University of Colorado **Anschutz Medical Campus**

A Provider's Guide to Monoclonal Antibody Therapy for COVID-19

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mAb Colorado

Disclosures

mAb Colorado funding

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3UL1TR002535-04S2

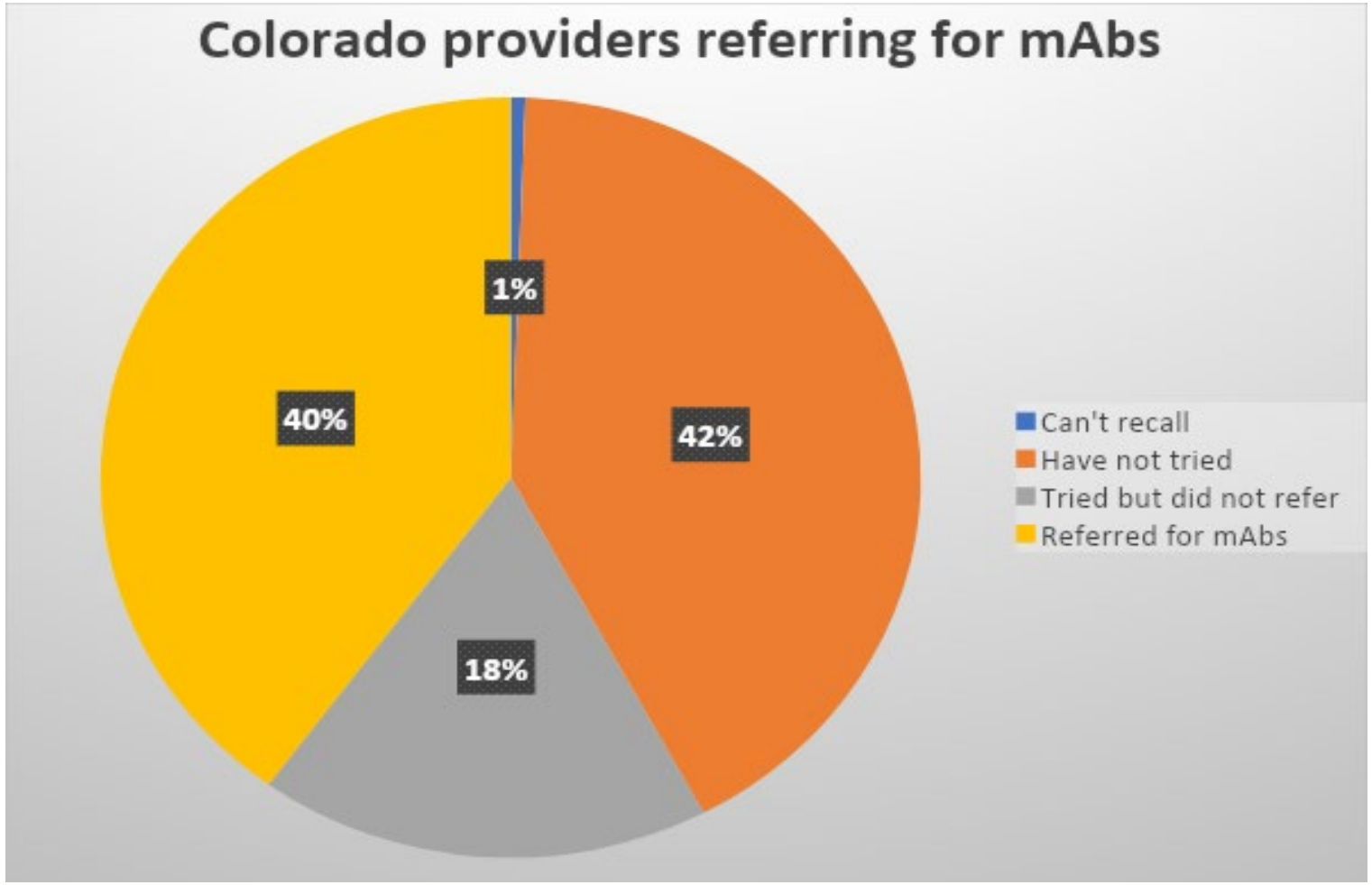
(03/15/2021-04/30/2022)

- No conflicts of interest (COI) to declare

Learning Objectives

- Data around current mAb use in Colorado
- How mAbs work in COVID-19
- Clinical data supporting efficacy for use with COVID
- Clinical pathways and guidelines for mAb use
- Essential logistics (infusion v. subQ, monitoring, adverse reactions, cost, insurance issues, how to communicate with patients)
- Resources for further questions

Provider survey results (N = 356)



Key Points:

- Need to simplify the ordering process
- Providers want more information about availability of treatment, cost, and need for timely action

mAb therapy available and efficacious for patients with:

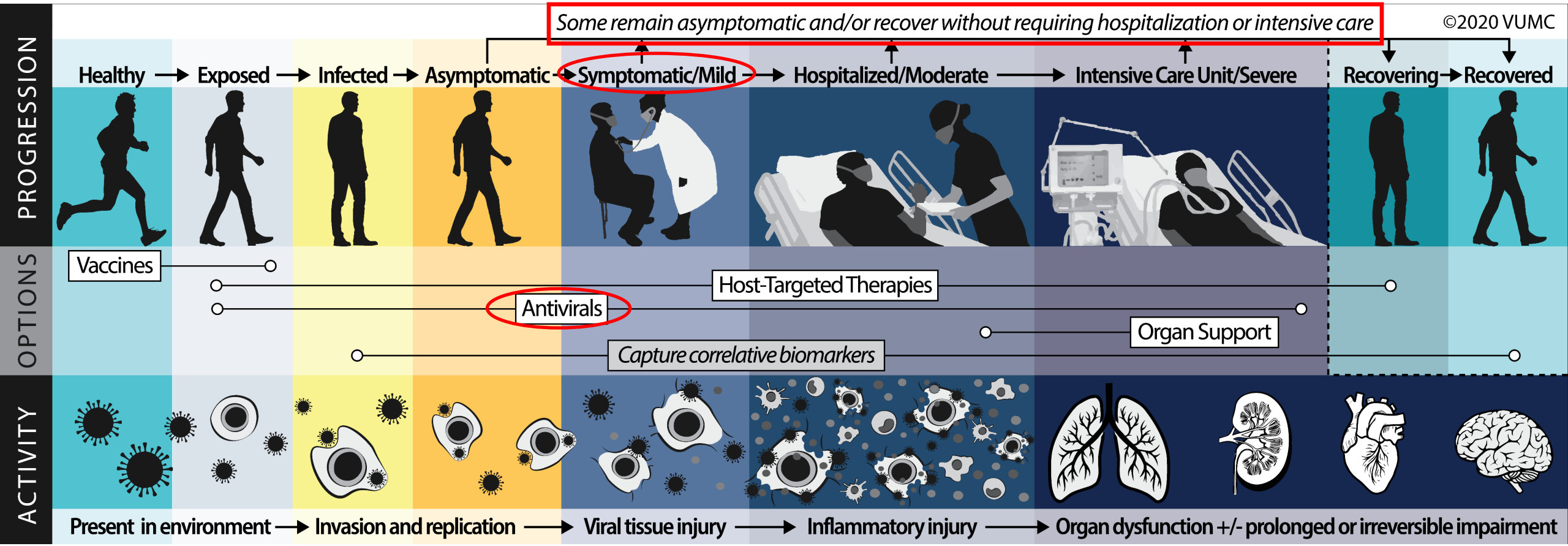
COVID-19 Treatment by monoclonal antibodies

