6th Annual

LEAD2024

Enriching Experiences for Women in Hematology & Oncology

Clinical Updates in Hematologic Malignancies

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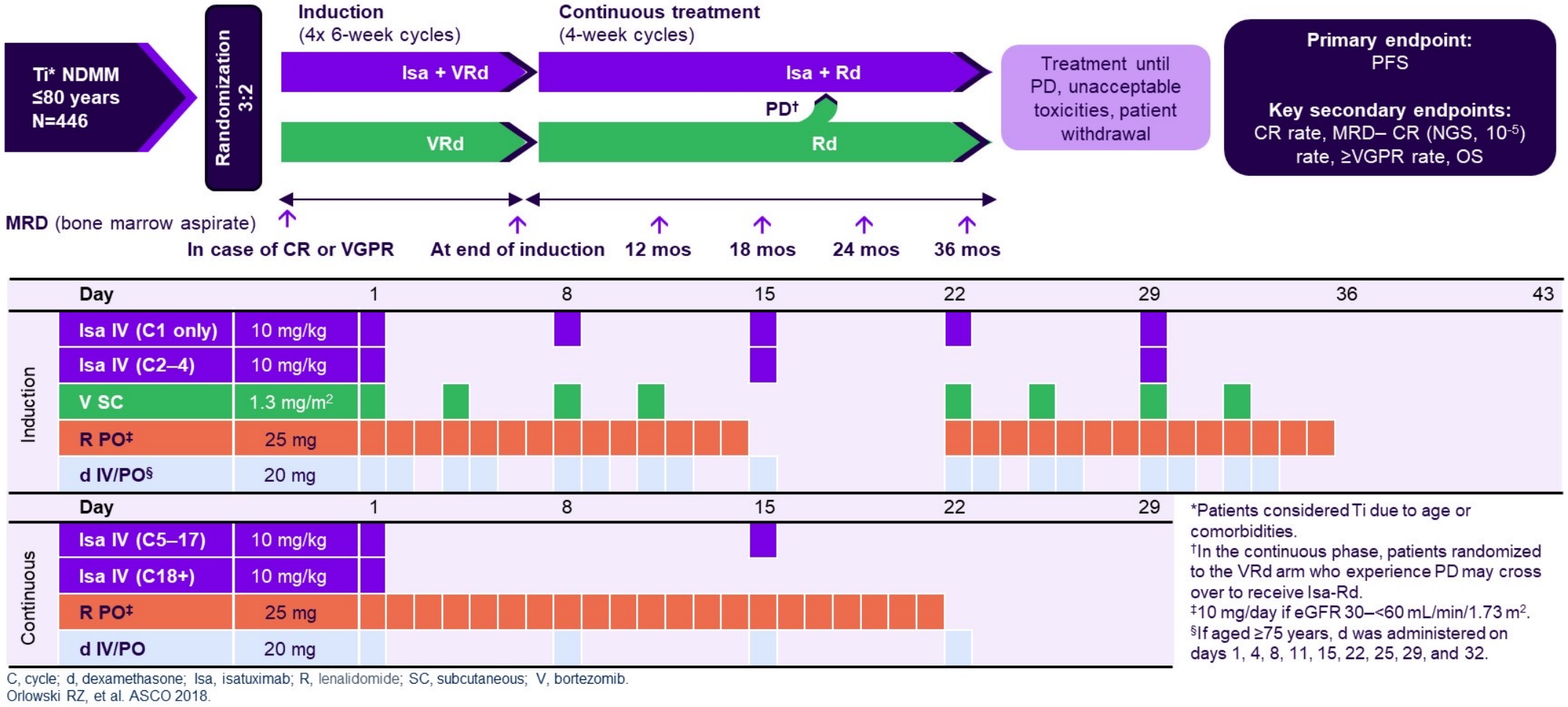
University of Nebraska Medical Center
Nebraska Medicine

Myeloma

Myeloma Updates

- **IMROZ**: Phase III Study of Isatuximab Plus VRd vs VRd for Transplant-Ineligible, Newly Diagnosed MM
- **BENEFIT**: Phase III Trial of Isa-VRd vs Isa-Rd in Patients With Transplant-Ineligible ND MM
- **PERSEUS**: MRD Analysis: VRd With or Without Daratumumab in ND MM Eligible for ASCT
- **DREAMM-8**: Phase III Trial of Belantamab Mafodotin Plus Pom/Dex vs Bortezomib Plus Pom/Dex in R/R MM

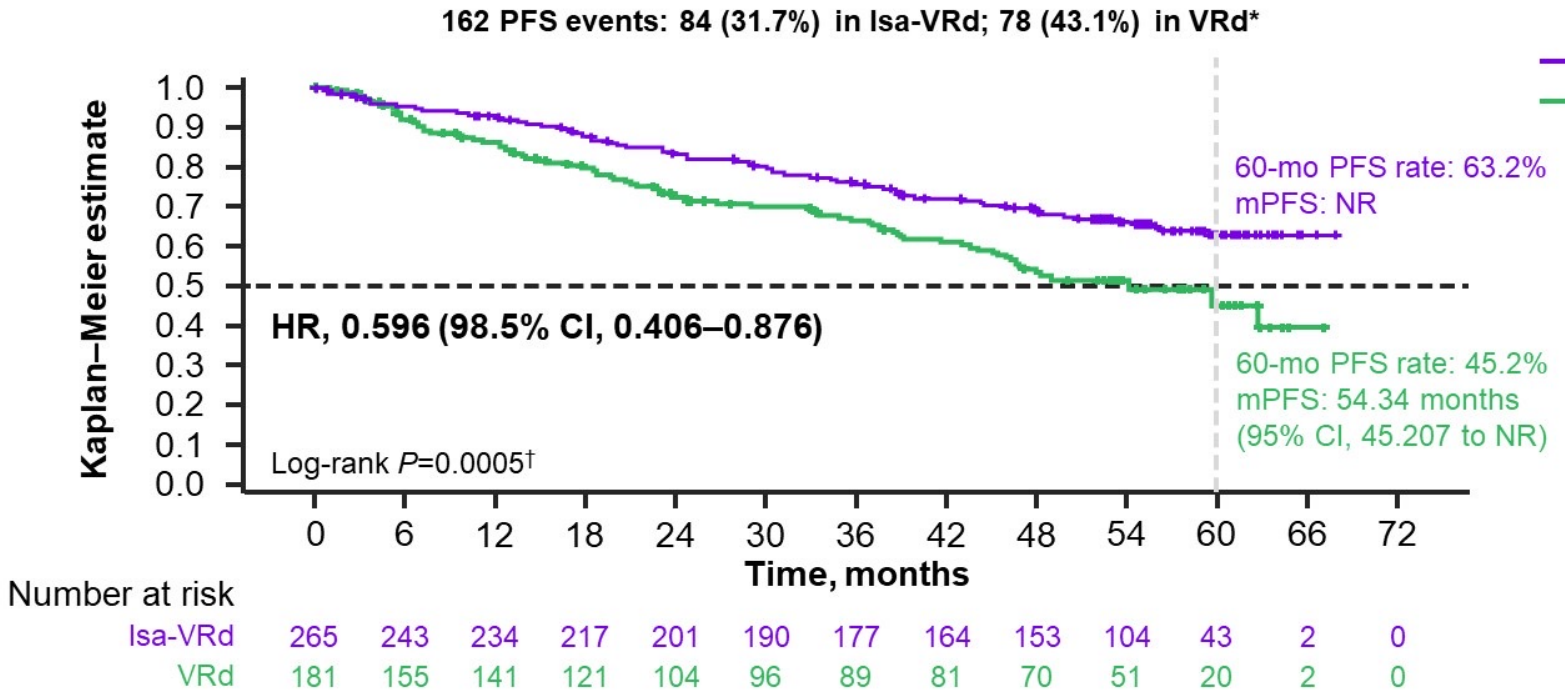
IMROZ Trial: Phase 3 Study Results of Isatuximab, Bortezomib, Lenalidamide, and Dexamethasone (Isa-VRd) versus VRd for Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma

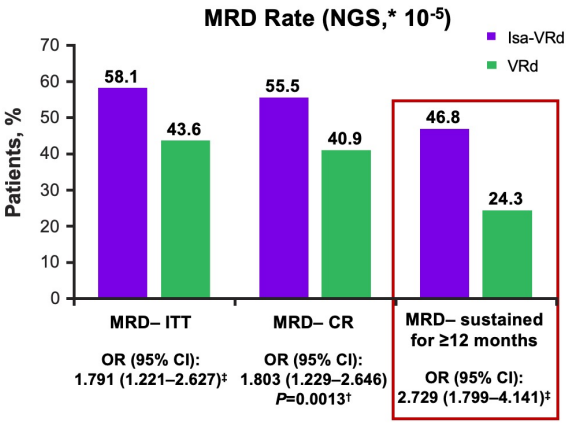


C, cycle; d, dexamethasone; Isa, isatuximab; R, lenalidomide; SC, subcutaneous; V, bortezomib.
Orlowski RZ, et al. ASCO 2018.

Source: Facon T et al. https://doi.org/10.1200/JCO.2024.42.16_suppl.7500

Primary endpoint met: Interim PFS analysis- IRC assessment in ITT population



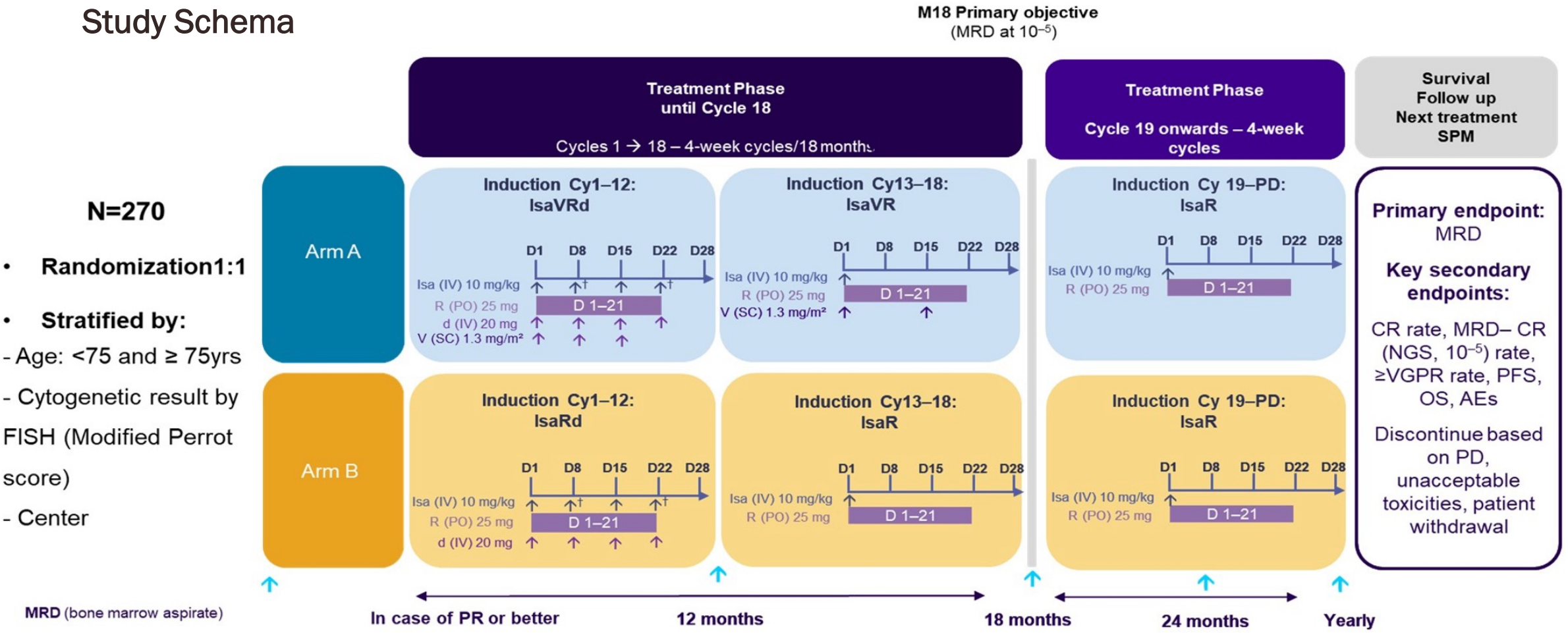


At a median follow-up of 5 years (59.7 months), Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or death by 40.4%

*Cutoff date for PFS analysis: September 26, 2023 (median follow-up, ~5 years). †Nominal one-sided *P* value.
NR, not reached.

BENEFIT: isatuximab (Isa) plus lenalidomide and dexamethasone (Rd) with bortezomib versus isard in patients with newly diagnosed transplant ineligible multiple myeloma

Study Schema

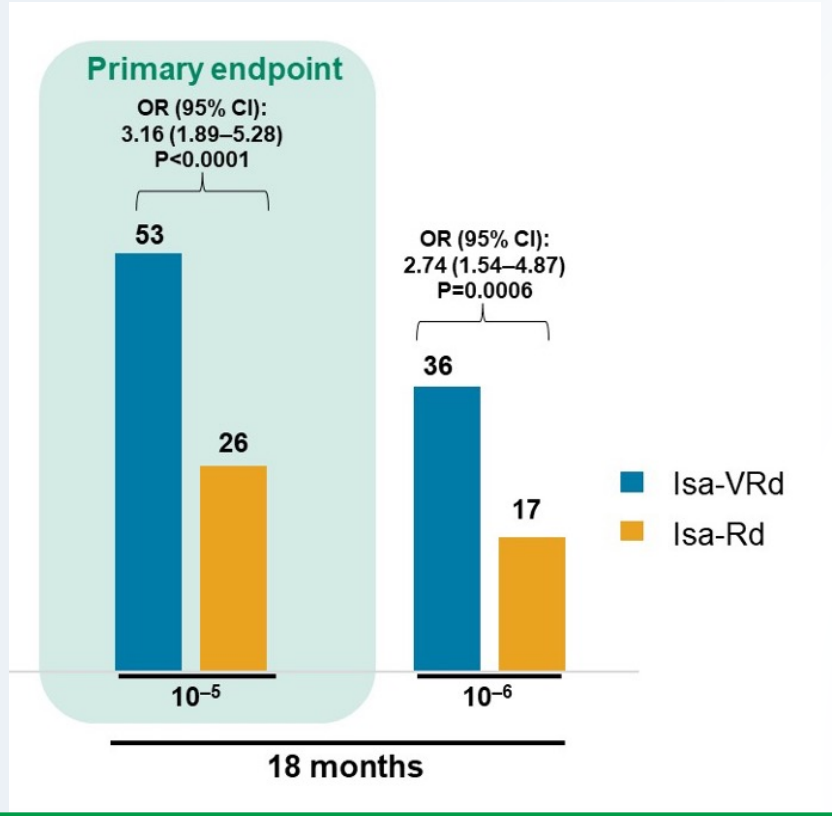


†Cycle 1 only. CR, complete response; Cy, cycle; d, dexamethasone; D, day; Isa, isatuximab; M, month; MRD, minimal residual disease; NDMM, newly diagnosed multiple myeloma; NGS, next generation sequencing; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; R, lenalidomide; SPM, second primary malignancy; Ti, transplant-ineligible; V, bortezomib; VGPR, very good partial response.

