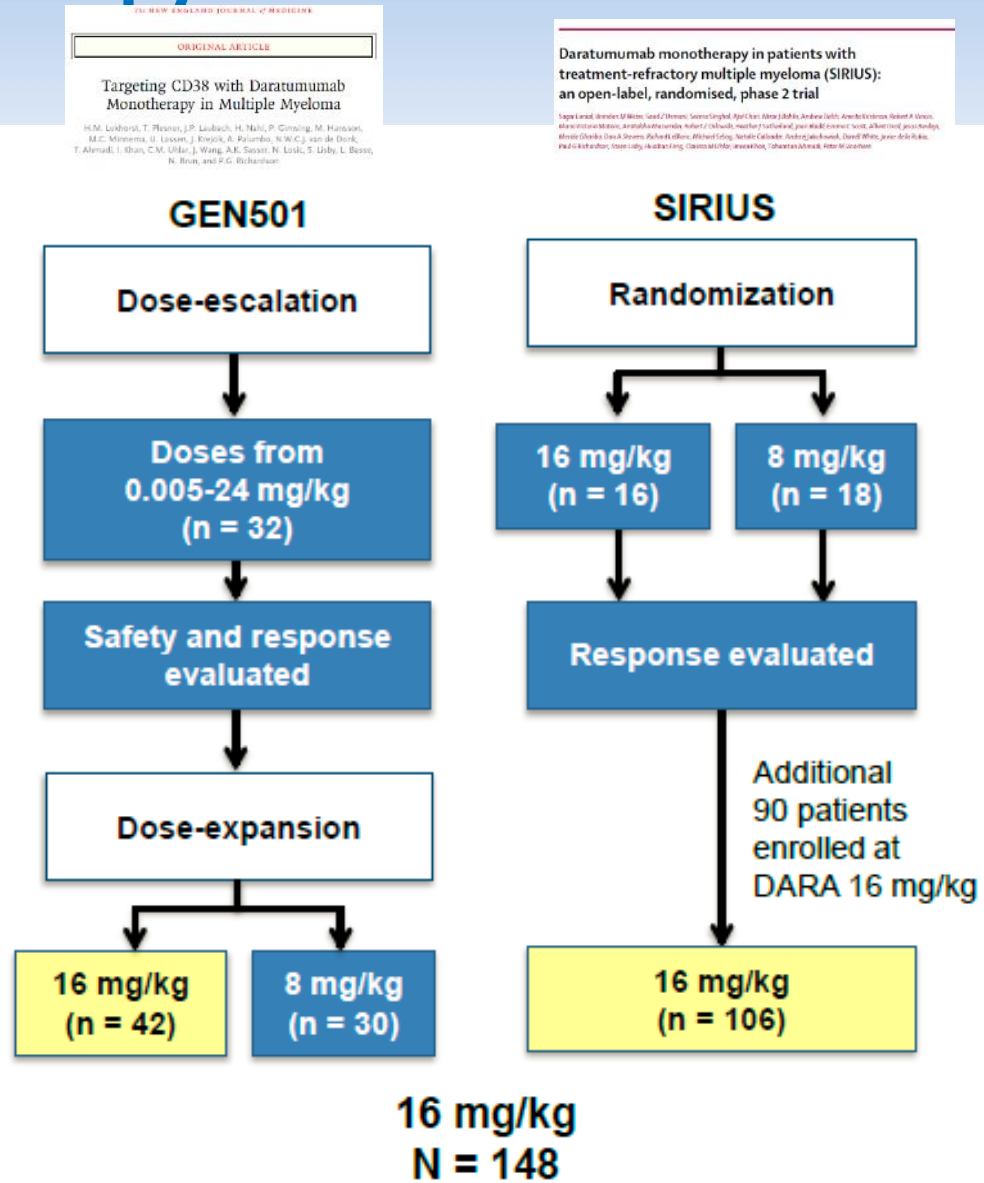


DARA Monotherapy Studies

- ≥ 18 years of age, ECOG status ≤ 2 ^{1,2}
- GEN501¹
 - Open-label, multicenter, phase 1/2, dose-escalation and dose-expansion study
 - Relapsed from or refractory to ≥ 2 prior lines of therapy including PIs and IMiDs
- SIRIUS²
 - Open-label, multicenter, phase 2 study
 - Patients had received ≥ 3 prior lines of therapy, including a PI and an IMiD, or were double refractory to a PI and an IMiD
- DARA was approved by the FDA on November 16, 2015, based on these studies



Baseline Characteristics

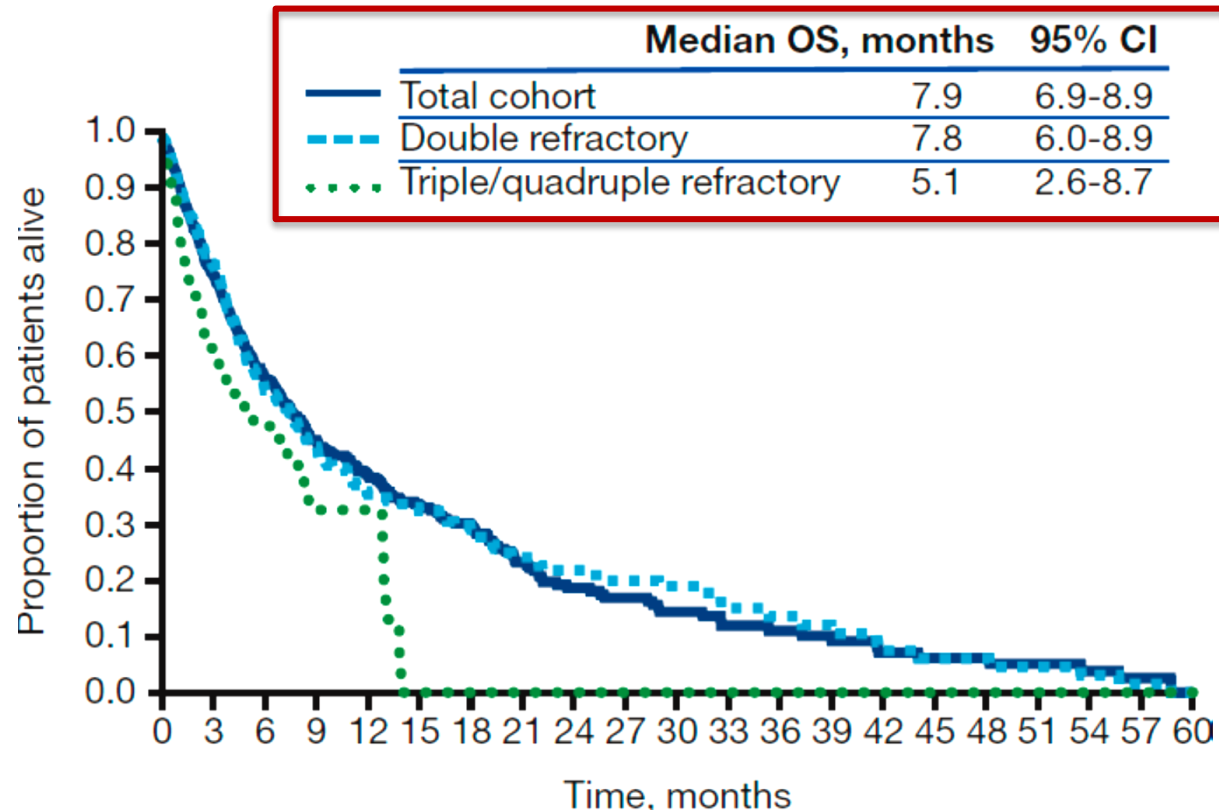
	16 mg/kg		
	GEN501, Part 2 n = 42	SIRIUS n = 106	Combined N = 148
Median (range) age, y	64.0 (44-76)	63.5 (31-84)	64 (31-84)
≥65 years of age, n (%)	20 (48)	48 (45)	68 (46)
Female/male sex, %	36/64	51/49	53/47
ECOG score, n (%)			
0	12 (29)	29 (27)	41 (28)
1	28 (67)	69 (65)	97 (66)
2	2 (5)	8 (8)	10 (7)
Median (range) time since diagnosis, y	5.8 (0.8-23.7)	4.8 (1.1-23.8)	5.1 (0.8-23.8)
Median (range) number of prior lines of therapy	4 (2-12)	5 (2-14)	5 (2-14)
>3 prior lines of therapy, n (%)	26 (62)	87 (82)	113 (76)
Prior ASCT, n (%)	31 (74)	85 (80)	116 (78)
Prior PI, n (%)	42 (100)	106 (100)	148 (100)
Bortezomib	42 (100)	105 (99)	147 (99)
Carfilzomib	8 (19)	53 (50)	61 (41)
Prior IMiD, n (%)	40 (95)	106 (100)	146 (99)
Lenalidomide	40 (95)	105 (99)	145 (98)
Pomalidomide	15 (36)	67 (63)	82 (55)
Thalidomide	19 (45)	47 (44)	66 (45)

Baseline Refractory Status

Refractory to, n (%)	16 mg/kg		
	GEN501, Part 2 n = 42	SIRIUS n = 106	Combined N = 148
Last line of therapy	32 (76)	103 (97)	135 (91)
Both PI and IMiD	27 (64)	101 (95)	128 (86)
PI only	3 (7)	3 (3)	6 (4)
IMiD only	4 (10)	1 (1)	5 (3)
PI + IMiD + alkylating agent	21 (50)	79 (75)	100 (68)
Bortezomib	30 (71)	95 (90)	125 (84)
Carfilzomib	7 (17)	51 (48)	58 (39)
Lenalidomide	31 (74)	93 (88)	124 (84)
Pomalidomide	15 (36)	67 (63)	82 (55)
Thalidomide	12 (29)	29 (27)	41 (28)
Alkylating agent only	25 (60)	82 (77)	107 (72)

Relapsed and Refractory MM

Median overall survival in the combined eligible population from the IMS LifeLink and OPTUM datasets (N = 662) and double refractory (n = 350) and triple/quadruple refractory (n = 93) patients.



Efficacy in Combined Analysis

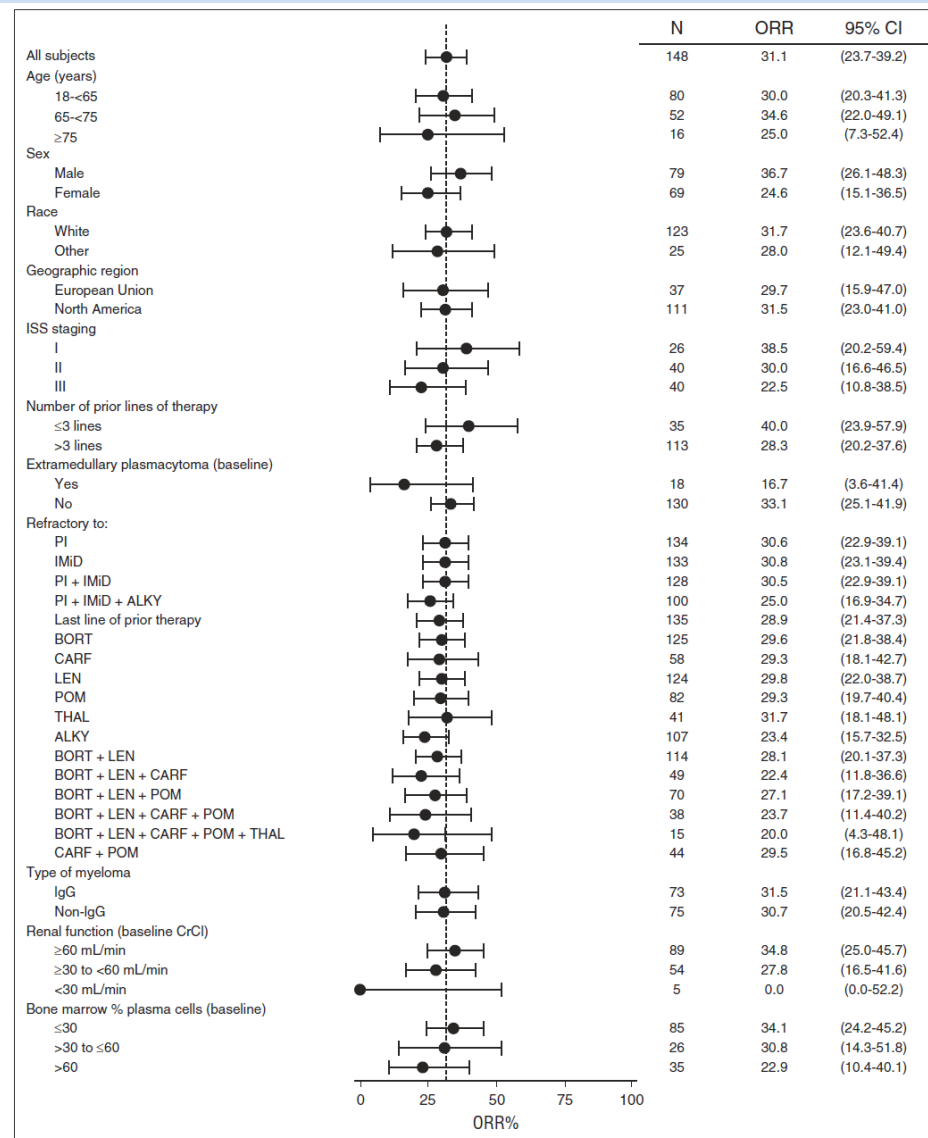
Median Follow up 20.7 months

		16 mg/kg (N = 148)	
Response	n (%)	95% CI	
ORR	46 (31.1)	23.7-39.2	
Clinical benefit (ORR + MR)	55 (37.2)	29.4-45.5	
VGPR or better (sCR+CR+VGPR)	20 (13.5)	8.5-20.1	
CR or better (sCR+CR)	7 (4.7)	1.9-9.5	
sCR	3 (2.0)	0.4-5.8	
CR	4 (2.7)	0.7-6.8	
VGPR	13 (8.8)	4.8-14.6	
PR	26 (17.6)	11.8-24.7	
MR	9 (6.1)	2.8-11.2	
SD	68 (45.9)	37.7-54.3	
PD	18 (12.2)	7.4-18.5	
NE	7 (4.7)	1.9-9.5	

83.1 %

- Median DOR = 7.6 (95% CI, 5.6-NE) months
- ORR = 31% and was consistent in subgroups including age, number of prior lines of therapy, refractory status, or renal function
- Time to response = 0.95 (0.5-5.6) months

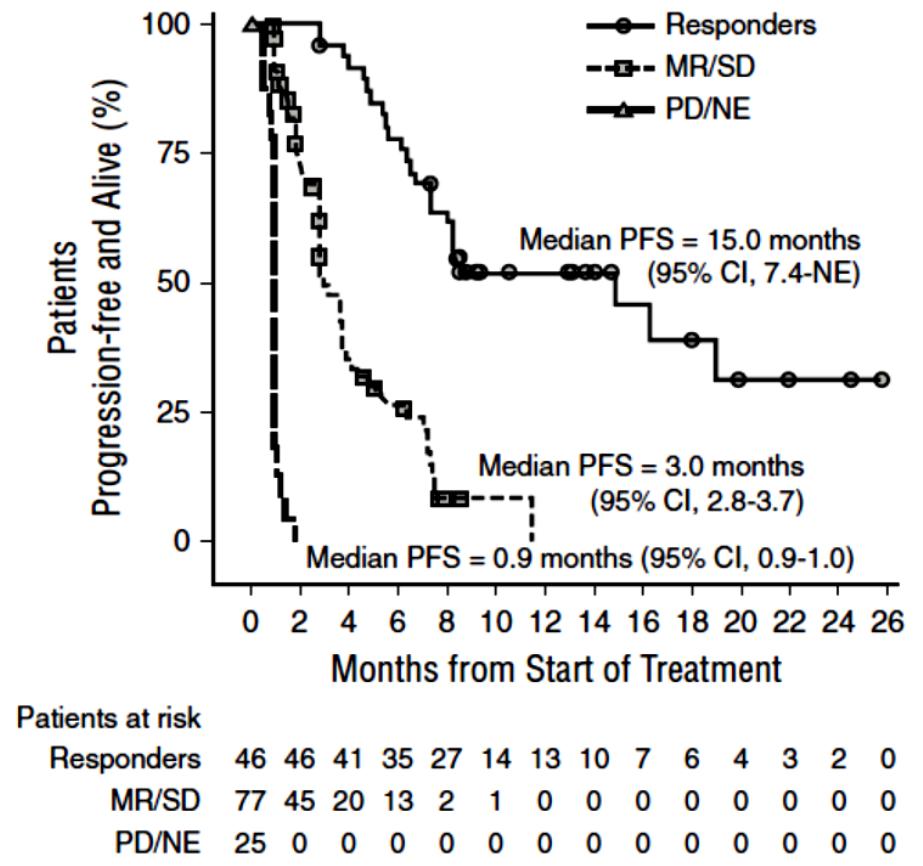
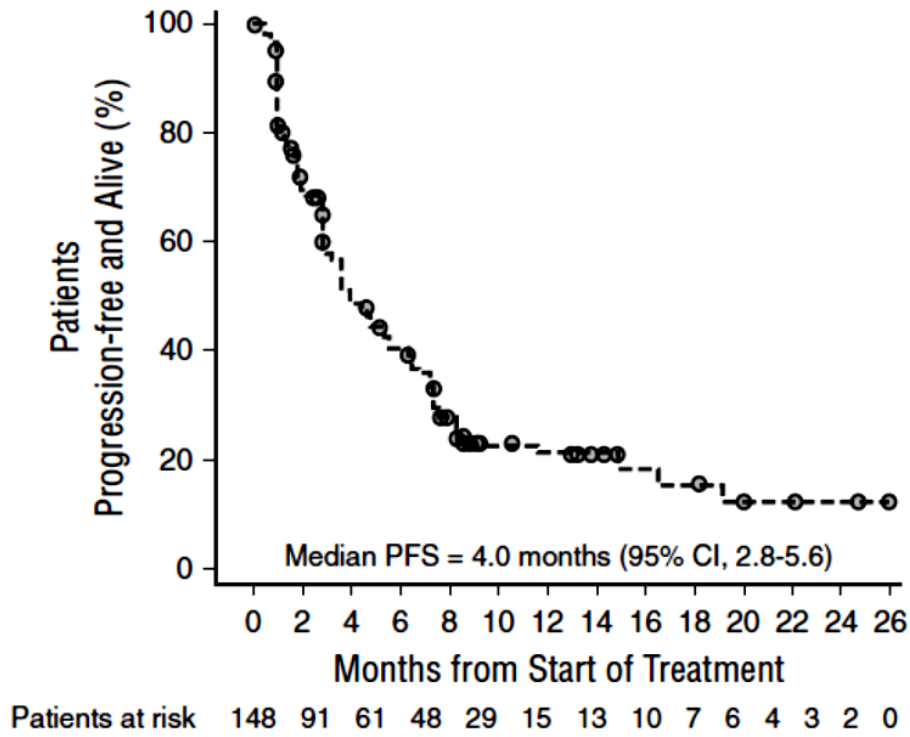
Efficacy in Combined Analysis - Subgroups