- Confirmed positive SARS-CoV-2 infection
- Mild-moderate COVID-19 disease
    - **NOT** hospitalized due to COVID-19
    - **NOT** requiring new oxygen therapy or increase in baseline O2 flow rate
- Symptom onset ≤ 10 days (ideally <7 days)
- At risk for progression to severe disease

Prophylaxis after COVID-19 exposure

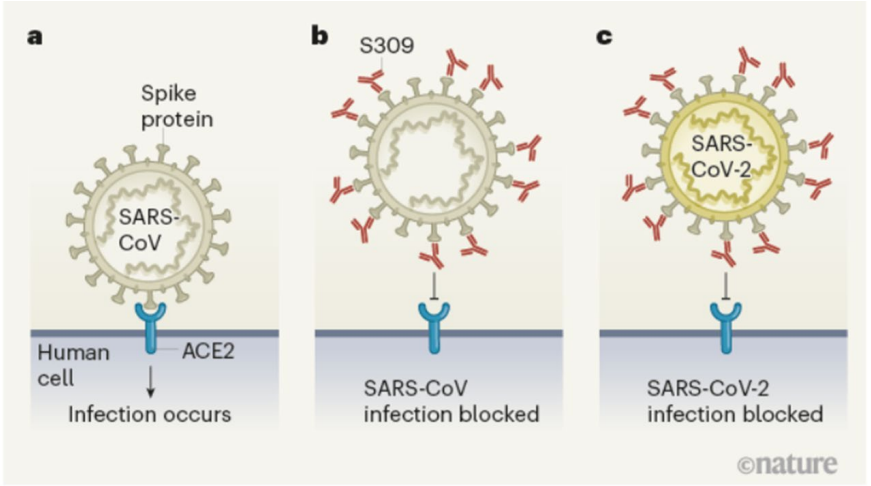
- Individuals with household or facility exposure to SARS-CoV-2 infection
- Possible vaccine augmentation in future

Early Intervention for Mild COVID-19 in Outpatient Setting to Prevent Hospitalization/Death



Neutralizing mAbs for COVID-19 treatment

- Laboratory-made human neutralizing IgG treatment to SARS-CoV-2
  - Originally isolated from B cells of recovered patients
- Binds to viral spike protein to block interaction with ACE2 receptor on host cells
- Combination treatment “cocktails” bind to separate non-overlapping spike protein regions to increase treatment efficacy and prevent escape mutations



Current mAb treatments available:

- Casirivimab/imdevimab (Regeneron)
- Bamlanivimab/etesevimab (Lilly)
- Sotrovimab (GSK/Vir)
- AZD7442 (AstraZeneca)

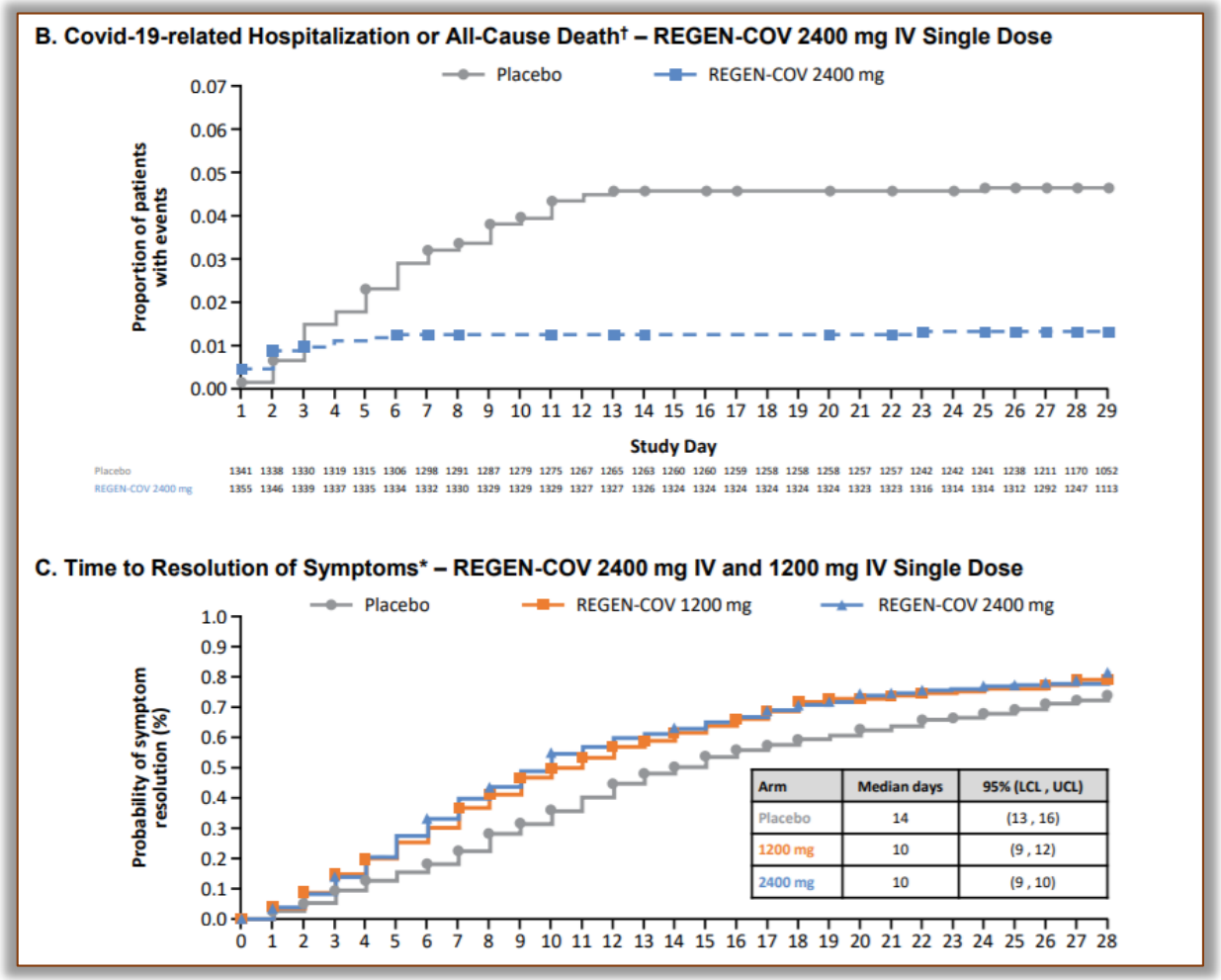
REGEN-COV Antibody Cocktail Clinical Outcomes Study in Covid-19 Outpatients

Study design

- 4,057 outpatients with one or more risk factors for severe disease
- Randomized to placebo or 2 possible doses of REGEN-COV
- Followed for 28 days

Study Results

- Median age 50 years (14% were ≥ 65 years)
- REGEN-COV reduced hospitalization/death vs placebo by **71%** (1.3% vs 4.6%; p<0.001)
- Symptoms resolved **4 days** faster vs placebo (10 vs 14 days; p<0.001)
- Infusion-related reactions rare (<0.3%)
- Study stopped by DSMB for efficacy



Weinreich et al. REGEN-COV Antibody Combination and Outcomes in Outpatients with COVID-19. NEJM, Sept 2021.

