Tocilizumab use in COVID 19 Patients

For full details refer to:

BACKGROUND

Tocilizumab has been investigated in the immune modulation arm of the REMAP-CAP and this demonstrated overall reduction in death of 24% and reduced the time in ITU/organ support by more than a week on average. There is currently a lack of data from patients out with an ITU/HDU setting, with research on going.

PATIENTS WHO MAY BENEFIT

Patients must meet all the eligibility criteria and none of the exclusion criteria

Eligible if:
- Aged at least 18 years
- Hospitalised
- Patient is in ITU/ACCU or is for escalation to ITU/ACCU if deteriorates in consultation with ICU team
- Within 24 hours of starting nasal high flow (NHF) oxygen with an FiO₂ of 0.6 or greater, continuous positive airway pressure (CPAP), non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV)
- Laboratory proven SARS-CoV-2 infection or high clinical suspicion of COVID-19 infection (clinical & radiological features)
- No medical history that might, in the opinion of the attending clinician, put the patient at significant risk

Exclusion criteria:
- Known hypersensitivity to tocilizumab
- Co-existing infection as this may be worsened by tocilizumab in particular bacterial infection
- >24hrs after starting respiratory support (NHF oxygen, CPAP, NIV, IMV)
- Patients who are not for escalation to ITU/ACCU in event of deterioration
- ALT or AST >5 times upper limit (caution if >1.5 times upper limit)
- Baseline platelet count <50 x 10⁹/l
- Baseline absolute neutrophil count of <2 x 10⁹/l
- Pre-existing condition or treatment resulting in ongoing immunosuppression
- Pregnancy unless clinically necessary, see section below for further information

PREGNANCY AND WOMEN OF CHILD BEARING AGE

The SmPC for tocilizumab currently states:- Women of childbearing potential must use effective contraception during and up to 3 months after treatment.”

In relation to use in pregnancy, the SmPC for tocilizumab states there is no adequate data for the use in pregnant women. A study in animals has shown an increased risk of spontaneous abortion/embryo-foetal death at a high dose with tocilizumab. REMAP-CAP excluded pregnant women from the trial, although RECOVERY has included pregnant women in the trial, data is not yet available.

Lead Author: Dr M Patel, Respiratory Consultant
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**DOSING AND ADMINISTRATION**

**Dose**

The recommended dose of tocilizumab is 8mg/kg to be administered as an intravenous infusion. The total dose should not exceed 800mg. Tocilizumab should be diluted in a 100mL bag of 0.9% sodium chloride, after removing an equivalent volume of sodium chloride 0.9% (total volume 100mL) and given over 1 hour.

<table>
<thead>
<tr>
<th>Weight</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;41kg</td>
<td>8mg/kg, rounded to 20mg</td>
</tr>
<tr>
<td>≥ 41kg and ≤ 45kg</td>
<td>360mg</td>
</tr>
<tr>
<td>≥ 46kg and ≤ 55kg</td>
<td>400mg</td>
</tr>
<tr>
<td>≥ 56kg and ≤ 65kg</td>
<td>480mg</td>
</tr>
<tr>
<td>≥ 66kg and ≤ 80kg</td>
<td>600mg</td>
</tr>
<tr>
<td>≥ 81kg and ≤ 90kg</td>
<td>680mg</td>
</tr>
<tr>
<td>≥91kg</td>
<td>800mg</td>
</tr>
</tbody>
</table>

Tocilizumab should not be infused concomitantly in the same IV line with other medications.

**Initiation & 2nd dose**

A single dose is to be administered, with the option to repeat a dose in 12-24 hours after the initial dose if there has not been sufficient clinical improvement.

MDT discussion should be undertaken between patient’s consultant, ITU/ACCU consultant and pharmacy (re availability) before initiation and before 2nd dose of tocilizumab if patient is outside critical care unit. For patients within a critical care unit two intensive care consultants and pharmacy should discuss this. If there has been improvement in clinical condition after 1st dose, there will usually not be a need for the 2nd dose – only 29% in REMAP-CAP study were administered a 2nd dose.

**DRUG SPECIFIC CONTRAINDICATIONS**

No interaction of tocilizumab and dexamethasone, prednisolone, hydrocortisone or remdesivir reported.

**MONITORING AND REPORTING**

Any suspected adverse drug reactions (ADRs) for patients receiving tocilizumab for this indication can be reported directly to the MHRA via the dedicated COVID-19 Yellow Card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

Hospitals managing COVID19 patients are encouraged to submit data through the ISARIC 4C Clinical Characterisation Protocol (CCP) case report forms (CRFs), as coordinated by the COVID19 Clinical Information Network (CO-CIN) (https://isaric4c.net/protocols/)

**ADDITIONAL INFORMATION**

SmPC for Tocilizumab: https://www.medicines.org.uk/emc/product/6673/smpc

Consideration should be made for blood borne viruses and/or TB. Please take bloods for a blood borne virus screen prior to administration but **DO NOT DELAY** administration of tocilizumab waiting for results. If concerns over latent (or active) TB, please liaise with ID/respiratory team for further advice.

**GOVERNANCE**

Tocilizumab delivered intravenously has marketing authorisation for use in moderate to severe active rheumatoid arthritis, some forms of juvenile idiopathic arthritis and for cytokine release syndrome as part of CAR-T therapy. NHS England also commissions off-label use of tocilizumab for Takayasu arteritis and Still’s Disease.

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