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

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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

NJ Bahlis [a], SZ Usmani [b], T Facon [c], S Zweegman [d], C Venner [e], M Braunstein [f], L Pour [g], J Marti [h], A Maiolino [i], V Hungria [j]

[a] *Arnie Charbonneau Cancer Research Institute, University of Calgary, Calgary, Canada*
[b] *Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, United States*
[c] *University of Lille, CHU Lille, Lille,France*
[d] *Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands*
[e] *Cross Cancer Institute, University of Alberta, Edmonton, Canada*
[f] *Perlmutter Cancer Center, NYU Langone Health, New York, United States*
[g] *University Hospital Brno, Brno, Czech Republic*
[h] *Hospital Universitario Mútua de Terrassa, Terrassa, Spain*
[i] *Instituto Americas de Ensino, Pesquisa e Inovação, Rio de Janeiro, Brazil*
[j] *Clínica Médica São Germano, São Paulo, Brazil*

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.

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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

T Facon [a], S Zweegman [b], V Hungria [c], NJ Bahlis [d], CP Venner [e], M Braunstein [f], L Pour [g], J Marti [h], A Maiolino [i], SZ Usmani [j]

[a] *University of Lille, CHU Lille, Lille, France*
[b] *Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands*
[c] *Clínica Médica São Germano, São Paulo, Brazil*
[d] *Arnie Charbonneau Cancer Research Institute, University of Calgary, Calgary, Canada*
[e] *Cross Cancer Institute, University of Alberta, Edmonton, Canada*

[f] *Perlmutter Cancer Center, NYU Langone Health, New York, United States*
[g] *University Hospital Brno, Czech Republic*
[h] *Hospital Universitario Mútua de Terrassa, Spain - Spain*
[i] *Instituto Americas de Ensino, Pesquisa e Inovação, Rio de Janeiro, Brazil*
[j] *Memorial Sloan Kettering Cancer Center, New York, United States*

Introduction: After reading out of the PERSEUS and CEPHEUS trials, daratumumab-based therapy + VRd is emerging as the standard of care in NDMM treatment. In CEPHEUS (NCT03652064), DVRd improved minimal residual disease negativity (MRD neg) and progression-free survival (PFS) vs VRd in patients (pts) with TIE or transplant-deferred (TD) NDMM. As transplant deferral is not a common clinical pathway in many regions, here we report a post hoc analysis of DVRd efficacy in TIE pts. **Objectives:** In this analysis, the primary endpoint of overall MRD neg rate (MRD neg at 10-5 and complete response or better [≥CR]), and key secondary endpoints, including PFS and sustained MRD neg (confirmed MRD neg ≥12 months [mo] apart without MRD positivity in between) were assessed. **Material and methods:** CEPHEUS enrolled pts with TIE or TD NDMM, ECOG performance status (PS) 0–2, and an International Myeloma Working Group (IMWG) frailty score of 0 or 1. Pts were randomized (1:1) to DVRd or VRd. **Results:** Of 395 pts, 289 were TIE (DVRd, n = 144; VRd, n = 145). TIE population baseline (BL) characteristics were generally well balanced between DVRd vs VRd. In the TIE vs intent-to-treat (ITT) population, median age was older (72 vs 70 years [y]), and a higher percentage of pts were intermediate fit per IMWG criteria (41.2% vs 35.2%). In TIE pts, overall MRD neg rate at 10−5 was 60.4% for DVRd and 39.3% for VRd (odds ratio [OR] 2.37; 95% CI 1.47–3.80; p < 0.0001); at 10−6, it was 45.8% vs 26.9% (OR 2.28; 95% CI 1.40–3.73; p = 0.001). Sustained MRD neg rate (10−5) was 46.5% vs 27.6% (OR 2.27; 95% CI 1.39–3.70; p = 0.0010). Overall ≥CR rate was 80.6% vs 61.4% (OR 2.73; 95% CI 1.71–4.34; p < 0.0001). At 58.7-mo median follow-up, median PFS was NR for DVRd and 49.6 mo for VRd, and the 54-mo PFS rate was 69.0% vs 48.0% (HR 0.51; 95% CI 0.35–0.74; p = 0.0003); OS favored DVRd vs VRd (HR 0.66; 95% CI 0.42–1.03); after censored for deaths due to COVID-19, HR 0.55; 95% CI 0.34–0.90). Treatment effect was generally consistent across subgroups MRD neg(10-5) rate, %: DVRd, VRd: ISS Stage III (55 vs 30), Cytogenetic risk high(50 both), ECOG ≥1 (621 vs 36.4) Median PFS, mo VRd: 60.6 Stage 1 and 33.6 Stage III, Cytogenetic risk High: 31.7, Standard:60.6. ECOG 0:60.6, ECOG ≥1:47.2. Safety profile was consistent with ITT and the known profile for daratumumab subcutaneous and VRd. **Discussion and conclusion:** In CEPHEUS TIE pts, the ≥CR rate was 80.6% and overall MRD neg rate (10−5) was 60.4%, with ∼50% of pts sustaining MRD neg for ≥1 y. Nearly 70% of pts were alive and progression free at 4.5 y. These subgroup data reinforce the strong efficacy of DVRd in the TIE population.

