Monoclonal Antibodies for COVID-19

Updates from April 21st, 2021

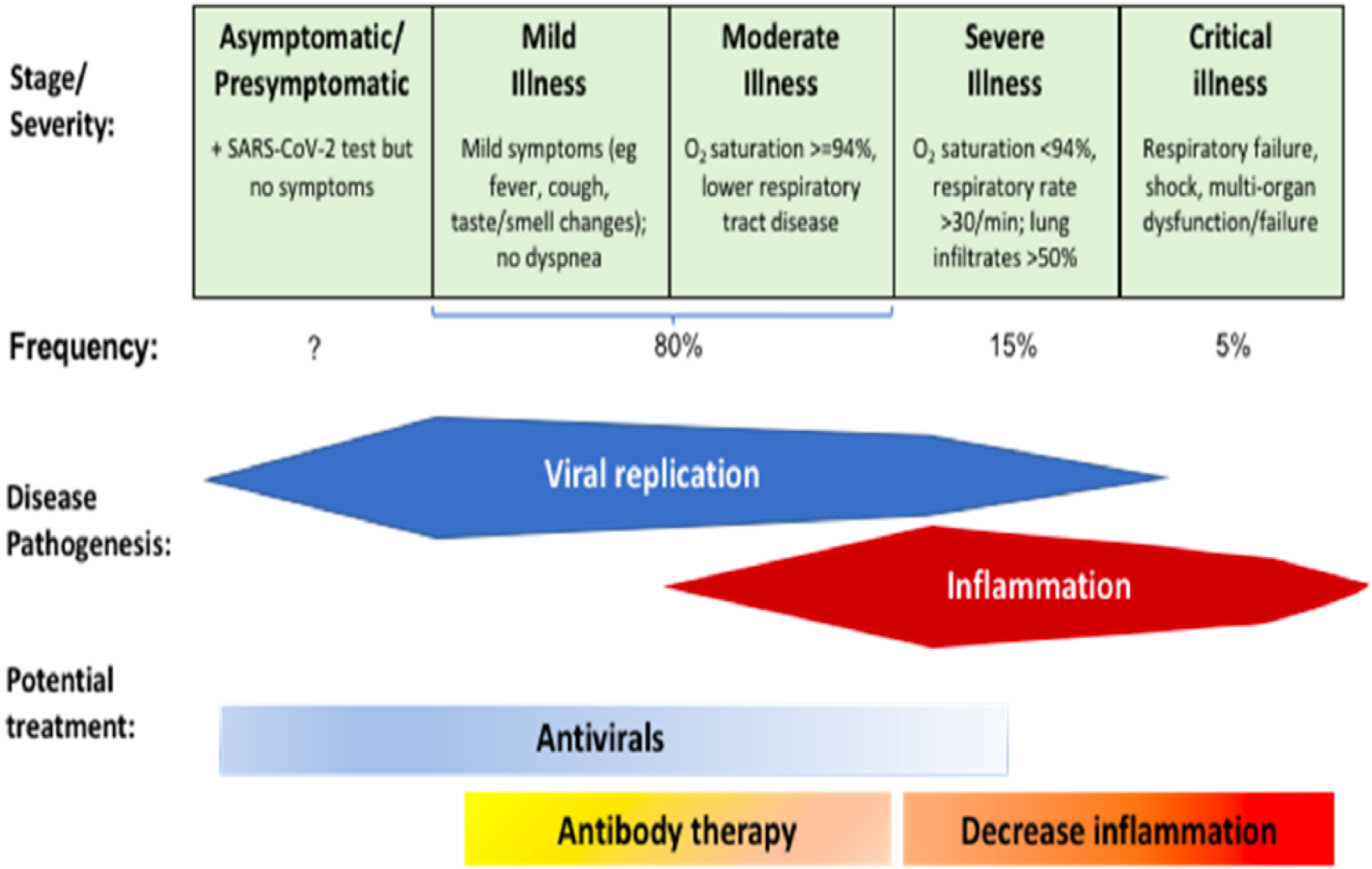
NIH, HHS, and FDA

Audience Response

Are you offering monoclonal Antibody therapy at your site?

