Chemotherapy Protocol

HAEMATOLOGY – HSCT AUTOGRAFT

InP - MELPHALAN and BORTEZOMIB (IV)

Please confirm correct protocol with transplant schedule

Regimen

- HSCT – InP - Melphalan-Bortezomib (IV)

Indication

- Conditioning for haematopoeitic stem cell transplant in patients with multiple myeloma

Toxicity

Drug	Adverse Effect
Melphalan	Nausea, vomiting, diarrhoea, stomatitis, alopecia and myelosuppression
Bortezomib	GI disturbances, peripheral neuropathy, hypotension, dizziness, blurred vision, headache, musculoskeletal pain, pyrexia

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to initiating treatment
- GFR measurement done by Nuclear Medicine or creatinine clearance calculation prior to first day of treatment.

Dose Modifications

The dose modifications listed are for liver and renal function. Dose adjustments may be necessary for other co-morbidities as well which will involve discussions with the Transplant Director, Senior Transplant Clinician or patient's consultant.

Haematological

Confirm with transplant consultant before proceeding if there are signs of disease relapse.

Hepatic Impairment

Drug	Bilirubin µmol/L	AST/ALT units/L	Dose (% of original dose)
Bortezomib	1.5xULN or below	N/A	100%
	greater than 1.5xULN	N/A	Consider initiating treatment at 0.7mg/m2

No information is available on melphalan in hepatic impairment. No dose changes recommended.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Melphalan	greater than 50ml/min	200mg/m^2
	30 – 50ml/min	140 mg/m^2
	less than 30 ml/min	Clinical decision, high dose melphalan is not recommended
Bortezomib	greater than 20	100%
	20 and below	Clinical decision

Other

Bortezomib

Neuropathic pain and/or peripheral neuropathy

For patients experiencing NCI-CTC grade 1 neuropathy continue with full dose

For NCI-CTC grade 1 with pain or grade 2 neuropathy reduce the dose of bortezomib to 1mg/m^2.

Regimen

Drug	Dose	Days	Administration
Melphalan	200mg/m^2	-1	Intravenous infusion in 500ml sodium chloride 0.9% over 30 minutes
Bortezomib	1.3mg/m^2	-1 and +4	Intravenous bolus over 5 seconds Day -1 to be given at least 12 hours after melphalan infusion

Dose Information

- The melphalan dose is rounded **down** to the nearest 10mg. The National Dose Banding Team have advised not to use dose banding tables for this product in view of the 90 minute expiry (must be made locally for individual patient), the 50mg vial size and frequent stock shortages.
- Bortezomib will be dose banded in accordance with the national dose bands

Administration Information

- Bortezomib IV on day -1 to be given at least 12 hours after melphalan infusion

Extravasation

- Melphalan – non-vesicant

Additional Therapy

- Antiemetics

- aprepitant 125mg once a day prior to melphalan followed by 80mg once a day for the subsequent two days oral
-dexamethasone 4mg each morning for three days oral
-metoclopramide 10mg three times a day oral or intravenous until nausea subsides
- ondansetron 8mg twice a day oral or intravenous for ten days then review

- Antimicrobials

Antimicrobials should be prescribed according to the institution guideline and may include:

-ciprofloxacin 250mg twice daily from day +5 to continue whilst neutropenic
-antifungal for example fluconazole 100mg once daily from admission until recovery from neutropenia
- antivirals for example aciclovir 400mg twice or three times a day from admission to continue after discharge

- Growth factors according to local formulary choice.
  For example:
  - filgrastim or bioequivalent 30million units subcutaneous once a day starting from day +7 to continue until neutrophils are more than 0.5.
  - lenograstim or bioequivalent 33.6million units subcutaneous once a day starting from day +5 to continue until neutrophils are more than 0.5.

- Gastric protection with a proton pump inhibitor should be prescribed throughout admission

- Mouthwashes including:

  - nystatin 1ml four times a day to continue until count recovery
  - sodium chloride 0.9% 10ml four times a day to continue until count recovery

- Thromboprophylaxis -in accordance with individual transplant schedule

- Premedication for stem cell transfusion -chlorphenamine 10mg intravenous -paracetamol 1000mg oral

- Intravenous hydration before and after melphalan infusion prescribed on inpatient prescribing system or using paper proforma (appendix 1)

The evening before melphalan infusion (to be completed by 0930 on the morning of the infusion)

sodium chloride 0.9% with potassium chloride 27mmol 1000ml

The day of melphalan infusion

0900hrs Start fluid chart and daily weights. Contact pharmacy to make melphalan infusion for delivery to ward at 1045hrs

0930hrs 1000ml sodium chloride 0.9% intravenous infusion over 90 minutes

1010hrs 20mg furosemide intravenous bolus

1045hrs Measure urine output since 0900hrs ·

If more than 500ml continue with melphalan infusion ·

If less than 500ml give second furosemide 20mg intravenous bolus dose and check urine output since 0900hrs again at 1100hrs:

• if more than 500ml go ahead with melphalan

• if less than 500ml contact the prescriber.

