

Phase 3 MAIA Study: Overall Survival Results With Daratumumab, Lenalidomide, and Dexamethasone vs Lenalidomide and Dexamethasone in Patients With Transplant-Ineligible Newly Diagnosed Multiple Myeloma



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Background

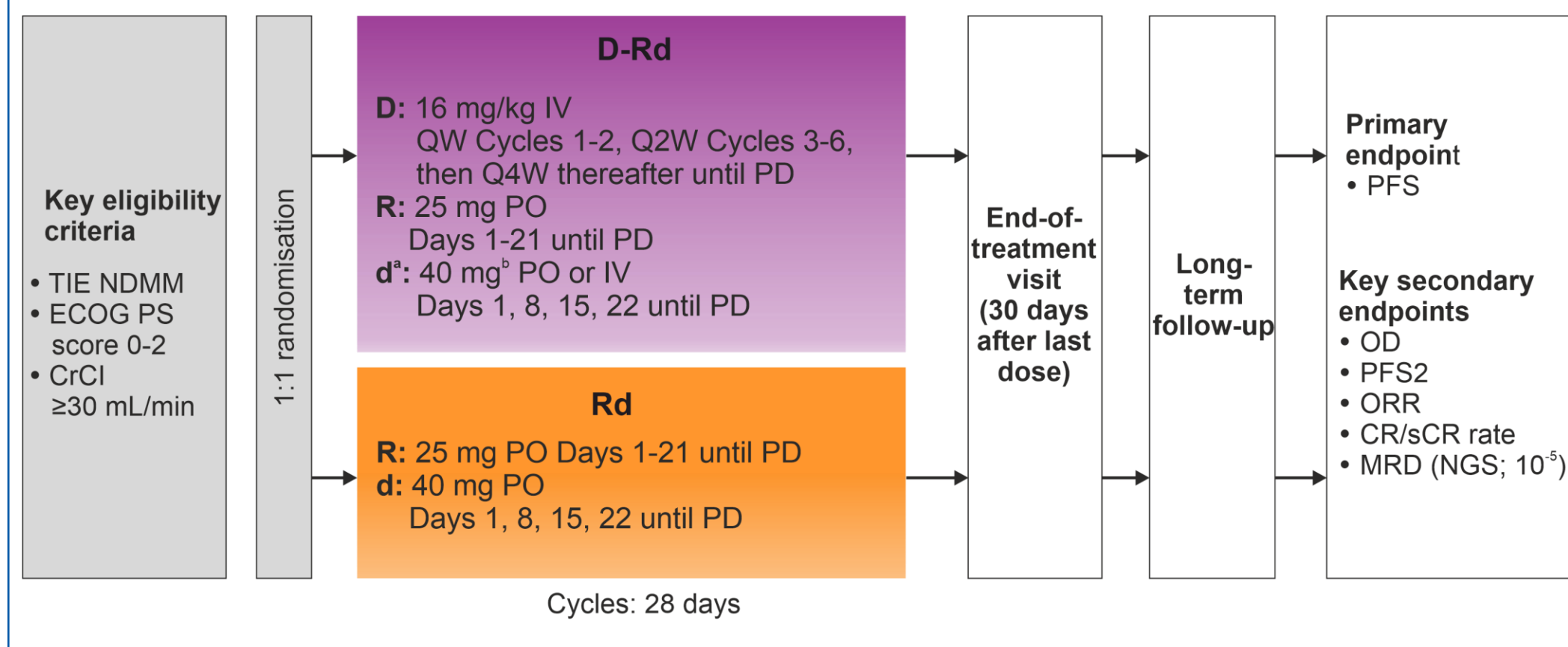
- The phase 3 ALCYONE, MAIA, and CASSIOPEIA studies established the progression-free survival (PFS) benefit of daratumumab (DARA) in combination with standard of care (SOC) vs SOC alone for patients with newly diagnosed multiple myeloma (NDMM)¹⁻³; ALCYONE also established, for the first time, an overall survival (OS) benefit of a DARA-based regimen in NDMM⁴
- The phase 3 SWOG S0777 study in patients with NDMM without intent for immediate transplant (69% of whom were intended for eventual transplant) established bortezomib/lenalidomide/dexamethasone (VRd) as a SOC regimen for elderly patients⁵
 - At a median follow-up of 84 months, median PFS was 41 months for VRd and 29 months for Rd (hazard ratio [HR], 0.742); median OS was not reached vs 69 months (HR, 0.709)⁶
 - 43% of patients in SWOG S0777 were ≥65 years (vs 99% in MAIA); however, a significant OS benefit in this subgroup was not observed for VRd vs Rd (median, 65 months vs 56 months; HR, 0.769; P = 0.168)⁶
- Real-world data indicate that >50% of nontransplant elderly patients with NDMM do not receive any subsequent therapy, suggesting that the most effective therapy should be used upfront and not saved for relapse,⁷ at which time additional genetic mutations conferring resistance may have been acquired⁸
- In the last MAIA update (Kumar SK, et al. ASH 2020), D-Rd prolonged PFS and also PFS on the next subsequent line of therapy (PFS2) vs Rd alone; OS data were not yet mature⁹

