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For Immediate Release

CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel) is the first BCMA-targeted treatment approved by the European Commission for patients with relapsed and refractory multiple myeloma who have received at least one prior line of therapy

Expanded indication for this one-time infusion may provide patients with a potential period away from their multiple myeloma treatment as early as first relapse[1]

Approval is based on results from the PHASE 3 CARTITUDE-4 study, in which treatment with cilta-cel in 1-3 prior lines of therapy reduced the risk of disease progression or death by 74 percent compared to standard therapies[1]

BEERSE, BELGIUM (22 April 2024) – Janssen-Cilag International NV, a Johnson & Johnson company, announced today that the European Commission (EC) has approved a Type II variation for CARVYKTI®▼ (ciltacabtagene autoleucel; cilta-cel). This latest approval is for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM), who have received at least one prior therapy, including an immunomodulatory agent (IMiD) and a proteasome inhibitor (PI), have demonstrated disease progression on the last therapy, and are refractory to lenalidomide.[1]

Cilta-cel is an innovative chimeric antigen receptor T-cell (CAR-T) therapy directed against B-cell maturation antigen (BCMA), a protein that is highly expressed on myeloma cells.[1] With this approval, cilta-cel becomes the first BCMA CAR-T therapy approved in Europe for the treatment of eligible patients as early as first relapse.[1]

More than 35,000 new cases of multiple myeloma, an incurable blood cancer, were diagnosed in the European Union in 2022.[2] Most patients with multiple myeloma relapse after standard treatment.[3] Each additional line of therapy is associated with lower response rates, shorter treatment-free intervals, and increased rates of toxicities and comorbidities.[4] The rate and aggressiveness of relapse with multiple myeloma means new therapies, that attack the disease in different ways, earlier in the treatment pathway, are needed.[3]

“Cilta-cel is a highly innovative, personalised cell therapy, that continues to deliver positive outcomes in patients in need of new therapeutic options,” said Edmond Chan, MBChB, M.D. (Res), EMEA Therapeutic Area Lead Haematology, Johnson & Johnson Innovative Medicine. “Today’s approval marks important progress for eligible patients with multiple myeloma, who may now benefit from treatment with cilta-cel earlier in their treatment pathway, where it has the potential to transform outcomes and change the trajectory of their disease.”

The expanded indication for cilta-cel is based on positive results from the Phase 3 CARTITUDE-4 study (NCT04181827), evaluating the efficacy and safety of cilta-cel in patients with relapsed and lenalidomide-refractory multiple myeloma.[5] Data from the study were previously published in *The New England Journal of Medicine*.[6] The CARTITUDE-4 study included patients (n=419) with relapsed and lenalidomide-refractory multiple myeloma, who had received at least one prior line of therapy (range, 1-3), including a PI and an IMiD.[1] Patients were randomised to receive either a sequence of apheresis, bridging therapy, lymphodepletion and cilta-cel (n=208) or standard of care (SOC), which included daratumumab, pomalidomide and dexamethasone (DPd) or pomalidomide, bortezomib and dexamethasone (PVd) (n=211).[1]

At a median follow-up of 15.9 months, a single infusion of cilta-cel resulted in a significantly lower risk of disease progression or death versus SOC (hazard ratio [HR]: 0.26; 95 percent confidence interval [CI], 0.2-0.4).[1] The median duration of progression-free survival (PFS) was not reached in the cilta-cel arm and was 11.8 months in the SOC arm (95 percent CI, 10-14).[1] At 12 months, estimated PFS rate was 76 percent in the cilta-cel arm (95 percent CI, 69-81) and 49 percent in the SOC arm (95 percent CI, 42-55).[1] Patients in the cilta-cel arm achieved an 85 percent overall response rate (ORR) and 73 percent achieved a complete response (CR) or better.[1] Among patients in the SOC arm, the ORR was 67 percent and CR or better was 22 percent.[1] Overall minimal residual disease (MRD) negativity rate was higher in the cilta-cel arm (61 percent) than the SOC arm (16 percent).[1] After a median follow-up of 28.7 months, median overall survival was not estimable in the cilta-cel (95 percent CI, NE-NE) and SOC (95 percent CI, 34-NE) arms but trended in favour of cilta-cel (HR: 0.57; 95 percent CI, 0.4-0.8).[1]

“Patients with lenalidomide-refractory multiple myeloma tend to experience early resistance to standard treatments and their disease worsens exponentially with each additional line of therapy,” said Professor Jesús San Miguel, Director of Clinical & Translational Medicine, Universidad de Navarra, Spain‡ “A single infusion of cilta-cel has been shown to significantly lower the risk of progression or death compared to current treatment options, as early as after first relapse.”

