RECOVERY
Randomised Evaluation of COVID-19 Therapy

Intervention

Tocilizumab

In the RECOVERY Trial we are testing tocilizumab which is an interleukin-6 receptor antagonist. It is being tested in a second randomisation after entry into the main trial (but within 21 days of randomisation) when participants fulfil certain criteria:

- Receiving supplemental oxygen or oxygen saturations <92% on air
- CRP ≥75 mg/L
- No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in this aspect of the RECOVERY trial.

Rationale for inclusion of tocilizumab in RECOVERY

Tocilizumab is licensed for use in patients with rheumatoid arthritis and for use in people aged at least 2 years with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

Severe COVID-19 is associated with a hyper-inflammatory state with elevated ESR, C-reactive protein, D-dimers, lactate dehydrogenase, ferritin, and increased levels of pro-inflammatory cytokines including as IL-1 and IL-6.[1-3] There have been published and unpublished (pre-print) case series reports of the successful treatment of COVID-19 patients with IL-6 inhibitors.[1,4] IL-6 inhibitors have not been evaluated for the treatment of COVID-19 in randomised controlled trials.

Potential harm

Tocilizumab does suppress the immune system, so should be used with caution in patients with evidence of a superimposed bacterial infection.

Frequently asked questions

1. Is tocilizumab safe in pregnancy?
   Two pharmaceutical global safety registry database studies have reported on tocilizumab use in pregnancy, including outcomes from 288 pregnancies [5] and 61 pregnancies,[6] typically for rheumatoid or other arthritides, and with the majority having received the drug in the first trimester. These data suggest that the rates of congenital abnormality, spontaneous pregnancy loss and other adverse outcomes were not higher than in the general population.[6] Small studies have shown that tocilizumab is transferred to the fetus with serum concentrations approximately 7-fold lower than those observed in maternal serum at the time of birth.[7] Very low concentrations of tocilizumab are identified in breast milk and no

drug is transferred into the serum of breast fed infants.[7,8] Women should be advised that if treated after 20 weeks' gestation, their infant should not be immunised with live vaccines (rotavirus and BCG) for the first 6 months of life. All non-live vaccinations are safe and should be undertaken.[9]

2. In renal impairment, is any dose adjustment required?
   No.

3. Are there any drug interactions?
   For patients receiving warfarin it is advisable to ensure they have an INR checked before discharge and shortly thereafter as tocilizumab may interfere with warfarin's effects. Other drugs which may be affected (and may need an increased dose for some weeks after tocilizumab) include phenytoin and ciclosporin.

References

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