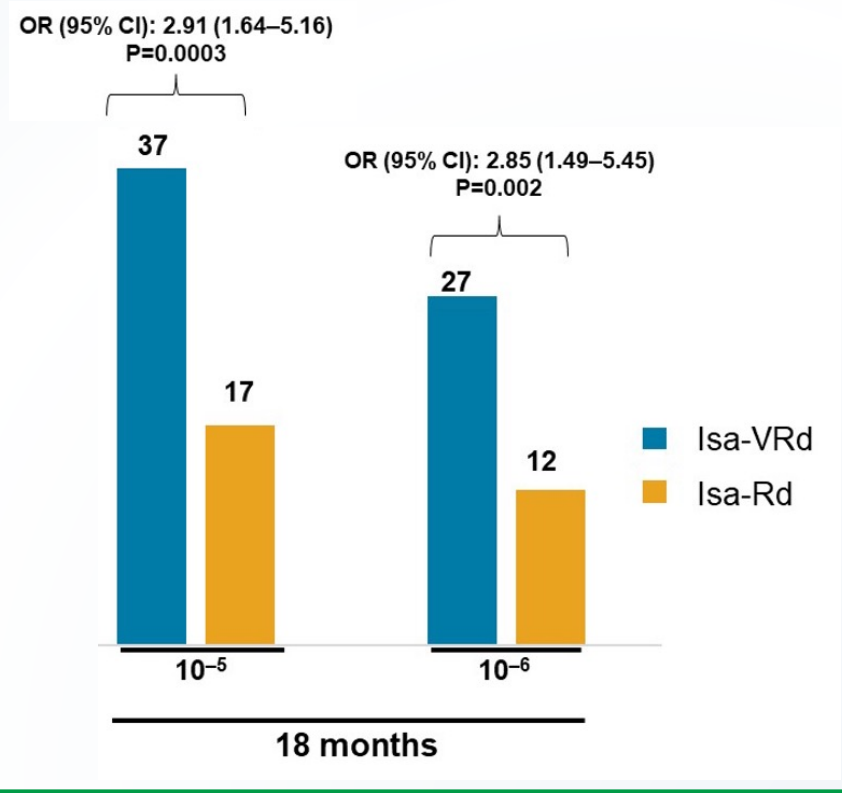
Leleu et al. https://doi.org/10.1200/JCO.2024.42.16_suppl.750

BENEFIT Trial: Isa-VRd vs. Isa-RD in TI NDMM

Results: Primary Endpoint MRD(-)



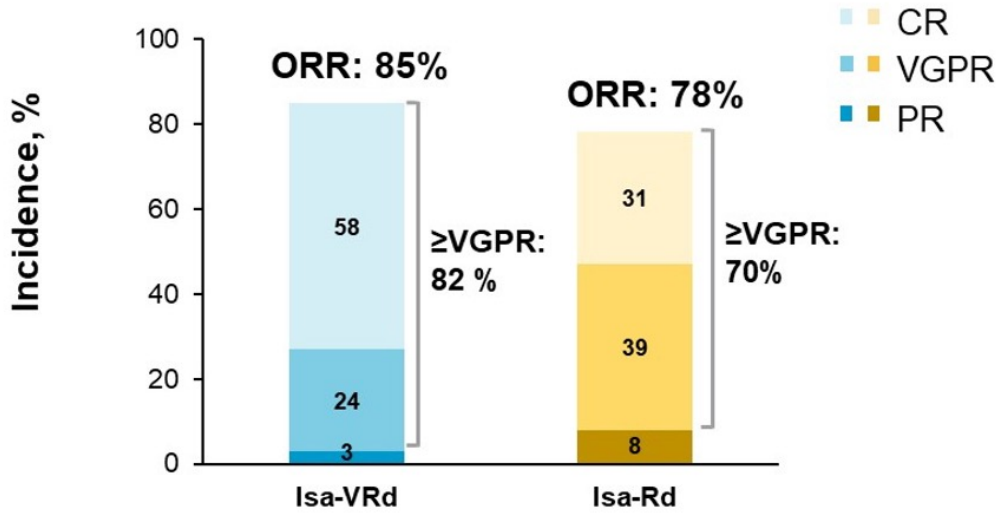
Secondary Endpoint MRD(-) CR rates



Isa-VRd resulted in significant improvements in MRD- and MRD- CR rates at 18 months and at the 10^{-5} and 10^{-6} levels

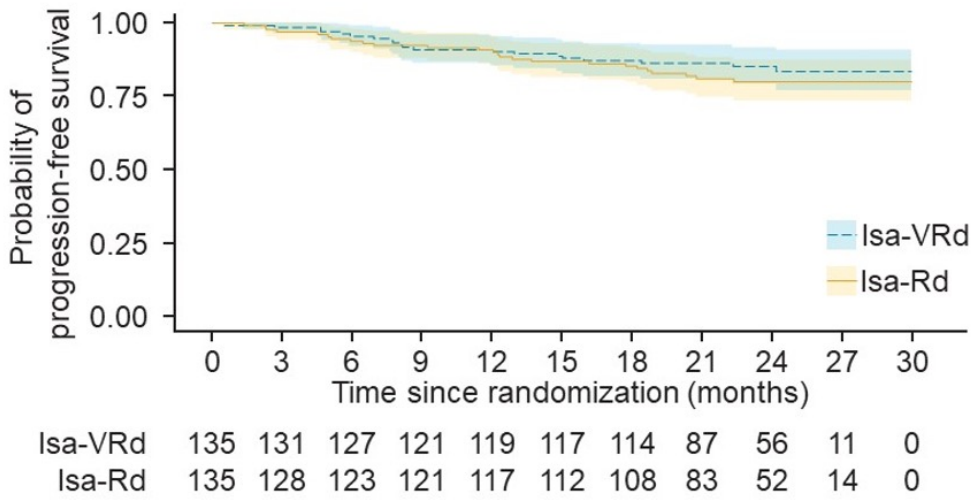
BENEFIT Trial: Isa-VRd vs. Isa-RD in TI NDMM

Results: Depth of Response (at 18 mos)



≥CR rate 58% vs. 31%, OR (95% CI): 2.97 (2–5), p<0.0001

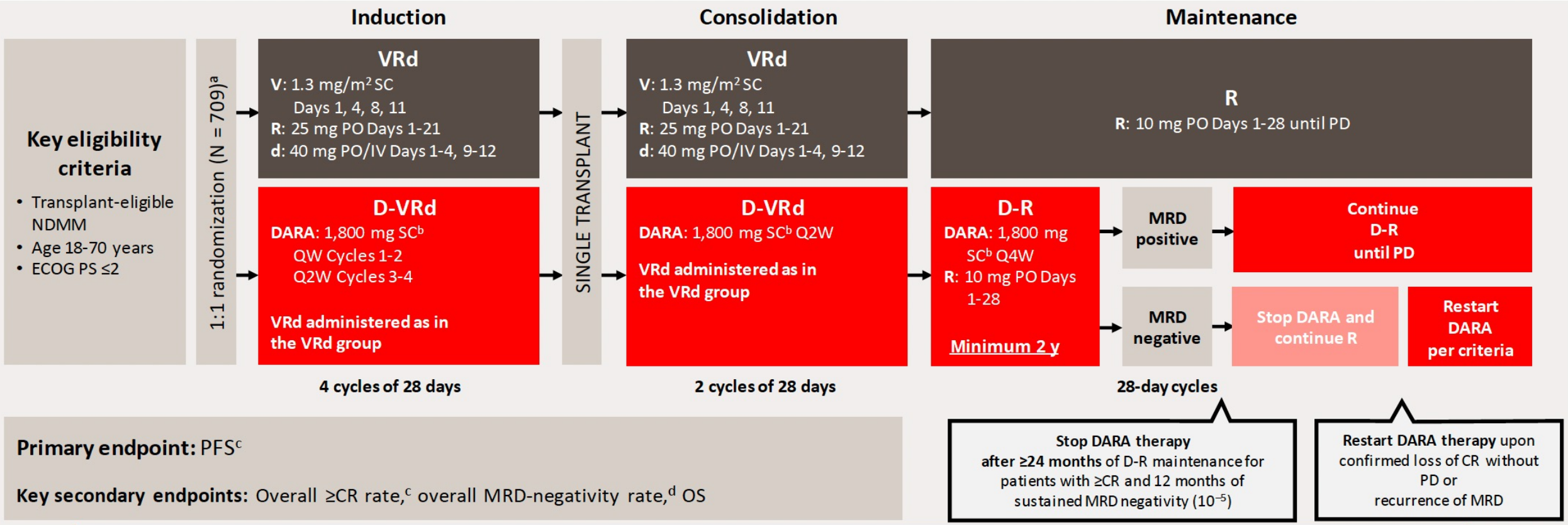
Preliminary PFS (Median F/U 23.5 mos)



Estimated 24 months PFS
85.2% (95%CI 79.2–91.7) for Isa-VRd
80.0% (95% CI 73.3–87.4) for Isa-Rd

Isa-VRd resulted in deep response rates, particularly CR at 18 months and PFS is still immature

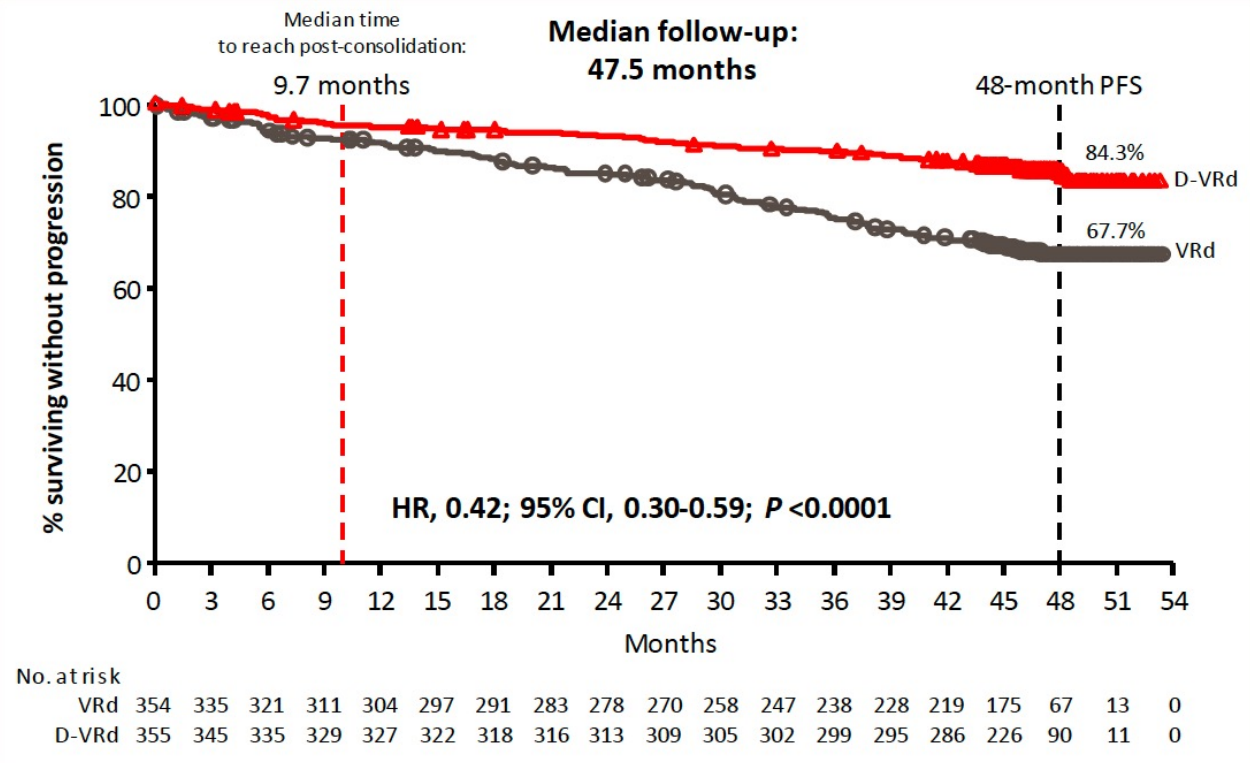
PERSEUS: Study Design

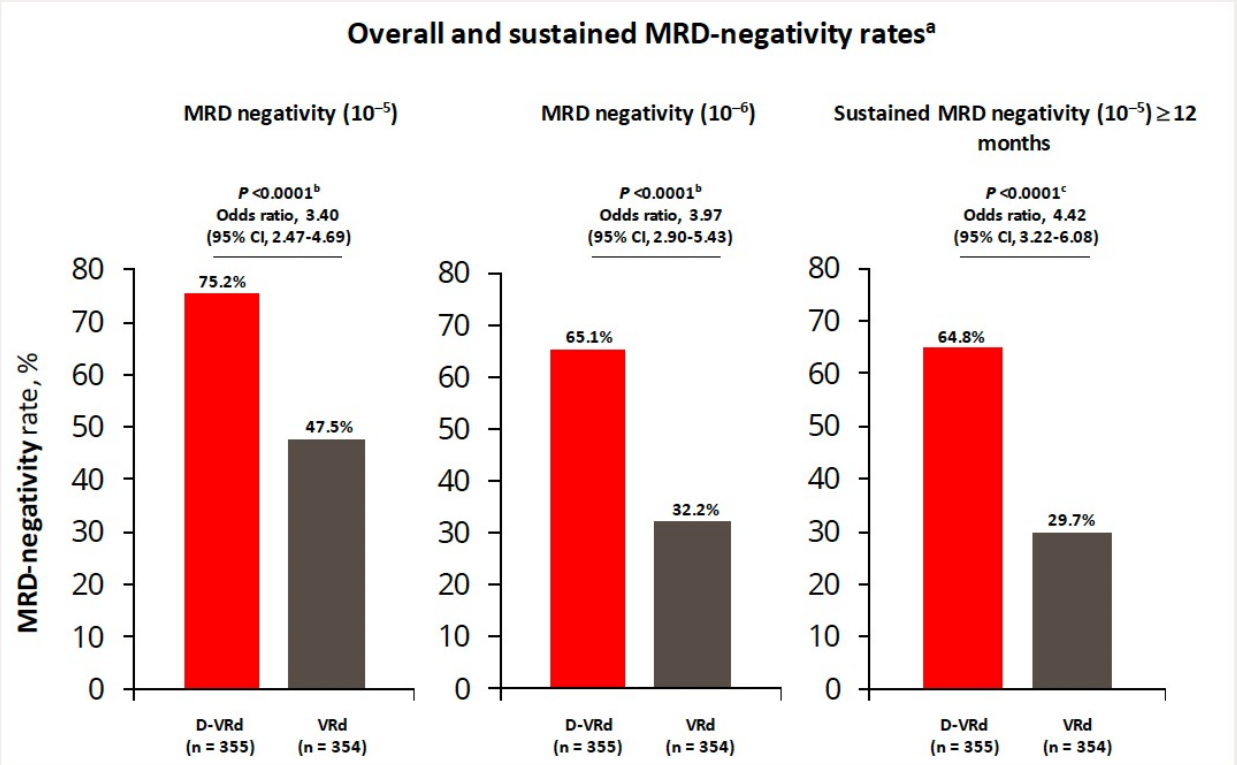


MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR in the ITT population. Patients who were not evaluable or had indeterminate results were considered MRD positive.

Sonnefeld P. DOI: 10.1056/NEJMoa2312054

PERSEUS Primary Analysis: D-VRd Followed by D-R Maintenance Significantly Improved PFS and Depth of Response Versus VRd Followed by R Maintenance[1]

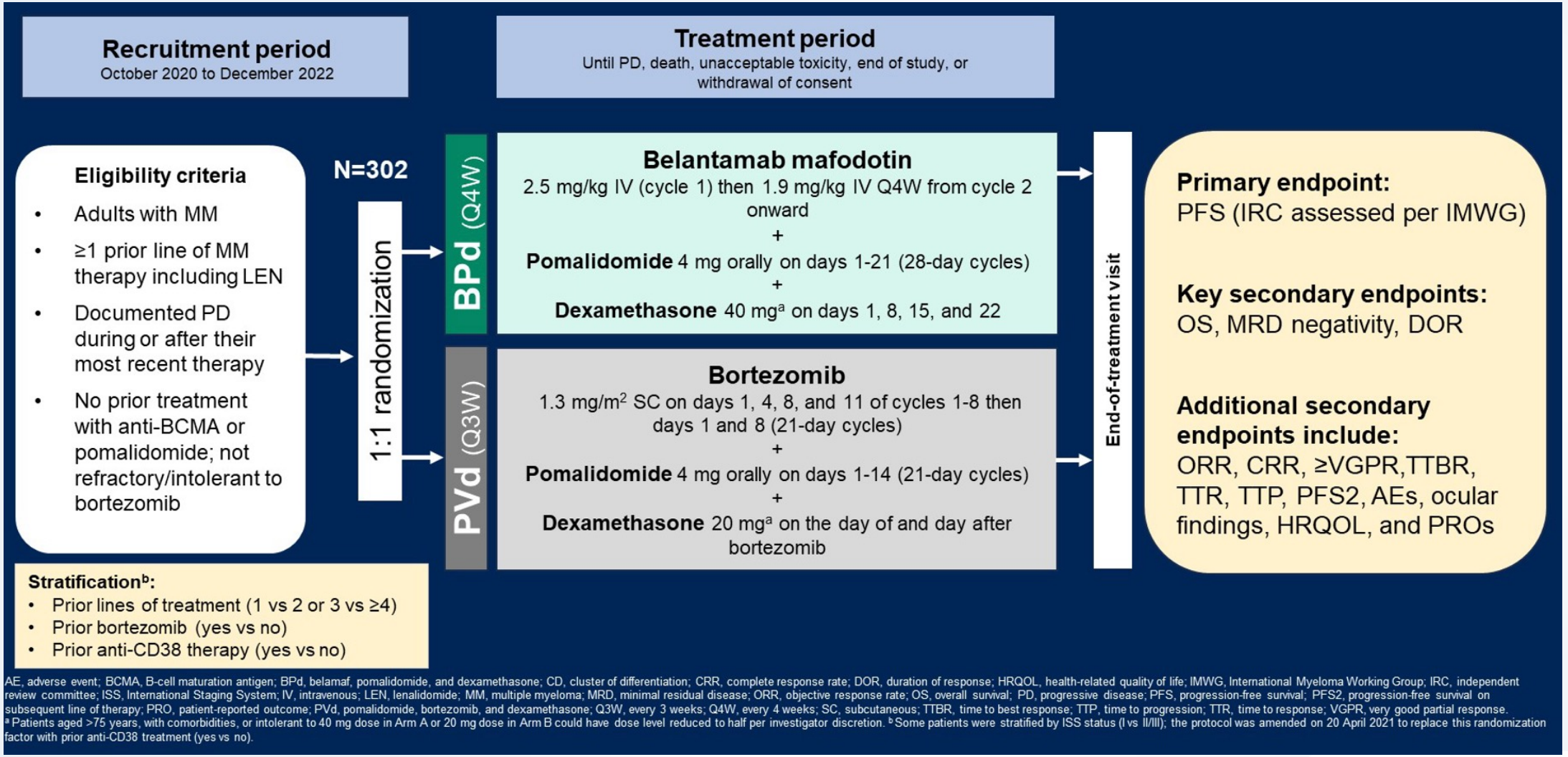




58% reduction in the risk of progression or death in patients receiving D-VRd

Deep and durable MRD negativity achieved with D-VRd

DREAMM-8: Phase III Trial of Belantamab Mafodotin Plus Pom/Dex vs Bortezomib Plus Pom/Dex in R/R MM



AE, adverse event; BCMA, B-cell maturation antigen; BPd, belamaf, pomalidomide, and dexamethasone; CD, cluster of differentiation; CRR, complete response rate; DOR, duration of response; HRQOL, health-related quality of life; IMWG, International Myeloma Working Group; IRC, independent review committee; ISS, International Staging System; IV, intravenous; LEN, lenalidomide; MM, multiple myeloma; MRD, minimal residual disease; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PFS2, progression-free survival on subsequent line of therapy; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; Q3W, every 3 weeks; Q4W, every 4 weeks; SC, subcutaneous; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.
[a] Patients aged >75 years, with comorbidities, or intolerant to 40 mg dose in Arm A or 20 mg dose in Arm B could have dose level reduced to half per investigator discretion. [b] Some patients were stratified by ISS status (I vs II/III); the protocol was amended on 20 April 2021 to replace this randomization factor with prior anti-CD38 treatment (yes vs no).

