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Janssen Announces Results from Phase 3 MAIA Study Showing Significant Overall Survival Benefits for Treatment with DARZALEX® (daratumumab) in Patients with Newly Diagnosed Multiple Myeloma Who are Transplant Ineligible

After nearly five years of follow-up, median progression-free survival was not reached, and a significant overall survival benefit was observed; data will be presented as a late-breaking abstract at the European Hematology Association (EHA) Virtual Congress

Raritan, N.J., June 12, 2021 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced overall survival (OS) results from the Phase 3 MAIA (NCT02252172) study showing the addition of DARZALEX® (daratumumab) to lenalidomide and dexamethasone (D-Rd) resulted in a statistically significant survival benefit over lenalidomide and dexamethasone (Rd) alone in patients with newly diagnosed multiple myeloma (NDMM) who were ineligible for autologous stem cell transplant (ASCT) and were treated to progression.[1] These data were featured in the European Hematology Association (EHA) 2021 Virtual Press Briefing and will be presented as a late-breaking abstract during the EHA Virtual Congress (Abstract #LB1901).

The prespecified interim analysis for OS found that after a median follow-up of nearly five years (56.2 months), a 32 percent reduction in the risk of death was observed in the D-Rd treatment arm vs. Rd arm.[1] Median OS was not reached in either arm [hazard ratio (HR): 0.68, 95 percent

confidence interval (CI), 0.53-0.86; p=0.0013].[1] Median progression-free survival (PFS) was not reached after nearly five years and the PFS benefit observed with D-Rd was maintained, with a 47 percent reduction in risk of disease progression or death [HR: 0.53; 95 percent CI, 0.43-0.66; p<0.0001].[1] These data are expected to form the basis of future regulatory submissions.

"The treatment of multiple myeloma becomes more complex with each relapse. Therefore, it is critical to achieve deep treatment responses and improved survival with frontline therapy," said Thierry Facon, M.D.*, Professor of Haematology at Lille University Hospital, Lille, France and study investigator. "These results strongly support the use of daratumumab, lenalidomide and dexamethasone as a new standard of care to extend survival and improve clinical outcomes in transplant ineligible patients with newly diagnosed multiple myeloma."

All patients enrolled in the MAIA study (n=737) were diagnosed with NDMM, were ineligible for high-dose chemotherapy and ASCT, and received 28-day cycles of D-Rd (n=368) or Rd (n=369). Patients were treated until disease progression or unacceptable toxicity.[1] The median age of patients was 73 years (range, 45-90 years). Median PFS was not reached with D-Rd vs. 34.4 months with Rd [HR, 0.53; 95 percent CI, 0.43-0.66; p<0.0001]. Of the 186 patients in the Rd arm who received subsequent therapy, 46 percent received DARZALEX®.

Additional New Findings from the MAIA Longer-Term Follow-Up Analysis:

- Estimated five-year OS rate of 66 percent with D-Rd vs. 53 percent with Rd [HR: 0.68; 95 percent CI, 0.53-0.86; p=0.0013].[1]
- Estimated five-year PFS rate of 53 percent with D-Rd vs. 29 percent with Rd [HR: 0.53; 95 percent CI, 0.43-0.66; p<0.0001].[1]
- Median time to next treatment was not reached with D-Rd vs. 42.4 months with Rd [HR: 0.47; 95 percent CI, 0.37-0.59; p<0.0001].[1]
- Updated overall response rate (ORR) of 93 percent with D-Rd vs. 82 percent with Rd.[1]

No new safety concerns were identified in the D-Rd arm. The most common Grade 3 or 4 treatment-emergent adverse events were neutropenia (D-Rd: 54 percent; Rd: 37 percent); pneumonia (D-Rd: 19 percent; Rd: 11 percent); anemia (D-Rd: 17 percent; Rd: 22 percent); and lymphopenia (D-Rd: 16 percent; Rd: 11 percent).[1]

"These latest findings from the MAIA study demonstrate the impact of this DARZALEX combination regimen on long-term survival in the frontline setting, further establishing the importance of DARZALEX as a backbone therapy in the treatment of multiple myeloma," said Craig Tendler, M.D.,

Vice President, Late Development and Global Medical Affairs, Oncology, Janssen Research & Development, LLC. "These results provide hope and confidence for newly diagnosed patients with multiple myeloma seeking effective treatment regimens that improve long-term outcomes and reflect our commitment to continuing to explore the full potential of DARZALEX in multiple myeloma."

About the MAIA Trial

The randomized, open-label, multicenter Phase 3 study included 737 newly diagnosed patients with multiple myeloma ineligible for high-dose chemotherapy and ASCT, aged 45-90 years (median age of 73).[1] Patients were randomized to receive either DARZALEX®-Rd (D-Rd) or Rd alone in 28-day cycles. In the D-Rd arm, patients received DARZALEX® 16 milligrams per kilogram (mg/kg) IV weekly for cycles 1 – 2, every two weeks for cycles 3 – 6 and every 4 weeks for cycle 7 and thereafter.[1] Patients in the D-Rd and Rd treatment arms received 25 mg of lenalidomide on days 1 – 21 of each 28-day cycle, and dexamethasone at 40 mg once a week for each cycle. Patients in both treatment arms continued until disease progression or unacceptable toxicity.[1]

Earlier results from the MAIA study supported the U.S. Food and Drug Administration (FDA) approval of DARZALEX® in combination with Rd, marking the first approval of a CD-38 monoclonal antibody for patients with transplant ineligible NDMM. These data were also published in *The New England Journal of Medicine* in 2019.