JAMA | Original Investigation

June 3, 2021

Effect of Bamlanivimab vs Placebo on Incidence of COVID-19 Among Residents and Staff of Skilled Nursing and Assisted Living Facilities

A Randomized Clinical Trial

Myron S. Cohen, MD; Ajay Nirula, MD, PhD; Mark J. Mulligan, MD; Richard M. Novak, MD; Mary Marovich, MD; Catherine Yen, MD; Alexander Stemer, MD;

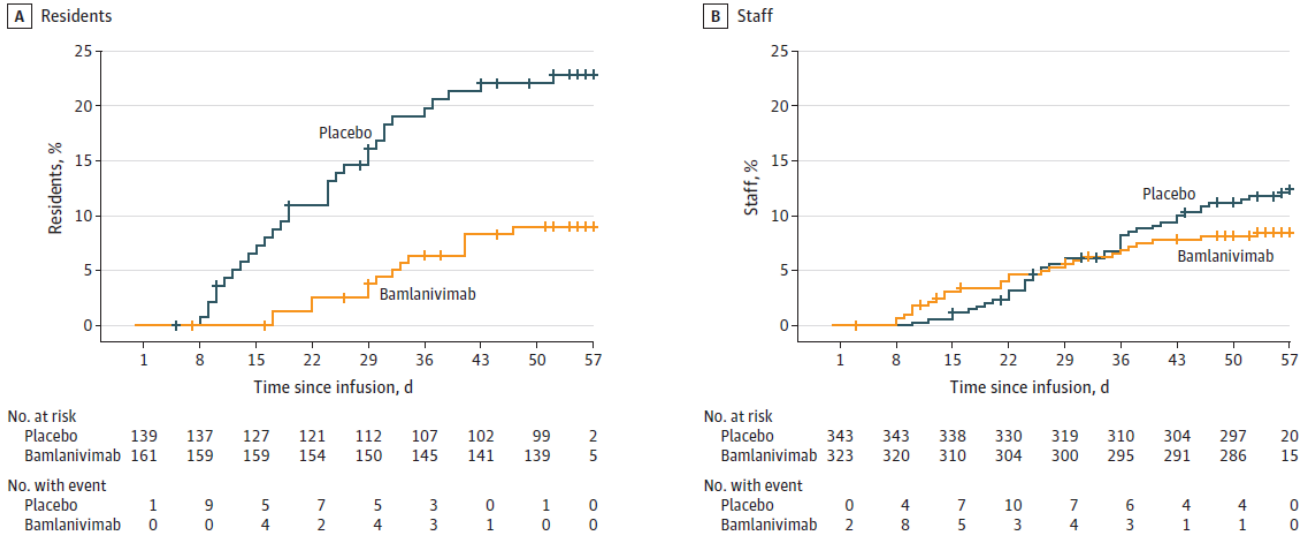
Study design

- 966 SARS-CoV-2 negative residents or staff of SNFs/ALFs with ≥1 positive SARS-CoV-2 infection
- Randomized to placebo or bamlanivimab (IV)
- Followed for 57 days (symptomatic SARS-CoV-2)

Study Results

- Median age: 75 yrs (residents) and 43 yrs (staff)
- Bamlanivimab reduced symptomatic SARS-CoV-2 vs placebo by **57%** (15.2% vs 8.5%; p<0.001)
  - **80%** reduction for residents (p<0.001)
  - **42%** reduction for staff (p=0.06)

Figure 2. Time From Infusion to Development of Mild or Worse COVID-19 With Bamlanivimab vs Placebo Among Resident and Staff Participants



AZD7442 PROVENT Phase III prophylaxis trial met primary endpoint in preventing COVID-19

20 August 2021 07:00 BST

77% reduced risk of developing symptomatic COVID-19

First long-acting antibody combination to prevent COVID-19

Design

- **5172 community dwelling individuals without SARS-CoV-2** (exposure not required for entry)
  - 43% age ≥65 years
  - 75% with co-morbidities
- 2:1 randomization to AZD7442 (***intramuscular***) or placebo for primary prevention
- Followed for 6 months (primary); follow-up to continue for 15 months

Results

- **77%** (95%CI 46-90) reduction in symptomatic SARS-CoV-2 infection
  - 0 severe cases/deaths in AZD7442 group
  - 3 severe cases (2 deaths) in placebo group

- Half-life extension (YTE mutation)—may be viable strategy to augment vaccination

https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-prophylaxis-trial-met-primary-endpoint.html

Available Monoclonal Antibodies

	Use		Formulation	
Product	Treatment	Post-exposure Prophylaxis	IV	SQ
Casirivimab/imdevimab	✓	✓	✓	✓[1]
sotrovimab	✓		✓	
bamlanivimab/etesevimab[2]	✓	✓	✓	

1 - For treatment, IV is preferred but SQ may be used if administering IV would delay treatment
2 - Distribution and use of bamlanivimab/etesevimab was recently restarted

Early and Ongoing Challenges

- Limited availability of mAbs
  - Random allocation system (late 2020)
  - Direct ordering from Federal supply (early 2021)
  - State-based distribution (Sept 2021 – present)
- Initial limited utilization of treatment
- Ongoing equity issues
  - Mostly non-Hispanic white patients with robust access to care
- Frequent shifting of guidance and distribution
- **Lingering uncertainty about benefit and risk – RESOLVED?!**

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Clinical Workflows for Monoclonal Antibody Therapy for COVID-19 in Colorado

