Daratumumab, Lenalidomide, and Dexamethasone (DRd) vs Lenalidomide and Dexamethasone (Rd) in Relapsed or Refractory Multiple Myeloma (RRMM): Efficacy and Safety Update (POLLUX)

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Introduction: Daratumumab (D) is a human CD38-targeting mAb that significantly prolongs progression-free survival (PFS) when added to standard-of-care regimens in patients (pts) with RRMM. We examined updated efficacy and safety data from POLLUX (NCT02076009), a randomized phase 3 study of DRd vs Rd in RRMM.

Methods: Pts with ≥1 prior line of therapy (LOT) received Rd (25 mg PO lenalidomide on days 1-21 of each q4w cycle; 40 mg dexamethasone weekly) ± D (16 mg/kg IV qw for cycles 1 and 2, q2w for cycles 3-6, then q4w until disease progression). Pts refractory to lenalidomide were ineligible. Minimal residual disease (MRD) was assessed on bone marrow samples at time of suspected complete response (CR) and at 3 and 6 months post-suspected CR at sensitivities of 10^{-4}, 10^{-5}, and 10^{-6} via next-generation sequencing (Adaptive Biotechnologies, Seattle, WA).

Results: Pts received a median (range) of 1 (1-11) prior LOT. 55% received prior IMiDs (18% lenalidomide). Based on previous median follow-up of 17.3 months, DRd significantly prolonged PFS (median: not reached vs 17.5 months; HR, 0.37; 95% CI, 0.28-0.50; P<0.0001) and significantly improved overall response rate (ORR; 93% vs 76%, P<0.0001) vs Rd. DRd induced higher rates of deep responses vs Rd (≥very good partial response [VGPR]: 78% vs 45%; ≥CR: 46% vs 20%; all P<0.0001) and included MRD negativity, which was >3-fold higher across all 3 sensitivity thresholds for DRd vs Rd (25% vs 6% at the 10^{-5} threshold). MRD-negative pts demonstrated longer PFS vs MRD-positive pts. Follow up for overall survival (OS) is ongoing (OS events: 40 [14%] in DRd and 56 [20%] in Rd). No new safety signals were

identified with longer follow up. Updated efficacy and safety data based on approximately 25-months follow up will be presented at the meeting.

Conclusions: DRd provided significant benefits vs Rd in terms of PFS, ORR, and MRD negativity, and the favorable safety profile of DRd was maintained with longer follow up. These data further validate the use of DRd in RRMM pts who received ≥1 prior therapy.

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