

## **LENVATINIB PHASE III RESULTS SHOW SIGNIFICANT IMPROVEMENT IN PROGRESSION-FREE SURVIVAL IN PATIENTS WITH RADIOIODINE-REFRACTORY DIFFERENTIATED THYROID CANCER**

*Phase III data for lenvatinib to be presented in a Head and Neck Cancer oral session at ASCO*

Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today the results from the Phase III SELECT trial of lenvatinib (E7080), a novel investigative anti-cancer agent for patients with progressive radioiodine-refractory differentiated thyroid cancer (RR-DTC). Progression-free survival (PFS) with lenvatinib was extended significantly compared to placebo (Hazard Ratio (HR) 0.21; 99% CI: 0.14-0.31;  $p < 0.0001$ ). The median PFS with lenvatinib and placebo were 18.3 months and 3.6 months respectively. These data will be presented at the 50th Annual Meeting of the American Society of Clinical Oncology (ASCO) in a Head and Neck Cancer oral session on Monday, June 2, and as part of the official press program on Saturday, May 31 (Abstract No. LBA6008).

Lenvatinib 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, in addition to other proangiogenic and oncogenic pathway-related RTKs involved in tumor proliferation. The SELECT (Study of E7080 "LEnvatinib" in Differentiated Cancer of the Thyroid) study confirmed a statistically significant benefit for treatment with lenvatinib on PFS in all predefined subgroups. Secondary endpoints included overall response rate (ORR\*), overall survival (OS) and safety. Rates of complete response were 1.5% (4 patients) for the lenvatinib group and zero in the placebo group. The results for partial response were 63.2% (165 patients) in the lenvatinib group and 1.5% (2 patients) in the placebo group. The median exposure duration was 13.8 months for lenvatinib and 3.9 months for placebo, and the median time to response for lenvatinib was 2.0 months. Median OS has not been reached yet.

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

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%). 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%).

Differentiated thyroid cancer is the most common form of thyroid cancer and accounts for approximately 95% of all thyroid cancers. Among these differentiated thyroid cancers, some are radioiodine-refractory (RR-DTC) and cannot easily be cured with surgery and radioactive iodine treatment, which presents a significant unmet medical need as treatment options are limited for RR-DTC.

"These positive Phase III results show the benefit of lenvatinib for this aggressive form of thyroid cancer where for which there are currently limited options for treatment," commented Professor Martin Schlumberger, Primary Investigator and M.D. Institut Gustave Roussy, University Paris Sud, Paris, France.

Eisai will submit regulatory applications for lenvatinib to health authorities in Japan, the United States (U.S.) and Europe. Lenvatinib was granted Orphan Drug Designation for thyroid cancer in Japan, Europe and the U.S. 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.

**[Please refer to the following notes on lenvatinib, the SELECT study and thyroid cancer.]**

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 PDGFR $\alpha$ ; KIT; and RET) involved in tumor proliferation. It is currently under development as a potential treatment for thyroid cancer, hepatocellular carcinoma (Phase III), non-small cell lung cancer (Phase II) and other solid tumor types. Lenvatinib was granted Orphan Drug Designation in Japan for thyroid cancer in August 2012, in the United States for 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 study**

The SELECT (**S**tudy of (**E**7080) **L**envatinib in Differentiated **C**ancer of the **T**hyroid) study was a multicenter, randomized, double-blind, placebo-controlled Phase III study to compare the PFS of patients with RR-DTC and radiographic evidence of disease progression within the prior 13 months, treated with once-daily, oral lenvatinib (24mg) versus placebo. The study enrolled 392 patients in over 100 sites in Europe, North and South America and Asia and was conducted by Eisai in collaboration with the SFJ Pharmaceuticals Group.

Participants were stratified by age ( $\leq 65$ ,  $> 65$  years), region and  $\leq 1$  prior VEGFR-targeted therapies and randomized 2:1 to either lenvatinib or placebo therapy (24mg/d, 28-d cycle). The primary endpoint was PFS assessed by independent radiologic review. The secondary endpoints of the study included overall response rate (ORR), overall survival (OS) and safety.

### **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 and usually occurs between the ages of 25 and 65. 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. There are limited treatment options for this difficult-to-treat, life-threatening and treatment-refractory form of thyroid cancer.