COVID-19 Treatment

Do This, Don’t Do That

Sept. 2022 Ellie Sukerman, MD

Disclosures

- I have no disclosures

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Objectives

- Review current COVID-19 treatment guidelines for hospitalized patients

- Brief update on COVID-19 monoclonal antibodies

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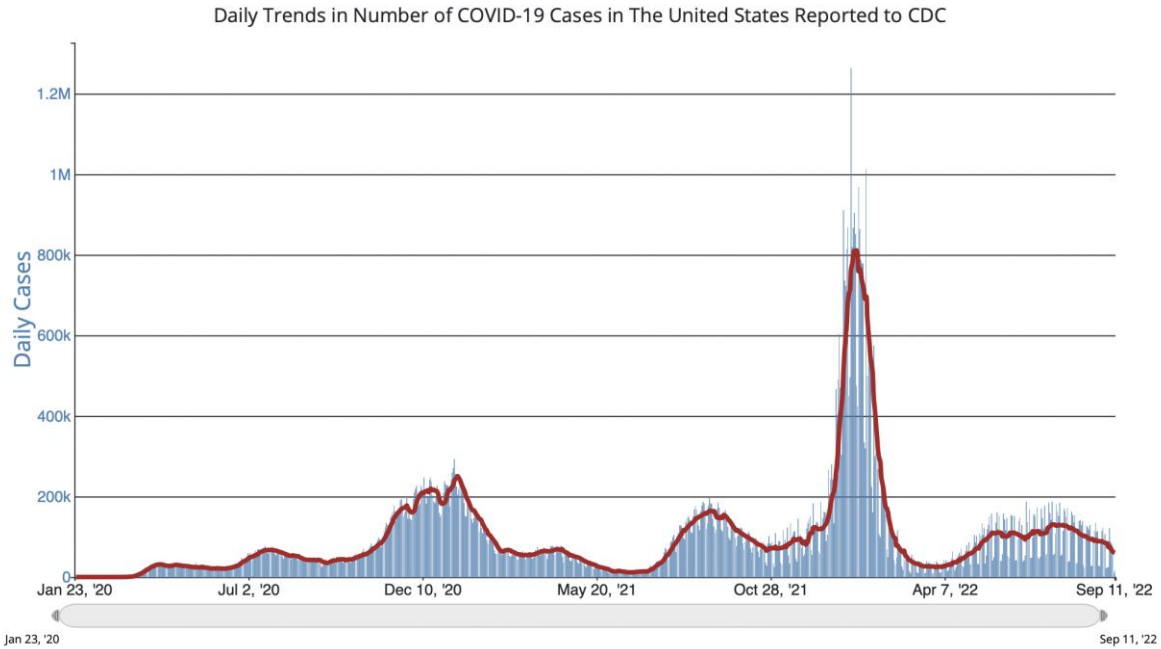
COVID-19 Trends

United States
At a Glance

Cases Total	**95,075,392**	**Deaths** Total	**1,045,253**	Current **Hosp.**	**15,457**
Case Trends		Death Trends		Admission Trends	



https://covid.cdc.gov/covid-data-tracker/#trends_dailycases_select_00 Accessed 9/12/22.

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Case 1

An 89yo is admitted to the hospital for a hip fracture. She has mild sinus congestion x 2d. SpO2 is 99% on room air. eGFR ~60. COVID-19 PCR is detected. What is the most appropriate treatment to offer?

A. No treatment
B. COVID-19 monoclonal antibody
C. Dexamethasone
D. Remdesivir

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Admitted *with* COVID or *due to* COVID??

- Patients with mild to moderate COVID admitted for reasons other than COVID may be eligible for ambulatory therapies

- Remdesivir (RDV) may be feasible in this circumstance

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Pts with COVID Hospitalized for Reason Other Than COVID…

- Look to guidelines for non-hospitalized pts with mild-moderate infection

- Meet **all** of the following:
  - Positive COVID test (PCR or antigen)
  - Sxs consistent with mild to moderate COVID-19
  - 1+ risk factors for severe COVID (per CDC guidance)
  - Within 5 days of sx onset for Paxlovid, 7 days for remdesivir

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html Accessed 9/12/22.

