a frequência de detecção de CTPCs por NGF em pacientes com MM recém-diagnosticado e sua associação com os sistemas prognósticos clínicos ISS e Durie- Salmon, investigando seu potencial valor como marcador de risco. **Material e métodos:** Ao diagnóstico, foram analisadas 18 amostras pareadas de MO e SP por citometria de fluxo (NGF) para detecção de PC clonais na MO e CTPC no SP. Todas as amostras foram processadas de acordo com os protocolos Euroflow (www.euroflow.org) e marcadas com o painel de dois tubos de 8 cores, NGF para MM (BD Biosciences). Para a análise do SP, foram adquiridos ≥ dez milhões de eventos por amostra utilizando o FACS Canto II (BD Biosciences) ou FACS Lyric (BD Biosciences). As análises foram realizadas através do software Infinicity™. **Resultados:** Entre os 18 pacientes avaliados, 13 (72%) apresentavam MM, 3 (17%) gamopatia monoclonal de significado indeterminado (MGUS) e 2 (11%) mieloma assintomático (SMM). Todos apresentaram plasmócitos clonais na MO. As CTPCs foram detectadas em 10 dos 13 pacientes com MM (77%) e em 2 dos 3 pacientes com MGUS (67%), estando ausentes nos casos de SMM. Entre os pacientes com MM, a presença de CTPCs foi observada em 2/3 (66,7%) com ISS I (faixa: 0,0025−0,01%), 4/6 (66,7%) com ISS II (0,002−0,30%) e 4/4 (100%) com ISS III (0,001−1,50%). Pela classificação de Durie-Salmon, CTPCs foram detectadas em 1/2 (50%) dos casos com DS IIA (0,02%), 8/9 (89%) com DS IIIA (0,001−1,50%) e 1/1 (100%) com DS IIIB (0,006%). **Discussão e conclusão:** A detecção de CTPCs por NGF foi frequente entre pacientes com MM ao diagnóstico, inclusive em estágios iniciais segundo o ISS, o que sugere seu potencial como marcador adicional de carga tumoral. A maior frequência e carga observadas em pacientes com ISS III e DS III reforçam sua possível associação com doença mais avançada. Embora este estudo não tenha avaliado desfechos clínicos como sobrevida, os achados estão alinhados com estudos prévios que indicam correlação entre níveis elevados de CTPCs e maior agressividade biológica da doença. A NGF demonstrou ser uma ferramenta sensível e viável para essa avaliação. Estudos prospectivos com maior número de casos e análise de prognóstico serão necessários para validar o papel das CTPCs como biomarcador complementar nos sistemas de estadiamento atuais.

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EFFICACY AND SAFETY OF BCMA-DIRECTED BISPECIFIC ANTIBODIES IN RELAPSED/ REFRACTORY MULTIPLE MYELOMA PATIENTS WITH RENAL IMPAIRMENT: A REVIEW

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Introduction: Renal impairment is frequent in relapsed/ refractory multiple myeloma (RRMM) due to light chain −mediated tubular injury, hypercalcemia, infection, and treatment-related toxicity. Patients with moderate/severe chronic kidney disease, especially on dialysis, are underrepresented in trials, limiting evidence for therapeutic decisions. BCMA-directed bispecific antibodies, such as teclistamab and elranatamab, show high response rates in heavily pretreated RRMM, but data in renal impairment remain scarce. This review synthesizes available evidence to guide treatment selection, monitoring, and supportive care. **Objectives:** The objective was to evaluate efficacy and safety of BCMA-directed bispecific antibodies in RRMM with renal impairment, including dialysis. Outcomes included overall response rate (ORR), progression-free survival (PFS), acute kidney injury (AKI), cytokine release syndrome (CRS), and ICANS. **Material and methods:** A PubMed search (to August 2025) used the terms “teclistamab,” “elranatamab,” “bispecific antibody,” “BCMA,” “multiple myeloma,” “renal impairment,” and “hemodialysis.” Eligible studies reported outcomes in RRMM with creatinine clearance <40 mL/min or on dialysis. Three were included: a multicenter real-world teclistamab analysis, a retrospective teclistamab vs CAR-T AKI comparison, and an elranatamab dialysis case report. **Discussion and conclusion:** In the largest cohort, 384 RRMM patients received teclistamab; 21% had renal impairment (<40 mL/min), 18% severe (<30 mL/min), and 5% dialysis. ORR was 52% in renal impairment vs 56% without (NS). Median PFS was 4.6 vs 6.5 months (NS). Safety was similar: CRS in 51% vs 59% (grade ≥3: 1.2% vs 1.0%), ICANS in 16% vs 13% (grade ≥3: 2.5% vs 2.6%). Hematologic toxicity was more frequent with renal impairment, but renal worsening was mainly disease- related. A retrospective study of 64 RRMM patients (34 teclistamab, 30 CAR-T) found AKI in 22% overall: 10 teclistamab vs 4 CAR-T. AKI-free survival at 180 days was 68% vs 90% (HR 3.38; p = 0.065), suggesting a non-significant trend toward higher AKI risk with teclistamab. In a case report, an elranatamab-treated dialysis patient achieved a very good partial response within 7 weeks. CRS grade 1 during step-up dosing was managed with tocilizumab and dexamethasone. Treatment was otherwise well tolerated; available data suggest moderate renal impairment does not significantly alter pharmacokinetics. These findings suggest that BCMA-directed bispecific antibodies maintain efficacy in RRMM with renal impairment, including dialysis, with ORR and PFS comparable to patients with preserved renal function. Toxicities, including high-grade CRS and ICANS, are not increased, though hematologic events are more common. A possible higher AKI risk with teclistamab than with CAR-T warrants monitoring. Limitations include the small number of severe renal impairment cases, predominance of retrospective data, and lack of robust pharmacokinetic analyses. Prospective studies stratifying by renal function and dialysis status are needed to refine dosing, monitoring, and supportive care. In conclusion, teclistamab and elranatamab appear effective and safe in RRMM with renal impairment, including dialysis. While efficacy is preserved and major toxicities

