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Covid-19 Treatment Guidelines update: alternatives to Tocilizumab

Context

Two main processes drive the pathogenesis of COVID-19. Early in the clinical course, the disease is primarily driven by the replication of SARS-CoV-2. Later in the clinical course, the disease appears to be driven by a dysregulated immune/inflammatory response to SARS-CoV-2 that leads to tissue damage. Based on this understanding, immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later stages of COVID-19.

Combination of tocilizumab plus dexamethasone has shown mortality benefit among patients with rapid respiratory decompensation who require oxygen delivery through a high-flow device or noninvasive ventilation.

In view of global shortage of tocilizumab, the acceptable alternatives are baricitinib or tofacitinib (if baricitinib is not available). Both belong to the same class of anti-inflammatory drugs, the Janus kinase (JAK) inhibitors. Baricitinib (or tofacitinib) should only be given in combination with dexamethasone or another corticosteroid

Baricitinib

Dose and duration:

Dependent on eGFR; duration of therapy is up to 14 days or until hospital discharge.

- eGFR ≥ 60 mL/min/1.73 m²: Baricitinib 4 mg PO once daily
- eGFR 30 to <60 mL/min/1.73 m²: Baricitinib 2 mg PO once daily
- eGFR 15 to <30 mL/min/1.73 m²: Baricitinib 1 mg PO once daily
- eGFR <15 mL/min/1.73 m²: Baricitinib is **not recommended**.

Adverse reactions ($\geq 1\%$) include: upper respiratory tract infections, nausea, herpes simplex, and herpes zoster. Serious venous thrombosis, including pulmonary embolism, and serious infections have been observed in COVID-19 patients treated with baricitinib and are known adverse drug reactions of baricitinib. It is not recommended for patients with known active tuberculosis infections, who are on dialysis, have end-stage renal disease, or have acute kidney injury and those with severe hepatic impairment.

WARNINGS AND PRECAUTIONS

Gastrointestinal Perforations: Use with caution in patients at risk



- Laboratory Assessment: Monitor for changes in lymphocytes, neutrophils, hemoglobin, liver enzymes, and lipids.
- Vaccinations: Avoid use with live vaccines.
- Hypersensitivity: Serious reactions have been reported.

Tofacitinib

Dose and duration: Tofacitinib 10 mg PO twice daily for up to 14 days or until hospital discharge

- Use as an alternative if baricitinib is not available or not feasible to use.
- eGFR <60 mL/min/1.73 m²: Tofacitinib 5 mg PO twice daily

Adverse effects

Similar to those for baricitinib. Risk of thrombosis and serious infections.

References

1. <https://www.covid19treatmentguidelines.nih.gov/>
2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/207924s002lbl.pdf
3. <http://labeling.pfizer.com/ShowLabeling.aspx?id=959>