CDC/IDSA Clinician Call

Nov. 12, 2022

Welcome & Introductions

Dana Wollins, DrPH, MGC
Vice President
Clinical Affairs & Practice Guidelines
Infectious Diseases Society of America

- 94th in a series of calls, initiated in 2020 as a forum for information sharing among frontline clinicians caring for patients with COVID-19.
- The views and opinions expressed here are those of the presenters and do not necessarily reflect the official policy or position of the CDC or IDSA. Involvement of CDC and IDSA should not be viewed as endorsement of any entity or individual involved.
- This webinar is being recorded and can be found online at www.idsociety.org/cliniciancalls.

CDC/IDSA Clinician Call:

SARS-CoV-2 Subvariants & the Future of Monoclonal Antibodies; Plus Monkeypox Update

1. Opening Remarks

Carlos del Rio, MD, FIDSA
IDSA President
Executive Associate Dean, Emory School of Medicine & Grady Health System
Distinguished Professor, Department of Medicine, Division of Infectious Diseases,
Emory University School of Medicine

2. Monkeypox Treatment Update

Jennifer R. Cope, MD, MPH
Captain, U.S. Public Health Service
Co-Lead, Clinical Escalations Team, Clinical Task Force
2022 Multinational Monkeypox Response
U.S. Centers for Disease Control & Prevention

Christina L. Hutson, PhD, MS
Laboratory and Testing Task Force Lead
2022 Multinational Monkeypox Response
Chief, Poxvirus and Rabies Branch
U.S. Centers for Disease Control & Prevention

3. SARS-CoV-2 Subvariants & the Future of Monoclonal Antibodies

Current SARS-CoV-2 Lineages & Trends

Natalie J. Thornburg, PhD
Respiratory Virus Immunology Team Lead
Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
U.S. Centers for Disease Control and Prevention

Impact of SARS-CoV-2 Subvariants on Therapeutic Effectiveness

Update on Anti-SARS CoV-2 Monoclonal Antibodies

Rajesh T. Gandhi, MD, FIDSA
Director, HIV Clinical Services and Education,
Massachusetts General Hospital
Co-Director, Harvard Center for AIDS Research
Professor of Medicine, Harvard Medical School

Impact of Subvariant Evolution on COVID-19 Outpatient Therapeutic Decision-Making

William A. Werbel, MD
Assistant Professor of Medicine, Division of Infectious Diseases, Johns Hopkins University

Antibody Susceptibility Testing

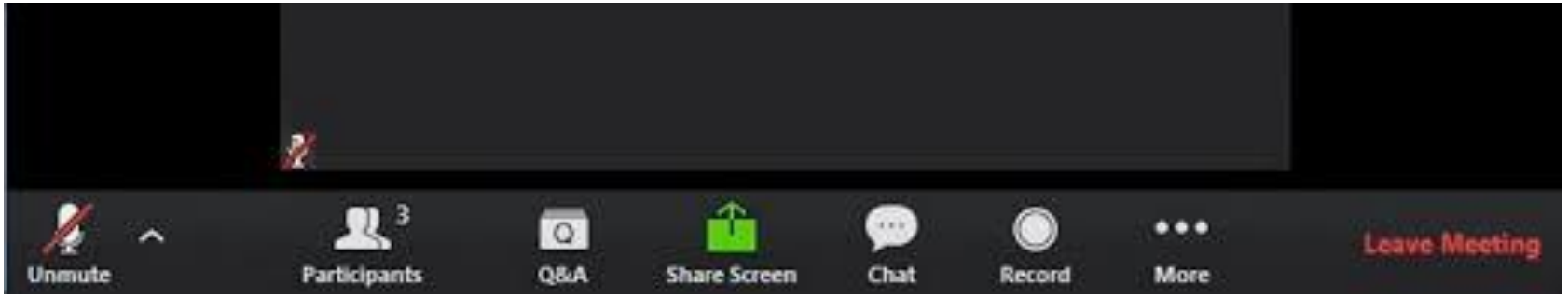
Robert W. Shafer, MD
Professor of Medicine
Division of Infectious Diseases
Stanford University

COVID-19 Therapeutics Update

Meghan E. Pennini, PhD
Therapeutics Director
Administration for Strategic Preparedness and Response
U.S. Department of Health & Human Services

Question?
Use the “Q&A” Button

Comment?
Use the “Chat” Button



Opening Remarks

Carlos Del Rio, MD, FIDSA

Flu, RSV & COVID
A “Tripledemic” in our Path this Winter

Increased Respiratory Virus Activity, Especially Among Children, Early in the 2022-2023 Fall and Winter

Print

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH ADVISORY

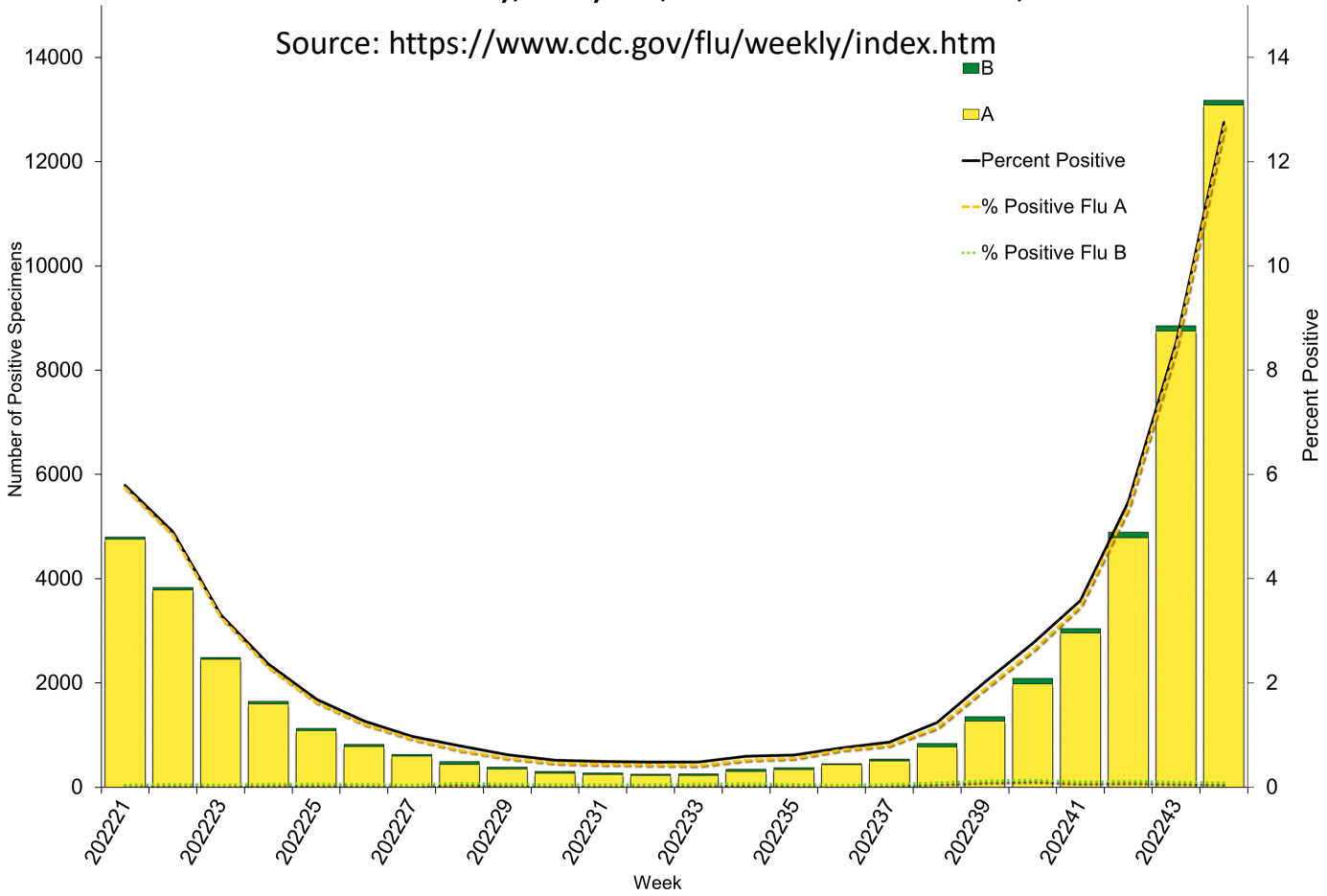
Distributed via the CDC Health Alert Network
November 04, 2022, 3:30 PM ET
CDCHAN-00479

Summary
The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory about early, elevated respiratory disease incidence caused by multiple viruses occurring especially among children and placing strain on healthcare systems. Co-circulation of respiratory syncytial virus (RSV), influenza viruses, SARS-CoV-2, and others could place stress on healthcare systems this fall and winter. This early increase in disease incidence highlights the importance of optimizing respiratory virus prevention and treatment measures, including prompt vaccination and antiviral treatment, as outlined below.

Background
Many respiratory viruses with similar clinical presentations circulate year-round in the United States and at higher levels in

Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, May 22, 2022 – November 5, 2022

Source: https://www.cdc.gov/flu/weekly/index.htm

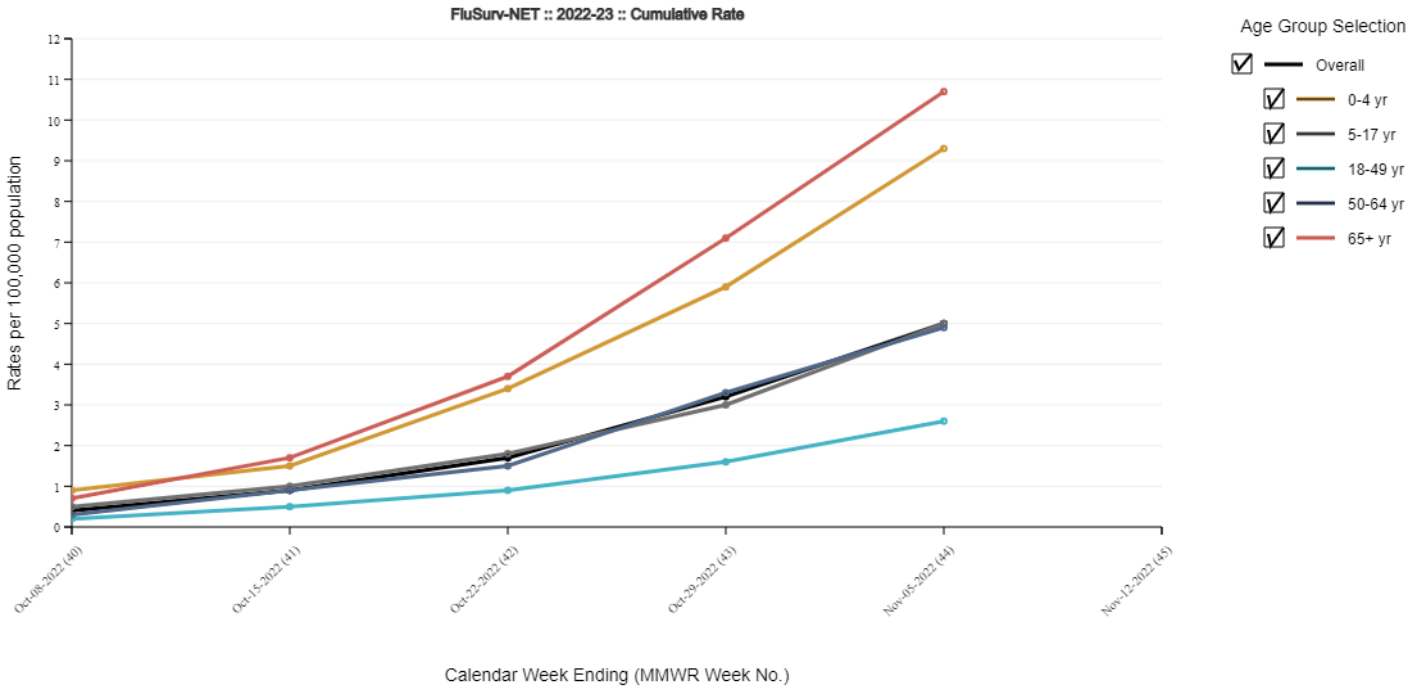


FLUVIEW interactive

CDC

Laboratory-Confirmed Influenza Associations, FluSurv-NET, 2022-23

Preliminary cumulative rates as of Nov 05, 2022



Source: https://www.cdc.gov/flu/weekly/index.htm

Key Points:

- Influenza activity continues to increase.
  - Regions 4 (Southeast) and 6 (South-Central) are reporting the highest levels of flu activity, followed by regions 3 (Mid-Atlantic) and 9 (south-central West Coast).
- Most cases are Influenza A (H3N2)
- Three influenza-associated pediatric deaths were reported this week.
- CDC estimates that, so far this season, there have been at least 2.8 million illnesses, 23,000 hospitalizations, and 1,300 deaths from flu.
- The cumulative hospitalization rate in the FluSurv-NET system is higher than the rate observed in week 44 during every previous season since 2010-2011.