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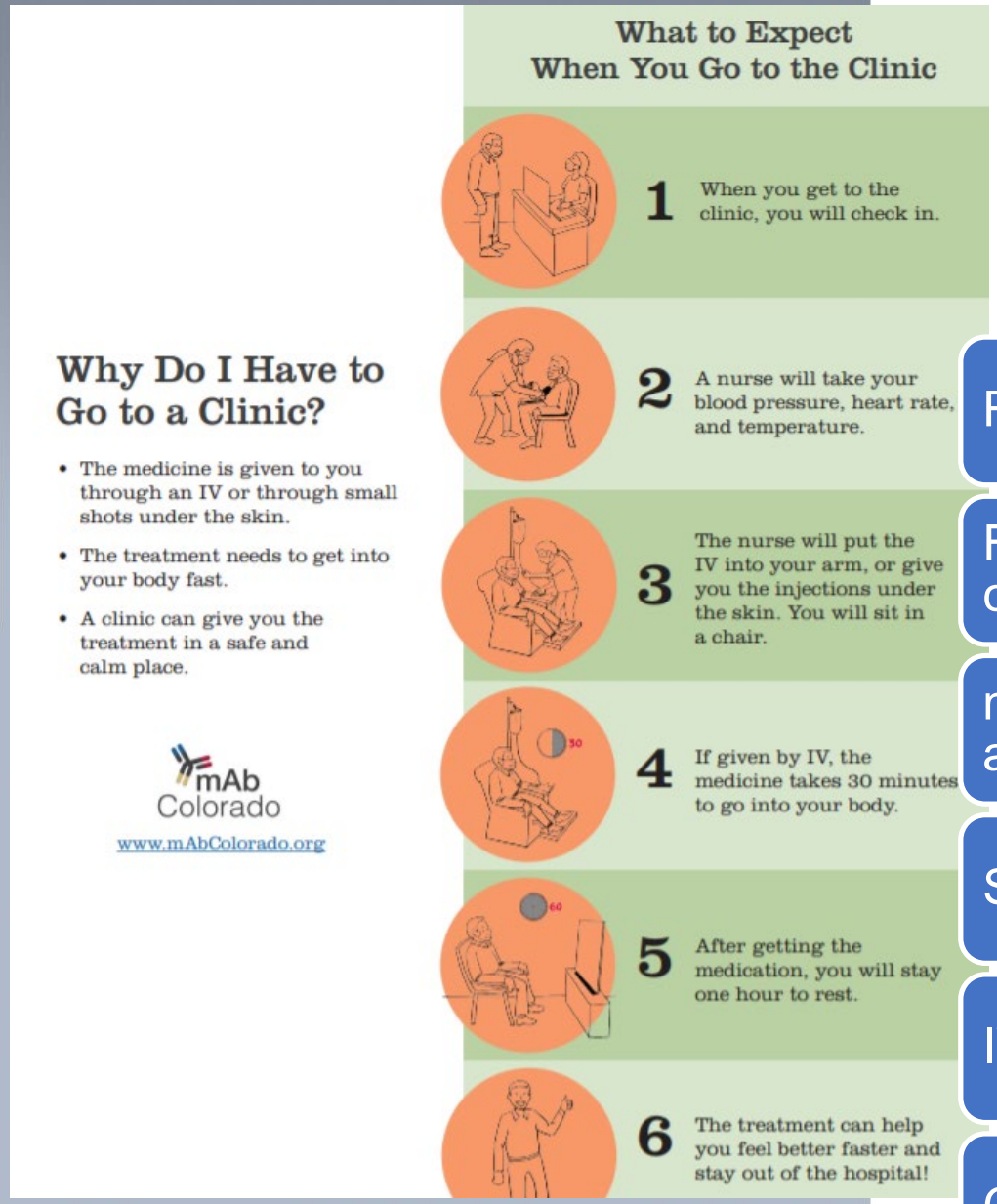
COVID-19 mAbs Summary

- Studies show mAbs reduce risk of hospitalizations and deaths by **70%**
- mAbs decrease symptoms by **four days**
- Adverse events are rare, often within 30 min
- CAS/IMD (REGEN-COV2) can be given as **subcutaneous injection** if IV is not feasible
- mAb therapy can be given **regardless of vaccination status**
- Vaccination can occur 90 days after mAb
- mAbs can be given as **post-exposure prophylaxis**



The Basics to Administer mAb

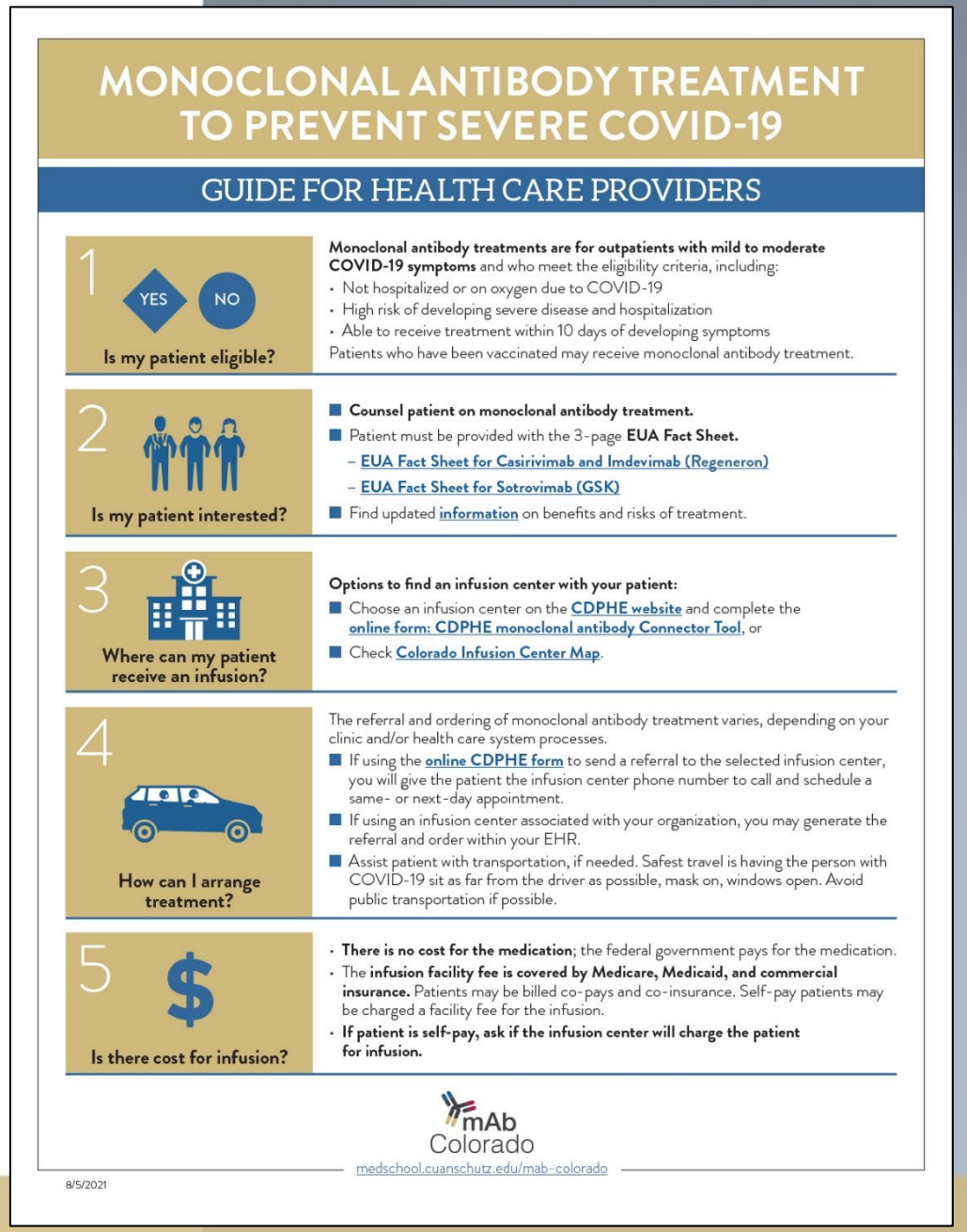
- Read the EUAs for helpful and specific information
- For COVID-19 treatment, IV is preferred for COVID-19 but SQ can be used
- mAb stored in refrigerator, out for 20 minutes prior to administration and must be used within 4 hours
- SQ requires 4 separate injections of 2.5ml
- IV requires 20-30 minutes
- Courtesy – Dr. Lindsey Fish, Denver Health Pena Urgent Care

