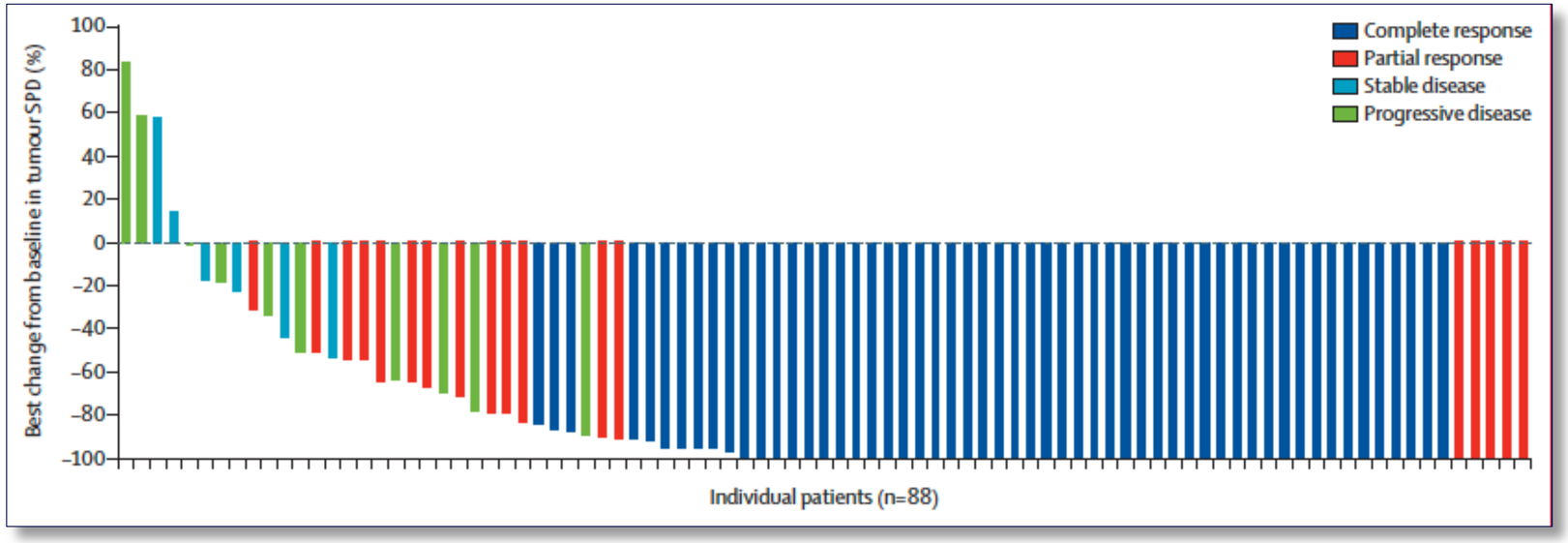
Mosunetuzumab

Follikuläres Lymphom (FL) Rezidiv/Refraktär



Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study

Lihua E Budde, Laurie H Sehn, Matthew Matasar, Stephen J Schuster, Sarit Assouline, Pratyush Giri, John Kuruvilla, Miguel Canales, Sascha Dietrich, Keith Fay, Matthew Ku, Loretta Nastoupil, Chan Yoon Cheah, Michael C Wei, Shen Yin, Chi-Chung Li, Huang Huang, Antonia Kwan, Elicia Penuel, Nancy L Bartlett

