

COVID 19 TREATMENT

Severity of Illness Categories

Asymptomatic or Presymptomatic	<ul style="list-style-type: none">• Positive PCR• No symptoms
Mild	<ul style="list-style-type: none">• Fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell <u>without</u> shortness of breath, dyspnea or abnormal chest imaging
Moderate	<ul style="list-style-type: none">• Respiratory disease by clinical assessment or imaging + SpO2 $\geq 94\%$ on room air at sea level
Severe	<ul style="list-style-type: none">• Individuals who have RR > 30 /minute, SpO2 $< 94\%$ on room air at sea level, PaO2/FiO2 < 300 mmHg OR• Lung infiltrates $> 50\%$
Critical	<ul style="list-style-type: none">• Respiratory failure, septic shock, and/or multiple organ dysfunction

Comorbid Conditions

Older age $\geq 65y$

Cardiovascular disease

Chronic lung disease

Diabetes

Cancer

Obesity

Chronic kidney disease

Sickle cell disease

Immunosuppressive therapy

Solid organ transplant or BMT

Management



Mild

- Ambulatory setting or at home through telemedicine or remote visits
- Patients with underlying comorbidities are at higher risk of disease progression



Moderate

- Close monitoring
- If bacterial pneumonia or sepsis is strongly suspected, administer empiric antibiotic



Severe

- Rapid clinical deterioration
- Oxygen therapy should be administered immediately using a nasal cannula or a high-flow oxygen device



Critical

- ICU care

Pharmacologic Interventions

Antiviral Therapy (Remdesivir)

Immune-Based Therapy (Corticosteroids)

Empiric Broad-Spectrum Antimicrobial Therapy

Empiric Broad-Spectrum Ab Therapy

- In patients with COVID-19 and severe or critical illness



Insufficient data

to recommend empiric broad-spectrum antimicrobial therapy in the absence of another indication

Empiric Broad-Spectrum Ab Therapy

- If antimicrobials are initiated, reassess their use daily in order to minimize the adverse consequences of unnecessary antimicrobial therapy

Empiric Broad-Spectrum Ab Therapy

Some experts routinely administer broad-spectrum antibiotics as empiric therapy for bacterial pneumonia to all patients with COVID-19 and moderate or severe hypoxemia

Other experts administer antibiotics only for:

- ✓ Lobar infiltrate on a chest X-ray
- ✓ Leukocytosis
- ✓ Elevated serum lactate level
- ✓ Microbiologic data
- ✓ Shock

Therapeutic Management of Patients with COVID-19

Disease severity	Recommendation
Not hospitalized OR hospitalized without supplement oxygen requirement	<ul style="list-style-type: none">➤ <u>No specific</u> antiviral or immunomodulatory therapy recommended➤ The Panel recommends <u>against the use</u> of dexamethasone (AI) or other corticosteroids (AIII)

Therapeutic Management of Patients with COVID-19

Clinician judges for
hospitalized patient with
moderate disease

Remdesivir



A person who is at a particularly
high risk for clinical deterioration

Therapeutic Management of Patients with COVID-19

Disease severity

Recommendation

Hospitalized patients +
Supplemental oxygen requirement

but

not a high-flow device:

- NIV
- Mechanical ventilation
- ECMO

- Remdesivir for 5 days or until discharge, whichever comes first (AI); or
- Remdesivir + dexamethasone for up to 10 days or until hospital discharge (BIII); or
- If remdesivir cannot be used, dexamethasone may be used instead (BIII).

Therapeutic Management of Patients with COVID-19

- Remdesivir may be extended to up to 10 days if no substantial clinical improvement is seen at Day 5
- There are theoretical reasons for adding dexamethasone to the drug regimen of patients who are currently receiving remdesivir but who are clinically deteriorating

Therapeutic Management of Patients with COVID-19

Disease severity

Recommendation

Hospitalized patients +
Supplemental oxygen requirement
through high-flow device:

- NIV

But not

- Mechanical ventilation
- ECMO

- A combination of dexamethasone plus remdesivir (AIII); or
- Dexamethasone alone (AI).

