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Study Investigating Darzalex®▼ (daratumumab) Shows Improved Depth of Response and Progression-Free Survival in Patients with Newly Diagnosed Multiple Myeloma Who are Eligible for a Transplant

- *Pivotal Phase 3 data presented in ASCO oral session and simultaneously published in The Lancet*
- *The Phase 3 CASSIOPEIA study is one of the largest transplant studies ever conducted in multiple myeloma, and the largest study conducted with daratumumab to date*

BEERSE, BELGIUM, June 2, 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson announced today results from the Phase 3 CASSIOPEIA (MMY3006, NCT02541383) study, an Intergroupe Francophone du Myelome (IFM) study in collaboration with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology (HOVON) and Janssen Research & Development, LLC., showing that the addition of Darzalex® (daratumumab) to bortezomib, thalidomide and dexamethasone (VTd) before and after autologous stem cell transplantation (ASCT) resulted in higher response rates and longer progression-free survival (PFS) compared to VTd alone in patients with newly diagnosed multiple myeloma (Abstract #8003).[1]

The data, being presented for the first time as part of an oral session at the 55th American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, have also been simultaneously published in *The Lancet*.

"CASSIOPEIA is the first study to investigate the clinical benefit of daratumumab in combination with a standard of care treatment regimen in patients with newly diagnosed multiple myeloma undergoing autologous stem cell transplant," said Dr Philippe Moreau, CASSIOPEIA primary investigator and Head of the Hematology Department at the University Hospital of Nantes, France. "There is a need for new treatment options for newly diagnosed patients, potentially including this combination therapy with daratumumab. This study adds to the growing body of evidence for daratumumab in the frontline setting."

The Phase 3 CASSIOPEIA trial is a two-part study. Results from this first part of the trial showed that after consolidation, the stringent complete response (sCR) rate was significantly higher in the daratumumab-VTd arm (29 percent) compared to VTd alone (20 percent) (Odds Ratio [OR] = 1.60; 95 percent confidence interval [CI], 1.21-2.12; P<0.0010).[1] At a median follow-up of 18.8 months, PFS was significantly improved in the daratumumab-VTd group compared to VTd alone (Hazard Ratio [HR] = 0.47; 95 percent CI, 0.33-0.67; P<0.0001), and the median PFS was not reached in either arm.[2] The addition of daratumumab to VTd resulted in an 18-month PFS rate of 93 percent compared to 85 percent for VTd alone.[1]

Daratumumab-VTd increased the rate of very good partial response or better (83 percent vs. 78 percent) (OR = 1.41; 95 percent CI, 1.04-1.92;[2] P = 0.0239) and complete response or better (39 percent vs. 26 percent) (OR = 1.82; 95 percent CI, 1.40-2.36;[2] P<0.0001) compared to VTd alone, respectively.[1] Daratumumab-VTd resulted in a higher rate of minimal residual disease (MRD) negativity at a sensitivity threshold of 10^{-5} compared to VTd post-consolidation (64 percent vs. 44 percent, respectively).[1]

The most common (≥10%) Grade 3/4 treatment-emergent adverse events (TEAEs) for daratumumab-VTd and VTd, respectively, were neutropenia (28 percent vs. 15 percent), lymphopenia (17 percent vs. 10 percent), stomatitis (13 percent vs. 16 percent) and thrombocytopenia (11 percent vs. 7 percent).[1] In the daratumumab-VTd combination arm, infusion-related reactions occurred in 35 percent of patients.[1]

"We are incredibly excited by these results, which highlight the benefit daratumumab could offer to transplant-eligible newly diagnosed multiple myeloma patients, and we continue to follow patients closely in part two of the study," said Dr Patrick Laroche, Europe, Middle East and Africa (EMEA)

Haematology Therapeutic Area Lead, Janssen-Cilag France. "These data formed the basis for recent regulatory submissions to both the European Medicines Agency and U.S. Food and Drug Administration, seeking to expand the current indication for daratumumab. We are now working closely with health authorities to bring this important combination to patients who need new options, as soon as possible."

ENDS

In Europe, daratumumab is indicated:[3]

- 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 CASSIOPEIA Trial[4]

The randomised, open-label, multicentre, Phase 3 study is sponsored by the French Intergroupe Francophone du Myelome in collaboration with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology and Janssen Research & Development, LLC. The study included 1,085 newly diagnosed patients with previously untreated, symptomatic multiple myeloma who were eligible for high-dose chemotherapy and stem cell transplant. In the first part of the study, patients were randomised to receive induction treatment with VTd alone or in combination with daratumumab, high-dose therapy and ASCT, and consolidation therapy with VTd alone or in combination with daratumumab. The primary endpoint in this part of the study is the proportion of patients who achieve an sCR 100 days after transplant. In the second part of the study, which is ongoing, patients who achieved a partial response or better in part one will undergo a second randomisation to receive maintenance treatment with daratumumab 16 mg/kg every eight weeks for up to two years or will be observed with no further treatment. The primary endpoint in this part of the study is PFS.

About daratumumab

Daratumumab is a first-in-class[5] biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[6] 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.[3] A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[3] 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.[4,7,8,9,10,11,12,13] 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 Biotech, Inc., Janssen-Cilag France and Janssen Research & Development, LLC 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 projections 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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