molecular genetics. **Results:** Multiple myeloma (MM) begins from an asymptomatic precursor stage, relating complex genetic and microenvironmental changes that transform plasma cells into a malignant neoplasm. It was reported that its silencing suppressed cell proliferation and increased apoptosis by transcriptionally regulating the miRNA hsa-miR138-5p, targeting caspase-3, a potential target for the early diagnosis and treatment of MM. The KIAA1191 gene was associated with improved overall survival and progression-free survival. Furthermore, its high expression suppressed the proliferation and migration of MM cells and had a synergistic effect with bortezomib on the cells' proliferation capacity. Initial therapies include VRd or Dara-VRd, followed by autologous stem cell transplantation (ASCT) in suitable candidates. **Discussion:** The clinical findings of this study showed that clinical history and investigation of the initial symptoms are needed. Multiple myeloma is more common in men above 65 years. The main symptoms are bone pain, anemia, leukocyte dysfunction and renal function alterations. To confirm the diagnosis, some additional tests are needed for therapeutic planning, including prothrombin time, activated partial thromboplastin time, fibrinogen, d-dimer, total bilirubin and fractions, alkaline phosphatase, transaminases and gamma-gt. **Conclusion:** This research underscores the complexity of multiple myeloma (MM) and the importance of early diagnosis and personalized treatment, beginning from an asymptomatic precursor stage with genetic and microenvironmental changes that transform plasma cells into malignant neoplasms. Initially, the progression from monoclonal gammopathy of undetermined significance to latent MM is marked by increasing genetic instability, exacerbated in patients with high-risk chromosomal abnormalities. Additionally, the Twist1 protein and miRNA hsa-miR138-5p emerge as potential targets for early diagnosis and treatment. Moreover, the KIAA1191 gene is associated with improved overall and progression-free survival, especially when combined with bortezomib. Risk stratification, including del(17p) and p53 mutation, guides initial therapies such as VRd or Dara-VRd, followed by autologous stem cell transplantation (ASCT). Therefore, treatment personalization, based on biomarkers and risk stratification, is crucial for improving outcomes in MM, ensuring more effective and targeted disease management.

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MULTI-OMIC ANALYSIS OF MULTIPLE MYELOMA BY T(11;14) STATUS

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Aims: To characterize the genomic and transcriptomic profiles associated with t(11;14) status in NDMM and RRMM. **Methods:** The global, non-interventional MEDICI study (NCT04721002) enrolled pts aged ≥18 years who provided informed consent and had BM aspirates collected at diagnosis and/or relapse. In this analysis (data cutoff October 31, 2023), BM aspirates were subjected to plasma cell enrichment and next-generation RNA sequencing (RNAseq) followed by differential gene expression analysis. *P* values were corrected by the Benjamini and Hochberg method. **Results:** A total of 525 pts were included. Among 110 pts with t(11;14)-positive (NDMM, n = 56; RRMM, n = 54), the median age was 64.5 years (range, 38.0–89.0), 60.0% of pts were male, and 74.5% of pts were White. Among 376 pts with t(11;14)-negative (NDMM, n = 235; RRMM, n = 141), the median age was 67.0 years (range, 37.0–90.0), 54.0% of pts were male, and 75.8% of pts were White. ECOG performance status for pts with t(11;14)-positive vs t(11;14)-negative status was 0–1 in 72.7% vs 69.7%. ISS stages I, II, and III disease were present in 34.5%, 21.8%, and 23.6% of pts with t(11;14)-positive and 30.9%, 24.7%, and 25.0% of pts with t(11;14)-negative status, respectively. Of the 525 pts, 369 had samples subjected to RNAseq for whole transcriptome sequencing (WTS). Differential gene expression analysis showed overexpression of *CCND1* (encodes cyclin D1) in pts with t(11;14)-positive vs t(11;14)-negative status in both NDMM and RRMM, as expected. Evaluation of BCL-2 family genes revealed increased expression of the pro-apoptotic BH3 sensitizer *PMAIP1* (encodes NOXA) in pts with t(11;14)-positive vs t(11;14)-negative status with NDMM and RRMM. Comparison of differentially expressed genes among pts with t(11;14)-positive NDMM vs RRMM, showed that while *BCL2* (encodes BCL-2) expression was similar in both disease settings, *MCL1* (encodes MCL-1) and *BCL2A1* (encodes BFL-1) expression were significantly increased in RRMM. Overexpression of *MCL1* and *BCL2A1* have been shown to drive Ven resistance in hematologic malignancies. Whole-exome sequencing analysis will be presented at the meeting. **Discussion:** The selective, potent, oral BCL-2 inhibitor venetoclax (Ven) has demonstrated efficacy in patients (pts) with t(11;14)-positive relapsed/refractory MM (RRMM) and is currently being evaluated as biomarker-directed therapy in this population. Clinical trials estimate 15%–20% of pts with MM carry t(11;14); however, t(11;14)-positive MM prevalence has yet to be established in a real-world setting. Using BM aspirates from MEDICI, WTS and differential expression analysis of key apoptotic pathway genes showed significantly higher *PMAIP1* expression in t(11;14)-positive NDMM and RRMM. Comparison among pts with t(11;14)-positive showed increased *MCL1* and *BCL2A1* expression in RRMM; further evaluation may offer insights into acquired genomic heterogeneity in RRMM and guide optimal combinations with Ven. **Conclusion:** The pro-apoptotic BH3 sensitizer PMAIP1 (NOXA) was overexpressed in t(11;14)-positive vs t(11;14)-negative disease in both NDMM and RRMM. Although BCL2 (BCL-2) expression levels were similar, MCL1 (MCL-1) and BCL2A1

(BFL-1) expression levels were higher in t(11;14)-positive in RRMM vs NDMM, and overexpression of these genes has been shown to drive BCL-2 inhibitor resistance in hematologic malignancies.