Responses were seen across all subgroups regardless of prior lines of therapy, refractory status, renal function, and baseline percentage of plasma cells in the bone marrow

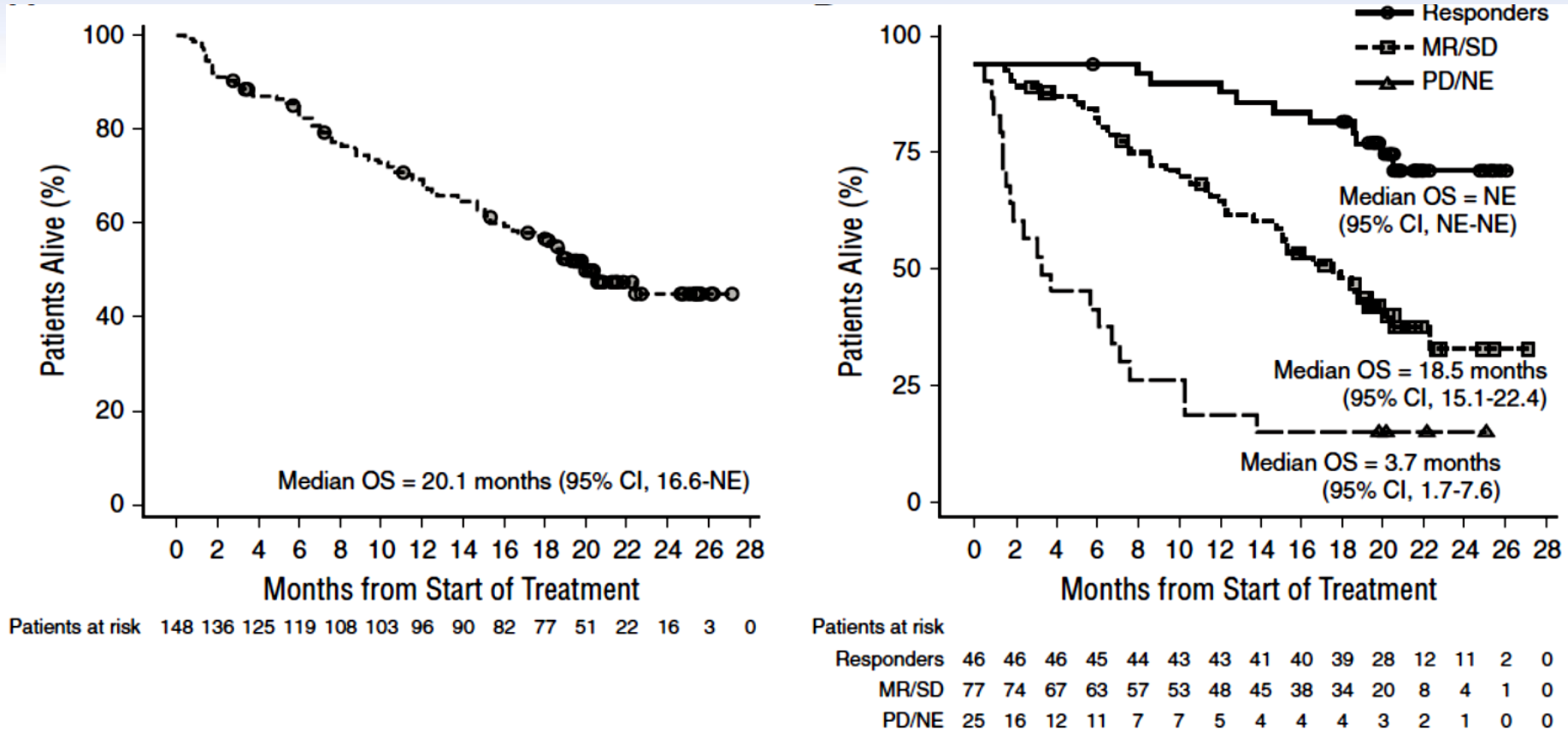
PFS

median follow-up 20.7 months



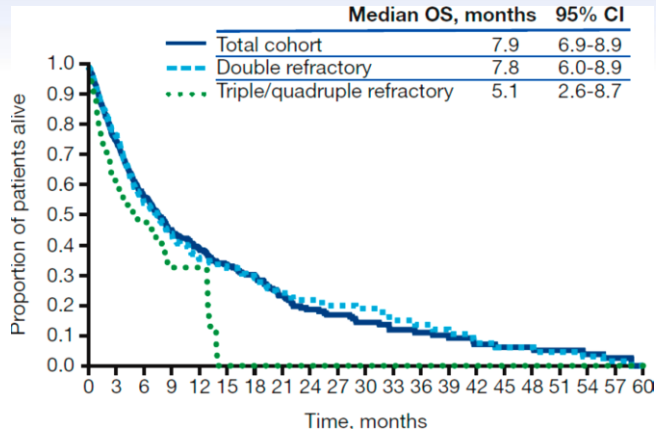
OS

median follow-up 20.7 months

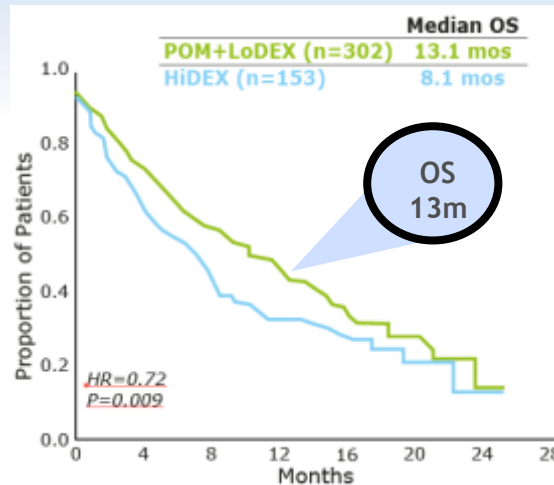


- For the combined analysis, **median OS = 20.1 months (95% CI, 16.6-NE months)**
- 18-month and 24-month OS rate = 56.5% and 45% respectively

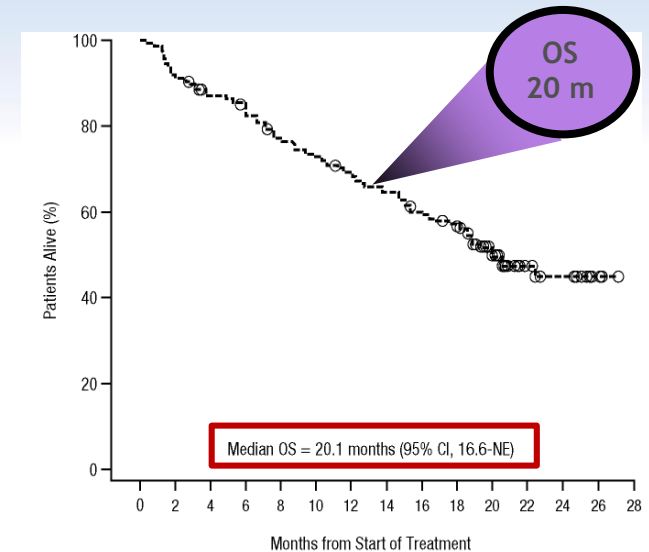
The Breakthrough (BT) population outcome



mOS 5-8 months in patients relapsed or refractory MM after ≥ 3 prior lines of therapy, including IMiD and PI



Pomalidomide: mOS 13,1months in patients relapsed or refractory MM after ≥ 2 prior lines of therapy, including IMiD and PI



Daratumumab: mOS of 20 months in patients with relapsed or refractory, double refractory or relapsed after ≥ 3 L, including pomalidomide and carfilzomib

COMPARATIVE EFFICACY OF DARATUMUMAB MONOTHERAPY AND POMALIDOMIDE PLUS LOW-DOSE DEXAMETHASONE (POM+LoDex) IN THE TREATMENT OF MULTIPLE MYELOMA: A MATCHING ADJUSTED INDIRECT COMPARISON (MAIC)

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¹Janssen Health Economics & Market Access DMEA Statistics & Modeling, Beerse, Belgium; ²Janssen Health Economics & Market Access DMEA, High Wycombe, UK; ³Janssen EMA Medical Affairs, Neuss, Germany

INTRODUCTION

Despite the introduction of proteasome inhibitors (PI) and immunomodulatory drugs (IMiD), multiple myeloma (MM) remains a fatal disease with a median overall survival (OS) of 16.7 months.¹ Daratumumab (Dara) is a novel anti-CD38 monoclonal antibody (mAb) that has shown promising results in phase III clinical trials. In the DREAMM2 study, Dara monotherapy was compared against Pomalidomide plus low-dose dexamethasone (POM+LoDex) in MM patients who had received at least two prior lines of therapy. The primary endpoint was OS. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS. In addition, Dara monotherapy was associated with a higher rate of adverse events (AE) compared to POM+LoDex. The results of this study suggest that Dara monotherapy may be a viable treatment option for MM patients who have received at least two prior lines of therapy.

OBJECTIVE

To compare the OS of Dara monotherapy with POM+LoDex in patients who have received at least two prior lines of therapy.

METHODS

Patients Treated With Dara

Inclusion Criteria:
 - MM patients receiving Dara monotherapy in phase III clinical trials (DREAMM2, DREAMM3, and DREAMM4).
 - Age ≥ 18 years.
 - Eastern Cooperative Oncology Group (ECOG) performance grade 0-2.
 - Patients received at least two prior lines of therapy.
Exclusion Criteria:
 - Patients who received Dara monotherapy in phase II clinical trials.
 - Patients who received Dara monotherapy in phase I clinical trials.
Study Population:
 - 100 MM patients receiving Dara monotherapy in phase III clinical trials.
 - 100 MM patients receiving Dara monotherapy in phase II clinical trials.
Study Population:
 - 100 MM patients receiving Dara monotherapy in phase I clinical trials.

Patients Treated With POM+LoDex

Inclusion Criteria:
 - MM patients receiving POM+LoDex in phase III clinical trials (DREAMM2, DREAMM3, and DREAMM4).
 - Age ≥ 18 years.
 - ECOG performance grade 0-2.
 - Patients received at least two prior lines of therapy.
Exclusion Criteria:
 - Patients who received POM+LoDex in phase II clinical trials.
 - Patients who received POM+LoDex in phase I clinical trials.

Matching Adjusted Treatment Comparison

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.

Table 1. Baseline Characteristics and Characteristics of MM Patients Treated With Dara and POM+LoDex. (Continued)

Characteristic	Dara (n=100)	POM+LoDex (n=100)
Median age (years)	68	68
ECOG performance grade		
0	10	10
1	40	40
2	50	50
Median number of prior lines of therapy	2	2
Median time to progression (months)	12.5	12.5
Median OS (months)	16.7	16.7

RESULTS

Matching Adjusted Treatment Comparison

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.

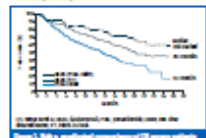


Figure 1. Overall survival (OS) for Dara monotherapy (n=100) and POM+LoDex (n=100). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

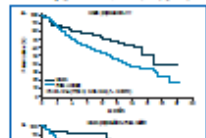


Figure 2. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by age (≤65 vs >65). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

Figure 3. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by ECOG performance grade (0-1 vs 2). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

Additional OS Analysis Based on Depth of Response

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.

Additional OS Analysis Based on Depth of Response

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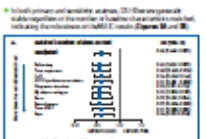


Figure 4. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by depth of response (CR vs non-CR). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

Additional OS Analysis Based on Depth of Response

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.

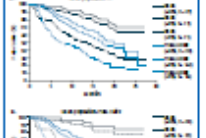


Figure 5. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by depth of response (CR vs non-CR) and ECOG performance grade (0-1 vs 2). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

Figure 6. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by depth of response (CR vs non-CR) and ECOG performance grade (0-1 vs 2). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

CONCLUSIONS

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.

Additional OS Analysis Based on Depth of Response

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.



Figure 7. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by depth of response (CR vs non-CR) and ECOG performance grade (0-1 vs 2). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

Additional OS Analysis Based on Depth of Response

The MAIC analysis was conducted using the R package 'MatchIt'. The analysis was stratified by age, ECOG performance grade, and number of prior lines of therapy. The results showed that Dara monotherapy was non-inferior to POM+LoDex in terms of OS.

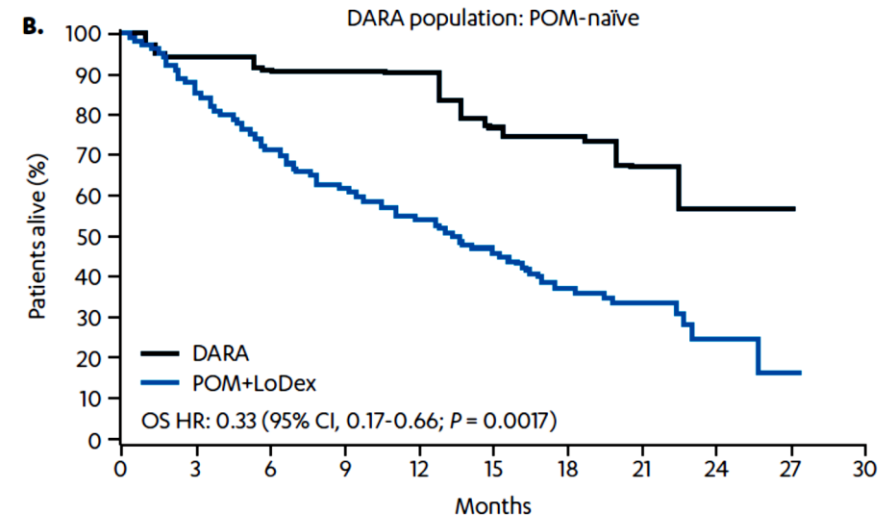
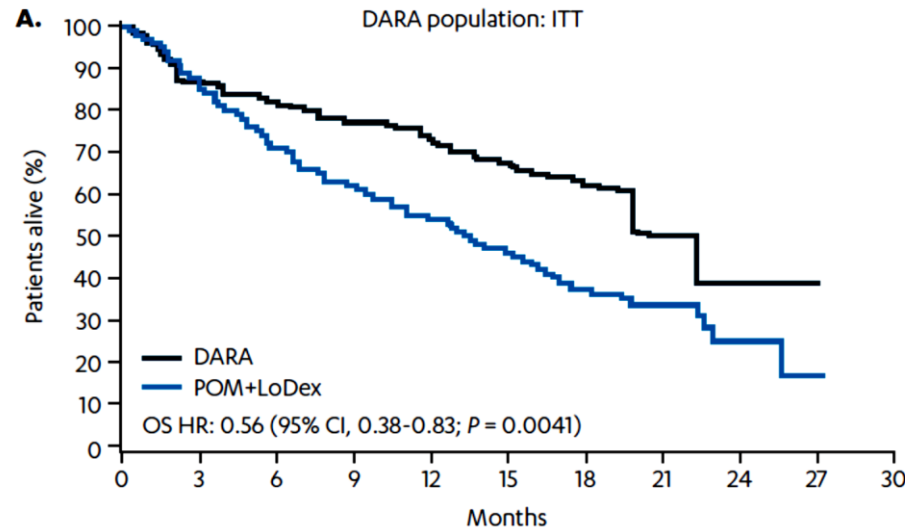


Figure 8. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by depth of response (CR vs non-CR) and ECOG performance grade (0-1 vs 2). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

Figure 9. OS for Dara monotherapy (n=100) and POM+LoDex (n=100) stratified by depth of response (CR vs non-CR) and ECOG performance grade (0-1 vs 2). The Dara monotherapy group showed a median OS of 16.7 months, while the POM+LoDex group showed a median OS of 16.7 months.

