Chemotherapy Protocol

LUNG CANCER – NON-SMALL CELL (NSCLC)

CARBOPLATIN-VINORELBINE

(Intravenous and Oral)

Regimen

- NSCLC – Carboplatin-Vinorelbine (Intravenous and Oral)

Indication

- First line therapy of stage III or IV NSCLC
- WHO Performance status 0, 1, 2
- Palliative intent

Toxicity

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Neuropathy, thrombocytopenia</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>Neuropathy, stomatitis, transient elevation of LFTs, pain, constipation</td>
</tr>
</tbody>
</table>

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Disease

- A baseline chest x-ray should be performed before starting treatment and up to date (ideally within 1 month) cross section imaging should also be performed

Regimen

- EDTA or calculated creatinine clearance before the first cycle
- FBC, LFTs and U&Es day 1 and 8
- A chest x-ray should be performed before each cycle

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.
In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

**Haematology**

Prior to prescribing cycle one the following treatment criteria must be met:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Eligible Level</th>
</tr>
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<tbody>
<tr>
<td>Neutrophil</td>
<td>Greater than or equal to 1.5x10^9/L (unless due to bone marrow impairment)</td>
</tr>
<tr>
<td>Platelets</td>
<td>Greater than or equal to 100x10^9/L (unless due to bone marrow impairment)</td>
</tr>
</tbody>
</table>

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL

If the neutrophils are less than 1.5x10^9/L, then in the first instance delay treatment for 7 days. If counts recover at this point continue at the initial dose. If counts remain low continue with treatment using a 20% dose reduction. If the myelosuppression recurs despite this dose reduction stop treatment.

If the platelets are less than 100x10^9/L then in the first instance delay treatment for 7 days. If the counts recover at this point continue at the initial dose. If the counts still fall within this range continue using a 20% dose reduction. If the platelet level falls below 50x10^9/L reduce the dose by 50%.

Dose adjustments for day eight should be made according to local practice guidelines or procedures.

**Hepatic Impairment**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>No dose reduction necessary</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>For the intravenous preparation consider a dose reduction to 20mg/m² in severe liver impairment</td>
</tr>
<tr>
<td></td>
<td>For the oral preparation consider a dose of 50mg/m²/week in moderate liver impairment</td>
</tr>
</tbody>
</table>
Renal Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>Significant changes in GFR (of more than 10%) may require dose adjustment</td>
</tr>
<tr>
<td></td>
<td>Do not administer if the CrCl is less than 20ml/min</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>No dose adjustment is necessary</td>
</tr>
</tbody>
</table>

Regimen

The starting dose of carboplatin AUC6 is used with calculated GFR. AUC5 may be considered with EDTA clearance, seek advice from the appropriate consultant before prescribing. The recommended maximum dose when using a calculated creatinine clearance at AUC6 is 900mg. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant.

It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

The maximum dose of oral vinorelbine is 120mg for the 60mg/m² dose and 160mg for the 80mg/m² dose. The capsules are available in 20mg and 30mg strengths. It must be clear to all professionals and patients taking this treatment that it is a short term therapy that must not be supplied from primary care.

The maximum dose of intravenous vinorelbine is 60mg.

21 day cycle for 4 cycles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>AUC6</td>
<td>1</td>
<td>Intravenous infusion in 500ml glucose 5% over 60 minutes</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>25mg/m² (max dose 60mg)</td>
<td>1</td>
<td>Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>60mg/m² (max dose 120mg)</td>
<td>8</td>
<td>Oral</td>
</tr>
</tbody>
</table>

Dose Information

- Carboplatin will be dose rounded to the nearest 50mg (up if halfway)
- Vinorelbine (intravenous) will be dose banded as per the CSCCN agreed bands
- Vinorelbine (oral) will be dose rounded to the nearest 20mg (up if halfway)
Administration

Extravasation

- Carboplatin – irritant
- Vinorelbine - vesicant

Other

- Oral vinorelbine capsules must be swallowed whole with food without chewing, sucking or dissolving the capsule.

Additional Therapy

- Antiemetics
  15-30 minutes prior to chemotherapy on day one only;
  - ondansetron 8mg oral or intravenous
  - dexamethasone 8mg oral or intravenous
  As take home medication;
  - dexamethasone 4mg twice a day oral for 3 days
  - metoclopramide 10mg three times a day when required
  15–30 minutes prior to vinorelbine on day eight only;
  - metoclopramide 10mg oral
- Gastric protection with PPI or H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed
- Prophylactic antibiotics can be considered if required

Additional Information

- The National Patient Safety Alert on oral chemotherapy (NPSA/2008/RRR001) must be followed in relation to oral vinorelbine.

Coding

- Procurement – X70.4
- Delivery – X72.3 / X72.4

References
REGIMEN SUMMARY

Carboplatin (AUC6)-Vinorelbine IV/PO

Day One

1. Dexamethasone 8mg oral or intravenous
2. Ondansetron 8mg oral or intravenous
3. Vinorelbine 25mg/m\(^2\) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
4. Carboplatin AUC6 intravenous infusion in 500ml glucose 5% over 60 minutes

Take Home Medicines

5. Dexamethasone 4mg twice a day oral for 3 days starting on day two of the cycle
6. Metoclopramide 10mg three times a day when required oral

Day Eight

7. Metoclopramide 10mg oral
8. Vinorelbine 60mg/m\(^2\) oral
<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Amendment</th>
<th>Written By</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>9th Jan 2014</td>
<td>Header changed to NHS badge AUC6 added to name and “and” replaced with dash Adverse effects put in table and toxicity removed &gt;and &lt; written in full Dose modification tabulated Renal and hepatic function tabulated. Vinorelbine information updated from SPC Carboplatin paragraph amended under regimen Regimen tabulated Vinorelbine changed to intravenous bolus over 10 minutes Twice daily now twice a day Bolus removed from injection Regimen name added to summary Metoclopramide dose changed to 10mg Starting on day two of the cycle added to dexamethasone Document control tabulated Hospital representation and disclaimer added</td>
<td>Dr Deborah Wright Pharmacist</td>
<td>Donna Kimber Pharmacy Technician</td>
</tr>
<tr>
<td>1.1</td>
<td>23rd Sept 2010</td>
<td>Font changed to Arial Header altered to include “Strength through Partnership” Drug names given capitals in regimen Extravasation moved to under Administration Information Footer changed to include regimen name and review date removed Standard paragraph added to introduction in dose modifications Dose modifications format (not information) changed Dose information added to reflect super user agreements Granisetron removed from antiemetics Coding added Summary page added</td>
<td>Dr Deborah Wright Pharmacist</td>
<td>Donna Kimber Pharmacy Technician</td>
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</table>
This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts:

- Hampshire Hospitals NHS Foundation Trust
- NHS Isle of Wight
- Portsmouth Hospitals NHS Trust
- Salisbury Hospitals NHS Foundation Trust
- University Hospital Southampton NHS Foundation Trust
- Western Sussex Hospitals NHS Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.