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LONG-TERM FOLLOW-UP FROM THE PHASE 1/2 MAJESTEC-1 TRIAL OF TECLISTAMAB IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: SUBGROUP ANALYSIS BY LINES OF THERAPIES

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Background: Teclistamab is the first approved B-cell maturation antigen × CD3 bispecific antibody (BsAb) for the treatment of triple-class exposed (TCE) relapsed/refractory multiple myeloma (RRMM), with weight-based dosing and the longest study follow-up of any BsAb in MM. In the pivotal phase 1/2 MajesTEC-1 study (NCT03145181/NCT04557098), teclistamab demonstrated rapid, deep, and durable responses (overall response rate [ORR], 63.0%; complete response or better [≥CR] rate, 46.1%; median duration of response [mDOR], 24 mo) and a low rate of discontinuations due to adverse events (AEs; 4.8%). This subgroup analysis of MajesTEC-1 reports the overall safety and efficacy of RRMM patients (pts) who received 2-3 prior lines of therapy vs. pts with 4 or more prior lines of therapies, with extended follow-up of 30 months. **Methods:** Pts received the recommended phase 2 dose (RP2D) of teclistamab (1.5 mg/kg QW) and could switch to Q2W dosing if in partial response or better after ≥4 cycles of therapy (phase 1) or in ≥CR for ≥6 mo (phase 2). The primary endpoint was ORR (assessed per IMWG 2016 criteria). AEs were graded per CTCAE v4.03. CRS and ICANS were graded per ASTCT. Safety was reported in the overall population and efficacy was evaluated in pts who received 2-3 prior lines of therapy (≤3 LoT) vs. pts who received more than 3 prior lines of therapies (> 3 LoT). **Results:** Of 165 pts who had received teclistamab as of Aug 2023, 26% (43/165) pts received ≤ 3 prior LoT and 74% (122/165) patients received > 3 prior LoT. Pts characteristics were similar between the groups, especially in terms of high-risk features. At 30.4 mo mFU, pts that received ≤3 prior LoT achieved an ORR of 74.4% with 60.5% of pts achieving ≥ CR [sCR 46.5% and CR 14%]. mPFS was 21.7 mo (95% CI, 13.8–NR), mDOR was 24.0 mo (95% CI, 14.0–NE) and median overall survival was not reached (95% CI, 18.3–NE). Pts who had > 3 prior LoT had an ORR of 59%, with 41% of pts achieving ≥CR [sCR 36.1% and CR 4.9%], mPFS was 9.7 mo (95% CI, 6.4–13.1), mDOR was 22.4 mo (95% CI, 14.9–NE) and median overall survival was 17.7 mo (95% CI, 12.2–29.7). In the overall population, hematologic AEs (any grade/grade 3/4) included neutropenia (72%/65%), anemia (55%/38%), thrombocytopenia (42%/23%), and lymphopenia (36%/35%). Infections occurred in 79% of pts (55% grade 3/4). Of grade 5 infections, 18/22 were due to COVID-19, reflecting study conduct during the COVID-19 pandemic. Onset of new grade ≥3 infections generally decreased over time, which aligned approximately with the median time of switch to Q2W dosing; other factors, such as increasing use of IVIG, may also contribute to this trend. AEs leading to dose reduction (n = 1) or discontinuation (n = 8; 5 due to infection) were infrequent. No new safety signals were reported. **Conclusion:** With the longest follow-up of any BsAb in MM, teclistamab continues to demonstrate deep and durable responses, especially in the subgroup of less heavily treated patients (≤3 prior LoT), which demonstrates even better PFS and complete response rates results than those patients in later lines of treatment (> 3 prior LOT). The safety profile of teclistamab remains consistent with that of BCMA-targeted bispecific therapies, with an important decrease in new onset of severe infections with time. **Acknowledgments:** This study was funded by Johnson & Johnson Innovative Medicine.

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SÍNDROME DE POEMS ASSOCIADA À DOENÇA DE CASTLEMAN VARIANTE PLASMOCITÁRIA: UM RELATO DE CASO

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Introdução: Síndrome de POEMS (SP) é uma doença rara com incidência incerta, acometendo mais frequentemente homens entre 50 e 60 anos. De acometimento sistêmico, sua patogênese ainda não é completamente entendida. Para o diagnóstico são necessários 2 critérios obrigatórios (polirradiculopatia e disfunção de células plasmocitárias), 1 critério maior (doença de Castleman, lesões ósseas escleróticas e elevação de fator de crescimento endotelial) e 1 critério menor (congestão extravascular, endocrinopatia, alterações cutâneas, papiledema e trombocitemia/policitemia). **Objetivo:**