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PRELIMINARY RESULTS OF DARATUMUMAB, CYCLOPHOSPHAMIDE, THALIDOMIDE AND DEXAMETHASONE: A QUADRUPLET INTENSIED TREATMENT FOR NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM) TRANSPLANT ELIGIBLE (TE) PATIENTS

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Background: The inclusion of the CD38-targeting antibody daratumumab (Dara) increases the depth and duration of the response, as demonstrated by Dara-VTd and Dara-VRd protocols to treat NDMM - TE patients (pts). However, the access to new drugs is a challenge for some countries in Latin America. There are many induction protocols and one of the most used inductions worldwide is cyclophosphamide (C), thalidomide (T) and dexamethasone (d)- (CTd). We hypothesized that the combination of Dara and CTd could be safe and allow deeper activity in NDMM TE pts. **Objective:** The primary endpoint was the attainment of VGPR after two consolidation cycles post-autologous stem cell transplantation (ASCT). Secondary endpoints were the overall response rate during all treatment phases and minimal residual disease (MRD), based on the IMWG criteria that includes the next-generation ow by the EuroFlow®and PET-CT and the safety prole. An exploratory endpoint was the analysis of the immunologic change in the lymphocyte prole during the treatment. **Methods:** This is a phase II, open-label single-center clinical trial. The main inclusion criteria were: NDMM TE, creatinine clearance > 30 mL/min, normal cardiac, renal and liver function and the ECOG performance status = 0 - 2. The protocol scheme was Dara-CTd for up to four 28-day induction cycles: C-500 mg oral (PO) on days 1,8 and 15, T at 100-200 mg PO on days 1 to 28, Dex at 40 mg PO on days 1,8,15 and 22 and Dara at 16 mg/kg/dose intravenous (IV) on days 1,8,15 and 22 during cycles 1 - 2 and every other week in cycles 3 – 4, followed by ASCT. Consolidation was started at D+30 aftek 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. All patients received antiviral, antipneumocystis and anti-thrombotic prophylaxis. **Results:** The rst patient was enrolled in November 2018. A total of 21 pts were included, the median age being 56 (range 38-67 years), 18 (85%) 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, 18 pts have completed induction, 12 have received ASCT and 10 have completed D+90 post-ASCT assessment. In an intention to treatment analysis, after the end of induction (cycle 4), 17 (95%) of the pts obtained > PR and 7 (33%) obtained VGPR or better. Ten patients have completed two consolidation cycles after transplant and 100% obtained > VGPR as best response, 8 (80%) obtained MRD = -10 negative remission by ow cytometry and 6 (60%) had negative PET-CTs. Five (50%) patients had both ow and PET-CT negativity. Two patients died from infection, one post-ASCT, 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 = 6), infection (n = 2), hypertension (n = 1) and rash (n = 1). **Conclusion:** This is the first study that combined daratumumab with CTd as induction for NDMM TE patients. This preliminary data has shown that the association of Dara-CTd achieved a deep response with a safety prole.

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REAÇÕES ADVERSAS RELACIONADAS AO TRATAMENTO COM LENALIDOMIDA EM PACIENTES COM MIELOMA MÚLTIPLO

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Introdução: A lenalidomida é indicada como terapia combinada para pacientes com mieloma múltiplo (MM) que não receberam tratamento anterior ou que não são elegíveis ao transplante de células tronco ou ainda para pacientes com doença recidivada ou em esquema de monoterapia. Dentre as reações relacionadas ao medicamento (RAM) destacam-se as hematológicas como a neutropenia, anemia e leucopenia, e dentre as não hematológicas destacam-se a astenia, fadiga, constipação e diarreia. **Objetivo:** O objetivo deste trabalho consistiu na avaliação das reações adversas apresentadas por pacientes com Mieloma Múltiplo em tratamento com lenalidomida. **Método**: Foi realizada análise retrospectiva em prontuários em uma clínica oncológica privada, no período de janeiro de 2019 a julho de 2020. Nesta análise, foram avaliados 37 pacientes de 66 a 80 anos, sendo 23 homens e 14 mulheres, de 1ª a 8ª linha de tratamento, elegíveis para tratamento com lenalidomida. As indicações avaliadas foram MM pós transplante autólogo de células-tronco (5 pacientes), MM refratário/recidivado (24 pacientes), MM recém diagnosticado NÃO elegível à transplante (6 pacientes), MM refratário/recidivado (MM IgG Lambda) (1 paciente) e MM manutenção (1 paciente). **Resultados:** No estudo, as reações ocorreram em 51% dos pacientes, onde 11% pacientes com menos de 65 anos, 58% em pacientes de 65 a 75 anos e 31% em pacientes acima de 75 anos. Foi evidenciado que 26% dos pacientes apresentaram astenia, 11% reações cutâneas, 53% mielotoxicidade, 5% reações do TGI e 5% apresentaram outras reações. As reações foram divididas de acordo com a indicação de cada tratamento. **Conclusão:** As reações predominantes no tratamento com lenalidomida são a mielotoxicidade e astenia, principalmente em pacientes MM refratários/recidivados e em idosos. Em ambos os casos, quando estas reações são apresentadas pelo paciente O tratamento foi interrompido, pausado ou a dose foi reduzida conforme necessário para controlar a toxicidade.