# Because tomorrow is still unwritten

## Start their next treatment line with LONSURF® (FTD/TPI) tablets, a balanced treatment option that offers extended survival with an established safety profile[1]

LONSURF 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.

FTD/TPI=trifluridine/tipiracil.

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.

### Selected Important Safety Information

**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 on page 10 and full Prescribing Information in pocket.**

**Find contact information for your LONSURF representative on back cover**

Lonsurf®
(trifluridine and tipiracil) tablets

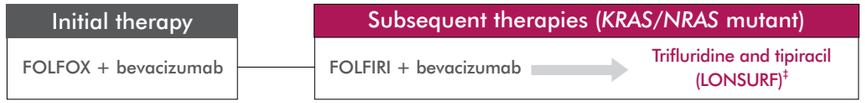
*Actor portrayal.*

*For patients with previously treated mCRC*

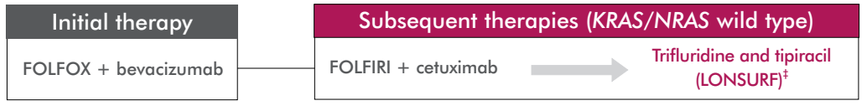
# Trifluridine and tipiracil (LONSURF) is recommended as a third-line or subsequent treatment option* for mCRC per the National Comprehensive Cancer Network® (NCCN®)[2,3]

Trifluridine and tipiracil (LONSURF®) tablets are a Category 2A† recommended option for third-line or subsequent therapy* for mCRC in the *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer* and the *NCCN Guidelines® for Rectal Cancer*.

Sample*§ treatment algorithm for third-line use (*KRAS/NRAS* mutant)




Sample*§ treatment algorithm for third-line use (*KRAS/NRAS* wild type)




*Trifluridine + tipiracil is a treatment option for patients who have progressed through all available regimens.
†Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
‡These treatment algorithms are examples only; other treatment options are recommended in the NCCN Guidelines.
§These example patients are BRAF WT, pMMR/MSS, not HER2-amplified, and NTRK gene fusion–negative.



## Selected Important Safety Information

**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.

 **Please see additional Important Safety Information on page 10 and full Prescribing Information in pocket.**



# Consider LONSURF in your treatment plan

**LONSURF was studied under TAS-102 in the RECOURSE trial[1,4]**

- Patients, ranging from 27 to 82 years of age, had ≥2 lines of prior treatment and had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- 98% of patients in the LONSURF arm were refractory to or were failing on a fluoropyrimidine-based therapy in a prior treatment regimen

## LONSURF patient considerations[1,5]

- Has already received multiple types of treatment, including fluorouracil (5-FU)
- Wants to maintain their ECOG performance status
- Is a candidate for oral chemotherapy

RECOURSE was an international, randomized, double-blind, placebo-controlled phase 3 trial.‡ All patients were ≥18 years of age, had 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, if *RAS* wild type, an anti-EGFR therapy, which could have included adjuvant chemotherapy if a tumor had recurred within 6 months after the last administration of this therapy. The primary efficacy endpoint was overall survival (OS). Key secondary endpoints included progression-free survival (PFS) and safety and tolerability.[1,4,6]

Patients were randomized 2:1 to receive either LONSURF 35 mg/m$^2$ (n=534) or placebo (n=266) twice daily after meals for 5 days a week with 2 days rest for 2 weeks, followed by a 14-day rest, repeated every 4 weeks plus best supportive care (BSC).[1]

All patients were followed for survival at scheduled 8-week intervals with computed tomography (CT) scans until 12 months after the first dose of study medication from the last patient randomized. After the end of treatment, all patients were followed for survival at scheduled 8-week time intervals until death.[6]

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

Lonsurf® (trifluridine and tipiracil) tablets

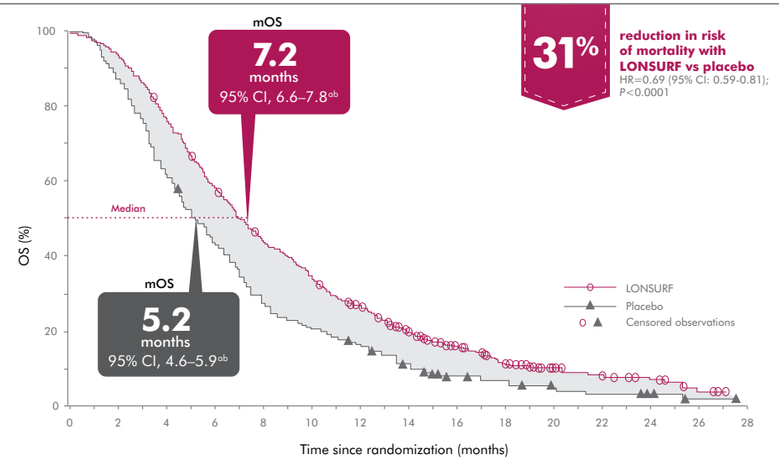
*For patients with previously treated mCRC*

# Help extend survival with LONSURF[1,6,7]

**In the final survival analysis, LONSURF® (FTD/TPI) tablets maintained a 2-month benefit in mOS vs placebo**

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

Final survival analysis: OS in patients with previously treated mCRC




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.