MAIC of OS among patients treated with DARA versus POM+LoDex in the ITT population and POM-naïve population

Due to the high percentage of POM-refractory patients (55%) treated with DARA in GEN501 and SIRIUS who were not included in the POM-naïve MM-003 study, the OS advantage of DARA may be a conservative estimate



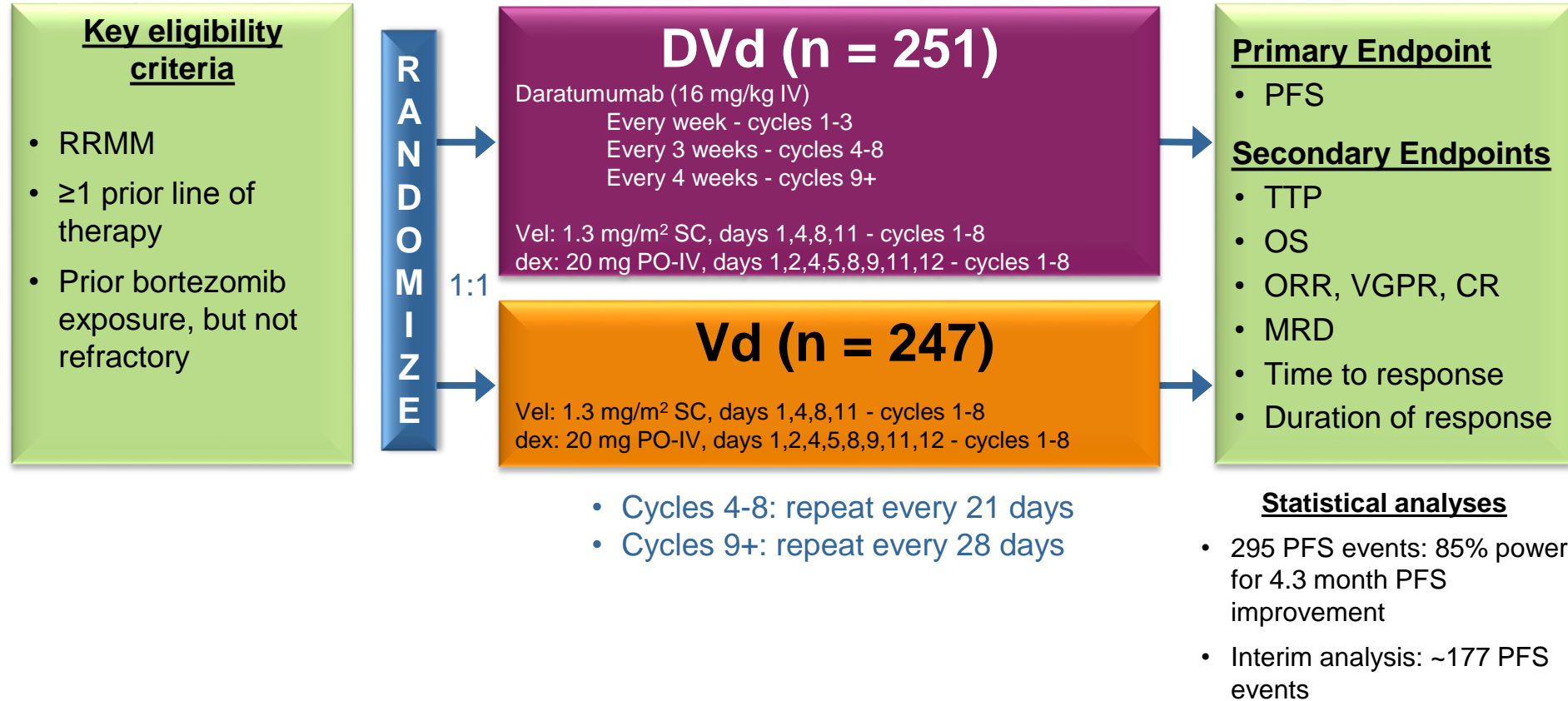
HR 0.56 (0.38-0.83);p= 0.0041

HR 0.33 (0.17-0.66);p= 0.0017

- **The primary analysis suggests a 44% reduction in the risk of death compared with POM+LoDex**
- **Comparison of POM-naïve patients from both studies suggests a 67% reduction in the risk of death compared with POM+LoDex**

CASTOR: Study Design

Multicenter, randomized, open-label, active-controlled phase 3 study



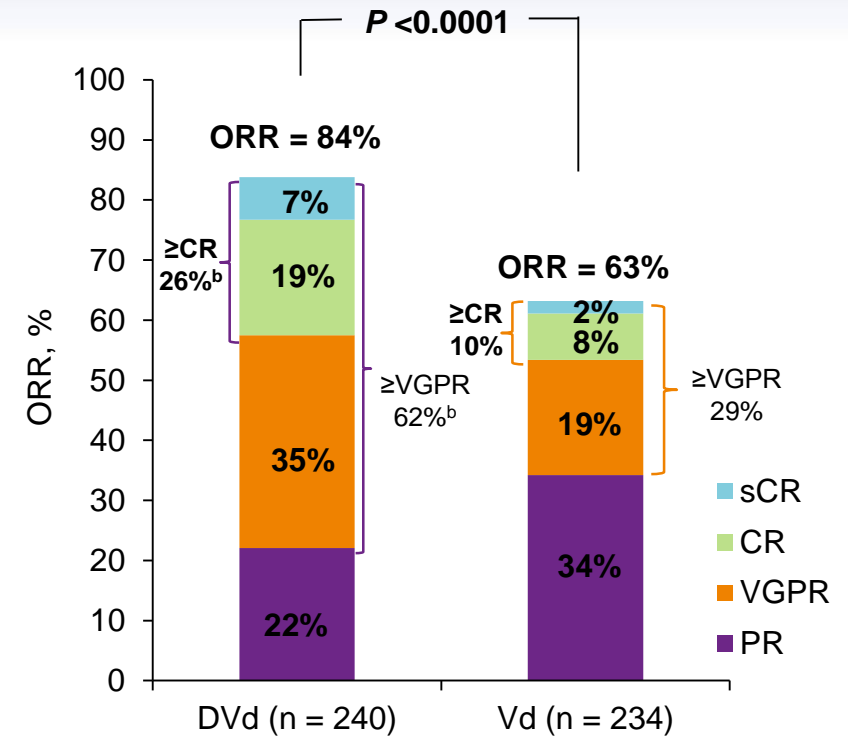
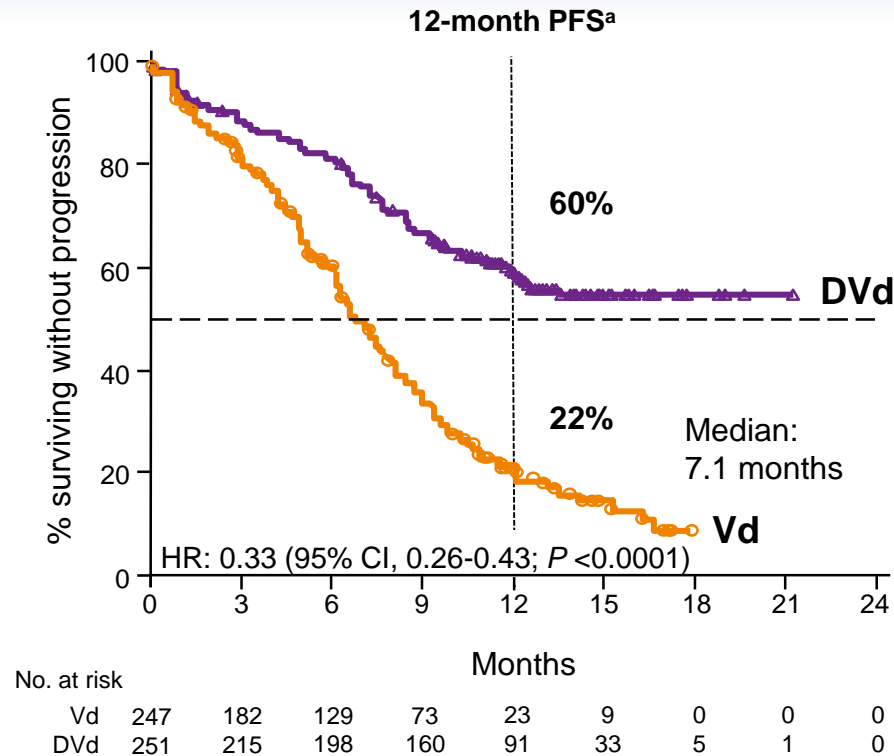
Daratumumab IV administered in 1000 mL to 500 mL; gradual escalation from 50 mL to 200 mL/hour permitted

Baseline Demographics and Clinical Characteristics

Characteristic	DVd (n = 251)	Vd (n = 247)
Age, years		
Median (range)	64 (30-88)	64 (33-85)
≥75, n (%)	23 (9)	35 (14)
ISS staging, n (%) ^a		
I	98 (39)	96 (39)
II	94 (38)	100 (41)
III	59 (24)	51 (21)
Cytogenetic profile, n (%) ^b		
Del17p	28 (16)	21 (12)
t(4;14)	14 (8)	15 (9)
Time from diagnosis, years	3.87	3.72
Median (range)	(0.7-20.7)	(0.6-18.6)

Characteristic	DVd (n = 251)	Vd (n = 247)
Prior lines of therapy, n (%)		
1	122 (49)	113 (46)
2	70 (28)	74 (30)
3	37 (15)	32 (13)
>3	22 (9)	28 (11)
Prior ASCT, n (%)	156 (62)	149 (60)
Prior PI, n (%)	169 (67)	172 (70)
Prior IMiD, n (%)	179 (71)	198 (80)
Prior PI + IMiD, n (%)	112 (45)	129 (52)
Refractory to IMiD, n (%)	74 (30)	90 (36)
Refractory to last line of therapy, n (%)	76 (30)	85 (34)

Updated Efficacy

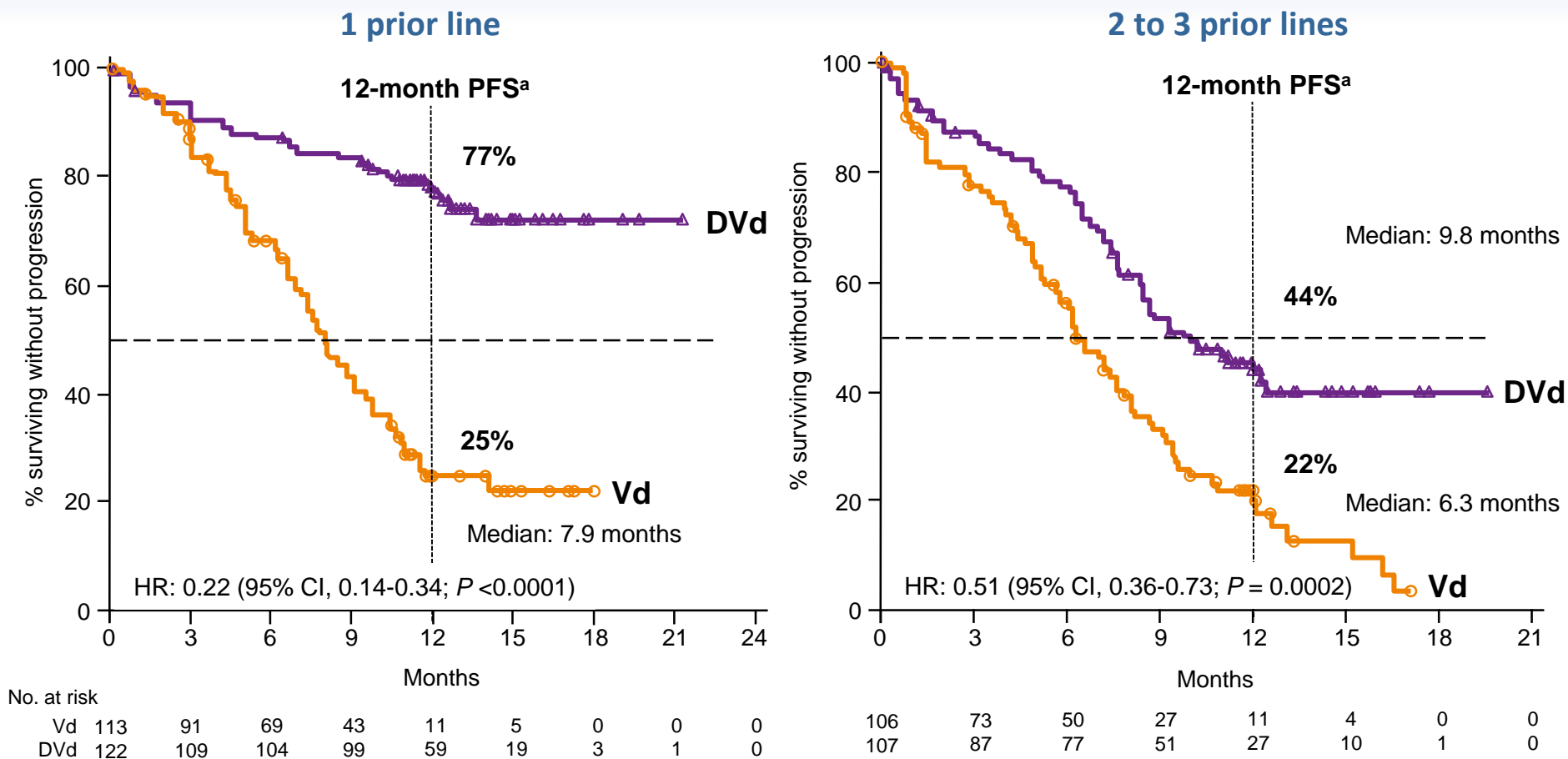


- Median (range) follow-up: 13.0 (0-21.3) months
- An additional 7% of patients receiving DVd achieved \geq CR with longer follow-up

Responses continue to deepen in the DVd group with longer follow-up

ITT, intent-to-treat.
 Note: PFS = ITT population; ORR = response-evaluable population.
^aKaplan-Meier estimate.
^b $P < 0.0001$ for DVd versus Vd.

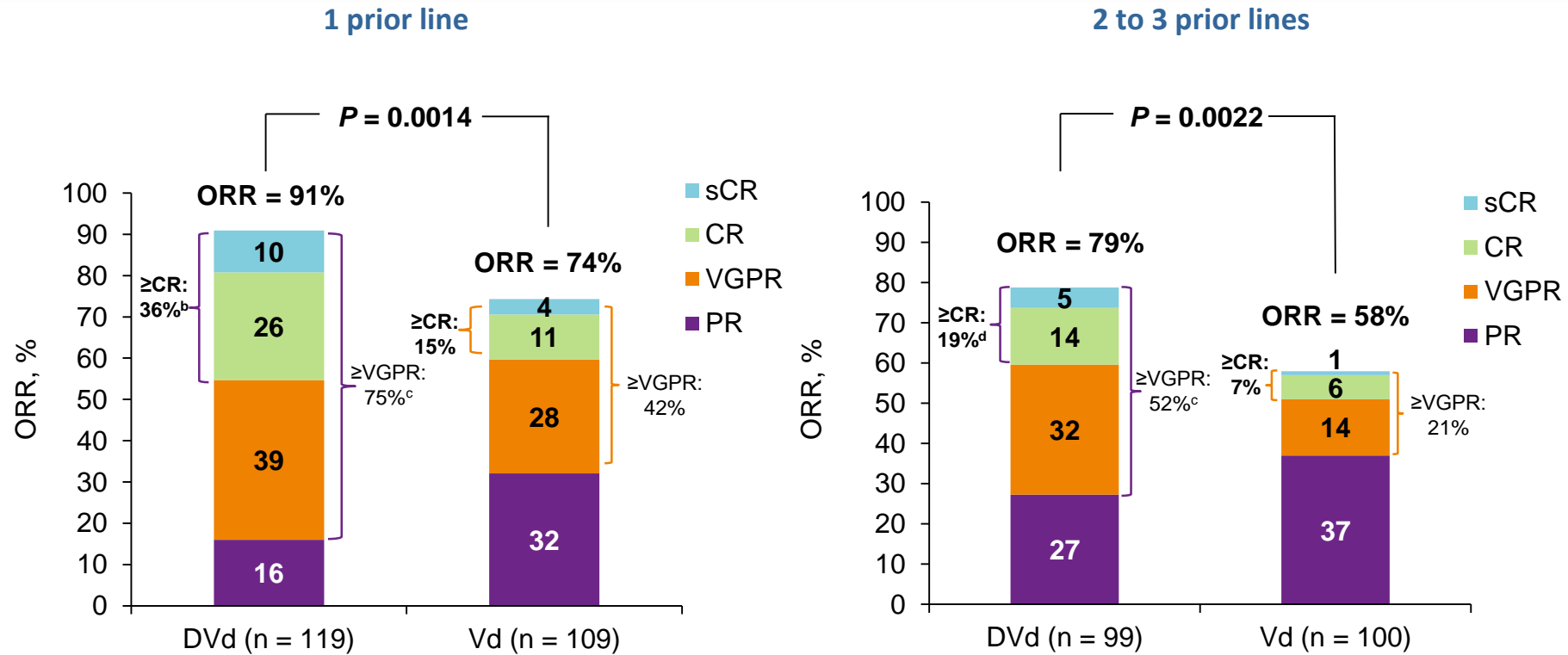
PFS: Prior Lines of Treatment



DVd is superior to Vd regardless of prior lines of therapy, with greatest benefit observed in 1 prior line

^aKaplan-Meier estimate.

