Monoclonal Antibodies in Coronavirus Disease 2019

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Objectives for Pharmacists & Nurses

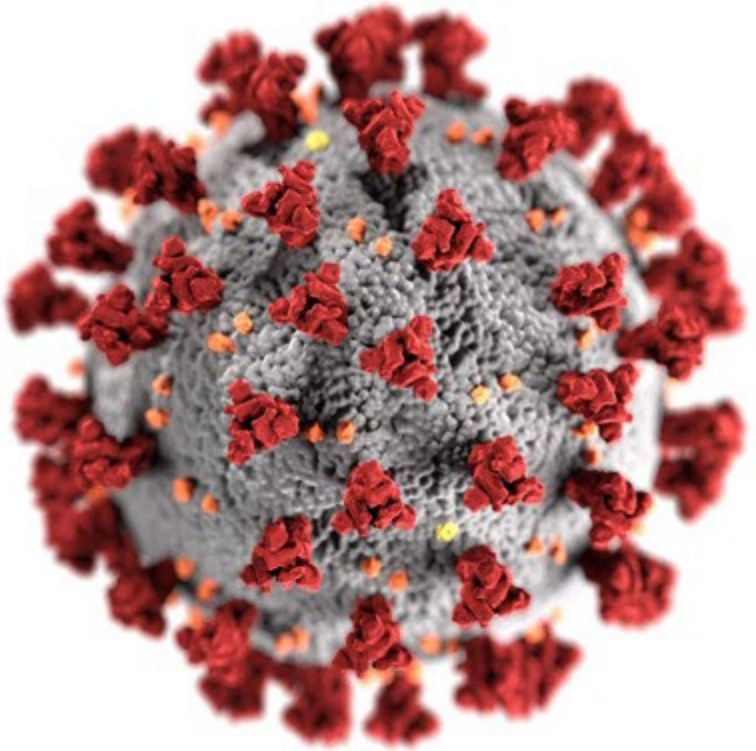
- Recall current treatment guidelines for COVID-19
- Identify eligibility criteria for each monoclonal antibody (mAB) used in the treatment of COVID-19
- Recognize the mechanism of action for mABs in the treatment of COVID-19

Objectives for Pharmacy Technicians

- Recall current treatment guidelines for COVID-19
- Identify proper dosing for monoclonal antibodies (mAB) used in the treatment of COVID-19
- Recognize proper compounding methods for monoclonal antibodies

COVID-19

- Infectious disease caused by the SARS-CoV-2 virus
- Most common symptoms include
  - Fever
  - Cough
  - Fatigue
- More severe symptoms
  - Difficulty breathing or shortnes of breath (SOB)
  - Altered mental status
  - Chest pain



Coronavirus [Internet]. World Health Organization. World Health Organization; [cited 2022Mar29]. Available from: https://www.who.int/health-topics/coronavirus#tab=tab_3

COVID-19 Severity Classifications

- **Asymptomatic/presymptomatic**
  - Test positive, but have no symptoms
- **Mild**
  - Have signs and symptoms of COVID-19
  - Do not experience any shortness of breath, dyspnea, or abnormal chest rising
- **Moderate**
  - Show evidence of lower respiratory disease
  - Have oxygenation saturation (SpO_2) ≥ 94 on room air
- **Severe**
  - SpO_2 < 94% on room air at sea level
  - Ratio of arterial partial pressure of oxygen to fraction of inspired oxygen < 300 mmHg
  - Respiratory rate > 30 bpm
  - Lung infiltrates > 50%
- **Critical**
  - Respiratory failure, septic shock, and/or multiple organ dysfunction

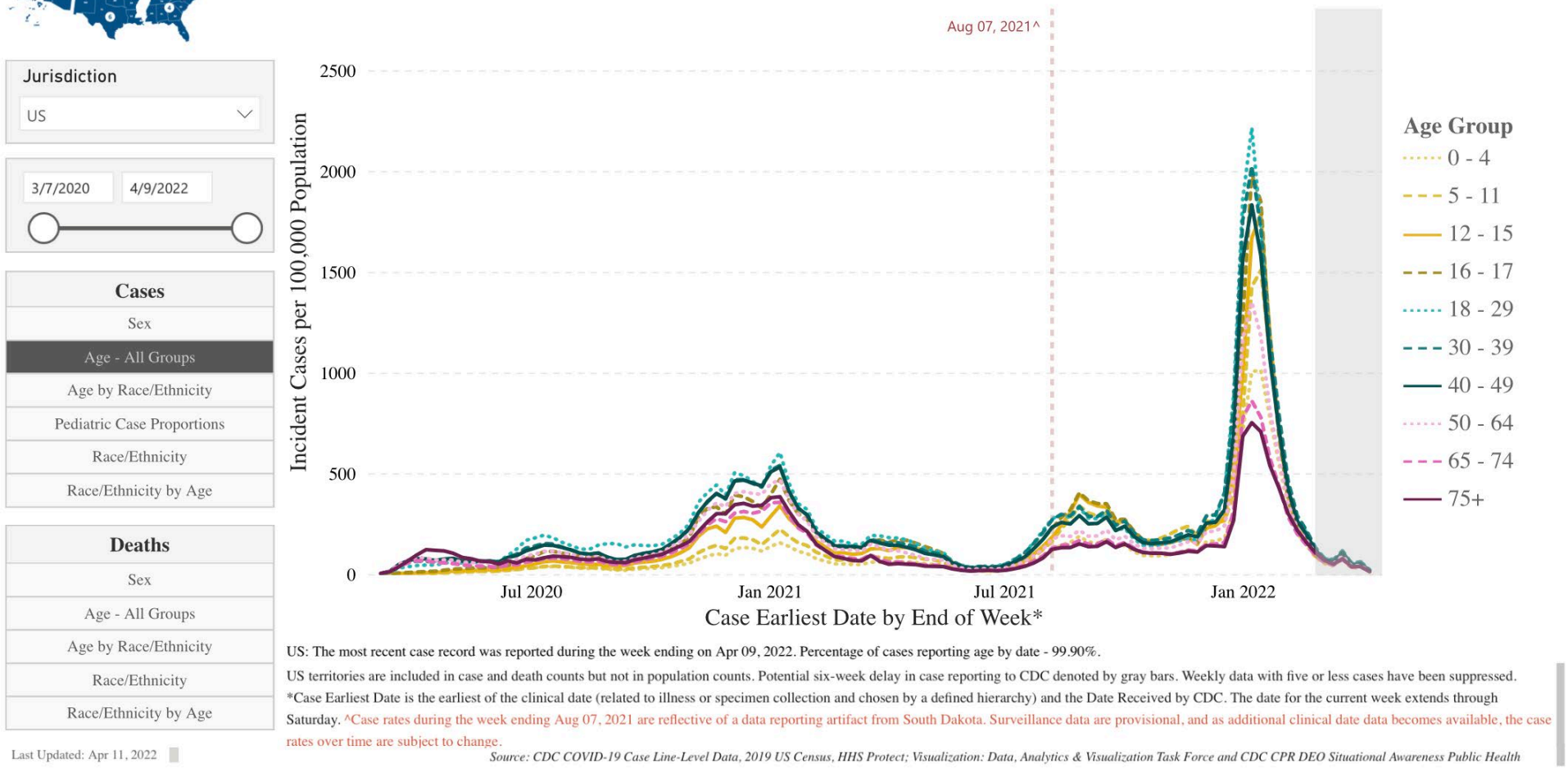
COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed March 25, 2022.

