Cyclophosphamide Priming Prior to PBSC Harvest

Indication
Stem cell harvesting for patients with myeloma, amyloidosis and POEMS syndrome

Pre-Assessment
- Liaise with BMT nurse practitioner (BMT NP) for timing of priming therapy and possible transplant slot
- Venous access should be assessed well in advance of collection. Every effort should be made not to use antecubital fossa veins in the run up to harvest. If venous access is poor, liaise with the line team to assess patient. Consider organising insertion of a femoral apheresis line before the day of harvest. Note that line must have two lumens.
- Record stage of disease and consider bone marrow aspiration and trephine
- Ensure the following investigations have been performed recently: FBC, ESR, U+E, creatinine, LDH, urate, calcium, magnesium and LFTs, Immunoglobulins, Serum free light chains, β2 microglobulin
  - CMV, VZV, EBV and Toxoplasma , IgG
  - Urine for Bence-Jones Protein
- **Infected agent screen.** Peripheral blood stem cells for autologous use are cryopreserved in liquid nitrogen. In order to eliminate the risk of transmitting infected agents during storage, the following tests are mandatory within 30 days of the harvesting procedure and results must be known before priming:
  - HepBs Antigen, HepBc Antibody, HIV 1+2, HCV, HTLV 1, TPHA - NHSBT virology tubes should be used and sent to Stem Cell Services laboratory, NHSBT with consent form 2B (there is a link on NSSG>Links to: Forms & Leaflets from ‘Haemopoietic Stem Cell Services’)
- ECG +/- Echocardiogram if clinically indicated
- Pregnancy test for women of child-bearing potential
- Record performance status (WHO/ECOG)
- Record height and weight
- Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects (see below). Document in medical notes (EPR) all information that has been given. Obtain written consent prior to or on the day of treatment on OUH consent form 3.
- Fertility – it is very important the patient understands the potential risk of infertility, all patients should be offered fertility advice/storage and early referral to a fertility specialist where appropriate
- BMT NP to e-mail the following forms to NHSBT:
  - Completed Final Donor Clearance (FRM3721)
  - Referral (FRM5071) to request to collect, test and process peripheral blood stem cells
- Therapeutic Apheresis Services request for collection of stem cells (FRM5110) Medical team to inform blood bank to ensure blood products are irradiated from 7 days prior to harvest
- All relevant forms to be scanned to patient EPR notes
Drug Regimen
Encourage 3L oral fluids

<table>
<thead>
<tr>
<th>Day 1</th>
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<tbody>
<tr>
<td>T – 30mins</td>
<td>Ondansetron</td>
<td>8mg IV/PO</td>
</tr>
<tr>
<td>T 0</td>
<td>Cyclophosphamide</td>
<td>1.5g/m² in 500mL sodium chloride 0.9% IV infusion over 30-60 minutes.</td>
</tr>
<tr>
<td>T 0</td>
<td>Mesna</td>
<td>0.3g/m² IV bolus</td>
</tr>
<tr>
<td>T +2 hours</td>
<td>Mesna</td>
<td>0.6g/m² PO</td>
</tr>
<tr>
<td>T + 6 hours</td>
<td>Mesna</td>
<td>0.6g/m² PO</td>
</tr>
<tr>
<td>Days 2 to 10</td>
<td>GCSF (filgrastim)</td>
<td>SC Daily. Refer to: NSSG&gt;BMT&gt; B.36 Filgrastim-Biosimilar protocol</td>
</tr>
</tbody>
</table>

Dose modifications
There is not a great deal of evidence to guide on correct dosage in renal impairment. The largest series of cyclophosphamide-primed patients in this setting is the Arkansas series in which doses of 3 g/m² were used. It is probably acceptable not to dose reduce in this setting although it is possible that there may be a slight increase in associated toxicity. This, however, should not be detrimental to PBSC mobilisation.

Investigations
Check FBC, U+Es, creatinine, LFTs prior to administration and discuss with consultant if unsure whether to proceed.

Concurrent medication

<table>
<thead>
<tr>
<th>Antiemetics</th>
<th>Ondansetron 8mg BD/PO for 3 days</th>
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<tbody>
<tr>
<td></td>
<td>Metoclopramide 10 - 20mg QDS/PO/prn for 5 days</td>
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<tr>
<td>Mesna</td>
<td>0.6g/m² at +2hr and +6 hr following cyclophosphamide</td>
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<tr>
<td>GCSF</td>
<td>SC Daily from Days 2-10. Refer to: NSSG&gt;BMT&gt; B.36 Filgrastim protocol</td>
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Harvesting
Day 9
If venous access is a problem, arrange for a femoral apheresis line to be inserted. The line should be removed post-harvest on day 11. Arrange for the patient to be admitted overnight if a temporary line is required.

