Updates in Hodgkin's and Non-Hodgkin's Lymphoma

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Tulane University

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Disclosure of Conflicts of Interests

Nakhle Saba, MD has the following financial relationships to disclose:

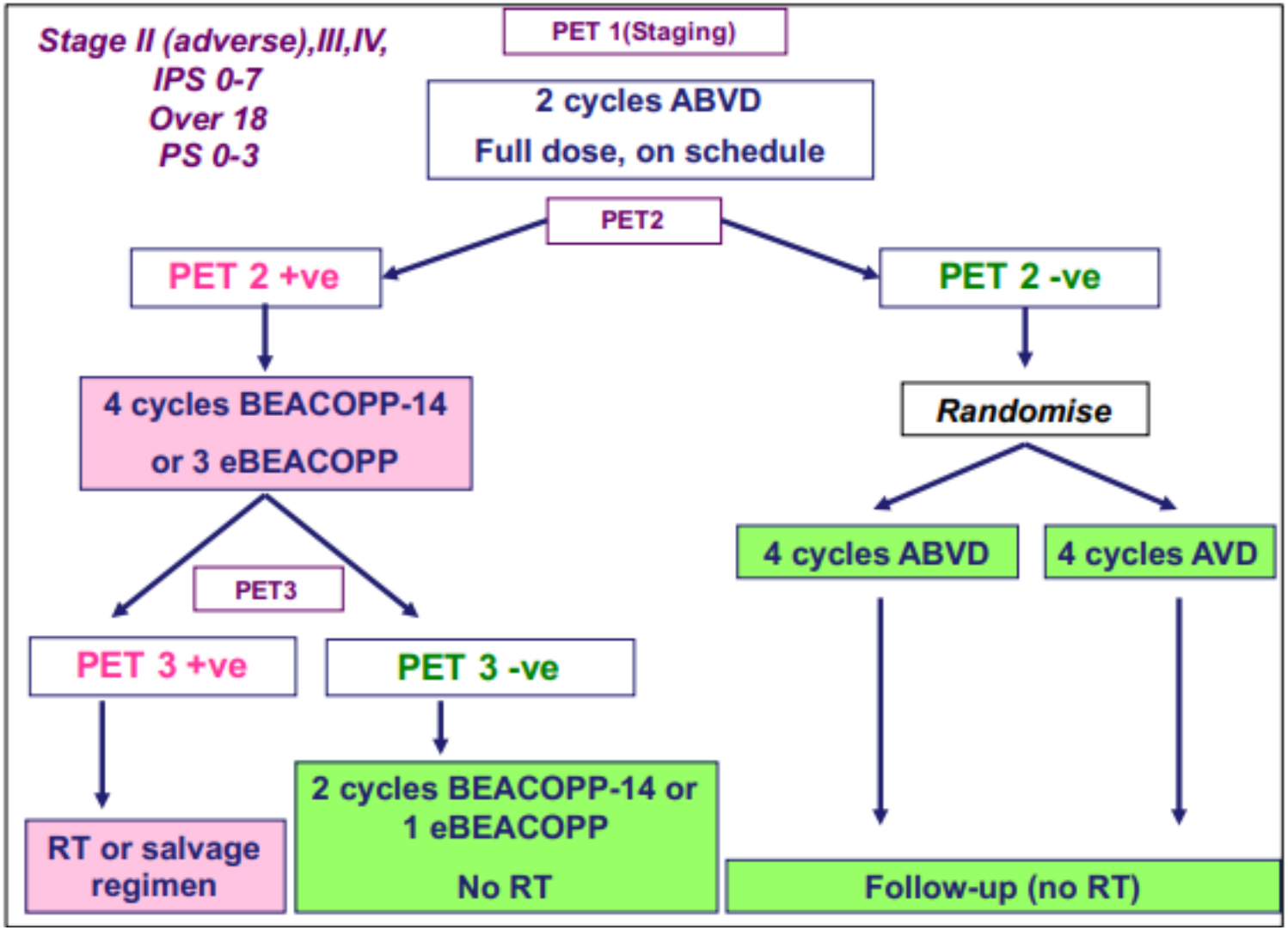
Consultant – ADC therapeutics, BeiGene, Ibrutinib (AbbVie/PCYC/Janssen); Innocare, KyowaKirin, TG Therapeutics, venetoctax (AbbVie)

Speaker–Ibrutinib (AbbVie/PCYC/Janssen), venetoctax (AbbVie)

Agenda

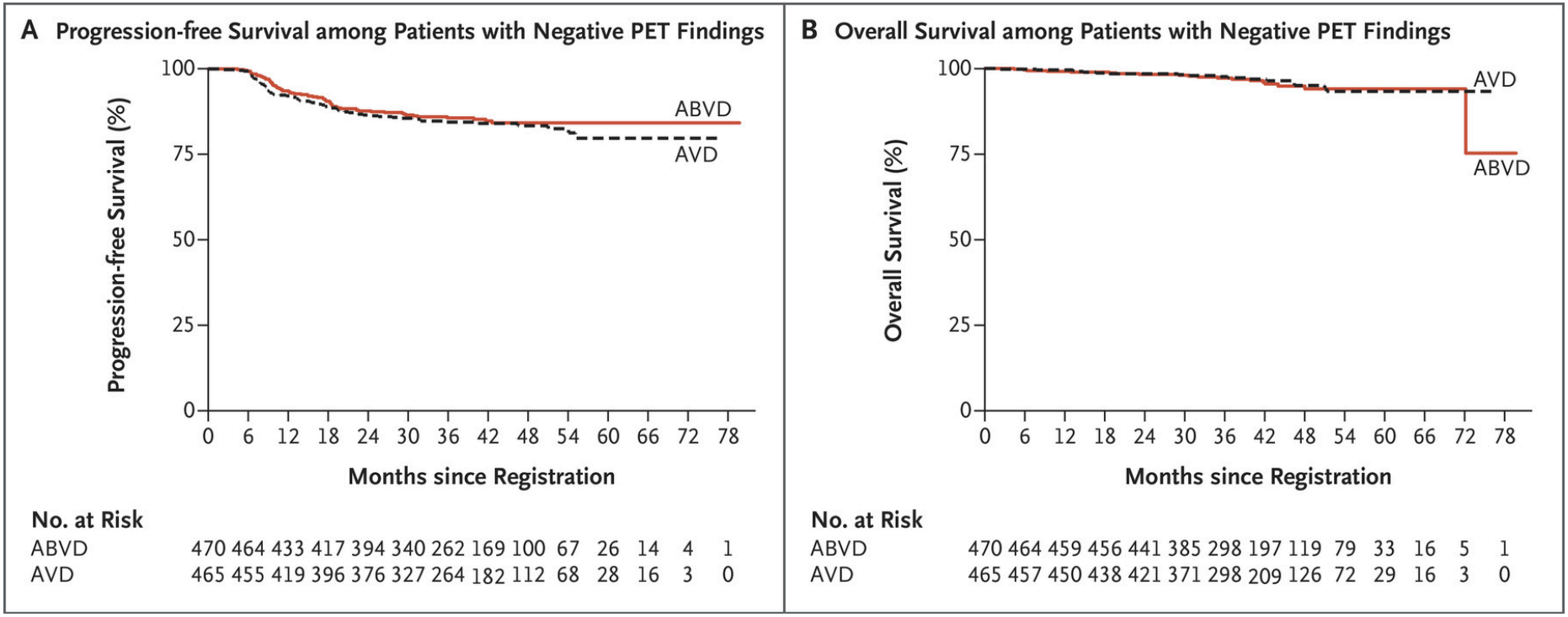
- **Hodgkin's**
  - **RATHL**
  - **ECHELON-1**
- **DLBCL**
  - **Novel agents approved in R/R DLBCL**
    - Polatuzumab vedotin
    - Selinexor
    - Loncastuximab
    - Tafasitamab-cxix
  - **Chimeric antigen receptor T cells**

RATHL trial: N=1214, TN
PET-adapted approach



Johnson et al. NEJM 2016

RATHL trial: N=1214, TN PET-adapted approach



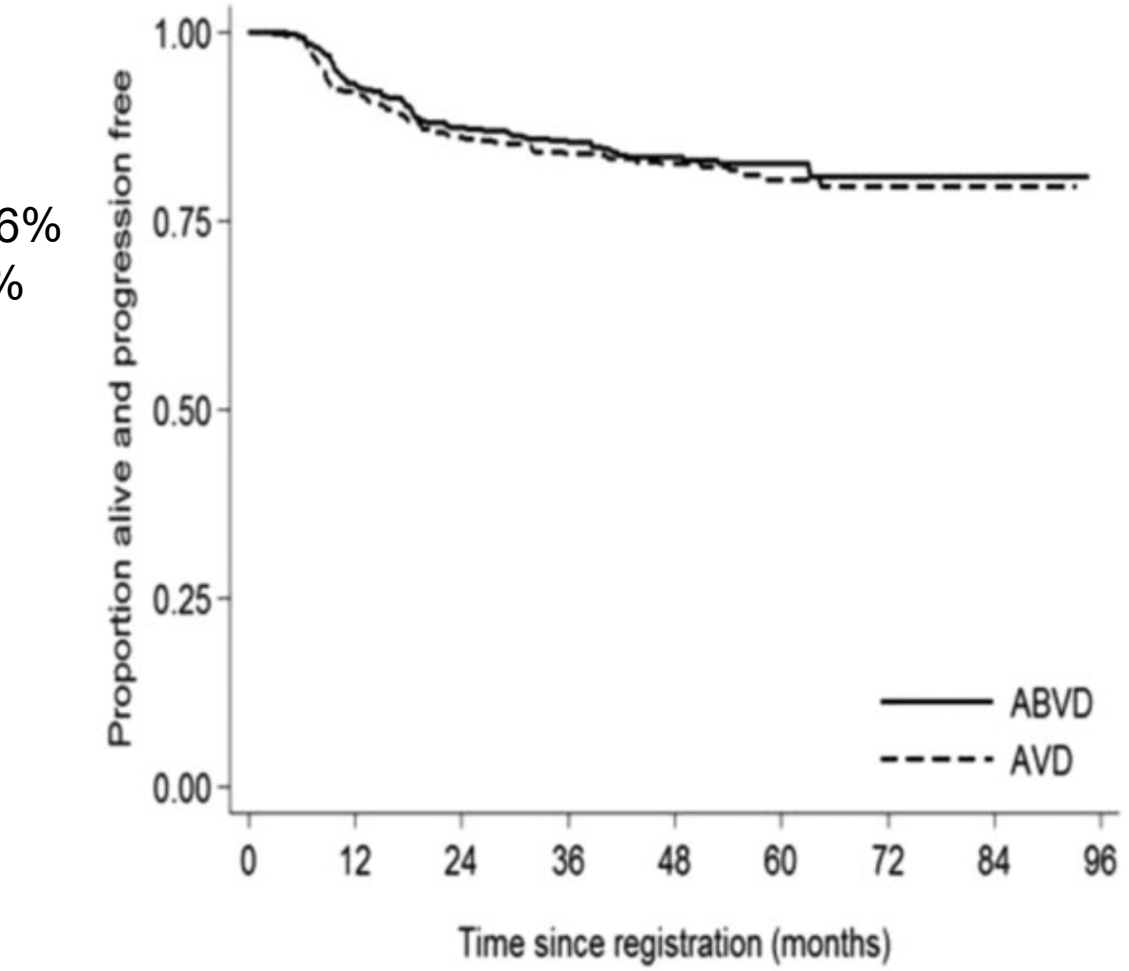
G3-4 lung events: 3% vs. 1%; P<0.05
DLCO difference: −7.4 percentage points (95% CI, 5.1 to 9.7; P<0.001)

