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Taiho Pharmaceutical Co., Ltd.
Servier

Taiho and Servier Announce Positive Results from LONSURF® (trifluridine/tipiracil) Study Presented at ESMO 2018 Congress and Published in The Lancet Oncology

Taiho Pharmaceutical Co., Ltd. and Servier announced that the clinical data from the pivotal Phase III (TAGS) trial were presented at the ESMO 2018 Congress held in Munich, Germany, from October 19 to 23. The study results were simultaneously published in *The Lancet Oncology.* Based on the results, Servier filed a new application for an additional indication for gastric cancer to the European Medicines Agency (EMA) for LONSURF®.

The TAGS trial evaluates LONSURF (trifluridine/tipiracil, TAS-102) versus placebo and best supportive care in patients with heavily pretreated metastatic gastric/gastroesophageal junction (GEJ) cancers who have progressed or are intolerant to previous lines of therapy. The trial met its primary endpoint of prolonged overall survival (OS) and secondary endpoint measures of progression-free survival (PFS) consistently supported the OS results, as well as continued to demonstrate LONSURF's predictable safety and tolerability profile. *TAGS, a phase 3, randomised, double-blind study of trifluridine/tipiracil (TAS-102) versus placebo in patients with refractory metastatic gastric cancer (Abstract #LBA25)*, data were presented by Hendrik-Tobias Arkenau, MD, PhD, from the Sarah Cannon Research Institute UK at the ESMO 2018 Congress during an oral session on Sunday, October 21 at 11:10 AM CEST.

In the TAGS trial, patients treated with LONSURF showed a clinically meaningful and statistically significant improvement in OS compared with placebo, a 31 percent risk reduction of death (HR 0.69), which translated into a prolongation of median survival of 2.1 months (5.7 months for trifluridine/tipiracil versus 3.6 months for placebo). In addition, LONSURF demonstrated a statistically significant improvement in PFS and time to deterioration of ECOG performance status versus placebo, as well as a predictable and manageable safety profile consistent with that previously reported in patients with metastatic colorectal cancer (mCRC).

Taiho Pharmaceutical and Servier remain committed to making further contributions to patients and to medical practitioners engaged in the treatment of cancer.

About TAGS

The TAGS (***TA***S-102 ***G***astric ***S***tudy) trial is a Taiho-sponsored pivotal Phase III multinational, randomized, double-blind study evaluating LONSURF (trifluridine/tipiracil), also known as TAS-102, plus best supportive care (BSC) versus placebo plus BSC in patients with metastatic gastric cancer, including gastroesophageal junction cancer, refractory to standard treatments. The primary endpoint in the TAGS trial is overall survival (OS), and the main secondary endpoint measures include progression-free survival (PFS), and safety and tolerability, as well as quality of life.

The TAGS trial aimed to enroll 500 adults 18 years and older, with metastatic gastric cancer who had previously received at least two prior regimens for advanced disease. The trial enrolled 507 subjects and was conducted in Japan, the United States, the European Union, Russia, Belarus, Israel, and Turkey.

For more information on the TAGS trial, please visit www.ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT02500043). The ClinicalTrials.gov Identifier is NCT02500043.

About Gastric Cancer

Gastric cancer is the fifth most common cancer worldwide and the third most common cause of cancer-related death (after lung and liver cancer), with an estimated 723,000 deaths annually[1]. In Japan, gastric cancer is the most common cancer and the third most common cause of cancer-related death (after lung and colorectal cancer), causing around 45,000 deaths annually[2].

In recent years, the outcome for gastric cancer has improved remarkably, and survival has increased dramatically over the past 10 years. As cancer progresses, however, numerous complications can limit the usable drugs and preclude intensive chemotherapy. Prolonging survival and relieving symptoms in late-stage treatment for metastatic gastric cancer are issues for which it is thought important to increase the options for new therapeutic drugs. At present, nivolumab and irinotecan are recommended in Japan as the standard third line treatment for metastatic gastric cancer.

About LONSURF

LONSURF (trifluridine/tipiracil) is an oral anticancer drug, which utilizes the combination of trifluridine (FTD) and tipiracil (TPI), whose dual mechanism of action is designed to maintain clinical activity and differs from conventional fluoropyrimidines. FTD is an antineoplastic nucleoside analogue, which is incorporated directly into the DNA, thereby interfering with the function of DNA. The blood concentration of FTD is maintained via TPI, which is an inhibitor of the FTD-degrading enzyme, thymidine phosphorylase.

In Japan, Taiho Pharmaceutical has been marketing LONSURF for the treatment of unresectable advanced or recurrent colorectal cancer since 2014. In the United States, beginning in 2015, Taiho Oncology, Inc., a U.S. subsidiary of Taiho Pharmaceutical, began marketing the drug for the treatment of patients with mCRC who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy. In 2015, Taiho Pharmaceutical and Servier entered into an exclusive license agreement for the co-development and commercialization of LONSURF in Europe and other countries outside of the United States, Canada, Mexico and Asia. In parts of Asia outside of Japan, Taiho Pharmaceutical's business partner TYY Biopharm launched LONSURF in Taiwan in July 2018, and Jeil Pharmaceutical is preparing to bring the drug to market in South Korea.

As of October 2018, LONSURF has been approved as a treatment for mCRC in 61 countries and regions worldwide.

About Servier

Servier is an international pharmaceutical company governed by a non-profit foundation, with its headquarters in France (Suresnes). With a strong international presence in 149 countries and a turnover of 4.152 billion euros in 2017, Servier employs 21,700 people worldwide. Entirely independent, the Group reinvests 25% of its turnover (excluding generic drugs) in research and development and uses all its profits for development. Corporate growth is driven by Servier's constant search for innovation in five areas of excellence: cardiovascular, immune-inflammatory and neuropsychiatric diseases, cancer and diabetes, as well as by its activities in high-quality generic drugs. Servier also offers eHealth solutions beyond drug development.

Becoming a key player in oncology is part of Servier's long-term strategy. Currently, there are twelve molecular entities in clinical development in

this area, targeting gastro-intestinal and lung cancers and other solid tumors, as well as various leukemias and lymphomas. This portfolio of innovative cancer treatments is being developed with partners worldwide, and covers different cancer hallmarks and modalities, including cytotoxics, proapoptotics, and targeted therapies, to deliver life-changing medicines to patients.

For more information about Servier, please visit www.servier.com.

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Int J Cancer. 2015;136:E359-86.
2. "Latest Cancer Statistics," a cancer information service of the National Cancer Center Japan (in Japanese). https://ganjoho.jp/reg_stat/statistics/stat/summary.html Last accessed October 2018