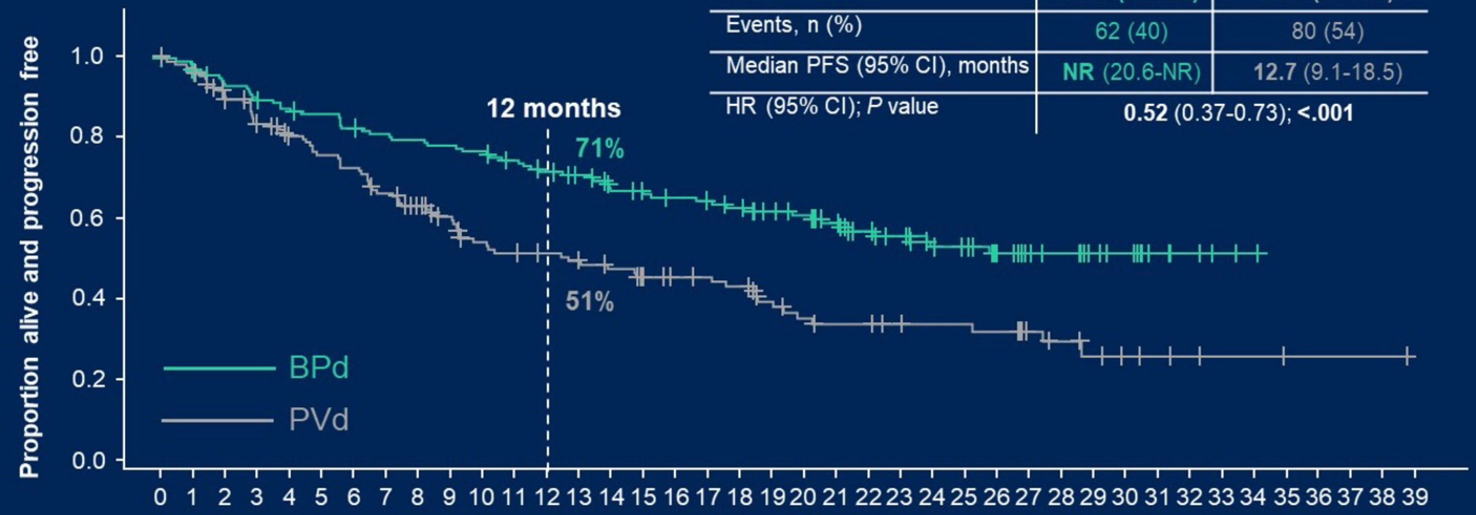
Dimopoulos MA et al. **DOI: 10.1056/NEJMoa2403407**

Baseline characteristics	ITT population	
	BPd (N=155)	PVd (N=147)
Age, median (range), years	67 (40-82)	68 (34-86)
<65, n (%)	64 (41)	53 (36)
65 to <75, n (%)	72 (46)	59 (40)
≥75, n (%)	19 (12)	35 (24)
Male/female, n (%)	99 (64)/56 (36)	82 (56)/65 (44)
White/Black/Asian/Mixed race, n (%)[a]	133 (86)/0/20 (13)/1 (<1)	127 (87)/0/17 (12)/0
ECOG PS ≤1, n (%)[b]	146 (97)	140 (97)
ISS stage at screening, n (%)		
I	93 (60)	85 (58)
II	39 (25)	40 (27)
III	22 (14)	22 (15)
Unknown	1 (<1)	0
Years since diagnosis, median (range)	4.04 (0.4-16.7)	3.43 (0.4-17.7)
Cytogenetic abnormalities, n (%)		
Standard risk[c]	72 (46)	75 (51)
High risk[d]	52 (34)	47 (32)
Missing or nonevaluable	31 (20)	25 (17)
Time to relapse after initiation of 1L treatment		
≤12 months	22 (14)	20 (14)
>12 months	133 (86)	127 (86)
Extramedullary disease, n (%)		

Prior treatments, n (%)	ITT population			
	BPd (N=155)		PVd (N=147)	
Prior LOT				
1	82 (53)		77 (52)	
2 or 3	54 (35)		48 (33)	
≥4	19 (12)		22 (15)	
Prior ASCT	99 (64)		82 (56)	
Prior treatment	Exposed	Refractory	Exposed	Refractory
Prior proteasome inhibitor	140 (90)	40 (26)	136 (93)	35 (24)
Bortezomib	134 (86)	16 (10)	130 (88)	8 (5)
Carfilzomib	34 (22)	18 (12)	37 (25)	23 (16)
Ixazomib	11 (7)	8 (5)	15 (10)	11 (7)
Prior immunomodulatory drug[a]	155 (100)	127 (82)	147 (100)	111 (76)
Lenalidomide	155 (100)	125 (81)	147 (100)	111 (76)
Thalidomide	49 (32)	9 (6)	48 (33)	6 (4)
Prior anti-CD38 monoclonal antibody[b]	38 (25)	35 (23)	42 (29)	36 (24)
Daratumumab	36 (23)	33 (21)	39 (27)	34 (23)
Isatuximab	2 (1)	2 (1)	3 (2)	2 (1)

BPD led to a significant PFS benefit vs. PVd

PFS	BPd (N=155)	PVd (N=147)
Events, n (%)	62 (40)	80 (54)
Median PFS (95% CI), months	**NR** (20.6-NR)	**12.7** (9.1-18.5)
HR (95% CI); *P* value	**0.52** (0.37-0.73); **<.001**	



No. at risk (no. of events)

Month	0	1	2	3	4	5	6	7	8	9
BPd	155 (0)	143 (5)	135 (10)	130 (15)	125 (19)	122 (21)	117 (26)	113 (28)	111 (30)	109 (32)
PVd	147 (0)	138 (4)	123 (14)	111 (23)	102 (27)	96 (33)	92 (37)	83 (45)	75 (49)	68 (52)

Month	10	11	12	13	14	15	16	17	18	19
BPd	107 (34)	102 (37)	97 (41)	93 (42)	82 (47)	80 (47)	77 (49)	75 (50)	72 (52)	67 (53)
PVd	59 (59)	56 (62)	54 (62)	51 (64)	47 (66)	43 (68)	40 (68)	39 (68)	37 (70)	30 (73)

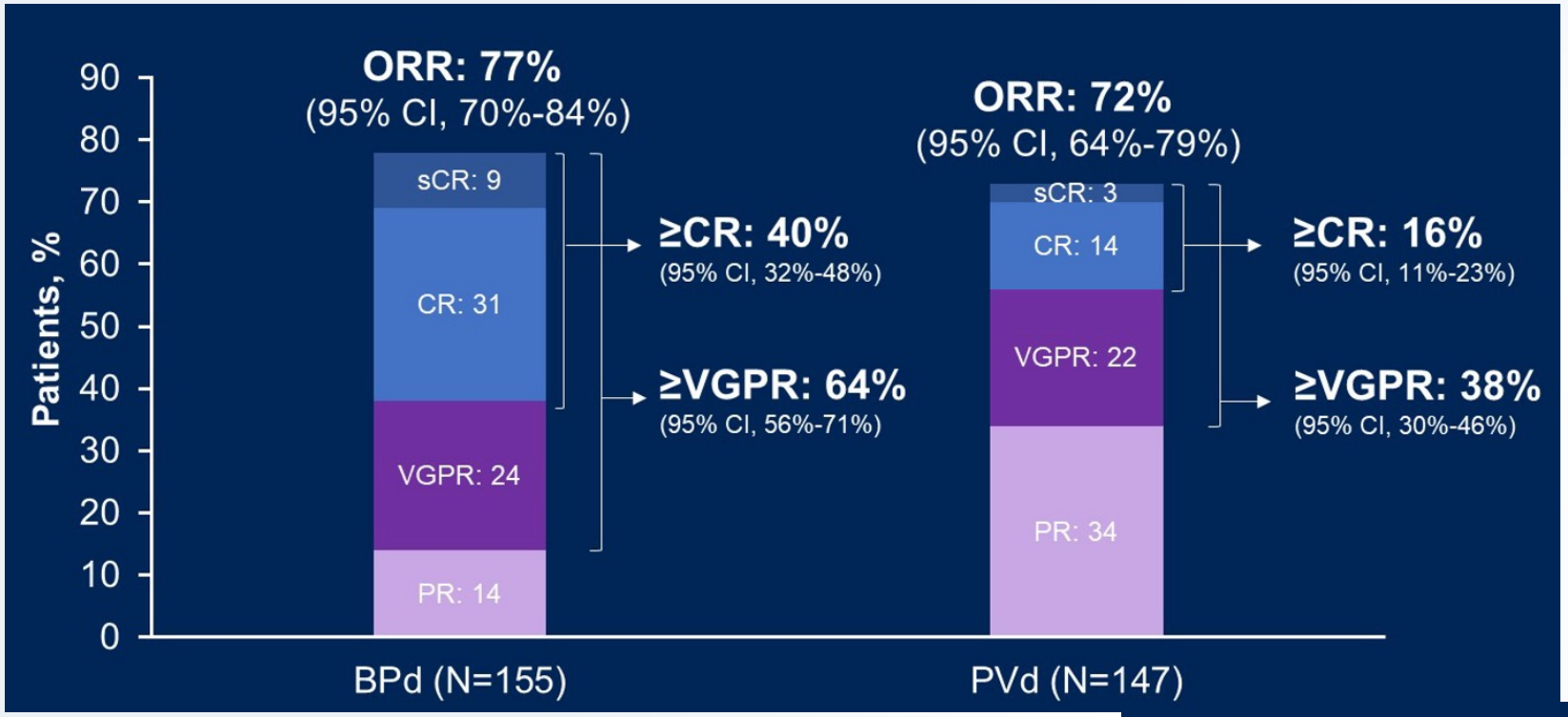
Month	20	21	22	23	24	25	26	27	28	29
BPd	64 (54)	59 (56)	50 (58)	45 (59)	38 (61)	36 (61)	28 (62)	23 (62)	21 (62)	16 (62)
PVd	25 (76)	22 (77)	22 (77)	19 (77)	18 (77)	18 (77)	17 (78)	13 (78)	11 (79)	7 (80)

Month	30	31	32	33	34	35	36	37	38	39
BPd	13 (62)	8 (62)	4 (62)	2 (62)	1 (62)	0 (62)	0 (62)	0 (62)	0 (62)	0 (62)
PVd	5 (80)	4 (80)	3 (80)	2 (80)	2 (80)	1 (80)	1 (80)	1 (80)	1 (80)	0 (80)

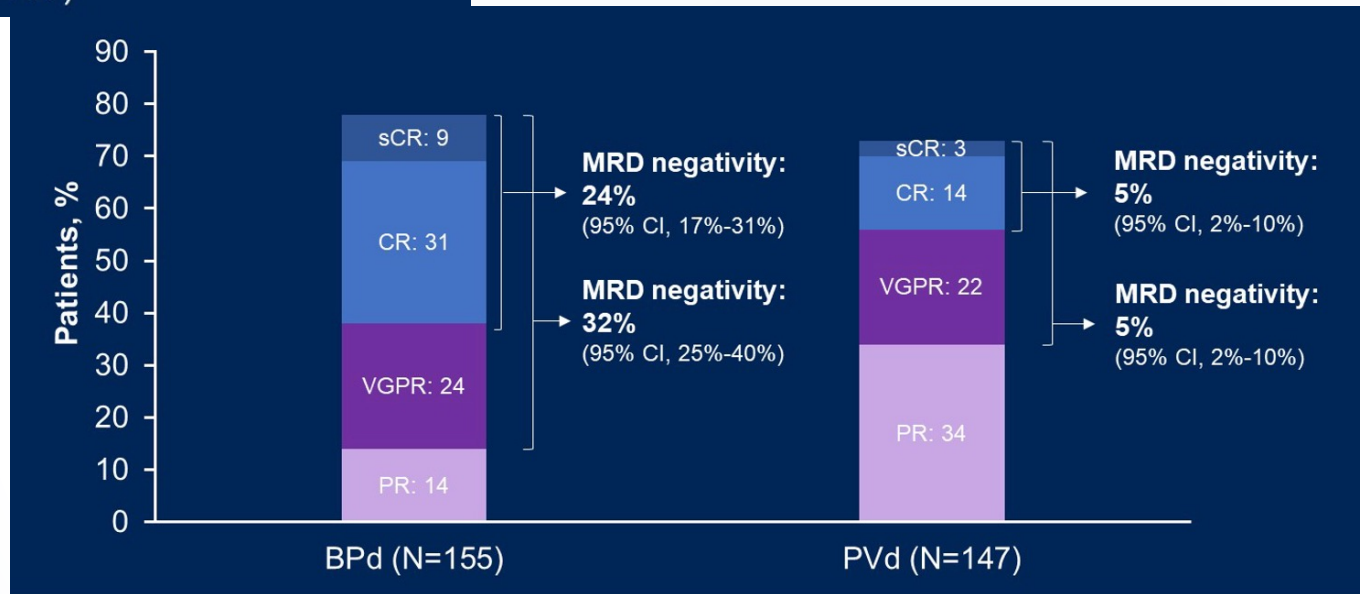
BPd led to a statistically significant and clinically meaningful reduction in risk of disease progression or death vs PVd (HR, 0.52; 95% CI, 0.37-0.73; *P*<.001)

Median follow-up, 21.8 months (range, 0.03-39.23 months)
The treatment effect (HR and corresponding 95% CIs) was estimated using the stratified Cox proportional hazards model, and the *P* value was produced based on the 1-sided stratified log-rank test. Stratified analyses were adjusted for number of prior lines of therapy and prior bortezomib use.
BPd, belamaf, pomalidomide, and dexamethasone; HR, hazard ratio; NR, not reported; PFS, progression-free survival; PVd, pomalidomide, bortezomib, and dexamethasone.

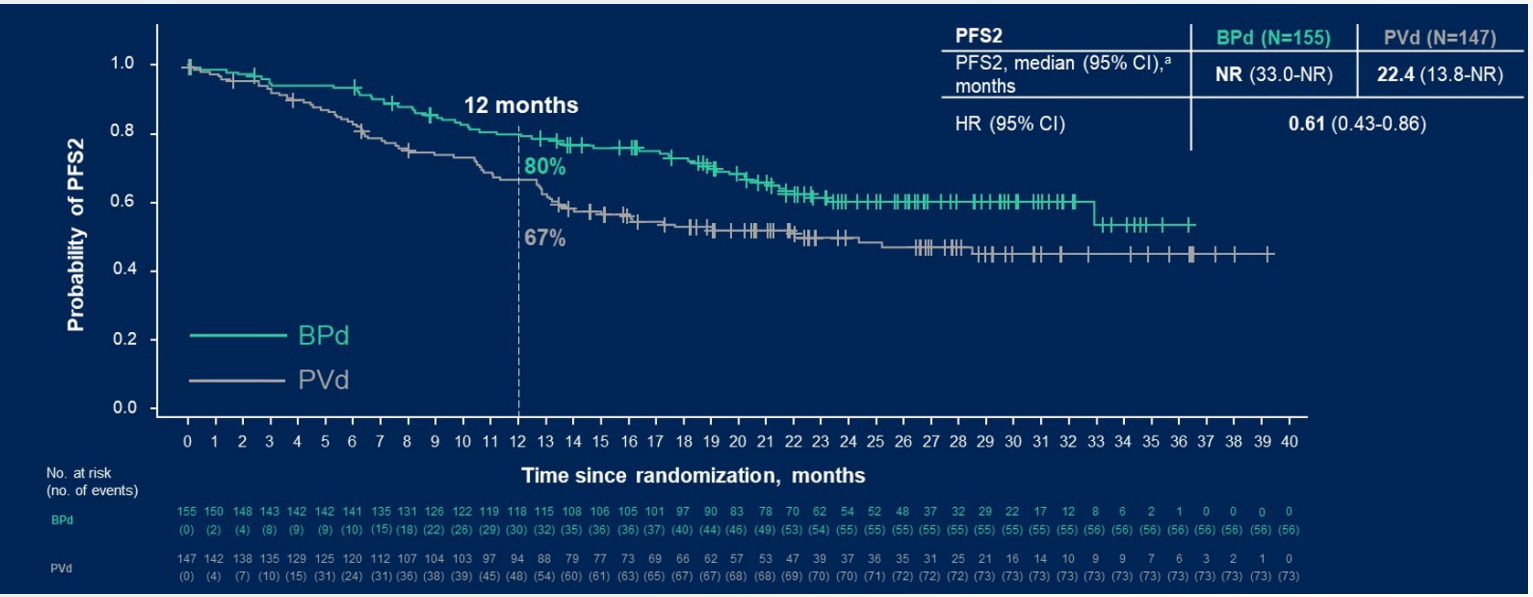
Deeper responses with BPD v. PVd



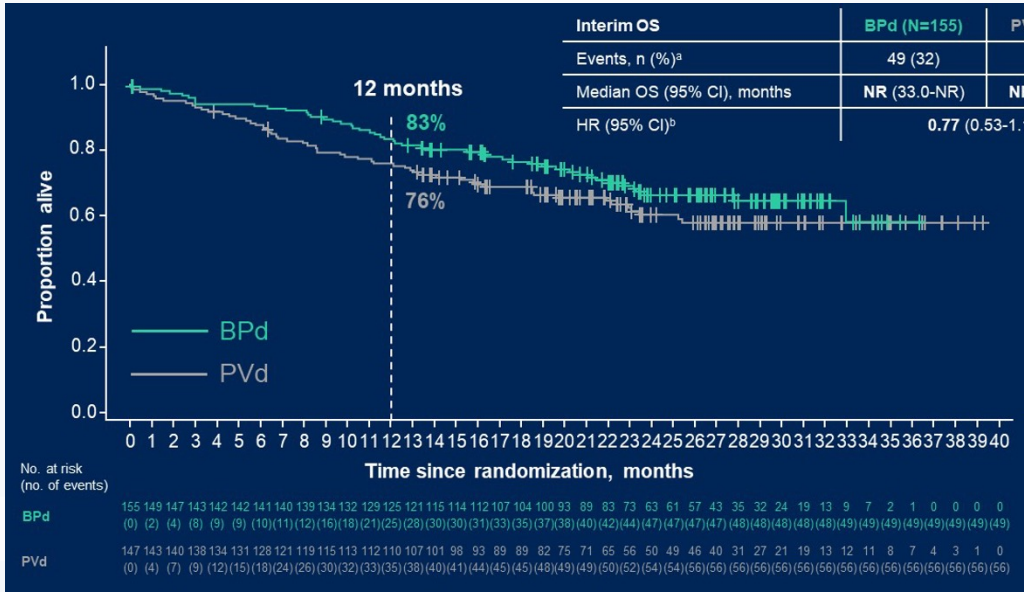
Higher MRD negativity with BPD v. PVd



Longer DOR & Time to Second Progression or Death w/ BPD v. PVd



Positive OS Trend Favoring w/ BPD v. PVd



Subsequent antimyeloma therapy, n (%)[c]	ITT population	
	BPd (N=155)	PVd (N=147)
Steroids	37 (24)	59 (40)
Anti-CD38 antibodies	23 (15)	49 (33)
Proteasome inhibitor	26 (17)	36 (24)
Immunomodulator	14 (9)	29 (20)
BCMA-targeting therapy[d,e]	1 (<1)	20 (14)
Chemotherapy	16 (10)	25 (17)
Transplant	1 (<1)	5 (3)

