

August 28, 2019

ONO Submits an Application for Manufacturing and Marketing Approval for Tirabrutinib Hydrochloride (ONO-4059), a BTK inhibitor, for Treatment of Recurrent or Refractory Primary Central Nervous System Lymphoma in Japan

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; President and Representative Director: Gyo Sagara; “ONO”) announced today that ONO submitted an application of tirabrutinib hydrochloride (ONO-4059) (“Tirabrutinib”), a Bruton’s tyrosine kinase (“BTK”) inhibitor, for the manufacturing and marketing approval for the treatment of recurrent or refractory primary central nervous system lymphoma (“PCNSL”) in Japan.

This application is based on the result from a multi-center, open-label, uncontrolled Phase I/II study (ONO-4059-02) in 44 patients with recurrent or refractory PCNSL, receiving Tirabrutinib orally once daily. Tirabrutinib was designated as an orphan drug for the planned indication of “primary central nervous system lymphoma” by the Ministry of Health, Labour and Welfare (MHLW) in Japan on August 20, 2019.

PCNSL is a malignant lymphoma in which the lesion is localized in the cerebrospinal cord (including the eyes) at the first onset. It is estimated that there are approximately 980 new cases with PCNSL per year in Japan^{*1, 2}. The signs and symptoms presented by patients with PCNSL vary depending on the site of the lesion, and include localized neuropathy, neuropsychiatric symptoms, symptoms associated with increased intracranial pressure, seizure, eye symptoms, headache, difficulty in movement, cranial neuropathy and radiculopathy.

Currently, untreated PCNSL patients receive high-dose methotrexate-based treatment followed by whole-brain radiation therapy, by which a certain patient population shows long-term remissions, but many patients will relapse. There are also refractory patients who do not respond to the initial treatment. Standard treatment has not been established for patients with recurrent or refractory PCNSL, and treatment options are limited for them. Therefore, a new treatment option is expected for patients with recurrent or refractory PCNSL^{*3}.

Tirabrutinib, discovered and developed by ONO, is a highly selective, oral BTK inhibitor and has been developed for the treatment of patients with B-cell tumors and autoimmune diseases in Japan. B cell receptor (BCR) signaling plays a core role in the survival, activation, proliferation, maturation and differentiation of B cell lymphocyte. The BCR signaling pathway is known to be permanently activated, particularly B cell non-Hodgkin lymphoma (B-NHL) and chronic lymphocytic leukemia (CLL). Tirabrutinib is expected to have a therapeutic effect because it inhibits BTK, a mediator located downstream of BCR.

In December 2014, ONO out-licensed Tirabrutinib to Gilead Sciences, Inc. (Gilead) to allow Gilead the right to develop and commercialize the product in all countries of the world, except Japan, South Korea, Taiwan, China and ASEAN countries where ONO retains the development and commercialization rights of the product.

*1: Neurol Med Chir (Tokyo). 2017;57(Supplement 1):9-102.

*2: Jpn J Neurosurg VOL.24 NO.10 2015.10

*3: Practical Guidelines for Neuro-Oncology 2019

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