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OVERALL SURVIVAL RESULTS WITH DARATUMUMAB, LENALIDOMIDE, AND DEXAMETHASONE VERSUS LENALIDOMIDE AND DEXAMETHASONE IN TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA: PHASE 3 MAIA STUDY

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Background: The primary analyses of the phase 3 ALCYONE, MAIA, and CASSIOPEIA studies established the superior clinical efficacy of daratumumab (DARA) in combination with standard-of-care regimens versus standard of care alone for patients with newly diagnosed multiple myeloma (NDMM). In ALCYONE, after longer follow-up, an overall survival (OS) benefit was observed; adding DARA to bortezomib, melphalan, and prednisone significantly reduced the risk of death by 40%. In the primary analysis of MAIA, DARA plus lenalidomide and dexamethasone (D-

Rd) reduced the risk of disease progression or death by 44% versus lenalidomide and dexamethasone (Rd).

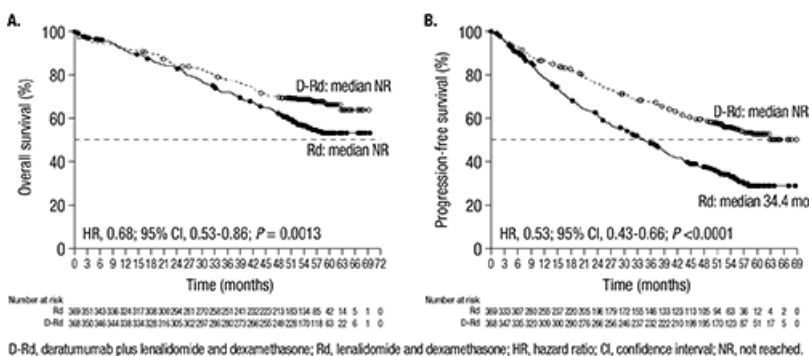
Aims: To report the updated efficacy and safety of D-Rd versus Rd after almost 5 years of median follow-up in transplant-ineligible patients with NDMM from the prespecified interim OS analysis of MAIA (NCT02252172).

Methods: Patients with NDMM ineligible for high-dose chemotherapy and autologous stem cell transplantation due to age ≥ 65 years or comorbidities were randomized 1:1 to D-Rd or Rd. All patients received 28-day cycles of Rd (R: 25 mg orally once daily on Days 1-21; d: 40 mg orally on Days 1, 8, 15 and 22) with or without DARA (16 mg/kg intravenously once weekly for Cycles 1-2, once every 2 weeks for Cycles 3-6, and once every 4 weeks thereafter). In both arms, patients were treated until disease progression or unacceptable safety events. The primary endpoint was progression-free survival (PFS). Key secondary endpoints included overall response rate (ORR), OS, and safety.

Results: 737 patients (D-Rd, 368; Rd, 369) were enrolled in this study. Baseline characteristics were well balanced between arms. The median age was 73 (range, 45-90) years. After a median follow-up of almost 5 years (56.2 months), a significant 32% reduction in the risk of death was observed with D-Rd versus Rd; median OS was not reached (NR) in either arm (hazard ratio [HR], 0.68; 95% confidence interval [CI], 0.53-0.86; $P=0.0013$ [crossing the prespecified stopping boundary of $P=0.0414$]). The estimated 5-year OS rate was 66.3% with D-Rd and 53.1% with Rd (Figure A). The updated median PFS was NR with D-Rd versus 34.4 months with Rd (HR, 0.53; 95% CI, 0.43-0.66; $P<0.0001$; Figure B). The estimated 5-year PFS rate was 52.5% with D-Rd and 28.7% with Rd. The updated ORR was 92.9% with D-Rd versus 81.6% with Rd ($P<0.0001$). No new safety signals were identified with longer follow-up. The most common (in $>15\%$ of patients in either arm) grade 3/4 treatment-emergent adverse events for the D-Rd/Rd arms were neutropenia (54.1%/37.0%, respectively), pneumonia (19.2%/10.7%), anemia (16.8%/21.6%), and lymphopenia (16.5%/11.2%).

Image:

Figure: Overall survival (A) and progression-free survival (B) with D-Rd and Rd.



Summary/Conclusion: After almost 5 years of follow-up, a significant and clinically meaningful OS improvement was demonstrated with the use of D-Rd versus Rd in patients with NDMM who are transplant ineligible, representing a 32% reduction in the risk of death. The significant PFS benefit of D-Rd versus Rd from the primary analysis (median follow-up, 28 months) was maintained, with a 47% reduction in risk of disease progression or death and a median PFS for D-Rd NR. The favorable benefit-risk profile observed supports the use of D-Rd in transplant-ineligible patients with NDMM. These results, together with the OS benefit observed in ALCYONE, support the use of frontline DARA-based combination regimens to maximize PFS for optimal long-term outcomes.

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