Source: https://www.cdc.gov/flu/weekly/index.htm

CDC recommends that everyone ages 6 months and older get a flu vaccine annually

Flu Vaccine Doses Distributed:

- As of October 22, 2022, 137.0 million doses of flu vaccine have been distributed in the U.S.
- Vaccine manufacturers have projected that they will supply the U.S. with 173.5 to 183.5 million doses of influenza vaccines for the 2022-2023 season.

Flu Vaccination Coverage:

- *Children = 24.8%.* Similar to last year at this time (25.2%) and lower than in 2020 (32.1%).
  - Coverage among states and DC ranges from 12.6% to 35.7%
- *Pregnant persons = 21%.* 5.4 percentage points lower compared to same time last year (21.0% vs 26.4%) and 17 percentage points lower than in 2020 (21.0% vs 38.0%).
- *Persons > 65 years = 54.0%.* Lower than at the same time in 2021 (57.8%) and 2020 (56.2%).

COCA Call

CDC Clinician Outreach and Communication Activity

2022-2023 Seasonal Influenza Testing and Treatment During the COVID-19 Pandemic

When:
Tuesday, November 15, 2022,
2:00 PM – 3:00 PM ET

Webinar Link:
https://www.zoomgov.com/j/1605388275
Webinar ID: 160 538 8275

Passcode: 620862
Telephone:
US: +1 669 254 5252 or +1 646 828 7666 or +1 669 216 1590 or +1 551 285 1373

To learn more, go to www.emergency.cdc.gov/COCA

Monkeypox Treatment Update

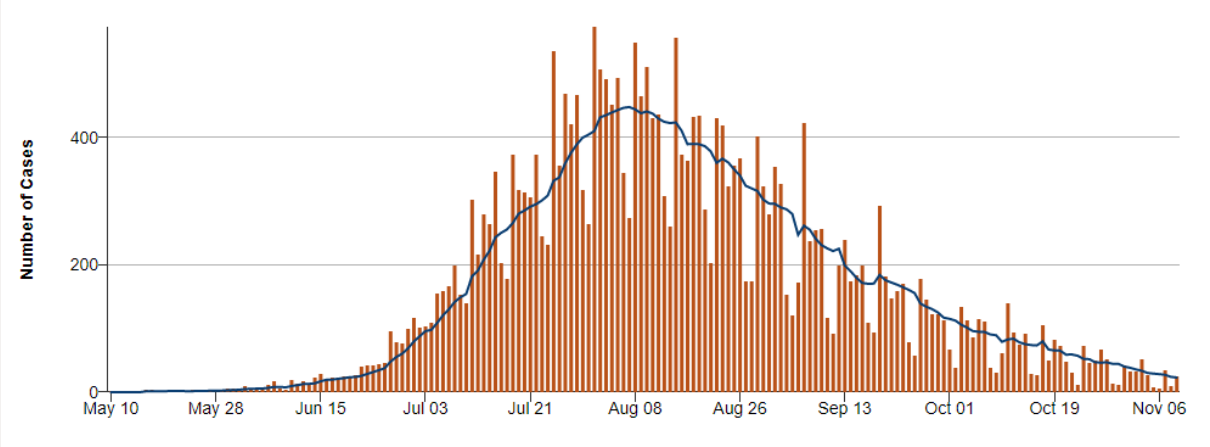
Jennifer R. Cope, MD, MPH
Christina L. Hutson, PhD, MS

MONKEYPOX

CDC Monkeypox Update
CDC/IDSA Clinician Call
November 12, 2022

MONKEYPOX

Daily Monkeypox Cases Reported and 7 Day Daily Average
(as of 11/9/2022)



U.S. Monkeypox Case Trends Reported to CDC | Monkeypox | Poxvirus | CDC

MONKEYPOX

CDC's Monkeypox Clinical Consultations Service – What We Do

Clinical consult service is staffed by CDC clinicians to respond to physicians/local public health inquiries on unusual/severe cases of monkeypox.

We provide the following:

1. **Knowledge sharing** with treatment teams of our understanding of Monkeypox
2. Facilitation of **monkeypox treatments** from the Strategic National Stockpile
3. Feedback to CDC response leadership on **emerging clinical phenotypes**

In October 2022, the Clinical Consultations Team conducted consultations for 66 patients – from 23 states + DC

Recent MMWR on Severe Monkeypox Cases

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022

Weekly / November 4, 2022 / 71(44);1412–1417

On October 26, 2022, this report was posted online as an MMWR *Early Release.*

Maureen J. Miller, MD[1,*]; Shama Cash-Goldwasser, MD[1,2,3,*]; Grace E. Marx, MD[1]; Caroline A. Schrodt, MD[1]; Anne Kimball, MD[1]; Kia Padgett, MPH[1]; Rebecca S. Noe, MPH[1]; David W. McCormick, MD[1,2]; Joshua M. Wong, MD[1,2]; Sarah M. Labuda, MD[1]; Brian F. Borah, MD[1,2,4]; Isaac Zulu, MD[1]; Amimah Asif, MBBS[1]; Gurpreet Kaur, MD[1,2]; Janet M. McNicholl, MD[1]; Athena Kourtis, MD[1]; Andrew Tadros, MD, PhD[1]; Sarah Reagan-Steiner, MD[1]; Jana M. Ritter, DVM[1]; Yon Yu, PharmD[1]; Patricia Yu, MPH[1]; Rachel Clinton, MS[1]; Corrine Parker, PharmD[1]; Eleanor S. Click, MD, PhD[1,2]; Johanna S. Salzer, DVM[1]; Andrea M. McCollum, PhD[1]; Brett Petersen, MD[1]; Faisal S. Minhaj, PharmD[1,2]; Ericka Brown, MD[5]; Michael P. Fischer, MD[6]; Robert L. Atmar, MD[7]; Andrew R. DiNardo, MD[7]; Ya Xu, MD, PhD[7]; Cameron Brown, PhD[7]; Jerry Clay Goodman, MD[7]; Ashley Holloman, MD[7]; Julia Gallardo, MD[7]; Hanna Siatecka, MD[7]; Georgia Huffman, MD[7]; John Powell, MD[7]; Philip Alapat, MD[7]; Pralay Sarkar, MD[7]; Nicola A. Hanania, MD[7]; Or Bruck, MD[7]; Steven D. Brass, MD[7,8]; Aneesh Mehta, MD[9]; Alexandra W. Dretler, MD[10]; Amanda Feldpausch, DVM[11]; Jessica Pavlick, DrPH[11]; Hillary Spencer, MD[2,12]; Isaac Ghinai, MBBS[12]; Stephanie R. Black, MD[12,13]; Laura N. Hernandez-Guarin, MD[13]; Sarah Y. Won, MD[13]; Shivanjali Shankaran, MD[13]; Andrew T. Simms, MD[13]; Jemma Alarcón, MD[2,14]; Jesse G. O'Shea, MD[1]; John T. Brooks, MD[1]; Jennifer McQuiston, DVM[1]; Margaret A. Honein, PhD[1]; Siobhán M. O'Connor, MD[1]; Kevin Chatham-Stephens, MD[1]; Kevin O'Laughlin, MD[1]; Agam K. Rao, MD[1]; Elliot Raizes, MD[1]; Jeremy A. W. Gold, MD[1,*]; Sapna Bamrah Morris, MD[1,*]; CDC Severe Monkeypox Investigations Team (VIEW AUTHOR AFFILIATIONS)

Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022 | MMWR (cdc.gov)

Characteristics Of Hospitalized Patients With Severe Manifestations of Monkeypox* (N = 57) For Whom CDC Provided Clinical Consultation — United States, August 10–October 10, 2022

Characteristic	No. (%)
Median age, yrs (range)	34 (20–61)
Sex	
Male	54 (94.7)
Race and ethnicity	
Black or African American, non-Hispanic	39 (68.4)
White, non-Hispanic	8 (14.0)
Hispanic or Latino	8 (14.0)
Asian, non-Hispanic	1 (1.8)
Multiple races, non-Hispanic	1 (1.8)
Experiencing homelessness†	13 (22.8)
Any immunocompromising condition§	51 (89.5)
HIV infection	47 (82.5)
History of solid organ transplantation	3 (5.3)
Hematologic malignancy (current chemotherapy)	2 (3.5)
Pregnant	3 (5.3)

*See HAN Archive - 00475 | Health Alert Network (HAN) (cdc.gov) for listing of severe manifestations

Laboratory and Treatment Characteristics of Hospitalized Patients With HIV Infection and Severe Monkeypox for Whom CDC Provided Clinical Consultation (N = 47) — United States, August 10–October 10, 2022

Characteristic (no. with information available)	No. (%)
HIV CD4, cells/mm^3 (43)	
<50	31 (72.1)
50–200	9 (20.9)
>200	3 (7.0)
HIV Treatment (47)	
On ART at the time of monkeypox diagnosis	4 (8.5)

Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022 | MMWR (cdc.gov)

Characteristics of Hospitalized Patients with Severe Manifestations of Monkeypox (N = 57) for Whom CDC Provided Clinical Consultation — United States, August 10–October 10, 2022

Clinical manifestation[¶]	
Dermatologic	57 (100.0)
Mucosal**	39 (68.4)
Pulmonary	12 (21.1)
Ocular	12 (21.1)
Deep tissue (muscle or bone)	5 (8.8)
Neurologic	4 (7.0)
Monkeypox-directed therapy[††]	
Tecovirimat (oral)	53 (93.0)
Tecovirimat (intravenous)	37 (64.9)
VIGIV	29 (50.9)
Cidofovir††	13 (22.8)
Received ICU-level care	17 (29.8)
STI coinfection[§§]	16 (28.1)

** Mucosal involvement might include oral, urethral, rectal, vaginal, or other lesions.

†† Patients could receive more than one treatment. All patients who received VIGIV or cidofovir also received tecovirimat.

§ § STI coinfection included concurrent diagnosis of syphilis, gonorrhea, chlamydia, herpes simplex virus type 2, or shigellosis

Outcomes among the 57 Patients

- Twelve (21%) died:
  - **5 deaths**, monkeypox was a **cause of death** or contributing factor,
  - **6 deaths** remain **under investigation** to determine whether monkeypox was a causal or contributing factor,
  - **1 death**, monkeypox was **not a cause** or contributing factor.

Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022 | MMWR (cdc.gov)

Clinical Consultations Service – Emerging Phenotypes

The Clinical Consultations Service has observed different phenotypes in terminal cases

1. **Fulminant, rapid progression**

   Characterized by death within <4 weeks of cumulative therapy. Have diffuse, whole-body lesions. Terminal events characterized by shock/profound inflammation or gastrointestinal hemorrhage.