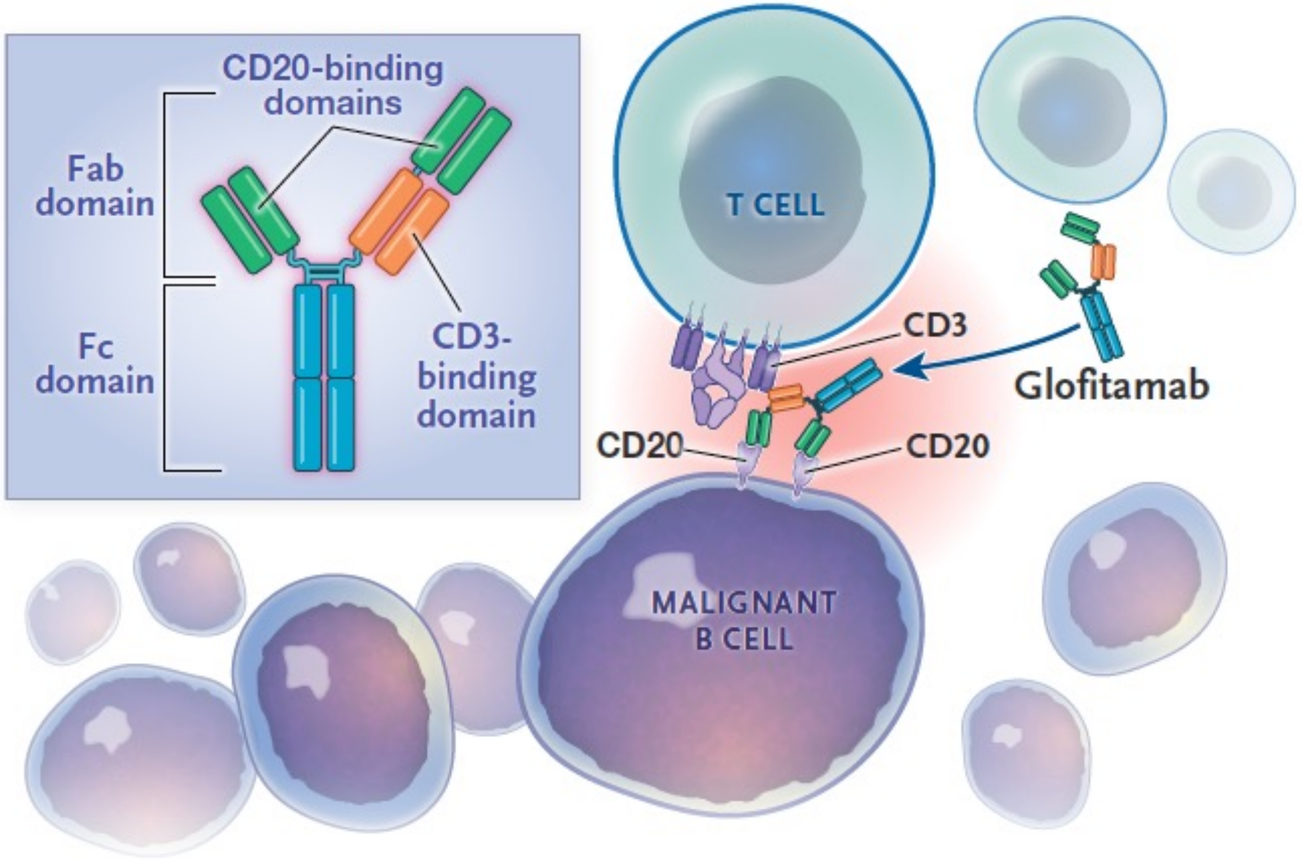


Number of previous lines of therapy	3 (2–4)
Two previous lines	34 (38%)
Three previous lines	28 (31%)
More than three previous lines	28 (31%)
Previous lymphoma therapy	
Alkylator therapy	90 (100%)
Anti-CD20 therapy	90 (100%)
Immunochemotherapy (anti-CD20 plus alkylator or anthracycline)	88 (98%)
Anthracyclines	74 (82%)
PI3K inhibitors	17 (19%)
Immunomodulatory drugs	13 (14%)
Chimeric antigen receptor T-cell therapy	3 (3%)
Previous autologous stem cell transplant	19 (21%)
Refractory to last previous therapy	62 (69%)
Refractory to any previous anti-CD20 therapy	71 (79%)
Refractory to any previous anti-CD20 therapy and an alkylator therapy (double refractory)	48 (53%)
POD24	47 (52%)