Objective: To report updated efficacy and safety results from a prespecified interim OS analysis of MAIA after a median follow-up of approximately 56 months

Study Design

- MAIA is a multicenter, randomized, open-label, active-controlled, phase 3 study of D-Rd vs Rd alone in patients with NDMM who are transplant ineligible
- Patients were enrolled in MAIA from March 2015 through January 2017

Figure 1. Study design



BMI, body mass index; CrCl, creatinine clearance; CR, complete response; D/DARA, daratumumab; d, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MRD, minimal residual disease; NGS, next-generation sequencing; ORR, overall response rate; PD, progressive disease; PO, oral; QW, once weekly; Q2W, once every 2 weeks; Q4W, once every 4 weeks; R, lenalidomide; sCR, stringent complete response; T1E, transplant-ineligible. *On days when DARA is administered, dexamethasone will be administered to patients in the D-Rd arm and will serve as the treatment dose of steroid for that day, as well as the required pre-infusion medication. ^aFor patients >75 years of age or with BMI <18.5 kg/m², dexamethasone was administered at a dose of 20 mg QW.

Results

Demographics and baseline characteristics were well balanced between arms

Table 1. Demographics and Baseline Characteristics

	D-Rd (n = 368)	Rd (n = 369)
Age, years, median (range)	73.0 (50-90)	74.0 (45-89)
Age, n (%)		
<65	4 (1)	4 (1)
65-<70	74 (20)	73 (20)
70-<75	130 (35)	131 (36)
≥75	160 (43)	161 (44)
ECOG PS score, n (%)		
0	127 (35)	123 (33)
1	178 (48)	187 (51)
2 ^a	63 (17)	59 (16)
ISS stage, n (%)		
I	98 (27)	103 (28)
II	163 (44)	156 (42)
III	107 (29)	110 (30)
Type of measurable disease, n (%)		
IgG	225 (61)	231 (63)
IgA	65 (18)	66 (18)
Other ^b	9 (2)	10 (3)
Detected in urine only	40 (11)	34 (9)
Detected as serum-free light chain only	29 (8)	28 (8)
Cytogenetic profile, n/total n (%)		
Standard risk	271/319 (85)	279/323 (86)
High risk	48/319 (15)	44/323 (14)
Median time since initial diagnosis of MM (range), months	0.95 (0.1-13.3)	0.89 (0-14.5)

D, daratumumab; ECOG PS, Eastern Cooperative Oncology Group performance status; Ig, immunoglobulin; ISS, International Staging System; MM, multiple myeloma; Rd, lenalidomide/dexamethasone. ^a2 patients had an ECOG PS score >2 (1 patient each with an ECOG PS score of 3 and 4). ^bIncludes IgG, IgA, IgM, and biconal. Note: percentages may not add up to 100% due to rounding.

Median duration of follow-up, 56.2 months

Table 2. Treatment Exposure

Safety population (received ≥1 dose of study treatment)	D-Rd (n = 364)	Rd (n = 365)
Median duration of study treatment, months (range)	47.5 (0.10-69.26)	22.6 (0.03-69.22)
Lenalidomide median RDI, % (range)	66 (8-206)	86 (5-239)
Discontinued lenalidomide only while continuing other study treatment, n (%)	33 (9)	14 (4)
Intravenous daratumumab median RDI, % (range)	98 (3-107)	—
Discontinued daratumumab only while continuing other study treatment, n (%)	5 (1)	—

42% of patients in the D-Rd arm and 18% of patients in the Rd arm remained on treatment; more patients discontinued Rd for AEs.