Epidemiology in America (As of April 2022)

- Total cases: 80,191,020
  - New: 25,913
- Total deaths: 982,663
  - New: 891
- Current hospitalizations: 8,280
  - New: 1,394
- Vaccinations: 82% (at least 1 dose)

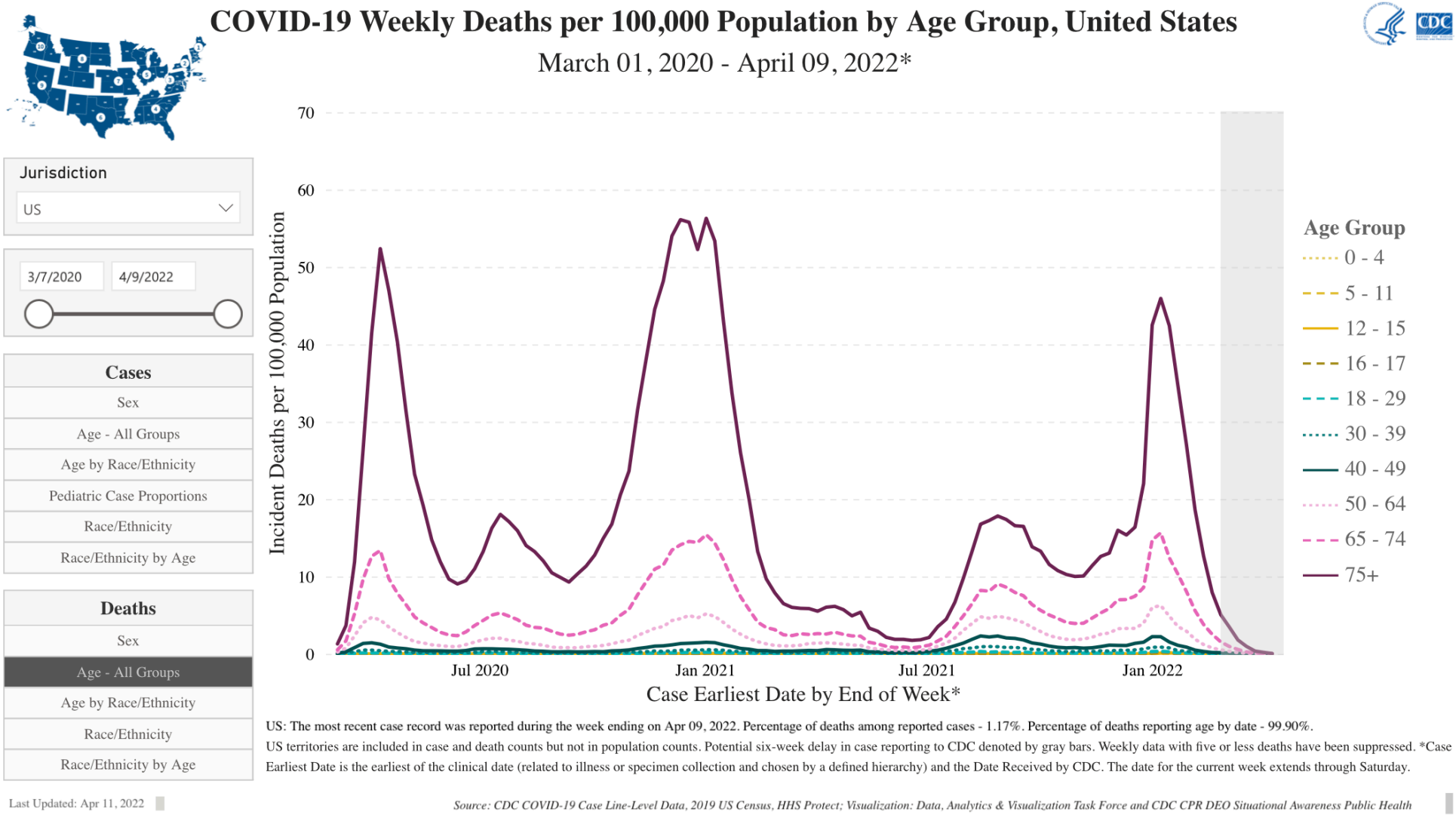
Covid-19 epidemiology [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022April11]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/science/about-epidemiology/index.html

Epidemiology



CDC Covid Data tracker [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022April11]. Available from: https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

Epidemiology



CDC Covid Data tracker [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Mar30]. Available from: https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

Adaptive Immunity

Active

Natural

Vaccine-induced

Passive

Mother-to-baby

Antibody-containing products (i.e. immunoglobulins)