Budde et al. Lancet Oncol 2022;23:1055-65

Glofitamab

DLBCL Rezidiv/Refraktär



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

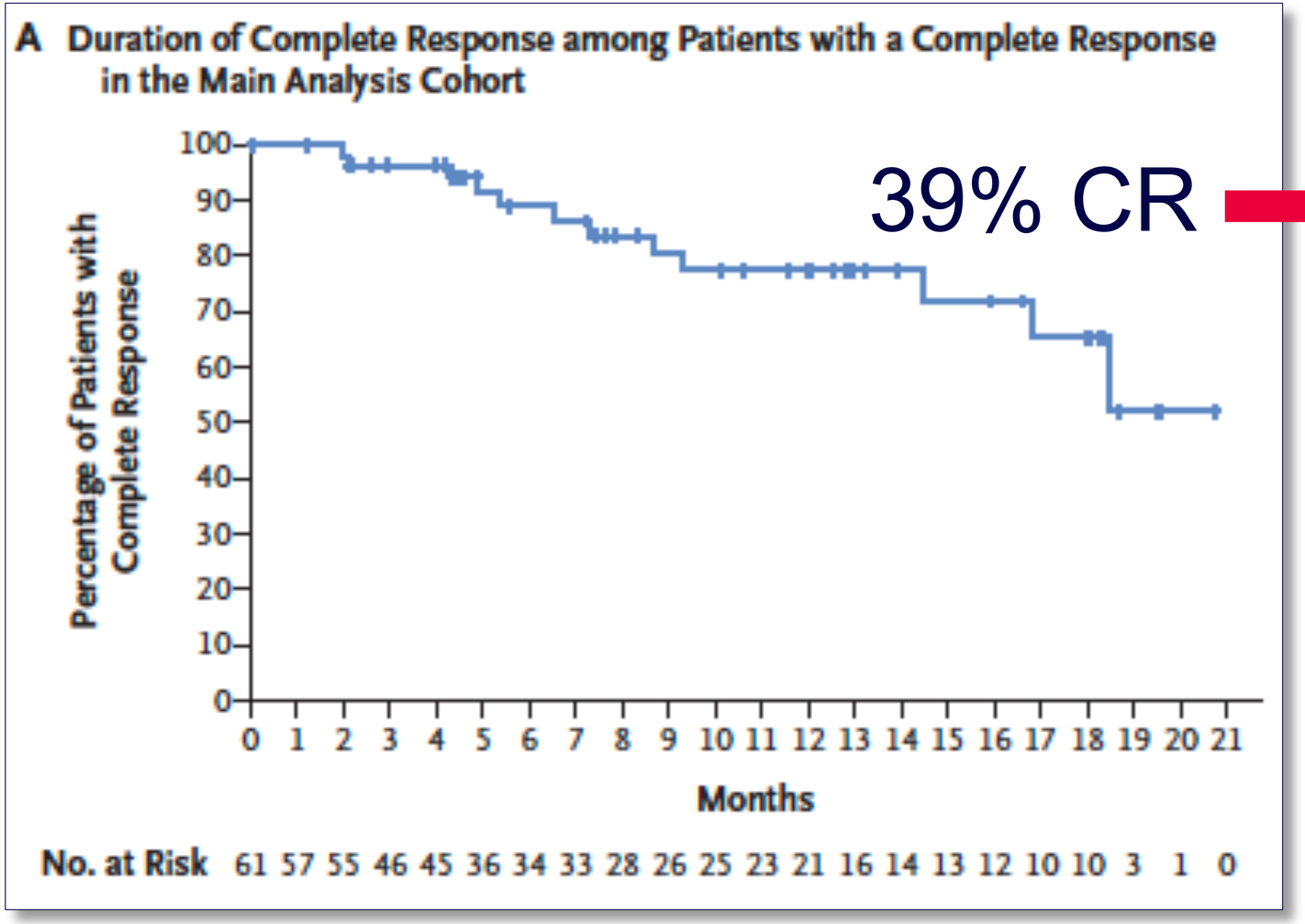
Michael J. Dickinson, M.B., B.S., D.Med.Sc., Carmelo Carlo-Stella, M.D.,

Table 1. Demographic and Clinical Characteristics at Baseline of All 154 Patients Treated at the Phase 2 Dose (Safety Population).*

