

Servier and Taiho announce Phase III Trial Data Demonstrates Significant Overall Survival Benefit of LONSURF® (trifluridine and tipiracil) in Patients with Metastatic Gastric Cancer

Data from TAGS presented at ESMO 20th World Congress on Gastrointestinal Cancer 2018

Paris, France, June 21, 2018 – Servier and Taiho Pharmaceutical Co., Ltd. today announced clinical data from the pivotal Phase III trial (TAGS) for LONSURF® (trifluridine and tipiracil, TAS-102) which showed significant improvement in overall survival (OS) for the treatment of patients with refractory metastatic gastric cancer (HR=0.69 [95% IC 0.56-0.85], p=0.0003). The median overall survival in patients treated with trifluridine/tipiracil and best supportive care (BSC) was 5.7 months as compared to 3.6 months when treated with placebo and BSC, and they had a 31% risk reduction of death. At 12-months, OS rates were 21.2% in the trifluridine/tipiracil group and 13.0% in the placebo group. In addition, the risk for disease progression measured by PFS, a key secondary endpoint, was reduced by 43% (HR: 0.57).

The overall safety profile was consistent with the known safety profile of trifluridine/tipiracil in metastatic colorectal cancer (CRC), with mainly hematological adverse events reported.

“The results presented today from TAGS demonstrate the potential of trifluridine/tipiracil in this group of patients with late-stage metastatic gastric cancer”, said Professor Josep Tabernero, Head of the Medical Oncology Department, Vall d’Hebron University Hospital, Barcelona and Director of the Vall d’Hebron Institute of Oncology (VHIO). “Patients at this stage of the disease have very few remaining therapeutic options and it is important that efficacious and manageable treatments are available to expand patient’s survival.”

Ali Zeaiter, Head of Servier Oncology Clinical Development Department added, “We are pleased that trifluridine/tipiracil has shown significant benefit for patients with metastatic gastric cancer who are in need of effective treatments when there are few options remaining. We are committed to improving patients’ outcomes and to providing access to new therapeutic options. We will continue to collaborate with regulatory bodies to progress our mission to make trifluridine/tipiracil accessible to patients and medical professionals.”

Trifluridine/tipiracil is currently indicated in Europe for the treatment of adult patients with metastatic CRC who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents.¹

About TAGS

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

TAGS enrolled 507 adult patients with metastatic gastric cancer who had previously received at least two prior regimens for advanced disease. The trial was conducted in Europe, Russia, Turkey, Japan, and North America.

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

About Metastatic Gastric Cancer

Gastric cancer, also known as stomach cancer, is a disease in which malignant cells form in the lining of the stomach. It 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.ⁱⁱ Approximately 50 percent of patients with gastric cancer have advanced disease at the time of diagnosis.ⁱⁱⁱ

Standard chemotherapy regimens for advanced gastric cancer include fluoropyrimidines, platinum derivatives, and taxanes, or irinotecan. The addition of trastuzumab to chemotherapy is standard of care for patients with HER2-neu-positive advanced gastric cancer. However, after failure of first- and second-line therapies, standard third line treatments are limited.

About LONSURF[®] (trifluridine and tipiracil, TAS-102)

LONSURF[®] is an oral anticancer drug, comprising a combination of trifluridine (FTD) and tipiracil (TPI), whose dual mechanism of action is designed to maintain clinical activity. LONSURF[®] is registered in Japan, USA, European Union and in many other countries. In the European Union, LONSURF[®] is indicated for the treatment of adult patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan- based chemotherapies, anti-VEGF agents, and anti-EGFR agents.ⁱ

LONSURF[®] is recommended by the National Institute for Health and Care Excellence (NICE),^{iv} NCCN^{v,vi} and ESMO Guidelines^{vii} for the treatment of adult patients with metastatic colorectal cancer.

In June 2015, Servier and Taiho Pharmaceutical entered into an exclusive license agreement for the co-development and commercialization of LONSURF[®].

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 148 countries and a turnover of 4.152 billion euros in 2017, Servier employs 21,600 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 nine molecular entities in clinical development in this area, targeting gastric and lung cancers and other solid tumors, as well as different types of leukemia and lymphomas. This portfolio of innovative cancer treatments is being developed with partners worldwide, and covers different cancer hallmarks and modalities, including cytotoxics, proapoptotics, immune, cellular and targeted therapies, to deliver life-changing medicines to patients.

More information: www.servier.com

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About Taiho Pharmaceutical Co., Ltd. (Japan)

Taiho Pharmaceutical, a subsidiary of Otsuka Holdings Co., Ltd. (<https://www.otsuka.com/en/>), is an R&D-driven specialty pharma focusing on the three fields of oncology, allergy and immunology, and urology. Its corporate philosophy takes the form of a pledge: "We strive to improve human health and contribute to a society enriched by smiles." In the field of oncology, in particular, Taiho Pharmaceutical is known as a leading company in Japan for developing innovative medicines for the treatment of cancer, a reputation that is rapidly expanding through their extensive global R&D efforts. In areas other than oncology, as well, the company creates and markets quality products that effectively treat medical conditions and can help improve people's quality of life. Always putting customers first, Taiho Pharmaceutical also aims to offer consumer healthcare products that support people's efforts to lead fulfilling and rewarding lives.

For more information about Taiho Pharmaceutical, please visit: <https://www.taiho.co.jp/en/>.

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ⁱ European Medicines Agency. Lonsurf. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/003897/human_med_001975.jsp&mid=WC0b01ac058001d124 Last accessed May 2018.

ⁱⁱ Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>

ⁱⁱⁱ National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Gastric cancer. V.1.2018.

^{iv} NICE TA405. Available at: www.nice.org.uk/guidance/TA405 Last accessed May 2018.

^v National Comprehensive Cancer Network (NCCN). NCCN Guidelines Insights: Colon Cancer, Version 2.2018.

^{vi} National Comprehensive Cancer Network (NCCN). NCCN Guidelines for Patients: Rectal Cancer, Version 1.2017.

^{vii} ESMO consensus guidelines for the management of patients with metastatic colorectal cancer: Van Cutsem E et al. Ann Oncol. 2016;27:1386-422.