

CAR-T Cell Therapy

Version: 3.1

No 1: Assessment and management of Cytokine Release Syndrome (CRS) following CAR-T Cell Therapy

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Uploaded to Wessex Haematology Website 2/2/23

Contents

Summary	2
1. Scope and Purpose	3
2. Definitions/Abbreviations:	3
3. Identification, assessment and management of cytokine release syndrome	4
3.1 Clinical Symptoms, Laboratory Diagnosis, Differential Diagnosis, and Predictive Factors	4
3.2 Monitoring for CRS	4
3.2.1 Medical Review, Observations and Grading	4
3.2.2 Laboratory investigations	5
3.2.3 Summary of routine observations and investigations	6
4. Management of CRS	6
4.1 EHA/EBMT algorithm	6
4.2 Management of CRS/MAS	7
4.3 Supportive Measures	8
5. Recovery, de-escalation and ambulatory care	9
6. Roles and responsibilities	9
7. Related Trust Policies	10
8. Communication Plan	10
9. Process for Monitoring Compliance/Effectiveness	10
10. Arrangements for Review of the Policy	10
Appendices	11
Appendix A Clinical features of cytokine release syndrome	11
Appendix B Drugs used in the treatment of CRS and ICANS	12
Appendix C Integrated CRS/ICANS Assessment Chart – front sheet and continuation	14

Summary

Cytokine release syndrome (CRS) is caused by a rapid and mild to massive release of cytokines from immune cells involved in immune reactions, particularly after immunotherapy, such as CAR-T cell therapy. The frequency and severity of CRS after CAR-T varies between products (any grade: 37–93%, G3/4: 1–23%).^{1,2,3}

This policy is adapted from the EHA/EBMT guidelines on identification and management of cytokine release syndrome,⁴ and the EBMT CAR-T handbook.⁵

This policy should be used in conjunction with the ICANS policy: [Management of CAR-T cell Therapy No.2 – Diagnosis and Management of Immune Effector Cell Associated Neurotoxicity Syndrome \(ICANS\) Post CAR-T Cell Therapy](#)

CAR-T SOPs and Policies available :-

Transplant Q Pulse 7

Metavision

Neurology TEAMS folder

¹ Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene CiloleuceL CAR-T cell therapy in refractory large B-cell lymphoma. *N Engl J Med.* 2017;377(26):2531–44.

² Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med.* 2019;380(1):45–56

³ Abramson JS, Palomba ML, Gordon LI, et al. Lisocabtagene maraleuceL for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. *Lancet.* 2020;396(10254):839–52.

⁴ Hayden et al. Management of adults and children receiving CAR T-cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the European Haematology Association (EHA). *Ann Oncol.* 2022 Mar;33(3):259-275

⁵ https://www.ebmt.org/sites/default/files/2022-02/2022_Book_TheEBMTEHACAR-TCCellHandbook.pdf

1. Scope and Purpose

To provide guidance on the identification and management of cytokine release syndrome (CRS) to all staff caring for patients undergoing CAR-T cell therapy; to ensure that patients with CRS receive appropriate care.

2. Definitions/Abbreviations:

ASTCT	American Society for Transplantation and Cellular Therapy
BiPAP	Bilevel positive airway pressure
CAR-T	Chimeric antigen receptor T-cell
CNS	Central nervous system
CPAP	Continuous positive airway pressure
CRP	C-reactive protein
CRS	Cytokine release syndrome
DIC	Disseminated intravascular coagulopathy
EDC	Emergency drugs fridge
G-CSF	Granulocyte colony stimulating factor
GICU	General Intensive Care Unit
GvHD	Graft versus host disease
HDU	High Dependency Unit
HLH	Haemophagocytic lymphohistiocytosis
ICANS	Immune effector cell-associated neurotoxicity syndrome
ICE	Immune effector cell-associated encephalopathy
ICU	Intensive Care Unit
IEC	Immune effector cell
IL-6	Interleukin-6
IL-10	Interleukin-10
MAS	Macrophage activation syndrome
NCI	National Cancer Institute
PCT	Procalcitonin
QM	Quality Manager
SPC	Summary of product characteristics
WBMTCT	Wessex Blood and Marrow Transplantation and Cellular Therapy

3. Identification, assessment and management of cytokine release syndrome

3.1 Clinical Symptoms, Laboratory Diagnosis, Differential Diagnosis, and Predictive Factors

According to the UK real world experience, the median time from infusion to onset of CRS is 2 days for Axicel and Tecartus, 3 days for Tisagen, and 5 days for Lisocel.⁶

Fever is the cardinal sign of CRS

CRS usually manifests with fever. This precedes, or is accompanied by, general symptoms such as malaise, headache, arthralgia, anorexia, rigours, and fatigue. CRS can rapidly progress to hypoxia, tachypnoea, tachycardia, hypotension, arrhythmia, culminating in shock and cardiorespiratory organ dysfunction or failure. A more comprehensive list of signs and symptoms associated with CRS may be found in appendix A.

