evasão, impossibilidade de tratamento, óbito. Somado a isso, é necessário buscar esclarecimentos sobre os achados deste estudo, como sexo, faixa etária e distribuição geográfica da doença. Por fim, os idosos merecem uma atenção maior na investigação por mieloma múltiplo, visto que eles representam 61,30% dos casos.

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## SAFETY OF DARATUMUMAB IN FRAIL PATIENTS WITH MULTIPLE MYELOMA

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**Introduction:** Frailty in elderly is associated with negative outcomes and high mortality. In frail patients diagnosed with Multiple Myeloma (MM), it's advisable to adjust the dosages of antineoplastic treatments to minimize associated toxicities. **Objective:** This study aims to present two clinical cases emphasizing the safety profile of Daratumumab in frail patients with MM. **Materials and methods:** MM patients receiving Daratumumab underwent a specialized geriatric assessment protocol. For frailty assessment, the modified Fried frailty criteria and the Frail Scale were utilized. The Lawton scale gauged functionality in instrumental activities of daily living (IADL), while sarcopenia assessment was conducted following the updated guidelines from the European Working Group on Sarcopenia. The study included elderly patients meeting three or more criteria on the Frail Scale. **Results:** Two frail patients diagnosed with MM were assessed during treatment with Daratumumab, Bortezomib, an alkylating agent, and corticosteroids, followed by Daratumumab maintenance. The first patient, S.N.C., aged 64, had type 2 diabetes mellitus, history of falls, osteoporosis with lytic bone lesions, and spinal fractures. She also had severe IADL dependence (scored 11 out of 27 on the Lawton scale) and used a wheelchair, having been independent earlier. She also displayed signs of sarcopenia. On the Frail Scale, she scored 3 of the 5 points. The initial treatment spanned seven cycles before transitioning to monthly maintenance. No dose modifications were required. After 6 months of therapy, the patient reported symptomatic relief, improved motor functions, regained walking abilities, and increased independence in IADL. The second patient, G.P.F., aged 78, had no notable comorbidities, but had several osteolytic lesions and fractures evident on CT scans. He was frail, dependent on IADL, exhibited nutritional risk and history of falls. He underwent a four-drug treatment for six cycles, subsequently establishing monthly maintenance. Upon reevaluation after completing the treatment cycles, he reported no outstanding complaints, regained his ambulation, and cited feeling well with a noted improvement in his IADL dependence. **Discussion:** Patients exhibiting frailty syndrome generally experience poorer outcomes and a higher rate of complications linked to therapeutic interventions across multiple clinical contexts. The efficacy of Daratumumab has been substantiated in the MAIA and ALCYONE trials for non-eligible patients per investigator subjective criteria. In the "frailty" sub-analysis of the MAIA study, geriatric assessment was not performed, and patients with high comorbidity scores were included. We present two cases with geriatric assessments and established frailty syndrome criteria who showed favorable outcomes with the chosen regimen, without need for dose adjustments. **Conclusion:** The administration of Daratumumab to frail patients in this study was safe and results in swift clinical responses. Thiago Xavier Carneiro receives honoraria from Janssen.

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## COMPREHENSIVE CIRCRNA ANALYSIS REVEALS MOLECULAR INTERACTIONS RELATED TO POOR OVERALL SURVIVAL IN MULTIPLE MYELOMA

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Multiple myeloma (MM) is one of the most common hematologic malignancies, characterized by uncontrolled proliferation of plasma cells in the bone marrow. Investigating MM epigenetics at the non-coding RNAs (ncRNAs) level and their interactions can be a key factor in understanding this disease. Circular RNAs (circRNAs) are ncRNAs whose 5'and 3'ends are covalently joined and have been mostly investigated in MM by acting as microRNAs (miRs) sponges, but it is known that they also interact with RNA binding proteins (RBPs). This study aimed to investigate the differentially expressed (DE) circRNAs in MM, their relationship with RBPs and miRs, and their biological implications. Public RNA-Seq datasets (PRJNA634534, PRJNA472759) were downloaded from ENA and the reads were treated to obtain the circRNA count matrix. The DE circRNAs were identified using the CircTest package and then submitted in circAtlas3.0 to obtain their interactions with miRs and RBPs. Furthermore, only miRs that interacted with two or more circRNAs were considered. miRTarBase was used to identify the target genes, selecting those validated by strong evidence. Functional enrichment analyses (FEA) were performed, using ReactomePA, for each circRNA considering both their RBP and miR-targets. Lastly, by combining the circRNAs'expression results and their interaction with RBPs or miRs, genes were selected to be investigated in a bigger RNA-Seq dataset of MM patients, available in TCGA. Gene expression was compared according to the patient's vital status and ISS stage, and the DE genes were selected for a Kaplan-Meier survival analysis. All analyses were performed on R and p-values<0.05 were considered statistically significant. First, 6 circRNAs were found as downregulated in MM

