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Chugai Files New Drug Application in Japan for Crovalimab for Paroxysmal Nocturnal Hemoglobinuria

- The application was submitted based on several studies, including the global phase III clinical studies COMMODORE 2 and COMMODORE 1
- Filed as a subcutaneously administered C5 inhibitor (maintenance phase) in Japan

TOKYO, June 14, 2023 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it filed regulatory applications with the Ministry of Health, Labour and Welfare for the anti-C5 antibody crovalimab for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) on June 14, 2023.

"We are very pleased that crovalimab, our in-house developed project, has been submitted for regulatory approval in Japan for the indication of paroxysmal nocturnal hemoglobinuria," said Chugai's President and CEO, Dr. Osamu Okuda. "Anti-C5 inhibitors are defined as a standard of care in PNH, and subcutaneous crovalimab aims to bring new values. A subcutaneous administration once every four weeks of crovalimab in the maintenance phase demonstrated favorable efficacy and safety, bringing a new treatment option possibly decreasing the treatment burden on patients, such as reducing the dosing time. We will continue working with the authorities to deliver this drug to patients as quickly as possible."

The application is based on the results of the COMMODORE 2 study in people with PNH not previously treated with C5 inhibitors and the COMMODORE 1 study in people with PNH who switched to crovalimab from currently approved C5 inhibitors. Both are global phase III clinical studies conducted in collaboration with Roche, with participation from Japan.

Crovalimab has been created using Chugai's Recycling Antibody® technology. While a typical antibody can bind to an antigen only once, crovalimab is engineered to bind to the antigen repeatedly, enabling sustained complement inhibition at a low dose and achieving subcutaneous administration every four weeks.

[Reference]

New Data Presented at EHA Show Chugai's Subcutaneously Administered Crovalimab Achieved Disease Control and was Well-Tolerated in People with Paroxysmal Nocturnal Hemoglobinuria (PNH) (Press release issued on June 12, 2023)
https://www.chugai-pharm.co.jp/english/news/detail/20230612170001_992.html

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

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not been treated previously with C5 inhibitors. The 204 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 six participants under 18 years old were included in a descriptive arm to be treated with SC crovalimab every four weeks.[1]

*Including two patients aged less than 18 years old enrolled before the revision of the protocol

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 included 89 people (18 years of age or older) currently treated with eculizumab, randomized in a 1:1 ratio to be treated with either SC crovalimab every four weeks or IV eculizumab every two weeks. 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 antibody drugs, it can be an effective treatment option for patients with a specific C5 gene mutation (appears in approximately 3.2% of Japanese patients with PNH), which causes existing antibody drugs not to bind to C5.[3,4]

In addition to PNH, clinical trials are ongoing for atypical hemolytic uremic syndrome (aHUS). Overseas, Roche is conducting trials for sickle cell disease (SCD) and lupus nephritis.

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.[5] 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.[6]

References:

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5. 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 2022.
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