COVID-19 Update

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What is a COVID-19 Variant?

- **A virus with specific genetic markers associated with:**
  - Changes to receptor binding
  - Reduced neutralization by antibodies generated against previous infection or vaccination
  - Reduced efficacy of treatments
  - Potential diagnostic impact, or
  - Predicted increase in transmissibility or disease severity
- **Classification**
  - Variant of Interest (VOI)
  - Variant of Concern (VOC)
  - A variant of high Consequence

https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html
Accessed December 1, 2021

Variant of Interest (VOI)

- It is the cause of an increased proportion of cases or outbreak clusters
- Limited prevalence or expansion in the US or in other countries
- Might require enhanced sequence surveillance or laboratory characterization, or epidemiological investigations to assess:
  - Transmission
  - Severity of disease
  - Efficacy of therapeutics and currently approved or authorized vaccine protection.
- Currently, there are no SARS-CoV-2 Variants of Interest in the US

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Variants of Concern (VOC)

- Impact on diagnostics, treatments, or vaccines
- Widespread interference with diagnostic test
- Substantially decreased susceptibility to one or more class of therapies or neutralization by antibodies from previous infection or vaccination
- Reduced vaccine-induced protection from severe disease
- Increased transmissibility
- Increased disease severity
- **Might require** notification to WHO, reporting to CDC, local or regional efforts to control spread, increased testing, or research

- **Current VOC in the US is the Delta,** B.1.617.2
  - Increased transmissibility
  - Potential reduction in neutralization by some EUA monoclonal antibody treatments
  - Potential reduction in neutralization by post-vaccination sera

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VOC: Omicron Variant

- On 26 November 2021, WHO designated the variant B.1.1.529 a variant of concern, named Omicron
- On November 30, 2021, the U.S. government SARS-CoV-2 Interagency Group made the decision to classify the Omicron variant as a Variant of Concern (VOC).
- This decision is based on multiple factors, including:
  - The detection of Omicron cases in multiple countries (23)
  - Transmission and displacement of Delta in South Africa
  - Mutations in the virus that could indicate a reduction in the effectiveness of COVID-19 vaccines and certain monoclonal antibody treatments.
- No cases of this variant have been identified in the U.S. to date.

https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html
Accessed December 1, 2021

Current knowledge about Omicron Compared With Other Variants Including Delta

- **Transmissibility:**
  - It is not yet clear whether Omicron is more transmissible
  - The number of people testing positive has risen in areas of South Africa affected by this variant
- **Severity of disease:**
  - It is not yet clear whether infection with Omicron causes more severe disease compared to infections
  - Preliminary data suggests that there are increasing rates of hospitalization in South Africa
  - There is currently no information to suggest that symptoms associated with Omicron are different from other variants.
- **Effectiveness of prior SARS-CoV-2 infection**
  - Preliminary limited information suggests there may be an increased risk of reinfection with Omicron (ie, people who have previously had COVID-19 could become reinfected more easily with Omicron).
- **Effectiveness of vaccines:**
  - Work in progress. Current vaccines remain effective against severe disease and death overall, data on Omicron pending
- **Effectiveness of current tests:**
  - PCR tests continue to detect Omicron infection
  - Studies on Impact on other types of tests are pending
- **Effectiveness of current treatments:**
  - Corticosteroids and IL6 Receptor Blockers will still be effective for managing patients with severe COVID-19.
  - Other treatments still need to be assessed.
- **Studies underway**
  - At the present time, WHO is coordinating with a large number of researchers around the world to better understand Omicron. Including assessing transmissibility, severity of infection, performance of vaccines and diagnostic tests, and effectiveness of treatments.

https://www.who.int/news/item/28-11-2021-update-on-omicron

Accessed December 1, 2021

WHO Recommended Actions for Countries Regarding Omicron

- **Enhancing surveillance** and sequencing of cases; sharing genome sequences on publicly available databases, such as GISAID; reporting initial cases or clusters to WHO
- **Performing field investigations and laboratory assessments** to better understand if Omicron has different transmission or disease characteristics, or impacts effectiveness of vaccines, therapeutics, diagnostics or public health and social measures
- Countries should **continue to implement the effective public health measures** to reduce COVID-19 circulation overall, using a risk analysis and science-based approach.
- They should **increase some public health and medical capacities** to manage an increase in cases.
- **Inequities in access to COVID-19 vaccines are urgently addressed** to ensure that vulnerable groups everywhere, including health workers and older persons, receive their first and second doses, alongside equitable access to treatment and diagnostics.

