Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Monoclonal Antibody Therapies in Leukemia and Lymphoma 2022

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#LearnACI

Disclosures

Consulting Fees: Abbvie, Amgen, BMS, Pfizer

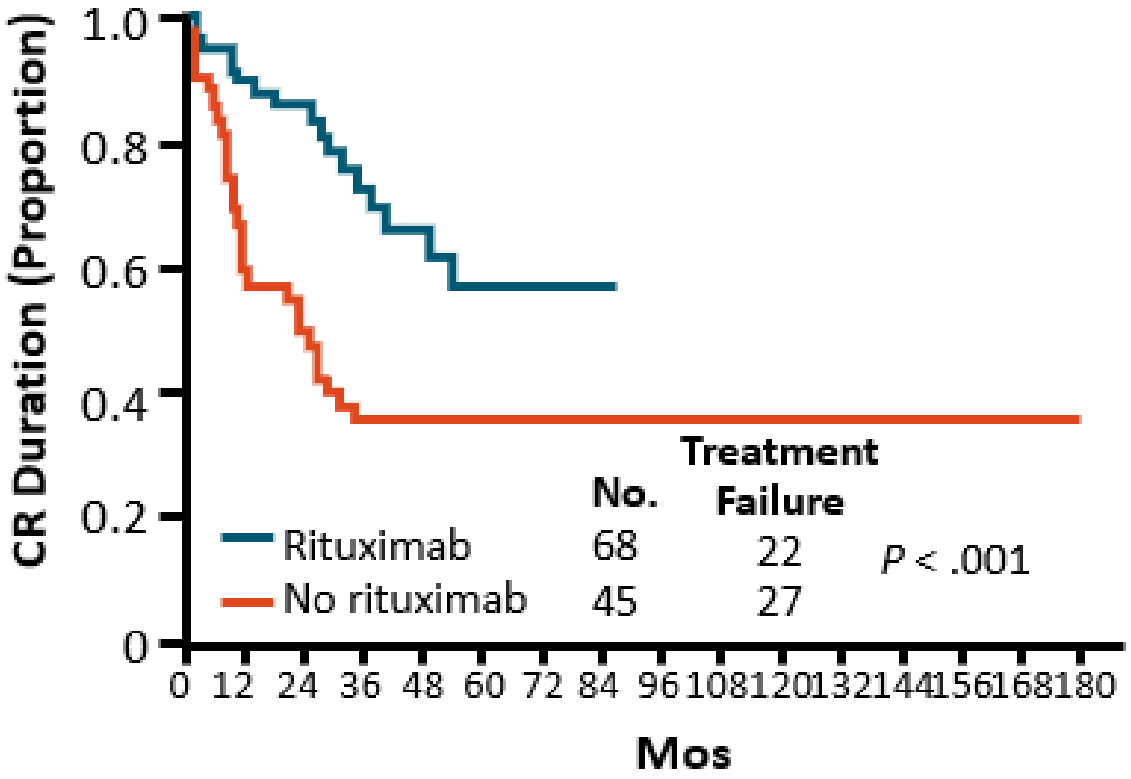
Contracted Research: Autolus, Amphivena, Astellas, Jazz, Kadmon, Kite, Pharmacyclics, Talaris

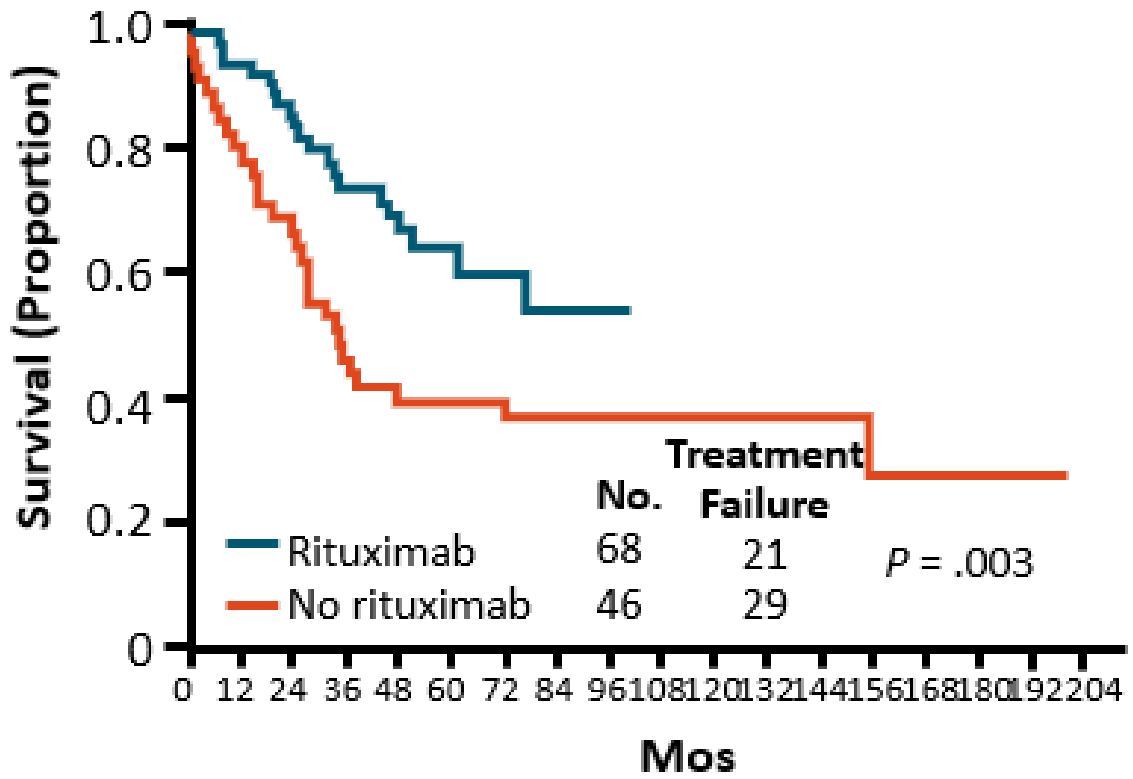
I will be discussing non-FDA approved indications during my presentation.

Acute Lymphoblastic Leukemia

Rituximab Improves Outcome for CD20+ (>20% blasts) ALL

Rituximab + Hyper-CVAD

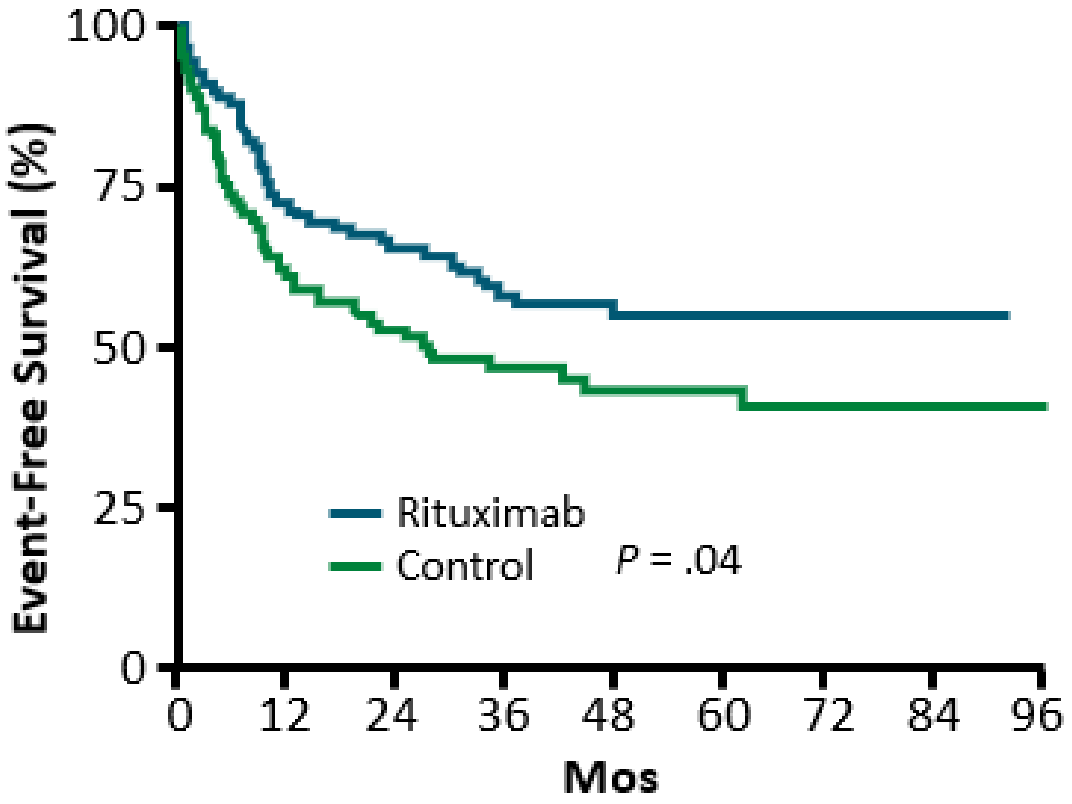


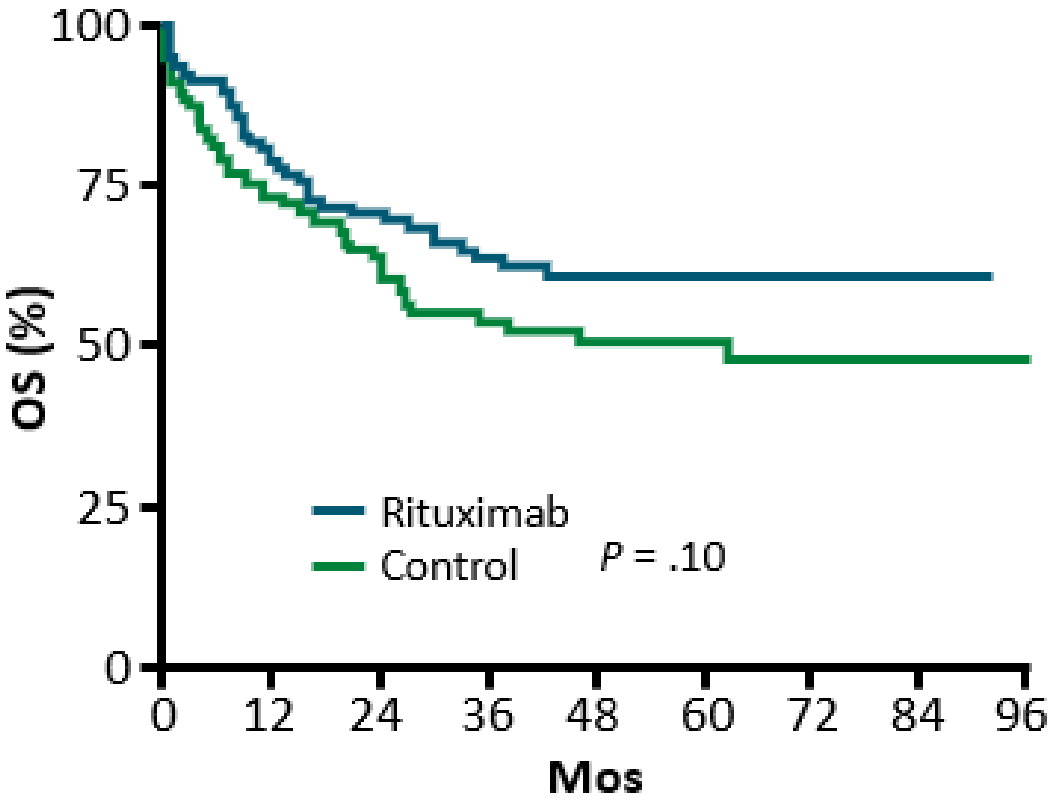


Thomas DA, et al. J Clin Oncol. 2010;28:3880-3889.

GRAALL: Rituximab Improves Outcome for CD20+ ALL

Rituximab + BFM-like Regimen

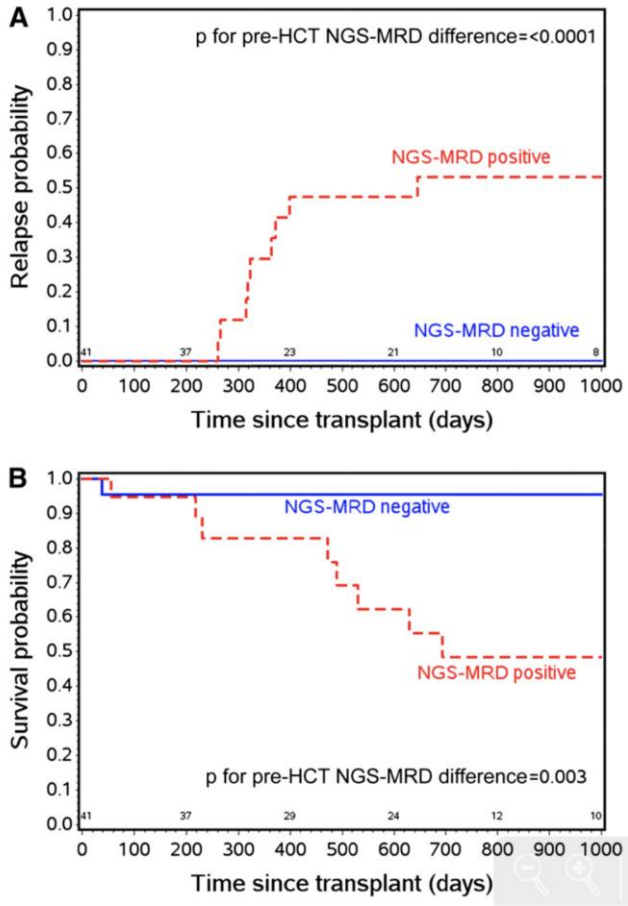




Maury S, et al. NEJM. 2016;375:1044-1053.

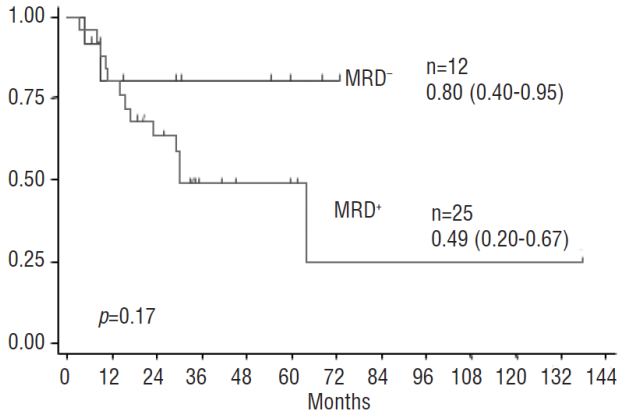
MRD Status Pre-HCT Predicts RFS and OS in B-ALL

- N=56, age 1-21
- COG ASCT0431
- MRD Quant: NGS

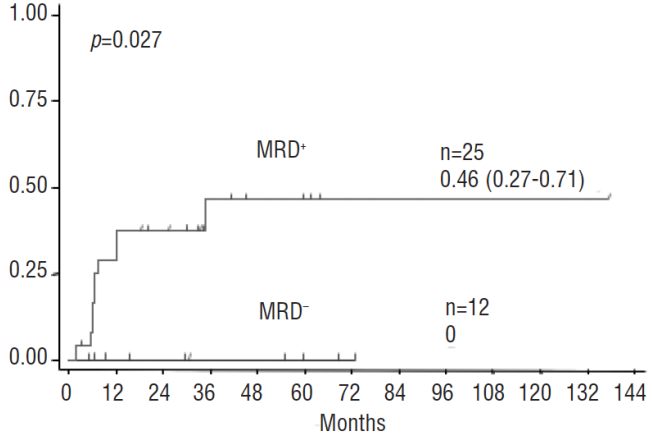


n=43, age 18-63
MAC alloHCT in CR1
MRD quant:
TCR/Ig ASO-PCR or BCR/ABL Q-PCR or
MLL/AF4 Q-PCR

