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Eisai Co., Ltd.

ANTICANCER AGENT "TASFYGO® TABLETS 35mg" (TASURGRATINIB SUCCINATE) APPROVED IN JAPAN FOR BILIARY TRACT CANCER WITH *FGFR2* GENE FUSIONS OR REARRANGEMENTS

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has obtained manufacturing and marketing approval for fibroblast growth factor receptor (FGFR) selective tyrosine kinase inhibitor "TASFYGO® Tablets 35mg" (tasurgratinib succinate) in Japan for the treatment of patients with unresectable biliary tract cancer with *FGFR2* gene fusions or rearrangements that progressed after cancer chemotherapy. In Japan, it has received orphan drug designation from the Ministry of Health, Labour and Welfare (MHLW), and the marketing authorization application was submitted in December 2023.

This approval is based on data such as the results of a multicenter, open-label, single-arm clinical phase II trial (Study 201) conducted by Eisai in Japan and China. Study 201 enrolled 63 patients with unresectable advanced or metastatic cholangiocarcinoma with *FGFR2* gene fusions or rearrangements previously treated with gemcitabine-based combination chemotherapy. The primary endpoint of this study was objective response rate (ORR), and secondary endpoints included safety.[1] This study achieved its primary endpoint and exceeded a prespecified tumor response threshold (15%) with statistical significance: ORR of patients treated with TASFYGO was 30.2% (90% confidence interval (CI): 20.7-41.0) as assessed by independent imaging review. Treatment-emergent adverse events (incidence of 25% or more) observed in this study were hyperphosphataemia (81.0%), palmar-plantar erythrodysaesthesia syndrome (44.4%), diarrhoea (36.5%), aspartate aminotransferase increase (31.7%), alanine aminotransferase increase (28.6%) and stomatitis (25.4%).

The estimated number of patients in Japan with biliary tract cancer is approximately 22,000[2,3] with approximately 25% of the five-year relative survival rate,[2] making it an intractable cancer with the second worst prognosis following pancreatic cancer. Since drug therapy options are limited in comparison with other cancers, it is a disease with significant unmet medical needs. *FGFR2* gene fusions or rearrangements are observed in approximately 14% of intrahepatic cholangiocarcinoma, which accounts for 15-30% of biliary tract cancers.[4] FGFR genetic aberrations such as the gene fusions are known to be deeply involved in the proliferation, survival and migration of cancer cells as well as tumor angiogenesis and drug resistance. As these genetic aberrations in FGFRs have been observed in various other types of cancers as well as biliary tract cancer, there is growing interest in FGFRs as a promising target for cancer therapy. TASFYGO is thought to show tumor growth inhibition by selectively inhibiting FGFR1, 2 and 3, and blocking those signals.[5,6] In non-clinical studies, the antitumor activity of TASFYGO was confirmed in cells expressing the *FGFR2*-fusion genes, which were identified by the National Cancer Center Japan (Headquarters: Tokyo) through large-scale genomic analysis of Japanese biliary tract cancer. The companion diagnostic test to detect *FGFR2* gene fusions or rearrangements for the use of TASFYGO in biliary tract cancer, "AmoyDx® FGFR2 Break-apart FISH Probe Kit" by Nihon Stery, Inc. (Headquarters: Tokyo) was approved in August 2024.[7]

Eisai aims to make continuous efforts to meet the diversified needs of and increase the benefits provided to patients with cancer, their families, and healthcare professionals, by delivering TASFYGO as a new treatment option for biliary tract cancer with *FGFR2* gene fusions or rearrangements.

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[Notes to editors]

1. Product Information

1) Brand name

TASFYGO® Tablets 35mg

2) Generic name

Tasurgratinib succinate

3) Indications

Unresectable biliary tract cancer with *FGFR2* gene fusions or rearrangements that progressed after cancer chemotherapy

4) Dosage and Administration

The usual adult dose of tasurgratinib is 140mg orally once daily under fasting conditions. The dose may be reduced appropriately according to the condition of the patient.

2. About "TASFYGO® Tablets 35mg" (tasurgratinib succinate, Development Code: E7090)

Discovered in-house by Eisai's Tsukuba Research Laboratories, TASFYGO is an orally available novel tyrosine kinase inhibitor that demonstrates selective inhibitory activity against fibroblast growth factor receptors (FGFR) FGFR1, FGFR2 and FGFR3. Distinct from prior known FGFR inhibitors, TASFYGO has a basic structure which lacks the dimethoxyphenyl moiety, and in a kinetic interaction analysis study, it was observed that TASFYGO demonstrates antitumor activities due to inhibition of kinase activity with a binding mode (Type V) that exhibits rapid and potent binding as well as high selectivity to FGFR. [5,6]

In non-clinical studies for biliary tract cancer, NIH/3T3 cells expressing *FGFR2-AHCYL1*, *FGFR2-KCTD1*, *FGFR2-BICC1* or *FGFR2-TXLNA* as *FGFR2*-fusion genes, provided by the National Cancer Center Japan, were used. The antitumor activity of TASFYGO against *FGFR2* gene fusion-positive cancers was confirmed in these models by evaluating its effect on anchorage-independent growth and subcutaneously transplanted tumor growth in mice.[6]

A Phase I clinical trial is underway in Japan in patients with estrogen receptor-positive and HER2-negative breast cancer.

1. Furuse J. et al. Pivotal single-arm, phase 2 trial of tasurgratinib for patients with fibroblast growth factor receptor (FGFR)-2 gene fusion-positive cholangiocarcinoma (CCA). 2024 ASCO Gastrointestinal Cancers Symposium; Abstract No. 471. https://ascopubs.org/doi/pdf/10.1200/JCO.2024.42.3_suppl.471
2. Latest statistics, Cancer Information Service, National Cancer Center, Japan. (Japanese only)
3. The 23rd Follow-up Survey Reports for Primary Liver Cancer Cases in Japan (2014-2015), 2023. (Japanese only)
4. Arai Y. et al., Fibroblast growth factor receptor 2 tyrosine kinase fusions define a unique molecular subtype of cholangiocarcinoma, *Hepatology*, 2014, 59, 1427-1434.
5. Miyano SW. et al., E7090, a Novel Selective Inhibitor of Fibroblast Growth Factor Receptors, Displays Potent Antitumor Activity and Prolongs Survival in Preclinical Models, *Molecular Cancer Therapeutics*, 2016, 15, 2630-2639.
6. Kawano S. et al., Antitumor Activity of Tasurgratinib as an Orally Available FGFR1-3 Inhibitor in Cholangiocarcinoma Models With FGFR2-fusion, *Anticancer Research*, 2024, 44, 2393-2406.
7. AmoyDx® FGFR2 Break-apart FISH Probe Kit Approved as Companion Diagnostic for Eisai's Tasurgratinib in Japan. Available at: https://www.amoydiagnostics.com/about/press-releases/245 Last accessed: September 2024.