CAPECITABINE

1. An option for patients with locally advanced or metastatic breast disease
2. Adjuvant use in patients with triple negative breast cancer and an incomplete response to neo-adjuvant chemotherapy

Drug/Dosage/ Frequency:

Schedule 1 (licensed):

Capecitabine 1250 mg/m^2 PO twice daily from Day 1 to Day 14, followed by 7 days rest
21 day cycle

Schedule 2 (7 days on and 7 days off):

An option for patients experiencing problems with GI toxicity on the licensed dosing:

Capecitabine 1250* mg/m^2 PO twice daily from Day 1 to Day 7, and from Day 15 to Day 21

**but consider any previous dose reduction*

28 day cycle

Advanced setting: continue according to response
Adjuvant setting: 6 – 8 cycles (in the Phase 3 study, only 38% of patients completed the 8 cycles)

Administration: Tablets should be swallowed whole with water within 30 minutes after a meal.

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 (*renal function should be closely monitored)
	LFTs	Day 1
	CA 15-3	on alternate cycles **only** if elevated prior to treatment.
	ECG	if previous history of angina, MI or rhythm disturbances
	CT scan	after 3 months

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.

Reason for Update: adjuvant cape indication amended to TNBC only	Approved by Consultant: Dr T Crook
Version: 7	Approved by Lead Chemotherapy Nurse: S Wills-Percy
Supersedes: Version 6	Date: 12.2.18
Prepared by: S Taylor	Checked by: C Tucker

Doses of capecitabine omitted for toxicity are not replaced or restored. Instead the patient should resume the planned treatment cycle.

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:

O'Shaughnessy, JA et al, Annals of Oncology: 12:1247 – 1254, 2001
Blum, JL et al, Cancer, Oct 1, 2001; Vol 92; (7): 1759 - 1768
Blum, JL et al: JCO, 17; (2):485 – 493, 1999
Masuda, N et al; NEJM 2017; 376: 2147 – 2159 (adjuvant use)
Cadoo, K et al; Nature 2016; published online:
http://www.nature.com/articles/npjbcancer20166 (7 days on, 7 days off)