

# BC Cancer Protocol Summary for Third- or Later-Line Therapy of Advanced Gastroesophageal Carcinoma Using Trifluridine-Tipiracil

**Protocol Code**

**GIGAVTRFT**

**Tumour Group**

*Gastrointestinal*

**Contact Physician**

*GI Systemic Therapy*

## ELIGIBILITY:

- Metastatic gastric cancer or adenocarcinoma of gastroesophageal junction
- ECOG 0-1
- At least two prior lines of therapy including fluoropyrimidine, platinum, taxane or irinotecan and HER2 directed therapy if positive – if relapse within 6 months of peri-operative or pre-operative treatment that will count as a line of therapy.

## EXCLUSIONS:

- Patients with CNS metastases

## TESTS:

- Baseline: CBC, differential, platelets, sodium, potassium, creatinine, urea, bilirubin, ALT, alkaline phosphatase, LDH, dipstick urine protein. Optional : CEA, 19-9
- Prior to each cycle: CBC, differential, platelets, sodium, potassium, creatinine, urea, bilirubin, ALT, alkaline phosphatase, LDH.
- Day 15 : CBC, differential and platelets
- If clinically indicated: dipstick urine protein, CEA, 19-9

## PREMEDICATIONS:

- Antiemetic protocol for low emetogenic chemotherapy protocols (see SCNAUSEA)

## TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
trifluridine-tipiracil	35* mg/m <sup>2</sup> BID on days 1-5 and days 8-12	PO

\* based on the trifluridine component; up to maximum of 80 mg/dose.

Repeat every 28 days (one cycle) until progression or unacceptable toxicity.

**Dose Levels:**

Starting dose	Dose level -1	Dose level -2	Dose level -3
35 mg/m <sup>2</sup>	30 mg/m <sup>2</sup>	25 mg/m <sup>2</sup>	20 mg/m <sup>2</sup>

- Dose escalation is not permitted after it has been dose reduced.
- Round dose to nearest 5 mg.
- A total daily dose of 50 mg should be taken as 1 x 20 mg tablet in the morning and 2 x 15 mg tablets in the evening.

**Suggested Dose Dispensing Table:**

Dose (mg)* (given BID)	Number of Tablets per Dose	
	15 mg Tablet	20 mg Tablet
35	1	1
40	0	2
45	3	0
50	2	1
55	1	2
60	0	3
65	3	1
70	2	2
75	1	3
80	0	4

\* based on the trifluridine component; up to maximum of 80 mg/dose.

15 mg tablet = trifluridine-tipiracil 15 mg-6.14 mg tablet

20 mg tablet = trifluridine-tipiracil 20 mg-8.19 mg tablet

**DOSE MODIFICATIONS:****1. Hematological:****Table 1: Dose interruption and resumption criteria for hematological toxicities**

Parameter	Interruption Criteria	Resumption Criteria*
ANC	Less than 0.5 x 10 <sup>9</sup> /L	Greater than or equal to 1.5 x 10 <sup>9</sup> /L
Platelets	Less than 50 x 10 <sup>9</sup> /L	Greater than or equal to 75 x 10 <sup>9</sup> /L

\* Resumption Criteria applied to the start of the next cycle

Toxicity				Dose
Grade	ANC (x10 <sup>9</sup> /L)		Platelets (x10 <sup>9</sup> /L)	
1	greater than or equal to 1.5	or	greater than or equal to 75	100%
2	1.0 to less than 1.5	or	50 to less than 75	100%
3	0.5 to less than 1.0	or	25 to less than 50	100%
4	less than 0.5	or	less than 25	Delay until resolution to Grade 1 or baseline and then reduce one dose level. (minimum dose of 15 mg/m <sup>2</sup> twice daily in severe renal impairment)
Febrile neutropenia				Delay until resolution to Grade 1 or baseline and then reduce one dose level. (minimum dose of 15 mg/m <sup>2</sup> twice daily in severe renal impairment)

Dose escalation is not permitted after it has been dose reduced.

## 2. Non-Hematological toxicity:

CTCAE*- Grade	Dose
Grade 3 or 4 toxicity (except for Grade 3 nausea and/or vomiting controlled by antiemetic therapy or diarrhea responsive to antidiarrheal therapy)	Hold dose until symptoms resolve to Grade 1 or baseline and then reduce one dose level. (minimum dose of 15 mg/m <sup>2</sup> twice daily in severe renal impairment)
Interstitial Lung Disease/Pneumonitis (treatment-related)	Hold dose and investigate. If confirmed, discontinue treatment permanently.

\* CTCAE : Common terminology criteria for adverse events.

Dose escalation is not permitted after it has been dose reduced.

### 3. Renal dysfunction:

Creatinine Clearance (mL/min)	Dosage recommendation
Greater than or equal to 60	No adjustment required
30 to 59	No adjustment required; monitor for increased hematologic toxicity
15 to 29	Recommend dose reduction to 20** mg/m <sup>2</sup> (based on the trifluridine component); monitor for increased hematologic toxicity
Less than 15	no information found

\*\* Reduce dose to 15 mg/m<sup>2</sup> twice daily in patients with severe renal impairment who are unable to tolerate a dose of 20 mg/m<sup>2</sup> twice daily. Dose escalation should not be considered after the dose has been reduced. Permanently discontinue in patients who are unable to tolerate a dose of 15 mg/m<sup>2</sup> twice daily.

$$\text{calculated creatinine clearance} = \frac{N^* \times (140 - \text{Age}) \times \text{weight in kg}}{\text{serum creatinine in micromol/L}}$$

For males N=1.23;

For females N=1.04

### 4. Hepatic dysfunction:

No dose adjustment is required in patients with mild hepatic impairment (Child-Pugh class A). No information found in patients with moderate or severe hepatic impairment (Child-Pugh class B or C). Higher incidence of grade 3 or 4 hyperbilirubinemia was observed in patients with baseline moderate hepatic impairment.

### PRECAUTIONS:

1. Patients who received **prior radiotherapy** may be at higher risk of hematological and myelosuppression related adverse reaction including febrile neutropenia.
2. **Myelosuppression** can be severe and life-threatening. Fatal events related to neutropenic infection, sepsis, or septic shock have occurred. Monitor closely for signs of infection and treat as indicated.
3. **Pregnancy/Lactation:** Trifluridine-tipiracil is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least 6 months after the last dose. Women using a hormonal contraceptive must also use a barrier contraceptive, as it is unknown whether trifluridine-tipiracil may reduce the effectiveness of hormonal contraceptives. Breastfeeding is not recommended during treatment and for one day following the final dose.

**Call the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair [Dr. Theresa Chan](#) at (604) 930-2098 with any problems or questions regarding this treatment program.**

### References:

1. Shitara, K, Doi, T, 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: 1437–1448.
2. LONSURF® Product monograph, Taiho Pharma Canada Inc. Submission Control No. 235999, Date of revision: 29 Oct 2020.