Although the diagnosis of CRS cannot be established or ruled out by laboratory diagnostics, they can be used to monitor organ dysfunction.

CRS/MAS overlap can be considered as related hyperinflammatory syndrome, typically identified patients with refractory CRS. It is characterised by fever, organomegaly, hyperferritinemia, liver dysfunction, hypertriglyceridemia and pancytopenia. Many of these features are indistinguishable from CRS, but CRS/MAS overlap should be considered in those patients with CRS refractory to tocilizumab and corticosteroids.

CRS symptoms and laboratory findings closely mimic infection; therefore, infection workup (e.g. cultures, CXR, septic screen) and treatment are of primary importance.

Other relevant differential diagnoses include tumour lysis syndrome and progression of the underlying malignancy.

Prediction of CRS in an individual patient is not yet possible. However, the UK experience suggests ECOG performance status >0, or raised LDH at infusion, are predictors of more severe CRS and ICANS grade, and increased steroid usage.⁶

3.2 Monitoring for CRS

3.2.1 Medical Review, Observations and Grading

Patients undergoing CAR-T therapy are monitored on the cell therapy ward with routine observations 4-hourly from the time of infusion, with documentation of CRS/ICANS grade every 8 hours. In addition, CRS/ICANS grade should be documented whenever the patient's clinical status changes.

Grading should be documented on the CRS/ICANS Integrated Assessment Chart ([click to link to documents on Staffnet](#)). A sample can be seen in [Appendix B](#).

⁶ Sanderson et al. CAR-T Toxicity Management and Steroid Use in High-Grade B-Cell Lymphoma: Impact on Real-World Survival Outcomes in the UK. *Blood* (2021) 138 (Supplement 1): 531.

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CRS grading is based on a combination of routine observations and interventions (see figure 1).

Grade 1	Grade 2	Grade 3	Grade 4
Temperature $\geq 38^{\circ}\text{C}$ and no hypotension and no hypoxia	Temperature $\geq 38^{\circ}\text{C}$ and hypotension not requiring vasopressors and/or hypoxia requiring low-flow nasal cannula at ≤ 6 l/min or blow-by	Temperature $\geq 38^{\circ}\text{C}$ and hypotension requiring vasopressor and/or hypoxia requiring high-flow nasal cannula >6 l/min, facemask, nonrebreather mask, or Venturi mask	Temperature $\geq 38^{\circ}\text{C}$ and hypotension requiring multiple vasopressors (excluding vasopressin) and/or hypoxia requiring positive pressure (e.g. CPAP, BiPAP, intubation and mechanical ventilation)

Figure 1: Consensus grading of cytokine release syndrome⁷

Fever is defined as temperature $\geq 38^{\circ}\text{C}$. In patients with CRS who subsequently receive antipyretics or anti-cytokine therapy such as tocilizumab or steroids, fever is no longer required to grade subsequent CRS severity. In this case, CRS grading is driven by hypotension, and/or hypoxia.

Patients with grade 1 CRS or ICANS should have observations 2-hourly and CRS/ICANS grading performed 4-hourly.

Patients with grade 1+ CRS or ICANS managed on the transplant ward should have twice-daily review by the attending and/or on-call CAR-T consultant.

Patients with grades 2-4 CRS or ICANS managed on GICU or neuro ICU will have continuous observations, which may include invasive monitoring. CRS/ICANS grading must continue to be documented on the integrated CRS/ICANS Assessment Chart whilst the patient is on GICU or neuro ICU.

3.2.2 Laboratory investigations

Patients without CRS/ICANS should have daily bloods including FBC, U&E, LFTs, bone profile, LDH, CRP and ferritin.

Patients with CRS/ICANS of any grade should have bloods performed at least every 12 hours, or more frequently at the discretion of the CAR-T/GICU consultant. Coagulation screen and peripheral/line blood cultures should be performed daily.

Patients receiving tocilizumab may have infection in the absence of fever or raised CRP/PCT.

⁷ Yakoub-Agha I, Chabannon C, Bader P, et al. Management of adults and children undergoing chimeric antigen receptor T-cell therapy: best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the joint accreditation committee of ISCT and EBMT (JACIE). *Haematologica*. 2020;105(2):297–316.