Current Barriers

- Difficult to navigate mAB Connector Tool/map
- Delayed response from referrals sites, putting patients outside of the treatment window
- Limited referral sites / limited # of practices offering this
- Some sites running out of mAb allocation early in the week and not being able to treat more patients
- Patients being charged substantial facility fees or infusion fees

Clinician Checklist

1. Determine eligibility
2. Discuss treatment with patient and care partners
3. Identify treatment location
4. Refer and order treatment
5. Address cost and access questions



MONOCLONAL ANTIBODY TREATMENT TO PREVENT SEVERE COVID-19

GUIDE FOR HEALTH CARE PROVIDERS

1 YES NO

Is my patient eligible?

Monoclonal antibody treatments are for outpatients with mild to moderate COVID-19 symptoms and who meet the eligibility criteria, including:

- Not hospitalized or on oxygen due to COVID-19
- High risk of developing severe disease and hospitalization
- Able to receive treatment within 10 days of developing symptoms

Patients who have been vaccinated may receive monoclonal antibody treatment.

2

Is my patient interested?

- **Counsel patient on monoclonal antibody treatment.**
- Patient must be provided with the 3-page **EUA Fact Sheet.**
  - EUA Fact Sheet for Casirivimab and Imdevimab (Regeneron)
  - EUA Fact Sheet for Sotrovimab (GSK)
- Find updated information on benefits and risks of treatment.

3

Where can my patient receive an infusion?

Options to find an infusion center with your patient:

- Choose an infusion center on the CDPHE website and complete the online form: CDPHE monoclonal antibody Connector Tool, or
- Check Colorado Infusion Center Map.

4

How can I arrange treatment?

The referral and ordering of monoclonal antibody treatment varies, depending on your clinic and/or health care system processes.

- If using the online CDPHE form to send a referral to the selected infusion center, you will give the patient the infusion center phone number to call and schedule a same- or next-day appointment.
- If using an infusion center associated with your organization, you may generate the referral and order within your EHR.
- Assist patient with transportation, if needed. Safest travel is having the person with COVID-19 sit as far from the driver as possible, mask on, windows open. Avoid public transportation if possible.

5 $

Is there cost for infusion?

- **There is no cost for the medication**; the federal government pays for the medication.
- The **infusion facility fee is covered by Medicare, Medicaid, and commercial insurance.** Patients may be billed co-pays and co-insurance. Self-pay patients may be charged a facility fee for the infusion.
- **If patient is self-pay, ask if the infusion center will charge the patient for infusion.**

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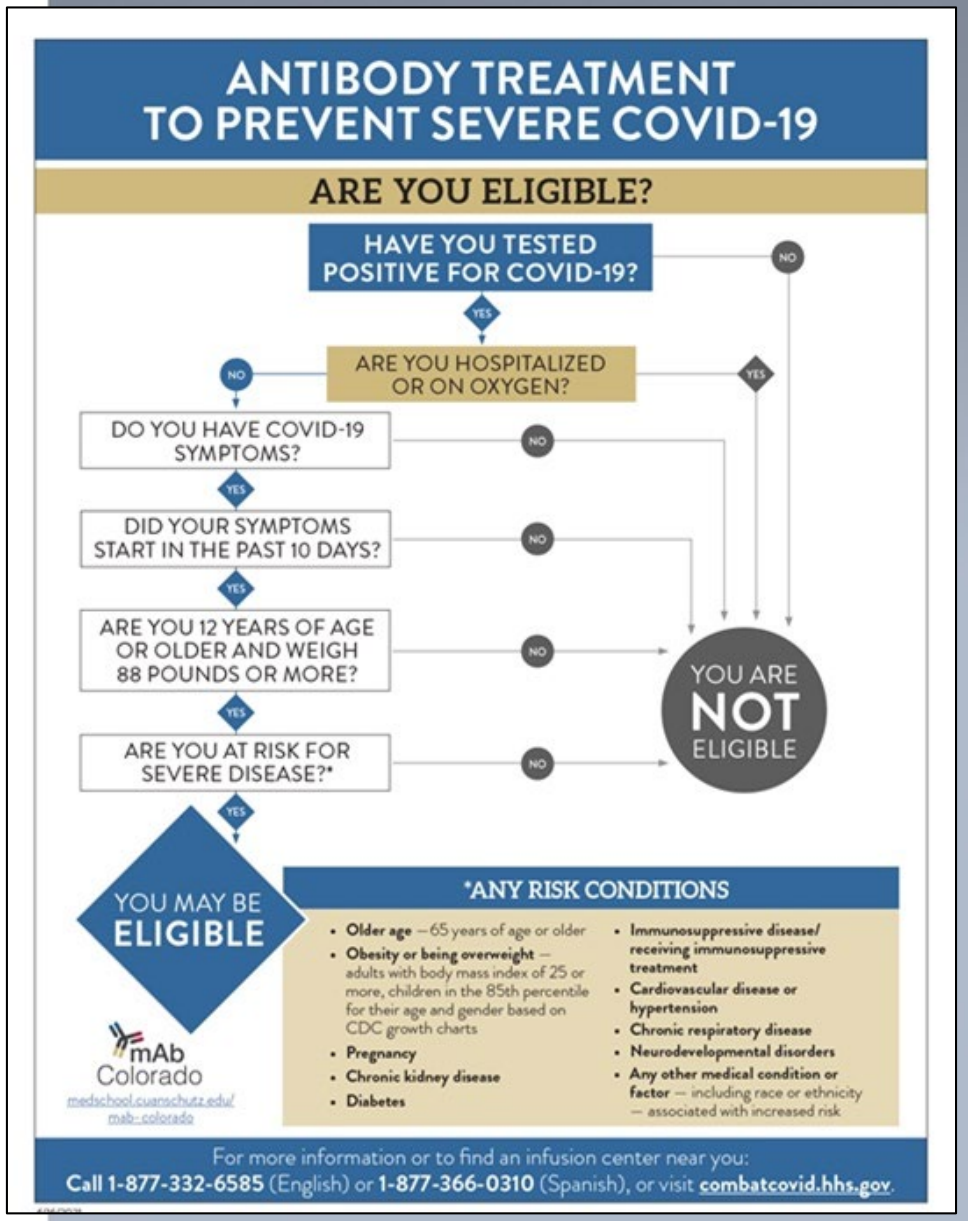
medschool.cuanschutz.edu/mab-colorado

