AMBULATORY CARE FOR LYMPHODEPLETION PRIOR TO CAR-T CELL INFUSION

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Clinical Standard Operating Procedure (SOP)

AMBULATORY CARE FOR LYMPHODEPLETION PRIOR TO CAR-T CELL INFUSION

SETTING	Stem Cell Transplant and Cellular Therapy Programme, Bristol Haematology and Oncology Centre
FOR STAFF	Any Haematology consultant, nursing and pharmacy personnel or junior medical staff involved in the care of CAR-T cell patients.
PATIENTS	CAR-T Cell Therapy patients

1. Indications for Practice

To provide a safe and effective framework by which lymphodepletion can be performed in the outpatient setting, prior to admission for CAR-T Cell infusion. This SOP details the following:

- Patient selection
- Criteria and procedures for re-admission
- Model of care
- Data collection
- Monitoring and support pre-cell reinfusion

Expected outcomes

- Safe administration of lymphodepletion pre CAR -T Cell infusion in selected patients in the outpatient setting
- Reduction or elimination of inpatient admissions for this procedure, improving the patient experience and releasing inpatient resources

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 CAR-T Cell patients.

2.2 Patient selection

Inclusion criteria:

- Aged over 16, deemed fit enough by frailty score criteria and as agreed by MDT. Patients must be receiving commissioned CAR-T Cell infusion
- Normal cardiac and lung function as usually performed before a conventional Autologous Stem Cell Transplant (ASCT).
- Absence of other relevant organ dysfunctions. (Liver impairment -defined in lymphodepletion protocols as AST/ALT >3 x ULN and Bili >34 or renal impairment, renal impairment defined as creatinine clearance <70 ml/min).

- Absence of advanced / bulky disease
- Any severe infection not completely microbiologically or clinically resolved is considered a contraindication to outpatient lymphodepletion
- Place of stay must be within 30 minutes' drive of the hospital.
- Suitable caregiver available 24 hours a day (specific to treatments)
- Access to a telephone 24 hours a day to be able to contact the transplant centre
- 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.
- Ability to understand spoken and written English in order to be able to communicate needs to transplant centre in the event of an emergency.
- ECOG score of 0-1.
- Patient/carer must be able to administer medications (oral)
- Patient/carer must be able to take and record temperature on a digital thermometer.
- Patient has Central Venous Access and is able to undertake basic care of line
- Patient and carer must be educated regarding nutrition, risk of infection and daily management during the treatment phase in ACA
- Patient and carer must have a clear understanding of the process to follow if the patient becomes unwell or if there is an emergency situation
- Patient must live within one hour's driving distance from the hospital (inclusion zone.)
- Patient must be able to get to appointments, without use of public transport and if they become unwell whilst at home (if this is an appropriate form of transport in an emergency).
- Informed consent including a detailed SOP for the caregiver and the outpatient management team.

Exclusion Criteria

- Patients with an ECOG score >2
- Patients with co-morbidities that will require medical monitoring or interventions during transplant (ie: unstable Diabetes)
- Patients who live more than an hour's driving time (outside the inclusion zone) from BHOC.

- Housing unsuitable
- No carer available (please check treatment protocol for confirmation of need for carer)
- No transport available
- Prior history of poor compliance with treatment/appointments
- Patients with CNS disease resulting in confusion and risk if cognitive impairment
- Patients deemed unable to participate due to lack of capacity
- History of drug abuse
- Patients at risk of self-harm
- Psychiatric illness, suicidal tendencies
- Physical disabilities which may prevent self-management of the treatment regimen (unless a carer is deemed able)
- Patients undergoing trials are to be excluded as are those patients receiving newly commissioned agents until further experience with these are gained.

3. Procedure

3.1 Equipment/Supplies

- Dedicated chair in outpatient unit for ambulatory BMT patients
- One bed will be identified for overnight admission. 3 outpatients 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 Process

- Patients will be selected as per the criteria for in section 2.2. They will be given an information sheet and consented to ambulatory care prior to attending for lymphodepletion. Consent should include risk assessments as mentioned above.
- Ensure adequate CAR-T Cell production has occurred and cells have been received at the NHSBT lab in Filton.
- Work up investigations are within acceptable limits and agreed at the BMT planning meeting.
- CVAD must be in situ

Timeline:

