Lymphoma: State of the Art

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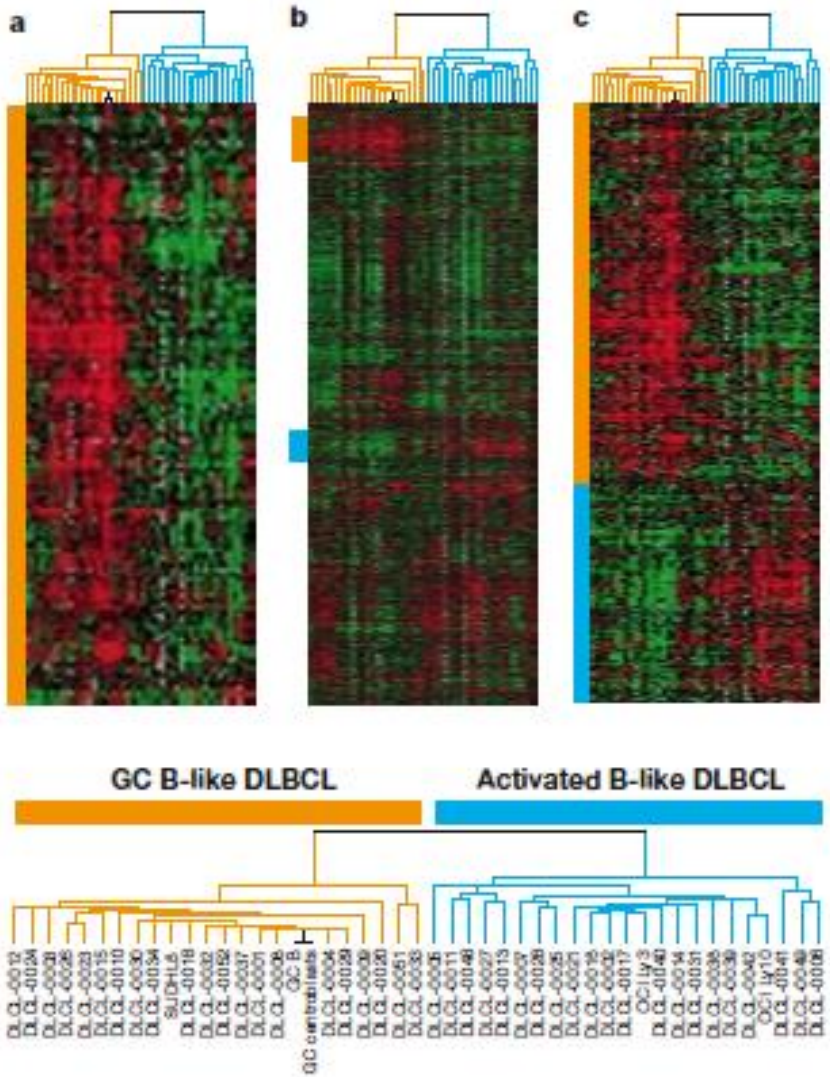
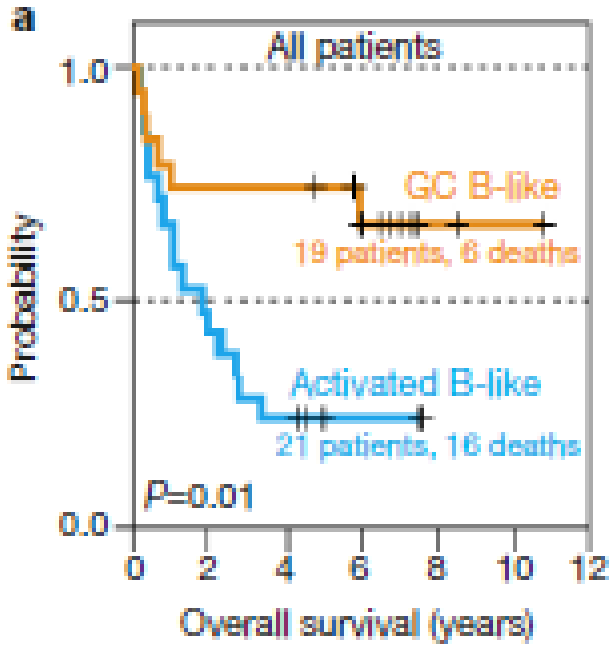
City of Hope Comprehensive Cancer Center

Aggressive NHL

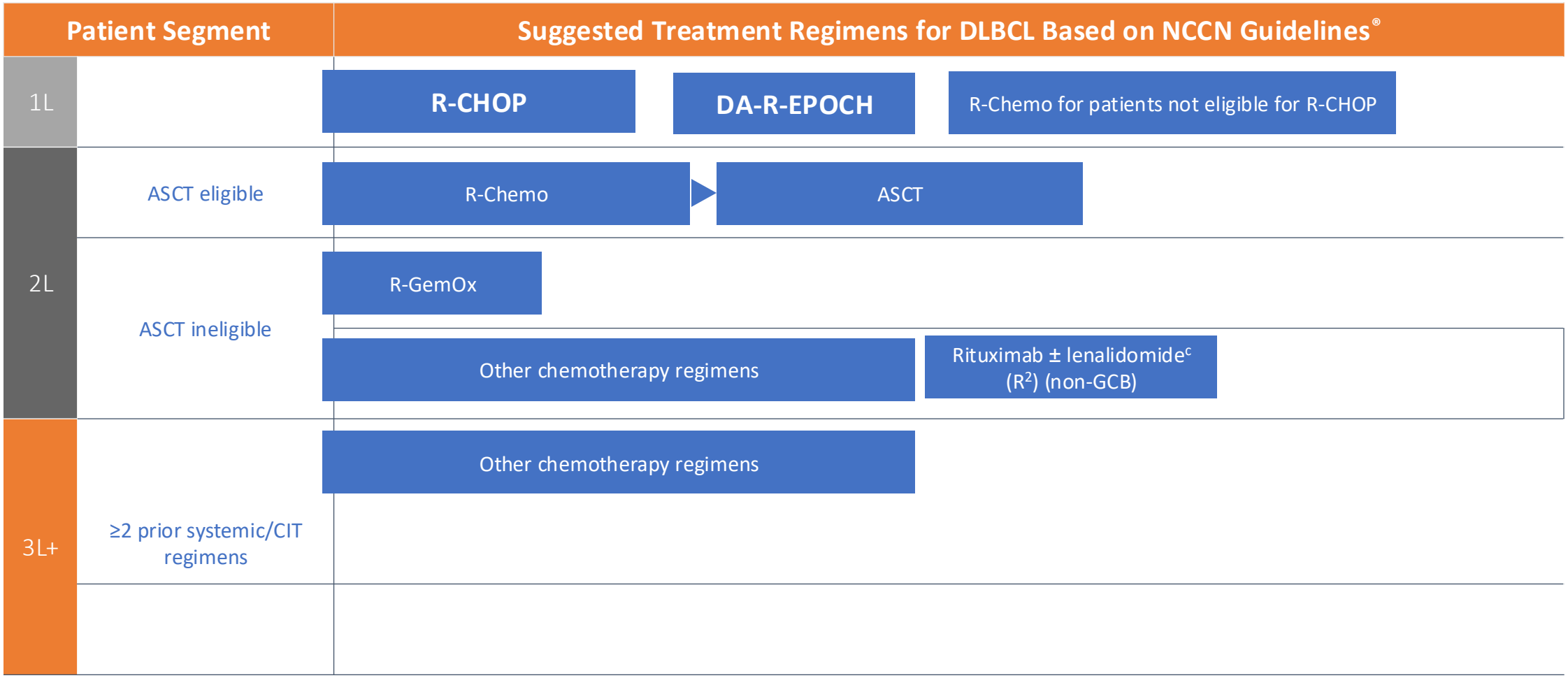
Cell of Origin (COO) predicts outcomes



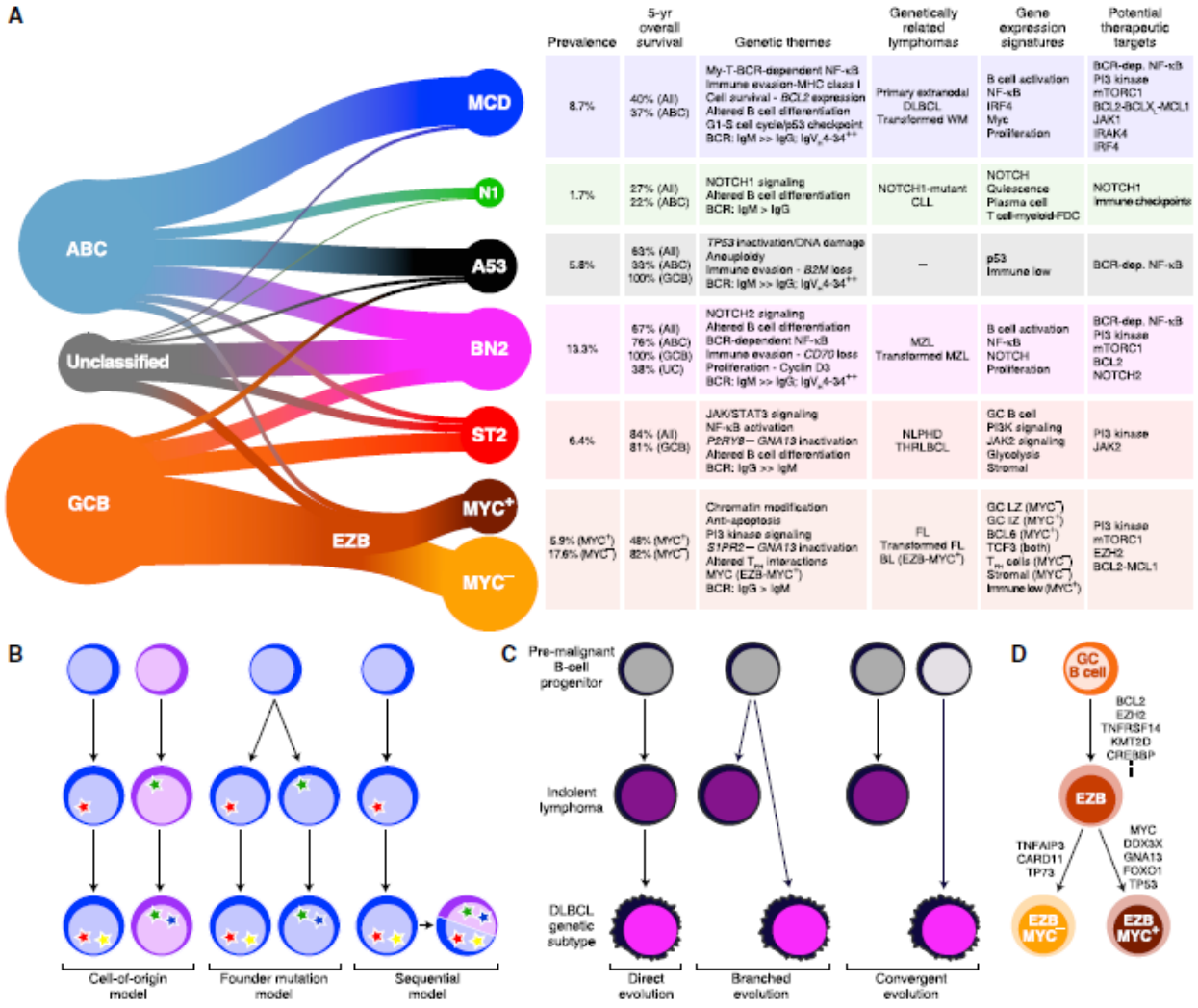


Alizadeh et al, 2000

DLBCL in 2000-2010



Genetic classifications of DLBCL



	Prevalence	5-yr overall survival	Genetic themes	Genetically related lymphomas	Gene expression signatures	Potential therapeutic targets
MCD	8.7%	40% (All) 37% (ABC)	MyT-BCR-dependent NF-κB Immune evasion-MHC class I Cell survival - *BCL2* expression Altered B cell differentiation G1-S cell cycle/p53 checkpoint BCR: IgM >> IgG; $IgV_H4\text{-}34^{++}$	Primary extranodal DLBCL Transformed WM	B cell activation NF-κB IRF4 Myc Proliferation	BCR-dep. NF-κB PI3 kinase mTORC1 BCL2-BCLX_L-MCL1 JAK1 IRAK4 IRF4
N1	1.7%	27% (All) 22% (ABC)	NOTCH1 signaling Altered B cell differentiation BCR: IgM > IgG	NOTCH1-mutant CLL	NOTCH Quiescence Plasma cell T cell-myeloid-FDC	NOTCH1 Immune checkpoints
A53	5.8%	63% (All) 33% (ABC) 100% (GCB)	*TP53* inactivation/DNA damage Aneuploidy Immune evasion - *B2M* loss BCR: IgM >> IgG; $IgV_H4\text{-}34^{++}$	–	p53 Immune low	BCR-dep. NF-κB
BN2	13.3%	67% (All) 76% (ABC) 100% (GCB) 38% (UC)	NOTCH2 signaling Altered B cell differentiation BCR-dependent NF-κB Immune evasion - *CD70* loss Proliferation - Cyclin D3 BCR: IgM >> IgG; $IgV_H4\text{-}34^{++}$	MZL Transformed MZL	B cell activation NF-κB NOTCH Proliferation	BCR-dep. NF-κB PI3 kinase mTORC1 BCL2 NOTCH2
ST2	6.4%	84% (All) 81% (GCB)	JAK/STAT3 signaling NF-κB activation *P2RY8*– *GNA13* inactivation Altered B cell differentiation BCR: IgG >> IgM	NLPHD THRLBCL	GC B cell PI3K signaling JAK2 signaling Glycolysis Stromal	PI3 kinase JAK2
MYC+ / MYC–	5.9% (MYC^+) 17.6% (MYC^-)	48% (MYC^+) 82% (MYC^-)	Chromatin modification Anti-apoptosis PI3 kinase signaling *S1PR2*– *GNA13* inactivation Altered T_{FH} interactions MYC (EZB-MYC^+) BCR: IgG > IgM	FL Transformed FL BL (EZB-MYC^+)	GC LZ (MYC^-) GC IZ (MYC^+) BCL6 (MYC^+) TCF3 (both) T_{FH} cells (MYC^-) Stromal (MYC^-) Immune low (MYC^+)	PI3 kinase mTORC1 EZH2 BCL2-MCL1

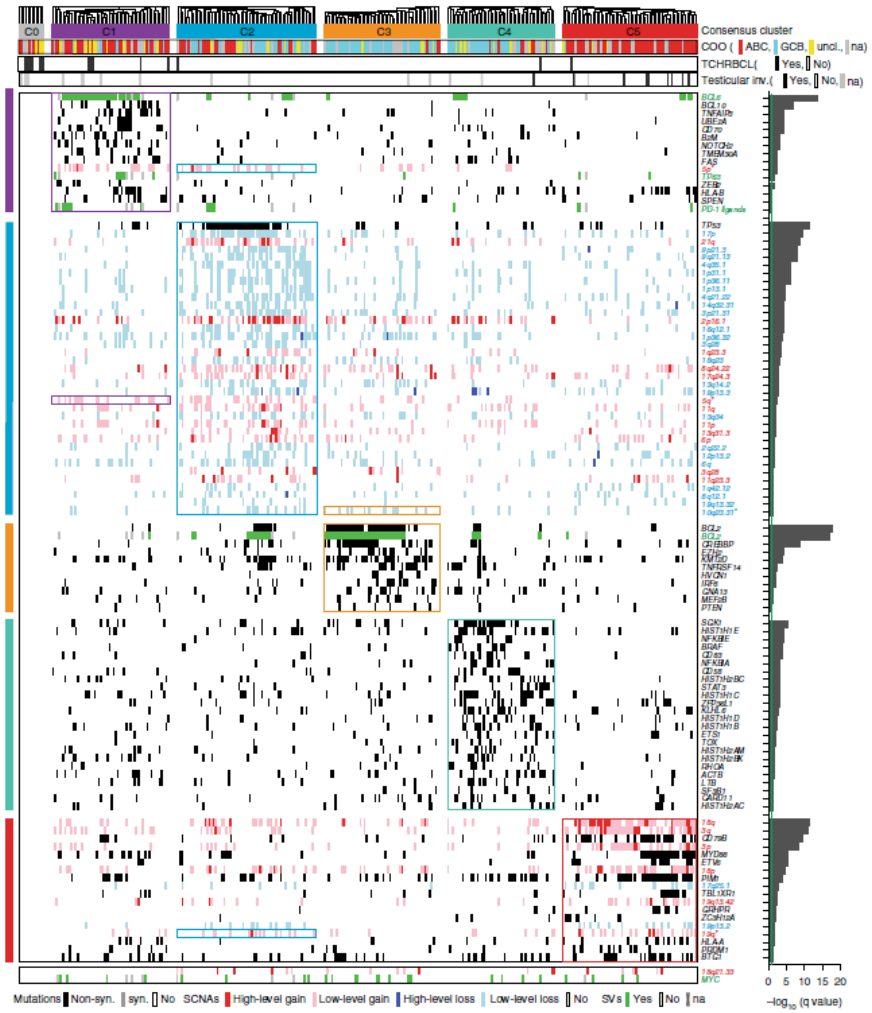


Figure 8. Implications of the DLBCL Genetic Subtypes for Pathogenesis and Therapy

(A) Summary of the relationship between DLBCL COO subgroups and the genetic subtypes (left). The genetic themes, phenotypic attributes, clinical correlates, and treatment implications of each subtype are shown at right. Prevalences were estimated using the NCI cohort, adjusting for a population-based distribution of COO subgroups (see STAR Methods). dep., dependent; FDC, follicular dendritic cell; LZ, light zone; IZ, intermediate zone.