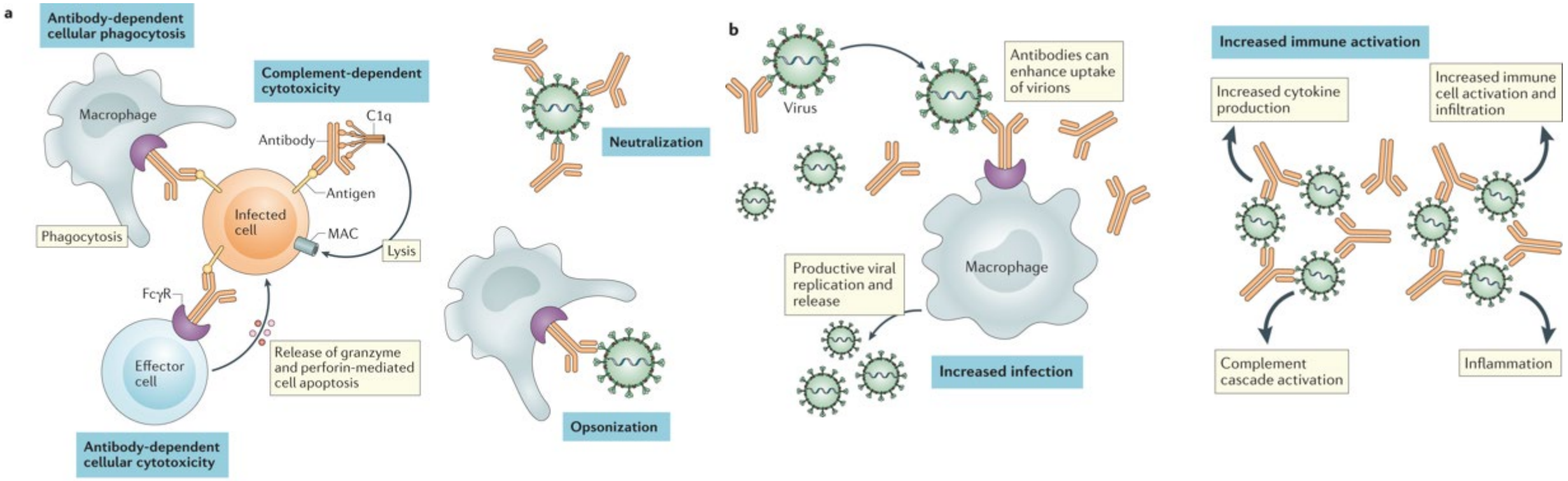
Types of immunity to a disease [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2021 [cited 2022Mar30]. Available from: https://www.cdc.gov/vaccines/vac-gen/immunity-types.htm

Monoclonal Antibodies

- Laboratory produced molecules that act as substitute antibodies
- Can restore, mimic, or enhance the immune system's attack on cells
- Created by identifying pathogen-specific B cells in patients who have recently recovered from the infection or by immunizing mice genetically modified to have a humanized immune system and harvesting effective antibodies from them

Taylor PC, et al. Nat Rev Immunol. 2021; 21:382-393

Pathophysiology



Taylor PC, et al. *Nat Rev Immunol.* 2021; 21:382-393

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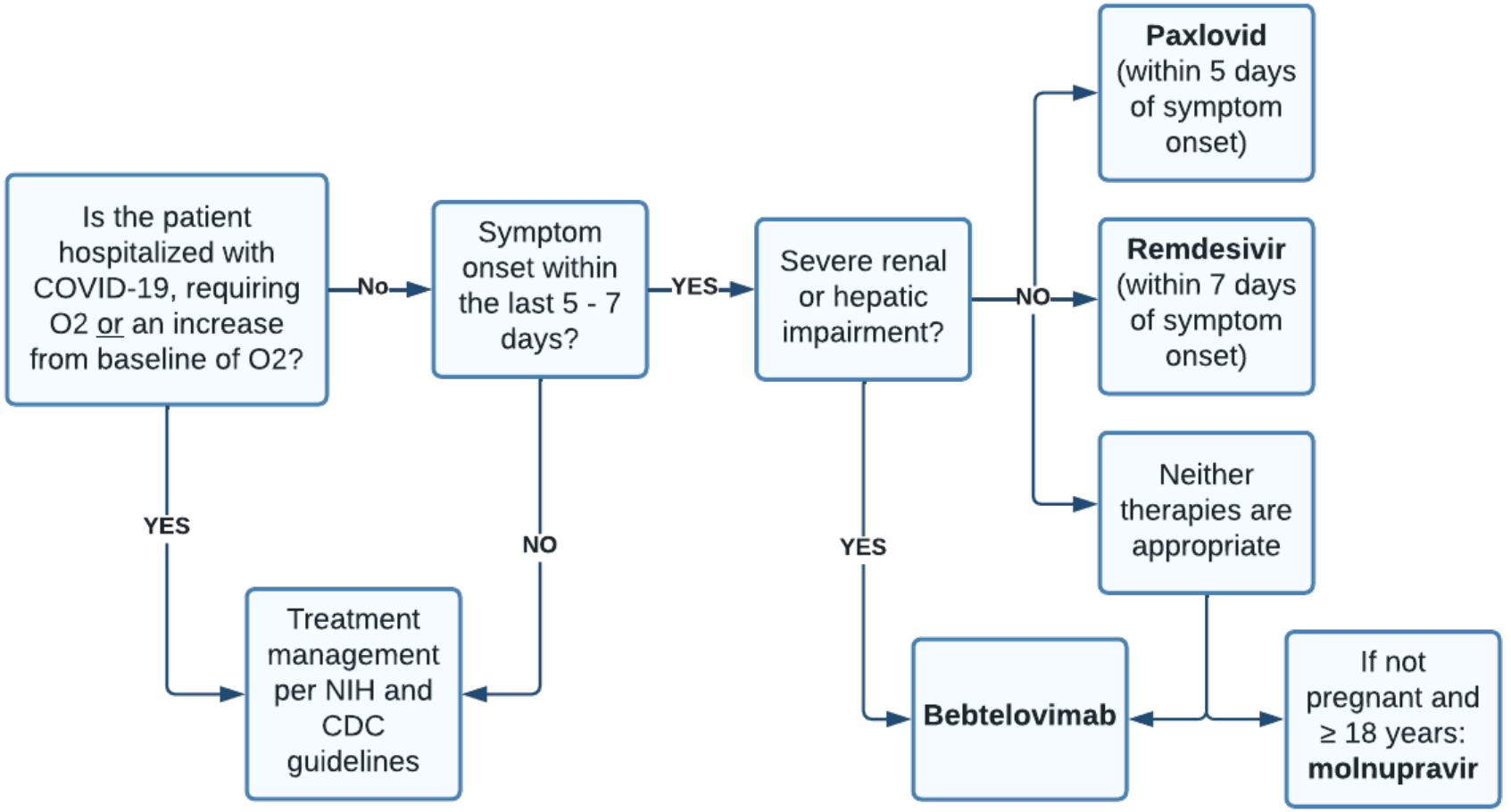
GUIDELINE DIRECTED THERAPY AND TREATMENT