DREAMM8: Safety overview

Event, n (%)	Safety population	
	BPd (N=150)	PVd (N=145)
Any AE	149 (>99)	139 (96)
Grade 3/4 AE[a]	136 (91)	106 (73)
Exposure adjusted, patients/100 person-years[b]	66	78
AEs leading to interruption/delay	136 (91)	109 (75)
Exposure adjusted, patients/100 person-years[b]	66	80
Any ocular (CTCAE/KVA) event leading to dose interruption/delay of any study treatment	124 (83)	2 (1)
AEs leading to dose reduction	92 (61)	88 (61)
Exposure adjusted, patients/100 person-years[b]	44	65
Any ocular (CTCAE/KVA) event leading to dose reduction of any study treatment	88 (59)	0
AEs leading to permanent discontinuation of any study treatment	22 (15)	18 (12)
Exposure adjusted, patients/100 person-years[b]	11	13
Any ocular (CTCAE/KVA) event leading to discontinuation of any study treatment	14 (9)	0
Any SAE	95 (63)	65 (45)
Exposure adjusted, patients/100 person-years[b]	46	48
Fatal SAEs	17 (11)[c]	16 (11)

ORIGINAL ARTICLE

Belantamab Mafodotin, Pomalidomide, and Dexamethasone in Multiple Myeloma

Meletios Athanasios Dimopoulos, M.D., Meral Beksac, M.D., Ludek Pour, M.D., Sosana Delimpasi, M.D., Vladimir Vorobyev, M.D., Hang Quach, M.D., Ivan Spicka, C.Sc., Jakub Radocha, M.D., Ph.D., Pawel Robak, M.D., Ph.D., Kihyun Kim, M.D., Michele Cavo, M.D., Kazuhito Suzuki, M.D., Ph.D., Kristin Morris, Pharm.D., Farrah Pompilus, Ph.D., Amy Phillips-Jones, M.Sc., Xiaoou L. Zhou, M.D., Ph.D., Giulia Fulci, Ph.D., Neal Sule, M.B., B.S., M.D., Brandon E. Kremer, M.D., Ph.D., Joanna Opalinska, M.D., Ph.D., María-Victoria Mateos, M.D., Ph.D., and Suzanne Trudel, M.D., for the DREAMM-8 Investigators*

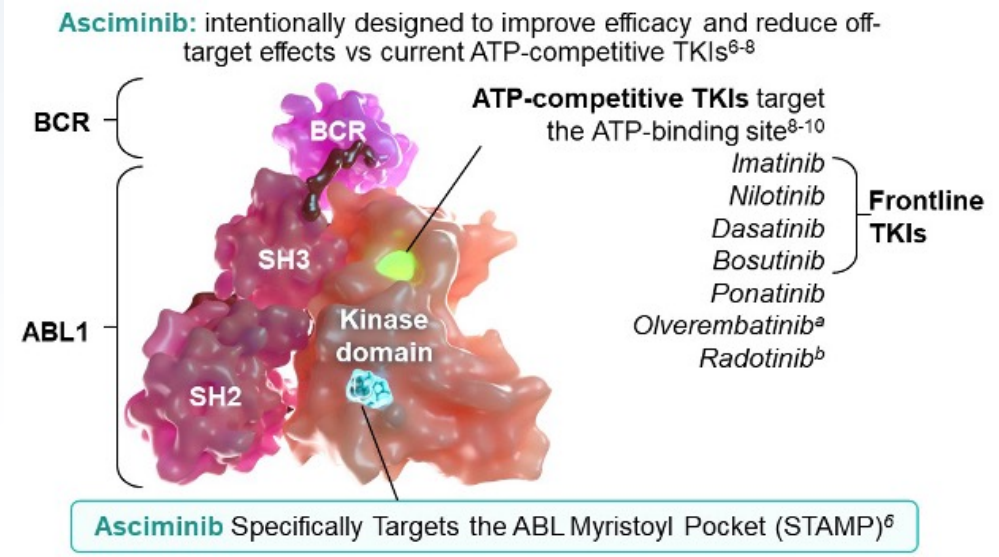
Ocular events managed by dose holds 83% and reduction in dosing frequency 59% and led to a low discontinuation rate9%.

Leukemia

Leukemia Updates

- **ASC4FIRST:** Asciminib vs Investigators' Choice of TKI in ND Ph+ CML
- Palliative Care in AML/MDS

ASC4FIRST: Phase 3 of Asciminib vs Investigators' Choice of TKI in ND Ph+ CML



NCT04971226

Key inclusion criteria

- Newly diagnosed Ph+ CML-CP with ***no*** prior TKIs[a]
- Age ≥18 years

Prerandomization TKI selection

- The TKI a patient will take if randomized to the investigator-selected (IS-TKI) arm
- Selected by the physician in consultation with the patient

Stratification by:

- Prerandomization TKI selection (IMA or 2G TKI)
- ELTS risk category (high, intermediate, low)

R 1:1
N=405

Asciminib (ASC) 80 mg QD
- Imatinib stratum: **ASC^{IMA}**
- 2G TKI stratum: **ASC^{2G}**

All IS-TKIs at label doses
- Imatinib stratum: **IS-TKI^{IMA}**
- 2G TKI stratum: **IS-TKI^{2G}**

End of study: LPFT + 5 years[b]

Data cutoff: Nov. 28, 2023

Primary endpoints:
- MMR at week 48 for asciminib vs all investigator-selected TKIs
- MMR at week 48 for asciminib vs investigator-selected TKI within the imatinib stratum

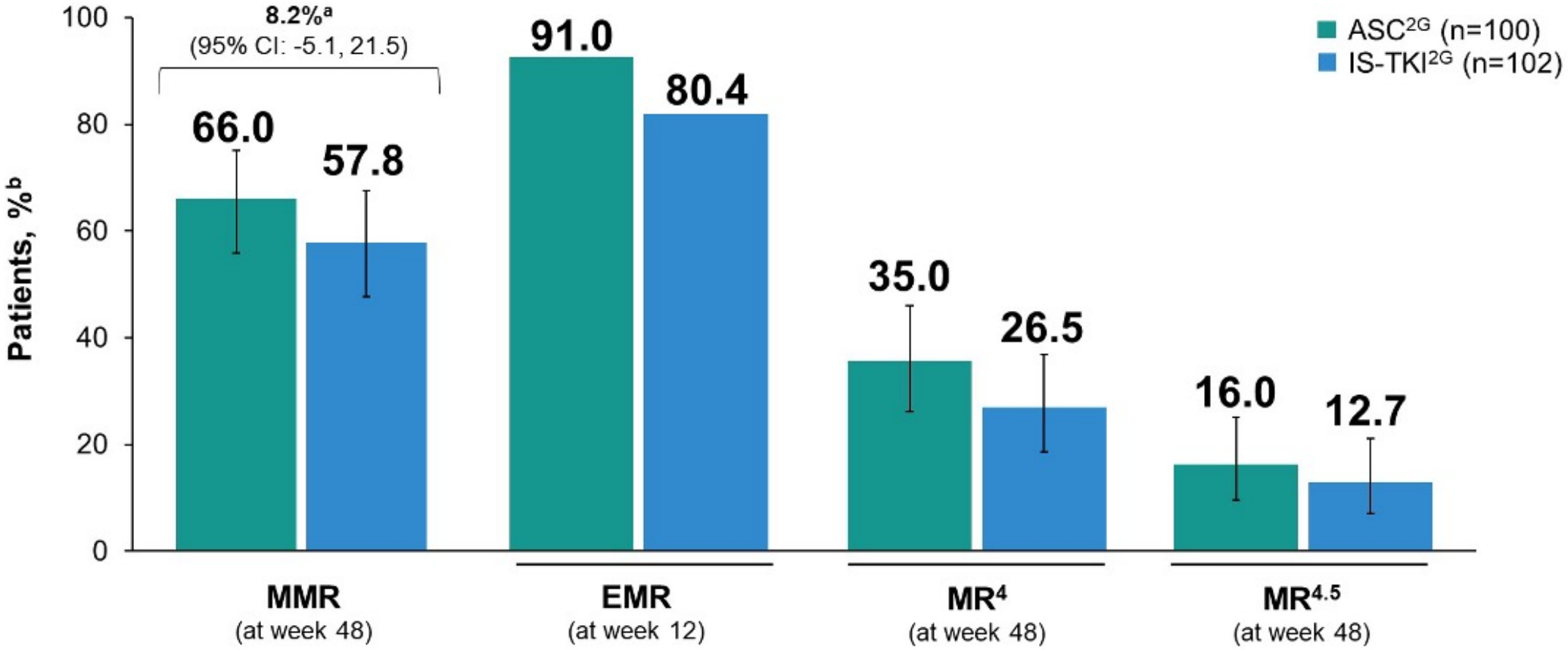
Hughes TP, Hochhaus A , Takahashi N, et al. ASCO 2024. LBA 6500.

Baseline Characteristics

Variable	Asciminib			IS-TKI		
	All asciminib (n=201)	Imatinib stratum (n=101)	2G TKI stratum (n=100)	All IS-TKI (n=204)	Imatinib stratum (n=102)	2G TKI stratum (n=102)
Median age (range), years	52.0 (18.0-79.0)	56.0 (21.0-79.0)	43.0 (18.0-76.0)	50.5 (19.0-86.0)	54.5 (20.0-86.0)	43.0 (19.0-83.0)
Age group, %						
18 to <65 years	77.1	68.3	86.0	76.0	68.6	83.3
65 to <75 years	17.9	23.8	12.0	16.7	21.6	11.8
≥75 years	5.0	7.9	2.0	7.4	9.8	4.9
Male, %	65.2	61.4	69.0	61.3	63.7	58.8
Framingham CV risk score, %[a]						
Low risk (<10%)	54.2	40.6	68.0	54.9	39.2	70.6
Intermediate risk (10%-20%)	15.9	20.8	11.0	21.6	28.4	14.7
High risk (≥20%)	29.9	38.6	21.0	23.5	32.4	14.7
ELTS, %[b]						
Low	60.7	61.4	60.0	61.3	62.7	59.8
Intermediate	27.9	29.7	26.0	27.9	29.4	26.5
High	11.4	8.9	14.0	10.8	7.8	13.7

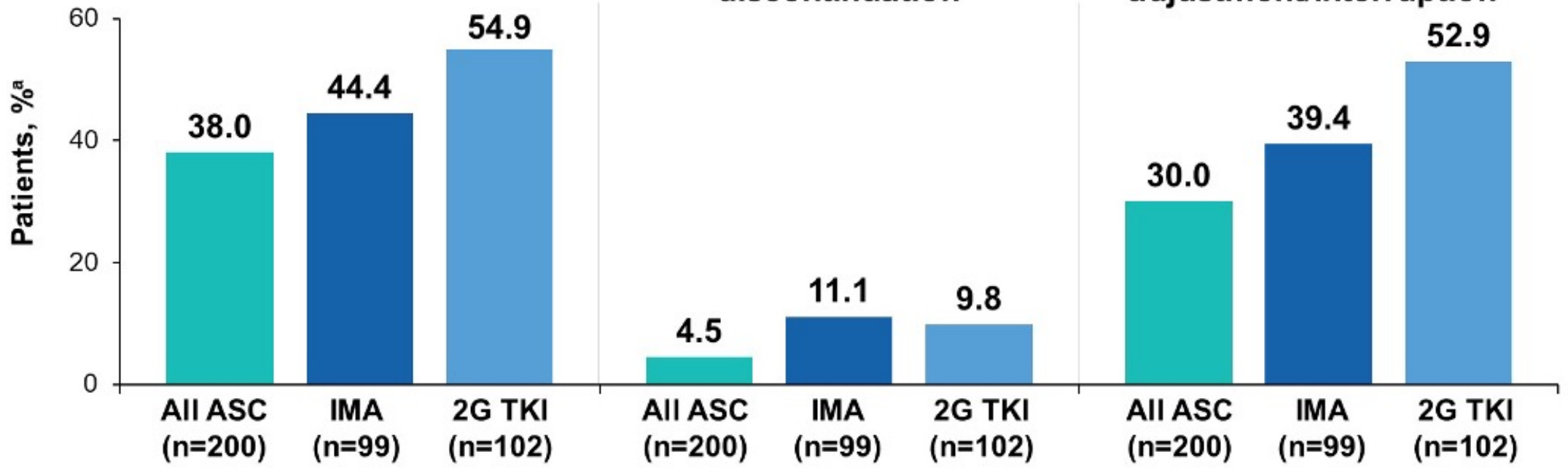
[a] Framingham estimated 10-year cardiovascular disease risk categories.
[b] Based on randomization data.

High proportion of patients with ASC achieved early and deep molecular responses vs. IS-TKI



Error bars represent 95% CIs.
[a] The common treatment difference and its 95% CI are estimated using the Mantel-Haenszel method after stratifying for baseline ELTS risk groups (IRT data).