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3.2.3 Summary of routine observations and investigations

CRS/ICANS grade	Grade 0	Grade 1	Grade 2	Grade 3-4
Routine observations from infusion (Temperature, HR, BP, SpO2 and RR)	4-hourly	2-hourly	2-hourly	Continuous
CRS grading	8-hourly	4-hourly	4-hourly	4-hourly
ICE score	8-hourly	4-hourly	4-hourly	4-hourly
Routine bloods from infusion, including FBC, U&E, LFT, bone, CRP, LDH, Ferritin	Daily (12-hourly if high risk for TLS*)	Daily	Daily	Daily
Fluid balance	4-hourly	Hourly	Hourly	Hourly
Additional investigations		Coagulation screen and peripheral/line cultures when first documented, and at any subsequent clinical deterioration	Coagulation screen and peripheral/line cultures when first documented, and at any subsequent clinical deterioration	Coagulation screen and peripheral/line cultures when first documented, and at any subsequent clinical deterioration

Table 1: Summary of routine observations and investigations post CAR-T infusion

*As directed by CAR-T consultant

4. Management of CRS

4.1 EHA/EBMT algorithm

CRS and ICANS are medical emergencies, and all grades of CRS or ICANS must be immediately escalated to the attending/on-call CAR-T consultant.

CRS management combines symptomatic measures (antipyretics e.g paracetamol, ibuprofen, and IV fluids, vasopressors, respiratory support) with tocilizumab (IL-6 receptor) +/- corticosteroids. Should two doses of tocilizumab fail to control CRS, dexamethasone should be administered.

Tocilizumab should be considered earlier in older and/or more frail patients who might tolerate higher grade CRS less well. However, there is to date no data to support routine early or prophylactic tocilizumab. Such an approach may be followed in some patients at the discretion of the attending CAR-T consultant, with discussion with the UHS CAR-T MDT.

Clinicians should remain vigilant for occult sepsis emerging post-tocilizumab. Gastrointestinal perforation has also been reported. Corticosteroids should be subject to rapid taper once CRS controlled.

Should CRS not respond to tocilizumab/corticosteroids, alternative therapeutic options include siltuximab and anakinra, but limited clinical data are available. There should in addition be high clinical suspicion for underlying/concurrent infection or CRS/MAS overlap.

UHS have adopted the universal management algorithm for CRS as laid out by EHA/EBMT consensus (Figure 2) (REF):

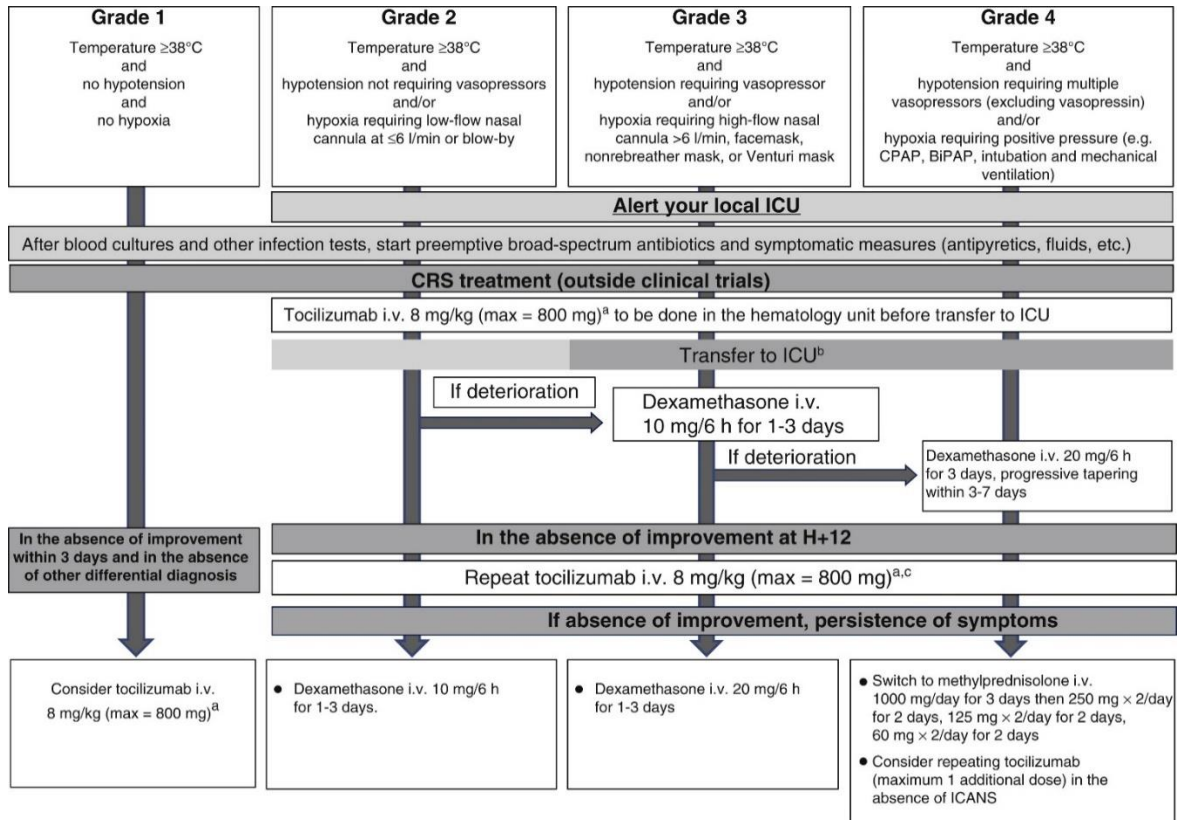


Figure 2: EHA/EBMT algorithm for grading and management of cytokine release syndrome.⁸

^ain children <30 kg, tocilizumab is given at the dose of 12 mg/kg.

