HIGH-DOSE MELPHALAN WITH STEM CELL RESCUE (AUTOLOGOUS STEM CELL TRANSPLANT, ASCT) IN THE OUTPATIENT SETTING

Creator: **University Hospitals Bristol and Western**

Author: Rebecca Hallam, Advanced Clinical Practitioner

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Clinical Standard Operating Procedure (SOP)

HIGH-DOSE MELPHALAN WITH STEM CELL RESCUE (AUTOLOGOUS STEM CELL TRANSPLANT, ASCT) IN THE OUTPATIENT SETTING

SETTING	Stem Cell Transplant and Cellular Therapy Programme, Bristol Haematology and Oncology Centre (BHOC)
FOR STAFF	Medical, nursing and pharmacy staff
PATIENTS	Patients receiving high-dose melphalan and autologous stem cell rescue as outpatients

1. Indications for Practice

To provide a framework by which high-dose melphalan and autologous stem cell rescue (autologous stem cell transplant, ASCT) can be performed in the outpatient setting. This SOP details the following:

- Describes the model
- Patient selection
- Prophylaxis during aplastic phase
- Monitoring and support in aplastic phase
- Criteria and procedures for re-admission
- Data collection

Expected outcomes

- Safe administration of high-dose melphalan and stem cell rescue in selected patients in the outpatient setting
- Reducing or eliminating inpatient admissions for this procedure will improve the patient experience, and release inpatient resources
- Overall mortality at Day+100 should not exceed 3%, as per common myeloma auto outcomes in published literature

> This SOP should be read in conjunction with the wider SOP Assessment of Suitability for Ambulatory Care BMT at BHOC.

2. Authorised Personnel / Training Required

2.1 Personnel & Responsibilities

Any Haematology Consultant, nursing and pharmacy personnel or junior medical staff involved in the care of stem cell transplant/bone marrow transplant (SCT/BMT) patients.

3. Procedure

3.1 Equipment/Supplies

- Dedicated chair in outpatient unit for ambulatory BMT patients
- One bed will be identified for overnight admission. 3 outpatient autografts can be done per identified bed
- If the bed is utilized overnight a new bed must be identified the next day
- Medicines cupboard and fridge

3.2 Patient selection

Inclusion criteria:

- Age between 18 and 65 years.
- Normal cardiac and lung function as usually performed before a conventional ASCT.
- Absence of other relevant organ dysfunctions. (Liver impairment, defined as total bilirubin > 30 µmol/L, or renal impairment, defined as creatinine clearance <60 ml/min.
- Absence of advanced disease (for example, <PR).
- Absence of Gram-negative multi drug resistant (MDR) pathogen colonisation or infection during the 3 months prior to ASCT. Any severe infection not completely microbiologically or clinically resolved is considered a contraindication to outpatient ASCT.
- Place of stay within a 60 minute drive of the hospital.
- Availability of a suitable caregiver 24 hours.
- A dedicated 24 hour phone line (triage) at transplant centre to allow patients or their caregivers to contact an expert physician on the transplant team.
- Informed consent including a detailed SOP for the caregiver and the outpatient management team.

3.3 Description of the process

1. Patients will be selected as per the criteria above. They will be given an information sheet and consented prior to ASCT. Consent should include risk assessments as mentioned above.
2. Ensure adequate stem cell dose of at least $\geqslant 2\times10^6$ CD34+ cells/kg is available.
3. Pre-transplant investigations are within acceptable limits and agreed at the BMT planning meeting.

4. Central venous access device (CVAD) must be in situ.

5. Transplant protocol sheets, Chemocare® prescription and drug chart, needs to be completed and handed to pharmacy a minimum of 72 hours prior to day -2, (not inclusive of weekends). Supportive medication can be prescribed on an outpatient prescription.

6. Patient has blood tests as recommended on transplant protocol on day-3.

7. Weight should be re-checked on day -3, and compared with transplant protocol. Supportive medication from pharmacy will be issued to the patient.

8. Patient arrives at 09:30 hrs on day-2 and receives melphalan on day unit, along with pre- and post- hydration.

9. Patient comes in for further hydration, and receives stem cells as per protocol as a minimum 24 hrs after melphalan on day 0.

10. Patient is sent home on Day 0.

11. Patient attends day unit area daily and is assessed by BMT Associate Specialist /Advanced Clinical Practitioner daily until ANC>0.5×10^9/L and platelets>20×10^9/L.

12. Patient is not sent home if their personnel circumstances have changed and any of the inclusion criteria are not met.