ORR by Prior Lines^a



More patients achieve a deeper response with DVd after 1 prior line of treatment

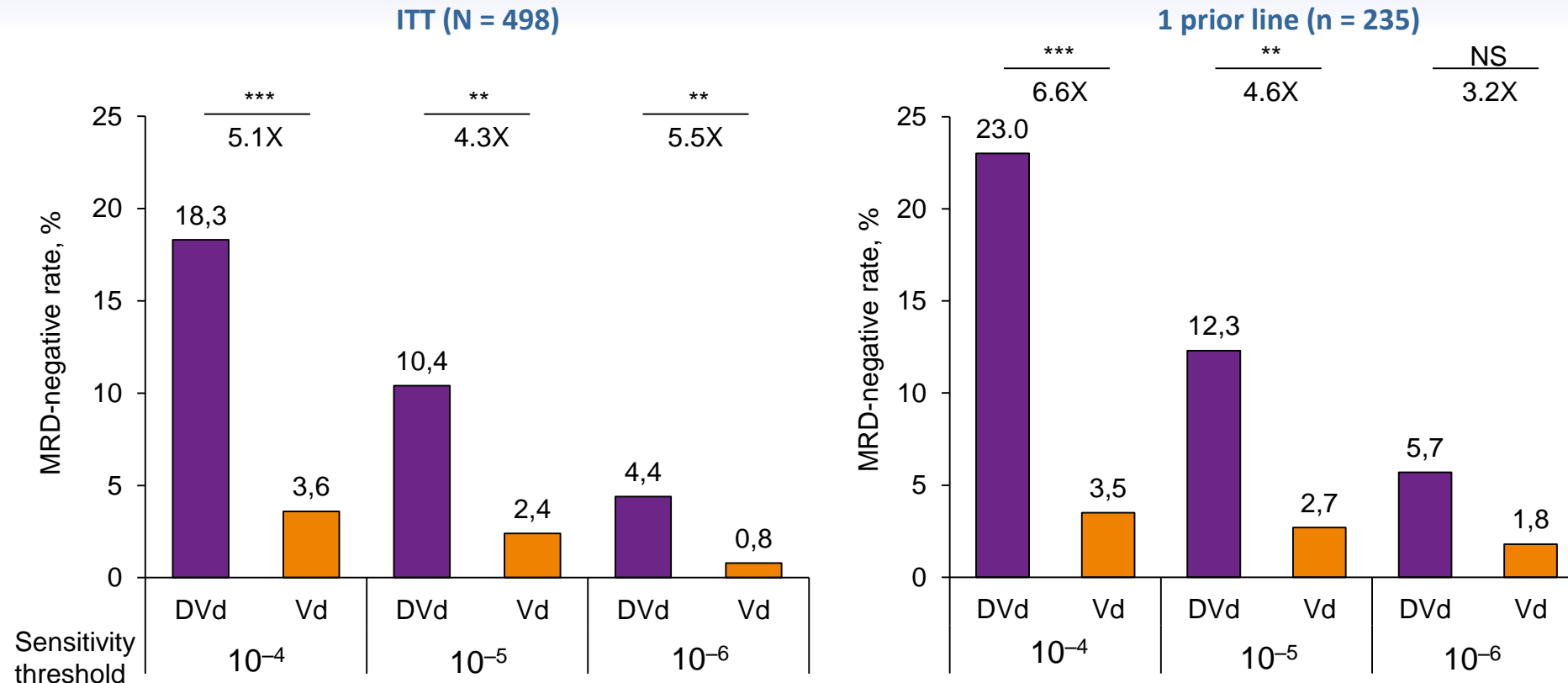
^aResponse-evaluable population.

^bP = 0.0006 for DVd vs Vd.

^cP < 0.0001 for DVd vs Vd.

^dP = 0.0133 for DVd vs Vd.

MRD rates by prior lines of therapy

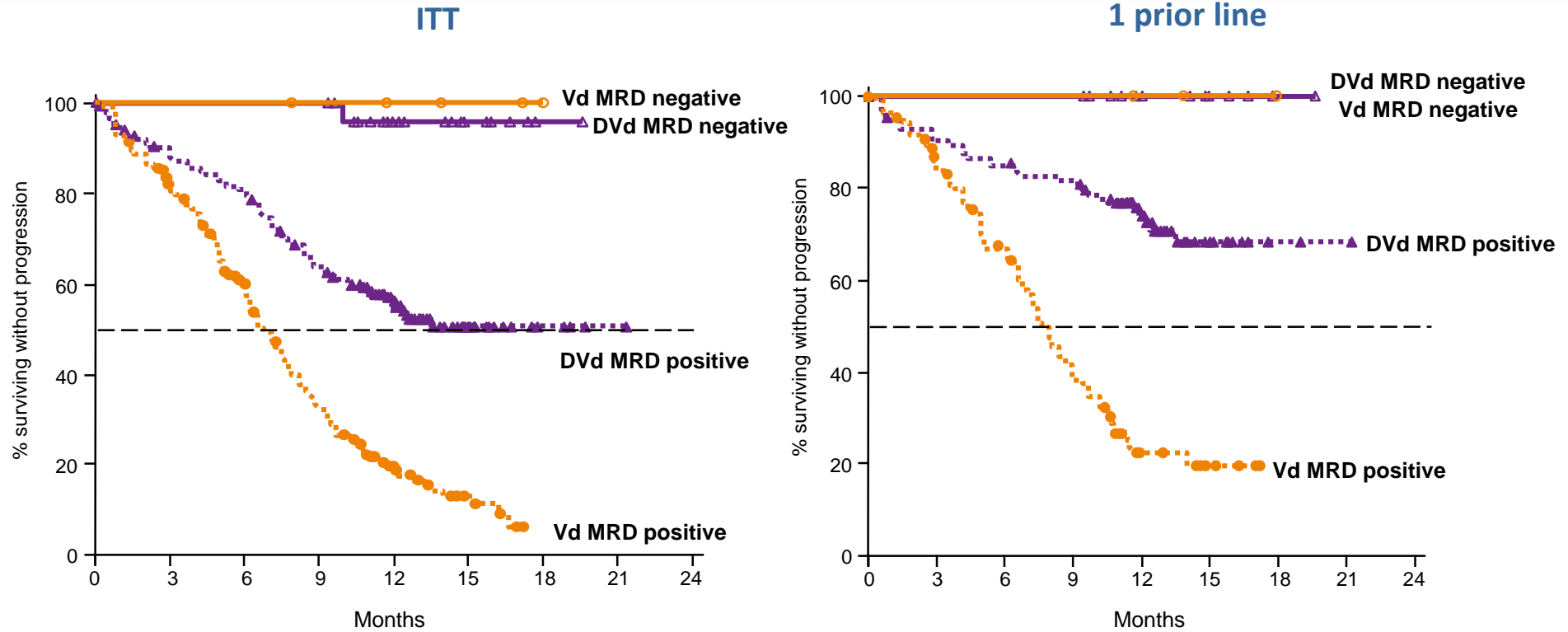


- MRD was evaluated by ClonoSEQ-NGS-based assay in a central laboratory at 3 sensitivity thresholds, for patients with suspected CR and also for patients who maintain CR at Cycle 9 and Cycle 15

MRD-negative rates for DVd were ≥3-fold higher across all thresholds

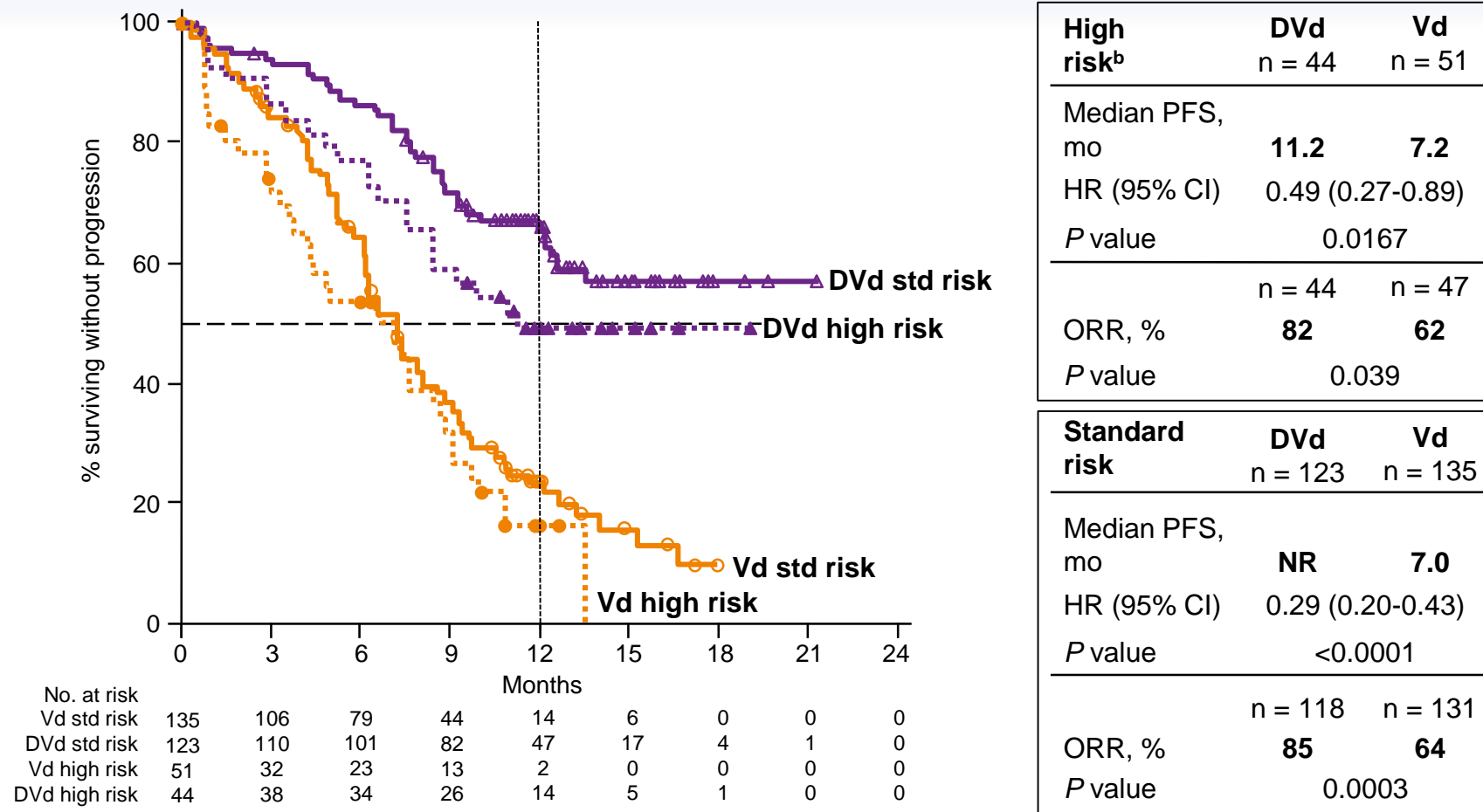
***P < 0.0001. **P < 0.01. NS, not significant; NGS, next-generation sequencing.
 P values calculated using likelihood-ratio chi-square test.
 MRD-negativity rate = proportion of patients with negative MRD test results at any time during treatment.

PFS: MRD Status (10^{-5})



MRD negativity is associated with better outcomes

PFS: Cytogenetic Risk in All Evaluable Patients^a



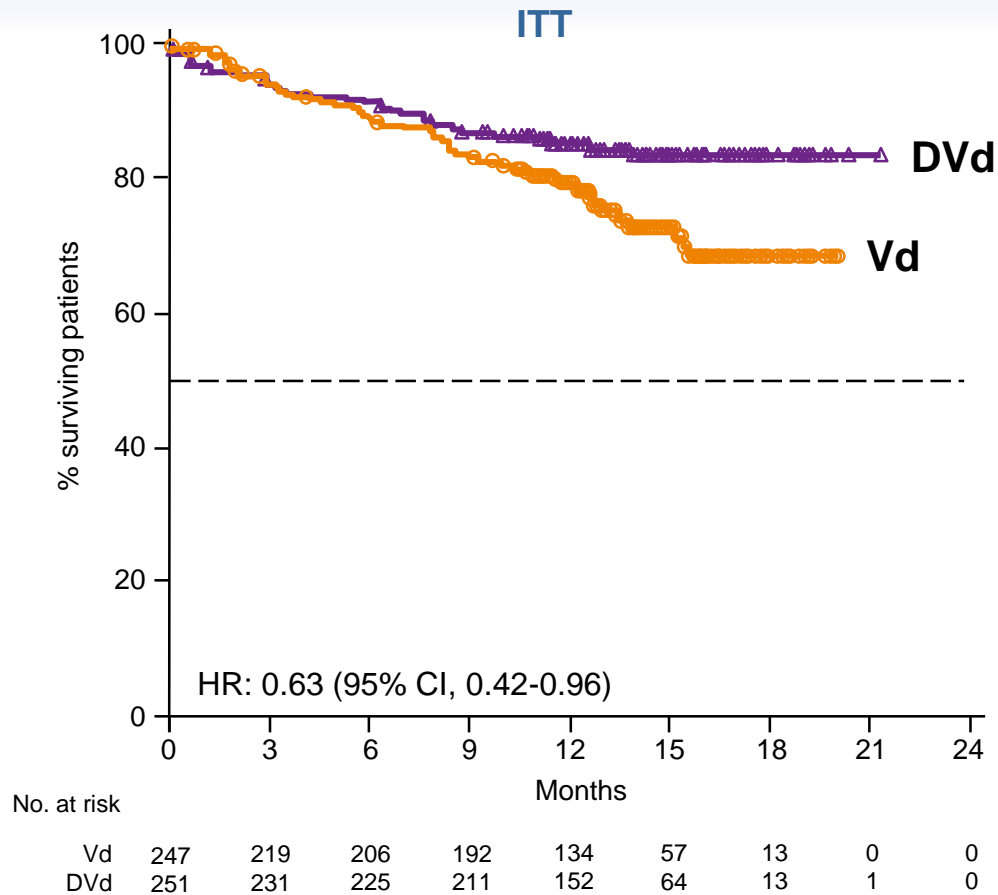
DVd improves outcomes regardless of cytogenetic risk

NR, not reached.

^aITT/Biomarker risk-evaluable analysis set.

^bCentral NGS. High-risk patients had any of t(4;14), t(14;16), or del17p. Standard-risk patients had an absence of high-risk abnormalities.

OS



OS events

— 37 (15%) in DVd

— 58 (24%) in Vd

OS HR for DVd versus Vd by prior lines:

— 1 prior line = HR: 0.42

(95% CI, 0.19-0.93)

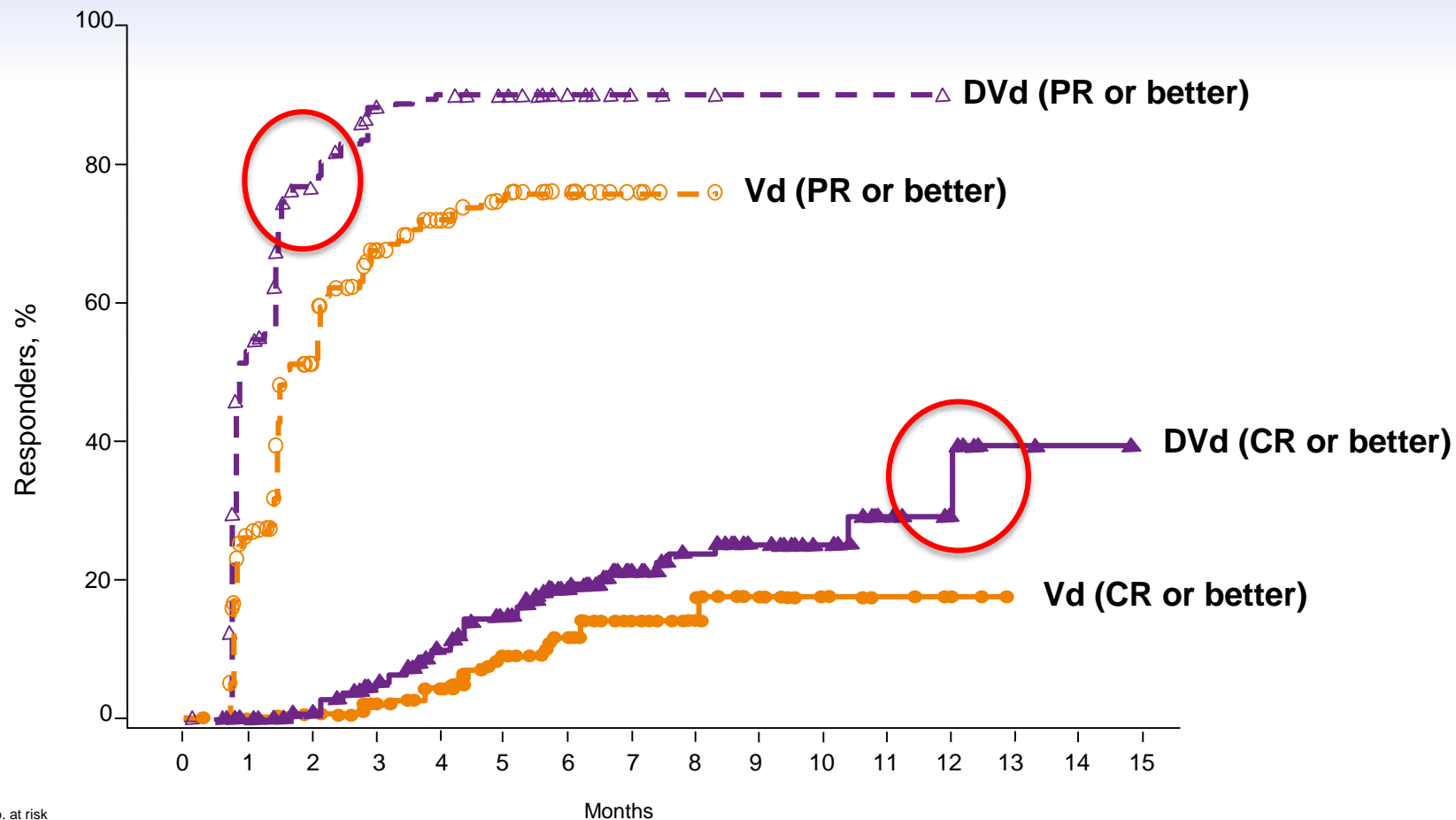
— 1 to 3 prior lines = HR: 0.54

(95% CI, 0.34-0.84)

Curves are beginning to separate, but OS data are immature

Median OS was NR; results did not cross the prespecified stopping boundary.

