Concordance grade (0,927) between HLCr and IFE qualitative results were analyzed with Cohen k coefficient. Hevylite allowed accurate identification and quantification of M protein in 10 IgA MM patients that couldn't be resolved by CZE. Case#1. IgAκ: 3,849 g/L, IgAλ: 0,032 g/L. HLCr: 120,28. CZE β1-2 fraction alteration without signs of monoclonal component. Hevylite solved this patient's evaluation. **Conclusions:** The performance of Hevylite assay as a biomarker in IgA monoclonal gammopathies allow us: To use a full automated lab assay, easy to run in daily routine. To better discriminate monoclonal components that co-migrates in CZE, especially IgA monoclonal proteins. To increase the sensitivity to detect monoclonal protein compared to CZE, given a quantitative and reproducible results of both monoclonal isotype (involved) and non-monoclonal isotype (uninvolved) in the patient serum sample. To use as a clinical tool to overcome traditional methods'limitations on monoclonal gammopathies detections and follow up. Overall, our results showed that Hevylite could be a useful clinical tool, with increased sensitivity compared with electrophoretic methods and that can provide additional clinical information overcoming electrophoresis limitations and allowing more MM serum samples to be accurate evaluated and, and the end, to better manage IgA MM patients.

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ELRANATAMAB, A B-CELL MATURATION ANTIGEN-CD3 BISPECIFIC ANTIBODY, FOR PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: EXTENDED FOLLOW UP AND BIWEEKLY ADMINISTRATION FROM THE MAGNETISMM-3 STUDY

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Introduction/Objectives: To report the findings of extended follow-up and biweekly administration of elranatamab monotherapy in patients (pts) with relapsed/refractory multiple myeloma (RRMM) naïve to BCMA-directed therapies enrolled in Cohort A of MagnetisMM-3. **Materials and methods:** MagnetisMM-3 (NCT04649359) is an open-label, multicenter, registration phase 2 study evaluating the efficacy and safety of elranatamab monotherapy in pts with RRMM. Eligible pts were refractory to at least 1 proteasome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody. Pts received subcutaneous elranatamab in 28-d cycles with step-up doses of 12 mg on cycle 1 day 1 (C1D1) and 32 mg on C1D4 followed by 76 mg once-weekly beginning C1D8. Pts treated for 6 cycles and achieving partial response (PR) or better, lasting ≥2 mo, were switched to 76 mg once every two weeks (Q2W). **Results:** Overall, 123 pts received elranatamab. Median pt age was 68.0 y (range, 36-89); 63.4% of pts had an ECOG PS ≥1. The median number of prior lines of therapy was 5.0 (2-22), with 96.7% and 42.3% of pts having triple-class- and penta-drug refractory disease, respectively. At data cutoff (≈12 mo after last pt initial dose), the median follow up was 12.8 mo (0.2-22.7); 34.1% of pts remained on treatment. The most common reasons for treatment discontinuation were progressive disease (39.0%) and adverse events (AE; 13.8%). Objective response rate per blinded independent central review (BICR) was 61% (95% CI 51.8-69.6), with 39 (31.7%) pts with complete response (CR) or stringent CR (sCR); very good partial response (VGPR) and PR were achieved in 29 (23.6%) and 7 (5.7%) pts, respectively. MRD-negativity (threshold 10−−5) was achieved by 92.0% (n = 23/25) of evaluable pts. Median duration of response (mDOR) has not been reached (95% CI 12.9-NE), and DOR at 12 mo was 74.1% (95% CI 60.5-83.6). In pts with CR/sCR or VGPR, mDOR was not reached by 12 mo; in pts with PR, mDOR was 5.2 mo (95% CI 1.6-NE). There were 46 responders by BICR who switched to Q2W dosing ≥24 wk prior to the data cutoff; among these pts, 80.4% maintained/improved their response ≥24 wk after the switch. Median progression-free and overall survival have not been reached by 12 mo, and the respective rates (95% CI) at 12 mo were 57.1% (47.2-65.9) and 62.0% (52.8-70.0). Most common grade 3/4 treatment emergent AEs were hematologic; grade 3/4 nonhematologic events reported in ≥5% of pts were COVID-pneumonia (10.6%), hypokalemia (9.8%), pneumonia (7.3%), sepsis (6.5%), hypertension (6.5%), ALT increased (5.7 %), and SARS-COV-2 test positive (5.7%). Among pts who switched to Q2W dosing (n = 58), the incidence of grade 3/4 AEs decreased

by >10% after the switch. **Discussion:** Elranatamab remains efficacious and well tolerated in pts with RRMM after >1 y of follow-up. Updated analysis with a median follow-up of ≈15 mo, the longest of all phase 2 BCMA-CD3 bispecific antibody studies, including the outcome of pts who switched to the Q2W dosing, will be presented. **Conclusion:** These results support continued elranatamab development for pts with MM.