MRD status pre-HCT: OS



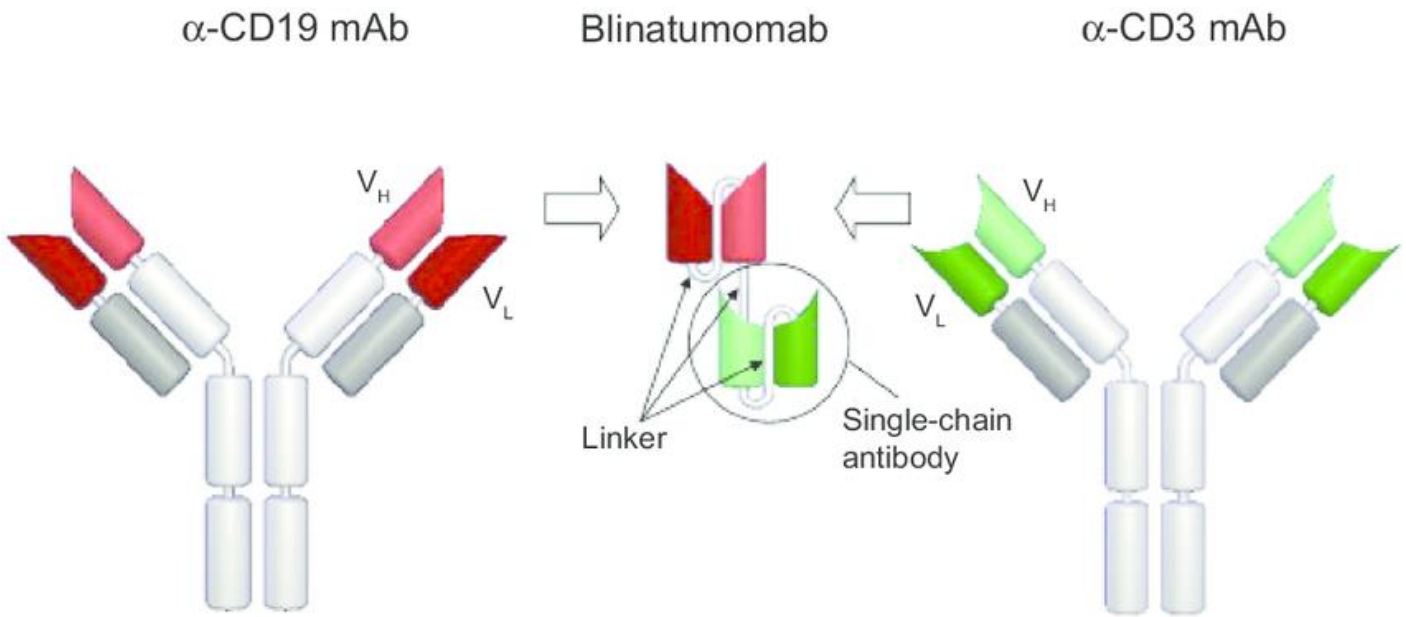
MRD status pre-HCT: CIR

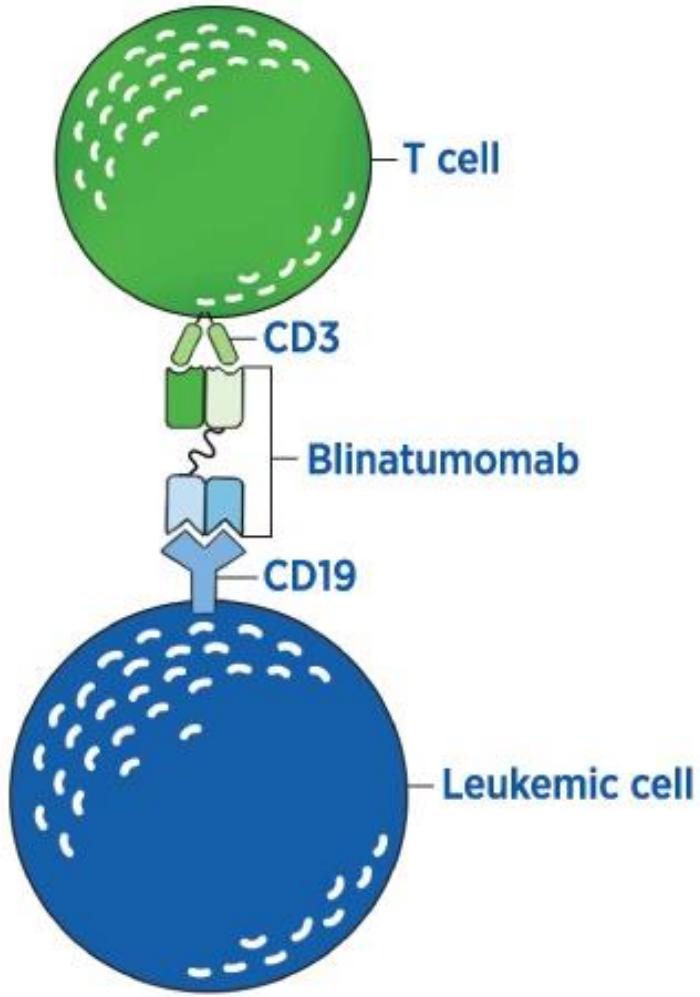


Pulsipher *et al*. Blood 2015; 125:3501-3508

Spinelli *et al*. Haematologica 2007; 92:612-618

Blinatumomab BLAST Trial: Preemption of ALL Relapse Using MRD-Directed Treatment



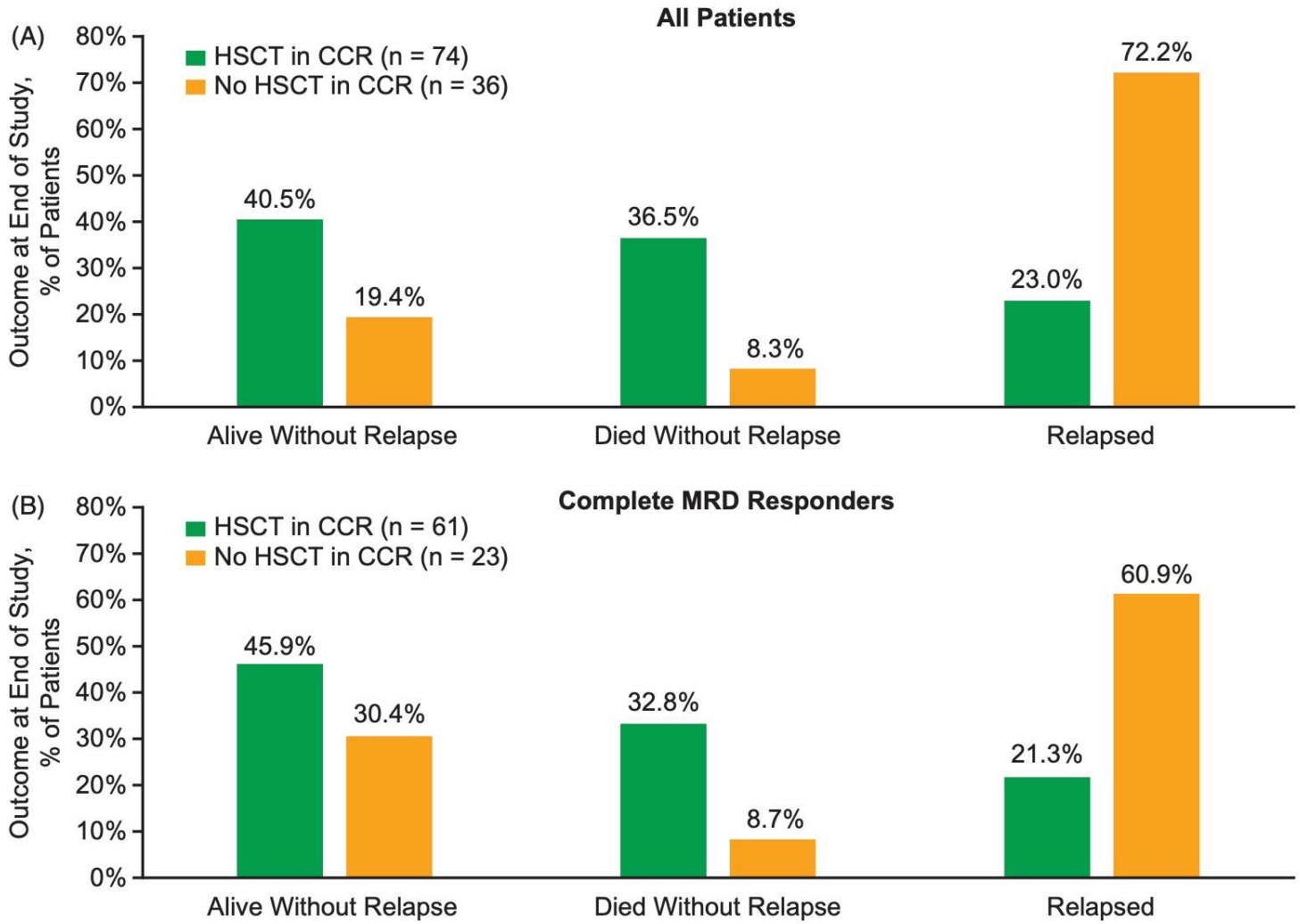


Honey K. AACR.ORG

Blinatumomab BLAST Trial: Preemption of ALL Relapse Using MRD-Directed Treatment

Blinatumomab administered for >10^{-3} MRD after ≥ 3 blocks of chemotherapy

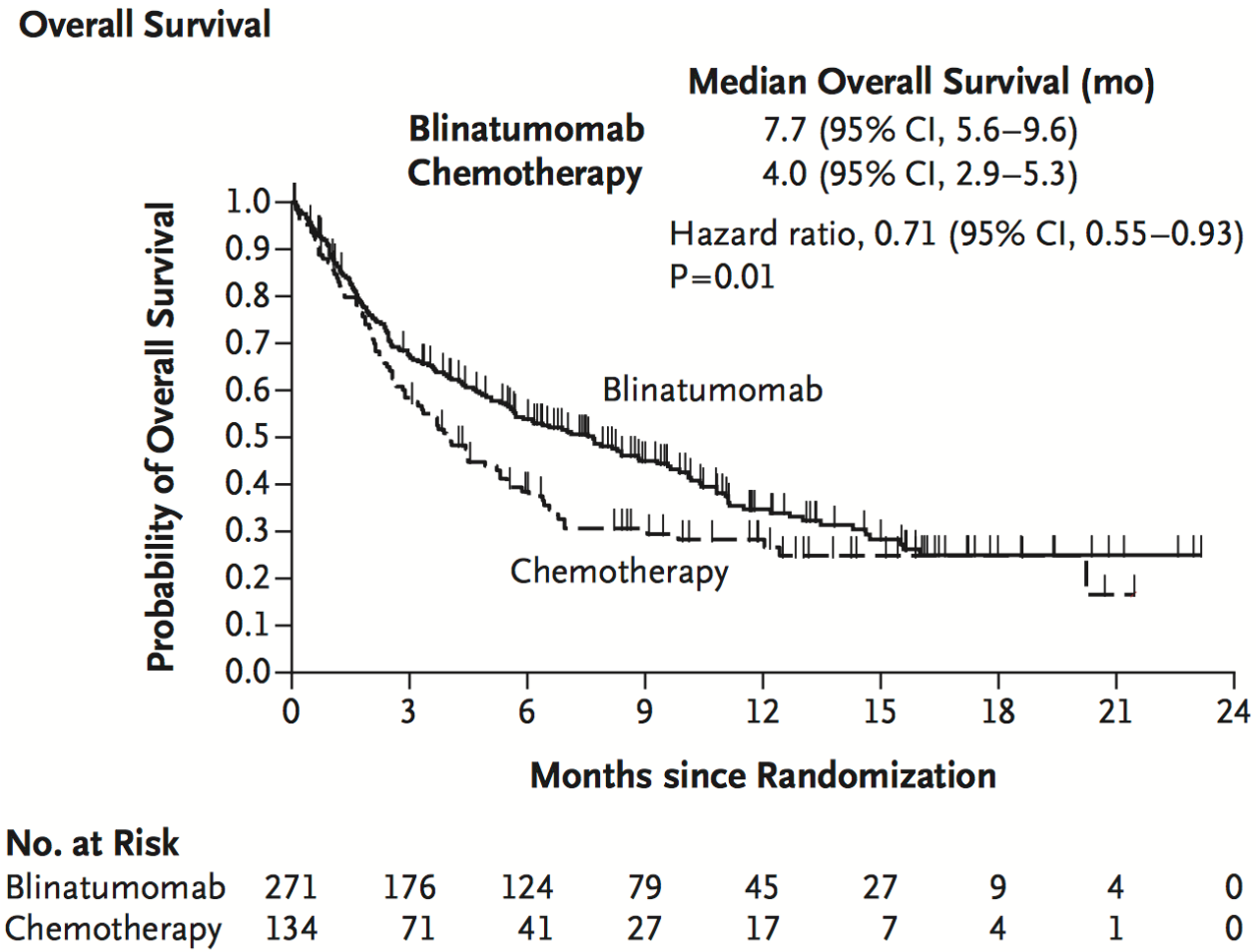
- 80% MRD response (achieved MRD <10^{-4})
- 72% underwent alloHCT



Gökbuget et al. Blood 2018; 131:1522-1531

Gökbuget et al. Leuk Lymph 2020; 61(11):2665-2673.

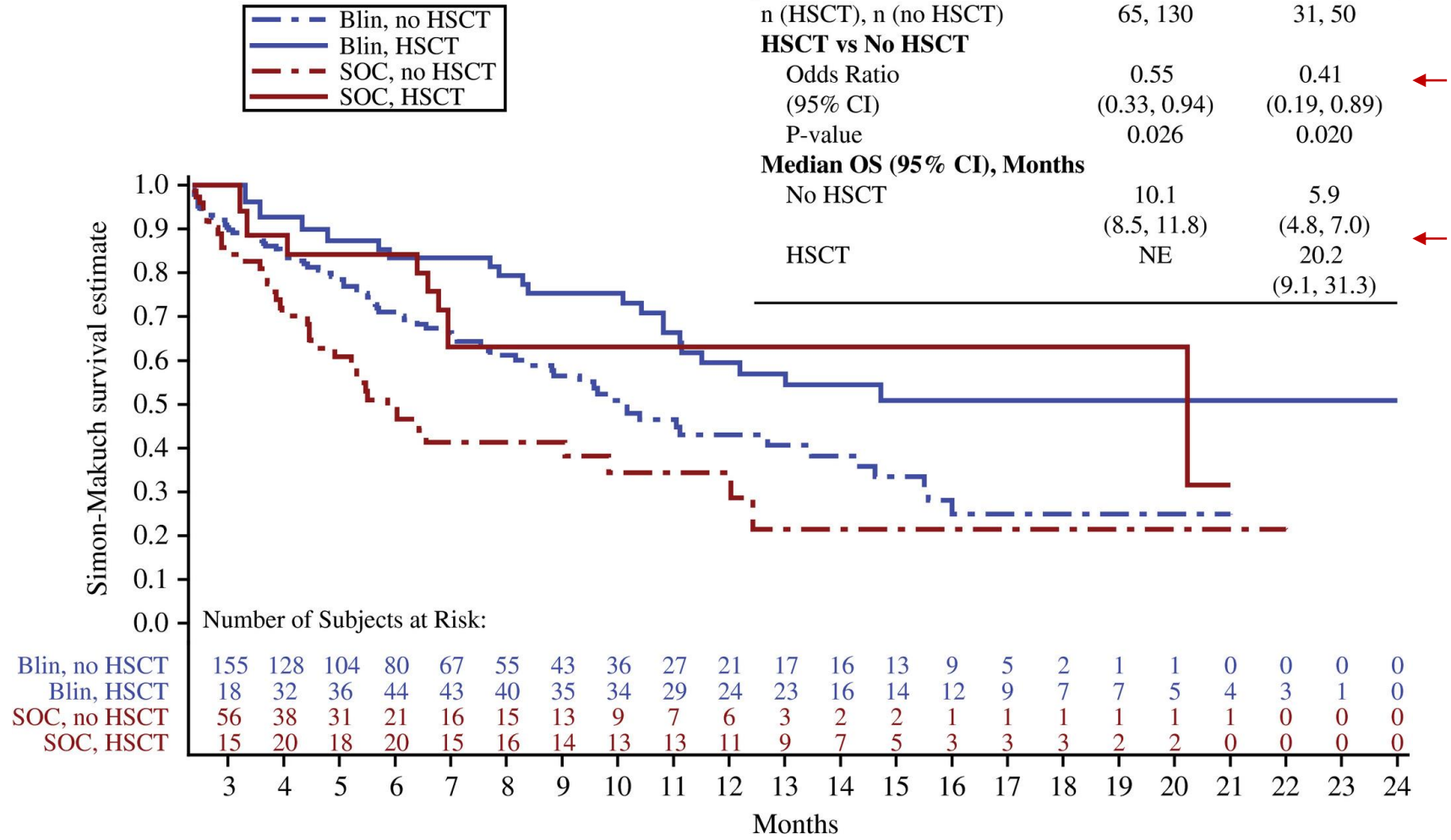
Treatment of Relapsed/Refractory ALL — Blinatumomab



Kantarjian et al., N Engl J Med 2017; 376:836-847

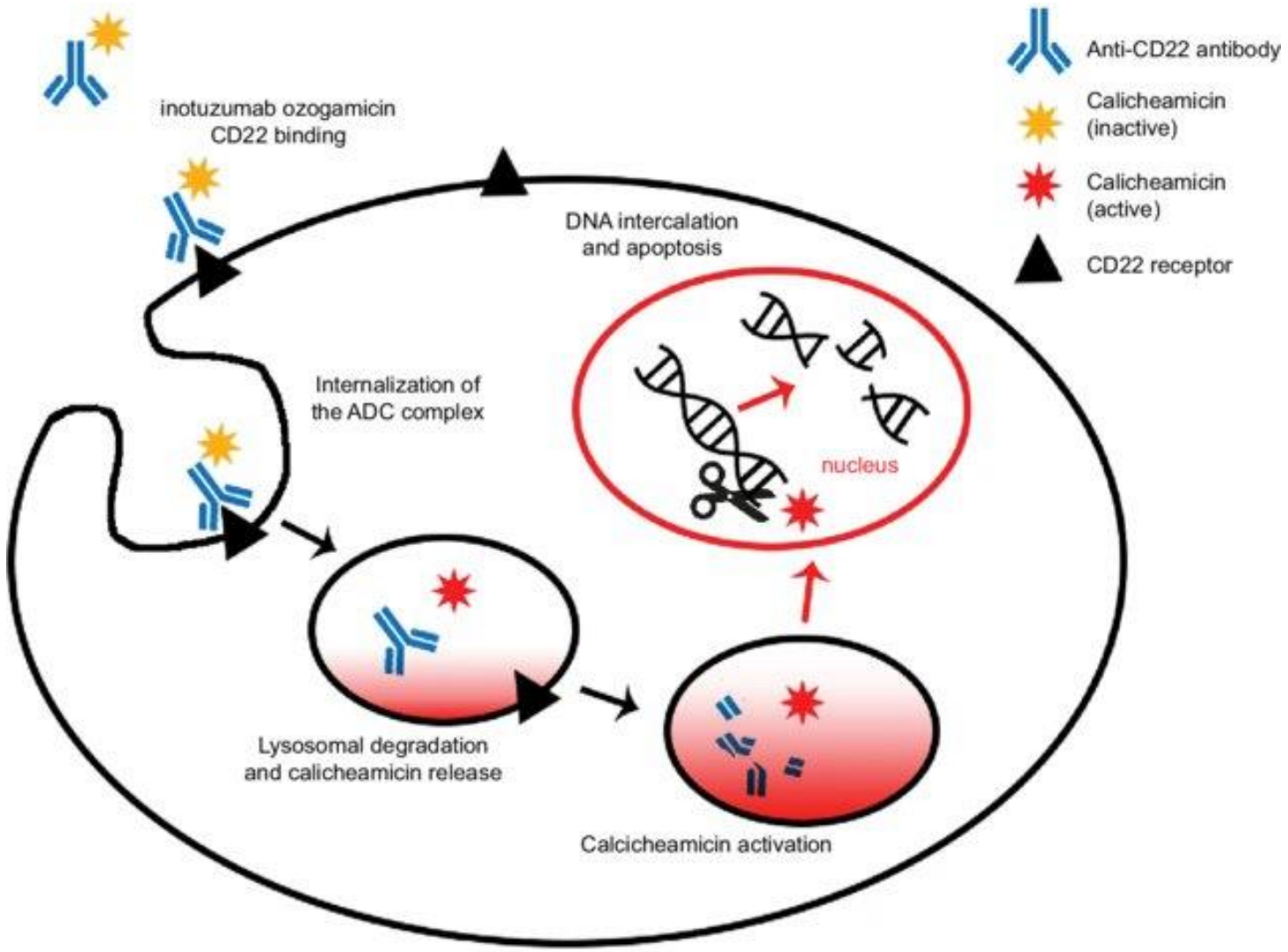
Blinatumomab as Bridge to Allo-HCT in R/R ALL

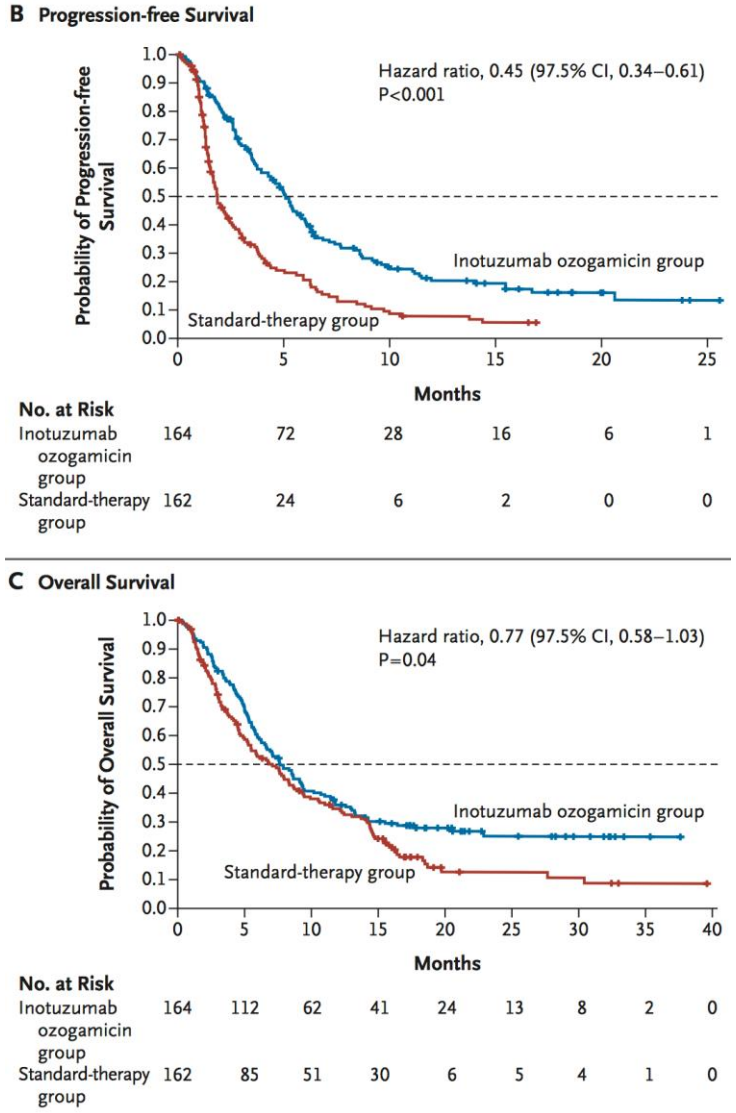
	Blin n = 195	SOC n = 81
n (HSCT), n (no HSCT)	65, 130	31, 50
HSCT vs No HSCT		
Odds Ratio	0.55	0.41
(95% CI)	(0.33, 0.94)	(0.19, 0.89)
P-value	0.026	0.020
Median OS (95% CI), Months		
No HSCT	10.1 (8.5, 11.8)	5.9 (4.8, 7.0)
HSCT	NE	20.2 (9.1, 31.3)



Jabbour et al. Cancer 2019; 125(23):4181-4192

Inotuzumab Treatment for Relapsed/Refractory ALL

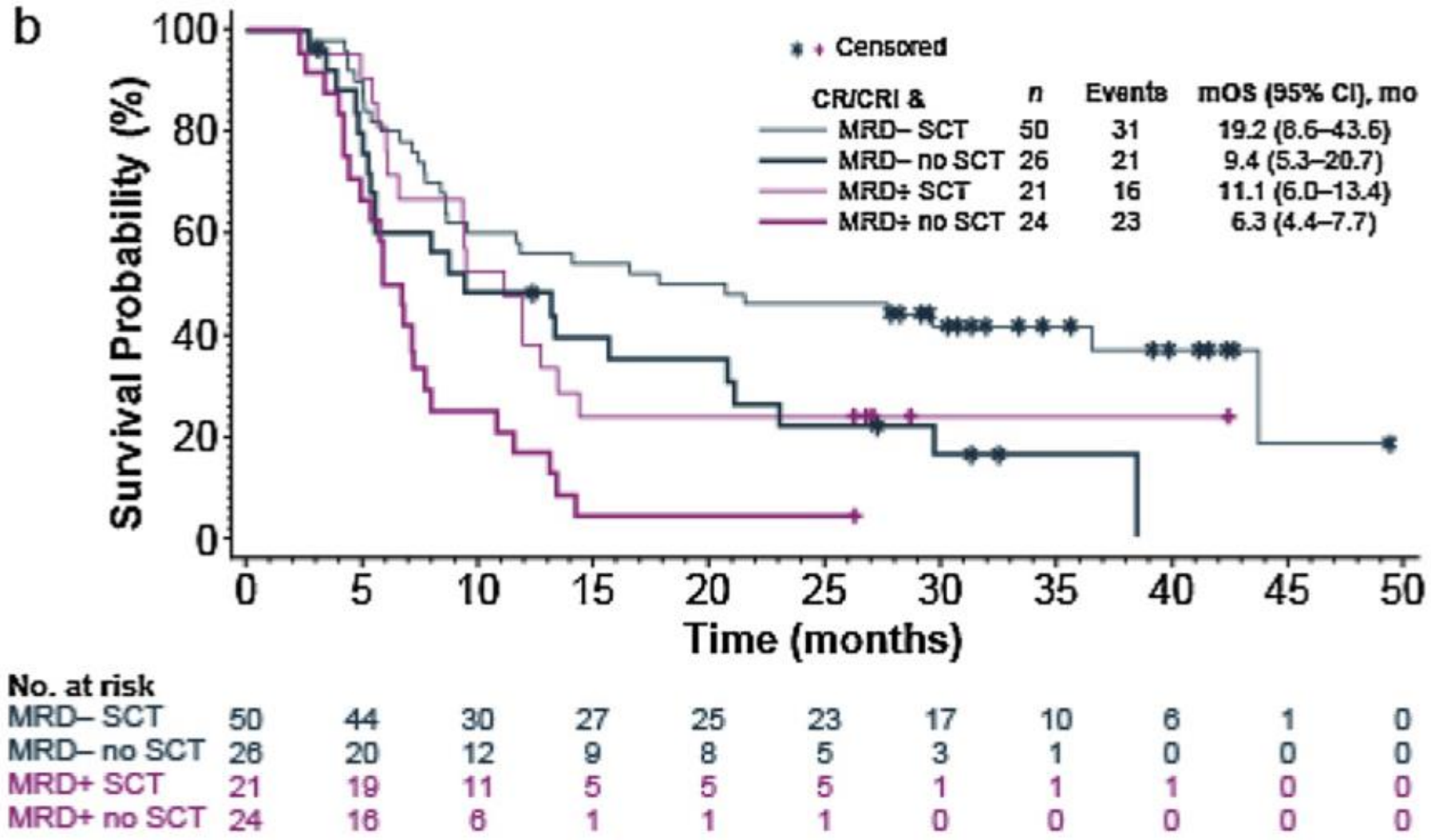




Uy et al., J Blood Med 2018; 9:67-74

Kantarjian et al., N Engl J Med 2016; 375:740-753

Inotuzumab as Bridge to Allo-HCT in R/R ALL



Jabbour et al. Leukemia Res 2020; 88:106283

Sequencing of Novel Agents in R/R B-ALL: Blin and Ino have comparable efficacy as first/second salvage therapy

Study Objective

Analyze clinical outcomes for adult patients ≥18 years of age with R/R B-cell ALL treated with blinatumomab, InO, or both outside of clinical trials between 2013 and 2019

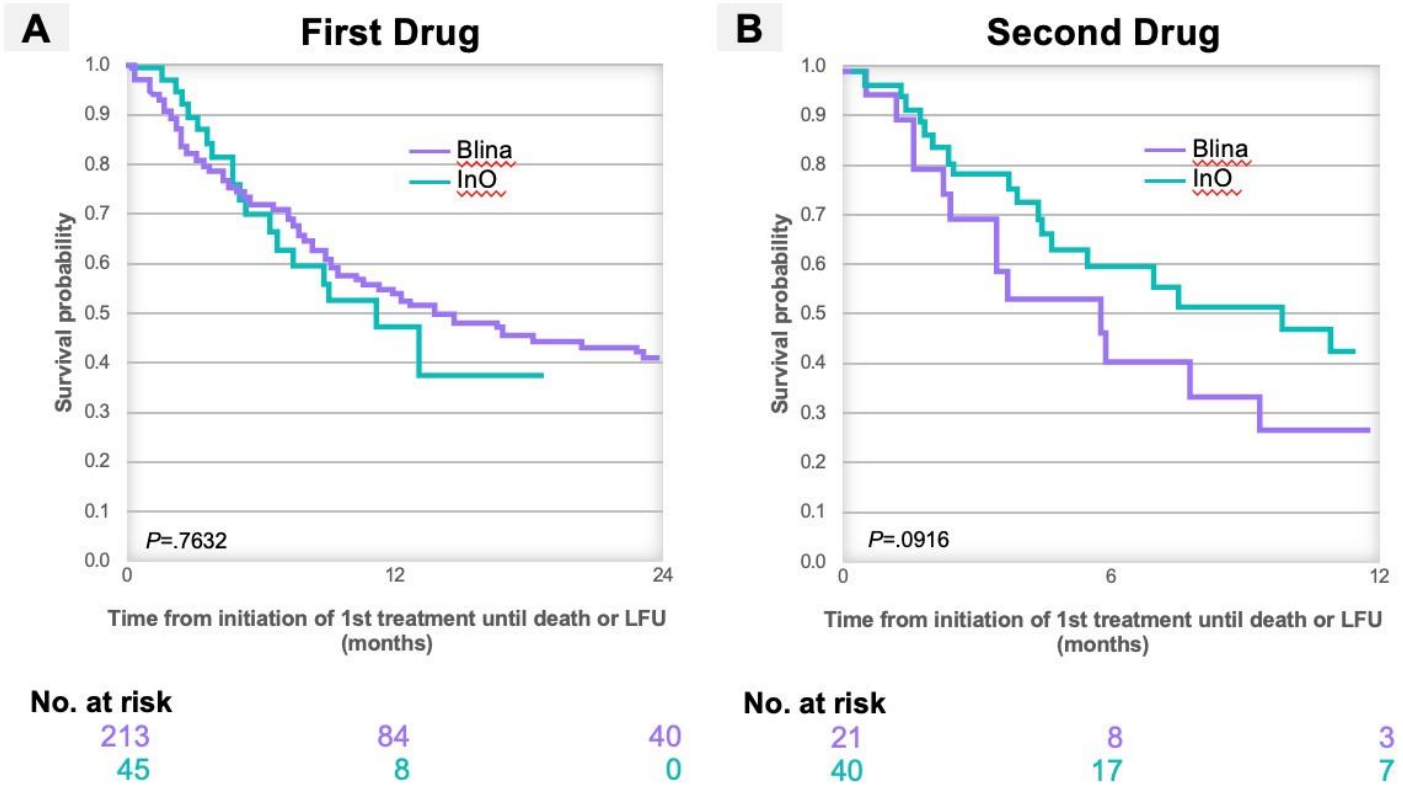
Analyses Performed

Response rate, duration of response, discontinuation rates due to adverse events, and survival outcomes were evaluated for a 276-patient cohort