- Yes
- No
- No, but I would like to offer it

Management Across the COVID-19 Spectrum



Gandhi RT, CID, 2020; Gandhi RT, Lynch J, del Rio C. NEJM 2020

Boost immune responses

Monoclonal Antibodies

- Monoclonal antibodies against SARS-CoV-2 being studied for treatment and prevention
- Target spike protein of SARS-CoV-2
- Emergency Use Authorizations for treatment of ambulatory patients with mild to moderate COVID-19 at high risk of progression and within 10 days of symptom onset:
  - ~~Bamlanivimab (700 mg)~~
  - Casirivimab + Imdevimab (2400 mg)
  - Bamlanivamab (700 mg) and Etesevimab (1400 mg)

FDA U.S. FOOD & DRUG ADMINISTRATION

Variants of Concern

Table 3: Pseudovirus Neutralization Data for SARS-CoV-2 Variant Substitutions with Bamlanivimab and Etesevimab Together (1:2 Molar Ratio)

Lineage with Spike Protein Substitution	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y	no change[b]
B.1.351 (South Africa origin)	K417N + E484K + N501Y	>45[c]
P.1 (Brazil origin)	K417T + E484K + N501Y	>511[c]
B.1.427/B.1.429 (California origin)	L452R	7.4
B.1.526 (New York origin)[d]	E484K	17

[a] For variants with more than one substitution of concern, only the one(s) with the greatest impact on activity is(are) listed.

[b] No change: <5-fold reduction in susceptibility.

[c] No activity observed at the highest concentration tested. Bamlanivimab and etesevimab together are unlikely to be active against variants from this lineage.

[d] Not all isolates of the New York lineage harbor the E484K substitution (as of February 2021).

It is not known how pseudovirus data correlate with clinical outcomes. Given the similarities between the substitutions in B.1.351 and P.1, it is unlikely that bamlanivimab and etesevimab together will be active against these variants.

From EUA Healthcare provider information

Phase 3 Clinical Data in Outpatients with mild/moderate COVID

Participants	Primary Outcome: Day 29 hospitalization/death	Day 29 all-cause mortality
BAM + ETE [2800/2800mg] (n=518) Placebo (n=517)	BAM + ETE (2.1%) Placebo (7.0%) p=0.0004	BAM + ETE (0%) Placebo (1.9%) P<0.001
CAS + IMD [600/600mg] (n=736) Placebo (n=748) CAS + IMD [1200/1200mg] (n=1335) Placebo (n=1341)	CAS + IMD [600/600] (1.0%) Placebo (3.2%) p=0.0024 CAS + IMD [1200/1200] (1.3%) Placebo (4.6%) P<0.0001	CAS + IMD [600/600] (0.1%) CAS + IMD [1200/1200] (0.05%) Placebo (0.3%)

No comparative data to determine whether there are differences in clinical efficacy or safety between bamlanivimab plus etesevimab and casirivimab plus imdevimab.

Adapted from https://www.covid19treatmentguidelines.nih.gov/outpatient-management/

FDA update

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FDA revocation of bamlanivimab on April 16, 2021

- On April 16, 2021, FDA revoked the emergency use authorization **(EUA)** that allowed for use of the investigational monoclonal antibody therapy bamlanivimab, **when administered alone**
  - Due to the **sustained increase in variants resistant to bamlanivimab alone** resulting in the increased risk for treatment failure and **availability of alternative authorized mAbs**

- USG **stopped the distribution of bamlanivimab alone** on March 24, 2021

- Sites that only have bamlanivimab and are administering monoclonal antibodies, should either
  - Order etesevimab to pair with the current supply of bamlanivimab
    OR
  - order and use the casirivimab + imdevimab monoclonal antibody cocktail

- **Information on direct ordering process available at:**
  https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/direct-order-process-covid19-mAb.aspx

Revised NIH COVID-19 treatment guidelines | April 8, 2021

- The NIH has **strongly recommended (AIIa)** the following for use in non-hospitalized COVID-19 patients:
  - Casirivimab + imdevimab (Regeneron)
  - Bamlanivimab + etesevimab (Eli Lilly)

- Updated NIH COVID-19 guidelines can be found at: https://www.covid19treatmentguidelines.nih.gov/statement-on-anti-sars-cov-2-monoclonal-antibodies-eua/

Expanded Use Authorization Criteria: Ambulatory Patients with Mild to Moderate COVID-19 at High Risk for Progression - 1