https://www.who.int/news/item/28-11-2021-update-on-omicron
Accessed December 1, 2021

WHO Recommended Actions for People Regarding Omicron

- The most effective steps individuals can take to reduce the spread of the COVID-19 virus is to:
  - **Get Vaccinated**
  - Keep a physical distance of at least 3 feet from others
  - Wear a well-fitting mask
  - Improve ventilation of shared areas
  - Avoid poorly ventilated or crowded spaces
  - Keep hands clean; cough or sneeze into a bent elbow or tissue

https://www.who.int/news/item/28-11-2021-update-on-omicron
Accessed December 1, 2021

Variants of High Consequence

- Has clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness relative to previously circulating variants.
- Demonstrated failure of diagnostic test targets
- Significant reduction in vaccine effectiveness
- Significantly reduced susceptibility to approved or authorized therapeutics
- More severe clinical disease and increased hospitalizations
- Would require notification to WHO, reporting to CDC, and announcement of strategies to prevent or contain transmission, and recommendations to update treatments and vaccines.
- Currently there are no variants of high consequence

https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html
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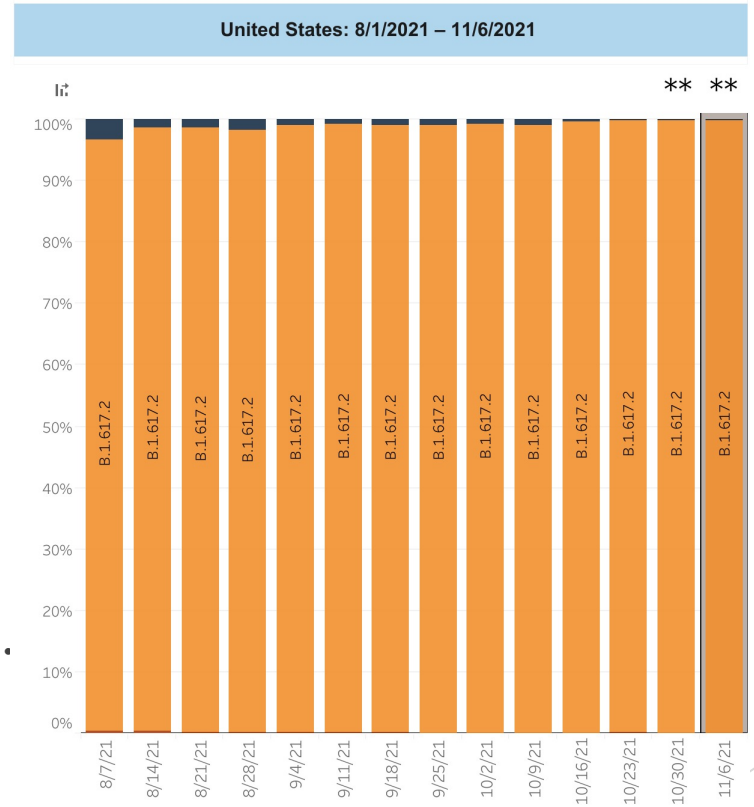
Variants in the US

- Delta Variant
  - Makes up 99.9% of USA variants
- AY.4.2 Variant Under Investigation
  - Derived from Delta; first seen in UK
  - Transmits in UK better than parent Delta
  - Should transmit in the USA
  - Does not evade vaccines or monoclonal Abs
- Omicron variant as a Variant of Concern (VOC). identified in the US yet.



https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html

https://www.idsociety.org/science-speaks-blog/2021/ay.4.2-delta-subvariant-spreading-in-uk--15000-cases-and-found-in-usa-get-vaccinated/

COVID-19 VACCINES

- COVID-19 and SARS-CoV-2 Infection
  - Recommended for everyone previously infected aged 5 years and older
    - Vaccinate when recovered and off isolation
- Don’t vaccinate people as post exposure prophylaxis
- Vaccinate people getting non-COVID-19 medical care (no symptoms and no close contact)
- Vaccinate all people who are pregnant or are lactating

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

NIH COVID-19 Guidelines Update

Influenza Vaccine:

- For symptomatic COVID-19 patients consider deferring influenza vaccination until the patients have completed their COVID-19 isolation period and are no longer moderately or severely ill.
- People with SARS-CoV-2 infection who are not moderately or severely ill (including those who are asymptomatic) should seek influenza vaccination when they no longer require isolation. They can be vaccinated sooner if they are in a health care setting for other reasons.
- Influenza vaccine and a COVID-19 vaccine may be administered concurrently at different injection sites.

