News Release

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Janssen Presents Efficacy and Subgroup Analyses from MAIA Study Showing Long-Term Results of DARZALEX® (daratumumab)-based Regimen in Newly Diagnosed, Transplant-Ineligible Multiple Myeloma

Updated analyses report on progression-free survival, minimal residual disease negativity, overall response and overall survival across patient types, regardless of age or cytogenetic risk

Five-year follow-up highlights health-related quality of life data in a subgroup of frail patients

NEW ORLEANS, December 12, 2022 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced new analyses from the Phase 3 MAIA study of DARZALEX® (daratumumab) in combination with lenalidomide and dexamethasone (D-Rd), evaluating progression-free survival (PFS), minimal residual disease (MRD) negativity and overall response rate (ORR) at a median follow-up of 64.5 months, and overall survival (OS) at a median follow-up of 73.6 months in newly diagnosed, transplant-ineligible (TIE) patients with multiple myeloma, regardless of patients' age and across clinically important subgroups, as well as health-related quality of life (HRQoL) among frail TIE patients.[1,2,3,4] These findings were presented in oral and poster presentations at the American Society of Hematology (ASH) 2022 Annual Meeting, and strengthen previous data from the MAIA study across clinically relevant study endpoints and patient populations.[5]

"Initial data from the MAIA study were instrumental in establishing the D-Rd regimen as a standard of care for the treatment of patients with newly diagnosed, transplant-ineligible multiple myeloma," said study author, Shaji Kumar, M.D.[†], Consultant, Division of Hematology, Department of Internal Medicine, Mayo Clinic. "These updated findings continue to reinforce the overall survival benefit with the D-Rd regimen and provide important insights across key patient populations at varying ages and levels of cytogenetic risk."

An updated efficacy analysis from the MAIA study reports data after 64.5 and 73.6 months of median follow-up on the primary study endpoint, PFS, and the secondary endpoints of MRD negativity, ORR, and OS (Abstract #4559).[1] Additional new post hoc efficacy analyses report on critical subgroups, including by age (Abstract #4553) and by cytogenetic risk factors, including Gain(1q21) and Amp(1q21) (Abstract #3245).[2,3]

"DARZALEX-based combination regimens are foundational in the treatment of newly diagnosed multiple myeloma, and the data presented at ASH provide further insight into the treatment of transplant-ineligible patients with the D-Rd regimen in the frontline setting," said Mark Wildgust, Ph.D., Vice President, Global Medical Affairs, Janssen Research & Development, LLC. "Building on Janssen's deep legacy in the treatment of multiple myeloma, we remain committed to evaluating the full potential of DARZALEX in combination with lenalidomide and dexamethasone to meet the unique needs of various patient populations."

The median age of the 737 patients enrolled in the MAIA trial was 73 (range: 45 to 90) years, with 44 percent of participants over the age of 75 years. Findings from the post-hoc subgroup analysis were consistent with previously reported data from the MAIA study on age and showed D-Rd improved OS, PFS, MRD-negativity, and ORR compared to Rd alone in all three age groups examined, including patients under 70 years of age, between 70 and 75 years of age, and under the age of 75.[2]

- In patients under 75 years (D-Rd, n=208; Rd, n=208) who were treated with D-Rd, median PFS was not reached vs. 37.5 months in the Rd arm [hazard ratio (HR): 0.52, 95 percent confidence interval (CI), 0.39-0.68]. MRD-negativity was 36.1 percent vs. 12.0 percent [odds ratio (OR), 4.13; 95 percent CI, 2.49-6.84]. The ORR was 95.2 percent vs. 81.7 percent.[2]
- In patients under 70 years of age (D-Rd, n=78; Rd, n=77) who were treated with D-Rd, median PFS was not reached vs. 39.2 months in the Rd arm (HR, 0.35; 95 percent CI, 0.21-0.56). MRD-negativity was 35.9 percent vs. 11.7 percent (OR, 4.23; 95 percent CI, 1.84-9.75). The ORR was 93.6 percent vs. 80.5 percent.[2]