8/5/2021

1. Determine Eligibility for Treatment

- Must be positive and symptomatic for COVID-19
- Not hospitalized
- Must not have (new) oxygen requirement due to COVID-19
- Must be within 10 days of symptom onset
- Must be age of 12 or older and weigh at least 88 lbs
- At high risk for severe COVID-19



ELIGIBILITY: High Risk Conditions

- Older age ≥65 y.o.
- Obesity or overweight (Adults BMI >25 kg/m2 , or if age 12-17, BMI ≥85th percentile)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or treatment
- Cardiovascular disease or hypertension
- Chronic lung diseases
- Sickle cell disease
- Neurodevelopmental disorders or other conditions that confer medical
- Having a medical-related technological dependence
- Other medical conditions or factors (for example, race or ethnicity)

COVID-19 Treatment and Post-exposure prophylaxis:
*Which of my patients are **not** eligible for mAb?*

2. Discuss Treatment with Patients or Care Partners

Example language for patient counseling:

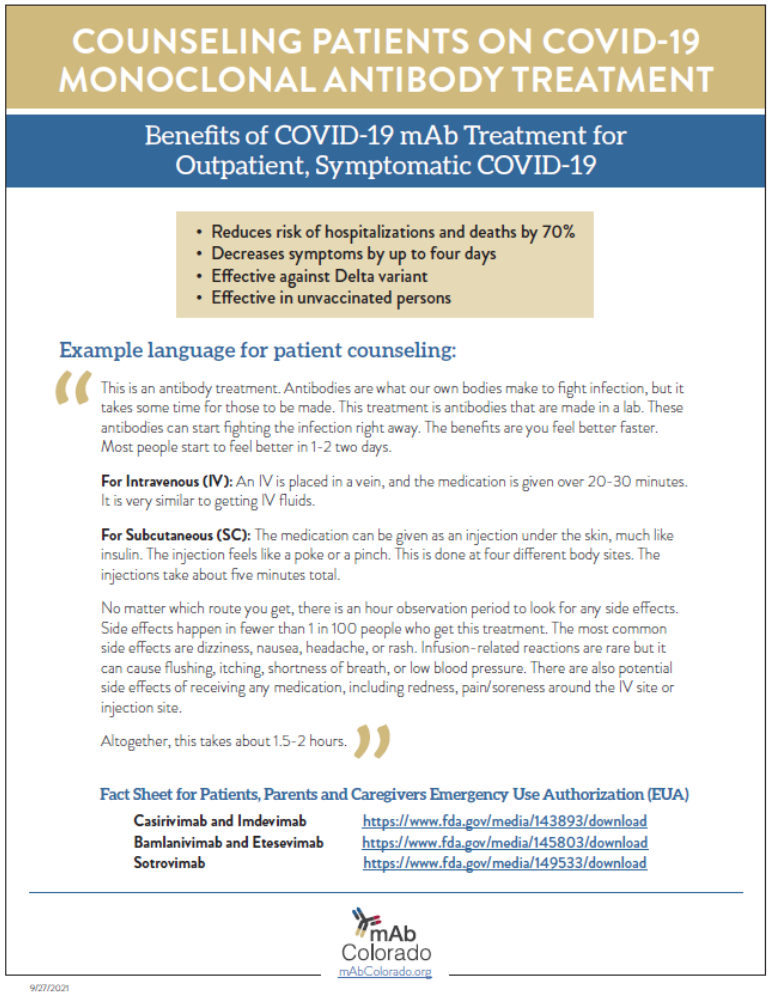
"This is an antibody treatment. Antibodies are what our own bodies make to fight infection, but it takes some time for those to be made. This treatment is antibodies that are made in a lab. These antibodies can start fighting the infection right away. The benefits are you feel better faster. Most people start to feel better in 1-2 two days.

For Intravenous (IV): An IV is placed in a vein, and the medication is given over 20-30 minutes. It is very similar to getting IV fluids.

For Subcutaneous (SC): The medication can be given as an injection under the skin, much like insulin. The injection feels like a poke or a pinch. This is done at four different body sites. The injections take about five minutes total.

No matter which route you get, there is an hour observation period to look for any side effects. Side effects happen in fewer than 1 in 100 people who get this treatment. The most common side effects are dizziness, nausea, headache, or rash. Infusion-related reactions are rare but it can cause flushing, itching, shortness of breath, or low blood pressure. There are also potential side effects of receiving any medication, including redness, pain/soreness around the IV site or injection site.

Altogether, this takes about 1.5-2 hours."



COUNSELING PATIENTS ON COVID-19 MONOCLONAL ANTIBODY TREATMENT

Benefits of COVID-19 mAb Treatment for Outpatient, Symptomatic COVID-19

- Reduces risk of hospitalizations and deaths by 70%
- Decreases symptoms by up to four days
- Effective against Delta variant
- Effective in unvaccinated persons

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Fact Sheet for Patients, Parents and Caregivers Emergency Use Authorization (EUA)

Casirivimab and Imdevimab	https://www.fda.gov/media/143893/download
Bamlanivimab and Etesevimab	https://www.fda.gov/media/145803/download
Sotrovimab	https://www.fda.gov/media/149533/download

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9/27/2021

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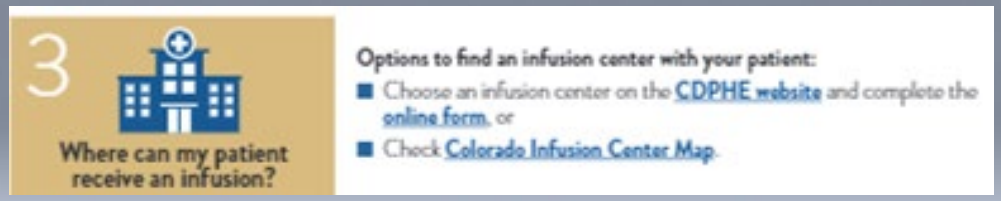
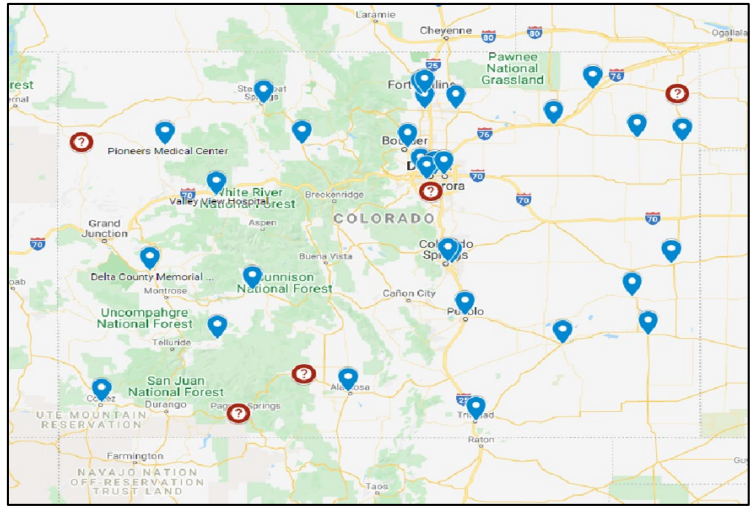
3. Find Infusion Sites



