Supplementary Material

Adjusted Indirect Treatment Comparison of Progression-free Survival with D-Rd and VRd Based on MAIA and SWOG S0777 Individual Patient-level Data

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Table S1. Alignment of key inclusion/exclusion criteria for the MAIA and SWOG S0777 trials

Criterion	MAIA	SWOG S0777	Alignment
NDMM and treatment naïve	Required	Required	Aligned
MM diagnostic criteria	≥1 CRAB criteria met	≥1 CRAB criteria met	Aligned
Transplant eligibility	Ineligible	Ineligible and eligible	Restrict both trial populations to patients aged ≥65 years (proxy for transplant ineligibility)
Measurable disease per IMWG at baseline [1,2]	Required	Required	Aligned
ECOG PS score	0-2	0-3	To harmonize the inclusion criteria, patients with a baseline ECOG PS score >2 were excluded from the comparative analyses (MAIA, n = 2; SWOG S0777, n = 4)
Hemoglobin	≥7.5 g/dL	≥9 g/dL	In terms of inclusion criteria, the MAIA trial required a baseline hemoglobin ≥7.5 g/dL and the SWOG S0777 trial required a hemoglobin ≥9 g/dL, but both trials included patients with hemoglobin <9 g/dL (14% and 8% of MAIA and SWOG S0777 patients, respectively, aged ≥65 years). In the primary analysis of PFS, propensity-score weighting was used to adjust for baseline hemoglobin, but no restriction based on hemoglobin was applied; in a sensitivity analysis, only patients with hemoglobin ≥9 g/dL were included
Neutrophil count	$\geq 1.0 \times 10^9$/L	$\geq 1.0 \times 10^9$/L	Aligned
Creatinine clearance	≥30 mL/min	>30 mL/min	Aligned
Exclusion: NYHA class III/IV cardiac status or recent AMI	Excluded	Excluded	Aligned

Exclusion: uncontrolled infection, HIV infection, hepatitis B or hepatitis C infection	Excluded all	Excluded all	Aligned
Exclusion: prior cancer	Patients with another malignancy within prior 5 years excluded	Excluded	Aligned
Exclusion: poorly controlled diabetes	Yes	Yes	Aligned

SWOG, Southwest Oncology Group; NDMM, newly diagnosed multiple myeloma; MM, multiple myeloma; CRAB, calcium elevation, renal impairment, anemia, bone involvement; IMWG, International Myeloma Working Group; ECOG PS, Eastern Cooperative Oncology Group performance status; PFS, progression-free survival; NYHA, New York Heart Association; AMI, acute myocardial infarction; HIV, human immunodeficiency virus.

Table S2. Baseline patient characteristics before and after multiple imputation and propensity-score weighting for the MAIA trial

	Unweighted	
Covariate	**D-Rd (n = 363)**	**Rd (n = 364)**
Age, mean (SD), years	74.19 (5.11)	74.38 (5.39)
Female, n (%)	178 (49.0)	171 (47.0)
ISS disease stage, n (%)		
I	97 (26.7)	102 (28.0)
II	163 (44.9)	153 (42.0)
III	103 (28.4)	109 (29.9)
ECOG PS score, n (%)		
0	126 (34.7)	121 (33.2)
1	176 (48.5)	186 (51.1)
≥2	61 (16.8)	57 (15.7)
Hemoglobin, n (%)		
<10 g/dL	134 (36.9)	122 (33.5)
eGFR, n (%)		
<60 mL/min/1.73 m^2	137 (37.7)	102 (28.0)
LDH		
≥190 U/L, n/N (%)[a]	176/346 (50.9)	181/355 (51.0)
Missing, n (%)	17 (4.7)	9 (2.5)
Cytogenetic risk		
High risk, n/N (%)[b]	47/315 (14.9)	44/318 (13.8)
Missing, n (%)	48 (13.2)	46 (12.6)

D-Rd, daratumumab plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; SD, standard deviation; ISS, International Staging System; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; LDH, lactate dehydrogenase.

[a]The denominator for the LDH ≥190 U/L percentage calculation was n = 346 for the D-Rd arm and n = 355 for the Rd arm due to missing data.

[b]High cytogenetic risk was defined in MAIA as the presence of ≥1 high-risk cytogenetic abnormality (del17p, t[14;16], or t[4;14]). The denominator for the high cytogenetic risk percentage calculation was n = 315 for the D-Rd arm and n = 318 for the Rd arm due to missing data.