- Lastly, in patients ages 70 through 75 (D-Rd, n=130; Rd, n=131), who were treated with D-Rd, median PFS was reached at 61.9 months vs. 37.5 months in the Rd arm (HR, 0.64; 95 percent CI, 0.45-0.89; *P* = 0.0079). MRD-negativity was 36.2 percent vs. 12.2 percent (OR, 4.07; 95 percent CI, 2.16-7.67). The ORR was 96.2 percent vs. 82.4 percent.[2]

A second analysis in key clinical subgroups (Abstract #3245) reported increased PFS, MRD-negativity and ORR following treatment with D-Rd in patients 75 or older, with International Staging System (ISS) stage III disease, with high cytogenetic risk, with renal insufficiency, and with extramedullary plasmacytomas.[3] Key highlights include:

- Patients with high cytogenetic risk, defined as having one or more of the abnormalities t[4;14], t[14;16] or del17p, had a median PFS of 45.3 months following treatment with D-Rd vs. 29.6 months with Rd alone (HR, 0.57; 95 percent CI, 0.34-0.96) (D-Rd, n=48; Rd, n=44). MRD-negativity was 25.0 percent compared to 2.3 percent (OR, 14.33, 95 percent CI, 1.78-115.59) and the ORR was 91.7 percent vs. 75 percent (OR, 3.67, 95 percent CI, 1.07-12.55).[3]
- Patients with Gain(1q21) or Amp(1q21) had a median PFS of 53.2 months following treatment with D-Rd vs. 32.3 months with Rd alone (HR, 0.63; 95 percent CI, 0.46-0.88) (D-Rd, n=127; Rd, n=120). MRD-negativity was 33.1 percent compared to 11.7 percent (OR, 3.74, 95 percent CI, 1.92-7.30) and the ORR was 95.3 percent vs. 85 percent (OR, 3.56, 95 percent CI,1.36-9.30).[3]
- The rates of Grade 3/4 and serious treatment-emergent adverse events (TEAEs) were similar in both treatment groups for patients 75 years of age or older, with a lower rate of discontinuation due to TEAEs for patients treated with D-Rd compared to Rd alone.[3]

In a fourth analysis presented from the MAIA study, patient-reported outcomes (PRO) data were highlighted in an oral presentation, and showed sustained improvements in HRQoL and physical functioning among a subgroup of frail patients treated with D-Rd compared to Rd, with a notable reduction in pain throughout the duration of treatment (Abstract #472).[4] A higher percentage of patients continued treatment with D-Rd, compared to those receiving Rd alone.[4]

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 autologous stem cell transplant (ASCT), aged 45-90 years (median age of 73).[6] Patients were randomized to receive either 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 four weeks for cycle 7 and thereafter.[6] 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.[7]

Earlier results from the MAIA study supported the U.S. Food and Drug Administration (FDA) approval of DARZALEX® in combination with Rd. These data were also published in *The New England Journal of Medicine* in 2019. An updated OS analysis was published in *The Lancet Oncology* in 2021.

About DARZALEX®

DARZALEX® (daratumumab) received U.S. FDA approval in November 2015 and is approved in eight indications in multiple myeloma, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.[7]

DARZALEX® is the first CD38-directed antibody approved to treat multiple myeloma.[7] DARZALEX® is approved in more than 100 countries and DARZALEX®-based regimens have been used in the treatment of more than 300,000 patients worldwide and more than 68,000 patients in the U.S. alone.[7] There are more than 37 company-sponsored clinical trials, including 14 Phase 3 studies, evaluating the efficacy and safety of DARZALEX®.[7]

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement which granted Janssen an exclusive license to develop, manufacture and commercialize daratumumab.