- Body mass index (BMI) ≥35
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or receiving immunosuppressive treatment
- ≥65 years of age
- ≥55 years of age AND have
  - cardiovascular disease, OR
  - hypertension, OR
  - chronic obstructive pulmonary disease/other chronic respiratory disease

http://pi.lilly.com/eua/bamlanivimab-eua-factsheet-hcp.pdf
https://www.regeneron.com/sites/default/files/treatment-covid19-eua-fda-letter.pdf

Administration details

Drug	Infusion time	Monitoring time
Bamlanivimab/ Etesevimab	21- 60 minutes depending on the volume	1 hour after infusion is complete
Casirivimab and Imdevimab	60 minutes	1 hour after infusion is complete

Other requirements:

1. PROVIDE a "fact sheet" to the patient
2. INFORM that this is an unapproved drug
3. DISCUSS Risk/ Benefits/ Alternatives
4. Mandatory reporting for any SERIOUS adverse events https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

Infection Preventions Considerations for setting up infusions for COVID pts

- Ensure clinic staff at all levels are aware of the arrival and status of the COVID+ patient. Consider sharing at a morning huddle.
- Follow your institution's guidelines for care for known COVID-19 + patients
- Consider having mock scenarios where clinics practice a COVID-19+ pt arrival

How COVID + patients are handled in ambulatory care settings in UW system:

- When possible, patients are seen at designated "respiratory plus" clinics that routinely test/see patients with COVID-19.

- For other clinic types:

  1.) the patient is met by a masked staff member at a designated entrance, one that is the least public facing with fastest access to the clinic.

  2.) At point of entry, the patient is given a procedure mask and instructed to perform hand hygiene.

  3.) The staff member escorts the patient into a private room in the clinic.

  4.) The visit is conducted in appropriate COVID-19 precautions

  5.) After the visit , the patient is escorted out of the building.

  6.) Room is cleaned per EVS protocols

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mAb administration not limited to hospital setting

Potential administration sites

Hospital

- Hospital-based infusion centers
- Emergency departments
- Alternate care sites

Ambulatory center

- Infusion centers
- Urgent care clinics
- Dialysis centers
- FQHCs

Congregate living

- Skilled nursing facilities
- Long-term care facilities
- Others (Correctional facilities, etc.)

Mobile sites

- Trailer, etc.
- Other mobile sites

Home

- At patient's home with home infusion provider

Expansion to add'l sites

Ask:
Expand number of mAb administration sites within your jurisdiction

Expansion via:

- State-directed allocations
- Order product
  - Direct order *available soon* for infusion centers and urgent care clinics
  - Currently available through SPEED for SNFs/LTC, FQHC, correctional facilities, and dialysis centers

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Reporting via TeleTracking on COVID-19 therapeutics

Distribution to individual sites dependent on **mandatory therapeutics reporting**

Bam / ete quantity reporting became **mandatory on April 7**

Reporting via TeleTracking

- For each of the products, enter in quantities of **product remaining on hand** and of **product used in the last week**
- Quantity reported should be in **patient courses**
- Bamlanivimab solo usage and inventory **should exclude** bam part of bam / ete combos

For bam / ete quantities – please report **all quantities remaining on hand & utilized week to date** when reporting for the **first time**

If you need assistance setting up a Teletracking account or learn of sites having challenges reporting, email support at (COVID19Therapeutics@hhs.gov)

Helpful information

- **HHS/ASPR Website:** https://www.phe.gov
- **HHS Website:** https://combatcovid.hhs.gov/
- **ASPR Regional Teams**
  - Consult the ASPR Regional Team in your area for questions regarding COVID-19 medical countermeasures
- **HHSProtect Therapeutics Dashboard:** https://protect.hhs.gov/workspace/module/view/latest/ri.workshop.main.module.084a09b4-bcd0-4a6b-817a-90afb7a3cd1d
- **Direct Ordering Link via ABC:** https://app.smartsheet.com/b/form/255d164d67834793b4ab549e160941e8
- **Treatment Site locator tool** https://protect-public.hhs.gov/pages/therapeutics-distribution
- **Reach the Federal COVID-19 Response Therapeutics Team:** COVID19Therapeutics@hhs.gov

Find a location near you…

- https://protect-public.hhs.gov/pages/therapeutics-distribution#distribution-locations