between these two anti-CD38 mAbs, therapeutic choice should be based on factors other than efficacy. Protocol Registration: CRD420250618823.

https://doi.org/10.1016/j.htct.2025.104822

ID - 821

DARATUMUMAB + BORTEZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (DVRD) VS VRD IN TRANSPLANT-INELIGIBLE (TIE)/TRANSPLANT-DEFERRED (TD) NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): PHASE 3 CEPHEUS TRIAL CYTOGENETIC SUBGROUP ANALYSIS

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Introduction: In CEPHEUS, DVRd significantly improved overall MRD negativity (MRD neg + ≥CR) and sustained MRD neg rates and PFS in patients (pts) with TIE/TD NDMM. In this post hoc analysis, we report outcomes in cytogenetic risk subgroups. **Objectives:** To gain additional insight into those patients who had long-term clinical benefit ≥5 years after a single cilta-cel infusion, we conducted a post hoc analysis. We report OS, ≥5-year progression-free outcomes, associated biomarkers, and safety from CARTITUDE-1, with 61.3-month median follow-up. **Material and methods:** Pts with TIE/TD NDMM were randomized 1:1 to DVRd or VRd. High-risk (HiR) cytogenetic abnormalities (HRCAs) were assessed by FISH. HiR was ≥1 of: del(17p); t(4;14); t(14;16). Revised HiR (R-HiR) was ≥1 of above or gain (3 copies) or amp(1q) (≥4 copies). Standard risk (SR) was 0 HRCAs; revised SR (R-SR) was 0 revised HRCAs. Additional risk groups included: gain or amp(1q) + other HRCAs; 1 and ≥2 revised HRCAs. We assessed overall MRD neg rate, sustained MRD neg, ≥CR rate, and PFS. We reported all MRD neg rates at 10-5 unless noted. **Results:** Of 395 randomized pts (DVRd, n = 197; VRd, n = 198), 298 had SR (DVRd, n = 149; VRd, n = 149) and 52 HiR (DVRd, n = 25; VRd, n = 27). 184 pts had R-SR (DVRd, n = 94; VRd, n = 90) and 167 R-HiR (DVRd, n = 83; VRd, n = 84). At median 58.7-month (mo) follow-up, overall MRD neg rate was higher with DVRd vs VRd in SR (64% vs 38%; P < 0.0001) and R-SR pts (68% vs 38%; P < 0.0001). Rates by treatment (tx) arm in HiR (48% vs 56%; P = 0.7816) and R-HiR pts (55% vs 45%; P = 0.2169) were comparable. DVRd improved ≥1-year (y) sustained MRD neg rate vs VRd in SR (51% vs 26%; P < 0.0001) and R-SR pts (54% vs 24%; P < 0.0001). Sustained MRD neg rates by tx arm were comparable in HiR (40% vs 37%; P = 1.0000) and R-HiR pts (43% vs 30%; P = 0.0782). PFS was improved with DVRd vs VRd in SR (HR = 0.61 [95% CI, 0.41−0.91]; P = 0.01) and R-SR (HR = 0.54 [95% CI, 0.32−0.91]; P = 0.01) pts and was comparable by tx arm in HiR (HR = 0.88 [95% CI, 0.48−1.84]; P = 0.73); and R-HiR HR = 0.73 [95% CI, 0.46−1.15]; P = 0.17; pts (), including in MRD neg pts (R-SR: (HR = 0.63 [95% CI, 0.26−1.52]; P = 0.30); R-HiR: HR = 0.71 [95% CI, 0.32−1.58]; P = 0.39. Gain(1q)+otherHRCAs HR = 0.80 [95% CI, 0.45−1.42]; P = 0.044; Amp(1q)+other HRCAs HR = 0.97 [95% CI, 0.38−2.47]; P = 0.95. 1 revised HRCA HR = 0.63[95% CI, 0.37−1.09]; P = 0.09; ≥2 revised HRCA (HR = 1.01[95% CI, 0.42 −2.44]; P = 0.98) Remaining outcomes, including rates of ≥CR, ≥2-y sustained MRD neg, and overall and ≥1-y sustained MRD neg at 10-6, were improved with DVRd in SR and R-SR pts and comparable by tx arm in HiR and R-HiR pts. **Discussão e conclusão:** In CEPHEUS, DVRd consistently improved the key response outcomes of MRD neg and PFS in (R-)SR pts. In HiR pts, MRD and PFS outcomes trended lower in both tx arms vs those in SR pts. Here, DVRd mostly improved PFS outcomes vs VRd; however, pt numbers were small, with the study underpowered for HiR pts. These data support use of DVRd for TIE/TD NDMM regardless of cytogenetic risk status. **Funding:** This study was funded by Johnson & Johnson. Medical writing support was provided by Maggie Hartman, PharmD, of Eloquent Scientific Solutions, and funded by Johnson & Johnson.

https://doi.org/10.1016/j.htct.2025.104823

ID - 765

DARATUMUMAB PLUS BORTEZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (DVRD) IN PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM): SUBGROUP ANALYSIS OF TRANSPLANT-INELIGIBLE (TIE) PATIENTS IN THE PHASE 3 CEPHEUS STUDY

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