Clinical Guideline
Sarilumab for patients admitted to ICU with COVID-19 pneumonia (adults)

Overview

Sarilumab is a recombinant humanised monoclonal antibody that binds specifically to both soluble and membrane-bound interleukin-6 (IL-6) receptors. IL-6 is a pleiotropic pro-inflammatory cytokine produced by a variety of cell types including T- and B-cells, monocytes and fibroblasts [4]. In COVID-19, sarilumab may mitigate the cytokine release syndrome and prevent progression in severe disease. Currently, sarilumab is licensed for the use in moderately to severely active rheumatoid arthritis. [1,2,3, 4].
Sarilumab use in COVID-19 is OFF-LABEL.

Eligibility criteria

Patients have been admitted with severe pneumonia requiring respiratory support, such as high-flow nasal oxygen, non-invasive ventilation, or invasive mechanical ventilation; and with COVID-19 infection that is confirmed by microbiological testing or where staff are confident that COVID-19 is the most likely diagnosis based on clinical and radiological features [1,2,3].

Patients are receiving or have completed a course of dexamethasone or equivalent corticosteroid, unless contraindicated [7]

And they EITHER:

- need supplemental oxygen and have a C-reactive protein level of 75 mg/litre or more, OR
- are within 48 hours of starting high-flow nasal oxygen, continuous positive airway pressure, non-invasive ventilation or invasive mechanical ventilation. [7]

Exclusion criteria [1,2,3]

- Previously treated with other IL-6 inhibitors, such as tocilizumab within the current admission
- Hypersensitivity to sarilumab
- Evidence of co-existing bacterial or viral infection (other than SARS-CoV-2) that might be worsened by sarilumab
- It's been more than 48 hours since commencement of respiratory support Pre-existing condition or treatment resulting in ongoing immunosuppression

- Baseline alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than 5 times the upper limit of normal (ULN)
- Baseline absolute neutrophil count (ANC) below 2 x 10^9/L
- Baseline platelet count below 150 x 10^9/L. Consider tocilizumab for patients with a baseline platelet count of 50-150 x 10^9 /L.

Caution [1, 4]

- Patients with latent or active tuberculosis should be treated with standard therapy before starting sarilumab
- Patients with ALT or AST more than 1.5 times the ULN
- Patients with a history of recurring or chronic infections or with underlying conditions (e.g. diverticulitis, diabetes and interstitial lung disease) which may predispose patients to infections.
- Patients with platelet count below 100 x 10^9/L). If platelets reach 50 x 10^9 /L or less, discontinue sarilumab.
- Viral activation (e.g. Hepatitis B) has been reported with biologic therapies
- Live and live attenuated vaccines should not be given concurrently with sarilumab as clinical safety has not been established
- Increased risk of bowel perforation in patients with diverticular disease. [8]

A full list of cautions can be found on
https://www.medicines.org.uk/emc/product/8144/smpc

Stopping criteria [1,3, 4]

Patients who develop:

- an ANC < 0.5 x 10^9/ L or a platelet count < 50 x 10^9/L
- ALT or AST more than 5 times the ULN
- an anaphylactic reaction or other serious hypersensitivity / serious infusion related reaction

Dose and method of administration

The recommended dose of sarilumab is 400mg as a single intravenous infusion. This is an off label indication and use for sarilumab.

Sarilumab is available as a pre-filled syringe. For a 400mg dose two 200mg pre-filled syringes should be injected into a 100mL sodium chloride 0.9% infusion bag. The bag should be inverted at least 10 times to ensure thorough mixing and given over 60 minutes.

Sarilumab should not be infused concomitantly in the same IV line with other medications[4, 5, 6].

Method of administration can be found on Medusa: https://injmed.wales.nhs.uk/ or via SharePoint

Sarilumab is a monoclonal antibody and so reduce direct handling to a minimum and wear appropriate personal protective equipment. Patients can develop hypersensitivity reactions, therefore monitor for anaphylaxis signs such as flushing, fever, chills, rash, pruritus, urticaria, headache and hypertension.

Adverse drug effects

Commonly reported adverse effects include neutropenia; infections such as upper respiratory tract infections, urinary tract infection, nasopharyngitis or oral herpes; increased ALT, injection site reaction.

Any suspected ADRs for patients receiving sarilumab should be reported directly to the MHRA via the new dedicated COVID-19 yellow card reporting site at: https://coronavirus-yellowcard.mhra.gov.uk/

Pregnancy and breastfeeding

Women of childbearing potential must use effective contraception during and up to 3 months after treatment. The excretion of sarilumab in milk has not been studied in animals. The decision on whether to continue/ discontinue breastfeeding or treatment should be made based on the benefit of breastfeeding and the benefit of patient [3, 4].

Co-administration

There is no interaction of sarilumab with dexamethasone/ hydrocortisone or remdesivir [1, 4].

For further information on interactions, please visit the university of Liverpool covid-19 drug interactions website: https://www.covid19-druginteractions.org/

Ongoing Monitoring

Patients who have been treated with sarilumab should be given an information leaflet and advised to report any signs of infection. The infection risk remains for approximately 3 months after the last dose. The Information leaflet is available at https://www.sps.nhs.uk/wp-content/uploads/2021/03/COVID-19-Patient-Discharge-Information-Leaflet-Tocilizumab-Sarilumab.pdf

This information should also be shared with the patient's GP, who should be made aware of the infection risk and escalate if appropriate.

References

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7. NICE Guidance COVID-19 rapid guideline: managing COVID-19 Published: 23 March 2021 [Accessed 30th September 2021] Available from: https://www.nice.org.uk/guidance/ng1918.NHS England Covid- 19 Guidance Discharge information [Accessed 30th September 2021] Available from: https://www.sps.nhs.uk/wp-content/uploads/2021/03/COVID-19-Patient-Discharge-Information- Leaflet-Tocilizumab-Sarilumab.pdf
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