LONDON CANCER ALLIANCE West and South

Breast Pathway Group – MVCarbo (Mitomycin C / Vinblastine / Carboplatin) in Advanced Breast Cancer

Indication: Fourth line therapy in patients with advanced breast cancer previously treated with anthracyclines or taxanes

Regimen details:

Mitomycin C	8mg/m^2 (max. 14mg)	IV	Day 1 **(cycles 1, 2, 4 & 6 only)**
Vinblastine	6mg/m^2 (max. 10mg)	IV	Day 1
Carboplatin	AUC 5*	IV	Day 1

*Carboplatin dose is calculated using the Calvert formula:
Dose = Target AUC x (25 + GFR)
GFR should be measured using EDTA wherever possible. If not available, Cockcroft & Gault equation may be used to estimate GFR; if the calculated GFR <60 or >120ml/min measure EDTA clearance or creatinine clearance before prescribing. Monitor trends in serum creatinine between treatments: if >25% from baseline value re-calculate GFR using the Cockcroft & Gault equation.

Administration:
Mitomycin C IV bolus injection via a fast-running Sodium Chloride 0.9% infusion
Vinblastine in 50 ml Sodium Chloride 0.9% IV infusion over 5 – 10 minutes
Carboplatin in 500ml Glucose 5% IV over 1 hour

Carboplatin Infusion-related hypersensitivity reactions may occur, such as flushing, rash with or without pruritus, chest tightness, dyspnoea and fever or chills 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.

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

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Frequency: Day 1, every 21 days, for 6 cycles

Pre-medication: Paracetamol / Chlorphenamine / Hydrocortisone can be given for administration-related reactions such as chills / fever

Anti- emetics: Moderate emetogenicity
Follow local anti-emetic policy

Extravasation: Mitomycin C: vesicant
Vinblastine: vesicant
Carboplatin: irritant
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)
EDTA	Prior to cycle 1

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; nausea; vomiting; anorexia; diarrhoea; peripheral neuropathy; alopecia; hypersensitivity reactions

DOSE MODIFICATIONS

Haematological Toxicity

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

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Non-haematological Toxicities

Renal Impairment

Mitomycin C

GFR (ml/min)	Mitomycin C Dose
> 10	100%
< 10	75%

Vinblastine: No dose reduction necessary

Carboplatin: Contraindicated if creatinine clearance is < 20 ml/min

Hepatic Impairment

Mitomycin C: Dose reduction probably not necessary. Discuss dose with Consultant when AST levels > 2 x ULN

Vinblastine

Bilirubin (µmol/L)		AST/ALT (units)	Vinblastine Dose
26 – 51	**or**	60 – 180	Give 50%
> 51	**&**	Normal	Give 50%
> 51	**&**	> 180	Omit

Carboplatin: No dose reduction necessary

Location of regimen delivery: Out-patient setting
Availability of resuscitation equipment must be ensured as a standard precaution.

Comments:

Haemolytic-uremic syndrome – Mitomycin C

A syndrome of renal failure and microangiopathic haemolytic anaemia with hypertension and neurological symptoms (haemolytic-uremic syndrome) has been reported in 10% patients. This syndrome usually appears after 6 months of therapy of Mitomycin C, and may be exacerbated with blood transfusions. Patients should be monitored for development of renal failure or haemolysis.

Pulmonary toxicity – Mitomycin C

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Pulmonary toxicity typically presents as dyspnoea and non-productive cough. Administration of vinca alkaloids to patients who have previously or simultaneously received Mitomycin C may cause severe or life-threatening dyspnoea and bronchospasm within minutes to hours. Bronchodilators, steroids and/or oxygen have produced symptomatic relief

Drug interactions:

Carboplatin

Concurrent therapy with nephrotoxic drugs or ototoxic drugs such as aminoglycosides, may increase / exacerbate toxicity due to carboplatin induced changes in renal clearance.

Mitomycin C

Clozapine: increased risk of agranulocytosis, avoid concomitant use
Tamoxifen: haemolytic anaemia, thrombocytopenia, renal impairment
Vinca alkaloids: shortness of breath and bronchospasm. Bronchodilators, steroids and/or oxygen have produced symptomatic relief

Vinblastine

Anticonvulsants: serum levels of anticonvulsants may be reduced by vinblastine
Cisplatin: cause higher plasma concentration of vinblastine
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Erythromycin: may increase the toxicity of vinblastine, avoid concomitant use
Itraconazole: increased risk of neurotoxicity
Mitomycin C: acute respiratory distress and pulmonary infiltration

References:

Urruticoechea A *et al*. British Journal of Cancer (2005)92: 475-479
Paccagnella A *et al*. Cancer (1996) 78: 1701-1707
UCLH-Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009
UCLH-Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009
LCA Breast Cancer Clinical Guidelines October 2013

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