Table S3. Baseline patient characteristics before multiple imputation and propensity-score weighting for the SWOG S0777 trial

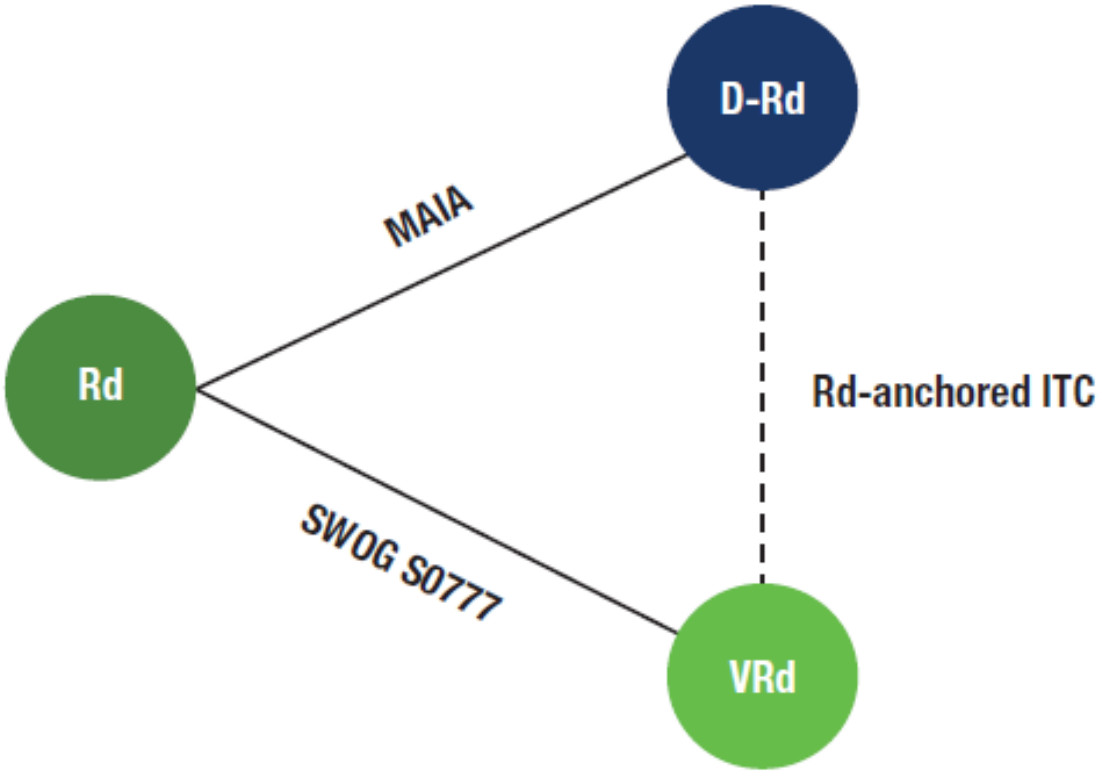
	Unweighted	
Covariate	**VRd (n = 91)**	**Rd (n = 107)**
Age, mean (SD), years	73.36 (5.58)	72.07 (5.0)
Female, n (%)	33 (36.3)	47 (43.9)
ISS disease stage, n (%)		
I	20 (22.0)	19 (17.8)
II	38 (41.8)	52 (48.6)
III	33 (36.3)	36 (33.6)
ECOG PS score, n (%)		
0	36 (39.6)	42 (39.3)
1	49 (53.8)	53 (49.5)
≥2	6 (6.6)	12 (11.2)
Hemoglobin, n (%)		
<10 g/dL	29 (31.9)	33 (30.8)
eGFR, n (%)		
<60 mL/min/1.73 m^2	45 (49.5)	48 (44.9)
LDH		
≥190 U/L, n/N[a]	39/90 (43.3)	37/107 (34.6)
Missing, n (%)	1 (1.1)	0
Cytogenetic risk		
High risk, n/N[b]	6/54 (11.1)	11/68 (16.2)
Missing, n (%)	37 (40.7)	39 (36.4)

SWOG, Southwest Oncology Group; VRd, bortezomib plus lenalidomide/dexamethasone; Rd, lenalidomide/dexamethasone; SD, standard deviation; ISS, International Staging System; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; LDH, lactate dehydrogenase.

[a]The denominator for the LDH ≥190 U/L percentage calculation was n = 90 for the VRd arm due to missing data.

[b]High cytogenetic risk was defined in SWOG S0777 as the presence of ≥1 high-risk cytogenetic abnormality (del[17p], t[14;16], or t[4;14]). The denominator for the high cytogenetic risk percentage calculation was n = 54 for the VRd arm and n = 68 for the Rd arm due to missing data.

Figure S1. Anchored ITC study design for MAIA versus SWOG S0777.



ITC, indirect treatment comparison; SWOG, Southwest Oncology Group;
Rd, lenalidomide/dexamethasone; D-Rd, daratumumab plus lenalidomide/dexamethasone;
VRd, bortezomib plus lenalidomide/dexamethasone.

References

1. Durie BGM, Harousseau JL, Miguel JS, et al. International uniform response criteria for multiple myeloma. Leukemia. 2006;20(9):1467-73.

2. Rajkumar SV, Harousseau JL, Durie B, et al. Consensus recommendations for the uniform reporting of clinical trials: report of the International Myeloma Workshop Consensus Panel 1. Blood. 2011;117(18):4691-5.