Johnson&Johnson

NEWS RELEASE

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj)-based regimens demonstrate improved rates of minimal residual disease (MRD) negativity and progression-free survival in patients with newly diagnosed multiple myeloma

2024-12-08

New analysis from Phase 3 CEPHEUS study demonstrates 85 percent of patients who achieved MRD negativity (10^{-6}) with DARZALEX FASPRO® were progression free at 4.5 years

Subgroup analysis from Phase 3 AURIGA study show higher rates of MRD-negative conversion in patient populations disproportionately impacted by multiple myeloma

SAN DIEGO, Dec. 8, 2024 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) today announced data highlighting that DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj)-based regimens improve overall and sustained minimal residual disease (MRD) negativity rates and progression-free survival (PFS) in patients with newly diagnosed multiple myeloma (NDMM), regardless of transplant status.[1,2] These findings were demonstrated in an expanded MRD analysis of the Phase 3 CEPHEUS study (**Abstract #362**) and a post hoc analysis of clinically relevant subgroups in the Phase 3 AURIGA study (**Abstract #675**), which were both featured as oral presentations at the 2024 American Society of Hematology (ASH) Annual Meeting.

Data from the expanded MRD analysis of the Phase 3 CEPHEUS study show the addition of DARZALEX FASPRO® to bortezomib, lenalidomide and dexamethasone (D-VRd) leads to improved and deepened rates of overall and sustained MRD negativity (both 10^{-5} and 10^{-6} sensitivity thresholds in patients who achieved a complete response or better) versus VRd alone, and shows significantly improved progression-free survival.[1] CEPHEUS is the fifth Phase

3 study showing the addition of DARZALEX® improves depth and duration of response, leading to improved progression-free survival.[1,3,4,5]

At a median follow-up of 58.7 months, overall MRD-negativity rates were significantly higher with D-VRd versus VRd at both 10^{-5} (60.9 percent vs. 39.4 percent; odds ratio [OR], 2.37; 95 percent confidence interval [CI], 1.58-3.55; P<0.0001) and 10^{-6} (46.2 percent vs. 27.3 percent; OR, 2.24; 95 percent CI, 1.48-3.40; P=0.0001) sensitivity thresholds. Treatment with D-VRd shows continued benefit of sustained MRD negativity for two years (10^{-5}: 42.1 percent vs. 22.7 percent; 10^{-6}: 27.9 percent vs. 13.6 percent). Additionally, the deeper and more sustained MRD negativity rates with D-VRd trended with improved progression-free survival (PFS) rates – the estimated 54-month PFS rates were 86.2 percent for D-VRd patients versus 79 percent for VRd in MRD negative (10^{-6}) patients, and 51 percent versus 36.5 percent for MRD-positive patients.[1]

"This analysis from the CEPHEUS study comparing daratumumab-VRd versus VRd, showed higher rates of both overall and sustained MRD negativity alongside promising trends in progression-free survival," said Sonja Zweegman, MD, PhD, head of the Department of Hematology, Amsterdam University Medical Center.* "This regimen has the potential to improve outcomes for patients with newly diagnosed multiple myeloma who are ineligible for transplant or for whom transplant is not planned as initial therapy."

Addition of DARZALEX FASPRO® to maintenance regimens resulted in higher MRD negativity rates across clinically relevant subgroups by age, race, disease stage and cytogenetic risk

In a post hoc analysis of the Phase 3 AURIGA study, an investigational maintenance regimen of DARZALEX FASPRO® combined with lenalidomide (R) resulted in consistently improved MRD-negative conversion rates after 12 months. These results were consistent across anti-CD38 naïve patient subgroups who were MRD-positive post-autologous stem cell transplant (ASCT). In patients older than 65 years, MRD-negative rates were higher when treated with D-R maintenance therapy compared to R alone (52.6 percent vs. 17.5 percent; OR, 5.24; 95 percent CI, 1.86-14.74). Maintenance therapy with D-R showed a consistently higher conversion to MRD negativity in Black patients (n=20) compared to R alone (60.0 percent vs 16.7 percent; OR, 7.50; 95 percent CI, 1.85-30.34) and white patients (n=67) (46.3 percent vs. 20.6 percent; OR, 3.32; 95 percent CI, 1.55-7.10).[2]

