Chemotherapy Protocol

COLORECTAL CANCER

TRIFLURIDINE-TIPIRACIL

Regimen

- Colorectal Cancer – Trifluridine-Tipiracil

Indication

- Trifluridine-tipiracil is recommended as a third or subsequent line of therapy for treating metastatic colorectal cancer in adults who have had previous treatment with available treatments including a fluoropyrimidine, oxaliplatin or irinotecan based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-epidermal growth factor receptor (EGFR) agents, or when these therapies are not suitable, only when the company provides trifluridine–tipiracil hydrochloride with the discount agreed in the patient access scheme.

- Performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Trifluridine-Tipiracil	Diarrhoea, nausea, neutropenia, thrombocytopenia, proteinuria, fatigue, decreased appetite

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

- FBC, U&Es and LFTs prior to day one of treatment.

- Urine testing for protein on day one

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Dosing adjustments may be required based on individual safety and tolerability.

A maximum of three dose reductions are permitted, at 5mg/m^2 increments, from 35mg/m^2 to

30mg/m^2, 25mg/m^2 to a minimum dose of 20 mg/m^2 of trifluridine twice a day. Dose escalation is not permitted after it has been reduced.

In the event of haematological toxicities patients should follow the dose interruption, resumption and reduction criteria stated in the table below.

Parameter	Interruption criteria	Resumption criteria
Neutrophils	less than 0.5×10^9/L	greater than or equal to 1.5×10^9/L
Platelets	less than 50×10^9/L	greater than or equal to 75×10^9/L

Resumption criteria applied to the start of the next cycle for all patients regardless of whether or not the interruption criteria were met.

Adverse reaction	Recommended dose modifications
Febrile neutropenia or a CTCAE grade 4 neutropenia (less than 0.5x10^9/L) or thrombocytopenia (less than 25×10^9/L) that results in more than one week's delay in the start of next cycle.	• Interrupt dosing until toxicity resolves to CTCAE grade 1 or baseline. • When resuming dosing, decrease the dose level by 5 mg/m^2 of the trifuridine dose from the previous dose level to a minimum of 20mg/m^2 trifluridine

Consider blood transfusion or erythropoietin if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Hepatic Impairment

No adjustment of the starting dose is recommended in patients with mild hepatic impairment. It is not recommended in patients with moderate or severe hepatic impairment.

Renal Impairment

No adjustment of the starting dose is recommended in patients with mild or moderate renal impairment. Administration is not recommended in severe renal impairment or end stage renal disease.

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Regimen

28 day cycle until disease progression or intolerance (12 cycles will be set in Aria)

The dose is calculated based on the trifluridine dose.

Drug	Dose	Days	Administration
Trifluridine-Tipiracil	35mg/m^2 twice a day	1, 2, 3, 4, 5, 8, 9, 10, 11, 12	Oral

Dose Information

- The dose is calculated based on the trifluridine dose
- The maximum dose is 80mg of trifluridine
- The minimum dose is 20mg/m^2 of trifluridine
- Doses will be rounded to the nearest 5mg (up if half way)

Administration Information

- The dosage schedule is easier to remember if it is started on a Monday and taken through to the Friday with the weekend off.
- If a dose is missed or with held the patient must not make up the doses
- The tablets are available in two strengths, 15mg/6.14mg and 20mg/8.19mg trifluridine and tipiracil (as the hydrochloride) respectively.

Additional Therapy

- Anti-emetics are not routinely required but you may consider adding
    - metoclopramide 10mg three times a day oral when required
- Antidiarrhoeal agents such as loperamide or codeine.
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.
- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.

Coding

- Procurement – X71.5
- Delivery – X73.1

References

1. Mayer R, van Cutsem E, Falcone A, Yoshino T, Garcia-Carbonero R, Mizunuma N et al. Randomized Trial of TAS-102 for Refractory Metastatic Colorectal Cancer. N Engl J Med 2015;372:1909-19.

REGIMEN SUMMARY

Trifluridine-Tipiracil

Take Home Medicines

Cycle 1 onwards

Day 1, 2, 3, 4, 5, 8, 9, 10, 11, 12

1. Trifluridine – Tipiracil 35mg/m^2 twice a day oral
   Administration Instructions
   The dose is based on the dose of trifluridine

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	Oct 2016	None	Dr Deborah Wright Pharmacist	Dr Tim Iveson Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospital NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors that occur as a result of following these guidelines.