had an entry for the start date of LOT2. The LOT3 Population comprised all pts from the LOT2 Population who had an entry of the start date of LOT3. We defined TCE pts as those who had received ≥1 proteasome inhibitor (PI), ≥1 immunomodulatory drug (IMiD), and ≥1 anti-CD38 antibody, regardless of tx duration. We analyzed TCE pts with at least one subsequent LOT after becoming TCE. We analyzed time to next treatment (TTNT) and overall survival (OS), with TTNT measured between Day 1 of the LOT of interest and Day 1 of the subsequent LOT. **Resultados:** Of the 1029 pts originally analyzed, 405 and 167 entered the LOT2 and LOT3 Populations, respectively. In LOT2, the most frequently used PI, IMiD, and anti-CD38 were bortezomib (41.0%), lenalidomide (41.0%) and daratumumab (26.2%). Other agents used in >10% were carfilzomib (17.0%) and thalidomide (19.3%). The median TTNT was 21.2 months (mo), and median OS was 26.1 mo. In LOT3, Carfilzomib (26.9%), Lenalidomide (34.7%), and Daratumumab (18.6%) were, respectively, the most common PI, IMiD, and anti-CD38. Bortezomib (25.7%) and thalidomide (10.8%) were the next most frequent. The median TTNT was 12.2 mo, median OS was 14.5 mo. A total of 166 (16.1%) pts had a record of tx with ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 at some point. Of these pts, 48 (48/166=28.9%) initiated a subsequent LOT after TCE and entered the TCE Population. These pts became TCE after LOT1 (n = 5), LOT2 (n = 27), LOT3 (n = 8), or later (n = 8). Considering agents belonging to the PI, IMID, and anti-CD38 classes, Carfilzomib was the agent most frequently used in the first LOT after TCE (52.1%), followed by Lenalidomide (22.9%), pomalidomide (20.8%), Daratumumab (18.8%), and Thalidomide (10.4%). Forty-five TCE pts could be analyzed for TTNT and OS. The median TTNT was 9.5 mo (95% CI, 5.9 to 19.4 mo). The median OS was 13.4 mo (95% CI, 10.6 to 17.7 mo). **Discussion and conclusion:** This snapshot of pts with MM treated in Latin America shows heterogeneity in txs used in LOT2, LOT3, and after TCE status, suggesting a lack of standard of care in the real world. The difference between real-life drug use and international guidelines could also be determined by access barriers. The short OS, especially after TCE, highlights the importance of more effective tx options to improve outcomes. **Funding:** This study was funded by Johnson & Johnson and Legend Biotech USA In.

