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Janssen Seeks Expanded Use of DARZALEX®▼ (daratumumab) Combination Therapy for Newly Diagnosed, Transplant Eligible Patients with Multiple Myeloma

First DARZALEX combination regimen being pursued as frontline treatment option for transplant eligible patients with multiple myeloma

BEERSE, BELGIUM, 27 March 2019 – The Janssen Pharmaceutical Companies of Johnson & Johnson today announced the submission of a Type II variation application to the European Medicines Agency (EMA) for DARZALEX®▼ (daratumumab) in combination with bortezomib, thalidomide and dexamethasone (VTd) for newly diagnosed patients with multiple myeloma who are eligible for autologous stem cell transplant (ASCT).

The submission is supported by data from the Phase 3 CASSIOPEIA (MMY3006) study. Additional information about this study can be found at www.ClinicalTrials.gov (NCT02541383).

"With this regulatory submission, Janssen could help redefine treatment for transplant eligible patients by providing the opportunity to be treated with a daratumumab regimen for the very first time," said José Antonio Burón Vidal, Vice President, Medical Affairs, Europe, Middle East and Africa (EMEA), Janssen-Cilag, S.A. "We continue to deliver advances in multiple myeloma, and if approved, this could offer a broader range of frontline patients a new treatment option and improved outcomes."

Janssen has also submitted an application to the U.S. Food and Drug Administration (FDA) seeking approval of daratumumab-VTd for newly diagnosed patients with multiple myeloma who are eligible for autologous stem cell transplant (ASCT).

In Europe, daratumumab is indicated: [1]

- 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[2]

The randomised, open-label, two-arm, multicentre, Phase 3 study includes participants with previously untreated multiple myeloma eligible for high dose chemotherapy and ASCT. In the first part of the study, on which the filing was based, participants were randomised to receive either induction (before transplantation) and consolidation (after transplantation) treatment with daratumumab combined with bortezomib, thalidomide and dexamethasone or bortezomib, thalidomide and dexamethasone alone. The primary endpoint is the number of patients that achieve a stringent Complete Response (sCR) rate after consolidation therapy. In the second part of the study, patients that achieved a response will undergo a second randomisation to either receive maintenance treatment of daratumumab or no further treatment (observation). The primary endpoint of this part of the study is progression free survival (PFS). The total duration for each participant in the study will be approximately 138 weeks. The end of the study will occur approximately five years after the last participant is randomised in the second phase of the study. Disease assessments will be performed every 4 weeks in the first phase of the study and then every 8 weeks in the second phase of the study.

About daratumumab

Daratumumab is a first-in-class[3] biologic targeting CD38, a surface protein that is highly expressed across multiple myeloma cells, regardless of disease stage.[4] 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.[1] A subset of myeloid derived suppressor cells (CD38+ MDSCs), CD38+ regulatory T cells (Tregs) and CD38+ B cells (Bregs) were decreased by daratumumab.[1] 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.[2,5,6,7,8,9,10,11] 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.[12,13] 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.[14]

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.[15] In Europe, more than 48,200 people were diagnosed with MM in 2018, and more than 30,800 patients died.[16] Almost forty percent of patients with MM do not reach five-year survival.[17]

Although treatment may result in remission, unfortunately, patients will most likely relapse as there is currently no cure.[18] Refractory MM is when a patient's disease progresses within 60 days of their last therapy.[19,20] Relapsed cancer is when the disease has returned after a period of initial, partial or complete remission.[21] 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.[22] Patients who relapse after treatment with standard therapies, including proteasome inhibitors and immunomodulatory agents, have poor prognoses and few treatment options available.[23]

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. and Janssen-Cilag S.A. 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 a recommendation to broaden the existing marketing authorisation for daratumumab. 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 Biotech, Inc., Janssen-Cilag S.A., the 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. 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.

References

[1] European Medicines Agency. DARZALEX summary of product characteristics. Available at: https://www.ema.europa.eu/documents/product-information/darzalex-epar-product-information_en.pdf Last accessed March 2019.

[2] ClinicalTrials.gov. A study to evaluate daratumumab in transplant eligible participants with previously untreated multiple myeloma (Cassiopeia). NCT02541383. Available at: https://clinicaltrials.gov/ct2/show/NCT02541383 Last accessed March 2019.

[3] Sanchez L, et al. Daratumumab: a first-in-class CD38 monoclonal antibody for the treatment of multiple myeloma. J Hematol Oncol. 2016 Jun 30;9(1):51. doi: 10.1186/s13045-016-0283-0.

[4] Fedele G, di Girolamo M, Recine U, et al. CD38 ligation in peripheral blood mononuclear cells of myeloma patients induces release of protumorigenic IL-6 and impaired secretion of IFNgamma cytokines and proliferation. *Mediat Inflamm*. 2013;2013:564687.