Data also show that the investigational maintenance regimen of D-R resulted in higher MRD-negative conversion rates for patients with advanced-stage disease (Stage III) as defined by the International Staging System (ISS) (65.2 percent vs. 13 percent; OR, 12.50; 95 percent CI, 2.83-55.25) and patients with high cytogenetic risk per the standard definition (31.8 percent vs. 6.7 percent; OR, 6.53; 95% CI, 0.71-60.05) or the revised definition (43.8 percent vs. 13.3 percent; OR, 5.06; 95 percent CI, 1.43-17.88).[2]

"Patients over 65, Black individuals, and those with advanced or high-risk disease are disproportionately impacted

by multiple myeloma and historically have had fewer treatment options that yield deep and durable results," said Imran Khan, M.D., Ph.D., Vice President, Medical Affairs, Hematology, Johnson & Johnson Innovative Medicine. "Evaluating MRD negativity in these patients underlies its importance as a recognized predictor of long-term progression-free survival. The data being presented at ASH this year emphasize the potential of DARZALEX FASPRO in helping newly diagnosed patients achieve MRD negativity."

Final analysis of Phase 3 ANDROMEDA study reinforces DARZALEX FASPRO®-based regimen showing significant overall survival in patients with newly diagnosed light chain (AL) amyloidosis

The final analysis of the Phase 3 ANDROMEDA study was also presented (**Abstract #891**), showing that the addition of DARZALEX FASPRO® to bortezomib, cyclophosphamide, and dexamethasone (D-VCd) demonstrated deeper and more rapid hematologic responses, resulting in a statistically significant improvement in both OS and major organ deterioration progression-free survival (MOD-PFS) (i.e., end-stage renal or cardiac disease, hematologic progression, or death) for patients with newly diagnosed AL amyloidosis, a rare plasma cell disorder associated with the deterioration of vital organs. Patients treated with D-VCd showed a 56 percent reduction in the risk of progression or death (hazard ratio [HR] = 0.44, P< 0.0001). The median MOD-PFS was not reached for D-VCd, while it was 30.2 months for VCd. Additionally, D-VCd also provided significant survival benefits with a HR of 0.62 (P=0.0121), indicating a 38 percent reduction in the risk of death compared to VCd. The 5-year survival rate was 76.1 percent for D-VCd versus 64.7 percent for VCd.[6]

In the CEPHEUS, AURIGA and ANDROMEDA studies, the safety profiles were consistent with the known safety profile for DARZALEX FASPRO®.

About the CEPHEUS Study

CEPHEUS (**NCT03652064**) is an ongoing, multicenter, randomized, open-label, Phase 3 study comparing the efficacy and safety of D-VRd vs VRd in patients with newly diagnosed multiple myeloma who are transplant-ineligible or for whom transplant is not intended as initial therapy. Primary endpoint is MRD negativity rate at 10^{-5} sensitivity threshold. Secondary endpoints include PFS, MRD-negative rate at one year, durable MRD negativity, ORR, time to and duration of response, PFS on next line of therapy, overall survival and safety. The trial has enrolled 396 patients in 13 countries.

About the AURIGA Study

The randomized study (**NCT03901963**) included 200 patients aged 18-79 years with newly diagnosed multiple myeloma who are minimal residual disease (MRD)-positive after frontline autologous stem cell transplant. Patients received investigational 1,800 milligram (mg) daratumumab by subcutaneous (SC) injection in combination with lenalidomide (orally) as maintenance therapy for a maximum of 36 cycles. Each cycle is 28 days. Patients in the

comparative arm will receive lenalidomide (orally) alone as maintenance therapy for a maximum of 36 cycles. Each cycle is 28 days.[4]

About the ANDROMEDA Study

ANDROMEDA (**NCT03201965**) is an ongoing Phase 3, randomized, open-label study investigating the safety and efficacy of DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd), compared to VCd alone, for the treatment of adult patients with newly diagnosed light chain (AL) amyloidosis. The study includes 388 patients with newly diagnosed AL amyloidosis with measurable hematologic disease and one or more organs affected. The primary endpoint is overall complete hematologic response rate by intent-to-treat (ITT). Patients received DARZALEX FASPRO® 1,800 mg/30,000 units administered subcutaneously once weekly from weeks one to eight, once every two weeks from weeks nine to 24 and once every four weeks starting with week 25 until disease progression or unacceptable toxicity or a maximum of two years. Among patients who received D-VCd, 74 percent were exposed for 6 months or longer and 32 percent were exposed for greater than one year.