(B) Models of selection for shared genetic features in DLBCL subtypes.

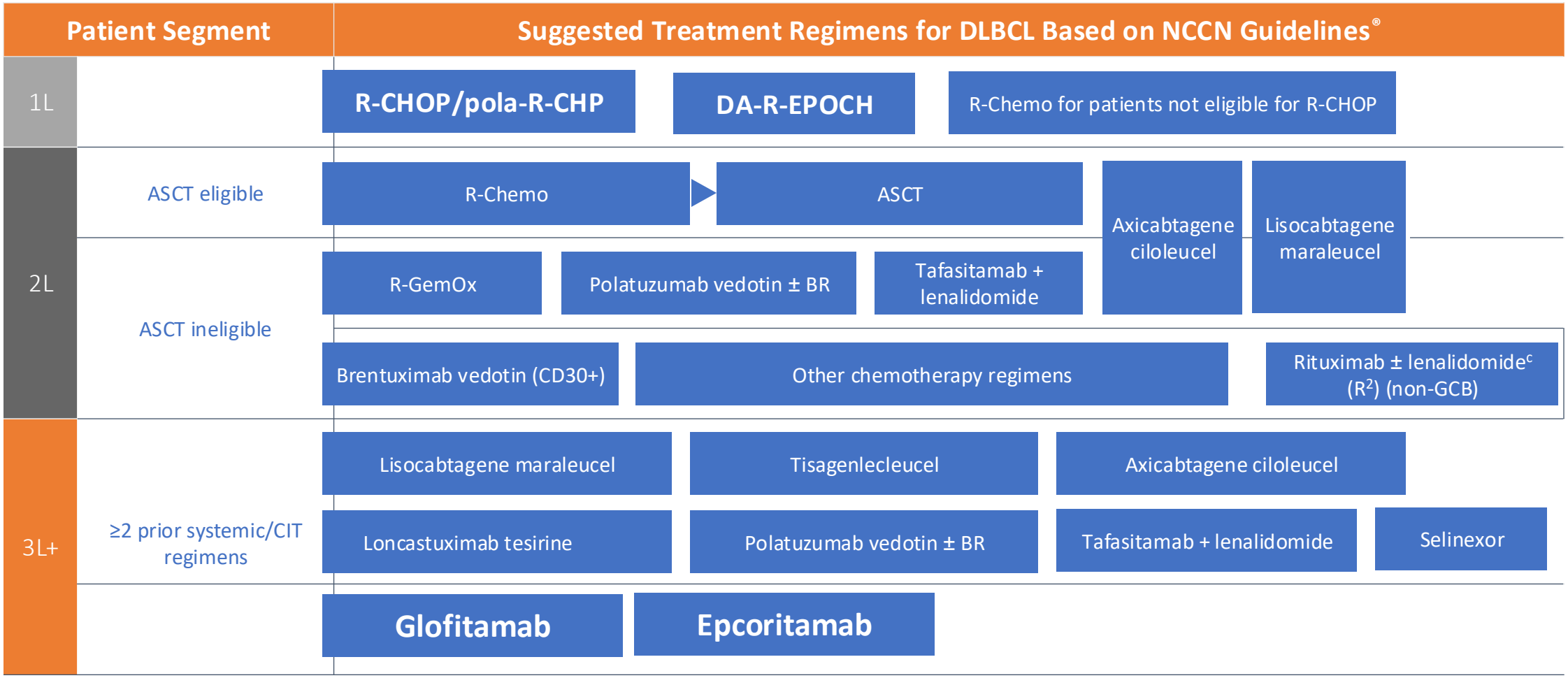
(C) Models accounting for genetic attributes shared by DLBCL genetic subtypes and indolent NHLs.

(D) Model of EZB-MYC^+ and EZB-MYC^- evolution.

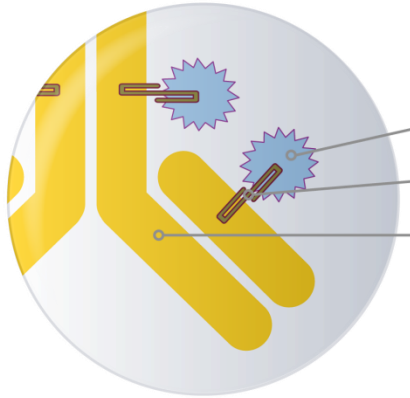
Wright et al, 2020

Chapuy et al, 2018

Current treatment landscape in DLBCL



Polatuzumab Vedotin – an ADC (Antibody-Drug conjugate)

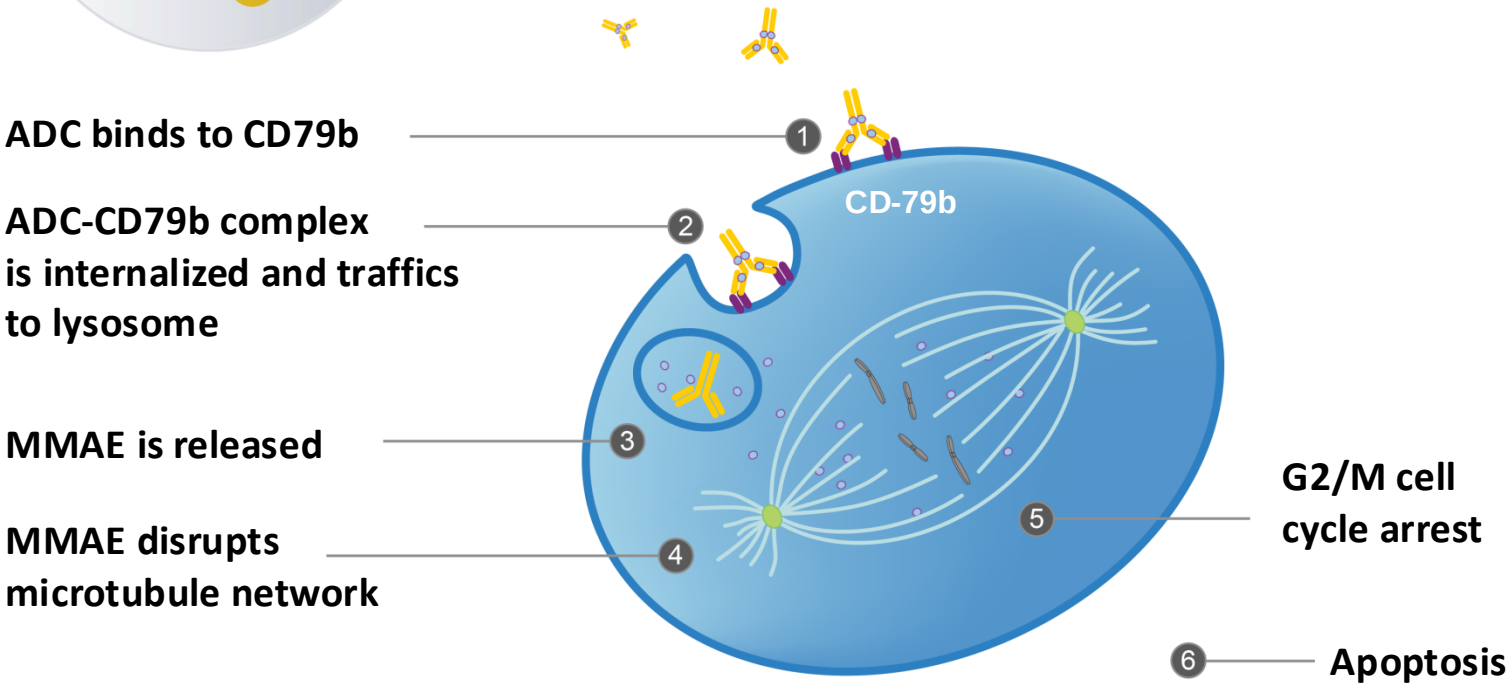


Polatuzumab vedotin antibody-drug conjugate (ADC)

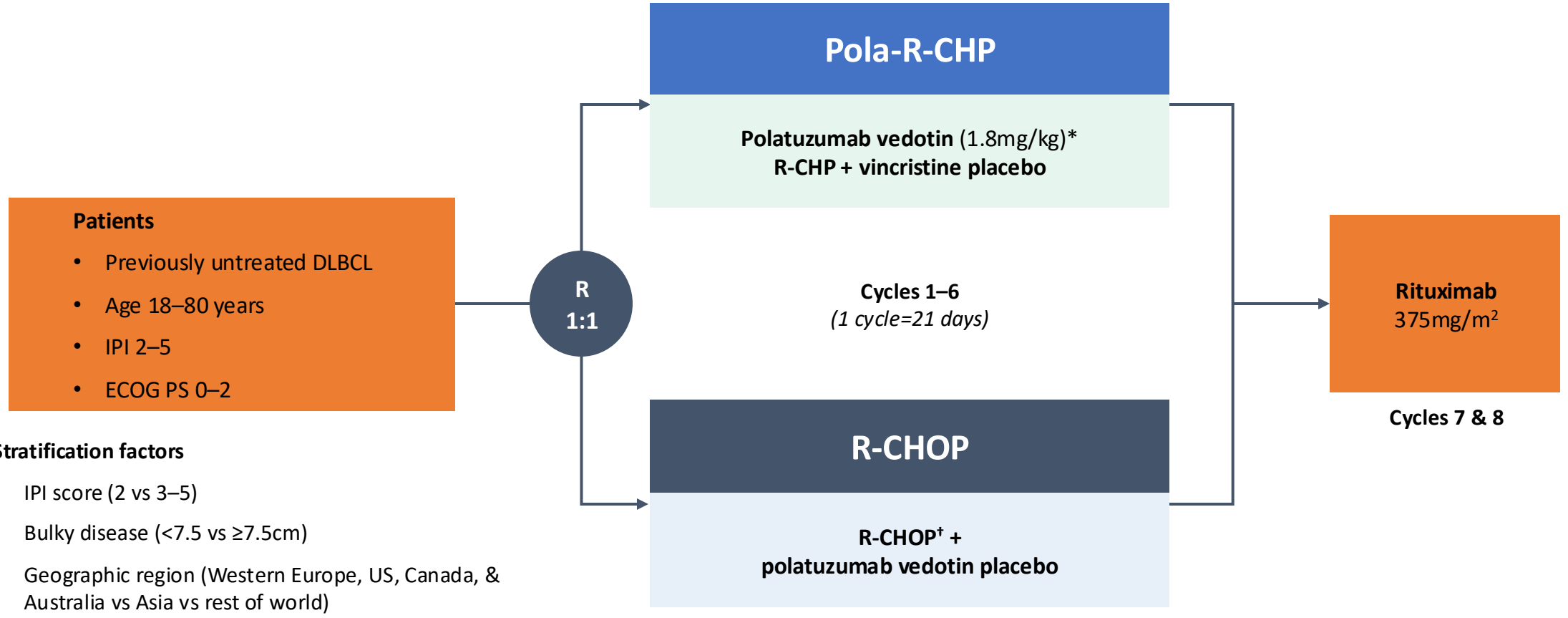
Monomethyl auristatin E (MMAE), microtubule-disrupting agent

Protease-cleavable linker

Anti-CD79b monoclonal antibody



POLARIX – a randomized double-blinded study



Stratification factors

- IPI score (2 vs 3–5)
- Bulky disease (<7.5 vs ≥7.5cm)
- Geographic region (Western Europe, US, Canada, & Australia vs Asia vs rest of world)

*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.

IPI, International prognostic index; ECOG PS, Eastern Cooperative Oncology Group performance status; R, randomized.