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DENOSUMABE VERSUS ACIDO ZOLEDRÔNICO NA PREVENÇÃO DOS EVENTOS RELACIONADOS AO ESQUELETO EM PACIENTES COM MIELOMA MÚLTIPLO: UMA REVISÃO INTEGRATIVA

TS Pereira, ALN Gomes, DMSL Silva

Hospital Amaral Carvalho (HAC), Jaú, SP, Brasil

Introdução: Os eventos relacionados ao esqueleto (EREs) são uma das complicações mais comuns associadas ao mieloma múltiplo. Esses eventos estão relacionadas à destruição óssea, resultando em fraturas patológicas, compressão da medula espinhal, hipercalcemia e dor, sendo uma das principais causas de morbidade e mortalidade. A escolha padrão de tratamento é o uso de Bifosfonatos, devido à sua capacidade de inibir a atividade dos osteoclastos, sendo o mais conhecido, o ácido zoledrônico. Estudos recentes identificaram novas drogas que não somente interferem na biologia da destruição óssea, mas também com a sobrevida. O denosumabe é um anticorpo monoclonal humano que atua na via de sinalização RANKL-RANK, levando à supressão da formação, função e sobrevivência de osteoclastos, reduzindo a reabsorção óssea. Essa via está envolvida no desenvolvimento de doenças ósseas em pacientes com mieloma múltiplo, sendo portanto um alvo para tratamento promissor das EREs nessa população. **Objetivos:** Discutir os resultados de eficácia e segurança do denosumabe versus ácido zoledrônico na prevenção de eventos relacionados ao esqueleto (EREs) em pacientes com mieloma múltiplo. **Material e métodos:** O presente trabalho trata-se de uma revisão integrativa. O trabalho seguiu os preceitos do estudo exploratório, por meio de uma pesquisa bibliográfica. Baseando-se na busca de artigos indexados na seguinte base de dados: PUBMED. Foram aplicados os seguintes descritores: denosumab, multiple myeloma, zoledronic, com o operador booleano "AND". Sendo selecionados meta-análises, e revisões sistemáticas no idioma inglês, com recorte temporal de janeiro de 2020 até julho de 2025. Os dados obtidos foram selecionados e sistematicamente classificados de acordo com a classificação dos níveis de evidencia. A utilização da estratégia de busca na base de dados resultou em 6 estudos incluídos. **Discussão e conclusão:** A presente revisão integrativa evidenciou que os estudos incluídos corroboram com a hipótese de que o Denosumabe apresenta-se como uma escolha promissora na prevenção das EREs em pacientes com mieloma múltiplo. Como destaque, temos que o tempo até a ocorrência do primeiro ERE foi ligeiramente maior com o uso de denosumabe em comparação ao ácido zoledrônico. Um dos estudos notavelmente indicou que o denosumabe proporcionou uma melhora estatisticamente significativa na sobrevida livre de progressão (SLP) em comparação com o ácido zoledrônico, essa vantagem pode estar relacionada a menor toxicidade óssea e melhor controle de remodelação óssea pelo denosumabe. Além disso, o denosumabe foi associado a menor riscos de eventos adversos renais, sendo uma escolha preferencial para pacientes com