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For Immediate Release

DARZALEX® (daratumumab)-SC based quadruplet regimen approved by the European Commission for patients with newly diagnosed multiple myeloma who are transplant-eligible

Phase 3 PERSEUS study of daratumumab subcutaneous (SC) formulation in combination with bortezomib, lenalidomide and dexamethasone induction and consolidation, followed by daratumumab SC and lenalidomide maintenance showed a 58 percent reduction in risk of disease progression or death[1]

New regimen reinforces daratumumab SC as a foundational element for optimising frontline treatment of patients with newly diagnosed multiple myeloma, and significantly delaying disease progression[2]

BEERSE, BELGIUM (23 October 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, today announced that the European Commission (EC) approved the indication extension for DARZALEX® (daratumumab) subcutaneous (SC) formulation in combination with bortezomib, lenalidomide and dexamethasone (daratumumab-VRd) in patients with newly diagnosed multiple myeloma (NDMM) who are eligible for an autologous stem cell transplant (ASCT).[3] Patients will have the opportunity to receive this daratumumab SC-based quadruplet therapy at initial diagnosis, providing them with a new treatment shown to significantly improve outcomes.

This approval is supported by data from the Phase 3 PERSEUS study, which evaluated daratumumab SC-based quadruplet regimen for induction and consolidation therapy, followed by daratumumab SC and lenalidomide (D-R) maintenance therapy, compared to bortezomib, lenalidomide and dexamethasone (VRd) during induction and consolidation, followed by lenalidomide (R) maintenance in 709 patients with NDMM eligible for ASCT.[4]

“Multiple myeloma is a complex and highly varied disease, which reinforces the need for continuous innovation in first-line treatment strategies to deepen responses, reduce relapse and ultimately improve long-term outcomes,” said Dr. Paula Rodriguez-Otero, Department of Hematology, Cancer Center Clínica Universidad de Navarra, Pamplona, Navarra, Spain.* “The EC approval of this daratumumab SC-based quadruplet regimen offers a practice-changing new option, that has shown the potential to significantly improve progression-free survival, complete response rates, and MRD-negativity status compared to the current standard of care.”

Findings from the PERSEUS study, after a median follow-up of 47.5 months, demonstrated a significant improvement in the primary endpoint of progression-free survival (PFS), with the daratumumab-VRd regimen reducing the risk of disease progression or death by 58 percent compared to VRd (hazard ratio [HR], 0.42; 95 percent confidence interval [CI], 0.30-0.59; $p<0.0001$).[1] Treatment with daratumumab-VRd resulted in deeper responses compared to VRd with overall minimal residual disease (MRD)-negativity rate assessed at 10^{-5} of 75.2 percent vs. 47.5 percent ($p<0.001$), complete response or better of 87.9 percent vs 70.1 percent ($p<0.001$) and importantly, sustained MRD negativity for ≥12 months of 64.8 percent vs 29.7 percent, respectively.[1]

“The European Commission’s approval of this daratumumab quadruplet regimen marks a pivotal step forward in the treatment of newly diagnosed multiple myeloma,” said Edmond Chan, MBChB, M.D. (Res), Senior Director, EMEA

Therapeutic Area Lead Haematology, Innovative Medicine, Johnson & Johnson. “By incorporating daratumumab SC into this regimen we are further optimising frontline therapy for patients, building on our aim to transform outcomes, and establish new standards of care for eligible patients from induction through to maintenance.”

The overall safety profile of daratumumab-VRd was consistent with the known safety profiles for daratumumab SC and VRd.[2] The most common haematologic adverse reactions (≥20 percent) in patients with multiple myeloma who received daratumumab-VRd vs VRd were neutropenia (69.2 percent vs 58.8 percent), thrombocytopenia (48.4 percent vs 34.3 percent) and anaemia (22.2 percent vs 20.7 percent).[2] The most common non-hematologic adverse reactions (≥20 percent) in patients with multiple myeloma who received daratumumab-VRd vs VRd were peripheral neuropathy (53.6 percent vs 51.6 percent), fatigue (23.9 percent vs 26.5 percent), peripheral oedema (20.5 percent vs 21.3 percent), pyrexia (31.6 percent vs 31.4 percent), upper respiratory infection (31.6 percent vs 25.1 percent), COVID-19 (35 percent vs 23.9 percent), constipation (33.9 percent vs 34.0 percent), diarrhoea (61.0 percent vs 54.2 percent), back pain (22.8 percent vs 19.0 percent), insomnia (27.1 percent vs 17.6 percent), asthenia (26.8 percent vs 25.6 percent) and rash (23.4 percent vs 27.1 percent).[2]

