mCRC efficacy and safety information inside

Lonsurf® (trifluridine and tipiracil) tablets

A balanced choice for today and tomorrow

See the proven results your adult patients with previously treated mCRC may experience

LONSURF® tablets—FTD/TPI—is indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) 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 (GEJ) 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.

Study design

RECOURSE was an international, randomized, double-blind, placebo-controlled phase 3 study.* All patients were ≥18 years of age, had histologically confirmed mCRC, had ECOG PS of 0 or 1, and had received ≥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, if *RAS* wild type, an anti-EGFR therapy. The primary endpoint was OS. Key secondary endpoints included PFS and safety and tolerability.

Treatment arms were LONSURF plus BSC vs placebo plus BSC.[1]
RECOURSE=**Re**fractory **Co**lo**re**ctal Cancer **S**tudy.

Selected 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.

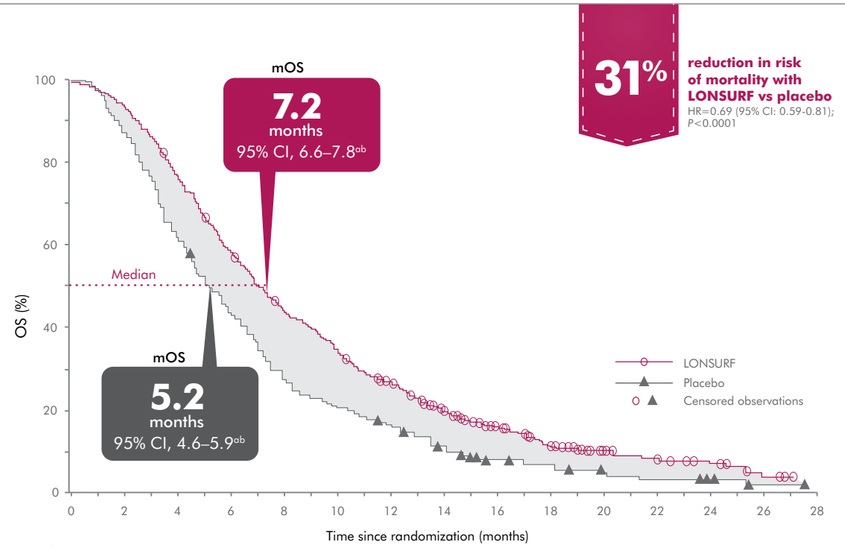
Please see additional Important Safety Information throughout and full Prescribing Information in pocket.

Help extend survival with LONSURF[1,3,4]

In the final survival analysis, LONSURF® tablets—FTD/TPI—maintained a **2-month** benefit in mOS vs placebo[3]

- The final survival analysis was conducted 9 months after the initial RECOURSE analysis

Final survival analysis: OS in patients with previously treated mCRC[3]



n at risk:

LONSURF	534	521	499	459	406	355	308	267	231	212	180	156	137	117	95	74	59	49	38	29	20	17	14	12	10	7	4	1	0
Placebo	266	259	232	198	163	137	114	94	71	62	56	51	43	36	27	21	16	15	14	10	8	7	6	6	4	3	1	1	0

OS was defined as the time (in months) from randomization until death.
mOS=median OS.

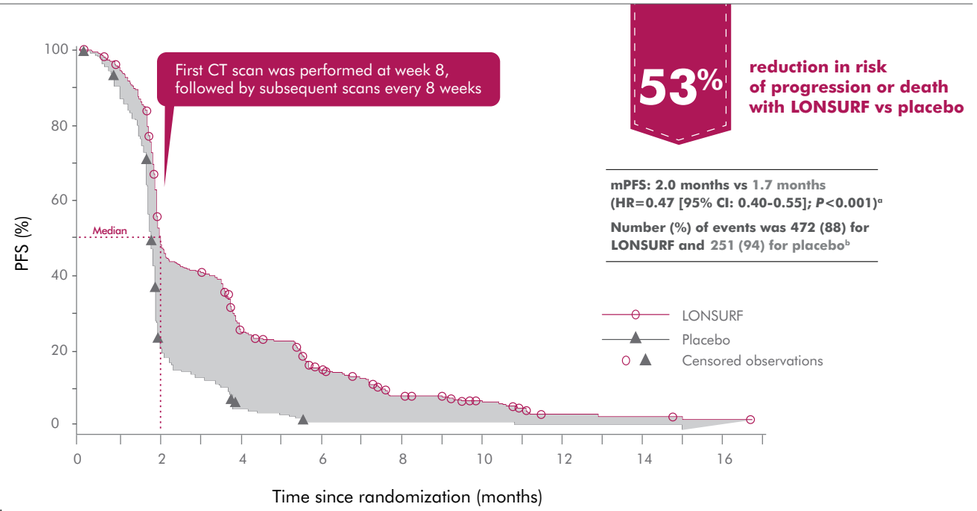
[a]Kaplan-Meier estimates.
[b]Methodology of Brookmeyer and Crowley.

