Chemotherapy Protocol

LYMPHOMA

GEMCITABINE-VINORELBINE

Regimen

- Lymphoma – Gemcitabine-Vinorelbine

Indication

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

Toxicity

Drug	Adverse Effect
Gemcitabine	Peripheral oedema, diarrhoea, constipation, rash, respiratory problems, influenza-like symptoms, radiosensitising
Vinorelbine	Neuropathy, stomatitis, transient elevation of LFTs, pain, constipation

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

Neutrophils ($x10^9$/L)	**Dose Modifications (gemcitabine and vinorelbine)**
1 or greater	100%
Less than 1	1st Occurrence 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. 2nd Occurence consider dose reduction to 75% of the original dose and give prophylactic growth factors
Platelets ($x10^9$/L)	**Dose Modifications (gemcitabine and vinorelbine)**
75 or above	100%
50 – 74	1st Occurrence Give 75% dose of the original dose 2nd Occurrence Give 50% dose of the original dose
Less than 50 or signs of active haemorrhage	1st Occurrence Delay until the platelets are 75 or above then give 75% of the original dose 2nd Occurrence Delay until the platelets are 75 or above then give 50% of the original dose

Hepatic Impairment

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

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Gemcitabine	more than 30*		N/A	Initiate treatment with a dose of 800mg/m^2
Vinorelbine	more than 2xULN		more than 5xULN	67%

*Limit reflects local practice and may vary from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Gemcitabine	more than or equal to 30	100%
	less than 30	Consider dose reduction
Vinorelbine	N/A	No dose reduction needed

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/m^2

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/m^2. 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/m^2. For persistent symptoms the dose may be further reduced to 15mg/m^2 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/m^2. 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

Drug	Dose	Days	Administration
Gemcitabine	1000mg/m^2	1, 8	Intravenous infusion in 250ml sodium chloride 0.9% over 30minutes
Vinorelbine	25mg/m^2	1, 8	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

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 1x10^9/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

1. Spencer A, Reed K, Arthur C. Pilot study of an outpatient-based approach for advanced lymphoma using vinorelbine, gemcitabine and filgrastim. Internal Medicine Journal 37 (2007) 760–766

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/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

4. Gemcitabine 1000mg/m^2 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/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

3. Gemcitabine 1000mg/m^2 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/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

3. Gemcitabine 1000mg/m^2 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/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

7. Gemcitabine 1000mg/m^2 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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Jan 2015	Header changed Toxicities removed Hepatic impairment table updated Metoclopramide dose changed to 10mg Growth factor units updated Bolus removed from intravenous bolus throughout text Mucositis recommendation changed OPCS codes updated “Warning – Check blood transfusion status”” added to cycle 1 Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	July 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist Dr Alison Milne Consultant Haematologist

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.