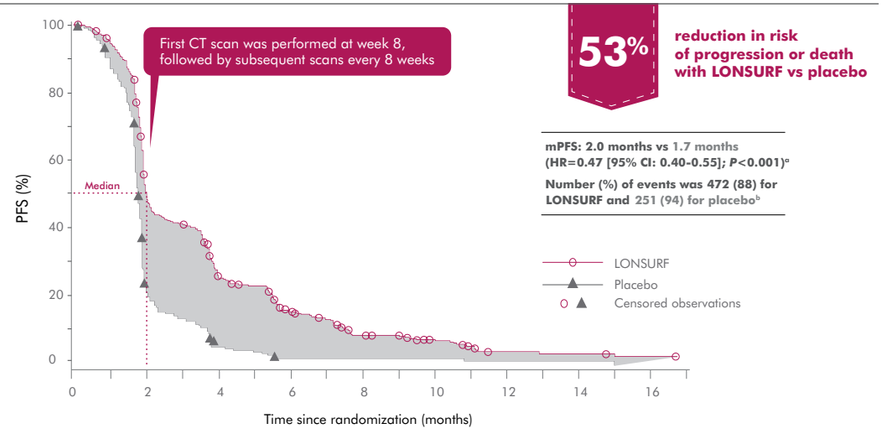
6-month survival with LONSURF was **58%** vs 44% for placebo

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



# Help prolong PFS[1,4,6]

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

**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.

**Please see additional Important Safety Information on page 10 and full Prescribing Information in pocket.**

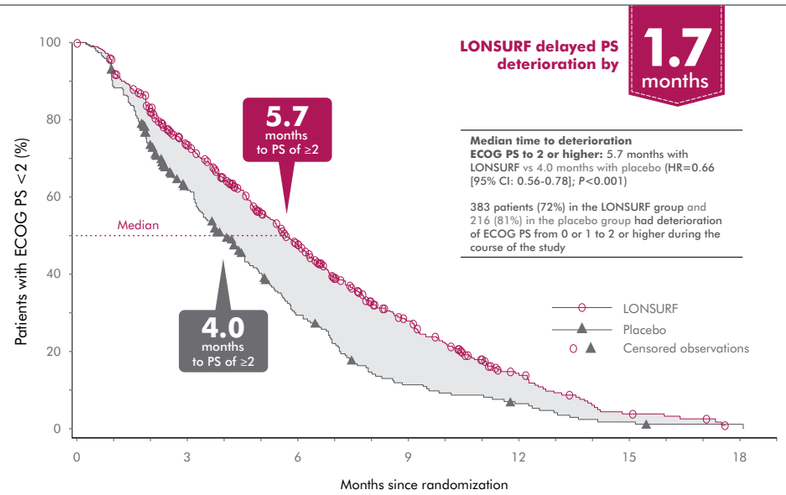
Lonsurf® (trifluridine and tipiracil) tablets

*For patients with previously treated mCRC*

# Give patients the potential to maintain performance status[4]

**LONSURF® (FTD/TPI) tablets provided a statistically significant reduction in risk of deterioration to ECOG performance status ≥2 (34%)***

Median time to deterioration of ECOG PS to ≥2, based on a post hoc analysis




n at risk:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| LONSURF | 534 | 352 | 188 | 84 | 28 | 7 | 0 |
| Placebo | 266 | 134 | 57 | 21 | 11 | 3 | 1 |

PS=performance status.
Time to worsening of PS was prespecified in the statistical analysis plan before the data were unblinded.

***ECOG PS scale:** Grade 0=fully active and able to carry on all predisease performance without restriction; Grade 1=restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature; Grade 2=ambulatory and capable of all self-care, but unable to carry out any work activities; up and about >50% of waking hours; Grade 3=capable of only limited self-care and confined to a bed or chair >50% of waking hours; Grade 4=completely disabled and cannot carry on any self-care and totally confined to a bed or chair.[8]



# Preserve the potential for additional active treatment

- **42%** of patients in the LONSURF arm went on to receive subsequent therapy at the end of the trial[4]
- Approximately **16%** of these patients received a regimen containing regorafenib[6]

## Selected Important Safety Information

**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.

**Please see additional Important Safety Information on page 10 and full Prescribing Information in pocket.**

Lonsurf® (trifluridine and tipiracil) tablets

*For patients with previously treated mCRC*

# Consider an option with a demonstrated safety profile

AEs* in ≥5% of patients treated with LONSURF® (FTD/TPI) tablets 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.

AE=adverse event.

*Treatment arms were LONSURF plus BSC vs placebo plus BSC.