compared with health controls (referred to as circs-down), and 4 circRNAs were specifically expressed in MM (referred to as circs-spe). In RBP analyses, 47 RBPs interacted with circs-down, and 51 with circs-spe. FEA resulted in 35 pathways, in which one pathway was exclusively enriched by circs-down, and 7 others by circs-spe. From 12 RBPs that interacted exclusively with circs-down, 5 genes were DE in the vital status analysis, and 2 genes were DE in the ISS stage analysis. And from 16 RBPs exclusively to circs-spe, 8 genes were DE in the vital status analysis, and 2 genes were DE in the ISS stage analysis. In miR analyses, 24 miRs and 172 targets interacted with 5 circs-down, while 18 miRs and 79 targets interacted with 3 circs-spe. FEA resulted in 396 pathways, 242 only for circs-down and 61 exclusively to circs-spe. From 198 exclusive axes formed by 5 circs-down, 7 miRs, and 94 targets; 8 genes were deregulated in both analyses (vital status and ISS stage). 2 axes were formed by 2 circs-spe, 1 miR, and 1 target. Altogether (RBPs and miR-targets), 22 genes (when upregulated) and 4 genes (when downregulated), were significantly associated with poor overall survival. This study highlighted potential molecular interactions in which circRNAs are key players. Through their interactions with RBPs and miRs, circRNAs can be involved in important cancer-related functions. Furthermore, we identified genes that are associated with poor survival in patients with multiple myeloma, which may help in the prognosis assessment and development of new therapies for this disease.

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## ANÁLISE EPIDEMIOLÓGICA DOS DIAGNÓSTICOS DE MIELOMA MÚLTIPLO NO BRASIL NO PERÍODO 2013-2022

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**Objetivo:** O mieloma múltiplo é o segundo tumor hematológico mais prevalente no Brasil e no mundo, sendo, assim, um problema de saúde pública que merece maior enfoque. Esse trabalho busca descrever a epidemiologia de tais enfermidades no país e suas respectivas distribuições por sexo, faixa etária, entre as unidades federativas da região e as modalidades terapêuticas adotadas, entre os anos de 2013 e 2022. **Material e estudo:** Efetuou-se um estudo descritivo transversal acerca dos diagnósticos de mieloma no país entre 2013 e 2022. A obtenção de dados ocorreu por meio do Sistema de Informações Hospitalares do SUS (SIH/SUS). Foram filtradas e combinadas as informações: sexo, faixa etária, região do diagnóstico, unidade federativa do diagnóstico e modalidade terapêutica. **Resultados:** Entre 2013 e 2022, foram reportados 30.843 diagnósticos de mieloma múltiplo no Brasil, sendo a região sudeste aquela com o maior número absoluto de casos (14.927), representando 48,39% do total de casos. O estado com maior número absoluto de casos foi São Paulo (7.806), representando 25,3% dos diagnósticos dessa patologia no país. Em relação ao sexo, os homens receberam maior número de diagnósticos: 16.233 (52,63%), em relação a 14.610 mulheres (47,36%). Em relação à faixa etária, o intervalo com maior concentração de diagnósticos foi entre 65 e 69 anos, com 5.145 diagnósticos (16,68%). Interessante pontuar que a população geriátrica correspondeu ao maior grupo epidemiológico da doença. Indivíduos com idade maior ou igual a 60 anos correspondem a 19.449 diagnósticos (63.05%). Quanto às modalidades terapêuticas, a quimioterapia foi a mais adotada, com 24.150 tratamentos realizados (78,29%), seguido de radioterapia, com 2.757 tratamentos realizados (8,93%). Importante salientar que em 3.811 casos não temos informações sobre o tratamento (12,35%). **Discussão:** É inevitável não associar o envelhecimento da população brasileira com a epidemiologia do mieloma múltiplo. Em 2013, foram efetuados 2.449 diagnósticos da doença, enquanto em 2022 foram efetuados 4.480. Isso confere um aumento de 89,93% de novos casos no período. Esse aumento nos remete à maior necessidade das autoridades públicas no investimento em políticas voltadas tanto à população idosa quanto ao diagnóstico precoce e à maior acessibilidade do tratamento mais utilizado (quimioterapia) aos pacientes com tal enfermidade. Além disso, os idosos correspondem a mais da metade dos indivíduos afetados, o que necessita de maior atenção às políticas de saúde, devido à negligência histórica que essa população sobre, assim como a transição demográfica em curso na nação e as peculiaridades fisiológicas que tal grupo etária apresenta. **Conclusões:** O período analisado evidenciou 30.843 diagnósticos de mieloma múltiplo, sendo a região sudeste aquela com maior concentração de casos, em números absolutos, com 14.927 diagnósticos, representando 48,39% do total nesse período. A faixa etária com maior número de diagnósticos foi entre 65 e 69 anos, com 5.145 diagnósticos (16,68%). Além disso, a população idosa, de maneira geral, é a mais acometida pela doença, representando 63.05% do número de diagnósticos no país entre 2013 e 2022. Portanto, é necessário maior enfoque e investimento de políticas públicas para o diagnóstico precoce e tratamento do mieloma múltiplo, pois a população geriátrica é a mais afetada pela doença, em um contexto de envelhecimento demográfico e aumento da expectativa de vida no Brasil.

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## A PHASE 3, TWO-STAGE, RANDOMIZED STUDY OF MEZIGDOMIDE, CARFILZOMIB, AND DEXAMETHASONE (MEZIKD) VERSUS CARFILZOMIB AND DEXAMETHASONE (KD) IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): SUCCESSOR-2

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