LB1901 OVERALL SURVIVAL RESULTS WITH DARATUMUMAB, LENALIDOMIDE, AND DEXAMETHASONE VERSUS LENALIDOMIDE AND DEXAMETHASONE IN TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA: PHASE 3 MAIA STUDY

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

Keywords: Monoclonal antibody Multiple myeloma Survival

Authors: Thierry Facon[1], Shaji K. Kumar[2], Torben Plesner[3], Robert Z. Orlowski[4], Philippe Moreau[5], Nizar Bahlis[6], Supratik Basu[7], Hareth Nahi[8], Cyrille Hulin[9], Hang Quach[10], Hartmut Goldschmidt[11], Michael O'Dwyer[12], Aurore Perrot[13], Christopher P. Venner[14], Katja Weisel[15], Joseph R. Mace[16], Noopur Raje[17], Mourad Tiab[18], Margaret Macro[19], Laurent Frenzel[20], Xavier Leleu[21], Tahamtan Ahmadi[22], Jianping Wang[23], Rian Van Rampelbergh[24], Clarissa M. Uhlar[25], Brenda Tromp[26], Maria Delioukina[25], Jessica Vermeulen[26], Saad Z. Usmani[27]

[1] University of Lille, CHU Lille, Service des Maladies du Sang, Lille, France
[2] Department of Hematology, Mayo Clinic Rochester, Rochester, MN, United States
[3] Vejle Hospital and University of Southern Denmark, Vejle, Denmark
[4] Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, United States
[5] Hematology, University Hospital Hôtel-Dieu, Nantes, France
[6] Arnie Charbonneau Cancer Research Institute, University of Calgary, Calgary, AB, Canada
[7] Royal Wolverhampton NHS Trust and University of Wolverhampton, Wolverhampton, United Kingdom
[8] Karolinska Institute, Department of Medicine, Division of Hematology, Karolinska University Hospital at Huddinge, Stockholm, Sweden
[9] Department of Hematology, Hôpital Haut Lévêque, University Hospital, Pessac, France
[10] University of Melbourne, St Vincent's Hospital, Melbourne, Australia
[11] University Hospital Heidelberg, Internal Medicine V and National Center for Tumor Diseases (NCT), Heidelberg, Germany
[12] Department of Medicine/Haematology, NUI, Galway, Ireland
[13] CHU de Toulouse, IUCT-O, Université de Toulouse, UPS, Service d'Hématologie, Toulouse, France
[14] Cross Cancer Institute, University of Alberta, Edmonton, AB, Canada
[15] Department of Oncology, Hematology and Bone Marrow Transplantation with Section of Pneumology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[16] Florida Cancer Specialists, St. Petersburg, FL, United States
[17] Center for Multiple Myeloma, Massachusetts General Hospital Cancer Center, Boston, MA, United States
[18] CHD Vendée, La Roche sur Yon, France

[19] Centre Hospitalier Universitaire (CHU) de Caen, Caen, France
[20] Department of Clinical Haematology, Hopital Necker-Enfants Malades, Paris, France
[21] CHU Poitiers, Hôpital la Milétrie, Poitiers, France
[22] Genmab US, Inc., Plainsboro, NJ, United States
[23] Janssen Research & Development, LLC, Raritan, NJ, United States
[24] Janssen Research & Development, Beerse, Belgium
[25] Janssen Research & Development, LLC, Spring House, PA, United States
[26] Janssen Research & Development, LLC, Leiden, Netherlands
[27] Levine Cancer Institute/Atrium Health, Charlotte, NC, United States

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).

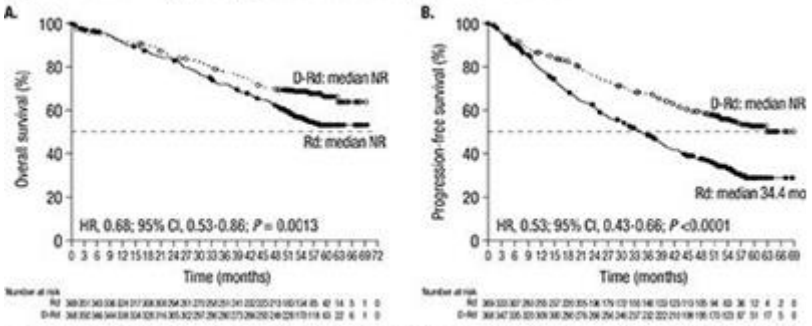
Methods: Patients with NDMM ineligible for high-dose chemotherapy and autologous stem cell transplantation due to age ≥65 years or comorbidities were randomized 1:1 to D-Rd or Rd. All patients received 28-day cycles of Rd (R: 25 mg orally once daily on Days 1-21; d: 40 mg orally on Days 1, 8, 15 and 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%).

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



D-Rd, daratumumab plus lenalidomide and dexamethasone; Rd, lenalidomide and dexamethasone; HR, hazard ratio; CI, confidence interval; NR, not reached.

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.