Since 2020, the National Comprehensive Cancer Network® (NCCN®) has recommended DARZALEX®-based combination regimens for the treatment of newly diagnosed multiple myeloma and relapsed and refractory multiple myeloma. For newly diagnosed multiple myeloma, the NCCN® guidelines recommend DARZALEX® in combination with lenalidomide and dexamethasone as a preferred regimen in Category 1; DARZALEX® in combination with bortezomib, melphalan, and prednisone as a recommended regimen for non-transplant candidates in Category 1; and DARZALEX® in combination with bortezomib, thalidomide and dexamethasone as useful in certain circumstances for transplant candidates in Category 2A. In relapsed/refractory myeloma, four DARZALEX® regimens are listed as preferred regimens for early relapses (1-3 prior therapies) in Category 1: DARZALEX® in combination with lenalidomide and dexamethasone; DARZALEX® in combination with bortezomib and dexamethasone; DARZALEX® in combination with carfilzomib and dexamethasone; and DARZALEX® in combination with pomalidomide and dexamethasone [after two prior therapies, including lenalidomide and a proteasome inhibitor (PI)]. The NCCN® recommends DARZALEX® in

Category 2A after at least three prior therapies, including a PI and an immunomodulatory agent, or for patients who are double refractory to a PI and an immunomodulatory agent.

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.[8,9] In multiple myeloma, these plasma cells change, spread rapidly and replace normal cells in the bone marrow with tumors. In 2022, it is estimated that more than 34,000 people will be diagnosed with multiple myeloma, and more than 12,000 will die from the disease in the U.S.[9] While some people diagnosed with multiple myeloma have no symptoms, most patients are diagnosed due to symptoms that can include bone fracture or pain, low red blood cell counts, tiredness, high calcium levels, kidney problems or infections.[10]

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

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. These reactions can be life-threatening, and fatal outcomes have been reported. 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, tachycardia, headache, laryngeal edema, pulmonary edema, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Signs and symptoms may include respiratory symptoms, such as nasal congestion, cough, throat irritation, as well as chills, vomiting, and nausea. Less common signs and symptoms were wheezing, allergic rhinitis, pyrexia, chest discomfort, pruritus, hypotension and blurred vision.

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, i.e., 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.

Ocular adverse reactions, including acute myopia and narrowing of the anterior chamber angle due to ciliochoroidal effusions with potential for increased intraocular pressure or glaucoma, have occurred with DARZALEX® infusion. If ocular symptoms occur, interrupt DARZALEX® infusion and seek immediate ophthalmologic evaluation prior to restarting DARZALEX®.

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 immunoglobulin G (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 & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

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

[†]Shaji Kumar, M.D., 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 product development and the potential benefits and treatment impact of DARZALEX® (daratumumab). 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 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Reports on Form 10-Q, and other 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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[1] Kumar SK, Usmani SZ. Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) Alone in Transplant-ineligible Patients with Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of the Phase 3 MAIA Study. To be presented at the 2022 American Society of Hematology Annual Meeting.

[2] Facon T, Goldschmidt H. Daratumumab Plus Lenalidomide and Dexamethasone in Patients with Transplant-ineligible Newly Diagnosed Multiple Myeloma: MAIA Age Subgroup Analysis. To be presented at the 2022 American Society of Hematology Annual Meeting.
[3] Moreau P, Kumar SK. Daratumumab Plus Lenalidomide and Dexamethasone (D-Rd) Versus Lenalidomide and Dexamethasone (Rd) in Transplant-ineligible Patients (Pts) With Newly Diagnosed Multiple Myeloma (NDMM): Clinical Assessment of Key Subgroups of the Phase 3 MAIA Study. To be presented at the 2022 American Society of Hematology Annual Meeting.
[4] Facon T, Weisel K. Health-Related Quality of Life for Frail Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma Treated With Daratumumab, Lenalidomide and Dexamethasone: Subgroup Analysis of MAIA Trial. To be presented at the 2022 American Society of Hematology Annual Meeting.
[5] Facon T, Kumar SK, Plesner T, et al. Daratumumab, lenalidomide, and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2021;22(11)
[6] ClinicalTrials.gov Identifier NCT02076009. https://clinicaltrials.gov/ct2/show/NCT02076009. Accessed December 10, 2022.
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[8] Kumar, SK et al. Risk of progression and survival in multiple myeloma relapsing after therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. Leukemia. 2012 Jan; 26(1):149-57.
[9] American Cancer Society. "What Is Multiple Myeloma?" Available at: http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-multiple-myeloma. Accessed December 10, 2022.
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