^bin centres with little experience, it is recommended to transfer the patients to ICU from grade 2

^cin grade 2 CRS, dexamethasone can be concurrently administered with the second dose of tocilizumab if needed

4.2 Management of CRS/MAS

Persistent fever despite tocilizumab with organomegaly, cytopenias, hyperferritinemia ($>10,000$ ng/ml), liver dysfunction, coagulopathy and hypertriglyceridemia favour a CRS/MAS overlap syndrome rather than CRS.

⁸ Hayden et al. Management of adults and children receiving CAR T-cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the European Haematology Association (EHA). Ann Oncol. 2022 Mar;33(3):259-275

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Patients with CRS/MAS should be treated with anakinra in combination with corticosteroids, as per the EHA/EBMT algorithm (figure 3). Cytotoxic IV or intrathecal chemotherapy may be considered in refractory cases or those with CNS involvement, although the evidence base is lacking for this approach, and there is a risk of CAR-T cells ablation with loss of therapeutic efficacy. It is recommended that use of cytotoxics in this case should, where possible, be discussed by the attending CAR-T consultant with the HLH MDT at UCLH.

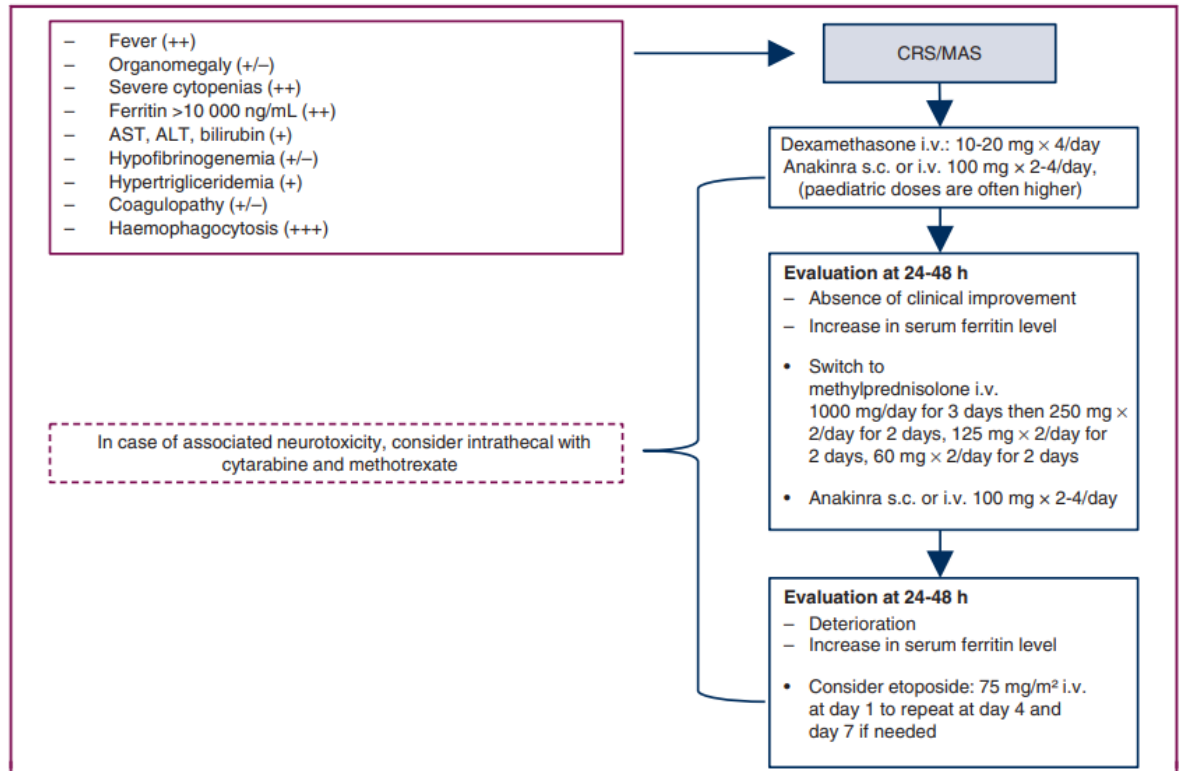


Figure 3. Recommended management of CRS/MAH overlap syndrome.⁹

4.3 Supportive Measures

In addition to measures outlined above, the following measures should be taken in all patients following CAR-T infusion:

Urgent Review should be requested if:

- Systolic blood pressure >140mmHg or <90mmHg
- Heart rate >120bpm or <60bpm, or arrhythmia
- Respiratory rate >25 breaths/min or <12 breaths/min
- Upward trend in creatinine or liver function tests
- Change in mental status, or tremors or jerky movements in extremities.

