SUBCUTANEOUS DARATUMUMAB + BORTEZOMIB, CYCLOPHOSPHAMIDE, AND DEXAMETHASONE (VCD) IN PATIENTS WITH NEWLY DIAGNOSED LIGHT CHAIN (AL) AMYLOIDOSIS: UPDATED RESULTS FROM THE PHASE 3 ANDROMEDA STUDY

EQ Crusoe [a], E Kastritis [b], V Sanchorawala [c], GMOBOTAS Group [d]

[a] *Clínica CEHON, Rede D'Or Oncologia, Salvador, BA, Brazil*
[b] *Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Athens, Greece*
[c] *Amyloidosis Center, Boston University School of Medicine and Boston Medical Center, Boston, Massachusetts, United States*
[d] *Amyloidosis Research and Treatment Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy*

Objectives: Systemic AL amyloidosis is a plasma cell disease characterized by the deposition of insoluble amyloid fibrils causing organ dysfunction and death. Primary results from the ANDROMEDA study showed that addition of subcutaneous (SC) daratumumab (DARA) to the standard of care combination of bortezomib, cyclophosphamide, and dexamethasone (VCd) was superior to VCd alone, with higher rates of hematologic complete response (CR) and an acceptable safety profile. DARA-VCd was approved for newly diagnosed AL amyloidosis in January 2021. Here we present an update of the primary ANDROMEDA study results with longer follow-up. **Methods:** ANDROMEDA is a randomized, open-label, active-controlled phase 3 study. Adult patients with newly diagnosed AL amyloidosis were randomized 1:1 to DARA-VCd or VCd and were treated for 6 cycles 28 days each. Bortezomib (1.3 mg/m^2), cyclophosphamide (300 mg/m^2; maximum weekly dose 500 mg), and dexamethasone (40 mg) were given weekly. DARA SC was given weekly (cycle 1–2) and every 2 weeks (cycle 3–6). After cycle 6, patients in the DARA-VCd group received DARA SC alone every 4 weeks for up to 24 cycles from first dose. Disease status was evaluated every 4 weeks in cycle 1–6 and every 8 weeks after cycle 7. The primary endpoint was overall hematologic CR rate in the intent-to-treat population. Secondary endpoints were major organ deterioration progression-free survival (PFS), organ response rate, time to hematologic response, survival, and safety. **Results:** Of 388 randomized patients, 195 were randomized to DARA-VCd and 193 to VCd. As of November 2020, the median follow-up was 20.3 months (mo), with a median treatment duration of 18.5 mo for DARA-VCd and 5.3 mo for VCd; 78 patients (40%) in the DARA-VCd group were still on treatment. The overall hematologic CR rate continued to be higher with DARA-VCd than VCd (59% vs 19%; odds ratio [OR] 5.9; 95% CI 3.7–9.4; $p < 0.0001$). More patients achieved a very good partial response or better (≥VGPR) with DARA-VCd than VCd (79% vs 50%; OR 3.7; 95% CI 2.4–5.9; $p < 0.0001$). Among responders, median time from randomization to ≥VGPR was shorter for DARA-VCd than VCd (0.56 vs 0.82 months). Cardiac response rates were higher with DARA-VCd than VCd at 6 months (42% vs 22%) and at 12 months (57% vs 28%); renal response rates were 54% vs 27% at 6 months and 57% vs 27% at 12 months. A total of 71 deaths occurred (DARA-VCd, n = 31; VCd, n = 40). From cycle 7 onward in the DARA-VCd group, no grade 3/4 treatment-emergent adverse events occurred in ≥5% of patients. There were no systemic administration-related reactions with DARA-VCd after cycle 6. Analysis of major organ deterioration PFS will be updated after 200 events have occurred. **Discussion:** DARA-VCd (versus VCd alone) demonstrated robust hematologic and organ responses with no new safety concerns with longer follow-up. **Conclusion:** Updated results from the ANDROMEDA study reinforce the clinical superiority of DARA-VCd over VCd in pts with newly diagnosed AL amyloidosis. Based on its recent approval, DARA-VCd represents a new standard of care in AL amyloidosis. This trial was registered at www.clinicaltrials.gov as NCT03201965.

https://doi.org/10.1016/j.htct.2021.10.364

TALQUETAMAB, A G PROTEIN-COUPLED RECEPTOR FAMILY C GROUP 5 MEMBER D (GPRC5D) CD3 BISPECIFIC ANTIBODY FOR RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM): UPDATED PHASE 1 STUDY RESULTS

JG Berdeja [a], AY Krishnan [b], A Oriol [c], NWV Donk [d], P Rodríguez-Otero [e], E Askari [f], M Mateos [g], MC Minnema [h], LJ Costa [i], R Verona [j], BW Hilderq [j], S Girgisq [j], T Prior [j], JS Russell [j], JD Goldberg [k], A Chari [l]

[a] *Sarah Cannon Research Institute and Tennessee Oncology, Nashville, United States*
[b] *City of Hope Comprehensive Cancer Center, Duarte, United States*
[c] *Institut Català d'Oncologia and Institut Josep Carreras. Hospital Germans Trias i Pujol, Barcelona, Spain*
[d] *Amsterdam University Medical Center, VU University Medical Center, Amsterdam, Netherlands*
[e] *Clínica Universidad de Navarra, Navarra, Spain*
[f] *Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain*
[g] *Hospital Clínico Universitario de Salamanca, Salamanca, Spain*
[h] *University Medical Center Utrecht, Utrecht, Netherlands*
[i] *University of Alabama at Birmingham, Birmingham, United States*
[j] *Janssen R&D, Spring House, United States*
[k] *Janssen R&D, Raritan, United States*
[l] *Mount Sinai School of Medicine, New York, United States*

Objectives: Patients with MM continue to relapse on current therapies, stressing the need for new immunotherapy targets. GPRC5D is an orphan receptor that is expressed on malignant

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.

https://doi.org/10.1016/j.htct.2021.10.365

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

ABDS Salgado [a,b], RJP Magalhães [b], RM Pontes [a,c], E Barbosa [a], GS Pimenta [b], J Flores-Montero [d,e], LDCS Flores [e,f], A Orfao [d,e], ES Costa [a,g], A Maiolino [a,b]

[a] *Internal Medicine Postgraduate Program, Faculty of Medicine, Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*
[b] *Department of Clinical Haematology, Hospital Universitário Clementino Fraga Filho (HUCFF), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*
[c] *Hospital da Criança de Brasília, Brasília, DF, Brazil*
[d] *Translational and Clinical Research Program, Cancer Research Center, Cytometry Service and Department of Medicine, University of Salamanca (USAL), Salamanca, Spain*
[e] *Centro de Investigación Biomédica en Red de Cáncer, Instituto Carlos III, Madrid, Spain*
[f] *Institute of Biomedicine of Seville, Department of Hematology, University of Seville, Seville, Spain*
[g] *Cytometry Service, Instituto de Puericultura e Pediatria Martagão Gesteira (IPPMG), Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*

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