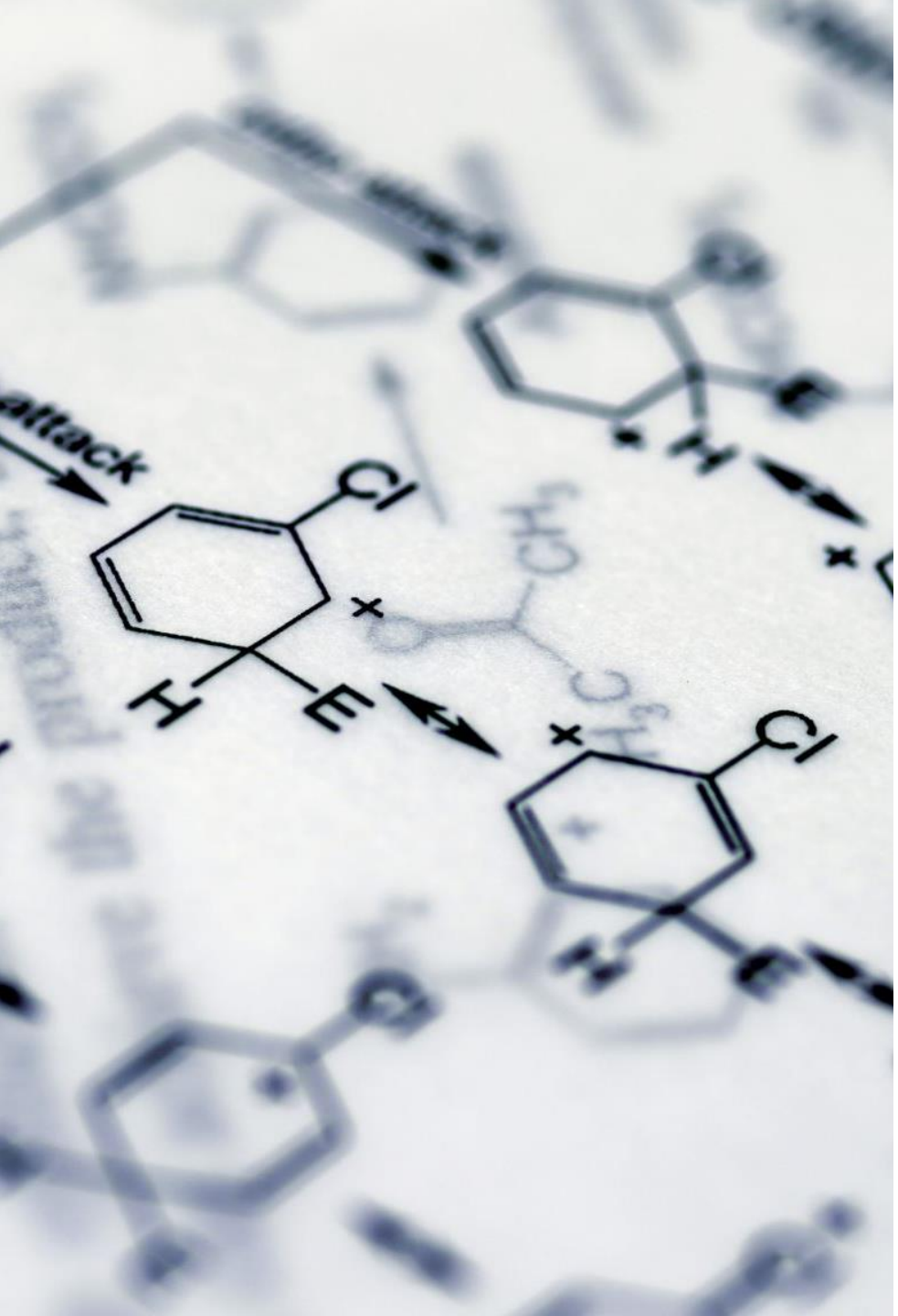
ASCO 2024 Hematologic malignancy

SUZANNE FANNING, DO

PRISMA HEALTH CANCER INSTITUTE



Outline

Myeloid malignancies

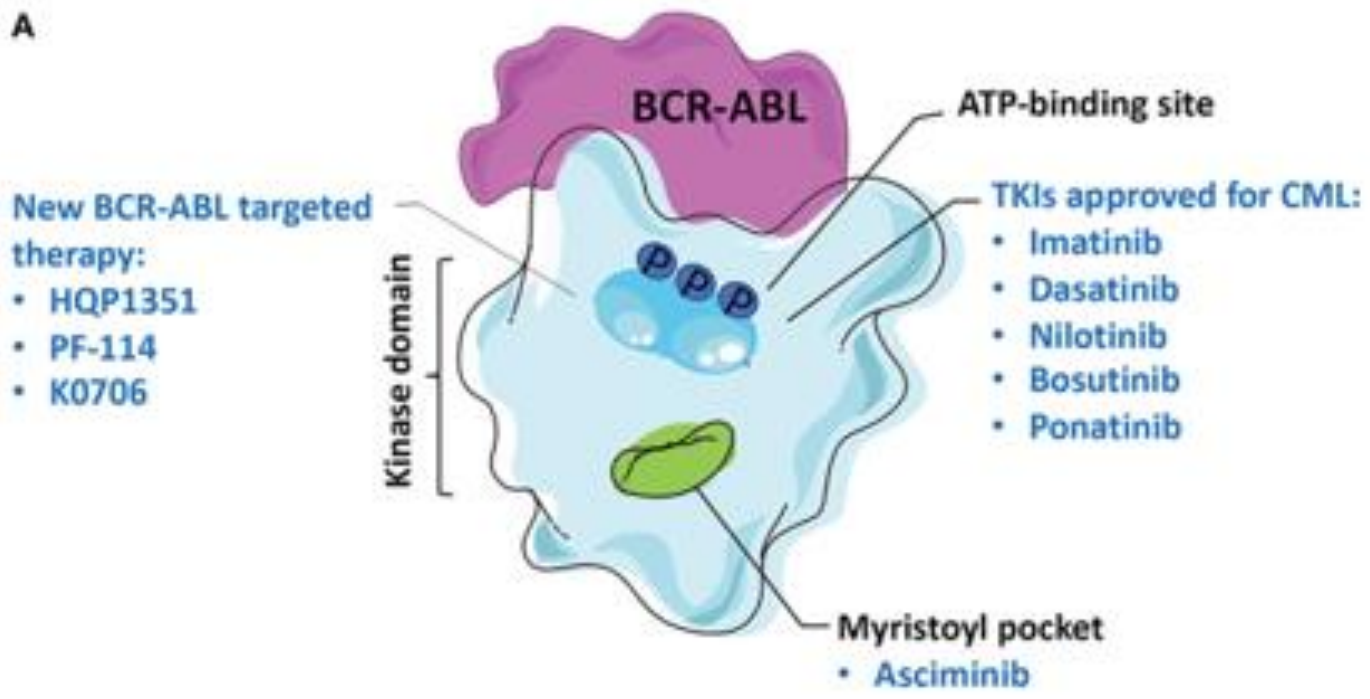
- a. CML
- b. AML

NHL

- a. Mantle cell
- b. Follicular

Multiple myeloma

- a. NDMM
- b. RRMM



ASC4FIRST, a pivotal phase 3 study of asciminib (ASC) vs investigator-selected tyrosine kinase inhibitors (IS TKIs) in newly diagnosed patients (pts) with chronic myeloid leukemia (CML): Primary results

Timothy P. Hughes, Andreas Hochhaus, Naoto Takahashi, Ghayas C. Issa, Richard A. Larson, Felice Bombaci, Jianxiang Wang, Dong-Wook Kim, Dennis Dong Hwan Kim, Jiri Mayer, Yeow Tee Goh, Phillipp D. Le Coutre, David Jacob Andorsky, Shruti Kapoor, Tracey McCulloch, Kamel Malek, Lillian Yau, Sophie Ifrah, Jorge E. Cortes, ASCO 2024

ASC4FIRST, a pivotal phase 3 study of asciminib (ASC) vs investigator-selected tyrosine kinase inhibitors (IS TKIs) in newly diagnosed patients (pts) with chronic myeloid leukemia (CML): Primary results

- 1:1 randomization of ascinimib vs. investigator choice TKI
- At data cutoff, treatment was ongoing in 86% on ASC
- ASC had highest MMR rate at 48 weeks
- ASC with deepest response –MR4 and MR 4.5
- ASC with less grade ≥3 AE's
- ASC with half the rate of AE's leading to discontinuation
- Rate of arterial occlusive events 1% ASC, 0% IM, 2% 2G TKI's

Timothy P. Hughes, Andreas Hochhaus, Naoto Takahashi, Ghayas C. Issa, Richard A. Larson, Felice Bombaci, Jianxiang Wang, Dong-Wook Kim, Dennis Dong Hwan Kim, Jiri Mayer, Yeow Tee Goh, Phillipp D. Le Coutre, David Jacob Andorsky, Shruti Kapoor, Tracey McCulloch, Kamel Malek, Lillian Yau, Sophie Ifrah, Jorge E. Cortes, ASCO 2024

Efficacy and Safety of Ibrutinib Plus Venetoclax in Patients With Mantle Cell Lymphoma and *TP53* Mutations in the SYMPATICO Study

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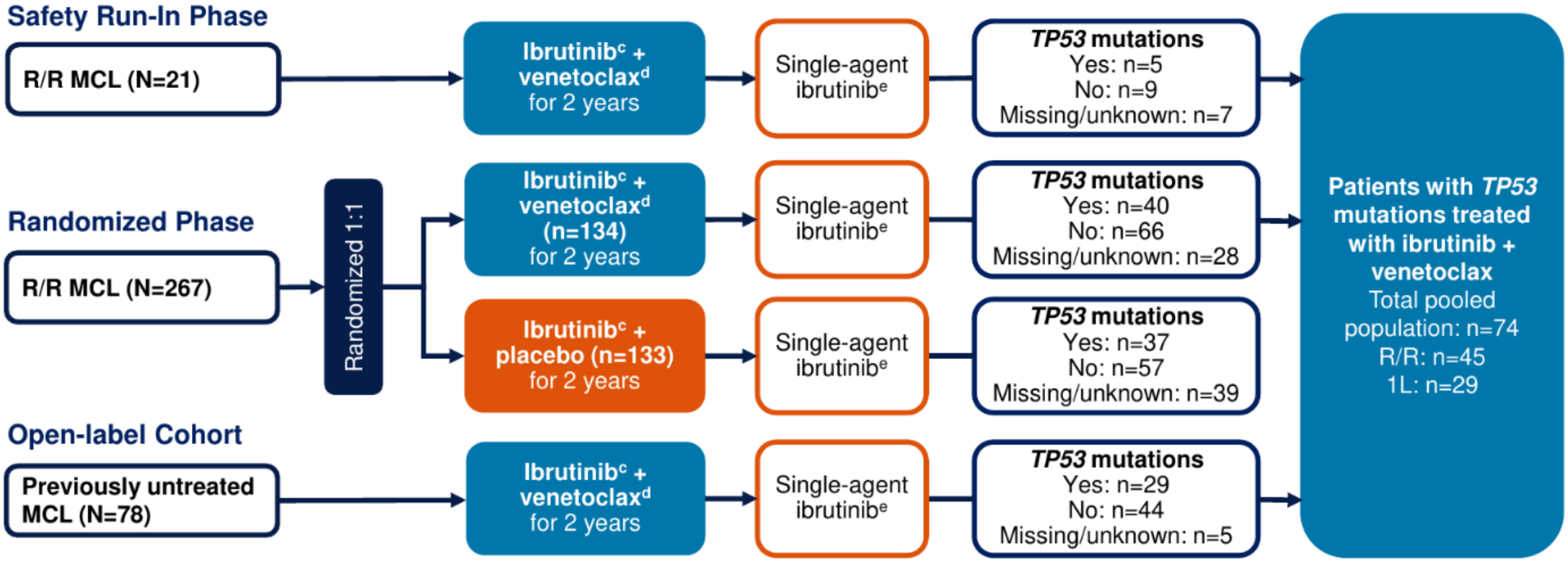
2024 ASCO Annual Meeting; May 31–June 4, 2024; Chicago, IL, USA

Abstract 7007

- SYMPATICO[a] is a multinational, randomized, double-blind, placebo-controlled, Phase 3 study
- Data were pooled (3 cohorts) for patients with *TP53* mutations (no deletions)[b] treated with ibrutinib + venetoclax



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.

