foram estudados de pacientes diagnosticados com mieloma múltiplo em centros de referência: o Laboratório de Genética e Genômica do SOLCA Quito e a Faculdade de Ciências da Saúde Eugenio Espejo da Universidade UTE, Quito, Equador, e o Laboratório Díaz Gill S.A., em Assunção, Paraguai. Variáveis demográficas (idade, sexo) e resultados de citogenética convencional e FISH foram avaliados. **Resultados:** Um total de 106 pacientes do Equador e 104 pacientes do Paraguai com diagnóstico confirmado de MM foram analisados. A média de idade foi de 59 anos (variação: 37-98 anos; mediana: 59,5) no Equador e 61,5 anos (variação: 26-83; mediana: 63) no Paraguai. A proporção homens/mulheres na coorte equatoriana foi de 68%/32%, enquanto, na coorte paraguaia, foi de 47%/53%. Um cariótipo normal estava presente em > 50% dos casos no Equador e em 46% no Paraguai. A classificação citogenética em hiperdiploide e não hiperdiploide ocorreu em 6% e 94% dos casos no Equador e 15% e 85% no Paraguai, respectivamente. A seleção positiva de células foi usada em ambos os países, o que permitiu a detecção de anormalidades em mais de 20% dos casos com cada uma das sondas RB, IGH, TP53, 1p (CDKN2C) e 1q (CKSB1). Uma vez identificada a alteração de IGH, foram identificadas uma alta frequência de t(4;14) FGFR3/IGH e uma baixa frequência de t(11;14) CCND1/IGH em ambas as coortes em comparação com outras populações. Estudos mostram diferenças entre pacientes com MM no Equador e no Paraguai em termos de idade no diagnóstico e porcentagem de apresentação de acordo com o gênero, o que pode estar associado à composição genética de cada população. Pacientes da América Central e da região andina têm uma idade média no diagnóstico de 55,8 anos, em comparação com uma idade média de 62,8 anos nos países do Cone Sul. Em relação à razão de gênero, nos países da América Central e dos Andes a porcentagem média de homens com MM é de 55,3% contra 44,3% dos homens nos países do Cone Sul. Em relação aos achados citogenéticos, há uma diferença na apresentação de casos hiperdiploides entre o Equador e o Paraguai, embora a porcentagem seja geralmente baixa em comparação com outras populações. Da mesma forma, ambas as coortes latino- americanas mostram semelhanças na apresentação de translocações envolvendo o gene IGH. **Discussão e conclusão:** Esta análise ressalta a necessidade de padronizar os sistemas de coleta de dados clínico-genéticos na região, fortalecer a integração de informações entre os países e promover a pesquisa multicêntrica. A unificação dos critérios diagnósticos e o uso complementar de ferramentas genômicas melhorariam o diagnóstico precoce, otimizariam os tratamentos e avançariam em direção à medicina personalizada contextualizada na América Latina.

https://doi.org/10.1016/j.htct.2025.104821

ID - 528

COMPARATIVE EFFICACY OF ANTI-CD38 MONOCLONAL ANTIBODIES IN MULTIPLE MYELOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS SOUTO

JTD Filho [a], A Doshi [b], A Grimshaw [c], S Giri [d], LJ Costa [d]

[a] *Faculdade de Medicina de Campos (FMC), Campos dos Goytacazes, Brazil*
[b] *Jacobi Medical Center/Albert Einstein College of Medicine, United States*
[c] *Cushing / Whitney Medical Library, Yale University, United States*
[d] *Division of Hematology and Oncology, Department of Medicine, University of Alabama, Birmingham, United States*

Introduction: The introduction of anti-CD38 monoclonal antibodies (mAb) has significantly advanced treatment of multiple myeloma (MM). Both daratumumab (D) and isatuximab (I) have demonstrated substantial efficacy and improved outcomes in newly diagnosed and relapsed/refractory MM. Although widely evaluated with similar backbone regimens, direct comparative evidence between these agents remains unavailable. In the absence of head-to-head trials, network meta-analysis (NMA) provides a rigorous framework for indirect comparisons to support evidence-based selection of CD38-targeted strategies. **Objectives:** We conducted a systematic review (SR) and NMA of randomized clinical trials (RCT) to compare efficacy and survival outcomes of daratumumab- versus isatuximab-based regimens in MM. **Material and methods:** A structured search of Cochrane Library, Embase, Google Scholar, Medline, PubMed, Scopus, Web of Science, clinical trial registries, and major conference abstracts (2022 −2025) was performed in January 2025. Eligible phase II/III RCT evaluated either antibody in combination with a shared therapeutic backbone and reporting progression-free survival (PFS) as endpoint. Two authors extracted and quality-checked data. We estimated hazard ratios (HR) for PFS and overall survival (OS) using a frequentist NMA model based on aggregate-level data, for each indirect comparison between regimens sharing a common backbone. Subsequently, we pooled the results using a random-effect model to summarize the overall treatment effect. Heterogeneity was assessed using Cochran's Q and I^2 statistics. **Results:** Six phase III trials comprising 2,587 patients met inclusion criteria. To enable an indirect comparison between D and I, studies were grouped into three networks based on identical backbone regimens: carfilzomib and dexamethasone (Kd), pomalidomide and dexamethasone (Pd), and bortezomib, lenalidomide and dexamethasone (VRd). No significant differences in PFS were observed across regimens: D-Kd vs. I-Kd (HR 1.10, 95% CI: 0.73−1.66), D-Pd vs. I-Pd (HR 1.11, 95% CI: 0.75−1.63), and D-VRd vs. I- VRd (HR 0.95, 95% CI: 0.60−1.49). Similarly, no differences in OS were detected: D-Kd vs. I-Kd (HR 0.91, 95% CI: 0.59−1.40), D-Pd vs. I-Pd (HR 1.05, 95% CI: 0.70−1.58), and D-VRd vs. I-VRd (HR 1.09, 95% CI: 0.65−1.82). In the pooled analysis, no significant differences were found between daratumumab- and isatuximab-based regimens for either PFS (HR 1.06, 95% CI: 0.86 −1.30; p = 0.36) or OS (HR 1.01, 95% CI: 0.79−1.28; p = 0.91). Heterogeneity was low in both analyses (PFS: Cochran's Q, p = 0.86; I^2 = 0%; and OS: Cochran's Q, p = 0.84; I^2 = 0%). Risk of bias was low across all studies, and effect modifiers were sufficiently balanced to support transitivity. **Discussion and conclusion:** This is the first NMA to indirectly compare daratumumab and isatuximab in MM using RCT-level evidence. In absence of significant differences in PFS or OS

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

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.

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

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*