2. **Prolonged, progressive course**

   Characterized by death with >4 weeks of therapy. Generally, have persistent, necrotic lesions that do not resolve vs progress slightly. Underwent sequential therapy w/ PO tecovirimat → IV tecovirimat → vaccinia immunoglobulin + IV tecovirimat. Terminal events characterized by comfort care vs septic shock.
   Median time of Monkeypox onset to death = ~64 days.

3. **Incidental cases**

   Deaths that can occur after many viral illness (e.g., influenza), need to distinguish from background rates.

Brincidofovir (also known as CMX001 or Tembexa) is now available

- Prodrug of cidofovir that is approved by FDA for the treatment of human smallpox disease in adult and pediatric patients, including neonates (no data on effectiveness in human Monkeypox infection)
- Should not be used simultaneously with cidofovir
- Made available from the SNS for treatment of Monkeypox to clinicians who request and obtain an FDA-authorized single-patient emergency use IND (e-IND)

Treatment Information for Healthcare Professionals | Monkeypox | Poxvirus | CDC

FDA's review criteria for brincidofovir e-IND requests

- Patients with positive test results for human monkeypox viral testing who:
  - Have severe disease OR are at high risk for progression to severe disease
  - AND meet either of the following:
    - Experience clinically significant disease progression while receiving tecovirimat or who develop recrudescence (initial improvement followed by worsening) of disease after an initial period of improvement on tecovirimat, *OR*
    - Are otherwise ineligible or have a contraindication for oral or intravenous tecovirimat

Treatment Information for Healthcare Professionals | Monkeypox | Poxvirus | CDC

Single-patient emergency use IND (EIND) request for brincidofovir to treat patients with human monkeypox disease

Kirk Chan-Tak, MD
U.S. Food and Drug Administration

https://societycentral.zoom.us/rec/share/lwGP3XMUCXcF4bxqVrBWz2EeO2M9lLSmNgGng3-2RukWUUML2t2gKoNsjkDU7_jV.FRGPMimWRP_NtzAJ?startTime=1668026706000

Passcode: pFvdP4%^

MONKEYPOX

CDC Monkeypox Clinical Consultation Service

Call CDC Emergency Operations Center at 770.488.7100

1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348   www.cdc.gov

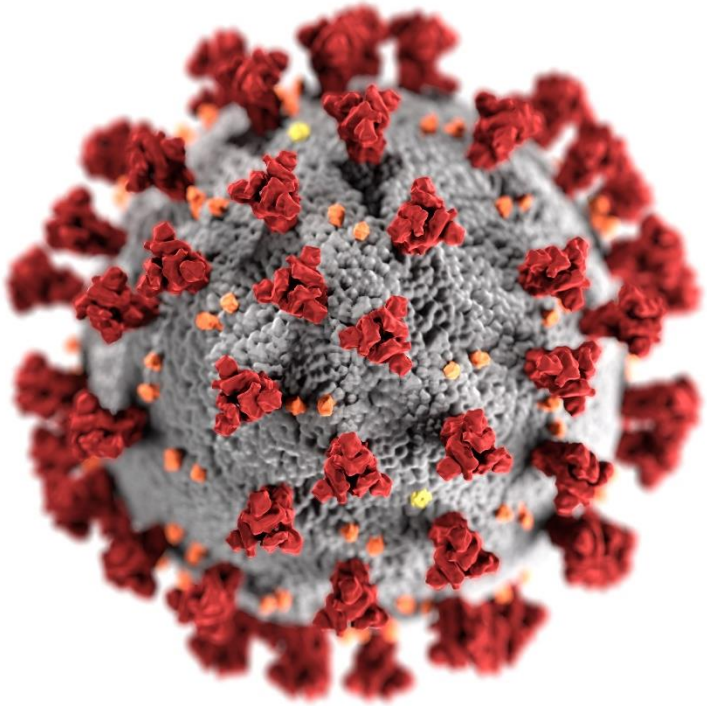
Current SARS-CoV-2 Lineages & Trends

Natalie J. Thornburg, PhD

Current SARS-CoV-2 lineages and trends

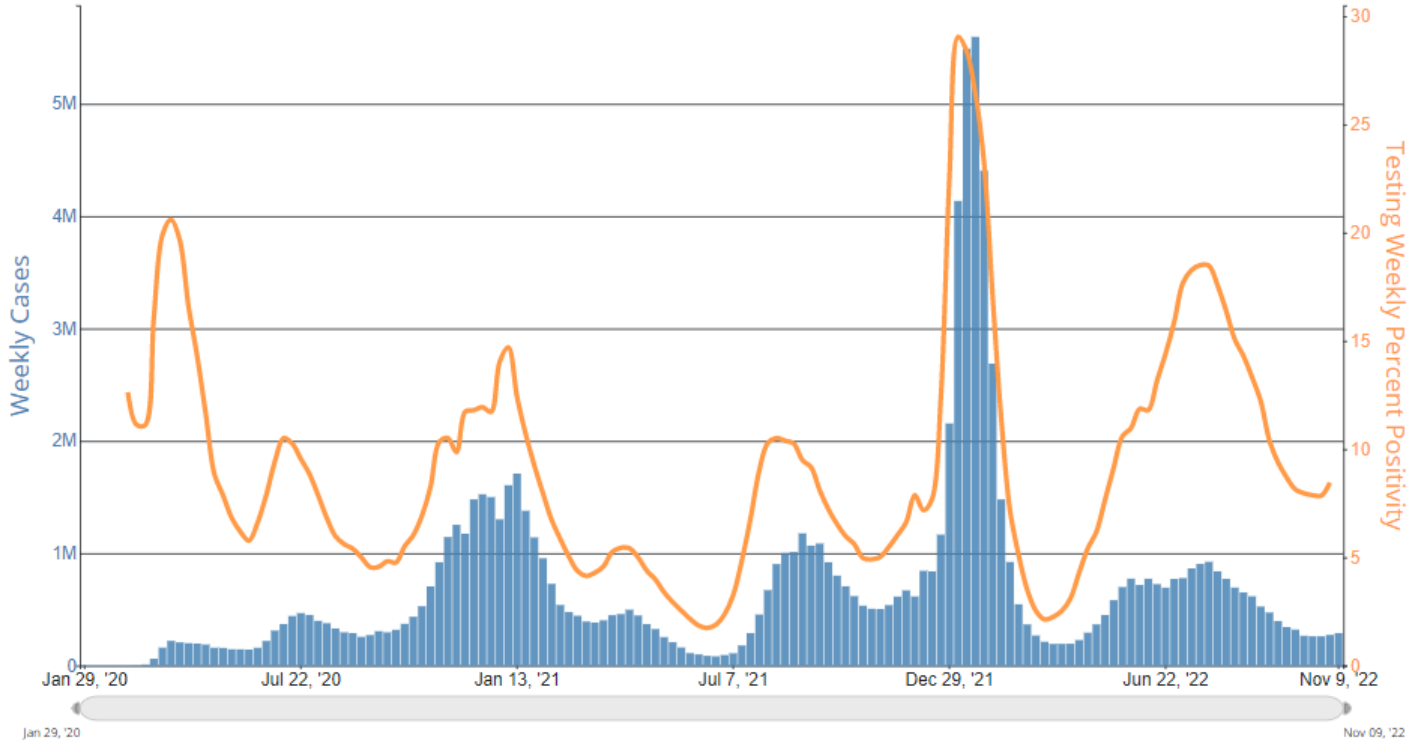
IDSA clinician call

Natalie J. Thornburg, PhD
Respiratory virology lead
NCIDR/CORVD (proposed)
Saturday November 12, 2022



cdc.gov/coronavirus

Weekly Trends in Reported COVID-19 Cases and Test Percent Positivity (7-day Moving Average), United States



Convergent Evolution of Different Omicron Sub-lineages
Key changes in the spike receptor binding domain

>90% of circulating lineages BA.4/BA.5
(spike component included in bivalent vaccine)

BA.5 – L452R, F486V
- BF.7 – R346T
- BA.5.2.6 – R346T
- **BQ.1 – K444T, N460K**
- **BQ.1.1 – R346T, K444T, N460K**

BA.4 – L452R, F486V
- BA.4.6 – R346T

BA.2
- BA.2.75 – D339H, G446S, N460K, R493Q
- BA.2.75.2 – D339H, R346T, G446S, N460K, F486S, R493Q
- **BN.1 – D339H, R346T, K356T, G446S, N460K, F490S, R493Q**
- ***XBB** – D339H, R346T, L368I, V445P, G446S, N460K, F486S, F490S, R493Q

Bolded sub-lineages are expanding in U.S.
Change impacts some monoclonal antibody treatments
* Sub-lineage <1% weighted estimate in U.S. as of November 11, 2022

- https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-omicron-subvariants/

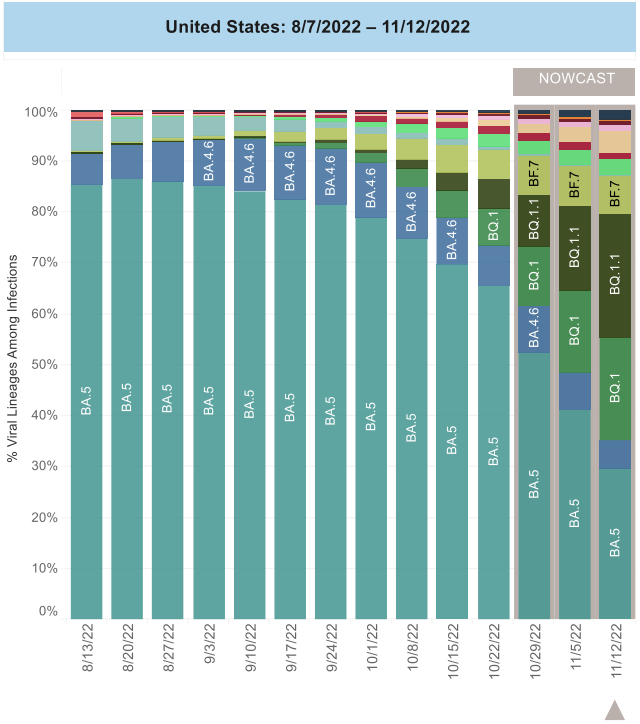
National Nowcast Estimates of SARS-CoV-2 Lineages

- Omicron estimated at ≥ 99% of circulating viruses

- BA.4 and BA.5 lineages and sub-lineages >90% of circulating viruses
- BA.2 lineage viruses make up about 8% of circulating viruses

New lineages >1% separated from parent

- **BN.1 (BA.2.75.5.1)**
  - BN.1 growing and predicted to account for 4.3% (3.0-6.2%) of cases
  - Mutations in Spike RBD, relative to BA.2 : D339H, **R346T**, K356T, **G446S**, N460K, F490S, R493Q



United States: 11/6/2022 – 11/12/2022 NOWCAST

USA

WHO Label	Lineage	US Class	%Total	95%PI
Omicron	BA.5	VOC	29.7%	27.2-32.3%
	BQ.1.1	VOC	24.1%	21.3-27.3%
	BQ.1	VOC	20.1%	17.2-23.4%
	BF.7	VOC	7.8%	6.8-9.0%
	BA.4.6	VOC	5.5%	5.0-6.2%
	BN.1	VOC	4.3%	3.0-6.2%
	BA.5.2.6	VOC	2.9%	2.5-3.4%
	BA.2	VOC	1.3%	0.8-1.9%
	BA.2.75	VOC	1.2%	1.0-1.5%
	BA.2.75.2	VOC	0.9%	0.6-1.2%
	BA.4	VOC	0.1%	0.1-0.1%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		2.0%	1.1-3.3%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1 and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, BN.1 was aggregated with BA.2.75. Lineages BA.2.75.2, BN.1, BA.4.6, BF.7, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