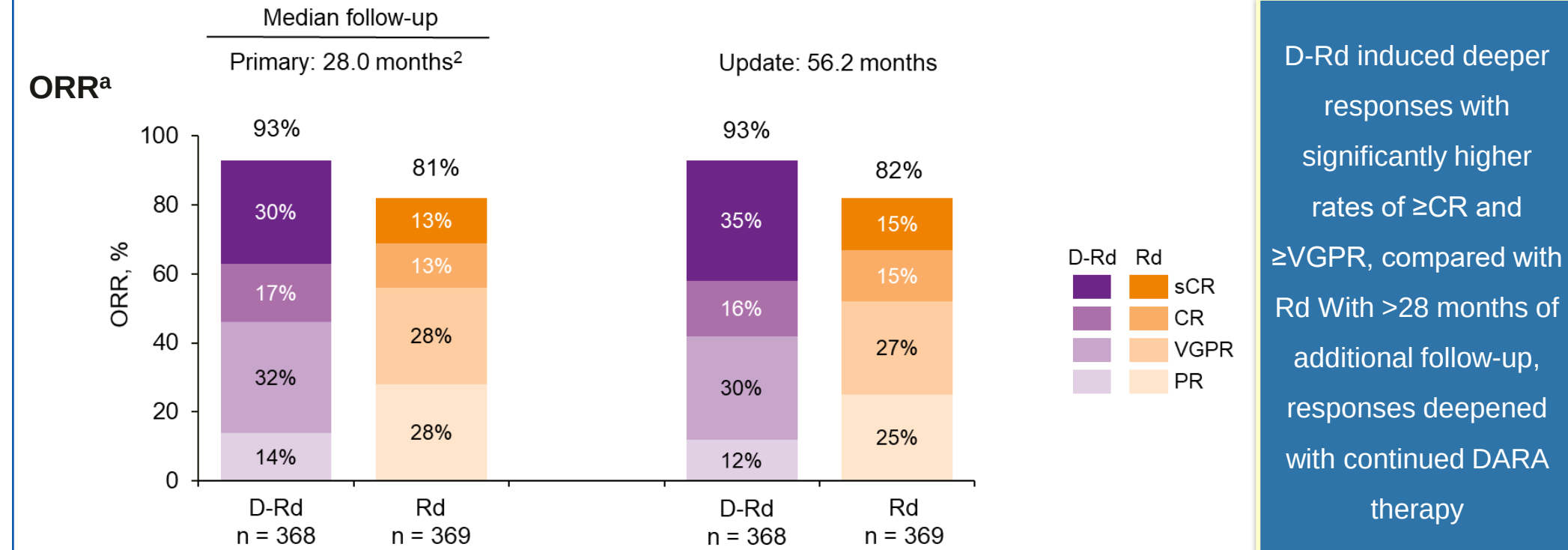
AE, Adverse event; D, daratumumab; Rd, lenalidomide/dexamethasone; RDI, relative dose intensity

