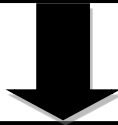


CRS treatment algorithm

Every patient should have baseline and regular monitoring of:

- temperature
- blood pressure
- oxygen saturation



If CRS is suspected, **immediately** contact the CAR-T Team
If concurrent ICANS also follow the ICANS management algorithm



If CRS is suspected, the following additional investigations should be performed:

- | | |
|------------|--|
| • Ferritin | • Coagulation |
| • FBC | • Daily ECG |
| • U&Es | • Appropriate imaging (e.g. chest X-ray) |
| • LFTs | • Blood and urine cultures |
| • CRP | • Bone profile (if TLS in differential) |



Follow CRS management table

Patients must be monitored closely and treatment rapidly escalated if there is lack of clinical response or further deterioration.

CAR-T toxicity treatment decisions should be undertaken by the attending consultant / CAR-T team and escalation plan pre-empted where possible to support rapid treatment escalation when required.

(If part of a clinical trial, contact the trial team and follow the specific trial protocol for management of CRS)

CRS management table

Grade 1 CRS Temp $\geq 38^{\circ}\text{C}$ No hypotension No hypoxia	• Monitor vital signs every 4 hours or as per NEWS score • Treat as per neutropenic sepsis guidelines • If persistent grade 1 consider tocilizumab 8mg/kg (max 800mg) IV - see drug monograph • After 2 doses of tocilizumab, any further treatment should include dexamethasone and avoid tocilizumab monotherapy • If persistent grade 1 for > 48-72 hrs, consider a single dose of dexamethasone 10mg
Grade 2 CRS Temp $\geq 38^{\circ}\text{C}$ <i>AND</i> Hypotension responsive to fluids, not requiring vasopressors <i>AND/OR</i> Hypoxia requiring low-flow <6L/min oxygen	• Monitor vital signs every 4 hours or as per NEWS score • Treat as per neutropenic sepsis guidelines • Administer oxygen and fluids as required • Inform ICU team • Administer tocilizumab 8mg/kg (max 800mg) IV - see drug monograph • Administer a single dose of dexamethasone 10mg IV • If no response after >12-24hrs, increase IV dexamethasone to 10mg QDS • If refractory, consider anakinra – see drug monograph
Grade 3 CRS Temp $\geq 38^{\circ}\text{C}$ <i>AND</i> Hypotension requiring 1 vasopressor <i>AND/OR</i> Hypoxia requiring high-flow >6L/min oxygen	The management of grade 3 & 4 CRS can be merged to permit rapid escalation of management if there is lack of clinical response or further deterioration • Treat as per neutropenic sepsis guidelines • Continuous cardiac monitoring, consider ECHO • Administer vasopressors and oxygen as required • Transfer to ICU • Administer tocilizumab 8mg/kg (max 800mg) IV- see drug monograph • Administer dexamethasone 10mg IV QDS • If no response within 24hrs, administer anakinra - see drug monograph • If no response within further 24hrs consider switching dexamethasone to methylprednisolone IV and consider alternative agents
Grade 4 CRS Temp $\geq 38^{\circ}\text{C}$ <i>AND</i> Hypotension requiring multiple vasopressors <i>AND/OR</i> Hypoxia requiring positive pressure	