Key Results

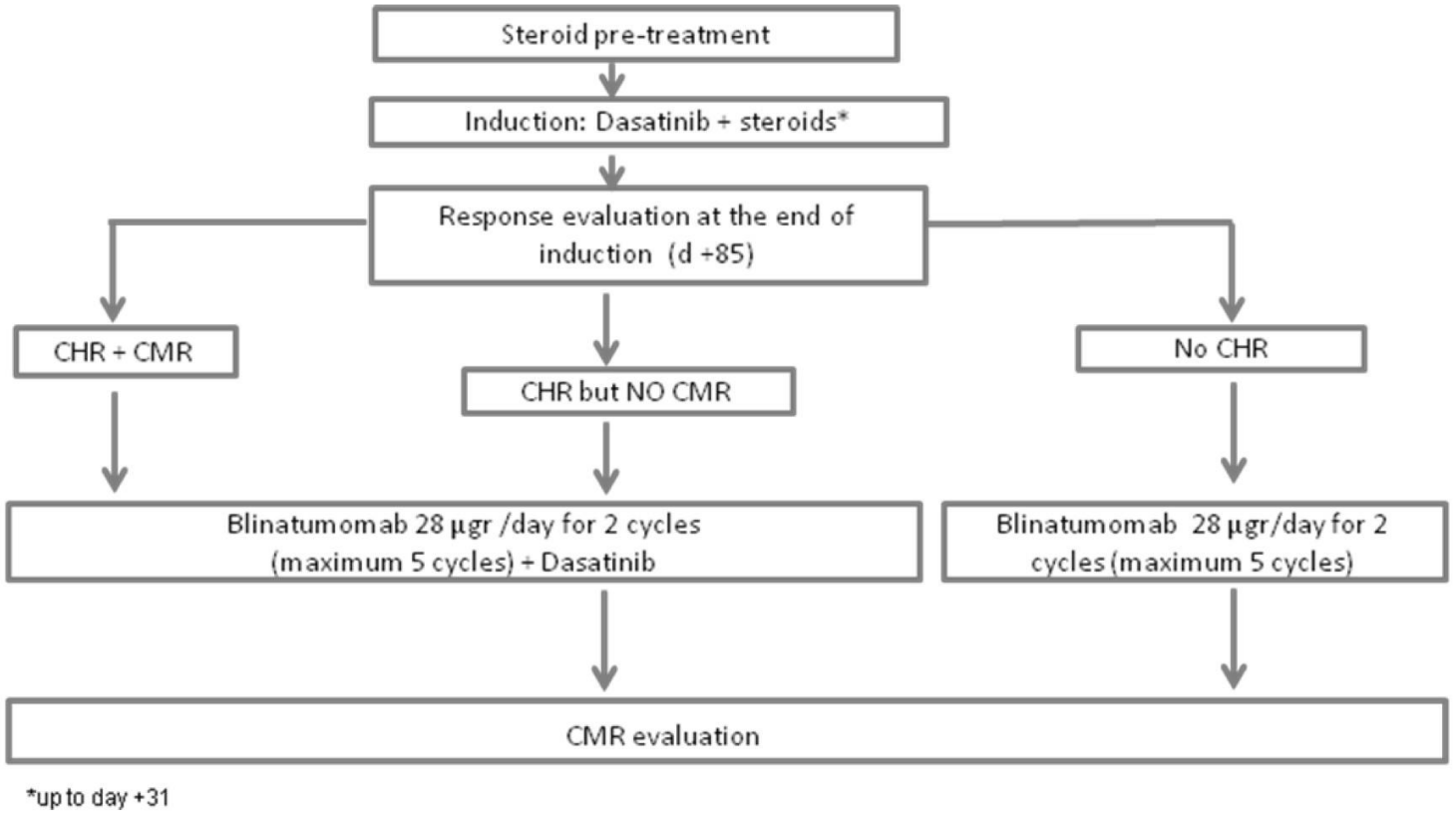
- 221 (80%) patients received blinatumomab as a first novel agent and 55 (20%) patients received InO
- Overall response rate (CR+CRi): 65% with blinatumomab and 67% with InO (*P*=.73)
- CR with MRD negativity with the first novel agent: 47% in the blinatumomab group and 46.5% in the InO group (*P*=.68)
- CR with MRD negativity after second novel agent: 24% for blinatumomab and 42% for InO (*P*=.29)

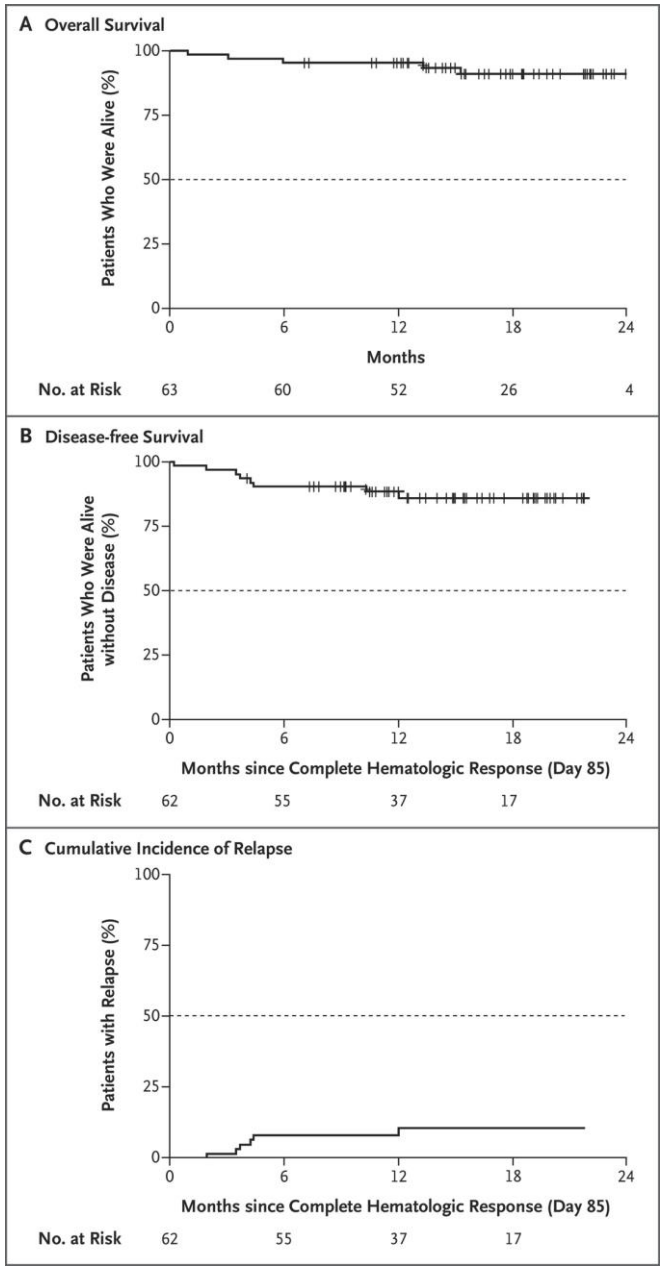
Overall survival after first novel agent therapy and second novel agent therapy



Badar T, et al. Cancer. 2021;127(7):1039-1048

Frontline Blinatumomab + Dasatinib for Ph+ ALL — D-ALBA study

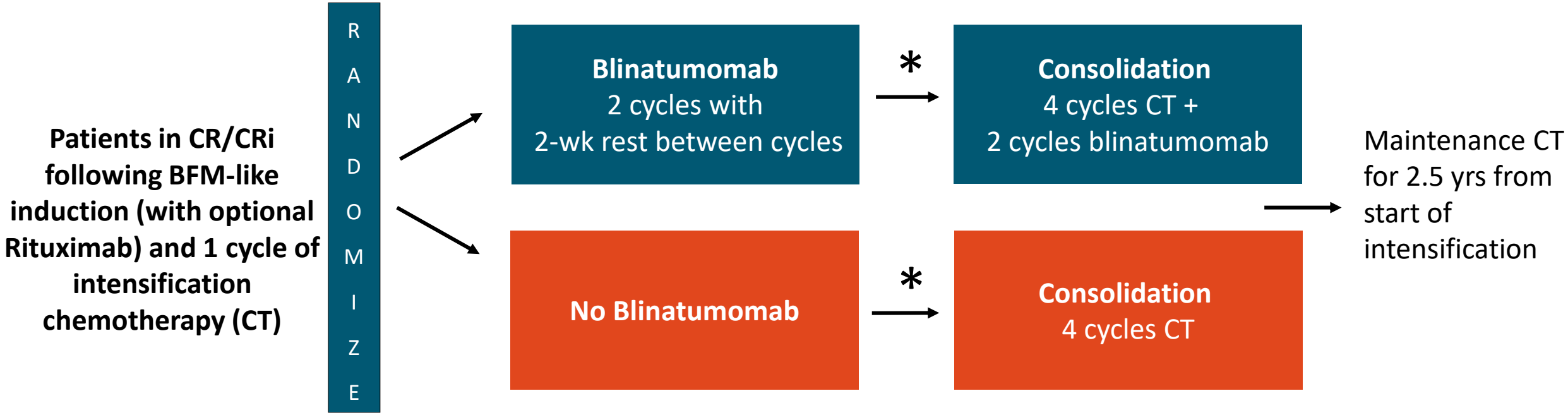




Foa R et al. NEJM 2020; 383:1613-1623.

ECOG 1910: Blinatumomab in Front-Line Therapy for Newly Diagnosed Ph-neg B-ALL (Age 30-70)

- Phase III, randomized trial

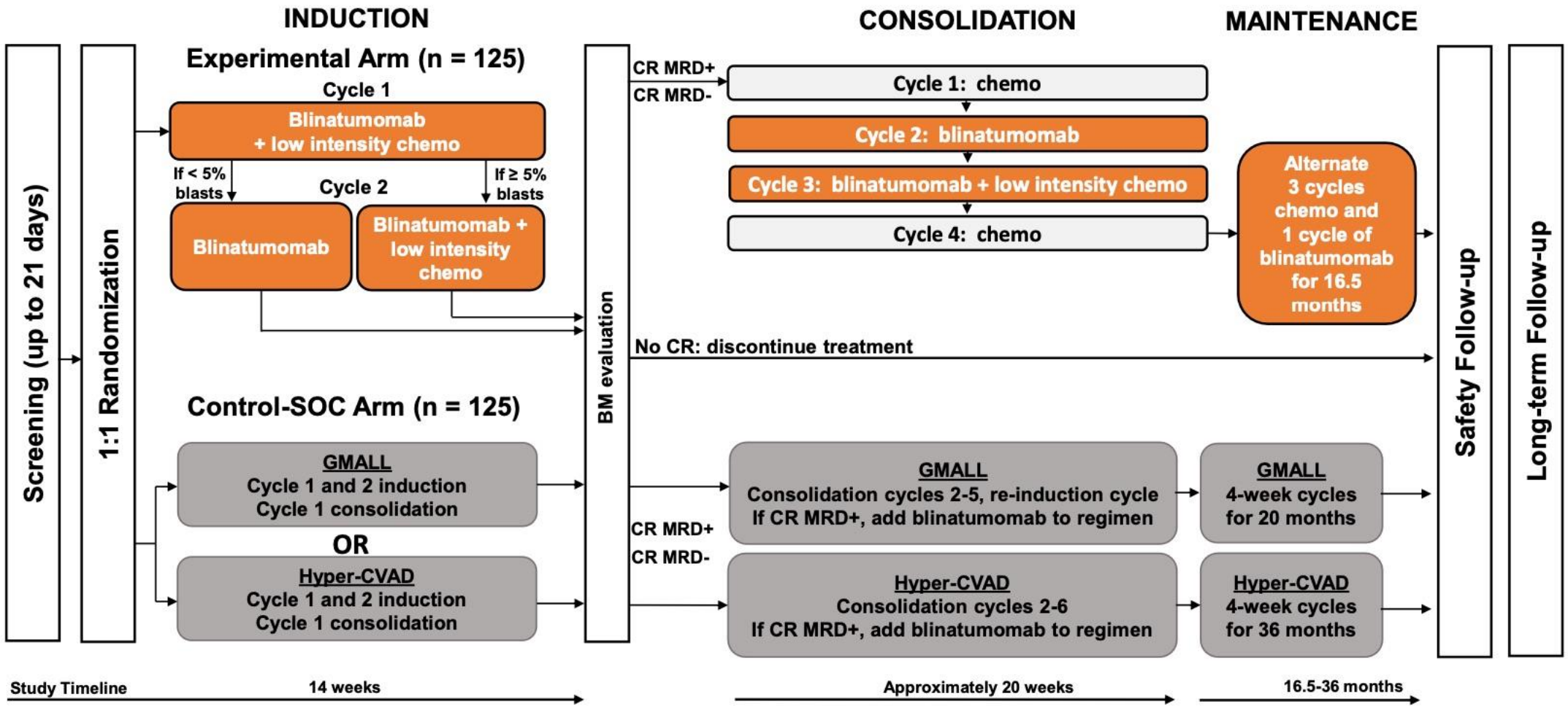


*Pts can proceed to BMT if recommended and suitable donor found

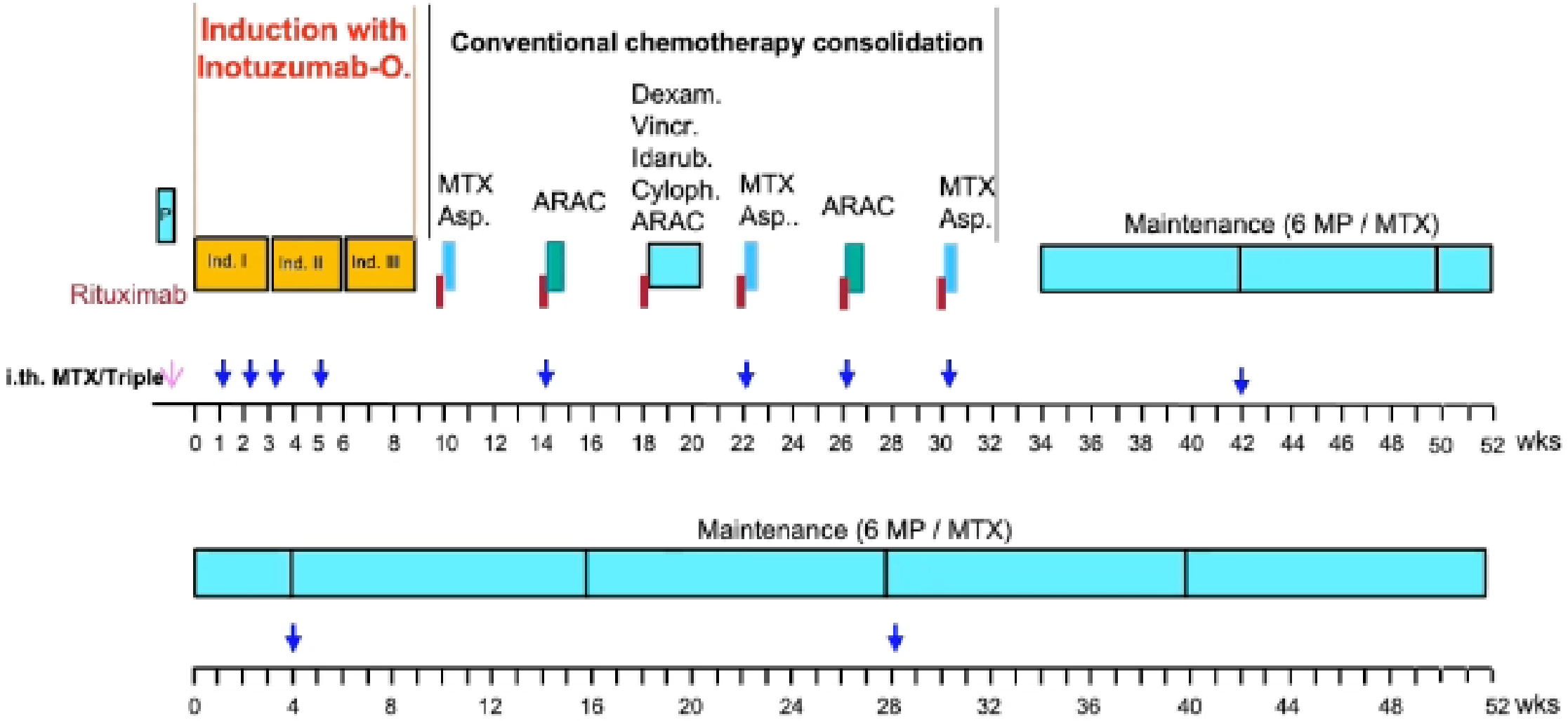
NCT0200322.

Low-intensity chemo + Blin vs GMALL or hCVAD in Age 55+

- Phase III, randomized trial

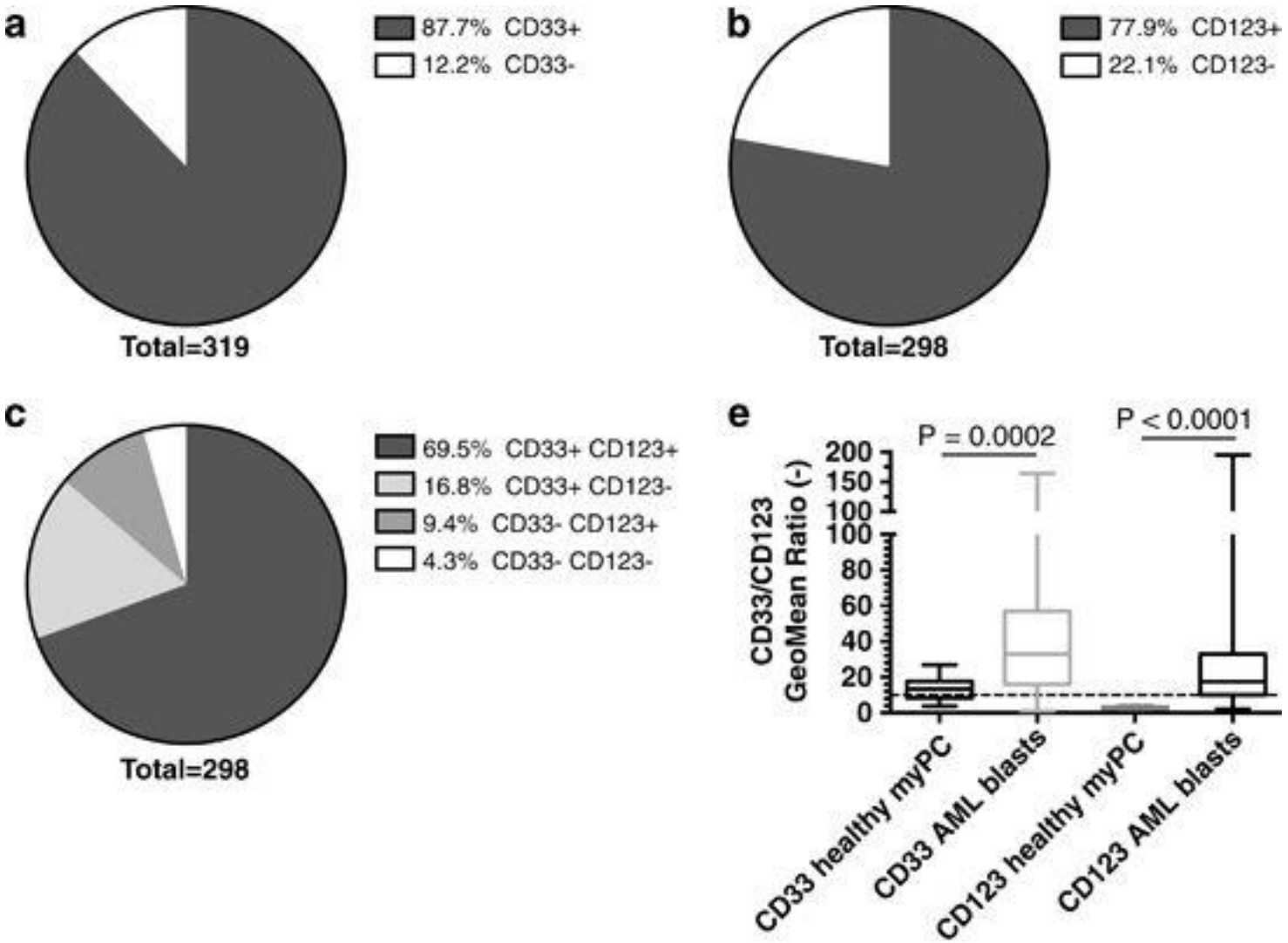


Initial-1: Inotuzumab for Induction Therapy Followed by Conventional Chemo, Age 55+, Phase II



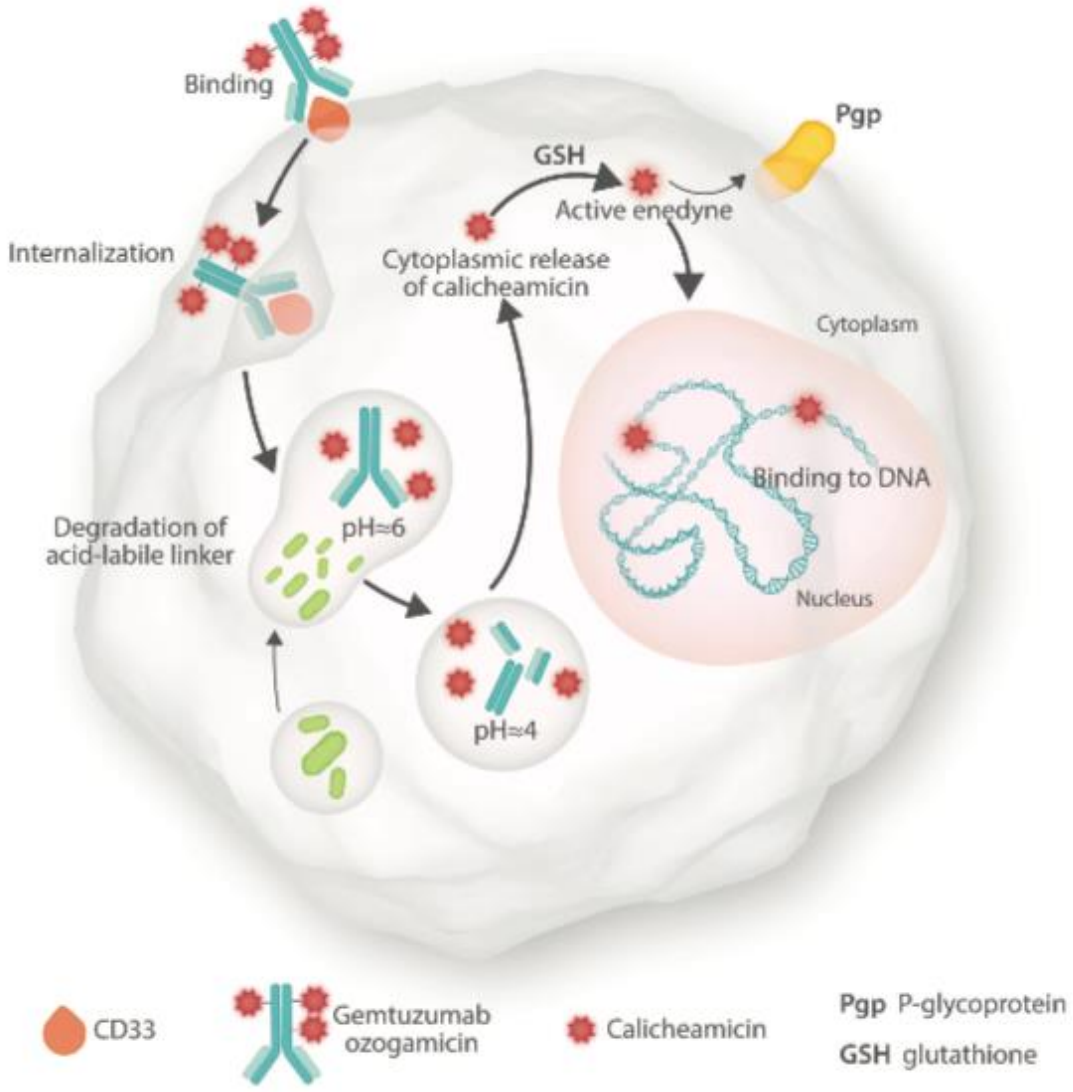
Acute Myelogenous Leukemia

Immunotherapy Targets in AML: CD33 and CD123



Ehninger et al. Blood Cancer J 2014, 4:e218.