- **COVID-19 Vaccines**
  - Vaccination remains the most effective way to prevent SARS-CoV-2 infection.
  - CDC recommends giving an additional dose of an mRNA COVID-19 vaccine to people who are at high risk of having suboptimal immune responses to a two-dose series.
  - This dose should be given at least 28 days after the person receives the second dose of the two-dose series.

https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
Accessed December 1, 2021

SARS-COV-2 Post Exposure Prophylaxis (PEP)with Monoclonal Antibodies

- **Either bamlanivimab plus etesevimab or casirivimab plus imdevimab can be given as PEP**
  - For those who have a history of exposure to individuals with SARS-CoV-2 infection and who are at high risk of progression to serious disease if they acquire the infection.[1]
- **REGEN-COV Phase 3 Prophylaxis trial[2]**
  - 1200 mg given (4 subcutaneous injections) to COVID-19 uninfected persons
  - 586 enrolled and randomized
  - 81.4% COVID-19 risk reduction already reported in NEJM article at one month
  - At 2-8 months, there is a persistent 81.6% risk reduction of laboratory confirmed COVID-19
  - Among those who got the Infusion, there were…
    - Zero Hospitalizations (vs 6 in controls)
    - Zero Deaths
    - Zero Safety signals

1. https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/Accessed December 1, 2021
2.https://newsroom.regeneron.com/news-releases/news-release-details/new-phase-3-analyses-show-single-dose-regen-covr-casirivimab-

Prophylaxis (PEP) and SARS-COV-2 Treatment with Monoclonal Antibodies

- Bamlanivimab plus etesevimab has been added as an anti-SARS-CoV-2 mAb combination option for the treatment of nonhospitalized patients with mild to moderate COVID-19 who are at high risk of progression to severe disease.
  - In June 2021, the distribution of bamlanivimab plus etesevimab was paused in the US because of the increase in the combined frequencies of two circulating SARS-CoV-2 variants: Gamma (P.1) and Beta (B.1.351).
  - The Delta (B.1617.2, non-AY.1/AY.2) variant has become the predominant variant circulating in all states. Bamlanivimab plus etesevimab retains activity against the Delta variant, the distribution of these anti-SARS-CoV-2 mAbs has resumed.

https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
Accessed December 1, 2021

JAMA Network | Open

Research Letter | Infectious Diseases

Outcome Comparison of High-Risk Native American Patients Who Did or Did Not Receive Monoclonal Antibody Treatment for COVID-19

Ryan M. Close, MD, MPH; T. Shaifer Jones, BS; Christopher Jentoft, MD; James B. McAuley, MD, MPH

- QI study conducted at the Whiteriver Service Unit, a rural acute care facility that serves as the primary hospital and public health department on the Fort Apache Indian Reservation in eastern Arizona.
- During the observation period, 983 WRSU patients received a positive COVID-19 test result.
- Of the 983 patients, 481 (48.9%) met EUA high-risk criteria for treatment and 201 high-risk patients (41.8%) received mAb treatment.
- The median time from COVID-19 test collection to mAb treatment was 23 hours (IQR, 3-45 hours), and 182 of 201 patients (90.5%) received treatment within 72 hours.
- The median time from symptom onset to treatment was 2 days (IQR, 1-3 days), and 113 of 149 symptomatic patients (75.8%) were treated within 3 days
- Compared with nonrecipients, the mAb-treated patients had
  - A lower proportion of acute medical visits (59 [29.4%] vs 136 [48.6%])
  - Hospitalizations (35 [17.4%] vs 120 [42.9%])
  - Transfers to outside facilities (4 [2%] vs 26 [9.3%])
  - Intensive care unit admissions (0 vs 12 [4.3%])
  - Deaths (0 vs 8 [2.9%])
    - Of the 8 deaths during the observation period, these patients all met the EUA high-risk criteria but did not receive mAb treatment.