Tilly et al. *NEJM* 2021

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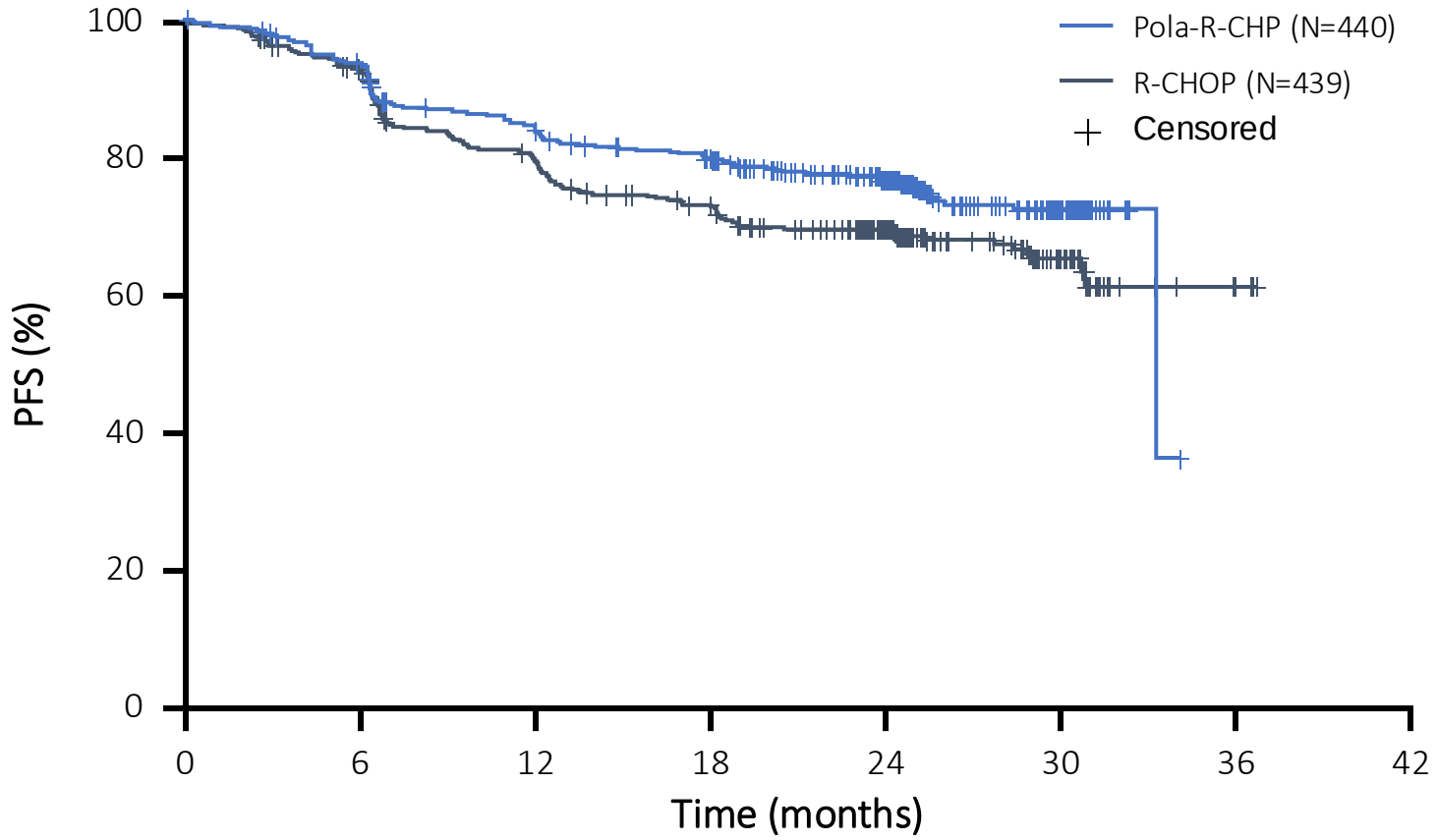
POLARIX Primary endpoint: Progression-free survival



No. of patients at risk								
Pola-R-CHP	440	404	353	327	246	78	NE	NE
R-CHOP	439	389	330	296	220	78	3	NE

HR 0.73 **(P<0.02)**

95% CI: 0.57, 0.95

- Pola-R-CHP demonstrated a **27% reduction in the relative risk of disease progression, relapse, or death** versus R-CHOP
- **24-month PFS:** 76.7% with Pola-R-CHP versus 70.2% with R-CHOP (**Δ=6.5%**)

ITT population. Data cut-off: June 28, 2021; median 28.2 months' follow-up.
NE, not evaluable.

Tilly et al. *NEJM* 2021

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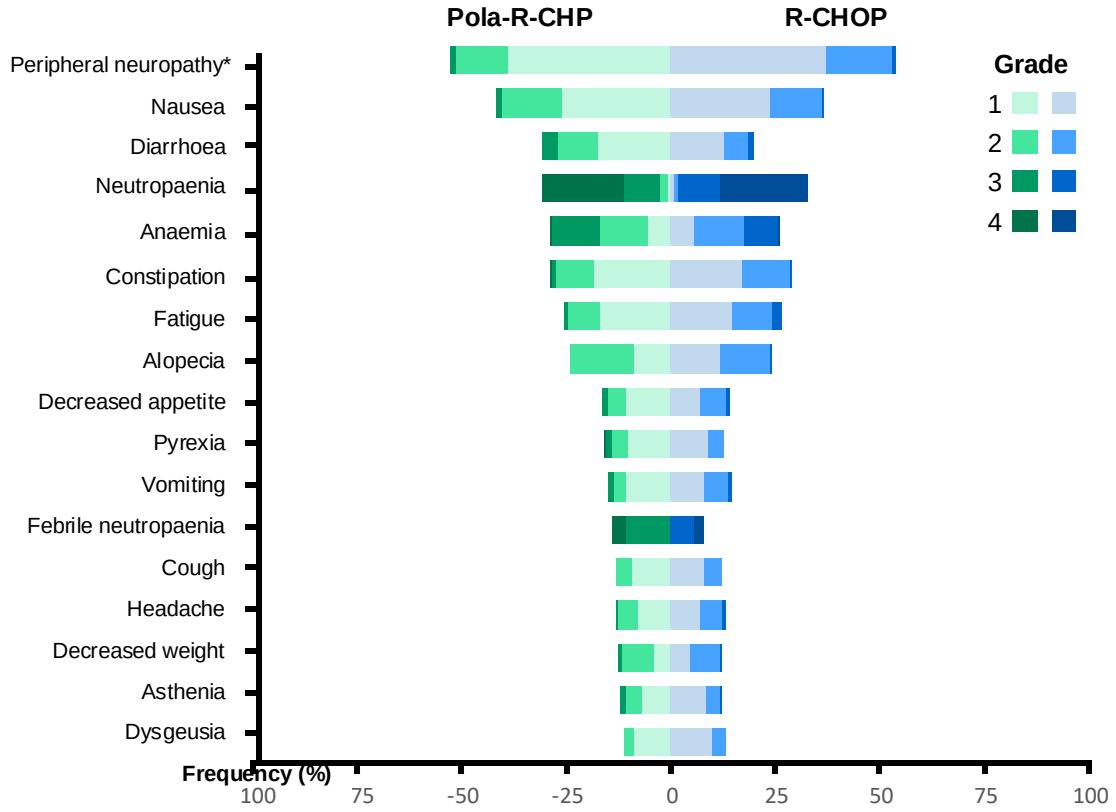
POLARIX: Safety summary

n (%)	Pola-R-CHP (N=435)	R-CHOP (N=438)
Any-grade adverse events	426 (97.9)	431 (98.4)
Grade 3–4	251 (57.7)	252 (57.5)
Grade 5	13 (3.0)	10 (2.3)
Serious adverse events	148 (34.0)	134 (30.6)
Adverse events leading to:		
Discontinuation of any study drug	27 (6.2)	29 (6.6)
Polatuzumab vedotin / vincristine	19 (4.4)	22 (5.0)
Dose reduction of any study drug	40 (9.2)	57 (13.0)

Common adverse events



Tilly et al. *NEJM* 2021

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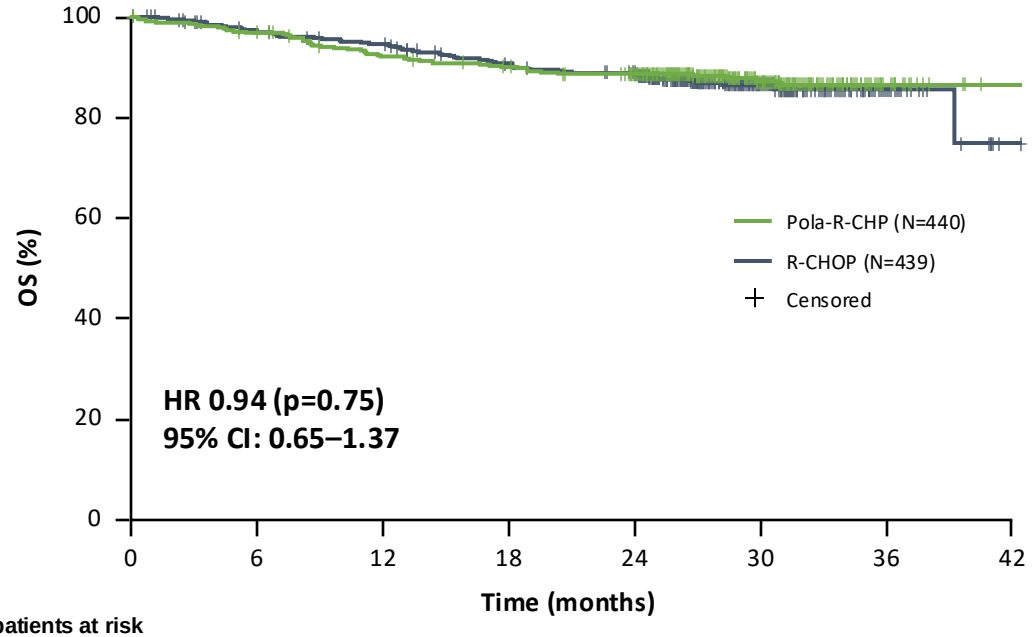
POLARIX: Overall Survival

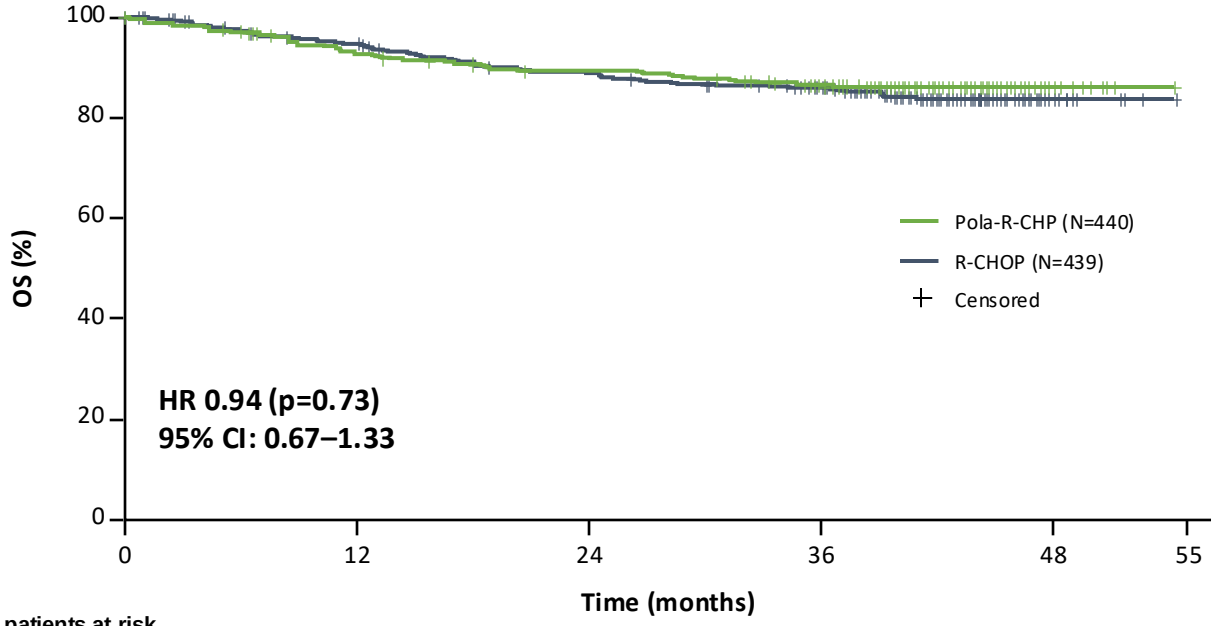
Primary analysis (CCOD: June 28, 2021)[1]
Median follow-up: 28.2 months



No. of patients at risk

Pola-R-CHP	440	423	397	384	362	140	15	1
R-CHOP	439	414	401	376	355	132	20	1

Updated results (CCOD: June 15, 2022)
Median follow-up: 39.7 months



No. of patients at risk

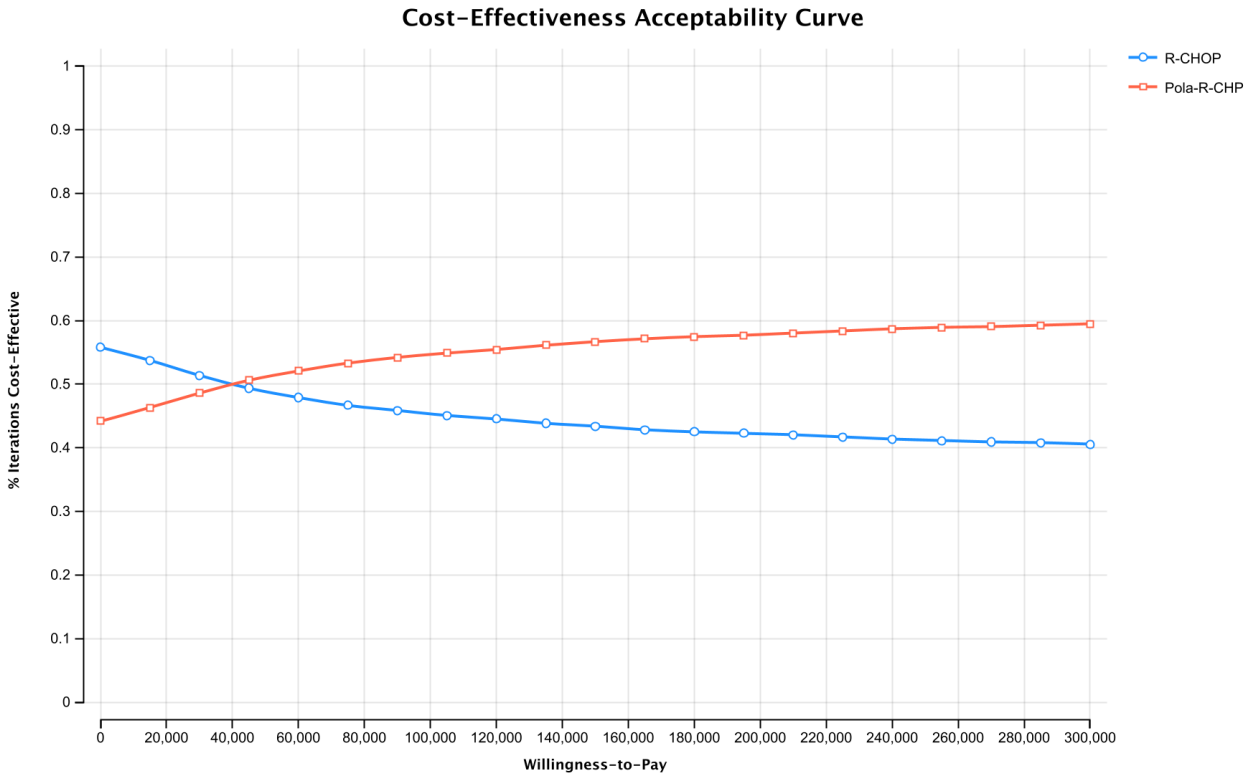
Pola-R-CHP	440	423	398	387	379	371	338	129	13	1
R-CHOP	439	415	403	382	372	361	329	124	18	1

No new safety signals have been identified with longer follow-up compared with the primary analysis

Analysis based on the ITT population. Analysis of OS was time-driven, and was a prespecified, statistically tested analysis.