13. Patient is discharged when transplant physician deems suitable as per engraftment criteria and microbiology advice.

3.4 Supportive care

Antimicrobial/antiviral/antifungal prophylaxis

To be prescribed on an outpatient prescription, and started on day -1.

- Ciprofloxacin 500mg PO BD until neutrophil engraftment.
- Fluconazole 100mg PO OD until neutrophil engraftment.
- Aciclovir 400mg PO BD until 3-months post-autograft
- Co-trimoxazole 480mg PO BD and folic acid 5mg PO weekly (Saturday) from Day +28 provided neutrophils ≥1 x 10^9/L and platelets ≥50 x 10^9/L until 3-months post autograft (consider nebulised pentamidine or atovaquone PO if intolerant of co-trimoxazole or blood counts inadequate)

Antiemetic

- Netupitant and palonosetron hydrochloride (Akynzeo®). (To be collected from pharmacy on day -2. To be taken a minimum of one hour prior to melphalan).
- Metoclopramide 10mg PO TDS PRN from Day -1, review on Day +3.

GI protection

- Omeprazole 20mg PO OD from Day -1 until discharge from service unless symptomatic of a GI complication or platelets ≤50 x 10^9/L.

Post-transplant granulocyte-colony stimulating factor (G-CSF)

- Filgrastim (Zarzio®) 0.5 million units/kg SC OD from day +6 until neutrophils are ≥1.5 x 109/L for two consecutive days.

Tumour Lysis Syndrome (TLS) prophylaxis

- Allopurinol 300mg OD from Day -1 until D0 (if needed, i.e. disease not in complete remission).

Allergies and infusion-related reactions (IRRs)

- Chlorphenamine 4mg PO QDS PRN or 10mg IV TDS PRN
- Hydrocortisone (Solu-Cortef®) 100mg IV Q6H PRN
- Paracetamol PO/IV QDS PRN
- Pethidine 6.25-25mg Q4H PRN

Fluid overload

- Furosemide 20-40mg PO BD PRN

3.5 Daily assessments

Include review of:

- Patient held temperature chart - Patient advised to check temperature QDS and report if experiences a temperature of 37.5°C on two occasions one hour apart, or one fever>38°C.
- 24 hr fluid intake and output.
- Oral assessment and intake.
- Sickness control.
- Daily assessment by day unit ACP/ward doctor. Consultant review on Tuesday in clinic- BMT ward Consultant to be given daily verbal report for bed management purposes.
- All observations done by nursing team including daily weights.
- Blood tests for full blood count, urea and electrolytes including serum creatinine, bone profile, CRP, magnesium, liver function tests, to be done daily and reviewed by the BMT Associate Specialist / BMT Advanced Clinical Practitioner.

3.6 Readmission criteria (Patient recalled or not sent home):

- Severe mucositis not managed, and pain not managed by Morphine Sulphate Oral Solution.
- Fever>37.5°C on two occasions one hour apart, or one fever>38°C.
- All NEWS2 scores ≥2 must be discussed with BMT consultant on ward duties.
- Uncontrolled sickness.
- Poor nutritional input.
- Profound diarrhoea, (> 4-5 episodes daily).
- If patient unable to cope with out-patient care (e.g. poor compliance, inability in tolerating PO medication) then consider in-patient admission.

3.7 Data

It is the responsibility of the ambulatory care team to collect the following data from the start of conditioning until discharge back to referring consultant.

- Number of days spent as full inpatient.
- Number of units of RBC/platelets transfused.
- Failure of antiemetic protocol- defined by admission for IV anti-emetics.
- Neutropenic days and admissions for neutropenic fever.
- Organisms cultured from CVAD/peripheral blood cultures

REFERENCES	Holbro A., Ahmad I., Cohen S., et al. Safety and cost-effectiveness of outpatient autologous stem cell transplantation in patients with multiple myeloma. Biol Blood Marrow Transplant. 2013; 19: 547-51. Martino M., Lemoli RM., Girmenia C., et al. Italian consensus conference for the outpatient autologous stem cell transplantation management in multiple myeloma. Bone Marrow Transplant. 2016; 51: 1032-40.
RELATED DOCUMENTS AND PAGES	SOP 2.23 Adult Autologous Stem Cell Transplant Pathway Assessment of Suitability for Ambulatory Care BMT at BHOC.
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QUERIES AND CONTACT	Rebecca Hallam, Advanced Clinical Practitioner Rebecca.Hallam@uhbw.nhs.uk Tel: x21529 Adult Stem Cell Transplant Co-ordination Team: Email: BMTCo-Ordination@UHBW.nhs.uk Tel: x21118 or x21525

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