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Anti-C5 Recycling Antibody Crovalimab Obtains Priority Review in China for the Treatment of Paroxysmal Nocturnal Hemoglobinuria

- China's NMPA accepted the world's first filing of regulatory application for crovalimab and granted priority review
- The application is submitted by Roche China based on a Chinese phase III clinical trial (COMMODORE 3 study) for paroxysmal nocturnal hemoglobinuria
- Crovalimab is designated in China as a Breakthrough Therapy for the disease in July 2021

TOKYO, August 10, 2022 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that the National Medical Products Administration (NMPA) of People's Republic of China accepted an application for regulatory approval of crovalimab (development code: SKY59/RG6107) for paroxysmal nocturnal hemoglobinuria (PNH) and granted priority review. Crovalimab is a humanized complement inhibitor C5 monoclonal antibody discovered by Chugai. As F. Hoffmann-La Roche Ltd. (hereafter "Roche") [Head Office: Basel, Switzerland. CEO: Severin Schwan] is responsible for the development of crovalimab outside Japan and Taiwan, the regulatory application was filed by a China affiliate of Roche. In China, crovalimab was designated as a Breakthrough Therapy for PNH in July 2021.

PNH is a disease caused by abnormal destruction of red blood cells (hemolysis) due to an acquired gene mutation affecting hematopoietic stem cells. It is listed among the designated intractable diseases in Japan (Designated intractable disease 62). Major symptoms include anemia, hemoglobinuria and thrombosis. Moreover, hemolysis may cause various organ disorders. PNH is a rare disease with an incidence of about one to ten cases per million people in China.[1]

"We are delighted to announce that China's regulatory authorities accepted the world's first application for regulatory approval of crovalimab. Paroxysmal nocturnal hemoglobinuria is an intractable disease and was long known as a potentially life-threatening disease with limited effective treatment options. In China, patients are mainly treated with blood transfusion and symptomatic therapies. Crovalimab has obtained Breakthrough Therapy Designation in China for the disease, and the filing of crovalimab is a great step forward to contribute to patients who are in need of new treatment options," said Dr. Osamu Okuda, Chugai's President and CEO. "Two global phase III clinical trials are ongoing for paroxysmal nocturnal hemoglobinuria. We will continue to work closely with Roche to deliver a new drug to patients in China and the rest of the world as soon as possible."

Crovalimab was created with one of Chugai's antibody engineering technologies called recycling antibody technology. Recycling antibodies are designed to allow antibodies to bind with the target antigen multiple times and to act longer in the body. Crovalimab is the second recycling antibody developed by Chugai following Enspryng®, a treatment for neuromyelitis optica spectrum disorder. Chugai's research company

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in Singapore, Chugai Pharmabody Research, played a leading role in the discovery of crovalimab.

The filing was based on the primary analysis of COMMODORE 3 study, a multicenter, single-arm, phase III clinical trial conducted in China. The study evaluated the efficacy, safety, pharmacokinetics, and pharmacodynamics of crovalimab administered subcutaneously every 4 weeks in patients with PNH who has not been previously treated with anti-C5 antibodies. Approximately 50 patients aged 12 years and older were enrolled and received crovalimab for at least 24 weeks. The primary endpoints were the percentage of patients who achieved predetermined hemolytic control based on LDH level between week 5 through week 25, and the change in the percentage of patients achieving predetermined transfusion avoidance from baseline at week 25. Detailed results of the study are to be presented at a future medical meeting.

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 by subcutaneous administration.

Currently, two global phase III clinical trials for paroxysmal nocturnal hemoglobinuria are underway: COMMODORE 1 study in patients who switched from anti-C5 antibodies, and COMMODORE 2 study in untreated patients. Clinical trials for atypical hemolytic uremic syndrome and sickle cell disease are ongoing as well. 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.[2] 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, the rare disease is listed as one of the designated intractable diseases (designated intractable disease 62). 927 individuals have been granted the medical care recipient certificate for PNH as of end of 2020.[3]

Source:

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2. 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.
3. Japan Intractable Diseases Information Center. Available from: https://www.nanbyou.or.jp/. Accessed

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