LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Docetaxel & Capecitabine in Advanced Breast Cancer

Indication:	Alternative palliative treatment for advanced breast cancer in patients previously treated with an anthracycline or for whom an anthracycline is not suitable.			
Regimen details:	Docetaxel	75mg/m^2	IV	Day 1
	Capecitabine	*1000mg/m^2 BD	PO	Days 1 to 14 followed by 7 day rest period
	*Start with 900mg/m^2 in patients > 60 years of age, dose may be escalated if well tolerated.			
Administration:	Docetaxel in 250ml or 500ml Sodium Chloride 0.9% depending on final concentration IV over 1 hour Capecitabine tablets orally twice a day, swallow whole with water within 30 minutes after a meal and approximately 12 hours apart. Capecitabine available as 150mg and 500mg tablets. Hypersensitivity reactions may occur with docetaxel, such as flushing, rash with or without pruritus, chest tightness, back pain, dyspnoea and fever or chills, usually during the first and second infusions and within a few minutes following the start of the infusion; the infusion should be slowed down or interrupted and the necessary supportive medication should be administered. Severe reactions such as hypotension and/or bronchospasm or generalised rash/erythema requires immediate discontinuation. Availability of resuscitation equipment must be ensured as a standard precaution.			
Frequency:	Docetaxel on Day 1, capecitabine taken from Days 1 to 14, every 21 days, for 6 cycles			

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Reason for Update: LCA Protocol Development	Approved by LCA Joint Delivery Subgroup Co-Chairs: Pauline McCalla & Rebecca Johl
Prepared by: Lisa Yuen	Approved by LCA Medicines & Chemotherapy Steering Group Chair: Jamie Ferguson
Second check by: Laura Cameron	Date prepared: November 2014 Review Date: November 2016

Pre-medication:	Oral dexamethasone 8mg BD for 3 days, starting the day before docetaxel administration to reduce the incidence and severity of fluid retention and hypersensitivity reactions. If the patient has not taken the oral pre-medication, clinicians may prescribe dexamethasone IV 20mg, chlorphenamine IV 10mg and ranitidine IV 50mg to be administered 1 hour prior to chemotherapy. *(note: there is no data available to support the use of IV steroids in this setting, responsibility remains with the prescribing clinician).* Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever.
Anti- emetics:	Moderate emetogenicity Follow Local Anti-emetic Policy
Supportive medication:	Diarrhoea can be managed with loperamide Mouthcare as per Local Policy
Extravasation:	Docetaxel: vesicant Docetaxel should be administered with appropriate precautions to prevent extravasation. If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation
Regular investigations:	Prior to cycle 1

FBC	Day 1 (within 14 days)
LFTs	Day 1 (within 14 days)
U&Es	Day 1 (within 14 days)

Prior to Day 1 (all cycles)

FBC	Day 1 (within 72 hours)
LFTs	Day 1 (within 72 hours)
U&Es	Day 1 (within 72 hours)
CT scan	Every 3 cycles

Toxicities:	Neutropenia (reversible), anaemia, nausea, vomiting, diarrhoea, stomatitis, asthenia, peripheral neuropathy, hypersensitivity reactions, fluid retention, cutaneous reactions, palmar-plantar

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erythrodysesthesia, alopecia, nail disorder, cystoid macular oedema, ovarian failure, infertility.

DOSE MODIFICATIONS

Haematological Toxicity

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Dose
≥ 1.5	&	≥ 100	100%
< 1.5	& / or	< 100	Delay for 1 week. Repeat FBC - if recovered to above these levels, resume treatment with 100% doses Consider dose reduction for >1 delay.