Gemtuzumab Ozogamicin (anti-CD33 ADC) Treatment in AML

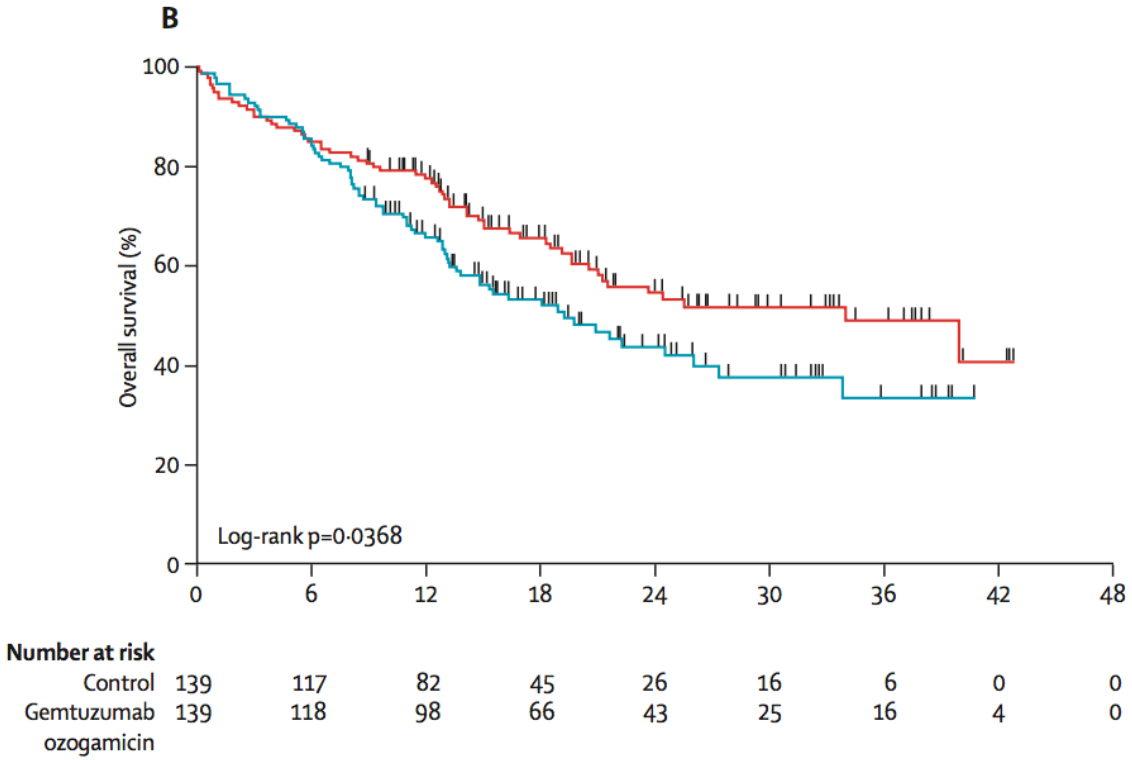


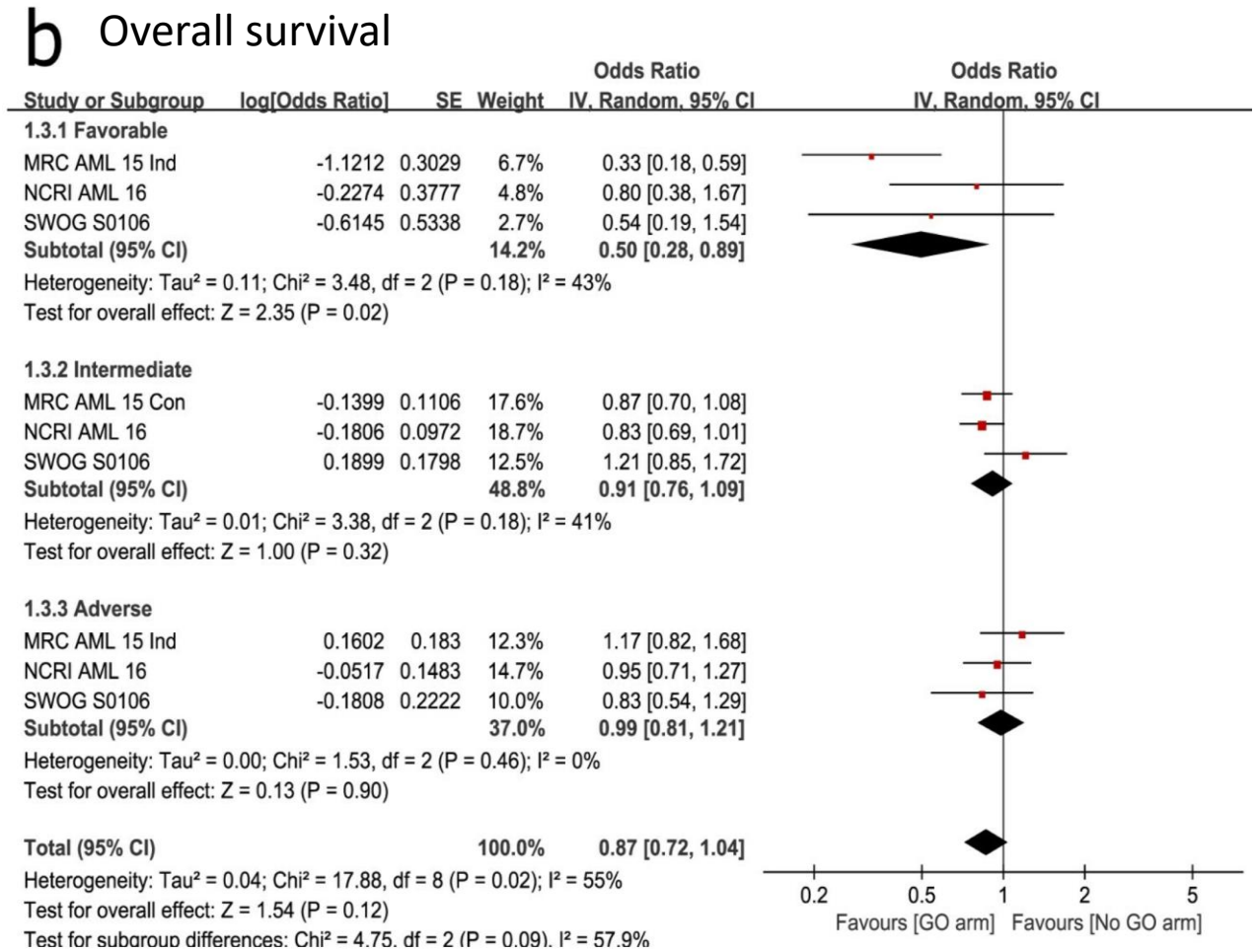
Hitzler and Estey. Haematologica 2019, 104(1):7-9

Gemtuzumab Ozogamicin (anti-CD33 ADC) Treatment in AML

ALFA-0701 Trial — Ph3 RCT 7+3 +/- GO

CR 75% (control) vs 81% (with GO), p=0.25
OS 19.2 vs 34 mos, HR 0.69, p=0.0368
RFS HR 0.58, p=0.0003

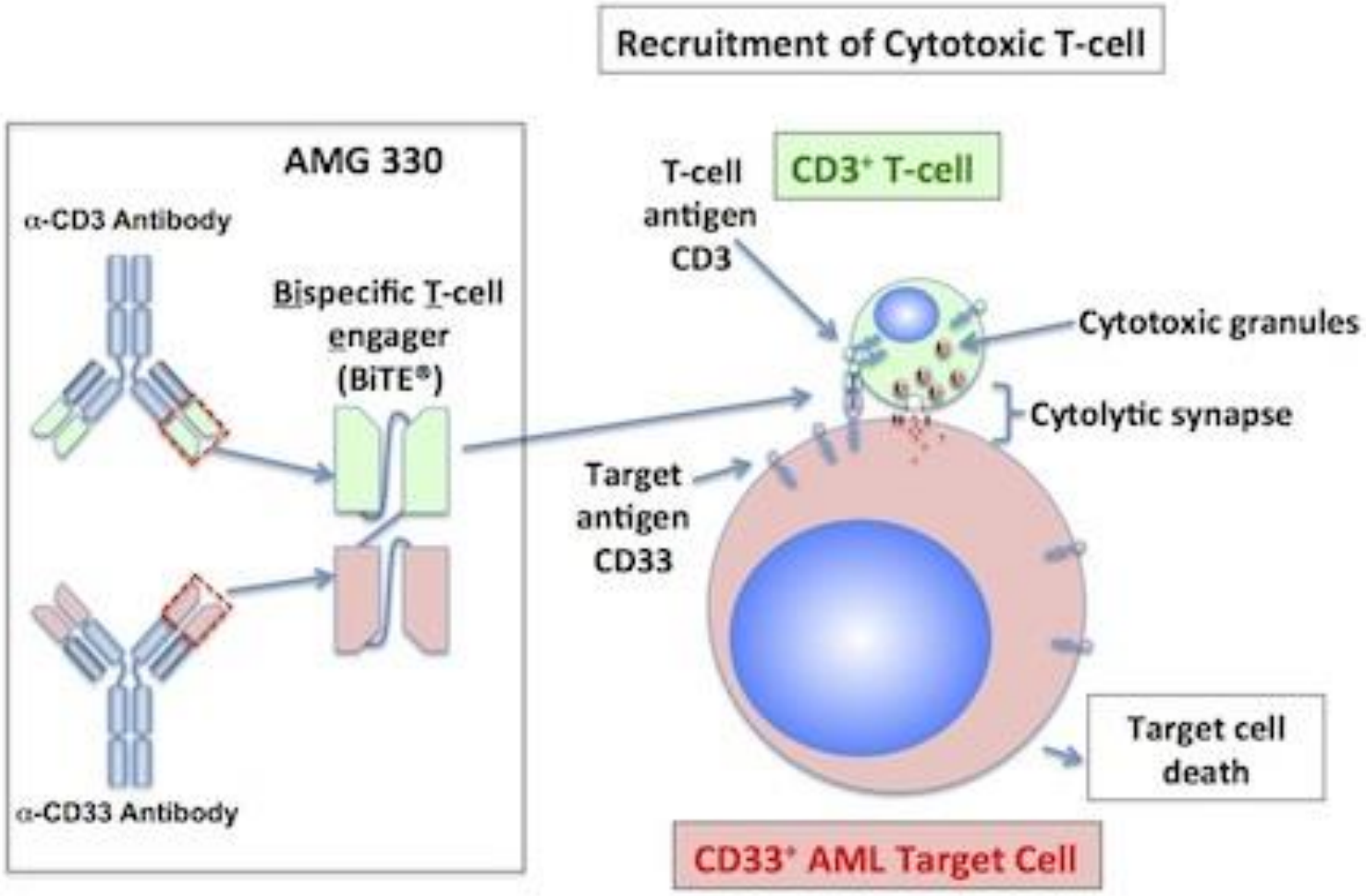




Castaigne et al. Lancet 2012; 379:1508-1516.

Guo et al. Hematol 2022; 27:53-64.

AMG330 — CD33:CD3 BiTE

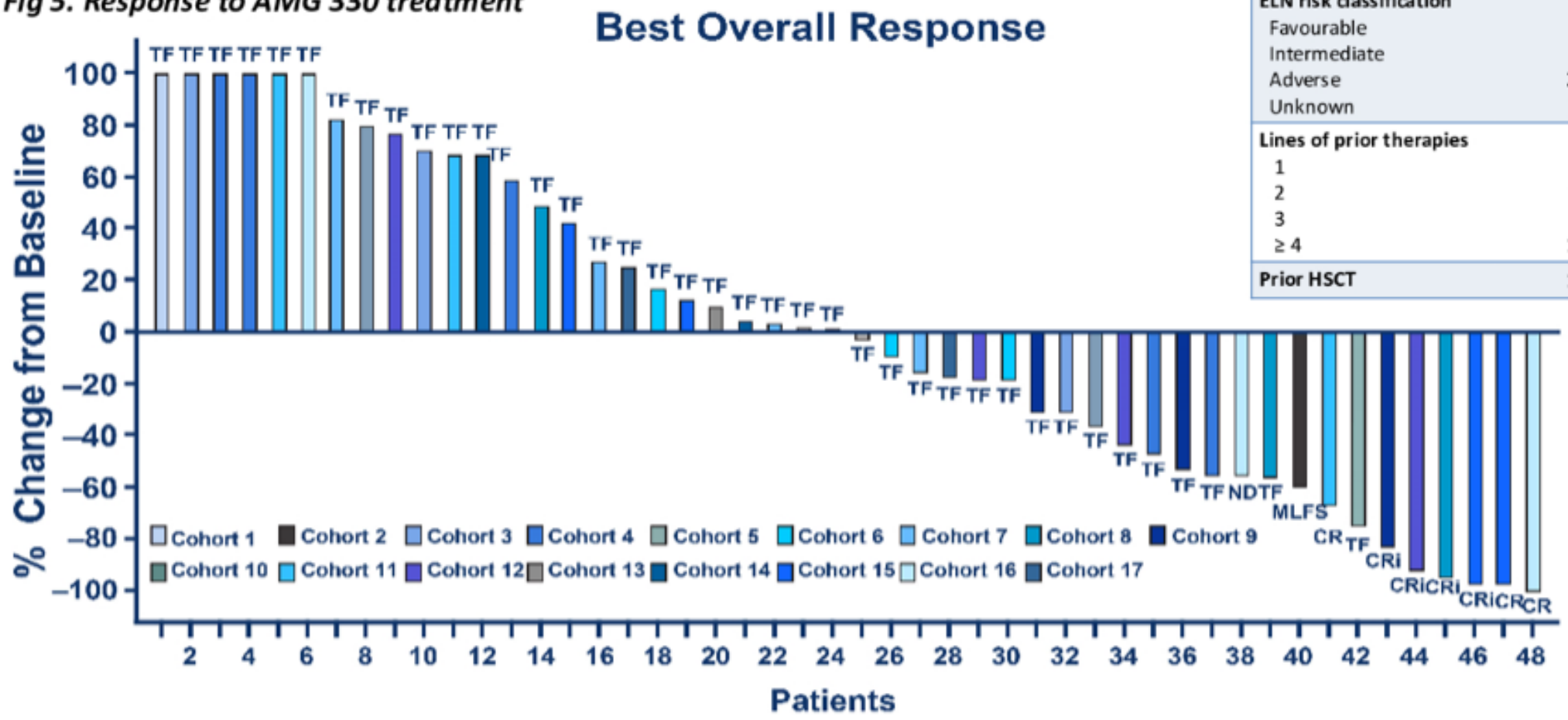


http://authors.fhcrc.org/699/1/A%20New%20Drug%20Bites%20AML.pdf

AMG330 — CD33:CD3 BiTE — Phase I results

Characteristics	Non-responders[a] at TD ≥ 120 µg, N=35; n (%)	Responders[b] at TD ≥ 120 µg, N=7; n (%)
ELN risk classification		
Favourable	2 (6)	0
Intermediate	3 (9)	2 (29)
Adverse	22 (63)	4 (57)
Unknown	8 (23)	1 (14)
Lines of prior therapies		
1	5 (14)	1 (14)
2	5 (14)	2 (29)
3	6 (17)	1 (14)
≥ 4	19 (54)	3 (43)
Prior HSCT	14 (40)	4 (57)

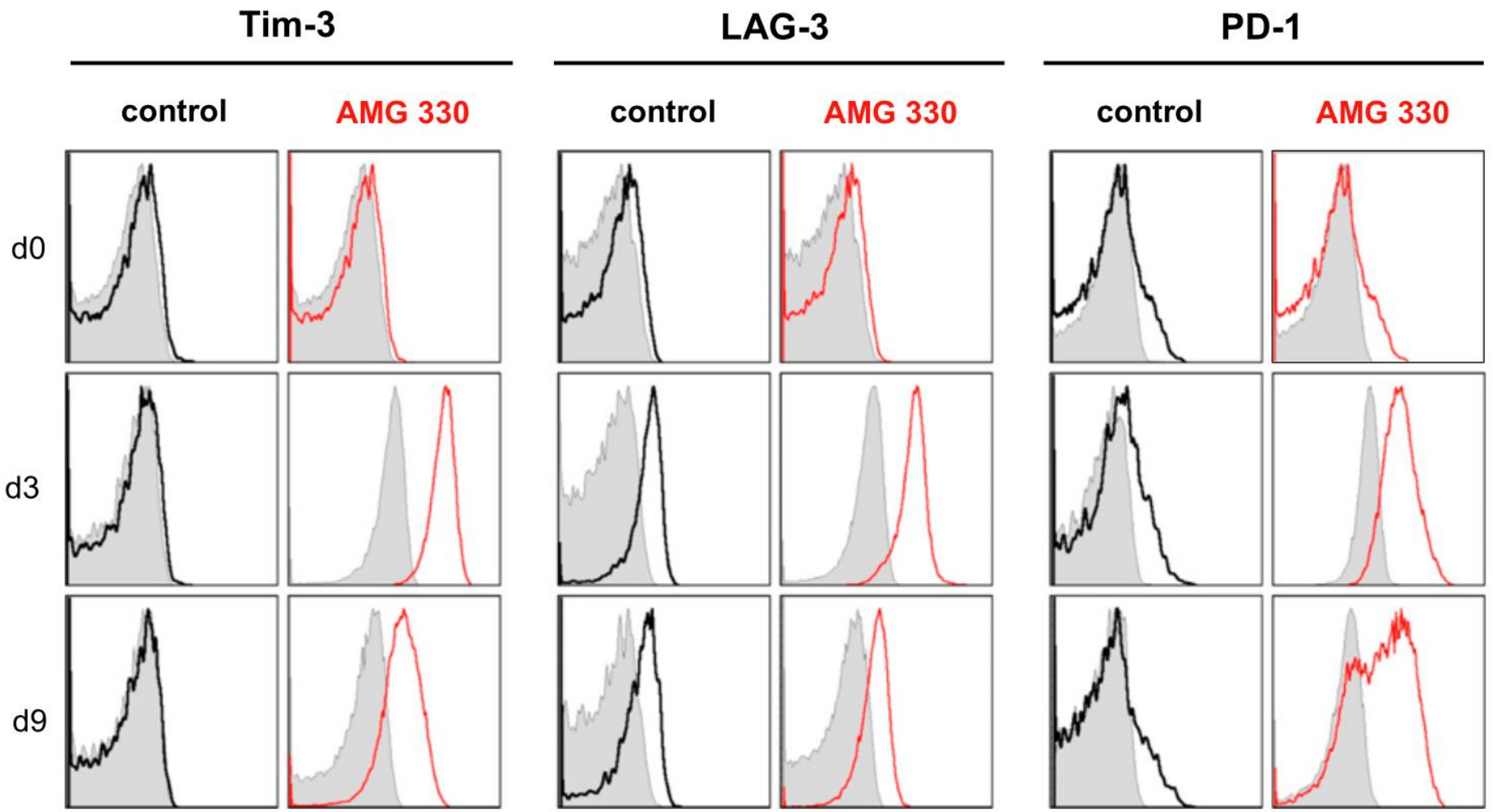
Fig 5. Response to AMG 330 treatment



CRS
67% gr1+
15% gr3+

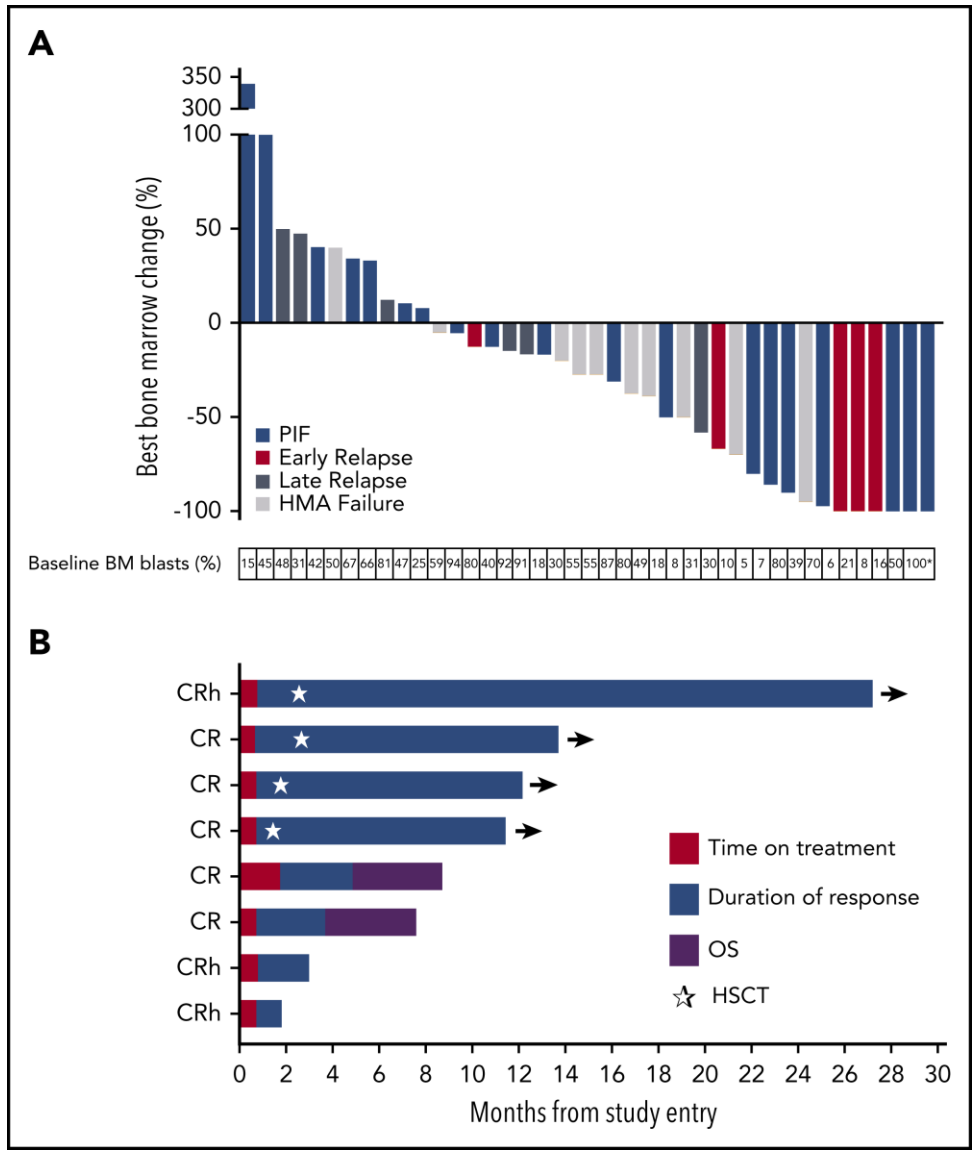
Ravandi et al., EHA 2020, Abstract EP582