[5] ClinicalTrials.gov. A study comparing daratumumab, lenalidomide, and dexamethasone with lenalidomide and dexamethasone in relapsed or refractory multiple myeloma. NCT02076009. Available at: https://clinicaltrials.gov/ct2/show/NCT02076009 Last accessed March 2019.

[6] ClinicalTrials.gov. Addition of daratumumab to combination of bortezomib and dexamethasone in participants with relapsed or refractory multiple myeloma. NCT02136134. Available at: https://clinicaltrials.gov/ct2/show/NCT02136134 Last accessed March 2019.
[7] ClinicalTrials.gov. A study of combination of daratumumab and Velcade (bortezomib) melphalan-prednisone (DVMP) compared to Velcade melphalan-prednisone (VMP) in participants with previously untreated multiple myeloma. NCT02195479. Available at: https://clinicaltrials.gov/ct2/show/NCT02195479 Last accessed March 2019.
[8] ClinicalTrials.gov. Study comparing daratumumab, lenalidomide, and dexamethasone with lenalidomide and dexamethasone in participants with previously untreated multiple myeloma. NCT02252172. Available at: https://clinicaltrials.gov/ct2/show/NCT02252172 Last accessed March 2019.
[9] ClinicalTrials.gov. A study of Velcade (bortezomib) melphalan-prednisone (VMP) compared to daratumumab in combination with VMP (D-VMP), in participants with previously untreated multiple myeloma who are ineligible for high-dose therapy (Asia Pacific region). NCT03217812. Available at: https://clinicaltrials.gov/ct2/show/NCT03217812 Last accessed March 2019.
[10] ClinicalTrials.gov. Comparison of pomalidomide and dexamethasone with or without daratumumab in subjects with relapsed or refractory multiple myeloma previously treated with lenalidomide and a proteasome inhibitor daratumumab/pomalidomide/dexamethasone vs pomalidomide/dexamethasone (EMN14). NCT03180736. Available at: https://clinicaltrials.gov/ct2/show/NCT03180736 Last accessed March 2019.
[11] ClinicalTrials.gov. Study of carfilzomib, daratumumab and dexamethasone for patients with relapsed and/or refractory multiple myeloma (CANDOR). NCT03158688. Available at: https://clinicaltrials.gov/ct2/show/NCT03158688 Last accessed March 2019.
[12] ClinicalTrials.gov. A study to evaluate 3 dose schedules of daratumumab in participants with smoldering multiple myeloma. NCT02316106. Available at: https://clinicaltrials.gov/ct2/show/NCT02316106 Last accessed March 2019.
[13] ClinicalTrials.gov. An efficacy and safety proof of concept study of daratumumab in relapsed/refractory mantle cell lymphoma, diffuse large B-cell lymphoma, and follicular lymphoma. NCT02413489. Available at: https://clinicaltrials.gov/ct2/show/NCT02413489 Last accessed March 2019.
[14] Johnson & Johnson. Janssen Biotech announces global license and development agreement for investigational anti-cancer agent daratumumab. Press release August 30, 2012. Available at: https://www.jnj.com/media-center/press-releases/janssen-biotech-announces-global-license-and-development-agreement-for-investigational-anti-cancer-agent-daratumumab Last accessed March 2019.
[15] American Society of Clinical Oncology. Multiple myeloma: introduction. Available at: https://www.cancer.net/cancer-types/multiple-myeloma/introduction Last accessed March 2019.
[16] GLOBOCAN 2018. Cancer Today Population Factsheets: Europe Region. Available at: https://gco.iarc.fr/today/data/factsheets/populations/908-europe-fact-sheets.pdf Last accessed March 2019.
[17] De Angelis R, Minicozzi P, Sant M, et al. Survival variations by country and age for lymphoid and myeloid malignancies in Europe 2000-2007: results of EUROCARE-5 population-based study. *Eur J Cancer.* 2015;51:2254-68.
[18] Abdi J, Chen G, Chang H, et al. Drug resistance in multiple myeloma: latest findings and new concepts on molecular mechanisms. *Oncotarget*. 2013;4:2186–207.
[19] National Cancer Institute. NCI dictionary of cancer terms: refractory. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=350245 Last accessed March 2019.
[20] Richardson P, Mitsiades C, Schlossman R, et al. The treatment of relapsed and refractory multiple myeloma. *Hematology Am Soc Hematol Educ Program*. 2007:317-23.
[21] National Cancer Institute. NCI dictionary of cancer terms: relapsed. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms?CdrID=45866 Last accessed March 2019.
[22] American Cancer Society. Multiple myeloma: early detection, diagnosis and staging. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8740.00.pdf Last accessed March 2019.
[23] Kumar SK, Lee JH, Lahuerta JJ, et al. Risk of progression and survival in multiple myeloma relapsing after therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. *Leukemia*. 2012;26:149-57.