- Dose reduction and / or delay is more appropriate in the advanced setting
- If during the preceding cycle, the patient has experienced neutrophils < 0.5 x 10^9/L or has febrile neutropenia diagnosed, GCSF should be considered.
- If platelets persistently < 100 x 10^9/L on Day 1 despite dose delay - seek Consultant advice and consider dose reduction by 25%

Non-haematological Toxicities

Renal Impairment

Docetaxel No dose adjustment required

Capecitabine

Creatinine Clearance	Capecitabine Dose
> 50ml/min	100%
30 - 50	Give 75% dose
< 30	Omit

Hepatic Impairment

Docetaxel

ALP		AST / ALT		Bilirubin (µmol/L)	Docetaxel Dose
≤ 2.5 x ULN	&	≤ 1.5 x ULN	& / or		100% dose
2.5 – 6 x ULN		1.6 – 3.5 x ULN			75% dose
> 6 x ULN		> 3.5 x ULN		> 22	Not recommended. Discuss with consultant.

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Capecitabine

In the absence of safety and efficacy data in patients with hepatic impairment, capecitabine use should be carefully monitored in patients with mild to moderate liver dysfunction, regardless of the presence or absence of liver metastasis.

Bilirubin (treatment-related elevation)		**ALT / AST (treatment-related elevation)**	**Capecitabine Dose**
> 3 x ULN	**or**	> 2.5 x ULN	Omit until recovers and discuss with consultant

Dose modifications for other toxicities as appropriate

Docetaxel

NCI CTCAE Grade	**Cutaneous Reactions**	**Docetaxel Dose**
1	Erythema without associated symptoms	100%
2	Localised erythema of the palms of the hands and soles of the feet with oedema followed by desquamation	Consider dose reduction to 75% dose
3	Severe, generalised eruptions followed by desquamation	Delay until recovery to ≤ Grade 2, reduce by 25% For 2nd occurrence, discontinue docetaxel
4	Generalised exfoliative, ulcerative or bullous dermatitis	Discontinue docetaxel permanently

NCI CTCAE Grade	**Sensory Neuropathy**	**Docetaxel Dose**
1	Paraesthesia (including tingling), but not interfering with function	100% dose
2	Paraesthesia interfering with function, but not interfering with activities of daily living	Consider dose reduction to 75% dose
3	Paraesthesia interfering with activities of daily living	Delay until recovery to ≤ Grade 2, reduce by 25% For 2nd occurrence, discontinue docetaxel

4	Disabling	Discontinue docetaxel permanently

Capecitabine

NCI CTCAE Grade		Capecitabine Dose
1	Any appearance	100%
2	1st appearance	Interrupt until resolved to Grade 0-1, then give 100%
	2nd appearance	Interrupt until resolved to Grade 0-1, then give 75%
	3rd appearance	Interrupt until resolved to Grade 0-1, then give 50%
	4th appearance	Discontinue permanently
3	1st appearance	Interrupt until resolved to Grade 0-1, then give 75%
	2nd appearance	Interrupt until resolved to Grade 0-1, then give 50%
	3rd appearance	Discontinue permanently
4	1st appearance	Discontinue or if clinician considers in best interest of patient to continue, interrupt until resolved to Grade 0-1, then give 50%
	2nd appearance	Discontinue permanently

Location of regimen delivery:

Outpatient setting.
Availability of resuscitation equipment must be ensured as a standard precaution.
Capecitabine to be supplied to the patient for oral self-administration. Ensure that the patient has an information pack and the treatment plan.

Comments:

Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced metabolism of capecitabine. Ensure patient is informed of action to take if signs of toxicity (e.g. severe mucositis, diarrhoea) develop within the first few days of treatment, as this is often an early indication of DPD deficiency.

Severe skin reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported during treatment with capecitabine. Some cases were fatal. Capecitabine should be discontinued if a serious skin reaction occurs, and the reaction should be treated promptly

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Capecitabine contains anhydrous lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Drug interactions:

Docetaxel

Concomitant administration of substrates, inducers or inhibitors of cytochrome P450-3A e.g. ciclosporin, terfenadine, ketoconazole, erythromycin etc may alter the pharmacokinetics of docetaxel presenting a potential interaction.

Capecitabine

Allopurinol: avoid concomitant use (reduced efficacy of capecitabine)
Folinates: avoid concomitant use (enhanced capecitabine toxicity)
Phenytoin: monitor plasma phenytoin levels (increase phenytoin level)
Warfarin / coumarin anticoagulants: switch to low molecular weight heparin (altered coagulation parameters and /or bleeding including death)

References:

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