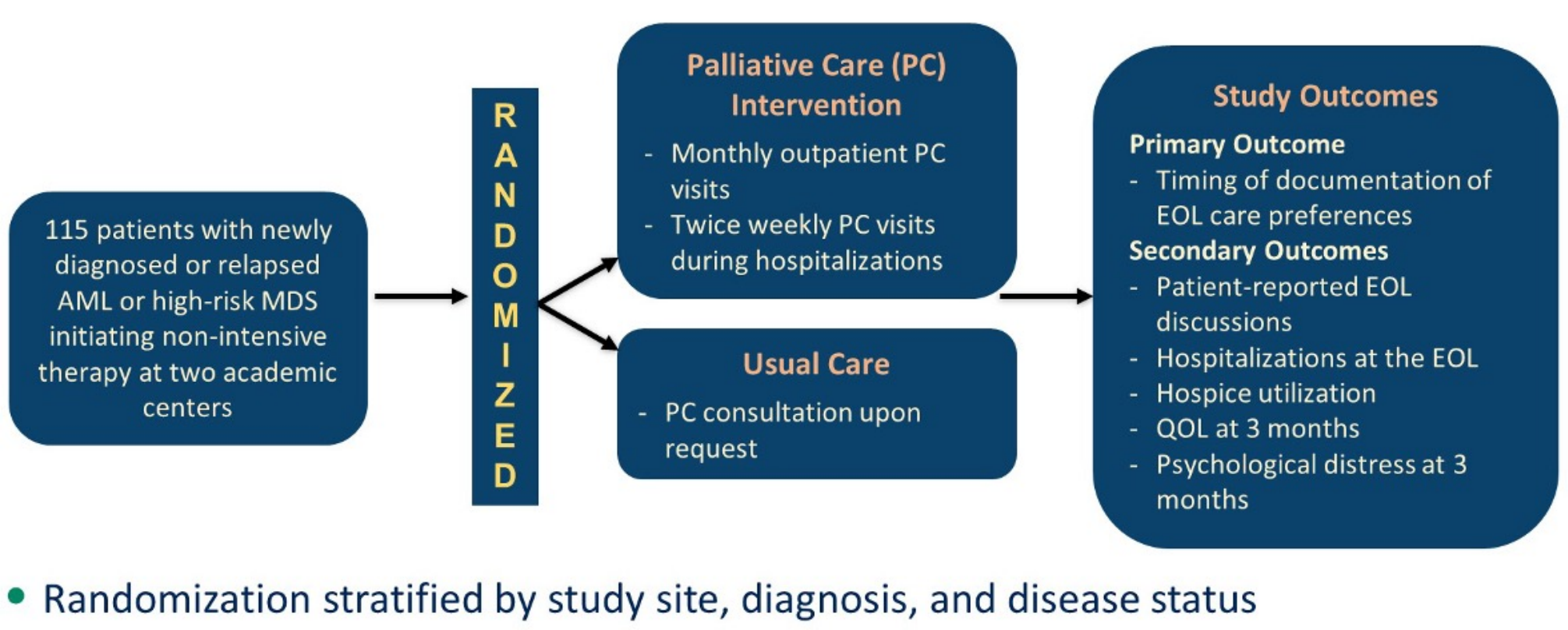
Safety Profile



- The median dose intensity was 80.0 mg/day with ASC, 400.0 mg/day with IMA, 595.1 mg/day with NIL, 98.9 mg/day with DAS, and 341.8 mg/day with BOS
- The most common AEs leading to treatment discontinuation were increased lipase with ASC (1.5%), diarrhea and lymphopenia with IMA (2.0% each), and pleural effusion with 2G TKIs (2.0%)

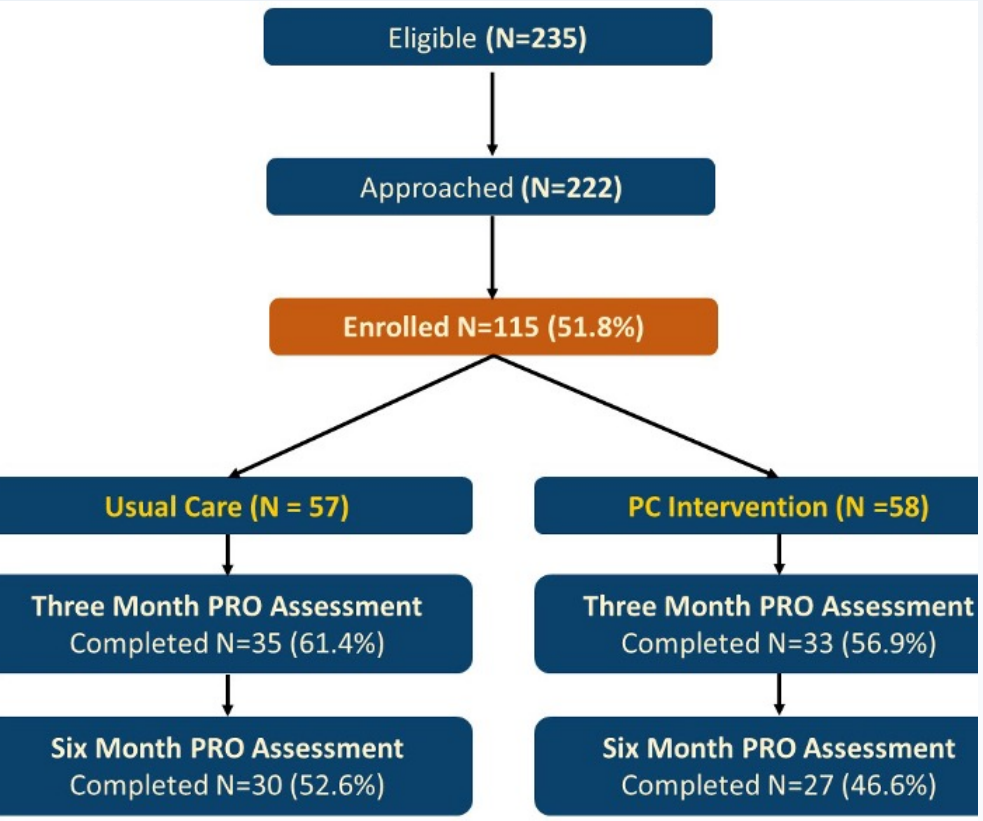
Multi-Site Randomized Trial of a Collaborative Palliative Care and Oncology Care Model for Patients with AML/MDS Receiving Non-Intensive Therapy

Can palliative care improve EOL care in AML & MDS?



El-Jawahri A et al. ASCO 2024. LB 6508

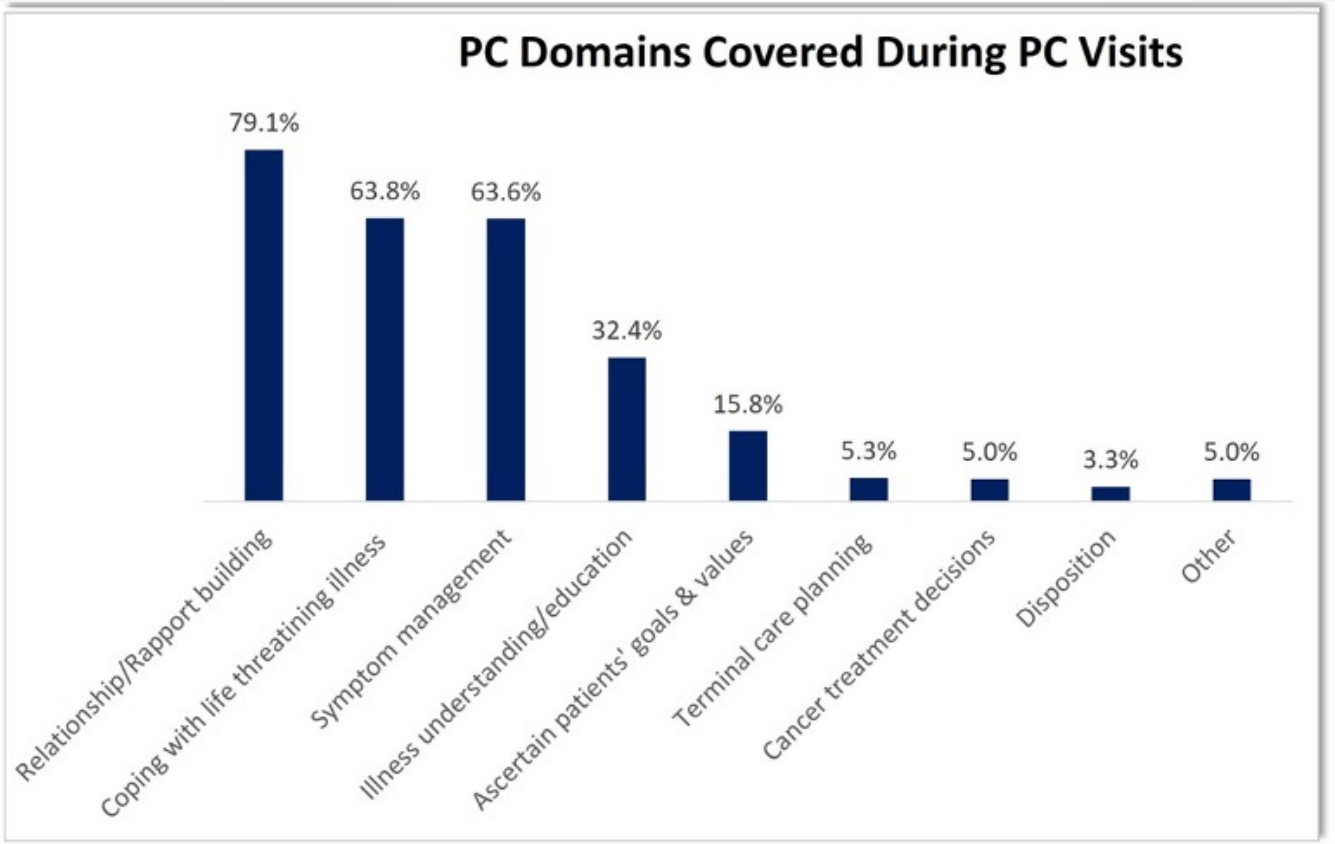
Patient Characteristics



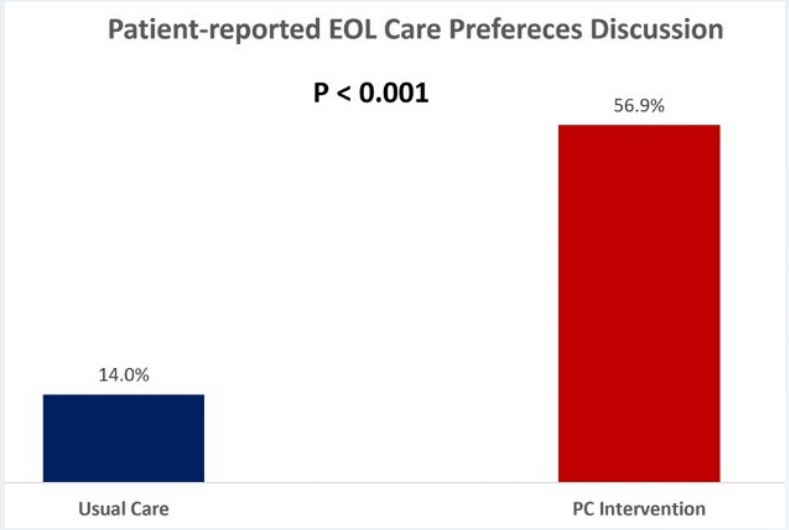
Characteristic	Usual Care (N=57)	PC Intervention (N=58)
Age, Median Years (range)	69.5 (35.5-90.5)	69.8 (29.3-87.4)
Man	30 (52.6%)	37 (63.8%)
Woman	27 (47.4%)	21 (36.2%)
White	53 (93.0%)	49 (84.5%)
Black	2 (3.5%)	3 (5.2%)
Native American	0	1 (1.7%)
Other	0	3 (5.2%)
Missing	2 (3.5%)	2 (3.4%)
Hispanic or Latino/x	3 (5.3%)	6 (10.3%)
Married/Partnered	42 (73.7%)	84 (73.0%)
Single	5 (8.9%)	11 (9.6%)
Divorced/Separated	3 (5.3%)	9 (7.8%)
Widowed	5 (8.8%)	8 (7.0%)
Missing	2 (3.5%)	3 (2.6%)
New diagnosis AML	20 (35.1%)	19 (32.8%)
Relapsed/refractory AML	17 (29.8%)	15 (25.9%)
New diagnosis MDS	13 (22.8%)	18 (31.0%)
Relapsed/persistent MDS	7 (12.3%)	6 (10.3%)
ECOG = 0	19 (33.3%)	20 (34.5%)
ECOG = 1	26 (45.6%)	23 (39.7%)
ECOG = 2	9 (15.8%)	12 (20.7%)
ECOG = 3	0	1 (1.7%)
ECOG Missing	3 (5.3%)	2 (3.4%)
HMA-based therapy at enrolment	37 (64.9%)	42 (72.4%)
Clinical trial therapy at enrollment	20 (35.1%)	16 (27.6%)

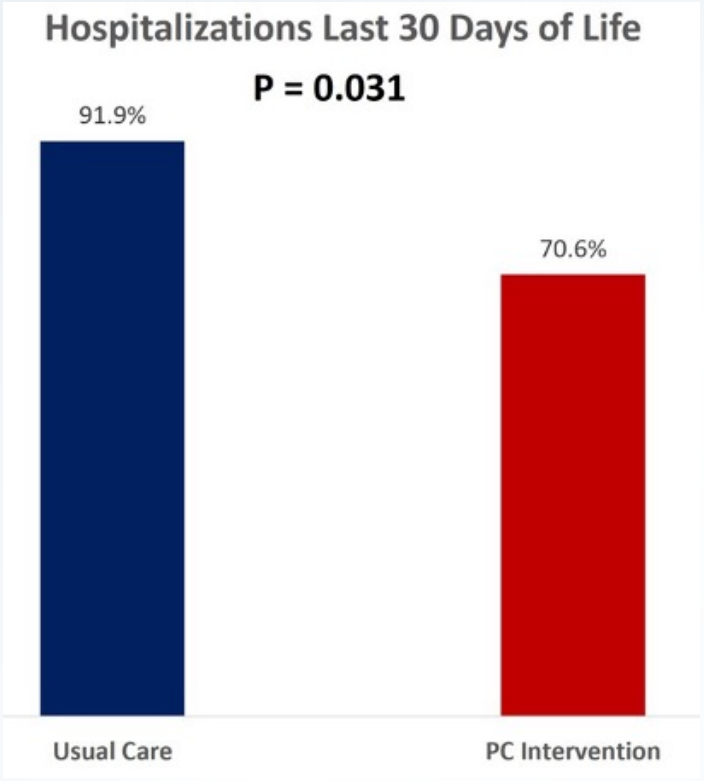
Intervention Delivery & Fidelity

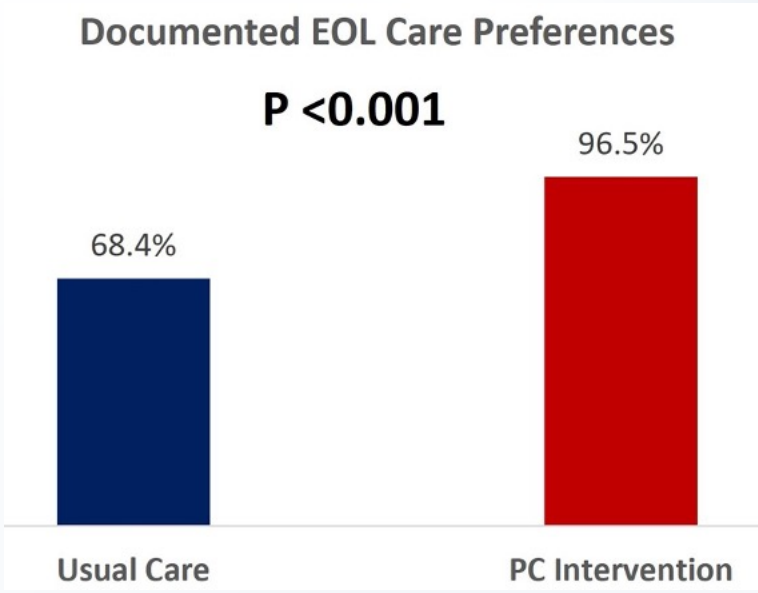
- 76.9% of initial PC visits occurred on inpatient setting
- Median time spent on initial PC consult = 60 minutes (range 15-132 minutes)
- Median time spent on PC visits during hospitalization per week = 35 minutes (range 1-200 minutes)

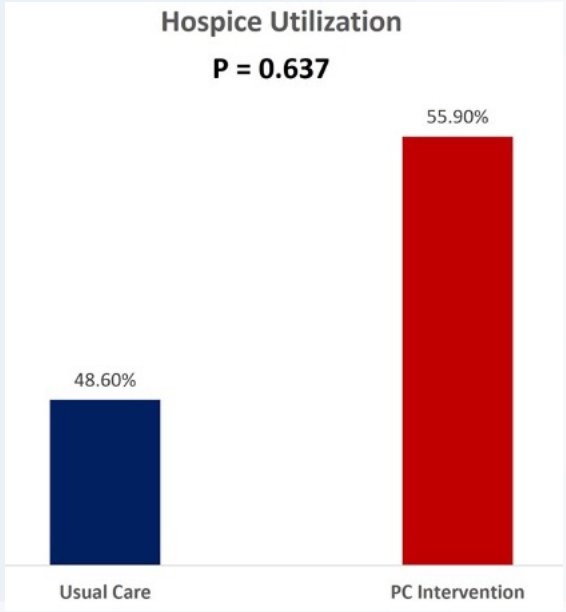


EOL Outcomes





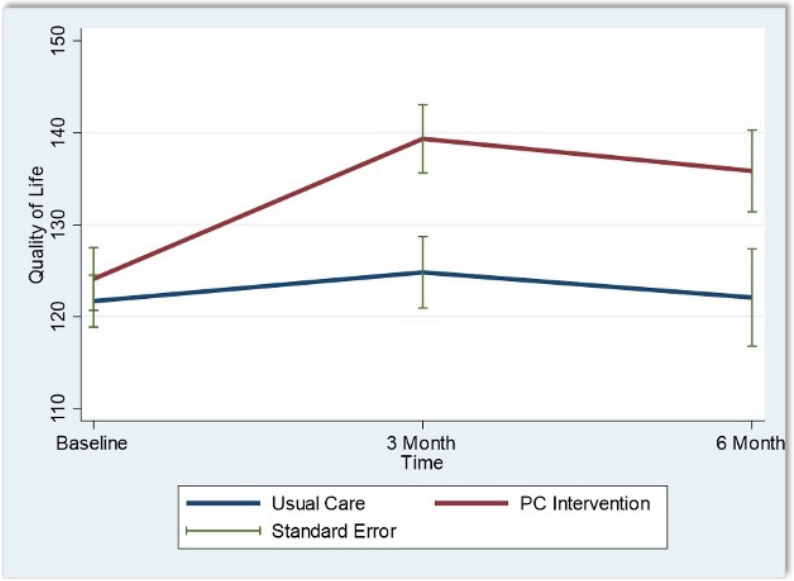




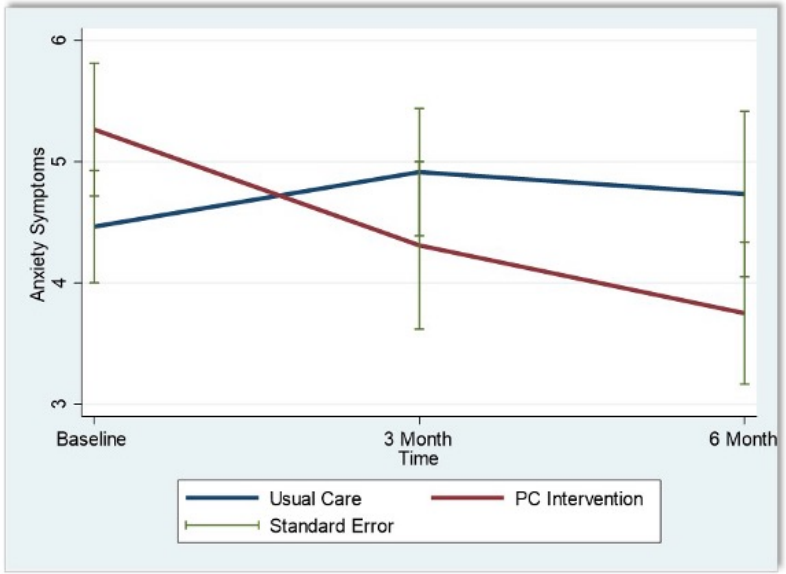
Longitudinal Secondary Outcomes

Longitudinal Secondary Outcomes

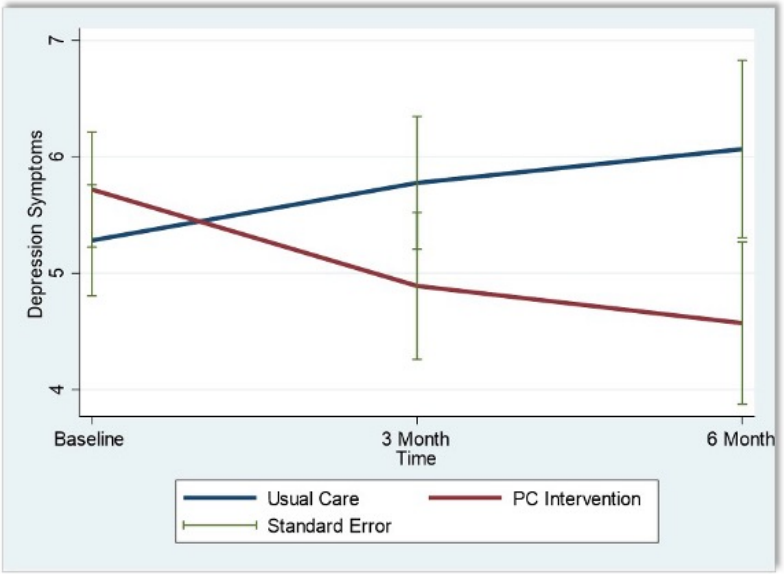
Qualify of Life (QOL): Group X Time
B = 6.4 (95%CI 0.3 – 12.2), P=0.041



