November 23, 2022

FDA Updates on Treatment and Prophylaxis of Emerging Omicron Subvariants *(November 4, 2022)*

A newly published study indicated that emerging omicron subvariants had developed resistance to most or all monoclonal antibodies, including those currently authorized in the U.S. as COVID-19 treatments.

The study highlights the neutralization effect of a range of antibody treatments against multiple omicron subvariants, including the emerging BQ.1.1 "escape variant." Overall, the tested mAbs or mAb cocktails did not cause appropriate neutralization. Treatment with mAbs alone might not provide enough protection, especially for high-risk individuals.

Maui Health has been offering outpatient mAb therapies for several months and we will be discontinuing outpatient treatments effective December 17, 2022. There are still many community providers available for these outpatient therapies that residents can access. However, we did want to provide an important update on mAb efficacy, notably Bebtelovimab and Evusheld and the new, emerging variants and resistance against SARS-CoV-2 variants, including Omicron subvariants BQ.1 and BQ.1.1

There are several **alternative treatments** that are authorized or approved to treat certain patients with mild-to-moderate COVID-19 which are expected to retain activity against currently circulating variants, including Omicron subvariants BQ.1 and BQ.1.1. (E.g., oral Paxlovid (nirmatrelvir/ritonovir), oral Lagevrio (molnupiravir), IV Veklury (Remdesivir)

Health care providers should assess whether these treatments are right for their patient in the event the patient develops mild-to-moderate COVID-19.

FDA updated the Health Care Provider Fact Sheet for Bebtelovimab (included) with specific information regarding expected reduced activity against certain emerging Omicron subvariants of SARS-CoV-2. This information shows that Bebtelovimab is not expected to neutralize Omicron subvariants BQ.1 and BQ.1.1.

Update on Evusheld (Pre-exposure Prophylaxis)
Evushield loses neutralization potency against BA.4.6 (confirmed() and potentially also against BF.7, BA.2.75.2 and BQ subvariants (preliminary); retains activity against BA.2.75 and BA.4 (confirmed). Please note, breakthrough infections are possible, advise patients to have a treatment plan in place and to seek timely medical attention is symptoms occur.

New! Updated Bebtelovimab Fact Sheet and FDA Update

Fact Sheet Update: Clinical Pharmacology, Microbiology (12.4): updated neutralizing data (Nov 4)

- Bebtelovimab not active against BQ.1, BQ.1.1; activity confirmed against BF.7, BA.2.75.2