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Baseline Characteristics of Patients With *TP53* Mutations Treated With Ibrutinib + Venetoclax

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)

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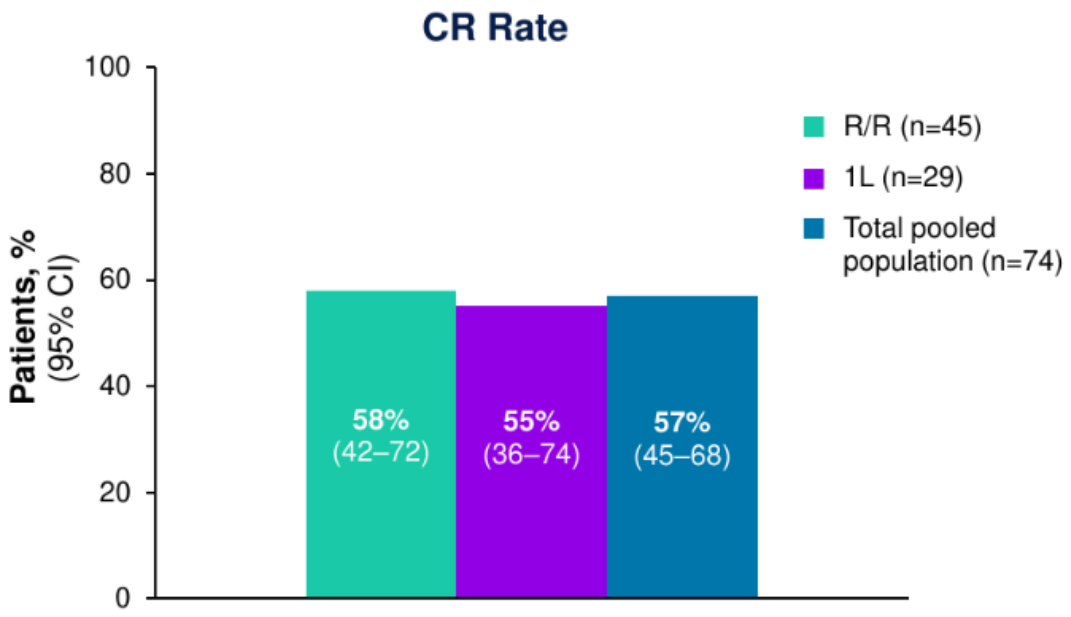
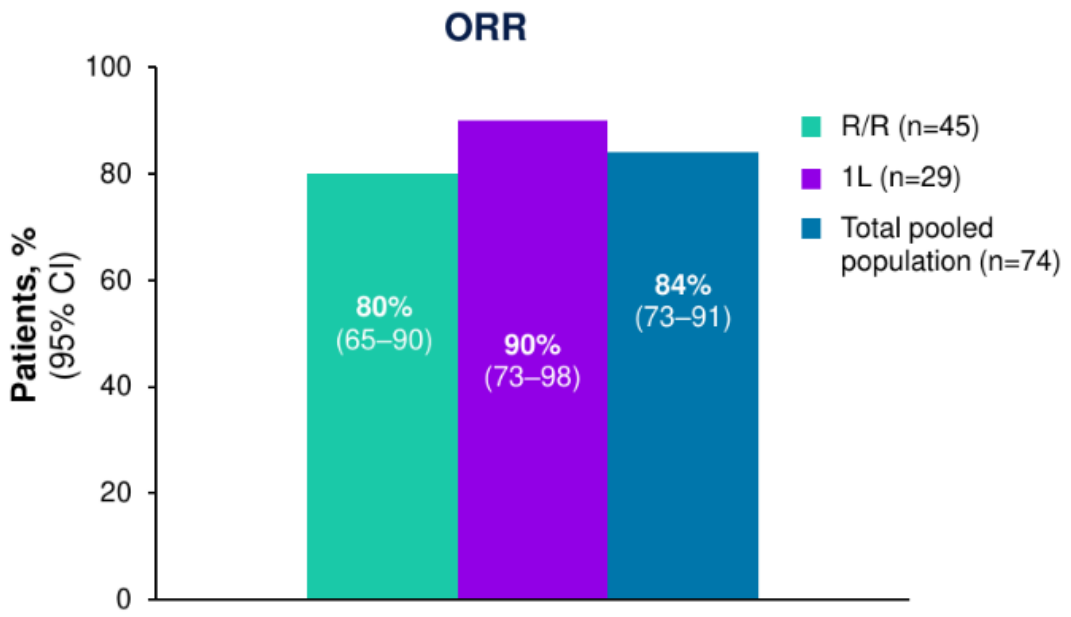
with *TP53* Mutations





	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)

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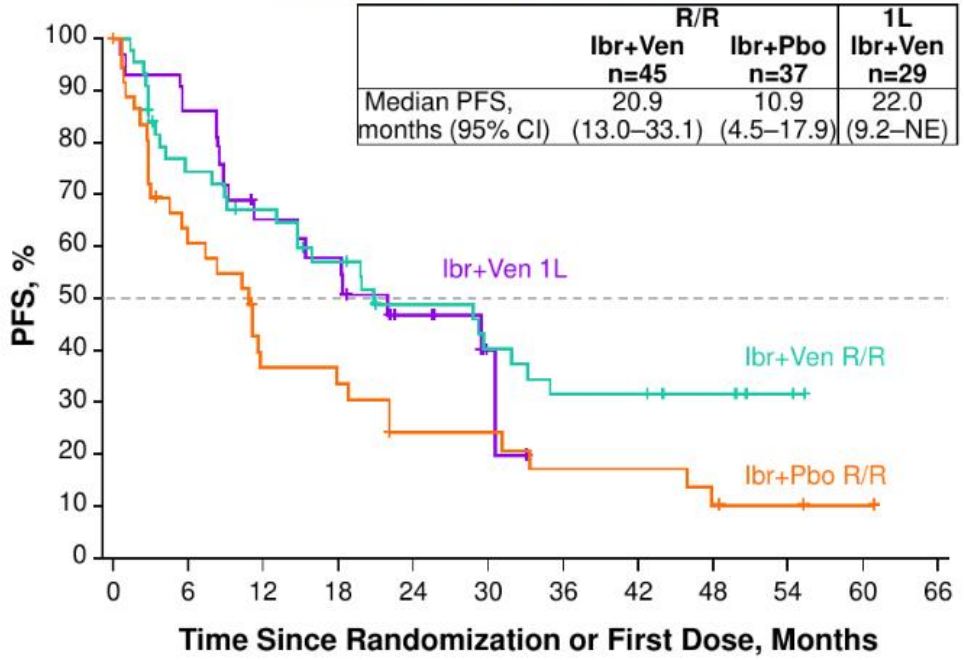
PFS Benefit Was Observed With Ibrutinib + Venetoclax in Patients With and Without *TP53* Mutations

Patients With *TP53* Mutations

	R/R		1L
	Ibr+Ven n=45	Ibr+Pbo n=37	Ibr+Ven n=29
Median PFS, months (95% CI)	20.9 (13.0–33.1)	10.9 (4.5–17.9)	22.0 (9.2–NE)

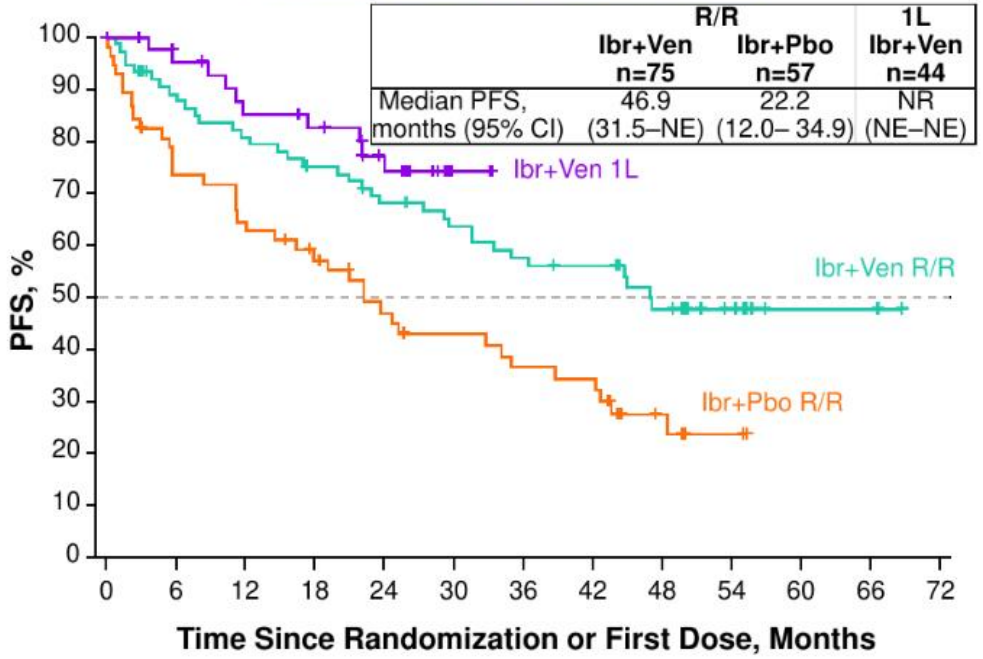


Patients at risk

Ibr+Ven R/R	45	31	27	22	17	14	11	11	7	2	0	0
Ibr+Pbo R/R	37	21	12	11	7	7	5	5	3	2	1	0
Ibr+Ven 1L	29	25	18	16	9	2	0	0	0	0	0	0

Patients Without *TP53* Mutations

	R/R		1L
	Ibr+Ven n=75	Ibr+Pbo n=57	Ibr+Ven n=44
Median PFS, months (95% CI)	46.9 (31.5–NE)	22.2 (12.0– 34.9)	NR (NE–NE)



Ibr+Ven R/R	75	64	58	53	47	42	38	36	23	11	2	2	0
Ibr+Pbo R/R	57	41	36	30	23	20	17	16	7	3	0	0	0
Ibr+Ven 1L	44	39	34	32	26	5	0	0	0	0	0	0	0

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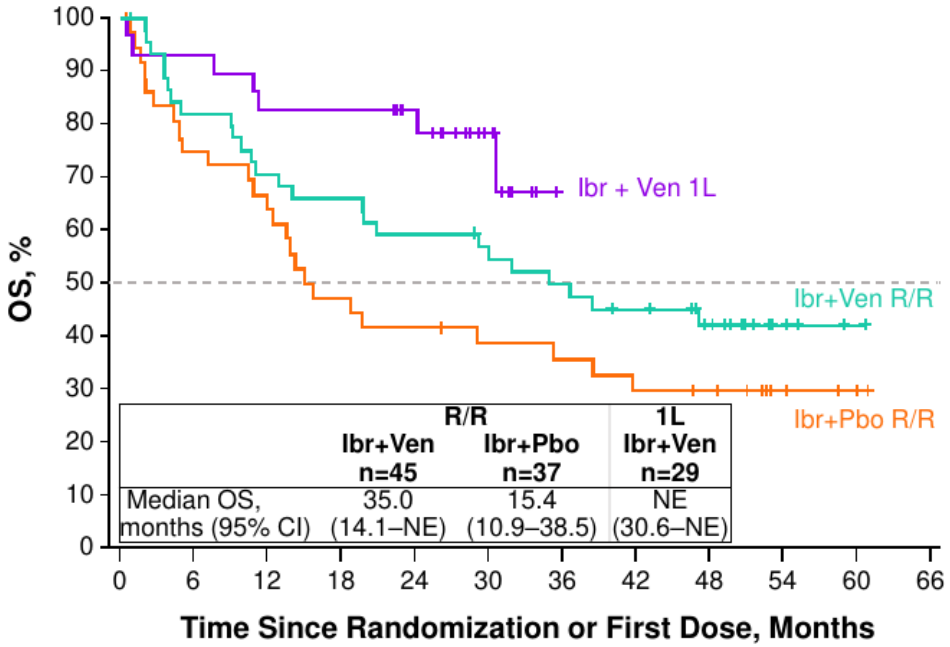
OS Benefit With Ibrutinib + Venetoclax in Patients With and Without *TP53* Mutations

Patients With *TP53* Mutations

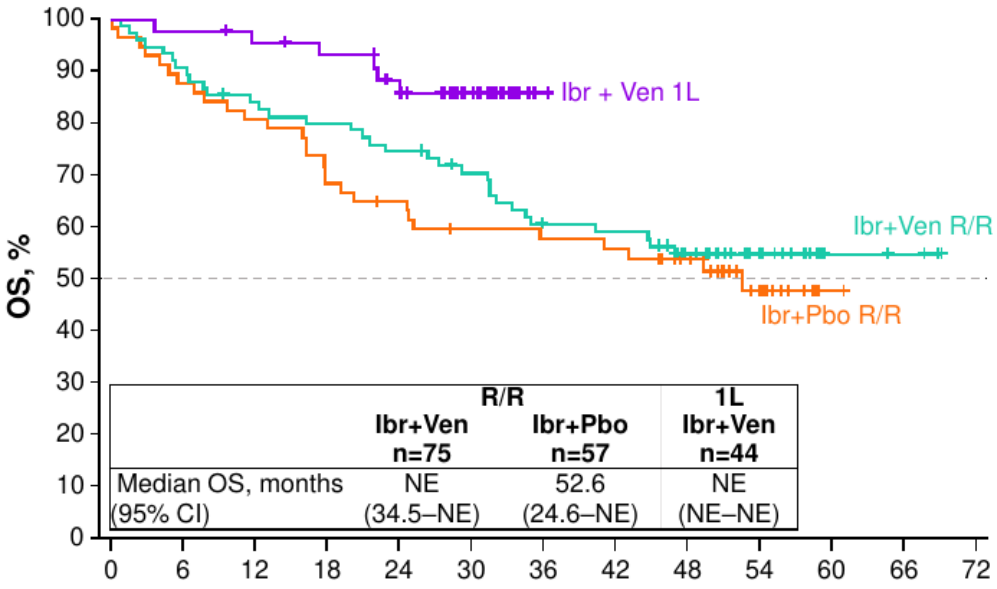


	R/R		1L
	Ibr+Ven n=45	Ibr+Pbo n=37	Ibr+Ven n=29
Median OS, months (95% CI)	35.0 (14.1–NE)	15.4 (10.9–38.5)	NE (30.6–NE)

