

COVID-19 Therapy for the Hospitalized Patient

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Objectives

- Analyze current evidence based therapies being used in practice
- Discuss investigational therapies being used in practice
- Identify patient specific markers for appropriate utilization of therapies

If your loved one was hospitalized with a COVID-19 infection, which of these would you want for them?

All the treatments possible. I would want everything!

Treatment based on what their symptoms are.

None of the current treatments. Evidence is everything.

Treatments that sound cool. Baricitinib anyone?

Therapies for hospitalized patient

NO oxygen requirement

- ± convalescent plasma

Oxygen requirement

- Steroids
- ± convalescent plasma
- ± Tocilizumab
- Remdesivir
- ± Baricitinib

Mechanical ventilation

- Steroids
- Remdesivir (uncertain benefit in population)
- ± Tocilizumab

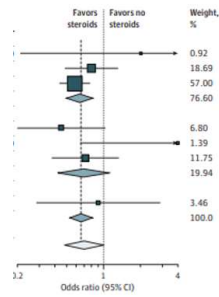
Jose 62 yo male

PMH – HTN, HLD, CAD, DMII
Presented with shortness of breath and fever
Diagnosed with COVID-19
Labs were within normal limits
Chest Xray showed bilateral airspace disease
O2 saturations >94% on room air

Steroids ⁽¹⁾

Backbone of therapy options

Drug and trial	ClinicalTrials.gov Identifier	Initial dose and administration	No. of patients Steroids	No. of deaths/fatal No. steroids	Odds ratio (95% CI)
Dexamethasone					
DECISION	NCT04335061	High: 20 mg/d intravenously	317	312	2.00 (0.31-18.69)
CORTEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/124	283/683	0.59 (0.44-0.78)
Subgroup fixed effect					
			166/459	361/823	0.64 (0.50-0.82)



REACT work group. JAMA 2020;324(13):1310-1345.

Why do we use it?

RECOVERY trial

- Dexamethasone resulted in a 28-day mortality reduction
 - Mechanically ventilated - 29.3% vs 41.4% (0.64:95% CI 0.51-0.81)
 - NNT 8
 - Oxygen - 22.9 vs 25.7% (0.82: 95% CI 0.72-0.94)
 - NNT 36
 - No oxygen requirement - Not helpful
- Secondary outcomes
 - Improved hospital discharge at 28 days
 - ↓ chance of renal replacement therapy

RECOVERY-NEJM 2021;384(1):69-79

Steroids (3): Dexamethasone

Dose	Duration	ADR	Benefit:
<ul style="list-style-type: none"> • 6mg daily (IV/PO) 	<ul style="list-style-type: none"> • While needing oxygen OR • 10 days 	<ul style="list-style-type: none"> • Hyperglycemia • Psychosis • Gastritis 	<ul style="list-style-type: none"> • Mortality • Earlier discharge from hospital • ↓ risk of renal replacement therapy

Agatha 92 yo female

PMH – Dementia, HLD, HTN
 Diagnosed with COVID in the ED
 7 days later returned with worsening agitation and SOB
 Labs notable for AKI and mildly elevated COVID labs
 CT chest showed bilateral ground glass opacities
 Saturations of 91% on RA with tachypnea
 Placed on 2L of O₂

Remdesivir (1)

- Backbone (#2) of therapy options
- Available October 1, 2020 as an Emergency Use Authorization
- Developed in 2009 for Ebola use
- MOA: inhibits the transcription of viral RNA

Why do we use it?

- ACTT: 10 days of remdesivir had faster clinical improvement than standard of care
- 3 SIMPLE I: No difference between 10-day and 5-day therapy with remdesivir in hospitalized patient's with hypoxia
- 3 SIMPLE II: 5 days of remdesivir showed clinical improvement on day 11 vs. usual care clinical status improvement on day 15 in patients with moderate COVID infection

Regep J. NEJM 2020;383:1813-1826.

Remdesivir (3)

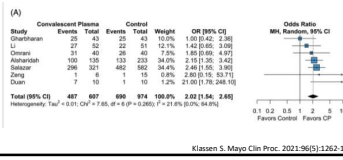
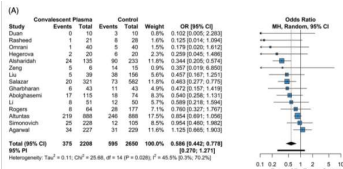
Dose	Duration	ADR	Benefit:
<ul style="list-style-type: none"> 200mg IV once, then 100mg IV x 4 days 	<ul style="list-style-type: none"> 5 days while hospitalized 	<ul style="list-style-type: none"> GI symptoms QTc prolongation 	<ul style="list-style-type: none"> Accelerated clinical improvement

Convalescent plasma (CP)

- Convalescent= recovering from an illness
- Collected from donors who have recovered
 - Antibodies could protect by binding to virus → neutralizing the pathogen
- Has been useful in other viral illness
 - SARS-CoC-1, influenza, MERS-CoV

Why do we use it?