“Since its first approval in 2016, over half a million patients worldwide have been treated with daratumumab, and today’s approval reinforces our commitment to bringing this transformative therapy to more patients as a first-line treatment, where it has the greatest potential for impact,” said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, Innovative Medicine, Johnson & Johnson. “At Johnson & Johnson, we continually challenge ourselves to one day eliminate cancers like multiple myeloma, and today’s milestone marks a significant step toward achieving that goal.”

About the PERSEUS study

The PERSEUS study (NCT03710603) is being conducted in collaboration with the European Myeloma Network as the sponsor.[4] PERSEUS is an ongoing, randomised, open-label, Phase 3 study comparing the efficacy and safety of daratumumab-VRd and autologous stem cell transplant (ASCT) followed by D-R maintenance vs VRd and ASCT followed by R maintenance in patients with TE NDMM (n=355).[2] The primary endpoint is PFS, and secondary endpoints include overall complete response or better rate, overall MRD-negativity (in patients with complete response or better), and OS.[2] Daratumumab SC was discontinued after at least 24 months of D-R maintenance therapy in patients who had a complete response or better and had sustained MRD-negative status for at least 12 months.[2] The median age is 61.0 (range, 32-70) years for patients in the daratumumab-VRd arm and 59.0 (range, 31-70) years for patients in the VRd arm.[2] The study is being conducted in 13 countries in Europe and Australia.[4]

Data from the PERSEUS study were featured as a late-breaking oral presentation (LBA-1) at the 2023 American Society of Hematology (ASH) Annual Meeting and were simultaneously published in *The New England Journal of Medicine* in 2023.

About Daratumumab and Daratumumab SC

Johnson & Johnson is committed to exploring the potential of daratumumab for patients with multiple myeloma across the spectrum of the disease.

In August 2012, Janssen Biotech, Inc., a Johnson & Johnson company and Genmab A/S entered a worldwide agreement, which granted Johnson & Johnson an exclusive licence to develop, manufacture and commercialise daratumumab. Since launch, daratumumab has become a foundational therapy in the treatment of multiple myeloma, having been used in the treatment of more than 548,000 patients worldwide.[5] Daratumumab is the only CD38-directed antibody approved to be given subcutaneously to treat patients with multiple myeloma.[2] Daratumumab SC is co-formulated with recombinant human hyaluronidase PH20 (rHuPH20), Halozyme's ENHANZE® drug delivery technology.[6]

CD38 is a surface protein that is present in high numbers on multiple myeloma cells, regardless of the stage of disease.[3] Daratumumab binds to CD38 and inhibits tumour cell growth causing myeloma cell death.[3] Daratumumab may also have an effect on normal cells.[3] Data across ten Phase 3 clinical trials, 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.[7,8,9,10,11,12,13,14,15,16]

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

About Multiple Myeloma

Multiple myeloma is currently an incurable blood cancer that affects a type of white blood cell called plasma cells, which are found in the bone marrow.[17,18] In multiple myeloma, these malignant plasma cells continue to proliferate, accumulating in the body and crowding out normal blood cells, as well as often causing bone destruction and other serious complications.[18] In the European Union, it is estimated that more than 35,000 people were diagnosed with multiple myeloma in 2022, and more than 22,700 patients died.[19] Whilst some patients with multiple myeloma initially have no symptoms, others can have common signs and symptoms of the disease, which can include bone fracture or pain, low red blood cell counts, fatigue, high calcium levels, infections, or kidney damage.[20]

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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 www.innovativemedicine.jnj.com/emea. Follow us at www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen-Cilag International NV, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., and Janssen Research & Development, LLC are 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 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-Cilag International NV, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & Development, LLC 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; competition, including technological advances, new products and patents attained by competitors; challenges to patents; 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 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 http://www.sec.gov/, http://www.jnj.com/ or on request from Johnson & Johnson. None of Janssen-Cilag International NV, Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen Research & Development, LLC nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.

** Dr. Paula Rodriguez-Otero, Department of Hematology, Cancer Center Clínica Universidad de Navarra, has provided consulting, advisory, and speaking services to Janssen; she has not been paid for any media work.*

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