Table 3. Patient Disposition

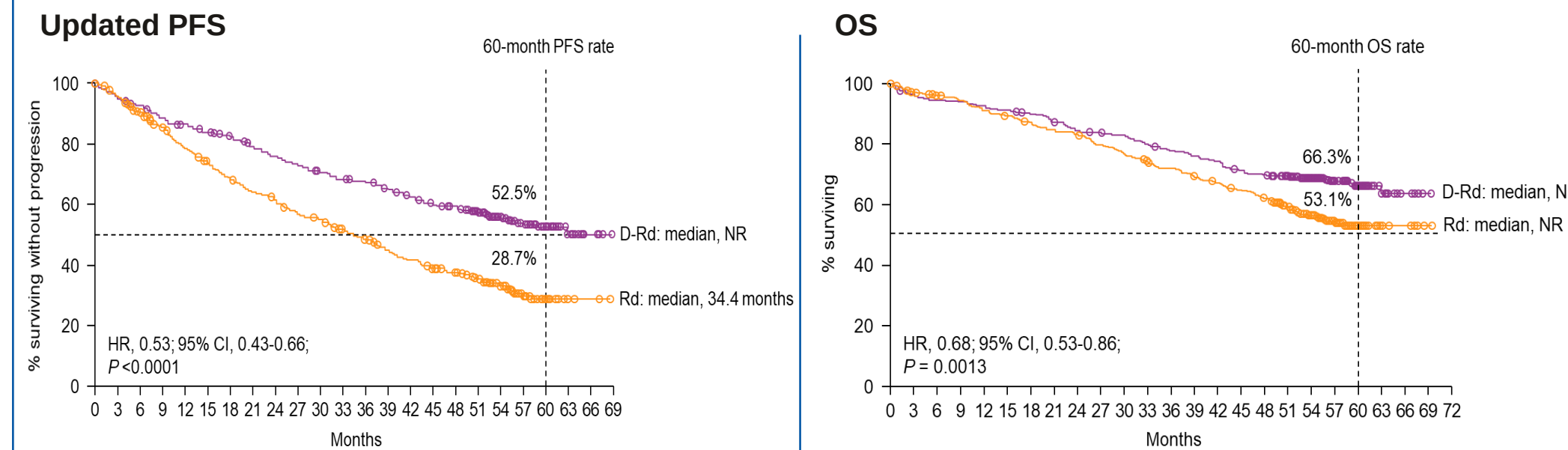
ITT population	D-Rd (n = 368)	Rd (n = 369)
Remaining on study treatment, %	42	18
Discontinued study treatment, %	57	81
Progressive disease	27	34
Adverse event	13	23
Death	7	7
Noncompliance with study drug	5	8
Physician decision	4	6
Other	1	1
Lost to follow-up	<1	1
Patient withdrawal	0	2

D, daratumumab; ITT, intent-to-treat; Rd, lenalidomide/dexamethasone

Figure 2. Efficacy



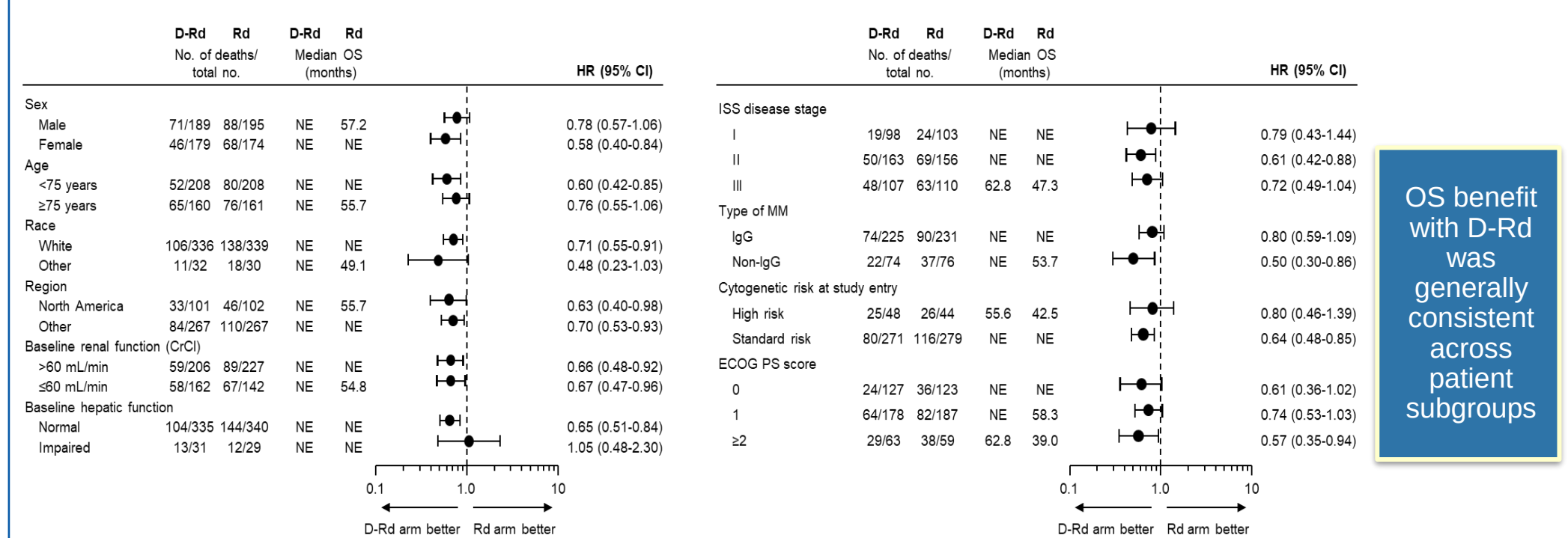
CR, complete response; DARA (D), daratumumab; ORR, overall response rate; PR, partial response; Rd, lenalidomide/dexamethasone; sCR, stringent complete response; VGPR, very good partial response. *ITT population. Note: percentages may not add up to the total due to rounding.



