MVCarbo: Mitomycin C / Vinblastine / Carboplatin in Advanced Breast Cancer

Indication: Fourth line palliative therapy in patients with Metastatic Breast Cancer previously treated with anthracyclines or taxanes

Regimen details: Mitomycin C 8mg/m² (max. 14mg) IV D1 (on cycles 1, 2, 4 and 6 only) 
Vinblastine 6mg/m² (max. 10mg) IV D1 
Carboplatin AUC 5 (EDTA) IV D1 (see Comments)

Administration: Mitomycin C IV Bolus injection via a fast-running Sodium Chloride 0.9% infusion 
Vinblastine in 50mls Sodium Chloride 0.9% IV infusion over 5 – 10 minutes 
Carboplatin in 500mls Glucose 5% IV over 30 – 60 minutes

Frequency: 21 days, 6 cycles

Extravasation: Mitomycin C and Vinblastine are vesicants 
Carboplatin: Non-vesicant

Anti-emetics: Moderate emetogenic 
Follow Local Anti-emetic Policy

Regular investigations: FBC D1 
LFTs D1 
U&Es D1 
CT scan Every 3 cycles 
EDTA Prior to 1st cycle 
Repeat if renal function becomes abnormal

Comments: Carboplatin: The total dose should be calculated in milligrams, using the Calvert formula 
Dose= Target AUC x (25 + GFR) 
GFR should be calculated by EDTA prior to cycle 1. For subsequent cycles the GFR can be calculated by using the Cockcroft & Gault equation; if the calculated GFR < 60 or > 120ml/min, measure EDTA clearance before prescribing. Monitor trends in serum creatinine between treatments: if 25% from baseline value, re-calculate GFR using the Cockcroft & Gault equation or measure EDTA clearance

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
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.

**DOSE MODIFICATIONS**

**Haematological Toxicity**

**Day 1**

| WBC < 3.0 x 10^9/l or Neutrophils < 1.5 x 10^9/l or Platelets < 100 x 10^9/l | Delay for 1 week. Repeat FBC - If within normal parameters, resume treatment and discuss possible dose reduction with Consultant |

**Renal Impairment:**

- **Mitomycin C:** Renal function should be monitored before each cycle.

<table>
<thead>
<tr>
<th>GFR (ml/min)</th>
<th>Mitomycin C Dose</th>
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<tbody>
<tr>
<td>&gt; 10</td>
<td>Give 100%</td>
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<tr>
<td>&lt; 10</td>
<td>Give 75%</td>
</tr>
</tbody>
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**Carboplatin** is contraindicated if CrCl < 20ml/min

**Hepatic Impairment:**

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

**Carboplatin:** No dose reduction necessary.

- **Vinblastine:** It is excreted principally by the liver, it may be necessary to reduce Vinblastine dose in the presence of significantly impaired hepatic or biliary function.

<table>
<thead>
<tr>
<th>Bilirubin (µmol/L)</th>
<th>AST/ALT (units)</th>
<th>Vinblastine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 – 51 or 60 – 180</td>
<td>Give 50%</td>
<td></td>
</tr>
<tr>
<td>&gt; 51 and Normal</td>
<td>Give 50%</td>
<td></td>
</tr>
<tr>
<td>&gt; 51 and &gt; 180</td>
<td>Omit</td>
<td></td>
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</tbody>
</table>
DOSE MODIFICATIONS FOR OTHER TOXICITIES AS APPROPRIATE

PERIPHERAL NEUROPATHY- VINBLASTINE

In instances of Grades 1 or 2 peripheral neuropathy, the Vinblastine dose was given as 50% dose
For Grade 3 or 4 neuropathy, discontinue Vinblastine

Toxicities: Myelosuppression; nausea; vomiting; anorexia; diarrhoea; peripheral neuropathy; alopecia (reversible); hearing impairment; nephrotoxicity; haemolytic-uremic syndrome; pulmonary toxicity

Drug interactions: Mitomycin C
- Clozapine : increased risk of agranulocytosis, avoid concomitant use
- Tamoxifen : haemolytic anaemia, thrombocytopenia, renal impairment
- Vinca alkaloids : shortness of breath and bronchospasm
Bromchodilators, 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

Carboplatin
- Aminoglycoside antibiotics : increased risk of nephrotoxicity and ototoxicity
- Clozapine : increased risk of agranulocytosis, avoid concomitant use
- Diuretics : increased risk of nephrotoxicity and ototoxicity
- Nephrotoxic drugs : increased incidence of renal dysfunction ; not recommended
- Phenytin : reduced absorption of the antiepileptic
- Warfarin : increased anticoagulant effect of warfarin

References:
www.medicines.org.uk
Royal Marsden Hospital. Breast Unit guidelines. MVCarbo regimen. October 2008
GSTT guidelines for treating nausea and vomiting in adult patients. September 2007
UCLH- Dosage Adjustment for Cytotoxics in Renal Impairment. November 2003
UCLH- Dosage Adjustment for Cytotoxics in Hepatic Impairment. November 2003
CTCAE v3.0. August 2006