Linages with 346 and / or 444 substitutions Implications for Therapeutics

- Bebtelovimab may lose potency against viruses with Spike substitution at 444
  - BQ.1 and BQ.1.1 have K444T
  - Comprise ~ 44% circulating viruses nationally
- Evusheld may lose potency against viruses with Spike substitution at 346 or 444
  - BA.4.6, BF.7, B.5.2.6, and BA.2.75.2, have R346T substitutions without 444 substitution
  - BQ.1 has K444T substitution, but not R346T
  - BQ.1.1 has both R346T and K444T
  - Combined these lineages make up approximately 61% of circulating viruses

WHO Label	Lineage	US Class	%Total	95%PI
Omicron	BA.5	VOC	29.7%	27.2-32.3%
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	BN.1	VOC	4.3%	3.0-6.2%
	BA.5.2.6	VOC	2.9%	2.5-3.4%
	BA.2	VOC	1.3%	0.8-1.9%
	BA.2.75	VOC	1.2%	1.0-1.5%
	BA.2.75.2	VOC	0.9%	0.6-1.2%
	BA.4	VOC	0.1%	0.1-0.1%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
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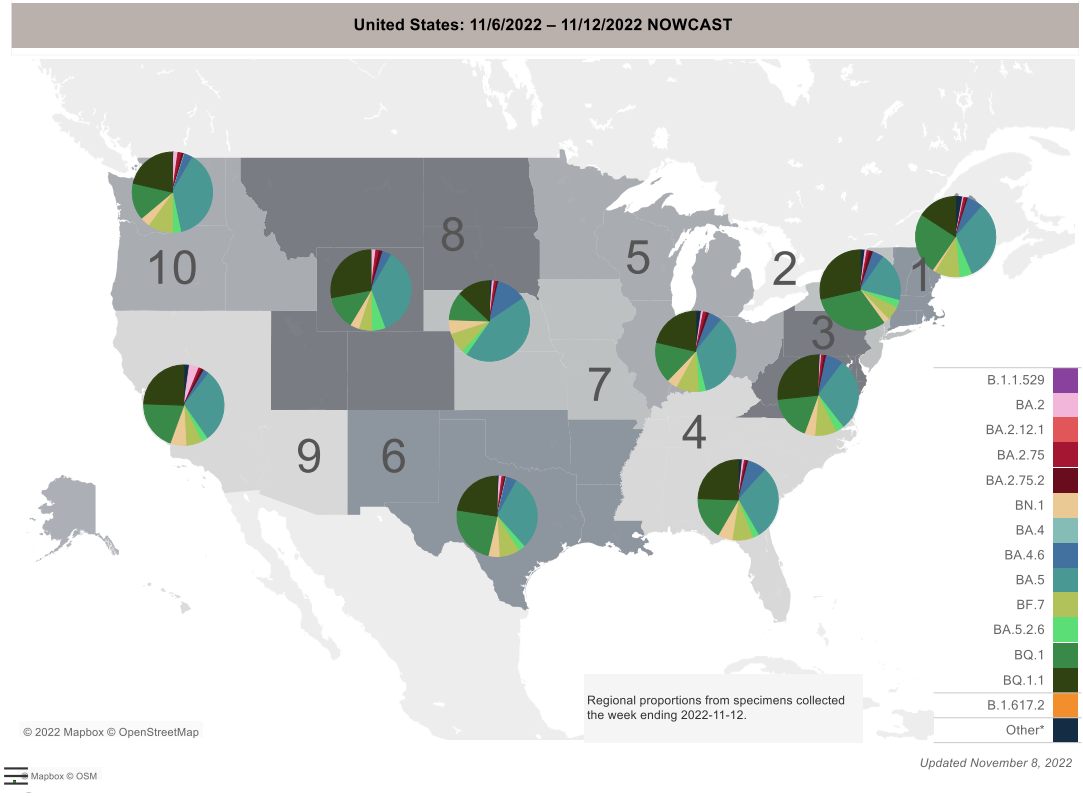
Nowcast estimates of SARS-CoV-2 lineages by HHS region

- BQ.1 and BQ.1 are increasing in every region
  - BQ.1 ranges from 11-25% in each region
  - BA.1.1 from 13-29% per region

- BQ.1 and BQ.1.1 make up over half of SARS-CoV-2 infections in HHS Region 2



Week over Week Growth Analysis

BA.4/5 lineage viruses

- **BQ.1.1** has a doubling time of ~14 days, which is slower than last week's 9 days
- **BQ.1** has a doubling time of ~26 days, which is slightly slower than last week's 13 days

BA.2 lineage viruses

- **BN.1** (BA.2.75.5.1) has a doubling time of ~14 days, but the absolute number of sequences is low so confidence intervals are wide
- **XBB** (and XBB.1) growth is increasing with a doubling time of ~12 days, but absolute number of sequences is low, so confidence intervals are wide and weighted estimates still below 1%

- There are some other sublineages with growth rates above zero that have not met the 1% threshold. All are BA.5 or BA.2 lineage viruses.

Viral surveillance key takeaways

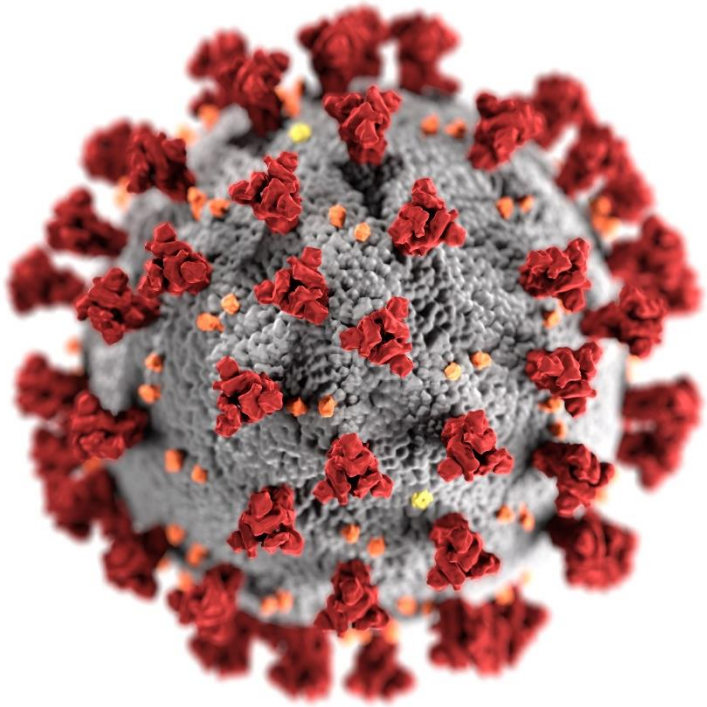
- Currently, there is a lot of lineage diversity, but we are observing convergent evolution
- There is no one “stand out” sublineage
- BA.5 parental lineage is decreasing in prevalence
- BA.4 and BA.5 sublineage viruses continue to predominate
- **BQ.1 and BQ.1.1 are increasing in proportion** in the US and were the fastest growing lineages, though growth is slowing
    - Doubling time for BQ.1 ~26 days
    - Doubling time for BQ.1.1 ~14 days

New sublineage that has been be added to the data tracker this week

- **BN.1** - D339H, **R346T**, K356T, **G446S**, N460K, F490S, Q493R

New sublineage that may be added in coming weeks

- **XBB** - D339H, **R346T**, L368I, V445P, **G446S**, N460K, F486S, F490S, R493Q



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Impact of SARS-CoV-2 Subvariants on Therapeutic Effectiveness

Rajesh T. Gandhi, MD, FIDSA
William A. Werbel, MD
Robert W. Shafer, MD
Meghan E. Pennini, PhD

Update on anti-SARS CoV-2 monoclonal antibodies (as of Nov 12, 2022)

Rajesh T. Gandhi, MD

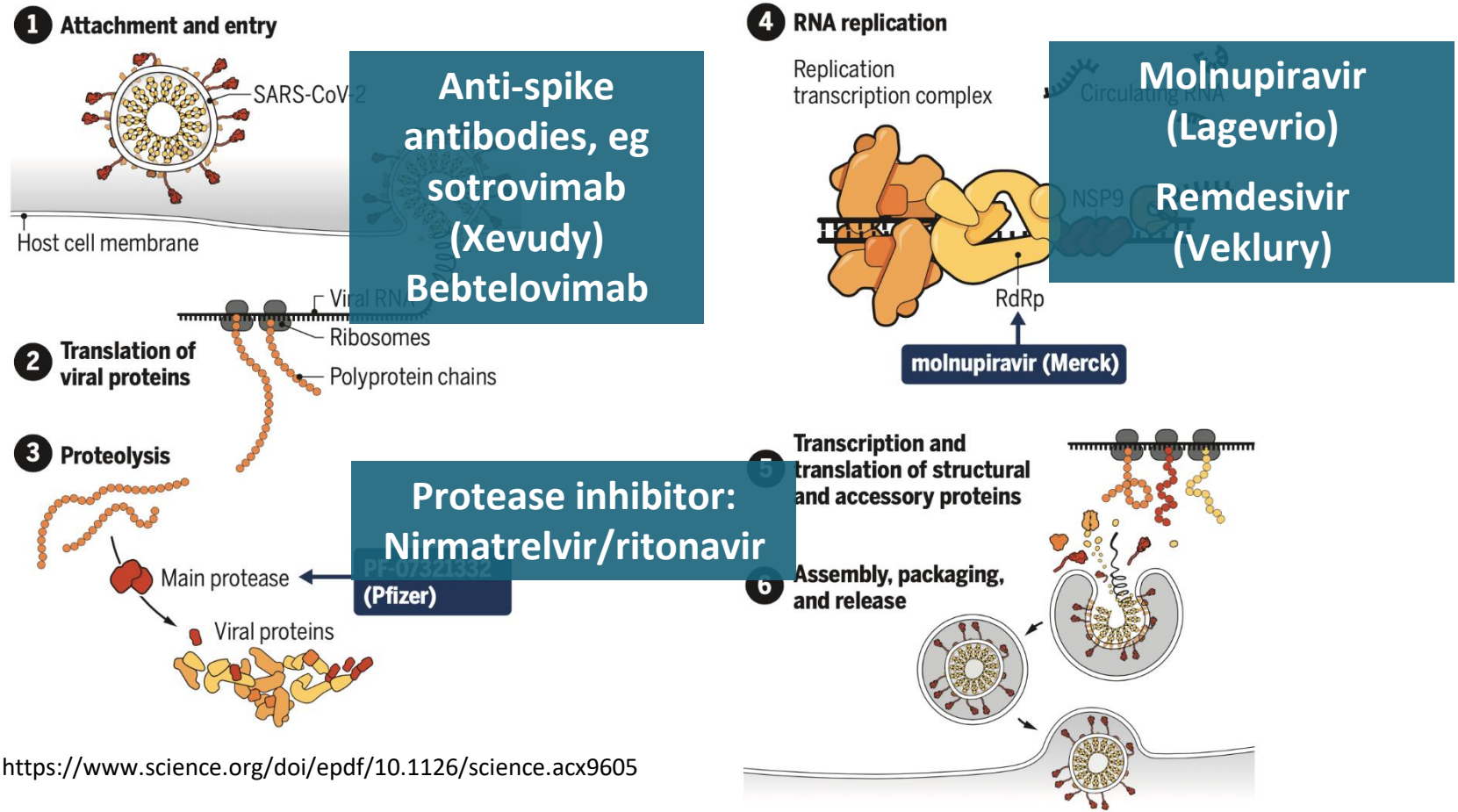
Director, HIV Clinical Services and Education, Massachusetts General Hospital

Director, Harvard University Center for AIDS Research

Disclosures (past 2 years):
Member, NIH & Infectious Diseases Society of America COVID-19 Treatment Guidelines Panels; Recommendations in this talk are my own and not necessarily those of the Panels

Acknowledgments: Arthur Kim, Jon Li, Courtney Tern

SARS CoV-2 Antivirals

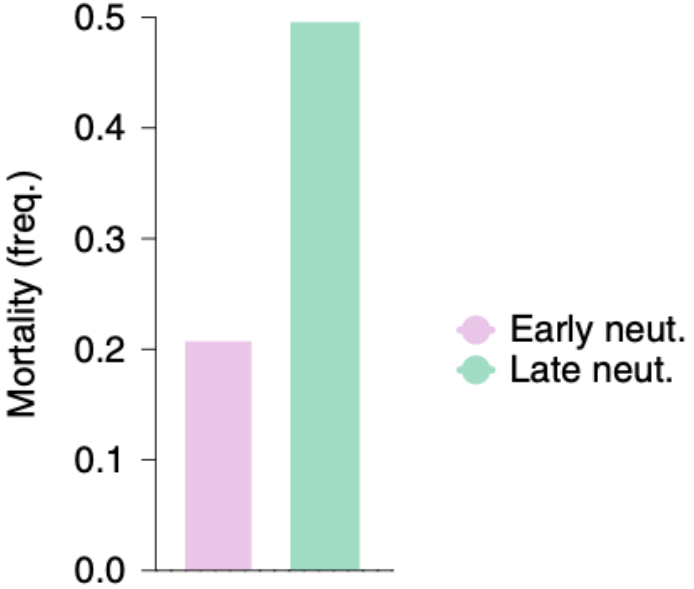


Modified from https://www.science.org/doi/epdf/10.1126/science.acx9605

Anti-SARS CoV-2 Monoclonal Antibodies for Treatment: Rationale

- Delayed production of neutralizing antibodies correlates with fatal COVID-19

- Would providing passive immunity through antibody therapy improve clinical outcomes?



