No. 20-15

March 26, 2020
Eisai Co., Ltd.

EISAI SUBMITS MARKETING AUTHORIZATION APPLICATION IN JAPAN FOR ANTICANCER AGENT DENILEUKIN DIFTITOX (GENETIC RECOMBINANT) FOR CUTANEOUS T-CELL LYMPHOMA AND PERIPHERAL T-CELL LYMPHOMA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has submitted in Japan a marketing authorization application of the anticancer agent denileukin diftitox (genetic recombinant) (generic name, development code: E7777) for relapsed or refractory Cutaneous T-cell Lymphoma (CTCL) and Peripheral T-cell Lymphoma (PTCL).

This application is based on data from a multicenter, open-label, single-arm Phase II clinical study (study 205) conducted in Japan for patients with relapsed or refractory CTCL or PTCL to evaluate the efficacy and safety of this agent.
This study achieved the primary endpoint and exceeded a predetermined threshold with statistical significance: the objective response rate (ORR) of CTCL and PTCL patients in total (n=36) was 36.1% (95% confidence interval (CI): 20.8-53.8). The ORRs of each subtype were 31.6% (95% CI : 12.6-56.6) for CTCL (n=19) and 41.2% (95%CI: 18.4-67.1) for PTCL (n=17).
The five most frequent adverse events observed in this study were increased aspartate aminotransferase (AST) (89.2%), increased alanine aminotransferase (ALT) (86.5%), hypoalbuminaemia (70.3%), lymphopenia (70.3%), and pyrexia (51.4%).

Denileukin diftitox (genetic recombinant) is a fusion protein of the receptor-binding portion of interleukin-2 (IL-2) and diphtheria toxin that specifically binds to the IL-2 receptor on the surface of tumoral lymphocyte. The antitumor effect of denileukin diftitox depends on the intracellular delivery of diphtheria toxin which inhibits protein synthesis and induces cell death. The agent has been evaluated as a drug with high medical need by the "Study Group for Unapproved Drugs/Off-Label Drugs for High Medical Needs"*, and Eisai has been requested to develop it by the Ministry of Health, Labour and Welfare.

Eisai positions oncology as a key franchise area and aims to create innovative drugs that act towards curing cancer. Eisai aims to make continuous efforts to meet the diversified needs of and increase the benefits provided to patients with cancer, their families, and healthcare professionals.

* The Study Group set up within the Ministry of Health, Labour and Welfare with the purpose of contributing to enhancing the development of drugs and indications that have not been approved in Japan (unapproved drugs/off-label drugs) by pharmaceutical companies. In addition to evaluating the medical needs of unapproved drugs/off-label drugs, their responsibilities include evaluating the applicability of the drug to an Application with Public Knowledge, and the adequacy of additional clinical studies that need to be conducted for filing applications for approval, and so on.

Media Inquiries:
Public Relations Department,
Eisai Co., Ltd.
+81-(0)3-3817-5120

[Notes to editors]

1. About Denileukin Diftitox (Genetic Recombinant) (generic name, development code: E7777)

Denileukin diftitox (genetic recombinant) is a fusion protein of the receptor-binding portion of interleukin-2 (IL-2) and diphtheria toxin that specifically binds to the IL-2 receptor on the surface of tumoral lymphocyte. The antitumor effect of denileukin diftitox depends on the intracellular delivery of diphtheria toxin which inhibits protein synthesis and induces cell death.

Eisai retains exclusive development and marketing rights for the agent in Japan and Asia, and in other regions, Dr. Reddy's Laboratories Ltd. has development and marketing rights.

2. About Phase II Clinical Study (Study 205)

Study 205 is a multicenter, open-label, single-arm phase II clinical study evaluating the efficacy and safety of denileukin diftitox (genetic recombinant) conducted in Japan for patients with relapsed or refractory Cutaneous T-cell Lymphoma (CTCL) or Peripheral T-cell Lymphoma (PTCL). The patients who participated in this study received a final histopathological definitive diagnosis by the Central Committee for Pathological Diagnosis, which is independent of the clinical study site. The histopathological subtypes of participants consisted of 19 in CTCL, 17 in PTCL, and 1 other malignant lymphoma. The efficacy of this drug was evaluated in 36 patients with CTCL or PTCL, and the safety was evaluated in 37 patients. The drug was administered by intravenous drip infusion at a dose of 9μg / kg / day for five consecutive days from day 1 to day 5 to complete a cycle, with one cycle every three weeks and a maximum of up to 8 cycles conducted. In this study, the primary endpoint was objective response rate, and the efficacy of the agent was evaluated on the basis that the lower limit of the confidence interval (CI) was above a predetermined threshold.

3. About Cutaneous T-cell Lymphoma (CTCL)

CTCL is a type of non-Hodgkin's lymphoma of primary cutaneous with various forms. In CTCL, some of the T cells (a type of lymphocyte involved in the immune system) become cancerous, causing skin lesions and reducing the patient's QOL (Quality of Life) due to pain and pruritus. CTCL is generally a low-grade lymphoma, but it progresses slowly and advances to the tumor stage over several years to several decades. CTCL is still one of the diseases with extremely high unmet medical needs because it has a high malignancy when it reaches the tumor stage and has a poor prognosis such as infiltration of lymph nodes and internal organs.

4. About Peripheral T-cell Lymphoma (PTCL)

PTCL is a type of T-cell non-Hodgkin's lymphoma that is classified as an intermediate-grade lymphoma. PTCL is often detected in advanced stages, and has symptoms such as swelling and lumps in the lymph nodes, fever, heavy night sweats, and weight loss. Among PTCLs, Anaplastic Lymphoma Kinase (ALK)-positive anaplastic large cell lymphoma, which occurs in the 20s and 30s, has a favorable prognosis and is curable. However, other types of PTCL often occur around the age of 60, and may have a poor prognosis or may be difficult to treat. Therefore, PTCL is still one of the diseases with extremely high-unmet medical needs.