Patients at risk

Ibr+Ven R/R	45	36	31	29	26	24	21	18	13	5	1	0
Ibr+Pbo R/R	37	27	23	17	15	13	12	10	9	4	2	0
Ibr+Ven 1L	29	27	24	24	19	10	0	0	0	0	0	0

Patients Without *TP53* Mutations



	R/R		1L
	Ibr+Ven n=75	Ibr+Pbo n=57	Ibr+Ven n=44
Median OS, months (95% CI)	NE (34.5–NE)	52.6 (24.6–NE)	NE (NE–NE)

	75	68	62	59	55	50	42	41	29	15	4	3	0
	57	50	46	39	36	32	31	30	24	12	1	0	0
	44	43	41	39	35	23	1	0	0	0	0	0	0

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Safety in Patients With *TP53* Mutations was Consistent With Known Safety Profiles of Ibrutinib and Venetoclax

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

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Epcoritamab With Rituximab + Lenalidomide (R^2) in Previously Untreated (1L) Follicular Lymphoma (FL) and Epcoritamab: EPCORE NHL-2 Arm 6

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Presented at the American Society of Clinical Oncology Annual Meeting; May 31–June 4, 2024; Chicago, IL

Background

- Patients with advanced 1L FL remain incurable[1]:
  - R^2 is a recommended treatment that has shown improved outcomes compared with rituximab alone,[2] and outcomes are comparable with rituximab + chemotherapy (CR rates, ~50%)[3,4]
  - Outcomes are still suboptimal, and novel, chemotherapy-free combinations that induce deep and durable responses translating to favorable long-term outcomes in a larger proportion of patients with 1L FL are needed[5]

In EPCORE NHL-2, we assessed the long-term safety and efficacy of fixed-duration epcoritamab + R^2 in 1L FL (updated data from arm 6)

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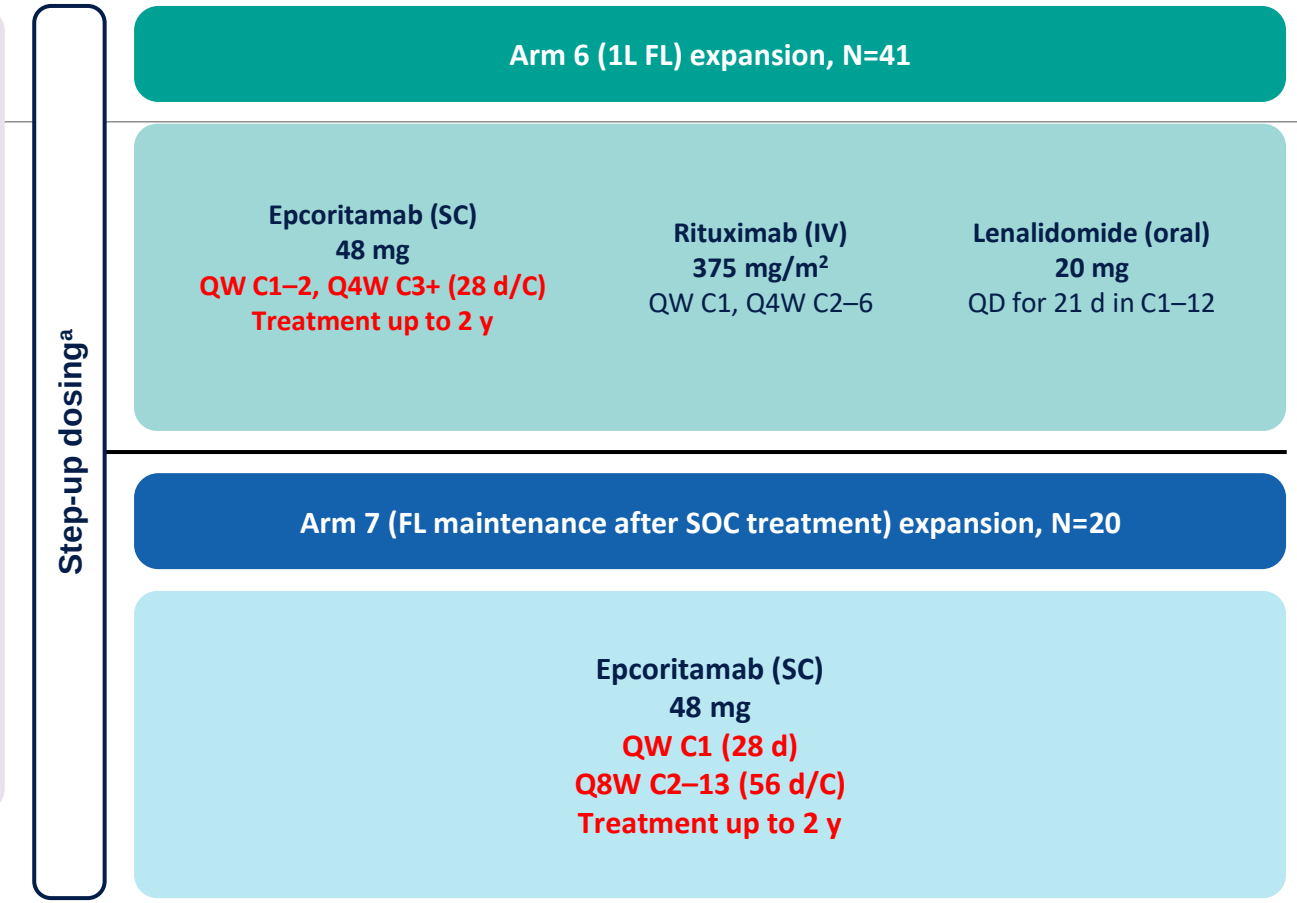
1L, previously untreated; CR, complete response; FL, follicular lymphoma; OS, overall survival; R^2, rituximab + lenalidomide; SOC, standard of care; y, year(s). **1.** Ghione P, et al. *Haematologica*. 2023;108:822-32. **2.** Zucca E, et al. *Blood.* 2019;134:353-62. **3.** Delfau-Larue MH, et al. *Blood Adv*. 2020;4:3217-23. **4.** Morschhauser F, et al. *N Engl J Med*. 2018;379:934-47. **5.** Dixon JG, et al. *Clin Lymphoma Myeloma Leuk*. 2022;22;e1009-18. **6.** Rule S, et al. *Haematologica*. 2022;107:500-9. **7.** Kahl BS, et al. *J Clin Oncol*. 2024;42:774-8.

Study Design

Key inclusion criteria

- CD20+ FL
  - Grade 1, 2, or 3A
- 1L FL **(arm 6, 1L FL)**
- In CR or PR after 1–2 lines of SOC treatment **(arm 7, FL maintenance)**
- ECOG PS 0–2
- Measurable disease by CT or MRI **(arm 6, 1L FL)**
- Adequate organ function

Data cutoff: January 31, 2024



- **Primary objective:**
  - **Arm 6:** Antitumor activity (ORR)[b]
  - **Arm 7:** Safety/tolerability
- **Key secondary endpoints:**
  - **Arm 6:** Safety/tolerability, DOR, DOCR, PFS, OS
  - **Arm 7:** CR rate,[c] DOCR

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Arm 6 (1L FL): Baseline Characteristics, Treatment Exposure, and Follow-Up

Characteristic	N=41
Median age, y (range)	57 (39–78)
Male, n (%)	21 (51)
Ann Arbor stage, n (%)[a]	
III	16 (39)
IV	22 (54)
FLIPI, n (%)[b]	
2	15 (37)
3–5	14 (34)
ECOG PS, n (%)	
0	34 (83)
1	6 (15)
2	1 (2)

Treatment Exposure and Follow-Up	N=41
Median follow-up, mo (range)	22.8 (1.4+ to 25.6)
Epcoritamab treatment exposure[c]	
Median number of treatment cycles initiated (range)[d]	23 (1–27)
Median duration of treatment, mo (range)	22.0 (0.5–24.2)
Ongoing treatment, n (%)	12 (29)
Completed treatment per protocol, n (%)	14 (34)
Discontinued treatment, n (%)	15 (37)
AE	9 (22)
Patient withdrawal	2 (5)
PD	1 (2)
Other[e]	3 (7)

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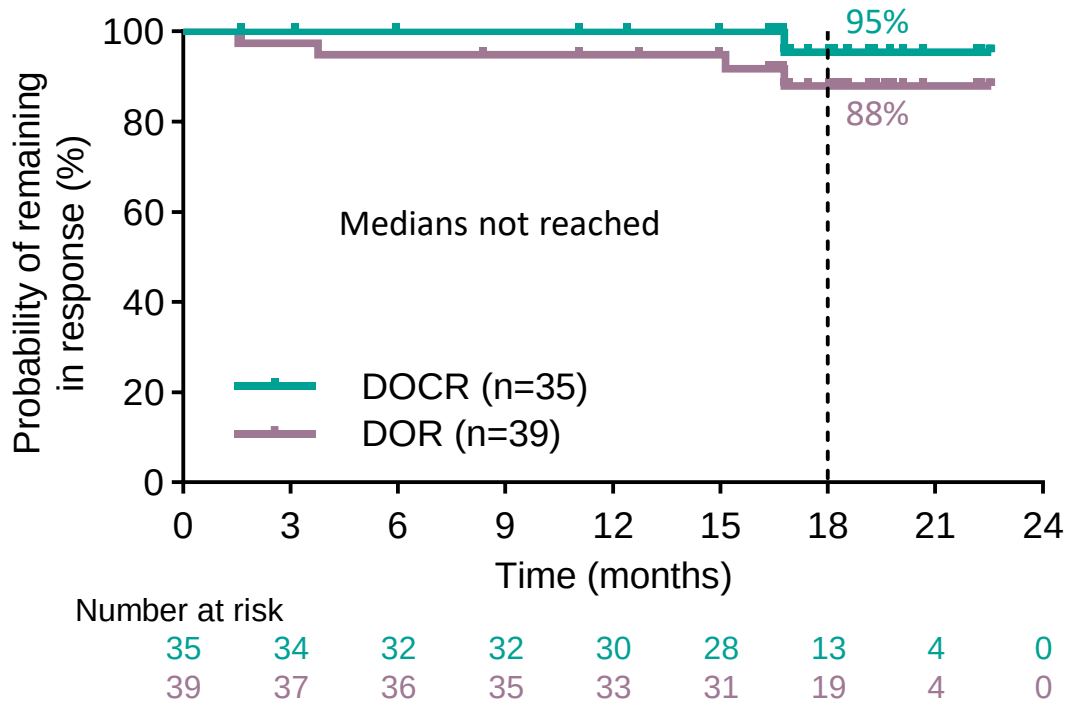
Arm 6 (1L FL): Epcoritamab + R^2 Continued to Show Deep, Durable Responses

	N=41[a]
Overall response, n (%)	39 (95)
Complete response, n (%)	35 (85)
Partial response, n (%)	4 (10)
Progressive disease, n	0
Median time to response, mo (range)	2.7 (1.2–5.5)
Median time to complete response, mo (range)	2.8 (1.4–11.4)



High rates of patients remaining in response and complete response were observed at 18 months

