CAPECITABINE AND DOCETAXEL

Locally advanced or metastatic breast disease in patients for whom initial chemotherapy (including anthracycline) has failed; NICE Approved May 2003

Drugs/Dosage:	Capecitabine:	**Age < 60:** 1000-1250mg/m^2 }	PO	twice daily Day 1 – Day 14,
		Age ≥ 60: 950mg/m^2 }		followed by 7 days rest
	Docetaxel	75mg/m^2	IV	Day 1

Administration: Capecitabine, available as 500mg and 150mg tablets, should be swallowed with water within 30 minutes after a meal
For docetaxel doses ≤ 185mg, in 250ml sodium chloride 0.9% over 1 hour
For docetaxel doses > 185mg, in 500ml sodium chloride 0.9% over 1 hour

Frequency: 3 weekly cycle, with clinical review prior to each cycle and CT scan after 4 cycles

Main Toxicities: myelosuppression; diarrhoea; palmar-plantar erythema (PPE); stomatitis; cardiotoxicity (uncommon); alopecia; myalgia/arthralgia; hypersensitivity reactions (infusion-related and ↑ risk with 1st/2nd treatment); fluid retention; skin reactions & nail changes; peripheral neurotoxicity; ovarian failure/infertility

Anti- emetics: Docetaxel: moderately emetogenic
Capecitabine: mildly emetogenic

Regular Investigations:	FBC	Day 1
	U&Es & 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

Comments: Offer scalp cooling.

Pre-medication (to prevent hypersensitivity reactions and fluid retention):
Dexamethasone 8 mg po bd for 3 days, commencing the morning of the day prior to chemotherapy.
If the patient has not taken the oral pre-med for any reason, intravenous dexamethasone is not recommended and can only be substituted if prescribed by a Consultant.

Dose Modifications

Haematological Toxicity: If WBC < 3.0 x 10^9/l or Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l, delay treatment for 1 week.
If neutrophils < 0.5 x 10^9/l for more than 1 week or if febrile neutropenia occurs, reduce docetaxel dose to 55 mg/m^2 for subsequent cycles.
Docetaxel should be discontinued if neutrophils < 0.5 x 10^9/l or febrile neutropenia occurs at a dose of 55 mg/m^2 docetaxel.

Give **ciprofloxacin 250mg bd x 5 days**, starting on day 5, on subsequent cycles if patient suffers neutropenic sepsis or has chemotherapy deferred due to neutropenia.

Reason for Update: general review	Approved by Consultant: Dr S Houston
Version: 4	Approved by Lead Chemotherapy Nurse: P Deery
Supersedes: Version 3	Date: 13.9.13
Prepared by: S Taylor	Checked by: C Tucker

Non-Haematological 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), as specified below. 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.

Non-haematological toxicity	Action
First appearance of any Grade 2	Interrupt treatment until resolved to Grade 0 – 1. Dose reduction is not required.
Any Grade 3 or 2nd occurence of any Grade 2	Interrupt treatment until resolved to Grade 0 – 1, and then restart with 75% dose of both capecitabine and docetaxel.
2nd occurence of any Grade 3 or 3rd occurrence of Grade 2 toxicity	Discontinue docetaxel and give 50% dose of capecitabine once toxicity resolved to Grade 0 - 1.
Any Grade 4 toxicity	Discontinue docetaxel and capecitabine (unless specific Consultant approval for capecitabine alone to be restarted at 50% dose once toxicity resolved to Grade 0 – 1)

Docetaxel-related myalgia/arthralgia:

Often co-exist, usually Grade 1 or Grade 2. Management consists of reassuring patients that it is self-limiting. Consider use of NSAIDs, although not always effective.

Cardiotoxicity:

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.

Renal Impairment:

Before every cycle, calculate CrCl using Cockcroft and Gault. If borderline, request an EDTA.

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

Hepatic Impairment:

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

Docetaxel should not be administered without consultant approval if bilirubin > ULN or ALT/AST > 3.5 x ULN, with ALP > 6 x ULN

References:

O'Shaughnessy, J et al; JCO 2002; 20 (12): 2812 - 2823