CARBOPLATIN & ETOPOSIDE

First-line in small cell lung cancer and other primary tumours with small cell histology
May also be used in bronchial neuroendocrine tumours and Merkel cell carcinoma
Third line use in glioblastoma patients who are still fit for further treatment and have no problems with myelosuppression

Drug / Dosage:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Route</th>
<th>Day(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC 5</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Etoposide</td>
<td>100mg/m²</td>
<td>IV</td>
<td>Day 1</td>
</tr>
<tr>
<td>Etoposide</td>
<td>200mg/m²</td>
<td>PO</td>
<td>once daily on Day 2 and Day 3</td>
</tr>
</tbody>
</table>

Primary G-CSF prophylaxis s/c once daily for 5 days, starting on Day 5

Administration:

Carboplatin diluted in 250ml 5% glucose over 30 - 60 minutes
Etoposide IV diluted in 500 – 1000ml 0.9% sodium chloride and infused over a minimum of 1 hour.
Oral etoposide is available as 50mg and 100mg soft capsules.
Each dose should be swallowed whole on an empty stomach or an hour before food.

As an alternative for patients who cannot swallow capsules;
Etoposide 100mg/m² IV on Days 2 and 3 can be prescribed or
Etopophos® injection can be taken orally at a dose of 70%¹ of the usual oral capsule dose on Day 2 and Day 3 (unlicensed use).
Syringes for oral use must be prepared in an aseptics unit.
The injection is unpleasant to take, so advise to dilute with orange juice or similar immediately prior to administration, to mask the taste.

Radiotherapy:

For SCLC patients with limited stage disease, concurrent radiotherapy may be administered with one of the cycles as follows:
40Gy in 15 fractions (2.67 Gy/#) over 3 weeks, on weekdays only.
This is usually initiated on Day 1 of the 2nd or 3rd cycle of chemotherapy.
Radiotherapy is to be given after chemotherapy on Day 1 of the cycle.

Frequency:

3 weekly cycle for 4 - 6 cycles

Main Toxicities:

myelosuppression; alopecia; ovarian failure / infertility

Anti-emetics: highly emetogenic

Patients with GBM:

These patients are often on long-term dexamethasone, and their daily dose of dexamethasone can be taken into account when prescribing and administering anti-emetic dex;

- for patients on a daily dose totalling 8mg or more of dexamethasone, no extra dexamethasone needs to be prescribed as an anti-emetic
- for patients on a total daily dose of less than 8mg dexamethasone, the daily dose needs to be increased to 8mg daily on Days 1 to 4 of the cycle only.
- On Days 2, 3 and 4, the dose may either be taken as 4mg bd, or the total dose may be taken once daily in the morning, whichever the patient is used to, or prefers.
Reason for Update: Cipro removed; primary G-CSF added; volume of etoposide changed; only Etopophos IV brand for oral use, with qualifying statement for dose conversion added

Approved by Consultant: Dr A Mehta

Approved by Lead Chemotherapy Nurse: S Wills-Percy

Date: 20.4.17

Checked by: C Tucker

Extravasation: non-vesicants

Regular Investigations:
- FBC: Day 1
- LFTs: Day 1
- U&Es: Day 1
- EDTA: Prior to 1st cycle
- CT scan: after 2nd cycle (after 3rd cycle in GBM)

Comments:
Carboplatin dose should be calculated using the Calvert Formula:
Dose = Target AUC x (25 + GFR)
Cycle 1 may be given using the Cockcroft and Gault formula to predict creatinine clearance if the EDTA is not yet available. When using C&G, a “cap” of 125 ml/min should be used for carboplatin dose calculations.

Carboplatin dose should be re-calculated using the EDTA result for subsequent cycles (do not “cap”). EDTA should only be repeated if there is a 30% change in serum creatinine.

Dose Modifications

Haematological Toxicity:
- Neutrophils < 1.5 x 10^9/l: Delay for 1 week. Repeat FBC and, if within normal parameters, resume treatment.
- Platelets < 100 x 10^9/l

If significant myelosuppression, consider reduction of oral etoposide dose to 100mg/m^2 on Day 2 and Day 3.

Renal Impairment: Carboplatin is contra-indicated if CrCl < 20 ml/min.

<table>
<thead>
<tr>
<th>CrCl (ml/min)</th>
<th>Etoposide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>Give 100%</td>
</tr>
<tr>
<td>15 – 50</td>
<td>Give 75%</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>Give 50%</td>
</tr>
</tbody>
</table>

Hepatic Impairment: Creatinine clearance is the strongest predictor of etoposide clearance. There is conflicting information about dose reduction with hepatic impairment. Use the table below but, if in doubt, discuss with Consultant.

<table>
<thead>
<tr>
<th>Bilirubin (µmol/l)</th>
<th>AST (units/l)</th>
<th>Etoposide Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 – 51 or &gt; 51</td>
<td>60 - 180</td>
<td>Give 50% dose</td>
</tr>
<tr>
<td>or &gt; 180</td>
<td></td>
<td>Clinical decision</td>
</tr>
</tbody>
</table>

References:

^1 Use of 70% of capsule dose is as historical practice with other etoposide intravenous products, to allow for increased bioavailability over the capsules; in the absence of published or unpublished data regarding bioavailability of Etopophos orally compared to etoposide capsules, our Consultants have agreed to continue this practice.