Johnson et al. NEJM 2016

RATHL trial: 5-year PFS

ABVD vs. AVD:
Similar 5Y PFS: 82.7% vs. 80.6%
Similar 5Y OS: 95.3% vs. 95.0%

Among 172 pts with PET2+:
5Y PFS 65.7%
5Y OS 85.1%

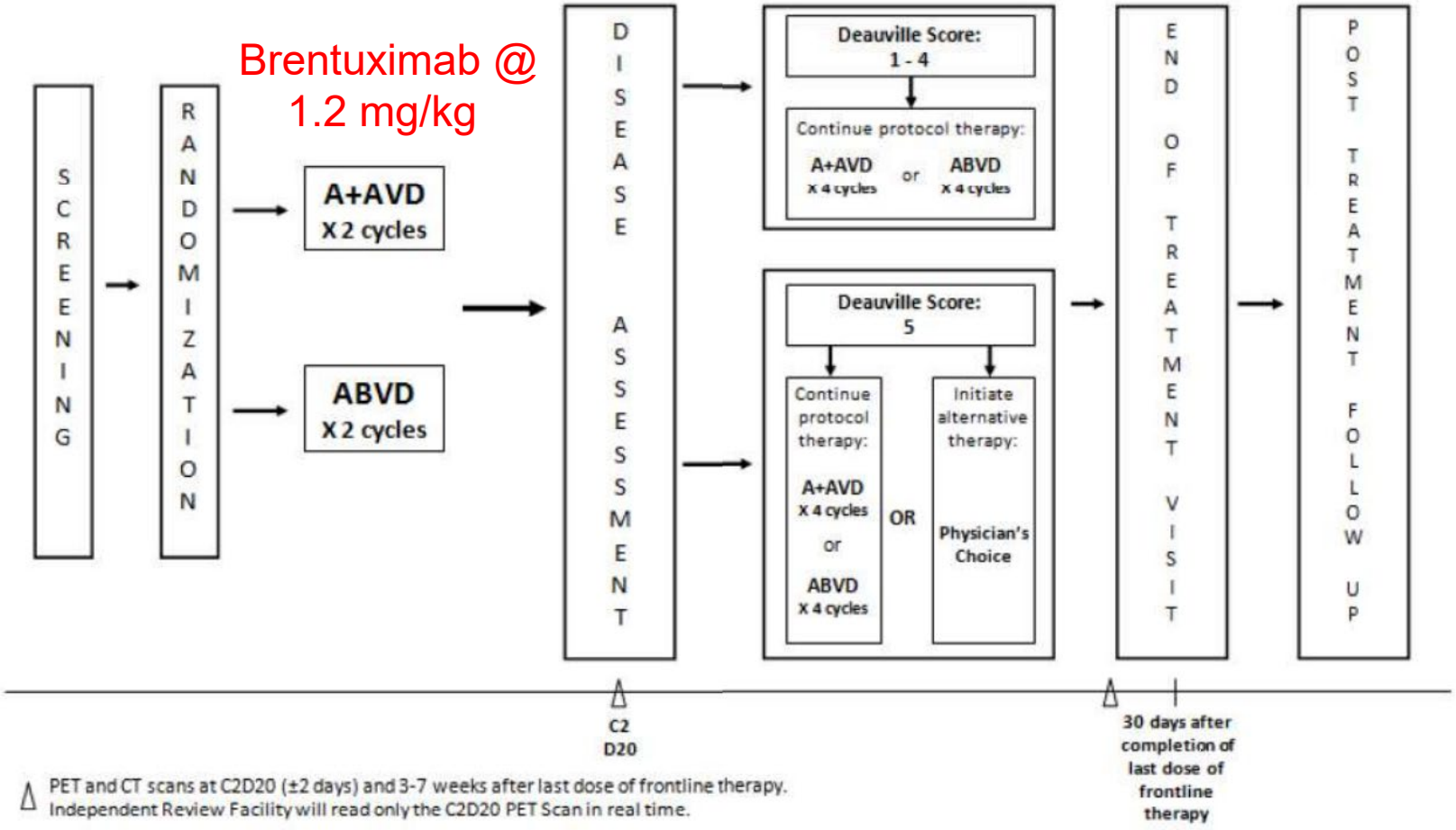


Number at risk

ABVD	470	433	396	350	228	107	35	7	0
AVD	464	420	379	349	239	115	40	8	0

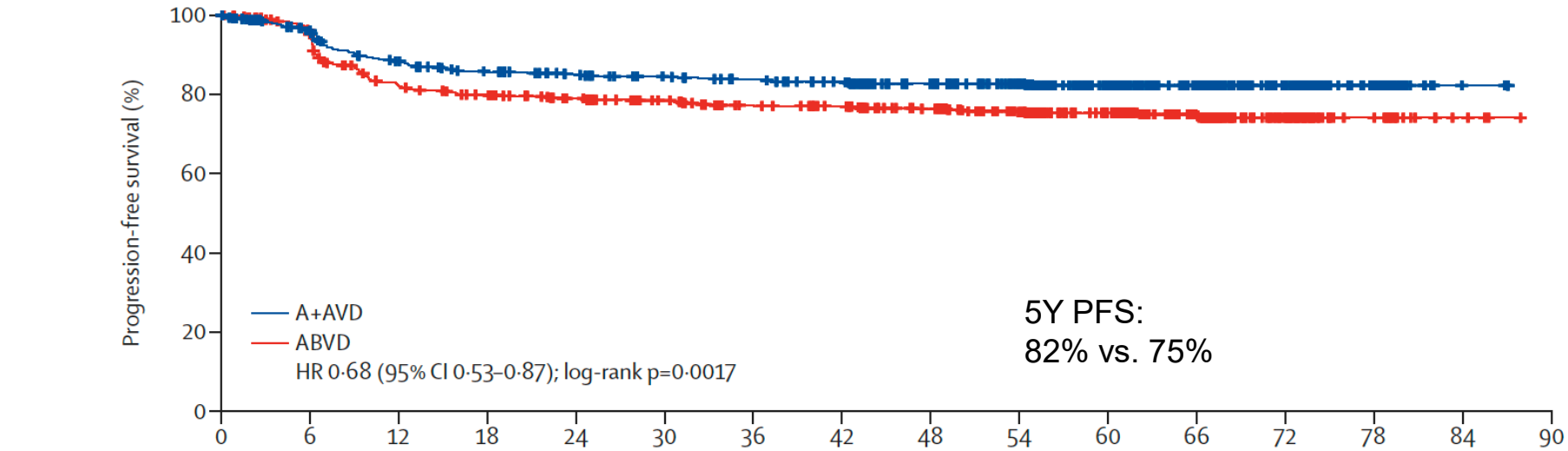
Trotman, Lugano 2017

ECHELON-1: randomized Phase III, N=1334, TN, Stage III-IV: A+AVD vs. ABVD



Strauss et al. Lancet Haematol 2021

ECHELON-1: 5Y updates



5Y PFS:
82% vs. 75%

Number at risk (number censored)

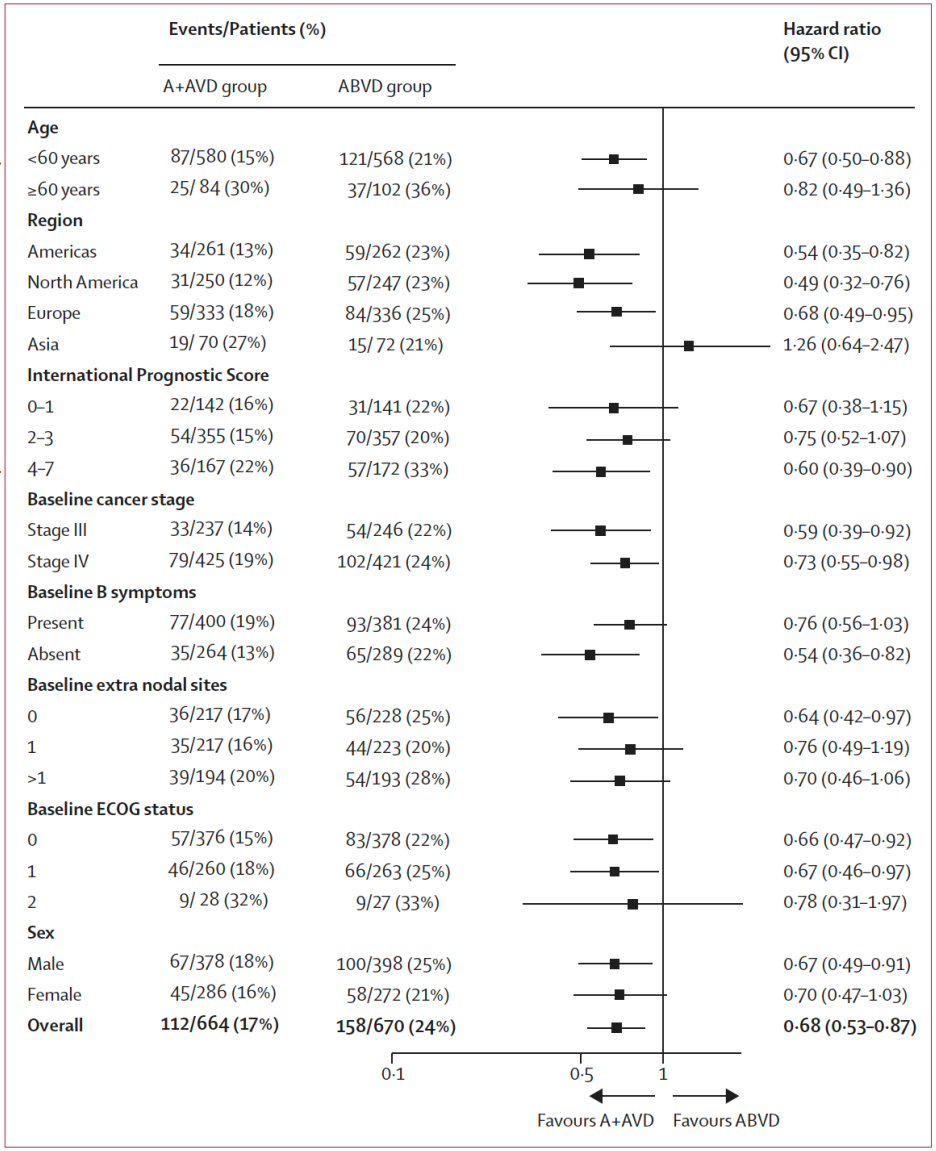
A+AVD	664 (0)	620 (19)	562 (27)	535 (37)	518 (50)	505 (60)	492 (69)	474 (83)	446 (108)	414 (140)	333 (219)	201 (351)	102 (450)	38 (514)	2 (550)	0 (552)
ABVD	670 (0)	613 (24)	521 (34)	500 (41)	478 (57)	456 (76)	432 (92)	423 (101)	397 (123)	360 (156)	292 (223)	179 (335)	73 (439)	22 (490)	4 (508)	0 (512)

A+AVD: 16 deaths and 96 progressive disease events.
ABVD: 30 deaths and 128 progressive disease events.

The number of confirmed deaths did not reach the prespecified number (112) to trigger analysis of overall survival.

Strauss et al. Lancet Haematol 2021

ECHELON-1: 5Y updates

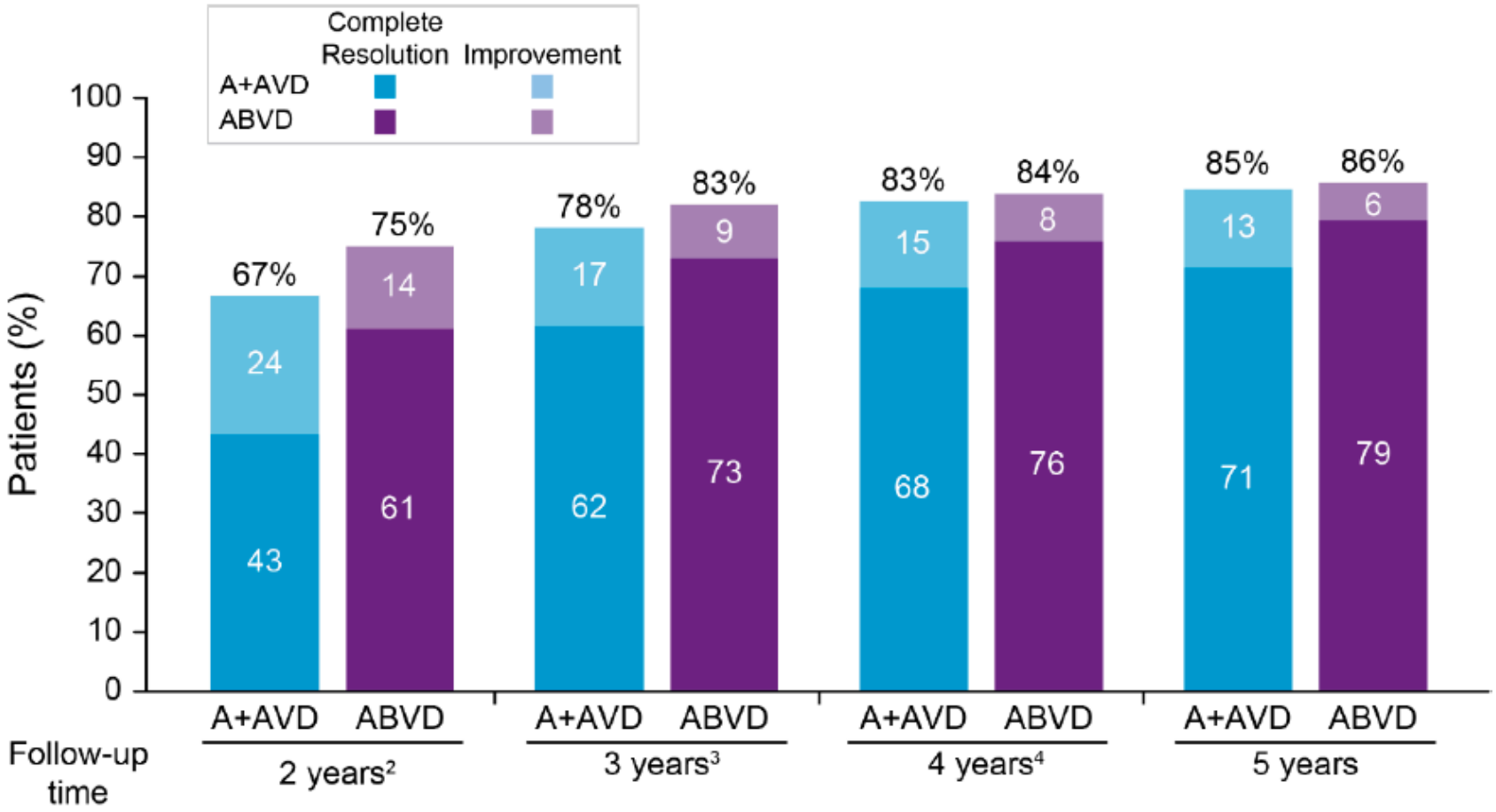


	Events/Patients (%)		Hazard ratio (95% CI)
	A+AVD group	ABVD group	
Age			
<60 years	87/580 (15%)	121/568 (21%)	0·67 (0·50–0·88)
≥60 years	25/ 84 (30%)	37/102 (36%)	0·82 (0·49–1·36)
Region			
Americas	34/261 (13%)	59/262 (23%)	0·54 (0·35–0·82)
North America	31/250 (12%)	57/247 (23%)	0·49 (0·32–0·76)
Europe	59/333 (18%)	84/336 (25%)	0·68 (0·49–0·95)
Asia	19/ 70 (27%)	15/ 72 (21%)	1·26 (0·64–2·47)
International Prognostic Score			
0–1	22/142 (16%)	31/141 (22%)	0·67 (0·38–1·15)
2–3	54/355 (15%)	70/357 (20%)	0·75 (0·52–1·07)
4–7	36/167 (22%)	57/172 (33%)	0·60 (0·39–0·90)
Baseline cancer stage			
Stage III	33/237 (14%)	54/246 (22%)	0·59 (0·39–0·92)
Stage IV	79/425 (19%)	102/421 (24%)	0·73 (0·55–0·98)
Baseline B symptoms			
Present	77/400 (19%)	93/381 (24%)	0·76 (0·56–1·03)
Absent	35/264 (13%)	65/289 (22%)	0·54 (0·36–0·82)
Baseline extra nodal sites			
0	36/217 (17%)	56/228 (25%)	0·64 (0·42–0·97)
1	35/217 (16%)	44/223 (20%)	0·76 (0·49–1·19)
>1	39/194 (20%)	54/193 (28%)	0·70 (0·46–1·06)
Baseline ECOG status			
0	57/376 (15%)	83/378 (22%)	0·66 (0·47–0·92)
1	46/260 (18%)	66/263 (25%)	0·67 (0·46–0·97)
2	9/ 28 (32%)	9/27 (33%)	0·78 (0·31–1·97)
Sex			
Male	67/378 (18%)	100/398 (25%)	0·67 (0·49–0·91)
Female	45/286 (16%)	58/272 (21%)	0·70 (0·47–1·03)
Overall	**112/664 (17%)**	**158/670 (24%)**	**0·68 (0·53–0·87)**

