TAIHO ONCOLOGY

National Comprehensive Cancer Network® Provides Updates on Use of LONSURF® (trifluridine and tipiracil) in NCCN Drugs and Biologics Compendium® for Colon Cancer and Rectal Cancer

PRINCETON, N.J., February 4, 2021 – Taiho Oncology, Inc. today announced that updated guidelines on the use of LONSURF® (trifluridine and tipiracil) have been included in the latest National Comprehensive Cancer Network® Drugs and Biologics Compendium (NCCN Compendium®) for Colon Cancer (Version 2.2021 - January 21, 2021) and Rectal Cancer (Version 1.2021 - December 22, 2020). Specifically, the "Colon Cancer"[a] and "Rectal Cancer"[b] sections of the NCCN Compendium, now include a Category 2A recommendation for trifluridine and tipiracil as subsequent therapy, either single agent or in combination with bevacizumab (per NCCN, an FDA-approved biosimilar is an appropriate substitute for bevacizumab), as treatment options for patients who have progressed through all available regimens.[1]

LONSURF is approved by the U.S. Food and Drug Administration (FDA) 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.[2]

The updated NCCN Compendium and Clinical Practice Guidelines are available at www.nccn.org.

About Metastatic Colorectal Cancer

Colorectal cancer is the fourth most commonly diagnosed cancer in the U.S.[3] In 2020, there were an estimated 147,950 new cases and 53,200 deaths in the U.S.[3] Approximately 22 percent of U.S. patients with colorectal cancer are diagnosed at the distant or metastasized stage.[3] Metastatic colorectal cancer (mCRC) is associated with poor prognosis with a five-year survival rate of approximately 14.3 percent.[3]

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.[4,5,6]

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[a] Regorafenib or trifluridine + tipiracil with or without bevacizumab are treatment options for patients who have progressed through all available regimens.

[b] Regorafenib or trifluridine + tipiracil with or without bevacizumab are treatment options for patients who have progressed through all available regimens.

About LONSURF[2]

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 Oncology has an oral oncology pipeline consisting of 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

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

For more information about Otsuka Holdings Co., Ltd., please visit:
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[1] National Comprehensive Cancer Network® Drugs and Biologics Compendium (NCCN Compendium®) for Colon Cancer (Version 2.2021 - January 21, 2021) and Rectal Cancer (Version 1.2021 - December 22, 2020). Available at http://www.nccn.org/. Accessed February 2021.

[2] LONSURF [US prescribing information]; Princeton, NJ: Taiho Oncology, Inc.; December 2019.

[3] National Cancer Institute Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Colon and Rectum Cancer. https://seer.cancer.gov/statfacts/html/colorect.html. Accessed January 2021.

[4] Brenner H, Kloor M, Pox CP. Colorectal cancer. *Lancet.* 2014;383(9927):1490-1502.

[5] Price TJ, Segelov E, Burge M, et al. Current opinion on optimal systemic treatment for metastatic colorectal cancer: outcome of the ACTG/AGITG expert meeting ECCO 2013. *Expert review of anticancer therapy*. 2014;14(12):1477-1493.

[6] Van Cutsem E, Cervantes A, Adam R, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. *Ann Oncol*. 2016;27(8):1386-1422.