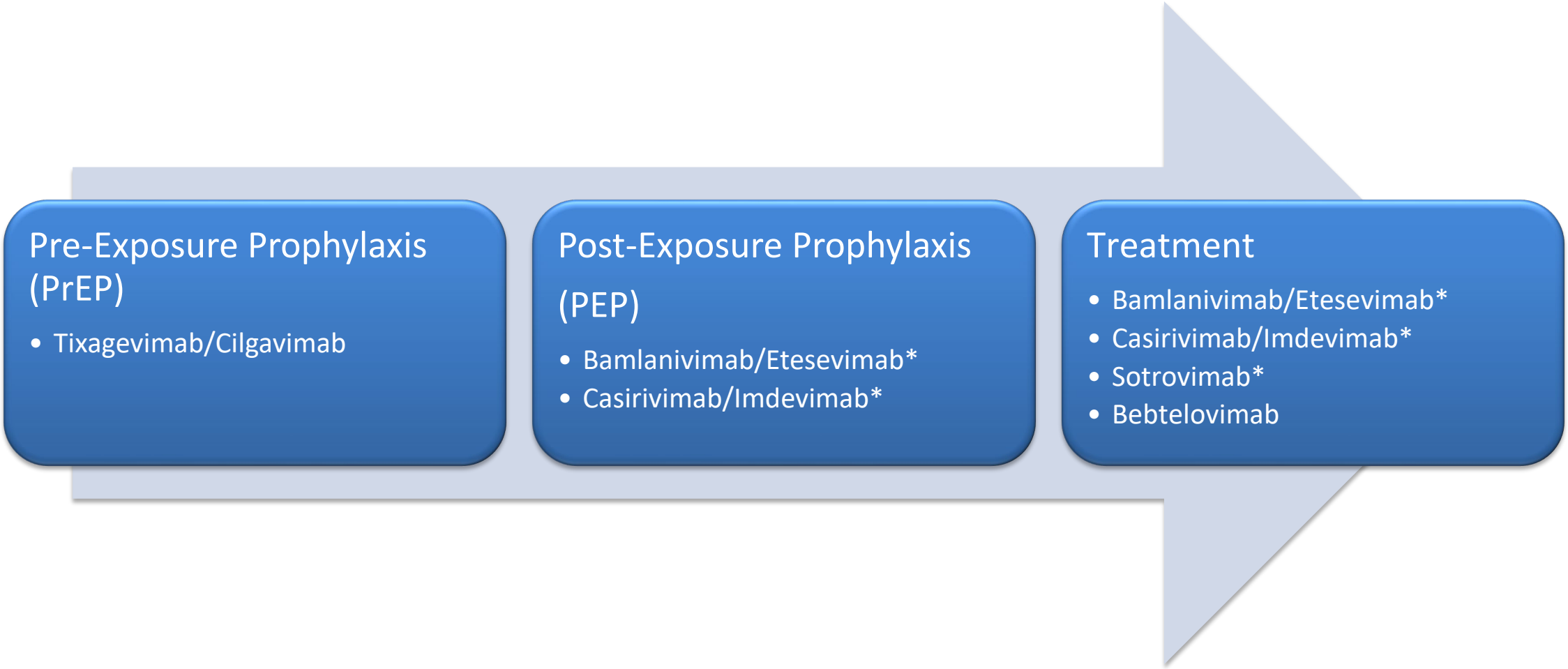
Current Recommendations: Mild to Moderate Disease (Outpatient)



COVID-19 Treatment Guidelines Panel. *NIH*. 2022.

Covid-19 Therapeutics: Decision Aid [Internet]. COVID-19 Therapeutics | HHS/ASPR. [cited 2022Apr6]. Available from: https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx

Monoclonal Antibody Therapy



PRE-EXPOSURE PROPHYLAXIS

Tixagevimab/Cilgavimab (Evusheld™)

- Manufacturer: AstraZeneca
- Emergency Use Authorization: PrEP (December 2021)
  - Not currently infected or have no known exposure to COVID-19
- Mechanism of Action (MOA): targets the receptor binding domain of the SARS-CoV-2 spike protein
- Duration of Action (DOA): depends on the circulating variant
  - Potential protective option
- Intramuscular injection
- Activity: Delta, Omicron, Mu

Euvosheld™. Fact Sheet for Healthcare Providers. AstraZeneca; 2022.

PROVENT (PrEP)

Objective	To assess the safety and efficacy of a single total dose of 300 mg AZD7442 (150 mg tixagevimab + 150 mg cilgavimab) compared to placebo for the prevention of COVID-19
Design	Phase III, randomized, double-blind, placebo-controlled, multi-center, international trial N = 5197
Population	Patients having increased risk for inadequate response to active immunization or having increased risk for COVID-19 infection • Patients whose locations or circumstances put them at risk of exposure to the virus • Unvaccinated and had a negative point-of-care serology test
Intervention	Single dose of tixagevimab 150 mg/cilgavimab 150 mg (2 IM injections) (n = 3460)
Comparator	Saline placebo (n = 1737)
Outcomes	The incidence of the first case of SARS CoV-2 RT-PCR positive symptomatic illness
Preliminary results	0.2% (tixagevimab/cilgavimab) vs. 1.0% (placebo); RRR 77% (95% CI 46 – 90) compared with placebo

Azd7442 Provent Phase III prophylaxis trial met primary endpoint in preventing COVID-19 [Internet]. AstraZeneca. 2021 [cited 2022Mar30]. Available from: https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-prophylaxis-trial-met-primary-endpoint.html
Phase III double-blind, placebo-controlled study of AZD7442 for pre-exposure prophylaxis of COVID-19 in adult. - tabular view [Internet]. Phase III Double-blind, Placebo-controlled Study of AZD7442 for Pre-exposure Prophylaxis of COVID-19 in Adult. - Tabular View - ClinicalTrials.gov. [cited 2022Mar30]. Available from: https://clinicaltrials.gov/ct2/show/record/NCT04625725

STORM CHASER (PEP)

Objective	To assess the safety and efficacy of AZD7442 (tixagevimab/cilgavimab) compared to placebo for the prevention of COVID-19 in patients recently exposed to the virus
Design	Phase III, randomized, double-blind, placebo-controlled, multi-center trial N = 1121
Population	Unvaccinated adults ≥ 18 years with confirmed exposure to a person with a case of the virus within the past eight days
Intervention	Single dose of tixagevimab 150 mg/cilgavimab 150 mg (2 IM injections) (n = 749)
Comparator	Saline placebo (n = 372)
Outcome	The incidence of the first case of SARS CoV-2 RT PCR positive symptomatic illness
Preliminary results	3.1% (tixagevimab/cilgavimab) vs. 4.6% (placebo); RRR 33% (95% CI -26 – 65) compared with placebo No indication for PEP

