Chemotherapy Protocol

SARCOMA

TRABECTEDIN

Regimen

- Sarcoma-Trabectedin

Indication

- Trabectedin is recommended as a possible treatment for people with advanced soft tissue sarcoma if:

  - treatment with anthracyclines and ifosfamide has failed, or
  - they cannot tolerate anthracyclines and ifosfamide, or
  - anthracyclines and ifosfamide are unsuitable.

Toxicity

Drug	Adverse Effect
Trabectedin	Anorexia, headache, peripheral neuropathy, hypotension, constipation, hepatobiliary disorders (hyperbilirubinaemia, raised ALT / AST)

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day one of treatment
- Additional monitoring of haematological parameters bilirubin, alkaline phosphatase, aminotransferases and CPK should occur weekly during the first two cycles of therapy, and at least once between treatments in subsequent cycles.

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.

The same dose should be given for all cycles provided that no NCI-CTC grade 3 or above toxicities are seen and that the patient fulfils the re-treatment criteria. Once a dose has been reduced because of toxicity, dose escalation in the subsequent cycles is not recommended. If any of these toxicities reappear in subsequent cycles in a patient exhibiting clinical benefit, the dose may be further reduced (see table).

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

Dose reductions are based on the table below.

Starting Dose	1.5mg/m^2
First Dose Reduction	1.2mg/m^2
Second Dose Reduction	1mg/m^2

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent.

Consider blood transfusion or the prescription of an erythropoietin produce according to NICE TA 323 if the patient is symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Prior to prescribing the following criteria must be met.

Criteria	**Eligible Level**
Neutrophil	equal to or more than 1.5x10^9/L
Platelets	equal to or more than 100x10^9/L

If any of the following events occur at any time between cycles, the dose must be reduced one level for subsequent cycles:

- neutrophils of less than 0.5x10^9/L lasting for more than 5 days or associated with fever or infection
- platelets of less than 25x10^9/L

Hepatic Impairment

The following criteria must be followed to treat with trabectedin:

- bilirubin within the normal range
- alkaline phosphatase less than or equal to 2.5xULN (consider hepatic isoenzymes 5 nucleotidase or GGT, if the elevation could be osseous in origin)
- albumin greater than 25g/L
- alanine aminotransferase (ALT) and aspartate aminotransferase (AST) less than 2.5xULN
- creatine phosphokinase (CPK) less than 2.5 x ULN

The same criteria as above must be met prior to re-treatment, otherwise treatment must be delayed for up to 3 weeks until these conditions criteria are met.

If any of the following events occur at any time between cycles, the dose must be reduced by one dose level, according to the table above for subsequent cycles;

- increase of bilirubin of more than the ULN and/or alkaline phosphatase of more than 2.5xULN

- increase of aminotransferases (AST or ALT) of more than 2.5xULN, which has not recovered by day 21

Renal Impairment

Trabectedin monotherapy may be only used if the creatinine clearance is equal to or greater than 30ml/min.

Regimen

21 day cycle until toxicity or disease progression occurs (six cycles will be set in Aria)

Drug	Dose	Days	Administration
Trabectedin	1.5mg/m^2	1	Continuous intravenous infusion in 240ml sodium chloride 0.9% over 24 hours (10ml/hour)

Dose Information

- Trabectedin will be dose banded according to the agreed bands

Administration Information

Extravasation

- Trabectedin – vesicant

Other

- The use of central venous access is strongly recommended. Patients may develop a potentially severe injection site reaction when trabectedin is administered through a peripheral venous line.

Additional Therapy

- Dexamethasone 4mg twice a day for one day on the day before trabectedin
- 30 minutes prior to the start of the trabectedin infusion administer dexamethasone 20mg intravenous
- Mouthcare for the prophylaxis or treatment of mucositis in accordance with local guidelines.
- 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.

Coding

- Procurement – X71.5
- Delivery – X72.3

References
1. Demetri G, Chawla S, von Mehren M et al. Efficacy and of trabectedin in patients with advanced or metastatic liposarcoma or leiomyosarcoma after failure of prior anthracyclines and ifosfamide: results of a randomised phase II study of two different schedules. J Clin Oncol 2009; 27 (25): 4188-4196.
2. National Institute of Health and Clinical Excellence. Technology Appraisal 185. Trabectedin for the treatment of advanced soft tissue sarcoma. DOH:London

REGIMEN SUMMARY

Trabectedin

Days 1

1.Dexamethasone 20mg intravenous
Administration Instructions
Administer 30 minutes prior to the start of the trabectedin infusion

2.Trabectedin 1.5mg/m^2 continuous intravenous infusion in 240mls sodium chloride 0.9% over 24 hours
Administration Instructions
Trabectedin should be administered via a central line

Take Home Medicines

3. Dexamethasone 4mg twice a day for 1 day on the day before the trabectedin infusion
Administration Instructions
This is the supply for the next cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	November 2015	None	Dr Deborah Wright Pharmacist	Dr Nicola Keay 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.