About Multiple Myeloma

Multiple myeloma is a blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[7] In multiple myeloma, these malignant plasma cells proliferate and replace normal cells in the bone marrow.[8] Multiple myeloma is the second most common blood cancer worldwide and remains an incurable disease.[9] In 2024, it is estimated that more than 35,000 people will be diagnosed with multiple myeloma in the U.S. and more than 12,000 will die from the disease.[10] People with multiple myeloma have a 5-year survival rate of 59.8 percent. While some people diagnosed with multiple myeloma initially 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.[11,12]

About AL Amyloidosis

Light chain (AL) amyloidosis is a rare and potentially fatal hematologic disorder that can affect the function of multiple organs. The disease occurs when bone marrow produces abnormal pieces of antibodies called light chains, which clump together to form a substance called amyloid. These clumps of amyloid are deposited in tissues and vital organs and interfere with normal organ function, eventually causing organ deterioration.[13,14] It is the most common type of amyloidosis. AL amyloidosis frequently affects the heart, kidneys, digestive tract, liver and nervous system, and is potentially fatal if left untreated.[15] Diagnosis is often delayed and prognosis is poor due to advanced, multi-organ, particularly cardiac, involvement.[16,17] Each year, an estimated 4,500 people develop AL amyloidosis in the U.S. alone.[18]

About DARZALEX FASPRO® and DARZALEX®

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) **received** U.S. FDA approval in May 2020 and is approved for eight indications in multiple myeloma, three of which are for frontline treatment in newly diagnosed patients who are transplant eligible or ineligible.[14] It is the only subcutaneous CD38-directed antibody approved to treat patients with MM. DARZALEX FASPRO® is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

DARZALEX® (daratumumab) received **U.S. FDA approval** in November 2015 and is approved in eight indications, three of which are in the frontline setting, including newly diagnosed patients who are transplant eligible and ineligible.[6]

DARZALEX® is the first CD38-directed antibody approved to treat multiple myeloma.[6] DARZALEX®-based regimens have been used in the treatment of more than 580,000 patients worldwide and more than 239,000 patients in the U.S. alone.

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

cyclophosphamide, bortezomib and dexamethasone as another Category 2A regimen for early relapses (1-3 prior therapies) and as monotherapy as a Category 2A regimen useful in certain circumstances for early relapse patients 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.

For more information, visit **www.DARZALEX.com**.

DARZALEX FASPRO® INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) is indicated for the treatment of adult patients with multiple myeloma:

- In combination with bortezomib, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed patients who are eligible for autologous stem cell transplant

- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant

- 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, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant

- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor (PI)

- 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 bortezomib and dexamethasone in patients who have received at least one prior therapy

- As monotherapy in patients who have received at least three prior lines of therapy including a PI and an immunomodulatory agent or who are double refractory to a PI and an immunomodulatory agent

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) is indicated for the treatment of adult patients with light chain (AL) amyloidosis

• In combination with bortezomib, cyclophosphamide and dexamethasone in newly diagnosed patients. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Limitations of Use:

DARZALEX FASPRO is not indicated and is not recommended for the treatment of patients with light chain (AL) amyloidosis who have NYHA Class IIIB or Class IV cardiac disease or Mayo Stage IIIB outside of controlled clinical trials.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX FASPRO® is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase, or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX FASPRO®. Fatal reactions have been reported with daratumumab-containing products, including DARZALEX FASPRO®.