In vitro coculture of T cells with AML + AMG 330 — Upregulation of checkpoint receptors

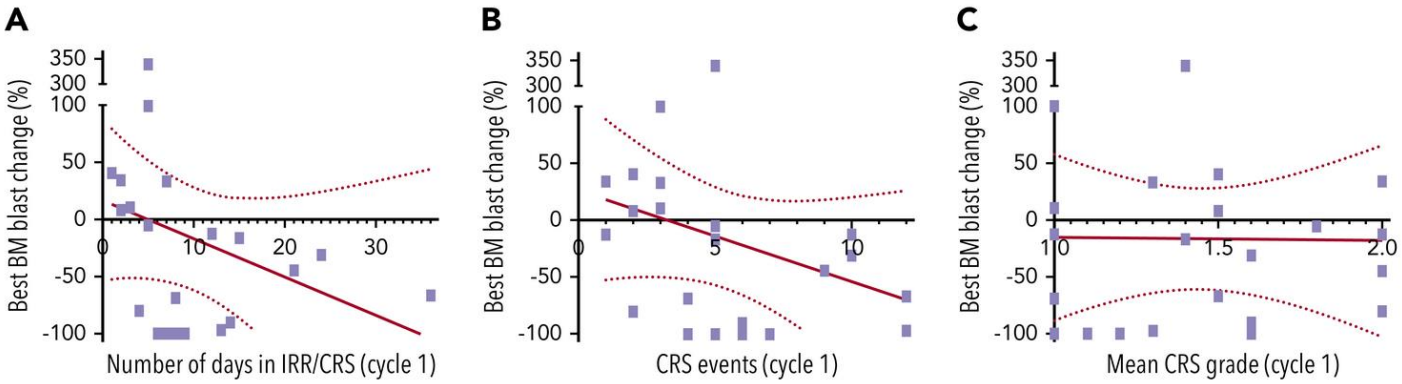


Krupka et al Blood 2014;123:356-365

Flotetuzumab – CD123 x CD3 DART

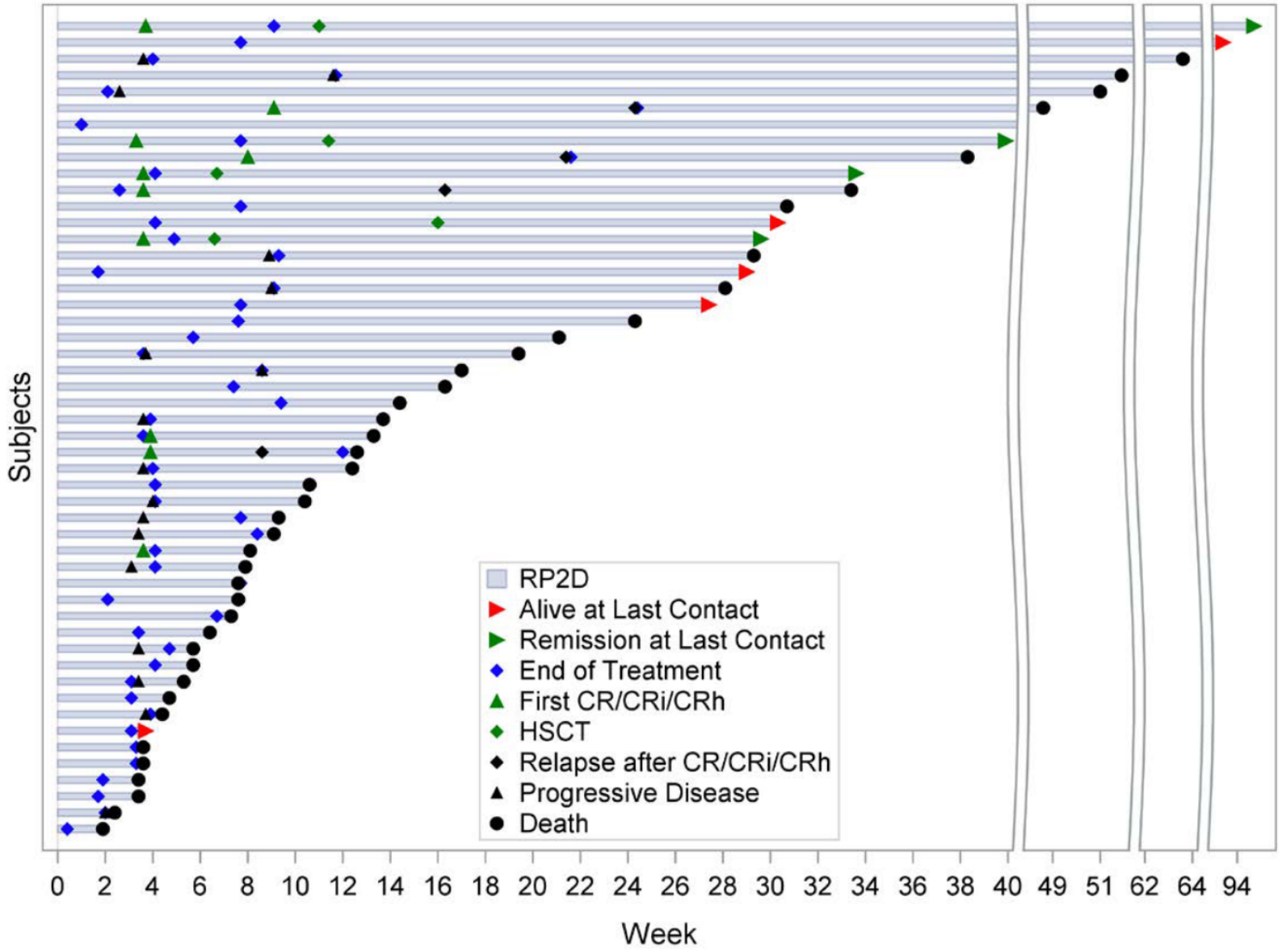


	R/R AML, % (n) n = 50	PIF/ER AML, % (n) n = 30
CR	12.0 (6)	16.7 (5)
CR/CRh	18.0 (9)	26.7 (8)
CR/CRh/CRi	20.0 (10)	30.0 (9)
CR/CRh/CRi/MLFS/PR	24.0 (12)	30.0 (9)



Uy et al. Blood 2021; 137(6):751-762.

Flotetuzumab – CD123 x CD3 DART

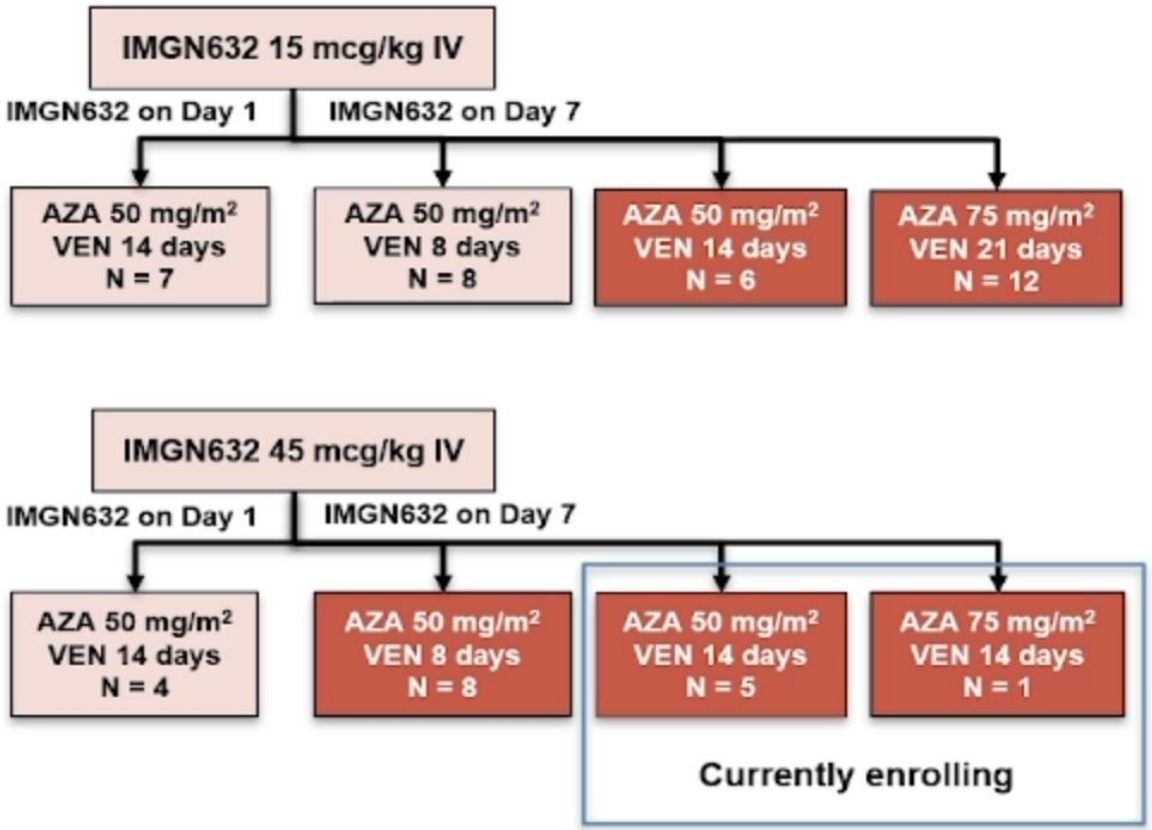


Uy et al. Blood 2021; 137(6):751-762.

IMGN632 (anti-CD123 ADC) in RR AML

Phase Ib/II

IMGN632 + Azacitidine + Venetoclax



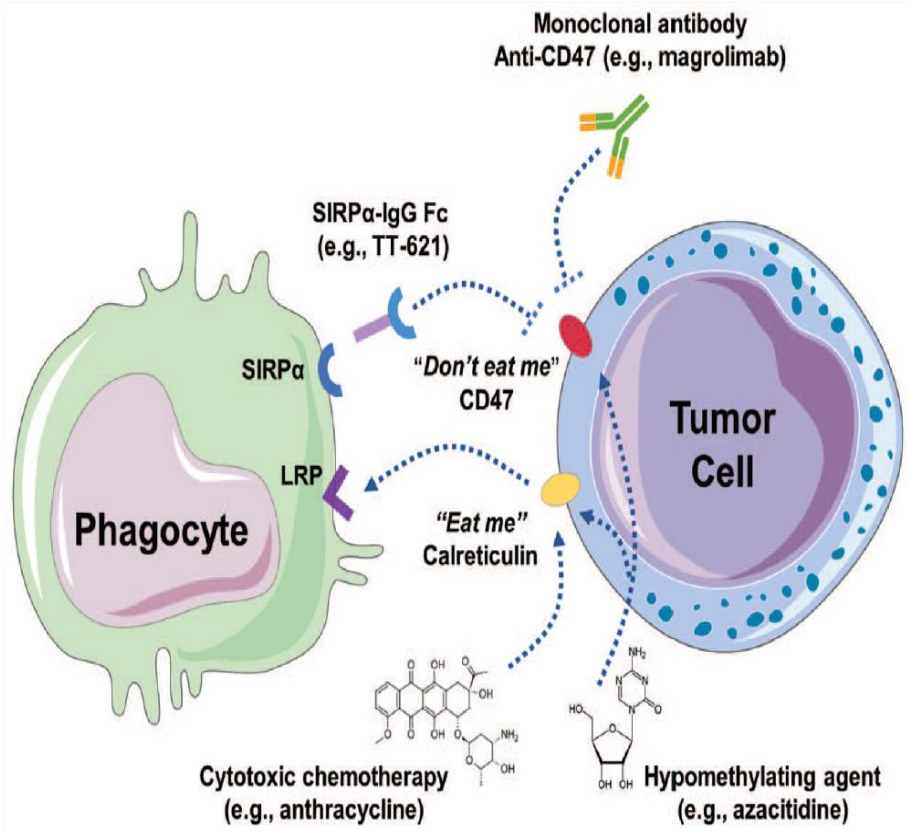
Efficacy evaluable population# (All doses and schedules)	N	ORR N	CCR N	CR N (%)	CRh N (%)	CRp N (%)	CRi N (%)
	46	22 (48%)	14 (30%)	4 (9)	8 (17)	1 (2)	1 (2)
Higher intensity cohorts#	**N**	**ORR N**	**CCR N**	**CR N (%)**	**CRh N (%)**	**CRp N (%)**	**CRi N (%)**
	29	17 (59%)	11 (38%)	4 (14)	6 (21)	1 (3)	0

Median duration on study: 9.1 weeks (Range 3-52.4 weeks)

Previous Treatments	N	ORR	CCR
VEN naïve	15	73%	53%
Prior VEN	14	43%	21%
Prior HMA + VEN	12	42%	25%
Prior Stem Cell Transplant	7	71%	71%
High Risk Cytogenetics	**N**	**ORR**	**CCR**
ELN Adverse Risk	14	64%	36%
FLT-ITD	9	89%	78%

Daver et al., ASH 2021, Abstract 372

Magrolimab (anti-CD47) in Untreated AML



<u>Phase Ib</u>

Newly diagnosed AML, ineligible for induction chemo
Magrolimab 1mg/kg priming, the 30mg/kg QW
Azacitidine 75mg/m2 Days 1-7

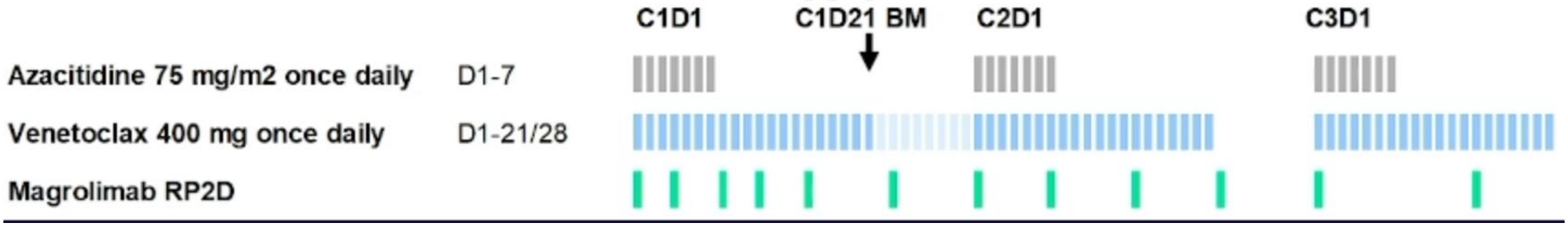
Outcome	All AML pts (n = 43)	*TP53*-mutant (n = 29)
ORR, n (%)	27 (63)	20 (69)
▪ CR	18 (42)	13 (45)
▪ CRi	5 (12)	4 (14)
▪ PR	1 (2)	1 (3)
▪ MLFS	3 (7)	2 (7)
▪ SD	14 (33)	8 (28)
▪ PD	2 (5)	1 (3)
Median time to response, mos (range)	1.95 (0.95-5.6)	NR
Median duration of response, mos	9.6	7.6
Complete cytogenic response, n/N (%)	9/20 (45)	7/16 (44)
MRD negativity in CR/CRi, n/N (%)	8/23 (35)	5/17 (29)

Wang and Sallman. Curr Opin Hematol 2022; 29(1): 44-52.

Sallman et al, ASH 2020, Abstract 330

Magrolimab (anti-CD47) in Untreated and RR AML

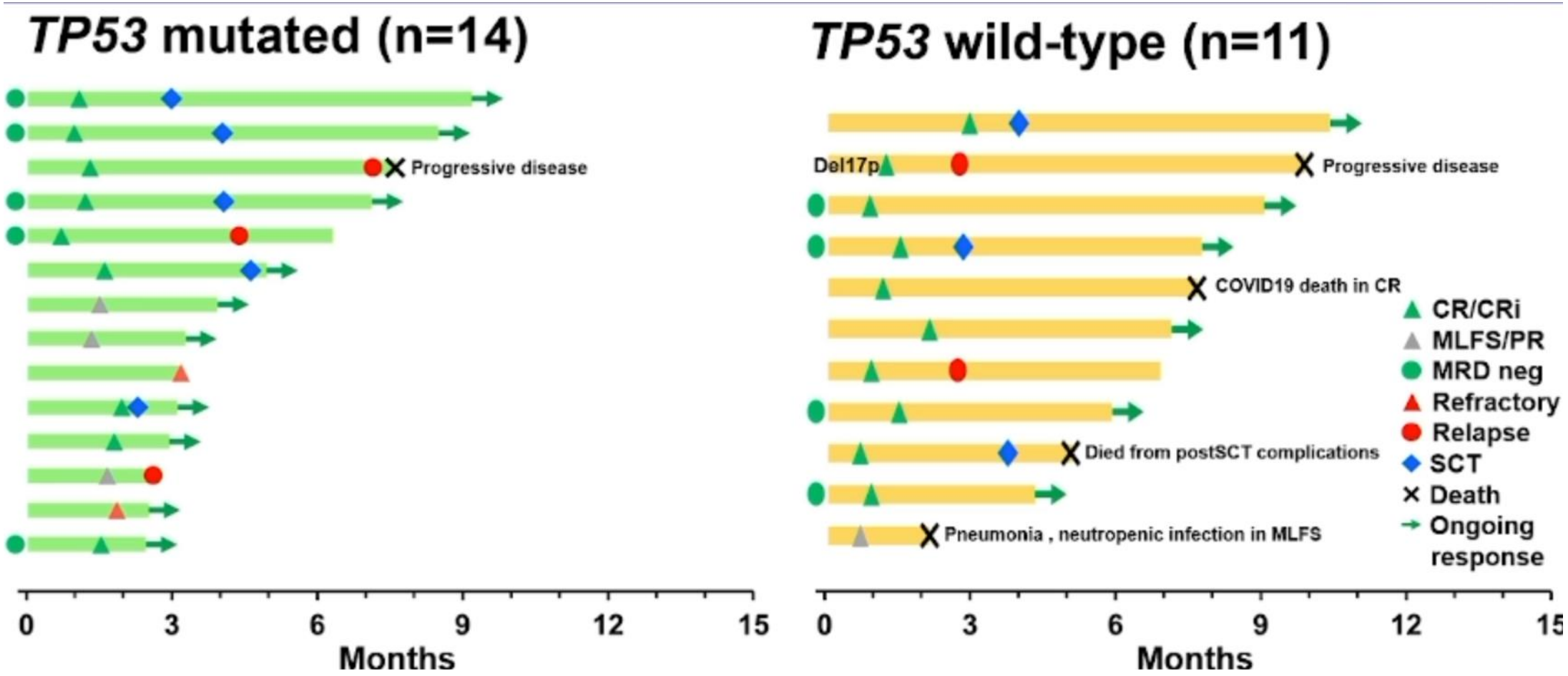
Phase I/II



Outcomes	Frontline Cohort (n=25)		R/R Cohort (n=23)	
	TP53 mutated (n=14)	*TP53* wild type (n=11)	VEN-naïve (n=8)	Prior VEN (n=15)
ORR	12 (86)	11 (100)	6 (75)	3 (20)
CR/CRi	9 (64)	10 (91)	5 (63)	3 (20)
CR	9 (64)	7 (64)	3 (38)	0
CRi	0	3 (27)	2 (25)	3 (20)
MLFS / PR[1]	3 (21)	1 (9)	1 (13)	0
MRD neg FCM	5/9* (55)	4/9 (45)	2/6 (33)	0
CCyR	4/9‡ (44)	5/6 (83)	3/5 (60)	1/2 (50)
No response	2 (14)	0	2 (25)	12 (80)
TT 1st response	0.7 [0.6-1.9]	0.7 [0.7-1.5]	0.7 [0.6-4.1]	2.2 [1.8-2.6]
TT Best response	1.5 [0.7-3.2]	1.1 [0.7-2.9]	1.5 [1.0-4.1]	2.0 [1.2-3.9]

Daver et al., ASH 2021, Abstract 371

Magrolimab (anti-CD47) in Untreated and RR AML



Daver et al., ASH 2021, Abstract 371

Checkpoint Inhibitors in AML

Table 1. Selected completed trials of immune checkpoint blockade monotherapy in AML/MDS. (Table view)

Drug	Target/mechanism	Phase [ref]	N	Patient characteristics	Outcomes
Pidilizumab	Anti-PD-1 antibody	I[57]	17 (8 AML, 1 MDS)	Advanced hematologic malignancies, age <65	1 AML patient with reduction in peripheral blasts
Nivolumab	Anti-PD-1 antibody	II[79]	15	MDS frontline and HMA failure	0% CR/CRp; 25% 1-year survival
		II[85]	14	HR-AML in CR ineligible for HSCT	71% 1-year CR rate
Pembrolizumab	Anti-PD-1 antibody	I[58]	28	MDS after HMA failure	ORR: 4% (1 PR); 49% 24-week survival
Ipilimumab	Anti-CTLA-4 antibody	I[13]	28 (12 pts w/AML)	Hematologic malignancies with relapse after HSCT	No response with 3 mg/kg Response with 10 mg/kg CR 23%, PR 9% 23% decrease in tumor burden CR in 1 AML patient secondary to MDS
		I[16]	29	MDS patients who failed HMAs	CR 3.4%, PSD for >46 weeks 27%, >54 weeks 10% Median OS 294 days (censoring at allogeneic HSCT),
		II[79]	20	MDS frontline and HMA failure	15% CR/CRp; 45% 1-year survival

Brewersdorf et al., Exp Rev Anticancer Ther 2019; 19(5):393-404.