Lucas C et al, Nat Med. 2021 May 5. doi: 10.1038/s41591-021-01355-0. PMID: 33953384.

Anti-SARS-CoV-2 Monoclonal Abs for Treatment

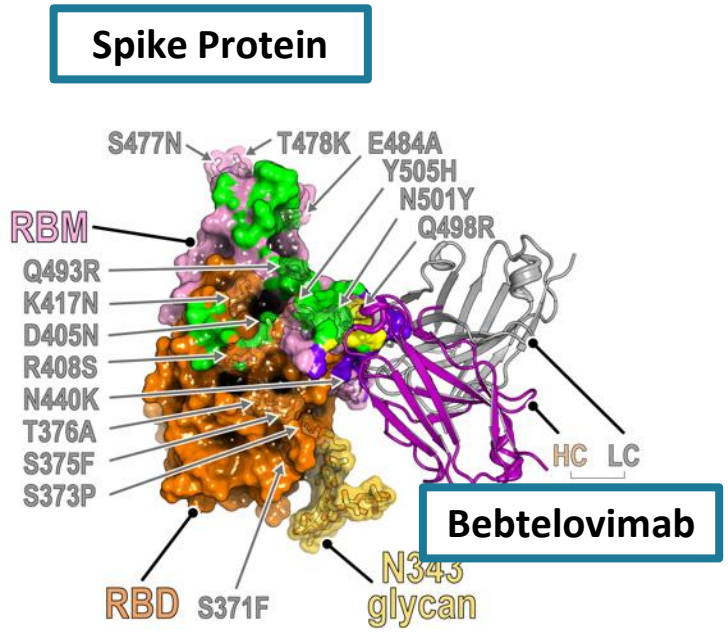
- Phase 3 placebo-controlled trials in non-hospitalized patients with mild to moderate COVID and ≥1 risk factor for severe disease

Antibody	% Reduction Hospitalization/Death
Bamlanivimab + Etesevimab	70%
Casirivimab + Imdevimab	70%
Sotrovimab	79%

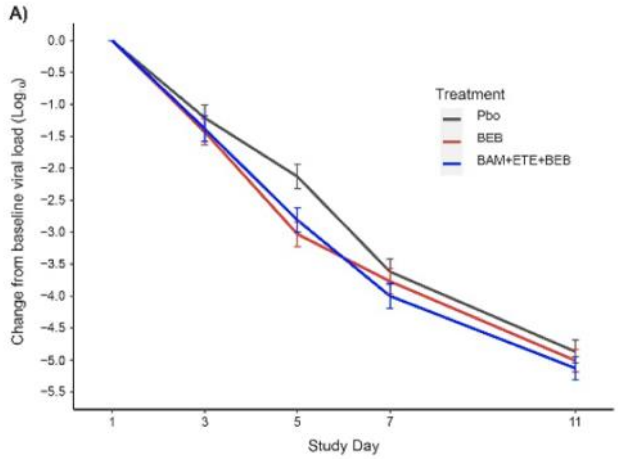
In lab studies, bamlanivimab/etesevimab, casirivimab/imdevimab not active against Omicron. Sotrovimab active vs. Omicron BA.1 but not against other subvariants

Dougan M et al, NEJM, 2021; Weinreich et al., NEJM 2021; Gupta A et al, NEJM, 2021;

Phase 2 Clinical Trial Data for Bebtelovimab

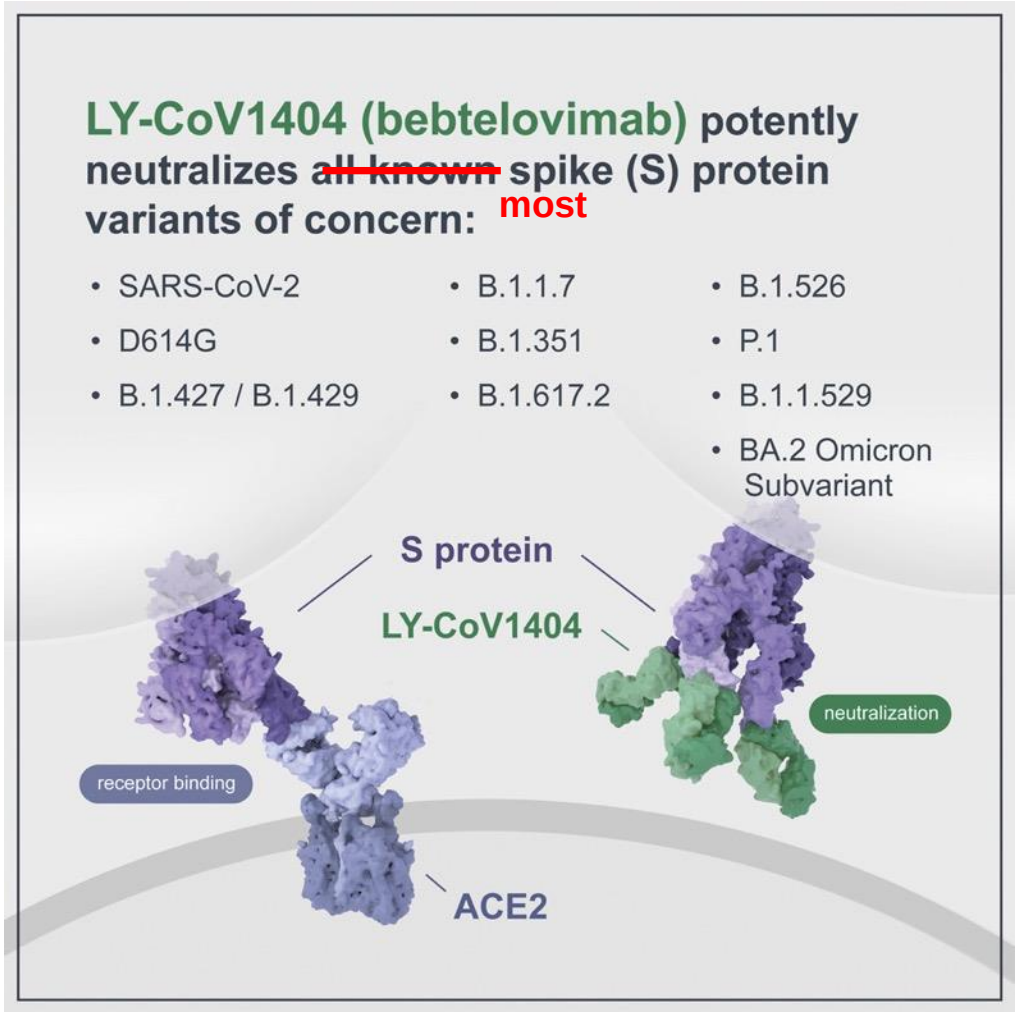


Change from baseline in SARS CoV-2 Viral Load



Low risk participants	BEB N=125	BEB+BAM+ ETE (n=127)	Placebo (n=126)
Symptom resolution, median days (95% CI)	6 (5,7)	7 (6, 8)	8 (7, 9)
COVID-19 Hospitalization/Death	2/125 (1.6%)	3/127 (2.4%)	2/128 (1.6%)

Iketani S et al, Nature, 2022;
doi: https://doi.org/10.1038/s41586-022-04594-4
https://twitter.com/abrahamlabhms
Westendorf, Cell Rep, 2022;
doi: https://doi.org/10.1016/j.celrep.2022.110812
Dougan, medRxiv, 2022



- Bebtelovimab active in vitro against BA.1-5.
- New variants (BQ.1, BQ.1.1) may be resistant to bebtelovimab

Modified from slide from Dr. Arthur Kim

Iketani Nature 2022; Arora Cell Host Microbe 2022; Dougan medRxiV 2022; NIH Treatment Guidelines; Westendorf Cell Rep 2022

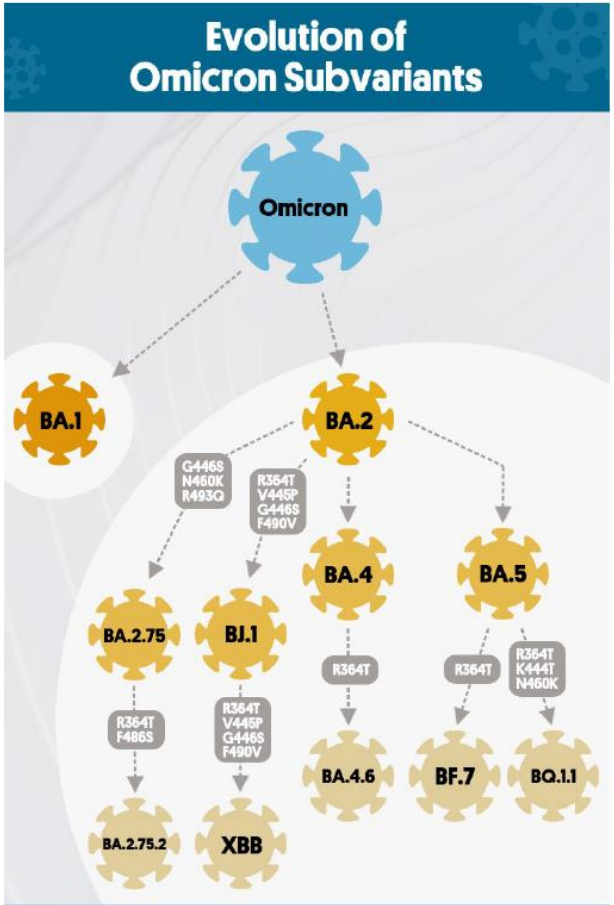


Figure 1. A. Schematic representation of the evolution of Omicron subvariants (adapted from @TRyanGregory). Similar mutations that evade antibody recognition have emerged in different sequence backgrounds. Only RBD mutations are indicated. See ref 5 for complete sequence information.