Tilly et al. *NEJM* 2022

Cost-effectiveness of Pola-R-CHP



Assuming a 5-year PFS of 69.6% with pola-R-CHP and 62.7% with RCHOP, pola-R-CHP was cost-effective at a willingness to pay of $150,000

Pola-R-CHP was no longer cost effective if its 5-year PFS was ≤66.1%

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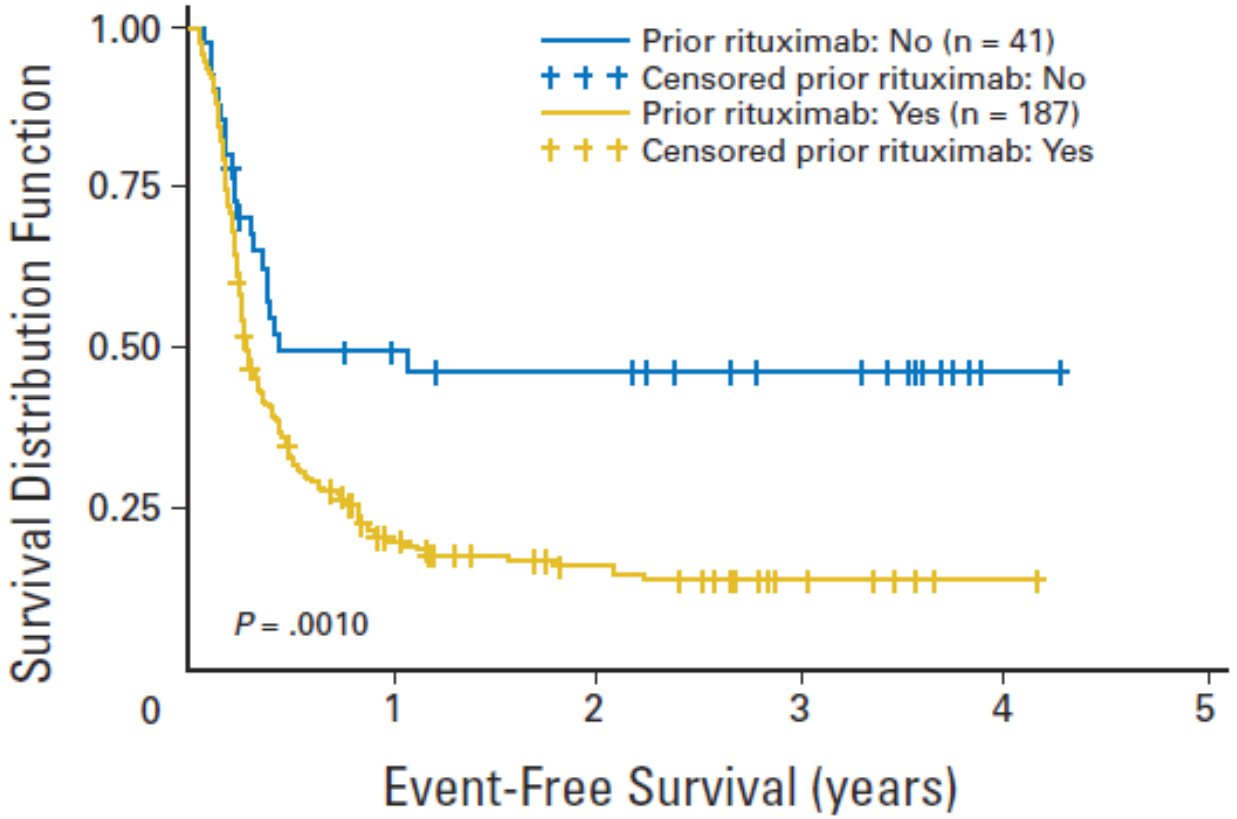
Kambhampati et al. *Blood* 2022

Early relapse after R-CHOP -> Poor outcomes

1º refractory/early relapse after prior rituximab

- 2L salvage intent-to-transplant outcomes:
  - ORR 46%
  - 3y EFS 20%
  - 3y OS 39%

CORAL



Greenbrecht et al, *JCO* 2010

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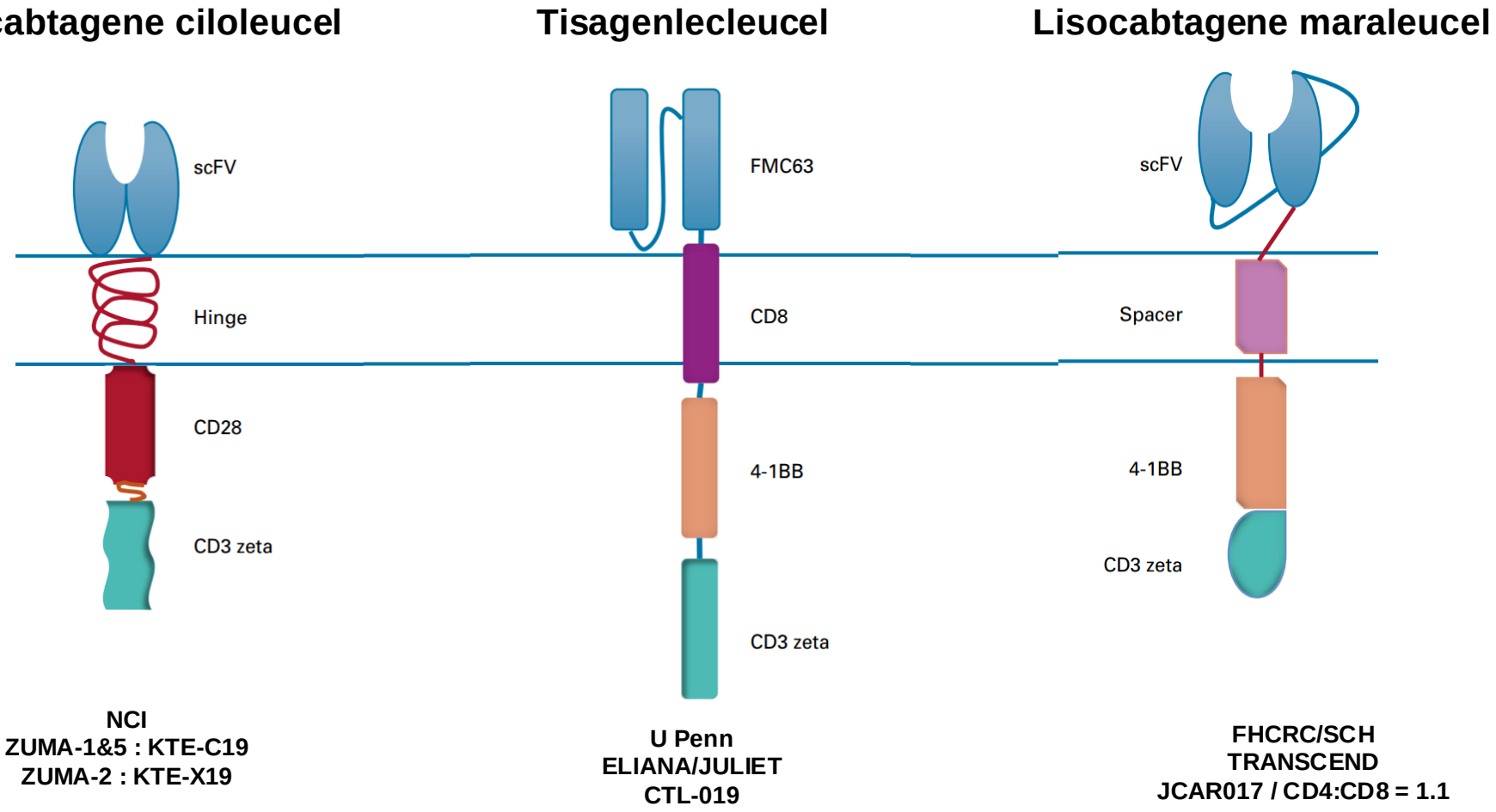
CAR T cell Vectors



Jacobson et al, *JCO* 2018

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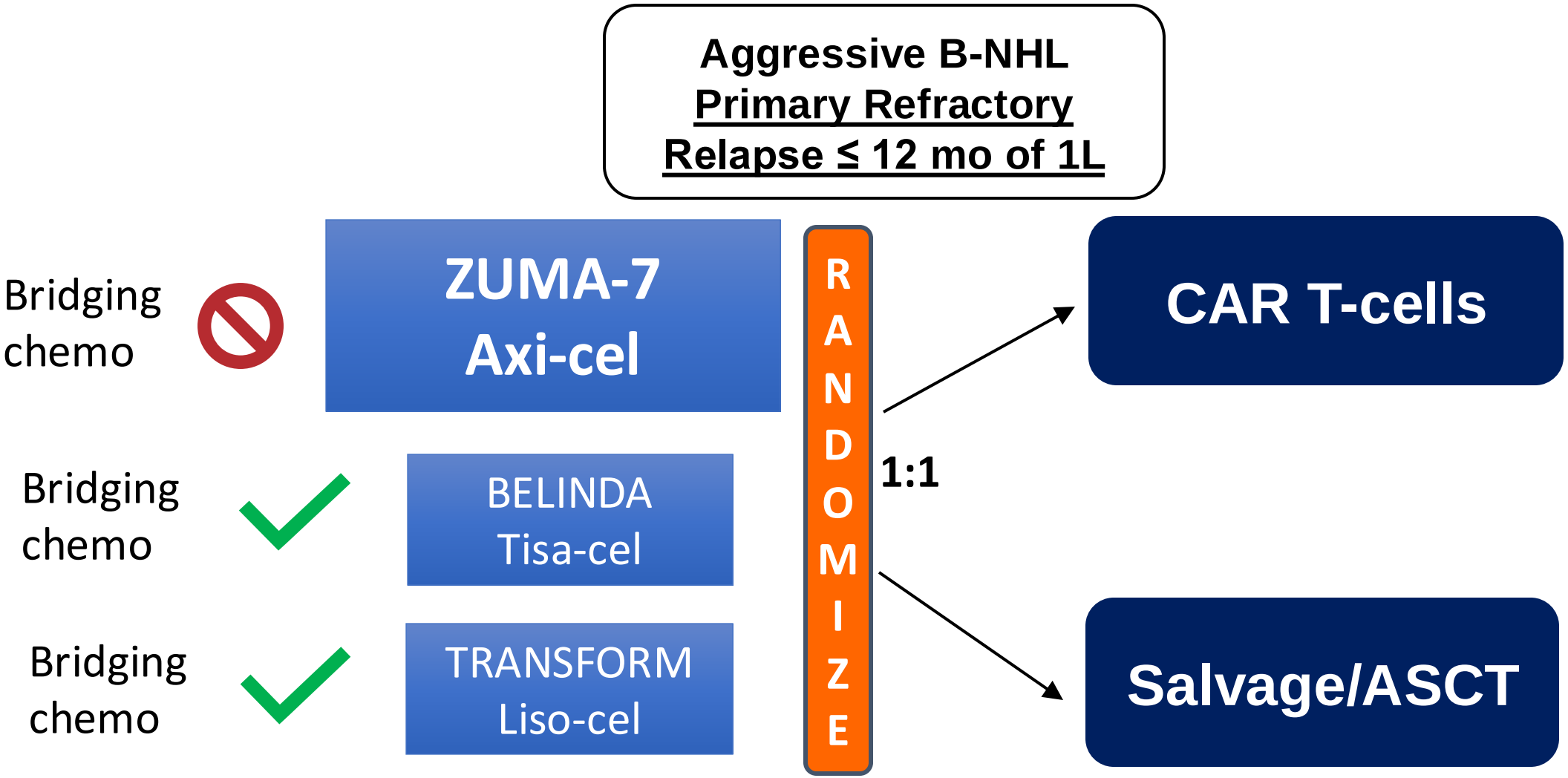
CAR T cells in 2nd line



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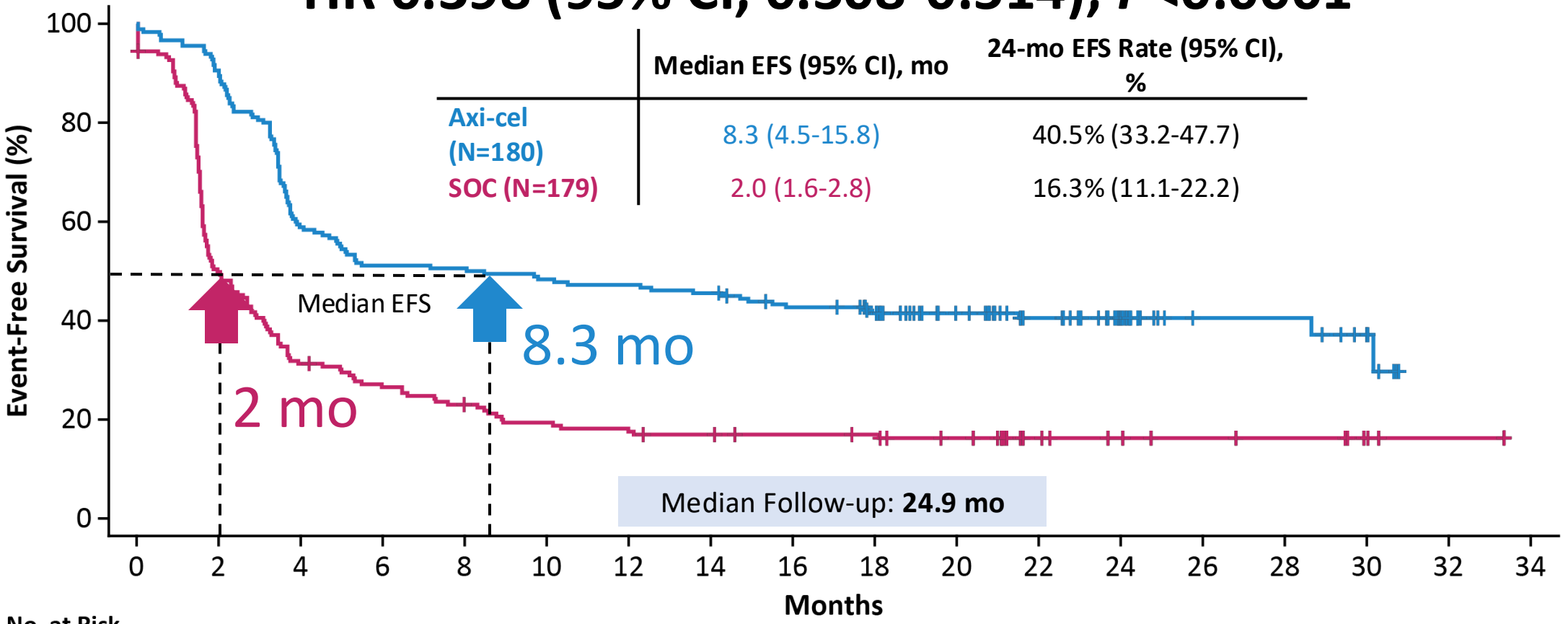
Primary EFS Endpoint: Axi-Cel Is Superior to SOC

HR 0.398 (95% CI, 0.308-0.514); *P*<0.0001

	Median EFS (95% CI), mo	24-mo EFS Rate (95% CI), %
Axi-cel (N=180)	8.3 (4.5-15.8)	40.5% (33.2-47.7)
SOC (N=179)	2.0 (1.6-2.8)	16.3% (11.1-22.2)



No. at Risk																
Axi-cel	180	163	106	92	91	87	85	82	74	67	52	40	26	12	12	6
SOC	179	86	54	45	38	32	29	27	25	24	20	12	9	7	6	3	1