Patients with neutropenia who develop fever should be prescribed broad spectrum antibiotics and have blood cultures taken in accordance with the infection prevention therapy protocols (adults)

⁹ Hayden et al. Management of adults and children receiving CAR T-cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the European Haematology Association (EHA). Ann Oncol. 2022 Mar;33(3):259-275

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version 4th July 2014. Broad spectrum antibiotics should also be considered in non-neutropenic patients.

Serum troponin, ECG, and echocardiogram should be considered in patients with fluid-refractory hypotension.

Red cell transfusion should be initiated to keep haemoglobin >80g/L

Platelet transfusion should be initiated to keep platelet count >20x10⁹/L

Consider FFP and/or cryoprecipitate in symptomatic coagulopathy

G-CSF may be considered and is not deemed unsafe in this setting. However, its use should be reserved for cytopenias persisting despite resolution of CRS. **G-CSF should not be administered without discussion with haematology consultant through Switchboard (100) Contact BMT and Cellular Therapy Haematology Consultant on call .**

5. Recovery, de-escalation and ambulatory care

Patients recovering from CRS and/or ICANS may have their care de-escalated at the discretion of the CAR-T and GICU consultants, typically after demonstrating normalisation of physiological parameters without organ support, along with acceptable improvement in laboratory parameters.

It is important to wean steroids quickly in recovering patients, in part due to the increased risk of invasive fungal and other atypical infections.

Patients with no evidence of CRS or ICANS by day 10 post-infusion are considered low-risk for further related events and according to drug label may be considered for ambulatory care from this point. All other patients may be considered for ambulatory care from day 14.

The SmPC for the three currently available commercial CAR-T products states patient must remain within 2 hours of the CAR-T centre up to and including day 28 post infusion. However, the [Interim Service Specification](#) provided by NHS England states patients must remain within 1 hour of the CAR-T centre. The EHA/EBMT recommendations are that patients stay within '30-60 minutes' of hospital up to day 28.

Until such time as NHS England issues revised guidance, all patients undergoing CAR-T therapy at UHS must remain inpatients for at least 10 days post infusion, and subsequently remain accompanied within 1 hour of the hospital, up to and including day 28 post infusion. Decisions to discharge patients to ambulatory care are made at the discretion of the attending CAR-T consultant, who should review the patient in person on the day of discharge.

6. Roles and responsibilities

This policy applies to all medical and nursing staff working in University Hospitals Southampton NHS Foundation Trust.

Contacts : CAR-T CNS mobile Amy Tooley or Alice Jenkins 07717138754
BMT and Cellular Therapy Consultant on call through switchboard (100)

7. Related Trust Policies

Infection prevention therapy protocols (adults) version 4th July 2014 **(add hyperlink to this)**

Management of CAR T cell therapies no 2– Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) – Post CAR-T cell therapy **(add hyperlink to this)**.

8. Communication Plan

Training sessions will be held throughout Cancer Care, Neurology and Intensive care based on the policies.

9. Process for Monitoring Compliance/Effectiveness

Compliance/understanding of the policies will be via acknowledgement of the policy on Q-Pulse

Key aspects of the procedural document that will be monitored:

What aspects of compliance with the document will be monitored	What will be reviewed to evidence this	How and how often will this be done	Detail sample size (if applicable)	Who will co-ordinate and report findings (1)	Which group or report will receive findings
Reading and acknowledgment of document by staff within the Southampton Wessex Blood and Marrow Transplant Service	Q Pulse document acknowledgment	Each time document updated and when new staff start. QM meetings held every 2 months	All WBMTCT staff	JACIE QM	WBMTCT Quality Meeting Group

