High Dose Melphalan for Autograft

Summary of Schedule

Date:

DRUG	-2	-1	0
Admission	*		
Melphalan *Chemotherapy*		*	
Bone marrow/stem cell re-infusion			*
Ondansetron (O) Dexamethasone (D) Aprepitant (A) Olanzapine (Z) *Different types of anti-sickness drugs*		O D A Z	O D A Z
Oral Cryotherapy *To prevent mucositis*		*	

Indications

Disease consolidation in patients with Multiple Myeloma

Patients with renal impairment are treated on protocol B.2.31 High dose Melphalan (renal impairment)

Selected patients with AL Amyloidosis and POEMS syndrome

Pre-assessment

- Ensure pre-transplant 'work-up' Investigation form (B.3.10d) is complete and results checked by Haematology SpR or appropriately trained and competent Physician Associate and recorded in patient record
- Ensure patient has an appropriate double lumen central line in situ
- High risk of early severe mucositis, consider early NG feeding/TPN
- Haematology SpR or appropriately trained and competent Physician Associate to complete electronic BMT front sheet. Administrator for BMT Nurses to distribute and file in patient record
- Prescribe chemotherapy, stem cells/bone marrow infusion and supportive treatment 10 days before admission
- Send NHSBT form ‘Request for Issue of Cyropreserved Products’ to NHSBT at least 7 days before planned infusion date and ensure copy of confirmation is placed in the patient’s record
- Perform a urine pregnancy test on Day -1, in all women of childbearing potential of age. Document results in patient record
- Ensure the patient receives irradiated bloods products from start of conditioning. See ‘Guidelines for the Use of Blood Components in Adult Haematology’ for further details and individual requirements/duration post autograft. Ensure irradiation sticker is attached to the patient’s notes and copy given to the patient
- Treatment should be agreed in the relevant MDT
- **Ambulatory delivery**: Ensure the patients meets the criteria in line with the Ambulatory Care Operational Policy

Chemotherapy and Fluids

Encourage 3L oral fluids daily, supplement with IV fluids if necessary

Day -2		Patient should drink 3L of oral fluids
Day –1 *08.00*	**Pre-hydration**	Commence oral fluids 1L or 1000ml sodium chloride 0.9% IV 2 hours prior to Melphalan
09.30	**Pre-medication**	Furosemide 20-40mg IV to ensure frequent diuresis
09:45 *10.00*	**Oral cryotherapy** **Melphalan**	Place the ice cubes/ice chips/ice lollies in the mouth, starting from approximately 15 minutes before melphalan infusion, during melphalan infusion and for 75 minutes after (~2 hours in total). Replenish with the new portion of the ice before it melts to keep the mouth constantly cool for the whole duration of oral cryotherapy **200mg/m²** OD in 100ml sodium chloride 0.9% IV infusion over 30mins
10.30	**Post-hydration**	1000ml sodium chloride 0.9% + 20mmol potassium chloride IV infusion over 2 hours.
12.30	**Post-hydration**	1000ml sodium chloride 0.9% + 20mmol potassium chloride IV infusion over 4 hours
16.30		Patient should be advised to continue drinking. At least 1L should be consumed over the evening. If nauseated, continue IV fluids
Day 0 *09.00*	**Pre-hydration**	1000ml sodium chloride 0.9% iv infusion over 4 hours
13:00	**Stem cell re-infusion should be a minimum of 24hrs post Melphalan dose**	Give hydrocortisone 100mg IV, chlorphenamine 10mg IV and cyclizine 50mg IV, 15 minutes before infusion.
Day +6	**G-CSF**	As per local policy. SC daily until engraftment

Extravasation risk: Neutral

Weight: BD from morning of day -1 for 48 hours then daily

Dose modification

Patients with renal impairment (CrCl <50ml/min) are to be treated using B.3.21 High Dose Melphalan for Autograft (Renal Impairment). Consider Melphalan dose reduction to140mg/m^2 in patients aged 70 years or older.

Anti-emetics

Regular antiemetics*	
5HT3 antagonist	Days -1 to +5 i.e. Ondansetron 8mg BD PO/IV
Dexamethasone	Days -1 to +1: Dexamethasone 8mg OD PO/IV on day -1, then dexamethasone 4mg OD PO on days 0 to +1
NK1 inhibitor	Days -1 to +1 i.e. Aprepitant 125mg OD on day -1, then 80mg on days 0 and +1
Olanzapine	5mg ON PO day -1 to day +2
When required antiemetics* form the start of conditioning for rescue antiemetic	
5HT3 antagonist	Ondansetron 8mg BD PO/IV PRN, maximum 32mg in 24hours
Cyclizine	50mg TDS PO/IV PRN
* Review antiemetic control and optimise in case of breakthrough N&V	

