Chemotherapy Protocol

LYMPHOMA

GEMCITABINE-VINORELBINE

**Regimen**

- Lymphoma – Gemcitabine-Vinorelbine

**Indication**

- Relapsed or refractory Non-Hodgkin’s Lymphoma
- Relapsed or refractory Hodgkin’s Lymphoma

**Toxicity**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza-like symptoms, radiosensitising</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>Neuropathy, stomatitis, transient elevation of LFTs, pain, constipation</td>
</tr>
</tbody>
</table>

Patients diagnosed with Hodgkin’s Lymphoma carry a lifelong risk of transfusion associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as a diagnosis is made and the patient must be issued with an alert card to carry with them at all times.

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

**Monitoring**

**Drugs**

- FBC prior to days one and eight of treatment
- LFTs and U&Es prior to day one of treatment

**Dose Modifications**

The dose modifications listed are for haematological, liver and renal function and drug specific toxicities 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.
**Haematological**

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. **Irradiated blood products must be used in Hodgkin’s Lymphoma patients.**

Prophylactic growth factors are recommended from day 9 until neutrophil recovery to greater than 1x10^9/L.

Dose modifications based on haematological parameters apply to gemcitabine and vinorelbine.

**Day 1 and 8**

<table>
<thead>
<tr>
<th>Neutrophils (x10^9/L)</th>
<th>Dose Modifications (gemcitabine and vinorelbine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 or greater</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Less than 1</strong></td>
<td><strong>1st Occurrence</strong>&lt;br&gt;Delay treatment until the neutrophils have recovered to 1x10^9/L. If this occurs within 7 days continue with full dose and give prophylactic growth factors. If recovery takes longer than 7 days or if febrile neutropenia develops then consider dose reduction to 75% of the original dose and give prophylactic growth factors. <strong>2nd Occurrence</strong> consider dose reduction to 75% of the original dose and give prophylactic growth factors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Platelets (x10^9/L)</th>
<th>Dose Modifications (gemcitabine and vinorelbine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 or above</td>
<td>100%</td>
</tr>
<tr>
<td><strong>50 – 74</strong></td>
<td><strong>1st Occurrence</strong>&lt;br&gt;Give 75% dose of the original dose&lt;br&gt;<strong>2nd Occurrence</strong>&lt;br&gt;Give 50% dose of the original dose</td>
</tr>
<tr>
<td><strong>Less than 50 or signs of active haemorrhage</strong></td>
<td><strong>1st Occurrence</strong>&lt;br&gt;Delay until the platelets are 75 or above then give 75% of the original dose&lt;br&gt;<strong>2nd Occurrence</strong>&lt;br&gt;Delay until the platelets are 75 or above then give 50% of the original dose</td>
</tr>
</tbody>
</table>
Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Bilirubin µmol/L</th>
<th>AST/ALT units/L</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>more than 30*</td>
<td>N/A</td>
<td>Initiate treatment with a dose of 800mg/m²</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>more than 2xULN</td>
<td>more than 5xULN</td>
<td>67%</td>
</tr>
</tbody>
</table>

*Limit reflects local practice and may vary from published sources

Renal Impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Creatinine Clearance (ml/min)</th>
<th>Dose (% of original dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine</td>
<td>more than or equal to 30</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>less than 30</td>
<td>Consider dose reduction</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>N/A</td>
<td>No dose reduction needed</td>
</tr>
</tbody>
</table>

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Vinorelbine

When a NCI-CTC grade 2 peripheral neuropathy develops withhold the vinorelbine only until it has recovered to grade 1 then reduce the dose to 20mg/m²

If the peripheral neuropathy is classified at NCI-CTC grade 3 again withhold the vinorelbine until recovered to NCI-CTC grade 1 then reduce the dose to 15mg/m². Discontinue the vinorelbine if there is no recovery following this decrease in dose.

Constipation should at a NCI-CTC grade 1-2 may be managed with dietary interventions or laxatives. For constipation occurring at NCI-CTC grade 3 and above in the first instance reduce the dose of vinorelbine to 20mg/m². For persistent symptoms the dose may be further reduced to 15mg/m² or treatment stopped.