Update on Azd7442 Storm Chaser trial in post-exposure prevention of symptomatic covid-19 [Internet]. AstraZeneca. 2021 [cited 2022Mar30]. Available from: https://www.astrazeneca.com/media-centre/press-releases/2021/update-on-azd7442-storm-chaser-trial.html
Phase III double-blind, placebo-controlled study of azd7442 for post- exposure prophylaxis of COVID-19 in adults - tabular view [Internet]. Phase III Double-blind, Placebo-controlled Study of AZD7442 for Post- Exposure Prophylaxis of COVID-19 in Adults - Tabular View - ClinicalTrials.gov. [cited 2022Mar30]. Available from: https://clinicaltrials.gov/ct2/show/NCT04625972

Tixagevimab/Cilgavimab

EUA: PrEP

- Who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS- CoV-2 and
- Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination
- For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

Dose

- 300 mg tixagevimab + 300 mg cilgavimab
  - Patients who previously received 150 mg tixagevimab + 150 mg cilgavimab should receive another dose of 150 mg/150 mg in order to complete the full dose

Euvosheld™. Fact Sheet for Healthcare Providers. AstraZeneca; 2022.

New Dosing Recommendations as of February 2022

300 mg tixagevimab + 300 mg cilgavimab initially as 2 consecutive IM injections

Per the EUA fact sheet, there is no safety or efficacy data for repeat dosing. Due to the uncertainty of the upcoming dominant variant in the US, **the recommended timing of the repeat dose cannot be made at this time.**

Euvosheld™. Fact Sheet for Healthcare Providers. AstraZeneca; 2022.

Tixagevimab/Cilgavimab

Compounding considerations

- Concentration: Tixagevimab 150 mg/3 mL + cilgavimab 150 mg/ 3mL
  - Solutions in vials should be pallescent, colorless to slightly yellow
  - Discard if cloudy, discolored, or has visible particles
- In 2 separate syringes:
  - 6 mL tixagevimab (2 vials) + 6 mL cilgavimab (2 vials)
- Prepared syringes should be administered immediately
- Patient should be monitored for ≥ 60 minutes after injection

Euvosheld™. Fact Sheet for Healthcare Providers. AstraZeneca; 2022.

Tixagevimab/Cilgavimab

Adverse reactions

- Headache
- Fatigue
- Cough

Euvosheld™. Fact Sheet for Healthcare Providers. AstraZeneca; 2022.

Knowledge Check

What is the mechanism of action for tixagevimab/cilgavimab?

a. Targets the receptor binding domain of the SARS-CoV-2 spike protein
b. Binds and sequesters the ACE-2 receptor
c. Cleaves the spike protein of the SARS-CoV-2 molecule
d. Downregulates the ACE-2 receptor

Knowledge Check

What is the mechanism of action for tixagevimab/cilgavimab?

a. Targets the receptor binding domain of the SARS-CoV-2 spike protein
b. Binds and sequesters the ACE-2 receptor
c. Cleaves the spike protein of the SARS-CoV-2 molecule
d. Downregulates the ACE-2 receptor making the virus less virulent

Knowledge Check

Patient NK is a 54-year-old, immunocompromised female who received tixagevimab/cilgavimab 150 mg/150 mg IM for pre-exposure prophylaxis 3 weeks ago. How should you proceed with this patient?

a. Do nothing, this patient received the full recommended dose
b. She should receive a second dose of 150 mg/150 mg to complete the full recommended dose
c. She should receive a second dose of 300 mg/300 mg to complete the full recommended dose

Knowledge Check

Patient NK is a 54-year-old, immunocompromised female who received tixagevimab/cilgavimab 150 mg/150 mg IM for pre-exposure prophylaxis 3 weeks ago. How should you proceed with this patient?

a. Do nothing, this patient received the full recommended dose
b. She should receive a second dose of 150 mg/150 mg to complete the full recommended dose
c. She should receive a second dose of 300 mg/300 mg to complete the full recommended dose

Knowledge Check

You are tasked with preparing the dose of tixagevimab/cilgavimab for NK. How should you proceed?

a. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 1 syringe and administer immediately
b. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 1 syringe and administer in 2 hours
c. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 2 separate syringes and administer immediately
d. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 2 separate syringes and administer in 2 hours

Knowledge Check

You are tasked with preparing the dose of tixagevimab/cilgavimab for NK. How should you proceed?

a. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 1 syringe and administer immediately
b. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 1 syringe and administer in 2 hours
c. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 2 separate syringes and administer immediately
d. Draw up 2 vials of tixagevimab and 2 vials cilgavimab in 2 separate syringes and administer in 2 hours

POST-EXPOSURE PROPHYLAXIS AND TREATMENT

Bamlanivimab/Etesevimab

- Manufacturer: Elli Lily
- EUA: November 2020
  - Outpatient with mild to moderate COVID-19 who are at high risk for severe COVID-19 and had tested positive
- Originally derived from the blood of one of the first patients to recover from the virus
- MOA: both mAbs are recombinant neutralizing agents directed against the spike protein and bind to different, but overlapping epitopes
- Variant activity: Alpha, Delta

Bamlanivimab/etesevimab. Fact Sheet for Health Care Providers. Eli Lilly and Company. 2022.

Bamlanivimab/Etesevimab

Post-Exposure Prophylaxis

- Adults, pediatrics, neonates
- Not fully vaccinated **OR** not expected to amount an appropriate immune response to the vaccine **AND** have been exposed to an individual exposed to COVID-19 **OR** at high risk of exposure to an individual infected with COVID-19

Treatment & Post-Exposure Prophylaxis Dose

- Adults: 700 mg bamlanivimab + 1,400 mg etesevimab
- Pediatrics:
  - > 20 kg to < 40 kg: 350 mg bamlanivimab + 700 mg etesevimab
  - > 12 kg to 20 kg: 175 mg bamlanivimab + 350 mg etesevimab

Bamlanivimab/etesevimab. Fact Sheet for Health Care Providers. Eli Lilly and Company. 2022.

Bamlanivimab/Etesevimab

Preparation & Administration

- Standard concentration: 700 mg/1400 mg in 150 mL 0.9% sodium chloride over ≥ 41 min
- Administer with 0.2- or 0.22-micron polyethersulfone in-line filter
- Monitor for infusion related reactions for 60 min after completion of infusion

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Bamlanivimab/etesevimab. Fact Sheet for Health Care Providers. Eli Lilly and Company. 2022.