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EFFICACY AND SAFETY OF ELRANATAMAB IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA AND PRIOR B-CELL MATURATION ANTIGEN–DIRECTED THERAPIES: A POOLED ANALYSIS FROM MAGNETISMM STUDIES

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Introduction/Objectives: To evaluate the efficacy and safety of elranatamab in a pooled analysis of patients (pts) enrolled in MagnetisMM trials with relapsed or refractory multiple myeloma (RRMM) who had prior exposure to B-cell maturation antigen (BCMA)-directed therapy. **Materials and methods:** Eligible pts received at least 1 proteasome inhibitor, 1 immunomodulatory drug, 1 anti-CD38 antibody, and 1 BCMA-directed therapy (antibody-drug conjugate [ADC] and/or chimeric antigen receptor [CAR]-T cells). The pooled analysis included pts in the MagnetisMM-1 trial (NCT03269136; n = 13) who received subcutaneous (SC) elranatamab 215-1000 μg/kg; MM-3 (NCT04649359; n = 64) and MM-9 (NCT05014412; n = 9) who received the recommended phase 2 dose of 76 mg SC once-weekly. Efficacy endpoints were evaluated by investigator per IMWG criteria. TEAEs were graded by CTCAE (MM-1, v4.03; MM-3 & MM-9, v5.0); CRS and ICANS were graded by ASTCT criteria. Results include data up through ≈10 months after last pt initial dose in all pooled studies. **Results:** In total, 86 pts were included. Median age was 66.0 y (range, 40-84); 47.7% male. At baseline, 69.8% had an ECOG PS ≥1; 24.4% had high risk cytogenetics; 54.7% had extramedullary disease. Pts received a median of 7.0 (3-19) prior lines of therapy, including BCMA-directed ADC (67.4%), CAR T-cells (41.9%); 9.3% received both. 96.5% and 54.7% of pts were triple-class and penta-drug refractory, respectively; among pts who received ADC and CAR-T cells respectively, 79.3% and 27.8% were refractory to ADC and CAR-T cells. After a median follow-up of 10.3 mo (0.3-32.3), median duration of treatment was 3.3 mo (0.03-30.4). At the cut-off date, 24.4% of pts remained on treatment; most common reason for permanent treatment discontinuation was progressive disease (44.2%). The overall response rate (ORR) was 45.3% (95% CI 34.6-56.5), with ≥CR achieved in 17.4% of pts. ORR for pts with prior BCMA-directed ADC and CAR-T cells was 41.4% (95% CI 28.6-55.1) and 52.8% (95% CI 35.5-69.6), respectively. Among responders, median time to objective response was 1.9 mo (0.3-9.3). Median duration of response (DOR) was not reached by 10 mo; the DOR rate at 9 mo was 72.4% (95% CI 54.7-84.2). DOR rate (95% CI) for pts with prior BCMA-directed ADC and CAR-T cells were 67.3% (43.1-83.0) and 78.9% (53.2-91.5) at 9 mo, respectively. Median progression-free survival was 4.8 mo (95% CI 1.9-7.7); median overall survival was not reached by 10 mo, with a rate of 60.1% (95% CI 48.9-69.6) at 9 mo. Most common (≥25% of pts) TEAEs were CRS (65.1% [G3 1.2%]), anemia (59.3% [G3/4, 46.5%]), neutropenia (44.2% [G3/4, 40.7%]), thrombocytopenia (40.7% [G3/4, 29.1%]), diarrhea (33.7% [G3/4, 0%], and lymphopenia (32.6% [G3/4, 30.2%]). 5.8% (G3, 2.3%) of pts. **Discussion:** In pts with RRMM and prior exposure to BCMA-directed therapies, elranatamab was efficacious and well tolerated; no new safety signals were observed vs the BCMA-naïve population. **Conclusions:** These results support treatment with elranatamab in pts with RRMM post BCMA-directed therapy.

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