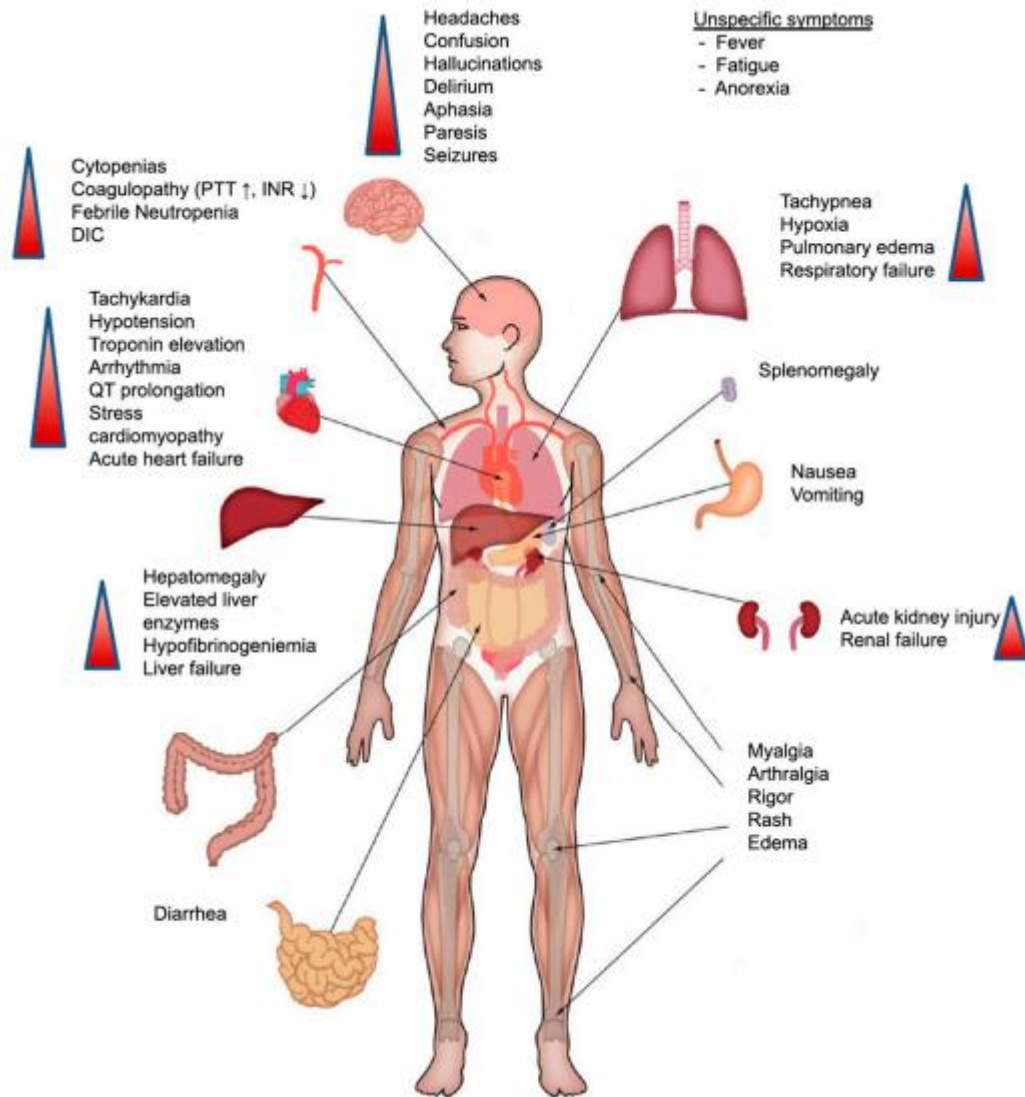
Where monitoring identifies deficiencies, actions plans will be developed to address them.

10. Arrangements for Review of the Policy

The policy will be reviewed every two years, or sooner if evidence or guidance changes.

Appendices

Appendix A Clinical features of cytokine release syndrome¹⁰



¹⁰ Mostafa Kamel, Y. CAR-T Therapy, The End of a Chapter or the Beginning of a New One? *Cancers* 2021, 13, 853. <https://doi.org/10.3390/cancers13040853>

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Appendix B Drugs used in the treatment of CRS and ICANS

Tocilizumab

Tocilizumab, an IL-6 receptor antagonist, can effectively diminish CRS-related toxicity with a rapid response. As a guide Tocilizumab should be dosed at 8mg/kg, and administered over 1hour. The dose may be repeated 8 hourly up to 4 times, at the discretion of the supervising consultant. Tocilizumab should be diluted in 100mls 0.9% sodium chloride. Tocilizumab comes in different size dose vials,

- 80mg in 4mls
- 200mg in 10mls
- 400mg in 20mls

Once Tocilizumab is added to the infusion bag, gently invert the infusion bag to avoid foaming. Dose should not exceed 800mg

Do not infuse with any other medicines

Tocilizumab does not cross the blood brain barrier and should not be used to treat ICANS in the absence of CRS. However, it may be given if CRS is also present.

Four doses of tocilizumab will be kept in the fridge on C6. This pack will contain information on dosing of tocilizumab, safe preparation of tocilizumab and equipment/devices to ensure safe preparation of tocilizumab. This will guide team collecting tocilizumab on how best to prepare dose for a patient of a given weight

Several strengths of tocilizumab will also be kept in the emergency drugs fridge (EDC). This is located behind pharmacy next to the security desk. A tocilizumab pack will be kept in the EDC. This will contain information on dosing of tocilizumab, safe preparation of tocilizumab and equipment/devices to ensure safe preparation of tocilizumab. This will guide team collecting tocilizumab on how best to prepare dose for a patient of a given weight

Storage of tocilizumab in the EDC ensures tocilizumab is available for patients at point of need and can be prepared and administered in safe way for patient and staff involved. Training on safe preparation of tocilizumab and use of safety needle free devices will be provided to staff

The staff member administering a dose of tocilizumab is responsible for informing pharmacy so that stocks can be replenished as soon as possible

Corticosteroids

Corticosteroids are a second-line therapy for CRS because the clinical response to corticosteroids is delayed compared to Tocilizumab. Furthermore, corticosteroids may lead to greater anti-tumour activity than Tocilizumab.