CDPHE - https://covid19.colorado.gov/for-coloradans/covid-19-treatments

- New in November: CDPHE Mobile buses for mAb treatment appointments
- Map includes sites registered with CDPHE
  - Contact local/ county public health department for administration sites not registered with the state, such as home health agencies, long-term care pharmacies
- Register to become an infusion site through CDPHE
  - Submit requests by 11:59 pm each Weds for the following week



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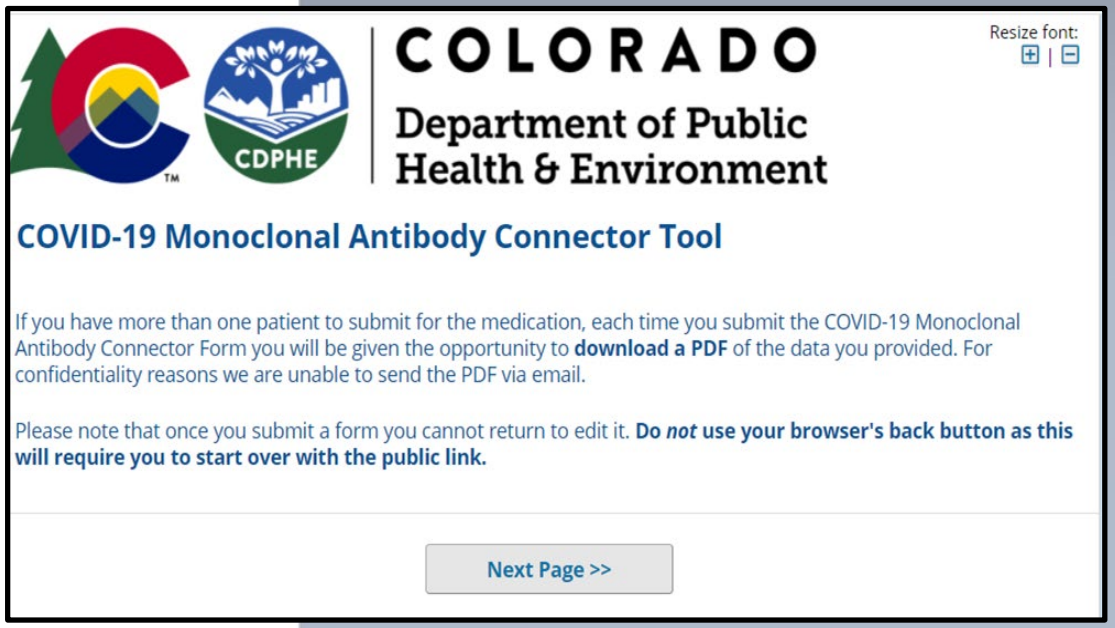
4. Refer and Order Treatment

Options:

- Prescription to patient
- Submit referral through CDPHE mAb Connector tool
- Direct order to infusion center within same health system

➢ No PCP? Use UC Health Virtual Health Center

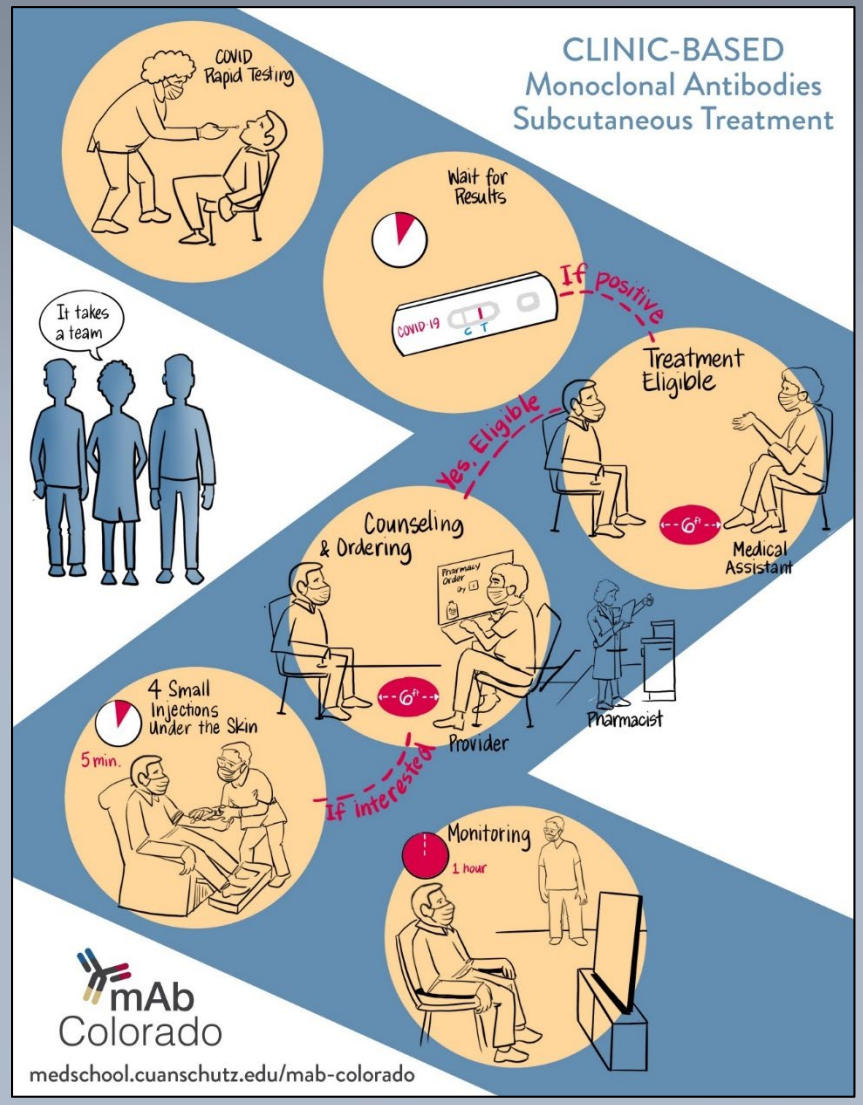


CDPHE Monoclonal Antibody Connector Tool

https://covid19.colorado.gov/for-coloradans/covid-19-treatments

5. Cost and Access Issues

- Federal government purchases doses of REGEN-COV and Bam/Ete
- No out of pocket cost for Medicare patients
- Deductibles apply; site charges vary (~$500-800)
- Costs for uninsured patients - may be waived or discounted
- Patients may face transportation issues
  - Some clinics may be able to offer subcutaneous
  - Home health administration may be available
  - CDPHE mobile units (buses)



Building new protocols

Place order (know the eligibility criteria)

Obtain consent (be able to describe the treatment)