# An established safety profile can help manage expectations

Hematologic abnormalities[1,4]

| | 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[4]
- **69%** of patients who developed neutropenia (any grade) during the RECOURSE trial developed it during cycle 1[6]
- In the RECOURSE trial, **9.4%** of patients in the LONSURF group received granulocyte-colony stimulating factor (G-CSF)[4]

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

**Please see Important Safety Information on page 10 and full Prescribing Information in pocket.**

Lonsurf® (trifluridine and tipiracil) tablets

## 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.

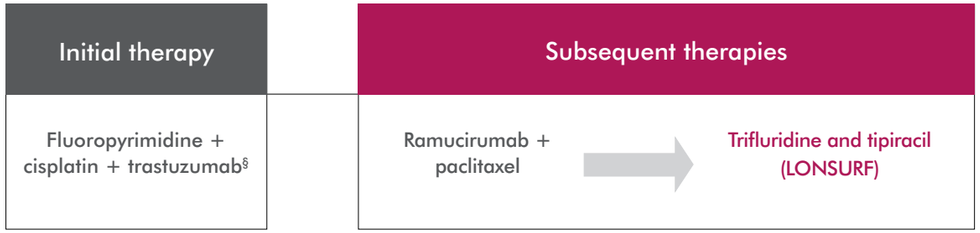
**Laboratory Test Abnormalities in Patients Treated With LONSURF:** The most common laboratory test abnormalities in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were anemia (77% vs 33%), neutropenia (67% vs 1%), and thrombocytopenia (42% vs 8%). In metastatic gastric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



# Trifluridine and tipiracil (LONSURF) is recommended as a third-line or subsequent treatment option for metastatic gastric cancer or esophagogastric junction adenocarcinoma per the NCCN[9,10]

Trifluridine and tipiracil (LONSURF®) tablets are a preferred regimen and a Category 1* recommended option for third-line or subsequent therapy for gastric cancer in the *NCCN Guidelines for Gastric Cancer* and for esophagogastric junction adenocarcinoma in the *NCCN Guidelines for Esophageal and Esophagogastric Junction Cancers*.

**Sample†‡ treatment algorithm (third-line use)**




*Category 1: Based upon high-level evidence, there is uniform NCCN consensus that intervention is appropriate.
†This suggested treatment plan is for patients with an ECOG performance status ≤2.
‡These treatment algorithms are examples only; other treatment options are recommended in the NCCN Guidelines.
§For HER2 overexpressing metastatic adenocarcinoma.



Lonsurf® (trifluridine and tipiracil) tablets

*For patients with previously treated metastatic gastric or GEJ cancer*

# LONSURF® (FTD/TPI) tablets were studied in the TAGS trial[1,11]

TAGS was a multinational, randomized, double-blind, placebo-controlled, phase 3 trial
**(N=507)**

## Inclusion criteria

- Patients with histologically confirmed, nonresectable metastatic gastric cancer or GEJ adenocarcinoma
- Patients received postoperative adjuvant chemotherapy and radiotherapy, or pre- and postoperative adjuvant chemotherapy if they had recurrence during or within 6 months of completion of the adjuvant chemotherapy
- ≥2 prior regimens, including:
  - Fluoropyrimidine
  - Platinum agent
  - Taxane and/or irinotecan
  - HER2 therapy in patients with HER2-positive tumors
- Refractory to/intolerant of last prior therapy
- ECOG performance status of 0 or 1
- Age ≥18 years (≥20 years in Japan)

**2:1 Randomization**

**LONSURF + BSC (n=337)**
35 mg/m$^2$/dose (up to 80 mg/dose) twice daily after meals on days 1-5 and 8-12 of each 28-day cycle

**Placebo + BSC (n=170)**
Twice daily after meals on days 1-5 and 8-12 of each 28-day cycle

## Endpoints

- Primary:
  - OS
- Key secondary:
  - PFS
  - Safety and tolerability
- Other secondary:
  - Overall response rate
  - DCR
  - Time to ECOG performance status ≥2

After the first dose of study medication, all patients were followed for progression at scheduled 8-week intervals with CT until progression. After the end of treatment, all patients were followed up for survival every 4 weeks until death or loss to follow-up, or until the targeted number of events (deaths) was met.

HER2=human epidermal growth factor receptor 2; TAGS=**TA**S-102 **G**astric **S**tudy.

## Selected Important Safety Information

**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%).



# Consider LONSURF as part of your treatment plan

Baseline characteristics of patients in the TAGS trial[6,11]

| | LONSURF (n=337) | Placebo (n=170) |
|---|---|---|
| **Age, years** | | |
| <65 | 54% | 56% |
| **Sex** | | |
| Male | 75% | 69% |
| Female | 25% | 31% |
| **ECOG performance status** | | |
| 0 | 36% | 40% |
| 1 | 64% | 60% |
| **HER2 status** | | |
| Positive | 20% | 16% |
| Negative | 61% | 62% |
| **Number of prior therapies** | | |
| 2 prior therapies | 37% | 38% |
| 3 prior therapies | 40% | 35% |
| ≥4 prior therapies | 23% | 27% |
| **Primary site** | | |
| Gastric | 71% | 71% |
| GEJ | 29% | 28% |
| **Number of metastatic sites** | | |
| 1-2 | 46% | 42% |
| ≥3 | 54% | 58% |
| **Prior systemic treatments** | | |
| Platinum therapy | 100% | 100% |
| Fluoropyrimidine-based therapy | >99%[a] | 100% |
| Taxane therapy[b] | 92% | 87% |
| Irinotecan therapy[b] | 54% | 58% |
| Ramucirumab therapy | 34% | 32% |
| Anti-HER2 therapy | 18% | 14% |
| Immunotherapy (anti–PD-1/PD-L1) | 7% | 4% |
| **Prior treatments** | | |
| Gastrectomy | 44% | 44% |

[a]1 patient did not receive a fluoropyrimidine.
[b]All patients received irinotecan or taxane or both.