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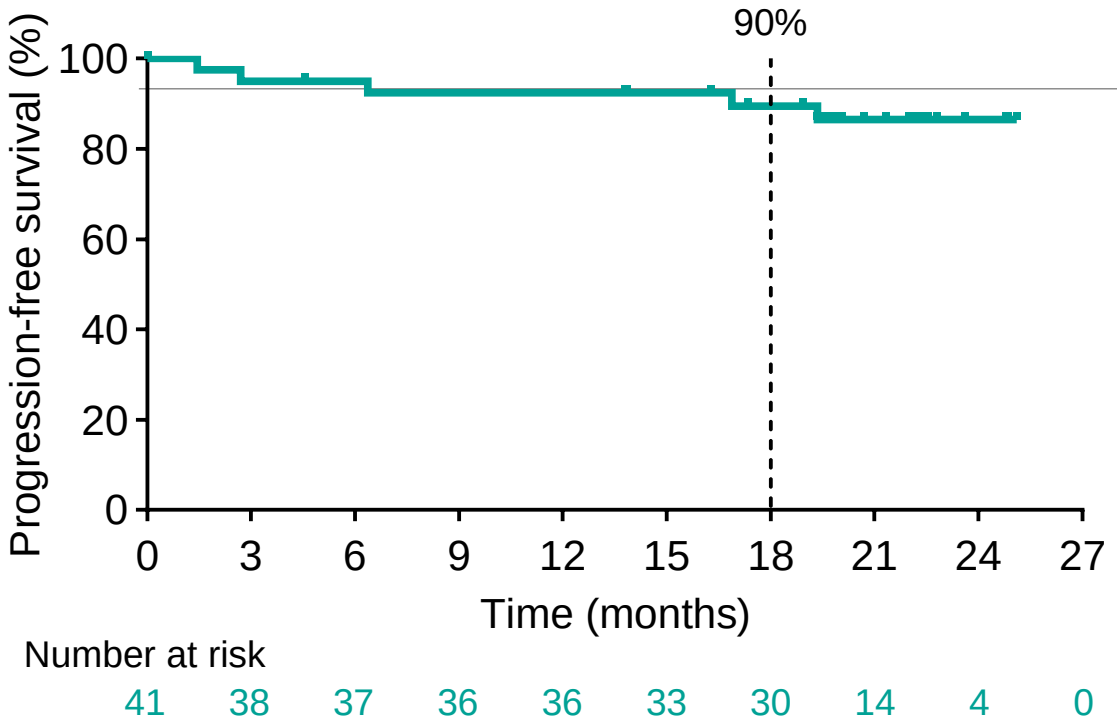
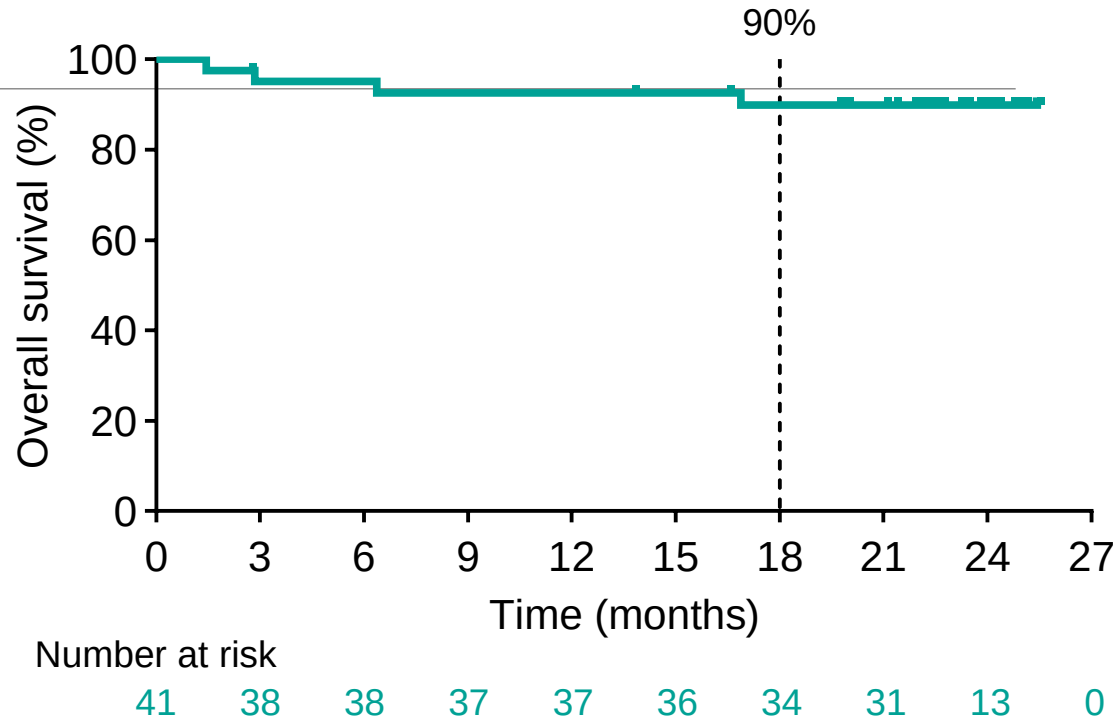
Arm 6 (1L FL): Progression-Free and Overall Survival





High rates of progression-free and overall survival were observed at 18 months

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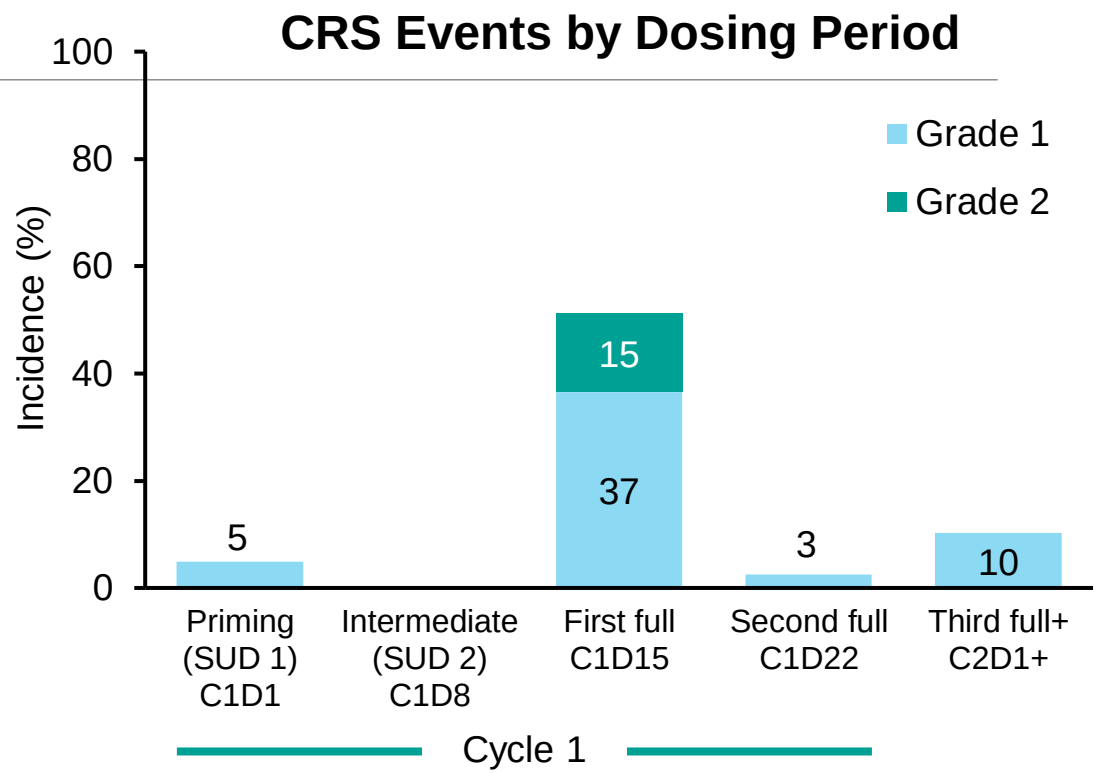
Arm 6 (1L FL): CRS Was Low Grade and Consistent With Prior Reports, With Predictable Timing

	N=41
CRS, n (%)[a]	23 (56)
Grade 1	17 (41)
Grade 2	6 (15)
Median time to onset after first full dose, d (range)	2 (1–6)
CRS resolution, n/n (%)	23/23 (100)
Median time to resolution,[b] d (range)	3 (1–6)
Treated with tocilizumab, n (%)	4 (10)
Leading to epcoritamab discontinuation, n (%)	0

[a]Graded by Lee et al 2019 criteria. [b]Median is based on longest CRS duration in patients with >1 CRS event.

- CRS timing was predictable; CRS events were primarily confined to cycle 1
- CRS events were low grade and resolved
- No ICANS or clinical tumor lysis syndrome



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Conclusions

- Longer follow-up showed that fixed-duration epcoritamab + R^2 in previously untreated FL leads to deep and durable responses that translate to favorable long-term outcomes
  - ORR 95%, CR rate 85%
  - At 18 months, an estimated 90% of patients remained progression free and alive

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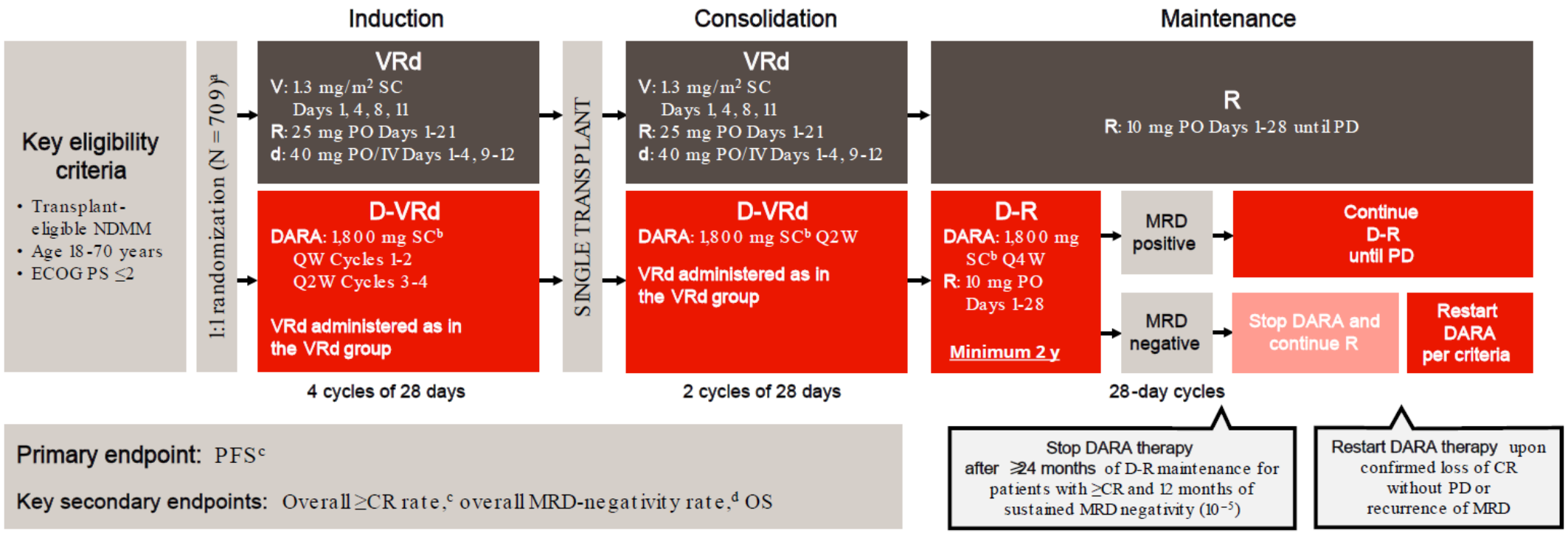
Rodriguez-Otero P et al. ASCO 2024 O7502

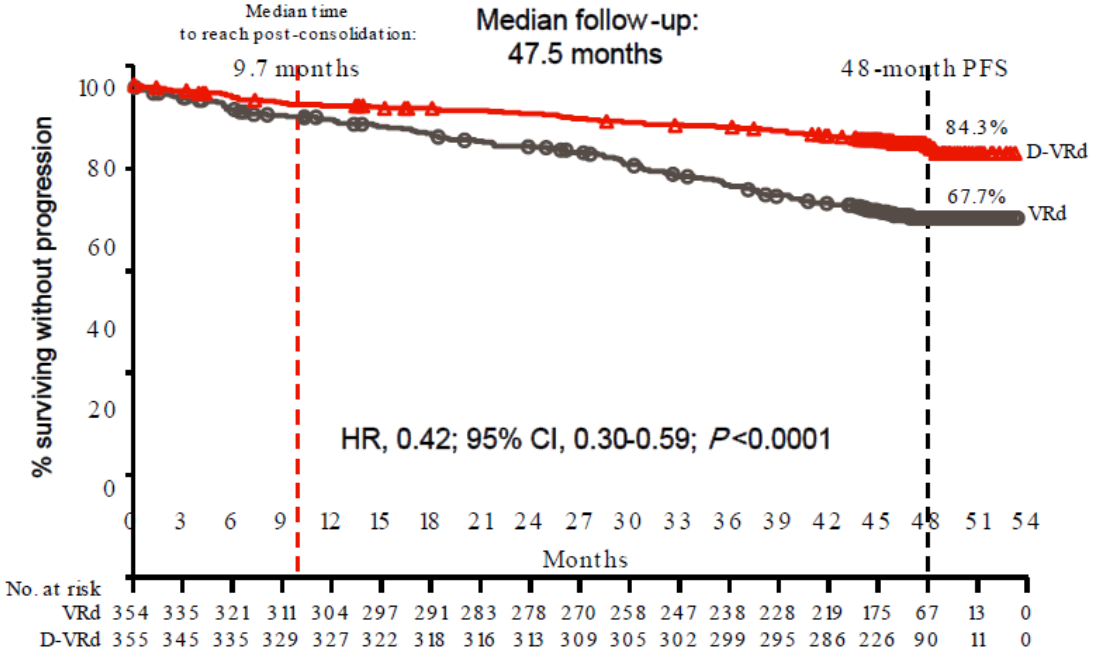
PERSEUS: Study Design

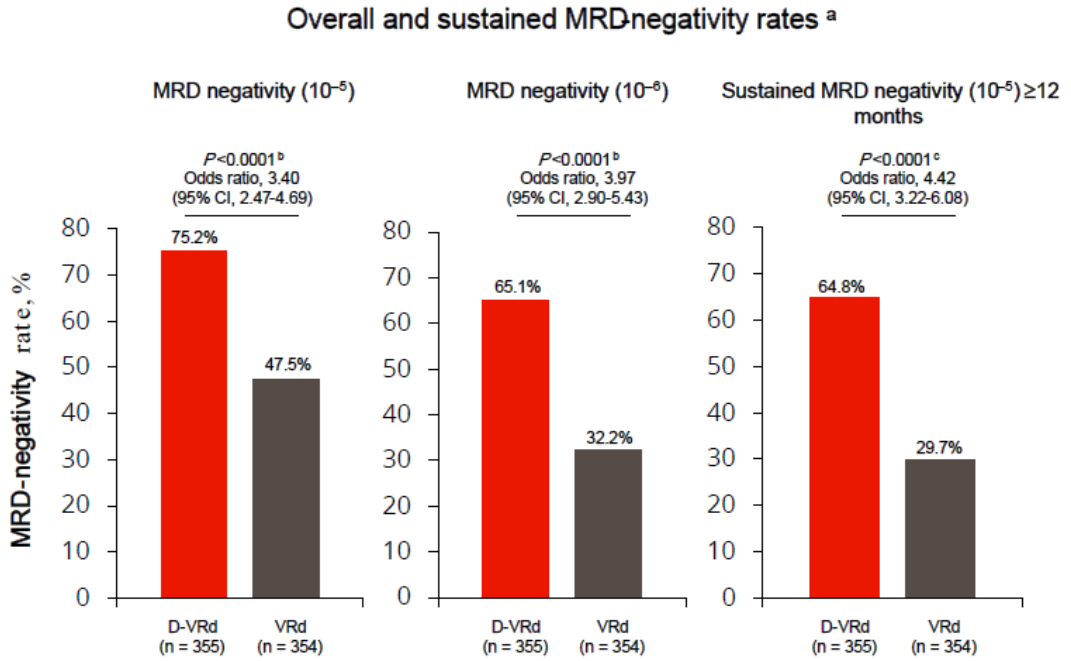


MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and ≥CR in the ITT population. Patients who were not evaluable or had indeterminate results were considered MRD positive.