Anxiety Symptoms: Group X Time
B = -0.7 (95%CI -1.4 – 0.1), P=0.088



Depression Symptoms: Group X Time
B = - 0.7 (95%CI -1.6 – 0.2), P=0.124



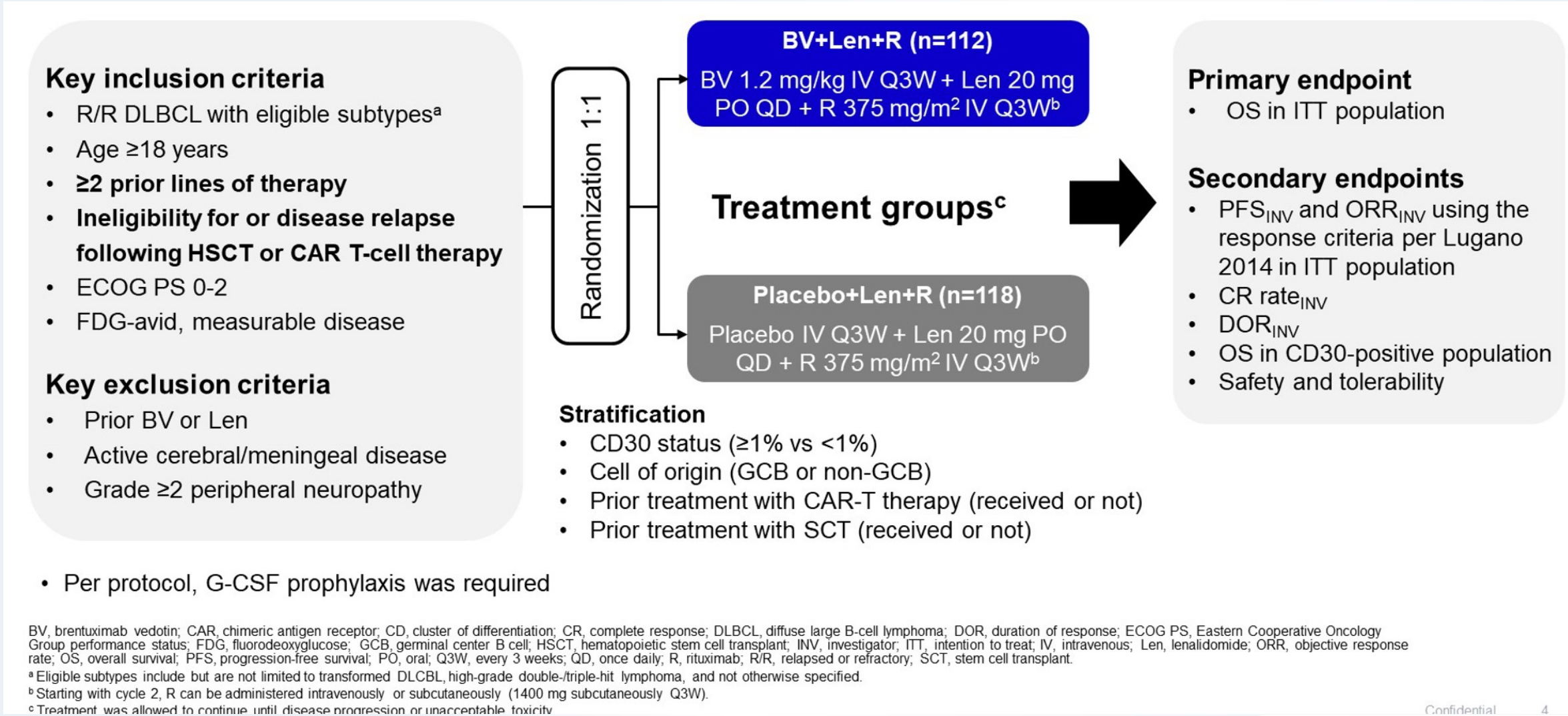
Lymphoma

Sub Text

Updates in Lymphoma

- **ECHELON-3:** Phase III Trial of Brentuximab Vedotin With Lenalidomide and Rituximab in R/R DLBCL
- **EPCORE NHL-1**: SC Epcoritamab in Patients With R/R Large B-Cell Lymphoma, extended results
- Phase I/II Study of **Glofitamab Retreatment** in Patients With Heavily Pretreated R/R NHL
- **SYMPATICO**: Ibrutinib + venetoclax

ECHELON-3: Phase III Study in Patients w/ R/R DLBCL



- Per protocol, G-CSF prophylaxis was required

BV, brentuximab vedotin; CAR, chimeric antigen receptor; CD, cluster of differentiation; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; GCB, germinal center B cell; HSCT, hematopoietic stem cell transplant; INV, investigator; ITT, intention to treat; IV, intravenous; Len, lenalidomide; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, oral; Q3W, every 3 weeks; QD, once daily; R, rituximab; R/R, relapsed or refractory; SCT, stem cell transplant.

[a] Eligible subtypes include but are not limited to transformed DLCBL, high-grade double-/triple-hit lymphoma, and not otherwise specified.

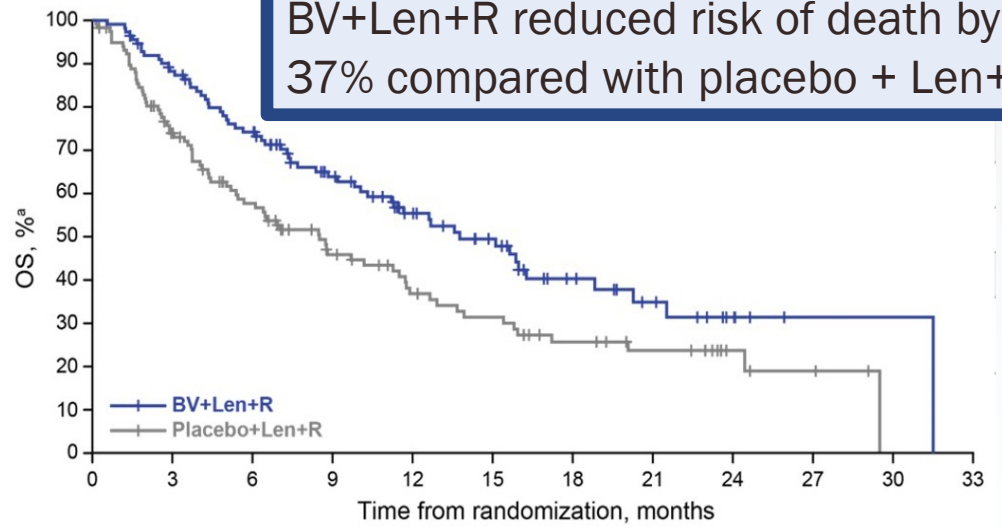
[b] Starting with cycle 2, R can be administered intravenously or subcutaneously (1400 mg subcutaneously Q3W).

[c] Treatment was allowed to continue until disease progression or unacceptable toxicity.

Kim JA, Hahn U, Kim W-S, et al. ASCO 2024. Abstract 7033.

Primary endpoint (OS) and key secondary endpoint PFS met

BV+Len+R reduced risk of death by 37% compared with placebo + Len+R



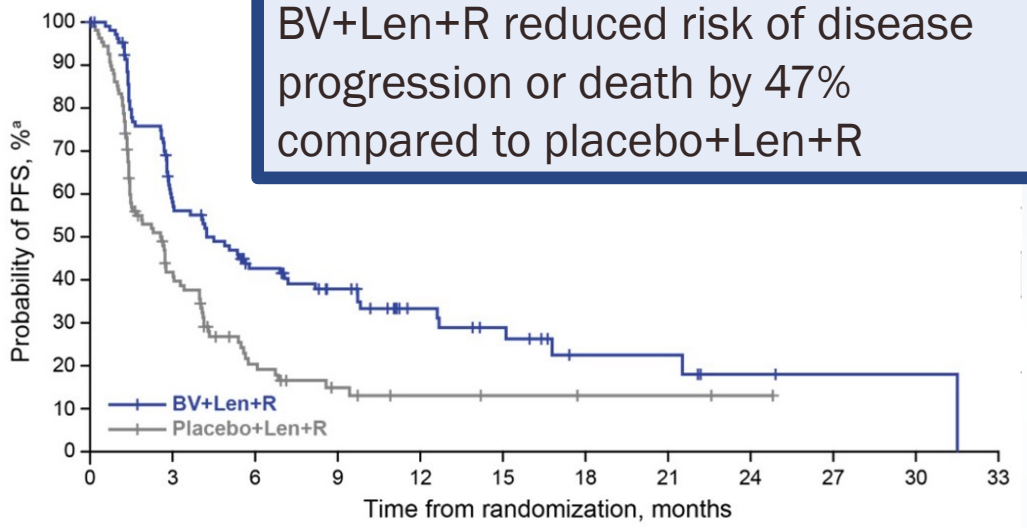
No. at risk

BV+Len+R	112	96	79	57	40	30	17	11	5	1	1	0
Placebo+Len+R	118	81	58	39	28	23	16	12	5	3	0	0

- BV+Len+R prolonged median OS by 5.3 months compared with placebo+Len+R
- Prespecified O'Brien-Fleming efficacy boundary was crossed at this interim analysis

	BV+Len+R (n=112)	Placebo+Len+R (n=118)
OS, median (95% CI), months	**13.8** (10.3-18.8)	**8.5** (5.4-11.7)
Hazard ratio (95% CI)[b]	0.629 (0.445-0.891)	
Log-rank *P* value[c]	.0085	
Events (deaths)	58	76
Follow-up, median (95% CI), months	15.5 (12.2-18.1)	18.9 (12.2-23.2)

BV+Len+R reduced risk of disease progression or death by 47% compared to placebo+Len+R



No. at risk

BV+Len+R	112	58	38	27	15	11	5	5	2	1	1	0
Placebo+Len+R	118	40	16	8	4	3	2	2	1	0	0	0

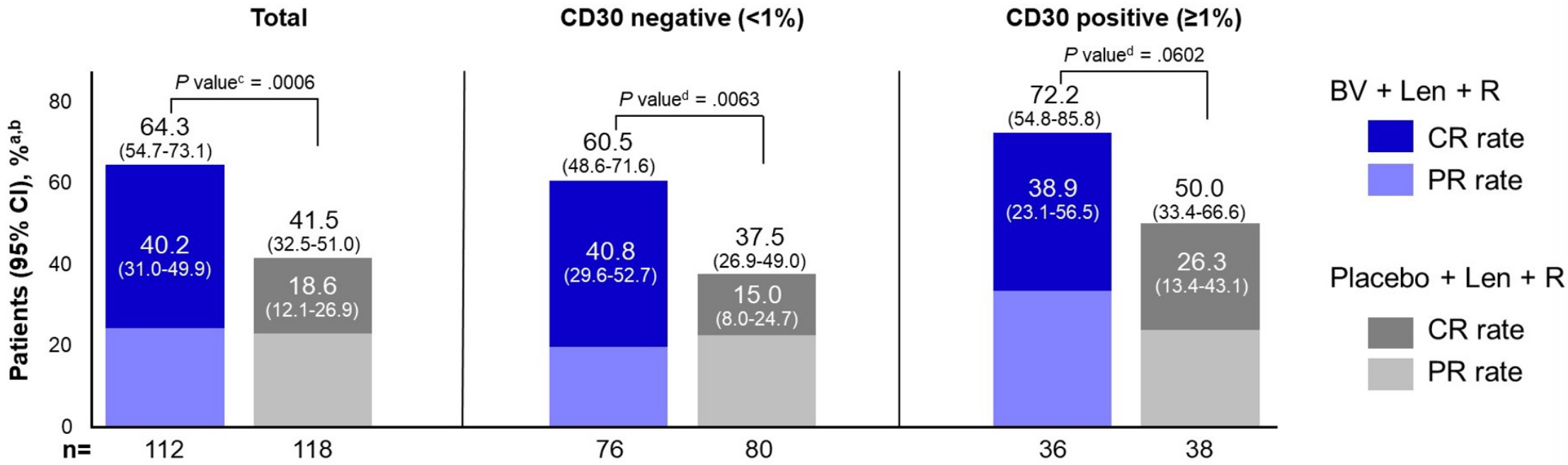
- PFS was an alpha controlled key secondary endpoint

	BV+Len+R (n=112)	Placebo+Len+R (n=118)
PFS, median (95% CI), months	**4.2** (2.9-7.1)	**2.6** (1.4-3.1)
Hazard ratio (95% CI)[b]	0.527 (0.380-0.729)	
Log-rank *P* value[c]	<.0001	
Events	71	85
Follow-up, median (95% CI), months	11.1 (8.6-14.2)	8.8 (6.9-10.9)

@christinemphmd

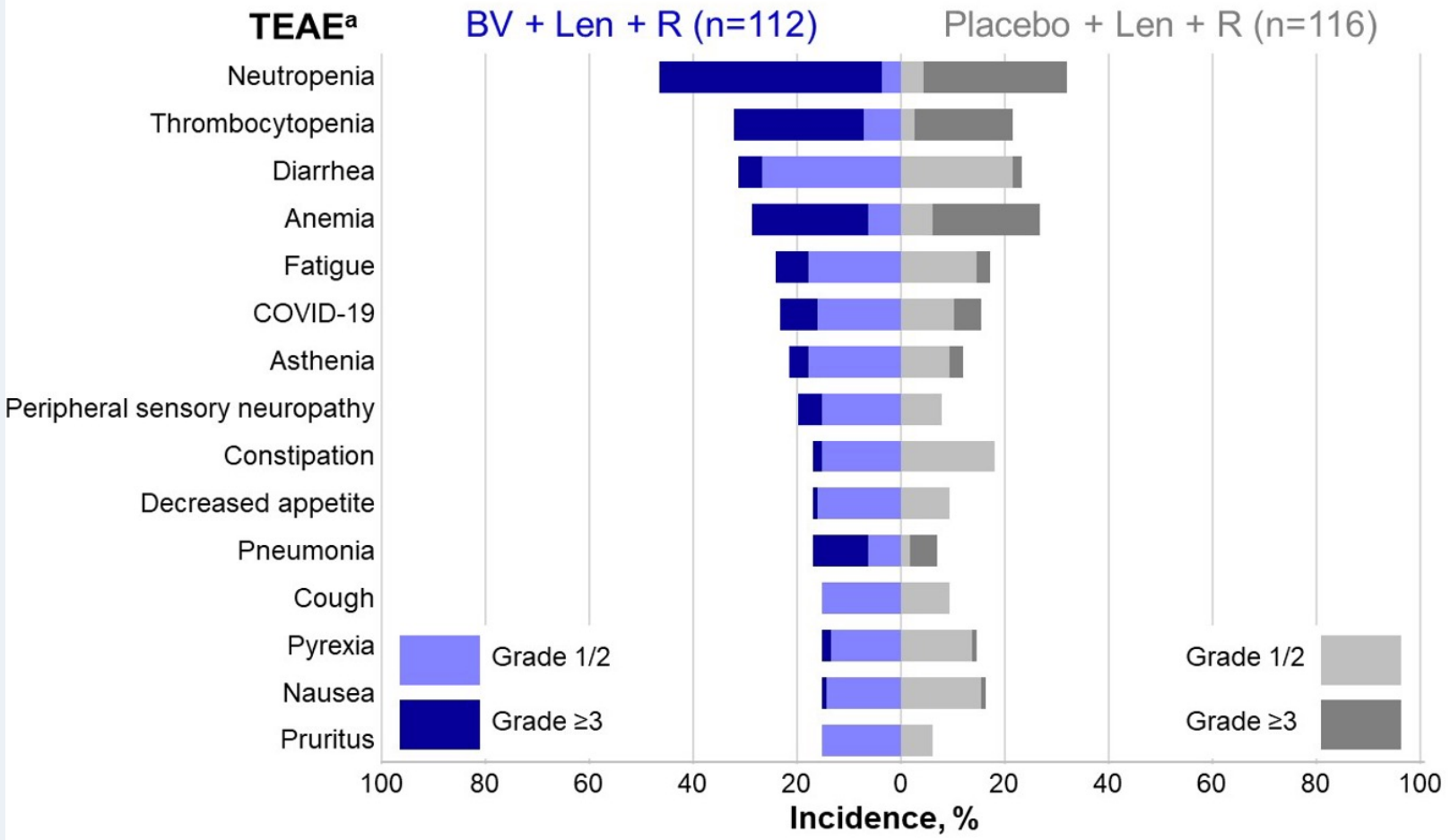
Overall Response Rate was significantly higher with BV+Len+R