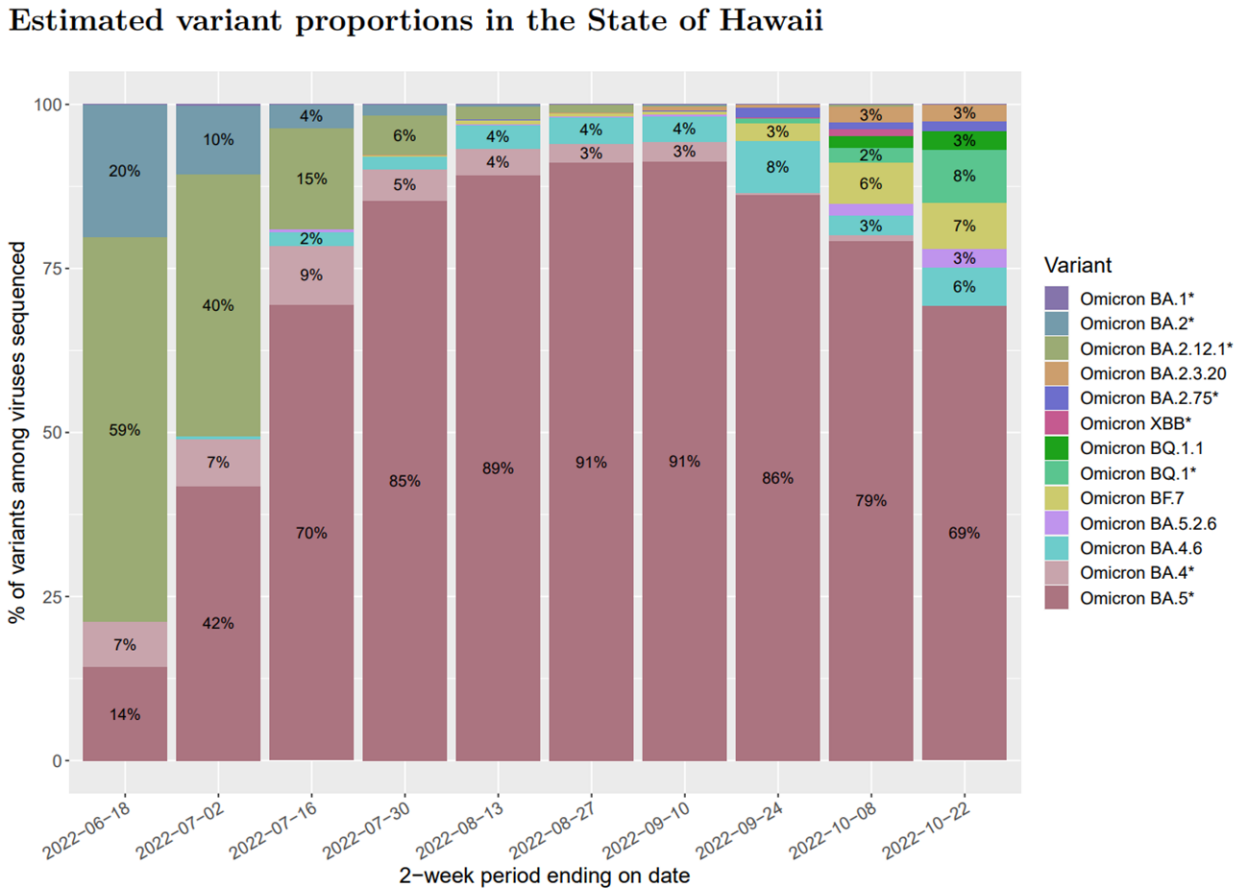
FDA Statement: FDA Updates on Bebtelovimab (Nov 4)

- At this time, bebtelovimab remains authorized in all U.S. regions until further notice by FDA. Prescribers should monitor CDC regional variant frequency, particularly Omicron subvariants BQ.1 and BQ.1.1.
- There are several treatments authorized or approved which are expected to retain activity against currently circulating variants, including Omicron subvariants BQ.1 and BQ.1.1.
  - Paxlovid is authorized for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg)
  - Veklury is approved for the treatment of adults and pediatric patients (28 days of age and older and weighing at least 3 kg) who are: hospitalized, or not hospitalized
  - Lagevrio is authorized for the treatment of mild-to-moderate COVID-19 in adults, and for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

Reminder: Bebtelovimab is not authorized for treatment of mild-to-moderate COVID-19 **in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant** based on available information including variant susceptibility to this drug and regional variant frequency.

Therapeutics Activity Against Emerging Variants

- **All products retain activity against most prevalent variant, BA.5**
  - All therapeutics also retain activity against BA.2.75*, BA.4 (BA.5+BA.2.75+BA.4 = ~42% prevalence)
  - There are currently no changes in authorization for use for any of the products
- Evusheld loses neutralization potency against BA.4.6 (confirmed) & potentially also against BF.7, BA.2.75.2 & BQ subvariants (preliminary) [~58%]; retains activity against BA.2.75* and BA.4 (confirmed)
  - Breakthrough infections are possible**, advise patients to have a treatment plan in place and to seek timely medical attention if symptoms occur**
- Bebtelovimab loses neutralization potency against BQ.1 and BQ.1.1 (confirmed); retains activity against BA.4.6, BA.2.75, BA.4, BA.5, BF.7, and BA.2.75.2 (confirmed)
  - BQ.1 + BQ.1.1 currently ~ 35% prevalence nationally
- Paxlovid/Lagevrio/Veklury expected to retain activity against all circulating variants based on preliminary data & sequence analysis; additional data pending
- mAbs currently not authorized for use (Regen-COV, bam/ete, sotrovimab) are routinely tested against emerging variants



References:

Updated Bebtelovimab fact sheet: https://www.fda.gov/media/156152/download

ASPR announcement: https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-04November2022.aspx

CDC variant report: https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Hawaii DOH variant report: https://health.hawaii.gov/coronavirusdisease2019/what-you-should-know/covid-19-data-reports/