CAPECITABINE & TEMOZOLOMIDE

An option for locally advanced or metastatic neuroendocrine tumours, including pancreas, small or large bowel

Drugs/Dosage:	Capecitabine 750mg/m^2	PO	twice daily on Day 1 to Day 14
	Temozolomide 150* - 200mg/m^2	PO	once daily on Day 10 – Day 14 (5 doses)

*Select the 150mg/m^2 dose for patients who have received prior chemotherapy or extensive radiation

Administration: Capecitabine tablets, available as 500mg and 150mg, should be swallowed whole with water within 30 minutes after a meal.
Information is available via Pharmacy regarding dispersing the tablets, for those patients with swallowing difficulties or with feeding tubes.
Temozolomide is available as 5mg, 20mg, 100mg, 140mg, 180mg and 250mg capsules.
To be taken on an empty stomach, swallowed whole with a glass of water.

Frequency: 4 weekly cycle for 6 cycles

Main Toxicities: myelosuppression; plantar/palmar syndrome (PPE); diarrhoea; mucositis; coronary artery spasm (uncommon); ovarian failure/infertility;

Anti-emetics: Capecitabine – mildly emetogenic
Temozolomide - highly emetogenic; ondansetron 8mg po once daily x 5 days, one hour before each dose of temozolomide (dexamethasone not routinely required)

Regular Investigations:	FBC	Day 1
	LFTs	Day 1
	U&Es	Day 1

Dose Modifications

Haematological Toxicity:	Neutrophils ≥ 1.5 x 10^9/l and Platelets ≥ 100 x 10^9/l	Proceed with the next cycle
	Neutrophils 1.0 - 1.4 x 10^9/l or Platelets 50 - 99 x 10^9/l	Delay treatment for 1 week. Repeat FBC and, if within normal parameters, continue with previous dose of both drugs.
	Neutrophils < 1.0 x 10^9/l or Platelets < 50 x 10^9/l	Delay treatment for 1 week. Repeat FBC and, once recovered, give 75% dose of capecitabine, and temozolomide at dose equivalent to 50mg/m^2 less than previous cycle, to a minimum of 100mg/m^2

Renal Impairment: Before every cycle, creatinine clearance should be calculated using Cockcroft and Gault. If borderline, an EDTA should be requested.

Reason for Update: New protocol	Approved by Consultant: Dr S Cummins
Version: 1	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: N/A	Date: 17.8.15
Prepared by: S Taylor	Checked by: C Tucker

CrCl (ml/min)	Capecitabine Dose
> 50	Give 100% dose
30 – 50	Give 75% dose
< 30	Regimen not recommended

Hepatic Impairment: If bilirubin > 3 x ULN or ALT/AST > 2.5 x ULN, omit capecitabine until liver function recovers.

No temozolomide dose reduction is routinely required in patients with hepatic impairment, but discuss with Consultant and consider the following:

- Hepatic injury, including fatal hepatic failure, has been reported in patients treated with temozolomide. If abnormal LFTs at baseline, the benefit/risk should be considered prior to initiating temozolomide, including the potential for fatal hepatic failure.
- For patients who develop significant liver function abnormalities after treatment has started, discuss the benefit/risk of continuing treatment with the Consultant. Liver toxicity may occur several weeks or more after the last treatment with temozolomide.

Non-Haematological Capecitabine Toxicities: **Note that severe diarrhoea and/or severe mucositis early in the first treatment cycle of capecitabine 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: Fine, RL et al; 2014 Gastrointestinal Cancers Symposium; Abstract 179