**Please see additional Important Safety Information on page 10 and full Prescribing Information in pocket.**

Lonsurf® (trifluridine and tipiracil) tablets

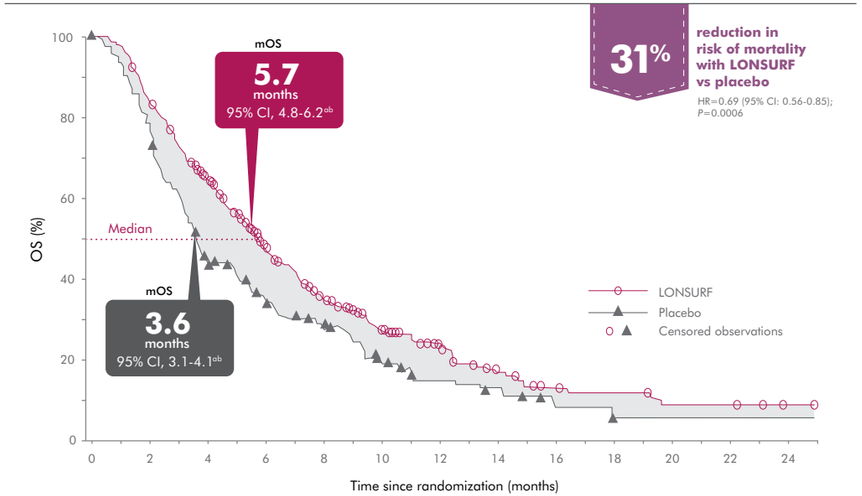
*For patients with previously treated metastatic gastric or GEJ cancer*

# Help extend survival with LONSURF[1,6,11]

**LONSURF® (FTD/TPI) tablets provided a statistically significant reduction in risk of mortality (31%)**

- In the TAGS study, LONSURF maintained a **2.1-month** benefit vs placebo

OS in patients with previously treated metastatic gastric or GEJ cancer




n at risk:

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LONSURF | 337 | 328 | 282 | 240 | 201 | 161 | 124 | 102 | 80 | 66 | 51 | 40 | 31 | 22 | 16 | 11 | 9 | 7 | 7 | 7 | 4 | 4 | 4 | 3 | 1 | 0 |
| Placebo | 170 | 158 | 131 | 101 | 71 | 60 | 47 | 40 | 34 | 29 | 17 | 12 | 10 | 9 | 7 | 5 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 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 **47%** vs 33% for placebo

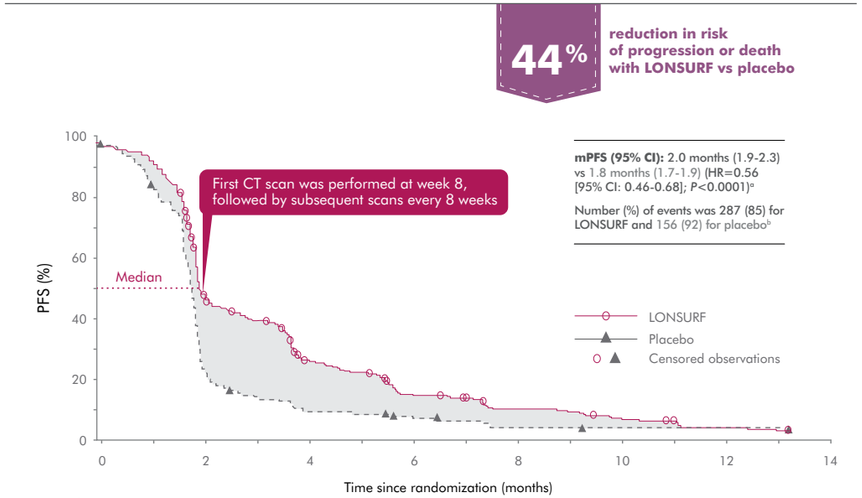
12-month survival with LONSURF was **21%** vs 13% for placebo



# Help prolong PFS[1,6,11]

**LONSURF provided a statistically significant reduction in the risk of progression or death (44%)**

Secondary endpoint: reduction in the risk of progression or death in patients with previously treated metastatic gastric or GEJ cancer




n at risk:

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| LONSURF | 337 | 314 | 154 | 122 | 72 | 60 | 37 | 32 | 20 | 18 | 12 | 9 | 4 | 2 | 0 |
| Placebo | 170 | 145 | 41 | 21 | 12 | 11 | 8 | 5 | 2 | 2 | 1 | 1 | 1 | 1 | 0 |

PFS was defined as the time (in months) from randomization to the first radiologic confirmation of disease events from any cause.
mPFS=median PFS.
[a]Kaplan-Meier estimates.
[b]Prespecified study endpoint.