Locke FL, et al ASH 2021. NEJM 2021

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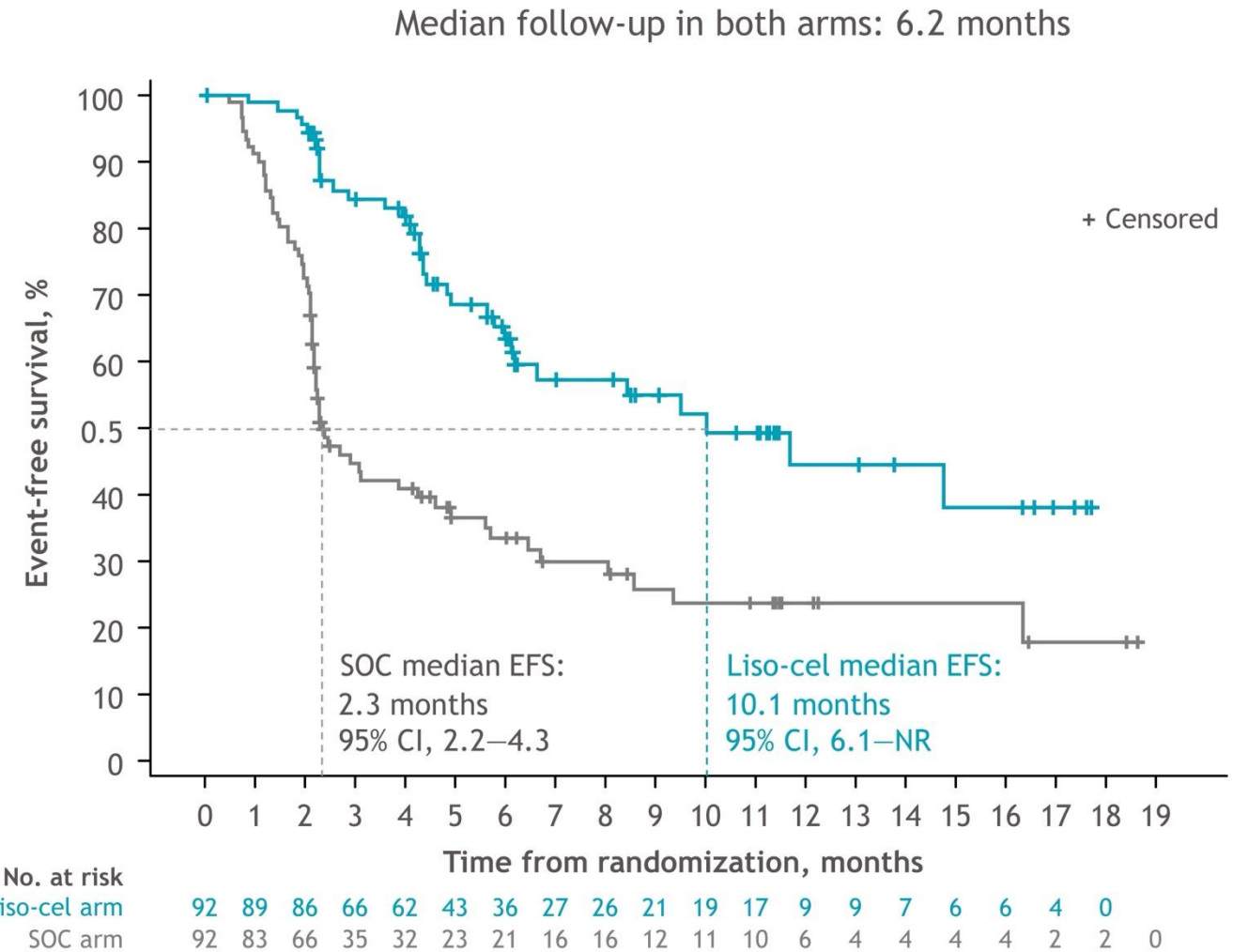
TRANSFORM: Event-free survival per IRC (ITT set; primary endpoint)



	Liso-cel arm (n = 92)	SOC arm (n = 92)
Patients with events, n	35	63
Stratified HR (95% CI)	**0.349** (0.229—0.530)	
	***P* < 0.0001**	
6-month EFS rate, % (SE)	63.3 (5.77)	33.4 (5.30)
Two-sided 95% CI	52.0—74.7	23.0—43.8
12-month EFS rate, % (SE)	44.5 (7.72)	23.7 (5.28)
Two-sided 95% CI	29.4—59.6	13.4—34.1

One-sided *P* value significance threshold to reject the null hypothesis was < 0.012

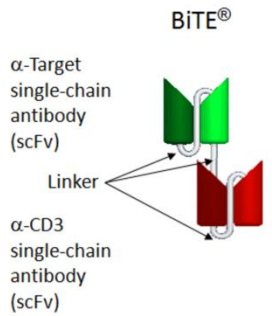
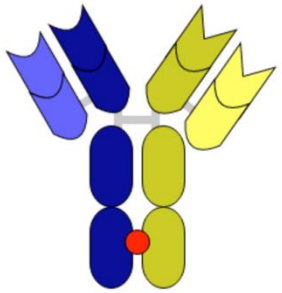
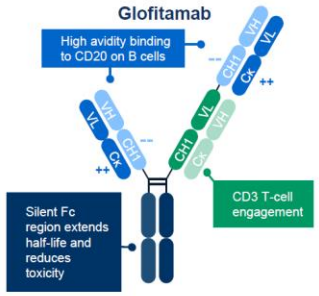
EFS is defined as the time from randomization to death due to any cause, progressive disease, failure to achieve CR or PR by 9 weeks post-randomization or start of a new antineoplastic therapy due to efficacy concerns, whichever occurs first.
CI, confidence interval; HR, hazard ratio; NR, not reached; SE, standard error.

Kamdar M, et al. ASH 2021 [Abstract #91]

CAR T cells in 2nd line: Safety

Safety	ZUMA-7[1] (N=338) R/R LBCL	BELINDA[2] (N=322) R/R aNHL	TRANSFORM[3] (N=183) R/R LBCL
Treatment arm	Axi-cel (n=170)	Tisa-cel (n=162)	Liso-cel (n=92)
Treatment-related deaths, n	1	10	1
CRS Any grade, n (%) Grade ≥3, n (%) Median time to onset, days Median time to resolution, days	 157 (92) 11 (6) 3 7	 95 (59) 8 (5) Not reported Not reported	 45 (49) 1 (1) 5 4
Neurologic events Any grade, n (%) Grade ≥3, n (%) Median time to onset, days Median time to resolution, days	 102 (60) 36 (21) 7 9	 16 (10) 3 (2) Not reported Not reported	 11 (12) 4 (4) 11 6

Bi-Specific antibodies in Non-Hodgkin lymphoma

The Original: Proof of Concept	Received regulatory approval		
Blinatumomab[1]	**Epcoritamab[2]**	**Mosunetuzumab[3]**	**Glofitamab[4]**
			
CD3 (scFV) x CD19 (scFV)	DuoBody- CD3 x CD20 BsAb	CD3 x CD20 Knobs-in-hole Fc BsAb	CD3 (Fab) x CD20 (Fab x2) Fc BsAb

Properties of the BsAbs vary by construct

Distinguishing features of BsAbs include:

- **Off-the-shelf** – rapid access, relative ease of delivery
- **Adaptable** – lack of persistence and ability to modulate dosing may improve tolerability

1. Queudeville M, et al. *Onco Targets Ther*. 2017;10:3567-3578. 2. Clausen MR, et al. *J Clin Oncol*. 2021;39(suppl 15):7518. 3. Budde LE, et al. *Blood*. 2018;132(suppl 1):399. 4. Hutchings M, et al. *Blood*. 2020;136(suppl 1):45-46.

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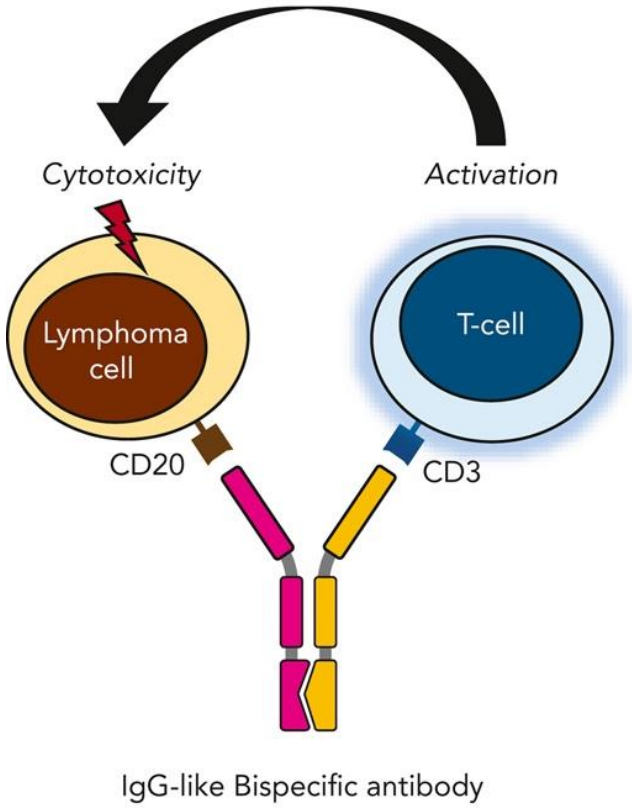
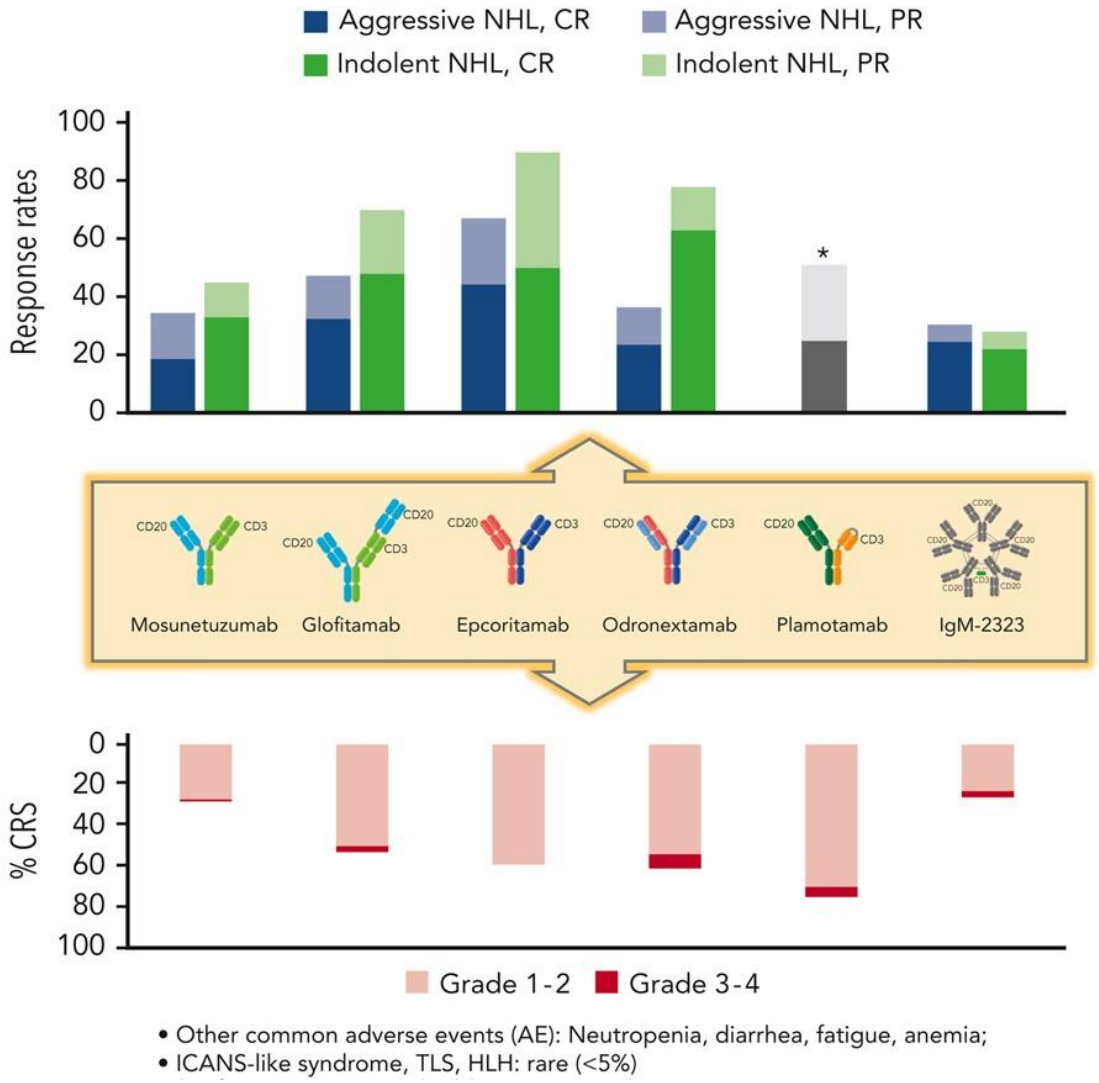
Bispecific Antibodies in B-cell NHL





*Data for aggressive NHL and indolent NHL reported in aggregate.

CR, complete response; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell-associated neurotoxicity syndrome; NHL, non-Hodgkin lymphoma; PR, partial response; TLS, tumor lysis syndrome

1. Falchi L, Vardhana SA, Salles GA. *Blood.* 2023;141:467-480.

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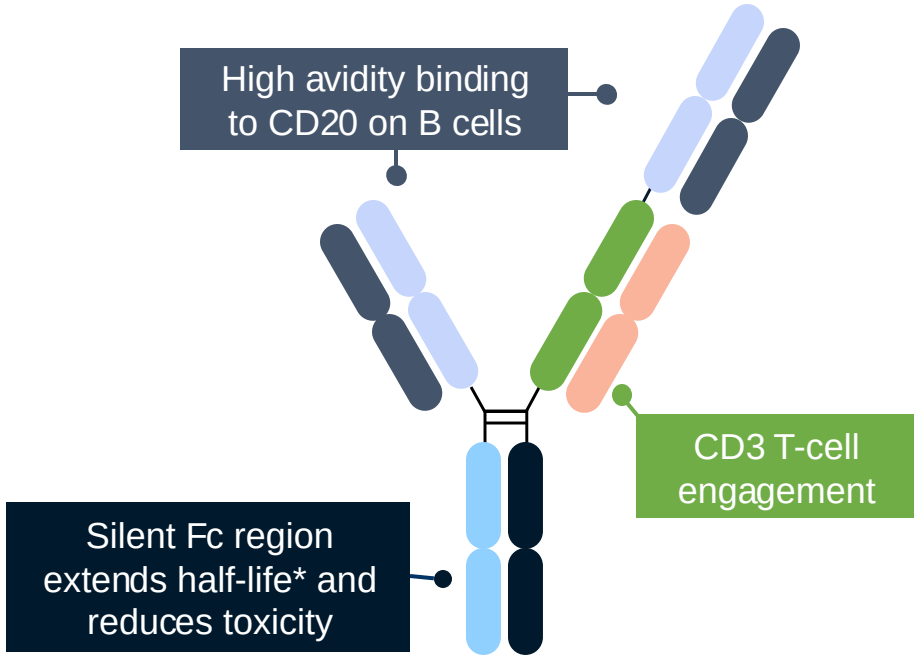
Glofitamab: a 2:1 CD20xCD3 bispecific antibody

- **Glofitamab**
  - Off-the-shelf treatment delivered in a fixed course of 12 three-weekly cycles[1,2]
- **Phase II experience (NCT03075696)[2]**
  - Glofitamab has induced high CR rates and demonstrated manageable toxicity in patients with R/R LBCL[3]

Glofitamab: *CD20xCD3 bispecific antibody with 2:1 format for increased potency vs 1:1 format[1]*



Aim: to report an extended follow-up and landmark analyses in patients with R/R LBCL who achieved a CR after receiving glofitamab monotherapy