manageable, careful monitoring for hematologic complications and AKI is advisable, particularly with teclistamab. Further prospective research is essential to optimize treatment protocols and confirm safety in this population.

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EFFICACY AND SAFETY OF ISATUXIMAB SUBCUTANEOUS (SC) PLUS CARFILZOMIB AND DEXAMETHASONE (ISA-KD) IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): RESULTS OF THE PHASE 2 STUDY IZALCO

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Introduction: Intravenous (IV) isatuximab (Isa) can provide benefit to patients (pts) in multiple combinations across the therapeutic spectrum for multiple myeloma. SC administration would offer a more convenient treatment option for pts and caregivers. Results of a Phase 1b study demonstrated safety and efficacy of Isa SC administration via an on-body delivery system (OBDS; an investigational wearable injector), plus pomalidomide and dexamethasone in RRMM pts. **Objectives:** In the Phase 2 IZALCO study (NCT05704049), we evaluated the efficacy (primary objective), safety, pharmacokinetics (PK), and pt preference for Isa SC administration by manual injection or OBDS, in combination with carfilzomib and dexamethasone (Kd), in RRMM pts. **Material and methods:** Isa SC 1400 mg was given weekly in cycle (C)1 then biweekly. In Part 1 of the study, pts received Isa injected SC manually. In Part 2, pts were randomized to Isa administered SC via OBDS (C1–C3) followed by manual injection (C4–C6), or to manual injection (C1–C3) followed by OBDS administration (C4–C6); from C7, pts could choose either treatment modality. All pts received treatment with carfilzomib (20 mg/m2 on D1-2 then 56 mg/m2 biweekly) and dexamethasone (20 mg). Primary study endpoint (EP) was overall response rate (ORR); pt preference for Isa SC administration modality was the key secondary EP. **Results:** Overall, 74 RRMM pts were enrolled: 8 in Part 1 and 66 in the randomized cohort (Part 2). At study entry, pts had a median age of 65 (44–85) yrs and a median of 1 prior therapy line (1–5); 56.8%, 32.4% and 10.8% had ISS stage I, II or III, respectively. The ORR rate was 79.7% (median follow-up 10.1 mo). After treatment with both modalities for Isa SC delivery, 74.5% of pts expressed a preference for the OBDS rather than manual injection (p = 0.0004); 8.5% had no preference. Treatment with Isa SC plus Kd was well tolerated. A single infusion reaction event (1 of Grade [G]1, 1 of G2) occurred in 2 pts (2.7%, both with manual injection at first dose). Six (8.1%) pts had 18 injection site reactions (17 of G1, 1 of G2) in 1297 (1.1%) manual or OBDS injections. Comparable PK exposure was observed between OBDS and manual administration. **Discussion and conclusion:** The study met its primary endpoint, demonstrating efficacy and safety of Isa SC administration in combination with Kd, either by manual injection or OBDS. Our study findings are comparable to those reported in the Phase 3 study IKEMA with Isa IV. Pts expressed a clear preference for receiving Isa SC by an OBDS.

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EFICÁCIA E SEGURANÇA DA TERAPIA QUÁDRUPLA INTEGRADA AO ANTI-CD38 VS. TERAPIA TRIPLA NO MIELOMA MÚLTIPLO RECÉM-DIAGNOSTICADO E INELEGÍVEL PARA TRANSPLANTE: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE DE ENSAIOS CLÍNICOS RANDOMIZADOS

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Introdução: O mieloma múltiplo é a segunda neoplasia hematológica mais comum. Anticorpos monoclonais anti-CD38, particularmente daratumumabe e isatuximabe, evoluíram do uso em casos recidivados ou refratários para a terapia de primeira linha, tanto em pacientes elegíveis quanto inelegíveis para transplante. Em casos recém-diagnosticados e