Checkpoint Inhibitors in AML

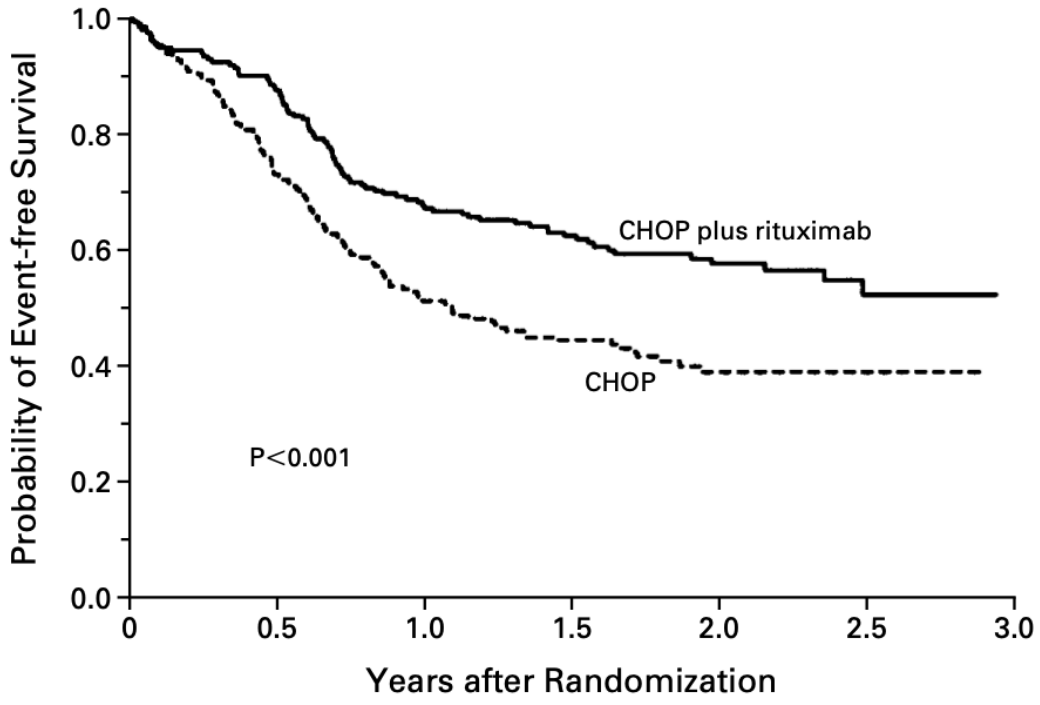
Table 2. Selected completed clinical trials of immune checkpoint blockade as part of combination therapy in AML/MDS. (Table view)

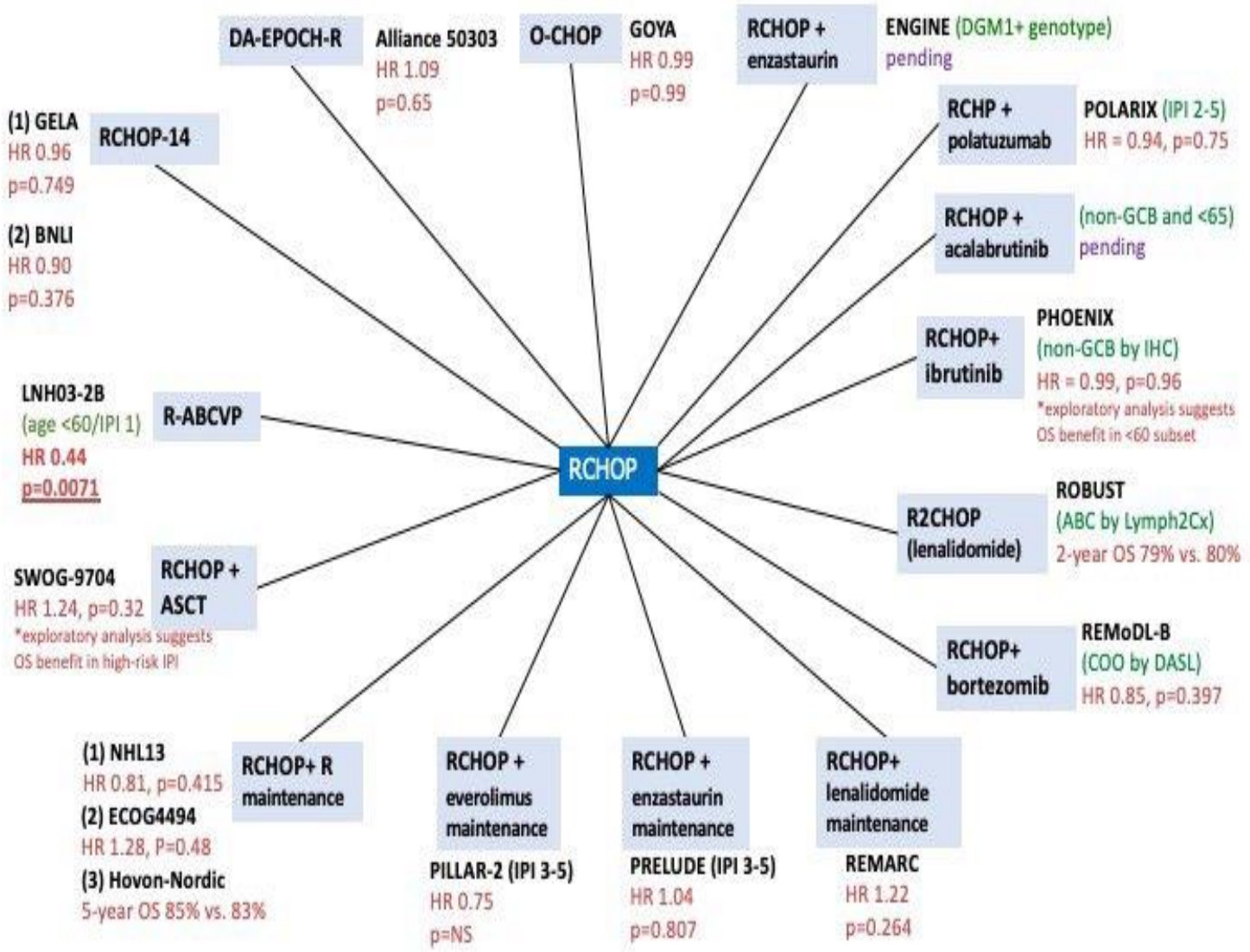
Drug	Target/mechanism	Phase [ref]	N	Patient characteristics	Intervention	Outcomes
Nivolumab	Anti-PD-1 antibody	II[79]	20	MDS frontline and HMA failure	Nivolumab + 5-AZA	75% CR/CRp; 50% 1-year survival
		II[75]	70	RR-AML	Nivolumab + 5-AZA	ORR: 33% (22% CR/CRi); median OS 6.3 months
		II[83]	41	Frontline AML or high-risk MDS; age<65	Idarubicin + cytarabine ± nivolumab	77% CR/CRi; median OS 18.54 (nivolumab group) vs 13.2 months (I + A alone), p = 0.2
Pembrolizumab	Anti-PD-1 antibody	I[77]	17	RR-AML	Pembrolizumab + decitabine	1 MRD-negative CR; median OS 7 months
Ipilimumab	Anti-CTLA-4 antibody	II[79]	21	MDS frontline and HMA failure	Ipilimumab + 5-AZA	71% CR/CRp; 68% 1-year survival

Brewersdorf et al., Exp Rev Anticancer Ther 2019; 19(5):393-404.

Non-Hodgkin Lymphoma

Front-Line DLBCL Therapy





Hazard Ratios for OS

Coiffier et al. NEJM 2002; 346:235-242.

Twitter: @MattCheungMD

Polatuzumab Vedotin (anti-CD79a ADC) in Front-Line DLBCL (POLARIX Trial)

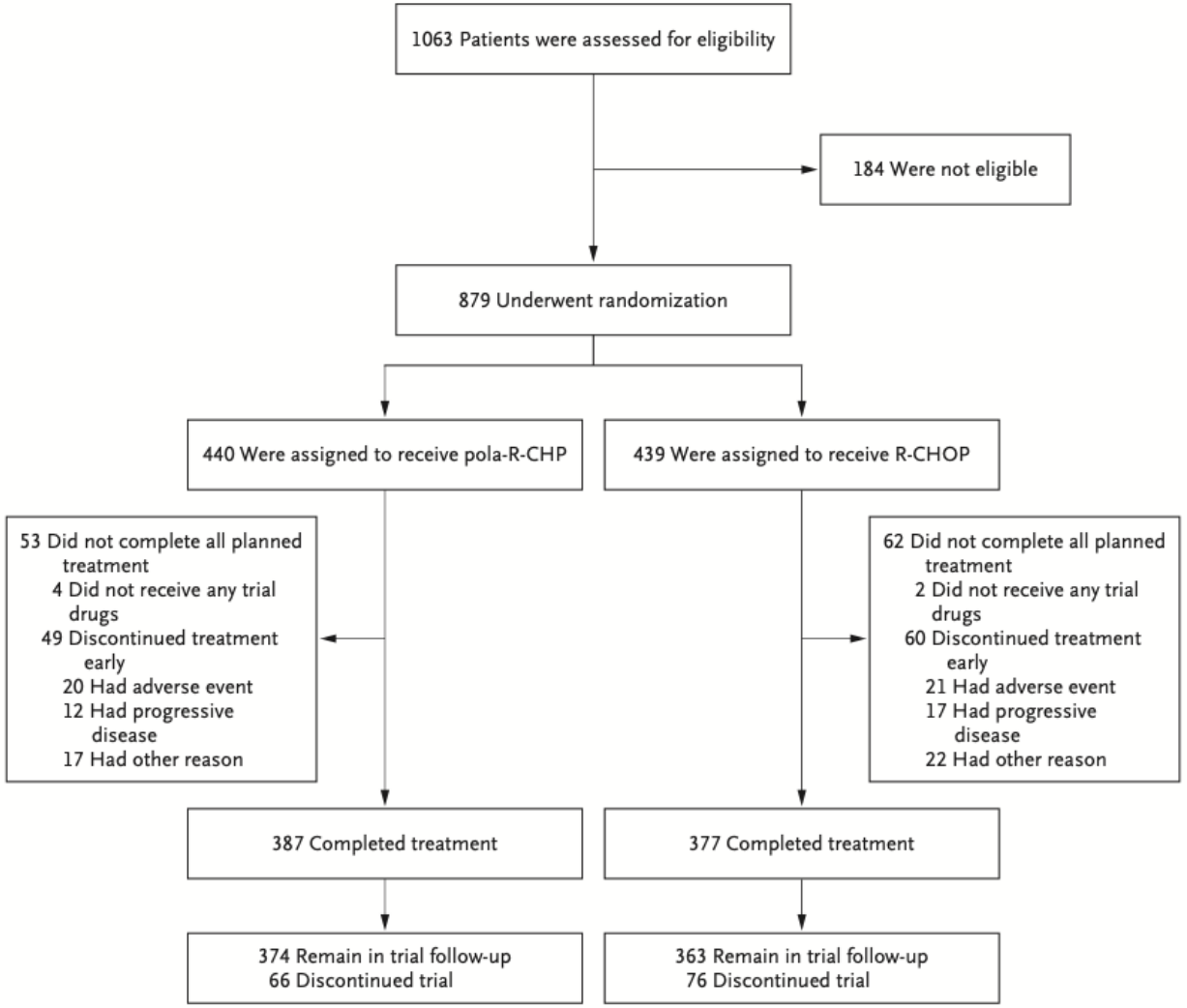


Table 1. Demographic and Clinical Characteristics at Baseline (Intention-to-Treat Population).*

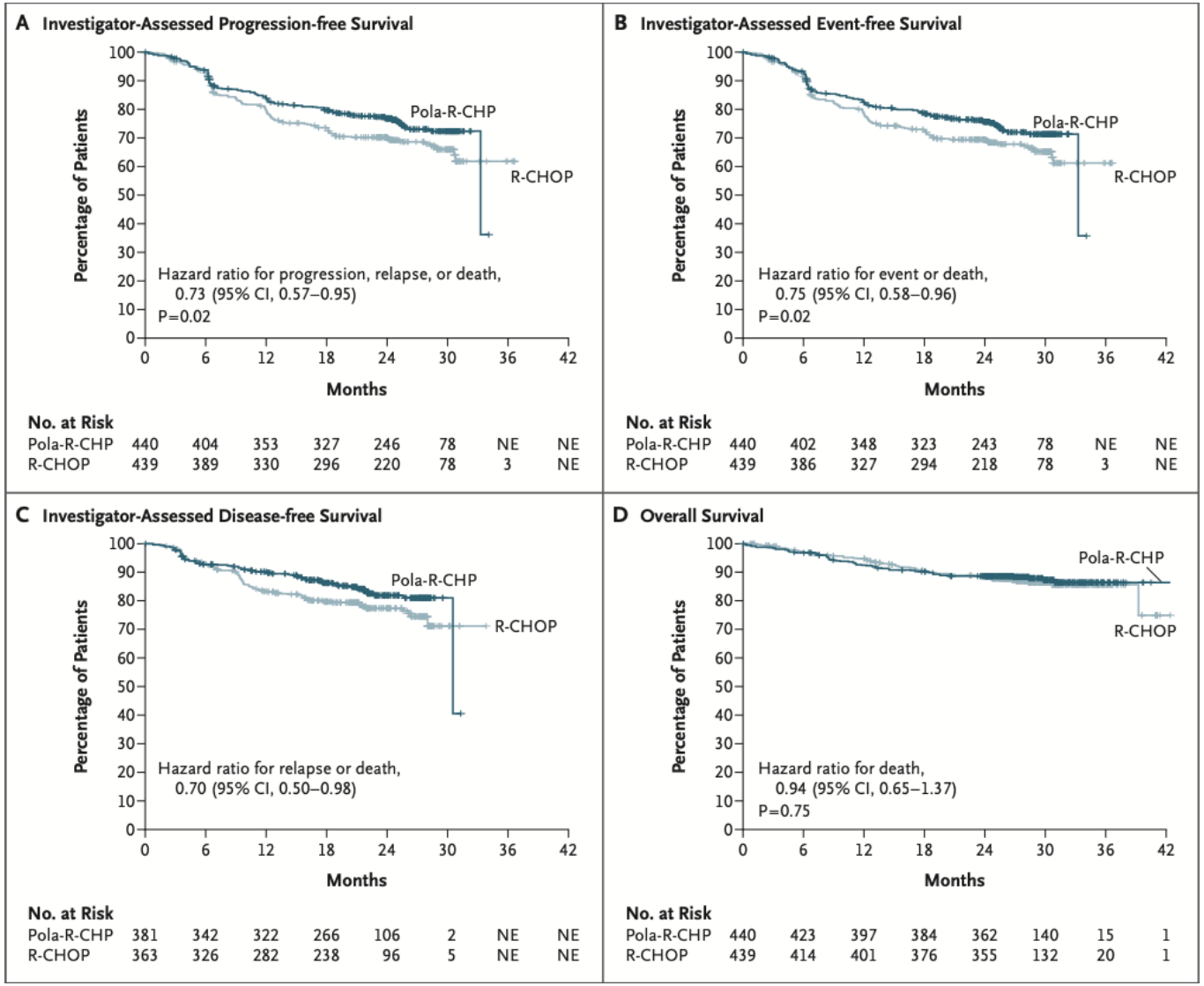
Characteristic	Pola-R-CHP (N=440)	R-CHOP (N=439)
Median age (range) — yr	65 (19–80)	66 (19–80)
Age category — no. (%)		
≤60 yr	140 (31.8)	131 (29.8)
>60 yr	300 (68.2)	308 (70.2)
Female sex — no. (%)	201 (45.7)	205 (46.7)
Geographic region — no. (%)†		
Western Europe, United States, Canada, and Australia	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)

Tilly et al. NEJM 2022; 386:351-363.

Polatuzumab Vedotin in Front-Line DLBCL (POLARIX Trial)

Table 2. Efficacy (Intention-to-Treat Population).

Variable	Pola-R-CHP (N=440)	R-CHOP (N=439)	Hazard Ratio (95% CI)	P Value
Progression-free survival*				
Patients who died or had progression or relapse — no. (%)	107 (24.3)	134 (30.5)	0.73 (0.57–0.95)	0.02
Earliest event — no.				
Death	19	20		
Progression or relapse	88	114		
Estimate at 1 year (95% CI) — %	83.9 (80.4–87.4)	79.8 (75.9–83.6)		
Estimate at 2 years (95% CI) — %	76.7 (72.7–80.8)	70.2 (65.8–74.6)		
Event-free survival*				
Patients who died, had progression or relapse, or had other events — no. (%)†	112 (25.5)	138 (31.4)	0.75 (0.58–0.96)	0.02
Earliest event — no.				
Death	18	20		
Progression or relapse	86	106		
Other†	8	12		
Estimate at 2 years (95% CI) — %	75.6 (71.5–79.7)	69.4 (65.0–73.8)		
Response status at treatment completion‡				
Overall response — no. (%)	376 (85.5)	368 (83.8)		
Complete response	343 (78.0)	325 (74.0)		
Partial response	33 (7.5)	43 (9.8)		
Stable disease — no. (%)	8 (1.8)	6 (1.4)		
Progressive disease — no. (%)	22 (5.0)	28 (6.4)		
Not evaluated or data missing — no. (%)	34 (7.7)	37 (8.4)		
Overall survival				
Patients who died — no. (%)	53 (12.0)	57 (13.0)	0.94 (0.65–1.37)	0.75
Estimate at 2 years (95% CI) — %	88.7 (85.7–91.6)	88.6 (85.6–91.6)		
Disease-free survival§				
No. of patients who could be evaluated¶	381	363		
Patients who died or had relapse — no. (%)	62 (16.3)	79 (21.8)	0.70 (0.50–0.98)	
Earliest event — no.				
Death	8	13		
Relapse	54	66		



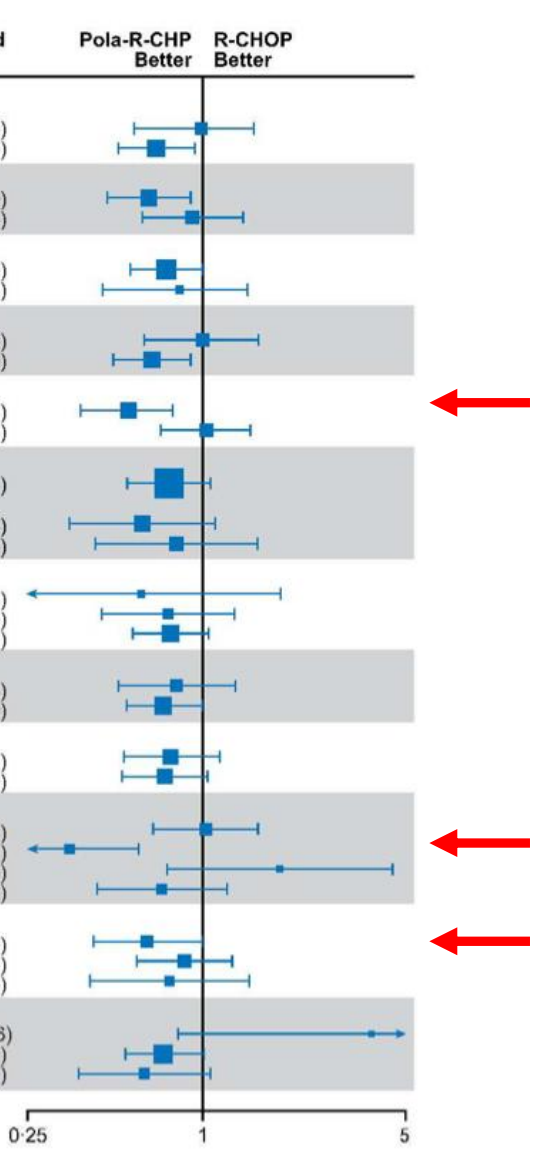
No safety signals

Tilly et al. NEJM 2022; 386:351-363.

Polatuzumab Vedotin in Front-Line DLBCL (POLARIX Trial)

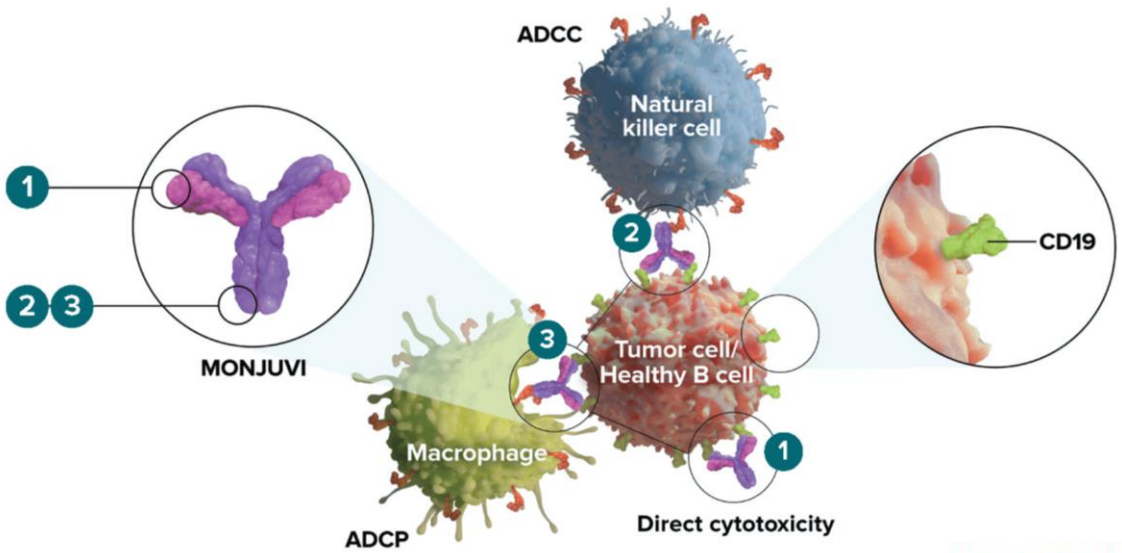
PFS

Baseline Risk Factors	Total N	Pola-R-CHP (N=440) n	Pola-R-CHP (N=440) 2-year Rate	R-CHOP (N=439) n	R-CHOP (N=439) 2-year Rate	Hazard Ratio	95% Wald CI
Age group							
≤60	271	140	74·1	131	71·9	0·9	(0·6 to 1·5)
>60	608	300	77·9	308	69·5	0·7	(0·5 to 0·9)
Sex							
Male	473	239	75·9	234	65·9	0·7	(0·5 to 0·9)
Female	406	201	77·7	205	75·2	0·9	(0·6 to 1·4)
ECOG PS							
0–1	737	374	78·4	363	71·2	0·8	(0·6 to 1·0)
2	141	66	67·2	75	65·0	0·8	(0·5 to 1·4)
IPI score							
IPI 2	334	167	79·3	167	78·5	1·0	(0·6 to 1·6)
IPI 3–5	545	273	75·2	272	65·1	0·7	(0·5 to 0·9)
Bulky disease							
Absent	494	247	82·7	247	70·7	0·6	(0·4 to 0·8)
Present	385	193	69·0	192	69·7	1·0	(0·7 to 1·5)
Geographic region							
Western Europe, United States, Canada, and Australia	603	302	78.6	301	72.0	0.8	(0·6 to 1·1)
Asia	160	81	74.3	79	65.6	0.6	(0·4 to 1·5)
Rest of world	116	57	70.8	59	67.3	0.9	(0·6 to 1·5)
Ann Arbor stage							
I–II	99	47	89·1	52	85·5	0·6	(0·2 to 1·8)
III	232	124	80·7	108	73·6	0·8	(0·5 to 1·3)
IV	548	269	72·6	279	66·1	0·8	(0·6 to 1·1)
Baseline LDH							
≤ULN	300	146	78·9	154	75·6	0·8	(0·5 to 1·3)
>ULN	575	291	75·4	284	67·2	0·7	(0·5 to 1·0)
No. of extranodal sites							
0–1	453	227	80·2	226	74·5	0·8	(0·5 to 1·1)
≥2	426	213	73·0	213	65·8	0·7	(0·5 to 1·0)
Cell-of-origin							
GCB	352	184	75·1	168	76·9	1·0	(0·7 to 1·5)
ABC	221	102	83·9	119	58·8	0·4	(0·2 to 0·6)
Unclassified	95	44	73·0	51	86·2	1·9	(0·8 to 4·5)
Unknown	211	110	73·8	101	64·3	0·7	(0·4 to 1·2)
Double expressor by IHC							
DEL	290	139	75·5	151	63·1	0·6	(0·4 to 1·0)
Non DEL	438	223	77·7	215	75·7	0·9	(0·6 to 1·3)
Unknown	151	78	76·0	73	69·8	0·8	(0·4 to 1·5)
Double- or triple-hit lymphoma							
Yes	45	26	69·0	19	88·9	3·8	(0·8 to 17·6)
No	620	305	76·8	315	70·3	0·7	(0·5 to 1·0)
Unknown	214	109	78·5	105	66·4	0·6	(0·4 to 1·1)



Tilly et al. NEJM 2022; 386:351-363.

