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Phase 3 COLUMBA Study Investigating a Subcutaneous Formulation of Darzalex® ▼ (daratumumab) Showed Non-Inferiority to Intravenous Administration in Patients with Relapsed/Refractory Multiple Myeloma

Subcutaneous formulation also showed reduced administration time and lower rates of infusion-related reactions compared to intravenous administration

BEERSE, BELGIUM, June 2, 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today results from the Phase 3 COLUMBA (MMY3012, NCT03277105) study, investigating a subcutaneously (SC) administered formulation of Darzalex® (daratumumab), co-formulated with recombinant human hyaluronidase PH20 (rHuPH20) [Halozyme's ENHANZE® drug delivery technology], in patients with relapsed/refractory multiple myeloma. The results showed non-inferior efficacy and pharmacokinetics for the SC administered formulation of daratumumab compared to intravenous (IV) administration, the only currently approved formulation of daratumumab (Abstract #8005).[1] The data presentation – the first for this Phase 3 study with SC formulation – is being featured in an oral session at the 55th American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, and was selected for the Best of ASCO 2019 Meetings.

"This study showed that the subcutaneous formulation of daratumumab resulted in non-inferior pharmacokinetics and efficacy compared to the current intravenous formulation, and also importantly offers the potential for a fixed-dose administration, shorter infusion times and a lower rate of infusion-related reactions," said Maria-Victoria Mateos, M.D., Ph.D., COLUMBA primary investigator and Director of the Myeloma Unit at University Hospital of Salamanca-IBSAL, Salamanca, Spain. "Daratumumab IV has proven to be an important medication in the treatment of multiple myeloma,

and a new subcutaneous formulation may offer patients a different experience, including a shorter administration time."

At a median follow-up of 7.5 months, the overall response rate (ORR) was 41 percent for the SC administered formulation of daratumumab compared to 37 percent for daratumumab IV (95 percent confidence interval [CI], 1.11 (0.89-1.37); P<0.0001).[1] The ORR was similar across all clinically relevant subgroups, including bodyweight.[1] The ratio of geometric means of C_{trough} for SC daratumumab over IV daratumumab was 108 percent (90 percent CI, 96 percent -122 percent).[1] The progression-free survival was comparable between the SC administered formulation of daratumumab and the current IV formulation of daratumumab (Hazard Ratio [HR] = 0.99; 95 percent CI, 0.78-1.26; P<0.9258).[1] The median duration for each SC injection was five minutes, compared to more than three hours with IV infusions.[1]

The most common (>5%) Grade 3/4 treatment-emergent adverse events (TEAEs) were thrombocytopenia (14 percent vs. 14 percent), anaemia (13 percent vs. 14 percent) and neutropenia (13 percent vs. 8 percent).[1] A lower rate of infusion-related reactions was observed in the arm that received the SC administered formulation of daratumumab compared to daratumumab IV (13 percent vs. 35 percent, respectively) (Odds Ratio = 0.28; 95 percent CI (0.18-0.44); P<0.0001).[1] The primary reasons for treatment discontinuation included progressive disease (43 percent in the SC arm vs. 44 percent in the IV arm) and adverse events (7 percent in the SC arm vs. 8 percent in the IV arm).[1]

"Our ambition in multiple myeloma has always focused on improving outcomes, but also experience for patients, and we are therefore incredibly pleased to see these results which confirm the potential for a new, and shorter, route of administration," said Dr Patrick Laroche, Europe, Middle East and Africa (EMEA) Haematology Therapeutic Area Lead, Janssen-Cilag France. "We look forward to submitting these data for regulatory review in coming months, to extend the reach of daratumumab to patients who could benefit from this novel formulation."

ENDS

In Europe, daratumumab is indicated:[2]

- in combination with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant

- as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy
- in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

About the COLUMBA Trial[3]

The randomised, open-label, multicentre Phase 3 study included 522 patients with multiple myeloma who had received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD), or whose disease was refractory to both a PI and an IMiD (median age of 67). In the arm that received the SC administered formulation of daratumumab (n=263), patients received a fixed dose of daratumumab 1,800 milligrams (mg) co-formulated with recombinant human hyaluronidase (rHuPH20) 2,000 Units Per millilitre (U/mL), subcutaneously weekly for Cycles 1 – 2, every two weeks for Cycles 3 – 6, and every four weeks for Cycle 7 and thereafter. In the daratumumab IV arm (n=259), patients received daratumumab for intravenous infusion 16 milligrams per kilogram (mg/kg) weekly for Cycles 1 – 2, every two weeks for Cycles 3 – 6, and every four weeks for Cycle 7 and thereafter. Each cycle was 28 days. Patients in both treatment arms continued until disease progression or unacceptable toxicity. Co-primary endpoints were ORR (analysed by Farrington-Manning test, with non-inferiority = 60 percent retention of ORR) and pre-dose C3D1 DARA C_{trough} (non-inferiority = lower bound of 90 percent CI for the ratio of the geometric means [GM] ≥80%).

About daratumumab

Daratumumab is a first-in-class[4] biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[5] Daratumumab is believed to induce tumour cell death through multiple immune-mediated mechanisms of action, including complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), as well as through apoptosis, in which a series of molecular steps in a cell lead to its death.[2] A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[2] Daratumumab is being evaluated in a comprehensive clinical development programme across a range of treatment settings in multiple myeloma, such as in frontline and relapsed settings.[6,7,8,9,10,11,12,13]

Additional studies are ongoing or planned to assess its potential in other malignant and pre-malignant haematologic diseases in which CD38 is expressed, such as smouldering myeloma.[14,15] For more information, please see www.clinicaltrials.gov.

For further information on daratumumab, please see the Summary of Product Characteristics at https://www.ema.europa.eu/documents/product-information/darzalex-epar-product-information_en.pdf.

In August 2012, Janssen Biotech, Inc. and Genmab A/S entered a worldwide agreement, which granted Janssen an exclusive licence to develop, manufacture and commercialise daratumumab.[16]

About Multiple Myeloma

Multiple myeloma (MM) is an incurable blood cancer that starts in the bone marrow and is characterised by an excessive proliferation of plasma cells.[17] In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.[18] Almost 60 percent of patients with MM do not survive more than five years after diagnosis.[19]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[20] Refractory MM is when a patient's disease progresses within 60 days of their last therapy.[21,22] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[23] While some patients with MM have no symptoms at all, most patients are diagnosed due to symptoms that can include bone problems, low blood counts, calcium elevation, kidney problems or infections.[24] Patients who relapse after treatment with standard therapies, including proteasome inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[25]

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/emea. Follow us at www.twitter.com/janssenEMEA for our latest news. Janssen R&D, LLC, Janssen Biotech and Janssen-Cilag France 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 the benefits of daratumumab for the treatment of patients with multiple myeloma. 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 materialise, actual results could vary materially from the expectations and of Janssen Research & Development, LLC., Janssen-Cilag France and 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 behaviour 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 30, 2018, 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. Neither the Janssen Pharmaceutical Companies of Johnson & Johnson 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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