ASCO 2024 7502

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

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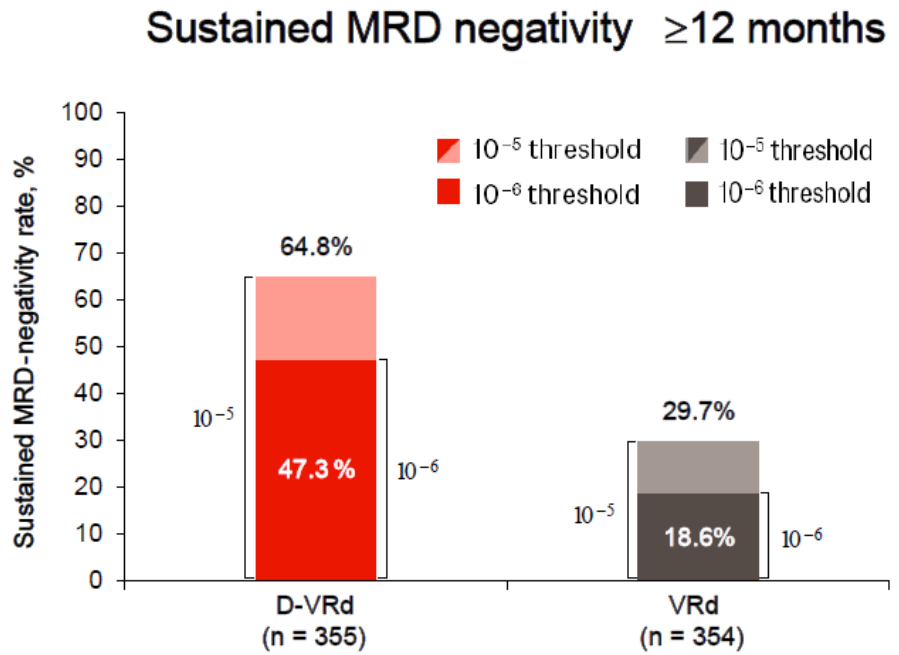
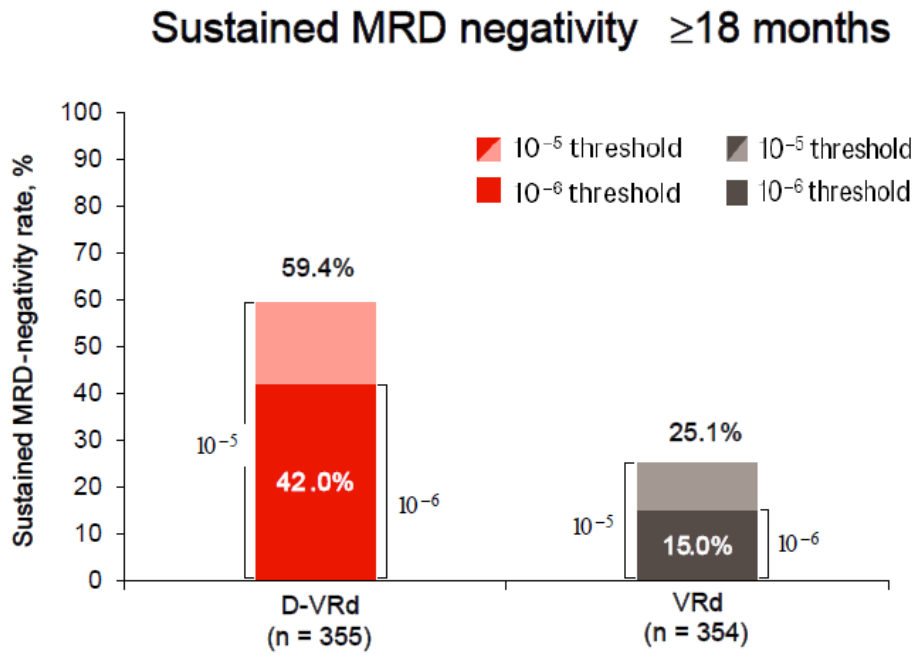
PERSEUS: Sustained MRD negativity Rates (10^{-5} and 10^{-6} ; ITT)





- Rates of sustained MRD negativity at 10^{-6} were 2.5-fold higher for D-VRd + D-R versus VRd + R
- More than 40% of patients had sustained MRD negativity at 10^{-6} for ≥18 months with D-VRd + D-R

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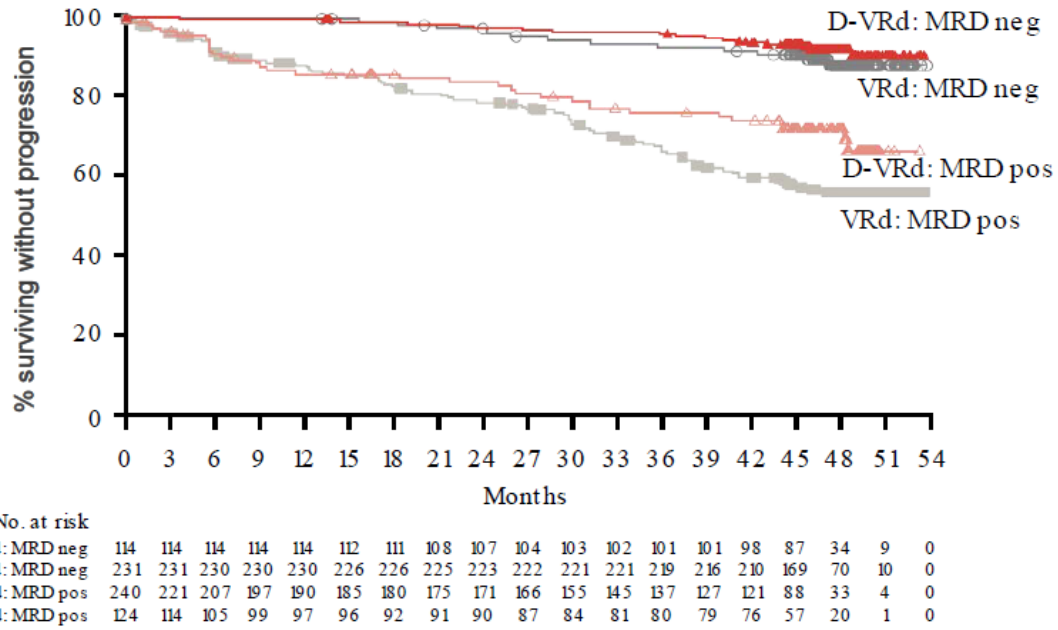
(10^{-6}; ITT)

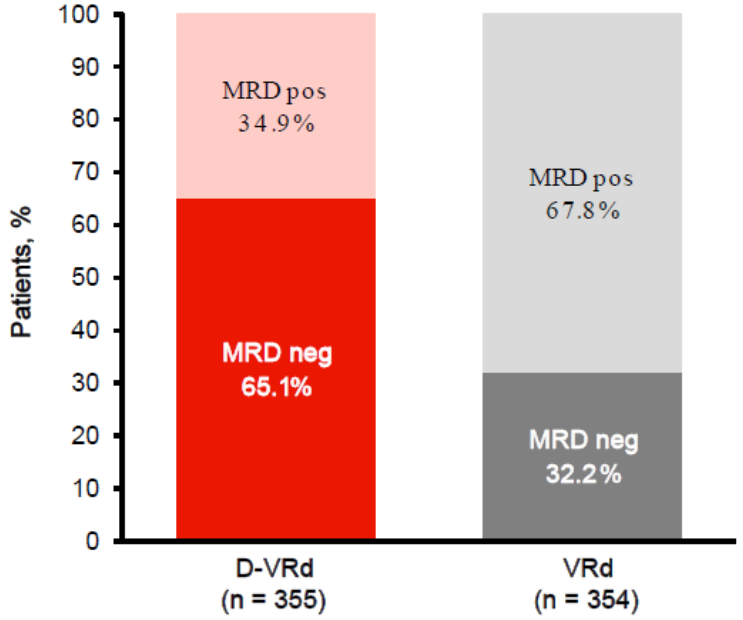
PFS according to MRD status (10^{-6})



No. at risk

VRd: MRD neg	114	114	114	114	114	112	111	108	107	104	103	102	101	101	98	87	34	9	0
D-VRd: MRD neg	231	231	230	230	230	226	226	225	223	222	221	221	219	216	210	169	70	10	0
VRd: MRD pos	240	221	207	197	190	185	180	175	171	166	155	145	137	127	121	88	33	4	0
D-VRd: MRD pos	124	114	105	99	97	96	92	91	90	87	84	81	80	79	76	57	20	1	0

Overall MRD negativity (10^{-6})



- MRD negativity at 10^{-6} was associated with improved long -term outcomes
- Twice as many patients achieved MRD negativity at 10^{-6} with D -VRd + D-R versus VRd + R
- Patients remaining MRD positive had improved PFS with D -R maintenance versus R alone

ASCO 2024 Abstract 7502

Oral presentation presented at ASCO 2024 meeting

IMROZ

2024 ASCO ANNUAL MEETING

Phase 3 Study Results of Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone (Isa-VRd) Versus VRd for Transplant-Ineligible Patients With Newly Diagnosed Multiple Myeloma (IMROZ)

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2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY: Thierry Facon, MD

Abstract 7500

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Disclaimer

- Presented at the American Society of Clinical Oncology (ASCO), taking place onsite in Chicago, IL, USA, May 31–June 4, 2024
- Some information may not be consistent with the approved product labeling for the products(s) being discussed; this information may relate to the indication or use, dosage and administration, patient population, combination use, or other potential unapproved uses. No conclusions regarding safety and efficacy can be made for such uses

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Background

- Bortezomib–lenalidomide–dexamethasone (VRd) is a standard frontline treatment for transplant-eligible and -ineligible patients,[1,2] and is commonly used in clinical practice[1]
- Phase 3 studies have shown improved outcomes with quadruplet regimens consisting of an anti-CD38 in combination with PI and IMiD agents for transplant-eligible patients with NDMM, reinforcing quadruplet therapies as the standard of care[3–6]
- Results of a Phase 1b study of isatuximab combined with VRd (Isa-VRd) showed a well-tolerated safety profile, preliminary clinical activity, and deep responses in transplant-ineligible patients or those with no immediate intent for autologous stem cell transplant[7]
- We report the results of a prespecified interim analysis of IMROZ (NCT03319667), the first global Phase 3 study investigating the efficacy and safety of Isa-VRd vs VRd in transplant-ineligible patients with NDMM

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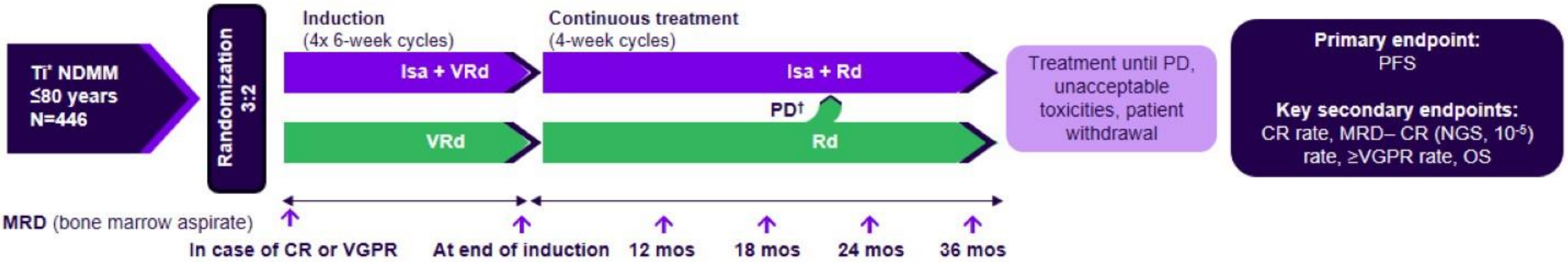
IMiD, immunomodulatory drug; PI, proteasome inhibitor.

