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Eisai Co., Ltd.

EISAI PRESENTS RESULTS OF PHASE III TRIAL OF LENVIMA® (LENVATINIB) IN UNRESECTABLE HEPATOCELLULAR CARCINOMA IN ORAL SESSION AT 20TH CSCO ANNUAL MEETING

RESULTS OF SUBPOPULATION ANALYSIS OF PATIENTS FROM GREATER CHINESE REGION (MAINLAND CHINA, HONG KONG, AND TAIWAN)

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") has announced that the results of a subpopulation analysis of patients from the Greater Chinese Region (mainland China, Hong Kong, and Taiwan) in a Phase III trial (REFLECT / Study 304)[1] of its in-house discovered and developed anticancer agent lenvatinib mesylate (product names: Lenvima® / Kisplyx®, "lenvatinib") versus sorafenib as a first-line treatment for unresectable hepatocellular carcinoma (HCC) were orally presented for the first time during the 20th Annual Meeting of the Chinese Society of Clinical Oncology (CSCO), which took place in Xiamen (Amoy) in the Fujian Province of China. Over half of the world's HCC patients come from the Greater Chinese Region.

In the subpopulation analysis, lenvatinib demonstrated efficacy based on extension of Overall Survival (OS) compared to sorafenib (nominal P = 0.026), with improvements also observed in Progression Free Survival (PFS), Time to Progression (TTP) and Objective Response Rate (ORR) (see table below). Approximately 80% of patients in the subpopulation were suffering from HCC resulting from chronic hepatitis B virus (HBV). For these patients, median OS in the lenvatinib group (123 patients) was 14.9 months, compared to 9.9 months in the sorafenib group (119 patients) (Hazard Ratio [HR] 0.72, 95% Confidence Interval [CI] = 0.53-0.97). These findings are consistent with the overall results of the Greater Chinese Region subpopulation.
HBV is considered to be a negative predictor of tumor response to existing drug therapies. However, this data supports the effect of lenvatinib in patients with HCC resulting from HBV. Since there are many patients suffering from HCC resulting from HBV in the Greater Chinese Region, lenvatinib is expected to be a new treatment option for HCC patients in this area.

Efficacy Outcome	Total Population		Patients from Greater Chinese Region	
	Lenvatinib (n = 478)	Sorafenib (n = 476)	Lenvatinib (n = 144)	Sorafenib (n = 144)
Median OS, months	13.6	12.3	15.0	10.2
HR(95% CI)	0.92 (0.79–1.06)		0.73 (0.55–0.96)	
Median PFS, months	7.4	3.7	9.2	3.6
HR(95% CI)	0.66 (0.57–0.77)		0.55 (0.42–0.72)	
Median TTP, months	8.9	3.7	11.0	3.7
HR(95% CI)	0.63 (0.53–0.73)		0.53 (0.40–0.71)	
ORR, %	24.1	9.2	21.5	8.3
Odds Ratio(95% CI)	3.13 (2.15–4.56)		3.17 (1.54–6.53)	

** CI: Confidence Interval, HR: Hazard Ratio, OR: Odds Ratio*

Additionally, lenvatinib's safety profile for the Greater Chinese Region subpopulation was consistent with previous studies.

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.[2] HCC accounts for 85% to 90% of primary liver cancer cases. Treatment options for unresectable HCC are limited and the prognosis is very poor, making this an area of high unmet medical need.

Following submissions in Japan (June 2017), the United States and Europe (July 2017), Eisai will submit a regulatory application for lenvatinib in HCC in China within the latter half of fiscal 2017. 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.

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

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) is underway. Additionally, a Phase Ib study of the agent in hepatocellular carcinoma is also underway.

2. About analysis of Greater Chinese Region subpopulation in REFLECT study

The results presented were based on a subpopulation analysis of 288 patients from the Greater Chinese Region (mainland China: 213, Hong Kong: 21, Taiwan: 54) out of the 954 HCC patients that participated in the REFLECT study. The subpopulation analysis revealed the following results: OS (lenvatinib 15.0 months versus sorafenib 10.2 months in median, HR 0.73, 95% CI = 0.55-0.96, nominal P=0.026), PFS (lenvatinib 9.2 months versus sorafenib 3.6 months in median, HR 0.55, 95% CI = 0.42-0.72, nominal P=0.00001), TTP (lenvatinib 11.0 months versus sorafenib 3.7 months in median, HR 0.53, 95% CI = 0.40-0.71, nominal P=0.00001) and ORR (lenvatinib 21.5% versus sorafenib 8.3%, odds ratio 3.17, 95% CI = 1.54-6.53, nominal P=0.0014).

Additionally, of the 288 patients in the subpopulation, approximately 80% (n = 231) were suffering from HCC resulting from HBV. An analysis of these patients revealed the following results: OS (lenvatinib [n = 123] 14.9 months versus sorafenib [n = 119] 9.9 months in median, HR 0.72, 95% CI = 0.53-0.97) and PFS (lenvatinib 9.2 months versus sorafenib 3.5 months in median, HR 0.52, 95% CI = 0.38-0.70). Additionally, lenvatinib's safety profile for the Greater Chinese Region subpopulation was consistent with previous studies.

[1] 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

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