LONSURF® (FTD/TPI) tablets dosing guide

Starting dose based on trial results in mCRC and metastatic gastric or GEJ cancer[1-5]*

Dosing guidelines[1]

Indicated dosage	35 mg/m^2 twice daily[ab]
Active treatment days	Days 1 to 5 and 8 to 12 of each 28-day treatment cycle
BSA-based calculation	• Round up to the nearest 5 mg increment • Do not exceed 80 mg/dose[a] or 160 mg/day[a]
Administration	• Taken orally twice daily with food • No restriction on food type
Missed or vomited doses	The patient should not make up for these doses
Handling	LONSURF is a cytotoxic drug. Follow applicable special handling and disposal procedures

[a]Based on the trifluridine component.
[b]In patients with severe renal impairment (CLcr of 15 to 29 mL/min), the recommended dosage is 20 mg/m^2.

28-day dosing schedule[1]

Week 1	Twice daily for 5 days with food	2 days rest
Week 2	Twice daily for 5 days with food	2 days rest
Week 3	Rest	
Week 4	Rest	

- Obtain complete blood cell counts prior to and on day 15 of each cycle

2 tablet strengths for personalized dosing[1]

15 mg trifluridine/
6.14 mg tipiracil tablet

20 mg trifluridine/
8.19 mg tipiracil tablet

Tablets shown at actual size.

BSA=body surface area; CLcr=creatinine clearance; FTD/TPI=trifluridine/tipiracil; GEJ=gastroesophageal junction; mCRC=metastatic colorectal cancer; OS=overall survival; PFS=progression-free survival; RECOURSE=Refractory Colorectal Cancer Study (Study 1); TAGS=TAS-102 Gastric Study.

*In the RECOURSE study: median OS (95% CI): 7.2 months (6.6-7.8) for LONSURF vs 5.2 months (4.6-5.9) for placebo (HR=0.69 [95% CI: 0.59-0.81]; $P<0.0001$). Number (%) of deaths was 364 (68) for LONSURF and 210 (79) for placebo. RECOURSE was a randomized, double-blind, placebo-controlled phase 3 study. Treatment arms were LONSURF plus best supportive care (BSC) vs placebo plus BSC. All patients were 18 years of age, had Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and had received at least 2 prior regimens of standard chemotherapy and were refractory to or were failing all of the following within 3 months: fluoropyrimidine, irinotecan, and oxaliplatin; an anti-VEGF biological therapy; and an anti-EGFR therapy (if *RAS* wild type). The primary efficacy endpoint was OS. Key secondary endpoints included PFS and safety and tolerability.[1-4]

In the TAGS study, median OS (95% CI): 5.7 months (4.8-6.2) for LONSURF vs 3.6 months (3.1-4.1) for placebo (HR=6.9 [95% CI: 0.56-0.85]; $P=0.0006$). TAGS was a multinational, randomized, double-blind, placebo-controlled, phase 3 trial. Treatment arms were LONSURF plus BSC vs placebo plus BSC. All patients were 18 years of age (≥20 years of age in Japan), had histologically confirmed, nonresectable, metastatic gastric or GEJ adenocarcinoma, had ECOG performance status of 0 or 1, had previously received 2 regimens of standard chemotherapy, and were refractory to or intolerant of their last previous therapy. Previous regimens must have included a fluoropyrimidine, a platinum agent, a taxane or irinotecan, or both, and, if HER2-positive, an anti-HER2 therapy. Adjuvant chemotherapy could be counted as 1 prior regimen in patients who had recurrence during or within 6 months of completion of the adjuvant chemotherapy. Both patients and investigators were masked to treatment allocation. The primary endpoint was OS. Key secondary endpoints included PFS and safety and tolerability.[1,3,5]

For assistance in calculating your patient's LONSURF starting dose, use the dosage calculator online at LONSURFhcp.com/calculator

Please see Important Safety Information on back cover and full Prescribing Information in pocket.

Lonsurf®
(trifluridine and tipiracil) tablets

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.

LONSURF is indicated for the treatment of adult patients with 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 in pocket.

References: 1. LONSURF [package insert]. Princeton, NJ: Taiho Oncology, Inc.; 2019. **2.** Van Cutsem E, Mayer RJ, Laurent S, et al; for the RECOURSE Study Group. The subgroups of the phase III RECOURSE trial of trifluridine/tipiracil (TAS-102) versus placebo with best supportive care in patients with metastatic colorectal cancer. *Eur J Cancer.* 2018;90:63-72. **3.** Data on file. Taiho Oncology, Inc., Princeton, NJ. **4.** Mayer RJ, Van Cutsem E, Falcone A, et al; for the RECOURSE Study Group. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. *N Engl J Med.* 2015;372(20):1909-1919. **5.** Shitara K, Doi T, Dvorkin M, et al. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2018;19(11):1437-1448.

TAIHO ONCOLOGY

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