About DARZALEX®

Janssen is committed to exploring the potential of DARZALEX® (daratumumab) for patients with multiple myeloma across the spectrum of the disease. DARZALEX® has been approved in eight indications, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.[2]

DARZALEX® has become a backbone therapy in the treatment of multiple myeloma, having been used in the treatment of more than 190,000 patients worldwide and more than 68,000 patients in the U.S. alone since its U.S. FDA approval in 2015.[3] DARZALEX® is the first CD38-directed antibody approved globally to treat multiple myeloma.[2]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[4] DARZALEX® binds to CD38 and inhibits tumor cell growth causing myeloma cell death.[4] DARZALEX® may also have an effect on normal cells.[4] Data across eight Phase 3 clinical

trials, in both the frontline and relapsed settings, have shown that DARZALEX®-based regimens resulted in significant improvement in progression-free survival and/or overall survival.[5,6,7,8,9,10,11,12]

About Multiple Myeloma

Multiple myeloma is an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[13,14] When damaged, these plasma cells rapidly spread and replace normal cells with tumors in the bone marrow. In 2021, it is estimated that more than 34,000 people will be diagnosed and close to 12,000 will die from the disease in the U.S.[15] While some patients with multiple myeloma have no symptoms, most patients are diagnosed due to symptoms, which can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.[15]

DARZALEX® INDICATIONS

DARZALEX® (daratumumab) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- In combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant
- In combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- In combination with carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy
- In combination with pomalidomide and dexamethasone in patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
- As monotherapy in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

DARZALEX® IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX® is contraindicated in patients with a history of severe hypersensitivity (eg, anaphylactic reactions) to daratumumab or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

DARZALEX® can cause severe and/or serious infusion-related reactions including anaphylactic reactions. In clinical trials (monotherapy and combination: N=2066), infusion-related reactions occurred in 37% of patients with the Week 1 (16 mg/kg) infusion, 2% with the Week 2 infusion, and cumulatively 6% with subsequent infusions. Less than 1% of patients had a Grade 3/4 infusion-related reaction at Week 2 or subsequent infusions. The median time to onset was 1.5 hours (range: 0 to 73 hours). Nearly all reactions occurred during infusion or within 4 hours of completing DARZALEX®. Severe reactions have occurred, including bronchospasm, hypoxia, dyspnea, hypertension, laryngeal edema, and pulmonary edema. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, and hypotension.

When DARZALEX® dosing was interrupted in the setting of ASCT (CASSIOPEIA) for a median of 3.75 months (range: 2.4 to 6.9 months), upon re-initiation of DARZALEX®, the incidence of infusion-related reactions was 11% for the first infusion following ASCT. Infusion-related reactions occurring at re-initiation of DARZALEX® following ASCT were consistent in terms of symptoms and severity (Grade 3 or 4: <1%) with those reported in previous studies at Week 2 or subsequent infusions. In EQUULEUS, patients receiving combination treatment (n=97) were administered the first 16 mg/kg dose at Week 1 split over two days, ie, 8 mg/kg on Day 1 and Day 2, respectively. The incidence of any grade infusion-related reactions was 42%, with 36% of patients experiencing infusion-related reactions on Day 1 of Week 1, 4% on Day 2 of Week 1, and 8% with subsequent infusions.

Pre-medicate patients with antihistamines, antipyretics, and corticosteroids. Frequently monitor patients during the entire infusion. Interrupt DARZALEX® infusion for reactions of any severity and institute medical management as needed. Permanently discontinue DARZALEX® therapy if an

anaphylactic reaction or life-threatening (Grade 4) reaction occurs and institute appropriate emergency care. For patients with Grade 1, 2, or 3 reactions, reduce the infusion rate when re-starting the infusion.

To reduce the risk of delayed infusion-related reactions, administer oral corticosteroids to all patients following DARZALEX® infusions. Patients with a history of chronic obstructive pulmonary disease may require additional post-infusion medications to manage respiratory complications. Consider prescribing short- and long-acting bronchodilators and inhaled corticosteroids for patients with chronic obstructive pulmonary disease.

Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive Indirect Antiglobulin Test may persist for up to 6 months after the last daratumumab infusion. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type is not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX®. Type and screen patients prior to starting DARZALEX®.

Neutropenia and Thrombocytopenia

DARZALEX® may increase neutropenia and thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX® until recovery of neutrophils or for recovery of platelets.

Interference with Determination of Complete Response

Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX® can cause fetal harm when administered to a pregnant woman. DARZALEX® may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive

potential to use effective contraception during treatment with DARZALEX® and for 3 months after the last dose.

The combination of DARZALEX® with lenalidomide, pomalidomide, or thalidomide is contraindicated in pregnant women, because lenalidomide, pomalidomide, and thalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide, pomalidomide, or thalidomide prescribing information on use during pregnancy.

ADVERSE REACTIONS

The most frequently reported adverse reactions (incidence ≥20%) were: upper respiratory infection, neutropenia, infusion-related reactions, thrombocytopenia, diarrhea, constipation, anemia, peripheral sensory neuropathy, fatigue, peripheral edema, nausea, cough, pyrexia, dyspnea, and asthenia. The most common hematologic laboratory abnormalities (≥40%) with DARZALEX® are: neutropenia, lymphopenia, thrombocytopenia, leukopenia, and anemia.

Please **click here** to see the full Prescribing Information.

About the Janssen Pharmaceutical Companies of Johnson & Johnson

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular & Metabolism, Immunology, Infectious Diseases & Vaccines, Neuroscience, Oncology, and Pulmonary Hypertension.

Learn more at www.janssen.com. Follow us at @JanssenUS and @JanssenGlobal. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

*Dr. Facon has served as a consultant to Janssen; he has not been paid for any media work.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding DARZALEX FASPRO®*. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or*

uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, Janssen Biotech, Inc., or any of the other Janssen Pharmaceutical Companies, and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2021, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in the company's most recently filed Quarterly Report on Form 10-Q, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

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