6-month survival with LONSURF was **58%** vs 44% for placebo[4]

12-month survival with LONSURF was **27%** vs 18% for placebo[4]

Help prolong PFS[1,2,4]

Secondary endpoint: reduction in risk of progression or death in patients with previously treated mCRC



n at risk:

LONSURF	534	488	238	205	121	107	66	52	30	26	18	11	5	4	4	2	2	0
Placebo	266	227	51	32	10	7	2	2	2	2	2	1	1	1	1	0		

PFS was defined as the time (in months) from randomization to the first radiologic confirmation of disease progression or death from any cause.

mPFS=median PFS.
[a]Kaplan-Meier estimates.
[b]Prespecified study endpoint.

Selected Important Safety Information

WARNINGS AND PRECAUTIONS

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.

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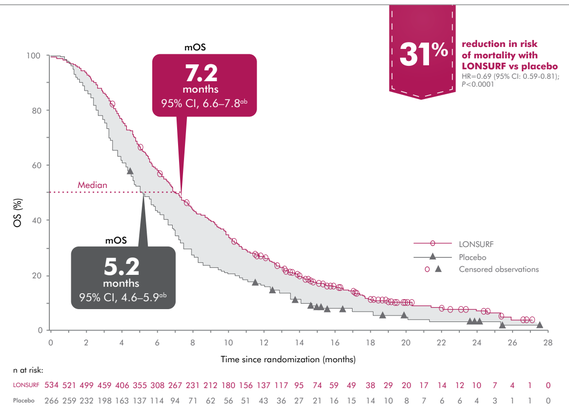

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Consider an option with a demonstrated safety profile

AEs* in ≥5% of patients treated with LONSURF® tablets—FTD/TPI—and occurring more commonly (>2%) than in patients taking placebo[1]

	LONSURF + BSC (n=533), %		Placebo + BSC (n=265), %	
	All Gr	Gr 3-4[a]	All Gr	Gr 3-4[a]
General				
Asthenia/fatigue	52	7	35	9
Pyrexia	19	1	14	<1
Gastrointestinal				
Nausea	48	2	24	1
Diarrhea	32	3	12	<1
Vomiting	28	2	14	<1
Abdominal pain	21	2	18	4
Stomatitis	8	<1	6	0
Metabolism and nutrition				
Decreased appetite	39	4	29	5
Infections[b]	27	6	16	5
Nervous system				
Dysgeusia	7	0	2	0
Skin and subcutaneous tissue				
Alopecia	7	0	1	0

[a]No Grade 4 definition for nausea, abdominal pain, or fatigue in National Cancer Institute Common Terminology.
[b]Incidence reflects 64 preferred terms in the Infections and Infestations system organ class.
*Treatment arms were LONSURF plus BSC vs placebo plus BSC.

An established safety profile can help manage expectations

Hematologic abnormalities[1,2]

	LONSURF + BSC (n=533), %		Placebo + BSC (n=265), %	
	All Gr[a]	Gr 3-4	All Gr[a]	Gr 3-4
Anemia[b]	77	18	33	3
Neutropenia	67	38	1	0
Thrombocytopenia	42	5	8	<1
Febrile neutropenia	4	4	0	0

[a]Worst Grade ≥1 grade higher than baseline, with percentages based on number of patients with postbaseline samples, which may be <533 (LONSURF) or 265 (placebo).
[b]One Grade 4 anemia adverse reaction based on clinical criteria was reported.

- In the RECOURSE trial, hand-foot syndrome was reported in 2% of patients in the LONSURF group, and 2% of patients in the placebo group. No Grade 3/4 was reported[2]
- **69%** of patients who developed neutropenia (any grade) during the RECOURSE trial developed it during cycle 1[4]
- In the RECOURSE trial, **9.4%** of patients in the LONSURF group received granulocyte-colony stimulating factor (G-CSF)[2]

3.6% of patients taking LONSURF discontinued treatment due to an AE in RECOURSE trial[1]

Selected Important Safety Information

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.

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Lonsurf® (trifluridine and tipiracil) tablets

Learn more at **LONSURFhcp.com/mcrc-treatment/efficacy**

Important Safety Information (cont'd)

USE IN SPECIFIC POPULATIONS (cont'd)

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%).

LONSURF is available in 2 strengths[1]

Tablets:

- 15 mg trifluridine/6.14 mg tipiracil
- 20 mg trifluridine/8.19 mg tipiracil

Please see full Prescribing Information in pocket.

References: 1. LONSURF [package insert]. Princeton, NJ: Taiho Oncology, Inc.; 2019. **2.** 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. **3.** 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. **4.** Data on file. Taiho Oncology, Inc., Princeton, NJ.