Strauss et al. Lancet Haematol 2021

ECHELON-1: 5Y updates

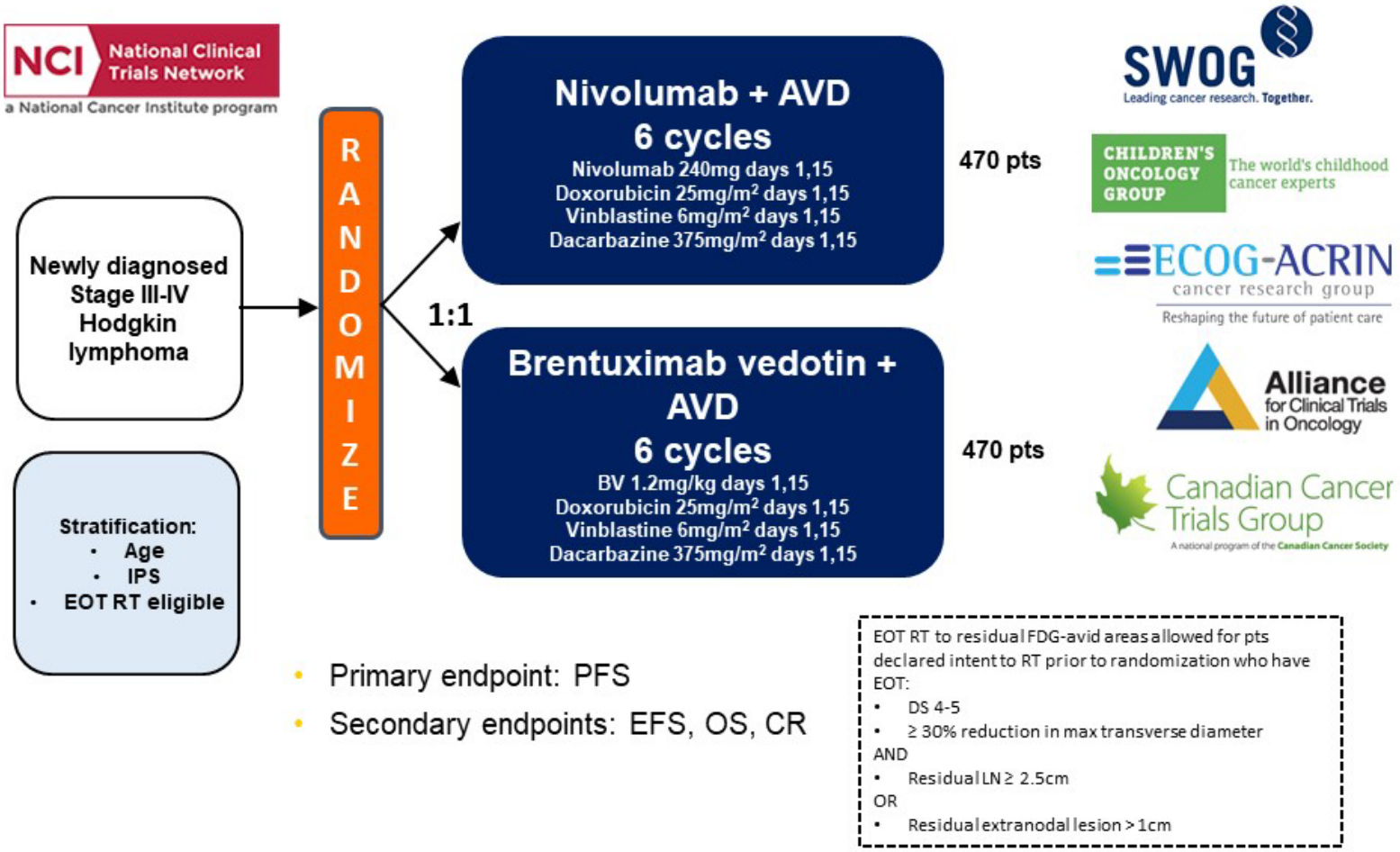
Peripheral neuropathy occurred in 67% of A+AVD group 43% in the ABVD group



Strauss et al. Lancet Haematol 2021

S1826 (NCT03907488)

Randomized, open-label, phase III study of N-AVD versus BV-AVD in pts with newly diagnosed advanced stage HL



- Primary endpoint: PFS
- Secondary endpoints: EFS, OS, CR

EOT RT to residual FDG-avid areas allowed for pts declared intent to RT prior to randomization who have EOT:

- DS 4-5
- ≥ 30% reduction in max transverse diameter

AND

- Residual LN ≥ 2.5cm

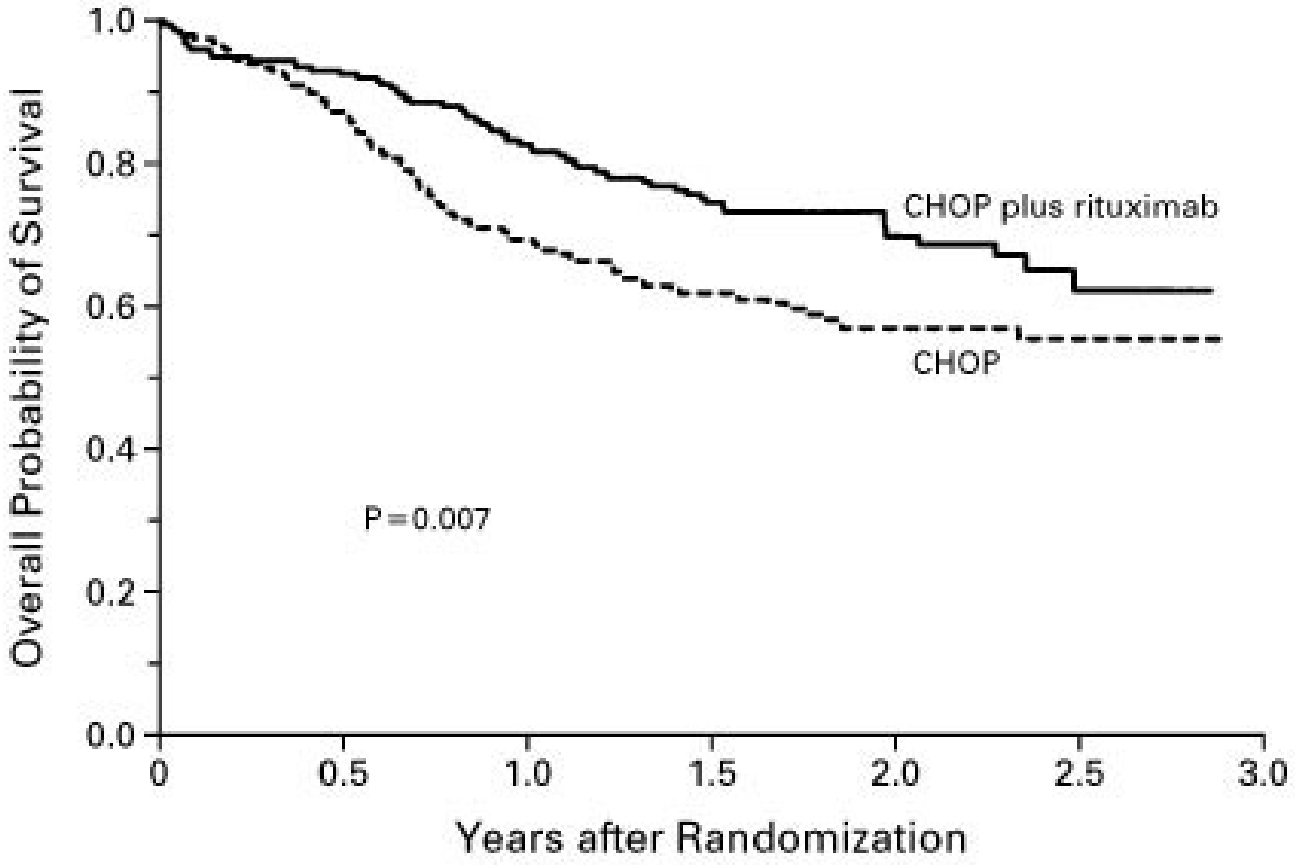
OR

- Residual extranodal lesion > 1cm

Herrera et al. ASH 2020, A#2969

DLBCL

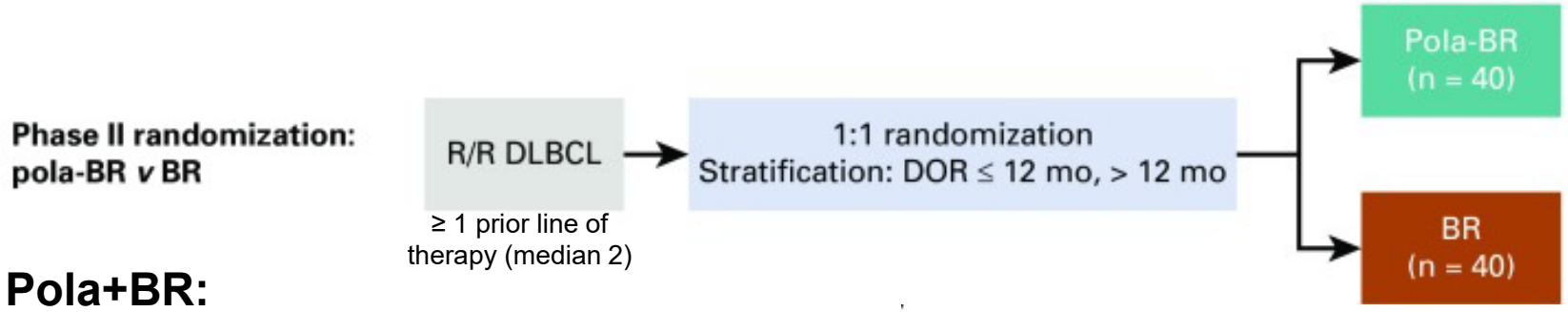
R-CHOP is superior to CHOP



No. at Risk						
CHOP plus rituximab	202	187	167	118	64	21
CHOP	197	171	136	96	58	16

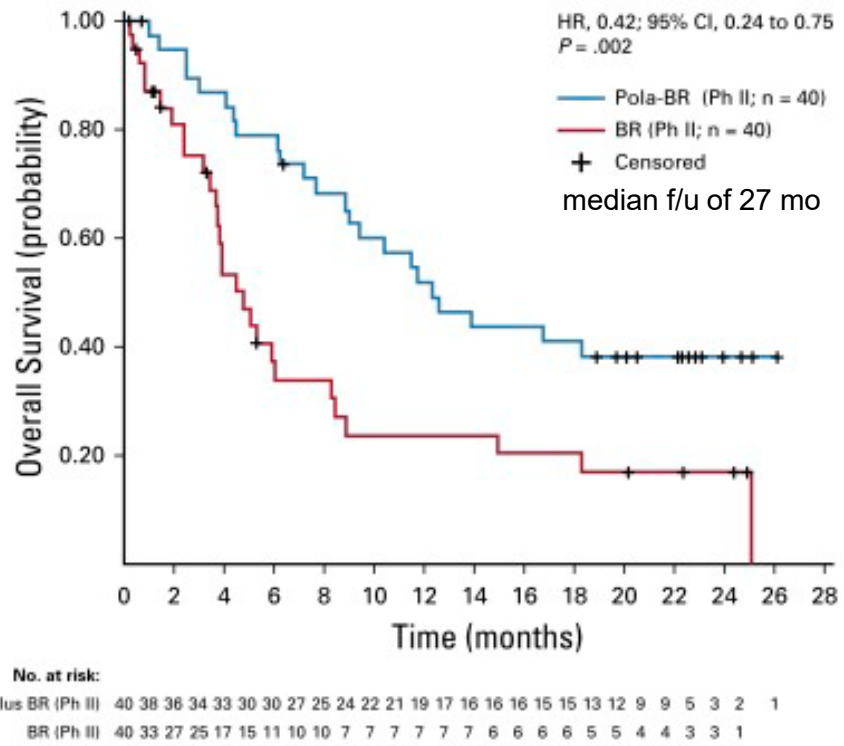
Coiffer et al. NEJM 2002

Polatuzumab in R/R DLBCL



Pola+BR:

- ORR: 45% (CR : 40%)
- mPFS: 9.5 mo
- mOS of 12.4 mo
- Higher rates of G3-4 neutropenia (46.2% vs. 33.3%), anemia (28.2% vs.17.9%), and thrombocytopenia (41% vs. 23.1%), similar grade 3-4 infections (23.1% vs. 20.5%).
- Peripheral neuropathy associated with Pola (43.6% of patients) all G1-2 and resolved in most patients.
- Discontinuation due to AE: 33%



Rituximab IV 375 mg/m^2 on D 1; Bendamustine 90 mg/m^2 IV on D2&3 of C1, then D1&2 of subsequent cycles; Polatuzumab vedotin 1.8 mg/kg IV on D 2 of C1 and D1 of subsequent cycles. Patients were treated for up to six 21-day cycles.

Sehn et al. JCO 2020

Selinexor in R/R DLBCL

SADAL: a single-arm, multicenter, open-label, phase 2 trial

DLBCL (127)
N=127, Line of prior therapy: 2-5 (median 2)

Selinexor
60 mg orally D1&3 weekly, until PD or unacceptable toxicity

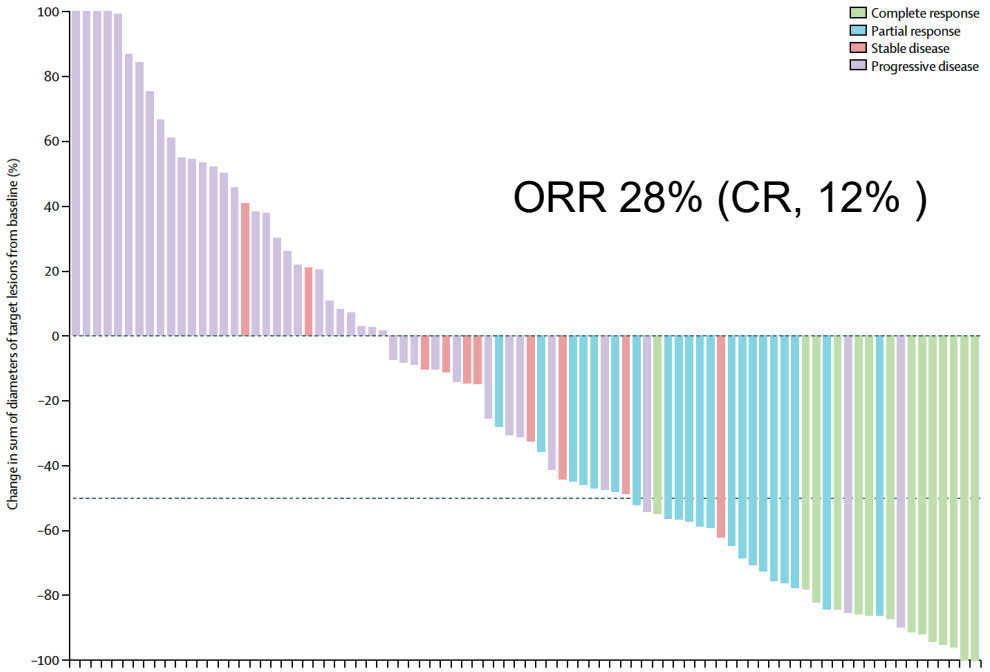
Primary endpoint: ORR
Other endpoints: DOR, PFS, OS

Efficacy

- Median f/u: 11.1mo
- mPFS: 2.6 mo
- mOS: 9 mo
- Median time to first response: 56d

Toxicity

- Most common G≥3 TEAE: thrombocytopenia (46%), neutropenia (24%), anemia (22%), fatigue (11%), hyponatremia (8%), and nausea (6%)
- Discontinuation due to AE: 17%
- Dose modification due to AE: 70%



ORR 28% (CR, 12%)

All patients were required to receive 8 mg of ondansetron (or equivalent) before the first dose of selinexor and continued two to three times daily, as needed. Supportive care was provided at the discretion of the investigator.

