CEPHEUS: Depth and durability of MRD response with DVRd (NCT03652064)

N = 395

The CEPHEUS trial previously demonstrated improved depth of response and PFS with DVRd vs VRd. This final analysis, with a median follow up of 76 months, evaluated the depth, durability, and clinical meaningfulness of the DVRd MRD benefit.

Primary endpoint: Overall MRD (≥CR) negativity

Eligibility: Newly diagnosed MM; transplant-ineligible or transplant-deferred; ECOG PS 0–2; IMWG frailty score 0–1

STUDY DESIGN

Induction: 8 × 21-day cycles
Maintenance: 28-day cycles until disease progression or unacceptable toxicity

1:1 randomization

DVRd | n = 197

Induction	Maintenance
Daratumumab	Daratumumab
Bortezomib	Lenalidomide
Lenalidomide	Dexamethasone
Dexamethasone	

VRd | n = 198

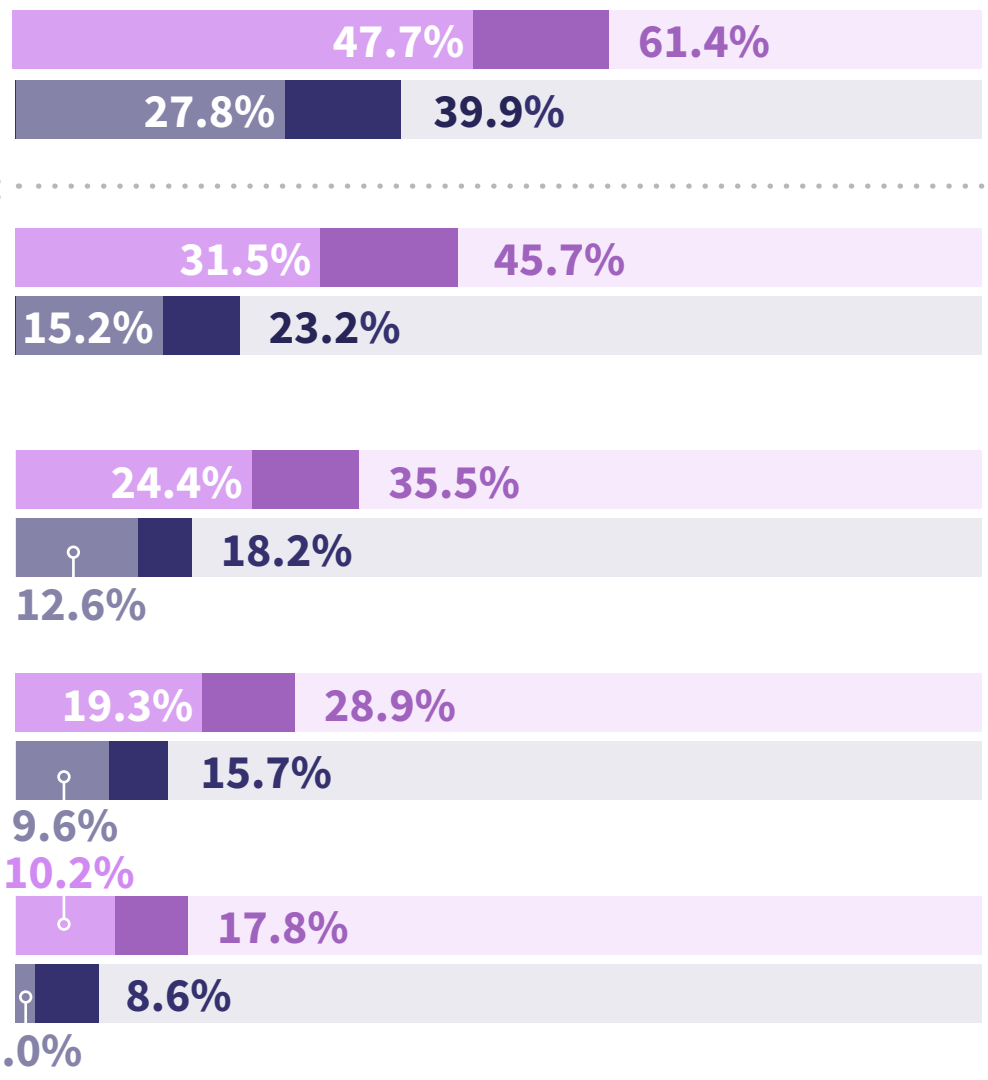
Induction	Maintenance
Bortezomib	Lenalidomide
Lenalidomide	Dexamethasone
Dexamethasone	

EFFICACY

Sustained MRD negativity rates (ITT population)

DVRd Thresholds: 10^{-6} 10^{-5} | VRd Thresholds: 10^{-6} 10^{-5}

MRD (≥CR) negativity rate by threshold



	10^{-6}	10^{-5}
Overall	OR, 2.33 (95% CI, 1.54–3.54) p < 0.0001	OR, 2.36 (95% CI, 1.58–3.54) p < 0.0001
Sustained:		
≥24 months	OR, 2.57 (95% CI, 1.57–4.21) p = 0.0001	OR, 2.78 (95% CI, 1.80–4.29) p < 0.0001
≥36 months	OR, 2.19 (95% CI, 1.29–3.71) p = 0.0029	OR, 2.47 (95% CI, 1.55–3.94) p = 0.0001
≥48 months	OR, 2.21 (95% CI, 1.23–3.96) p = 0.0065	OR, 2.16 (95% CI, 1.33–3.52) p = 0.0017
≥60 months	OR, 5.37 (95% CI, 1.82–15.84) p = 0.0006	OR, 2.27 (95% CI, 1.23–4.20) p = 0.0074

PFS: DVRd vs VRd by sustained MRD negativity status (10^{-5} threshold, ITT population)

mPFS after >6 years:

DVRd: Not reached	HR, 0.59; 95% CI, 0.44–0.80; p = 0.0005	VRd: 52.6 months

HR for PFS	Sustained MRD negativity: Achieved	Sustained MRD negativity: Not achieved
12 months	**HR, 0.65**; 95% CI, 0.34–1.26	**HR, 0.85**; 95% CI, 0.60–1.20
24 months	**HR, 0.92**; 95% CI, 0.40–2.12	**HR, 0.80**; 95% CI, 0.57–1.12

Sustained MRD negativity was associated with improved PFS. Furthermore, in patients with sustained MRD negativity, PFS was improved in those who received DVRd vs VRd.

After >6 years of follow-up, DVRd-treated patients achieved deeper and more sustained MRD negativity and improved PFS compared with those receiving VRd.

CI, confidence interval; CR, complete response; DVRd, daratumumab + bortezomib + lenalidomide + dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IMWG, International Myeloma Working Group; ITT, intent-to-treat; MM, multiple myeloma; mPFS, median PFS; MRD, minimal residual disease; OR, odds ratio; PFS, progression-free survival; VRd, bortezomib + lenalidomide + dexamethasone.

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