
SHARED CARE FOR ADULT CAR-T PATIENTS

Creator: **University Hospitals Bristol and Western**

Author: Rebecca Hallam, Advanced Clinical Practitioner

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Clinical Standard Operating Procedure (SOP)

SHARED CARE FOR ADULT CAR-T PATIENTS

SETTING	Stem Cell Transplant Programme
FOR STAFF	All qualified medical and nursing staff may be required to be involved in the shared care of patients post CAR-T therapy
PATIENTS	Patients receiving CAR-T Cell Therapy

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1. Indications for Practice

1.1 GENERAL PRINCIPLES OF SHARED CARE OF ADULT CAR-T PATIENTS

Adult patients will be referred to University Hospitals Bristol and Weston for CAR-T therapy which will now be referred to as the “treatment centre”. Effective shared care between the treatment centre and referring centre is essential before, during and after therapy. This requires:

1. Good communication between treatment centre and referring centre (email/mobile)
2. Preliminary discussions of potential patients encouraged
3. Early referral to treatment centre is important to allow scheduling of apheresis and manufacturing slots
4. Treatment centre contracted to provide 30 days of post treatment care in Bristol
5. Intensity of post CAR-T care patient dependent and flexibility required
6. Treatment centre should be involved in complications after return back to referral centre
7. The Treatment centre will formally ‘hand-over’ patients at day 30 to referring centre. The referring centre should specify a designated individual to receive hand-over.

2. Authorised Personnel / Training Required

All qualified medical and nursing staff may be required to be involved in the shared care of patients post CAR-T therapy.

3. Procedure

3.1 PRE CAR-T

The following investigations and procedures will be performed by either the referring centre or the transplant centre depending on the individual patient circumstances:

3.1.1 INVESTIGATIONS

- Microbiological markers: Hep B Surface Ag, Hep B core Ag, Hep C Ab, Syphilis, HTLV 1+2 Ab, HIV 1+2 Ag/Ab, HIV NAT, HBV NAT, HCV NAT, Hep E RNA
- Documentation of disease status: PET scan/marrow as close to admission for CAR-T therapy as possible
- CXR
- Pulmonary function tests (spirometry, lung volumes, transfer factor, 6 min walking test)
- Echocardiogram
- Assessment of renal and liver function
- Baseline immunoglobulin levels
- FBC, U+Es, LFTs, CRP, ferritin, clotting screen, Ca²⁺, Mg²⁺, PO₄⁻ and LDH
- Blood bank to be informed of need for irradiated blood products due to fludarabine

3.1.2 Vascular Access Requirements

Tunnelled double lumen central venous catheter

3.2 FOLLOW-UP POST CAR-T INFUSION

Discharge summary documenting inpatient course and medication on discharge to outpatient setting to be completed according to SOP. Clinic letters to referring centre copied to GP.

3.2.1 Day -6 – 0

CAR-T patients will be admitted to D703 to receive their conditioning chemotherapy

3.2.2 Day 0-14

CAR-T cell recipients will remain inpatients for a minimum of 14 days post cell infusion and will only be discharged once any cytokine release syndrome (CRS) has resolved and they have an Immune Effector Cell Encephalopathy (ICE) score of 10/10.

3.2.3 Day 14-30

From day 14-30 CAR-T cell recipients will reside in near-hospital accommodation if their home address is more than a 30 minute drive from the hospital.

CAR-T recipients will be reviewed daily from discharge until day +30. As a minimum, patients will have a face to face assessment twice weekly up to D+30 for clinical review including:

- ICE score
- Physical examination
- Review of medication
- FBC, U+Es, LFTs, CRP, ferritin, clotting screen, Ca²⁺, Mg²⁺, PO₄⁻ and LDH.

On the week days not attending in person, a video/phone call will be made to the patient and carer for daily review including completion of the ICE score
On a Sunday the On-call registrar will call the patient and their carer.

Additionally, on a Friday the patient will attend the CAR-T clinic.

