Taiho Oncology Presents Data on LONSURF® (trifluridine and tipiracil) and Futibatinib (TAS-120) at ASCO 2020 Gastrointestinal Cancers Symposium (ASCO GI)

Data include pooled safety analysis of Phase III trials of LONSURF in patients with metastatic colorectal cancer and metastatic gastric/gastroesophageal junction cancer, updates on futibatinib trials in progress

PRINCETON, N.J., January 25, 2020 – Taiho Oncology, Inc. announced today the presentation of a pooled analysis for hematologic adverse events of the global Phase III TAGS and RECOURSE trials evaluating LONSURF® (trifluridine and tipiracil) in patients with metastatic colorectal cancer (mCRC) and metastatic gastric or gastroesophageal junction cancer (mGC/GEJC), respectively. The company also presented updates on two trials in progress with futibatinib, the Phase III FOENIX-CCA3 study of futibatinib as first-line treatment for patients with advanced cholangiocarcinoma (CCA) harboring *FGFR* 2 gene rearrangements and a Phase II basket study of futibatinib in patients with advanced solid tumors harboring *FGFR* genomic aberrations.

These data were highlighted at the ASCO 2020 Gastrointestinal Cancers Symposium (ASCO GI) in San Francisco on January 23-25, 2020.

LONSURF Pooled Safety Analysis

The pooled safety analysis of the TAGS and RECOURSE trials determined that hematologic adverse events with LONSURF in subgroups of patients with mild to moderate renal impairment and mild hepatic impairment were manageable and similar to those in the overall patient population.

“Beyond the therapeutic effects of treatment and its impact on disease progression and survival in people living with cancer, the safety and tolerability of our medicines are the highest priority to us,” said Karin Blakolmer, MD, MBA, Senior Vice President and Head of Medical Affairs, Taiho Oncology, Inc. “For patients treated with LONSURF in the TAGS and RECOURSE trials, we are pleased to see that hematologic adverse events for certain subgroups were in line with what we saw in the overall patient population and, as important, were manageable. This is good news for people living with metastatic colorectal cancer and metastatic gastric cancer who are receiving treatment with LONSURF.”

Futibatinib Trials in Progress

The first trial in progress is FOENIX-CCA3, a Phase III multicenter, open-label, randomized study that will be conducted in patients with metastatic or unresectable intrahepatic CCA harboring *FGFR*2 rearrangements. Approximately 216 patients will be randomized to receive first-line therapy with 20 mg futibatinib once daily or gemcitabine and cisplatin for up to 8 cycles. Patients are to be treated until the first occurrence of

disease progression, death or other protocol specified discontinuation criteria. The primary endpoint is progression-free survival (PFS). Secondary endpoints include objective response rate (ORR) and disease control rate and safety.

The second trial in progress is a Phase II global, open-label study that will explore treatment with futibatinib in patients (n=~60) with metastatic or locally advanced solid tumors, except primary brain tumors or intrahepatic CCA, harboring *FGFR*1–4 rearrangements and with disease progression after standard treatment (Cohort A), and in patients (n=~35) with metastatic or locally advanced gastric tumors harboring *FGFR*2 amplifications and with two or more lines of prior therapy (Cohort B). Patients will receive 20 mg of futibatinib once daily in a continuous 28-day cycle until disease progression, unacceptable toxicity or other discontinuation criteria are met. The primary endpoint is independently assessed ORR. Secondary endpoints include ORR per investigator, disease control rate, duration of response, PFS, overall survival and safety.

About TAGS

The TAGS (***TA***S-102 ***G***astric ***S***tudy) trial was a Taiho-sponsored, global, pivotal Phase III, multinational, randomized, double-blind study evaluating LONSURF (trifluridine and tipiracil, FTD/TPI), 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 was overall survival (OS), and the main secondary endpoint measures included progression-free survival (PFS), safety and tolerability, as well as quality of life.

The TAGS trial enrolled 507 adult patients with metastatic gastric cancer who had previously received at least two prior regimens for advanced disease. The study was conducted in 17 countries and 110 sites around the world.

About RECOURSE

The RECOURSE trial was a global, randomized, double-blind, placebo-controlled Phase III comparison trial evaluating the efficacy and safety of orally administered LONSURF in patients with previously treated mCRC. The trial enrolled 800 patients in North America, Japan, Europe and Australia. Patients were randomized (2:1) to receive LONSURF (35 mg/m^2) or placebo, plus BSC, twice daily. The study met its primary and secondary endpoints of OS and PFS versus placebo.

