plasma cells in MM. Talquetamab (JNJ-64407564) is a bispecific IgG4 antibody that binds to GPRC5D and CD3, redirecting T cell killing to MM cells. Updated phase 1 results of talquetamab at the recommended phase 2 dose (RP2D) in patients with RRMM are presented. **Material and methods:** Eligible patients had RRMM or were intolerant to standard therapies. Patients received talquetamab intravenously (IV; range 0.5–180 μg/kg) or subcutaneously (SC; range 5.0–800 μg/kg) weekly or biweekly. The primary objectives of the study were identification of the RP2D in part 1 and talquetamab safety and tolerability at the RP2D in part 2. Adverse events (AEs) were graded by CTCAE v4.03; cytokine release syndrome (CRS) was graded per Lee 2014 criteria. Response was assessed per IMWG criteria. **Results:** As of Feb 8, 2021, 174 patients had received talquetamab, 102 by IV and 72 by SC. Across parts 1 and 2 of the study, 28 patients were treated at the RP2D of weekly SC 405 μg/kg, with 10.0 and 60.0 μg/kg step-up doses. Patients treated at the RP2D had a median age of 61.5 years (range 46–80) and a median of 5.5 prior lines of therapy (range 2–14), with 100%/79% triple-class/penta-drug exposed; 71%/18% triple- class/penta-drug refractory; 86% refractory to last line of therapy; and 21% with prior B- cell maturation antigen–directed therapy. No dose-limiting toxicities at the RP2D occurred in part 1. At the RP2D, most common AEs were CRS (79%; grade 3 4%; median time to onset was day after SC injection), neutropenia (64%; grade 3/4 54%), anemia (57%; grade 3/4 29%) and dysgeusia (57%; all grade 1/2). Infections were reported in 32% of patients (grade 3/4 4%) and neurotoxicity in 7% (grade 3/4 none). 75% of patients dosed at the RP2D had skin-related AEs (grade 3/4 none), including 18% with nail disorders. In response-evaluable patients (n = 24), the overall response rate at the RP2D was 63%, with 50% ≥very good partial response; 9/17 (53%) evaluable triple-class refractory patients and 3/3 (100%) penta-drug refractory patients responded. Median time to first confirmed response at the RP2D was 1.0 mo (range 0.2–3.8); responses were durable and deepened over time (median follow-up 6.2 mo [range 2.7–9.7 +] for responders at the RP2D). At the RP2D, exposure was maintained over the maximum EC90 target level and consistent T cell activation was observed. **Discussion:** The promising efficacy, safety profile, and convenience of SC dosing support monotherapy development and combination approaches with talquetamab. Based on pharmacokinetic data, other SC dosing strategies are being explored. **Conclusions:** Talquetamab showed a high clinical response rate and was well-tolerated in patients with RRMM treated at the RP2D of weekly 405 μg/kg SC.

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THE ROLE OF LENALIDOMIDE MAINTENANCE AND MEASURABLE RESIDUAL DISEASE IN A REAL LIFE MULTIPLE MYELOMA TRANSPLANTED POPULATION RECEIVING DIFFERENT STRATEGIES GUIDED BY ACCESSIBLE TREATMENTS IN BRAZIL

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Multiple myeloma (MM) treatment and monitoring with MRD-Next Generation Flow (NGF) has evolved fast in the last decade. Nevertheless, its incorporation by low-middle income countries remains challenging. Despite Lenalidomide maintenance (M-Len) after ASCT improves PFS and OS of MM, and MRD-NGF monitoring can discriminate patients with better outcomes, there is no data about these approaches in real-world patients in Brazil (BR) and Latin America. Here we evaluated in two cohorts of patients guided by drug access, the benefit in outcomes of M-Len and MRD-NGF monitoring after ASCT. The study enrolled patients from public and private healthcare systems (HS). A total of 53 patients with symptomatic MM receiving up-front CTD n = 27 or VCD n = 26. All pts had a BM sample at D+100 for MRD-NGF following the EuroFlow SOPs with a limit of detection of 10^{-6} and a complete protein profile to meet the IMWG response and MRD criteria. Median patient age was 58 (40-70) years, 51% were females. At D+100 the conventional responses were: PR, 5 (9%); VGPR, 21 (40%); CR, 6 (11%); sCR, 21 (40%). Residual plasma-cells were detected by MRD-NGF in 60% of all studied patients and in 44% of those in CR/sCR. MRD^+ patients showed a significantly inferior outcome in this setting with median PFS of 26 months vs NR (p = 0.05). Since Len was recently approved in BR and restricted to private HS, we evaluated the impact of this practice in a subset of 18 patients (30%), with a median treatment time of 20.5 months. In this group only, 2/18 (11%) cases progressed whereas in those without maintenance, progression occurred in 19/35 (54%) cases with median PFS NR *vs.* 21 months (p = 0.001). This benefit also extended to OS, since in the M-len group had no deaths, in contrast to 11/35 (31%) (p = 0.01) deaths in the absence of this drug. Combining the M-Len and MRD-NGF monitoring post ASCT allowed the recognition of groups of patients with different outcomes: M-Len $/MRD^-$ (n = 7) *vs.* no M-Len/MRD^+ (n = 21) with medianPFS NR *vs* 16 months (p = 0.003). Interestingly, the benefit of maintenance was particularly clear among MRD^+ these patients had

