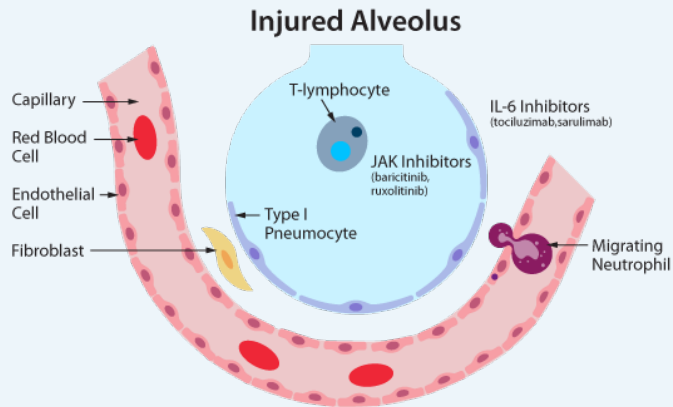


IMMUNE MODULATION FOR INFECTIONS INCLUDING COVID-19

COVID-19 provokes a dysregulated inflammatory response in patients with critical illness.

Multiple immune-modulating drugs have been studied for the treatment of patients with severe hypoxemia.



GLUCOCORTICOIDS

- Dexamethasone, methylprednisolone, hydrocortisone
- Reduced mortality in landmark RECOVERY trial in patients with COVID-19¹
 - Mortality decrease in patients with hypoxemia
 - Signal for harm in patients without hypoxemia
- Advocated by NIH, IDSA, & SSC guidelines
- Standard dose is
 - Dexamethasone 6 mg IV or PO daily for up to 10 days
- Not recommended for outpatients

JANUS KINASE (JAK) INHIBITORS

- Baricitinib, ruxolitinib
- Broad-spectrum anti-inflammatory drugs
- Potential antiviral effects
- Benefit seen in ACTT-2: Improved time to recovery, especially in patients on NIV or HHFNC
- Limited benefit in patients on mechanical ventilation
- NIH and IDSA recommend baricitinib plus remdesivir only for nonintubated patients who require oxygen supplementation and for whom dexamethasone is contraindicated

IL-6 INHIBITORS

- Tocilizumab, sarilumab
- Early interest due to anecdotal reports of similarities between COVID-19 critical illness and cytokine storm seen in CAR-T cell therapy
- Industry-sponsored trials stopped due to lack of benefit
- Multiple conflicting RCTs, although interest recently renewed by evidence of decreased ICU mortality by the REMAP-CAP and RECOVERY groups
- Conditional recommendation by IDSA for use in severe and critical disease

INTERFERONS

- Enhanced host immune response to viral infections
- Early evidence of benefit in trial in Hong Kong²
- Improved clinical outcomes with inhaled IFN-beta in a UK RCT³ and enhanced virologic clearance seen in outpatients with IFN-lambda⁴
- No benefit seen to SC or IV IFN-beta in the open-label WHO Solidarity trial⁵
- Not currently recommended by NIH, IDSA, or SSC guideline panels

¹The RECOVERY Collaborative Group. *N Engl J Med*. 2020.

²Hung, et al. *Lancet*. 2020.

³Monk, et al. *Lancet Respir Med*. 2020.

⁴Feld, et al. *Lancet Respir Med*. 2021.

⁵WHO Solidarity Trial Consortium. *N Engl J Med*. 2020.