Kalakonda et al. Lancet Hematol. 2020

Loncastuximab in R/R DLBCL

LOTIS-2: a multicenter, open-label, single-arm, phase 2 trial

DLBCL
N=145; ≥ 2 prior line of therapy (median 3)

Loncastuximab tesirine
IV D1 Q21D-cycle, at 150 µg/kg for 2 cycles, then 75 µg/kg thereafter, for up to 1Y

ORR

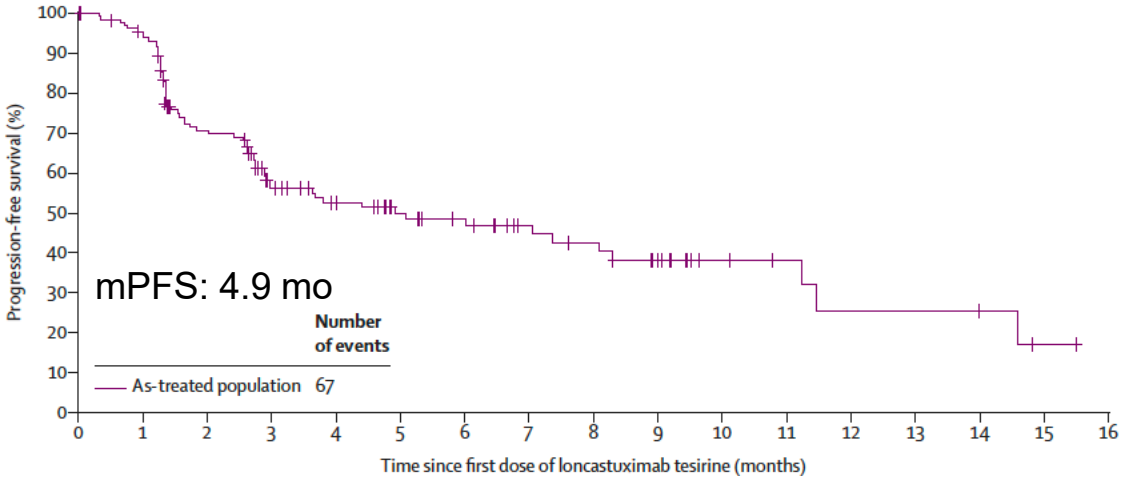
ORR: 48.3% (24.2% CR)

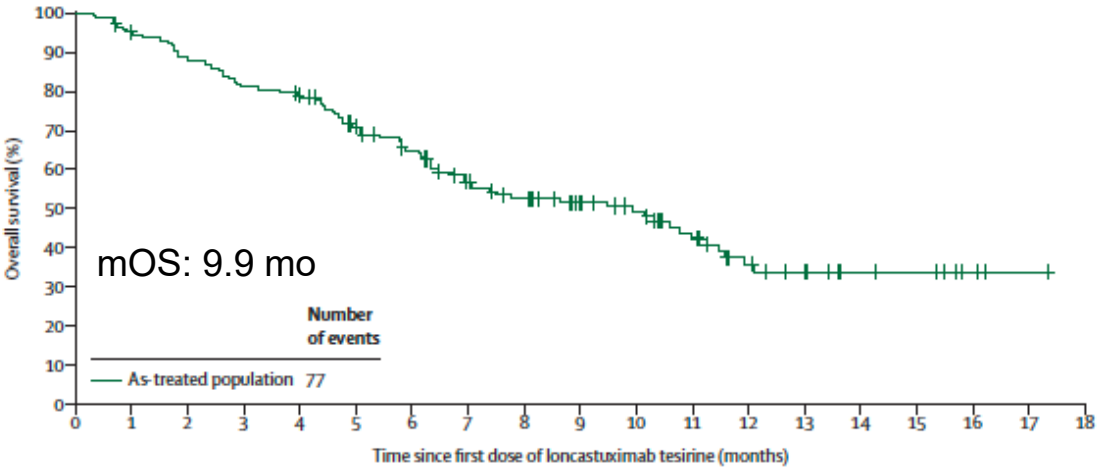
Efficacy

- Median time to first response: 41d

Toxicity

- Most common G≥3 TEAE: Neutropenia (26%), thrombocytopenia (18%), and increased GGT (17%)
- Edema or effusion (31%, G≥3: 5%)
- Discontinuation due to AE: 23%





Caimi et al. Lancet Oncol. 2021

Tafasitamab +lenalidomide in R/R DLBCL

L-MIND: a multicenter, open-label, single-arm, phase 2 trial

DLBCL
N=80; ≥ 1 prior line of therapy (median 2)

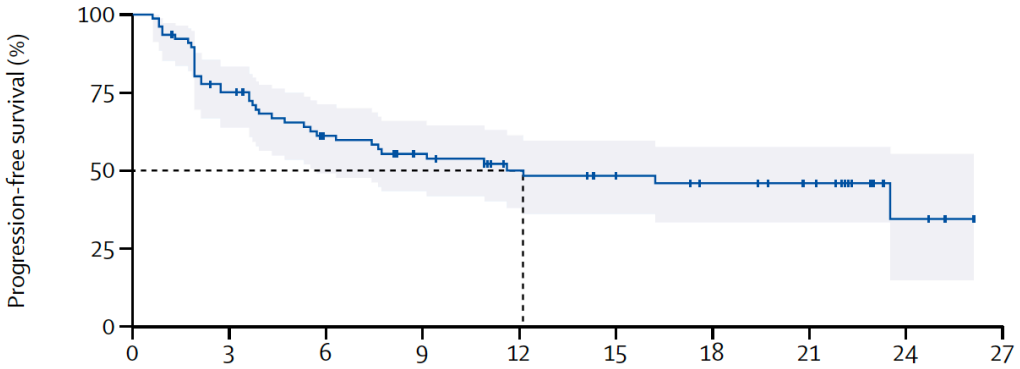
Tafasitamab + lenalidomide
for up to 12 cycles (28 days each)*

ORR

ORR: 60%
(43% CR)

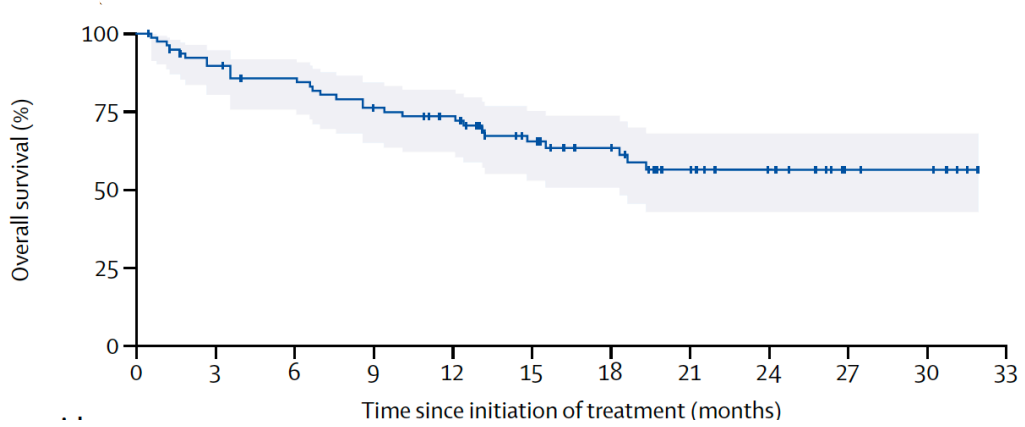
Efficacy

- Median f/u: 13.2 mo
- Median time to first response: 60d
- mPFS: 12.1 mo
- mOS: NR



Toxicity

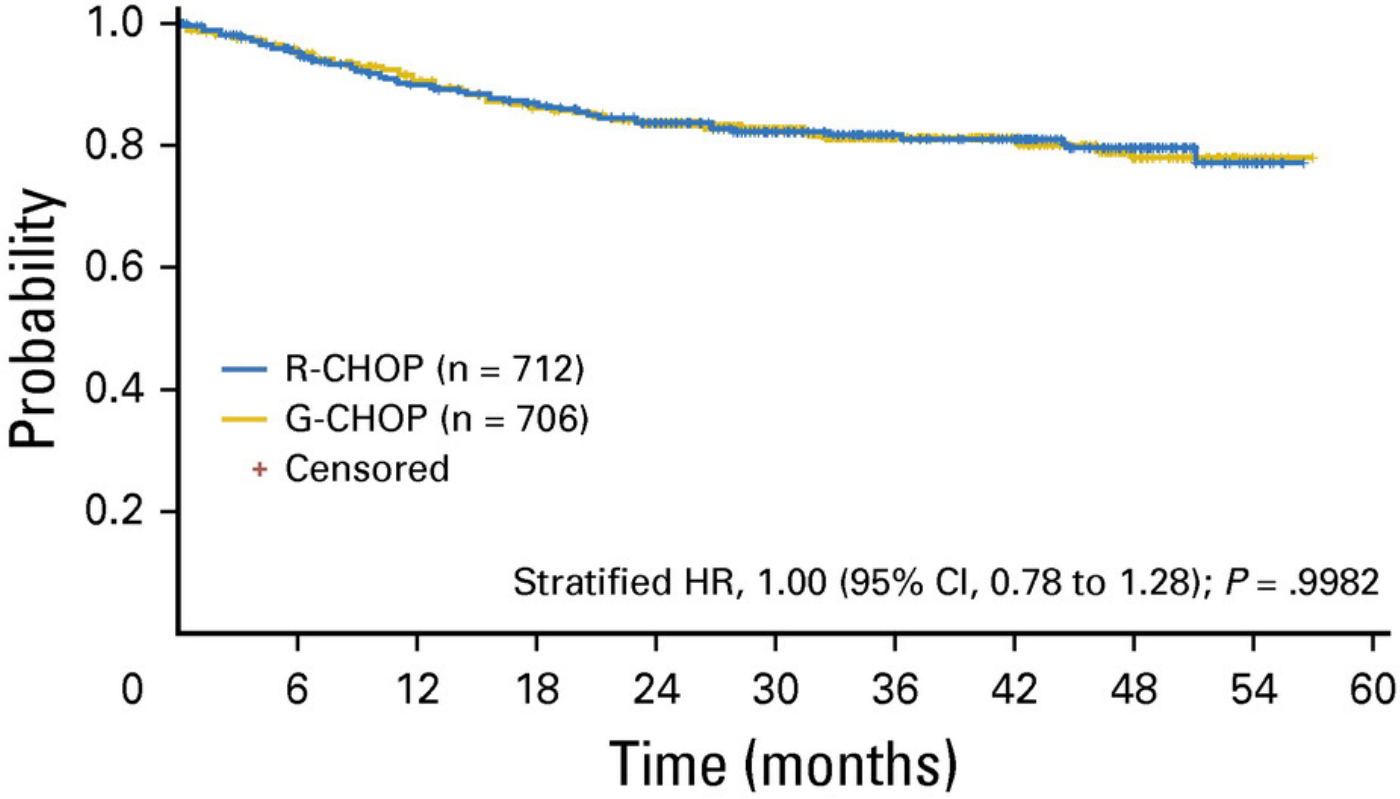
- Most common G≥3 TEAE: Neutropenia (48%), thrombocytopenia (17%), Feb. Neutropenia (6%), PE (4%), A.Fib/CHF (2% each)
- Discontinuation due to AE: 25%



*Tafasitamab IV at 12 mg/kg: days 1, 8, 15, and 22 for C1–3, an additional loading dose was administered on day 4 of cycle 1. From cycle 4, tafasitamab was administered every 14 days,17 on days 1 and 15 of each cycle. Premedication comprised antipyretics, histamine (H1 and H2) receptor blockers, glucocorticoids, and meperidine.

Caimi et al. Lancet Oncol. 2021

R-CHOP vs. G-CHOP (GOYA trial)

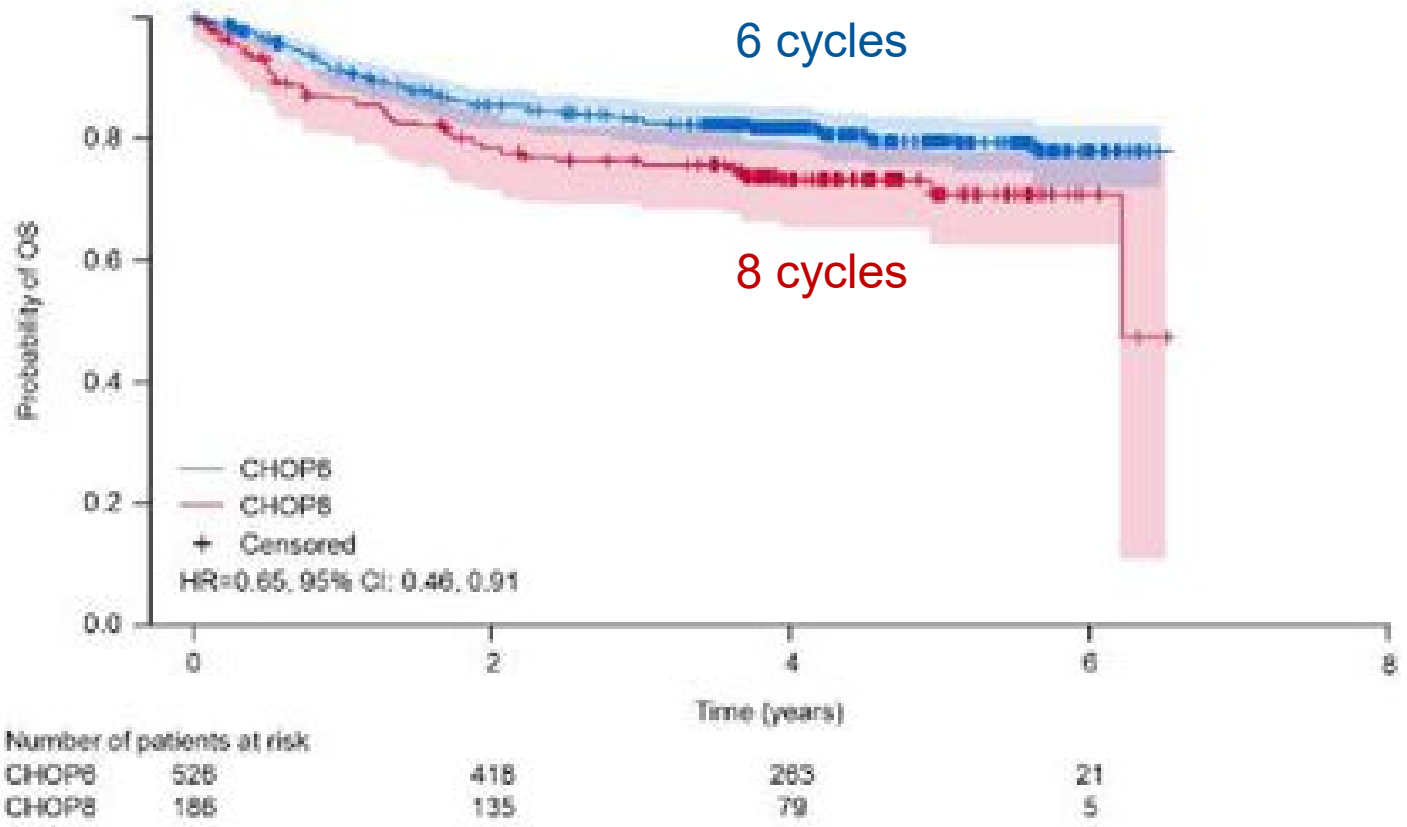


No. at risk:

R-CHOP	712	663	617	586	540	319	190	138	71	9
G-CHOP	706	659	616	582	552	316	201	138	67	8

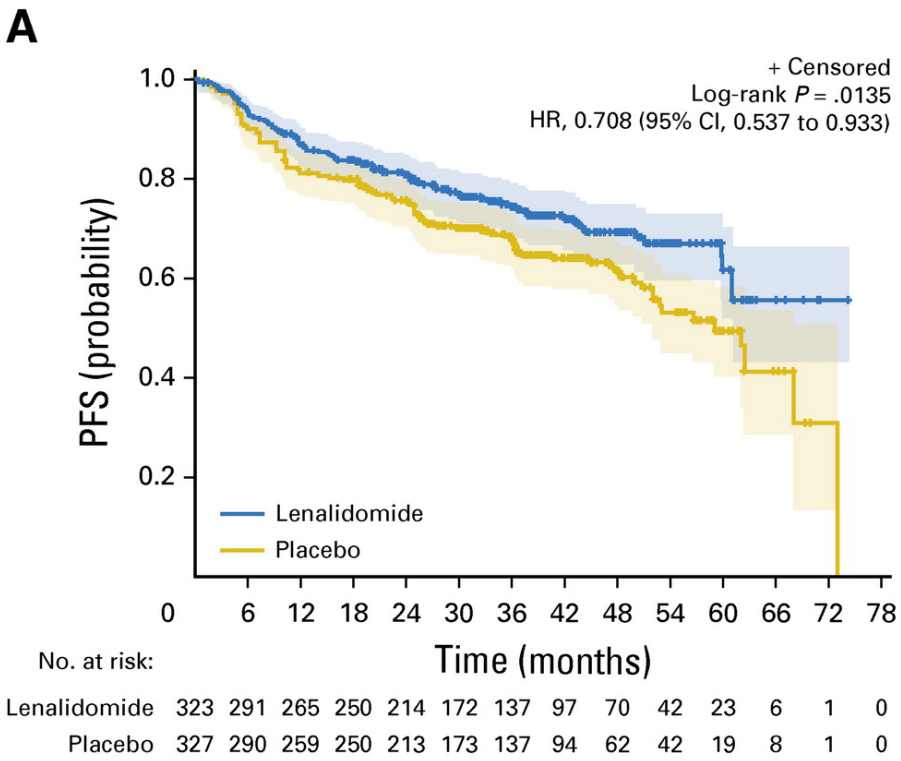
Vitolo et al. JCO 2017

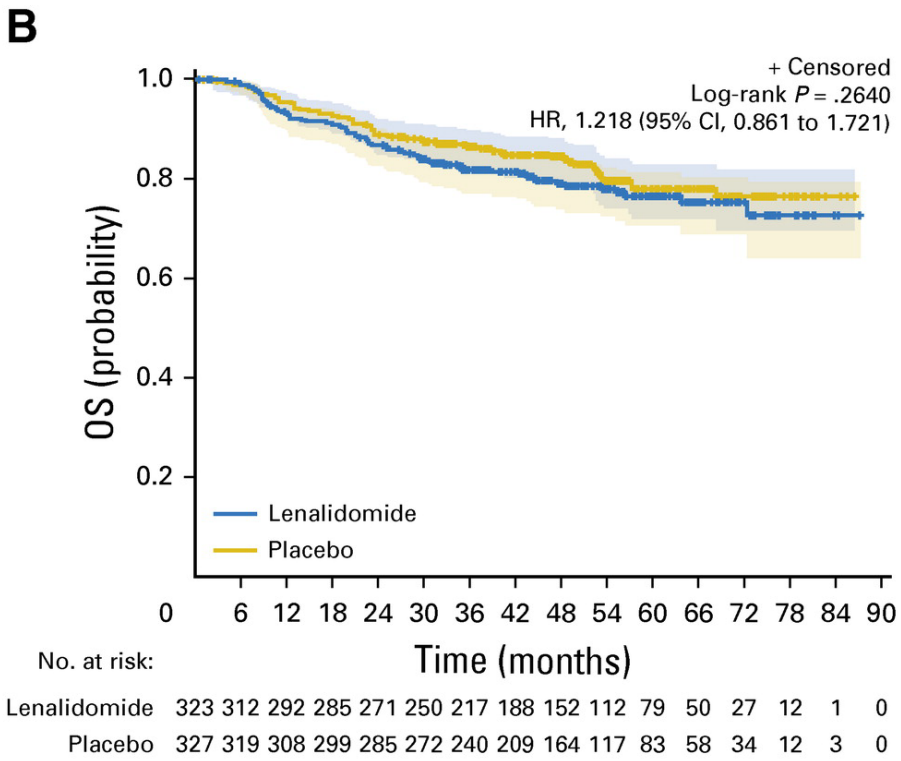
R-CHOP 6 vs. 8 cycles (GOYA trial)



Sehn ASH 2018 A#783

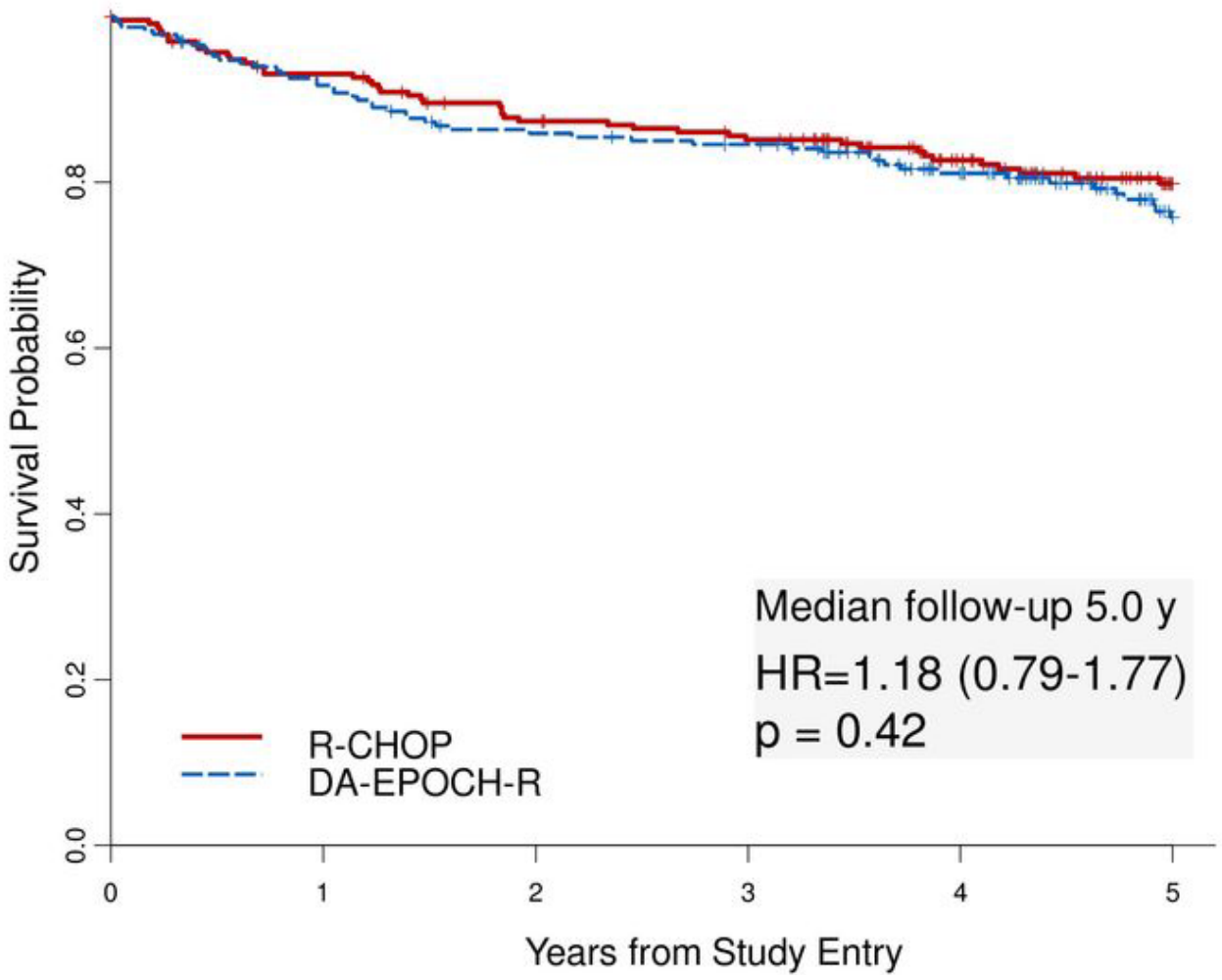
Lenalidomide vs. Placebo maintenance post R-CHOP (LYSARC trial)





Thieblemont et al. JCO 2017

R-CHOP vs. R-EPOCH (50303 trial)



Coiffer et al. NEJM 2002

Combinable with RCHOP?

	N	Median # prior therapies	ORR (%)	CR (%)	mPFS
Pola +R[1]	39	3	54	21	5.6
Pola +BR[2]	40	2	45	40	9.5
Selinexor[3]	127	2	28	12	2.6
Lonca[4]	145	3	48	24	4.9
Tafa+Len[5]	80	2	60	43	12.1

Head-to-head studies between these regimen are lacking. Therefore, direct comparisons cannot be made.

1. Sehn et al. JCO 2020; 2. Morschhauser et al. Lancet Haematol. 2019; 3. Kalakonda et al. Lancet Hematol. 2020; 4. Caimi et al. Lancet Oncol. 2021; 5. Caimi et al. Lancet Oncol. 2021.

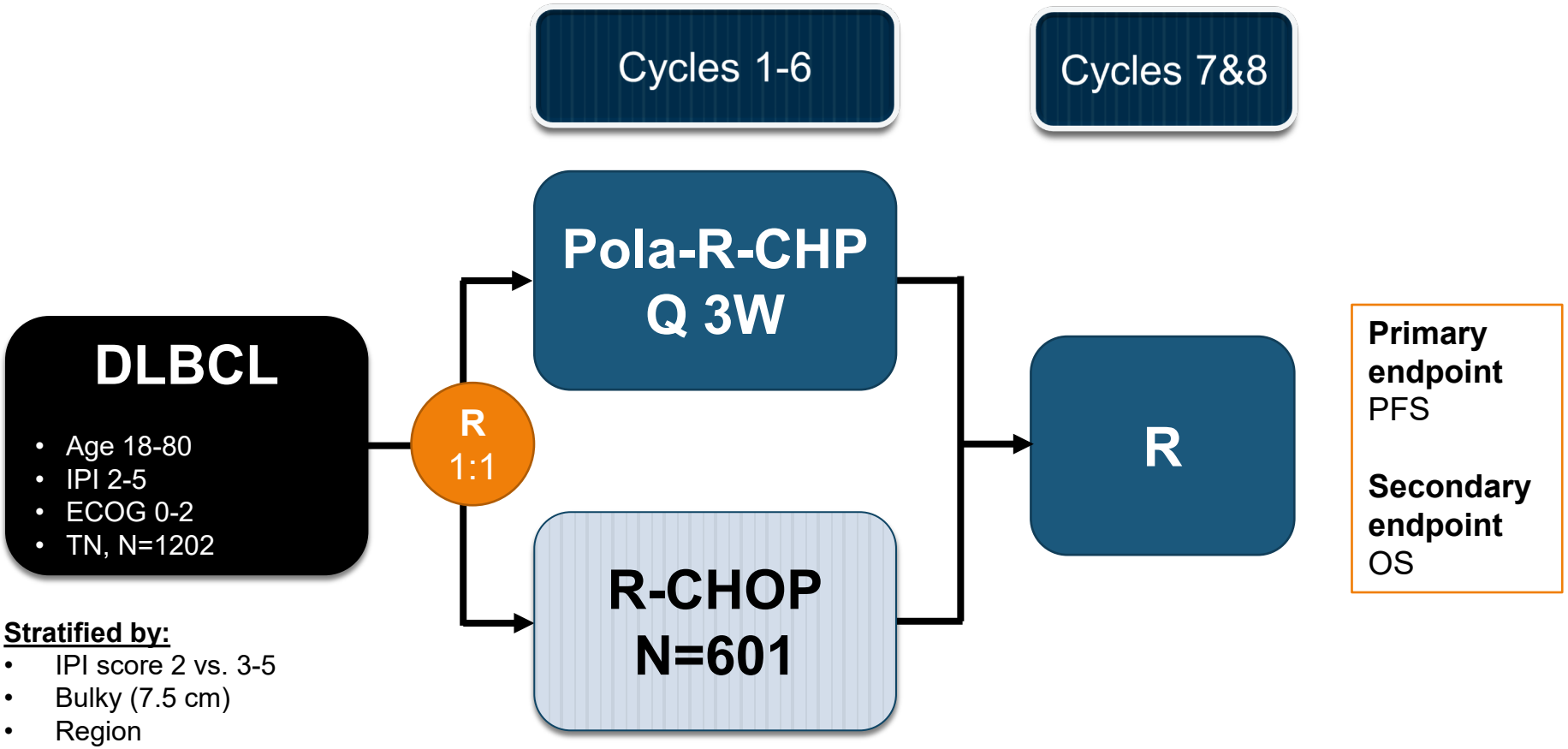
Frontline Trials in DLBCL

	Phase	Name	Comparator	ClinicalTrials.gov Id
Pola + RCHP	III Double-blinded	POLARIX	Placebo + RCHOP	NCT03274492
Selinexor + RCHOP	Ib/II	-	-	NCT03147885
Lonca + RCHOP	II	LOTIS-8	-	NCT04974996
Tafa+Len+ RCHOP	III Double-blinded	frontMIND	Placebo + RCHOP	NCT04824092

ClinicalTrials.gov

POLARIX:

Phase III, randomized, placebo-controlled study in frontline DLBCL



D1: IV Pola 1.8 mg/kg and placebo matching intravenous vincristine (Pola-R-CHP group) or a placebo matching pola and IV vincristine at 1.4 mg/m^2 (maximum of 2 mg) (R-CHOP group), plus IV rituximab (375 mg/m^2), cyclophosphamide (750 mg/m^2), and doxorubicin (50 mg/m^2). Prednisone 100 mg daily d1-5. Cycles 7&8, patients in both groups received rituximab (375 mg/m^2) monotherapy

