CARBOPLATIN HYPERSENSITIVITY GUIDELINES AND DESENSITISATION REGIMEN

The risk of developing a carboplatin hypersensitivity reaction (HSR) is related to increased exposure to the drug, with a peak incidence observed during cycle 2 of a patient’s second course of carboplatin-based treatment.¹

To minimise the incidence and severity of a HSR, it has been decided to standardise practice such that all carboplatin doses are infused over a minimum of 1 hour.

Grading of Hypersensitivity Reactions (HSRs)

<table>
<thead>
<tr>
<th>Symptoms of Allergic Reaction (any of)</th>
<th>Grade 1 MILD</th>
<th>Grade 2 MODERATE</th>
<th>Grade 3 SEVERE</th>
<th>Grade 4 Life-threatening</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient flushing or rash, temp &lt; 38⁰</td>
<td></td>
<td></td>
<td>Symptomatic bronchospasm; allergy-related oedema / angio-oedema; hypotension OR prolonged unresolving moderate symptoms.</td>
<td>Anaphylaxis</td>
<td>Death</td>
</tr>
</tbody>
</table>

+ Back pain is a common symptom - if it presents as the only symptom, treat as Grade 1

Grade 1-2 HSR to carboplatin: following a mild to moderate HSR, re-challenge should be carried out as follows:

a) Patients who recover within 30 minutes of receiving IV hydrocortisone and IV chlorphenamine;
   - the infusion may be re-started on the same day at 50% rate for 30 minutes, then increased up to 100% rate again.
   - For subsequent treatment cycles, use increased oral and IV HSR prophylaxis as below, along with a standard carboplatin bag for infusion, given over 2 – 4 hours.

b) Patients whose symptoms do not resolve 30 minutes post IV hydrocortisone and IV chlorphenamine;
   - re-book patient to return one week later (if < 20% dose given before HSR) and supply oral prophylaxis as below to start the day before administration.
   - Also prescribe IV prophylaxis as below, along with a standard carboplatin bag, given over 2 – 4 hours.
   - If there is any further Grade 1 – 3 reaction, the desensitisation regimen should be considered for any further doses.

HSR Prophylaxis to be used before carboplatin re-challenge:

Starting 24 hours before carboplatin i.e. Day -1:
- Cetirizine 10mg po om x 2 doses
- Ranitidine 150mg po bd x 3 doses
- Dexamethasone 8mg po bd x 3 doses

PLUS, 30 minutes before carboplatin:
- Chlorphenamine 10mg IV
- Ranitidine 50mg IV
- Dexamethasone 8mg IV

Grade 3 HSR to carboplatin: see overleaf

Grade 4 HSR to carboplatin: for any life-threatening Grade 4 reaction, the patient should not be re-challenged with carboplatin, and substitution with cisplatin should be considered.
CARBOPLATIN DESENSITISATION REGIMEN

For all subsequent cycles after a Grade 3 (severe) reaction to carboplatin, depending on an assessment of the patient and a detailed discussion with the patient regarding the risks and benefits.

Note: For patients on 3-weekly paclitaxel and carboplatin, the paclitaxel should be given one Day 1 and the carboplatin desensitisation on Day 2.

Drugs/Dosage/ Administration: Starting 24 hours before carboplatin i.e. Day -1:
- Cetirizine 10mg po om x 2 doses
- Ranitidine 150mg po bd x 3 doses last dose on the morning of carboplatin
- Dexamethasone 8mg po bd x 3 doses administration

PLUS, 30 minutes before Carboplatin:
- Chlorphenamine 10mg IV
- Ranitidine 50mg IV
- Dexamethasone 8mg IV

Carboplatin IV infusion:

Bag 1: Carboplatin 1% of total dose (to nearest mg) in 250 ml glucose 5%
- Infuse 25 ml over 30 minutes
- then
- infuse 225 ml over 30 minutes

Bag 2: Carboplatin 10% of total dose (to nearest mg) in 100 ml glucose 5%
- Infuse 100 ml over 30 minutes

Bag 3: Carboplatin 89% of total dose in 500 ml glucose 5%
- Infuse 500 ml over 1 hour

Calculate total dose in mg, then divide dose between Bags 1, 2 and 3 as follows:

Patient must be monitored at least every 15 minutes throughout, and there must be adequate nursing and medical staff available during the whole desensitisation period.

If a reaction occurs at any step, stop the infusion and administer chlorphenamine 10mg IV and hydrocortisone 100mg IV. Start appropriate monitoring and supportive care.

For any Grade 1 – 2 reaction:
- observe for 30 minutes:
- If symptoms resolve completely after 30 minutes, re-start the infusion at 50% of the pre-reaction rate and complete the remaining steps at 50% rate also i.e. each dose level over 1 hour and the final dose level over 2 hours. Follow this slower schedule for subsequent cycles.
- If symptoms do not resolve after 30 minutes, or if they recur, do not re-start infusion.
- Consider a switch to cisplatin, or an alternative regimen.

For any Grade 3 – 4 reaction:
- do not re-start the infusion and consider a switch to cisplatin, or an alternative regimen.

References:
Adapted from RMH Management Protocol for adult Hypersensitivity Reactions associated with systemic anti-cancer therapy.
- Makrilia et al; Hypersensitivity Reactions Associated with Platinum Antineoplastic Agents: A Systematic Review; Metal Based Drugs 2010: 207084
- ICON 8 trial, Clinical management Guidance, May 2011

Reference:
Adapted from RMH Management Protocol for adult Hypersensitivity Reactions associated with systemic anti-cancer therapy.
- Makrilia et al; Hypersensitivity Reactions Associated with Platinum Antineoplastic Agents: A Systematic Review; Metal Based Drugs 2010: 207084
- ICON 8 trial, Clinical management Guidance, May 2011