About Metastatic Colorectal Cancer

Colorectal cancer is the 4th most commonly diagnosed cancer in the United States (U.S.).[1] In 2019, there were an estimated 145,600 new cases and 51,020 deaths in the U.S.[1] Approximately 22 percent of U.S. patients with colorectal cancer are diagnosed at the distant or metastasized stage.[1] Metastatic colorectal cancer (mCRC) is associated with poor prognosis with a five-year survival rate of approximately 14 percent.[1]

Over the last decade, clinical outcomes for patients with mCRC have improved considerably due to the advent of novel treatment agents, predictive biomarkers, and a more strategic approach to the delivery of systemic therapies. Currently, the median

overall survival for patients with mCRC being treated both in Phase III trials and in large observational series or registries is 30 months – more than double that of 20 years ago.[2,3,4]

About Cholangiocarcinoma
Cholangiocarcinoma (CCA), also known as bile duct cancer, is not common. About 8,000 people in the U.S. are diagnosed with CCA each year.[5] This includes both intrahepatic (inside the liver) and extrahepatic (outside the liver) cancers. CCA can occur at younger ages, but it is seen mainly in older people. The average age of people in the U.S. diagnosed with cancer of the intrahepatic bile ducts is 70, and for cancer of the extrahepatic bile ducts it is 72.[5] The chances of survival for patients with CCA depend to a large extent on its location and how advanced it is when it is found.[5]

The main treatment for CCA is surgery. Radiation therapy and chemotherapy may be used if the cancer cannot be entirely removed with surgery and in cases where the edges of the tissues removed at the operation show cancer cells (also called a positive margin). Both stage III and stage IV cancers cannot be completely removed surgically. Currently, standard treatment options are limited to radiation, palliative therapy, liver transplantation, surgery, chemotherapy and interventional radiology.[6]

About Metastatic Gastric Cancer
Gastric cancer, also known as stomach cancer, is the 15th most commonly diagnosed cancer in the U.S.[7] In 2019, there were an estimated 27,510 new cases and 11,140 deaths. Approximately 62 percent of U.S. patients with gastric cancer are diagnosed at advanced disease. Metastatic gastric cancer (mGC) is associated with a five-year survival rate of about 5 percent.[7]

In the U.S., standard chemotherapy regimens for advanced gastric cancer include fluoropyrimidines, platinum derivatives, and taxanes (with ramucirumab), or irinotecan. After failure of first- and second-line therapies, subsequent treatment options are limited.

About Gastroesophageal Junction Cancer
Gastroesophageal junction cancer is a type of cancer that begins in cells located near the gastroesophageal junction, the area where the esophagus connects to the stomach.[8] It remains a significant clinical problem that is increasing in incidence and is associated with a poor prognosis. The majority of patients present with advanced disease, and less than 50 percent undergo curative treatment.[9]

About Futibatinib (TAS-120)
Futibatinib (TAS-120) is an investigational, oral, potent, selective, and irreversible small-molecule inhibitor of FGFR1, 2, 3, and 4 being studied as a potential treatment for patients with advanced solid tumors, including cholangiocarcinoma, who were previously treated with chemotherapy or other therapies including other FGFR inhibitors. Futibatinib selectively and irreversibly binds to the ATP binding pocket of FGFR 1-4 resulting in the inhibition of FGFR-mediated signal transduction pathways,

reduced tumor cell proliferation and increased tumor cell death in tumors with *FGFR*1-4 genomic aberrations.

About LONSURF[10]
LONSURF is an oral nucleoside antitumor agent discovered and developed by Taiho Pharmaceutical Co., Ltd. LONSURF consists of a thymidine-based nucleoside analog, trifluridine, and the thymidine phosphorylase (TP) inhibitor, tipiracil, which increases trifluridine exposure by inhibiting its metabolism by TP. Trifluridine is incorporated into DNA, resulting in DNA dysfunction and inhibition of cell proliferation.

Since 2015, Taiho Pharmaceutical and Servier have been in 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.