Morschhauser et al. NEJM 2021

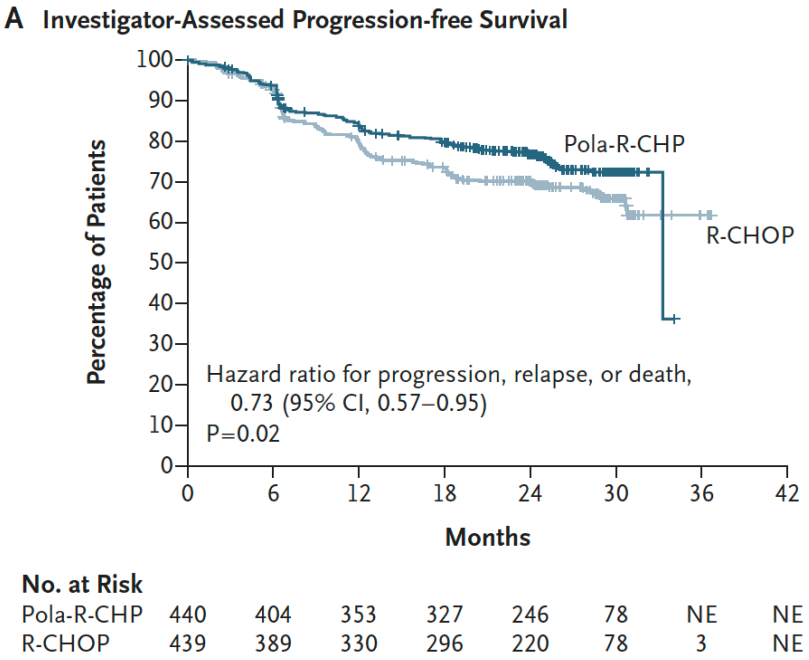
POLARIX

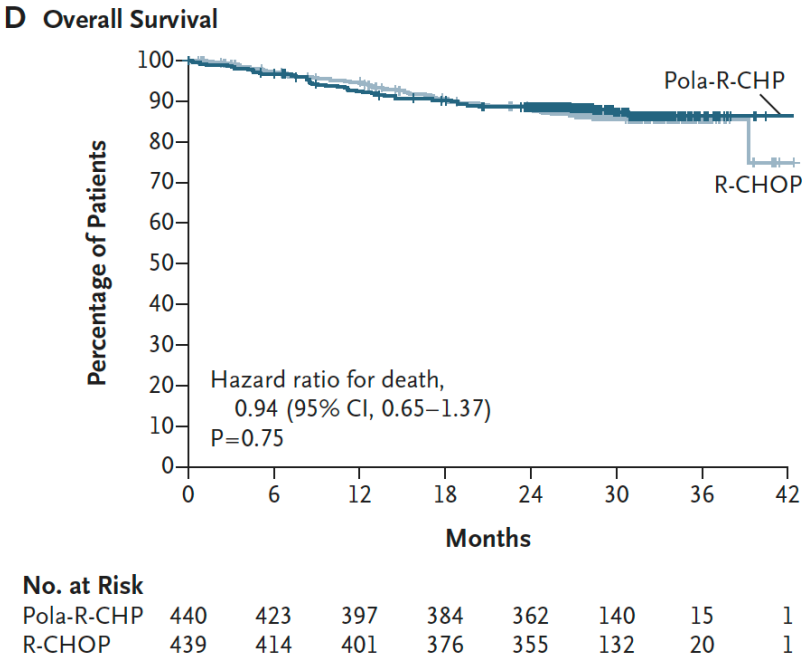
Table 1. Demographic and Clinical Characteristics at Baseline (Intention-to-Treat Population).*

Characteristic	Pola-R-CHP (N = 440)	R-CHOP (N = 439)
Median age (range) — yr	65 (19–80)	66 (19–80)
Age category — no. (%)		
≤60 yr	140 (31.8)	131 (29.8)
>60 yr	300 (68.2)	308 (70.2)
Female sex — no. (%)	201 (45.7)	205 (46.7)
Geographic region — no. (%)†		
Western Europe, United States, Canada, and Australia	302 (68.6)	301 (68.6)
Asia	81 (18.4)	79 (18.0)
Rest of world	57 (13.0)	59 (13.4)
Ann Arbor stage — no. (%)‡		
I or II	47 (10.7)	52 (11.8)
III or IV	393 (89.3)	387 (88.2)
No. of extranodal sites — no. (%)		
0 or 1	227 (51.6)	226 (51.5)
≥2	213 (48.4)	213 (48.5)
Bulky disease — no. (%)†§	193 (43.9)	192 (43.7)
ECOG performance status score — no. (%)¶		
0 or 1	374 (85.0)	363 (82.7)
2	66 (15.0)	75 (17.1)
Lactate dehydrogenase level — no. (%)‖		
Normal	146 (33.2)	154 (35.1)
Elevated	291 (66.1)	284 (64.7)
IPI score — no. (%)†**		
2	167 (38.0)	167 (38.0)
3 to 5	273 (62.0)	272 (62.0)
Median time from initial diagnosis to treatment initiation (IQR) — days	26 (16.0–37.5)	27 (19.0–41.0)
Cell of origin — no./total no. (%)††		
Germinal-center B-cell–like subtype	184/330 (55.8)	168/338 (49.7)
Activated B-cell–like subtype	102/330 (30.9)	119/338 (35.2)
Unclassified	44/330 (13.3)	51/338 (15.1)
Double-expressor lymphoma — no./total no. (%)††	139/362 (38.4)	151/366 (41.3)
Double-hit or triple-hit lymphoma — no./total no. (%)††	26/331 (7.9)	19/334 (5.7)

Morschhauser et al. NEJM 2021

POLARIX





Morschhauser et al. NEJM 2021

POLARIX

Table 3. Adverse Events during the Treatment Period (Safety Population).*

Adverse Event	Pola-R-CHP (N=435)		R-CHOP (N=438)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
	number of patients (percent)			
Peripheral neuropathy†	230 (52.9)	7 (1.6)	236 (53.9)	5 (1.1)
Nausea	181 (41.6)	5 (1.1)	161 (36.8)	2 (0.5)
Neutropenia	134 (30.8)	123 (28.3)	143 (32.6)	135 (30.8)
Diarrhea	134 (30.8)	17 (3.9)	88 (20.1)	8 (1.8)
Anemia	125 (28.7)	52 (12.0)	114 (26.0)	37 (8.4)
Constipation	125 (28.7)	5 (1.1)	127 (29.0)	1 (0.2)
Fatigue	112 (25.7)	4 (0.9)	116 (26.5)	11 (2.5)
Alopecia	106 (24.4)	0	105 (24.0)	1 (0.2)
Decreased appetite	71 (16.3)	5 (1.1)	62 (14.2)	3 (0.7)
Pyrexia	68 (15.6)	6 (1.4)	55 (12.6)	0
Vomiting	65 (14.9)	5 (1.1)	63 (14.4)	3 (0.7)
Febrile neutropenia	62 (14.3)	60 (13.8)	35 (8.0)	35 (8.0)
Headache	56 (12.9)	1 (0.2)	57 (13.0)	4 (0.9)
Cough	56 (12.9)	0	53 (12.1)	0
Decreased weight	55 (12.6)	4 (0.9)	52 (11.9)	1 (0.2)
Asthenia	53 (12.2)	7 (1.6)	53 (12.1)	2 (0.5)
Dysgeusia	49 (11.3)	0	57 (13.0)	0

Morschhauser et al. NEJM 2021

FDA-approved CAR-T in NHL

- Lisocabtagene maraleucel (DLBCL)
- Tisagenlecleucel (DLBCL, ALL <25 yo)
- Brexucabtagene autoleucel (MCL)
- Axicabtagene ciloleucel (DLBCL, FL)

FDA-approved CAR-T

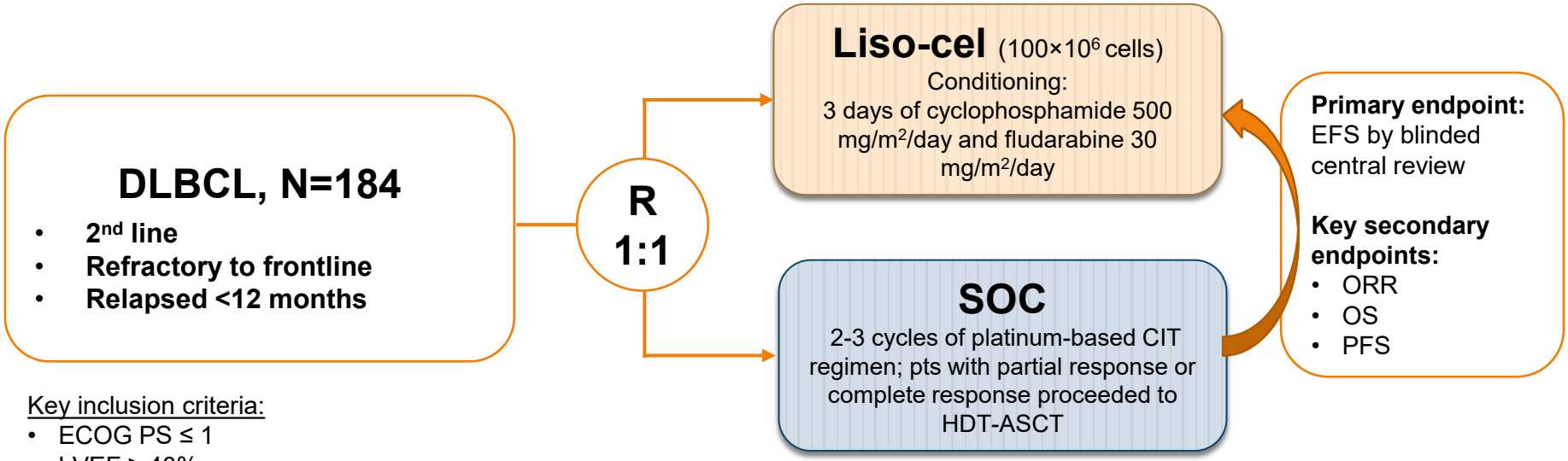
Product	Indication	Target	Trial/N	Median # prior Tx	ORR (CR)	mPFS (m)	mOS (m)	G3-4 CRS	G3-4 CRES
Axicabtagene ciloleucel[1]	DLBCL 3rd + line	CD19	ZUMA-1 P1-2/101	3	82 (54)	6	25.8	11%	32%
Lisocabtagene maraleucel[2]	DLBCL 3rd + line	CD19	TRANSCEND/192	3	73 (53)	16 (DOR)	21	2%	10%
Tisagenlecleucel[3]	DLBCL 3rd + line	CD19	JULIET P2/93	2	52 (40)	3	12	22%	12%
Brexucabtagene autoleucel[4]	MCL 2nd + line	CD19	ZUMA-2 P2/60	3	93 (67)	61% @1Y	83% @1Y	15%	31%
Axicabtagene ciloleucel[5]	FL 3rd + line	CD19	ZUMA-5 P2/124	3	94 (80)	78% @1Y	93% @1Y	6%	15%

Head-to-head studies between these regimen are lacking. Therefore, direct comparisons cannot be made.

[1]Locke Lancet Oncol 2019; [2]Abramson The Lancet 2020; [3]Schuster NEJM 2019; [4]Wang NEJM 2020; [5]Jacobson ASH 2020

TRANSFORM: Liso-cel Vs. SOC In R/R DLBCL

Phase III randomized trial



Key inclusion criteria:
- ECOG PS ≤ 1
- LVEF ≥ 40%
- CrCl > 45 mL/min
- Secondary CNS lymphoma was allowed

Key exclusion criteria:
- Prior gene or anti-CD19–targeted therapy,
- Active infection

EFS: time from randomization to death from any cause, PD, failure to achieve CR or PR by 9 weeks after randomization, or start of new antineoplastic therapy, whichever occurred first.

Kadmar et al. ASH 2021. Abstract #91

TRANSFORM: Patients' characteristics

Characteristic	Liso-cel arm n = 92	SOC arm n = 92
Male, n (%)	44 (48)	61 (66)
Age, years, n (%)		
Median (IQR)	60 (53.5–67.5)	58.0 (42–65)
< 65	56 (61)	67 (73)
≥ 65 to < 75	36 (39)	23 (25)
≥ 75	0	2 (2)
LBCL subtypes, n (%)		
DLBCL NOS	53 (58)	49 (53)
HGBCL with rearrangements in *MYC* and *BCL2*, *BCL6*, or both (DLBCL histology)	22 (24)	21 (23)
PMBCL	8 (9)	10 (11)
DLBCL transformed from any indolent lymphoma	7 (8)	8 (9)
THRBCL	1 (1)	4 (4)
FL3B	1 (1)	0
ECOG PS, n (%)		
0	48 (52)	57 (62)
1	44 (48)	35 (38)
sAAIPI, n (%)		
0 or 1	56 (61)	55 (60)
2 or 3	36 (39)	37 (40)
Prior response status, n (%)		
Refractory[a]	67 (73)	68 (74)
Relapsed[b]	25 (27)	24 (26)
Secondary CNS lymphoma, n (%)	1 (1)	3 (3)

[a]Defined as stable disease, progressive disease, PR, or CR with relapse < 3 months after 1L therapy; [b]Defined as CR with relapse on or after 3 months within 12 months after 1L therapy.
IQR, interquartile range.

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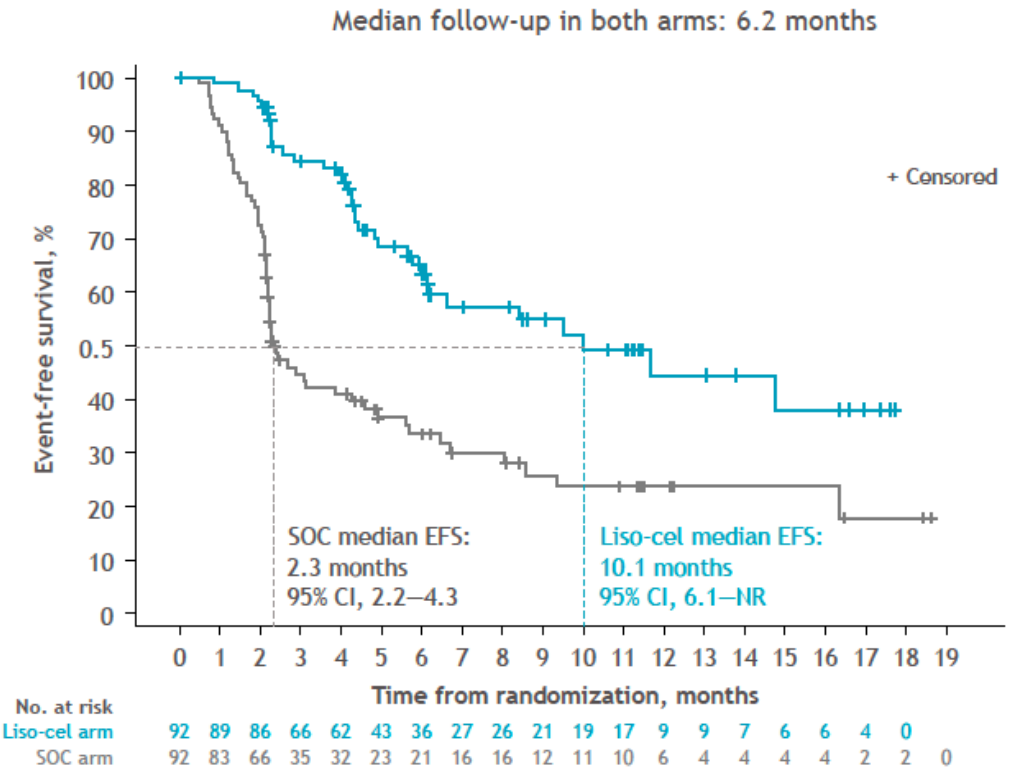
TRANSFORM: EFS, ITT analysis



