Daratumumab (DARA) in Combination with Carfilzomib, Lenalidomide, and Dexamethasone (KRd) in Patients (pts) With Newly Diagnosed Multiple Myeloma (MMY1001): an Open-label, Phase 1b Study

Andrzej Jakubowiak,[1] Ajai Chari,[2] Sagar Lonial,[3] Brendan Weiss,[4] Raymond L. Comenzo,[5] Kaida Wu,[6] Nushmia Z. Khokhar,[6] Jianping Wang,[7] Parul Doshi,[6] Saad Z. Usmani[8]

Affiliations: [1]University of Chicago Medical Center, Chicago, IL; [2]Tisch Cancer Institute, Mount Sinai School of Medicine, New York, NY, USA; [3]Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA, USA; [4]Abramson Cancer Center and Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [5]Division of Hematology/Oncology, John C. Davis Myeloma and Amyloid Program, Tufts Medical Center, Boston, MA; [6]Janssen Research & Development, LLC, Spring House, PA, USA; [7]Janssen Research & Development, LLC, Raritan, NJ, USA; [8]Levine Cancer Institute/Carolinas HealthCare System, Charlotte, NC, USA.

Introduction: DARA in combination with established standard of care regimens prolongs PFS, deepens responses, and demonstrates a favorable safety profile in relapsed or refractory multiple myeloma (MM). The tolerability and efficacy of DARA-KRd in newly diagnosed MM pts was examined.

Methods: Newly diagnosed pts regardless of transplantation eligibility were enrolled. Pts received DARA 16 mg/kg QW for Cycles 1-2, Q2W for Cycles 3-6, and Q4W thereafter. All pts received the 1st dose of DARA split over 2 days. Carfilzomib (K) was administered on Days 1, 8 and 15 of each 28-day cycle (20 mg/m^2 on C1D1, 36 or 70 mg/m^2 subsequently based on tolerability of first dose) for ≤13 cycles or elective discontinuation for ASCT. Lenalidomide 25 mg was given on Days 1-21 and dexamethasone 20-40 mg per week. The primary endpoint was tolerability.

Results: Twenty-two pts (median [range] age, 60 [34-74] y) were enrolled and received a median of 8 (1-10) treatment cycles. Nineteen pts escalated K dose to 70 mg/m^2 by C1D15. Median (range) duration of follow-up was 7.4 (4.0-9.3) months. Six (27%) pts discontinued treatment (1 AE [pulmonary embolism]; 1 PD; 4 other [ASCT]). Serious AEs occurred in 46% of pts, and 14% were possibly related to DARA; 18 (82%) experienced a grade 3/4 TEAE. The most common grade 3/4 TEAEs (>10%) were lymphopenia (50%) and neutropenia (23%); 1 (5%) cardiac grade 3 TEAE was observed (congestive heart failure) which resolved; pt quickly resumed study treatment with reduced K dose. No grade 5 TEAE was reported. All DARA-associated infusion reactions (27% of pts) were grade ≤2. Treatment with DARA-KRd yielded an ORR (≥partial response) of 100% (5% complete response, 86% ≥very good partial response) in 21 response-evaluable pts. The 6-month PFS rate was 100%.

Conclusions: The addition of DARA to KRd was well tolerated; the overall safety profile was consistent with that previously reported for KRd, with no additional toxicity observed with the addition of DARA. Deep and durable responses were observed. These data support further investigation of DARA-KRd as a frontline treatment regimen. Updated data will be presented based on longer follow up.

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