CI, confidence interval; D, daratumumab; HR, hazard ratio; NDMM, newly diagnosed multiple myeloma; NR, not reached; OS, overall survival; PFS, progression-free survival; Rd, lenalidomide/dexamethasone.

- D-Rd continued to demonstrate a significant PFS benefit, with median PFS not reached with D-Rd
- These data provide a new PFS benchmark in patients with NDMM who are transplant ineligible
- D-Rd demonstrated a significant benefit in OS, with a 32% reduction in the risk of death, in patients with NDMM who are transplant ineligible

Figure 3. Subgroup Analysis of OS



CI, confidence interval; D-Rd, daratumumab + lenalidomide/dexamethasone; ECOG PS, Eastern Cooperative Oncology Group (ECOG) performance status; HR, hazard ratio; Ig, immunoglobulin; ISS, International Staging System; NE, not estimated; MM, multiple myeloma; OS, overall survival; Rd, lenalidomide/dexamethasone.

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Subsequent Therapy

- Median time to next treatment was not reached with D-Rd vs 42.4 months with Rd (HR, 0.47; 95% CI, 0.37-0.59; P <0.0001)
- 114 patients in the D-Rd arm and 186 patients in the Rd arm received subsequent therapy; of these:
 - A PI-containing regimen without an IMiD was the most common first subsequent therapy (53% vs 54% with D-Rd and Rd, respectively)
 - 15% of patients in the D-Rd arm and 46% of patients in the Rd arm received daratumumab as any subsequent therapy

Safety

Table 4. Most Common Grade 3/4 (>5%) TEAEs^a

	D-Rd (n = 364)	Rd (n = 365)
Haematologic, n (%)		
Neutropenia	197 (54)	135 (37)
Anemia	61 (17)	79 (22)
Lymphopenia	60 (16)	41 (11)
Leukopenia	42 (12)	23 (6)
Thrombocytopenia	32 (9)	34 (9)
Nonhematologic, n (%)		
Pneumonia	70 (19)	39 (11)
Hypokalemia	46 (13)	36 (10)
Cataract	40 (11)	39 (11)
Diarrhea	32 (9)	22 (6)
Fatigue	32 (9)	17 (5)
Hypertension	31 (9)	16 (4)
Hyperglycemia	28 (8)	14 (4)
Pulmonary embolism	26 (7)	19 (5)
Asthenia	19 (5)	17 (5)
Acute kidney injury	19 (5)	12 (3)
Chronic kidney disease	19 (5)	10 (3)

No new safety concerns were identified with longer follow-up

A lower percentage of grade 3/4 and serious TEAEs occurred after 24 months vs during the first 24 months of treatment in both arms

D, daratumumab; Rd, lenalidomide/dexamethasone; TEAE, treatment emergent adverse event. ^aMedian duration of study treatment was 47.5 months in the D-Rd arm and 22.6 months in the Rd arm. Data are not exposure adjusted.

Conclusions

- After almost 5 years of follow-up, a significant OS benefit of D-Rd vs Rd given to progression was demonstrated in patients with transplant-ineligible NDMM, representing a 32% reduction in the risk of death
 - The estimated 5-year OS rate was 66.3% with D-Rd and 53.1% with Rd, which will likely lead to a substantial improvement of median OS in this patient population
- The significant PFS benefit of D-Rd vs Rd was maintained, with a 47% reduction in risk of disease progression or death (median PFS for D-Rd, not reached)
 - The estimated 5-year PFS rate was 52.5% with D-Rd and 28.7% with Rd
- These PFS and OS results have been achieved in a study population with 44% of patients aged 75 to 90 years
- No new safety concerns were identified with continuous therapy and longer follow-up

The results of MAIA study strongly support upfront D-Rd as a new standard of care for patients with transplant-ineligible NDMM

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Disclosure

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