Concurrent Medication

Norethisterone	5-10mg PO TDS from day 0 until platelets >50x10^9/L (menstruating women only)
Fluconazole	50mg PO OD from day 0 until neutrophils >1.0x10^9/L (or longer if on steroids)
Omeprazole	20mg PO/IV OD from start of conditioning until platelet count >50x10^9/L (or longer if on steroids)
Aciclovir	200mg PO TDS (or 250mg IV/TDS) from day 0 until day +90
G-CSF	SC daily starting from day +6 until stable engraftment as per local policy
Difflam 0.15% MW	Use 15ml as mouthwash QDS a day when required as directed
AS Saliva Orthana spray	Use 2-3 sprays when required for dry mouth
Oral cryotherapy	**On day -1**: Place the ice cubes/ice chips/ice lollies in the mouth, starting from approximately 15 minutes before melphalan infusion, during melphalan infusion and for 75 minutes after (~2 hours in total). Replenish with the new portion of the ice before it melts to keep the mouth constantly cool for the whole duration of oral cryotherapy

Medication on Discharge (TTO's)

Norethisterone	5-10mg PO TDS. Stop when platelets >50x10^9/L (menstruating women only)
Fluconazole	50mg PO OD. Stop when neutrophils >1.0x10^9/L (or longer if on steroids)
Omeprazole	20mg PO OD. Stop unless clinically indicated
Aciclovir	200mg PO TDS until day +90
Co-trimoxazole	960mg OD on Mon, Wed, Fri, until day +90. Start when neutrophils >1x10^9/L and platelet transfusion independent. Consider prophylaxis with Pentamidine monthly IV 4mg/kg (max dose 300mg), starting at day +30 if patient is allergic to co-trimoxazole or there are concerns over counts

Treatment Related Mortality: 1- 2%

References

1. Moreau P et al. Comparison of 200mg/m^2 melphalan and 8 Gy total body irradiation plus 140 mg/m^2 melphalan as conditioning regimens for peripheral blood stem cell transplantation in patients with newly diagnosed multiple Myeloma: final analysis of the Intergroupe Francophone du Myelome 9502 randomized trial. **Blood** 2002 Feb 1; 99 (3): 731-5.
2. Medical Research Council, **Myeloma IX,** Myelomatosis Therapy Trial; Version 1.1, January 13, 2002
3. Badros et al. Results of autologous stem cell transplant in multiple myeloma patients with renal failure. **Br J Haematol.** 2001 Sep; 114(4): 822-9.
4. High Dose Protocol: Melphalan 200mg Ambulatory Unit. The Royal Marsden NHS Trust. Myeloma Unit. V1.1 12.03.2012
5. E-mail correspondence The Royal Hallamshire Hospital, Sheffield

Author(s) of original protocol (B.2.3) from which this protocol has been adapted:

Tim Littlewood, BMT Programme Director - Version 3, 2005, Version 4 and 5, 2006
Marc Mitchell - Divisional Pharmacist - Version 3, 2005, Version 4 and 5, 2006
Pamela Roberts – Myeloma Nurse Specialist - Version 6, 2009

Audit: These processes are subject to OxBMT audit programme

Circulation: NSSG Haematology Website

Review

Name	Revision	Date	Version	Review date
Andy Peniket, BMT Programme Director Julia Wong, Cancer Pharmacist Rachel Miller, Clinical Haematology Ward Sister. Sandy Hayes, Quality Manager.	Development of a protocol suitable for Ambulatory care.	Sept 2013	1.0	Sept 2015
Dr Robin Aitchison, Dr Karthik Ramasamy, Haematologists Sandy Hayes, Quality manager	Amalgamation of standard and ambulatory protocols. Update format	Mar 2016	2.0	Mar 2018
Dr Karthik Ramasamy, Consultant Haematologist Rachel Miller, Deputy Matron	Minor amendments Generic changes Inclusion/exclusion criteria	May 2018	2.1	May 2020
Denise Wareham, BMT Coordinator	Minor amendment Addition of dose reduction for patient >70 years	Sept 2018 Not full review	2.2	May 2020
Nadjoua Maouche, Lead Haematology Pharmacist	Antiemetics, extravasation risk	June 2019	2.3	June 2020
Natalia Czub, Specialist Cancer Pharmacist Nadjoua Maouche, Lead Haematology Pharmacist	Addition of olanzapine, oral cryotherapy Difflam MW	Feb 2021	2.4	June 2021
Natalia Czub, Specialist Cancer Pharmacist Nadjoua Maouche, Lead Haematology Pharmacist	Minor editing. Added BD to ondansetron PRN dose. Added Saliva spray.	Apr 2021	2.5	June 2021
Natalia Czub, Specialist Cancer	Minor editing	May 2021	2.6	June 2023

