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NEWS RELEASE

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj)-based quadruplet regimen approved in the U.S. for patients with newly diagnosed multiple myeloma who are transplant-eligible

7/30/2024

Findings from first-ever quadruplet therapy study with subcutaneous DARZALEX FASPRO® showed 60 percent reduction in risk of disease progression or death

New regimen solidifies DARZALEX FASPRO® as a foundational frontline therapy in multiple myeloma with potential to significantly delay disease progression

HORSHAM, Pa., July 30, 2024 /PRNewswire/ -- Johnson & Johnson (NYSE:JNJ) announced today that the U.S. Food and Drug Administration (FDA) approved DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) in combination with bortezomib, lenalidomide and dexamethasone (D-VRd) for induction and consolidation in patients with newly diagnosed multiple myeloma (NDMM) who are eligible for an autologous stem cell transplant (ASCT).[1] Patients will have the opportunity to receive this DARZALEX FASPRO®-based quadruplet therapy at initial diagnosis, providing them with a new treatment that may significantly improve outcomes.

This approval is supported by data from the Phase 3 PERSEUS study evaluating DARZALEX FASPRO® in a regimen that included D-VRd induction and consolidation therapy compared to bortezomib, lenalidomide and dexamethasone (VRd) during induction and consolidation in patients with NDMM eligible for ASCT.[1] Following consolidation, patients received an investigational treatment regimen for maintenance that included DARZALEX FASPRO® in combination with lenalidomide or lenalidomide alone.[1]

"Multiple myeloma has a highly varied clinical course among patients and in each individual patient, and there is a continued need for innovation and therapies that employ different targets and combinations to provide patients with treatment options at diagnosis and throughout the course of their disease," said Amrita Y. Krishnan, M.D., Professor and Director of the Judy and Bernard Briskin Multiple Myeloma Center, City of Hope.* "The efficacy data supporting this new quadruplet regimen, combined with its established safety and tolerability profile, provide compelling evidence that adding D-VRd upon initial diagnosis as compared to VRd can deepen responses and prolong remissions in the context of autologous stem cell transplantation."

Findings from the PERSEUS study demonstrated a significant improvement in the primary endpoint of progression-free survival (PFS), with D-VRd reducing the risk of disease progression or death by 60 percent compared to VRd (HR [95% CI]: 0.40 [0.29, 0.57]; p-value < 0.0001).[1] Treatment with D-VRd induction and consolidation resulted in deeper responses at the end of consolidation compared to VRd: minimal residual disease (MRD) negativity rates of 57.5 percent vs. 32.5 percent, and MRD-negativity rates in patients with complete response (CR) or better of 76.6 percent vs. 58.5 percent, respectively.[1]

"This latest indication for DARZALEX FASPRO-based quadruplet therapy demonstrated a clinically significant reduction in disease progression or death during first-line treatment when patients are likely to experience their deepest responses," said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, Johnson & Johnson. "Today's approval embodies our commitment to setting new standards of care for patients newly diagnosed with multiple myeloma who are transplant eligible."

The overall safety profile of D-VRd was consistent with the known safety profiles for DARZALEX FASPRO® and VRd.[1] The most common adverse reactions (≥20%) in patients with multiple myeloma who received D-VRd are peripheral neuropathy, fatigue, edema, pyrexia, upper respiratory infection, constipation, diarrhea, musculoskeletal pain, insomnia, and rash.[1]

About the PERSEUS Study

The PERSEUS study is being conducted in collaboration with the European Myeloma Network as the sponsor. PERSEUS is an ongoing, randomized, open-label, Phase 3 study comparing the efficacy and safety of D-VRd during induction and consolidation versus VRd during induction and consolidation in patients with NDMM eligible for ASCT. Following consolidation, patients received an investigational treatment regimen for maintenance that included DARZALEX FASPRO® in combination with lenalidomide or lenalidomide alone. The trial was not designed to isolate the effect of DARZALEX FASPRO® in the maintenance phase of treatment. The efficacy of DARZALEX FASPRO® in combination with lenalidomide for maintenance has not been established. The primary endpoint is PFS, and secondary endpoints include overall CR or better rate, and overall MRD-negativity (in patients with CR or better). The median age is 61.0 (range, 32-70) years for patients in the D-VRd arm and 59.0 (range, 31-70) years for

patients in the VRd arm.[2] The study is being conducted in 14 countries in Europe and Australia.

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.[3] In multiple myeloma, these malignant plasma cells proliferate and replace normal cells in the bone marrow.[4] Multiple myeloma is the second most common blood cancer worldwide and remains an incurable disease.[5] 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.[6] People with multiple myeloma have a 5-year survival rate of 59.8 percent.[6] 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.[7,8]

About DARZALEX FASPRO®

DARZALEX FASPRO® (daratumumab and hyaluronidase-fihj) **received** U.S. FDA approval in May 2020 and is approved for nine indications in multiple myeloma, four of which are for frontline treatment in newly diagnosed patients who are transplant eligible or ineligible.[1] It is the only subcutaneous CD38-directed antibody approved to treat patients with multiple myeloma. DARZALEX FASPRO® is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.

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.

For more information, visit **https://www.darzalexhcp.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

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.

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 neuropathy, peripheral sensory neuropathy, constipation, pneumonia, edema, peripheral edema, musculoskeletal pain, and rash.

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 read full Prescribing Information for DARZALEX FASPRO®.

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.janssen.com/johnson-johnson-innovative-medicine**. Follow us at **@JanssenUS** and **@JNJInnovMed**. Janssen Research & Development, LLC and Janssen Biotech, Inc. are both 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 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 Janssen Research & Development, LLC, Janssen Biotech, Inc. 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., nor Johnson & Johnson undertake to update any forward-looking statement as a result of new information or future events or developments.

*Dr. Amrita Y. Krishnan has provided consulting, advisory, and speaking services to Johnson & Johnson; she has not been paid for any media work.

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[1] DARZALEX FASPRO® U.S. Prescribing Information.
[2] Pieter Sonneveld, Dimopoulos MA, Boccadoro M, et al. Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. The New England Journal of Medicine. Accessed July 2024. **https://www.nejm.org/doi/full/10.1056/NEJMoa2312054**
[3] Rajkumar SV. Multiple Myeloma: 2020 Update on Diagnosis, Risk-Stratification and Management. Am J Hematol. 2020;95(5):548-5672020;95(5):548-567. **http://www.ncbi.nlm.nih.gov/pubmed/32212178**
[4] National Cancer Institute. Plasma Cell Neoplasms. Accessed July 2024. Available at:

https://www.cancer.gov/types/myeloma/patient/myeloma-treatment-pdq
[5] Multiple Myeloma. City of Hope, 2022. Multiple Myeloma: Causes, Symptoms & Treatments. Accessed July 2024. Available at: **https://www.cancercenter.com/cancer-types/multiple-myeloma**
[6] American Cancer Society. Myeloma Cancer Statistics. Accessed July 2024. Available at: **https://cancerstatisticscenter.cancer.org/types/myeloma**
[7] American Cancer Society. What is Multiple Myeloma? Accessed July 2024. Available at: **https://www.cancer.org/cancer/multiple-myeloma/about/what-is-multiple-myeloma.html**
[8] American Cancer Society. Multiple Myeloma Early Detection, Diagnosis, and Staging. Accessed July 2024. Available at: **https://www.cancer.org/cancer/types/multiple-myeloma/detection-diagnosis-staging/detection.html**

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