Adverse events (AEs) were evaluated in the safety population (n=208 in each arm).[6] Results published in *The New England Journal of Medicine* demonstrated that the most common Grade 3 or 4 AEs in both groups were haematologic, including neutropenia (cilta-cel: 90 percent; SOC: 82 percent), thrombocytopenia (cilta-cel: 41 percent; SOC: 19 percent) and anaemia (cilta-cel: 36 percent; SOC: 14 percent).[6] Serious AEs were reported in 92 patients (44 percent) in the cilta-cel arm and in 81 patients (39 percent) in the SOC arm.[6] Infections occurred in 62 percent and 71 percent of patients in the cilta-cel and SOC arms, respectively.[6] Overall, 39 patients in the cilta-cel arm and 46 patients in the SOC arm died; ten cilta-cel and five SOC patients died due to treatment-emergent AEs.[6] Cytokine release syndrome (CRS) occurred in 76 percent (one percent Grade 3 or 4) of the 176 patients who received cilta-cel.[6]

The EC also today approved the conversion of the conditional marketing authorisation (MA) for cilta-cel to a standard MA, as the obligations of the conditional approval have now been met.[1]

“Our ambition is to progress the science to address patients’ needs at each stage of this complex disease,” said Jordan Schecter, M.D., Vice President, Disease Area Leader, Multiple Myeloma, Johnson & Johnson Innovative Medicine. “Cilta-cel is an important part of how we are working to redefine multiple myeloma and ultimately achieve sustained remissions for patients. We are determined to get in front of cancer and today’s approval represents an important step forward in achieving this goal.”

The EC approval follows the U.S. Food and Drug Administration (FDA) approval of cilta-cel for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least one prior line of therapy including a PI and an IMiD and are refractory to lenalidomide, on 5 April 2024.[7]

About the CARTITUDE-4 Study

CARTITUDE-4 is the first international, randomised, open-label Phase 3 study evaluating the efficacy and safety of cilta-cel versus PVd or DPd in adult patients with relapsed and lenalidomide-refractory multiple myeloma, who received 1-3 prior lines of therapy.[5] Participants in the study previously received 1-3 prior lines of therapy, including a PI and an IMiD, and were refractory to lenalidomide.[5] Patients were randomised to receive either a sequence of apheresis, bridging therapy, lymphodepletion and cilta-cel (n=208) or standard of care (SOC), which included PVd or DPd (n=211).[1,5] The primary outcome measure for the study is PFS, defined as the time from the date of randomisation to the date of first documented disease progression, as defined in the IMWG criteria, or death due to any cause.[5]

About Cilta-cel

Cilta-cel received an initial conditional MA from the EC in May 2022, for the treatment of adults with relapsed and refractory multiple myeloma who have received at least three prior therapies, including an IMiD, a PI and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy.[8] Furthermore, in February 2024, the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA) recommended by consensus that the orphan designation for cilta-cel be maintained. In February 2022, the U.S. FDA initially approved cilta-cel for the treatment of adults with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody.[9]

For a full list of adverse events and information on dosage and administration, contraindications and other precautions when using cilta-cel please refer to the Summary of Product Characteristics for further information.[1] In line with EMA regulations for new medicines and those given conditional approval, cilta-cel is subject to additional monitoring.[1]

Cilta-cel is a BCMA-directed, genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient’s own T-cells with a transgene encoding CAR that directs the CAR positive T-cells to eliminate cells that express BCMA.[10] BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B-cells and plasma cells.[11,12] The cilta-cel CAR protein features two BCMA-targeting single domains designed to confer high avidity against human BCMA.[10] Upon binding to BCMA-expressing cells, the CAR promotes T-cell activation, expansion and elimination of target cells.[13]

In December 2017, Janssen Biotech, Inc., a Johnson & Johnson Company, entered into a worldwide licence and collaboration agreement with Legend Biotech USA, Inc. to develop and commercialise cilta-cel.[14]

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.[15,16] 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.[16] 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.[2] While 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.[17]

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.janssen.com/emea. Follow us at https://www.linkedin.com/company/jnj-innovative-medicine-emea. Janssen Pharmaceutica NV, Janssen-Cilag Limited, Janssen Biotech, Inc., Janssen-Cilag International NV 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 cilta-cel. 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 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 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.

‡ Professor Jesús San Miguel has provided consulting, advisory, and speaking services to Johnson & Johnson; he has not been paid for any media work.

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