CAPECITABINE

Second-line use in advanced or metastatic biliary tract tumours, including gallbladder carcinoma and cholangiocarcinomas
Adjuvant use after complete surgical resection of cholangiocarcinoma or gall bladder cancer

Drug/Dosage:	***Advanced use:***		
	Capecitabine	1000mg/m^2	PO twice daily from Day 1 to Day 14, followed by 7 days rest
	Adjuvant use:		
	Capecitabine	1250mg/m^2	PO twice daily from Day 1 to Day 14, followed by 7 days rest
Administration:	Tablets should be swallowed whole with water within 30 minutes after a meal.		
Frequency:	Advanced:	3 weekly cycle for 6 – 8 cycles CT scan after 4 cycles	
	Adjuvant:	3 weekly cycle for 8 cycles	
Main Toxicities:	myelosuppression; diarrhoea; palmar-plantar erythema (PPE); stomatitis; cardiotoxicity (uncommon); ovarian failure/infertility		
Anti- emetics:	mildly emetogenic		
Regular Investigations:	FBC	Day 1	
	U&Es	Day 1	
	LFTs	Day 1	
	CA 19-9	Day 1 (if raised at baseline)	
	ECG	If previous history of angina, MI or rhythm disturbances	

Dose Modifications

Haematological Toxicity:	Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l	Delay treatment for 1 week. Repeat FBC. If recovered, restart capecitabine, using dose adjustment guidelines in table below, according to worst grade of haematological toxicity recorded.

Non-Haematological 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.

Reason for Update: adjuvant indication added; WBC cut-off removed	Approved by Consultant: Dr S Cummins
Version: 2	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 1	Date: 22.11.17
Prepared by: S Taylor	Checked by: C Tucker

Haematological and Non-Haematological Dose Adjustment Guidelines according to Common Toxicity Criteria

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

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

CrCl (ml/min)	Capecitabine Dose
> 50	Give 100% dose
30 – 50	Give 75% dose
< 30	Omit

Hepatic Impairment: Bilirubin > 3 x ULN
or
ALT/AST > 2.5 ULN
Omit capecitabine until liver function recovers

Cardiotoxicity: Has been associated with fluoropyrimidine therapy (including myocardial infarction, angina, arrhythmias, cardiogenic shock, sudden death and ECG changes). Therefore, exercise caution in patients with prior history of coronary heart disease, arrhythmias and angina pectoris.

References:
Thongprasert, S; Annals of Oncology 2005; 16 (Supplement 2): ii93 – ii96
Patt, Y et al; Cancer 2004; 101 (3): 578 – 586
Bilcap study, presented at ASCO 2017, Abstract 4006