1100hrs – give melphalan intravenous infusion over thirty minutes (this product has a short expiry so adhering to set timing is essential)

1130hrs - 1000ml sodium chloride 0.9% intravenous infusion over 120 minutes

1330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over 240 minutes

1730hrs - 1000ml sodium chloride 0.9% intravenous infusion over 360 minutes

2330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over 480 minutes

• The day after melphalan infusion:

0730hrs - 1000ml sodium chloride 0.9% intravenous infusion over 480 minutes then restart routine intravenous fluids

References

1. P-P-54 Wessex Blood and Marrow Transplant – Dose adjustments for stem cell transplant conditioning agents policy. Version 1.0
2. P-P-43 Wessex Blood and Marrow Transplant – WESSEX BLOOD AND MARROW TRANSPLANT – Conditioning schedule for High Dose Melphalan Policy. Version 1.4
3. Dosage Adjustments for Cytotoxics in Hepatic Impairment January 2009 University College London Hospitals
4. Summary of Product Characteristics for Melphalan (Aspen) – last updated 09 Dec 2014
5. Handbook of Systemic Treatments for Cancer 7th Edition 2012 Lilly Oncology
6. National Dose Banding Tables

REGIMEN SUMMARY

InP-Melphalan-Bortezomib IV

Day -1

1. Warning – Check supportive medication prescribed
Administration instructions

Please refer to the individual transplant schedule for full details of the required supportive medicines on inpatient prescribing system

1. Antibacterials in accordance with individual transplant schedule
2. Antifungals in accordance with the individual transplant schedule
3. Antivirals in accordance with the individual transplant schedule
4. Thromboprophylaxis in accordance with individual transplant schedule
5. Growth factors in accordance with the individual transplant schedule
6. Aprepitant 125mg once a day on the day of melphalan administration followed by 80mg once a day for two days afterwards
7. Dexamethasone 4mg in the morning with each dose of aprepitant
8. Metoclopramide 10mg three times a day oral or intravenous
9. Ondansetron 8mg twice a day oral or intravenous
10. Gastric protection in accordance with the individual transplant schedule
11. Nystatin mouthwash 1ml four times a day
12. Sodium chloride 0.9% mouthwash 10ml four times a day
13. Chlorphenamine 10mg intravenous when required as a premedication for stem cells
14. Paracetamol 1000mg oral when required as a premedication for stem cells
15. Furosemide 20mg up four times a day when required for the treatment of fluid overload intravenous
16. Melphalan hydration on paper chart (Appendix 1 of protocol)
17. Heparin line lock in accordance with local central venous access device management procedure
18. Reminders for melphalan and stem cells administration

2. Warning – Check hydration and fluid balance
Administration Instructions
See separate hydration prescription chart for the pre hydration (Appendix 1):
1. Overnight to be completed at 0930hrs on day of melphalan infusion, 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion The day of melphalan infusion:
2. 0900hrs on the day of melphalan start fluid chart and daily weights. Contact pharmacy to make melphalan infusion for delivery to ward at 1045hrs
3. 0930hrs 1000ml sodium chloride 0.9% intravenous infusion over 90 minutes
4. 1010hrs 20mg furosemide intravenous bolus
5. 1045hrs Measure urine output since 0900hrs If more than 500ml continue with melphalan infusion If less than 500ml give second furosemide 20mg dose intravenous bolus and recheck urine output since 0900hrs again at 1100hrs:
• if more than 500ml go ahead with melphalan
• if less than 500ml contact prescriber

3. Time– Administer melphalan at 1100hrs

4. Melphalan 200mg mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 30 minutes
   Administration Instructions - see separate hydration prescription chart for the post hydration (Appendix 1 of protocol)
   1. 1100hrs – give melphalan intravenous infusion over thirty minutes
   2. 1130hrs - 1000ml sodium chloride 0.9% intravenous infusion over two hours
   3. 1330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over four hours
   4. 1730hrs - 1000ml sodium chloride 0.9% intravenous infusion over six hours
   5. 2330hrs - 1000ml sodium chloride 0.9% with potassium chloride 27mmol intravenous infusion over eight hours
   6. The day after melphalan infusion: 0730hrs - 1000ml sodium chloride 0.9% intravenous infusion over eight hours and then restart routine intravenous fluids as clinically indicated.

5. Bortezomib 1.3mg/m^2 intravenous bolus over 5 seconds
   Administration instructions
   To be given at least 12 hours after melphalan infusion

Day +4

6. Bortezomib 1.3mg/m^2 intravenous bolus over 5 seconds

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	January 2021	None	Nanda Basker Haematology Pharmacist	Dr Matthew Jenner Haematology Consultant

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 that occur as a result of following these guidelines.