	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

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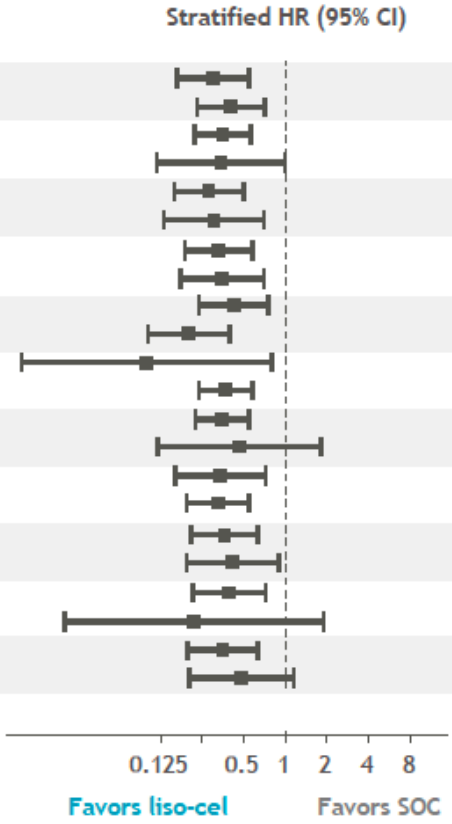
TRANSFORM: Subgroup analysis

Subgroup		Liso-cel arm n/N	SOC arm n/N	Stratified HR
sAAIPI	0 or 1	16/56	32/55	0.298
	2 or 3	19/36	31/37	0.404
Prior response status	Refractory	30/67	52/68	0.350
	Relapse to last prior therapy	5/25	11/24	0.343
Age group, years	< 65	17/56	46/67	0.277
	≥ 65 to < 75	18/36	15/23	0.301
Sex	Male	19/44	44/61	0.331
	Female	16/48	19/31	0.346
ECOG PS (at screening)	0	18/48	36/57	0.420
	1	17/44	27/35	0.201
SPD	> 50 cm²	3/10	9/10	0.099
	≤ 50 cm²	29/77	53/76	0.366
Lactate dehydrogenase	< 500 µ/L	30/79	53/81	0.350
	≥ 500 µ/L	4/10	10/11	0.460
Prior CT response status	Chemorefractory (PD, SD)	15/25	16/18	0.338
	Chemosensitive (PR, CR)	20/67	47/74	0.320
NHL type	DLBCL	21/60	36/57	0.357
	HGBCL	14/22	19/21	0.413
DLBCL subtype	DLBCL NOS de novo	19/53	30/49	0.395
	DLBCL transformed from indolent NHL	2/7	6/8	0.218
DLBCL subtype based on cell of origin	GCB	21/45	29/40	0.348
	ABC, non-GCB	7/21	22/29	0.477



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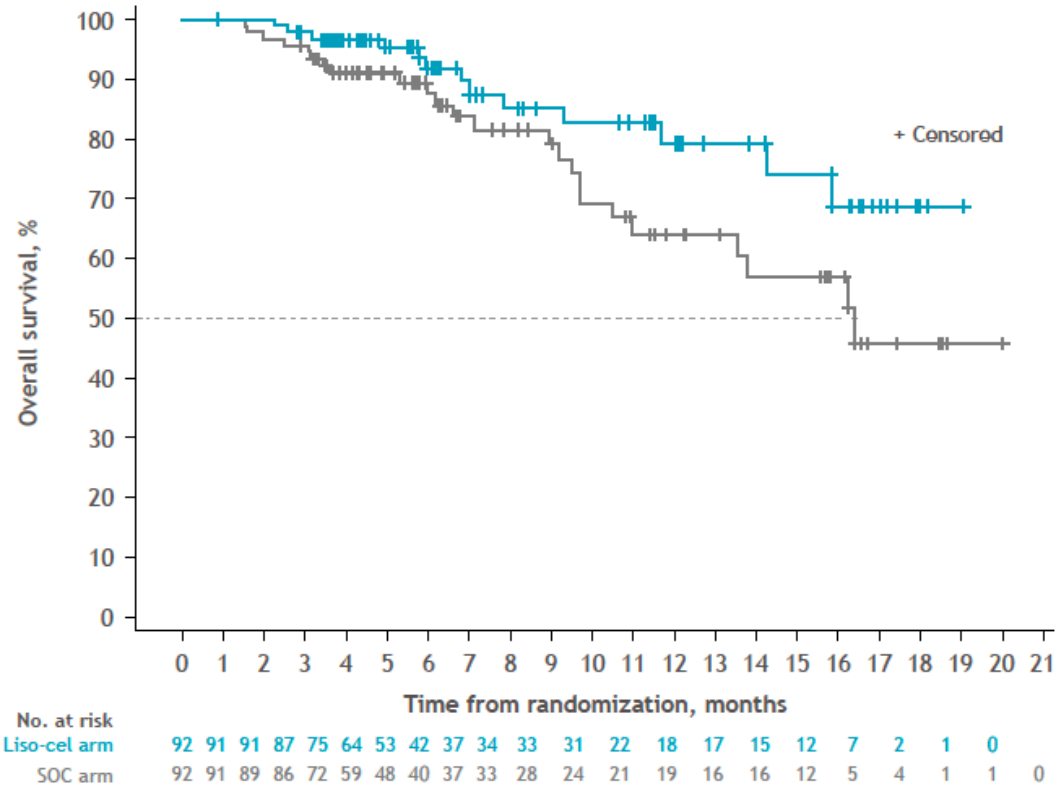
TRANSFORM: OS



	Liso-cel arm (n = 92)	SOC arm (n = 92)
Patients with events, n	13	24
Stratified HR (95% CI)	0.509 (0.258–1.004) *P* = 0.0257	
Median OS (95% CI), months	NR (15.8–NR)	16.4 (11.0–NR)
6-month OS rate, % (SE)	91.8 (3.29)	89.4 (3.36)
Two-sided 95% CI	85.4–98.2	82.9–96.0
12-month OS rate, % (SE)	79.1 (6.13)	64.2 (6.99)
Two-sided 95% CI	67.1–91.1	50.5–77.9

Patients in the SOC arm that crossed over to receive liso-cel continue to be followed for OS in the SOC arm

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

Kadmar et al. ASH 2021. Abstract #91

TRANSFORM: AEs

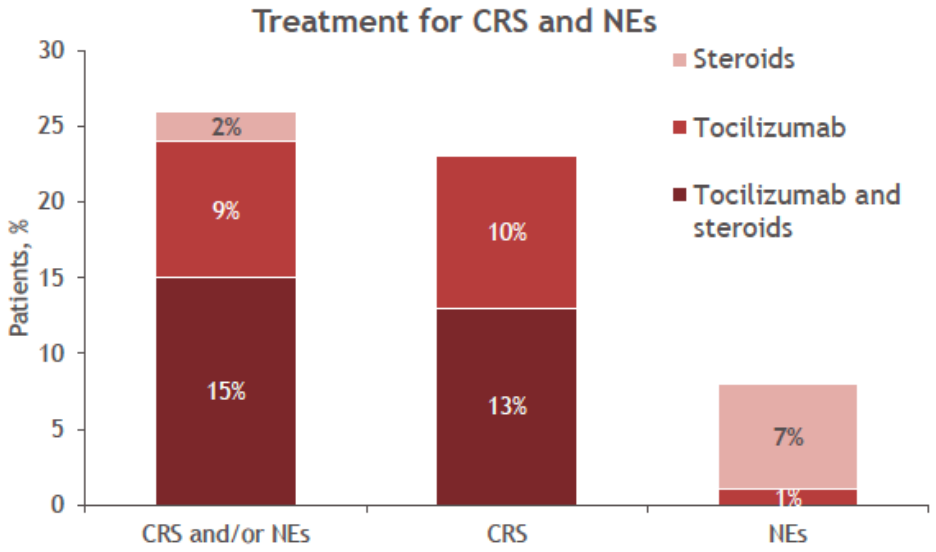
TEAEs	Liso-cel arm (n = 92)		SOC arm (n = 91)[a]	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Patients experiencing any TEAE, n (%)	92 (100)	85 (92)	90 (99)	79 (87)
Patients experiencing any serious TEAE, n (%)	44 (48)	N/A	44 (48)	N/A
Deaths due to TEAEs, n (%)	N/A	1 (1)[b]	N/A	2 (2)[b]
Most common TEAEs (occurring in ≥ 25% of patients in either arm), n (%)				
Neutropenia	75 (82)	74 (80)	49 (54)	46 (51)
Anemia	58 (63)	45 (49)	58 (64)	45 (49)
Thrombocytopenia	53 (58)	45 (49)	62 (68)	58 (64)
Nausea	49 (53)	3 (3)	52 (57)	3 (3)
CRS	45 (49)	1 (1)	N/A	N/A
Headache	39 (42)	4 (4)	20 (22)	1 (1)
Fatigue	36 (39)	0	35 (38)	2 (2)
Constipation	31 (34)	2 (2)	22 (24)	0
Pyrexia	27 (29)	0	21 (23)	0
Lymphopenia	25 (27)	23 (25)	10 (11)	8 (9)
Diarrhea	23 (25)	0	38 (42)	3 (3)
Decreased appetite	21 (23)	1 (1)	28 (31)	3 (3)
Vomiting	18 (20)	1 (1)	23 (25)	2 (2)

- Febrile neutropenia: 15% and 24% in the liso-cel and SOC arms, respectively

Kadmar et al. ASH 2021. Abstract #91

TRANSFORM: AEs

Patients with CRS and NEs	Liso-cel arm (n = 92)
CRS,[a] n (%)	
Any grade	45 (49)
Grade 1	34 (37)
Grade 2	10 (11)
Grade 3	1 (1)[b]
Grade 4/5	0
Time to onset, days, median (range)	5 (1–63)
Time to resolution, days, median (range)	4 (1–16)
NE,[c] n (%)	
Any grade	11 (12)
Grade 1	5 (5)
Grade 2	2 (2)
Grade 3	4 (4)
Grade 4/5	0
Time to onset, days, median (range)	11 (7–25)
Time to resolution, days, median (range)	6 (1–30)



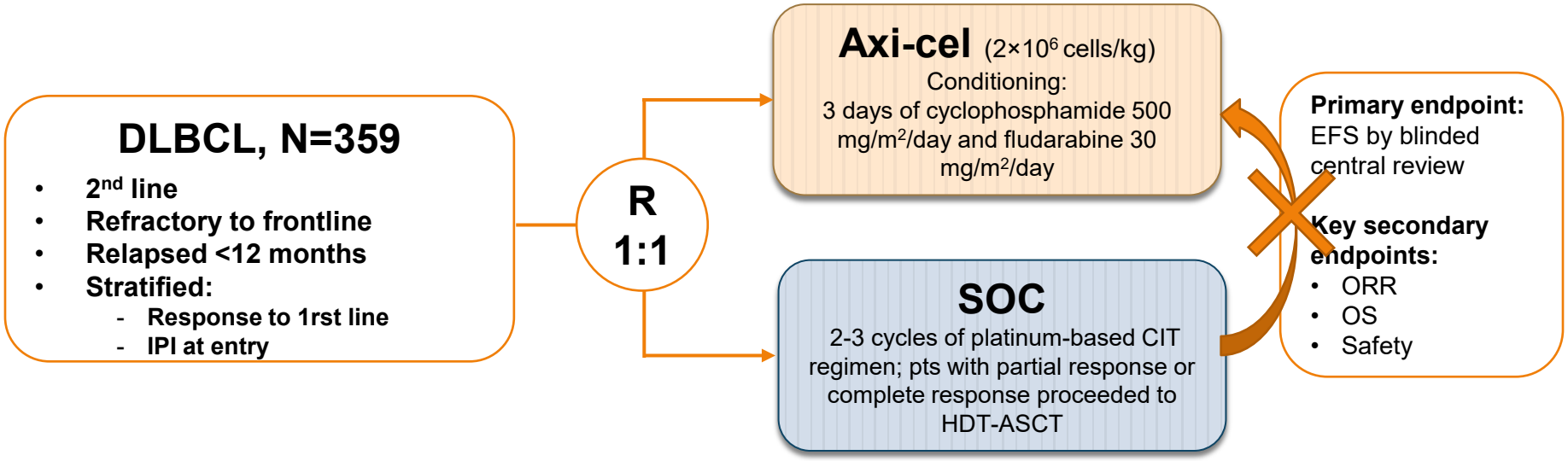
Other adverse events of special interest	Liso-cel arm (n = 92)	SOC arm (n = 91)
Prolonged cytopenia[d]	40 (43)	3 (3)
Grade ≥ 3 infection	14 (15)	19 (21)

[a]Graded according to the Lee 2014 criteria; [b]Grade 3 CRS event due to hypertransaminasemia, which resolved 2 days later; [c]Defined as investigator-identified neurological adverse events related to liso-cel. These were graded using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03; [d]Grade ≥ 3 anemia, neutropenia, or thrombocytopenia at 35 days after liso-cel infusion for the liso-cel arm or at 35 days after the start of the last CT for the SOC arm.

Kadmar et al. ASH 2021. Abstract #91

ZUMA-7: Axi-cel Vs. SOC In R/R DLBCL

Phase III randomized trial



EFS: time to earliest date of disease progression, death from any cause, or new lymphoma Tx)

Locke et al. ASH 2021. Abstract #2

ZUMA-7: Results

- Median f/u of 24.9 m: mEFS 8.3 m (95% CI, 4.5-15.8) for axi-cel vs with 2.0 m (95% CI, 1.6-2.8) for SOC (HR, 0.398; 95% CI, 0.308-0.514; *P* < .0001).
- ORR 83% for axi-cel vs 50% for SOC (OR, 5.31; 95% CI, 3.1-8.9; *P* < .0001).
- Strong trend toward improved OS favoring axi-cel over SOC, but did not yet meet statistical significance (median not reached vs 35.1 months, HR, 0.730; *P*=.027).
- Although the study did not include a crossover design, patients who failed on SOC and later received axi-cel could be confounding these results.

