CAPECITABINE & STREPTOZOCIN

Locally advanced or metastatic neuroendocrine tumours, predominantly pancreas, also small or large bowel

Drugs/Dosage:	Streptozocin	1000mg/m^2	IV	D1
	Capecitabine	625mg/m^2	PO	BD on Day 1 to Day 21

Administration: Streptozocin in 500ml 0.9% sodium chloride over 1 hour
Capecitabine tablets, available as 500mg and 150mg, should be swallowed whole with water within 30 minutes after a meal.
Information, provided by Roche, is available via Pharmacy regarding dispersing the tablets for those patients with swallowing difficulties or with feeding tubes.

Frequency: 3 weekly cycle for 6 cycles

Main Toxicities: myelosuppression; plantar/palmar syndrome (PPE); diarrhoea; mucositis; coronary artery spasm (uncommon); 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: streptozocin - highly emetogenic
capecitabine – mildly emetogenic

Extravasation: streptozocin is a vesicant

Regular Investigations:	FBC	Day 1
	LFTs	Day 1
	U&Es	Day 1
	Urinalysis for proteinuria	Day 1 - make sure result available for clinic doctor (see Renal Impairment section)

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.

Dose Modifications

Haematological Toxicity: If neutrophils < 1.0 x 10^9/l or platelets 100 x 10^9/l:

1st occurrence:	Stop capecitabine and defer streptozocin for one week. Repeat FBC and, if recovered, continue with 100% doses of capecitabine and 80% dose of streptozocin.
2nd occurrence:	Once FBC recovered, continue with 80% doses of both drugs
3rd occurrence:	Once FBC recovered, continue with 80% doses of capecitabine and 60% dose of streptozocin

Reason for Update: New protocol	Approved by Consultant: Dr S Cummins
Version: 1	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Any other versions, including FCiSt	Date: 20.8.13
Prepared by: S Taylor	Checked by: C Tucker

Renal Impairment: NB. Streptozocin is both renally excreted and nephrotoxic. Mild proteinuria is one of the first signs of renal toxicity due to streptozocin and may herald further deterioration of renal function.

CrCl (ml/min)	Dosing advice
>60	100% doses of both drugs
40 – 60	80% doses of both drugs
30 - 39	60% doses of both drugs
< 30	Discontinue treatment

Hepatic Impairment: If bilirubin > 3 x ULN or ALT/AST > 2.5 x ULN, omit capecitabine until liver function recovers.
No specific advice for streptozocin, but consider dose reduction or discontinuation in the event of significant hepatic toxicity.

Non-Haematological Capecitabine Toxicities: **Note that severe diarrhoea and/or severe mucositis early in the first treatment cycle can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.**

Toxicity due to capecitabine may be managed symptomatically and/or modification of the dose (treatment interruption or dose reduction). Use the table below for dose adjustment guidelines. Once the dose has been reduced, it should not be increased at a later time. Doses of capecitabine omitted for toxicity are not replaced or restored. Instead the patient should resume the planned treatment cycle.

Capecitabine Dose Adjustment Guidelines for Non-Haematological Toxicities

Common Toxicity Criteria*	During Course of Therapy	Dose adjustment for next cycle (% of start dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2: 1st Appearance	Interrupt until resolved to Grade 0 – 1	Give 100% dose
Grade 2: 2nd Appearance	Interrupt until resolved to Grade 0 – 1	Give 75% dose
Grade 2: 3rd Appearance	Interrupt until resolved to Grade 0 – 1	Give 50% dose
Grade 2: 4th Appearance	Discontinue treatment permanently	
Grade 3: 1st appearance	Interrupt until resolved to Grade 0 – 1	Give 75% dose
Grade 3: 2nd appearance	Interrupt until resolved to Grade 0 – 1	Give 50% dose
Grade 3: 3rd appearance	Discontinue treatment permanently	
Grade 4: 1st appearance	Discontinue permanently **or, with Consultant approval,** interrupt until resolved to Grade 0 – 1	Give 50% dose

Reference: Adapted from NET-01 trial