No. 17-69

December 6, 2017
Eisai Co., Ltd.

EISAI SUBMITS APPLICATION FOR EXPANDED INDICATION COVERING HEPATOCELLULAR CARCINOMA FOR ANTICANCER AGENT LENVIMA® IN TAIWAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced that it has submitted an application for its in-house discovered and developed anticancer agent lenvatinib mesylate (product names: Lenvima® / Kisplyx®, product name in Taiwan: 樂衛瑪®, "Lenvima") for an additional indication for use in the treatment of hepatocellular carcinoma (HCC) in Taiwan. This application for the HCC indication for Lenvima follows the submission of respective applications in Japan and China in Asia.

Liver cancer is the second leading cause of cancer related deaths and is estimated to be responsible for approximately 750,000 deaths per year globally. Additionally, approximately 780,000 cases are newly diagnosed each year, about 80% of which occur in Asian regions.[1] Specifically, in Taiwan, there are approximately 10,000 new cases and 8,000 deaths per year.[2] HCC accounts for 85% to 90% of primary liver cancer cases. Treatment options for unresectable HCC are limited. Therefore, HCC is extremely difficult to treat, and the development of new treatments is necessary.

Eisai submitted applications for an additional indication for Lenvima for the treatment of HCC in Japan (June 2017), the United States and Europe (July 2017), and China (October 2017). In Taiwan, Eisai obtained approval for Lenvima as a treatment for patients with radioactive iodine-refractory differentiated thyroid cancer in September 2016 and in combination with everolimus as a treatment for renal cell carcinoma (second-line) in July 2017.

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 cancer patients, their families, and healthcare providers worldwide.

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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 over 50 countries, including the United States, Japan, and in Europe. Additionally, Eisai has obtained approval for the agent in combination with everolimus as a treatment for renal cell carcinoma (second-line) in over 40 countries, including the United States and in Europe. In Europe, the agent was launched under the brand name Kisplyx for renal cell carcinoma.

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

2. About the RELECT study (Study 304) [3]

This application was based on the results of the REFLECT study (Study 304), a multicenter, open-label, randomized, global Phase III trial comparing the efficacy and safety of Lenvima versus sorafenib, a standard treatment for HCC, as a first-line treatment for the patients with unresectable HCC. The REFLECT study is a multicenter, open-label, randomized, global Phase III study comparing the efficacy and safety of Lenvima versus sorafenib. 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), overall response rate (ORR) and quality of life (QOL) were assessed as secondary endpoints.

According to the results of the study, Lenvima met the statistical criteria for non-inferiority in the primary endpoint of median OS compared to sorafenib (Lenvima 13.6 months versus 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 efficacy endpoints, doubling sorafenib's median values and ratios: 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, the European Organization for Research and Treatment of Cancer's (EORTC) health-related QOL questionnaires QLQ-C30 and QLQ-HCC18 were used for the assessment. In both groups, scores decreased after the administration of the agents. However, within three categories in EORTC QLQ-C30 (role functioning, pain, diarrhea) and two categories in QLQ-HCC18 (nutrition, body image), it was found that Lenvima helped to delay deterioration of QOL compared to sorafenib (nominal P-value < 0.01).

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

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

2 Taiwan Cancer Registry: Cancer Incidence and Mortality Rates in Taiwan. http://tcr.cph.ntu.edu.tw/main.php?Page=N2

3 Cheng A 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