Abstract: P974

Title: DARATUMUMAB (DARA)/BORTEZOMIB/LENALIDOMIDE/DEXAMETHASONE (D-VRD) WITH D-R MAINTENANCE (MAINT) IN TRANSPLANT-ELIGIBLE (TE) NEWLY DIAGNOSED MYELOMA (NDMM): ANALYSIS OF PERSEUS BASED ON CYTOGENETIC RISK

Abstract Type: Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

In the primary analysis of the phase 3 PERSEUS study, subcutaneous DARA (DARA SC) + VRd induction/consolidation (ind/consol) and D-R maint improved progression-free survival (PFS) and increased rates of deep and durable responses, including minimal residual disease (MRD) negativity and sustained MRD negativity, vs VRd ind/consol and R maint in TE NDMM, regardless of cytogenetic risk status.

Aims:

We report an expanded analysis of PERSEUS (PFS, overall MRD negativity, and sustained MRD negativity) based on the presence of high-risk cytogenetic abnormalities (HRCAs), including gain(1q21) and amp(1q21).

Methods:

TE patients (pts) with NDMM were randomly assigned 1:1 to D-VRd or VRd. Pts in both arms received up to six 28-day cycles (4 pre-ASCT ind, 2 post-ASCT consol) of VRd (V 1.3 mg/m2 SC on Days [D] 1, 4, 8, 11; R 25 mg PO on D 1-21; d 40 mg PO/IV on D 1-4, 9-12) and R maint (10 mg PO on D 1-28 until progressive disease [PD]). In the D-VRd arm, pts also received DARA SC (DARA 1,800 mg + recombinant human hyaluronidase PH20 [rHuPH20; 2,000 U/mL; Halozyme]) QW in Cycles 1-2, Q2W in Cycles 3-6, and Q4W during maint until PD.

Cytogenetic risk was assessed by FISH. High risk was defined per protocol as the presence of ^{3}1 of the following HRCAs: del(17p), t(4;14), t(14;16). Revised high risk was defined as the presence of ^{3}1 of the following HRCAs: del(17p), t(4;14), t(14;16), gain(1q21), amp(1q21). Cytogenetic risk subgroups included standard risk (0 HRCAs per the protocol definition); high risk (per the protocol definition); revised standard risk (0 HRCAs per the revised definition); revised high risk; gain(1q21) and amp(1q21) (3 copies and ≥4 copies, respectively, of chromosome 1q21 ± other HRCAs); and (only) 1 HRCA and ≥2 HRCAs (per the revised definition). MRD-negativity rate (clonoSEQ®) was defined as the percentage of pts in the intent-to-treat population who achieved both complete response or better and MRD negativity.

Results:

709 pts were randomized (D-VRd, n=355; VRd, n=354). At a median follow-up of 47.5 months, PFS favored D-VRd vs VRd across all cytogenetic risk subgroups (**Figure**).

Overall MRD-negativity rates (10–5) were higher with D-VRd vs VRd across subgroups: standard risk (77.3% vs 48.1%; *P*<0.0001), high risk (68.4% vs 47.4%; *P*=0.0086), revised standard risk (75.3% vs 47.3%; *P*<0.0001), revised high risk (73.1% vs 49.3%; *P*<0.0001), gain(1q21) (69.5% vs 46.5%; *P*=0.0086), amp(1q21) (85.7% vs 55.6%; *P*=0.0104), 1 HRCA (75.3% vs 50.0%; *P*=0.0002), and ≥2 HRCAs (66.7% vs 47.4%; *P*=0.1044).

Rates of sustained MRD negativity (10–5) for ≥12 months were higher with D-VRd vs VRd across subgroups: standard risk (69.3% vs 31.2%; *P*<0.0001), high risk (48.7% vs 25.6%; *P*=0.0032), revised standard risk (66.1% vs 31.7%; *P*<0.0001), revised high risk (59.2% vs 27.7%; *P*<0.0001), gain(1q21) (62.7% vs 29.6%; *P*=0.0002), amp(1q21) (71.4% vs 27.8%; *P*=0.0006), 1 HRCA (61.9% vs 28.2%; *P*<0.0001), and ≥2 HRCAs (51.5% vs 26.3%; *P*=0.0303).

Rates of overall MRD negativity and sustained MRD negativity for ^{3}12 months at 10–6 were higher with D-VRd

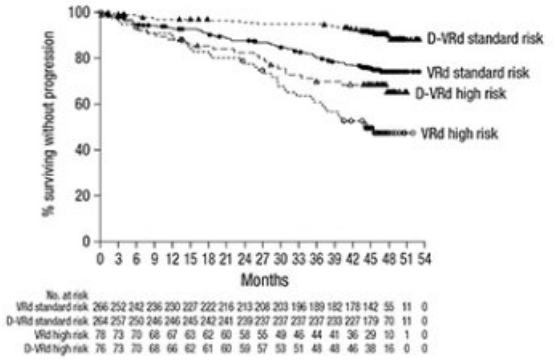
vs VRd across subgroups and will be presented at the meeting. Results for additional cytogenetic risk subgroups will also be presented.

Summary/Conclusion:

The addition of DARA SC to VRd ind/consol and to R maint provided clinical benefit in terms of PFS and induced higher rates of deep and sustained responses vs VRd ind/consol and R maint across all cytogenetic risk subgroups. These results support D-VRd ind/consol and D-R maint as a new standard of care for TE NDMM, regardless of cytogenetic risk status.

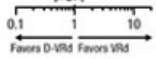
Figure. (A) Subgroup analysis of PFS based on protocol-defined cytogenetic risk status and (B) cytogenetic risk subgroup analysis of PFS in the ITT population.

A.



B.

	D-VRd		VRd			
	n/N	Median PFS (mo)	n/N	Median PFS (mo)	HR (95% CI)	*P* value
Standard risk	25/264	NE	62/266	NE	0.35 (0.22-0.56)	<0.0001
High risk	24/76	NE	38/78	44.1	0.59 (0.36-0.99)	0.0439
Revised standard risk	12/174	NE	35/167	NE	0.29 (0.15-0.56)	0.0001
Revised high risk	33/130	NE	62/148	NE	0.53 (0.35-0.81)	0.0027
Gain(1q21)	15/59	NE	26/71	NE	0.62 (0.33-1.18)	0.1400
Amp(1q21)	6/28	NE	17/36	46.7	0.37 (0.15-0.94)	0.0306
1 HRCA	21/97	NE	43/110	NE	0.47 (0.28-0.79)	0.0035
≥2 HRCAs	12/33	NE	19/38	44.1	0.73 (0.35-1.50)	0.3878



PFS, progression-free survival; ITT, intent-to-treat; D-VRd, daratumumab plus bortezomib/lenalidomide/dexamethasone; VRd, bortezomib/lenalidomide/dexamethasone; HR, hazard ratio; CI, confidence interval; NE, not estimable; HRCA, high-risk cytogenetic abnormality.

Keywords: Multiple myeloma, CD38, Minimal residual disease (MRD), Cytogenetic abnormalities