No.15-16

March 2, 2015
Eisai Co., Ltd.

EISAI LAUNCHES ANTICANCER AGENT LENVIMA™ IN THE UNITED STATES

FIRST COUNTRY IN THE WORLD TO GAIN ACCESS TO NEW TREATMENT OPTION

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that its U.S. subsidiary Eisai Inc. has launched its in-house developed novel anticancer agent Lenvima™ (lenvatinib mesylate) as a treatment for locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer in the United States on February 26, 2015. The United States is the first country in the world where the agent has been launched.

Discovered at Eisai's Tsukuba Research Laboratories and developed in-house, Lenvima is an orally administered molecular targeted agent that selectively inhibits the activities of several different molecules including VEGFR, FGFR, RET, KIT and PDGFR. In particular, the agent simultaneously inhibits VEGFR, FGFR and also RET which are especially involved in tumor angiogenesis and proliferation of thyroid cancer. Furthermore, Lenvima has been confirmed through X-ray crystal structural analysis to demonstrate a new binding mode (Type V) to VEGFR2, and exhibits rapid and potent inhibition of kinase activity, according to kinetic analysis[1]. In a Phase III placebo controlled study (SELECT study), Lenvima demonstrated a statistically significant improvement in progression-free survival compared to placebo as well as response rate. The five most common Lenvima treatment-related adverse events of any grade were hypertension, diarrhea, fatigue or asthenia, decreased appetite, and weight loss. Lenvima was approved in the United States by the U.S. Food and Drug Administration (FDA) on February 13, 2015, based on the FDA's priority review system.

Although treatment is possible for most types of thyroid cancer, there are few treatment options available once thyroid cancer has progressed, therefore it remains a disease with significant unmet medical needs. The number of patients newly diagnosed with thyroid cancer in 2012 in the United States was estimated to be approximately 52,000.

Currently the agent is undergoing regulatory review in Japan and the EU, as well as Switzerland, South Korea, Canada, Singapore, Russia, Australia and Brazil, and Lenvima was also granted accelerated assessment in the EU. Eisai will continue to file applications seeking regulatory approval for the agent in countries around the world, and the company will market the agent in those countries where approval has been received. Furthermore, Eisai is conducting a global Phase III trial of Lenvima in hepatocellular carcinoma as well as Phase II studies of Lenvima in several other tumor types such as renal cell carcinoma and non-small cell lung cancer.

In addition to providing Lenvima as a new treatment option for thyroid cancer, Eisai is committed to exploring the potential clinical benefits of Lenvima in order to further contribute to address the diverse needs of, as well as increase the benefits provided to, patients with cancer, and their families.

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[Notes to editors]

1. About Lenvima (lenvatinib mesylate)

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 (FLT1), VEGFR2 (KDR) and VEGFR3 (FLT4)) and fibroblast growth factor (FGF) receptors (FGFR1, 2, 3 and 4) 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. In particular, the agent simultaneously inhibits VEGFR, FGFR and also RET which are especially involved in tumor angiogenesis and proliferation of thyroid cancer. Furthermore, Lenvima has been confirmed through X-ray crystal structural analysis to demonstrate a new binding mode (Type V) to VEGFR2, and exhibits rapid and potent inhibition of kinase activity, according to kinetic analysis[1]. Lenvima has been approved for the treatment of refractory thyroid cancer in the United States, and is currently undergoing regulatory review for this indication in Japan, the EU, Switzerland, South Korea, Canada, Singapore, Russia, Australia and Brazil. Meanwhile, Eisai is currently conducting clinical studies of Lenvima in several types of cancer including hepatocellular carcinoma (Phase III), renal cell carcinoma (Phase II), non-small cell lung cancer (Phase II) and endometrial cancer (Phase II). Furthermore, Lenvima was granted Orphan Drug Designation in Japan for thyroid cancer, in the United States for treatment of follicular, medullary, anaplastic, and metastatic or locally advanced papillary thyroid cancer and in Europe for follicular and papillary thyroid cancer.

2. About Lenvima's Novel Binding Mode (Type V)[1]

Kinase inhibitors are categorized into several types (Type I to Type V) depending on the binding site and the conformation of the targeted kinase in complex with them. Most of the currently approved tyrosine kinase inhibitors are either Type I or Type II, however according to X-ray crystal structural analysis, Lenvima was found to possess a new Type V binding mode of kinase inhibition that is distinct from existing compounds. In addition, Lenvima was confirmed via kinetic analysis to exhibit rapid and potent inhibition of kinase activity, and it is suggested that this may be attributed to its novel binding mode.

3. About the SELECT study

The SELECT (**S**tudy of (**E**7080) **LE**nvatinib in Differentiated **C**ancer of the **T**hyroid) study was a multicenter, randomized, double-blind, placebo-controlled Phase III study to compare the progression-free survival (PFS) of patients with radioactive iodine-refractory differentiated thyroid cancer and radiographic evidence of disease progression within the prior 13 months, treated with once-daily, oral Lenvima (24mg) versus placebo. A total of 392 patients were randomized 2:1 to either Lenvima or placebo therapy. In the study's primary endpoint of PFS, Lenvima demonstrated a statistically significant extension in PFS compared to placebo ($p<0.001$; median PFS in the Lenvima group: 18.3 months, median PFS in the placebo group: 3.6 months; Hazard Ratio (HR) 0.21 [99% CI: 0.14-0.31]). In addition, Lenvima demonstrated a statistically significant improvement in response rate (sum of complete and partial responses) compared to placebo ($p<0.001$; Lenvima: 64.8% vs placebo: 1.5%). In particular, complete response was observed in 1.5% (4 patients) of the Lenvima group and zero in the placebo group. The most common Lenvima treatment-related adverse events of any grade, which occurred in more than 40% of patients in the Lenvima group, were hypertension (67.8%), diarrhea (59.4%), fatigue or asthenia (59.0%), decreased appetite (50.2%), weight loss (46.4%) and nausea (41.0%). The study enrolled patients at over 100 sites in Europe, North and South America and Asia, including Japan, and was conducted by Eisai in collaboration with SFJ Pharma Ltd.

4. About Thyroid Cancer

Thyroid cancer refers to cancer that forms in the tissues of the thyroid gland, located at the base of the throat near the trachea. It is more common in women than in men. The most common types of thyroid cancer, papillary and follicular (including Hürthle cell), are classified as differentiated thyroid cancer and account for approximately 95% of all cases. The remaining cases are classified as either undifferentiated (3-5% of cases) or medullary carcinoma (1-2% of cases). While most differentiated thyroid cancer patients are curable with surgery and radioactive iodine treatment, there are a small percentage of patients for which these types of therapies are not suitable.

[1] Okamoto K, et al. Distinct Binding Mode of Multikinase Inhibitor Lenvatinib Revealed by Biochemical Characterization. *ACS Med. Chem. Lett.;* 2015, 6, 89–94