General Considerations:

- CAR-T recipients will carry a CAR-T Cell Alert Card
- Day +30 PET/CT or BMA+T +/- imaging as appropriate for restaging.
- Avoid use of GCSF from Day 0 to Day 21 as may increase CRS
- Avoid use of steroid unless indicated for CRS/ICANS (discuss with consultant)
- Stop prophylactic levetiracetam at day 30
- Patient to refrain from driving, using machines or activities that require alertness for 8 weeks post CAR-T therapy
- For patients with hypogammaglobulinaemia (IgG <4g/L) and recurrent infections, IvIg replacement should be administered monthly (at referring centre).

3.2.3 Day 31-100 (Referring centre responsible for administering routine treatment support e.g. blood product support but Treatment centre to be contacted with any signs of ICANS or disease progression).

Minimum fortnightly follow-up at Treatment Centre

- Be alert to possibility of altered consciousness for 8 weeks
- FBC, U+Es, LFTs, BMT PCR (if previous allograft, EBV+ or late derangement of LFTs)
- IgG measurement (monthly)

Day 60 and day 90 bone marrow/ Day 90 PET-CT to be arranged by referral centre.

3.2.4 Day 100 onwards (Referring centre responsible for readmissions and outpatient follow up)

Minimum monthly clinical review at referring centre to 6 months (may be more frequent if ongoing problems)

3.3 STANDARD ANTI-INFECTIVE PROPHYLACTIC MEASURES

1. Aciclovir 400mg bd po till 6 months post
2. Antifungal prophylaxis until neutrophil recovery (>0.5)
3. Co-Trimoxazole 480mg bd Mon/Wed/Fri till 1 year post treatment (or until CD4 count >300) given with folic acid 5mg 1xweekly or nebulised pentamidine 3-4 weekly, if intolerant of septrin.
4. Seasonal flu vaccination may be administered 1 month after CAR-T infusion.
5. Seasonal flu vaccination should be administered to all household contacts of the patient.
6. Patients who have received previous Allogeneic-SCT should proceed with re-vaccination on resolution of B-cell aplasia.

3.4 FOLLOW-UP

Treatment centre review at landmarks of 3, 6, 9, and 12 months as a minimum and then annually thereafter.

3.5 LATE EFFECTS

- Relapse
- Prolonged cytopenias
- B-cell aplasia
- Hypogammaglobulinaemia
- Late infections
- Secondary malignancies
- Monitoring for immune-related events
- Psychiatric events
- Neurological events
- GvHD in previous allograft recipients

Referral to Late Effects Clinic initiated by treatment centre at around 5 years post CAR-T, dependent on responsible Consultant (see Long-Term Follow-up SOP for further information). Follow-up to continue at treatment centre for 15 years.

REFERENCES	<p>Brudno, J et al. Toxicities of chimeric antigen receptor T cells: recognition and management. Blood Vol 127;26 (2016) 3321-3329.</p> <p>Buitrago, J et al. Adult Survivorship. Considerations following CAR T-cell therapy. Clinical Journal of Oncology Nursing. Vol 23;2 (Apr 2019). 42-48.</p> <p>Cordeiro, A et al. Late Effects after Treatment with CD19-Targeted Chimeric Antigen Receptor Modified T Cells. Biology of Blood and Marrow Transplantation 00 (2019) 1-8.</p> <p>Hayden, P.J et al. An international survey on the management of patients receiving CAR T-cell therapy for haematological malignancies on behalf of the Chronic Malignancies Working Party of EBMT. Current Research in Translational Medicine 67 (2019) 79-88.</p> <p>Mahadeo, K et al. Management guidelines for paediatric patients receiving chimeric antigen receptor T cell therapy. Nature Reviews Clinical Oncology. Vol 16 (2019) 45-63.</p> <p>Neelapu, S et al. Chimeric antigen receptor T-cell therapy – assessment and management of toxicities. Nature Reviews Clinical Oncology. Vol 15 (Jan 2018) 47-62.</p>
RELATED DOCUMENTS AND PAGES	See also: Adult/TYA Car T Cell Supportive Care Guidelines
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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