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UPDATED RESULTS OF SONROTOCLAX + DEXAMETHASONE, AN ALL-ORAL TREATMENT, IN PATIENTS WITH T(11;14)-POSITIVE RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Introduction: Despite the clinical efficacy of BCL2 inhibition in t(11;14)-positive multiple myeloma (MM), no BCL2-targeted treatments are approved. Sonrotoclax (BGB- 11417), a next-generation BCL2 inhibitor, is a more selective and pharmacologically potent inhibitor of BCL2 than venetoclax, with a shorter half-life and no drug accumulation. BGB-11417-105 (NCT04973605) is an ongoing phase 1b/2 study of sonrotoclax mono- or combination therapy in patients (pts) with t(11;14)-positive relapsed/refractory (R/R) MM. **Objectives:** To assess safety and efficacy of sonrotoclax + dexamethasone (dex) in pts from BGB-11417-105. **Material and methods:** Eligible pts had R/R MM with centrally confirmed t(11;14) and received oral daily sonrotoclax (320 or 640 mg) and weekly dex (40 mg) until end of treatment. Adverse events (AEs) were graded by CTCAE v5.0, and efficacy was assessed by the investigator per IMWG criteria. **Results:** As of January 20, 2025, 14 and 36 evaluable pts were enrolled in sonrotoclax 320- and 640-mg cohorts, respectively; median (range) follow-up was 6.2 months (2.6- 34.5) and 12.1 months (0.1-28.9), respectively. In the 320- vs 640-mg cohorts, respectively, median age (range) was 69.5 y (44-86) vs 69.0 y (48-80); 42.9% vs 52.8% were male; and 57.1% vs 75.0% were White. Pts had a median of 3 prior treatment lines in both the 320-mg (range, 1-7) and 640-mg (range, 1-12) cohorts; 78.6% and 66.7% of pts were refractory to 3 treatment classes, respectively. At data cutoff, 7 pts (50.0%) in the 320-mg cohort and 14 (38.9%) in the 640-mg cohort remained on treatment; progression was the most common reason for discontinuation (35.7% and 41.7%, respectively). The ORR (95% CI) was 64.3% (35.1%-87.2%) for 320 mg and 80.6% (64.0%-91.8%) for 640-mg, with VGPR or better rates (95% CI) of 35.7% (12.8%-64.9%) and 55.6% (38.1%-72.1%), respectively. The median time to response was 0.7 months in both cohorts. Median (95% CI) duration of response was 5.9 months (1.8-not estimable [NE]) in the 320-mg cohort and 12.2 months (8.3-18.9) in the 640-mg cohort. Median (95% CI) progression- free survival was 6.6 months (2.9-NE) in the 320-mg cohort and 13.3 months (9.0-19.6) in the 640-mg cohort. The safety profile was tolerable and manageable for both cohorts. The most common TEAEs were fatigue (35.7%) in the 320-mg cohort, and insomnia (38.9%) and diarrhea (38.9%, all grade 1 or 2) in the 640-mg cohort. Grade ≥3 TEAEs occurred in 5 pts (35.7%) in the 320-mg cohort and 17 pts (47.2%) in the 640-mg cohort; serious TEAEs occurred in 3 (21.4%) and 10 (27.8%), respectively. Grade ≥3 hematologic TEAEs occurred in 1 (7.1%) and 9 (25.0%) and grade ≥3 infections in 3 (21.4%) and 4 (11.1%) pts, respectively. Two pts (14.3%) in the 320-mg cohort and 2 (5.6%) in the 640-mg cohort died during the treatment-emergent portion of the study for reasons unrelated to sonrotoclax or dex (320-mg: pneumonia RSV and COVID-19; 640-mg: hypoventilation due to lung-involved progressive disease and metastatic pancreatic cancer). Four additional deaths

occurred >30 days after the last 640-mg dose. **Discussion and conclusion:** The all-oral combination of sonrotoclax + dex continued to show a tolerable safety profile, with low rates of infection and hematologic toxicity, and promising efficacy, with an 81% ORR in the 640-mg cohort, in this t(11;14)-positive R/R MM population. The study is ongoing; additional treatment combinations with sonrotoclax are being investigated.

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USO DO BORTEZOMIBE EM PACIENTES COM MIELOMA MÚLTIPLO ELEGÍVEIS AO TRANSPLANTE AUTÓLOGO DE CÉLULAS-TRONCO HEMATOPOIÉTICAS

