No. 17-45

September 11, 2017
Eisai Co., Ltd.

EISAI PRESENTS NEW QUALITY OF LIFE FINDINGS IN HEPATOCELLULAR CARCINOMA PATIENTS FROM LENVATINIB VERSUS SORAFENIB STUDY IN ORAL SESSION AT ESMO CONGRESS

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") has announced that new findings indicating its in-house discovered and developed anticancer agent lenvatinib mesylate (product names: Lenvima® / Kisplyx®, "lenvatinib") delays deterioration in certain areas of health-related quality of life (QOL) in comparison to sorafenib were presented in an oral session at the European Society for Medical Oncology (ESMO) 2017 Congress[1], which took place in Madrid, Spain. These findings are based on an analysis of a Phase III study (REFLECT / Study 304)[2] for first-line treatment of unresectable Hepatocellular Carcinoma (HCC).

The oral presentation was based on the results of an analysis of responses to QOL questionnaires related to the symptoms, functioning, and overall well-being of patients enrolled in the REFLECT study. 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. While declined QOL was recorded in both the lenvatinib and sorafenib arms during the treatment. and for most domains the impact on QOL was generally similar between the two drugs, in the five domains of diarrhea (Hazard Ratio [HR] 0.53), general pain (HR 0.82), role functioning (HR 0.83), body image (HR 0.79) and nutrition (HR 0.81), lenvatinib demonstrated a delay in time to deterioration of QOL over the treatment period compared to sorafenib (nominal $p < 0.01$).

Cancer and cancer treatments greatly influence patient QOL, effecting ability to carry out roles in family life, utilize talents at work, and participate in general society. Appropriate monitoring of QOL and continuous treatment via anticancer agents allow for maximum patient benefit.

The QOL data accumulated in this study demonstrated the effects of different treatment methods on patients with HCC from a QOL perspective, and we anticipate that this information will support future decisions regarding appropriate treatment methods. Eisai remains committed to generating scientific evidence aimed at maximizing the value 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.

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

[Notes to editors]

1. About lenvatinib mesylate (product name: Lenvima / Kisplyx, "lenvatinib")

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 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 35 countries, including the United States and in Europe. In Europe, the agent was launched under the brand name Kisplyx for renal cell carcinoma.

Following the submission of applications for the hepatocellular carcinoma indication in Japan (June 2017), the United States and Europe (July 2017), Eisai also plans to submit an application in China within the latter half of fiscal 2017.

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 (non-small cell lung cancer, renal cell carcinoma, endometrial cancer, urothelial cancer, head and neck cancer, and melanoma) is underway. Additionally, a Phase Ib study of the combination in hepatocellular carcinoma is also underway.

2. About the REFLECT Study (Study 304) [1, 2]

The REFLECT study (A Multicenter, Randomized, Open-Label, Phase 3 Trial to Compare the Efficacy and Safety of Lenvatinib (E7080) Versus Sorafenib in First-Line Treatment of Subjects With Unresectable Hepatocellular Carcinoma) is a multicenter, open-label, randomized, global Phase III study comparing the efficacy and safety of lenvatinib versus sorafenib. 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), Objective 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).

Regarding QOL, when comparing clinically significant delays in time to deterioration for lenvatinib and sorafenib, an assessment based on EORTC QLQ-C30 indicated the following results (lenvatinib/sorafenib): diarrhea (4.6 months / 2.7 months, Hazard Ratio [HR] 0.53, 95% Confidence Interval [CI] = 0.449-0.630, nominal p<0.0001), pain (2.0 months / 1.8 months, HR 0.82, 95% CI = 0.697-0.953, nominal p=0.006), role function (2.0 months / 1.9 months, HR 0.83, 95% CI = 0.705-0.970, nominal p=0.0098). An assessment based on EORTC QLQ-HCC18 indicated the following results (lenvatinib/sorafenib): body image (2.8 months / 1.9 months, HR 0.79, 95% CI = 0.675-0.933, nominal p=0.0041), nutritional status (4.1 months / 2.8 months, HR 0.81, 95% CI = 0.681-0.952, nominal p=0.006).

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.

3. About Hepatocellular Carcinoma

Liver cancer is the second-leading cause of cancer deaths, estimated to be responsible for 750,000 deaths per year globally. Additionally, 780,000 cases are newly diagnosed each year. There is a large regional difference, with about 80% of new cases occurring in Asian regions, including China and Japan.[3] Hepatocellular carcinoma accounts for

85% to 90% of primary liver cancer cases. Hepatocellular carcinoma is associated with chronic liver disease, in particular cirrhosis. Major causes of cirrhosis include hepatitis B virus and hepatitis C virus. However, according to a recent investigation, non-B/non-C hepatocellular carcinoma is on the rise. Surgery is the first option for treatment, however, in many cases of recurrence after resection or when the cancer is deemed advanced at diagnosis, surgery is not applicable due to the disease having already metastasized throughout the body, and so it remains a condition with significant unmet medical needs. The only medicine approved for systemic therapy is sorafenib, making this a disease with unmet medical needs.

4. About EORTC QLQ-C30 and EORTC QLQ-HCC18

Questionnaires developed by the European Organisation for Research and Treatment of Cancer (EORTC) to assess QOL. EORTC QLQ-C30 consists of 30 items and is widely used in the field of oncology. EORTC QLQ-HCC18 consists of 18 items and is used for hepatocellular carcinoma patients.

[1] Vogel A et al. “Health-related quality of life and disease symptoms in patients with unresectable hepatocellular carcinoma treated with lenvatinib or sorafenib (REFLECT/Study 304)”, the European Society for Medical Oncology (ESMO) 2017 Congress, (September 2017), Abstract No: 6180

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

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