Time to Response



	No. at risk															
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Vd (PR or better)	234	155	89	49	35	21	14	4	1	0	0	0	0	0	0	0
DVd (PR or better)	240	108	48	22	17	14	9	4	2	1	1	1	0	0	0	0
Vd (CR or better)	234	215	197	177	161	121	91	48	27	17	8	5	3	0	0	0
DVd (CR or better)	240	229	220	203	185	163	116	76	55	40	27	13	7	2	1	0

Most Common TEAEs (All Patients): Updated Analysis

	DVd (n = 243)		Vd (n = 237)	
Hematologic, n (%)	All grade ≥25% ^a	Grade 3/4 ≥5% ^a	All grade ≥25% ^a	Grade 3/4 ≥5% ^a
Thrombocytopenia	145 (60)	110 (45)	105 (44)	78 (33)
Anemia	67 (28)	36 (15)	75 (32)	38 (16)
Neutropenia	45 (19)	32 (13)	23 (10)	11 (5)
Lymphopenia	32 (13)	24 (10)	9 (4)	6 (3)
Nonhematologic, n (%)				
Peripheral sensory neuropathy	120 (49)	11 (5)	90 (38)	16 (7)
Diarrhea	83 (34)	9 (4)	53 (22)	3 (1)
Upper respiratory tract infection	72 (30)	6 (3)	43 (18)	1 (0.4)
Cough	66 (27)	0	30 (13)	0
Fatigue	53 (22)	12 (5)	58 (25)	8 (3)
Pneumonia	33 (14)	22 (9)	28 (12)	23 (10)
Hypertension	22 (9)	16 (7)	8 (3)	2 (0.8)

- Grade 3/4 TEAEs: 79% of DVd patients versus 63% of Vd patients
- Discontinuations due to TEAEs: 9% of DVd patients versus 9% of Vd patients^b
- No new IRRs; incidence remains stable with longer follow-up (45%)

Infusion-related Reactions (IRRs)

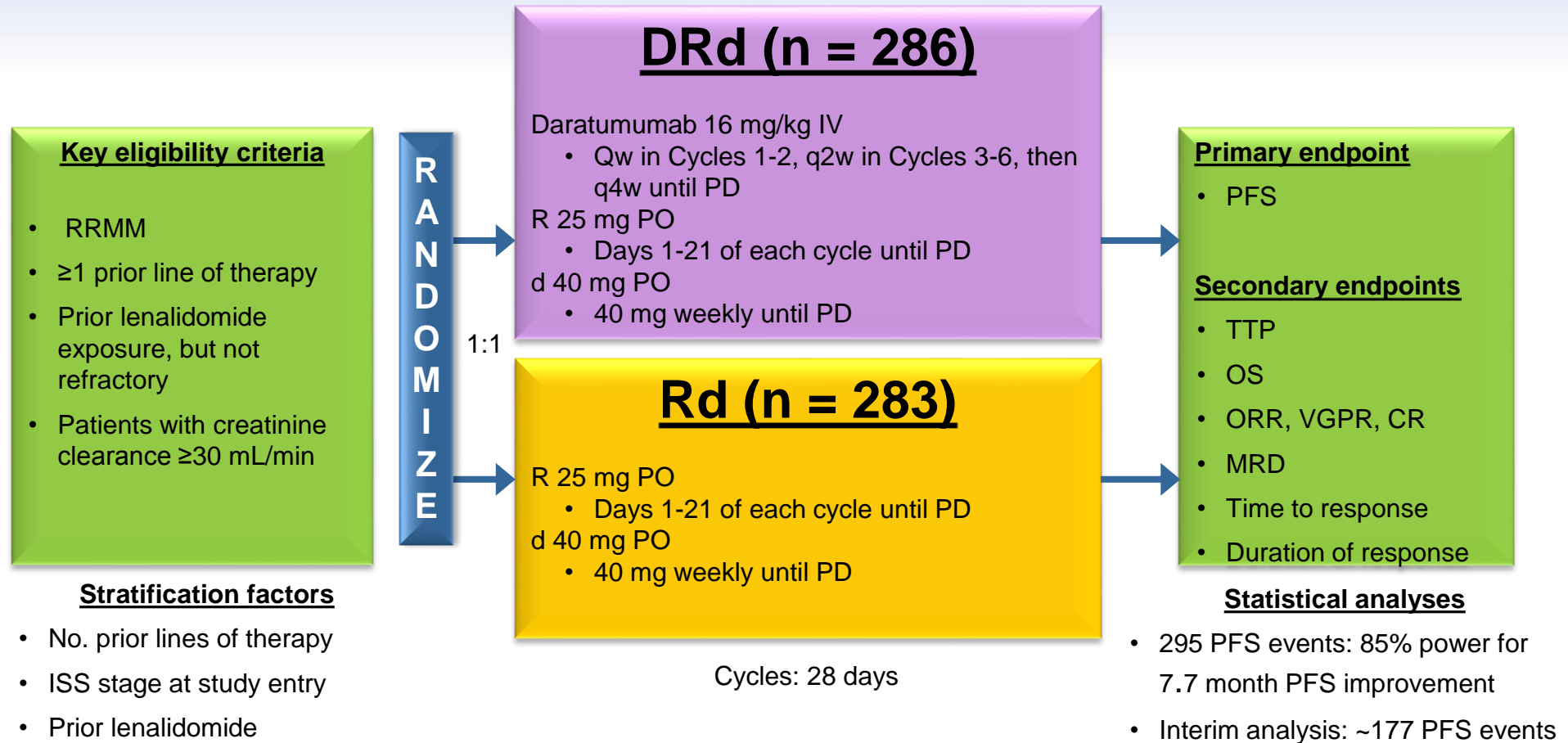
	Safety Analysis Set (n = 243)	
	All grades	Grade 3
Patients with IRRs, %	45	9
Most common (>5%) IRRs		
Dyspnea	11	2
Bronchospasm	9	3
Cough	7	0

- No grade 4 or 5 IRRs observed
- 98% of patients with IRRs experienced the event on the first infusion
- 2 patients discontinued due to IRRs
 - Bronchospasm in the first patient
 - Bronchospasm, laryngeal edema, and skin rash in the second patient

Preinfusion: dexamethasone 20 mg, paracetamol 650-1000 mg, diphenhydramine 25-50 mg
Stop infusion immediately for mild symptoms; once resolved, resume at half the infusion rate

POLLUX: Study Design

Multicenter, randomized (1:1), open-label, active-controlled phase 3 study



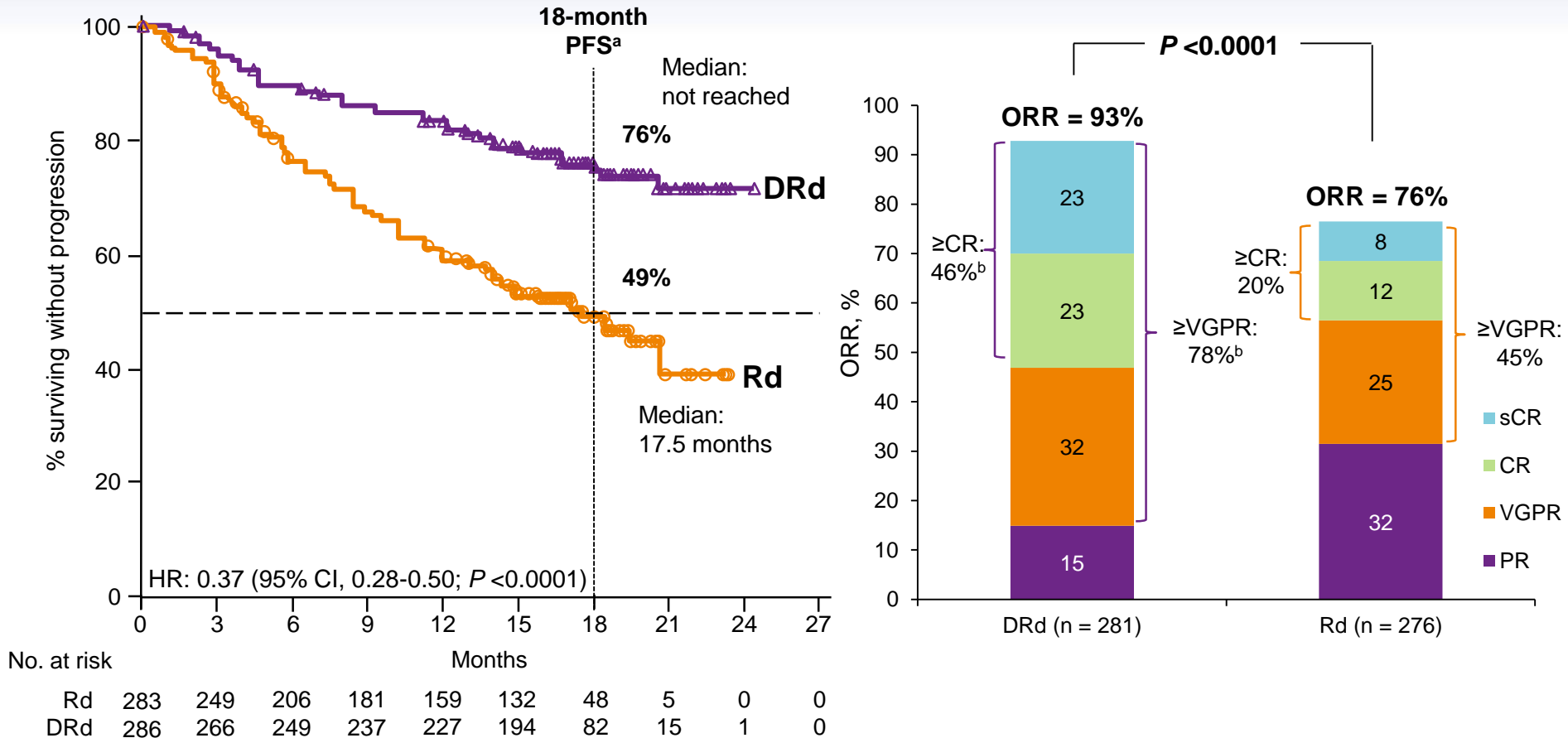
Pre-medication for the DRd treatment group consisted of dexamethasone 20 mg^a, paracetamol, and an antihistamine

Baseline Demographics and Clinical Characteristics (cont.)

Characteristic	DRd (n = 286)	Rd (n = 283)
Prior ASCT, %	63	64
Prior PI, %	86	86
Prior IMiD, %	55	55
Prior lenalidomide, %	18	18
Prior PI + IMiD, %	44	44
Refractory to PI, %	20	16
Refractory to last line of therapy, %	28	27

Updated Efficacy

Median (range) follow-up: 17.3 (0-24.5) months



Responses continue to deepen in the DRd group with longer follow-up

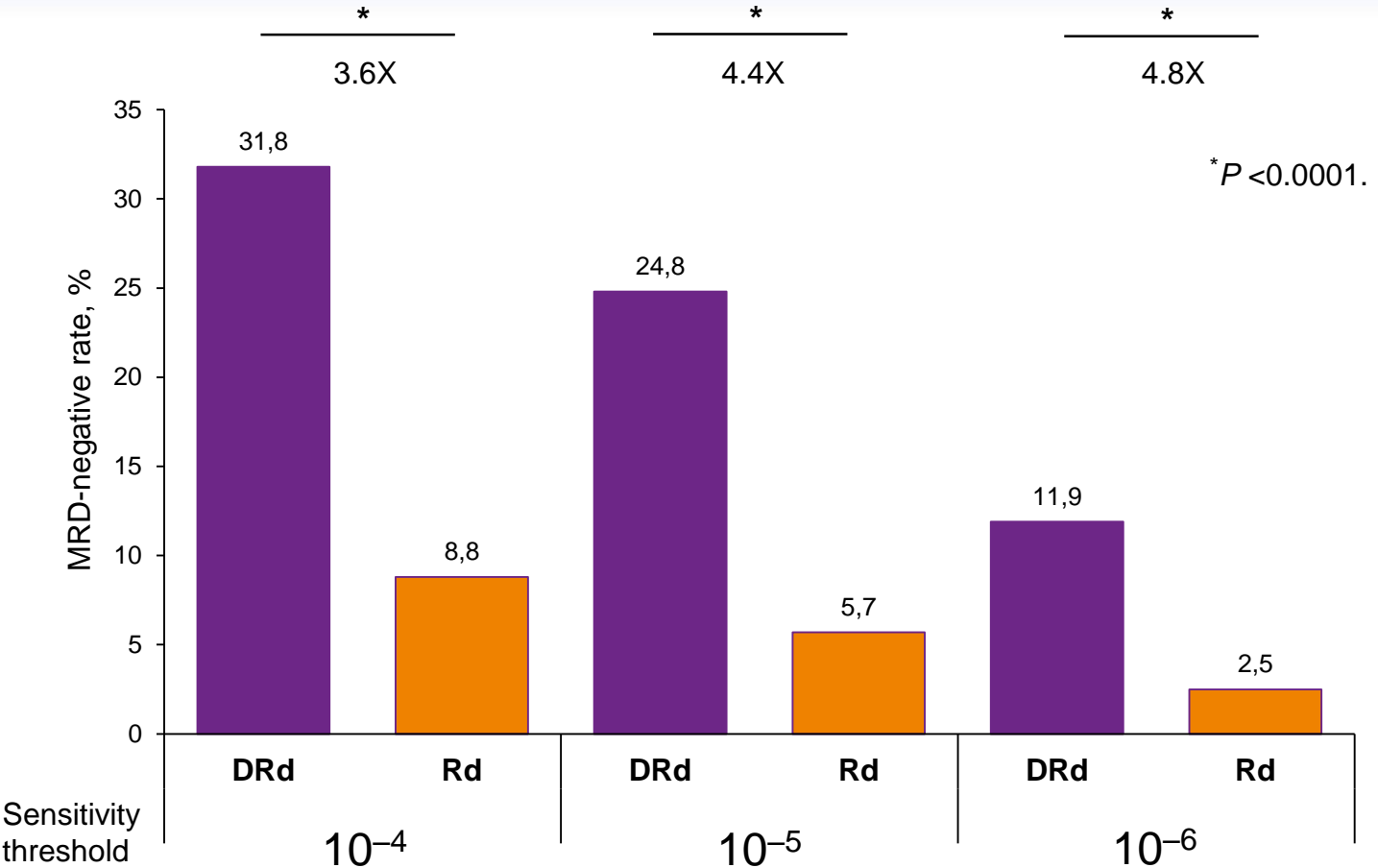
HR, hazard ratio; CI, confidence interval; sCR, stringent complete response; PR, partial response; ITT, intent-to-treat.

Note: PFS = ITT population; ORR = response-evaluable population.

^aKaplan-Meier estimate.

^bP < 0.0001 for DRd vs Rd.