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Introdução: O mieloma múltiplo (MM) é uma neoplasia progressiva originada da proliferação clonal de plasmócitos na medula óssea, alterando a hematopoiese. Essa condição leva a anemia, lesões ósseas líticas, insuficiência renal e sintomas como dor óssea, fraturas, fadiga, dispneia e palidez. A estratégia de tratamento é determinada pela elegibilidade do paciente para o Transplante Autólogo de Células Tronco Hematológicas (TACTH). Em 2022, o SUS disponibilizou o uso do Bortezomibe, um inibidor do proteassoma, para o tratamento de pacientes elegíveis ao TACTH, com destaque para o esquema VTD (Bortezomibe, Talidomida e Dexametasona). **Objetivos:** Analisar as características clínicas, laboratoriais, respostas terapêuticas e eventos adversos dos pacientes com MM elegíveis ao TACTH do ambulatório de hematologia de um hospital do SUS. **Material e métodos:** Estudo transversal e retrospectivo baseado na análise dos prontuários de pacientes com MM submetidos ao TACTH após uso do Bortezomibe. **Resultados:** O estudo abrangeu 31 pacientes entre 42 e 76 anos (média 60,1 anos; mediana 61 anos), sendo 74% homens e 23% mulheres. As comorbidades mais frequentes são Hipertensão Arterial Sistêmica (HAS) (31%), histórico de tabagismo (21%), Diabetes Mellitus (DM) (19%), histórico de etilismo (11%) e neoplasias malignas (11%). Os sintomas mais relatados no diagnóstico foram lombalgia (67,7%), perda ponderal (38,7%), astenia (38,7%), dor em membros inferiores (MMII) (22,6%) e parestesia e paresia em MMII (16,7%). Na avaliação laboratorial antes e após o TACTH, a Hb média variou de 11,34 para 13 g/dL; plaquetas de 231067 para 198161/mm3; creatinina de 1,07 para 1,14 mg/dL; beta2-microglobulina (B2M) de 4639 para 2938,26 ng/mL e cálcio iônico (Cai) de 1,51 para 1,21 mEq/L. Pelo estadiamento ISS (International Staging System), 21,4% foram classificados como ISS I, 32,1% como ISS II e 46,4% como ISS III. 22 pacientes foram tratados com VTD, 10 com VCD, 4 com CTD antes da implementação do Bortezomibe e 4 apresentaram recidiva após o TACTH. O tempo médio entre o diagnóstico e o TACTH foi de 12,9 meses e após isso, 67,7% não apresentaram proteína monoclonal na imunofixação, obtendo uma resposta completa. O tempo médio de seguimento foi de 38,5 meses, com apenas 1 (3,2%) óbito durante este seguimento (23 meses de sobrevida). **Discussão e conclusão:** A faixa etária e a predominância masculina seguem o perfil epidemiológico da literatura. A HAS e a DM são condições prevalentes para essa média de idade e os sintomas inespecíficos mostram a apresentação clínica insidiosa do MM, levando a um diagnóstico tardio. O aumento de Hb após o TACTH indica uma recuperação da função hematopoiética e a redução de B2M e Cai mostram uma boa resposta terapêutica. Houve uma discreta redução nas plaquetas e elevação da creatinina, possivelmente pela toxicidade da quimioterapia. A prevalência do ISS III sugere uma doença avançada, mas o predomínio da ausência de proteína monoclonal mostra uma boa resposta ao TACTH. Logo, os sintomas e as comorbidades do MM reforçam a necessidade da avaliação clínica multidimensional no manejo desses pacientes. A preferência pelo VTD e VCD está alinhada com as diretrizes terapêuticas atuais, no SUS, dada a eficácia do Bortezomibe. O TACTH é uma estratégia central no tratamento do MM, com impacto positivo na sobrevida e na qualidade de vida dos pacientes.

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UTILIZAÇÃO DA BIOLOGIA SISTÊMICA NA FISIOPATOLOGIA DO MIELOMA MÚLTIPLO: PAPEL DAS ANÁLISES MULTIÔMICAS NA COMPREENSÃO DOS MECANISMOS ENVOLVIDOS

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Introdução: O mieloma múltiplo (MM) é uma neoplasia hematológica incurável, caracterizada pela expansão clonal de plasmócitos aberrantes na medula óssea, sendo clinicamente definida pelos critérios de CRAB (anemia, lesão óssea, hipercalcemia e falência renal). Sua progressão dá-se a partir de entidades pré-malignas, como a gamopatia monoclonal de significado incerto (MGUS) e o mieloma smodering (SMM). Apresenta uma fisiopatologia complexa, onde muitos mecanismos genéticos e epigenéticos estão envolvidos e ainda parcialmente compreendidos. A utilização de abordagens integradas, como na biologia sistêmica, oferece uma visão mais abrangente da doença, pois permite a agregação de diferentes níveis de informações biológicas, trazendo resultados promissores. **Objetivos:** Abordar o papel das análises multiômicas na compreensão dos mecanismos envolvidos na fisiopatologia do mieloma múltiplo. **Material e métodos:** Trata-se de uma revisão integrativa de artigos publicados no período de 2020 a 2025, na base de dados PUBMED. Os termos