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

Protocol Code	*GIGAVTT*
Tumour Group	*Gastrointestinal*
Contact Physician	*GI Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Metastatic gastric cancer or adenocarcinoma of gastroesophageal junction,
- 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

Patients should have:

- ECOG 0 to 1

EXCLUSIONS:

Patients must not have:

- CNS metastases

TESTS:

- Baseline: CBC & Diff, creatinine, ALT, alkaline phosphatase, total bilirubin, albumin
- Baseline if clinically indicated: CEA, 19-9, GGT, ECG, dipstick or laboratory urinalysis for protein
- Prior to each cycle: CBC & Diff, creatinine, total bilirubin, ALT
- Day 15 of Cycle 1, and in subsequent cycles if dose modification: CBC & Diff
- If clinically indicated: CEA, CA 19-9, alkaline phosphatase, albumin, GGT, sodium, potassium, ECG, dipstick or laboratory urinalysis for protein, 24 hour urine for protein if occurrence of proteinuria dipstick urinalysis shows 2+ or 3+ or laboratory urinalysis for protein is greater than or equal to 1 g/L

PREMEDICATIONS:

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

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
trifluridine-tipiracil	35* mg/m^2 BID on Days 1 to 5 and Days 8 to 12	PO

* based on the trifluridine component; up to maximum of 80 mg/dose. Round dose to nearest 5 mg

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

Suggested Dose Dispensing Table:

Dose (mg)* (given BID)	Number of Tablets per Dose	
	15 mg Tablet	20 mg Tablet
20	0	1
25	**See note, below	
30	2	0
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

** 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

DOSE MODIFICATIONS:

Dose Levels (based on the trifluridine component):

Starting dose	Dose level -1	Dose level -2	Dose level -3
35 mg/m^2	30 mg/m^2	25 mg/m^2	20 mg/m^2

- Do not re-escalate dose after it has been reduced
- Round dose to nearest 5 mg

1. **Hematological:**

Day 1:

ANC (x 10^9/L)		Platelets (x 10^9/L)	Management
Greater than or equal to 1.5	and	Greater than or equal to 75	100%
1.0 to less than 1.5	or	50 to less than 75	▪ Delay until ANC 1.5 and platelets 75, then ▪ Restart at previous dose
0.5 to less than 1.0	or	25 to less than 50	
Less than 0.5	or	Less than 25	▪ Delay until ANC 1.5 and platelets 75, then ▪ Reduce one dose level when restarting*
Febrile neutropenia			

* do not re-escalate dose after it has been reduced

Day 15 (if ordered)**:**

- Doses are complete on Day 12 of each cycle. Day 15 labs provide guidance regarding dose for next cycle

ANC (x 10^9/L)		**Platelets (x 10^9/L)**	**Dose for Next Cycle**
Greater than or equal to 1.5	and	Greater than or equal to 75	100% of previous cycle dose
1.0 to less than 1.5	or	50 to less than 75	
0.5 to less than 1.0	or	25 to less than 50	
Less than 0.5	or	Less than 25	Reduce next cycle dose by one dose level*

* do not re-escalate dose after it has been reduced

2. Renal dysfunction:

- Monitor for increased hematologic toxicity if Creatinine Clearance (CrCl) less than 60 mL/min

CrCl (mL/min)	**Dose** (Twice Daily on Days 1 to 5 and 8 to 12)
Greater than or equal to 60	100%
30 to 59	100%
15 to 29	20* mg/m^2
Less than 15	Do not use. No information found.

* based on trifluridine component. Reduce dose to 15 mg/m^2 in patients with severe renal impairment who are unable to tolerate a dose of 20 mg/m^2. Do not re-escalate dose after it has been reduced. Permanently discontinue in patients who are unable to tolerate a dose of 15 mg/m^2

3. **Hepatic dysfunction**:

Total bilirubin	**Dose**
Less than or equal to 1.5 x ULN	100%
Greater than 1.5 x ULN	Do not use

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.

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.