VRd and markedly increased the depth andduration of the response. We hypothesized that the combination of Dara and CTd could be safe and allow deeper activityas an alternative protocol. **Aims:** The primary endpoint was to evaluate the VGPR after two consolidation cycles post-autologousstem cell transplantation (ASCT). Secondary endpoints were the overall response rate during alltreatment phases and minimal residual disease (MRD), based on the International Myeloma WorkingGroup (IMWG) criteria that includes the next-generation flow (NGF) by the EuroFlow®and PET-CTand the safety profile. **Methods:** This is a phase II, open-label single-center clinical trial. The main inclusion criteria were: TENDMM, creatinine clearance > 30 mL/min, normal cardiac, renal and liver function and the EasterCooperative Oncology Group (ECOG) performance status = 0 - 2. The protocol was Dara-CTd for upto four 28-day induction cycles: C-500 mg oral (PO) on days 1,8 and 15, T at 100-200 mg PO on days1 to 28, (d) at 40 mg PO on days 1,8,15 and 22 and Dara at 16 mg/kg/dose intravenous (IV) on days1,8,15 and 22 during cycles 1 - 2 and every other week in cycles 3 – 4, followed by ASCT. All ptsreceived up to four 28-day consolidation cycles that was started at D+30 after ASCT: Dara at 16 mg/kg and (d) at 40 mg every other week, associated with T at 100 mg PO on days 1 - 28. Dara at 16 mg/kg was used monthly as maintenance until progression or limiting toxicity. G-CSF was used forstem cell (SC) mobilization and plerixafor had been allowed whenever the pts need. All pts receivedantiviral, anti-pneumocystis and antithrombotic prophylaxis. **Results:** The first pts was enrolled in November 2018. A total of 21 pts were included, the median age being 56 (range 37– 67 years), 19 (90%) were non-white, 3 (14%) had an R-ISS = 1, 12 (57%) had an R-ISS = 2 and 3 (14%), an R-ISS = 3. Five (24%) pts had high-risk chromosomal abnormalities [del17p, t(4;14) or t(14;16)]. To date, all pts have completedinduction, 19 have received transplant and 17 have completed D+90 post-transplant assessment. No SC mobilizationfailure was observed, and five (26%) pts needed plerixafor use. In an intention to treatment analysis, after the end ofinduction (cycle 4), 19 (90%) of the pts obtained > PR and 8 (38%) obtained >VGPR, including three MRD negativity byNGF. 17 pts have completed two consolidation cycles after transplant and 94% obtained > VGPR as best response, 12(70%) obtained MRD negativity by NGF and nine (53%) had negative PET-CT. Seven (41%) pts had both flow and PETCTnegativity. Three pts died from infection, one before transplant because of Covid infection, on post-transplant, considered not related to the investigational agent, and another after consolidation, related to the investigational agent. The most common nonhematological adverse events (AEs) grades 3 and 4 before ASCT were neuropathy (n = 6), infusion reaction (n = 7), infection (n = 2), hypertension (n = 1) and rash (n = 1). **Summary/Conclusion:** This is the first study that combined Dara with CTd as induction for TE NDMM pts. This presentdata has shown that the association of Dara-CTd achieved the primary end point once > 90% of the pts achieved VGPRafter two consolidations cycles, and safety profile was acceptable. **Clinical trial information:** NCT03792620.

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EFFICACY AND SAFETY OF ELRANATAMAB (PF-06863135), A B-CELL MATURATION ANTIGEN (BCMA)-CD3 BISPECIFIC ANTIBODY, IN PATIENTS WITH RELAPSED OR REFRACTORY MULTIPLE MYELOMA

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Objectives: Elranatamab (PF-06863135) is a humanized bispecific monoclonal antibody (IgG2a) that targets BCMA, a member of the tumor necrosis factor receptor superfamily expressed in multiple myeloma, and CD3 on T cells. We reported results for intravenous (IV) dosing (Raje et al. Blood. 2019;134(S1):1869) and now update for subcutaneous (SC) dosing from the ongoing Phase 1 study (MagnetisMM-1; NCT03269136). **Materials and methods:** Patients received elranatamab at 80, 130, 215, 360, 600, and 1000 μg/kg SC weekly. A

