Nippon Shinyaku Co., Ltd.
Chugai Pharmaceutical Co., Ltd.

Humanized Anti-CD20 Monoclonal Antibody Gazyva Approved for Additional Indication of Chronic Lymphocytic Leukemia

Approval based on the results from the Phase III ELEVATE-TN *study evaluating Gazyva and acalabrutinib in patients with untreated chronic lymphocytic leukemia*

TOKYO, December 23, 2022 -- Nippon Shinyaku Co., Ltd. (TOKYO: 4516) and Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that Chugai obtained regulatory approval today from the Ministry of Health, Labour and Welfare (MHLW) for an anti-cancer agent/humanized anti-CD20 monoclonal antibody Gazyva® Intravenous Infusion 1000 mg [generic name: obinutuzumab (genetical recombination)] for an additional indication of CD20-positive chronic lymphocytic leukemia (including small lymphocytic lymphoma).

“We are very pleased that Gazyva has become a new option for the treatment of chronic lymphocytic leukemia (CLL), and to be able to meet medical needs,” said Nippon Shinyaku's President, Toru Nakai. “We hope for Gazyva to become a contribution for treating patients with CLL, and will continue to promote information provision activities for the proper use of Gazyva.”

“We are very pleased that this line extension enables us to offer the combination treatment as a new treatment option for patients with chronic lymphocytic leukemia (CLL),” said Chugai’s President and CEO, Dr. Osamu Okuda. “CLL has a long disease course. We will continue to provide information on efficacy and safety of Gazyva for the benefit of patients with CLL .”

The approval is based on data including the phase III ELEVATE-TN study, conducted by AstraZeneca, which evaluated the efficacy and safety of Gazyva and acalabrutinib (Bruton's tyrosine kinase (BTK) inhibitor, product name Calquence®) in patients with untreated CLL. The study showed that the combination of Gazyva and acalabrutinib significantly improved progression free survival compared to the combination of Gazyva and chlorambucil (hazard ratio: 0.10, 95% confidence interval: 0.06-0.17, p value < 0.0001). Major adverse reactions were neutropenia, headache, diarrhea, contusion, fatigue, nausea, thrombocytopenia, rash, arthralgia, petechiae, dizziness and anemia.

About ELEVATE-TN study

ELEVATE-TN (ACE-CL-007, NCT02475681) study is a randomized, multicenter, open-label Phase III trial evaluating the safety and efficacy of acalabrutinib in combination with obinutuzumab or acalabrutinib alone versus chlorambucil (unapproved) in combination with obinutuzumab in previously untreated patients with CLL. In the study, 535 patients are randomized 1:1:1 to following groups: chlorambucil plus obinutuzumab, acalabrutinib plus obinutuzumab, and acalabrutinib monotherapy.

The primary endpoint is IRC-assessed progression-free survival (PFS) with acalabrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab. The secondary endpoint is IRC-assessed PFS with acalabrutinib monotherapy versus chlorambucil plus obinutuzumab. Other secondary endpoints are overall response rate, time to next treatment, safety and overall survival etc.[1)]

Approval Information *Newly added description

Indications:

CD20-positive chronic lymphocytic leukemia (including small lymphocytic lymphoma)

Dosage and administrations:

When used in combination with acalabrutinib, the usual adult dose of obinutuzumab (genetical recombination) is 100 mg infused intravenously on Day 1 of Cycle 1 concomitant with acalabrutinib, 900 mg on Day 2, and 1000 mg on Days 8 and 15, and then 1000 mg on Day 1 of Cycle 2 and subsequent cycles. One cycle is 28 days, and administration is repeated for up to 6 cycles.

Precautions concerning dosage and administrations (Excerpt version):

Start administration of GAZYVA after administering acalabrutinib for 28 days.

About Gazyva (obinutuzumab)

Gazyva is a glycoengineered type II anti-CD20 monoclonal antibody designed to bind to CD20, a protein expressed on certain B cells, but not on stem cells or plasma cells. Gazyva is designed to attack and destroy targeted B cells both directly and together with the body's immune system. Nippon Shinyaku and Chugai jointly develop and market the product in Japan.

About chronic lymphocytic leukemia (CLL)

In CLL, blood stem cells in the bone marrow become excessive abnormal lymphocytes and these abnormal cells have difficulty fighting infections. As the number of abnormal cells grows there is less room for healthy white blood cells, red blood cells, and platelets.[2)] This could result in anemia, infection, and bleeding. Small lymphocytic lymphoma is the same type of cancer as CLL. When lymphocytes are not located in the peripheral blood or bone marrow, the disease is called small lymphocytic lymphoma.[3)] CLL/ small lymphocytic lymphoma is a rare type of lymphoma accounting for less than one case in 100,000 population annually in Japan.[4)] B-cell receptor signaling through BTK is one of the essential growth pathways for CLL.

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[Reference]

1. ClinicalTrials.gov. Elevate CLL TN: Study of Obinutuzumab + Chlorambucil, Acalabrutinib (ACP-196) + Obinutuzumab, and Acalabrutinib in Subjects With Previously Untreated CLL. https://clinicaltrials.gov/ct2/show/NCT02475681 [Internet. Accessed in December 2022]
2. National Cancer Institute. Chronic lymphocytic leukemia treatment (PDQ®)–Patient version. https://www.cancer.gov/types/leukemia/patient/cll-treatment-pdq [Internet. Accessed in December 2022]
3. Japanese Society of Hematology Practical Guidelines for Hematological Malignancies, 2018, Revisioned Version. http://www.jshem.or.jp/gui-hemali/table.html [Internet. Accessed in December 2022. Japanese only]
4. Center for Cancer Control and Information Services, National Cancer Center. Chronic lymphocytic leukemia/small lymphocytic lymphoma https://ganjoho.jp/public/cancer/CLL/index.html [Internet. Accessed in December 2022. Japanese only]

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