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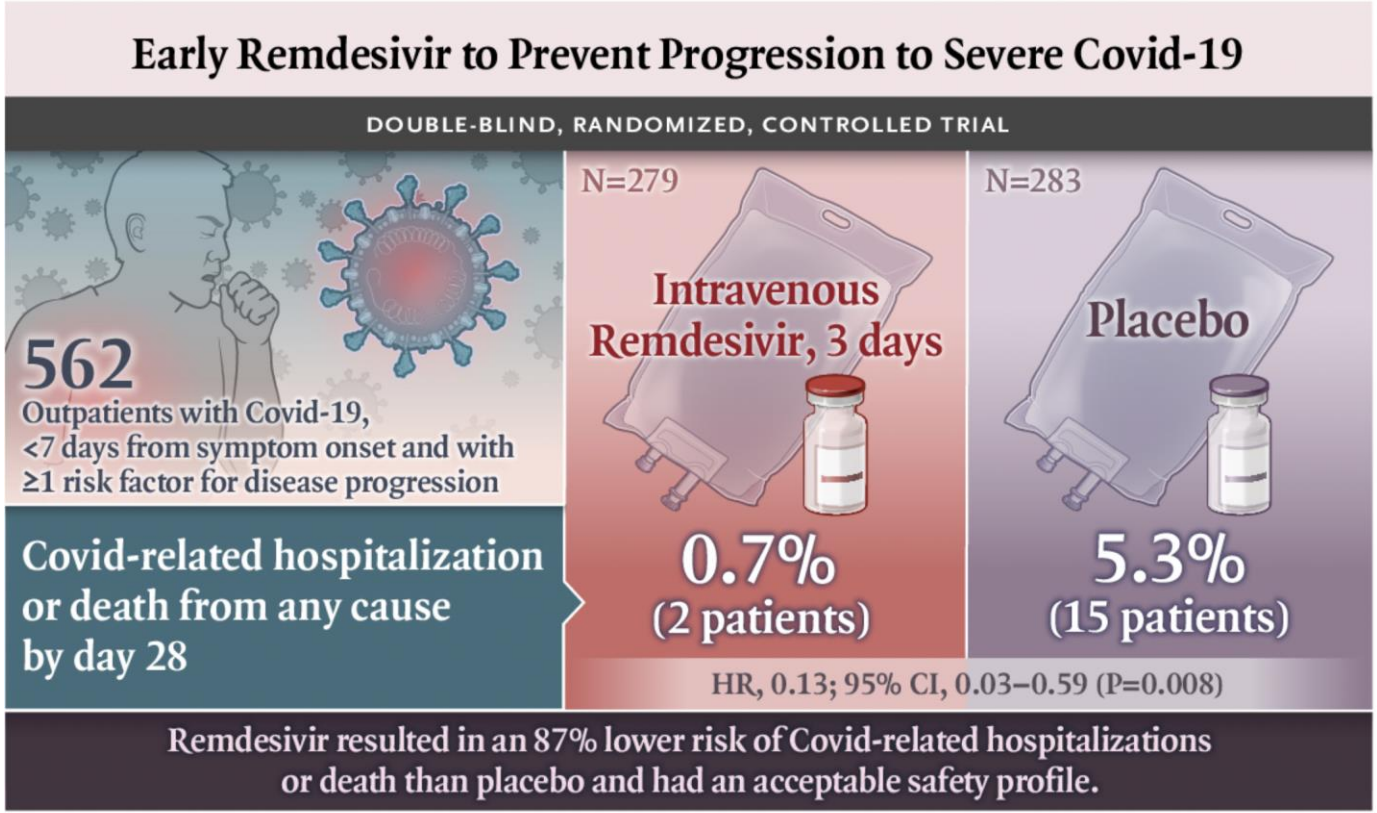
Remdesivir in Ambulatory Patients – PINETREE Trial



R.L. Gottlieb et al. 10.1056/NEJMoa2116846

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Remdesivir

- 200mg IV on day 1 -> 100mg daily on days 2 & 3

- Start ASAP and within 7d of sx onset

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What if our patient had an eGFR of 20?

- RDV package insert: not recommended in patients with eGFR <30mL/min

- Limited data suggest that RDV toxicity is similar in patients with vs. without severe renal impairment -> consider RDV in these pts

Pettit, et al. CID. 2021.

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Hospitalized Patients on Conventional O2

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NIH Recommendations

One of following options:

- RDV (BIIa) -> if minimal O2 requirement
- Dexamethasone + RDV (BIIa) -> most pts
- Dexamethasone alone if RDV not available (BI)

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Case 2

A 52yo woman with htn and DM is admitted for COVID-19 pna. She requires supplemental oxygen and is started on dexamethasone and remdesivir. Her O2 requirement is increasing quickly. What should be done next based on current evidence?

A. Increase her dexamethasone dose
B. Substitute baricitinib for dexamethasone
C. Add baricitinib
D. Increase steroid dose and add baricitinib

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Corticosteroid Dose?

COVID STEROID 2

- 6mg vs. 12mg dex
- No significant difference in days alive without life support at 28d

COVIDICUS

- 6mg vs. 20mg x 5d followed by 10mg x 5d
- No significant difference in 60d survival with high-dose dex

COVID Steroid 2 Trial Group. JAMA, 2021. Bouadma, et al. JAMA Intern Med. 2022.

