Systemic Anti Cancer Treatment Protocol

Docetaxel & Capecitabine Advanced Breast Cancer

PROTOCOL REF: MPHADOCABR
(Version No: 1.1)

Approved for use in:

Metastatic Breast Cancer: Criteria, very fit patients only PS 0-1

Visceral crisis disease that requires doublet treatment

Dosage:

Drug	Dosage	Route	Frequency
Docetaxel	75 mg/m² day 1	IV	Every 21 days, for 6 cycles
Capecitabine	1000mg/m² twice daily for 14 days from day 1 of cycle	Oral	

Supportive treatments:

Dexamethasone tablets 8mg twice daily for 3 days starting 24 hours before docetaxel (To reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions)

Loperamide 2mg when required after each loose stool

Domperidone 10mg tablets, up to three times a day when required

Notes - capecitabine

Tablets should be taken 12 hours apart

Swallow whole with water within 30 minutes of a meal

Do not add doses missed due to toxicity onto the end of the cycle. Continue according to the treatment plan and stop taking on the originally scheduled day.

Extravasation risk:

Docetaxel: exfoliant.

Administration:

Day	Drug	Dose	Route	Diluent and rate
1	**Docetaxel**	**75mg/m^2**	**IV Infusion**	Sodium chloride 0.9% 250mL over 60 minutes
1 to 14	**Capecitabine**	**1000mg/m^2 twice daily**	**Oral**	Every 12 hours

If oral dexamethasone has not been taken then an intravenous dose of 8mg can be administered on the day of treatment, in addition to the oral dose of 8mg

Main Toxicities:

Haematological	Neutropenia, thrombocytopenia and anaemia.
Gastrointestinal	Nausea, vomiting, stomatitis, diarrhoea
Cardiotoxicity	Capecitabine: myocardial infarction, angina, dysrhythmias, cardiogenic shock, sudden death and electrocardiographic changes (including very rare cases of QT prolongation).
Dermatological	Alopecia, normally reversible, although can be permanent following docetaxel. Capecitabine can cause hand-foot syndrome (PPE) Severe skin reactions such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. Capecitabine should be permanently discontinued in patients who experience a severe skin reaction.
Ocular	Watery eyes, gritty and irritated
Dermatological	Docetaxel: Brittle, chipped and ridged nails
Gastrointestinal	Mucositis, nausea and vomiting
Hypersensitivity reactions	Reactions may occur within a few minutes following the initiation of treatment with docetaxel, facilities for the treatment of hypotension and bronchospasm should be available. If hypersensitivity reactions occur, minor symptoms such as flushing or localised rash with or without pruritus do not require interruption of therapy. However, severe reactions, such as severe hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of docetaxel and appropriate treatment. Patients

	who have developed severe hypersensitivity reactions should not be re-challenged with docetaxel.
Nervous system	Docetaxel: peripheral neuropathy is very common
Musculoskeletal	Arthralgia, myalgia common with docetaxel

Investigations and Treatment Plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Comments
Medical Assessment	X		X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X		X	X	X	X	X	Every cycle
U&E & LFT	X		X	X	X	X	X	Every cycle
Dihydropyrimidine dehydrogenase (DPD) deficiency test	X							This test is normally only required if a patient has not had capecitabine, or fluorouracil in the past. However a consultant may still request this test if capecitabine or fluorouracil was not tolerated previously. The result must be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary. Treatment with capecitabine and fluorouracil is contraindicated in patients with known complete DPD deficiency.
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X		X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological Toxicity:

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Non-haematological toxicities

Hepatic Impairment:

Docetaxel
If Bilirubin >22µmol/L +/or ALT/AST >3.5 times ULN with ALP > 6 times ULN, docetaxel should not be used unless strictly indicated. ALT +/or AST > 1.5 times ULN and ALP > 2.5 times ULN – give 75mg/m^2

Renal Impairment: Before every cycle, calculate CrCl using Cockroft and Gault formula.

Creatinine Clearance (mL/min)	Capecitabine Dose
> 50	Give 100% dose
30 to 49	Give 75%
< 29	Omit

Capecitabine dose adjustment guidelines (according to CTCAE) for side effects including diarrhoea, vomiting, mucositis and PPE:

Capecitabine dose reduction schedule (3-weekly cycle) – table ref SPC;

Toxicity grades*	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
• *Grade 1*	Maintain dose level	Maintain dose level
• *Grade 2*		

-1st appearance	Interrupt until resolved to grade 0-1	100%
-2nd appearance		75%
-3rd appearance		50%
-4th appearance	Discontinue treatment permanently	Not applicable
• *Grade 3*		
-1st appearance	Interrupt until resolved to grade 0-1	75%
-2nd appearance		50%
-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%
-2nd appearance	Discontinue permanently	Not applicable

Note that severe diarrhoea and/or severe mucositis early in capecitabine treatment can be the first presenting toxicity due to DPD enzyme deficiency, in which case potentially fatal neutropenia can quickly follow.

References

Superior survival with capecitabine plus docetaxel

JCO 2002 20(12) 2812-23

O'Shaughnessy et al

SPC for Capecitabine (Actavis) available via Electronic Medicines Compendium at http://www.medicines.org.uk/emc/

Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH (Version 3 - updated January 2009)