## Selected Important Safety Information

**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.

**Please see additional Important Safety Information on page 10 and full Prescribing Information in pocket.**

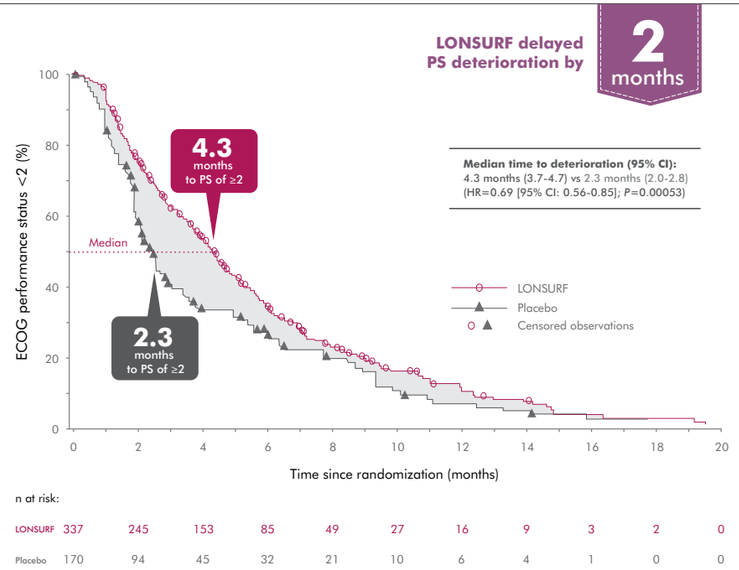
Lonsurf® (trifluridine and tipiracil) tablets

*For patients with previously treated metastatic gastric or GEJ cancer*

# Help delay time to performance status deterioration[11]

**LONSURF® (FTD/TPI) tablets provided a statistically significant reduction in risk of deterioration to ECOG performance status ≥2 (31%)***

Other secondary endpoint: median time to deterioration of ECOG performance status to ≥2




***ECOG PS scale**: Grade 0=fully active and able to carry on all predisease performance without restriction; Grade 1=restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature; Grade 2=ambulatory and capable of all self-care, but unable to carry out any work activities; up and about >50% of waking hours; Grade 3=capable of only limited self-care and confined to a bed or chair >50% of waking hours; Grade 4=completely disabled and cannot carry on any self-care and totally confined to a bed or chair.[8]



# Safety results seen in patients with metastatic gastric cancer were consistent with those in patients with mCRC[1,11]

AEs* in ≥5% of patients treated with LONSURF and occurring more commonly (>2%) than in patients taking placebo

| | LONSURF + BSC (n=335), % | | Placebo + BSC (n=168), % | |
|---|---|---|---|---|
| | All Gr | Gr 3-4[a] | All Gr | Gr 3-4[a] |
| **Gastrointestinal** | | | | |
| Nausea | 37 | 3 | 32 | 3 |
| Vomiting | 25 | 4 | 20 | 2 |
| Diarrhea | 23 | 3 | 14 | 2 |
| **Metabolism and nutrition** | | | | |
| Decreased appetite | 34 | 9 | 31 | 7 |
| Infections[b] | 23 | 5 | 16 | 5 |

[a]No Grade 4 definition for nausea or fatigue in National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.
[b]Incidence reflects 46 preferred terms in the Infections and Infestations system organ class.
*Treatment arms were LONSURF plus BSC vs placebo plus BSC.

Hematologic abnormalities

| | LONSURF + BSC (n=335), % | | Placebo + BSC (n=168), % | |
|---|---|---|---|---|
| | All Gr[a] | Gr 3-4 | All Gr[a] | Gr 3-4 |
| **Neutropenia** | 66 | 38 | 4 | 0 |
| **Anemia[b]** | 63 | 19 | 38 | 7 |
| **Thrombocytopenia** | 34 | 6 | 9 | 0 |
| **Febrile neutropenia** | 2 | 2 | 0 | 0 |

[a]Worst Grade ≥1 grade higher than baseline, with percent based on number of patients with postbaseline samples which may be <335 (LONSURF) or 168 (placebo).
[b]Anemia: No Grade 4 definition in CTCAE, v4.03.

- In the TAGS trial,16% of patients in the LONSURF group received granulocyte-colony stimulating factor (G-CSF)

**13%** of patients receiving LONSURF discontinued treatment due to an AE (any grade) vs 17% of patients receiving placebo

**Please see Important Safety Information on page 10 and full Prescribing Information in pocket.**

Lonsurf® (trifluridine and tipiracil) tablets

# Dosing with LONSURF[1]

## Dosing guidelines for LONSURF® (FTD/TPI) tablets

| | |
|---|---|
| Indicated dosage | 35 mg/m² 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<br>• Do not exceed 80 mg/dose[a] or 160 mg/day[a] |
| Administration | • Taken orally twice daily with food<br>• 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/m².

## 4-week dosing cycle (28 days)

| | | |
|---|---|---|
| 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

15 mg trifluridine/ 6.14 mg tipiracil tablet

20 mg trifluridine/ 8.19 mg tipiracil tablet

Tablets shown at actual size.

CLcr=creatinine clearance.