Characteristic	Value
Median age (range) — yr	66 (21–90)
Male sex — no. (%)	100 (65)
ECOG performance-status score — no. (%)†	
0	69 (45)
1	84 (55)
Ann Arbor stage at time of study entry — no. (%)	
I	10 (6)
II	25 (16)
III	31 (20)
IV	85 (55)
Missing data	3 (2)
Non-Hodgkin's lymphoma subtype — no. (%)	
Diffuse large B-cell lymphoma, not otherwise specified	110 (71)
Transformed follicular lymphoma	27 (18)
High-grade B-cell lymphoma	11 (7)
Primary mediastinal B-cell lymphoma	6 (4)
Bulky disease at study entry	
>6 cm	64 (42)
>10 cm	18 (12)
Previous lines of therapy	
Median no. of lines (range)	3 (2–7)
Only 2 previous lines — no. (%)	62 (40)
≥3 previous lines — no. (%)	92 (60)
Previous therapy for lymphoma — no. (%)	
Anti-CD20 antibody	154 (100)
Anthracycline	149 (97)
CAR T-cell therapy	51 (33)
Autologous stem-cell transplantation — no. (%)	28 (18)
Relapsed or refractory status — no. (%)‡	
Refractory to any previous therapy	139 (90)
Refractory to last previous therapy	132 (86)
Primary refractory	90 (58)
Refractory to any previous anti-CD20 therapy	128 (83)
Refractory to previous CAR T-cell therapy	46 (30)

Dickinson et al. NEJM 2022;387:2220-31

Glofitamab
DLBCL Rezidiv/Refraktär



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Michael J. Dickinson, M.B., B.S., D.Med.Sc., Carmelo Carlo-Stella, M.D.,

Table 2. Efficacy According to Independent Review Committee and Investigator Assessment (Intention-to-Treat Population).*

Outcome	Assessment According to Independent Review Committee (N=155)	Assessment According to Investigator (N=155)
Complete response		
No. of patients with response	61	58
Percentage of patients (95% CI)	39 (32–48)	37 (30–46)
Objective response		
No. of patients with response	80	89
Percentage of patients (95% CI)	52 (43–60)	57 (49–65)
Duration of complete response†		
Median (95% CI) — mo	NR (16.8–NR)	19.8 (18.2–NR)
Complete response at 12 mo (95% CI) — %	78 (64–91)	72 (59–86)
Duration of objective response‡		
Median (95% CI) — mo	18.4 (13.7–NR)	10.4 (6.8–NR)
Objective response at 12 mo (95% CI) — %	64 (51–76)	49 (37–61)
Median time to first complete response (range) — days†	42 (31–308)	43 (31–274)
Progression-free survival		
Median (95% CI) — mo	4.9 (3.4–8.1)	3.8 (3.3–5.4)
Alive without progression at 12 mo (95% CI) — %	37 (29–46)	30 (22–38)
Overall survival		
Median (95% CI) — mo	—	11.5 (7.9–15.7)
Alive at 12 mo (95% CI) — %	—	50 (41–58)

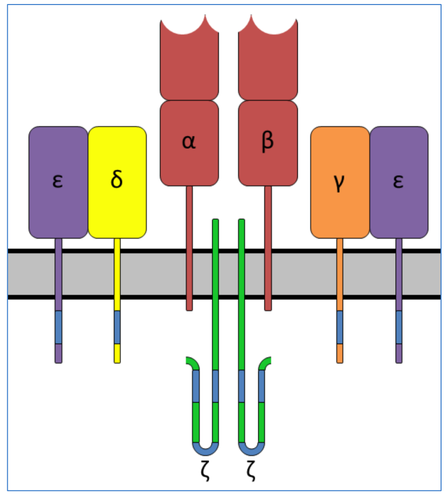
Toxizität:
- Zytokin-release Syndrom 63% (>Grad 2 4%)
- Neurologische Störungen 15% (>Grad 2 3%
- SAE 47%
- Todesfälle keine Therapie-bedingt