From BA.5: BQ.1, BQ.1.1, BF.7

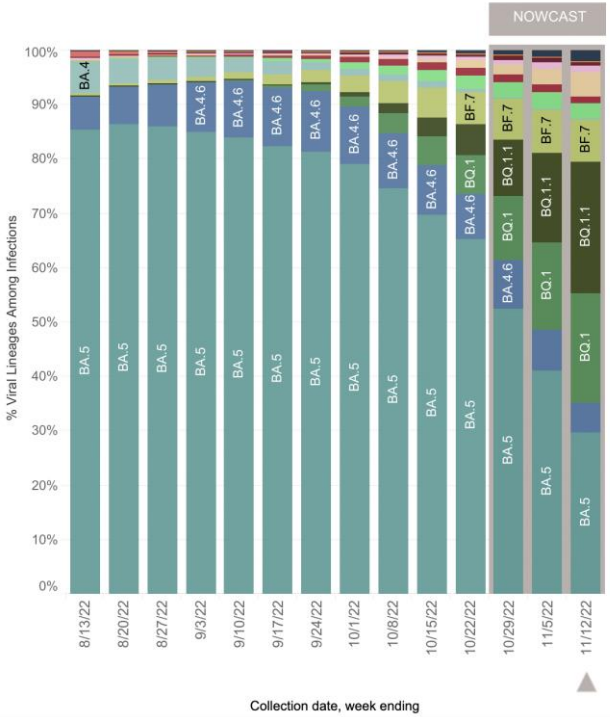
From BA.2: BA.2.75.2

From BA.4: BA.4.6

New Omicron variants resistant to bebtelovimab

Nov 12: BQ.1, BQ.1.1: about 44% of US isolates

United States: 8/7/2022 – 11/12/2022



United States: 11/6/2022 – 11/12/2022 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	29.7%	27.2-32.3%
	BQ.1.1	VOC	24.1%	21.3-27.3%
	BQ.1	VOC	20.1%	17.2-23.4%
	BF.7	VOC	7.8%	6.8-9.0%
	BA.4.6	VOC	5.5%	5.0-6.2%
	BN.1	VOC	4.3%	3.0-6.2%
	BA.5.2.6	VOC	2.9%	2.5-3.4%
	BA.2	VOC	1.3%	0.8-1.9%
	BA.2.75	VOC	1.2%	1.0-1.5%
	BA.2.75.2	VOC	0.9%	0.6-1.2%
	BA.4	VOC	0.1%	0.1-0.1%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		2.0%	1.1-3.3%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
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# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1 and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, BN.1 was aggregated with BA.2.75. Lineages BA.2.75.2, BN.1, BA.4.6, BF.7, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

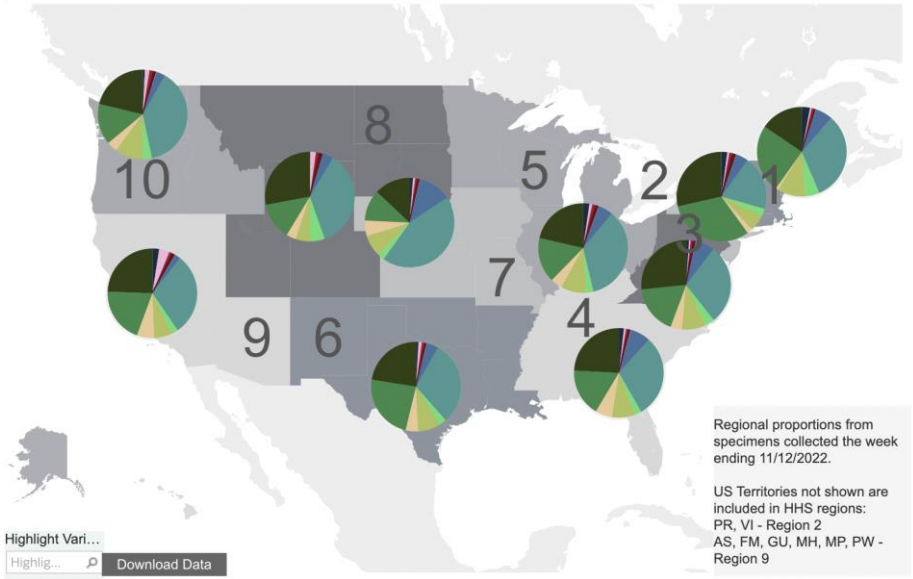
Omicron	Beb
BA.5	✓
BA.4.6	✓
BA.2.75.2	✓
BQ.1, 1.1	✗
XBB	✗

Modified from slide by Dr Jon Li

New variant susceptibility to Bebtelovimab

Lineage with spike protein substitution	WHO nomenclature	Key substitutions tested	Fold reduction in susceptibility
BQ.1	Omicron [BA.5+K444T+N460K]	BA.5 + K444T + N460K	>672
BQ.1.1	Omicron [BA.5+R346T+K444T+N460K]	BA.5 + R346T + K444T + N460K	>672

https://www.fda.gov/media/156152/download



CDC Nowcast (11/12/2022)

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	BA.2.75	VOC	1.2%	1.0-1.5%
	BA.2.75.2	VOC	0.9%	0.6-1.2%
	BA.4	VOC	0.1%	0.1-0.1%

Variants	All Regions	Region 1	Region 2	Region 3	Region 4	Region 5	Region 6	Region 7	Region 8	Region 9	Region 10
BQ.1	20.1%	24.6%	31.4%	17.8%	17.2%	16.3%	23.8%	11.2%	13.4%	20.0%	14.8%
BQ.1.1	24.1%	15.6%	28.5%	26.6%	24.2%	21.3%	22.5%	13.0%	27.9%	24.4%	21.2%
Total	44.2%	40.2%	**59.9%**	44.4%	41.4%	37.6%	46.3%	24.2%	41.3%	44.4%	36.0%

Table adapted from Marylu Schaffhauser, Alice Pau (NIH)

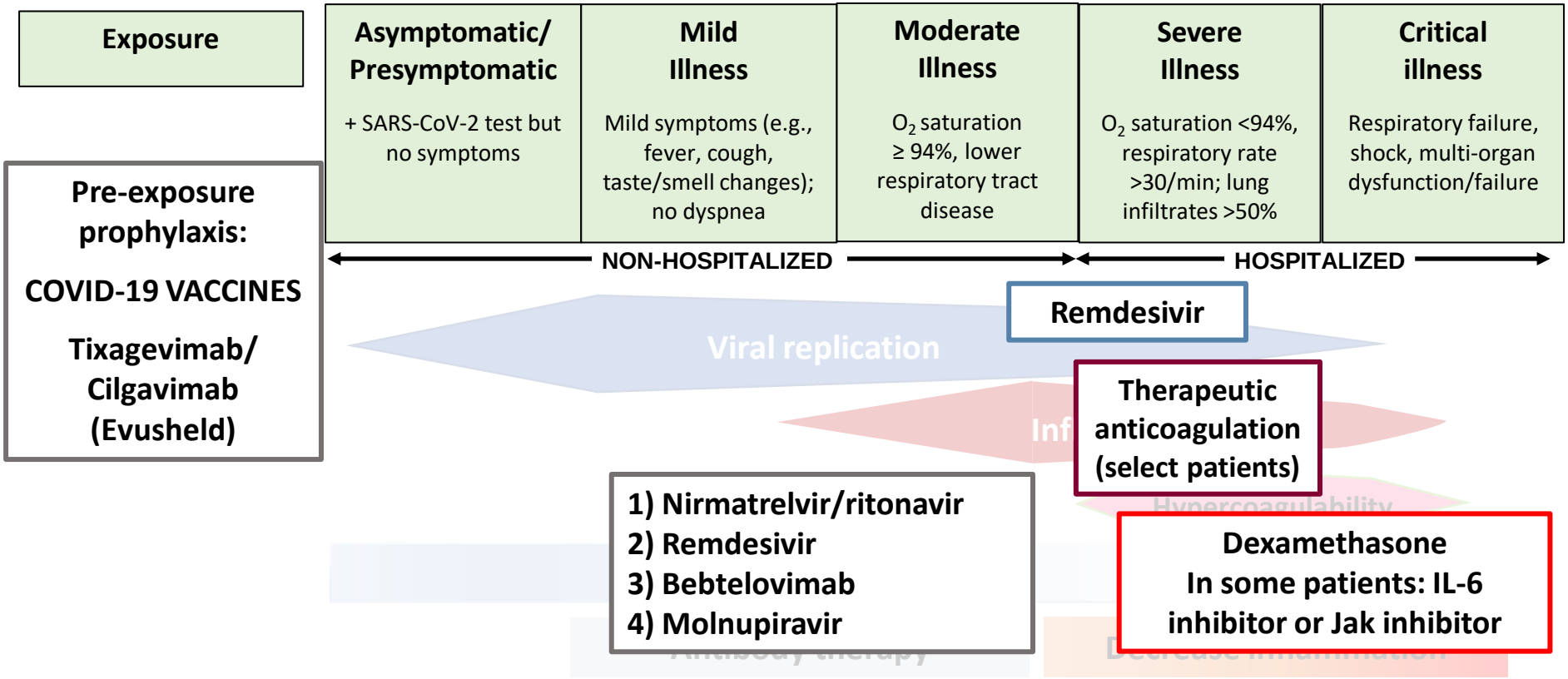
https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Small molecule antivirals anticipated to be active against new variants

	1) Nirmatrelvir/r	2) Remdesivir	3) Molnupiravir
Efficacy (prevention hospitalization or death)	• **Relative risk reduction: 88%** • Absolute risk: 6.3%→0.8% • NNT: 18	• **Relative risk reduction: 87%** • Absolute risk: 5.3%→0.7% • NNT: 22	• **Relative risk reduction: 30%** • Absolute risk: 9.7%→6.8% • NNT: 35
Pros	• Highly efficacious • Oral regimen • Ritonavir studied (safe) in pregnancy	• Highly efficacious • Studied in pregnancy • Few/no drug interactions	• Oral regimen • Not anticipated to have drug interactions
Cons	• Drug drug interactions	• Requires IV infusion on 3 consecutive days	• Lower efficacy • Concern: mutagenicity • Not recommended in pregnancy/children

Modified from Table in Gandhi RT, Malani P, del Rio C, JAMA, Jan 14, 2022

Treatment Across the COVID-19 Spectrum



Gandhi RT, CID, 2020; Gandhi RT, Lynch J, del Rio C. NEJM 2020

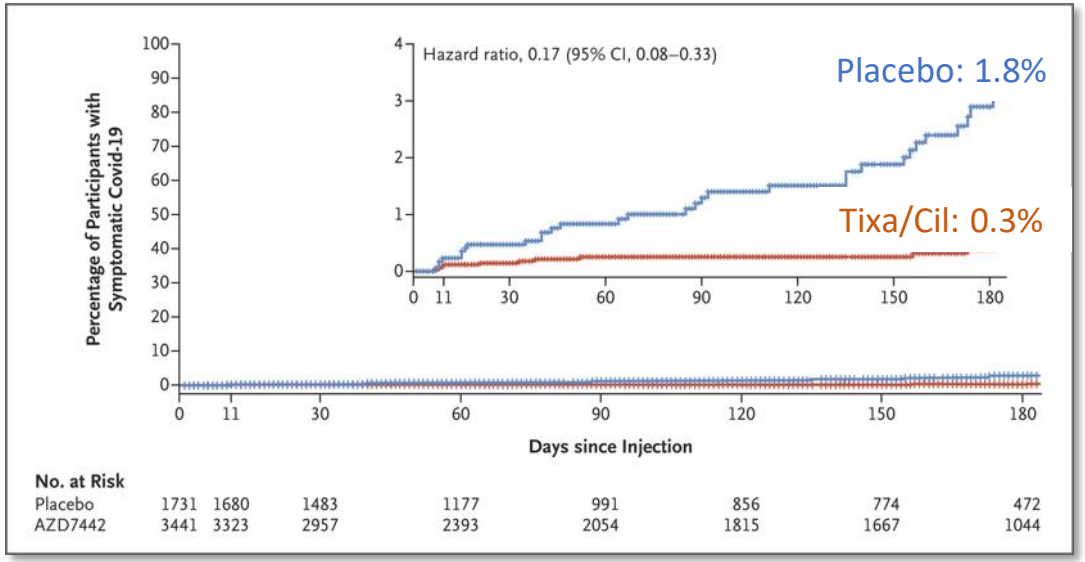
PROVENT: Tixagevimab/cilgavimab (AZD7442) for Pre-exposure prophylaxis