40% CR rate with BV+Len+R and ORR improvement regardless of CD30 expression



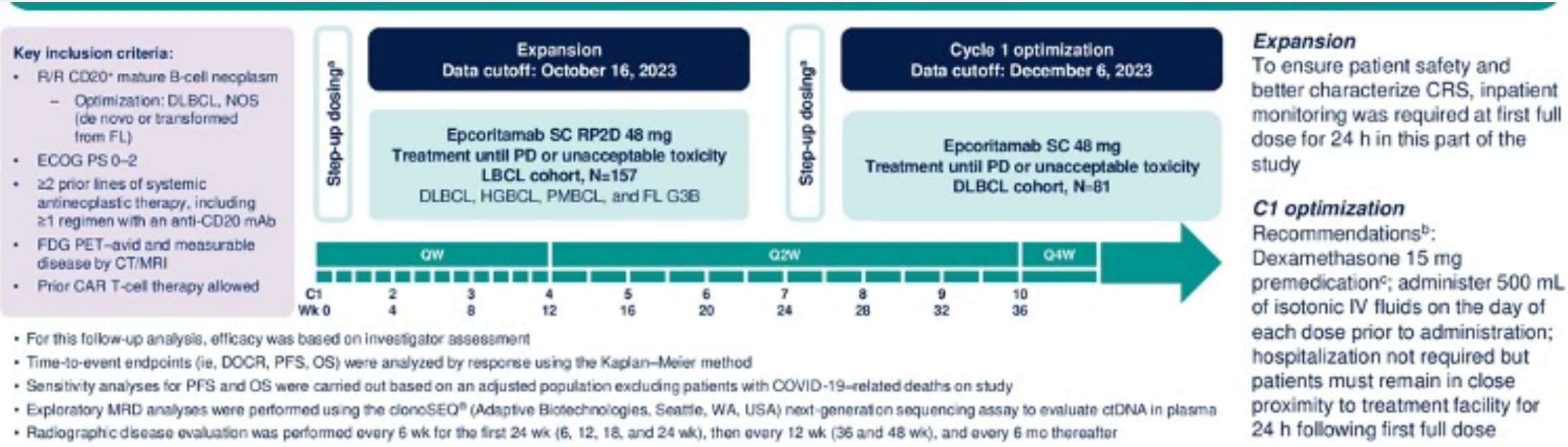
- In the total population, the median DOR (95% CI) was longer with BV+Len+R: 8.3 months (4.2-15.3 months) vs 3.0 months (2.8-5.4 months)
  - In patients who had a CR, the median DOR (95% CI) was 18.9 months (11.1 months-NR) with BV+Len+R and NR (2.8 months-NR) with placebo+Len+R
  - The median time to CR onset (range) was 1.58 months (1.2-7.3 months) with BV+Len+R and 1.61 months (0.7-4.6 months) with placebo+Len+R

No new safety signals with BV+Len+R



- TEAEs of any grade occurred in 97% of patients with each treatment
- Grade ≥3 TEAEs:
  - 88% with BV+Len+R
  - 77% with placebo+Len+R
  - 9% febrile neutropenia in each group
- Grade 5 TEAEs:
  - 12% with BV+Len+R
  - 8% with placebo+Len+R
- Any grade peripheral neuropathy TEAEs
  - 31% with BV+Len+R
  - 24% with placebo+Len+R
- Relative dose intensity
  - 94.4% for BV
  - 99.7% for placebo

Extended follow-up results beyond 2.5 years from the pivotal NHL-1 EPCORE trial: Subcutaneous epcoritamab monotherapy in patients with relapsed/refractory large B-cell lymphoma (R/R LBCL).



[a]SUD 1: priming, 0.16 mg; SUD 2: intermediate, 0.8 mg. Corticosteroid prophylaxis was used in cycle 1 to mitigate CRS. [b]Other recommendations include 2–3 L of fluid intake during the 24 h prior to and following each dose, holding antihypertensive medications for 24 h prior to each dose, and self-monitoring of temperature 3 times daily for 4 d following each dose. [c]On D1, D8, D15, and D22 and prophylaxis on D2–4, D9–11, D16–18, and D23–25. ClinicalTrials.gov: NCT03625037. EudraCT: 2017-001748-36.

Karimi Y. ASCO 2024. https://doi.org/10.1200/JCO.2024.42.16_suppl.703

Baseline Characteristics and Prior Treatments

	LBCL N=157	LBCL Complete Responders, n=65
Median age (range), y	64 (20–83)	68 (20–83)
≥75 y, n (%)	29 (18)	15 (23)
ECOG PS, n (%)		
0	74 (47)	36 (55)
1	78 (50)	29 (45)
2	5 (3)	0
DLBCL,[a] n (%)	139 (89)	58 (89)
De novo, n/n (%)	97/139 (70)	39/58 (67)
Transformed, n/n (%)	40/139 (29)	19/58 (33)
Ann Arbor stage IV disease, n (%)	96 (61)	38 (58)
Median time from initial diagnosis to first dose, y	1.6	2.1
Median time from end of last therapy to first dose, mo	2.4	2.9
Median prior lines of therapy (range)	3 (2–11)	3 (2–11)
≥3 prior lines of therapy, n (%)	110 (70)	47 (72)
Primary refractory[b] disease, n (%)	95 (61)	31 (48)
Refractory[b] to last systemic therapy, n (%)	130 (83)	48 (74)
Refractory[b] to ≥2 consecutive lines of therapy, n (%)	118 (75)	45 (69)
Prior ASCT, n (%)	31 (20)	15 (23)
Prior CAR T-cell therapy, n (%)	61 (39)	22 (34)

[a]Other disease types were FL G3B (n=5; CR, n=3), HGBCL (n=9; CR, n=2), and PMBCL (n=4; CR, n=2). DLBCL type was unknown in 2 patients. [b]Refractory disease is defined as disease that either progressed during therapy or progressed within 6 mo of completion of therapy.

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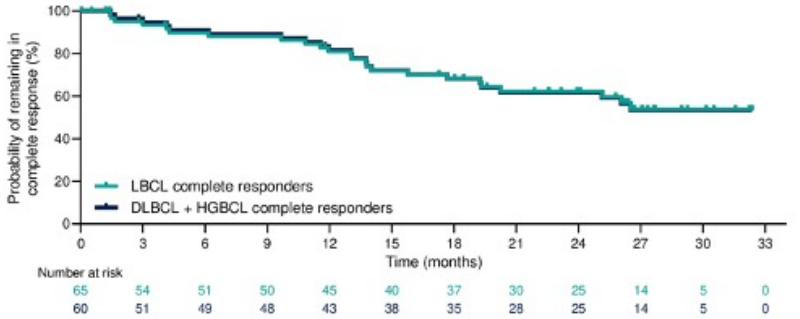
High Rates of Response and Durable CRs per Investigator

	LBCL N=157[a]	DLBCL + HGBCL[b] n=148[c]
ORR, n (%)	92 (59)	85 (57)
CR	65 (41)	60 (41)
PR	27 (17)	25 (17)
DOCR, median, mo	NR	NR
24-mo KM estimate, %	62	62
30-mo KM estimate, %	54	54
Follow-up, median, mo	26.4	26.7

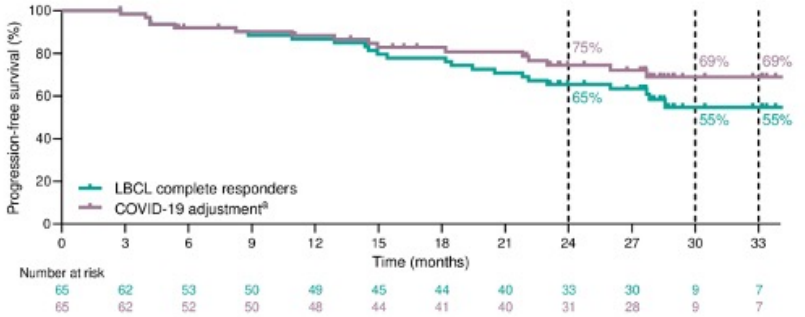
[a]Median study follow-up: 30.6 mo (range, 0.3 to 38.8+). [b]Population based on the FDA-approved indication of epcoritamab; 127 patients had DLBCL and 21 patients had HGBCL (including 12 patients who were enrolled with DLBCL but reclassified based on DH/TH status). [c]Median study follow-up: 31.1 mo (range, 0.3+ to 38.8).

Efficacy Results in Complete Responders

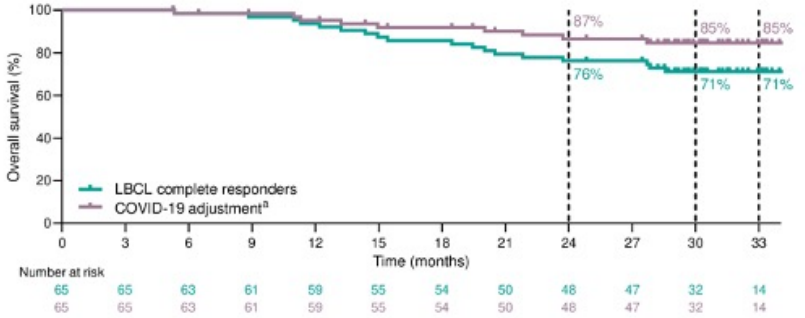
CRs Sustained Over Time



Favorable Long-Term Outcomes Among Complete Responders



Kaplan–Meier estimates are shown. [a]Based on COVID-19–adjusted sensitivity analyses, which censored deaths due to COVID-19.



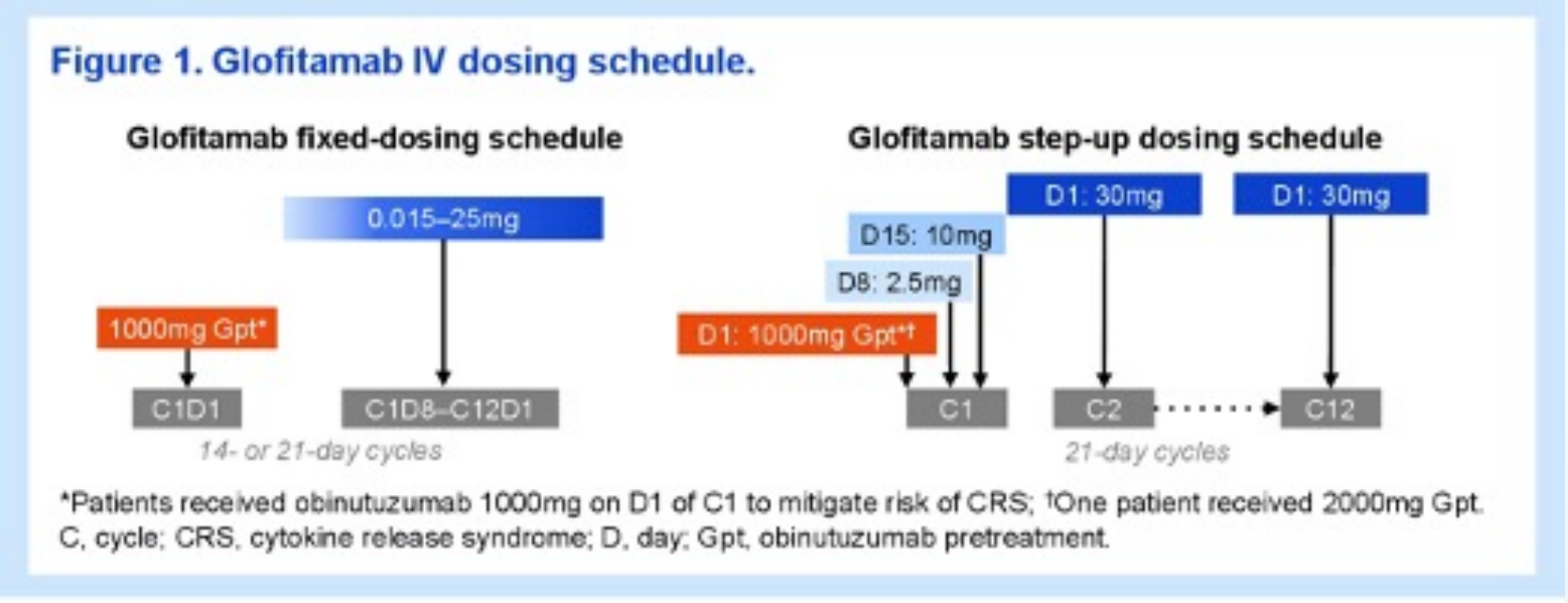
Kaplan–Meier estimates are shown. [a]Based on COVID-19–adjusted sensitivity analyses, which censored deaths due to COVID-19.

MRD Negativity in Complete Responders

MRD-Negativity Rate, n (%)	LBCL, n=49[a]
At C3D1	39 (80)
At any time	45 (92)

[a]Based on MRD-evaluable patients (patients had ≥1 baseline or on-treatment MRD result and MRD was not negative at baseline) with complete response.

Phase I/II: Glofitamab monotherapy retreatment in patients with heavily pre-treated relapsed or refractory (R/R) non-Hodgkin lymphoma (NHL)



Bartlett NL. ASCO 2024. Abstract 2020

Table 1. Patient and disease characteristics at study entry (prior to initial glofitamab treatment) amongst patients who received retreatment.

n (%) unless stated	N=13
Median age (range), years	63 (44–81)
Male	8 (61.5)
ECOG PS	
0	9 (69.2)
1	4 (30.8)
Histology	
DLBCL	4 (30.8)
FL	4 (30.8)
HGBCL	1 (7.7)
MCL	2 (15.4)
trFL	2 (15.4)
IPI score ≥3*	4 (30.8)
Ann Arbor stage	
I/II	5 (38.5)
III/IV	8 (61.5)

n (%) unless stated	N=13
Bulky disease	
>6cm	4 (30.8)
>10cm	1 (7.7)
Median prior lines of therapy (range)	3 (1–4)
Number of prior lines of therapy	
1	3 (23.1)
2	3 (23.1)
≥3	7 (53.8)
Prior CAR T-cell therapy	3 (23.1)
Refractory status	
Refractory to first prior therapy	8 (61.5)
Refractory to last prior therapy	8 (61.5)
Refractory to CAR-T cell therapy	3 (23.1)

*non-FL patients, n=7.
CAR, chimeric antigen receptor; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; HGBCL, high grade B-cell lymphoma; IPI, International Prognostic Index; MCL, mantle cell lymphoma; trFL, transformed FL.