Bamlanivimab/Etesevimab

- Significant adverse reactions
  - Hypersensitivity and infusion related reactions
    - Onset: Rapid
- Other adverse reactions
  - Pruritis
  - Nausea
  - Dizziness
  - Fever

Bamlanivimab/etesevimab. Fact Sheet for Health Care Providers. Eli Lilly and Company. 2022.

Casirivimab/Imdevimab (REGEN-COV)

- Manufacturer: Regeneron
- EUA: November 2020
  - Outpatients with mild to moderate COVID-19 who are at high risk for severe COVID-19
- MOA: Both mAbs bind to different spots regions of the SARS-CoV-2 spike protein receptor binding domain, blocking attachment to the human ACE2 receptor
- Variant activity: Alpha, Gamma, Delta

REGEN-COV®. Fact Sheet for HealthCare Providers. Regeneron Pharmaceuticals, Inc. 2021.

Casirivimab/Imdevimab

Treatment & PEP Dose

- Casirivimab 600 mg + imdevimab 600 mg IV infusion over 30 min

Compounding & Dispensing

- Standard concentration: 600 mg/600 mg per 10 mL
- 1.2 g in 100 mL 0.9% sodium chloride (total volume: 110 mL)
- Administer with 0.2- or 0.22-micron PES in line filter
- Monitor patient for 60 min following completion of infusion

REGEN-COV® Fact Sheet for HealthCare Providers. Regeneron Pharmaceuticals, Inc. 2021.

Casirivimab/Imdevimab

- Significant adverse reactions
  - Hypersensitivity
- Adverse reactions
  - Injection site reactions
  - Nausea
  - Vomiting

REGEN-COV® Fact Sheet for HealthCare Providers. Regeneron Pharmaceuticals, Inc. 2021.

Sotrovimab

- Manufacturer: GSK & Vir Biotechnology
- EUA (May 2021):
  - Mild-to-moderate COVID-19 in adults and pediatrics (≥ 12 years old and ≥ 40 kg) with a positive test result and are at high risk for progression of severe COVID-19
- MOA: Binds to a highly conserved epitope of the receptor binding domain of viral spike protein, inhibiting the step that occurs after virus attachment and prior to infusion of the virus with the cell membrane
- Activity: Alpha, Beta, Gamma, Delta, Omicron BA.1

Sotrovimab. Fact Sheet for Healthcare Providers. GlaxoSmithKline LLC. 2022.

COMET-ICE Study

Objective	To evaluate the efficacy and safety of sotrovimab in high-risk, ambulatory patients with mild-to-moderate Covid-19
Design	Multicenter, ongoing, phase 3 trial N = 583
Population	Non-hospitalized patients with symptomatic Covid-19 (≤5 days after the onset of symptoms) and at least one risk factor for disease progression
Intervention	Sotrovimab 500 mg IV infusion x 1 dose (n = 291)
Comparator	Placebo (n = 292)
Outcome	Hospitalization (for >24 hours) for any cause or death within 29 days after randomization
Results	1% sotrovimab vs. 7% placebo; p = 0.002
Conclusion	Among high-risk patients with mild-to-moderate Covid-19, sotrovimab reduced the risk of disease progression. No safety signals were identified.

Gupta A, et al. *NEJM*. 2021;385(21):1941–50.

COMET-PEAK: Sotrovimab Generation 2

Objective	To access the safety, tolerability and pharmacokinetics of second generation sotrovimab in non-hospitalized patients with mild to moderate COVID-19 disease
Design	Multicenter, randomized, double-blind, parallel group phase II study N = 342
Population	Non-hospitalized patients with symptomatic Covid-19 (≤5 days after the onset of symptoms) and at least one risk factor for disease progression
Intervention	Sotrovimab Generation 2: 500 mg IV infusion or IM injection x 1 dose (n = 291)
Comparator	Sotrovimab Generation 1: 500 mg IV infusion (n = 292)
Outcome	Occurrence of adverse events and serious adverse events
Results	No data has been posted yet

Safety, tolerability and pharmacokinetics of second generation VIR-7831 material in non-hospitalized participants with mild to moderate COVID-19 - Full Text View [Internet]. Safety, Tolerability and Pharmacokinetics of Second Generation VIR-7831 Material in Non-hospitalized Participants With Mild to Moderate COVID-19 - Full Text View - ClinicalTrials.gov. [cited 2022Mar30]. Available from: https://clinicaltrials.gov/ct2/show/NCT04779879

Sotrovimab

Dose

- 500 mg IV infusion over 15 or 30 min depending on the concentration

Preparation & Administration

- Concentration: 500 mg/8 mL
- Inject 8 mL from 1 vial into a prefilled infusion bag of 50- or 100-mL D5W or NS
  - 50 mL infused over 15 min
  - 100 mL infused over 30 min
- Administer with a 0.2-micron PES in line filter
- Monitor for ≥ 60 minutes after completion of infusion

Sotrovimab. Fact Sheet for Healthcare Providers. GlaxoSmithKline LLC. 2022.

Sotrovimab

- Significant adverse reactions
  - Hypersensitivity reaction
    - Onset: Immediate
- Other adverse reactions
  - Skin rash
  - Diarrhea

Sotrovimab. Fact Sheet for Healthcare Providers. GlaxoSmithKline LLC. 2022.

Bebtelovimab

- Manufacturer: Eli Lilly
- EUA (February 2022):
  - Treatment of mild to moderate COVID-19 in adults and pediatric patients (≥ 12 years old and ≥ 40 kg) with a positive COVID-19 test, and who are at high risk for progression to severe COVID-19 and for whom alternative COVID-19 treatment options approved or authorized by the FDA are not accessible or clinically appropriate
- MOA: binds to the spike protein and blocks attachment to the human ACE2 receptor
- Active variants: all except Mu

Bebtelovimab. Fact Sheet for Healthcare Providers. Eli Lilly and Company. 2022.

