STREPTOZOCIN CAPECITABINE

INDICATION (ICD10) M-8246/3

1. Metastatic neuroendocrine carcinoma (unlicensed indication)
PS 0, 1, 2

REGIMEN

Day 1	Prehydration sodium chloride 1000ml 0.9% IV infusion over 2 hours	
	STREPTOZOCIN*	1000mg/m^2 in 250ml sodium chloride 0.9% IV infusion over 1 hour
Days 1 to 21	CAPECITABINE	625mg/m^2 twice daily (1250mg/m^2/day) oral

*Named patient medicine

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days for 6 cycles (can be continued if well tolerated)

ADMINISTRATION

Tablets should be taken 12 hours apart.
Swallow with water within 30 minutes after a meal, or dissolve in 200ml luke warm water, stir thoroughly (squash may be added if unpalatable).

ANTI-EMETICS

High risk day 1
Low risk days 2 to 21

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Streptozocin	Ensure adequate hydration.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Streptozocin – vesicant

Peripheral line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine - GFR each cycle
DPD test

MAIN TOXICITES AND ADVERSE REACTIONS

Capecitabine	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. To minimise risk of anthracycline induced cardiac failure signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. All patients should be told to report any cardiac symptoms immediately and should be told to stop the medication immediately if any suspicion of cardiac problems. Stomatitis
Streptozocin	Burning along veins during rapid infusion Severe hyperglycaemia. Monitor BMs if signs of hyperglycaemia occur. Associated with renal tubule toxicity, hepatotoxicity and anaemia. Renal toxicity

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Capecitabine	Brivudine and analogues should be avoided Warfarin and caution with all oral anticoagulants Phenytoin Allopurinol
Streptozocin	Many interactions, check carefully

DOSE MODIFICATIONS
Haematological
Neutrophils <1.5x10^9/l or Platelets <100x10^9/l Delay treatment for 1 week.
Repeat FBC. If recovered, restart capecitabine, using dose adjustment guidelines below, according to worst grade of haematological toxicity recorded.

Non-haematological

Capecitabine

Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction).

Once the dose has been reduced it should not be increased at a later time.

When capecitabine is stopped for toxicity, the doses are omitted and not delayed.

Toxicity Grades	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
Grade 2 - 1st appearance	Interrupt until resolved to grade 0-1	100%
Grade 2 - 2nd appearance	Interrupt until resolved to grade 0-1	75%
Grade 2 - 3rd appearance	Interrupt until resolved to grade 0-1	50%
Grade 2 - 4th appearance	Discontinue treatment permanently	Not applicable
Grade 3 - 1st appearance	Interrupt until resolved to grade 0-1	75%
Grade 3 - 2nd appearance	Interrupt until resolved to grade 0-1	50%
Grade 3 - 3rd appearance	Discontinue treatment permanently	Not applicable
Grade 4 - 1st appearance	Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
Grade 4 - 2nd appearance	Discontinue treatment permanently	Not applicable

Hepatic impairment

Capecitabine

Bilirubin of >3xULN or ALT/AST >2.5xULN	Interrupt Capecitabine Treatment may be resumed when bilirubin decreases to <3xULN or hepatic aminotransferases decrease to <2.5xULN.

Renal impairment

Capecitabine

CrCl >50ml/min	give 100% dose
CrCl 30-50ml/min	give 75% dose
CrCl <30ml/min	contraindicated

Streptozocin

CrCl >60ml/min	give 100% dose
CrCl 46-60ml/min	give 50% dose
CrCl 31-45ml/min	Evaluation of risk / benefit
CrCl <30ml/min	contraindicated

REFERENCES

1. NET01 regimen
2. Eriksson. B., Oberg. K. 1993 An update of medical treatment of malignant endocrine pancreatic tumours. Acta Oncol. 32: 203-208