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Eisai Co., Ltd.

ANTICANCER AGENT LENVATINIB DESIGNATED FOR PRIORITY REVIEW AND APPROVAL BY CHINA FOOD AND DRUG ADMINISTRATION FOR HEPATOCELLULAR CARCINOMA

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced that its in-house discovered and developed anticancer agent lenvatinib mesylate (product names: Lenvima® / Kisplyx®, "lenvatinib") for use in the treatment of hepatocellular carcinoma (HCC), which was submitted for approval in China in October 2017, has been designated for Priority Review and Approval by the China Food and Drug Administration (CFDA) due to lenvatinib's significant clinical benefit compared to existing treatments.

The Priority Review and Approval procedure was implemented by the CFDA in February 2016 with the aim of accelerating research, development and launch of new medicines that have significant clinical value. Through designation for Priority Review and Approval, the period of time until approval is expected to be shortened.

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. Specifically, in China, there are approximately 395,000 new cases and 380,000 deaths per year, accounting for approximately 50% of cases worldwide.[1] HCC accounts for 85% to 90% of primary liver cancer cases. Unresectable HCC, for which treatment options are limited, is extremely difficult to treat, and the development of new treatments is necessary.

Eisai submitted applications for an additional indication for lenvatinib for the treatment of HCC in Japan (June 2017), the United States and Europe (July 2017), China (October 2017) and Taiwan (December 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 lenvatinib 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 lenvatinib mesylate (generic name, "lenvatinib", product name: Lenvima / Kisplyx)

Discovered and developed in-house, lenvatinib 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 lenvatinib as a treatment for refractory thyroid cancer in over 50 countries, including in the United States, Japan, Europe and Asia under the brand name Lenvima. 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 lenvatinib 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 was initiated in Japan.

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

The Priority Review and Approval designation in China was based on the results of a Phase III clinical study (REFLECT Study / Study 304).

The REFLECT study was a multicenter, open-label, randomized, global Phase III study comparing the efficacy and safety of lenvatinib versus sorafenib in first-line treatment of patients with unresectable HCC. In the study, 954 patients were randomized in a 1:1 ratio to receive lenvatinib 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, lenvatinib (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, lenvatinib showed statistically significant improvements in the three secondary efficacy endpoints, doubling sorafenib's median values and ratios: median PFS (lenvatinib 7.4 months versus sorafenib 3.7 months, HR 0.66, 95% CI = 0.57-0.77, P<0.00001), median TTP (lenvatinib 8.9 months versus sorafenib 3.7 months, HR 0.63, 95% CI = 0.53-0.73, P<0.00001) and ORR (lenvatinib 24% versus sorafenib 9%, P<0.00001).

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 lenvatinib.

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

[2] 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