Indications and Use
LONSURF is indicated for the treatment of adult patients with:

- metastatic colorectal cancer previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy
- metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Severe Myelosuppression:

LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of neutropenia (38%), anemia (18%), thrombocytopenia (5%), and febrile neutropenia (3%). Two patients (0.2%) died due to neutropenic infection. A total of 12% of LONSURF-treated patients received granulocyte-colony stimulating factors. Obtain complete blood counts prior to and on day 15 of each cycle of LONSURF and more frequently as clinically indicated. Withhold LONSURF for febrile neutropenia, absolute neutrophil count less than 500/mm^3, or platelets less than 50,000/mm^3. Upon recovery, resume LONSURF at a reduced dose as clinically indicated.

Embryo-Fetal Toxicity:

LONSURF can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 6 months after the final dose.

USE IN SPECIFIC POPULATIONS

Lactation: It is not known whether LONSURF or its metabolites are present in human milk. There are no data to assess the effects of LONSURF or its metabolites on the breast-fed infant or the effects on milk production. Because of the potential for serious adverse reactions in breast-fed infants, advise women not to breastfeed during treatment with LONSURF and for 1 day following the final dose.

Male Contraception: Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use condoms during treatment with LONSURF and for at least 3 months after the final dose.

Geriatric Use: Patients 65 years of age or over who received LONSURF had a higher incidence of the following compared to patients younger than 65 years: Grade 3 or 4 neutropenia (46% vs 32%), Grade 3 anemia (22% vs 16%), and Grade 3 or 4 thrombocytopenia (7% vs 4%).

Hepatic Impairment: Do not initiate LONSURF in patients with baseline moderate or severe (total bilirubin greater than 1.5 times ULN and any AST) hepatic impairment. Patients with severe hepatic impairment (total bilirubin greater than 3 times ULN and any AST) were not studied. No adjustment to the starting dose of LONSURF is recommended for patients with mild hepatic impairment.

Renal Impairment: No adjustment to the starting dosage of LONSURF is recommended in patients with mild or moderate renal impairment (CLcr of 30 to 89 mL/min). Reduce the starting dose of LONSURF for patients with severe renal impairment (CLcr of 15 to 29 mL/min) to a recommended dosage of 20 mg/m^2.

ADVERSE REACTIONS

Most Common Adverse Drug Reactions in Patients Treated With LONSURF (≥5%): The most common adverse drug reactions in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were asthenia/fatigue (52% vs 35%), nausea (48% vs 24%), decreased appetite (39% vs 29%), diarrhea (32% vs 12%), vomiting (28% vs 14%), infections (27% vs 16%), abdominal pain (21% vs 18%), pyrexia (19% vs 14%), stomatitis (8% vs 6%), dysgeusia (7% vs 2%), and alopecia (7% vs 1%). In metastatic gastric cancer or gastroesophageal junction (GEJ), the most common adverse drug reactions, respectively were, nausea (37% vs 32%), decreased appetite (34% vs 31%), vomiting (25% vs 20%), infections (23% vs 16%) and diarrhea (23% vs 14%).

Pulmonary emboli occurred more frequently in LONSURF-treated patients compared to placebo: in mCRC (2% vs 0%) and in metastatic gastric cancer and GEJ (3% vs 2%).

Interstitial lung disease (0.2%), including fatalities, has been reported in clinical studies and clinical practice settings in Asia.

Laboratory Test Abnormalities in Patients Treated With LONSURF: The most common laboratory test abnormalities in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were anemia (77% vs 33%), neutropenia (67% vs 1%), and thrombocytopenia (42% vs 8%). In metastatic gastric cancer or GEJ, the test abnormalities, respectively, were neutropenia (66% vs 4%), anemia (63% vs 38%), and thrombocytopenia (34% vs 9%).

Please see full Prescribing Information.
https://www.taihooncology.com/us/prescribing-information.pdf

About Taiho Oncology, Inc. (U.S.)
Taiho Oncology, Inc., a subsidiary of Taiho Pharmaceutical Co., Ltd. and Otsuka Holdings Co., Ltd., has established a world class clinical development organization that works urgently to develop innovative cancer treatments and has built a commercial business in the U.S. Taiho has an oral oncology pipeline consisting of both novel antimetabolic agents and selectively targeted agents. Advanced technology, dedicated researchers, and state of the art facilities are helping us to define the way the world treats cancer. It's our work; it's our passion; it's our legacy.

For more information about Taiho Oncology, please visit:
https://www.taihooncology.com/us/

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