Dexamethasone 10mg IV is the standard steroid used, with frequency of administration dictated by the grade of CRS/ICANS. Methylprednisolone IV at high doses may be used for high grades of CRS/ICANS.

Steroids should be rapidly weaned on clinical improvement, and attention should be paid to anti-fungal prophylaxis in any patient receiving high dose steroids.

Anakinra

Anakinra targets the IL-1 cytokine receptor and is able to cross the blood-brain barrier, potentially limiting the toxic side effects of CRS^{6,7}. Anakinra is not licensed for treatment of IEC-related CRS, but may be considered in patients with CRS refractory to tocilizumab and steroid. It is given as a fixed dose of 200mg subcutaneous once daily. This is dispensed in a pre-filled syringe.

Patients and their carers should be counselled to seek immediate attention should the signs or symptoms of ICANS occur post discharge.

If patients are admitted within 8 weeks of CAR T cell therapy with neurological symptoms then 4 hourly monitoring should be recommenced, using the integrated CRS/ICANS assessment sheet.

Appendix C EXAMPLE Integrated CRS/ICANS Assessment Chart – front sheet and continuation

Assessment Sheet to be printed off Q Pulse and placed in each patient's ward notes on admission. Controlled Copies available in C6 CAR-T folder.

Cytokine Release Syndrome (CRS) Grading and Action

Cytokine Release Syndrome (CRS) is graded on the basis of: pyrexia, hypotension and hypoxia.

The grade is determined by the more severe event.

In patients who have CRS who are receiving tocilizumab or steroids, fever is no longer required for grading.

See the table below for guidance.

CRS Parameter*	Grade 1	Grade 2	Grade 3	Grade 4
Fever#†	Temperature $\geq 38^{\circ}\text{C}$	Temperature $\geq 38^{\circ}\text{C}$	Temperature $\geq 38^{\circ}\text{C}$	Temperature $\geq 38^{\circ}\text{C}$
		With		
Hypotension#	None	Not requiring vasopressors	Requiring one vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
		And/ or‡		
Hypoxia#	None	Requiring low-flow nasal cannula [^] or blow-by	Requiring high-flow nasal cannula [^] , facemask, non-rebreather mask, or Venturi mask	Requiring positive pressure (eg: CPAP, BiPAP, intubation and mechanical ventilation)

*Not attributable to any other cause

†In patients who have CRS then receive tocilizumab or steroids, fever is no longer required to grade subsequent CRS severity

‡CRS grade is determined by the more severe event

[^]Low-flow nasal cannula is ≤ 6 L/min and high-flow nasal cannula is > 6 L/min

*Organ toxicities associated with CRS may be graded according to CTCAE v5.0 but they do not influence CRS grading

Lee et al. *Biol Blood Marrow Transplant*, 2019 Apr;25 (4):625-638

ANY abnormalities or any CRS/ICANS grade above 0 must be escalated immediately to physicians as require timely treatment.

IF IN DOUBT – ESCALATE TO PHYSICIAN

Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) Grading and Action

ICANS grading is completed by assessing multiple neurological functions of the patient. It uses a combination of the ICE Score, and presence of other neurological symptoms.

ICE Scoring Tool

Immune Effector Cell Associated Encephalopathy Tool		
Monitors	How	Points
Orientation	Ask the patient the year, month, city and hospital	1 point for each correct answer. Total of 4 points.
Naming	Point to 3 objects in the room and ask the patient to name them (e.g. pen, book, clock)	1 point for each correct answer. Total of 3 points.
Following commands	Ask the patient to do a command (e.g. show me three fingers or close your eyes and stick your tongue out)	1 point for the correct action
Writing	Ability to write a standard sentence (e.g. I took the dog for a walk in the woods)	Compare to the handwriting prior to cell infusion. 1 point for correct action.
Attention	Ask the patient to count backwards from 100 in tens	1 point for the correct answer.

Once all parts of the assessment are completed, add all points up to the maximum total of 10. Relate this to the grading tool below.