ORIGINAL ARTICLE

Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for Prevention of Covid-19

- Tixagevimab/cilgavimab: anti-SARS CoV-2 monoclonal antibodies (half life ≈90 days)
- 5197 participants randomized 2:1 to receive single IM dose of tixagevimab + cilgavimab (150/150 mg) or placebo
- Unvaccinated
- 3.8% immunocompromised

83% reduction in symptomatic Covid in tixagevimab/cilgavimab group



Levin M et al, NEJM, April 20, 2022

Tixagevimab/cilgavimab for COVID-19 Pre-Exposure Prophylaxis

U.S. FOOD & DRUG ADMINISTRATION

- **FDA EUA**:
  - 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 ***or***
  - For whom vaccination is not recommended due severe adverse reaction

- Wait 2 weeks *after* vaccination to administer tixagevimab/cilgavimab

https://www.fda.gov/media/154701/download

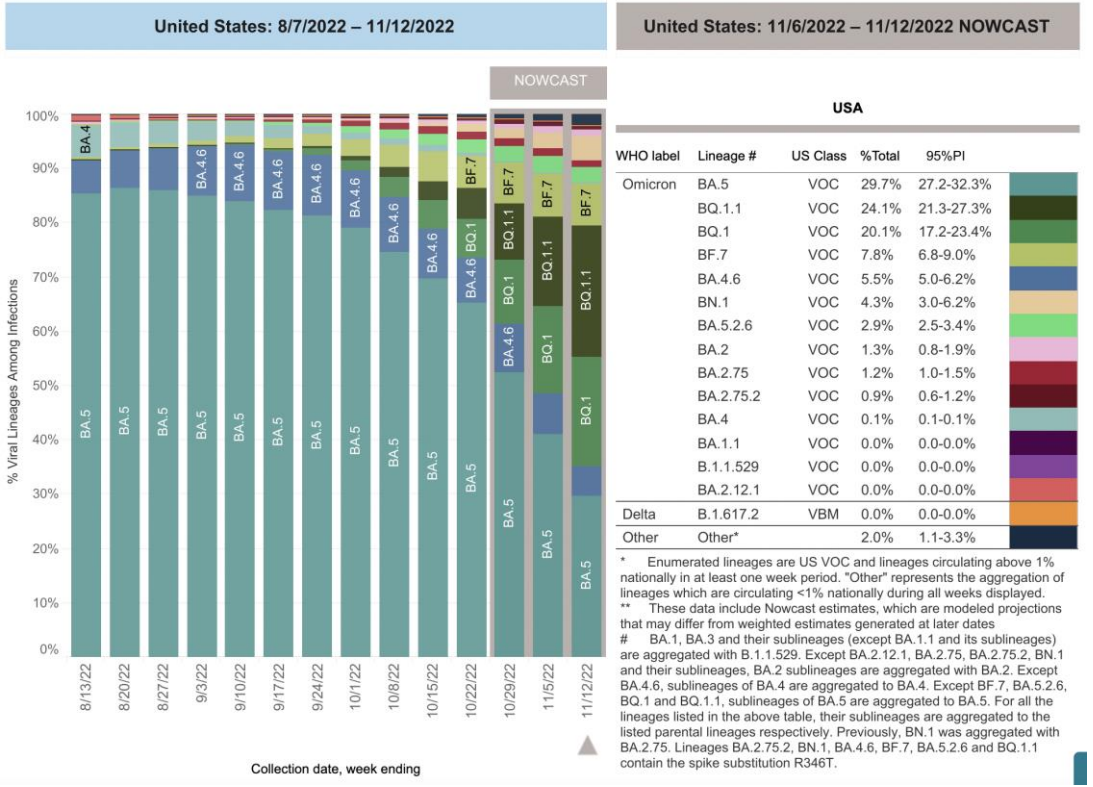
Moderate to Severe Immunocompromising Conditions and Treatments

- Active treatment for cancer
- Solid-organ transplant recipient and taking immunosuppressive therapy
- Receipt of CAR-T-cell or hematopoietic stem cell transplant
- Moderate or severe primary immunodeficiency
- Advanced or untreated HIV (CD4 <200; history of AIDS defining illness without immune reconstitution; clinical manifestations of symptomatic HIV)
- High-dose corticosteroids (>=20 mg prednisone/d for >=2 wk), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapy, TNF blockers, other immunosuppressive/immunomodulatory agents (e.g., B-cell depleting agents)

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

New Omicron variants resistant to tixagevimab/cilgavimab

Nov 12: BQ.1, BQ.1.1, BA.4.6, BF.7, BA.5.2.6 and BA.2.75.2: about 61.2% of US isolates



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* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
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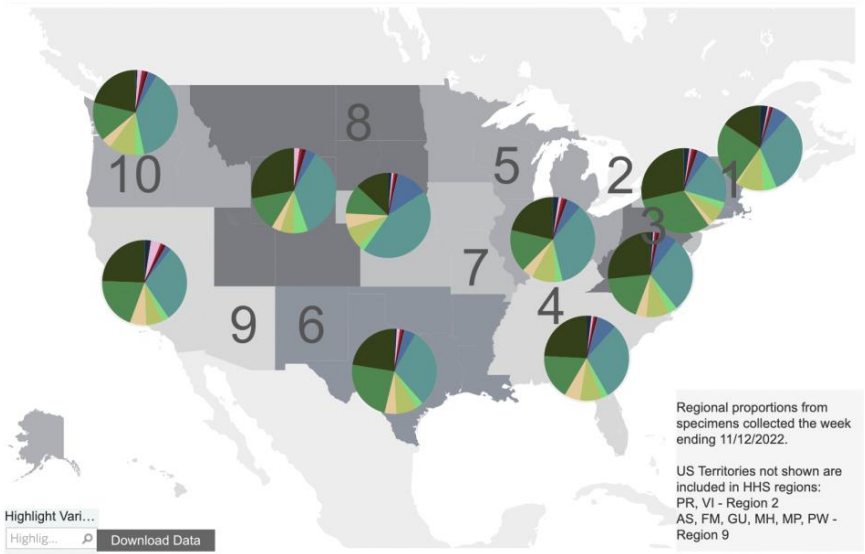
Omicron	Tixa/cil
BA.5	✓
BA.4.6	✗
BA.2.75.2	✗
BQ.1, 1.1	✗
XBB	✗

Modified from slide by Dr Jon Li



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Variants	All Regions	Region 1	Region 2	Region 3	Region 4	Region 5	Region 6	Region 7	Region 8	Region 9	Region 10
BA.2.75.2	0.9%	0.4%	1.2%	0.8%	0.7%	1.0%	0.5%	0.6%	1.2%	1.1%	0.9%
BA.4.6	5.4%	6.3%	4.5%	6.8%	7.4%	5.3%	4.2%	11.9%	3.7%	2.2%	3.4%
BQ.1	20.1%	24.6%	31.4%	17.8%	17.2%	16.3%	23.8%	11.2%	13.4%	20.0%	14.8%
BQ.1.1	24.1%	15.6%	28.5%	26.6%	24.2%	21.3%	22.5%	13.0%	27.9%	24.4%	21.2%
BA.5.2.6	2.9%	4.9%	2.9%	3.3%	2.5%	2.6%	2.9%	2.4%	5.3%	2.4%	3.5%
BF.7	7.8%	10.2%	5.7%	8.7%	8.4%	9.2%	7.8%	7.9%	5.2%	6.6%	10.0%
Total	**61.2%**	**62.0%**	**74.2%**	**64.0%**	**60.4%**	**55.7%**	**61.7%**	47.0%	**56.7%**	**56.7%**	**53.8%**

Table adapted from Marylu Schaffhauser, Alice Pau (NIH)

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

The COVID-19 Treatment Guidelines Panel's Statement on Omicron Subvariants, Pre-Exposure Prophylaxis, and Therapeutic Management of Nonhospitalized Patients With COVID-19. *Last Updated: November 10, 2022*

For Pre-Exposure Prophylaxis

- Tixagevimab + cilgavimab is the only agent authorized by the FDA for use as COVID-19 PrEP ….
- In the absence of an alternative option for PrEP, the Panel continues to recommend the use of tixagevimab plus cilgavimab as PrEP for eligible individuals (BIIb)
- Given the increasing prevalence of these resistant SARS-CoV-2 subvariants, the decision to administer tixagevimab plus cilgavimab to a given patient should be based on the regional prevalence of the resistant subvariants, the individual patient's risks, the available resources, and logistics.
- Individuals who receive tixagevimab plus cilgavimab as PrEP should continue to take precautions to avoid exposure to SARS-CoV-2. If they experience signs and symptoms consistent with COVID-19, they should be tested for SARS-CoV-2 infection and, if infected, promptly seek medical attention and treatment, if appropriate.

For Treatment of Mild to Moderate COVID-19 in Nonhospitalized Adults Who Are at High Risk of Progressing to Severe COVID-19

- The Panel continues to recommend the following anti-SARS-CoV-2 therapies as preferred treatments for COVID-19. These drugs are listed in order of preference:
  - Ritonavir-boosted nirmatrelvir (Paxlovid) (AIIa)
  - Remdesivir (BIIb)
- The following alternative therapies should be used ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. These drugs are listed in alphabetical order:
  - Bebtelovimab, but ONLY when the majority of circulating Omicron subvariants in the region are susceptible (CIII)
  - Molnupiravir (CIIa)

Conclusions

- Once high proportion of circulating variants are anticipated to be resistant, bebtelovimab is no longer reliable option for treating high-risk non-hospitalized patients with mild-to-moderate COVID-19
- Small molecule antivirals (nirmatrelvir/ritonavir, remdesivir, molnupiravir) anticipated to still be active
- Whenever possible, efforts should be made to manage nirmatrelvir/rit. drug-drug interactions or set up systems to provide remdesivir to high-risk patients
- Immunocompromised individuals who receive tixagivimab/cilgavimab for pre-exposure prophylaxis should be counseled to continue measures to avoid infection (including staying up to date with vaccination) and to seek testing and treatment if symptoms of COVID-19 develop

Impact of Subvariant Evolution on COVID-19 Outpatient Therapeutic Decision-Making

William A. Werbel, MD PhD

Assistant Professor of Medicine

Johns Hopkins School of Medicine

Associate Director of Epidemiology and Quantitative Sciences

Johns Hopkins Transplant Research Center

IDSA/CDC Clinician Call

November 12th, 2022

Funding and Disclosures

- National Institute of Allergy and Infectious Diseases
- NIH Center for AIDS Research