Tafasitamab in R/R DLBCL — Phase 2 L-MIND Study



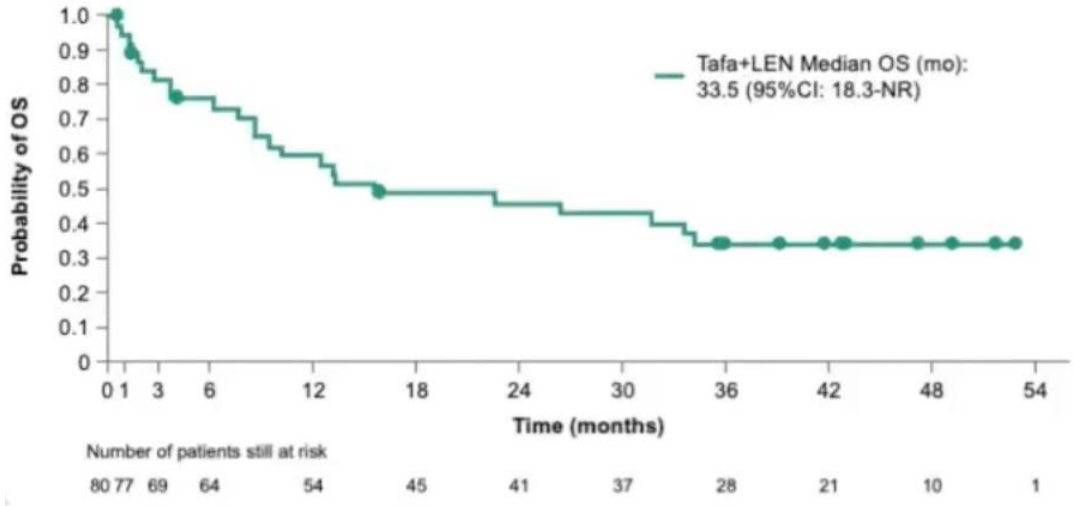
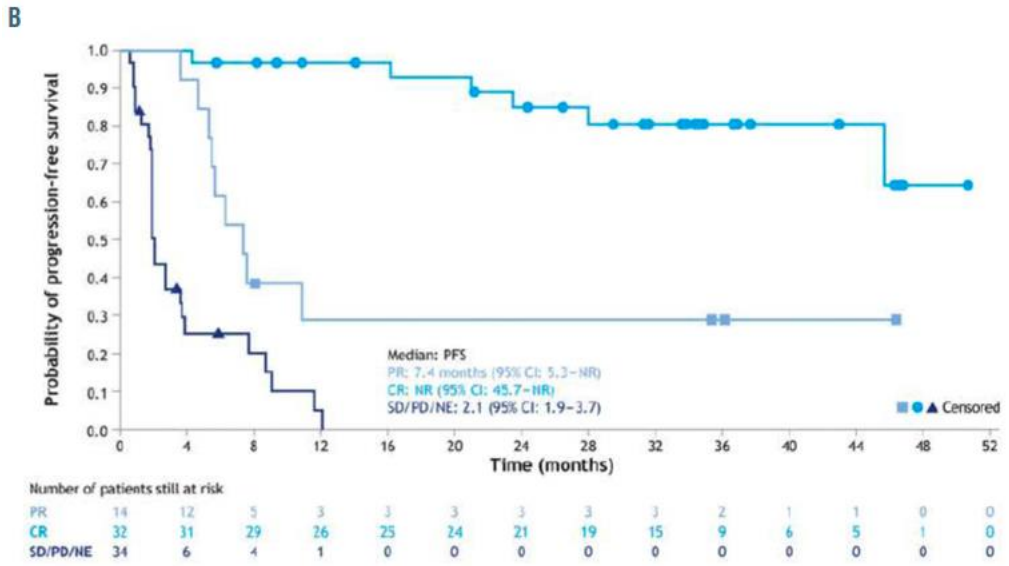


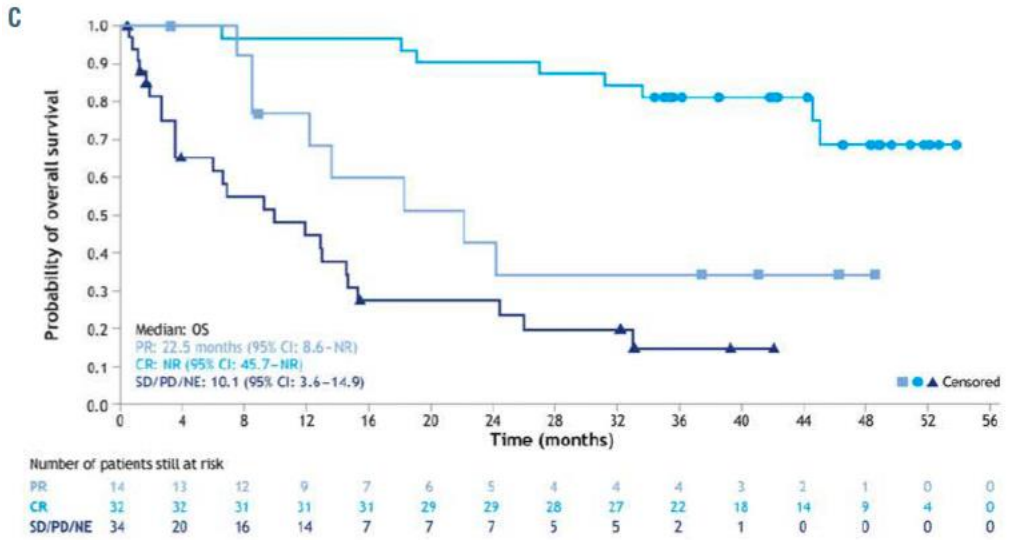
Table 2. **Efficacy outcomes in the primary and follow-up analyses.**

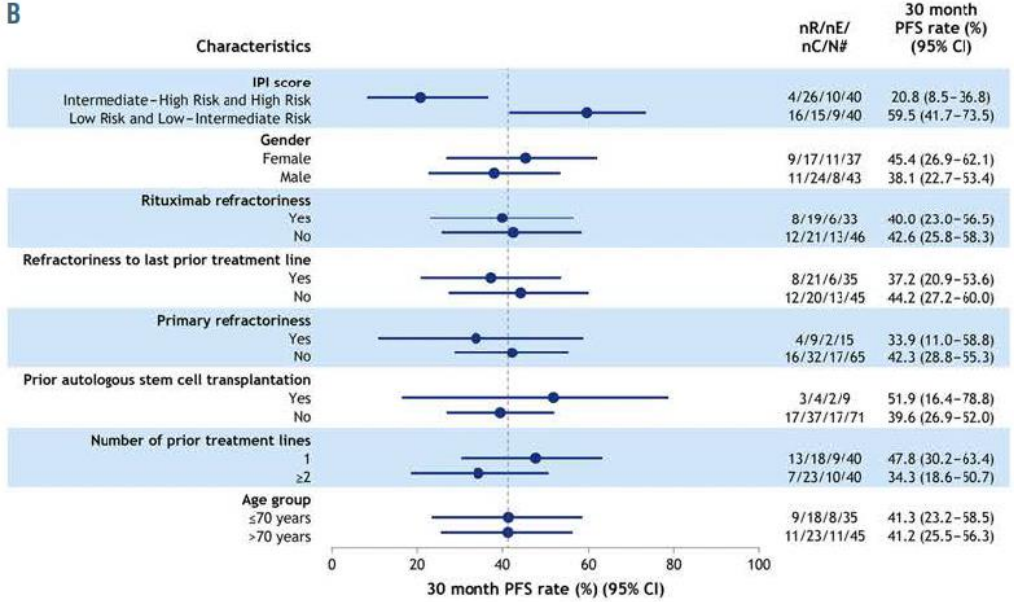
	Tafasitamab plus lenalidomide (N=80)‡		Clinically relevant subgroups (follow-up analysis)		
	Primary analysis (data cut-off: Nov 30, 2018)§	Follow-up analysis (data cut-off: Oct 30, 2020)	Primary refractory disease (n=15)	Rituximab-refractory disease (n=33)	Last-therapy-refractory (n=35)
Best objective response, n (%)					
Complete response	34 (42.5)	32 (40.0)	5 (33.3)	13 (39.4)	14 (40.0)
Partial response	14 (17.5)	14 (17.5)	3 (20.0)	5 (15.2)	7 (20.0)
Stable disease	11 (13.8)	13 (16.3)	2 (13.3)	4 (12.1)	3 (8.6)
Progressive disease	13 (16.3)	13 (16.3)	3 (20.0)	7 (21.2)	7 (20.0)
Not evaluable*	8 (10.0)	8 (10.0)	2 (13.3)	4 (12.1)	4 (11.4)
ORR (CR + PR), n (%) [95% CI]†	48 (60.0) [48.4-70.9]	46 (57.5) [45.9-68.5]	8 (53.3) [26.6-78.7]	18 (54.5) [36.4-71.9]	21 (60.0) [42.1-76.1]
Median DoR (IRC), months (95% CI)	21.7 (21.7-NR)	43.9 (26.1-NR)	NR (1.8-NR)	NR (5.8-NR)	NR (5.8-NR)
Median PFS (IRC), months (95% CI)	12.1 (5.7-NR)	11.6 (6.3-45.7)	5.3 (0.9-NR)	7.6 (2.7-NR)	7.6 (2.7-NR)
Median OS, months (95% CI)	NR (18.3-NR)	33.5 (18.3-NR)	13.8 (1.3-NR)	15.5 (8.6-NR)	15.5 (8.6-NR)

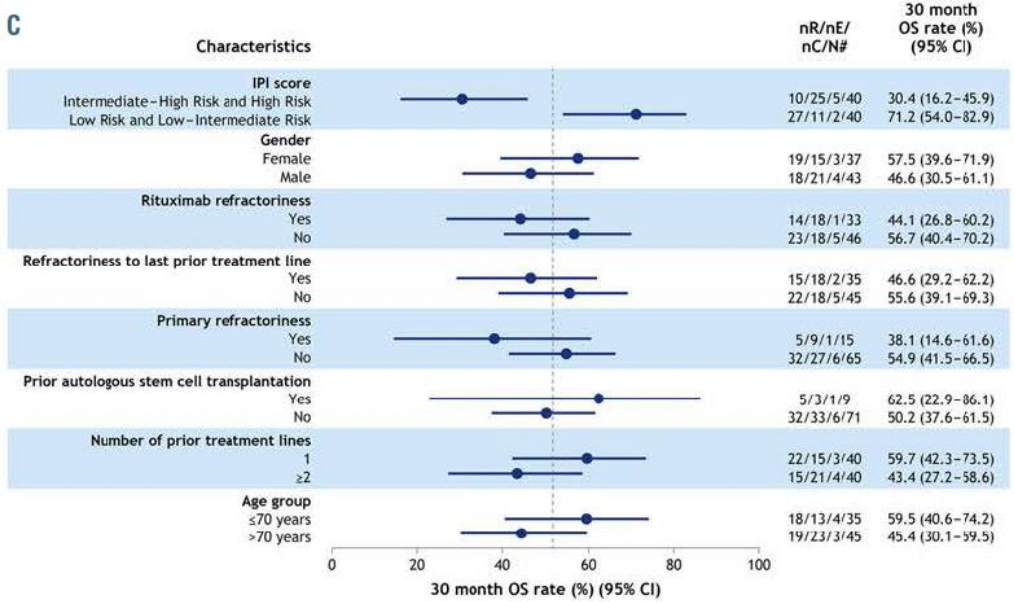
Salles et al. Lancet Oncol 2020; 21:978-988; Duell et al. Haematologica 2021; 106(9):2417-2426.

Tafasitamab in R/R DLBCL — Phase 2 L-MIND Study



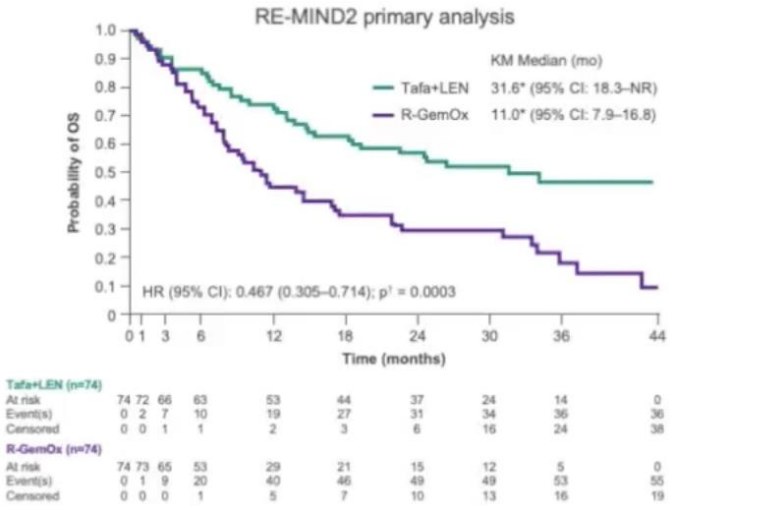


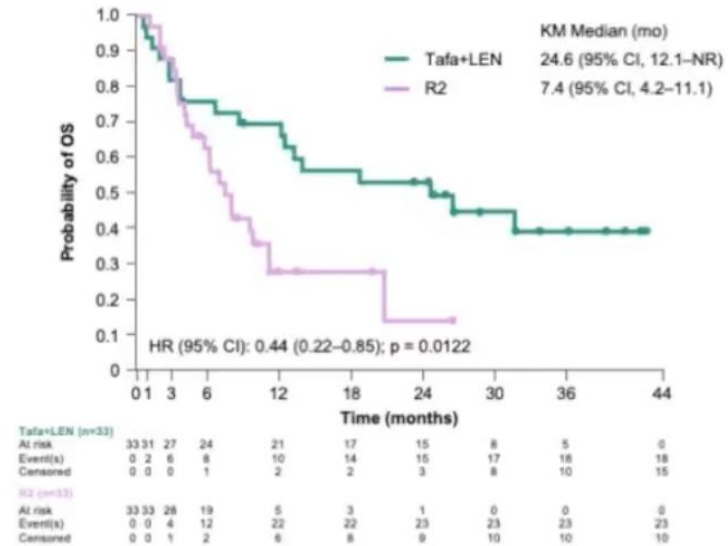




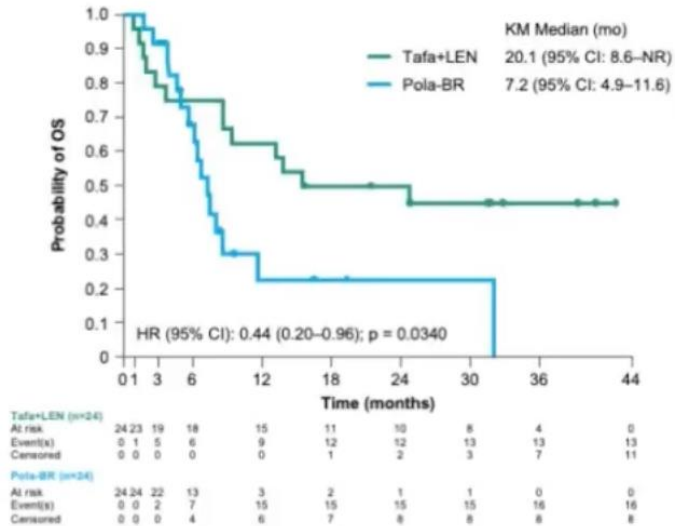
Duell et al. Haematologica 2021; 106(9):2417-2426.

Tafasitamab in R/R DLBCL —RWE RE-MIND2 Study

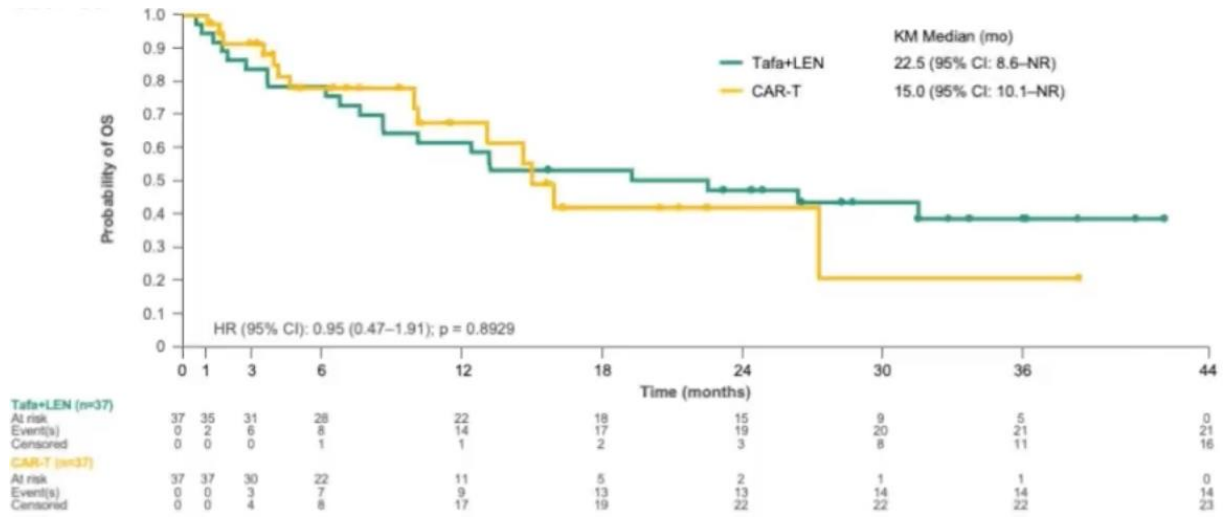




Median duration of follow-up: tafasitamab plus + LEN: 32; mo; R2: 13.4 mo



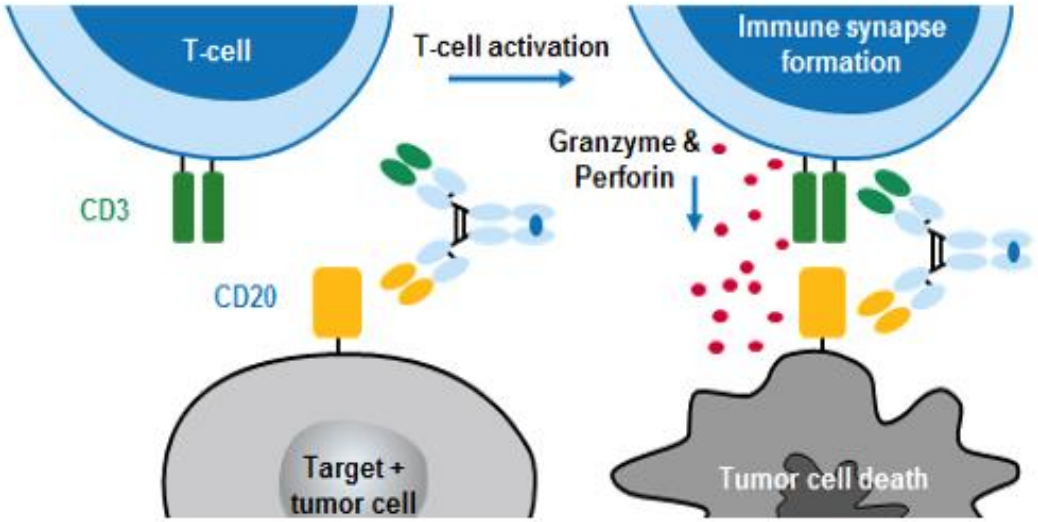
Median duration of follow-up: tafasitamab plus + LEN: 32 mo; Pola-BR: 16.6 mo

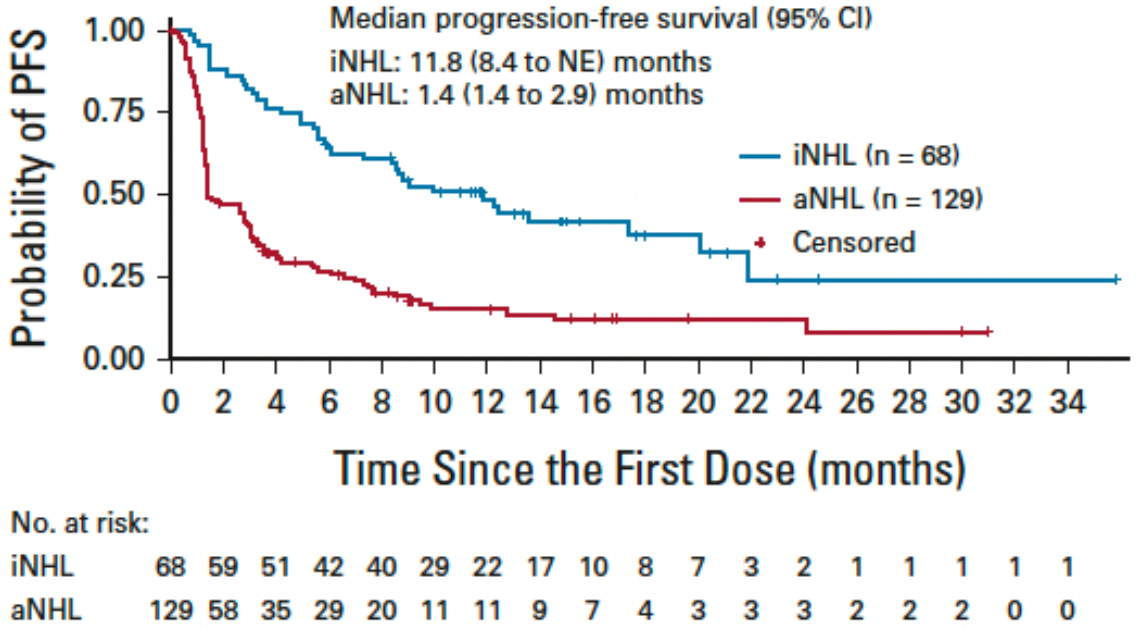


Median duration of follow-up: tafasitamab plus + LEN: 32 mo; CAR-T: 10.2 mo

Nowakowski et al. ASH 2021, Abstract 183

Mosunetuzumab in R/R NHL —

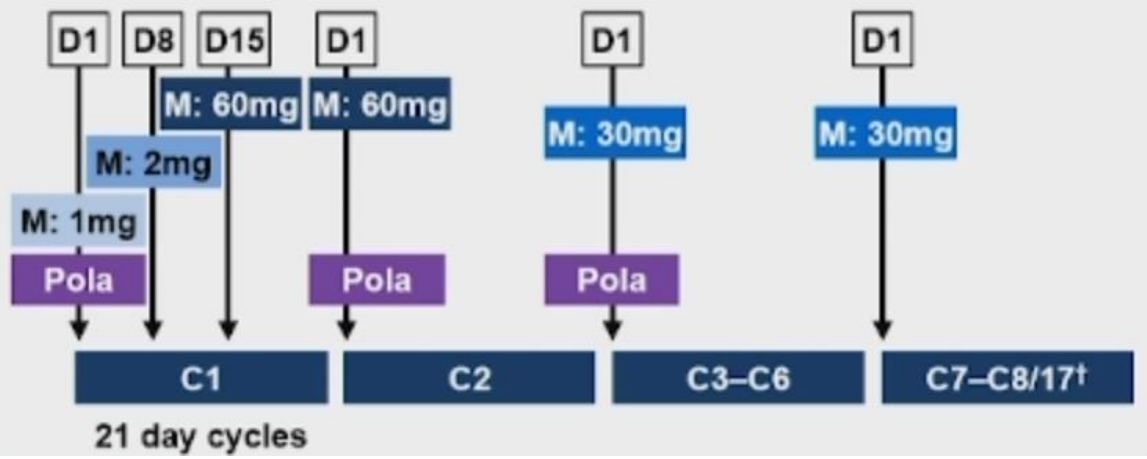




Best Objective Response[a]	Aggressive NHL[b] (n = 129)	Indolent NHL[c] (n = 68)	Post–CAR-T Therapy (n = 19)
ORR, No. (%) [95% CI]	45 (34.9) [26.7 to 43.8]	45 (66.2) [53.7 to 77.2]	7[d] (36.8) [16.3 to 61.6]
Complete response, No. (%) [95% CI]	25 (19.4) [13.0 to 27.3]	33 (48.5) [36.2 to 61.0]	5 (26.3) [9.2 to 51.2]
Partial response, No. (%) [95% CI]	20 (15.5) [9.7 to 22.9]	12 (17.6) [9.5 to 28.8]	2 (10.5) [1.3 to 33.1]
Stable disease, No. (%) [95% CI]	9 (7.0) [3.2 to 12.8]	13 (19.1) [10.6 to 30.5]	0 (0) [0.0 to 17.7]
Progressive disease, No. (%) [95% CI]	70 (54.3) [45.3 to 63.1]	9 (13.2) [6.2 to 23.6]	12 (63.2) [38.4 to 83.7]
Duration of response, median [95% CI], months	7.6 [5.6 to 22.8]	16.8 [11.7 to NE]	Not reported due to small sample size (n = 7)[d]
Duration of response in patients with complete response, median [95% CI], months	22.8 [7.6 to NE]	20.4 [16.0 to NE]	Not reported due to small sample size (n = 5)

