PHASE 3 RANDOMIZED STUDY OF DARATUMUMAB + BORTEZOMIB/THALIDOMIDE/DEXAMETHASONE (D-VTD) VERSUS VTD IN TRANSPLANT-ELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA: PART 1 CASSIOPEIA RESULTS

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Background
VTd is a standard of care for transplant-eligible newly diagnosed multiple myeloma (NDMM) patients. Daratumumab (DARA), a CD38 mAb, significantly reduced the risk of progression or death and improved complete response (CR) and minimal residual disease (MRD)-negative rates in relapsed refractory multiple myeloma or transplant-ineligible NDMM in phase 3 studies.

Aims
We report the primary and final analysis of Part 1 of the CASSIOPEIA trial for NDMM.

Methods
In Part 1, transplant-eligible NDMM patients 18-65 years old were randomized 1:1 to VTd (6 28-day cycles [C; 4 pre-autologous stem cell transplantation {ASCT} induction, 2 post-ASCT consolidation] of V 1.3 mg/m^2 SC BIW Week [W] 1-2; T 100 mg PO QD; d 40-80 mg/week PO or IV W 1-4 C 1-2, W 1-3 C 3-6) ± DARA (16 mg/kg IV QW C 1-2, Q2W C 3-6). Melphalan 200 mg/m^2 was pre-ASCT therapy. The primary endpoint was the rate of post-consolidation stringent complete response (sCR) assessed at Day 100 post-ASCT. Part 2 (maintenance) is ongoing.

Results

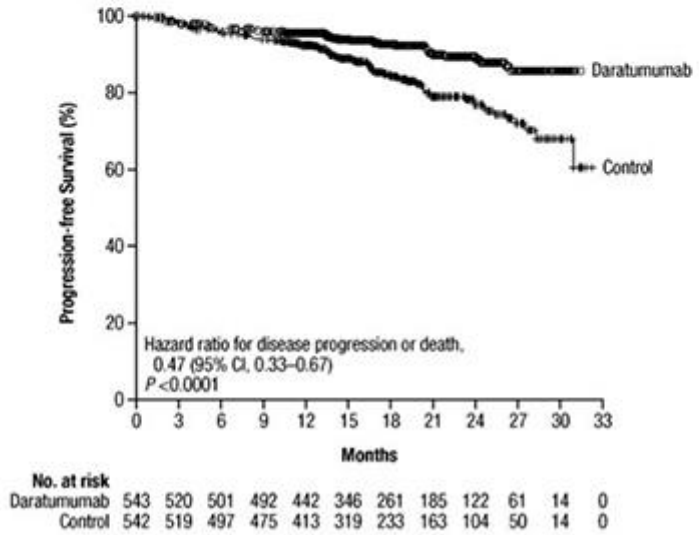
A cohort of 1085 patients (D-VTd, 543; VTd, 542) was randomized. The Day 100 post-ASCT sCR rate was significantly higher for the D-VTd arm versus the VTd arm (28.9% vs 20.3%; *P* = 0.0010; **Table**). With 18.8-months median follow-up, progression-free survival (PFS) from first randomization favored D-VTd with a hazard ratio (HR) of 0.47 (95% CI, 0.33-0.67; *P* <0.0001; **Figure**). With median PFS not reached in either arm, 18-month PFS rates were 92.7% versus 84.6% for D-VTd versus VTd. Rates of ≥CR, ≥VGPR, and MRD negativity supported sCR results (**Table**). Overall survival is immature with 46 deaths on study (D-VTd, 14; VTd, 32; HR, 0.43; 95% CI, 0.23-0.80). The most common (≥10%) grade 3/4 treatment-emergent adverse events (D-VTd/VTd) were neutropenia (27.6%/14.7%), lymphopenia (17.0%/9.7%), stomatitis (12.7%/16.4%), and thrombocytopenia (11.0%/7.4%). In the D-VTd arm, infusion-related reactions occurred in 35.4% of patients.

Table. Post-consolidation (Day 100 Post-ASCT) Response and MRD-negative Rates (10^{-5}): Intent-to-treat Population

	D-VTd, %	VTd, %	OR (95% CI)	*P*
sCR	28.9	20.3	1.60 (1.21-2.12)	0.0010
≥CR	38.9	26.0	1.82 (1.40-2.36)	<0.0001
≥VGPR	83.4	78.0	1.41 (1.04-1.92)	0.0239
MRD-negative	63.7	43.5	2.27 (1.78-2.90)	<0.0001
≥CR + MRD-negative	33.7	19.9	2.06 (1.56-2.72)	<0.0001

ASCT, autologous stem cell transplantation; MRD, minimal residual disease; D-VTd, daratumumab/bortezomib/thalidomide/dexamethasone; VTd, bortezomib/thalidomide/dexamethasone; OR, odds ratio; CI, confidence interval; sCR, stringent complete response; CR, complete response; VGPR, very good partial response.

Figure. PFS from first randomization regardless of second randomization.



Conclusion

D-VTd in induction prior to and consolidation after ASCT improved depth of response (sCR, ≥CR, and MRD negativity) and PFS with acceptable safety. The favorable benefit-risk profile supports the use of D-VTd in transplant-eligible NDMM. CASSIOPEIA is the first study to demonstrate the clinical benefit of daratumumab plus standard of care in transplant-eligible NDMM patients.