- Meta-analysis
 - 15 studies
 - Mortality at f/u
 - OR= 0.59 (95% CI= 0.44-0.78)
 - Unsure/controversial
- Clinical Improvement
 - OR = 2.11 (95% CI = 1.60-2.77)
 - Most significant when given within 48 hrs of admission
- Hospital Length of stay
 - No difference



Klassen S. Mayo Clin Proc. 2021;96(5):1262-1275.

CP: Considerations

- Differences in amount of titers in the specific plasma
 - The one study that showed mortality benefit had high Nab titers after plasma infusion (Duan et al)
- Differences in time to administration within disease process
 - Ranged from 1-20 days
 - Subgroup analysis showed improvement in mortality when given within 24-48 hours of hospital admission
 - Salazar et al showed infusion within 44 hours of admission had mortality benefit however benefit lost when >72 hours or intubated on day 0

CP (4)

Dose	Duration	ADR	Benefit:
<ul style="list-style-type: none"> 1 unit of high titer CP 	<ul style="list-style-type: none"> One infusion <48-72 hours into the admission Most will limit to < 48 hours admission to hospital 	<ul style="list-style-type: none"> infusion like reactions 	<ul style="list-style-type: none"> Accelerated clinical improvement Reduction in O2 needs Reduced progression to severe disease 16 vs 31% ? Mortality?

Baricitinib

Inhibits signaling to cytokines (IL-2, IL-6, IL-10) known to be high in COVID

Why do we use?

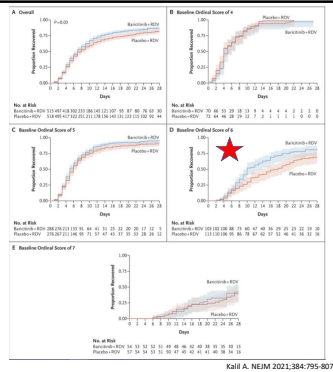
• ACTT-2 trial

• Outcomes

- Time to recovery
 - 7 vs 8 days RR 1.16 (1.01-1.32)
- Time to recover with patients on high-flow O2 needs
 - 10 vs 18 days RR 1.51 (1.1-2.08)

• ADR

- When in combination with steroids
 - New Infection 25.1 vs 5.5%



Bart 55 yo male

PMH – HTN, EtOH use d/o, Tobacco use d/o, Methamphetamine use
 Diagnosed with COVID19 in the ED after having symptoms for 9 days
 Returned with worsening shortness of breath 3 days later
 Labs showed Thrombocytopenia, Leukopenia, Transaminitis
 COVID labs with elevated Ddimer, ferritin, CRP, IL-6, and LD
 Chest Xray with patchy bilateral airspace disease and CTA with geographic ground-glass opacities
 Hypoxic to 89% on RA with tachypnea and increased WOB
 Requiring BiPap/HFNC

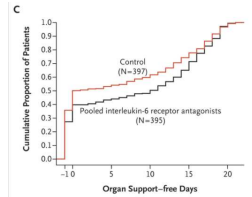
Tocilizumab (1)

Monoclonal antibody (MAB) so it inhibiting IL-6 receptor

Why do we use?

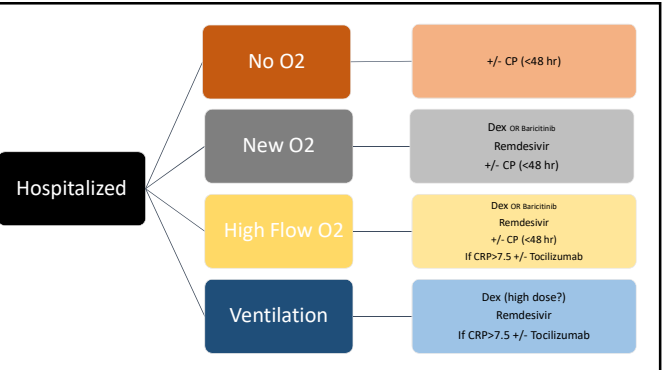
• REMAP-CAP

- Intervention:
 - tocilizumab + steroid vs placebo + steroid
 - started when in ICU and on organ support therapy
- Primary outcome: organ support free days at day 21
 - 10 vs 0
 - When just looking at survivors at 21 days, organ support days
 - 14 vs 13
- Previous studies have demonstrated no benefit in less severely ill patients



Tocilizumab (3)

Dose	Duration	ADR	Benefit:
<ul style="list-style-type: none"> • 8mg/kg • Most will limit to CRP > 7.5 & on steroids • Requiring organ support therapy 	<ul style="list-style-type: none"> • 1-2 doses 	<ul style="list-style-type: none"> • Long lasting neutropenia 	<ul style="list-style-type: none"> • Accelerated clinical improvement • ? Mortality ?



Fielding Questions from Patients

- I was treated for COVID in the hospital. Can I get still the vaccine?
- Can/should I donate plasma after having COVID-19?
- Should I be getting azithromycin, hydroxychloroquine, famotidine, ivermectin, (enter other meds here)?
- I was just diagnosed with COVID, can I get a Rx for steroids?
- What other questions have you had?

More Information

- [IDSA Guidelines on the Treatment and Management of Patients with COVID-19](#)