ical spectrum of AL presentation reflects the complexity of diagnostic approach: patients are seen by different specialists, require more than 2 biopsies and are diagnosed late in advanced stages with markers of poor prognosis. Moreover, proteasome inhibitor is not widely available in public system and few patients are eligible for ASCT. Altogether may explain poor outcomes of AL patients in our center. **Conclusions:** Diagnosis of systemic AL amyloidosis is a challenge in Brazil. Medical education, better tools for diagnosis, establishment of a multidisciplinary team and a registry, availability of disease-modifying drugs and ASCT may improve outcomes.

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POMALIDOMIDE, BORTEZOMIB, DEXAMETHASONE AFTER 1 PRIOR LINE OF THERAPY IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA: SUBANALYSIS OF OPTIMMISM BY AGE, PRIOR TRANSPLANT, AND HIGH-RISK CYTOGENETICS

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Goals: Upfront Lenalidomide (LEN) until disease progression is a standard treatment (Tx) for newly diagnosed multiple myeloma, regardless of patient (pt) age and transplant eligibility. However, pts who have exhausted the benefit of LEN at first relapse are a growing population in need of effective Tx options. In the OPTIMISMM trial (NCT01734928), pomalidomide (POM), bortezomib (BORT), and dexamethasone (DEX; PVd) significantly improved PFS vs Vd (median, 20.7 vs 11.6 mos; hazard ratio = 0.54 [95% CI, 0.36-0.82]; p = .0027) in an analysis of pts at first relapse. Here we report the efficacy and safety of PVd by age, prior stem cell transplant (SCT) status, and presence of high-risk cytogenetic abnormalities (HR CAs; defined as del[17p], t[4;14], or t[14;16]) in pts treated after 1 prior line of therapy (LOT). **Methods:** Pts received PVd or Vd (1:1) in 21-day cycles (C). POM 4 mg/d on d 1-14 (PVd arm only); BORT 1.3 mg/m^2 on d 1, 4, 8, and 11 of C 1-8 and on d 1 and 8 of C 9+; and DEX 20 mg/d (10 mg/d for pts aged > 75 yrs) on days of and after BORT. PFS was the primary endpoint. **Results:** 226 of 559 pts (40%) enrolled in OPTIMISMM had 1 prior LOT: 100 pts aged ≤ 65 yrs (49 PVd, 51 Vd) and 126 aged > 65 yrs (62 PVd, 64 Vd). In pts aged ≤ 65 yrs (PVd vs Vd), 55.1% vs 51.0% were LEN refractory and 83.7% vs 72.5% had prior BORT. In pts aged > 65 yrs, 59.7% vs 60.9% were LEN refractory and 41.9% vs 46.9% had prior BORT. After 1 prior LOT, PVd significantly improved PFS in pts aged ≤ 65 yrs (median, 22.0 vs 13.1 mos; HR = 0.49 [95% CI, 0.26-0.92], p =.0258) and those aged > 65 yrs (median, 17.6 vs 9.9 mos; HR = 0.57 [95% CI 0.34-0.97], p =.0369) vs Vd; data cutoff was 26 Oct 2017. In pts aged ≤ 65 yrs, ORR was 89.8% vs 54.9% (p <.001; ≥ VGPR 65.3% vs 17.6%) and in pts aged > 65 yrs, ORR was 90.3% vs 54.7% (p <.001; ≥ VGPR 58.1% vs 26.6%). Significant improvements in PFS and ORR with PVd vs Vd were also observed in pts with prior SCT (56 PVd, 54 Vd; median PFS, 22.0 vs 13.8 mos, p =.0241; ORR, 91.1% vs 57.4%, p < .001) or without prior SCT (55 PVd, 61 Vd; median PFS, 16.5 vs 9.5 mos, p =.0454; ORR, 89.1% vs 52.5%, p < .001). Pts with HR CAs had a median PFS of 14.7 mos with PVd (n = 18) vs 9.9 mos with Vd (n = 14); ORR was 94.4% vs 57.1% (p = .027), ≥ VGPR was 72.2% vs 35.7%. The most common grade 3/4 treatment-emergent adverse events (PVd vs Vd) were neutropenia (49.0% vs 6.3%), infections (system organ class; 30.6% vs 14.6%), and thrombocytopenia (26.5% vs 18.8%) in pts aged ≤ 65 yrs and neutropenia (25.8% vs 12.9%), infections (27.4% vs 16.1%), and thrombocytopenia (14.5% vs 22.6%) in pts aged > 65 yrs. **Discussion:** In pts with LEN-pretreated RRMM at first relapse, PVd reduced the risk of progression or death by 51% in pts aged ≤ 65 yrs and 43% in those > 65 yrs vs Vd, and led to significantly improved ORR and deeper responses. Similar outcomes were observed in pts regardless of prior SCT. Although limited by the number of pts, the high ORR and depth of response seen with PVd in pts with HR CAs are promising. The safety of PVd was consistent with the known profiles of POM, BORT, and DEX. **Conclusions:** These results support the use of PVd after first relapse in pts previously treated with LEN, regardless of age, prior SCT status, and presence of HR CAs.

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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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