Therapeutic Management of Patients with COVID-19

Disease severity

Recommendation

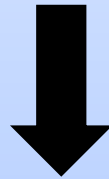
Hospitalized patients who require

- Mechanical ventilation
- ECMO

- Dexamethasone (AI); or
- Dexamethasone plus remdesivir for patients who have recently been intubated (CIII).

Therapeutic Management of Patients with COVID-19

For patients who received **remdesivir monotherapy** and progressed to requiring high-flow oxygen supplement or NIV or mechanical ventilation or ECMO



Dexamethasone should be initiated and remdesivir should be continued until the treatment course is completed

Antiviral Therapy

- Remdesivir:

- ✓ An investigational nucleotide prodrug of an adenosine analog
- ✓ Binds to the viral RNA-dependent RNA polymerase, inhibiting viral replication through premature termination of RNA transcription

Antiviral Therapy

- Remdesivir

Dose	200 mg IV over 30–120 minutes for 1 dose, followed by 100 mg IV on Day 2-5 5 mg/kg then 2.5/kg for children 3.5-40 kg
Duration	5 days or until discharge, whichever comes first. 10 days for who have not shown clinical improvement after 5 days of therapy
Route	IV

Antiviral Therapy

- During remdesivir use monitor for:
 - Infusion reactions
 - Renal and hepatic function

