No.14-35

June 26, 2014
Eisai Co., Ltd.

EISAI SUBMITS FIRST MARKETING AUTHORIZATION APPLICATION FOR ANTICANCER AGENT LENVATINIB IN JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has submitted its first marketing authorization application for its novel in-house developed anticancer agent lenvatinib mesylate ("lenvatinib") for the treatment of thyroid cancer in Japan. This application for Japan marks the first submission for lenvatinib in the world following the completion of a global clinical trial.

Lenvatinib is an oral multiple receptor tyrosine kinase (RTK) inhibitor with a novel binding mode that selectively inhibits the kinase activities of various RTKs including VEGFR, FGFR, PDGFRα, KIT and RET, involved in angiogenesis and tumor proliferation.

The application submitted in Japan was based on a Phase III clinical study known as the SELECT (Study of (E7080) LEnvatinib in Differentiated Cancer of the Thyroid) trial which was a multicenter, randomized, double-blind, placebo-controlled study of lenvatinib in patients with radioiodine-refractory differentiated thyroid cancer (RR-DTC) and radiographic evidence of disease progression within the prior 13 months (patients may have received ≤1 prior VEGFR-targeted therapies).

Compared to placebo, lenvatinib achieved a statistically significant improvement (Hazard Ratio (HR) 0.21, $p<0.0001$) in progression free survival (PFS), which was the primary objective of the study. The five most common lenvatinib treatment-related adverse events (TRAEs) of any grade were hypertension, diarrhea, decreased appetite, weight loss and nausea. The most common TRAEs of Grade 3 or higher (Common Terminology Criteria for Adverse Events) included hypertension, proteinuria, weight loss, diarrhea, and decreased appetite.

The number of patients with thyroid cancer in Japan is estimated to be between 13,000 and 29,000. 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.

Lenvatinib was granted Orphan Drug Designation for thyroid cancer in Japan, Europe and the U.S. Eisai is currently preparing to submit regulatory applications for lenvatinib to health authorities in the United States (U.S.) and Europe in the second quarter of fiscal 2014. Eisai has also initiated a global Phase III trial of lenvatinib in hepatocellular carcinoma and is conducting Phase II studies of lenvatinib in several other tumor types. Eisai is committed to exploring the potential clinical benefits of lenvatinib in order to further contribute to patients with cancer, including patients with thyroid cancer, and their families.

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

[Notes to editors]

1. About Lenvatinib (E7080)

Lenvatinib, discovered and developed by Eisai, is an oral 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)), in addition to other proangiogenic and oncogenic pathway-related RTKs (including fibroblast growth factor (FGF) receptors FGFR1, 2, 3 and 4; the platelet-derived growth factor (PDGF) receptor PDGFRα; KIT; and RET) involved in tumor proliferation. This potentially makes lenvatinib a first-in-class treatment, especially given that it simultaneously inhibits the kinase activities of FGFR as well as VEGFR. It is currently under development as a potential treatment for thyroid, hepatocellular (Phase III), non-small cell lung cancer (Phase II) and other solid tumor types. Lenvatinib was granted Orphan Drug Designation (ODD) in Japan for thyroid cancer in August 2012, in the United States for the treatment of follicular, medullary, anaplastic, and metastatic or locally advanced papillary thyroid cancer in December 2012, and in Europe for follicular and papillary thyroid cancer in April 2013.

2. About the SELECT Trial

The SELECT (Study of (E7080) LEnvatinib in Differentiated Cancer of the Thyroid) trial was a multicenter, randomized, double-blind, placebo-controlled Phase III study of lenvatinib in patients with RR-DTC and radiographic evidence of disease progression within the prior 13 months (patients may have received ≤1 prior VEGFR-targeted therapies). Patients were randomized 2:1 to either receive once-daily, oral lenvatinib (24 mg) or placebo therapy. The study enrolled 392 patients in over 100 sites in Europe, North and South America and Asia (including Japan) and was conducted by Eisai in collaboration with the SFJ Pharmaceuticals Group.

Compared to placebo, lenvatinib achieved a statistically significant improvement (Hazard Ratio (HR) 0.21; 99% CI: 0.14-0.31; $p<0.0001$) in progression free survival (PFS), which was the primary objective of the study. The median PFS with lenvatinib and placebo was 18.3 months and 3.6 months respectively. Secondary endpoints included overall response rate (ORR*), overall survival (OS) and safety. The results for overall response were 64.8% in the lenvatinib group and 1.5% in the placebo group. Complete response was observed in 1.5% (4 patients) of the lenvatinib group and zero in the placebo group. The median time to response for lenvatinib was 2.0 months. Median OS has not been reached yet.

The five most common lenvatinib treatment-related adverse events (TRAEs) of any grade were hypertension (67.8%), diarrhea (59.4%), decreased appetite (50.2%), weight loss (46.4%) and nausea (41.0%). The most common TRAEs of Grade 3 or higher (Common Terminology Criteria for Adverse Events) included hypertension (41.8%), proteinuria (10.0%), weight loss (9.6%), diarrhea (8.0%), and decreased appetite (5.4%).

*Overall Response Ratio (ORR): Sum of Complete Response and Partial Response

3. 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, a small percentage of patients do not respond to therapy.

4. About the SFJ Pharmaceuticals Group

The SFJ Pharmaceuticals Group, which includes SFJ Pharma Ltd., is a Global Drug Development Company, which provides a unique co-development partnering model for some of the world's top Pharmaceutical and Biotechnology companies. SFJ uses its financial strength and core team of pharmaceutical development experts to provide highly customized partnering models in which SFJ provides the funding and clinical development supervision, necessary to obtain regulatory approval for some of the most promising drug development programs of Pharmaceutical and Biotechnology companies.