# Calculate your patients' appropriate dosage[1]

## Dose according to body surface area (BSA)

| BSA (m²) | Morning dose | Evening dose | Total daily dose (mg) |
|---|---|---|---|
| < 1.07 | 1 x 20 mg | 1 x 20 mg | 70 |
| 1.07 - 1.22 | 2 x 20 mg | 2 x 20 mg | 80 |
| 1.23 - 1.37 | 3 x 15 mg | 3 x 15 mg | 90 |
| 1.38 - 1.52 | 2 x 15 mg + 1 x 20 mg | 2 x 15 mg + 1 x 20 mg | 100 |
| 1.53 - 1.68 | 1 x 15 mg + 2 x 20 mg | 1 x 15 mg + 2 x 20 mg | 110 |
| 1.69 - 1.83 | 3 x 20 mg | 3 x 20 mg | 120 |
| 1.84 - 1.98 | 3 x 15 mg + 1 x 20 mg | 3 x 15 mg + 1 x 20 mg | 130 |
| 1.99 - 2.14 | 2 x 15 mg + 2 x 20 mg | 2 x 15 mg + 2 x 20 mg | 140 |
| 2.15 - 2.29 | 1 x 15 mg + 3 x 20 mg | 1 x 15 mg + 3 x 20 mg | 150 |
| ≥ 2.30 | 4 x 20 mg | 4 x 20 mg | 160 |
| **For patients with severe renal impairment (20 mg/m² twice daily)** | | | |
| < 1.14 | 1 x 20 mg | 1 x 20 mg | 40 |
| 1.14 - 1.34 | 1 x 20 mg | 1 x 10 mg | 50[a] |
| 1.35 - 1.59 | 1 x 10 mg | 1 x 10 mg | 60 |
| 1.60 - 1.94 | 1 x 10 mg + 1 x 20 mg | 1 x 10 mg + 1 x 20 mg | 70 |
| 1.95 - 2.09 | 2 x 20 mg | 2 x 20 mg | 80 |
| 2.10 - 2.34 | 3 x 10 mg | 3 x 10 mg | 90 |
| ≥ 2.35 | 2 x 10 mg + 1 x 20 mg | 2 x 10 mg + 1 x 20 mg | 100 |
| **For patients with severe renal impairment (15 mg/m² twice daily)** | | | |
| < 1.15 | 1 x 15 mg | 1 x 15 mg | 30 |
| 1.15 - 1.49 | 1 x 20 mg | 1 x 20 mg | 40 |
| 1.50 - 1.84 | 1 x 20 mg | 1 x 10 mg | 50[a] |
| 1.85 - 2.09 | 1 x 10 mg | 1 x 10 mg | 60 |
| 2.10 - 2.34 | 1 x 10 mg + 1 x 20 mg | 1 x 10 mg + 1 x 20 mg | 70 |
| ≥ 2.35 | 2 x 20 mg | 2 x 20 mg | 80 |

Tablets shown are not actual size. Actual tablet size is 7 mm for 15-mg dose and 8 mm for 20-mg dose.
[a]For a total daily dose of 50 mg, instruct patients to take 1 x 20-mg tablet in the morning and 2 x 15-mg tablets in the evening.

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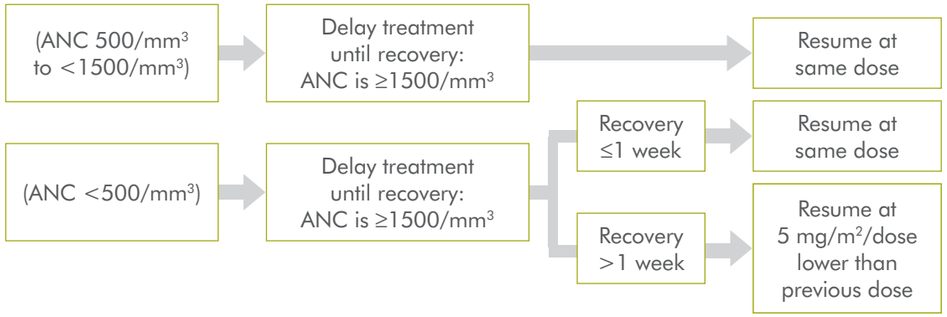
Lonsurf® (trifluridine and tipiracil) tablets

AE management at cycle start

# For AEs already present at cycle start, DELAY FIRST and then reinitiate as recommended[1,12]

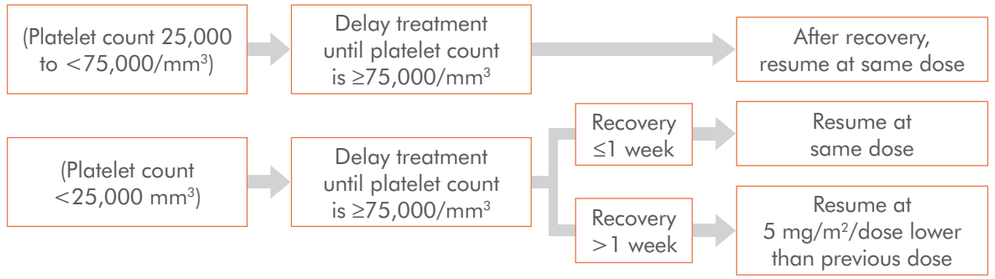
## Neutropenia




## Febrile neutropenia


In patients with **severe renal impairment** who are unable to tolerate a dose of 20 mg/m² twice daily, reduce dose to 15 mg/m² twice daily

## Thrombocytopenia




## Non-hematologic AEs[a]


[a]For all Grade 3 or 4 AEs except for Grade 3 nausea and/or vomiting controlled by antiemetic therapy or Grade 3 diarrhea responsive to antidiarrheal medication.[3]

ANC=absolute neutrophil count.



