Chemotherapy Protocol

NEUROENDOCRINE

CISPLATIN-FLUOROURACIL-FOLINIC ACID-STREPTOZOCIN

(FCiSt)

Regimen

- Neuroendocrine – Cisplatin-Fluorouracil-Folinic Acid-Streptozocin (FCiST)

Indication

- Metastatic or locally advance neuroendocrine tumours

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Fluorouracil	Palmar-plantar erythrodysesthesia, diarrhoea, chest pain, mucositis
Streptozocin	Nephrotoxicity, transient increases in LFTs, altered glucose tolerance, hypoglycaemia, confusion, depression

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

Monitoring

Drugs

- FBC prior to each cycle
- LFTs (including albumin) and U&Es prior to each cycle
- EDTA or calculated creatinine clearance prior to each cycle
- Regular monitoring of blood glucose levels
- Regular urinalysis for signs of proteinuria
- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with fluorouracil. All patients should be tested for DPD deficiency before initiation (cycle 1) to minimise the risk of these reactions

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

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 if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL.

Neutrophils ($x10^9$/L)	**Dose Modifications (cisplatin, fluorouracil and streptozocin)**
Greater than or equal to 1	100%
Less than 1 or febrile neutropenia	Delay chemotherapy until recovery then continue with 80% of the original dose.
Platelets ($x10^9$/L)	**Dose Modifications (cisplatin, fluorouracil and streptozocin)**
Greater than or equal to 100	100%
Less than 100 or bleeding	Delay chemotherapy until recovery then continue with 80% of the original dose.

Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	**Bilirubin µmol/L**		**AST/ALT units**	**Dose (% of original dose)**
Cisplatin	N/A		N/A	No dose adjustment needed
Fluorouracil	less than 85		less than 180	100%
	85 or greater		180 or greater	Contra-indicated
Streptozocin				Consider dose modification

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	60 or more	100%
	less than 60	Consider alternative
Fluorouracil	N/A	No dose adjustment needed
Streptozocin	60 or more	100%
	less than 60 or significant reduction from baseline	Consider dose reduction or ommission

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.

For all other non-haematological NCI-CTC grade 3 and above toxicities delay treatment until the adverse effect has resolved to NCI-CTC grade 1 or below. The dose of the causative agent should then be reduced to 80% of the original dose or discontinued as appropriate.

Regimen

21 day cycle for up to 6 cycles

Drug	Dose	Days	Administration
Cisplatin	70mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% + 20mmol potassium chloride at a rate of 1mg cisplatin/ min (min 120 minutes)
Fluorouracil	500mg/m^2	1	Intravenous bolus over 10 minutes
Folinic Acid	45mg	1	Intravenous infusion in 250ml glucose 5% over 120 minutes
Streptozocin	1000mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% over 120 minutes

Dose Information

- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)
- Fluorouracil will be dose banded in accordance with the national dose bands (25mg/ml PM)

- Streptozocin will be dose banded in accordance with the national dose bands (100mg/ml)

Administration Information

Extravasation

- Cisplatin - exfoliant
- Fluorouracil - inflammitant
- Streptozocin - vesicant

Other

Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy

- aprepitant 125mg oral
- dexamethasone 4mg oral or intravenous bolus
- ondansetron 8mg oral or intravenous bolus

As take home medication

- aprepitant 80mg oral once a day on days 2 and 3
- dexamethasone 4mg oral once a day for 3 days
- metoclopramide 10mg oral three times a day as required
- ondansetron 8mg oral twice a day for 3 days

- Cisplatin pre and post hydration as follows

  Pre

  Furosemide 40mg oral or intravenous bolus

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

  Post

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

  Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- Mouthcare for the prophylaxis or treatment of mucositis in accordance with CSCCN guidelines.

- Gastric protection with a proton pump inhibitor or a H2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

References
1. Turner N, Strauss S, Sarker D et al. Chemotherapy with 5-fluorouracil, cisplatin and streptozocin for neuroendocrine tumours. Br J Cancer 2010;102:1106-1112.

REGIMEN SUMMARY

Cisplatin-Fluorouracil-Folinic Acid-Streptozocin (FCiSt)

Day 1

1. Folinic acid 45mg intravenous infusion in 250ml glucose 5% over 120 minutes
2. Aprepitant 125mg oral
3. Dexamethasone 4mg oral or intravenous bolus
4. Ondansetron 8mg oral or intravenous bolus
5. Fluorouracil 500mg/m^2 intravenous bolus over 10 minutes
6. Streptozocin 1000mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% over 120 minutes
7. Furosemide 40mg oral or intravenous bolus
8. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes
9. Cisplatin 70mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride intravenous infusion over a minimum 120 minutes (maximum rate 1mg cisplatin/minute)
10. Sodium chloride 0.9% 1000ml with 20mmol potassium chloride and 16mmol magnesium sulphate intravenous infusion over 60 minutes

Take home medicines

11. Aprepitant 80mg once a day oral for 2 days, starting on day 2 of treatment
12. Dexamethasone 4mg once a day oral for 3 days, starting on day 2 of treatment
13. Metoclopramide 10mg three times a day oral as necessary
14. Ondansetron 8mg twice a day oral for 3 days, starting on the evening of day 1 of treatment

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Nov 2020	Updated monitoring with DPD testing Dose banding updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	Dec 2013	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Judith Cave Consultant Medical Oncologist Dr Luke Nolan 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 NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Trust

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