LONDON CANCER ALLIANCE West and South

Breast Pathway Group – Gemcitabine & Paclitaxel in Advanced Breast Cancer

Indication:	Alternative palliative treatment for advanced breast cancer in patients where docetaxel monotherapy or docetaxel/capecitabine are also considered appropriate			
Regimen details:	Paclitaxel	175 mg/m^2	IV	Day 1
	Gemcitabine	1250 mg/m^2	IV	Day 1 and Day 8
Administration:	Paclitaxel in 500ml Sodium Chloride 0.9% or Glucose 5% IV over 3 hrs Gemcitabine in 100-500ml Sodium Chloride 0.9% IV over 30 min Paclitaxel to be given via non-PVC infusion bag, with a 0.22 micron in-line filter. Paclitaxel must be diluted to a concentration of 0.3-1.2mg/ml to maintain stability in clinical practice.			
Frequency:	Day 1 & 8, every 21 days, for up to 6 cycles			
Pre-medication:	Dexamethasone	20mg	IV	30 – 60 minutes prior to paclitaxel administration
	OR			
	Dexamethasone	20mg	PO	6 hours and 12 hours prior to paclitaxel administration
	Chlorphenamine	10mg	IV	30-60 minutes prior to paclitaxel administration over at least 1 minute
	Ranitidine	50mg	IV	30-60 minutes prior to paclitaxel administration over at least 2 minutes
Anti- emetics:	Moderate emetogenicity Follow Local Anti-emetic Policy			
Supportive medication:	Mouthcare as per local policy			

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

Extravasation:	Paclitaxel – Vesicant Gemcitabine – Non-vesicant Paclitaxel 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 investigation:	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 8 (all cycles): FBC Day 8 (within 48 hours) 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)
Toxicities:	Myelosuppression, alopecia, mucositis, somnolence, proteinuria and haematuria, allergic skin rashes, oedema, arthalgia or myalgia, influenza like symptoms

DOSE MODIFICATIONS

Haematological Toxicity

Day 1

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

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Prior day 8 – Gemcitabine

Neutrophils (x 10^9/L)		Platelets (x 10^9/L)	Gemcitabine Dose
≥ 1.0	**&**	≥ 100	100% dose
0.5 – 0.9	**or**	75 - 100	75% dose
< 0.5	**or**	< 75	Omit Re-assess on day 1 of the next cycle

Non-haematological Toxicities

Renal Impairment

Creatinine Clearance	Gemcitabine Dose	Carboplatin Dose
> 30ml/min	100%	Contra-indicated if GFR <20ml/min.
< 30ml/min	Use with caution, however, no specific dosing recommendations have been made.	

Hepatic Impairment

Bilirubin (μmol/L)		ALT / AST	Paclitaxel Dose (mg/m^2)	Gemcitabine Dose
<22	**&**	< 10 x ULN	175	100% dose
22-26	**&**	Any	135	100% dose
27-51			75	AST elevations do not seem to cause dose limiting toxicities If bilirubin >27μmol/L, initiate treatment with 800mg/m^2
>51			50	

Dose modifications for other toxicities as appropriate

PERIPHERAL NEUROPATHY - Paclitaxel

NCI CTCAE Grade	Sensory Neuropathy	Paclitaxel 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	80% dose
3	Paraesthesia interfering with activities of daily living	Omit paclitaxel
4	Disabling	Discontinue paclitaxel

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		permanently

ARTHRALGIA / MYALGIA

NCI CTCAE Grade	Arthralgia/Myalgia	Action
1	Joint and muscle pain, not interfering with function	Consider use of NSAIDs
2	Joint and muscle pain, interfering with function, but not interfering with activities of daily living	Consider use of NSAIDs

Gemcitabine

Other toxicities	Dose
Grade 3-4 lethargy	Consider gemcitabine 25% dose reduction If does not respond to dose reduction: Stop treatment

Location of regimen delivery:

Outpatient setting
Availability of resuscitation equipment must be ensured as a standard precaution.

Comments:

Haemolytic anaemia
Gemcitabine should be discontinued at the first signs of any evidence of micro-angiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH, which may indicate development of haemolytic uraemic syndrome. Renal failure may not be reversible, even with discontinuation of therapy, and dialysis may be required

Drug interactions:

Paclitaxel and Gemcitabine are radiosensitisers
Increased risk of bleeding with warfarin. Caution with concurrent administration of active substances metabolised in the liver due to potential inhibition of the metabolism of paclitaxel. The metabolism of paclitaxel is catalysed, in part, by cytochrome P450 isoenzymes CYP2C8 and 3A4.

References:

Summerhayes M et al, Practical Chemotherapy a multidisciplinary guide 2003
Summary of Product Characteristics. Gemcitabine. Eli Lilly and Company Limited. Feb2006.

Summary of Product Characteristics. Paclitaxel. Wockhardt UK Ltd,Mayne Pharma Plc,2006

BCCA Protocol summary for Palliative Therapy for Metastatic Breast Cancer using Gemcitabine and Paclitaxel. Oct 2005.

CCO Formulary. Gemcitabine-Paclitaxel chemotherapy. Revised July 2006.

Micromedex review. Gemcitabine, Paclitaxel.

Khoo K.S et al. Eur J Cancer (2006) 42;12:1797-1806.

Colomer R. et al, Eur J Cancer suppl. (2005) 3;5:9-16.

Allouache D.et al, A phase II study. BMC Cancer (2005)5;151.

Moen M.D.et al, Am J Cancer (2005) 4;5:327-333

British Oncology Pharmacy Association (BOPA) Guidelines for Dose Adjustment of Cytotoxics in Hepatic and Renal impairment January 2009 accessed from www.bopawebsite.org

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