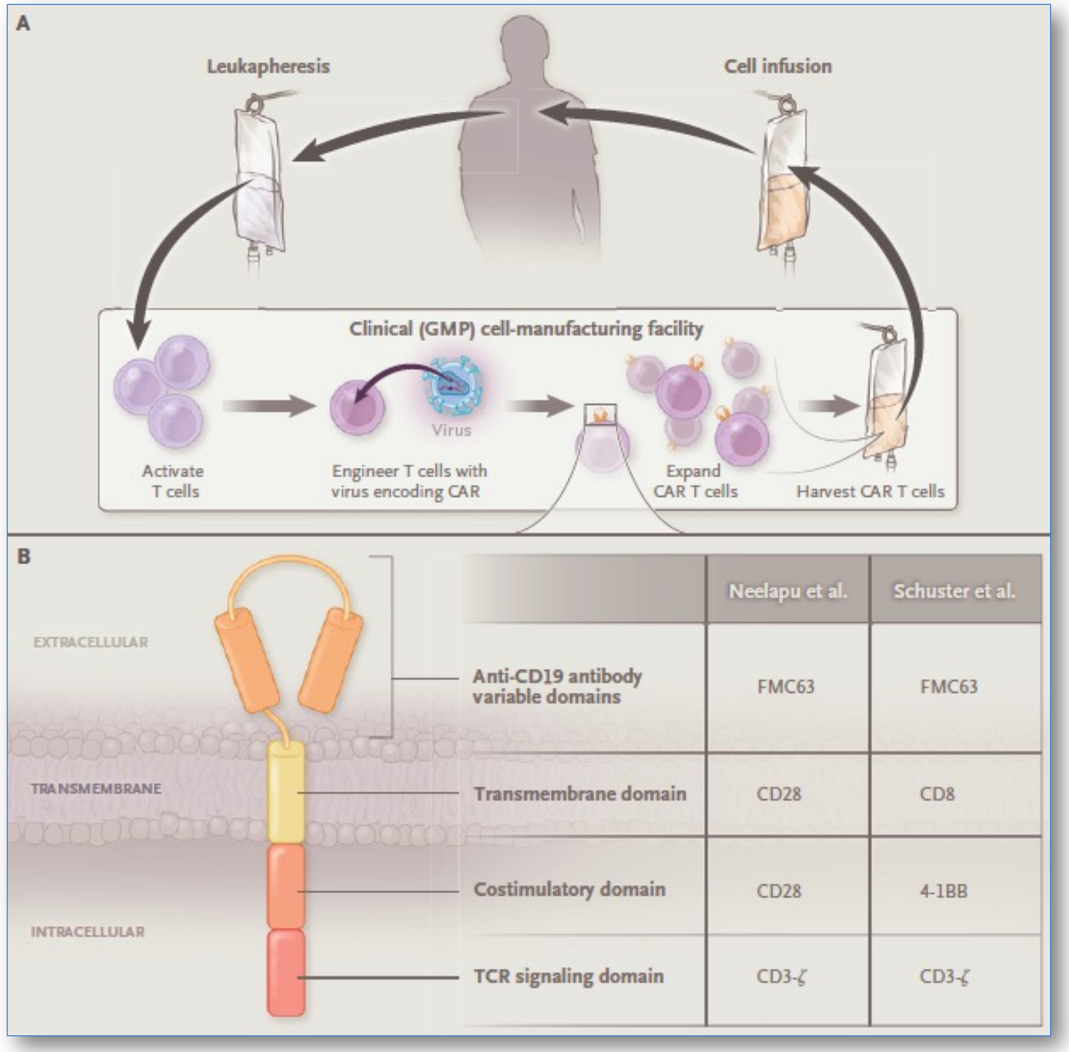
Dickinson et al. NEJM 2022;387:2220-31

Chimeric Antigen Rezeptor T-Zell Therapie (CAR-T Therapy)
DLBCL

CAR-T

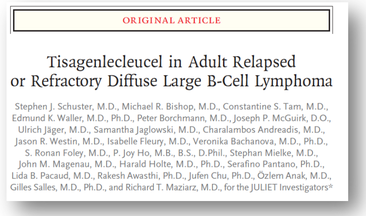
T-Zell-Rezeptor (TCR)