Efficacy of Retreatment Glofitamab Monotherapy

Table 2. Best overall response with retreatment by histology (INV assessment).

n (%)	All patients (N=13)	DLBCL (n=4)	FL (n=4)	HGBCL (n=1)	MCL (n=2)	trFL (n=2)
Objective response	9 (69.2)	2 (50)	3 (75)	0	2 (100)	2 (100)
Complete response	5 (38.5)	0	2 (50)	0	2 (100)	1 (50)

- Median follow up was 25.9 months (2.6-57.9)
- 9 patients (69.2% achied responsed by INV during retreatment, 5 pts (38.5%), 4 (30.8%) patients with PR

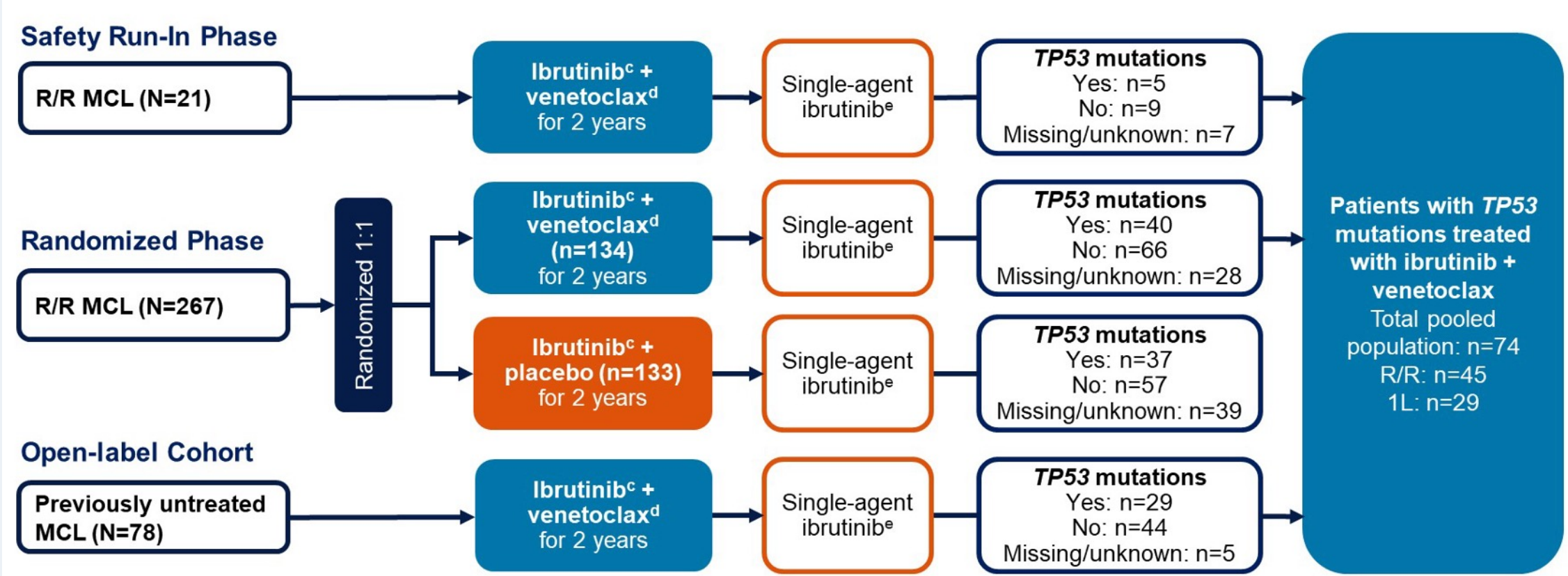
Safety Profile

Table 3. Safety summary with initial treatment and retreatment.

n (%)	Initial treatment (N=13)	Retreatment (N=13)
Any AE	13 (100)	13 (100)
Glofitamab related	13 (100)	10 (76.9)
Grade ≥3	8 (61.5)	6 (46.2)
Glofitamab related	7 (53.8)	4 (30.8)
Serious AE	7 (53.8)	5 (38.5)
Glofitamab related	7 (53.8)	5 (38.5)
Grade 5 AE	0	1 (7.7)*
Glofitamab related	0	1 (7.7)*
AE leading to interruption of glofitamab	3 (23.1)	3 (23.1)
Glofitamab related	3 (23.1)	2 (15.4)
AE leading to withdrawal of glofitamab	0	2 (15.4)
Glofitamab related	0	1 (7.7)
CRS	10 (76.9)	7(53.8)
Grade ≥2†	3 (23.1)‡	1 (7.7)§

*COVID-19 pneumonia; †American Society for Transplantation and Cellular Therapy grade; ‡Grade 3, n=1; §No Grade 3+ events. AE, adverse event.

SYMPATICO: Efficacy and Safety of Ibrutinib Plus Venetoclax in Patients with Mantle Cell Lymphoma and TP53 Mutations



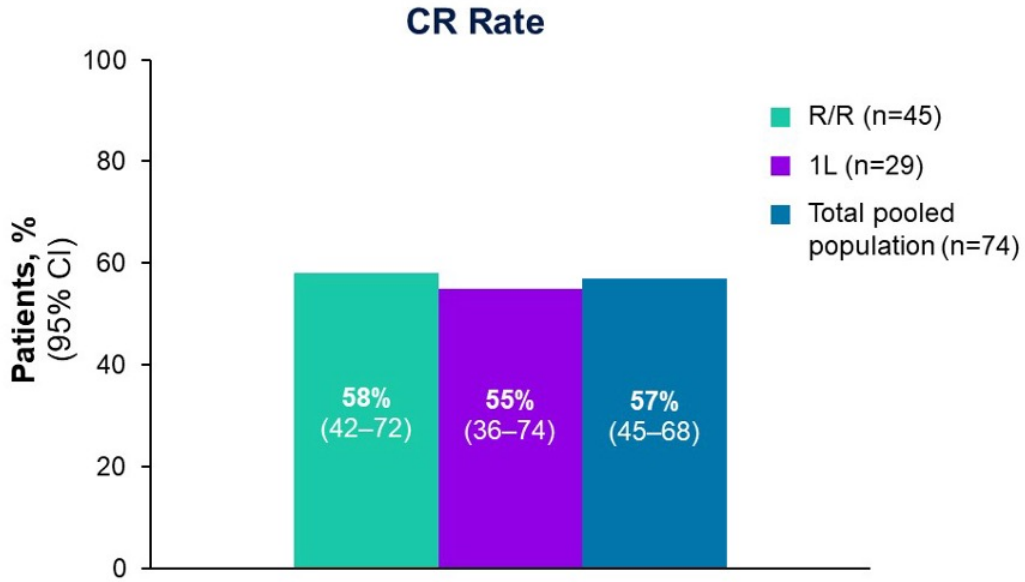
1L, first-line.
[a]NCT03112174. [b]Somatic mutations in exons 1–11 of *TP53* were evaluated by next-generation sequencing with a variant allele fraction cutoff of 2%. [c]560 mg once daily. [d]5-week ramp-up to 400 mg once daily. [e]560 mg once daily until PD or unacceptable toxicity.

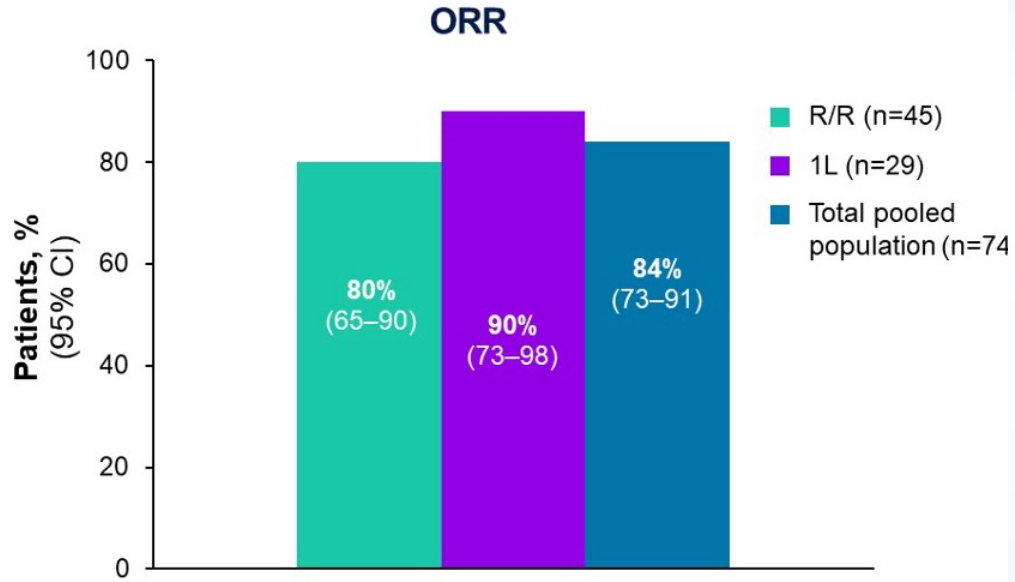
Baseline characteristics

Characteristic	R/R n=45	1L n=29	Total pooled population n=74
Age			
Median (range), years	67 (44–82)	66 (41–79)	67 (41–82)
≥65 years, n (%)	28 (62)	18 (62)	46 (62)
ECOG PS, n (%)			
0	25 (56)	15 (52)	40 (54)
1–2	20 (44)	14 (48)	34 (46)
MCL histology, n (%)			
Typical	29 (64)	18 (62)	47 (64)
Blastoid	8 (18)	0	8 (11)
Pleomorphic	3 (7)	5 (17)	8 (11)
Other	5 (11)	6 (21)	11 (15)
Simplified MIPI score, n (%)			
Low risk	7 (16)	5 (17)	12 (16)
Intermediate risk	15 (33)	13 (45)	28 (38)
High risk	21 (47)	11 (38)	32 (43)
Missing	2 (4)	0	2 (3)
Bulky disease, n (%)			
≥5 cm	18 (40)	9 (31)	27 (36)
≥10 cm	3 (7)	3 (10)	6 (8)
Extranodal disease, n (%)	24 (53)	13 (45)	37 (50)
BM involvement, n (%)	22 (49)	25 (86)	47 (64)
Splenomegaly, n (%)	16 (36)	13 (45)	29 (39)

BM, bone marrow; ECOG PS, Eastern Cooperative Oncology Group performance status; MIPI, MCL International Prognostic Index

Ibrutinib + Venetoclax Provided High CR Rates and Durable Remissions in Patients with TP53 Mutations



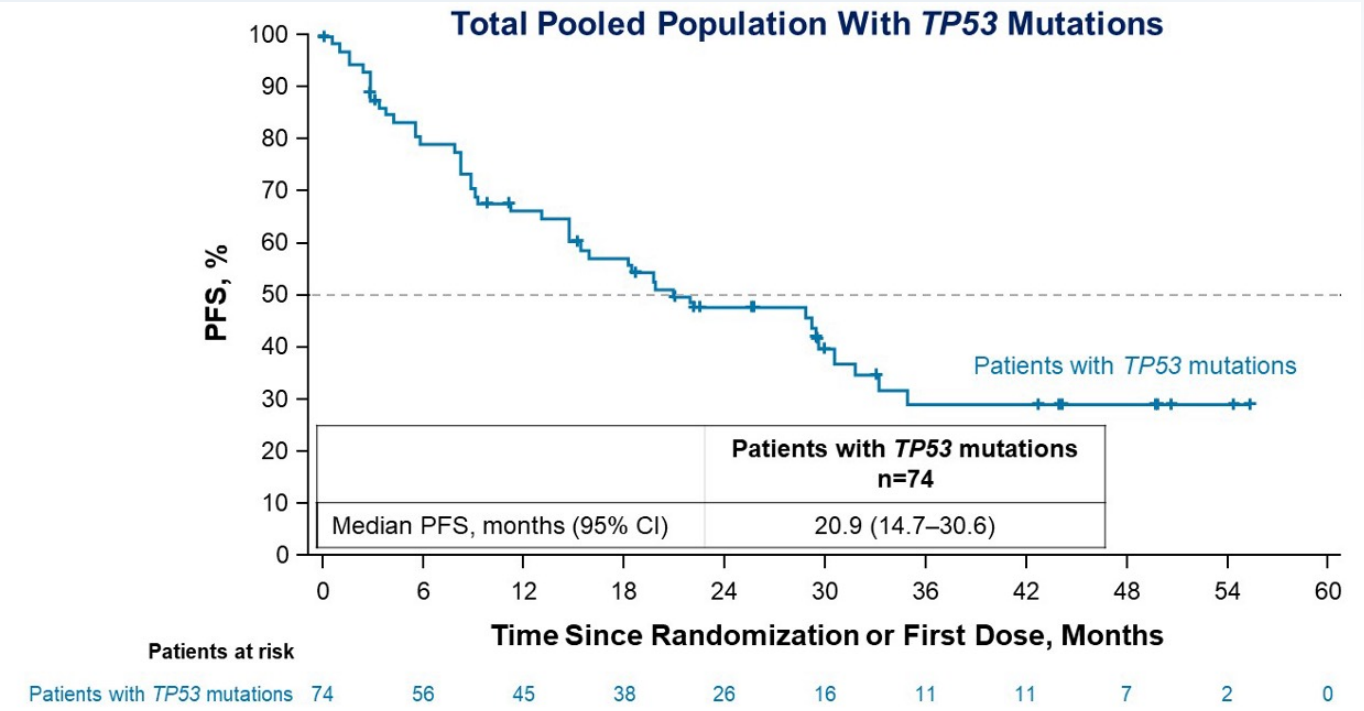


	R/R n=26	1L n=16	Total n=42
Median DOCR, months (95% CI)	NR (18.7–NE)	20.5 (5.4–NE)	32.2 (18.7–NE)

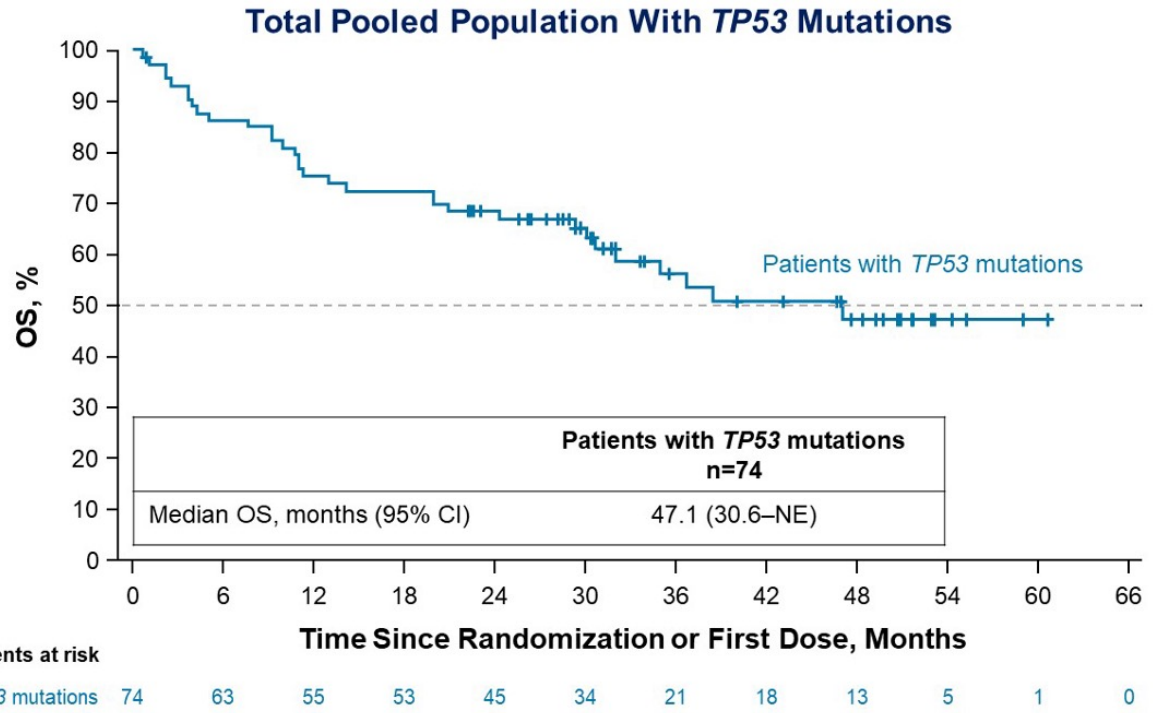
	R/R n=36	1L n=26	Total n=62
Median DOR, months (95% CI)	26.5 (16.8–NE)	20.5 (12.0–NE)	26.0 (16.8–32.2)

CR, complete response; DOCR, duration of complete response; DOR, duration of response; NE, not estimable; ORR, overall response rate.

Ibrutinib + Ven with Encouraging PFS & OS Benefit



Setting	Regimen	n	PFS
R/R	Ibrutinib + zilovertamab[1] Ibrutinib + venetoclax[2] Venetoclax[3]	7 11 NA	Median 17.3 months Median 5 months Median 3.2 months
1L	Zanubrutinib + venetoclax + obinutuzumab[4]	25	16-month rate: 75%



Setting	Regimen	n	OS
R/R	Ibrutinib + venetoclax[1] Venetoclax[2]	11 NA	Median 1.28 years Median 9.4 months
1L	Zanubrutinib + venetoclax + obinutuzumab[3]	25	16-month rate: 87%

Safety Profile

AE, n (%)	R/R n=45	1L n=29	Total n=74
Grade ≥3 AEs	37 (82)	22 (76)	59 (80)
Serious AEs	26 (58)	15 (52)	41 (55)
AEs leading to discontinuation	15 (33)	7 (24)	22 (30)
Ibrutinib only	4 (9)	3 (10)	7 (9)
Venetoclax only	2 (4)	0	2 (3)
Both	9 (20)	4 (14)	13 (18)
AEs leading to dose reduction	20 (44)	14 (48)	34 (46)
Ibrutinib only	9 (20)	5 (17)	14 (19)
Venetoclax only	6 (13)	3 (10)	9 (12)
Both	5 (11)	6 (21)	11 (15)
AEs leading to death	6 (13)	5 (17)	11 (15)
Ibrutinib related[a]	1 (2)	0	1 (1)
Venetoclax related[a]	0	0	0

AE, n (%)	R/R n=45	1L n=29	Total n=74
Most frequent any-grade AEs[b]			
Diarrhea	34 (76)	15 (52)	49 (66)
Neutropenia	18 (40)	9 (31)	27 (36)
Fatigue	13 (29)	12 (41)	25 (34)
Nausea	16 (36)	9 (31)	25 (34)
Thrombocytopenia	15 (33)	7 (24)	22 (30)
Anemia	13 (29)	8 (28)	21 (28)
COVID-19	7 (16)	11 (38)	18 (24)
Vomiting	9 (20)	8 (28)	17 (23)
Hypomagnesemia	6 (13)	9 (31)	15 (20)
Pyrexia	6 (13)	9 (31)	15 (20)
Most frequent grade ≥3 AEs[c]			
Neutropenia	17 (38)	7 (24)	24 (32)
Anemia	8 (18)	3 (10)	11 (15)
Thrombocytopenia	9 (20)	2 (7)	11 (15)
Tumor lysis syndrome			
Laboratory	2 (4)	3 (10)	5 (7)
Clinical	0	0	0

[a]Per investigator opinion. [b]Occurring in ≥20% of patients in the total population. [c]Occurring in ≥10% of patients in the total population.

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