No later than Day-8	Lymphodepletion protocol sheets, Chemocare® prescription and drug chart to be completed and handed to Pharmacy a minimum of **72 hours prior to Day -5** (not inclusive of weekends) Supportive medication can be prescribed on an outpatient prescription.	
Day-6	Patient has blood tests as recommended on lymphodepletion protocol Weight re-checked, and compared with lymphodepletion protocol. Supportive medication from Pharmacy issued to the patient. Drug history and medicines reconciliation to be undertaken by pharmacy medicines management technician	**Patient attends the day unit area daily and is assessed by BMT Associate Specialist, BMT ACP and Pharmacist trained in BMT / CAR-T cells.** Patient is sent home each day between Day -5 until Day - 1 unless their home or personal circumstances have changed and any of the inclusion criteria are not met or any of the exclusion criteria are now met. See section 3.4.
Day-5	Patient arrives at 09:30 and receives: • Fludarabine infused over 30 mins. • Normal saline 1L over 4 hours. Start 30 mins prior to infusion of cyclophosphamide infusion • Mesna – slow bolus given immediately prior to cyclophosphamide infusion • Cyclophosphamide and mesna infused over 1 hour • Oral mesna 2 hours after the start of cyclophosphamide • Oral mesna 6 hours after the start of cyclophosphamide.	
Day -4	Patient arrives at 09.30 and receives: • Fludarabine infused over 30 mins. • Normal saline 1L over 4 hours. Start 30 mins prior to infusion of cyclophosphamide • Mesna – slow bolus to be given immediately prior to cyclophosphamide infusion • Cyclophosphamide and mesna infused over 1 hour • Oral mesna to be given 2 hours after the start of cyclophosphamide • Oral mesna to be given 6 hours after the start of cyclophosphamide	
Day -3	Patient arrives at 09.30 and receives: • Fludarabine infused over 30 mins. • Normal saline 1L over 4 hours. Start 30 mins prior to infusion of cyclophosphamide • Mesna – slow bolus to be given immediately prior to cyclophosphamide infusion • Cyclophosphamide and mesna infused over 1 hour • Oral mesna to be given 2 hours after the start of cyclophosphamide • Oral mesna to be given 6 hours after the start of cyclophosphamide	
Day -2	Rest day	
Day -1	Patient admitted to the ward	
Day 0	CAR-T Cell infusion and monitoring for ICANS/CRS	

Patient is discharged from day 10 onwards, when transplant physician deems suitable as per engraftment criteria and microbiology advice.

3.3 Supportive care

Supportive care medications are to commence when patient starts on the Ambulatory Care pathway.

Refer to:

- Adult and TYA CAR-T Cell Therapy Supportive Care Guidelines
- Adult CAR-T Cell Therapy Antifungal Guidelines on Microguide
- BMT and CAR-T Antiemetics Guidelines

3.4 Daily Assessments

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 Friday in CAR T cell 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 ACP. In addition, on Monday, Wednesday and Friday test for clotting screen, fibrinogen, ferritin and LDH.

Readmission criteria (Patient recalled or not sent home):

- 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 of loose stool daily).
- If patient unable to cope with outpatient care (e.g. poor compliance, inability in tolerating oral medication) then consider in-patient admission.

Data

Collect the following data at all times

- Day of admission (if before Day –1)) and reason for early admission
- 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	External documents
RELATED DOCUMENTS AND PAGES	Adult CAR-T Cell Therapy Patient Pathway Revaccination SOP SOP 17.5 'Medical and nursing management of IEC toxicities' SOP 17.4 'Dosage and administration of tocilizumab' SOP 17.11 'Dosage and Administration of Anakinra for Refactory CRS and ICANS SOP 17.12 'Dosage and Administration of Siltuximab for Refactory CRS and ICANS' SOP 8.18 'Administration of nebulised pentamidine' Clinical Guidelines Adult and TYA CAR-T Cell Therapy Supportive Care Guidelines BMT and CAR-T Antiemetics Guidelines Clinical Guideline 'Prescribing granulocyte colony stimulating factor (GcSF) in BHOC' Clinical Guideline 'Neutropenic Sepsis' (opens MicroGuide) Clinical Guideline 'Adult BMT and CAR T-cell antifungal guidelines' (opens MicroGuide) Clinical Guideline 'Tumour lysis syndrome guidelines for prophylaxis and treatment'
AUTHORISING BODY	Adult BMT IEC Quality Group
SAFETY	Any additional safety concerns
QUERIES AND CONTACT	Stem Cell Transplant and CAR-T Coordination team BMTCo-Ordination@uhbw.nhs.uk

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Clinical Standard Operating Procedure (SOP)

ASSESSMENT OF SUITABILITY FOR AMBULATORY CARE BMT AT BHOC

SETTING	Stem Cell Transplant and Cellular Therapy Programme, Bristol Haematology and Oncology Centre
FOR STAFF	Clinical staff working in Stem Cell Transplant and Cellular Therapy
PATIENTS	Patients receiving autologous stem cell transplant or CAR-T Cell therapy at BHOC

1. Indications for Practice

Autologous transplants (such as Melphalan-conditioned Autologous BMT and CAR T cell transplants) were previously delivered as an elective inpatient admission treatment; patients would make scheduled day attendances to the hospital to receive all or part of the chemotherapy regime / supportive medications.

