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Eisai Co., Ltd.

EISAI SUBMITS APPLICATION FOR ADDITIONAL INDICATION OF ANTICANCER AGENT LENVIMA® FOR HEPATOCELLULAR CARCINOMA IN JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has submitted an application for an additional indication of its in-house discovered and developed anticancer agent Lenvima® (generic name: lenvatinib mesylate) for the treatment of hepatocellular carcinoma (HCC) in Japan, the first in the world.

This application is based on the results of a multicenter, open-label, randomized, global Phase III trial (Study 304) comparing the efficacy and safety of Lenvima versus sorafenib, a standard treatment for advanced HCC, as a first-line treatment for 954 patients with unresectable HCC. [1]

According to the results of this study, Lenvima met the statistical criteria for non-inferiority in the primary endpoint of Overall Survival (OS) compared to sorafenib. Additionally, Lenvima showed highly statistically significant and clinically meaningful improvements in the secondary endpoints of Progression Free Survival (PFS), Time To Progression (TTP), and Objective Response Rate (ORR), doubling sorafenib's median values and ratios. In this study, the five most common adverse events observed in the Lenvima arm were hypertension, diarrhea, decreased appetite, weight loss and fatigue, which is consistent with the known side-effect profile of Lenvima. Lenvima is the first agent to meet the statistical criteria for non-inferiority of OS compared to sorafenib since sorafenib was approved for the treatment of HCC 10 years ago.

Liver cancer is the second leading cause of cancer related deaths and is estimated to be responsible for 750,000 deaths per year globally.[2] Additionally, 780,000 cases are newly diagnosed each year, about 80% of which occur in Asian regions, including Japan and China.[2] HCC accounts for 85% to 90% of liver cancer cases. It is estimated that there are approximately 42,000 HCC patients in Japan,[3] with 26,000 deaths every year.[4] Treatment options for unresectable HCC are limited and the prognosis is very poor, meaning that this is an area of high unmet medical needs.

Following the application in Japan, Eisai plans to submit regulatory applications for Lenvima for the treatment of HCC in the United States and Europe during the first half of fiscal 2017, and in China within fiscal 2017.

Lenvima is approved as a treatment for refractory thyroid cancer in over 50 countries, including the United States, Japan, and in Europe. Additionally, Lenvima in combination with everolimus is approved for the treatment of renal cell carcinoma (RCC) in the United States, and in Europe. In Europe, Lenvima was launched under the brand name Kisplyx® for RCC.

Eisai positions oncology as a key therapeutic area, and is aiming to discover revolutionary new medicines with the potential to cure cancer. Eisai is committed to exploring the potential clinical benefits of Lenvima as it seeks to contribute further to addressing the diverse needs of, and increasing the benefits provided to, patients with cancer, their families, and healthcare providers.

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[Notes to editors]

1. About Lenvima® (generic name, lenvatinib mesylate)

Discovered and developed in-house, Lenvima is an orally administered multiple receptor tyrosine kinase (RTK) inhibitor with a novel binding mode that selectively inhibits the kinase activities of vascular endothelial growth factor (VEGF) receptors (VEGFR1, VEGFR2 and VEGFR3) and fibroblast growth factor (FGF) receptors (FGFR1, FGFR2, FGFR3 and FGFR4) in addition to other proangiogenic and oncogenic pathway-related RTKs (including the platelet-derived growth factor (PDGF) receptor PDGFRα; KIT; and RET) involved in tumor proliferation.

Currently, Eisai has obtained approval for Lenvima as a treatment for refractory thyroid cancer in 50 countries, including the United States, Japan, and in Europe. Additionally, Eisai has obtained approval for the agent in combination with everolimus in the United States, Europe, and other countries, as a treatment for renal cell carcinoma (second-line). In Europe, the agent was launched under the brand name Kisplyx® for RCC.

A Phase III study of Lenvima in separate combinations with everolimus and pembrolizumab in renal cell carcinoma (first-line) was initiated and is underway. A Phase Ib/II study to investigate the agent in combination with pembrolizumab in select solid tumors (non-small cell lung cancer, renal cell carcinoma, endometrial cancer, urothelial cancer, head and neck cancer, and melanoma) and a Phase Ib study in hepatocellular carcinoma are underway.

2. About Study 304 [1]

Study 304 is a multicenter, open-label, randomized, global Phase III study comparing the efficacy and safety of Lenvima versus sorafenib, a standard treatment for advanced hepatocellular carcinoma (HCC), as a first-line treatment for patients with unresectable HCC. In the study, 954 patients were randomized in a 1:1 ratio to receive Lenvima 12 mg (≥60 kg) or 8 mg (<60 kg) once a day, depending on baseline body weight (n= 478) or sorafenib 400 mg twice a day (n= 476). Treatment was continued until disease progression or unacceptable toxicity.

The primary endpoint of the study was Overall Survival (OS), with the goal of demonstrating non-inferiority. Other factors including Progression Free Survival (PFS), Time To Progression (TTP), Objective Response Rate (ORR) and Quality of Life (QOL) were assessed as secondary endpoints.

According to the results of the study, Lenvima (13.6 months) met the statistical criteria for non-inferiority in the primary endpoint of median OS compared to sorafenib (12.3 months). (Hazard Ratio [HR] 0.92, 95% Confidence Interval [CI] = 0.79-1.06)

Additionally, Lenvima showed statistically significant improvements in the three secondary endpoints compared to sorafenib: median PFS (Lenvima 7.4 months versus sorafenib 3.7 months, HR 0.66, 95% CI = 0.57-0.77, P<0.00001), median TTP (Lenvima 8.9 months versus sorafenib 3.7 months, HR 0.63, 95% CI = 0.53-0.73, P<0.00001) and ORR (Lenvima 24% versus sorafenib 9%, P<0.00001).

Furthermore, when overall QOL was evaluated based on the EORTC QLQ-C30 questionnaire, it was found that Lenvima helped to delay deterioration of QOL, such as pain and diarrhea, compared to sorafenib (nominal P-value < 0.05).

In this study, the five most common adverse events observed in the Lenvima arm were hypertension, diarrhea, decreased appetite, weight loss and fatigue, which is consistent with the known side-effect profile of Lenvima.

1 A. Cheng et al. “Phase 3 trial of lenvatinib vs sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma”, the 53rd Annual Meeting of the American Society of Clinical Oncology (ASCO), (June 2017), Abstract No: 4001

2 GLOBOCAN2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. http://globocan.iarc.fr/

3 Ministry of Health, Labour and Welfare, 2014 Patient Survey

4 Ministry of Health, Labour and Welfare, 2014 Population Trends Survey