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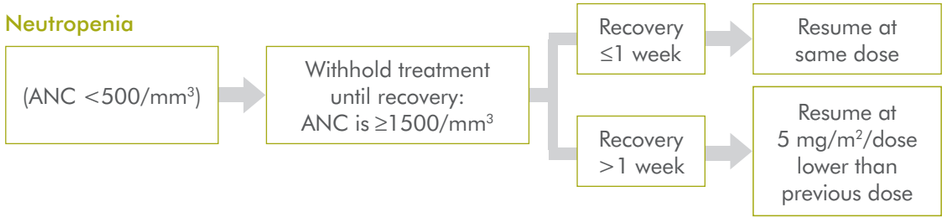
Lonsurf® (trifluridine and tipiracil) tablets

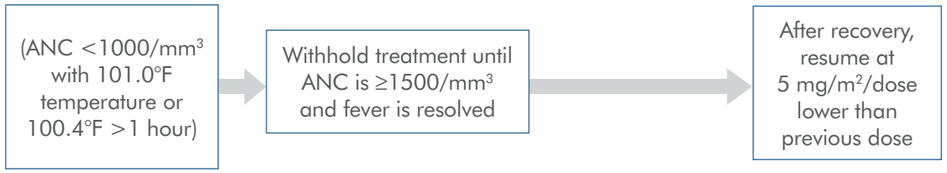
AE management during cycle

# For AEs occurring during active treatment, WITHHOLD FIRST and then reinitiate as recommended[1,12]*

## Neutropenia

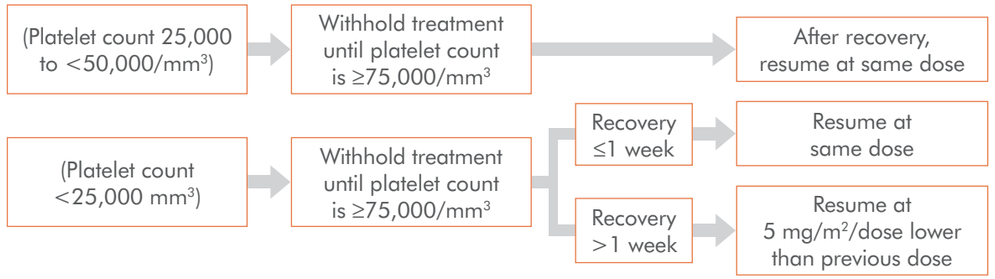



## Febrile neutropenia




With LONSURF® (FTD/TPI) tablets, **delay or withhold treatment** before determining whether a subsequent dose reduction is needed

## Thrombocytopenia




## Non-hematologic AEs[a]


[a]For all Grade 3 or 4 AEs except for Grade 3 nausea and/or vomiting controlled by antiemetic therapy or Grade 3 diarrhea responsive to antidiarrheal medication.

*Active treatment occurs on days 1 through 5 and days 8 through 12 of each 28-day cycle.

A maximum of 3 dose reductions are permitted. Permanently discontinue LONSURF in patients who are unable to tolerate a dose of 20 mg/m² orally twice daily. Do not escalate LONSURF dosage after it has been reduced.



**Please see Important Safety Information on page 10 and full Prescribing Information in pocket.**

Lonsurf® (trifluridine and tipiracil) tablets

# Tell your patients about Taiho Oncology Patient Support™: Eligible patients may pay $0

TAIHO ONCOLOGY PATIENT SUPPORT™

*A partner in your cancer care.*

We know getting patients access to LONSURF® (FTD/TPI) tablets is a critical step in their treatment. We strive to make this process as simple as possible.

## Co-pay support

- Eligible, privately insured patients can receive a Taiho Oncology Patient Support™ Co-pay Card for a $0 co-pay, no matter the dosage strength. This card can help with out-of-pocket expenses for LONSURF, to make access easier for patients. Register your patient at **TaihoOncologyCopay.com**

Making access easier for patients.

***$0 CO-PAY****

**No matter the dosage strength.*

## Access and reimbursement support

- Benefit investigations to determine and report patients' insurance coverage for LONSURF
- Prior authorizations to meet payer requirements
- Claims appeals assistance if coverage is denied



# Taiho Oncology Patient Support™: Designed to simplify patient access to LONSURF

## Specialty pharmacy (SP) prescription coordination

- Prescription triage
- Coordination with the in-network SP, self-dispensing practice, or hospital retail pharmacy
- Claims appeals assistance if coverage is denied

## Patient Assistance Program

- We research financial assistance for patients with no or insufficient prescription insurance coverage or insufficient resources to pay for LONSURF. Eligible patients may receive LONSURF at no cost based on assistance, financial, and medical criteria

