TRIFLURIDINE-TIPIRACIL (Lonsurf)

INDICATION (ICD10) C16, C18, C20

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (TRI1) (TR12)

1. Trifluridine–tipiracil for previously treated metastatic **colorectal** cancer, unsuitable for other available therapies, who have failed at least two prior regimens (fluoropyrimidine, oxaliplatin or irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-epidermal growth factor receptor (EGFR) agents) for advanced/metastatic disease (those patients relapsing during or within 6 months of completing adjuvant chemotherapy can count the adjuvant line as one line of therapy for advanced/metastatic disease). PS 0 or 1. (TA405)
2. Trifluridine plus tipiracil monotherapy for the third or more line of systemic therapy for locally advanced or metastatic adenocarcinoma of the **stomach** or **gastro-oesophageal junction**. PS 0 or 1. (TA852)

REGIMEN

Days 1 to 5 and 8 to 12	**TRIFLURIDINE-TIPIRACIL**	35mg/m^2 (maximum 80mg/dose)	oral	twice daily

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression (formal medical review by end of 2nd cycle)

ANTI-EMETICS

Low risk days 1 to 12

CONCURRENT MEDICATION REQUIRED

Trifluridine-tipiracil	-

ADMINISTRATION

Trifluridine-tipiracil	One tablet contains Trifluridine 15mg + Tipiracil 6.14mg or Trifluridine 20mg +Tipiracil 8.19mg. Tablets should be taken 12 hours apart. Swallowed with water within 1 hour after completion of the morning and evening meals.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs Neutrophils ≥1.5x10^9/L (and see dose modifications) Platelets ≥100x10^9/L (and see dose modifications)	baseline and every cycle (day 1)
Serum creatinine (and calculated CrCl)	baseline and every cycle (day 1)
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Trifluridine-tipiracil	Bone marrow suppression Diarrhoea Renal and hepatic impairment Stomatitis

DOSE MODIFICATIONS

Trifluridine-tipiracil

Dose level	Dose
Full dose	35mg/m^2
First dose reduction	30mg/m^2
Second dose reduction	25mg/m^2
Third dose reduction	20mg/m^2 (minimum dose 20mg/m^2 twice daily)

Dose escalation is not permitted after it has been reduced.

Haematological

Trifluridine-tipiracil

Neutrophils <0.5×10^9/L	interrupt treatment, resume once ≥1.5×10^9/L
Platelets <50×10^9/L	interrupt treatment, resume once ≥75×10^9/L
Febrile neutropenia	• Interrupt dosing until toxicity resolves to grade 1 or baseline. • When resuming dosing, decrease the dose level by 5mg/m^2 from the previous dose level. • Dose reductions are permitted to a minimum dose of 20mg/m^2 twice daily (or 15mg/m^2 twice daily in severe renal impairment).• Do not increase dose after it has been reduced.
CTCAE grade 4 neutropenia (<0.5x10^9/L) or thrombocytopenia (<25×10^9/L) that results in more than 1 week's delay in start of next cycle	• Interrupt dosing until toxicity resolves to grade 1 or baseline. • When resuming dosing, decrease the dose level by 5mg/m^2 from the previous dose level. • Dose reductions are permitted to a minimum dose of 20mg/m^2 twice daily (or 15mg/m^2 twice daily in severe renal impairment).• Do not increase dose after it has been reduced.

Non-haematological

Trifluridine-tipiracil

CTCAE non-haematologic grade 3 or grade 4 adverse reaction; except for grade 3 nausea and/or vomiting controlled by antiemetic therapy or diarrhoea responsive to antidiarrhoeal medicinal products	• Interrupt dosing until toxicity resolves to grade 1 or baseline. • When resuming dosing, decrease the dose level by 5mg/m^2 from the previous dose level. • Dose reductions are permitted to a minimum dose of 20mg/m^2 twice daily (or 15mg/m^2 twice daily in severe renal impairment).• Do not increase dose after it has been reduced.

Hepatic impairment

Trifluridine-tipiracil

Bilirubin of >1.5xULN	Not recommended

Renal impairment

Trifluridine-tipiracil

CrCl >30ml/min	give 100% dose
CrCl 15-29ml/min	Starting dose of 20mg/m^2 twice daily. One dose reduction to a minimum dose of 15mg/m^2 twice daily is permitted based on individual safety and tolerability. Dose escalation is not permitted after it has been reduced.

REFERENCES

1. SPC

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Ongoing
Informed consent	x				
Clinical assessment	x		Pre-C2		Alternate cycles, or at clinician's discretion
SACT assessment (PS and toxicities)	x	x	x	x	Every cycle
FBC	x	x	x	x	Every cycle
U&E & LFTs (including AST and ALP) & magnesium	x	x	x	x	Every cycle
CrCl	x	x	x	X	Every cycle
CT scan	x				At baseline, then CT-restaging at 3 cycles, or at clinician's discretion
Weight recorded	x	x	x	x	Every cycle
Height	x	x	x	x	Every cycle