Stem cell collection performed days 10 or 11

Yield
An adequate yield > 2.0 x 10⁶ CD34+ve cells/kg. An optimal yield would contain > 6.0 x 10⁶ CD34+ cells/kg, in those patients where 2 autografts are considered

If poor harvest on day 10, then consider Plerixafor rescue, refer to: NSSG>BMT>Priming> B.22 Plerixafor Use for Peripheral Blood Stem Cell Mobilisation protocol

Extravasation risk
Cyclophosphamide- Neutral.
Side Effects and Informed Consent

- Nausea, infection, anaemia, haemorrhagic cystitis, hair thinning, risk of reduced fertility, possible need for Plerixafor, risk of death <1%
- Patient should be warned about risk of failure to harvest of approximately 10-20%

Reference:

Author(s):
Pamela Roberts, Myeloma Specialist Nurse, Version 2, 2006
Denise Wareham, BMT Co-ordinator – Version 3, 2010
Sandy Hayes, Project Nurse, Amendments, Version 4, July 2010

Audit:
These processes are subject to the OxBMT/IEC audit programme

Circulation:
NSSG Haematology Website

Review

<table>
<thead>
<tr>
<th>Name</th>
<th>Revision</th>
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<th>Version</th>
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<tbody>
<tr>
<td>Julia Wong, Pharmacist</td>
<td>GCSF to daily G-CSF as per local policy. Removed Lenograstim, Lenograstim table, and reference 5HT3 frequency to bd Metoclopramide to 10 - 20mg qds/po/prn for 5 days</td>
<td>Aug 2014</td>
<td>5</td>
<td>2014</td>
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<tr>
<td>Sue Moore, BMT SNP Dr Karthik Ramasamy, Consultant</td>
<td>Changes as per protocols review 2013</td>
<td>Aug 2014</td>
<td>5.1</td>
<td>2014</td>
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<tr>
<td>Dr John Willan, SpR Sandy Hayes, Quality manager</td>
<td>Review, clarification of timing of Mesna, insertion of risk of mortality and harvest failure and side effects of treatment</td>
<td>Jan 2016</td>
<td>5.2</td>
<td>Jan 2018</td>
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<tr>
<td>Sandy Hayes, Quality manager</td>
<td>Incorporation of pharmacy comments, increase in optimal yield, insertion of hyperlinks</td>
<td>Apr 2016</td>
<td>5.3</td>
<td>Jan 2018</td>
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<tr>
<td>Cheuk-kie Cheung, Haematology Pharmacist</td>
<td>Separation of Mesna and Cyclo in view of stability data</td>
<td>May 2017</td>
<td>5.4</td>
<td>Jan 2018</td>
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<tr>
<td>Karthik Ramasamy, Consultant Nadjoua Maouche, Haematology Pharmacist</td>
<td>Addition of extravasation risk. Minor formatting/editing revisions.</td>
<td>June 2019</td>
<td>5.5</td>
<td>Jun 2021</td>
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<tr>
<td>Denise Wareham, BMT Senior Specialist Nurse</td>
<td>Minor amendments and clearer signposting to other documents Addition of nursing care plan as an integrated part of the document</td>
<td>Nov 2021</td>
<td>5.6</td>
<td>Nov 2023</td>
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</table>
Nursing Care Plan
Cyclophosphamide Priming

Indication: Priming prior to stem cell harvest for myeloma patients undergoing autograft.

**Cyclophosphamide** is an alkylating agent and is given to ‘mobilise’ stem cells into the peripheral blood circulation in preparation for stem cell harvest

**Side effects:**
Immediate: Nasal stuffiness (can be reduced by slowing rate of administration), dizziness
Short term: haemorrhagic cystitis, nausea and vomiting (high risk and may be delayed up to 48 hours after infusion), diarrhoea, anorexia, taste changes, neutropenia
Long term side effects: bone marrow suppression, alopecia, infertility (most cases reversible), renal and hepatic impairment

**Mesna:** Reduces risk of haemorrhagic cystitis due to high dose cyclophosphamide. Mesna reacts with a metabolite of cyclophosphamide in the urinary tract to prevent toxicity. Administered as IV bolus immediately prior to cyclophosphamide on Day 1. This is followed by 2 oral doses which will be given to the patient to take home.

**Regime Specific Considerations**
- Refer to clinical protocol above for additional information about medications
- Medical review: If the patient has been seen and consented in the out-patient clinic in preparation for priming, it is not necessary to review the patient on the day of chemotherapy, unless nursing staff or patient have new concerns
- Blood parameters: FBC/U&E’s results must be within 2 weeks of cyclopriming. No specific parameters given, discuss any concerns with clinician
- Advise patients to maintain fluid intake of 2-3 litres on the day, and for next few days.
- Advise patients to report haematuria.

**Day 1**
- **Record pregnancy test for women of child-bearing potential pre-chemotherapy administration.**
- Administer Ondansetron 30 mins prior to cyclophosphamide
- Administer IV bolus of Mesna followed by IV infusion of cyclophosphamide over 30 – 60 minutes
- **Inform patient of Oral Mesna dose schedule:**
  First dose, 2 hours after start of cyclophosphamide
  Second dose, 6 hours after start of cyclophosphamide
  e.g. cyclophosphamide starts at 1200, 1st Mensa is given at 1400, 2nd at 1800

**Days 2 -10**
- Administration of GCSF by patient, relative, district/practice nurse. GCSF should be administered in the evening at a similar time each day
- **Educate patient about side effects of GCSF:** bone pain, flu-like symptoms, headache and advise to take paracetamol regularly (unless allergic) and encourage to call triage if concerned

**Days 10-11:** PBSC Harvest at NHSBT.

**Author(s):** Pamela Roberts, Myeloma CNS, April 2016
**Circulation:** NSSG haematology website

**Audit:** These processes are subject to OxBMT/IEC audit programme

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<tr>
<td>Kirsten Rendall, Autologous BMT Specialist Nurse, Denise Wareham, BMT Senior Specialist Nurse</td>
<td>Format Mesna administration Bold emphasis of key information Nursing care plan previously N.32, now archived</td>
<td>Nov 2021</td>
<td>3.1</td>
<td>Nov 2023 Align with clinical protocol</td>
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