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Eisai Co., Ltd.

ANTICANCER AGENT "Remitoro® INTRAVENOUS DRIP INFUSION 300μg" (DENILEUKIN DIFTITOX (GENETIC RECOMBINANT)) APPROVED IN JAPAN FOR PERIPHERAL T-CELL LYMPHOMA AND CUTANEOUS T-CELL LYMPHOMA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has obtained manufacturing and marketing approval for the anticancer agent "Remitoro® for Intravenous Drip Infusion 300μg" (denileukin diftitox (genetic recombinant)) with the indications of relapsed or refractory Peripheral T-cell Lymphoma (PTCL) and relapsed or refractory Cutaneous T-cell Lymphoma (CTCL), in Japan. This agent was evaluated by the Ministry of Health, Labour and Welfare (MHLW) as a drug with high medical need at the "Study Group for Unapproved Drugs/Off-Label Drugs for High Medical Need". Hence, Eisai has been working on the development of the agent thereof in Japan, and applied for manufacturing and marketing approval in March 2020, based primarily on data from a Phase II clinical study (Study 205).

Study 205 is a multicenter, open-label, single-arm Phase II clinical study, conducted in Japan to evaluate the efficacy and safety of the agent in patients with relapsed or refractory PTCL or CTCL.
This study achieved the primary endpoint target and exceeded a prespecified tumor response threshold with statistical significance: the objective response rate (ORR) of PTCL and CTCL patients in total (n=36) was 36.1% (95% confidence interval (CI): 20.8-53.8). The ORRs of each subtype were 41.2% (95%CI: 18.4-67.1) for PTCL (n=17) and 31.6% (95% CI: 12.6-56.6) for CTCL (n=19).
The five most frequent treatment-emergent 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%).
Eisai will conduct a post-marketing special use results survey (all-case surveillance) in all patients who are administered the agent until a pre-determined number of patients has been reached in accordance with an approval condition imposed by the MHLW.

The agent is a fusion protein consisting of interleukin-2 (IL-2) and partial sequence of diphtheria toxin, and specifically binds to the IL-2 receptor on the surface of tumoral lymphocytes. The antitumor effect of denileukin diftitox depends on the intracellular delivery of diphtheria toxin fragment which inhibits protein synthesis and induces cell death. Eisai retains exclusive development and marketing rights for the agent in Japan and Asia.
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, by delivering "Remitoro" as a new treatment option for relapsed or refractory PTCL and relapsed or refractory CTCL in Japan.

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[Notes to editors]

1. About Remitoro for Intravenous Drip Infusion 300μg (Denileukin Diftitox (Genetic Recombinant))

This agent is a fusion protein consisting of interleukin-2 (IL-2) and partial sequence of diphtheria toxin. The antitumor effect of denileukin diftitox depends specific binding to the IL-2 receptor on the surface of tumoral lymphocytes followed by intracellular delivery and release of diphtheria toxin fragment 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 Peripheral T-cell Lymphoma (PTCL) or Cutaneous T-cell Lymphoma (CTCL). 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 17 patients with PTCL, 19 patients with CTCL, and 1 patient with other malignant lymphoma. The efficacy of the agent was evaluated in 36 patients with PTCL or CTCL, and the safety was evaluated in 37 patients. The agent was administered by intravenous drip infusion over 60 minutes 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 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 be difficult to treat. Therefore, PTCL is still a disease with extremely high-unmet medical need. It is estimated that the number of patients with PTCL in Japan is less than 6,000.[1]

4. About Cutaneous T-cell Lymphoma (CTCL)

CTCL is a type of non-Hodgkin's lymphoma of primary cutaneous disease with various other manifestations in additional sites like lymph nodes and peripheral blood. 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, with initial patch and plaque skin lesions, but it progresses slowly and advances to the tumor stage over several years to over a dozen years. CTCL is still a disease with extremely high unmet medical need because it has a high malignancy when it reaches the tumor stage and has a poor prognosis. It is estimated that the number of patients with CTCL in Japan is less than 4,000.[1]

5. About Study Group for Unapproved Drugs/Off-Label Drugs for High Medical Need

The Study Group was 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.

1. Vital Statistics/Patient Survey in 2017 (Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour and Welfare, Japan.) (available in Japanese only)