Locke et al. ASH 2021. Abstract #2

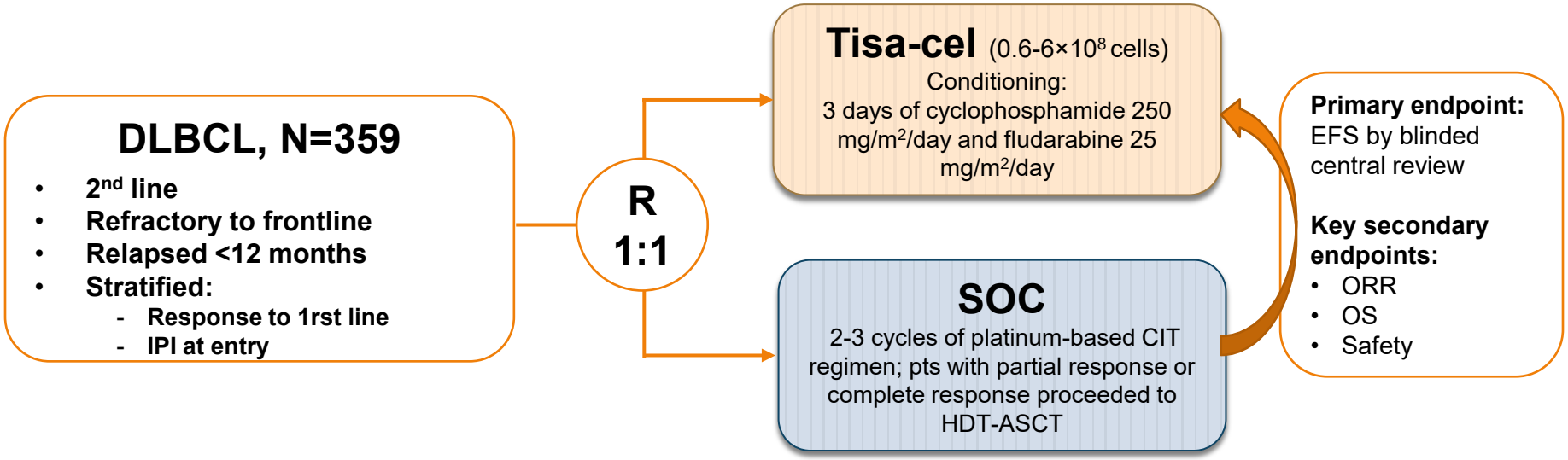
ZUMA-7: AEs

- G ≥3 neurologic events occurred in 21% of the axi-cel group and 1% of the SOC group; All were treated with corticosteroids. Median time to onset was 7 days with axi-cel and 23 days with SOC; median duration as 9 days vs 23 days.
  - tremor (26% vs 1%),
  - confusional state (24% vs 2%,),
  - aphasia (21% vs 0%).
- G ≥3 CRS was seen in 6% of axi-cel patients; CRS was managed with tocilizumab (65%) corticosteroids (24%) and vasopressors (6%).
- G ≥3 neutropenia (69% vs 41%) and anemia (30% vs 39%)
- The axi-cel arm had 1 treatment-related death; the SOC group had 2.

Locke et al. ASH 2021. Abstract #2

BELINDA: Tisa-cel Vs. SOC In R/R Aggressive B-cell lymphoma

Phase III randomized trial

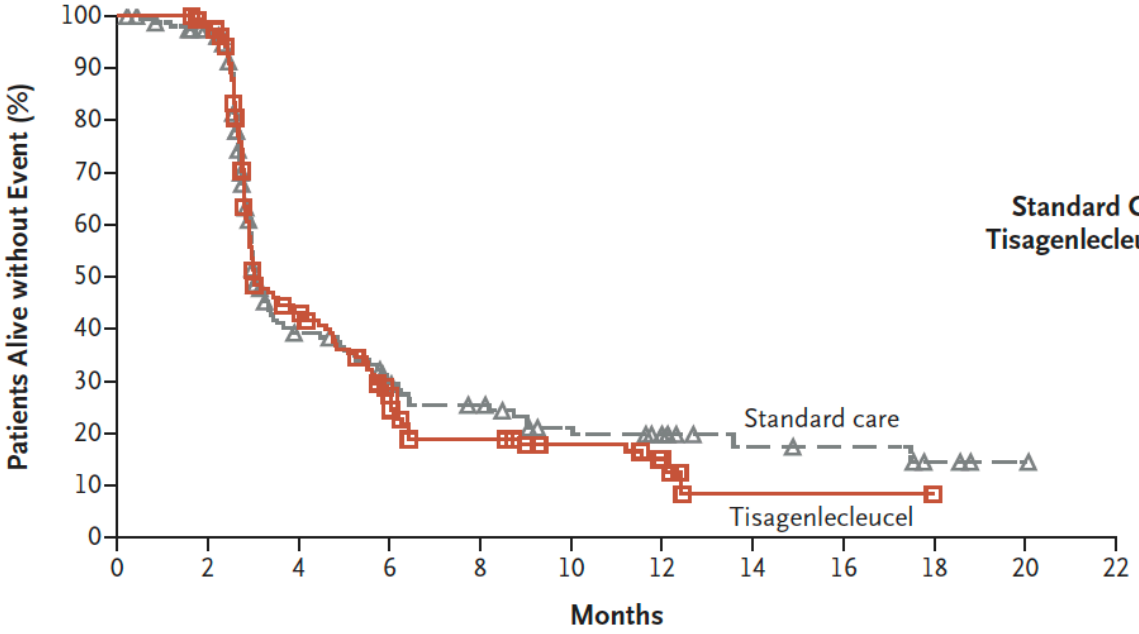


EFS: defined as the time from randomization to stable or progressive disease at or after the week 12 assessment or death

Bishop et al. NEJM 2022

BELINDA: Tisa-cel Vs. SOC In R/R Aggressive B-cell lymphoma

Phase III randomized trial



No. at Risk												
Standard care	160	148	45	31	25	17	12	7	6	3	1	0
Tisagenlecleucel	162	156	57	32	19	13	6	1	1	0	0	0

	No. of Patients	No. of Events	Median Event-free Survival (95% CI)
			mo
Standard Care	160	104	3.0 (3.0–3.5)
Tisagenlecleucel	162	117	3.0 (2.9–4.2)

Hazard ratio for event or death (tisagenlecleucel vs. standard care), 1.07 (95% CI, 0.82–1.40)
P=0.61

Bishop et al. NEJM 2022

BELINDA: Tisa-cel Vs. SOC In R/R Aggressive B-cell lymphoma

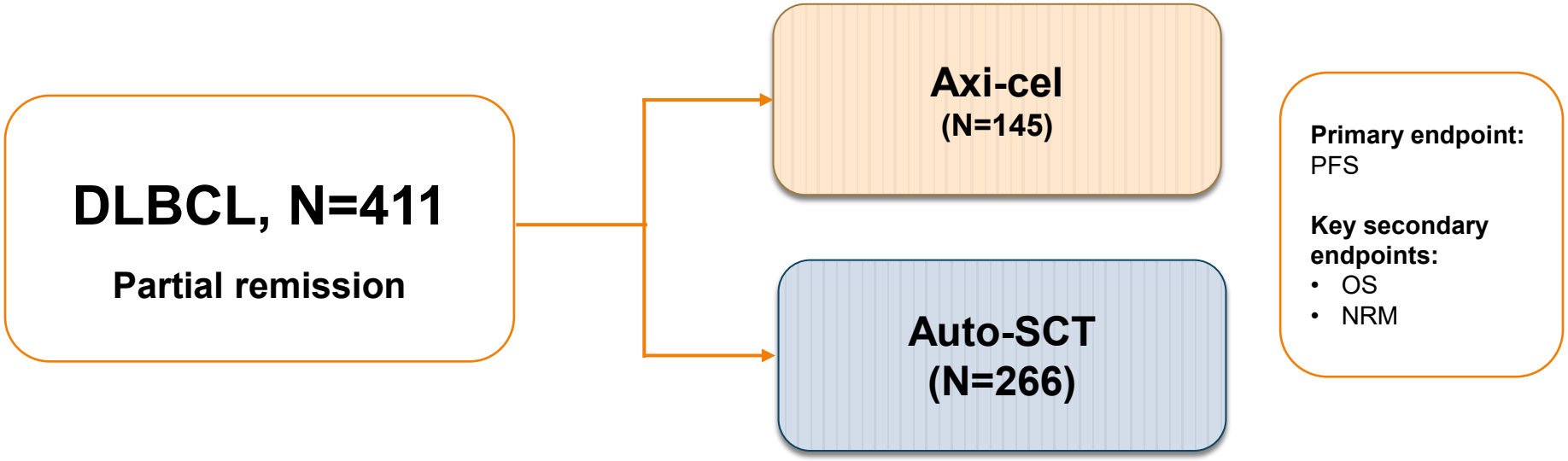
Phase III randomized trial

- A higher percentage of PD at week 6 (preinfusion) in the tisagenlecleucel group than in the SOC group (25.9% vs. 13.8%)
- lower number of chemotherapy cycles in the tisagenlecleucel group than in the SOC group
- A longer time to infusion and delayed response confounded the original definition of event-free survival in both groups at week 12

- G ≥3 neurologic events occurred in 1.9%
- G≥3 CRS occurred in 5.2%

Bishop et al. NEJM 2022

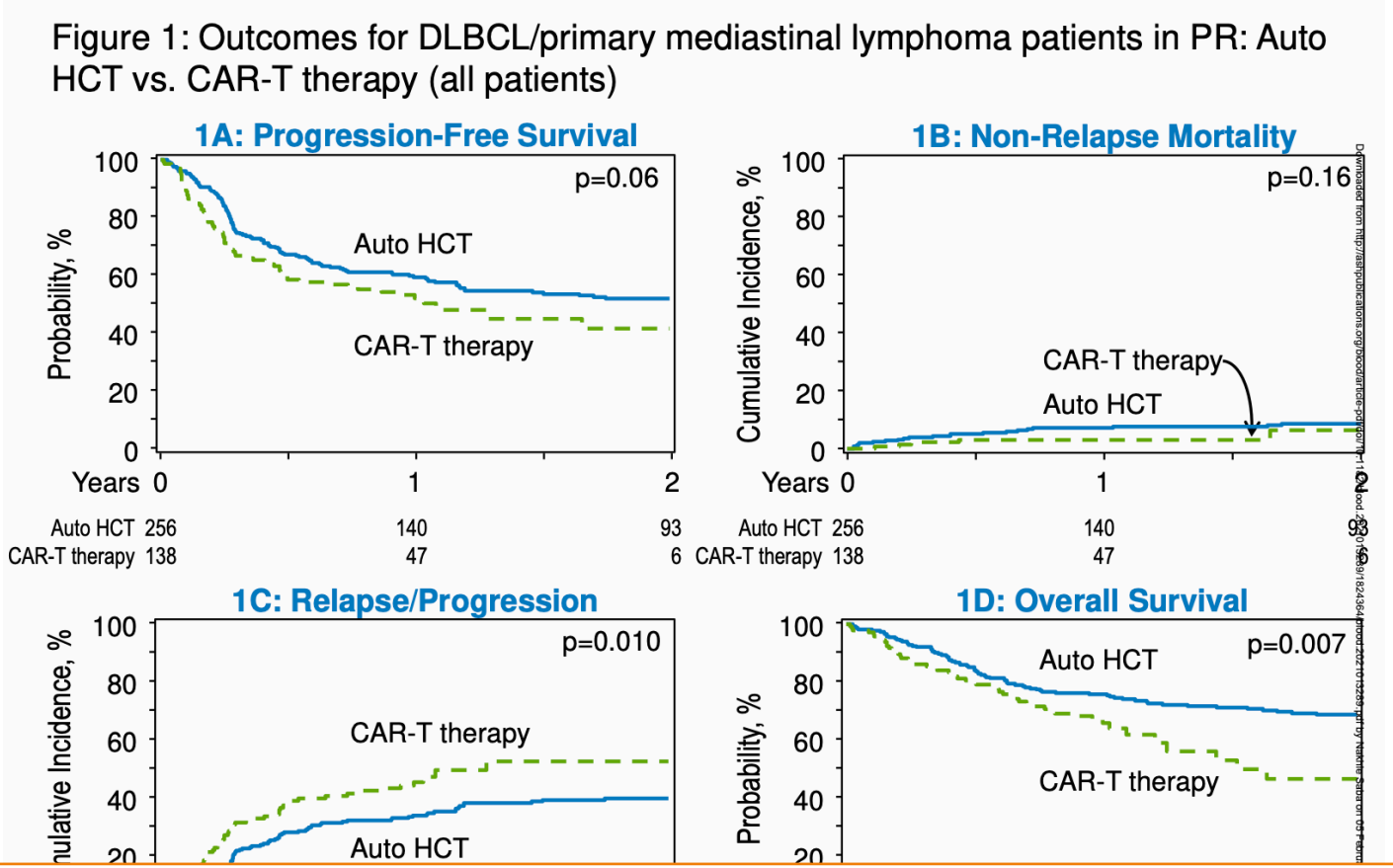
Autologous Transplant Vs. CAR T-cell For Relapsed DLBCL In Partial Remission: CIBMTR retrospective analysis



PFS: defined as time from either auto-HCT or CAR-T to relapse or death from any cause.

Shadman et al. Blood 2021

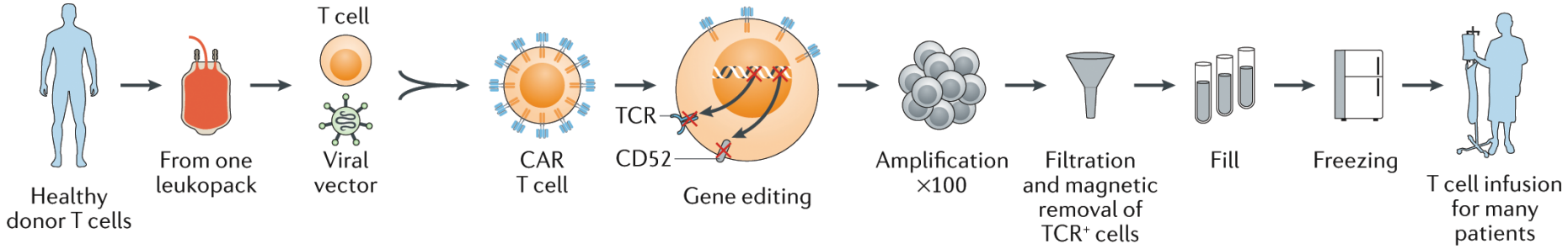
Autologous Transplant Vs. CAR T-cell For Relapsed DLBCL In PR



When analysis was limited to patients with early treatment failure (primary refractory disease or relapse within 12 months of diagnosis), auto-HCT (n=186) vs. CAR-T (n=110) cohorts had no significant difference in 2-year PFS.

Shadman et al. Blood 2021

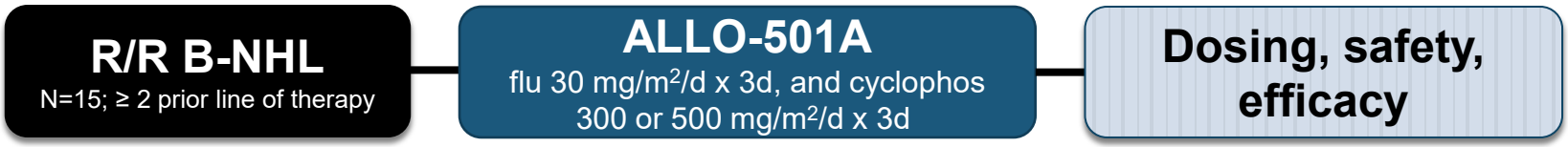
Manufacturing of allogeneic “off-the-shelf” CAR T cells



Depil et al. Nat Rev Drug Discov. 2020

ALPHA2 (NCT04416984):

Single-arm, open-label, Phase 1/2 trial of ALLO-501A in pts with DLBCL and transformed FL and MZL



- 12 evaluable patients
- No cases of GvHD
- No CRS, no ICANS, no GvHD, no DLTs, no dose reductions, no G≥3 infections and no SAEs
- Cytopenia was the most common AE and occurred in 72% of pts
- ORR 50% (all CR)

Lekatis et al. ASH 2021. Abstract #649

Thank you

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