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Second immunomodulatory agent for pts on *conventional O2*?

- Mixed results from studies of IL-6 inhibitors (e.g., tocilizumab) and JAK inhibitors (e.g., baricitinib)

- NIH Guidelines: recommend adding 2nd immunomodulatory agent to dexamethasone in pts with
  - Rapidly increasing O2 needs AND
  - Systemic inflammation (BIIa)

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Hospitalized Patients on High-Flow or Non-Invasive Ventilation (NIV)

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NIH Guidelines – High-Flow/NIV

Last update 8/8/22

- Dexamethasone + baricitinib (AI); OR
- Dexamethasone + tocilizumab (BIIa)

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RECOVERY Trial

- Baricitinib
  - 13% reduction in mortality in baricitinib group vs usual care (adjusted rate ratio 0.87, 95% CI 0.77-0.99, p=0.028)

- Tocilizumab
  - Pts with hypoxia and evidence of systemic inflammation
  - Mortality 31% in toci vs 35% usual care (rate ratio 0.85, 95%CI 0.76-0.94, p=0.0028)

RECOVERY Trial Group. Lancet, 7/2022.
RECOVERY Collaborative Group. Lancet. 5/2021.

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COV-BARRIER

- Decreased 28d all-cause mortality
  - 8% baricitinib + SOC vs. 13% placebo +SOC

- Decreased all-cause mortality in baricitinib group driven by those on high-flow/NIV

Marconi, et al. Lancet Respiratory Medicine. 2021.

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Remdesivir in High-Flow/NIV

NIH Guidelines

- For hospitalized patients who have certain medical conditions, recommend adding RDV to 1 of the recommended immunomodulator combinations (CIIa)

- Recommend **against** RDV without immunomodulators (AIIa)

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Mechanical Ventilation (MV)/ECMO

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NIH Guidelines – MV/ECMO

- Dexamethasone + baricitinib (BIIa); OR
- Dexamethasone + tocilizumab (BIIa)

- If RDV started previously, complete course

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COV-BARRIER Addendum Trial

- Pts on MV/ECMO at baseline
  - Reduction in 28d and 60d all-cause mortality
  - Numerically less vent days and shorter LOS (but not statistically sig)

Ely, et al. Lancet Respir Med. 2022.

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Back to case 2…

Our pt is now on dexamethasone, baricitinib and remdesivir and is on high-flow O2. Do we add a 3rd immunomodulatory agent?

A. Yes
B. No
C. Not sure

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NIH Guidelines

- Data insufficient to issue recommendation regarding combinations of 3 immunomodulators (e.g., dexamethasone + baricitinib + tocilizumab)

- Concern for additive risk of infection

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Case 3

A 64yo is admitted for COVID-19 and requires supplemental O2. He is started on dexamethasone and RDV. He is now ready for discharge. How do you manage his COVID-19 therapy?

A. Dc RDV and dexamethasone
B. Dc RDV and continue the dexamethasone to complete a 10d course
C. Continue the remdesivir to complete a 5d course and dexamethasone to complete a 10d course

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Tx Management on Discharge

- For dex/RDV/baricitinib -> stop on discharge if tx not already completed

- For pts still on O2 at discharge?
  - Insufficient evidence for or against continuation of dexamethasone
  - If continued, continue while on O2 and max 10d total

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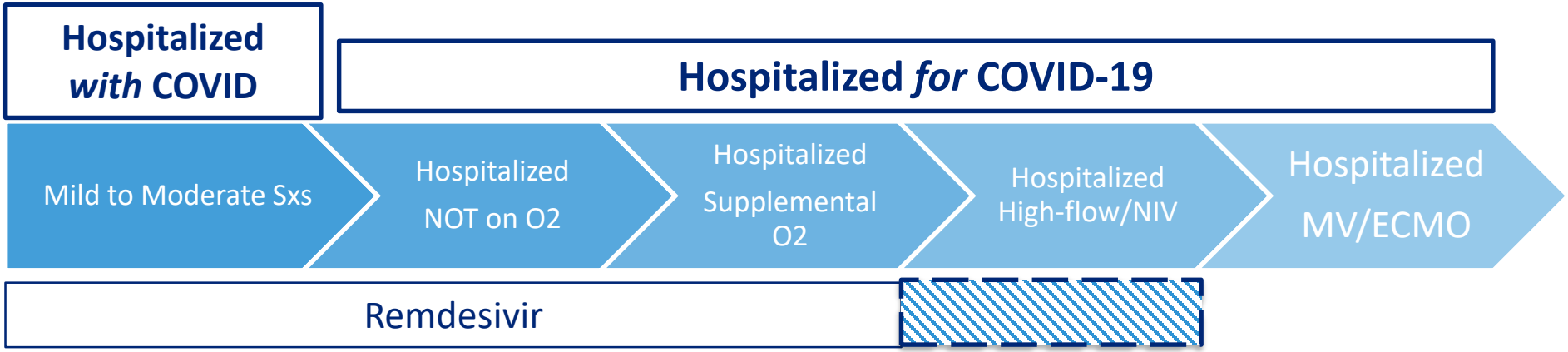