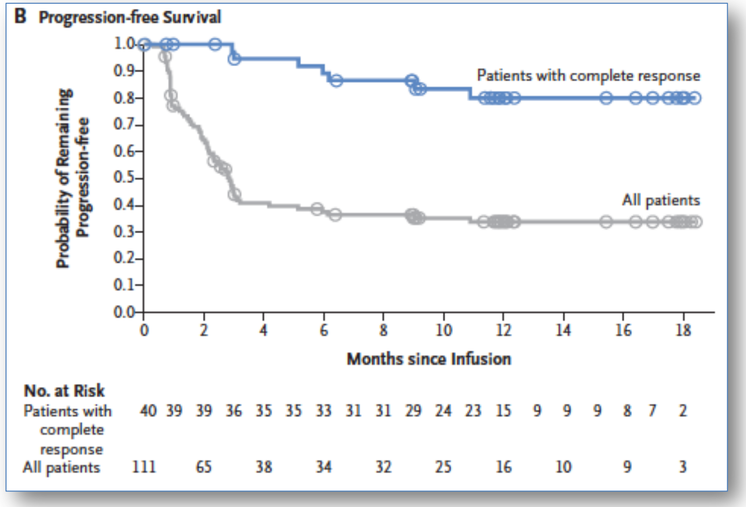
Tran et al. NEJM 2017;377:2393-6

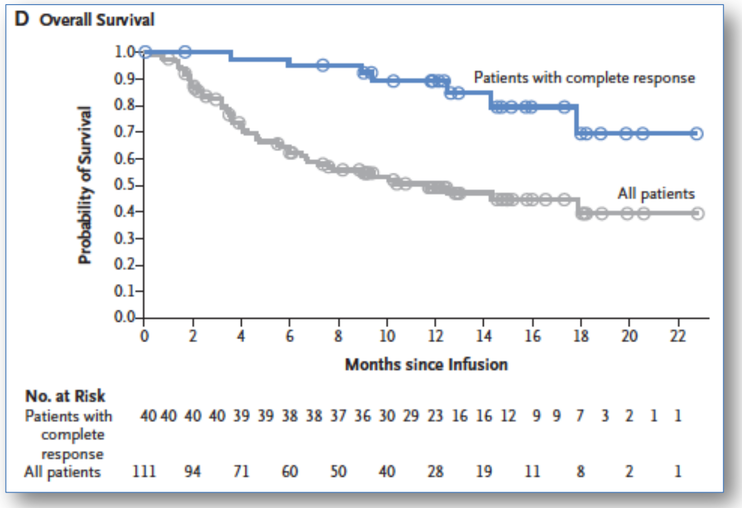
Tisagenlecleucel (Kymriah® Novartis)
DLBCL


ORIGINAL ARTICLE

Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Stephen J. Schuster, M.D., Michael R. Bishop, M.D., Constantine S. Tam, M.D., Edmund K. Waller, M.D., Ph.D., Peter Borchmann, M.D., Joseph P. McGuirk, D.O., Ulrich Jäger, M.D., Samantha Jaglowski, M.D., Charalambos Andreadis, M.D., Jason R. Westin, M.D., Isabelle Fleury, M.D., Veronika Bachanova, M.D., Ph.D., S. Ronan Foley, M.D., P. Joy Ho, M.B., B.S., D.Phil., Stephan Mielke, M.D., John M. Magenau, M.D., Harald Holte, M.D., Ph.D., Serafino Pantano, Ph.D., Lida B. Pacaud, M.D., Rakesh Awasthi, Ph.D., Jufen Chu, Ph.D., Özlem Anak, M.D., Gilles Salles, M.D., Ph.D., and Richard T. Maziarz, M.D., for the JULIET Investigators*





Type of Adverse Event	Patients with Any Event (N=111)	Patients with Events Starting ≤8 Wk after Infusion (N=111)	Patients with Events Starting >8 Wk after Infusion (N=96)
	number of patients (percent)		
Any adverse event	111 (100)	111 (100)	69 (72)
Adverse event suspected to be related to study drug	99 (89)	96 (86)	30 (31)
Serious adverse event	72 (65)	55 (50)	30 (31)
Serious adverse event suspected to be related to study drug	52 (47)	46 (41)	9 (9)
Grade 3 or 4 adverse event	99 (89)	94 (85)	47 (49)
Grade 3 or 4 adverse event suspected to be related to study drug	70 (63)	64 (58)	21 (22)
Adverse events of special interest†			
Cytokine release syndrome‡			
Any grade		64 (58)	0
Grade 3		15 (14)	0
Grade 4		9 (8)	0
Infection			
Any grade		38 (34)	37 (39)
Grade 3		20 (18)	13 (14)
Grade 4		2 (2)	4 (4)
Cytopenia not resolved by day 28§			
Any grade		49 (44)	NA
Grade 3		18 (16)	NA
Grade 4		18 (16)	NA
Neurologic event¶			
Any grade		23 (21)	5 (5)
Grade 3		8 (7)	3 (3)
Grade 4		5 (5)	0
Febrile neutropenia			
Any grade		17 (15)	2 (2)
Grade 3		14 (13)	1 (1)
Grade 4		2 (2)	1 (1)
Tumor lysis syndrome			
Any grade		1 (1)	0
Grade 3		1 (1)	0
Grade 4		0	0

Schuster et al. NEJM 2019;380:45-56

Vielen Dank

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