Pharmacist Nadjoua Maouche, Lead Haematology Pharmacist				
	Addition of care plan as an integrated part of the clinical protocol **Clinical protocol not reviewed**	Jan 2022	2.7	June 2023
Ana Rita Gomes, Advanced Cancer Pharmacist Jaimal Kothari, Lead Myeloma Consultant Alexandra Scott, BMT Specialist Nurse	Minor editing. Added cyclizine as stem cell pre-medication.	Nov 2024	2.8	Nov 2026

Care Plan On The Next Page

Nursing Care Plan

Ensure flush volumes are included in rate and volume calculations, i.e. drug and flush should be completed withing prescribed administration time.

Melphalan - is a cell-cycle non-specific alkylating chemotherapy agent given to suppress bone marrow production. The drug is unstable in solution so the infusion must be established as soon as the drug arrives on the ward.
Side effects: nausea and vomiting, bone marrow suppression, alopecia, mucositis and diarrhea

Day –1

With patient consent, oral cryotherapy should be implemented on day -1 with the aim of preventing/reducing occurrence of oral mucositis.

- 08.00: Infuse IV pre hydration or advise patient to drink 1L oral fluids
- 09.00: Contact Baxters to confirm delivery time
- 09.45: offer patient ice chips/lollies to suck for approximately 15 minutes pre melphalan and throughout the infusion
- 10.00: Administer melphalan infusion over 30 minutes
- 10.30: Administer IV post hydration
- Continue cryotherapy for 75 minutes after completion of Melphalan
- Ensure daily mucositis assessment is carried out and WHO score is documented on EPR in patient nursing notes.
- Refer to Oral Mucositis care plan for additional information: NSSG>BMT>Nursing Care Plan>N.26

Stem Cell Infusion of Cryopreserved (Frozen) Cells
Potential complications: Allergic reaction, fluid overload, hyperosmolarity, infusion of micro-aggregates, pulmonary oedema, nausea, vomiting, diarrhoea, abdominal pain, and facial flushing, headache, blurred vision, altered taste and smell due to DMSO.

Day 0

- **0800**: Cells will arrive at Laboratory Medicine and porters will bring to the clinical areas as outlined in Cell Management policy NSSG>BMT>Clinical Management> B.2.30. (must be >24 hours post-Melphalan)
- **0900**: Administer sodium chloride 0.9% 1 litre over 4 hours.
- **1245**: Administer pre-medications: chlorphenamine, hydrocortisone + antiemetics as prescribed a minimum of 15 minutes prior to stem cell reinfusion
- Ensure O2, suction, and call bell are checked, and anaphylaxis kit is in patient room
- **1300**: Peripheral Blood Stem Cell Infusion:
- Record baseline observations
- Positively identify the patient ID, against each bag of cells and on NHSBT Form 5071 (EPR under ‘BMT Coordination’)
- Check cells to ensure no clumping, or bag damage
- Take great care when spiking each bag, to prevent inappropriate puncturing. See Cell Management policy NSSG>BMT>Clinical Management> B.2.30 if bag is accidentally punctured
- Each bag of cells must be infused within 15 mins of thawing. The cells may be infused through a:

Peripheral cannula using a *blood administration giving set side-armed with Sodium Chloride 0.9%, using a Y connector, and gravity feed
OR
Central line using an **appropriate** infusion pump and associated double spike giving set (*filter size equivalent) side-armed with Sodium Chloride 0.9%

- Monitor patient closely and observe for any signs of reaction, fluid overload and/or respiratory compromise.
- Record: lot numbers of giving sets and saline, and volume of cells including start and completion time for each bag, on NHSBT form 'Summary of products issued for transplant'.
- On completion of cells, continue flushing the IV line with saline until it runs clear
- Ensure a copy of the NHSBT form 'Record of issue and infusion' and 'Summary of products issued for transplant' is scanned/filed in patient notes
- Ensure completion of NHSBT adverse event form is completed and returned to Haematology Ward Clerk who will forward to NHSBT/SCI

Author(s) Nursing Care Plan: Sally Springett, BMT IMPACT Research Nurse, Kirsten Rendall, Auto BMT Coordinator, Denise Wareham, BMT Senior Specialist Nurse

Authorised by: Denise Wareham, BMT Senior Specialist Nurse

Circulation: NSSG Haematology Website, patient medical notes

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

Review

	Revision	**Date**	**Version**	**Review date**
	Revised nursing care plan and added as an integrated part of the clinical protocol	Jan 2022	1.0	Align with clinical protocol
Alexandra Scott BMT Specialist Nurse	Removal of NHSBT scientist role and addition of PA role.	Nov 2024	1.1	Align with clinical protocol