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Data from the ANDROMEDA Study Show Hematologic Response for DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) in Newly Diagnosed Light Chain (AL) Amyloidosis

Further analyses from the Phase 3 ANDROMEDA study at ASH 2020 highlight potential of DARZALEX FASPRO® *in treatment of rare blood disease*

December 7, 2020 (RARITAN, N.J.) – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today new data from the Phase 3 ANDROMEDA study, which evaluated DARZALEX *FASPRO*® (daratumumab and hyaluronidase-fihj) as a treatment for patients with light chain (AL) amyloidosis, a rare disease associated with deterioration of vital organs, most notably the heart, kidneys and liver, for which there are no currently approved therapies.[1,2] The data, which were featured in an oral presentation at the American Society of Hematology (ASH) 2020 Annual Meeting, showed a significantly higher complete hematologic response rate with DARZALEX *FASPRO*® treatment in patients with this potentially fatal blood disorder compared to standard regimen and consistent decreases in markers of disease, indicative of deep hematologic responses (Abstract #552).[3]

These data supported the recent submission to the U.S. Food and Drug Administration (FDA) seeking approval for DARZALEX *FASPRO*® in combination with bortezomib (VELCADE®), cyclophosphamide and dexamethasone (D-VCd) for the treatment of patients with AL amyloidosis.

The submission is being reviewed under the Real-Time Oncology Review to seek the first approval for any drug to treat this disease.[4]

"AL amyloidosis is a rare blood disorder in which abnormal proteins build up in the tissues and organs and eventually cause major organ deterioration," said study investigator, Raymond L. Comenzo, M.D., Director, John C. Davis Myeloma and Amyloid Program, Tufts Medical Center. "The data being presented at ASH show the potential of this new treatment regimen. Compared to VCd alone, the D-VCd regimen increased hematologic response rates and prolonged major organ deterioration-progression-free survival (MOD-PFS) in patients with AL amyloidosis."

Key Findings from the ANDROMEDA Oral Presentation (Abstract #552):

- The primary endpoint of the Phase 3 ANDROMEDA study was complete hematologic response rate, classified by the absolute reduction of the involved free light chain (iFLC) and the difference between iFLC and uninvolved free light chain levels.[4] The overproduction of light chains by plasma cells leads to the deposit of an abnormal protein called amyloid in major organs, interfering with their function.
- The data showed that hematologic response rates were higher in patients with newly diagnosed AL amyloidosis who were treated with D-VCd compared to VCd alone (53 percent vs. 18 percent, respectively),[3] a current treatment regimen offered to patients with AL amyloidosis.
- Results consistently favor the daratumumab-containing regimen across various measures of deep hematological response:
    - Hematological response based upon iFLC ≤20 mg/L (regardless of FLC ratio) favored D-VCd vs. VCd (71 percent vs. 20 percent).[3]
    - Hematological response based upon the difference between iFLC and uninvolved FLC (dFLC)<10 mg/L (regardless of FLC ratio) favored D-VCd vs. VCd (64 percent vs. 31 percent).[3]
    - Time to MOD-PFS was longer in patients treated with D-VCd who achieved deep hematologic response by all criteria including complete hematological response, low iFLC, and low dFLC.[3]

Additionally, D-VCd had an acceptable safety profile, consistent with that previously observed for each of the agents alone.

"AL amyloidosis is a challenging disease to diagnose and treat, with symptoms that mimic other conditions. During that delay, major organ deterioration can occur," said Jessica Vermeulen, M.D., Ph.D., Global Medical Head/Clinical Leader, Hematology & Oncology, Janssen Research & Development, LLC. "It is our hope that the ANDROMEDA study contributes to raising awareness of AL amyloidosis among patients and providers, and that approval of DARZALEX *FASPRO*, pending health authority reviews, will bring a much-needed and effective treatment option to patients."

Extent of cardiac involvement at baseline has a major impact on clinical outcomes for patients with AL amyloidosis.[5] A separate poster presentation of the ANDROMEDA data focused on the impact of cardiac involvement in newly diagnosed AL amyloidosis patients (Abstract #1392).[6] Results found that rates of hematologic, cardiac and renal response at six months were higher in the D-VCd group than the VCd group regardless of baseline cardiac stage (I, II or III), with more than 76 percent of these patients having a baseline cardiac stage of II or higher.[6] Additionally, both MOD-PFS and major organ deterioration-event-free survival (MOD-EFS) favored D-VCd across baseline cardiac stages.[6]

About the ANDROMEDA Study[7]

ANDROMEDA (NCT03201965) is an ongoing Phase 3, randomized, open-label study investigating the safety and efficacy of daratumumab and hyaluronidase-fihj in combination with bortezomib, cyclophosphamide and dexamethasone (D-VCd), compared to VCd alone, for the treatment of 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). Secondary endpoints include MOD-PFS, MOD-EFS, organ response rate, overall survival and time to hematologic response, among others.

About DARZALEX *FASPRO*®

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 launch, it is estimated that more than 150,000 patients have been treated with daratumumab worldwide.[8] DARZALEX *FASPRO*® is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma.

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease. Daratumumab binds to CD38 and inhibits tumor cell growth, causing myeloma cell death.[9] Daratumumab may also have an effect on normal cells.[10] Data across nine Phase 3 clinical trials in multiple myeloma and AL amyloidosis, in both the frontline and relapsed settings, have shown that daratumumab-based regimens resulted in significant improvement in progression-free survival and/or overall survival.[11,12,13,14,15,16,17,18] Additional studies are underway to assess the efficacy and safety of DARZALEX *FASPRO*® in the treatment of other malignant and pre-malignant hematologic diseases in which CD38 is expressed, including smoldering myeloma and light chain (AL) amyloidosis.[19,20]

For the full U.S. Prescribing Information, please visit www.DARZALEX.com.

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.[21,22] 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.[23] Diagnosis is often delayed and prognosis is poor due to advanced, multi-organ, particularly cardiac, involvement.[24,25] Each year, an estimated 4,500 people develop AL amyloidosis in the U.S. alone.[26]

DARZALEX *FASPRO*™ 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 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

DARZALEX *FASPRO*™ 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*™.

Systemic Reactions

In a pooled safety population of 490 patients who received DARZALEX *FASPRO*™ as monotherapy or in combination, 11% of patients experienced a systemic administration-related reaction (Grade 2: 3.9%, Grade 3: 1.4%). Systemic administration-related reactions occurred in 10% of patients with the first injection, 0.2% with the second injection, and cumulatively 0.8% with subsequent injections. The median time to onset was 3.7 hours (range: 9 minutes to 3.5 days). Of the 84 systemic administration-related reactions that occurred in 52 patients, 73 (87%) occurred on the day of DARZALEX *FASPRO*™ administration. Delayed systemic administration-related reactions have occurred in less than 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. 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, pruritis, chills, vomiting, nausea, and hypotension.

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.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 7 minutes (range: 0 minutes to 4.7 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 is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide 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 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

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, pyrexia, cough, muscle spasms, back pain, vomiting, upper respiratory tract infection, peripheral sensory neuropathy, constipation, and pneumonia.

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

Please see full Prescribing Information at www.DARZALEX.com.

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 www.twitter.com/JanssenGlobal and www.twitter.com/JanssenUS. Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

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, 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 December 29, 2019, 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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