For other toxicities occurring at NCI-CTC grade 3 withhold the vinorelbine until recovered to NCI-CTC grade 1 then dose reduce to 20mg/m². If these toxicities occur at NCI-CTC grade 4 and above withhold the vinorelbine until the symptoms have resolved to NCI-CTC grade 1. Consultant advice should then be sought on whether to re-start therapy.
Regimen

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>Gemcitabine</td>
<td>1000mg/m²</td>
<td>1, 8</td>
<td>Intravenous infusion in 250ml sodium chloride 0.9% over 30minutes</td>
</tr>
<tr>
<td>Vinorelbine</td>
<td>25mg/m²</td>
<td>1, 8</td>
<td>Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes</td>
</tr>
</tbody>
</table>

Dose Information

- Gemcitabine will be dose banded according to the CSCCN agreed bands
- Vinorelbine will be dose banded according to the CSCCN agreed bands

Administration Information

Extravasation

- Gemcitabine – neutral
- Vinorelbine - vesicant

Additional Therapy

- Antiemetics
  15-30 minutes prior to chemotherapy
  - metoclopramide 10mg oral or intravenous

  As take home medication
  - metoclopramide 10mg three times a day when required oral

- Allopurinol 300mg once a day oral for the first cycle only

- Growth factors to be started on day 9 of the treatment cycle and continued until the neutrophil count is above 1x10⁹/L. For example
  - filgrastim or bioequivalent 30 million units once a day subcutaneous*
  - lenograstim or bioequivalent 33.6 million units once a day subcutaneous*
  - pegfilgrastim or bioequivalent 6mg once only subcutaneous*

  * a seven day supply will be issued on day 8 of each cycle.

- Consider anti-infective prophylaxis in high risk patients, including:
  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral
• Mouthwashes according to local or national policy on the treatment of mucositis

• Gastric protection with a proton pump inhibitor or a H2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

• The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

Coding (OPCS 4.6)

• Procurement – X71.3

• Delivery – X72.1, X72.4

References

REGIMEN SUMMARY

Gemcitabine-Vinorelbine

Cycle 1 Day 1

1. Warning – Check blood transfusion status
   Administration Instructions
   Patients with HODGKIN’S lymphoma carry a lifelong risk of transfusion associated graft versus host disease.
   Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life.
   Ensure transfusion departments are notified and the patient has been issued with an alert card to carry with them at all times.

2. Metoclopramide 10mg oral or intravenous injection

3. Vinorelbine 25mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

4. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Take Home Medicines

5. Metoclopramide 10mg three times a day when required oral

6. Allopurinol 300mg once a day oral for 21 days

Cycle 1 Day 8

1. Metoclopramide 10mg oral or intravenous injection

2. Vinorelbine 25mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

3. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Take Home Medicines

4. Growth factor as per local formulary choice. For example;
   - filgrastim or bioequivalent 30 million units once a day for seven days starting on day nine of the cycle subcutaneous
   - lenograstim or bioequivalent 33.6 million units once a day for seven days starting on day nine of the cycle subcutaneous
   - pegfilgrastim or bioequivalent 6mg once only on day nine of the cycle subcutaneous
Cycles 2, 3 and 4 Day 1

1. Metoclopramide 10mg oral or intravenous injection

2. Vinorelbine 25mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

3. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Take Home Medicines

4. Metoclopramide 10mg three times a day when required oral.

Cycles 2, 3 and 4 Day 8

5. Metoclopramide 10mg oral or intravenous injection

6. Vinorelbine 25mg/m² intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

7. Gemcitabine 1000mg/m² intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

Take Home Medicines

8. Growth factor as per local formulary choice. For example;*

   - filgrastim or bioequivalent 30 million units once a day for seven days starting on day nine of the cycle subcutaneous
   - lenograstim or bioequivalent 33.6 million units once a day for seven days starting on day nine of the cycle subcutaneous
   - pegfilgrastim or bioequivalent 6mg once only on day nine of the cycle subcutaneous

*Growth factors will appear as the drug in the regimen. The administration instructions reflect the guidance on agent, dose and duration
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 Foundation 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.