The Ambulatory Care (AC) BMT service primarily supports the administration of chemotherapy conditioning, administration of blood components and the need for blood tests and other investigations in the preparation phase and once treatment commences. This enables patients to receive their care in a timely fashion, receiving full access to specialist medical and nursing staff and pharmacy services, without staying in an inpatient environment.

The following SOP details the inclusion and exclusion criteria when referring patients to the AC BMT Service.

2. Authorised Personnel / Training Required

Bone Marrow Transplant Consultants, Associate Specialists, Fellows and Advanced Care Practitioners (ACP) can assess a patient for suitability for ambulatory care BMT.

3. Procedure

3.1 Assessment of Suitability for Ambulatory Care

Prior to initiating a patient on ambulatory chemotherapy, appropriate assessment of patient's suitability must be undertaken by the patient's referring consultant and/or ACP to ensure they are a safe candidate for administration of ambulatory chemotherapy conditioning and stem cell infusion.

On assessment, prior to commencing treatment in AC, the patient will sign an agreement of eligibility and self-care alongside the assessing nurse- a copy of which should remain in other

patient's notes and one for the patient to take.

If a patient is assessed as suitable for ambulatory BMT and agrees to ambulatory BMT, the consent form will list the treatment as 'Ambulatory'.

The exclusion and inclusion referral criteria listed below should be used alongside other individual protocol-specific requirements (or relating standard operating procedure) to establish patient eligibility for AC treatment. (For example, see also SOP 4.11 High Dose Melphalan With Autologous Stem Cell Rescue In The Outpatient Setting).

Any patient deemed to fulfil the referral criteria may have access to the service.

3.2 Referral Inclusion Criteria

- Patient has consented to ambulatory care and is aware of self-care requirements such as personal hygiene, nutrition, hydration during the transplant process.
- Patients undergoing Melphalan conditioned autografts or CAR T cell transplants
- ECOG score of 0-1.
- Full time carer available (specific to treatments)
- Patient/carer must be able to administer medications (oral)
- Patient/carer must be able to take and record temperature on a digital thermometer.
- Patient has Central Venous Access and is able to undertake basic care of line
- Patient and carer must be educated regarding nutrition, risk of infection and daily management during the treatment phase in ACA
- Patient and carer must have a clear understanding of the process to follow if the patient becomes unwell or if there is an emergency situation
- Patient and carer must understand spoken and written English
- Patient must live within one hour's driving distance from the hospital (inclusion zone.)
- Patient must be able to get to appointments, without use of public transport and if they become unwell whilst at home (if this is an appropriate form of transport in an emergency).
- Patient/carer must have access to a telephone 24 hours a day

The presence of pet animals/ small children in the home should be established - where this is the case counselling on heightened awareness of keeping animals at a distance from the patient for the duration of treatment must be mentioned.

All cytotoxic medication or contaminated equipment must be stored away from access to/risk of contact with women of childbearing potential, children, and pets.

3.3 Referral Exclusion Criteria

- Patients with an ECOG score >2
- Patients with co-morbidities that will require medical monitoring or interventions during transplant (i.e.: dialysis, unstable diabetes)
- Patients who live more than an hour's driving time (outside the inclusion zone) from BHOC.
- Housing unsuitable
- No carer available
- No transport available
- Prior history of poor compliance with treatment/appointments
- Patients with CNS disease resulting in confusion and risk if cognitive impairment
- Patients deemed unable to participate due to lack of capacity
- History of drug abuse
- Patients at risk of self-harm
- Psychiatric illness, suicidal tendencies
- Physical disabilities which may prevent self-management of the treatment regimen (unless a carer is deemed able)

3.4 Patient Education

- Patients must be educated regarding self-monitoring whilst an outpatient, ideally with their nominated family member or friend present
- Education is the responsibility of the nominated Consultant.
- Verbal information must be accompanied by written information including the BHOC patient leaflet: Ambulatory care for patients at BHOC undergoing bone marrow transplant.
- Patient must ensure access to an accurate thermometer (electronic preferred)
- Patients must be given the telephone number for the 24 hour Haematology advice line and have explained how the service works
- Patients must be told to contact the acute oncology service if unwell, if they have a fever >38C, or any symptoms of bleeding.

- Patients must be told to avoid taking paracetamol, NSAIDs or any anti-platelet drugs
- Patients must understand that readmission is common and prompt treatment of infections (IV antibiotics within 1 hour of fever) is essential

REFERENCES	NICE Guidance NG 47 Haematological Cancers: Improving Outcomes
RELATED DOCUMENTS AND PAGES	Autologous Pathway SOP 4.11 High Dose Melphalan With Autologous Stem Cell Rescue In The Outpatient Setting
AUTHORISING BODY	Adult BMT IEC Quality Group
SAFETY	No additional safety concerns
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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