1. Dimopoulos MA, et al. *Ann Oncol*. 2021;32:309–322. 2. Durie BGM, et al. *Lancet*. 2017;389:519–527. 3. Gay F, et al. *Blood*. 2023;142:4. 4. Goldschmidt H, et al. *Lancet Haematol*. 2022;9:e810–e821. 5. Sonneveld P, et al. *N Engl J Med*. 2024;390:301–313. 6. Moreau P, et al. *Lancet*. 2019;394:29–38. 7. Ocio EM, et al. *Leukemia*. 2023;37:1521–1529.

Study design: Isa-VRd vs VRd in transplant-ineligible NDMM



*Patients considered Ti due to age or comorbidities.
†In the continuous phase, patients randomized to the VRd arm who experience PD may cross over to receive Isa-Rd.
‡10 mg/day if eGFR 30–<60 mL/min/1.73 m^2.
§If aged ≥75 years, d was administered on days 1, 4, 8, 11, 15, 22, 25, 29, and 32.

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

ASCO 2024 abstract 7500

Baseline characteristics

ITT population	Isa-VRd (n=265)	VRd (n=181)
Age, median (range), years	72.0 (60–80)	72.0 (55–80)
Age by category, years, n (%)		
<65	8 (3.0)	9 (5.0)
65–<70	73 (27.5)	47 (26.0)
70–<75	115 (43.4)	68 (37.6)
75–80	69 (26.0)	57 (31.5)
ECOG PS, n (%)		
0	123 (46.4)	79 (43.6)
1	112 (42.3)	83 (45.9)
2*	29 (10.9)	19 (10.5)
eGFR <60 mL/min/1.73 m² (MDRD), n (%)	66 (24.9)	62 (34.3)

ITT population	Isa-VRd (n=265)	VRd (n=181)
R-ISS stage (IRT strata), n (%)		
I or II	234 (88.3)	157 (86.7)
III	29 (10.9)	21 (11.6)
Not classified	2 (0.8)	3 (1.7)
Cytogenetic risk, n (%)		
Standard	207 (78.1)	140 (77.3)
High†	40 (15.1)	34 (18.8)
High and 1q21+‡	19 (7.2)	15 (8.3)
1q21+/amplification 1q21,§ n (%)	95 (35.8)/ 32 (12.1)	70 (38.7)/ 23 (12.7)
Del(17p) (50% cutoff), n (%)	15 (5.7)	9 (5.0)
Extramedullary disease at study entry¶ (per IRC), n (%)	18 (6.8)	6 (3.3)

Patient characteristics were balanced in both arms

*One patient in the Isa-VRd arm had an ECOG PS of 3. †High risk defined as the presence of del(17p) and/or t(4;14) and/or t(14;16), with cutoffs defined in footnote ‡. ‡Abnormality defined as present in at least 30% of abnormal bone marrow plasma cells for t(4;14) and t(14;16) and 1q21+ (at least 3 copies), and at least 50% of abnormal plasma cells for del(17p). Only one patient had 2 high-risk cytogenetic abnormalities: del(17p) and t(4;14). §1q21+ defined as at least 3 copies of 1q21. Amplification 1q21 defined as at least 4 copies of 1q21. ¶In addition, there were 67 (25.3%; Isa-VRd) and 49 (27.1%; VRd) patients with paramedullary disease and 1 patient in each group with both extramedullary and paramedullary disease.
IRC, independent review committee; IRT, interactive response technology.

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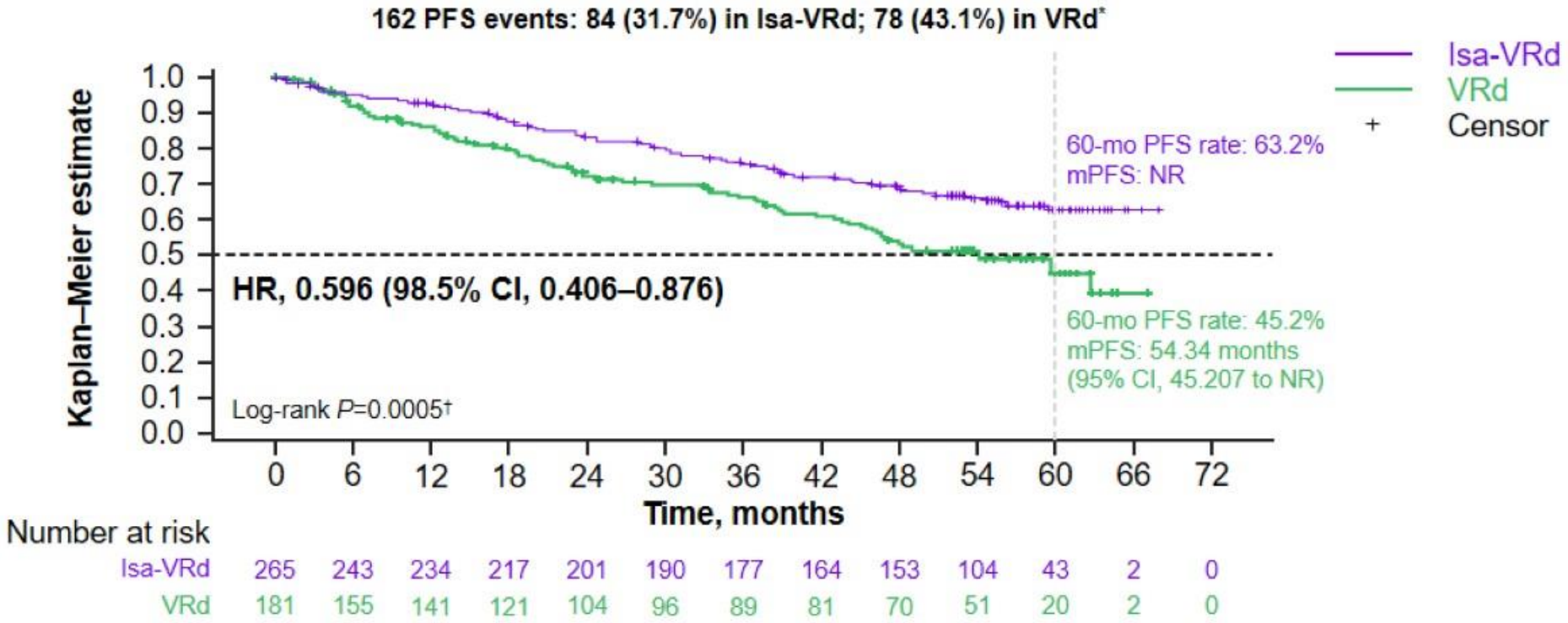
Primary endpoint met: Interim PFS analysis–IRC assessment in ITT population



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.

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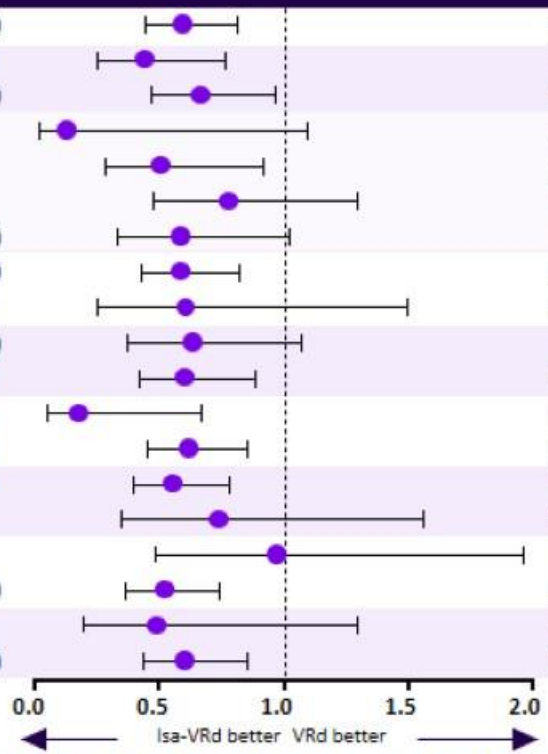
PFS subgroup analyses

Characteristic		Subgroup	Isa-VRd Events/total	Median PFS (95% CI)	VRd Events/total	Median PFS (95% CI)	Hazard ratio (95% CI)
All patients			84/265	NR (NR–NR)	78/181	54.341 (45.207–NR)	0.596 (0.438–0.812)
Age*	70-year threshold:	<70 years	22/80	NR (NR–NR)	27/56	53.914 (37.52–NR)	0.441 (0.251–0.775)
		≥70 years	62/185	NR (NR–NR)	51/125	54.341 (43.598–NR)	0.671 (0.463–0.972)
	Multiple subgroups:	<65 years	1/8	NR (48.066–NR)	5/9	31.524 (12.189–NR)	0.126 (0.014–1.095)
		65–<70 years	21/73	NR (NR–NR)	22/47	59.663 (37.52–NR)	0.503 (0.276–0.915)
		70–<75 years	39/115	NR (56.214–NR)	25/68	NR (45.207–NR)	0.781 (0.472–1.291)
		75–80 years	23/69	NR (53.06–NR)	26/57	45.864 (23.819–NR)	0.582 (0.331–1.02)
Baseline ECOG PS		0 or 1	74/235	NR (NR–NR)	69/162	54.341 (45.864–NR)	0.589 (0.424–0.818)
		>1	10/30	NR (29.503–NR)	9/19	43.598 (5.29–NR)	0.606 (0.246–1.493)
Baseline eGFR (MDRD)		<60 mL/min/1.73 m²	25/66	NR (48.066–NR)	31/62	43.598 (33.117–NR)	0.63 (0.371–1.068)
		≥60 mL/min/1.73 m²	59/197	NR (NR–NR)	47/119	59.663 (46.62–NR)	0.604 (0.412–0.887)
Extramedullary disease at baseline		Yes	6/19	NR (35.91–NR)	5/7	17.873 (2.825–NR)	0.174 (0.045–0.666)
		No	78/246	NR (NR–NR)	73/174	59.663 (46.16–NR)	0.618 (0.449–0.851)
R-ISS stage at study entry		I or II	67/234	NR (NR–NR)	65/157	59.663 (46.62–NR)	0.551 (0.391–0.776)
		III	16/29	45.602 (21.027–NR)	12/21	37.52 (4.6–NR)	0.736 (0.347–1.561)
Cytogenetic risk at baseline		High	18/40	NR (30.259–NR)	14/34	NR (37.454–NR)	0.971 (0.481–1.96)
		Standard	61/207	NR (NR–NR)	62/140	53.914 (43.006–NR)	0.517 (0.363–0.737)
HRCA† and 1q21+‡		Yes	8/19	NR (22.998–NR)	9/15	37.52 (5.782–NR)	0.491 (0.187–1.293)
		No	70/227	NR (NR–NR)	65/157	59.696 (45.864–NR)	0.604 (0.431–0.847)



A PFS benefit was observed with Isa-VRd vs VRd across most subgroups, including some difficult-to-treat populations with negative prognostic factors

*Age subgroups <70 and ≥70 years based on the randomization stratum as recorded based on interactive response technology. One patient in the Isa-VRd group stratified in the ≥70 category was 69 years old. Age subgroups <65, 65-<70, 70-<75, and 75-80 years based on age per the CRF. †Defined as del(17p) and/or t(4;14) and/or t(14;16). ‡1q21+ abnormality defined as at least 3 copies of 1q21.
HRCA, high-risk cytogenetic abnormality; MDRD, modification of diet in renal disease; NR, not reached.

