https://doi.org/10.1016/j.htct.2020.10.454

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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

E.Q. Crusoé[a,b,c], M.A. Salvino[a,d,e], S.Q. Silva[c], H.H.M. Santos[a,f], A.S. Santos[a,f], A.M. Almeida[a,d,e], L.O. Vieira[g], C.A. Fonseca[h], L.F. Lucas[a,b], J.S. Leal[b,c], M.M. Santos[a,f], J.A. Santos[b,c], E. Adorno[h], V.T.M. Hungria[i,j], M.G.B. Arruda[a,b,c]

[a] *Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[b] *Hematologia, Clínica CEHON, Rede D'Or Oncologia, Salvador, BA, Brazil*
[c] *Hematologia, Rede D'Or Oncologia, Salvador, BA, Brazil*
[d] *Hematologia e Unidade de TMO e Terapias Celulares, Rede D'Or Oncologia, Salvador, BA, Brazil*
[e] *Unidade de TMO, Hospital Universitário Professor Edgard Santos (HUPES), Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[f] *Laboratório de Imunologia, Molecular e Citometria, Instituto de Ciências da Saúde (ICS), Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[g] *Medicina Nuclear, Rede D'Or, Salvador, BA, Brazil*
[h] *Faculdade de Farmácia, Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[i] *Departamento de Hematologia, Clínica São Germano, São Paulo, SP, Brazil*
[j] *Hospital Central, Faculdade de Ciências Médicas da Santa Casa de São Paulo (FCMSCSP), São Paulo, SP, Brazil*

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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[a] *Universidade Federal da Bahia (UFBA), Salvador, BA, Brazil*
[b] *Hematologia, Clínica CEHON, Rede D'Or Oncologia, Salvador, BA, Brazil*
[c] *Hospital São Rafael, Hematologia Rede D'Or Oncologia, Salvador, BA, Brazil*
[d] *Hematologia e Unidade de TMO e Terapias Celulares, Rede D'Or Oncologia, Salvador, BA, Brazil*