## Alternate funding support

- We refer eligible, publicly insured patients to nonprofit foundations for co-pay assistance

## Personalized nurse support for treatment plan adherence upon request

- Our treatment plan adherence services are available as needed to support patient care, including refill reminders. We will quickly investigate each patient's LONSURF coverage, and help them get access to the LONSURF treatment they have been prescribed

For more information, visit **TaihoPatientSupport.com** or call **1-844-TAIHO-4U** (1-844-824-4648)

**Please see Important Safety Information on page 10 and full Prescribing Information in pocket.**

Lonsurf® (trifluridine and tipiracil) tablets

# Taiho Oncology provides useful tools for educating patients and caregivers to help them stay on track while taking LONSURF

## HCP Resources*

**Dosage Sheet**

Reminds patients of their active treatment days and their morning and evening doses. Print a Dosage Sheet and then fill it out with your patient.

**LONSURF Overview Brochure**

Provides an overview of the safety and efficacy data demonstrated by LONSURF® (FTD/TPI) tablets, the importance of dosing for proven results, and resources developed to support your patients. Available in English only.

**LONSURF Dosage Calculator**

Calculate your patients' personalized dosage and create personalized dosing calendars at **LONSURFhcp.com/calculator**.


**References: 1.** LONSURF [package insert]. Princeton, NJ: Taiho Oncology, Inc.; 2019. **2.** Referenced with permission from the *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer V.2.2021.* © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed January 27, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **3.** Referenced with permission from the *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Rectal Cancer V.1.2021.* © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed January 4, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **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.** Van Cutsem E, Falcone A, Garcia-Carbonero R, et al. Proxies of quality of life in metastatic colorectal cancer: analyses in the RECOURSE trial. *ESMO Open.* 2017;2(5):e000261. **6.** Data on file. Taiho Oncology, Inc., Princeton, NJ. **7.** 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. **8.** Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.* 1982;5(6):649-655. **9.** Referenced with permission from the *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer V.1.2021.* © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed February 22, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **10.** Referenced with permission from the *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers V.1.2021.* © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed February 22, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **11.** 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. **12.** National Cancer Institute. *Common Terminology Criteria for Adverse Events v4.03 (CTCAE).* Bethesda, MD: US Department of Health and Human Services; 2010. NIH publication 09-5410.



## Patient Resources†

**LONSURF Patient Starter Kit**

Contains useful resources and tools to help your patients start and stay on LONSURF, including:

- **Patient Brochure**
  Offers information on how LONSURF can help, how it is taken, tips on managing common side effects, and services that may be able to help with medication costs
- **Caregiver Brochure**
  Provides an overview of LONSURF and how it is taken, useful tips that may help manage common side effects, and strategies to help caregivers take care of themselves and their loved one
- **Thermometer**
  Encourages patients to check for fever while taking LONSURF
- **LONSURF Pillboxes**
  Designed to help patients organize their LONSURF tablets
- **Treatment Calendar**
  Allows patients to track their dosing habits and record side effects or questions

*Available at LONSURFhcp.com
†Available at LONSURF.com

TO REQUEST A **PATIENT STARTER KIT**, YOU CAN:

CALL **1-844-TAIHO-4U** (1-844-824-4648) or VISIT **TaihoPatientSupport.com** or ASK a representative

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Lonsurf® (trifluridine and tipiracil) tablets

# A balanced choice for today and tomorrow

for patients with previously treated

## mCRC

**LONSURF® (FTD/TPI) tablets provided a statistically significant reduction in risk of mortality (31%)[7]**

- mOS (95% CI): 7.2 months (6.6-7.8) vs 5.2 months (4.6-5.9) for placebo (HR=0.69 [95% CI: 0.59-0.81]; *P*<0.0001)*

**LONSURF helped prolong PFS[1,4,6]**

- mPFS (95% CI): 2.0 months vs 1.7 months for placebo (HR=0.47 [95% CI: 0.40-0.55]; *P*<0.001)*
- Number (%) of events was 472 (88) for LONSURF and 251 (94) for placebo†

for patients with previously treated

## metastatic gastric or GEJ cancer

**LONSURF provided a statistically significant reduction in risk of mortality (31%)[1,6,11]**

- mOS (95% CI): 5.7 months (4.8-6.2) vs 3.6 months (3.1-4.1) for placebo (HR=0.69 [95% CI: 0.56-0.85]; *P*=0.0006)*‡

**LONSURF helped prolong PFS[1,6]**

- mPFS (95% CI): 2.0 months (1.9-2.3) vs 1.8 months (1.7-1.9) for placebo (HR=0.56 [95% CI: 0.46-0.68]; *P*<0.0001)*
- Number (%) of events was 287 (85) for LONSURF and 156 (92) for placebo†

**LONSURF has a consistent safety profile across both indications[1,4,11]**

- Safety results in patients with metastatic gastric cancer were similar to those seen in patients with mCRC

*Kaplan-Meier estimates.
†Prespecified study endpoint.
‡Methodology of Brookmeyer and Crowley.

### Selected Important Safety Information

**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 on page 10 and full Prescribing Information in pocket.**

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Lonsurf® (trifluridine and tipiracil) tablets