Prophylaxis (PEP) and SARS-COV-2 Treatment with Monoclonal Antibodies with Supply and or Logistical Constraints

- Supply constraints, as well as logistical constraints, can make it impossible to administer anti-SARS-CoV-2 mAbs to all eligible patients
- Consider prioritizing the use of anti-SARS-CoV-2 mAb therapy for patients at highest risk of clinical progression.
- The NIH panel suggests prioritizing the use of anti-SARS-CoV-2 mAbs **only when triage becomes necessary due to logistical or supply constraints.**

https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
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Treatment

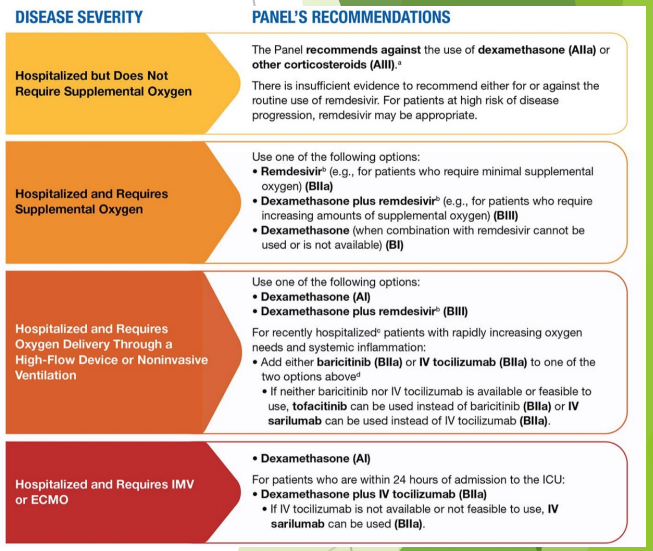
- **Pfizer's new oral drug:** PAXLOVID™ (PF-07321332; ritonavir)
  - EPIC-HR Phase 2/3 study evaluated non-hospitalized adults with COVID-19 at high risk to progress to severe illness
  - Drug given within three days of symptom onset
  - Risk of hospitalization and death was decreased 89% in those who received the drug
    - 0.8% who received drug were hospitalized (3/389) vs 7% placebo (27/385 hospitalized, 7 died)
  - Risk reduction was similar if drug given 5 days after symptom onset (1% vs 6.7%)
  - Severe adverse events requiring treatment were fewer in PAXLOVID vs placebozz
- **Merck's Molnupiravir also has requested EUA authorization**
- **Gilead's Remdesivir** showed 87% reduction in hospitalizations when used early as outpatient treatment in patients at risk for progression

https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate

- NIH Treatment Guidelines

NIH Treatment Guidelines Update

- Clinical management
  - No antibiotics up front (0-6% have CAP); look out for UTI, CLABSI, C diff, HAP /VAP later on and treat with antibiotics
  - Proning trials are a good idea but are not a substitute for intubation!
- ID Complications
  - TB and Hep B reactivation with immunomodulator Rx
  - Strongyloides superinfection: Ivermectin may finally have a role if locally endemic!
  - Aspergillus and Mucor risk present for patients on steroids



DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or **other corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[b] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone plus remdesivir**[b] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone** (when combination with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone (AI)** • **Dexamethasone plus remdesivir**[b] **(BIII)** For recently hospitalized[c] patients with rapidly increasing oxygen needs and systemic inflammation: • Add either **baricitinib (BIIa)** or **IV tocilizumab (BIIa)** to one of the two options above[d] • If neither baricitinib nor IV tocilizumab is available or feasible to use, **tofacitinib** can be used instead of baricitinib **(BIIa)** or **IV sarilumab** can be used instead of IV tocilizumab **(BIIa)**.
Hospitalized and Requires IMV or ECMO	• **Dexamethasone (AI)** For patients who are within 24 hours of admission to the ICU: • **Dexamethasone plus IV tocilizumab (BIIa)** • If IV tocilizumab is not available or not feasible to use, **IV sarilumab** can be used **(BIIa)**.

https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf

Thank You

Questions ?