FCiSt

Locally advanced or metastatic neuroendocrine tumours of pancreas, small or large bowel

Drugs/Dosage:	Folinic acid	45mg	IV	Day 1
	5-Fluorouracil	500mg/m^2	IV	Day 1
	Streptozocin	1000mg/m^2	IV	Day 1
	Cisplatin	70mg/m^2	IV	Day 1

Administration:
1 litre 0.9% sodium chloride +20mmol KCl +10mmol $MgSO_4$ IV over 2 hours
Folinic acid 45mg IV bolus, followed by:
5-Fluorouracil IV bolus
Streptozocin in 500ml 0.9% sodium chloride over 1 hour
Mannitol 20% 100ml IV over 15 minutes
Cisplatin in 1 litre 0.9% sodium chloride over 3 hours
1 litre 0.9% sodium chloride +20mmol KCl + 10mmol $MgSO_4$ IV over 2 hours
500ml sodium chloride 0.9% IV **or** 500mls – 1 litre water orally over 1 hour

Frequency: 3 weekly cycle for up to 6 cycles

Main Toxicities: myelosuppression; mucositis; nephrotoxicity; neuropathy / ototoxicity; palmar-plantar syndrome (PPE); diarrhoea; ovarian failure/infertility;
streptozocin side-effects:-
dose-related nephrotoxicity, with mild proteinuria one of the first signs of renal toxicity;
mild-moderate abnormalities of glucose tolerance, hypoglycaemia has been reported; transient increase in LFTs;
confusion, lethargy and depression have been reported in a limited number of patients on a continuous infusion 5 day regimen of streptozocin. Patients should be informed that there may be potential risk in driving or using complex machinery.

Antiemetics: highly emetogenic, including aprepitant

Extravasation: streptozocin is a vesicant

Regular Investigations:	FBC	Day 1
	LFTs	Day 1
	U&Es	Day 1
	Mg^{2+} and Ca^{2+}	Day 1
	EDTA	prior to 1st cycle
	Urinalysis for proteinuria	Day 1 - make sure result available for clinic doctor (see Renal Impairment)

Comments: Streptozocin is imported via IDIS. Please give pharmacy as much warning as possible about the intent to treat, as it may take at least one week to obtain supplies.

.

For patients on Cycle 1 whose EDTA is not yet available, Cockcroft & Gault may be used to predict GFR. Cisplatin dose should be adjusted if necessary once EDTA available. EDTA should only be repeated if the result is borderline at the start of treatment or if there is a 30% change in serum creatinine.

Reason for Update: indication and references updated; removed alopecia S/E; order of administration reviewed; aprepitant added; carboplatin option added, as Turner et al	Approved by Consultant: Dr S Cummins
Version: 3	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 2	Date: 10.10.13
Prepared by: S Taylor	Checked by: C Tucker

Check electrolytes – additional supplements of magnesium, potassium or calcium may be required.

Weight should be recorded prior to and at the end of cisplatin treatment, and a strict fluid balance chart should be maintained. An average urine output of at least 100ml/hr must be maintained throughout treatment, and cisplatin infusion should not be commenced unless this urine output is achieved. If the urine output is inadequate, the patient should be assessed and urine output increased by administering 500ml sodium chloride 0.9% IV +/- furosemide 20 – 40mg. Furosemide 20 – 40mg po may also be given if there is a positive fluid balance of 1.5 litres, a weight gain of 1.5kg or symptoms of fluid overload. The patient should be asked to drink 2 litres of fluid in the 24hrs following treatment, and to contact the hospital if this is impossible because of problems e.g. nausea and vomiting.

Dose Modifications

Haematological Toxicity:

WBC < 3.0 x 10^9/l
or
Neutrophils < 1.5 x 10^9/l
or
Platelets < 100 x 10^9/l

Defer for one week.
Repeat FBC and, if recovered, continue with treatment. If in doubt, discuss with Consultant.

Non-haem Toxicity: Following any Grade 3 non-haematological toxicity, reduce doses of all 3 cytotoxics by 20%, once the toxicity has resolved.

Renal Impairment: NB. Cisplatin is both eliminated primarily (>90%) in the urine and is nephrotoxic.

GFR (ml/min)	Cisplatin Dose
≥ 60	Give 100% dose
45 - 59	Give 75% dose, or substitute with carboplatin as below
20 – 44	Substitute with carboplatin AUC 5, administered in 250ml 5% Glucose over 30 minutes. It may be given according to this protocol, with however no requirement for pre- or post-hydration, nor fluid balance/urine monitoring
<20	Carboplatin contra-indicated

Although the effects of renal impairment on elimination of streptozocin have not been evaluated, some clinicians have suggested that patients with creatinine clearance of 10 – 50 ml/min receive 75% dose and those with creatinine clearance < 10 ml/min receive 50% dose[1].
Streptozocin is renally excreted and nephrotoxic. Mild proteinuria is one of the first signs of renal toxicity and may herald further deterioration of renal function. Reduction of the dose of streptozocin or discontinuation of treatment should be considered in the presence of significant renal toxicity. Discuss with Consultant.

Neuropathy: If patient develops Grade 2 neuropathy or ototoxicity, discuss with Consultant.

References:

Turner, N et al ; Br J Cancer 2010 ; 102 (7) : 1106 - 1112
[1]AHFS (American Hospital Formulary Service) on-line version