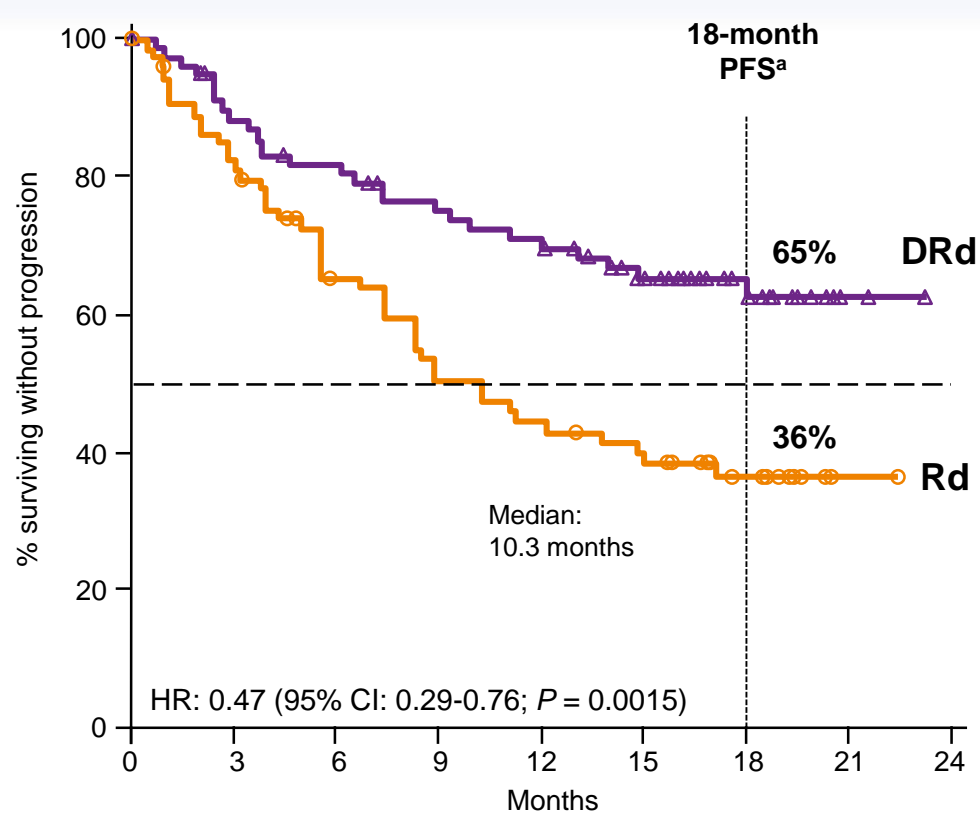
MRD-negative Rate



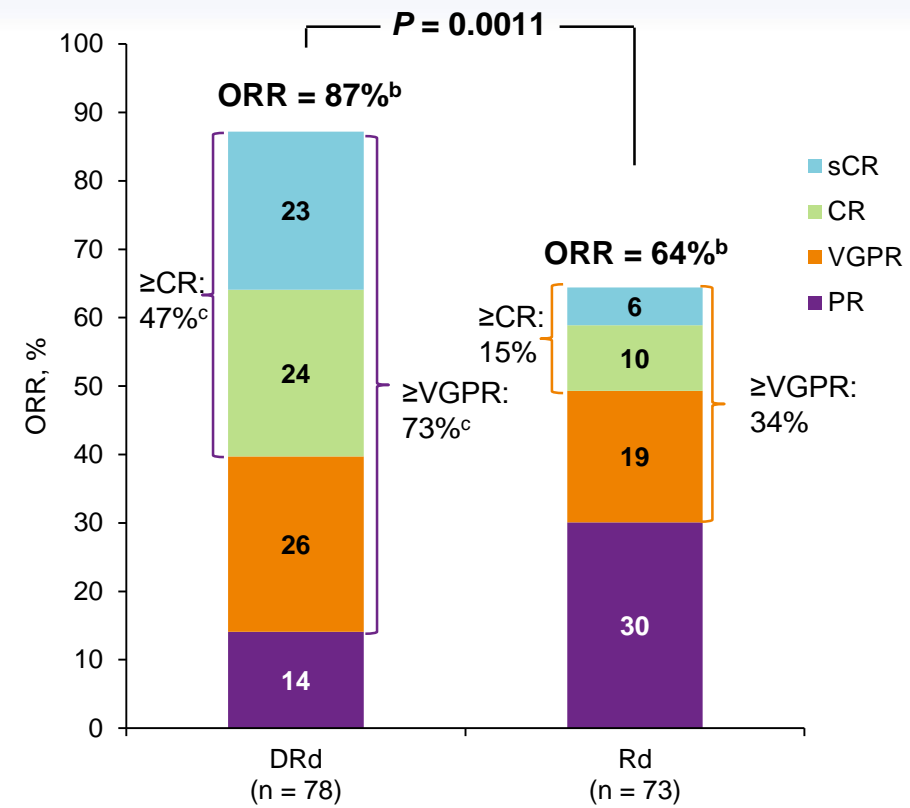
MRD-negative rates were >3-fold higher at all thresholds

ITT population.
P values are calculated using likelihood-ratio chi-square test.

Refractory to Last Line of Therapy



No. at risk	0	3	6	9	12	15	18	21	24
Rd	76	60	44	34	30	26	16	1	0
DRd	80	68	62	55	52	40	24	2	0

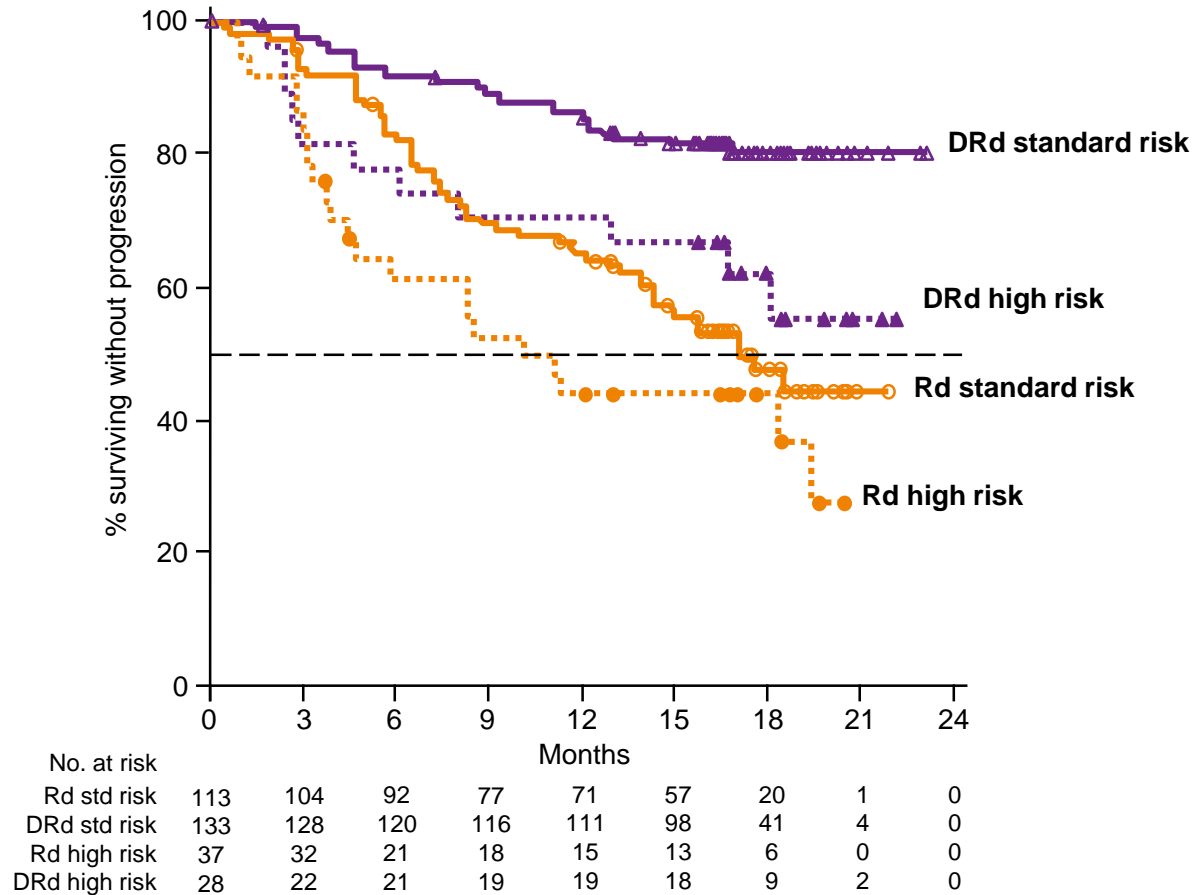


DRd benefits patients refractory to last line of therapy

^aKaplan-Meier estimate.
^bResponse-evaluable population.
^c $P < 0.0001$ for DRd vs Rd.

PFS: Cytogenetic Risk in All Evaluable Patients^a

■ Comparable results in 1 to 3 prior lines population



High risk	DRd n = 28	Rd n = 37
Median PFS, mo	NR	10.2
HR (95% CI)	0.44 (0.19-1.03)	
P value	0.0475	
ORR, %	85	67
P value	NS	

Standard risk	DRd n = 133	Rd n = 113
Median PFS, mo	NR	17.1
HR (95% CI)	0.30 (0.18-0.49)	
P value	<0.0001	
ORR, %	95	82
P value	0.0020	

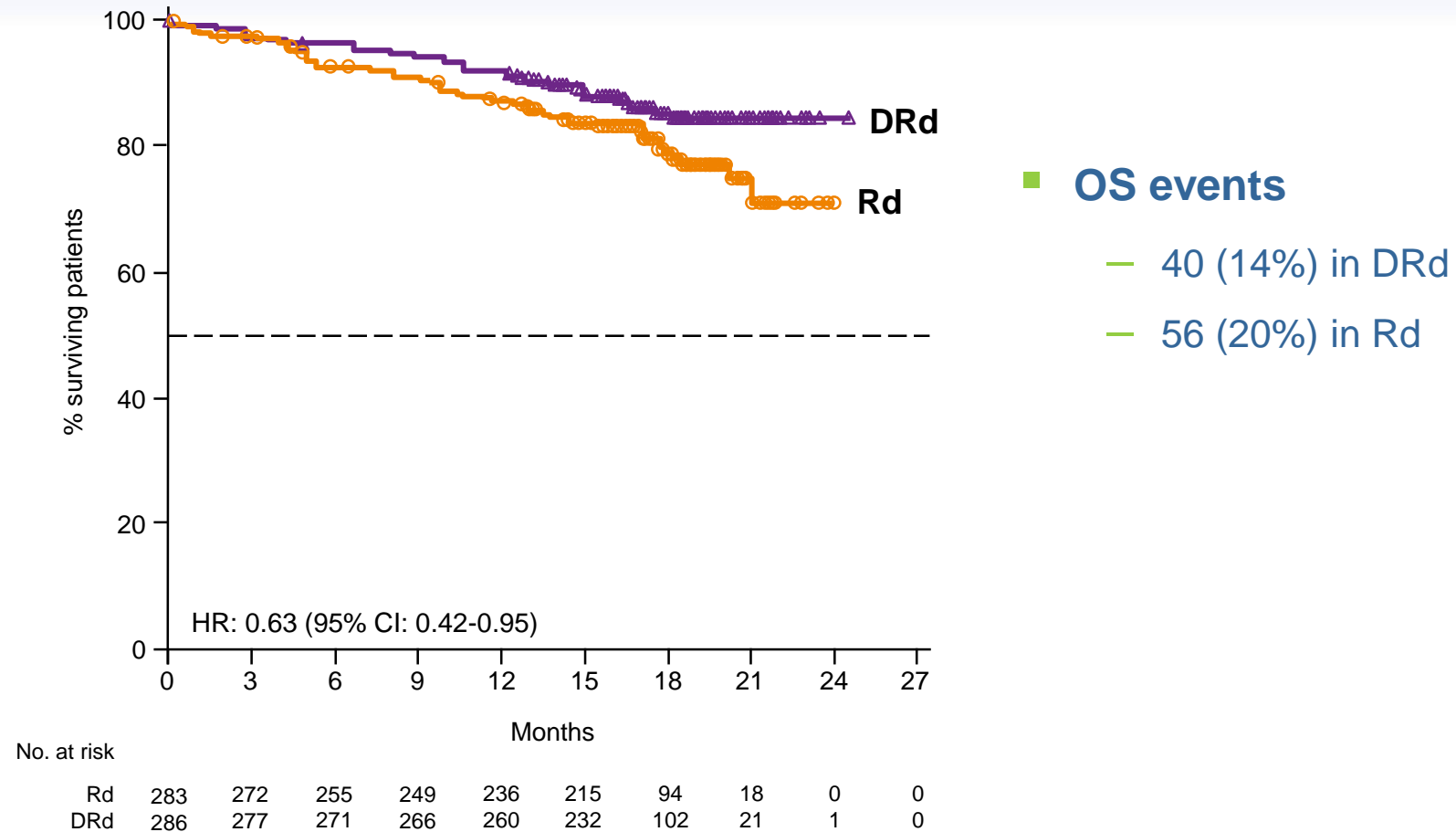
DRd improves outcomes regardless of cytogenetic risk

NR, not reached; NS, not significant.

^aITT/Biomarker risk-evaluable analysis set. High-risk patients had any of t(4;14), t(14;16), or del17p. Standard-risk patients had an absence of high-risk abnormalities.

OS

Median (range) follow-up: 17.3 (0-24.5) months

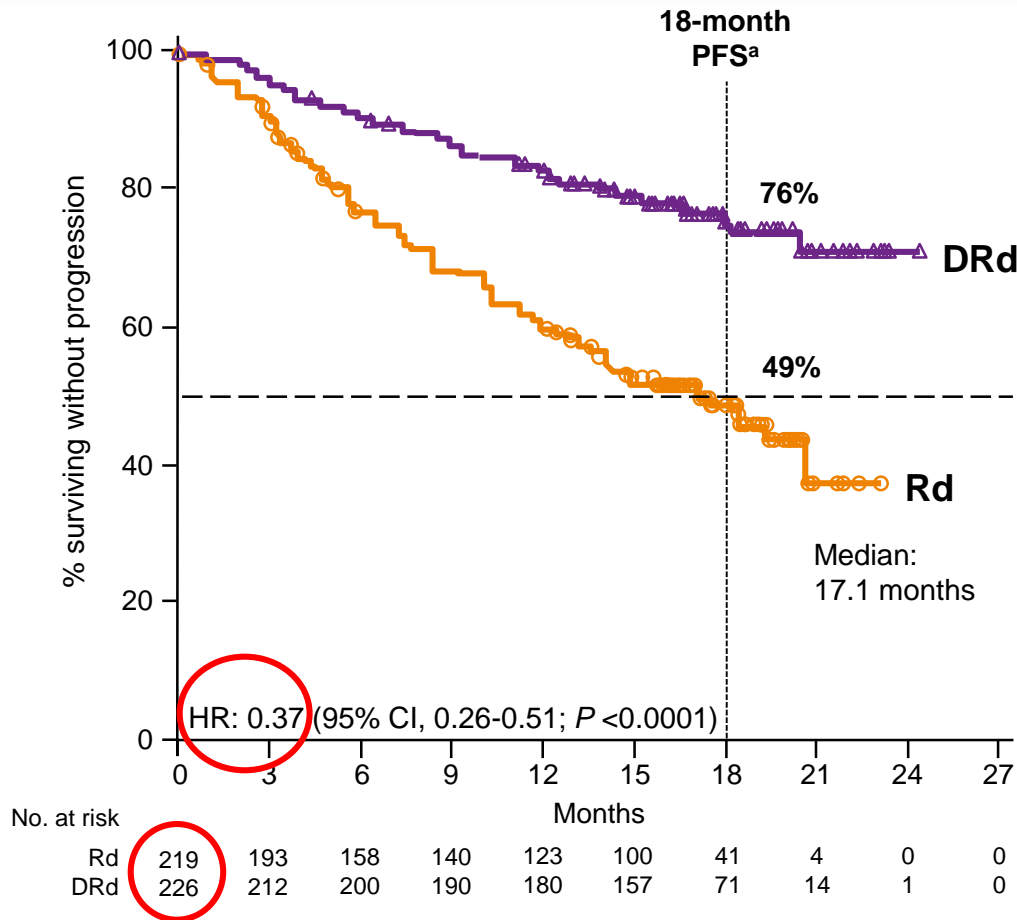


Curves are beginning to separate, but OS data are immature

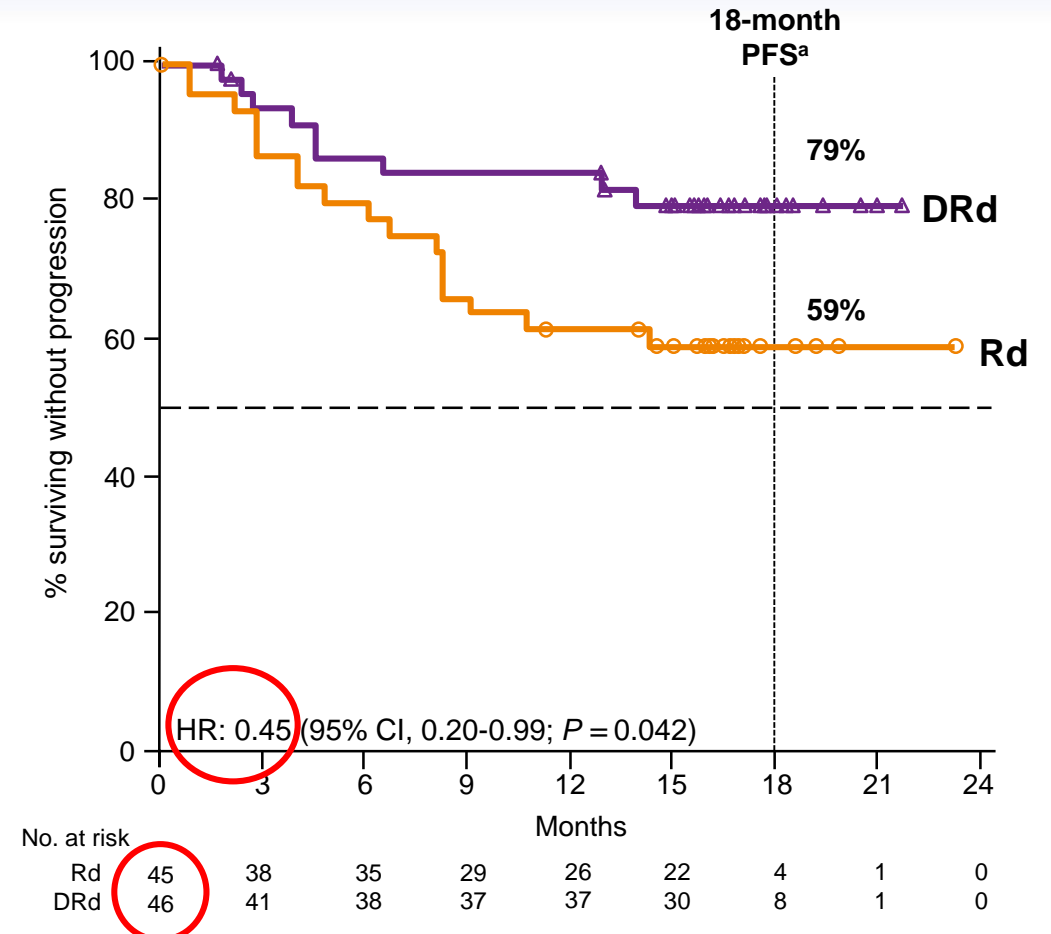
ITT population.
Median OS was not reached; results did not cross the prespecified stopping boundary.