BLAZE-4

Objective	To evaluate the safety and efficacy of mono- and combination monoclonal antibody therapy in patients with mild-to-moderate COVID-19 disease
Design	Phase 2, randomized, double blind, placebo controlled N = 1631
Population	Low and high risk non-hospitalized patients with mild to moderate COVID-19 infection
Interventions	Bebtelovimab 175 mg IV push + bamlanivimab 700 mg/etesevimab 1400 mg IV infusion
	Bebtelovimab 175 mg IV push alone
Comparator	Bamlanivimab 700 mg/etesevimab 1400 mg IV infusion Placebo
Outcome	Percentage of patients with viral load > 5.27 at day 7 • Bebtelovimab alone: 14%; RRR 34% (95% CI: -15 to 62%) • Bebtelovimab + bamlanivimab/etesevimab: 13%; RRR 38% (95% CI: -9 to 65) • Placebo: 21%

A study of immune system proteins in participants with mild to moderate COVID-19 illness - tabular view [Internet]. A Study of Immune System Proteins in Participants With Mild to Moderate COVID-19 Illness - Tabular View - ClinicalTrials.gov. [cited 2022Mar30]. Available from: https://clinicaltrials.gov/ct2/show/record/NCT04634409
Anti-SARS-cov-2 monoclonal antibodies [Internet]. IDSA Home. 2021 [cited 2022Mar30]. Available from: https://www.idsociety.org/covid-19-real-time-learning-network/therapeutics-and-interventions/monoclonal-antibodies/#Sotrovimab

Bebtelovimab

bebtelovimab
175 mg/2 mL injection

Dose

- 175 mg IV push over 30 seconds

Preparation & Administration

- Concentration: 175 mg/2 mL
- Solution should be opalescent and colorless to slightly yellow or brown (discard if cloudy, discolored, or contains particles)
- Draw up entire dose in a syringe
- Attach and prime polycarbonate and PVC DEHP-free IV extension set
- Administer over ≥ 30 seconds and flush extension set after
- Monitor for ≥ 60 min after completion of injection

Bebtelovimab. Fact Sheet for Healthcare Providers. Eli Lilly and Company. 2022.

Bebtelovimab

- Serious adverse events
  - Hypersensitivity
- Adverse reaction
  - Pruritis
  - Skin rash
  - Nausea
  - Vomiting
  - Infusion related action

Bebtelovimab. Fact Sheet for Healthcare Providers. Eli Lilly and Company. 2022.

Knowledge Check

Patient GD is to receive bebtelovimab. How should this medication be administered?

a. As a 60 min infusion through a 0.22-micron filter
b. As a 60 min infusion through a a primed polycarbonate and PVC DEHP-free IV extension set
c. As an IV push over ≥ 30 seconds directly into their IV catheter
d. As an IV push over ≥ 30 seconds through a primed polycarbonate and PVC DEHP-free IV extension set

Knowledge Check

Patient GD is to receive bebtelovimab. How should this medication be administered?

a. As a 60 min infusion through a 0.22-micron filter
b. As a 60 min infusion through a a primed polycarbonate and PVC DEHP-free IV extension set
c. As an IV push over ≥ 30 seconds directly into their IV catheter
d. As an IV push over ≥ 30 seconds through a primed polycarbonate and PVC DEHP-free IV extension set

VARIANTS

SARS-CoV-2 Variants

- Genetic lineages of the virus
- Routinely monitored by the United States via
  - Epidemiological investigations
  - Virus genetic sequence-based surveillance
  - Laboratory studies
- Variants being monitored (VBM)
- Variants of interest (VOI)
- Variants of concern (VOC)
- Variants of high consequence (VoHC)

SARS-COV-2 variant classifications and definitions [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Mar30]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvariants%2Fvariant-info.html#anchor_1632150752495

Variants Being Monitored & of Interest

- VBM
  - Data indicates there is a potential or clear impact on approved or authorized medical measures
  - Have been associated with severe disease or increased transmission
  - No longer detected or are circulating at very low levels
- VOI
  - Specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics, or immune escape
  - Evidence of increased proportion of cases or unique outbreak clusters
  - Limited prevalence or expansion in the US or in other countries
- VoHC

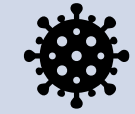
SARS-COV-2 variant classifications and definitions [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Mar30]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fvariants%2Fvariant-info.html#anchor_1632150752495

Characteristics of VOC

- Evidence of increased transmissibility
- More severe disease
- Reduction in neutralization by mAbs
- Reduced effectiveness of vaccines and treatments
- Diagnostic detection failure

SARS-COV-2 variant classifications and definitions [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Mar30]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html#concern

Variants of Concern

	Alpha	Beta	Gamma	Delta	Omicron		
					BA.1	BA.1.1	BA.2
Bamlanivimab/ Etesevimab							
Casirivimab/ Imdevimab							
Sotrovimab							
Tixagevimab/ Cilgavimab							
Bebtelovimab							

REGEN-COV®. Package Insert. Regeneron Pharmaceuticals, Inc. 2021.
Sotrovimab. Package Insert. GlaxoSmithKline LLC. 2022.
Bebtelovimab. Package Insert. Eli Lilly and Company. 2022.
Bamlanivimab/etesevimab. Package Insert. Eli Lilly and Company. 2022.
Evusheld™. Package Insert. AstraZeneca; 2022.