Neurotoxicity Domain [‡]	Grade 1	Grade 2	Grade 3	Grade 4
ICE Score	7-9	3-6	0-2	0 (patient is unarousable and unable to perform ICE)
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse or stupor or coma
Seizure	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly ; or Non-convulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min); or Repetitive clinical or electrical seizures without return to baseline in between
Motor findings	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Raised intracranial pressure / Cerebral edema	N/A	N/A	Focal/local edema on neuroimaging [#]	Diffuse cerebral edema on neuroimaging; Decerebrate or decorticate posturing; or Cranial nerve VI palsy; or Papilledema; or Cushing's triad

[‡]ICANS grade is determined by the most severe event (ICE score, level of consciousness, seizure, motor findings, raised ICP/cerebral edema) not attributable to any other cause

Lee et al. *Biol Blood Marrow Transplant*, 2019 Apr;25 (4):625-638

**If the patient's ICE score is 9 or below,
or there is a new a neurological symptom, or you are unsure,
escalate to physician.**

Assessment and grading should be done:

- Every 8 hours from CAR-T infusion;
- Every 4 hours if any grade CRS or ICANS
- Whenever a change in the patients' status is observed;

Affix patient label here:

BASELINE ASSESSMENT – TO BE PERFORMED IMMEDIATELY PRIOR TO CAR-T INFUSION

Date	CRS	Fever ≥38°C		Hypotension				Hypoxia O₂ required to maintain SpO₂ ≥92%				CRS Grade
	<i>circle</i>	N	Y	None	No pressor required	Requiring 1 pressor	Requiring >1 pressor	None	Low-flow < 6L/min	High flow ≥6L/min	NIV or I&V	
Time	<i>min grade</i>	0	1	0	2	3	4	0	2	3	4	Total
	ICANS	Year	Month	City	Hospital	Object 1	Object 2	Object 3	Follow command	Hand- writing	Attention	
Staff initials	ICE score											/10
	Handwriting											ICANS Grade

Date	CRS	Fever ≥38°C		Hypotension				Hypoxia O₂ required to maintain SpO₂ ≥92%				CRS Grade
	<i>circle</i>	N	Y	None	No pressor required	Requiring 1 pressor	Requiring >1 pressor	None	Low-flow < 6L/min	High flow ≥6L/min	NIV or I&V	
Time	<i>min grade</i>	0	1	0	2	3	4	0	2	3	4	Total
	ICANS	Year	Month	City	Hospital	Object 1	Object 2	Object 3	Follow command	Hand- writing	Attention	
Staff initials	ICE score											/10
	Handwriting											ICANS Grade

Date	CRS	Fever ≥38°C		Hypotension				Hypoxia O₂ required to maintain SpO₂ ≥92%				CRS Grade
	<i>circle</i>	N	Y	None	No pressor required	Requiring 1 pressor	Requiring >1 pressor	None	Low-flow < 6L/min	High flow ≥6L/min	NIV or I&V	
Time	<i>min grade</i>	0	1	0	2	3	4	0	2	3	4	Total
	ICANS	Year	Month	City	Hospital	Object 1	Object 2	Object 3	Follow command	Hand- writing	Attention	
Staff initials	ICE score											/10
	Handwriting											ICANS Grade

Date	CRS	Fever ≥38°C		Hypotension				Hypoxia O₂ required to maintain SpO₂ ≥92%				CRS Grade
	<i>circle</i>	N	Y	None	No pressor required	Requiring 1 pressor	Requiring >1 pressor	None	Low-flow < 6L/min	High flow ≥6L/min	NIV or I&V	
Time	<i>min grade</i>	0	1	0	2	3	4	0	2	3	4	Total
	ICANS	Year	Month	City	Hospital	Object 1	Object 2	Object 3	Follow command	Hand- writing	Attention	
Staff initials	ICE score											/10
	Handwriting											ICANS Grade

Management of CAR T cell Therapy No 1 Diagnosis and management of Cytokine Release Syndrome following CAR T cell therapy

Version: 3.1

Document Monitoring Information

Approval Committee:	Cancer Care Governance
Date of Approval:	
Ratification Committee:	Insert Name of Committee (Policy Ratification Group (PRG) for Level 1 documents)
Date of Ratification:	Insert Date
Signature of ratifying Committee Group/Chair:	
Lead Name and Job Title of originator/author or responsible committee/individual:	Robert Lown Consultant Haematologist CAR-T Lead for Lymphoma, WBMTCT unit
Policy Monitoring (Section 6) Completion and Presentation to Approval Committee:	Cancer Care Governance
Target audience:	Medical and nursing staff in cancer care, general intensive care and neurological intensive care
Key words:	CAR T cell, cytokine release syndrome (CRS)
Main areas affected:	Cancer Care, GICU, Neuro ICU
Summary of most recent changes if applicable:	N/A
Consultation:	D Richardson, A Davies, JH Falconer, JR Falconer, S Main, S Mutamba, M Norbury, A Dushianthan, B Skinner, N Basker, C Dalley, R Lown, P Silva, K Hudson, S Holtby, A Pinto, P Fernandez
Equality Impact Assessment completion date:	06.09.2019
Number of pages:	16
Type of document:	Procedure
Does this document replace or revise an existing document	N/A
Should this document be made available on the public website?	No
Is this document to be published in any other format?	No

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