Systemic Reactions

In a pooled safety population of 1249 patients with multiple myeloma (N=1056) or light chain (AL) amyloidosis (N=193) who received DARZALEX FASPRO® as monotherapy or in combination, 7% of patients experienced a systemic administration-related reaction (Grade 2: 3.2%, Grade 3: 0.7%, Grade 4: 0.1%). Systemic administration-related reactions occurred in 7% of patients with the first injection, 0.2% with the second injection, and cumulatively 1% with subsequent injections. The median time to onset was 2.9 hours (range: 5 minutes to 3.5 days). Of the 165 systemic administration-related reactions that occurred in 93 patients, 144 (87%) occurred on the day of DARZALEX FASPRO® administration. Delayed systemic administration-related reactions have occurred in 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension, tachycardia, and ocular adverse reactions, including choroidal effusion, acute myopia, and acute angle closure glaucoma. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritus, chills, vomiting, nausea, hypotension, and blurred vision.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen, and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX FASPRO®. Consider administering corticosteroids and other medications after the administration of DARZALEX FASPRO® depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

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 daratumumab-containing products. If ocular symptoms occur, interrupt DARZALEX FASPRO® and seek immediate ophthalmologic evaluation prior to restarting DARZALEX FASPRO®.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 7% of patients, including Grade 2 reactions in 0.8%. The most frequent (>1%) injection-site reaction was injection-site erythema. These local reactions occurred a median of 5 minutes (range: 0 minutes to 6.5 days) after starting administration of DARZALEX FASPRO®. Monitor for local reactions and consider symptomatic management.

Cardiac Toxicity in Patients with Light Chain (AL) Amyloidosis

Serious or fatal cardiac adverse reactions occurred in patients with light chain (AL) amyloidosis who received DARZALEX FASPRO in combination with bortezomib, cyclophosphamide and dexamethasone [see Adverse Reactions (6.1)]. Serious cardiac disorders occurred in 16% and fatal cardiac disorders occurred in 10% of patients. Patients with NYHA Class IIIA or Mayo Stage IIIA disease may be at greater risk. Patients with NYHA Class IIIB or IV disease were not studied. Monitor patients with cardiac involvement of light chain (AL) amyloidosis more frequently for cardiac adverse reactions and administer supportive care as appropriate.

Neutropenia

Daratumumab may increase neutropenia 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 FASPRO® until recovery of neutrophils. In lower body weight patients receiving DARZALEX FASPRO®, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX FASPRO® until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX FASPRO® can cause fetal harm when administered to a pregnant woman. DARZALEX FASPRO® 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 FASPRO® and for 3 months after the last dose.

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

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 administration. 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 are not impacted.

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX FASPRO®. Type and screen patients prior to starting DARZALEX FASPRO®.

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 DARZALEX FASPRO®-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

In multiple myeloma, the most common adverse reaction (≥20%) with DARZALEX FASPRO® monotherapy is upper respiratory tract infection. The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, headache, pyrexia, cough, muscle spasms, back pain, vomiting, hypertension, upper respiratory tract infection, peripheral sensory neuropathy, constipation, pneumonia, and peripheral edema.

The most common hematology laboratory abnormalities (≥40%) with DARZALEX FASPRO® are decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please **click here** to see the full Prescribing Information for DARZALEX FASPRO®.

DARZALEX® INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

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

- In combination with bortezomib, melphalan, and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant

- 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, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant

- In combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor

- 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 bortezomib and dexamethasone in patients who have received at least one prior therapy

- 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

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 lifethreatening, 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, 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.

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 Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow, and profoundly impact health for humanity. Learn more at **https://www.jnj.com/** or at **www.innovativemedicine.jnj.com**. Follow us at **@JanssenUS** and **@JNJInnovMed**. Janssen Research & Development, LLC,Janssen Biotech, Inc..,Janssen Global Services, LLC and Janssen Scientific Affairs, LLC are Johnson & Johnson companies.

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) and DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj). 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., Janssen Global Services, LLC, Janssen Scientific Affairs, LLC 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 December 31, 2023, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly 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 Janssen Research & Development, LLC, Janssen Biotech, Inc., Janssen Global Services, LLC, Janssen Scientific Affairs, LLC nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

[*] Sonja Zweegman, M.D., Ph.D., head of the Department of Hematology, VU University Medical Center, has provided consulting, advisory, and speaking services to Johnson & Johnson; she has not been paid for any media work.

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