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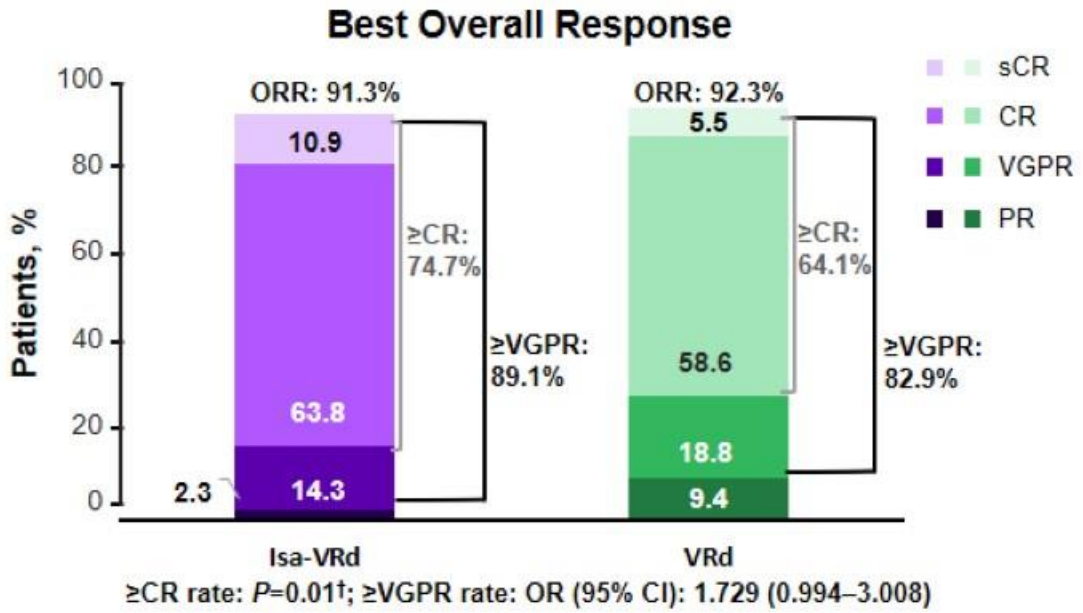
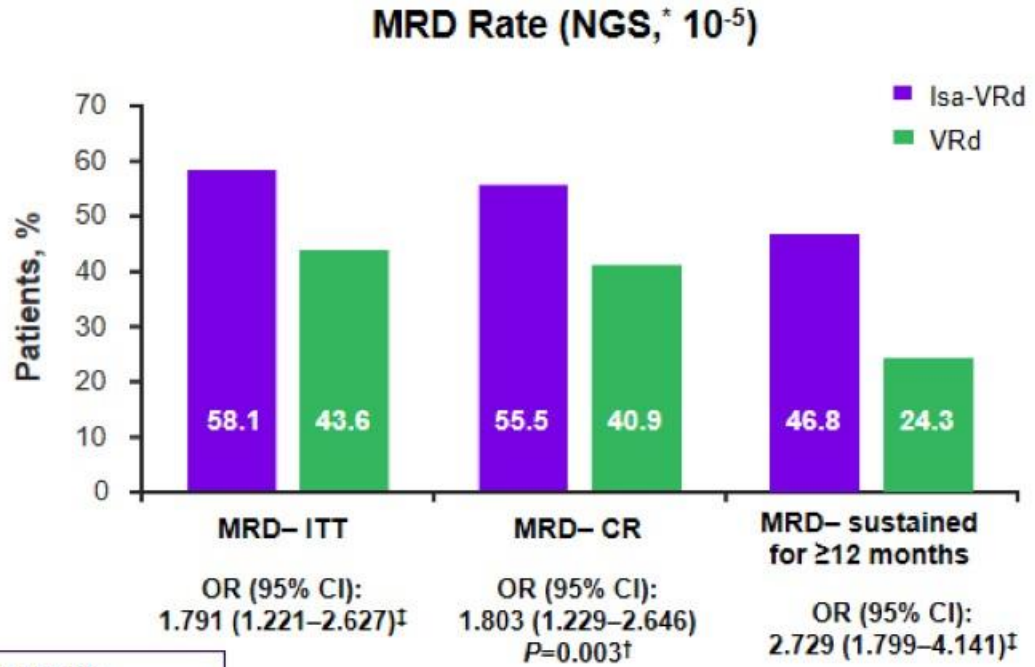
Depth of response in ITT population





Time to MRD–, median (95% CI)
Isa-VRd: 14.72 (11.53–24.08) months
VRd: 32.79 (17.51–45.11) months

Isa-VRd followed by Isa-Rd resulted in deep response rates, with a significant improvement in the MRD– CR rate, as well as higher rates of MRD– and sustained MRD– for ≥12 months

*Adaptive Biotechnologies clonoSEQ®. †Stratified Cochran-Mantel-Haenszel test. Two-sided significance level is 0.025. ‡*P* value not reported; not a key secondary endpoint. MRD–, minimal residual disease negativity.

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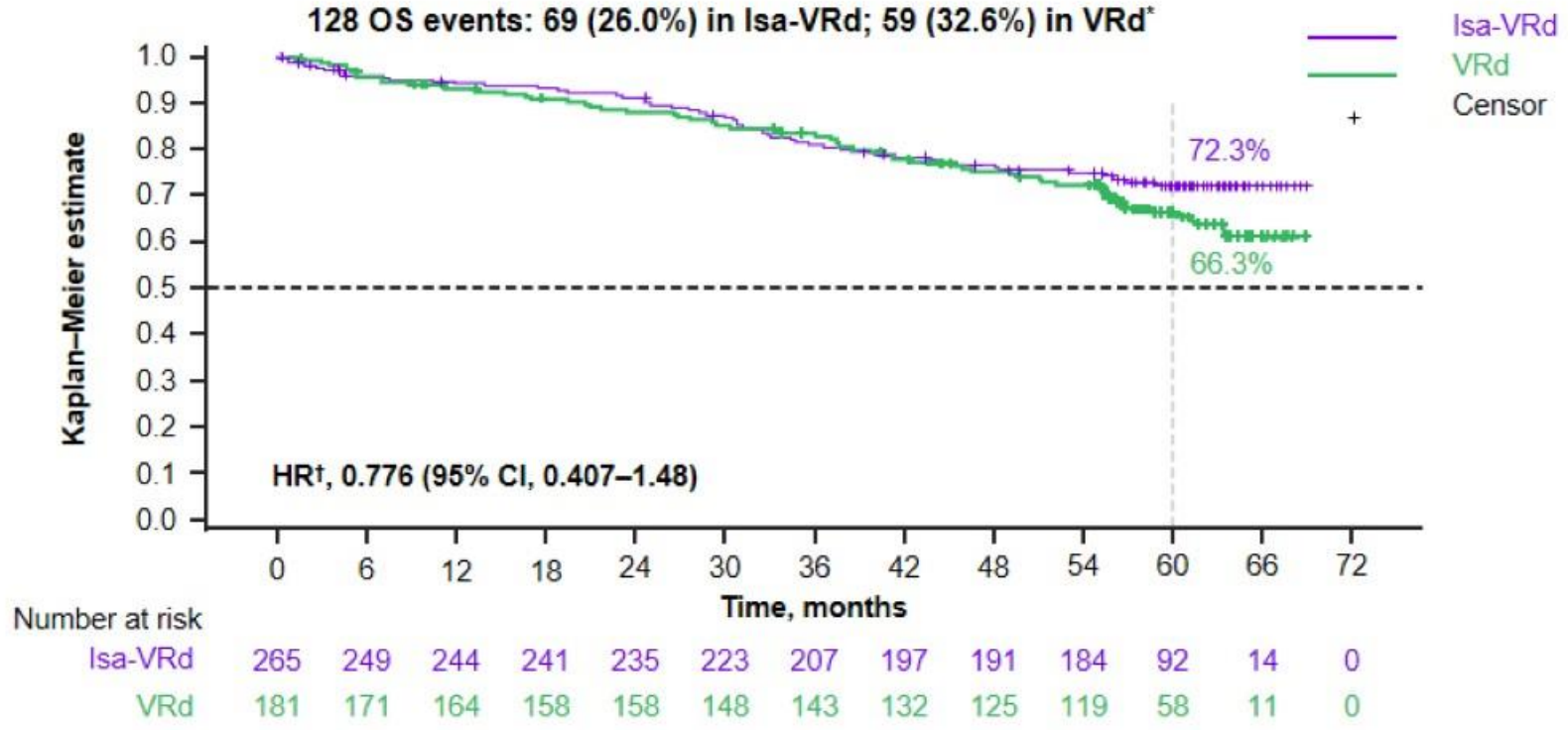
Interim OS analysis in ITT population



At a median follow-up of 5 years, OS is still immature; however, a favorable trend was observed for the Isa-VRd arm, with a 22.4% risk reduction compared with the VRd arm

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*Cutoff date for analysis: September 26, 2023. †HR passed the prespecified futility threshold (>1.1); follow-up is ongoing.

Safety summary (Safety population) (1/2)

TEAE overview, n (%)	Isa-VRd (n=263)	VRd (n=181)
Median treatment duration	**53.2 months**	**31.3 months**
Patients still on treatment	**125 (47.2)**	**44 (24.3)**
Any TEAE	262 (99.6)	178 (98.3)
Grade ≥3 TEAEs	241 (91.6)	152 (84.0)
Grade 5 TEAEs*	29 (11.0)	10 (5.5)
Serious TEAEs	186 (70.7)	122 (67.4)
Any TEAE leading to definitive treatment discontinuation	60 (22.8)	47 (26.0)
Event rate per patient-year†		
Any TEAE	13.39	12.69
Grade ≥3 TEAEs	1.17	0.99
Grade 5 TEAEs	0.03	0.02
Serious TEAEs	0.37	0.43
Any TEAE leading to definitive treatment discontinuation	0.07	0.09

The exposure-adjusted incidence rates suggest the difference in incidence of grade 5 TEAEs between arms was largely driven by the difference in treatment exposure ASCO 2024 Abstract 7500

*Causes of death occurring during the treatment period for the Isa-VRd group included COVID-19 pneumonia (n=7), COVID-19 pneumonia/multiorgan failure (n=1), renal tubular acidosis/TLS (n=1), septic shock (n=1), pneumonia (n=4), sudden death (n=4), undetermined (n=1), pneumonia pseudomonal (n=1), candida sepsis (n=1), hepatic cirrhosis (n=1), neuroendocrine carcinoma of the skin (n=1), pulmonary embolism (n=1), febrile neutropenia (n=1), pneumonia klebsiella and sepsis (n=1), respiratory failure (n=1), dyspnea (n=1), and sepsis (n=1). Causes of death occurring during the treatment period for the VRd group included pneumonia (n=2), COVID-19 (n=2), pneumonia aspiration (n=1), undetermined (n=1), pulmonary embolism (n=1), pleural effusion (n=1), sepsis (n=1), and bronchitis (n=1). †Calculated as number of patients with an event divided by total patient-years.

Safety summary (Safety population) (2/2)

Preferred term, n (%)	Isa-VRd (n=263)		VRd (n=181)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Hematologic laboratory abnormalities				
Neutropenia	230 (87.5)	143 (54.4)	145 (80.1)	67 (37.0)
Nonhematologic adverse events				
Infections	240 (91.3)	118 (44.9)	157 (86.7)	69 (38.1)
Pneumonia	79 (30.0)	53 (20.2)	35 (19.3)	23 (12.7)
Upper respiratory tract infection	90 (34.2)	2 (0.8)	61 (33.7)	2 (1.1)
Diarrhea	144 (54.8)	20 (7.6)	88 (48.6)	15 (8.3)
Peripheral sensory neuropathy	143 (54.4)	19 (7.2)	110 (60.8)	11 (6.1)
Cataract	100 (38.0)	41 (15.6)	46 (25.4)	20 (11.0)
Invasive second primary malignancies				
Solid tumors	22 (8.4)	14 (5.3)	8 (4.4)	6 (3.3)
Hematologic	3 (1.1)	1 (0.4)	2 (1.1)	2 (1.1)
Event rate per patient-year*				
Infections	1.181	-	1.166	-
Secondary primary malignancies†	0.041	-	0.026	-

Isa-VRd was well tolerated, and the safety profile remains consistent with the known safety profiles of each agent

ASCO 2024 Abstract 7500

*Calculated as number of patients with an event divided by total patient-years. Patients were followed yearly. †Including non-melanoma skin cancer.

Summary

- IMROZ is the first global Phase 3 study of an anti-CD38 mAb in combination with VRd in patients with transplant-ineligible NDMM
- Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or death by 40.4% (mPFS NR [Isa-VRd] vs 54.34 months [VRd]; HR, 0.596), highlighting an outstanding PFS benefit in patients with transplant-ineligible NDMM
- Isa-VRd resulted in deep response rates vs VRd, with a statistically significant improvement in the MRD– (NGS, 10^{-5}) CR as well as higher rates of MRD– and almost double sustained MRD– for ≥12 months
- Although OS is still immature, a trend in favor of Isa-VRd was also observed
- Isa-VRd was well tolerated, and the safety profile remains consistent with that of each agent

The improved efficacy of Isa-VRd followed by Isa-Rd, combined with a consistent safety profile, provides an important treatment option for frontline disease control, establishing Isa-VRd as a new SOC for patients aged ≤80 years with transplant-ineligible NDMM

