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Chugai Announces Positive Data from Global Phase III Program for Crovalimab in PNH, a Rare Life-Threatening Blood Condition

- The COMMODORE 2 study in people with paroxysmal nocturnal hemoglobinuria (PNH) who have not been previously treated with complement inhibitors, met its co-primary efficacy endpoints showing crovalimab achieved disease control
- The results of the phase III COMMODORE 1 study in people with PNH switching from currently approved C5 inhibitors, supported the favorable benefit-risk profile of crovalimab, as seen in the pivotal COMMODORE 2 study
- Results from both studies will be submitted to regulatory authorities around the world and presented at an upcoming medical meeting

TOKYO, February 7, 2023 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced positive results from the global phase III COMMODORE 2 study, evaluating the efficacy and safety of crovalimab in people with paroxysmal nocturnal hemoglobinuria (PNH) who have not been previously treated with complement inhibitors. The study met its co-primary efficacy endpoints of transfusion avoidance and control of hemolysis (the ongoing destruction of red blood cells measured by lactate dehydrogenase levels). Results showed that crovalimab, a novel, investigational anti-C5 recycling antibody, given as a subcutaneous injection every four weeks (maintenance dosing), achieved disease control and was non-inferior to eculizumab, a current standard of care, which is given intravenously every two weeks.

The efficacy and safety data from the separate global phase III COMMODORE 1 study in people with PNH switching from currently approved C5 inhibitors to crovalimab supported the favorable benefit-risk profile of crovalimab, as seen in the pivotal COMMODORE 2 study.

“We are delighted to see the non-inferiority of crovalimab compared to the standard of care in the treatment of paroxysmal nocturnal hemoglobinuria. In PNH, there are still unmet medical needs such as reducing the burden of treatment, and subcutaneous crovalimab may be a new treatment option for patients,” said Dr. Osamu Okuda, Chugai’s President and CEO. “We will work together with Roche to file for approval in Japan and globally to deliver the drug to patients as soon as possible.”

Data from both studies will be submitted to regulatory authorities around the world and presented at an upcoming medical meeting. Positive data from the phase III COMMODORE 3 study in China were presented at the American Society of Hematology (ASH) Annual Meeting and Exposition on 10 December 2022. Data from the COMMODORE 3 study have been submitted via China’s Center for Drug Evaluation Breakthrough Therapy Designation pathway. This submission has been accepted under Priority Review for approval consideration by China’s National Medical Products Administration.

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[Reference Information]

Anti-C5 Recycling Antibody Crovalimab Obtains Priority Review in China for the Treatment of Paroxysmal Nocturnal Hemoglobinuria (Press release issued on August 10, 2022)
https://www.chugai-pharm.co.jp/english/news/detail/20220810160000_942.html

Roche's subcutaneous crovalimab given every four weeks achieves disease control in people with PNH, a life-threatening blood condition (Press release issued by Roche on December 11, 2022)
https://www.roche.com/media/releases/med-cor-2022-12-11

About the COMMODORE 1 and 2 studies

The COMMODORE 2 study is a phase III, randomized, open-label study evaluating the efficacy and safety of crovalimab versus eculizumab in people with paroxysmal nocturnal hemoglobinuria (PNH) who have not been treated previously with C5 inhibitors. The study's co-primary efficacy endpoints measure transfusion avoidance and control of hemolysis (the ongoing destruction of red blood cells measured by lactate dehydrogenase levels). The adults enrolled in the study were randomized in a 2:1 ratio to be treated with either subcutaneous (SC) crovalimab every four weeks or intravenous (IV) eculizumab every two weeks. The participants who were less than 18 years old were included in a non-randomized treatment arm and were treated with SC crovalimab every four weeks.[1]

The COMMODORE 1 study is a phase III, randomized, open-label study evaluating the safety of crovalimab in people with PNH switching from currently approved C5 inhibitors. The study's outcome measures evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic properties of crovalimab. The study included people (18 years of age or older) currently treated with eculizumab. In a non-randomized arm, the study also included pediatrics (<18 years of age) currently treated with eculizumab, people currently treated with ravulizumab, people currently treated with off-label doses of eculizumab (higher than the approved dose for PNH: more than 900mg per dose and/or more frequently than every two weeks), or people with known mutations in the C5 gene who do not respond to current therapies.[2]

About Crovalimab

Crovalimab is an anti-C5 recycling antibody created with Chugai's recycling antibody technology. Recycling antibodies are designed to achieve pH-dependent antigen binding so that a single antibody molecule can bind with the antigen multiple times, enabling a longer efficacy compared with a conventional antibody. Crovalimab is designed to target C5, a key component of the complement system, and is expected to control complement activity. It is also expected to reduce the treatment burden for patients and their caregivers through subcutaneous administration. Since crovalimab binds to complement C5 at a different site from existing drugs, it can be an effective treatment option for patients with a specific C5 gene mutation (appears in approximately 3.5% of Japanese patients with PNH) which causes existing antibody drugs not to bind to C5.[3]

Clinical trials for atypical hemolytic uremic syndrome (aHUS) and sickle cell disease (SCD) are ongoing, other than for PNH. In addition, a clinical trial for lupus nephritis is in preparation.

About paroxysmal nocturnal hemoglobinuria

Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired hematopoietic stem cell disorder characterized by intravascular hemolysis due to complement activation. It is caused by the clonal expansion of hematopoietic stem cells, driven by acquired mutations in the *PIG-A* gene.[4] While symptoms may vary in each individual, there are typically two types. One is symptoms attributed to the characteristic hemolysis in PNH, such as hemoglobinuria and thrombosis. The other is hematopoietic failures similar to those associated with aplastic anemia. PNH may cause complications, including chronic kidney disease and pulmonary hypertension. In Japan, PNH is a rare disease that is listed as one of the designated intractable diseases (designated intractable disease 62). 959 individuals have been granted the medical care recipient certificate for PNH as of the end of 2021.[5]

References:

1. COMMODORE 2 (NCT04434092). [Internet; cited February 2023] Available at: https://www.clinicaltrials.gov/ct2/show/NCT04434092.
2. COMMODORE 1 (NCT04432584). [Internet; cited February 2023] Available at: https://www.clinicaltrials.gov/ct2/show/NCT04432584.
3. Fukuzawa T, et al. Long lasting neutralization of C5 by SKY59, a novel recycling antibody, is a potential therapy for complement-mediated diseases. 2017; Sci Rep 7, 1080.
4. Working group for the development of the reference guide revision of diagnostic criteria and practice for paroxysmal nocturnal hemoglobinuria (PNH). Referenced Guide to Paroxysmal Nocturnal Hemoglobinuria Treatment Revised 2019.
5. Portal Site of Official Statistics of Japan website (https://www.e-stat.go.jp/). Report on Public Health Administration and Services FY2021, Accessed February 2023. (Japanese only)

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