PFS: Prior Lenalidomide Treatment

No Prior Lenalidomide Treatment

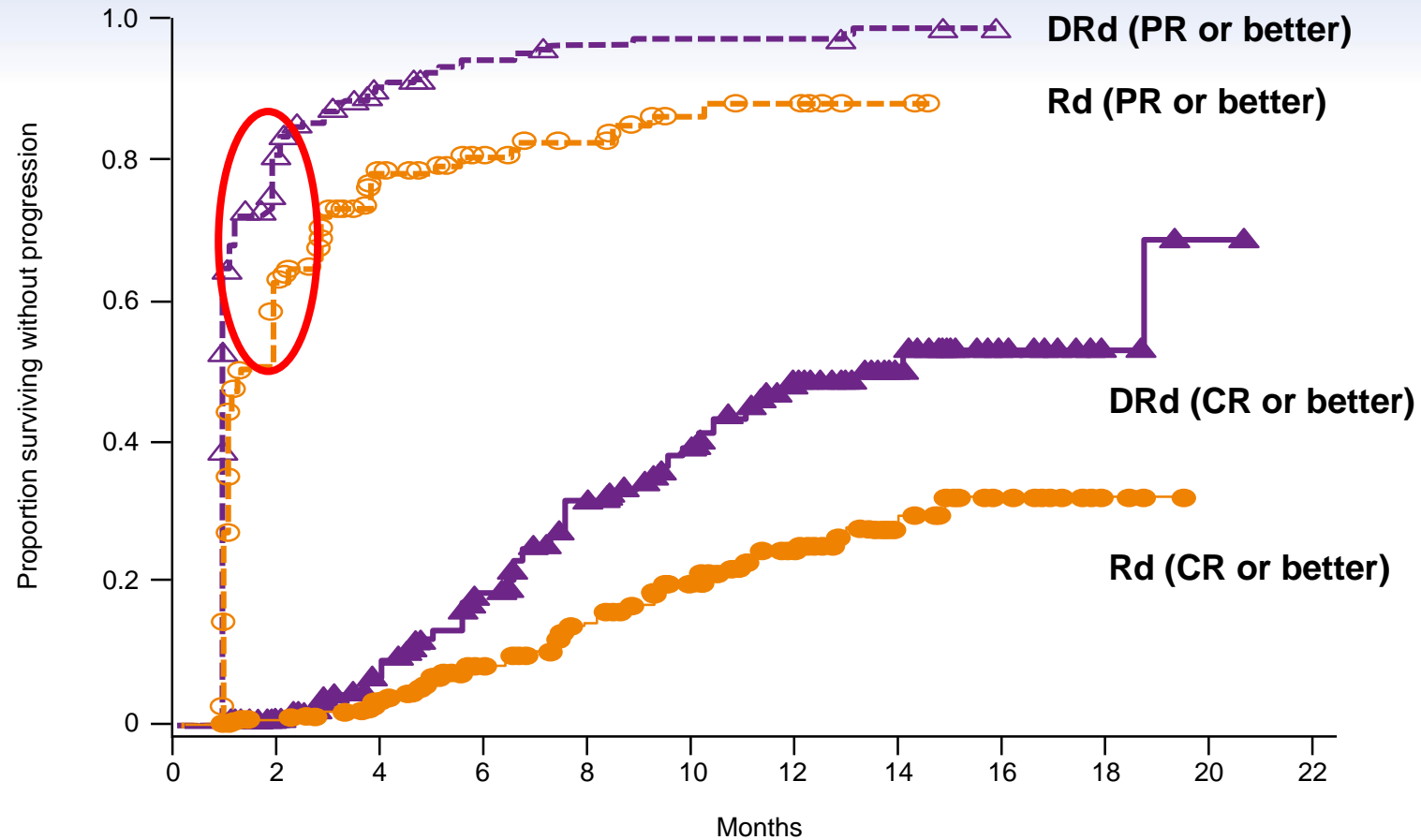


Prior Lenalidomide Treatment



Treatment effect is consistent regardless of prior lenalidomide exposure

Time to Response



No. at risk	0	2	4	6	8	10	12	14	16	18	20	22
Rd (PR or better)	276	95	35	23	16	8	6	2	0	0	0	0
DRd (PR or better)	281	46	19	10	6	5	5	2	0	0	0	0
Rd (CR or better)	276	262	220	187	159	133	100	36	14	3	0	0
DRd (CR or better)	281	271	237	201	162	132	100	37	12	4	1	0

Most Common AEs (All Patients): Updated Analysis

	DRd (n = 283)		Rd (n = 281)	
Hematologic, %	All grade $\geq 25\%^a$	Grade 3/4 $\geq 5\%^a$	All grade $\geq 25\%^a$	Grade 3/4 $\geq 5\%^a$
Neutropenia	60	53	44	38
Febrile neutropenia	6	6	3	3
Anemia	34	14	36	21
Thrombocytopenia	28	13	30	15
Lymphopenia	6	5	5	4
Nonhematologic, %				
Diarrhea	47	6	28	3
Fatigue	35	6	29	3
Upper respiratory tract infection	33	1	23	1
Cough	30	0	13	0
Constipation	30	1	26	0.7
Muscle spasms	27	0.7	20	2
Nasopharyngitis	26	0	17	0
Nausea	25	1	16	0.4
Pneumonia	16	9	13	8

No new safety signals reported

AE, adverse event.

^aCommon treatment-emergent AEs listed are either $\geq 25\%$ all grade OR $\geq 5\%$ grade 3/4.

Infusion-related Reactions (IRRs)

IRRs $\geq 2\%$	Safety Analysis Set (n = 283)	
	All grades (%)	Grade 3 (%)
Patients with IRRs	48	5
Cough	9	0
Dyspnea	9	0.7
Vomiting	6	0.4
Nausea	5	0
Chills	5	0.4
Bronchospasm	5	0.4
Pruritus	3	0.4
Throat irritation	3	0
Headache	3	0
Nasal congestion	3	0
Wheezing	2	0.7
Laryngeal edema	2	0.4
Rhinorrhea	2	0
Pyrexia	2	0

- No grade 4 or 5 IRRs were reported
- 92% of all IRRs occurred during the first infusion
- 1 patient discontinued daratumumab due to an IRR

Lenalidomide-based Studies

	POLLUX DRd vs Rd	ASPIRE KRd vs Rd ¹	ELOQUENT-2 ERd vs Rd ^{2,3}	TOURMALINE-MM1 NRd vs Rd ⁴
→ PFS HR (95% CI)	0.37 (0.27-0.52)	0.69 (0.57-0.83)	0.73 (0.60-0.89)	0.74 (0.59-0.94)
ORR	93%	87%	79%	78%
≥VGPR	76%	70%	33%	48%
→ ≥CR	43%	32%	4%	14%
Duration of response, mo	NE	28.6	20.7	20.5
OS HR (95% CI)	0.64 (0.40-1.01)	0.79 (0.63-0.99)	0.77 (0.61-0.97)	NE

1. Stewart AK, et al. *N Engl J Med*. 2015;372(2):142-152.

2. Lonial S, et al. *N Engl J Med*. 2015;373(7):621-631.

3. Dimopoulos MA, et al. *Blood*. 2015;126(23):Abstract 28.

4. Moreau P, et al. *N Engl J Med*. 2016;374(17):1621-1634.

Phase 1b Study of Daratumumab Plus Pomalidomide and Dexamethasone in Relapsed and/or Refractory Multiple Myeloma (RRMM) With ≥ 2 Prior Lines of Therapy

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Rationale for DARA + POM-D

- In a randomized, phase 3 study, pomalidomide plus low-dose dexamethasone (POM-D) in patients relapsed from or refractory to previous treatment with bortezomib or lenalidomide resulted in the following¹:
 - Overall response rate (ORR) = 31%
 - Median progression-free survival (PFS) = 4.0 months
 - Median overall survival (OS) = 12.7 months
- Pomalidomide increases CD38 expression in a time- and dose-dependent fashion in multiple myeloma (MM) cells²
- Increases in T-cell clonality were observed with DARA plus lenalidomide and dexamethasone (Rd) but not with Rd alone in POLLUX³

1. San Miguel J, et al. *Lancet Oncol.* 2013;14(11):1055-1066.

2. Boxhammer R, et al. Presented at: 51st American Society of Clinical Oncology (ASCO) Annual Meeting; May 29-June 2, 2015; Chicago, IL. Abstract 8588.

3. Chiu, C. et al. Presented at: 58th American Society of Hematology (ASH) Annual Meeting & Exposition; December 3-6, 2016; San Diego, CA. Abstract 4531.

MMY1001: DARA + POM-D Cohort

Eligibility criteria

- Refractory to last line of therapy
- ≥ 2 prior lines of therapy, including 2 consecutive cycles of lenalidomide and bortezomib
- Pomalidomide naïve
- Eastern Cooperative Oncology Group (ECOG) score ≤ 2
- Absolute neutrophil count $\geq 1.0 \times 10^9/L$, and platelet count $\geq 75 \times 10^9/L$ for patients with $>50\%$ plasma cells
- Calculated creatinine clearance (CrCl) ≥ 45 mL/min/1.73 m²

Open-label, multicenter, 6-arm, phase 1b study (28-day cycles)

DARA* IV 16 mg/kg +
Pomalidomide 4 mg (Days 1-21) +
Dexamethasone 40 mg QW

*QW for Cycles 1-2, Q2W for Cycles 3-6, and Q4W thereafter

Treat 6 patients with DARA + POM-D

Expansion cohort of an additional
97 patients (N = 103 total)

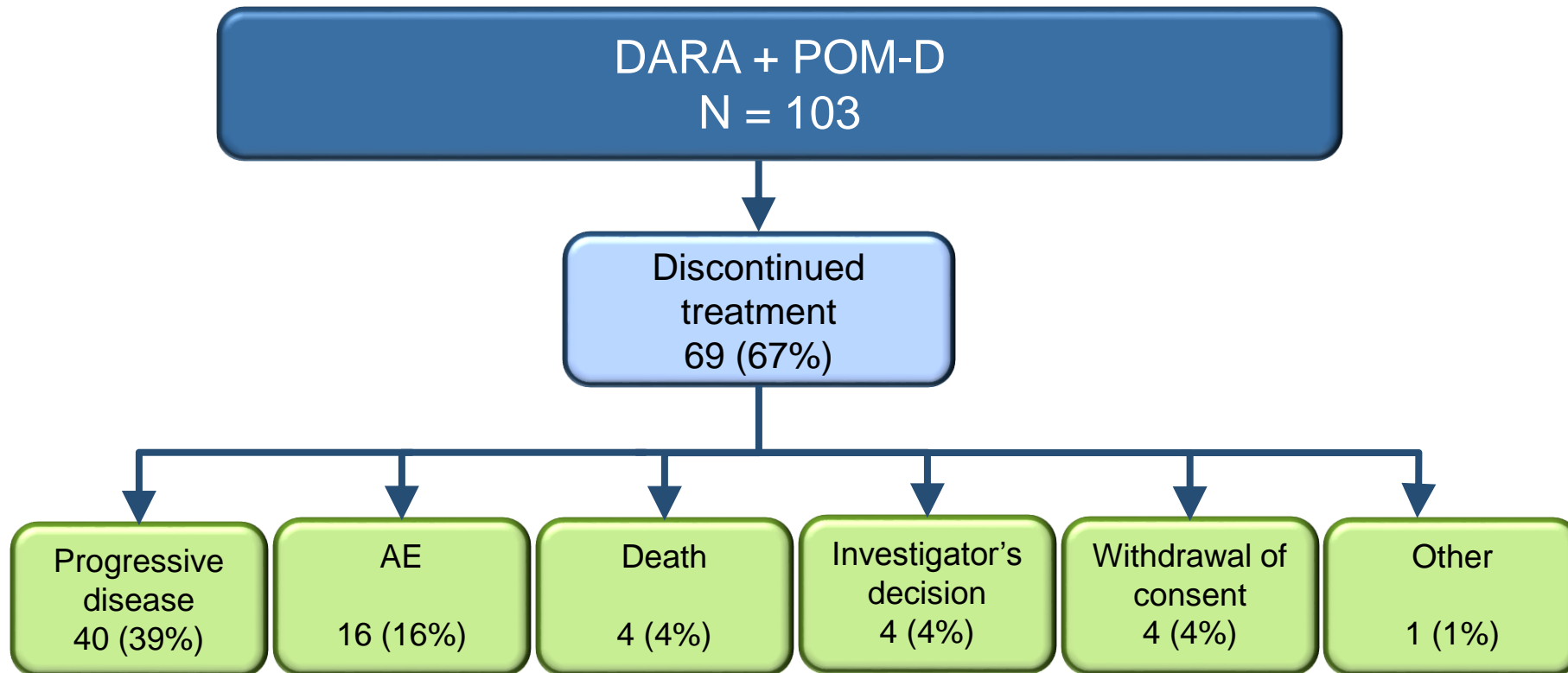
Baseline Demographics and Clinical Characteristics

Characteristic	DARA + POM-D N = 103
Age, y	
Median (range)	64 (35-86)
Category, n (%)	
<65	52 (51)
65-<75	43 (42)
≥75	8 (8)
Female/male, %	45/55
ECOG score, n (%)	
0	28 (27)
1	63 (61)
2	12 (12)
Cytogenetic profile, n (%)*	n = 87
Standard risk	65 (75)
High risk	22 (25)
del17p	16 (18)
t(4;14)	6 (7)
t(14;16)	1 (1)
Time from diagnosis, y	
Median (range)	5.13 (0.4-16.0)

Characteristic	DARA + POM-D N = 103
Prior lines of therapy, n (%)	
Median (range)	4 (1-13)
1	3 (3)
2	22 (21)
3	25 (24)
>3	53 (52)
Prior ASCT, n (%)	76 (74)
Prior PI, n (%)	102 (99)
Prior BORT	101 (98)
Prior CARF	34 (33)
Prior LEN, n (%)	103 (100)
Prior PI + IMiD, n (%)	102 (99)
Refractory to, n (%)	
LEN	92 (89)
BORT	73 (71)
CARF	31 (30)
Refractory to PI + IMiD, n (%)	73 (71)

Patient Disposition: DARA + POM-D*

- Median follow-up: 13.1 months (range: 0.2-25.8)
- Median duration of treatment: 6.7 months (range: 0.03-20.0+)



Safety Summary: DARA + POM-D

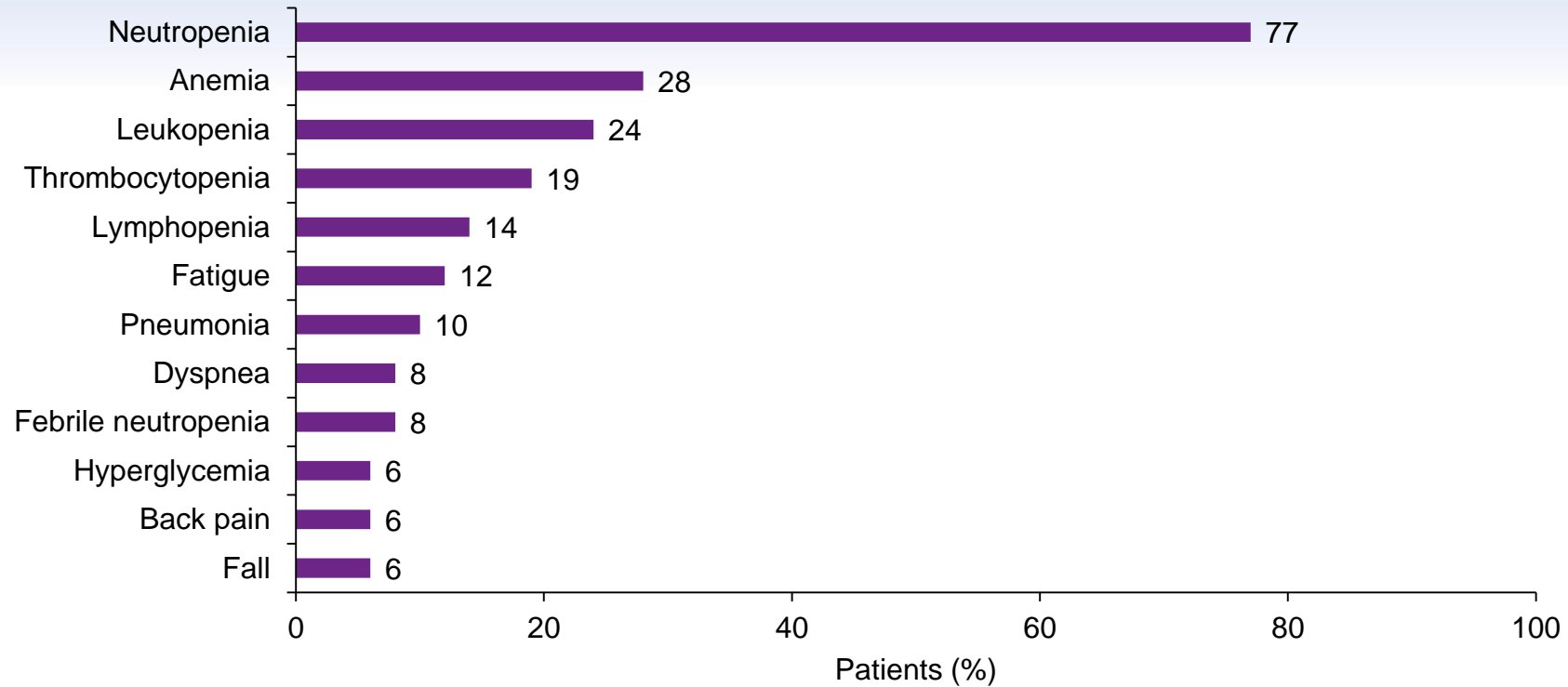
Most common (>25%) TEAEs

N = 103	n (%)
Neutropenia ^a	82 (80)
Anemia	56 (54)
Fatigue	54 (52)
Diarrhea	44 (43)
Thrombocytopenia	43 (42)
Cough	39 (38)
Leukopenia	38 (37)
Constipation	35 (34)
Dyspnea	33 (32)
Nausea	32 (31)
Pyrexia	31 (30)
Back pain	29 (28)
Upper respiratory tract infection	29 (28)
Muscle spasms	28 (27)