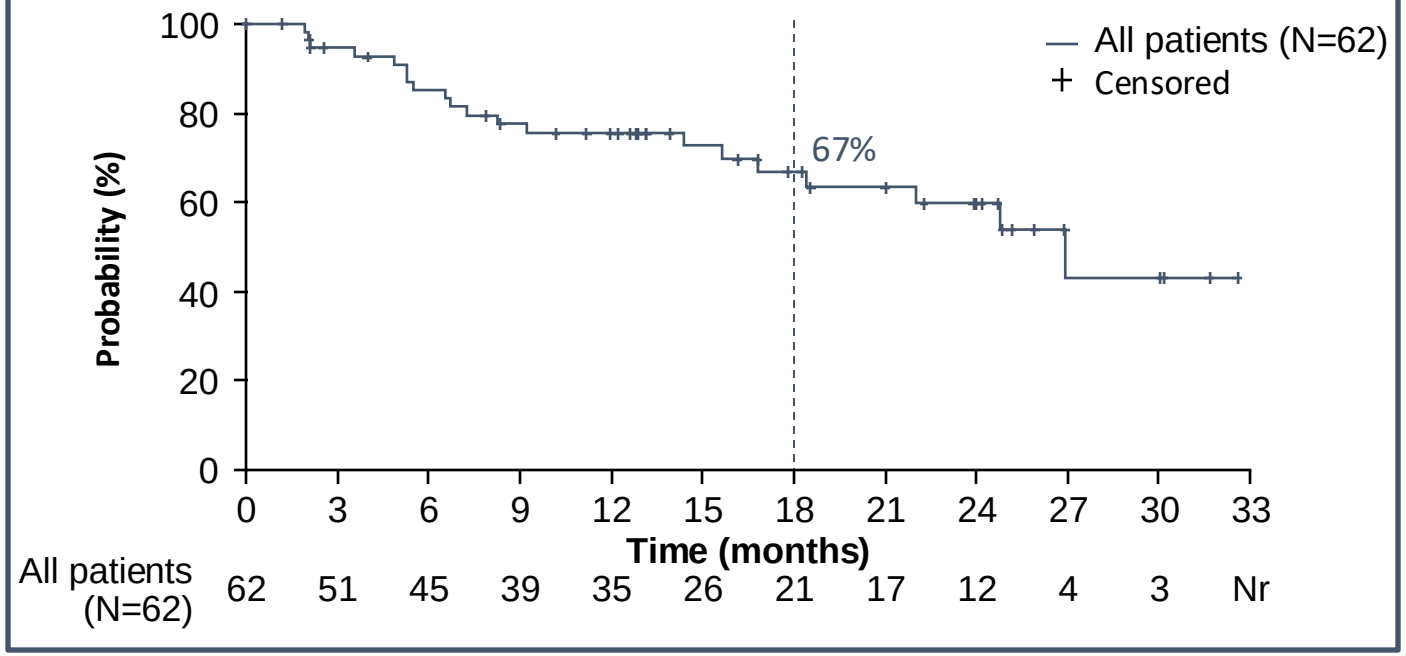
*Compared with non-Fc bearing T-cell engaging bispecific antibodies.[1,4] CR, complete response; Fc, fragment crystallized; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

1. Bacac, et al. Clin Cancer Res 2018; 2. NCT03075696. Available at: https://clinicaltrials.gov; 3. Dickinson MJ, et al. N Engl J Med 2022;387:2220–31; 4. Bacac M, et al. Oncoimmunol 2016;e1203498.

Complete responses to glofitamab were durable

	IRC (N=155)*
CR rate†, n (%) [95% CI]	62 (40) [32.2–48.2]
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]
Median CR follow-up, months (range)	18.2 (0–33)
18 months DoCR, n (%) [95% CI]	67.0 (53.3–80.8)
Ongoing CRs, n/N (%)	42/62 (68)
Median DoCR, months (95% CI)	26.9 (18.4–NR)

DoCR by IRC (n=62)



- The median time on study was 21.2 months (range: 0–34)

An estimated 67% of patients with a CR at any time remained in remission at 18 months

*Intent-to-treat population. †Best overall response. CI, confidence interval; NR, not reached.

Dickinson M, et al. ICML 2023.

DLBCL: Take-Home points

- Pola-R-CHP provides a novel first-line therapy with ↑ PFS
- Primary refractory/early relapsing patients:
  - CAR T-cell therapy is preferred
  - CAR T-cell therapy may be futile for uncontrollable disease
- ASCT suitable in pts with excellent response to salvage therapy and relapse > 12 months
- BsAb and novel therapies are available for patients who are not candidates or failed CAR T-cell therapy

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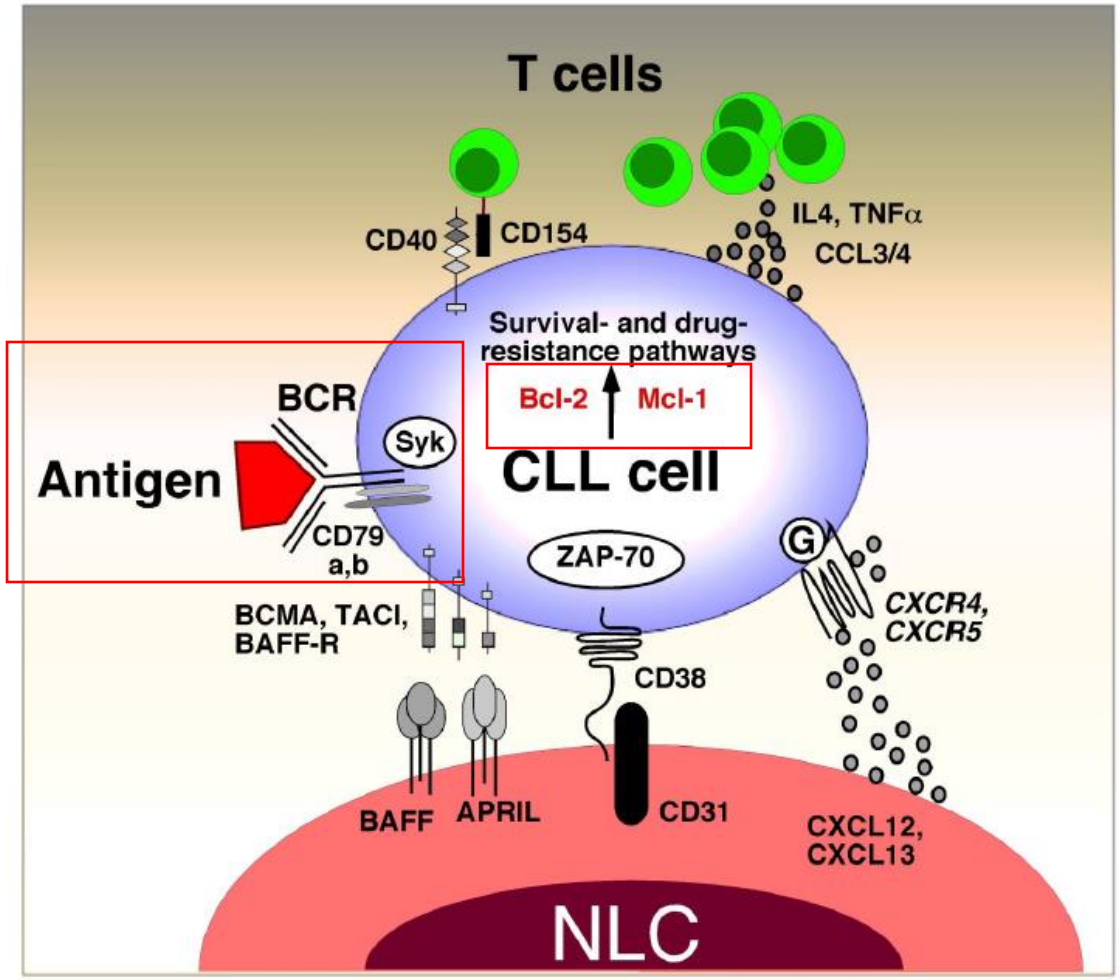
Indolent NHL

CLL cell survival is driven by microenvironment signaling



After Burger J, 2013

Frontline Phase III Randomized Trials in CLL

BTKi	BCL2i
RESONATE-2 (>65 or comorbidities) **Ibrutinib** *vs.* **Chlorambucil**	**CLL14** (CIRS >6; CrCl <70 mL/min) **Venetoclax + O** *vs.* **Chlorambucil + O**
iLLUMINATE (PCYC-1130) (>65 or comorbidities) **Ibrutinib + O** *vs.* **Chlorambucil + O**	
ECOG E1912 [<70; non-del(17p)] **Ibrutinib + R** *vs.* **FCR**	
Alliance A041202 (>65) **Ibrutinib** *vs.* **Ibrutinib + R** *vs.* **BR**	
ELEVATE-TN (>65 or comorbidities) **Acala** *vs.* **Acala + O** *vs.* **Chlorambucil + O**	
SEQUOIA [≥65 OR comorbidities; non-del(17p)] **Zanubrutinib** *vs.* **BR**	
FLAIR [≤75; non-del(17p)] **Ibrutinib + R** *vs.* **FCR**	

City of Hope.

ALPINE Study Design (NCT03734016)

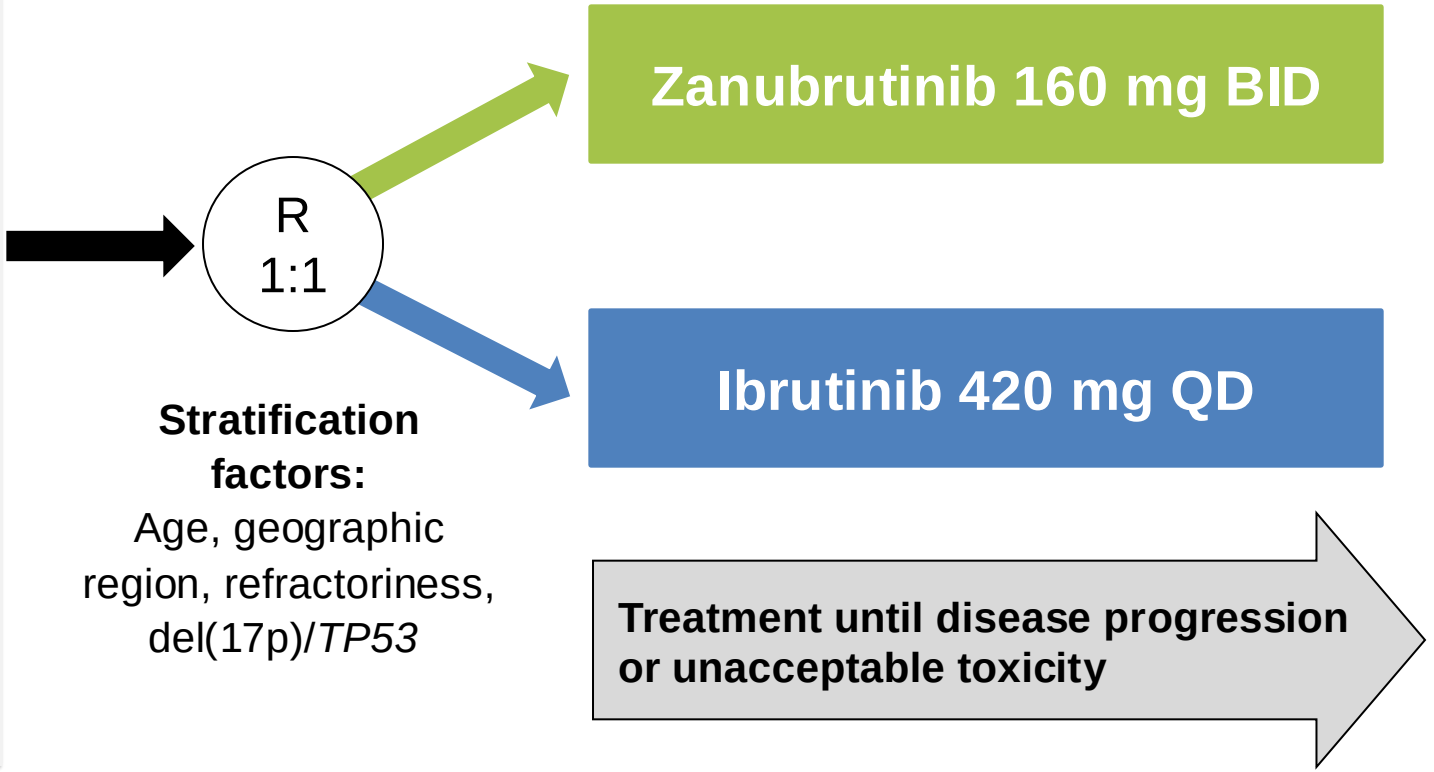
R/R CLL/SLL with ≥1 prior treatment
(N=652)

Key Inclusion Criteria

- R/R to ≥1 prior systemic therapy for CLL/SLL
- Measurable lymphadenopathy by CT or MRI
- Requires treatment per iwCLL

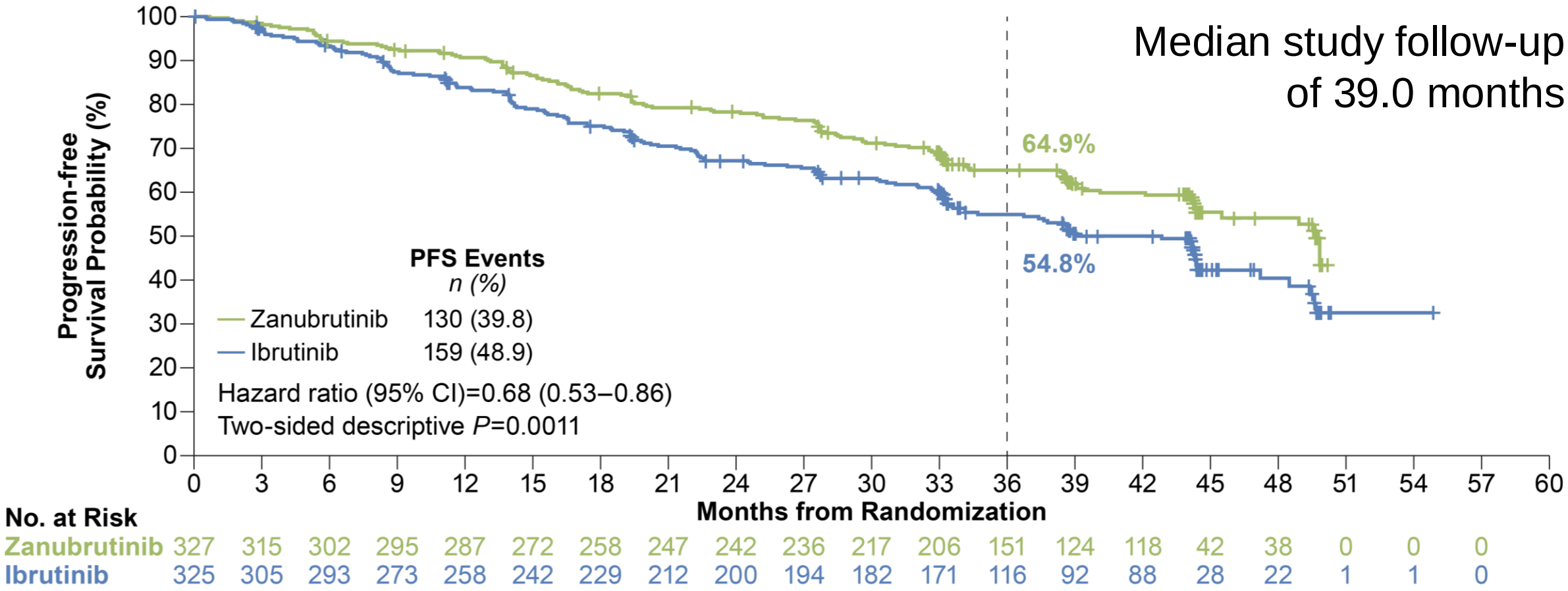
Key Exclusion Criteria

- Prior BTK inhibitor therapy
- Treatment with warfarin or other vitamin K antagonists



Brown JR, Eichhorst B, Hillmen P, et al. *N Engl J Med*. 2023;388:319-332.

