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Alaska Public Health Advisory

Monoclonal Antibody Antiviral Resistance Seen with SARS-CoV-2 Variants of Concern

March 29, 2021

Background

The FDA has issued EUAs for a number of investigational monoclonal antibodies that could help the immune system recognize and respond more effectively to the virus. They are intended for the treatment of outpatients with mild to moderate COVID-19 who are high risk for progressing to severe disease and/or hospitalization. The NIH COVID-19 Treatment Guidelines provide information about these drugs and describe what is known about their effectiveness. If used, they should be administered as soon as possible after diagnosis and within 10 days of symptom onset.

There are currently three recombinant human monoclonal antibody therapies (mAbs) indicated for the treatment of SARS-CoV-2 infection: bamlanivimab (Eli Lilly), bamlanivimab/etesevimab (Eli Lilly), and casirivimab/indevimab (Regeneron). All three mAbs preparations are given via IV infusion. The antibodies are directed against the SARS-CoV-2 spike protein and its receptor binding domain.[1,2,3,4,5]

In clinical trials, mAbs have shown considerable reduction in the need for hospitalization and emergency room visits.[1,2,4] Monoclonal antibody therapeutics are available for eligible high-risk adults and children (aged 12–17 years) who have tested positive for SARS-CoV-2 infection and have mild to moderate symptoms. They have been granted Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) to treat eligible, non-hospitalized COVID-19 patients. [1,2,4]

Emerging variants of concern (VOC) are now circulating worldwide. The U.S. Centers for Disease Control and Prevention (CDC) defines a VOC as, **"**A variant for which there is evidence of an increase in transmissibility, more severe disease (increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures". Cases of B.1.1.7, P.1, and B.1.429 have all been identified in Alaska since December 2020.[6,7]

The purpose of this advisory is to alert Alaska providers to how the presence of SARS-CoV-2 variants has impacted the use of mAbs.

Monoclonal Antibody Activity Against SARS-CoV-2 Variants of Concern

The available SARS CoV-2 monoclonal antibody products have been found to have varying effectiveness to current variants of concern. Applicable drug fact sheets for health care providers have been updated to include a section addressing resistance, as summarized below:[4,5,6]

- Bamlanivimab alone is unlikely to be effective against B.1.351 (S. Africa), P.1 (Brazil), B.1.427/B.1.429 (CA), and B.1.526 (NY). Given the sustained increase in SARS-CoV-2 viral variants in the United States that are resistant to bamlanivimab administered alone, and the

availability of other authorized monoclonal antibody therapies that are expected to retain activity to these variants, the U.S. Government, in coordination with Eli Lilly and Company, will stop the distribution of bamlanivimab alone. Etesevimab is available to pair with existing bamlanivimab doses that a facility may have in inventory.

- Modeling predicts bamlanivimab/etesevimab is maintaining its original activity against B.1.1.7, B.1.427/B.1.429, and B.1.526; however, it is unlikely to be effective against B.1.351 and P.1.
- Modeling predicts casirivimab/indevimab is maintaining is original activity against B.1.1.7, B.1.351, P.1, B.1.427/B.1.429, and B.1.526
- Both monoclonal combination therapies are commercially available to qualifying administration facilities. The Federal government has purchased the monoclonal antibody therapies so there is no cost to obtain the medication.

Recommendations for Providers

1. Consider offering monoclonal antibody *combination* therapy to high-risk outpatients who have tested positive for SARS-CoV-2, as per the NIH COVID-19 Treatment Guidelines.
2. Request mAbs from SOA using the form available online: http://dhss.alaska.gov/dph/Epi/id/SiteAssets/Pages/HumanCoV/COVID_Monoclonal_Antibody_Referral_Form.pdf

Resources

- Infectious Disease Society of America (IDSA) Guidelines on the Treatment and Management of Patients with COVID-19 (idsociety.org)
- Statement on Bamlanivimab Plus Etesevimab EUA | COVID-19 Treatment Guidelines (nih.gov)
- Direct order of etesevimab via AmerisourceBergen
- Alaska COVID Genomic Surveillance
- https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/default.aspx

References

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3. Eli Lilly, banlanivimab Fact sheet for medical providers, revised March 2021 https://www.fda.gov/media/143603/download
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5. Regeneron, casirivimab/indevimab Fact sheet for medical providers, revised March 2021 https://www.fda.gov/media/145611/download
6. CDC, "SARS-CoV-2 Variant Classifications and Definitions", Centers for Disease Control and Prevention, 24 March 2021, https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html#Concern
7. State of Alaska Department of Health and Social Services, Alaska COVID Genomic Surveillance, 18 March 2021, http://dhss.alaska.gov/dph/Labs/Documents/AKSeqCon_GenomicSituationReport.pdf

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