an improved disease control (n = 11) *vs* MRD+ patients with no M-Len(n = 21): medianPFS NR vs 16 months (p = 0.002) and median OS of NR *vs* NR (p = 0.02). In our cohort, the majority of patients admitted to the public HS had access to CTD induction without M-Len (n = 24; 45%), while in the private HS they were covered for Bortezomib induction and M-Len post-transplant (n = 15; 28%) with some patients having other mixed situations with VCD induction without M-Len (n = 11; 22%) or CTD+M-Len (n = 3; 5%). Firstly, the comparison between the strategies available by drug access CTD/no-M-len in public vs VCD/M-len in private had an impact on both PFS (median of 16 months vs NR; p = 0.003) and OS (median NR vs NR; p = 0.02). Similarly, patients that had access to PI in induction without M-len also had different outcomes: median PFS NR vs. 21 months for VCD/M-Len vs VCD/no M-Len, respectively (p = 0.01), with a trend in OS (p = 0.06). Finally, different induction regimens (CTD vs VCD without M-Len) showed no impact on PFS (median: 16 vs.21 months; p = 0.6). In real-life, the use of M-Len post-ASCT is associated with better survival outcomes, MRD-NGF was a reproductible and powerful tool to discriminate patients at higher and earlier relapse risk. Inequity of drug access remains a hurdle in countries with constraints, particularly in public HS with a negative impact on survival of MM.

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HEMOSTASIA E PAREDE VASCULAR: BIOLOGIA

AVALIAÇÃO DA INTEGRIDADE DA BARREIRA ENDOTELIAL E SUA RELAÇÃO COM AS MANIFESTAÇÕES CLÍNICAS E LABORATORIAIS NA COVID-19

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Objetivos: Os mecanismos fisiopatológicos que determinam a gravidade da Covid-19 estão associados a ativação da hemostasia e da imunidade inata, em um processo coletivamente referido como imunotrombose, e que envolve ativação plaquetária, geração de NETs (do inglês, *Nucleo extracelular traps*), expressão de fator tecidual, ativação do complemento e ativação endotelial. Um elemento importante da ativação endotelial é a quebra da barreira endotelial (BE), que ocorre para facilitar o acesso de leucócitos aos tecidos, onde contribuem para erradicação dos patógenos. No entanto, a avaliação da integridade da BE é desafiadora, exigindo o uso de modelos celulares. O objetivo desse estudo foi avaliar o efeito do soro de pacientes com Covid-19 sobre a integridade da BE em monocamadas de células endoteliais, e sua correlação com características clínicas da doença. **Materiais e métodos:** A população do estudo consistiu em 30 pacientes com Covid-19 que apresentavam comprometimento pulmonar confirmado por tomografia de tórax, e necessidade de internação hospitalar por hipoxemia e 30 controles saudáveis pareados por sexo e idade. Os pacientes recrutados fizeram parte de um estudo clínico (REBEC: U1111-1250-1843), e as amostras utilizadas nesta avaliação foram obtidas no momento da internação, antes de qualquer intervenção. Monocamadas de células endoteliais de duas fontes (HUVECs: células de cordão umbilical; HULECs: células endoteliais pulmonares) foram estimuladas com soro de pacientes e indivíduos saudáveis (diluição 15% em meio de cultura) e a integridade da BE foi avaliada por um sensor de impedância celular (ECIS; Eletric Cell-substrate Impedance Sensing System) continuamente por 36 horas. Biomarcadores de gravidade e relacionados à ativação da hemostasia foram avaliados por kits comerciais. Dados clínicos foram obtidos a partir dos prontuários digitais. **Resultados:** O soro de pacientes com Covid-19 induziu quebra de BE significativamente mais acentuada que o de indivíduos saudáveis em HUVECs nos tempos 15 min ($p < 0,01$); 30 min ($p \leq 0,001$); 1h ($p \leq 0,0001$); 2h ($p \leq 0,0001$); 3h ($p \leq 0,0001$); 4h ($p \leq 0,01$) e 5h ($p \leq 0,05$). Estes resultados foram confirmados no modelo de células endoteliais pulmonares (HULECs). A magnitude da quebra apresentou correlação significativa com desfechos clínicos relevantes como tempo de internação total (R_S até 0.57) e tempo de UTI ($R_S = 0,47$). Em relação a biomarcadores de interesse na Covid-19, a quebra da BE apresentou correlação significativa com neutrofilia, relação neutrófilo/linfócito, fator de Von Willebrand, fatores IX e XI, fibrinogênio, D-dímero e uPAR (Receptor de Uroquinase). **Discussão:** Através de um método considerado padrão-ouro para avaliação *in vitro* da integridade da BE nós demonstramos que componentes presentes no soro de pacientes com Covid-19 são capazes de promover a quebra da BE, e que a magnitude deste processo está relacionada à gravidade desta doença. A correlação com outros marcadores inflamatórios corrobora a conexão entre os mecanismos envolvidos na imunotrombose em pacientes com Covid-19. **Conclusão:** nossos resultados apontam a quebra da BE como um alvo terapêutico atrativo nestes pacientes.

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AVALIAÇÃO DOS NÍVEIS CIRCULANTES DE MEDIADORES DA INTEGRIDADE DA BARREIRA ENDOTELIAL NA COVID-19 E SUA RELAÇÃO COM A ATIVAÇÃO DA HEMOSTASIA

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Objetivos: a imunotrombose consiste no processo que envolve a ativação concomitante da imunidade inata, hemostasia e endotélio como parte da resposta a patógenos, e vem sendo colocada no centro da fisiopatologia da Covid-19. Um elemento menos explorado da imunotrombose é a ruptura da barreira endotelial (BE), que permite o acesso dos leucócitos aos tecidos inflamados. Entre os reguladores da integridade