Current Variants of Concern

Delta

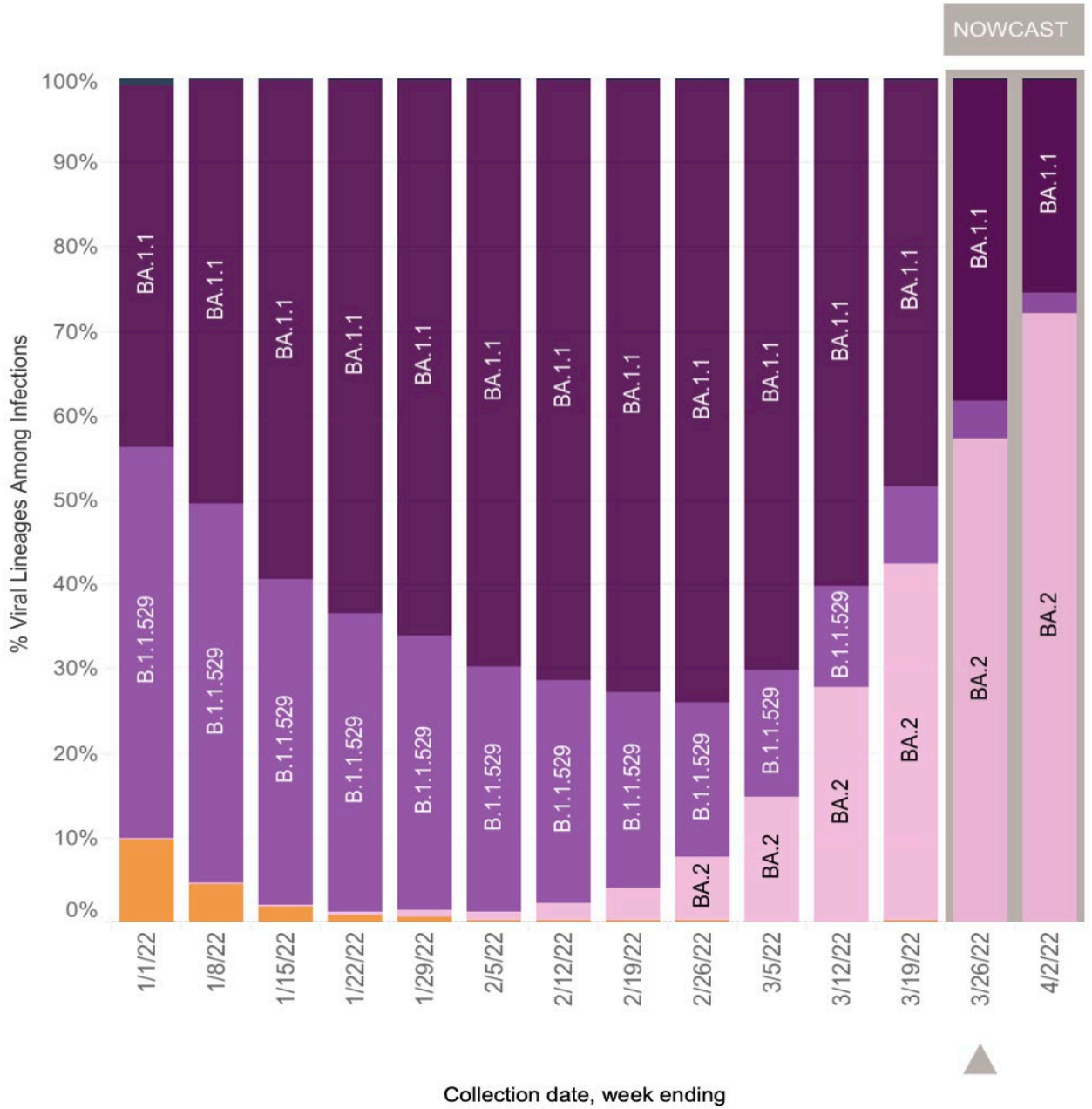
- Increased risk of transmissibility
- Most EUA mAbs are active against this variant
- Reduction in neutralization by vaccines

Omicron

- Potential increased risk of transmissibility
- Potential reduction in EUA mAb treatment
- Potential reduction in neutralization by vaccines

SARS-COV-2 variant classifications and definitions [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Mar30]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html#concern

Omicron Subvariants



CDC COVID Data tracker [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; [cited 2022Mar30]. Available from: https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Knowledge Check

Patient FD is a 27-year-old male who comes into the emergency room with a chief complaint of fever x 12 hours, chills, and cough. His COVID-19 test is positive. Assuming he meets EUA criteria, and the most likely variant is omicron BA.1, which monoclonal antibody should he receive?

a. Sotrovimab
b. Tixagevimab/cilgavimab
c. Bamlanivimab/etesevimab
d. Casirivimab/imdevimab

Knowledge Check

Patient FD is a 27-year-old male who comes into the emergency room with a chief complaint of fever x 12 hours, chills, and cough. His COVID-19 test is positive. Assuming he meets EUA criteria, and the most likely variant is omicron BA.1, which monoclonal antibody should he receive?

a. Sotrovimab
b. Tixagevimab/cilgavimab
c. Bamlanivimab/etesevimab
d. Casirivimab/imdevimab

FDA Criteria for Identifying High Risk Individuals Eligible for MAB Therapy

Medical conditions or other factors represented in clinical trials	Other conditions not represented in trials
• Age ≥ 65 • BMI > 30 • Diabetes • Cardiovascular disease or hypertension • Chronic lung disease	• Immunocompromised disease or treatment • Overweight (BMI 25 – 30) • Cancer • Chronic kidney disease • Chronic liver disease • Pregnancy • Sickle cell disease • Neurodevelopmental disorders • Medical related technology dependence • Infants < 1 year old • Cystic fibrosis • Dementia

COVID-19 Treatment Guidelines Panel. *NIH*. 2019.

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Knowledge Check

Of the following patients, who is eligible to receive a mAb?

a. 45-year-old male with hypertension
b. 56-year-old female with hyperlipidemia
c. 2-year-old child with otitis media
d. 64-year-old male with a chronic lung disease

Knowledge Check

Of the following patients, who is eligible to receive a mAb?

a. 45-year-old male with hypertension
b. 56-year-old female with hyperlipidemia
c. 2-year-old child with otitis media
d. 64-year-old male with a chronic lung disease

FDA Revoked or Currently Not Authorized EUA

- Due to increased resistance of current circulating variants, the following EUAs have been updated:
  - Revoked
    - Bamlanivimab monotherapy
  - Not authorized:
    - Bamlanivimab/etesevimab
    - Casirivimab/imdevimab
    - Sotrovimab

Commissioner Of the Coronavirus (COVID-19) update: FDA revokes emergency use authorization for monoclonal antibody bamlanivimab [Internet]. U.S. Food and Drug Administration. FDA; [cited 2022Mar30]. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab
Commissioner Of the. Emergency use authorization [Internet]. U.S. Food and Drug Administration. FDA; [cited 2022Apr1]. Available from: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

COVID-19 Vaccine and MAB Therapy

- COVID-19 vaccination can be given at any interval following receipt of passive antibody therapy
- Persons should wait 2 weeks after COVID-19 vaccination before receiving tixagevimab/cilgavimab for pre-exposure prophylaxis
- Persons who previously received antibody products (anti-SARS-CoV-2 mAb or convalescent plasma) as part of COVID-19 treatment, post-exposure prophylaxis, or pre-exposure prophylaxis can be vaccinated at any time

Interim clinical considerations for use of covid-19 vaccines [Internet]. Centers for Disease Control and Prevention; 2022 [cited 2022Mar30]. Available from: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Conclusion

- COVID-19 is an evolving virus with fast-paced changes to medication regimens
- There are currently only 2 mAbs with EUA status that have activity against the newest omicron BA.2 variant
- The key to staying ahead of the virus at your institution is to ensure you are up to date with the current data and literature as this information changes very quickly

Resources to Stay Up to Date

- Current EUAs: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs
- Current NIH guidelines: https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
- ASPR/HHS implementation guide: https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/USG-COVID19-Tx-Playbook.pdf
- ASPR/HHS decision aid: https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf
- ASPR/HHS side by side comparison: https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/side-by-side-overview.pdf

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Thank you!

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