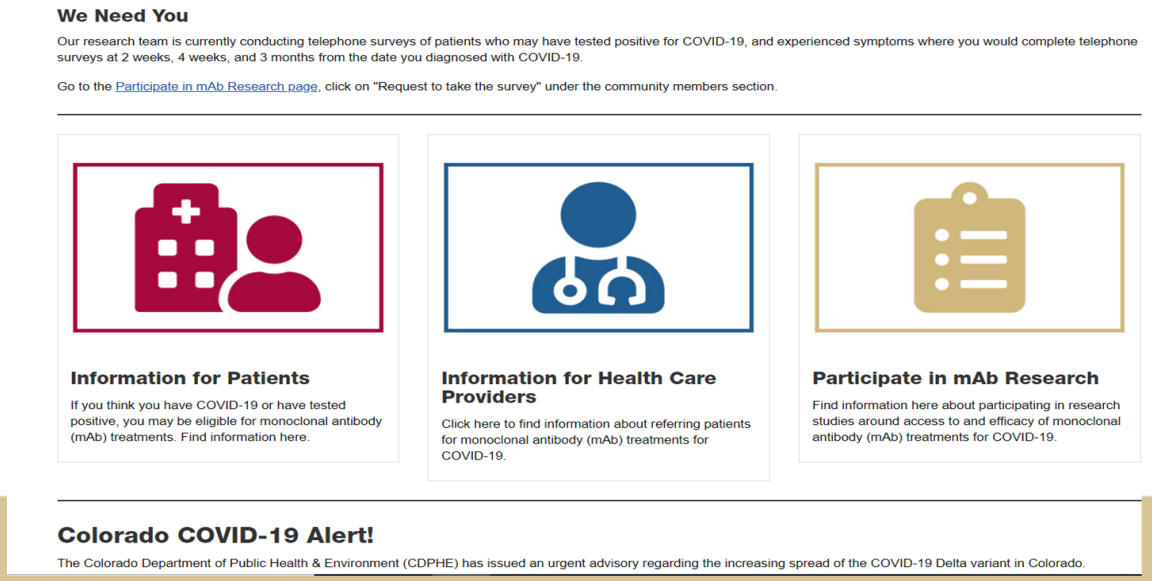
Administer infusion

Monitor for anaphylaxis

Access to infusion

Resources

- **CDPHE -** https://covid19.colorado.gov/for-coloradans/covid-19-treatments
- **UCHealth Virtual Health Center** (303-752-7732)
- **NIH treatment guidelines** https://www.covid19treatmentguidelines.nih.gov/
- **HHS Playbook** https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Documents/USG-COVID19-Tx-Playbook.pdf



We Need You

Our research team is currently conducting telephone surveys of patients who may have tested positive for COVID-19, and experienced symptoms where you would complete telephone surveys at 2 weeks, 4 weeks, and 3 months from the date you diagnosed with COVID-19.

Go to the Participate in mAb Research page, click on "Request to take the survey" under the community members section.

Information for Patients

If you think you have COVID-19 or have tested positive, you may be eligible for monoclonal antibody (mAb) treatments. Find information here.

Information for Health Care Providers

Click here to find information about referring patients for monoclonal antibody (mAb) treatments for COVID-19.

Participate in mAb Research

Find information here about participating in research studies around access to and efficacy of monoclonal antibody (mAb) treatments for COVID-19.

Colorado COVID-19 Alert!

The Colorado Department of Public Health & Environment (CDPHE) has issued an urgent advisory regarding the increasing spread of the COVID-19 Delta variant in Colorado.

mAb Colorado

Contact:

mAbColorado@cuanschutz.edu

Colorado website:

www.mAbColorado.org

COVID-19 Monoclonal Antibody Treatment Take Home Points

mAbs are available thru EUA for outpatient COVID-19 treatment (none are fully FDA-approved yet)

Early treatment is likely better

Proactively identify local treatment options

Use of mAb for Post-Exposure Prophylaxis, after exposure to SARS-CoV2

FDA authorizes REGEN-COV monoclonal antibody therapy for post-exposure prophylaxis (prevention) for COVID-19

Prophylaxis with REGEN-COV is not a substitute for vaccination against COVID-19

July 30, 2021

FDA authorizes bamlanivimab and etesevimab monoclonal antibody therapy for post-exposure prophylaxis (prevention) for COVID-19

Post-exposure prophylaxis with bamlanivimab and etesevimab, administered together, is not a substitute for vaccination against COVID-19

September 16, 2021

Aug 17, 2021: NIH guidance on PEP
https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-casirivimab-plus-imdevimab-as-pep/

NIH Treatment Guidelines

Updated September 24, 2021

Figure 1. Therapeutic Management of NonHospitalized Adults With COVID-19

All outpatients with COVID-19 who enter the health care system should have in-person or telehealth follow-up visits. Symptomatic treatments, including hydration, antipyretics, analgesics, and antitussives, can be initiated as needed.

Patients should be counseled about symptoms that warrant re-evaluation by a health care provider (e.g., new onset dyspnea, worsening dyspnea [particularly dyspnea that occurs while the patient is resting or that interferes with daily activities], mental status changes). Home resources should be assessed before patients are discharged from a clinic, urgent care center, ED, or hospital; outpatients should have access to housing, proper nutrition, a caregiver, and a device that is suitable for telehealth. If patients are discharged while they are still receiving oxygen supplementation, they should receive oximetry monitoring and close follow-up soon after discharge.

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Not Requiring Hospitalization or Supplemental Oxygen, As Determined by a Health Care Provider in ED or an In-Person or Telehealth Visit	Anti-SARS-CoV-2 monoclonal antibody products are recommended for outpatients with mild to moderate COVID-19 who are at high risk of disease progression, as defined by the EUA criteria (treatments are listed in alphabetical order):[a] • **Bamlanivimab plus etesevimab**; *or* • **Casirivimab plus imdevimab**; *or* • **Sotrovimab** The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in the absence of another indication **(AIII)**.[b]

https://www.covid19treatmentguidelines.nih.gov/

The COVID-19 Treatment Guidelines Panel's Statement on the Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS-CoV-2 Infection When There Are Logistical Constraints

Last Updated: September 3, 2021

The COVID-19 Treatment Guidelines Panel (the Panel) recommends using anti-SARS-CoV-2 monoclonal antibodies for the treatment of mild to moderate COVID-19 and for post-exposure prophylaxis (PEP) of SARS-CoV-2 infection in individuals who are at high risk for progression to severe COVID-19, as outlined in the Food and Drug Administration Emergency Use Authorizations (EUAs). See the individual EUAs for details.

While there are currently no shortages of these monoclonal antibodies, logistical constraints (e.g., limited space, not enough staff who can administer therapy) can make it difficult to administer these agents to all eligible patients. In situations where it is necessary to triage eligible patients, the Panel suggests:

- Prioritizing the treatment of COVID-19 over PEP of SARS-CoV-2 infection.
- Prioritizing the following groups over vaccinated individuals who are expected to have mounted an adequate immune response:
  - Unvaccinated or incompletely vaccinated individuals who are at high risk of progressing to severe COVID-19
  - Vaccinated individuals who are not expected to mount an adequate immune response (e.g., immunocompromised individuals).

Providers should use their clinical judgment when prioritizing treatment or PEP in a specific situation. When there are no logistical constraints for administering therapy, these considerations **should not** limit the provision of anti-SARS-CoV-2 monoclonal antibodies.