Antiviral Therapy

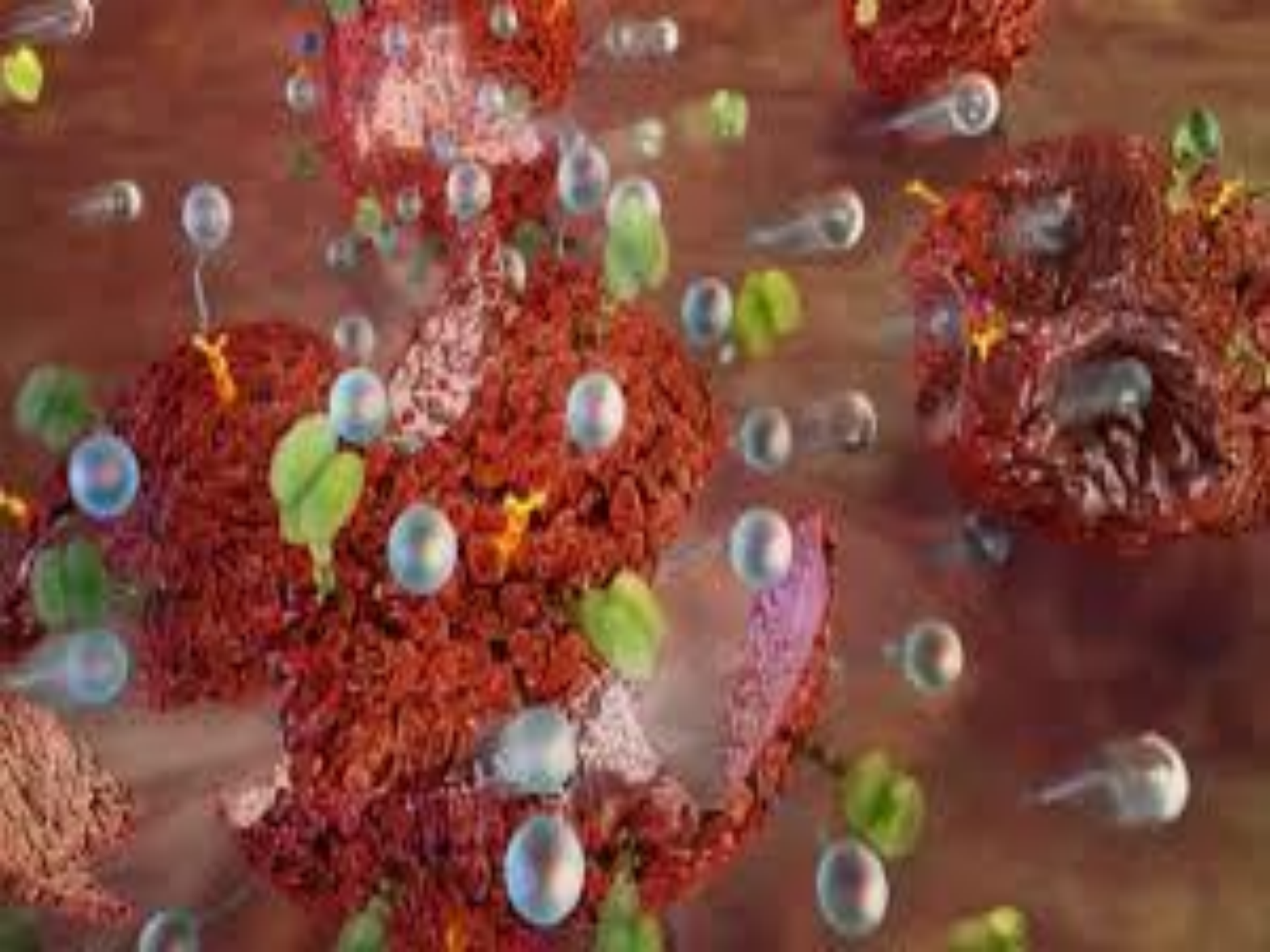
Do not administer remdesivir

- | | |
|--|--|
| | |
| | <ul style="list-style-type: none"><input type="checkbox"/> If eGFR is <30 mL/min<input type="checkbox"/> If patient is receiving dialysis<input type="checkbox"/> If ALT or AST level is >5 times ULN<input type="checkbox"/> With rifampin and chloroquine or hydroxychloroquine |

Potential Antiviral Drugs

- Recommendation against use of :
 - Chloroquine or hydroxychloroquine
 - Hydroxychloroquine plus azithromycin
 - Lopinavir/ritonavir or other HIV protease inhibitors
 - Ivermectin
 - Famotidine





Immune-Based Therapy

Given the hyperactive inflammatory effects of severe acute respiratory syndrome coronavirus 2 , agents that modulate the immune response are being explored as adjunctive treatments for the management of moderate to critical patients

Immune-Based Therapy

- Recommendation against the use of :
 - Mesenchymal stem cell
 - Anti-IL-6 receptor monoclonal antibodies (sarilumab, tocilizumab)
 - Interferon for severely or critically ill patients with COVID-19



Immune-Based Therapy

- There are insufficient data for the COVID-19 Treatment :

- ✓ COVID-19 convalescent plasma
- ✓ SARS-CoV-2 immunoglobulins
- ✓ IVIG
- ✓ Interleukin (IL)-1 inhibitors (e.g., anakinra)
- ✓ Interferon beta for the treatment of early (<7 days from symptom onset) mild and moderate COVID-19

Corticosteroids

- Dexamethasone

Dose	6-8 mg per day
Duration	Up to 10 days or until hospital discharge whichever comes first
Route	IV or PO IV rather than PO if intestinal dysfunction is suspected

Corticosteroids

- A dose of 6 mg of dexamethasone



- 150 mg of hydrocortisone (50 mg q 8 hours)
- 40 mg of prednisone
- 32 mg of methylprednisolone (8 mg q 6 hours or 16 mg q 12 hours)

Corticosteroids

Interventions compared

Usual
supportive care

No
corticosteroids

Corticosteroids
Suggested regimen

Acceptable alternative regimens

Dexamethasone

6 mg

Oral or intravenous



Daily for
7-10 days

Hydrocortisone

50 mg

Intravenous



Every 6 hours
for 7-10 days

Methylprednisolone

10 mg

Intravenous



Every 6 hours
for 7-10 days

Prednisone

50 mg

Oral



Daily for
7-10 days

Conclusion



Remdesivir ?

Dexamethasone

References

- Corticosteroids for COVID-19 Living guidance, September 2020, WHO
- COVID-19 Treatment Guidelines, NIH , October 2020
- BMJ 2020 ; 370:m3379 /doi: 10.1136/bmj.m3379
- Massachusetts General Hospital (MGH) COVID-19 Treatment Guidance. Version 6.2 9/23/2020
- JASN 2020 ; 31: 1384–1386
- <http://www.idsociety.org/COVID19guidelines>