Zanubrutinib Sustains PFS Benefit Over Ibrutinib At Extended Follow-up

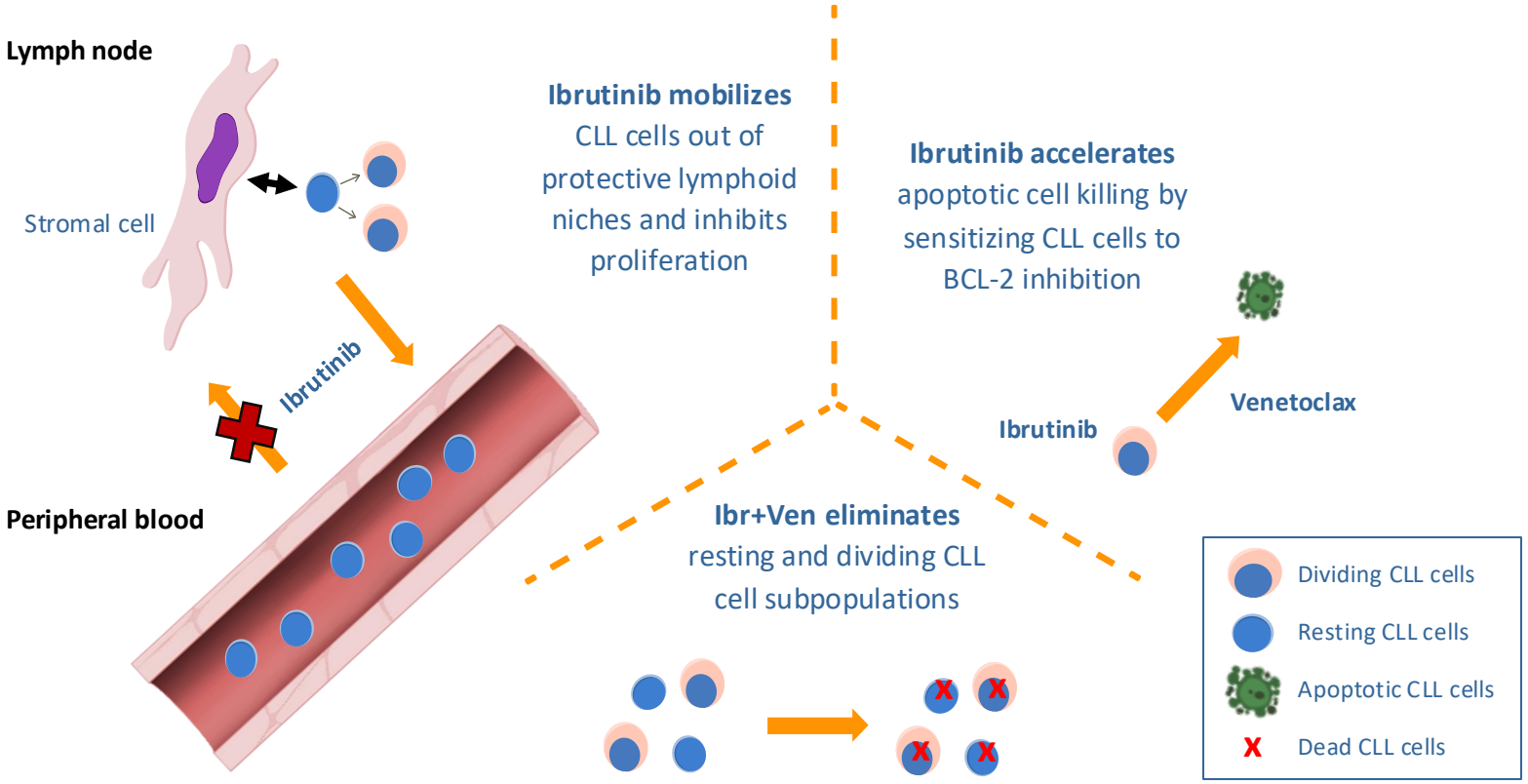


Data cutoff: 15 Sep 2023

Frontline Phase III Randomized Trials in CLL

BTKi	BCL2i	Novel-novel
RESONATE-2 (>65 or comorbidities) Ibrutinib *vs.* Chlorambucil **iLLUMINATE** (PCYC-1130) (>65 or comorbidities) Ibrutinib + O *vs.* Chlorambucil + O **ECOG E1912** [<70; non-del(17p)] Ibrutinib + R *vs.* FCR **Alliance** A041202 (>65) Ibrutinib *vs.* Ibrutinib + R *vs.* BR **ELEVATE-TN** (>65 or comorbidities) Acala *vs.* Acala + O *vs.* Chlorambucil + O **SEQUOIA** [≥65 OR comorbidities; non-del(17p)] Zanubrutinib *vs.* BR **FLAIR** [≤75; non-del(17p)] Ibrutinib + R *vs.* FCR	**CLL14** (CIRS >6; CrCl <70 mL/min) Venetoclax + O *vs.* Chlorambucil + O	**GLOW** (>65 or comorbidities) Ibrutinib + Venetoclax *vs.* Chlorambucil + O **CLL13** I+V+O *vs.* Ven+O *vs.* Ven+R *vs.* FCR/BR **MAJIC** A+V *vs.* V+O **CLL17** I *vs.* Ven+O *vs.* I+V

Ibrutinib + Venetoclax: Distinct and Complementary Modes of Action That Work Synergistically[1-9]

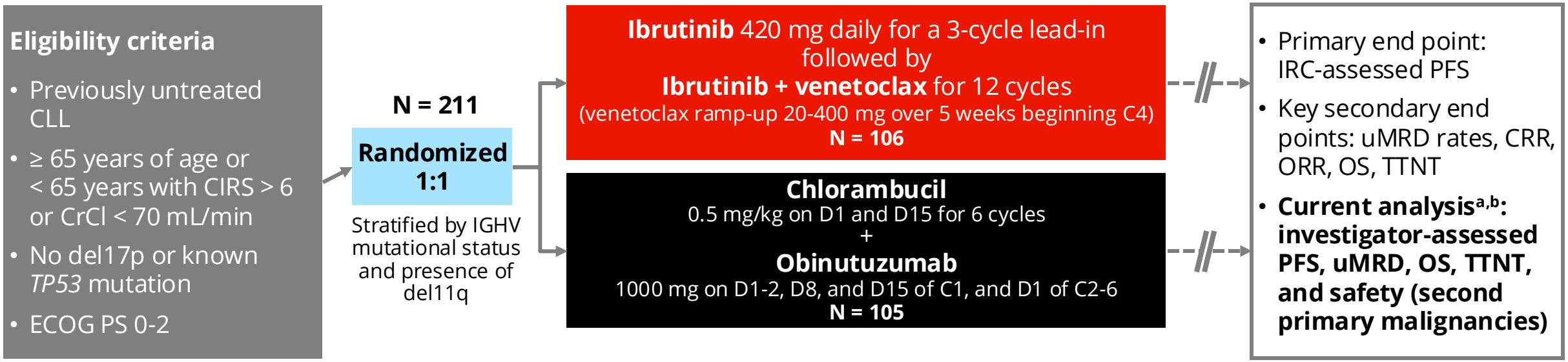


- MRD status is a predictor of PFS in CLL following CIT and FDT with venetoclax + an anti-CD20 antibody, but the relationship has not been explored for Ibr+Ven[10,11]
- We further investigated MRD outcomes and correlation with PFS in the phase 3 GLOW study

BCL-2, B-cell lymphoma-2; CIT, chemoimmunotherapy; CLL, chronic lymphocytic leukemia; FDT, fixed-duration treatment; Ibr+Ven, ibrutinib + venetoclax; MRD, minimal residual disease; PFS, progression-free survival.

1. Lu P, et al. *Blood Cancer J*. 2021;11:39; 2. Deng J, et al. *Leukemia*. 2017;31:2075-2084; 3. Herman ES, et al. *Clin Cancer Res*. 2015;21:4642-4651; 4. Burger JA, et al. *Leukemia*. 2020;34:787-798; 5. Shanafelt T, et al. *N Engl J Med*. 2019;381:432-443; 6. Cervantes-Gomez F, et al. *Clin Cancer Res*. 2015;21:3705-3715; 7. Kater AP, et al. *Blood Adv.* 2021 Sep 23 [Epub ahead of print]; 8. Haselager MV, et al. *Blood*. 2020;136:2918-2926; 9. Slinger E, et al. *Leukemia*. 2017;31:2601-2607; 10. Wierda WG, et al. *Leukemia*. 2021 Jun 24 [Epub ahead of print]; 11. Kater AP, et al. *J Clin Oncol*. 2019;37:269-277.

GLOW: Phase 3 Study (NCT03462719) Evaluating Fixed-Duration Ibr+Ven in Previously Untreated CLL



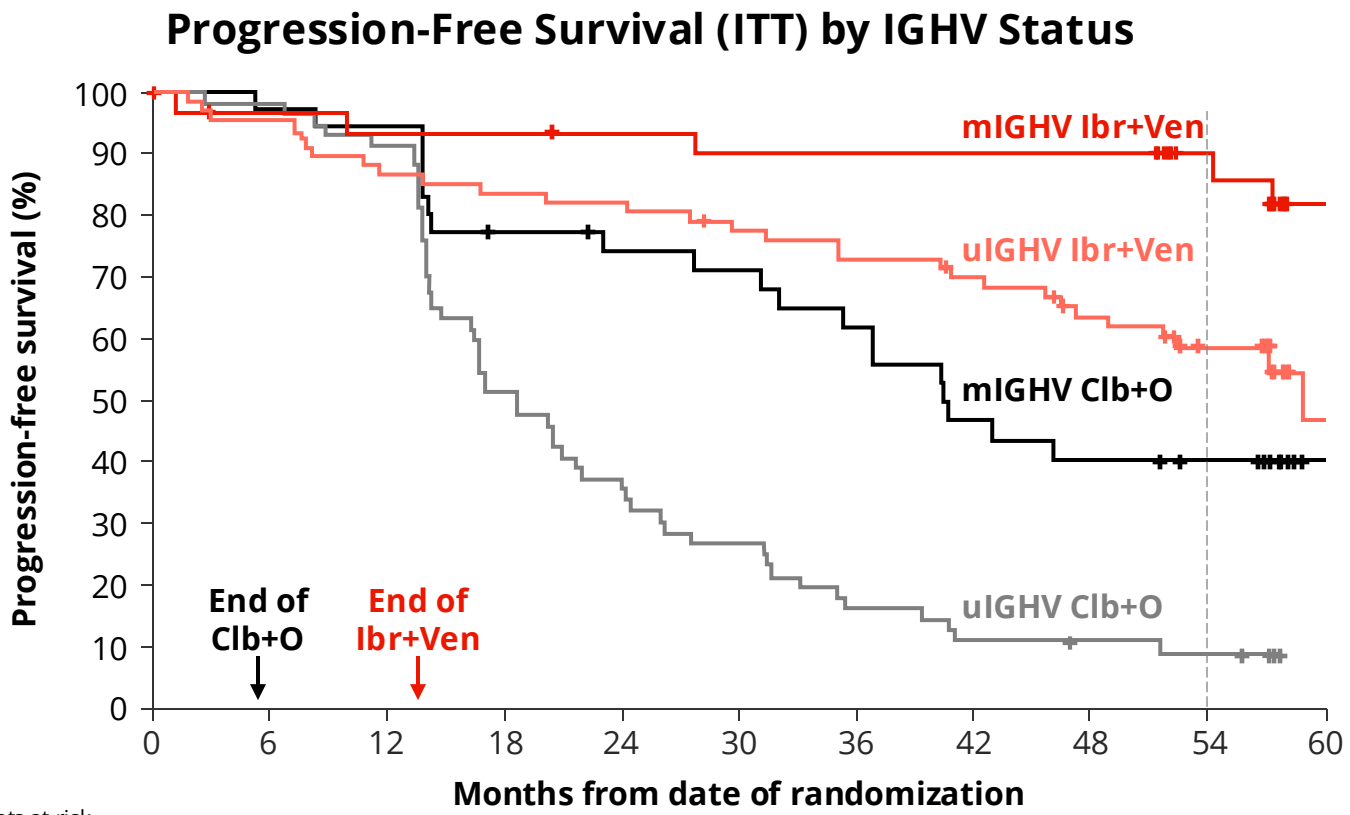
- **Here we present the updated clinical outcomes at a median follow-up of 57.3 months (range, 1.7-65.2)**
- Baseline characteristics (presented previously) were generally balanced between arms and reflective of an elderly and/or comorbid population[1]
- IGHV status at baseline:
  - Ibr+Ven arm: mIGHV 30.2%, uIGHV 63.2%
  - Clb+O arm: mIGHV 33.3%, uIGHV 54.3%

[a]All *p* values are nominal. [b]uMRD in PB by NGS via Clonoseq assay.
C, cycle (28 days); CIRS, Cumulative Illness Rating Scale score; CrCl, creatinine clearance; CRR, complete response rate; D, day; ECOG PS, Eastern Cooperative Oncology Group performance status; IRC, independent review committee; mIGHV, mutated IGHV; NGS, next-generation sequencing; ORR, overall response rate; PB, peripheral blood; uIGHV, unmutated IGHV.

1. Niemann CU, et al. *Lancet Oncol*. 2023;24:1423-1433.

Presented by G. Follows at the 65th ASH Annual Meeting and Exposition; December 9-12, 2023; San Diego, CA, USA

GLOW: At 57 Months of Follow-up, Ibr+Ven Improved PFS Versus Clb+O Regardless of IGHV Status



Patients at risk											
mIGHV Ibr+Ven	32	29	28	28	27	26	26	26	26	22	5
uIGHV Ibr+Ven	67	64	58	56	55	51	48	45	39	30	6
mIGHV Clb+O	35	34	33	26	24	23	20	15	13	9	2
uIGHV Clb+O	57	56	52	29	21	15	9	6	5	4	0

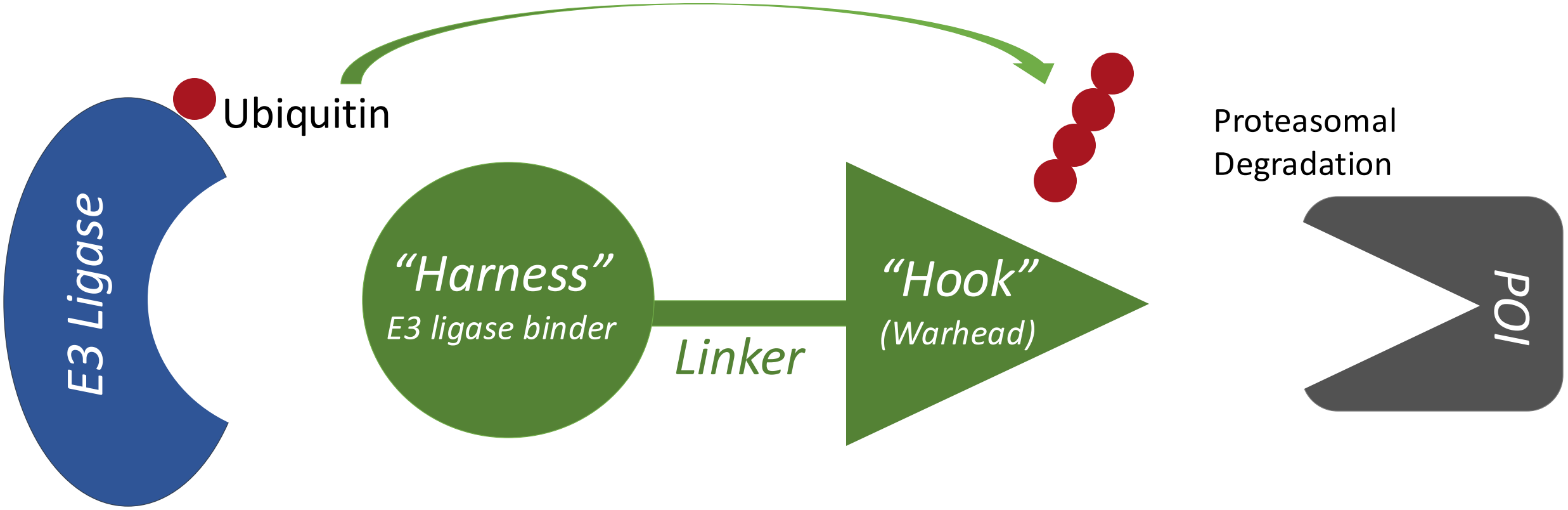
- Estimated 54-month PFS rates:
  - **Ibr+Ven:**
    - 90% for patients with mIGHV
    - 59% for patients with uIGHV
  - **Clb+O:**
    - 40% for patients with mIGHV
    - 8% for patients with uIGHV

Results based on updated IGHV reclassifications. Investigator-assessed progression-free survival was analyzed.