modified toxicity probability interval method was used for escalation, with monitoring for dose-limiting toxicity (DLT) to end of the first cycle. Treatment-emergent adverse events (TEAEs) were graded by Common Terminology Criteria for Adverse Events (v4.03), and cytokine release syndrome (CRS) by American Society for Transplantation and Cellular Therapy criteria (Lee et al. Biol Blood Marrow Transplant. 2019;25:625). Response was assessed by International Myeloma Working Group criteria. Pharmacokinetics, cytokine profiling, and T cell immunophenotyping were performed. **Results:** 30 patients had received elranatamab as of 4-Feb-2021 at 80 (n = 6), 130 (n = 4), 215 (n = 4), 360 (n = 4), 600 (n = 6), or 1000 (n = 6) μg/kg SC weekly. Patients had a median of 8 prior treatments; 87% had triple refractory disease, 97% had prior anti-CD38 therapy, and 23% (7 patients) had prior BCMA-directed antibody drug conjugate (6 of 7 patients) or chimeric antigen receptor T cell therapy (3 of 7 patients). The most common all causality TEAEs included lymphopenia (n = 25, 83%; 20% G3, 63% G4), CRS (n = 22, 73%; 57% G1, 17% G2, none ≥G3), anemia (n = 18, 60%; 50% G3, 0% G4), thrombocytopenia (n = 16, 53%; 17% G3, 20% G4), neutropenia (n = 16, 53%; 23% G3, 30% G4), and injection site reaction (n = 15, 50%; 43% G1, 7% G2, none ≥G3). Both CRS and immune effector cell-associated neurotoxicity syndrome (n = 6, 20%) were limited to ≤G2 with median durations of 3 and 2.5 days, respectively. No DLT was observed. Exposure increased with dose, and T_{max} ranged from 3–7 days. Cytokine increases occurred with the first dose, and increased T-cell proliferation was observed in peripheral blood. The overall response rate (ORR) for doses ≥215 μg/kg was 70% (n = 14/20) including partial response (PR; n = 1), very good PR (VGPR; n = 7), complete response (CR; n = 1), and stringent CR (sCR; n = 5). Median time to response was 22 days, and 3 of 4 patients (75%) with prior BCMA-directed therapy achieved response (VGPR, n = 2 and sCR, n = 1). Updated data, including duration of response, will be presented. **Discussion:** Elranatamab demonstrated a manageable safety profile and, across the efficacious dose range (≥215 μg/kg), achieved ORR of 70% with CR/sCR rate of 30%, including responses after prior BCMA-directed therapy. **Conclusion:** These results demonstrate the safety and efficacy of elranatamab in this relapsed/refractory population and support ongoing development of elranatamab for patients with multiple myeloma, both as monotherapy and in combination with standard or novel therapies.

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GAMOPATIA MONOCLONAL DE SIGNIFICADO RENAL: RELATO DE CASO

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Objetivo: descrever um caso de gamopatia monoclonal de significado renal (GMSR) em seus aspectos clínico-laboratoriais, diagnósticos e terapêuticos, pela raridade e potencial morbidade renal associada à condição. **Relato:** Mulher de 46 anos, branca, encaminhada em 2019 à nefrologia/HU-UFJF com picos hipertensivos, fadiga e edema periférico há 6 meses; sem história familiar ou pessoal relevante. Ao exame: anasarca e hipertensão arterial. Exames complementares: hemoglobina 10,4 g/dL; creatinina sérica 1,3 mg/dL; albumina 3,1 g/dL; PCR 6; VHS 56; colesterol total 358 mg/dL, triglicerídeos 432 mg/dL; EAS: proteína 4+/4, piócitos 30 p/c e hemácias 10 p/c; proteinúria 2164 mg/24h; sorologias virais, VDRL e provas reumatológicas negativas. Biópsia renal: glomerulonefrite (GN) membranoproliferativa mediada por imunocomplexos. Foi iniciada terapia antiproteinúrica e foram investigadas exaustivamente causas secundárias infecciosas, parasitárias e neoplásicas sem sucesso. A paciente teve intensificação de sintomas sistêmicos (fadiga, febre baixa, cefaleia, parestesias) e internações frequentes por hipervolemia nos meses seguintes, sendo medicada com prednisona e ciclofosfamida. Em setembro de 2020 houve aumento da proteinúria (4 g) e da creatinina (3,6 mg/dL), levando à hipótese de GN rapidamente progressiva superajuntada, indicando nova biópsia renal que, dessa vez, mostrou GN de padrão membranoproliferativo com deposição de imunocomplexos e restrição de cadeia leve (kappa). A propedêutica hematológica foi aprofundada. A imunofixação de proteínas mostrou padrão oligoclonal IgG, kappa e lambda no soro e monoclonal IgG/kappa na urina. A biópsia de medula óssea não demonstrou infiltrado plasmocitário anormal e a pesquisa de amiloide foi negativa. Nenhuma lesão óssea foi identificada, não havendo critérios diagnósticos de mieloma múltiplo. O tratamento da GMSR foi realizado com bortezomibe, dexametasona e ciclofosfamida, contudo a paciente evoluiu para diálise ainda sem recuperação de função renal. **Discussão:** GMSR foi um termo introduzido em 2012 para descrever desordens renais causadas por proteínas monoclonais secretadas por um clone de células B em pacientes que não apresentam critérios diagnósticos para mieloma múltiplo ou doenças linfoproliferativas. Diversas doenças renais decorrem de GMSR e são classificadas como de depósitos organizados, depósitos não organizados ou sem depósito. As manifestações variam de síndrome nefrítico-nefrótica a insuficiência renal aguda/crônica, devendo-se suspeitar de GMSR em pacientes com doença hematológica pré-maligna ou não maligna (gamopatia monoclonal de significado indeterminado) e disfunção renal e/ou proteinúria e nos pacientes com disfunção renal e triagem hematológica inconclusiva ou positiva para gamopatias. A biópsia renal é fundamental ao diagnóstico da GMSR e um grande desafio é diferenciá-la do mieloma. Pacientes com GMSR progridem para diálise em 60-65% dos casos e 71-89% deles recidivam no enxerto renal. O tratamento atualmente utilizado é baseado em opiniões de especialistas e visa a eliminação do clone celular produtor da proteína monoclonal com uma combinação de quimioterápicos. **Conclusão:** A GMSR é polimórfica, incomum e de diagnóstico laborioso, porém deve ser aventada precocemente como hipótese pela possibilidade de que o tratamento evite a elevada morbidade renal.

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