- 44% of patients had baseline grade 1/2 neutropenia
- 15% of patients discontinued due to treatment-emergent adverse events (TEAEs)
 - None of the TEAEs occurred in >1 patient
 - 3% were related to DARA
- 9% of patients had a TEAE leading to death
 - None were related to DARA
- No patients reported secondary primary malignancies

No new safety signals were reported with longer follow-up

Most Common (>5%) Grade 3/4 Adverse Events (AEs)



- Serious adverse events (SAEs) occurred in 53% of patients
 - 18% were related to DARA per investigator discretion
- The most common grade 3 or 4 infection/infestation TEAE was pneumonia (10%)
- There were relatively low rates of febrile neutropenia (8%)

Other than neutropenia, rates of grade ≥ 3 AEs were similar to those observed historically with POM-D alone

IRRs in >5% Patients: DARA + POM-D

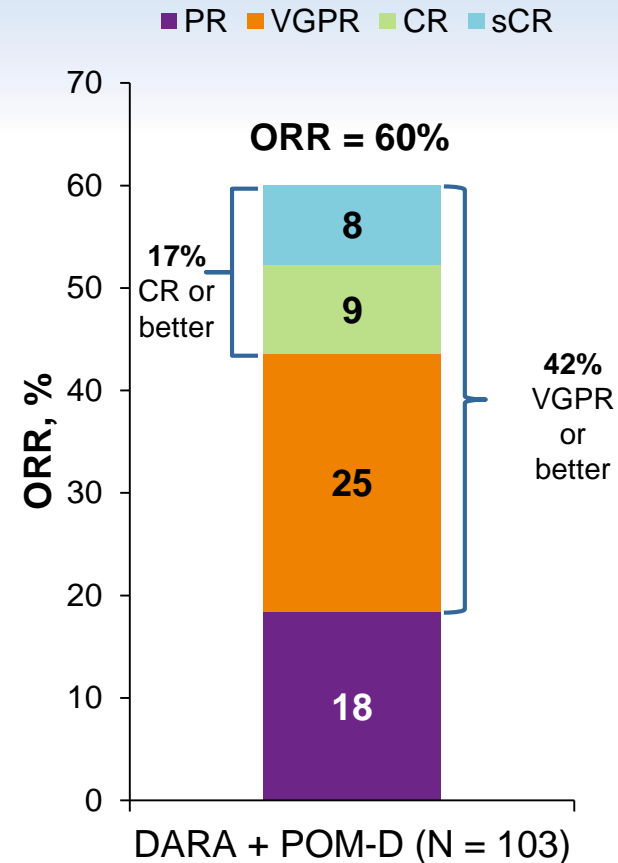
	N = 103	
IRR	Any grade, %	Grade 3, %
Any event	50	4
Chills	15	0
Cough	11	0
Dyspnea	11	0
Nausea	9	0
Nasal congestion	7	0
Throat irritation	7	0

- 4 (4%) patients had grade 3 infusion-related reactions (IRRs)
 - Hypertension (n = 2), hypoxia (n = 1), and increased blood pressure (n = 1)
- No grade 4 or 5 IRRs occurred
- 1 patient discontinued due to an IRR (grade 3 hypoxia)
- All IRRs occurred during the first infusion, except for 1 instance of laryngeal edema, which occurred during the second infusion

IRRs were mostly grade ≤ 2 and occurred predominantly during the first infusion

ORR^a: DARA + POM-D

	DARA + POM-D (N = 103)	
	n (%)	95% CI
ORR (sCR+CR+VGPR+PR)	62 (60)	50.1-69.7
Best response		
sCR	8 (8)	3.4-14.7
CR	9 (9)	4.1-15.9
VGPR	26 (25)	17.2-34.8
PR	19 (18)	11.5-27.3
MR	2 (2)	0.2-6.8
SD	26 (25)	17.2-34.8
PD	3 (3)	0.6-8.3
NE	10 (10)	4.8-17.1
VGPR or better (sCR+CR+VGPR)	43 (42)	32.1-51.9
CR or better (sCR+CR)	17 (17)	9.9-25.1

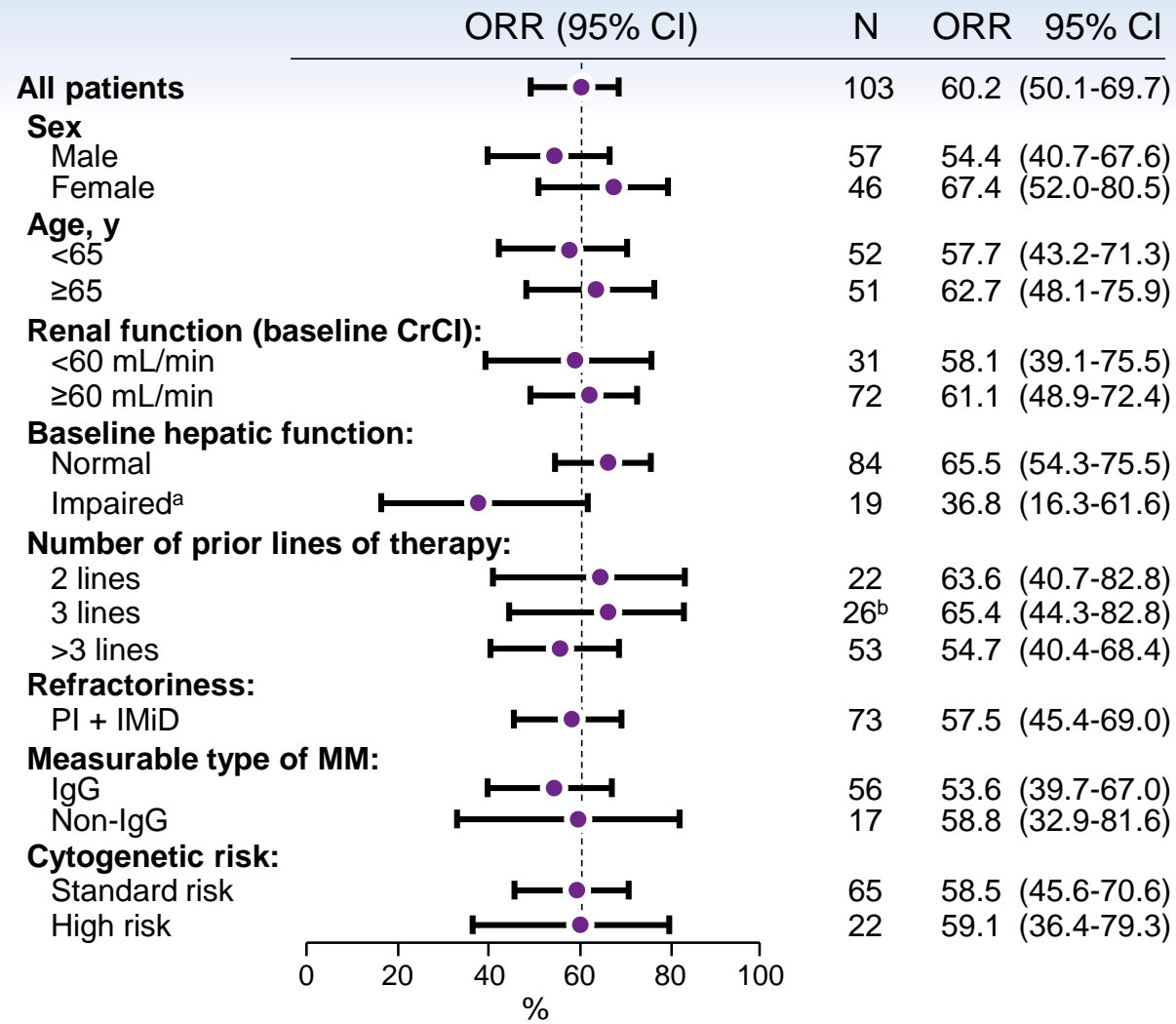


- Among patients with CR or better, the minimal residual disease negative rate at:
 - 10^{-4} threshold = 6/17 (35%)
 - 10^{-5} threshold = 5/17 (29%)
 - 10^{-6} threshold = 1/17 (6%)

Deep responses were observed with DARA + POM-D

^aBased on independent safety monitoring board assessment. Daratumumab IFE reflex assay was used to mitigate DARA-mediated interference with assessment of CR.

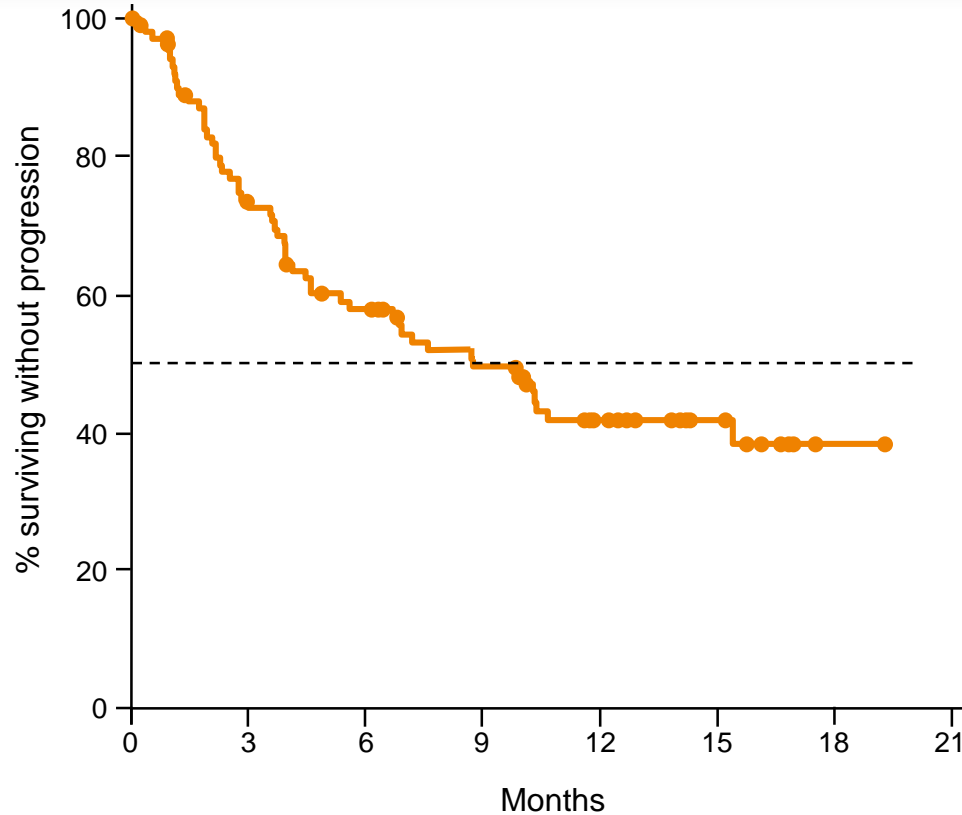
ORR Subgroup Analysis: DARA + POM-D



High response rate maintained across clinically relevant subgroups

^aClassified as mild, moderate, or severe; 17% had mild impairment; 1% had moderate impairment; 0% had severe impairment. Patients with impaired hepatic function received fewer doses of DARA versus patients with normal hepatic function. ^bDiscrepancy from demographics table due to update of concomitant medication data.

PFS: DARA + POM-D



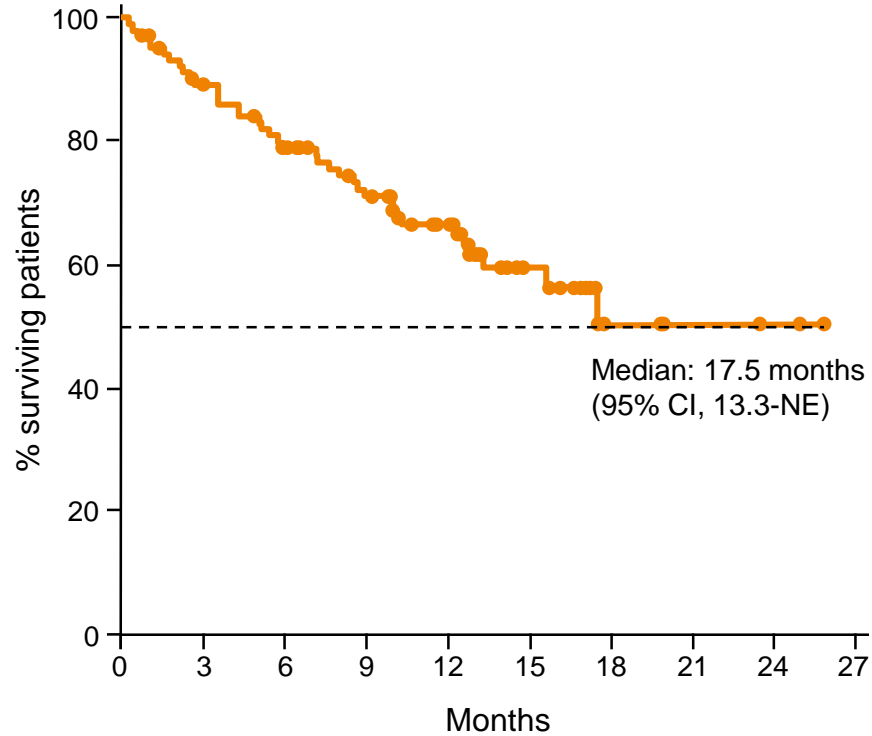
No. at risk 103 71 53 42 28 12 1 0

- Median PFS: 8.8 months (95% CI, 4.6-15.4)
- 6-month PFS rate: 57.8% (95% CI, 47.3-66.9)
- 12-month PFS rate: 41.9% (95% CI, 31.5-51.9)

~40% of patients maintain PFS after 1 year

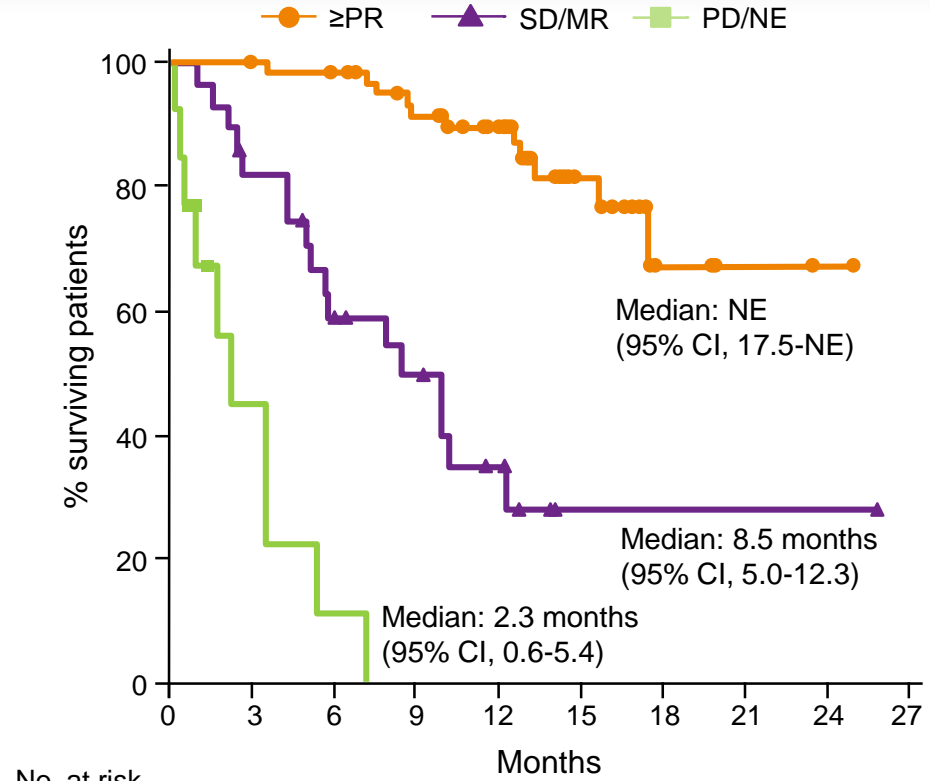
OS: DARA + POM-D

OS



No. at risk 103 88 75 63 49 18 5 3 2 0

OS by Response Category



No. at risk

	0	3	6	9	12	15	18	21	24	27
≥PR	62	62	59	52	43	17	4	2	1	0
SD/MR	28	22	15	11	6	1	1	1	1	0
PD/NE	13	4	1	0	0	0	0	0	0	0

- 12-month OS rate: 66.2% (95% CI, 55.6-74.8)

Patients with SD/MR derive survival benefit with DARA + POM-D

Conclusions: DARA + POM-D

- DARA can be safely combined with POM-D
 - High neutropenia rates in a population with 44% baseline neutropenia
 - Febrile neutropenia rates were consistent with POM-D alone
- DARA (16 mg/kg) + POM-D induced deep responses, including MRD negativity, in a heavily pretreated patient population
 - Median of 4 prior lines of therapy
 - 71% of patients were double refractory to a PI and an IMiD
 - High response rate is maintained in double-refractory and high-risk patients
- 40% of patients remain progression-free after 1 year
- The addition of DARA to POM-D is associated with encouraging OS

A phase 3 study is being planned