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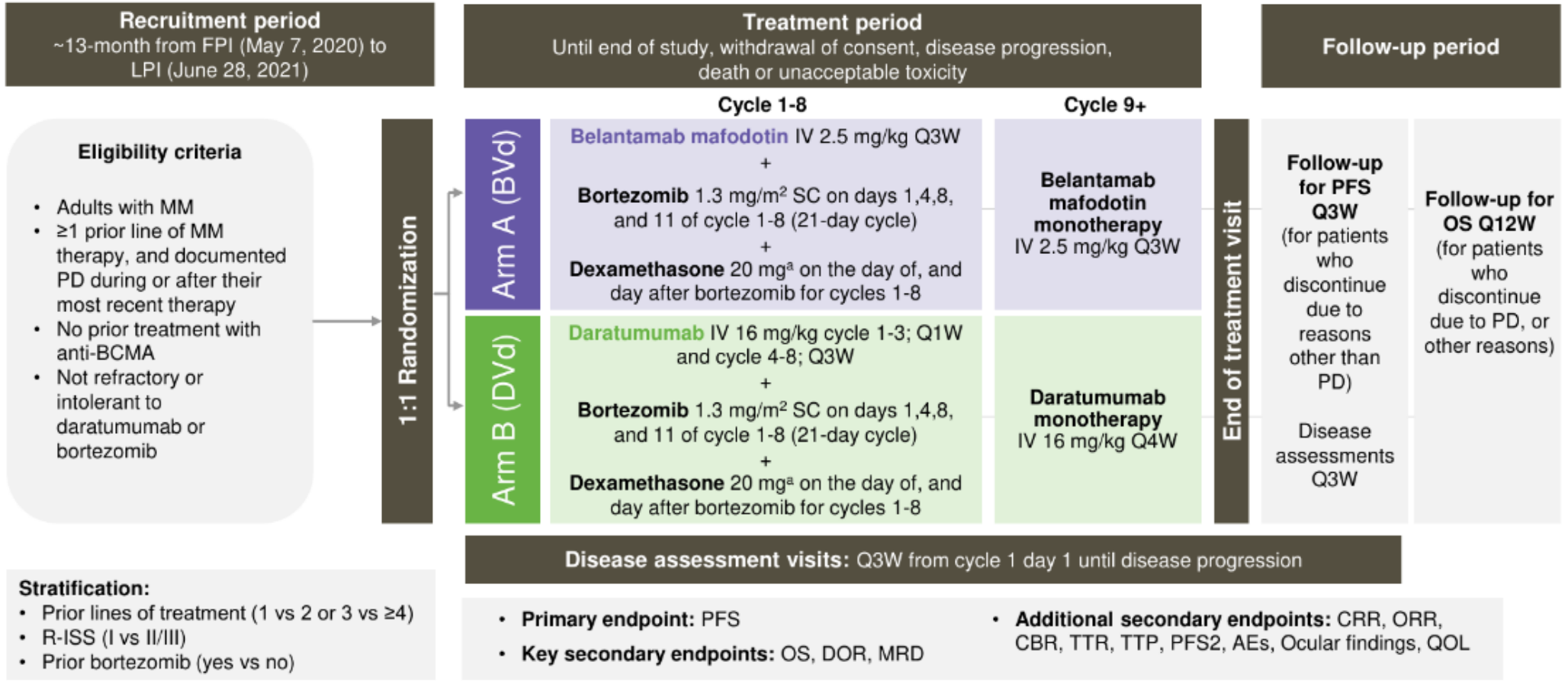
CD, cluster of differentiation; NR, not reached; SOC, standard of care.

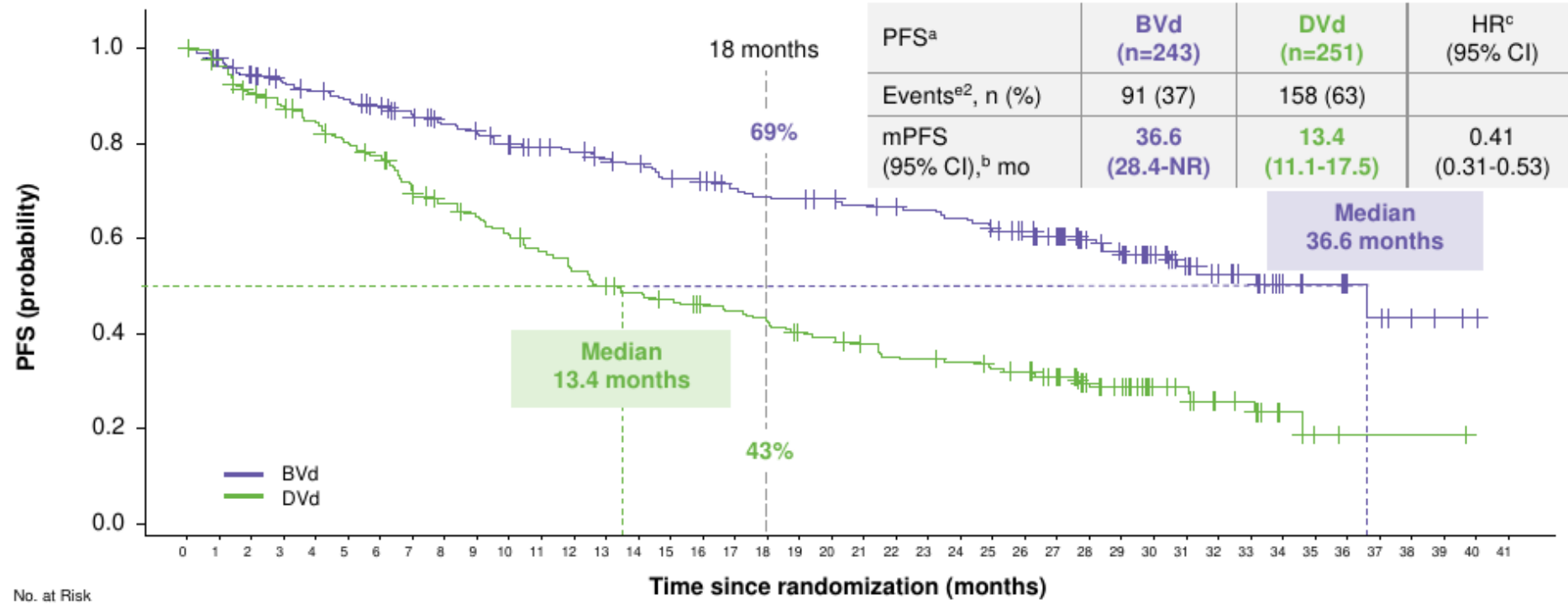
DREAMM-7 is a phase 3 study examining a belantamab mafodotin-based combination at first relapse in MM (NCT04246047)



ASCO 2024 Abstract 7503

DREAMM-7: BVd time to disease progression or death vs DVd[1]

PFS[a]	BVd (n=243)	DVd (n=251)	HR[c] (95% CI)	*p*-value[d]
Events[e2], n (%)	91 (37)	158 (63)		
mPFS (95% CI),[b] mo	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.00001

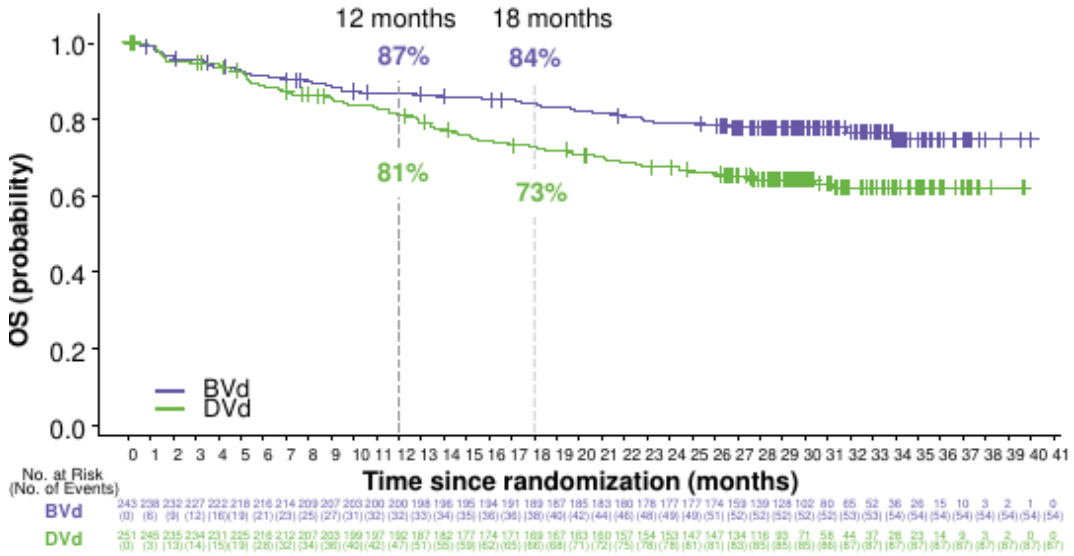


After median follow up of 28.2 months (range, 0.10-40) BVd demonstrated a mPFS that was 23 months longer than DVd (36.6 vs 13.4 months).

ASCO 2024 Abstract 7503

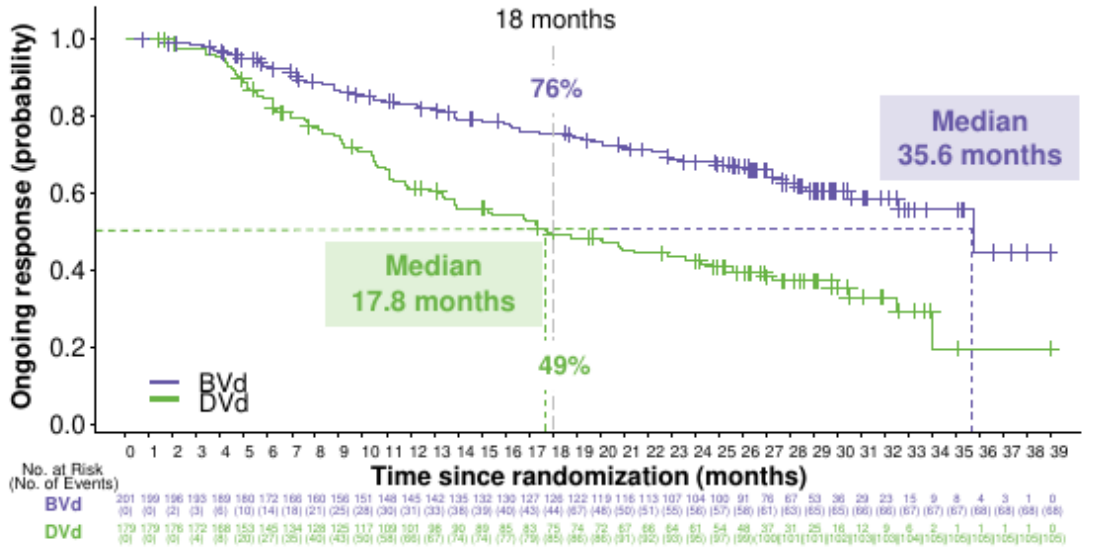
DREAMM-7: OS and DOR data - BVd vs DVd[2]

OS[a]	BVd (n=243)	DVd (n=251)	HR[c] (95% CI)	*p*-value[d]
Events, n (%)	54 (22)	87 (35)		
mOS (95% CI),[b] mo	NR	NR	0.57 (0.4-0.8)	.00049[e]



Although data is immature, OS showed a trend favoring the BVd arm; additional OS follow-up is ongoing

DOR[a]	BVd (n=201)	DVd (n=179)
Events, n (%)	68 (34)	105 (59)
Patients with ongoing response	106 (53)	52 (29)
mDOR (95% CI),[b] mo	35.6 (30.5-NR)	17.8 (13.8-23.6)



BVd median DOR 35.6 vs DVd 17.8 months.

A separate analysis of restricted mean DOR comparing DOR between arms showed a statistically significant benefit in favor of BVd ($p<.00001$).[f1]

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DREAMM-7: Safety Overview

n (%)	BVd (N=242)	DVd (N=246)
Any AE	242 (100)	246 (100)
AEs related to any study treatment[a]	242 (100)	234 (95)
Grade 3/4 AE	229 (95)	187 (76)
Exposure adjusted, events/person-years[b]	**68.8**	**62.4**
Related to any study treatment[a]	219 (90)	164 (67)
AEs leading to permanent discontinuation of any study treatment	75 (31)	46 (19)
Exposure adjusted, events/person-years[b]	**22.5**	**15.4**
AEs related to any study treatment leading to permanent discontinuation of any study treatment[a]	64 (26)	36 (15)
AEs leading to dose reduction	182 (75)	146 (59)
AEs leading to dose interruption/delay	228 (94)	185 (75)
Any SAE	121 (50)	90 (37)
Exposure adjusted, events/person-years[b]	**36.3**	**30.0**
Related to any study treatment[a]	47 (19)	30 (12)
Fatal SAEs	23 (10)	19 (8)
Fatal SAEs related to any study treatment[a]	7 (3)	2 (<1)

ASCO 2024 Abstract 7503

DREAMM-7: Ocular AEs (CTCAE)[1]

Grade ≥3 ocular events (CTCAE) in ≥5% of patients in either treatment group by preferred term and maximum grade

Ocular AESIs (by CTCAE) preferred terms, n (%)	BVd* (N=242)		DVd (N=246)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Any Event	191 (79)	82 (34)	72 (29)	7 (3)
Vision blurred	160 (66)	53 (22)	26 (11)	2 (<1)
Dry eye	123 (51)	17 (7)	17 (7)	0
Eye irritation	103 (43)	12 (5)	13 (5)	0
Visual impairment	26 (11)	13 (5)	4 (2)	1 (<1)

Ocular exams for patients in the BVd arm were assessed at screening/baseline and then every 3 weeks prior to dosing up to at least the 6th dose of belantamab mafodotin and then every three months if there were no significant ocular findings. For patients in the DVd arm, ocular exams were performed at screening/baseline with on treatment ocular exams performed at cycle 6 and then decreased to every 6 months.

The keratopathy and visual acuity (KVA) scale incorporates corneal examination findings (via slit lamp examination) and changes in best corrected visual acuity (BCVA) into a composite grade. The KVA scale was not initially utilized in DREAMM-7 and was introduced post-protocol amendment. Ocular events per overall KVA scale were 84% in the BVd arm.[2]

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Thank you!