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

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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.

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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

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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