Presented by G. Follows at the 65th ASH Annual Meeting and Exposition; December 9-12, 2023; San Diego, CA, USA

PROTAC therapies (Proteolysis-targeting chimera)

Catalytic ubiquitination and degradation of target



Baseline demographics/disease characteristics

Elderly population with multiple prior lines of targeted therapies

Characteristics	Patients with CLL (n=31)	Patients with NHL/WM (n=48)	Overall population (N=79)
Median age, years (range)	69.0 (35–88)	66.5 (42–87)	67.0 (35–88)
Male, n (%)	19 (61.3)	33 (68.8)	52 (65.8)
ECOG PS, n (%)			
0	13 (41.9)	13 (27.1)	26 (32.9)
1	18 (58.1)	33 (68.8)	51 (64.6)
CNS involvement, n (%)	2 (6.5)	10 (20.8)	12 (15.2)
Median prior lines of therapy (range)	4.0 (2–14)	4.0 (2–13)	4.0 (2–14)
Previous targeted treatments[a], n (%)			
BTKi	30 (96.8)	29 (60.4)	59 (74.7)
≥2 BTKi	11 (35.5)	NA	NA
Pirtobrutinib	7 (22.6)	7 (14.6)	14 (17.7)
BCL2i	28 (90.3)	7 (14.6)	35 (44.3)
BTKi and BCL2i	27 (87.1)	7 (14.6)	34 (43.0)
CAR-T therapy	2 (6.5)	11 (22.9)	13 (16.5)
Bispecific antibody	1 (3.2)	7 (14.6)	8 (10.1)
PI3Ki	9 (29.0)	4 (8.3)	13 (16.5)
Chemo/chemo-immunotherapies	24 (77.4)	48 (100.0)	72 (91.1)
Mutation status, n (%)			
TP53	14/30 (46.7)	4/42 (9.5)	18/72 (25.0)
BTK	13/30 (43.3)	0/42 (0.0)	13/72 (18.1)
PLCG2	6/30 (20.0)	2/42 (4.8)	8/72 (11.1)

[a]Patients could have received multiple prior treatments; NA, not applicable

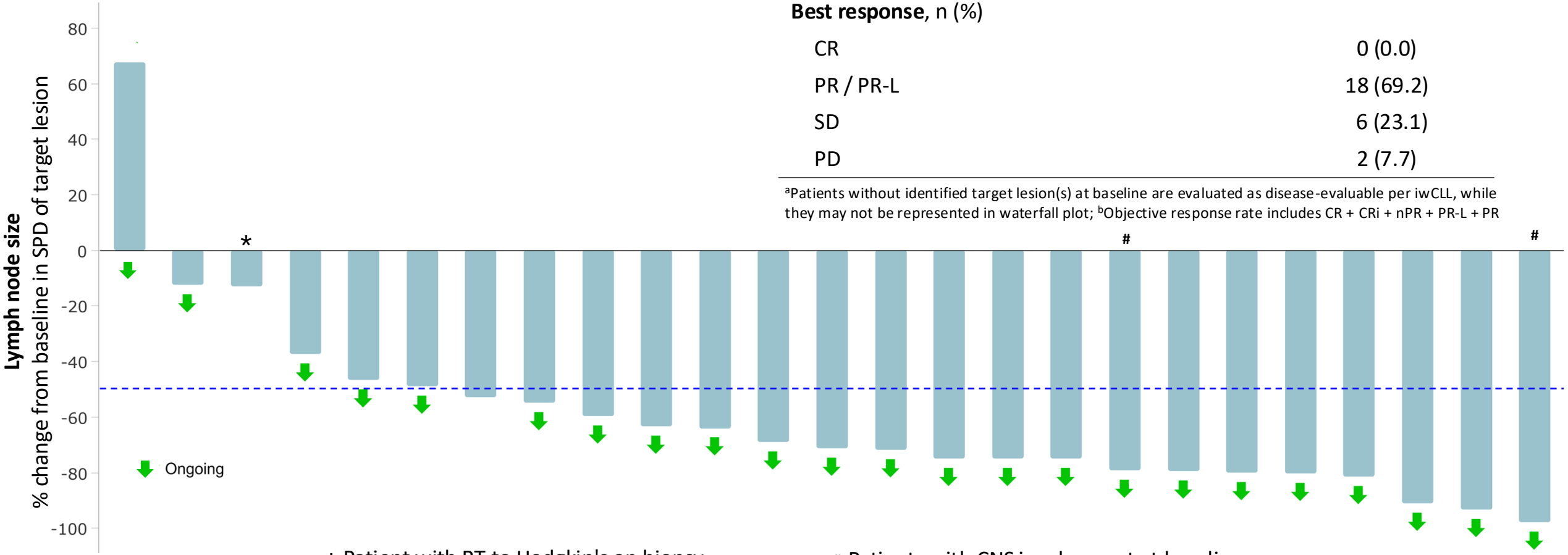
Linton et al, EHA 2024

NX-5948 efficacy: clinical response

Broad antitumor activity in CLL/SLL as demonstrated by significant lymph node reduction and ORR

CLL disease-evaluable patients[a]	n=26
Objective response rate[b], % (95% CI)	69.2 (48.2–85.7)
Best response, n (%)	
CR	0 (0.0)
PR / PR-L	18 (69.2)
SD	6 (23.1)
PD	2 (7.7)

[a]Patients without identified target lesion(s) at baseline are evaluated as disease-evaluable per iwCLL, while they may not be represented in waterfall plot; [b]Objective response rate includes CR + CRi + nPR + PR-L + PR



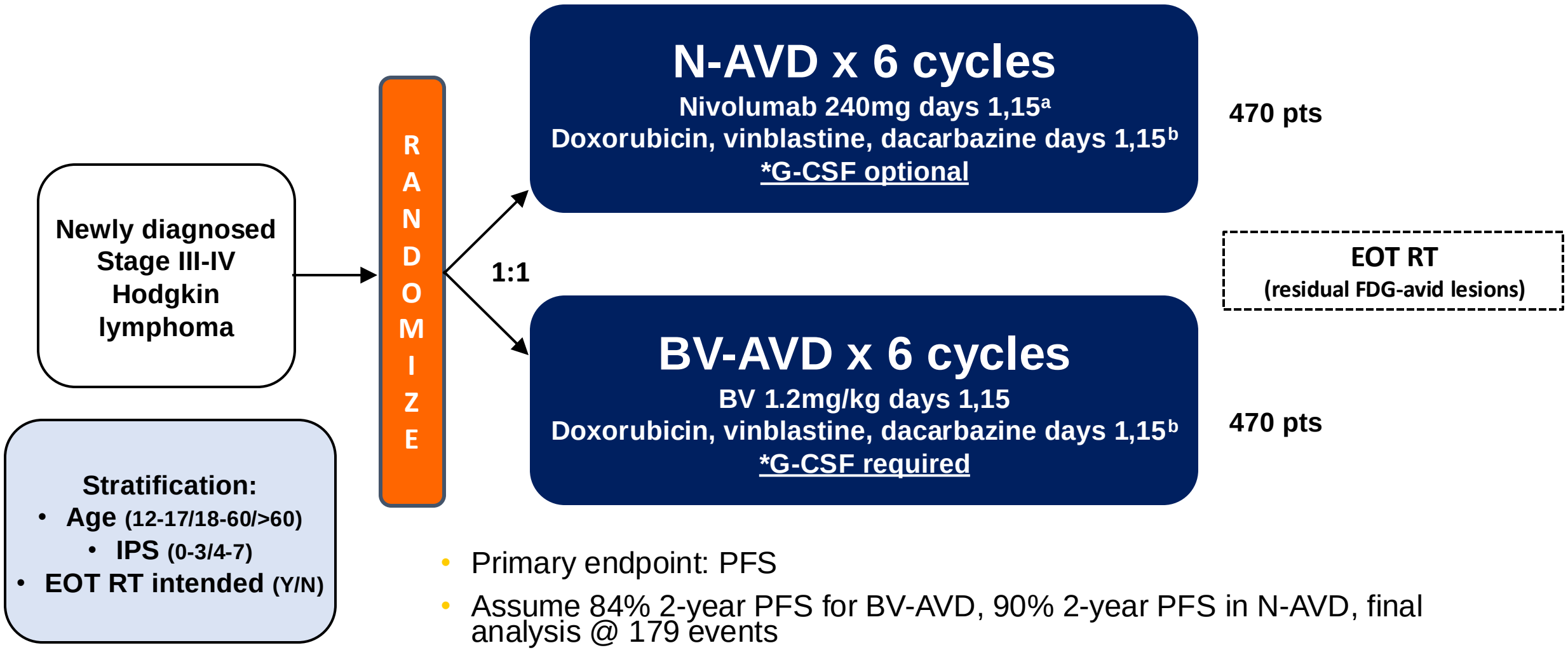
∗ Patient with RT to Hodgkin's on biopsy

Patients with CNS involvement at baseline

SPD, sum of products diameters

Linton et al, EHA 2024

HODGKIN LYMPHONA: S1826 Study

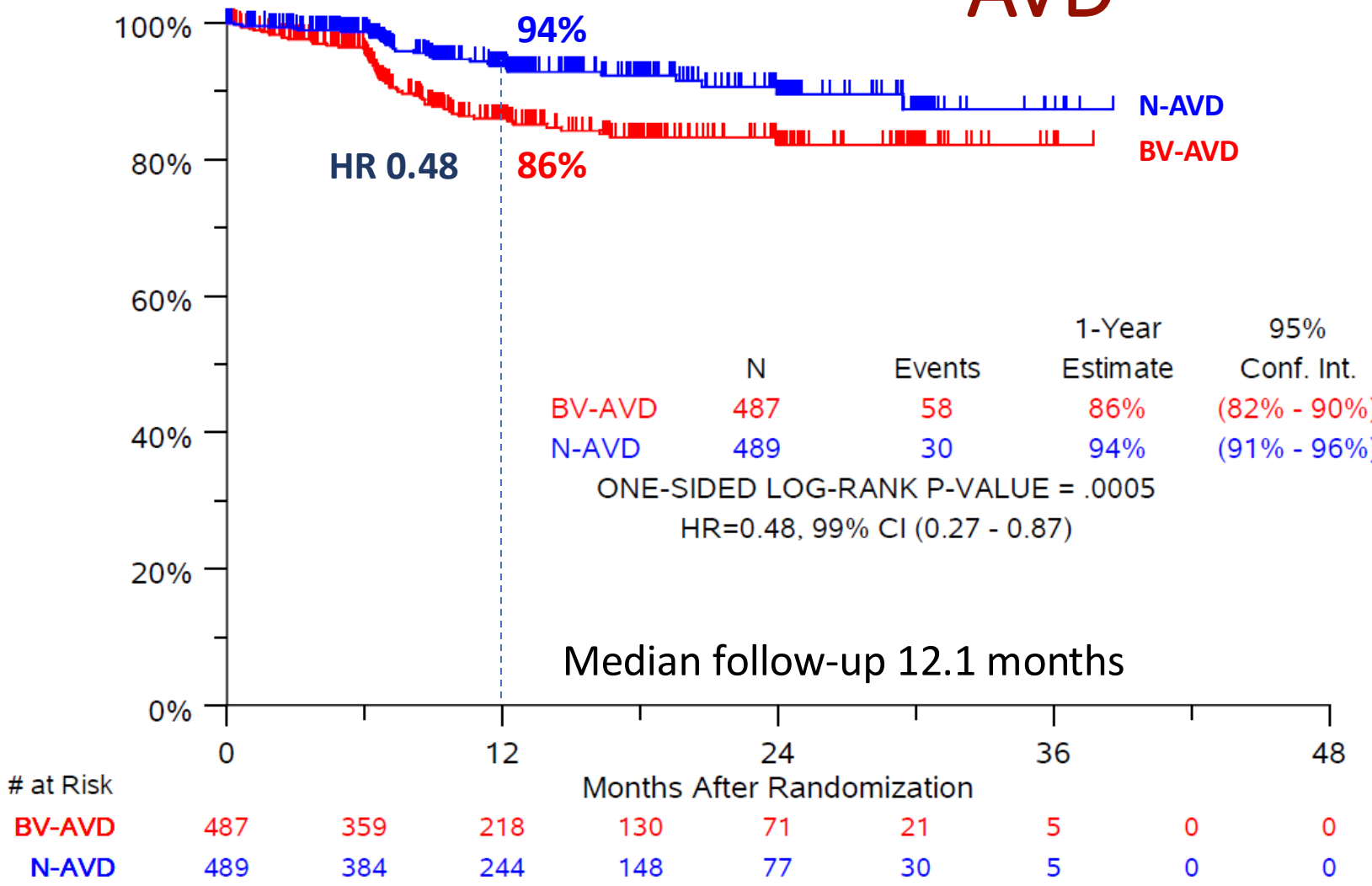


- Primary endpoint: PFS
- Assume 84% 2-year PFS for BV-AVD, 90% 2-year PFS in N-AVD, final analysis @ 179 events

Herrera AF, et al. *J Clin Oncol*. 2023;41(Suppl 17):LBA4.

[a] Nivolumab 3mg/kg for ages ≤ 17, max 240mg
[b] Conventional doses of AVD: Stephens DM et al Blood 2019, Ansell, NEJM 2022

N-AVD Improves PFS Compared to BV-AVD



1-year PFS
N-AVD 94%
BV-AVD 86%

Herrera AF, et al. *J Clin Oncol*. 2023;41(Suppl 17):LBA4.

Indolent NHL: Take-Home points

- Targeted therapy replaced chemo-immunotherapy in treatment of indolent NHL
  - BTK inhibitors
  - BCL2 inhibitors
  - EZH2 inhibitors
  - CRBN modulators
  - Bi-Specific Antibodies (follicular lymphoma, mantle cell lymphoma)
  - CAR T cells (follicular lymphoma, mantle cell lymphoma)
- Combination targeted therapies are making progress
- Resistance to targeted therapies is the new change
  - BTK degraders
  - Bi-specific antibodies

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