Adapted from Assistant Secretary for Preparedness and Response (ASPR) CDC/IDSA presentation 8/8/22.

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Dosing Regimens

Agent	Dose
Remdesivir	
• Ambulatory • Inpatient	• 200mg on day 1 then 100mg days 2-3 • 200mg on day 1 then 100mg days 2-5 (or hospital dc)
Dexamethasone	6mg daily for up to 10 days (or hospital dc)
Baricitinib	4mg PO daily for up to 14 days (or hospital dc) Renally dose adjusted; not recommended if eGFR <15
Tocilizumab	8mg/kg actual body weight (up to max 800mg) x 1 dose

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Stay tuned

- ACTIV-1 topline results
  - Immunomodulator vs placebo, both + SOC
  - Improvements in mortality and clinical status at day 28 for infliximab vs placebo and abatacept vs placebo

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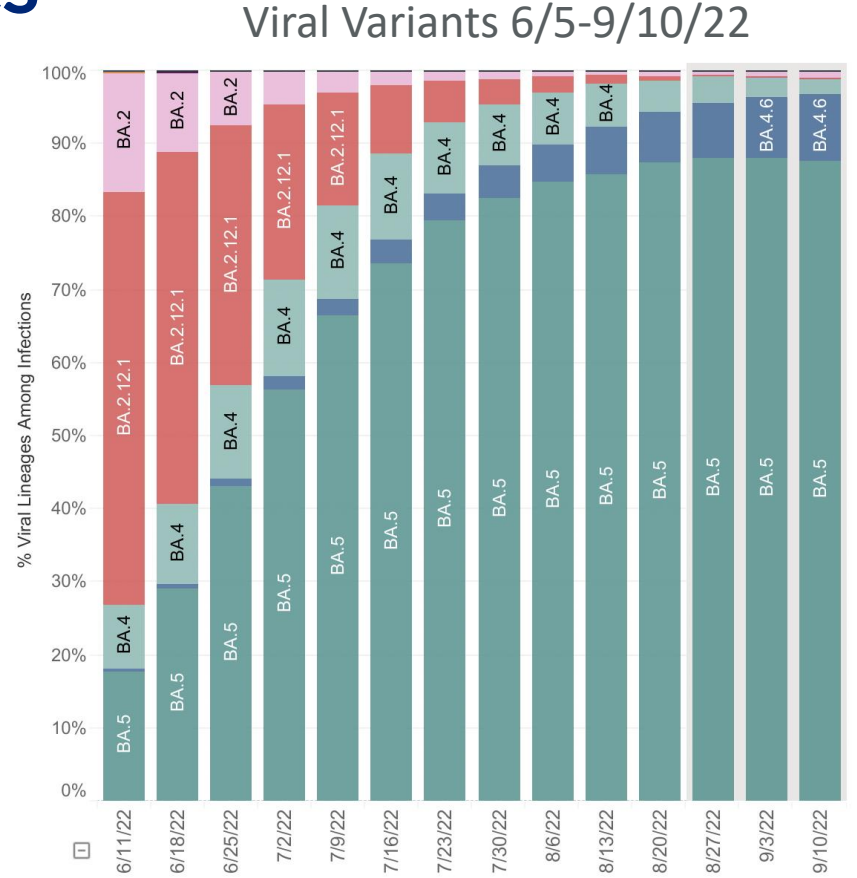
Monoclonal Ab Therapies

- Omicron BA.5 predominates
- Bebtelovimab retains activity against BA.4 and BA.5
- Tixagevimab + cilgavimab (Evusheld) still recommended as pre-exposure prophylaxis in select patients



Takashita, et al. NEJM. 8/2022.

Take-Home Points

- Do
  - Remember remdesivir 3d course in pts with mild to moderate COVID-19 admitted for reasons other than COVID
  - Consider remdesivir in pts with renal impairment with shared decision-making
  - Use admission as potential opportunity to provide Evusheld
- Don't
  - Forget about baricitinib/tocilizumab in patients on conventional O2 with rapidly progressing O2 requirements
  - Use remdesivir monotherapy in pts on HFNC/NIV

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Thank You