Budde et al. J Clin Oncol 2021; epub

Mosunetuzumab + Polatuzumab in R/R NHL —



N (%) unless stated	All patients N=63	DLBCL patients N=60
Median age, years (range)	68 (20–83)	68 (20–83)
Male	39 (61.9)	37 (61.7)
ECOG PS at entry		
0–1	59 (93.7)	56 (93.3)
2	4 (6.3)	4 (6.7)
Histology		
DLBCL	60 (95.2)	60 (100)
de novo DLBCL	44 (69.8)*	44 (73.3)
transformed FL	12 (19.0)†	12 (20.0)
Grade 3b FL	4 (6.3)	4 (6.7)
FL Grade 1–3a	3 (4.8)	0
Bulky disease (≥10 cm)	6 (9.5)	6 (10.0)

N (%) unless stated	All patients N=63	DLBCL patients N=60
Ann Arbor stage at entry		
I–II	13 (20.6)	12 (20.0)
III–IV	50 (79.4)	48 (80.0)
Number of prior lines of therapy		
1–2	24 (38.1)	24 (40.0)
3+	39 (61.9)	36 (60.0)
Median prior lines of therapy, range	3 (1–10)	3 (1–8)
Prior CAR-T therapy	25 (39.7)	24 (40.0)
Refractory to last prior therapy	48 (76.2)	46 (76.7)

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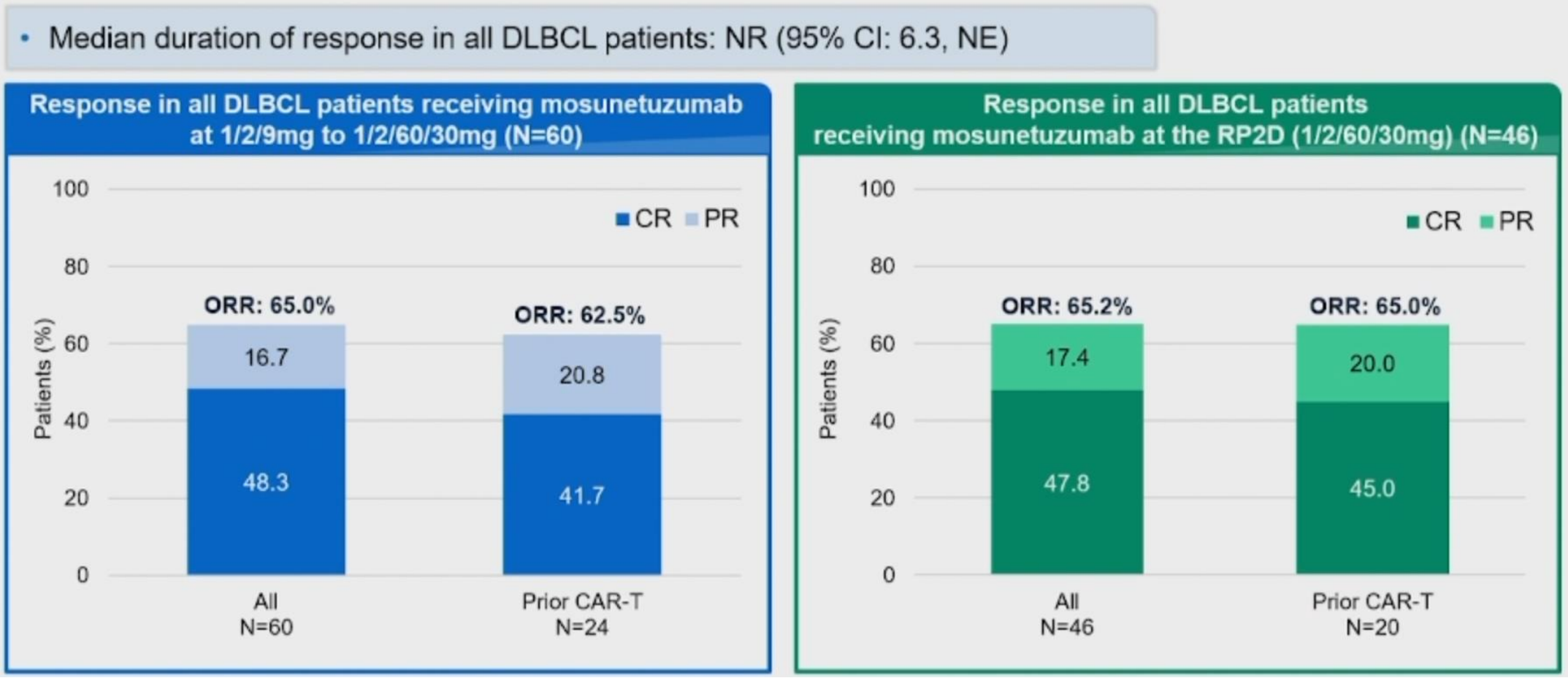
Mosunetuzumab + Polatuzumab in R/R NHL —

CRS: Grade 1 15.9%, Grade 2 1.6%, no Grade 3+
ICANS-like: Any grade 7.9%, Grade 3+ 3.2%



Budde et al. ASH 2021, Abstract 533

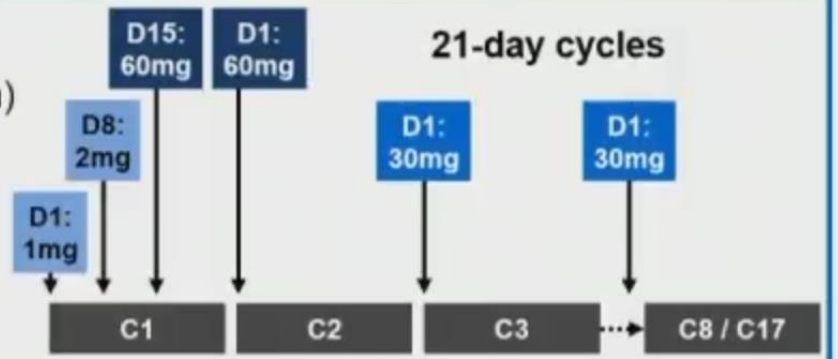
Mosunetuzumab in R/R iNHL —

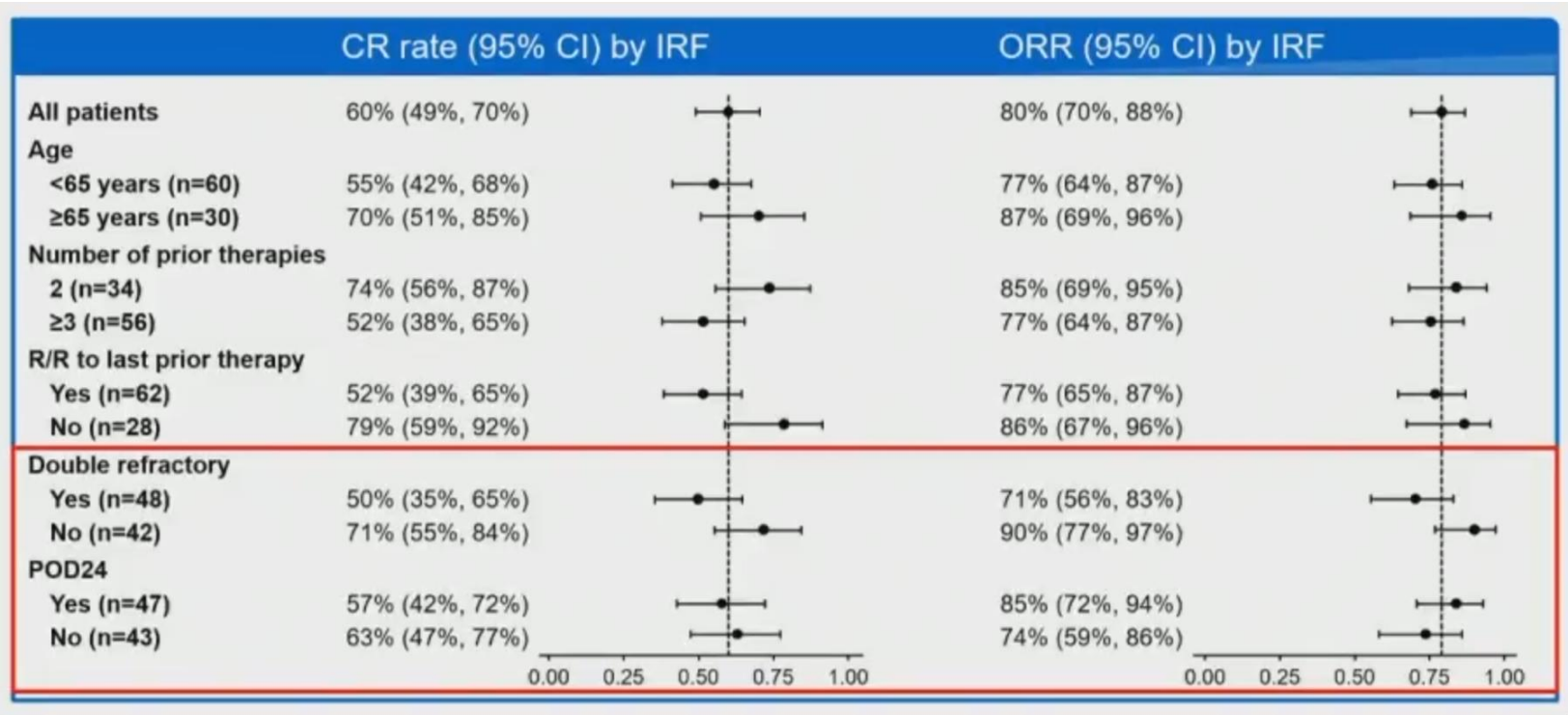
Key inclusion criteria

- FL (Grade 1–3a)
- ECOG PS 0–1
- ≥2 prior regimens, including
  - ≥1 anti-CD20 Ab
  - ≥1 alkylating agent

Mosunetuzumab administration

- Q3W intravenous administration
- C1 step-up dosing (CRS mitigation)
- **Fixed-duration treatment**
  - 8 cycles if CR after C8
  - 17 cycles if PR/SD after C8
- **No mandatory hospitalization**





Budde et al. ASH 2021, Abstract 127

Hodgkin Lymphoma

Brentuximab Vedotin in HL — Echelon-1 Study

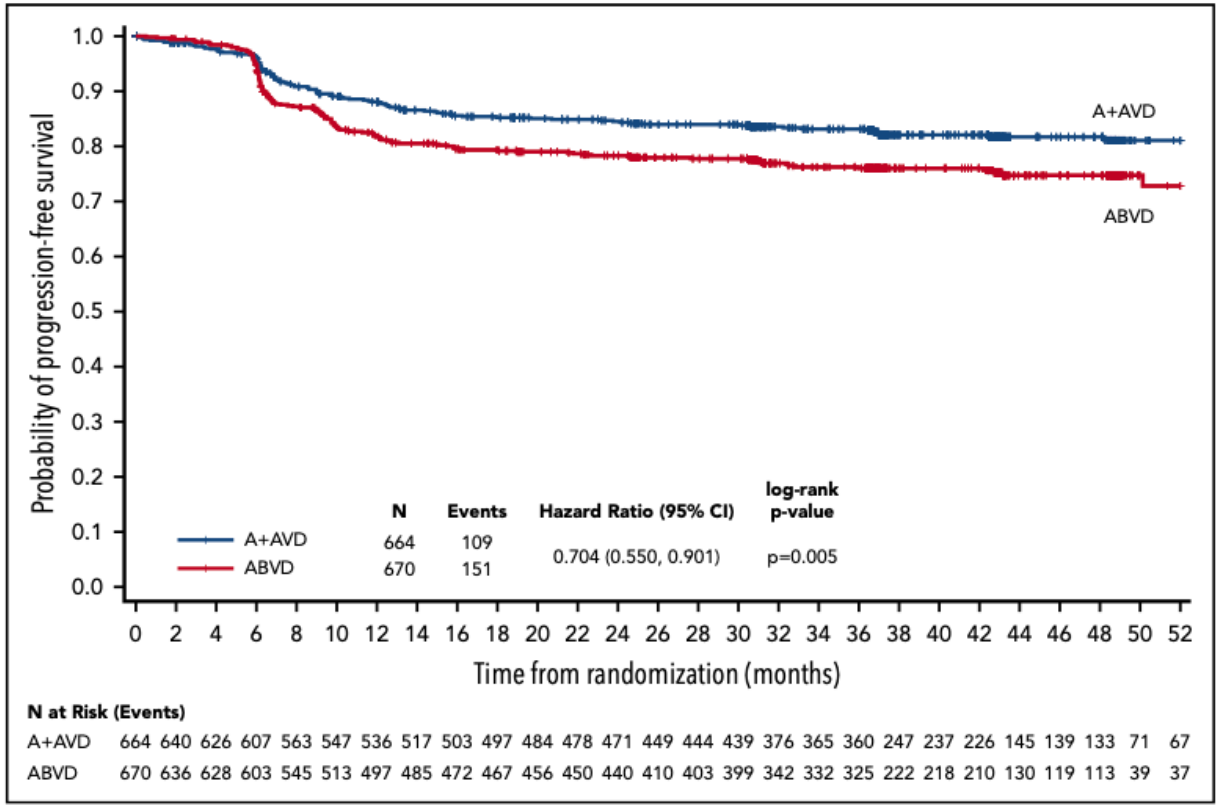
Characteristic	A+AVD, n = 664	ABVD, n = 670	Total, N = 1334
Male sex	378 (57)	398 (59)	776 (58)
Age, y	35 (18-82)	37 (18-83)	36 (18-83)
<60	580 (87)	568 (85)	1148 (86)
≥60	84 (13)	102 (15)	186 (4)
Regions			
Americas	261 (39)	262 (39)	523 (39)
Europe	333 (50)	336 (50)	669 (50)
Asia	70 (11)	72 (11)	142 (11)
IPS			
0 or 1	141 (21)	141 (21)	282 (21)
2 or 3	354 (53)	351 (52)	705 (53)
4 to 7	169 (25)	178 (27)	347 (26)
ECOG performance status			
0	376 (57)	378 (57)	754 (57)
1	260 (39)	263 (39)	523 (39)
2	28 (4)	27 (4)	55 (4)
PET2 status			
Positive	47 (7)	58 (9)	105 (8)
Negative	588 (89)	577 (86)	1165 (87)
Unknown/unavailable	29 (4)	35 (5)	64 (5)

Phase III

Brentuximab + Doxorubicin + Vinblastine + Dacarbazine

vs

Doxorubicin + Bleomycin + Vinblastine + Dacarabizine



Straus et al. Blood 2020, 135(10):735-742.

Pembrolizumab in HL —

Sequential Pembrolizumab and AVD in classical Hodgkin lymphoma, Phase 2 study

N=30

PET1

Pembrolizumab x 3

PET2

AVD x 2

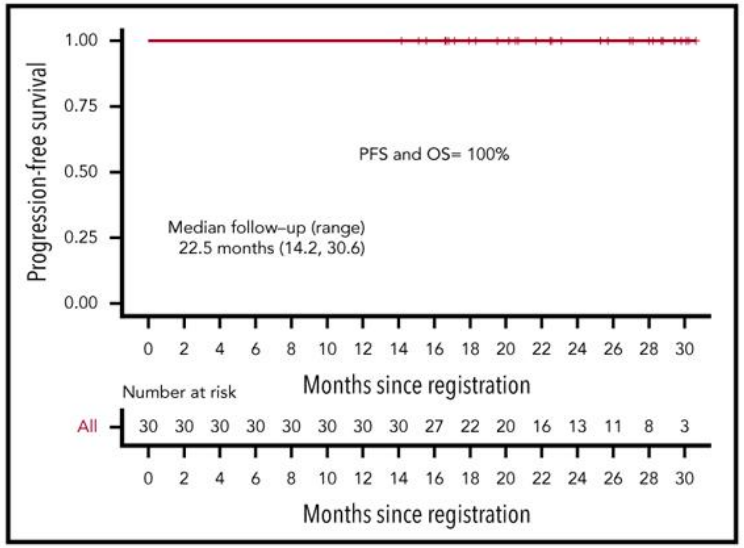
PET3

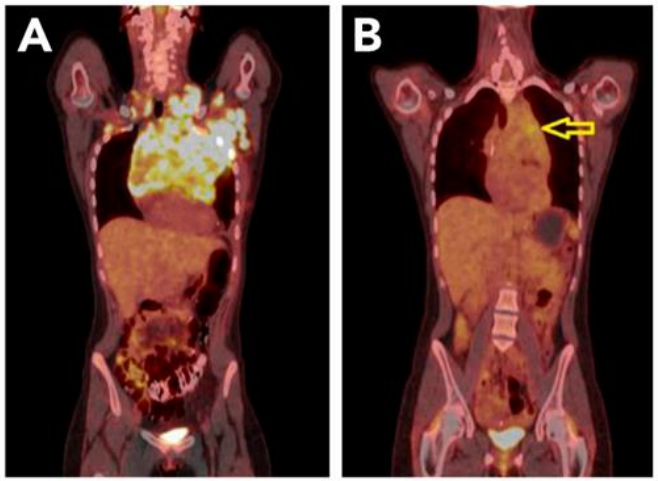
AVD x 2-4

End of Treatment PET

Newly diagnosed early unfavorable and advanced stage classical Hodgkin lymphoma

Follow up every 3 months x 2 years

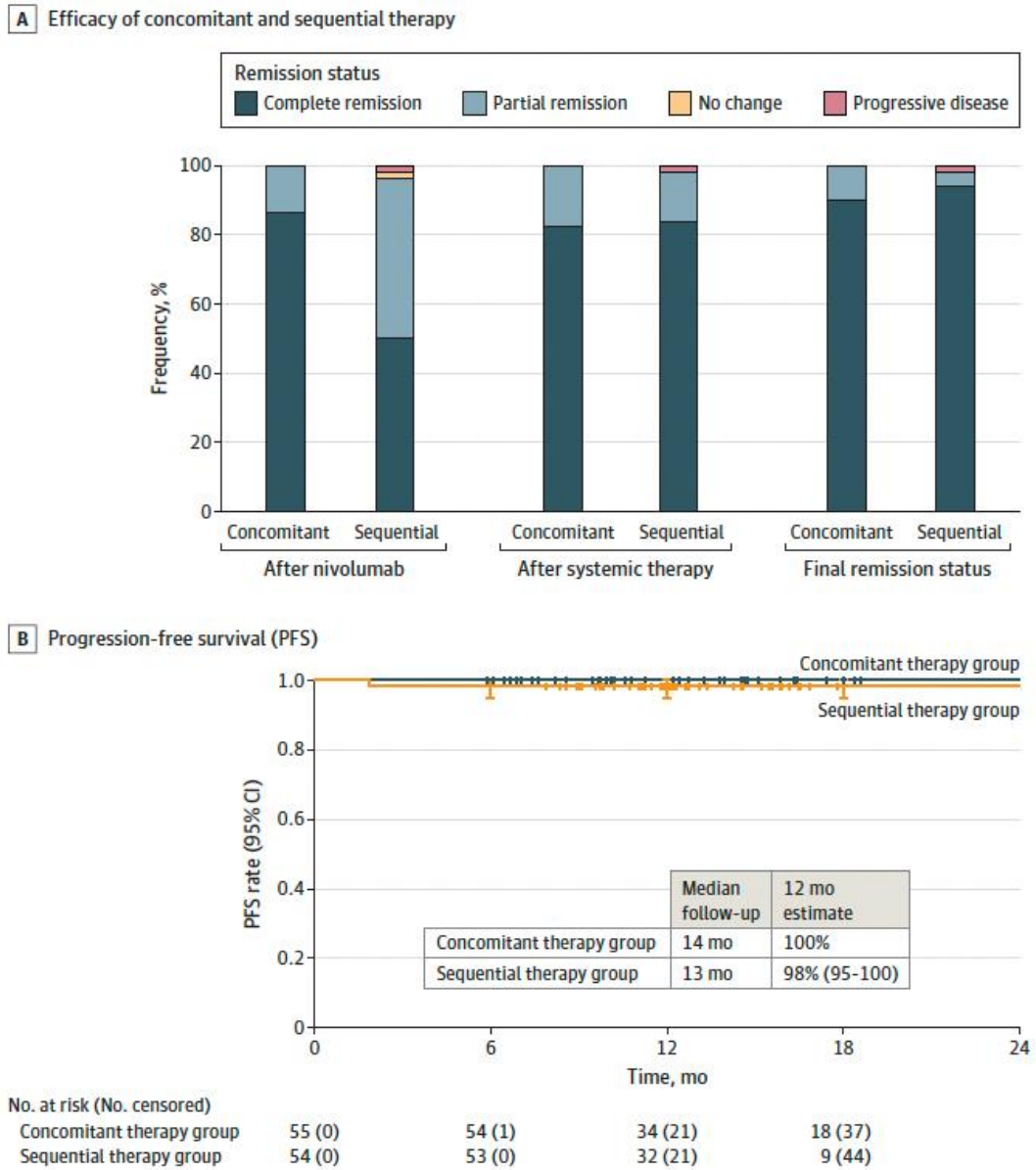




Response to single-agent pembrolizumab

Allen et al. Blood 2021, 137(10):1318-1326.

Nivolumab in HL —



Brockelmann et al. JAMA Oncol 2020, 6(6):872-880.

Monoclonal antibodies in Leukemia/Lymphoma:

- **ALL: monoclonal antibodies play an essential role in all lines of therapy, including, uniquely, MRD+ disease. No role for checkpoint inhibitors thus far.**
- **AML: monoclonal antibodies to CD33 and CD123 have been applied to enhance responses to chemotherapy, or serve as targets for T cell engagers. Other targets are emerging. Limited role for checkpoint inhibitors thus far.**
- **NHL: monoclonal antibodies have been essential for treatment for over 20yrs, but improving on R-CHOP outcomes has been difficult. Pola-R-CHP is a modest, but real improvement over R-CHOP. Additional ADC and bispecifics are on the horizon.**
- **HL: only blood cancer in which there is compelling evidence supporting for use of checkpoint inhibitors in front-line therapy. ADC may help**

Thank you!