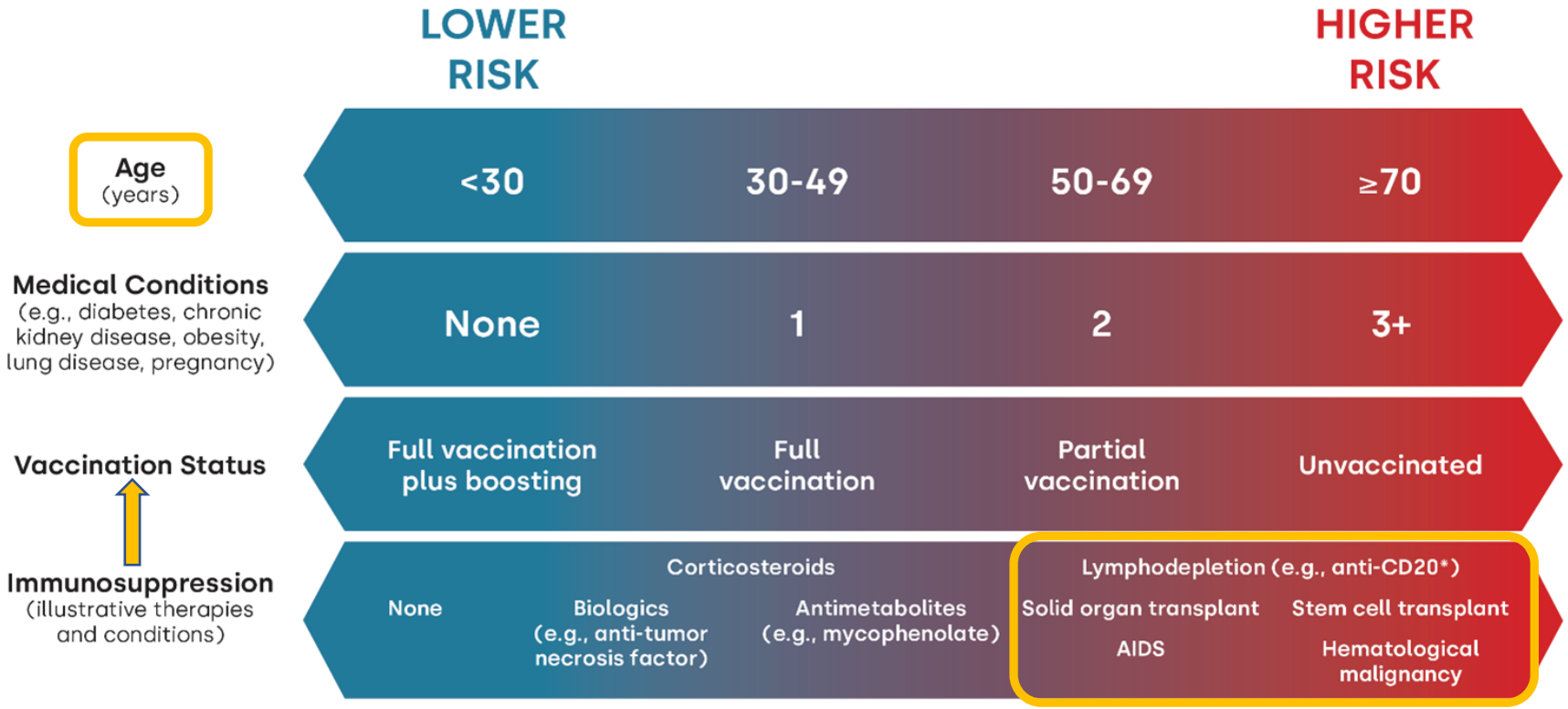
- Infectious Diseases Society of America
  - CDC/IDSA COVID-19 Real-Time Learning Network (section editor)
- AstraZeneca (speaking fees), Novavax (advisory board)

The content in this presentation represents my own views, not that my funders, employer, CDC, or IDSA.

Alternate Title:
"COVID-19 Treatment in a mAb-less Winter"

- Establish patient degree of risk for severe COVID-19
- Understand subvariant prevalence in region → mAb role?
- Connect ill and at-risk patients to appropriate authorized therapeutic
  - Antiviral: Intravenous and oral options
  - Antibody: mAb vs. high-titer convalescent plasma

COVID-19 Risk Continuum



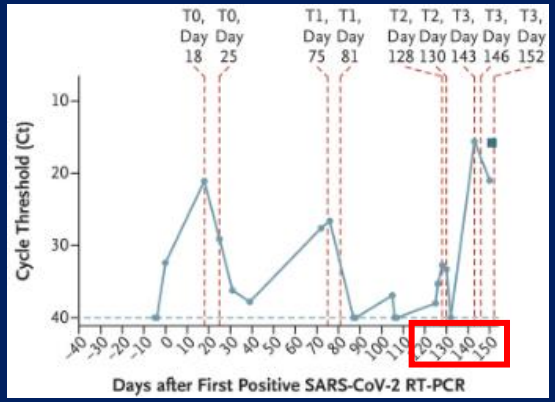
Sociodemographic factors and non-pharmaceutical interventions affect exposure risk

Original illustration by Dr. William Werbel. Adapted for the COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

Continued focus COVID-19 in the immunocompromised

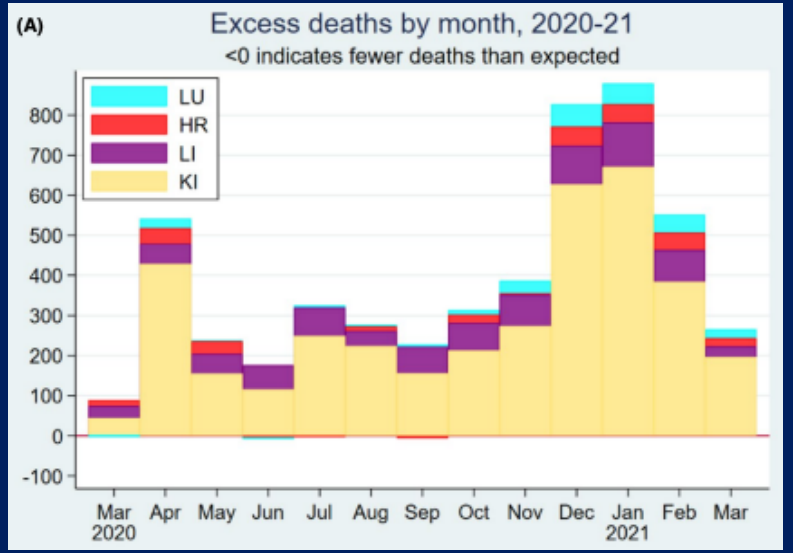
- Outsized morbidity and mortality, attenuated vaccine protection
- Potential for prolonged replication and disease (*months* with B cell depletion) → generate resistant variants?
- Lack of dedicated vaccine or therapeutic trials to confirm effectiveness



Massie et al., AJT, 2021
Hensley et al., CID, 2021
Choi et al., NEJM, 2021
Werbel & Segev, NYT, 2022

Illustrative Population: Solid Organ Transplant (SOT) Recipients

- Intersection of high-risk medical comorbidities and immunosuppression
  - Severe COVID-19 outcomes
  - End organ dysfunction, multiple medications
- Relatively common condition – ~400,000 SOTRs in US
- Immunosuppressants utilized in other common conditions (e.g., autoimmune disease, stem cell transplant)



Kates et al., CID, 2020
Raja et al., Txp Rev, 2020
Massie et al., AJT, 2022
Heldman et al., TID, 2021
Mehta et al., Transplantation, 2021

Example Case

- 72-year-old male with history of obesity (BMI 31), diabetes, and renal failure requiring kidney transplant 3 years ago.
- Calls your clinic with two days of malaise and new fever today. Denies dyspnea.
- Rapid home antigen test is positive for SARS-CoV-2 infection.
- Has received 2 mRNA vaccines (last 6 months ago, no bivalent booster)
- Takes prednisone, tacrolimus, mycophenolate, atorvastatin, losartan, aspirin

NIH COVID-19 Treatment Guidelines (9.26.22 Update)

Panel's Recommendations

For All Patients:

- All patients should be offered symptom management (**AIII**).
- The Panel **recommends against** the use of **dexamethasone**[a] or **other systemic corticosteroids** in the absence of another indication (**AIIb**).

For Patients Who Are at High Risk of Progressing to Severe COVID-19[b]

Preferred therapies. Listed in order of preference:

- **Ritonavir-boosted nirmatrelvir (Paxlovid)**[c,d] (**AIIa**)
- **Remdesivir**[d,e] (**BIIa**)

CDC/IDSA COVID-19 Real-Time Learning Network Outpatient Roadmap

https://www.idsociety.org/globalassets/covid-19-real-time-learning-network/outpatientroadmap-v10.pdf

Alternative therapies. For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:

- **Bebtelovimab**[f] (**CIII**)
- **Molnupiravir**[d,g,h] (**CIIa**)

Choosing the Right Antiviral

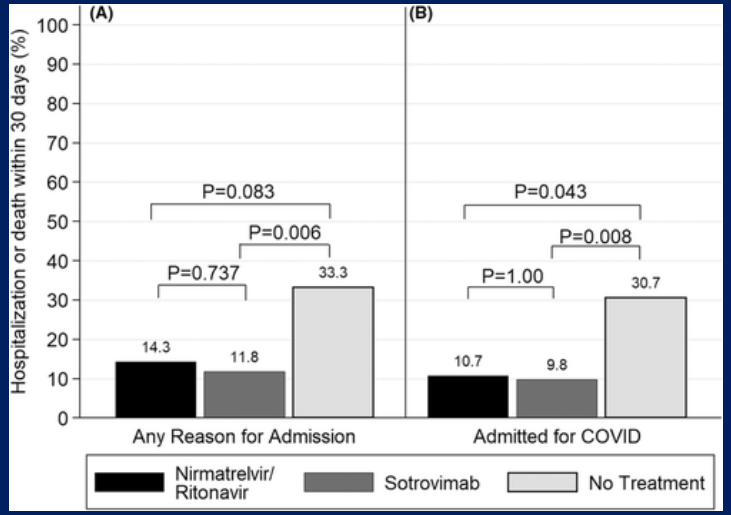
FDA Fact Sheets
NIH Treatment Guidelines
Solera et al., AJT 2022
Hedvat et al., AJT 2022
Radcliffe et al., AJT 2022

	Route	Effectiveness*	Patient Considerations	Major Issues	Other Notes
Remdesivir (Veklury®)	IV 3 days, daily	+++	Mild-mod transaminase ↑ common (inpt 5-10 dy course)	Logistics	FDA-approved, inc for infants >28 days **≤7 days** of sx onset
Nirmatrelvir/ Ritonavir (Paxlovid™)	Oral 5 days, twice daily	+++	Not recommended for Child C liver disease or GFR<30	Drug-drug interactions	½ dose N if GFR 30-59 **≤5 days** of sx onset GI AE, rebound?
Molnupiravir (Lagevrio™)	Oral 5 days, twice daily	+	No dose change for renal or liver disease	Lower effectiveness	?Mutagenicity ≠<18yr; + contraception **≤5 days** of sx onset

*Effectiveness data in immunocompromised persons consist primarily of case series

Can We Give Nirmatrelvir/Ritonavir (Paxlovid™) to this Patient?

- "Yes, but…"
- Significant interaction with calcineurin inhibitors, mTORi
  - *Not absolute contraindication*, but can be dangerous (levels ↑ ↑ ↑)
- Multiple other drug interactions must be evaluated (anticoagulants, anticonvulsant, statins, antiarrhythmics)



FDA EUA Fact Sheet
Hedvat et al., AJT, 2022
NIH Treatment Guidelines
AST Statement on Oral Antivirals

Know/Find Paxlovid™ Interactions!

- Liverpool Drug Interactions
- Ontario COVID-19 Science Table
- NIH Treatment Guidelines

- Talk to a pharmacist

- Make a plan *before* an acute illness (i.e., now, for your high-risk patients)

NIH Treatment Guidelines

Prescribe Alternative COVID-19 Therapy

For these medications, management strategies are not possible or the risks outweigh the potential benefits.

Anticonvulsants

- Carbamazepine
- Phenobarbital
- Phenytoin
- Primidone

Anti-infectives

- Glecaprevir/pibrentasvir
- Rifampin
- Rifapentine

Immunosuppressants

- Voclosporin

Cardiovascular

- Amiodarone
- Clopidogrel[a,b]
- Disopyramide
- Dofetilide
- Dronedarone
- Eplerenone
- Flecainide
- Ivabradine
- Propafenone
- Quinidine

Neuropsychiatric

- Clozapine
- Lurasidone
- Midazolam (oral)
- Pimozide

Pulmonar hyperten

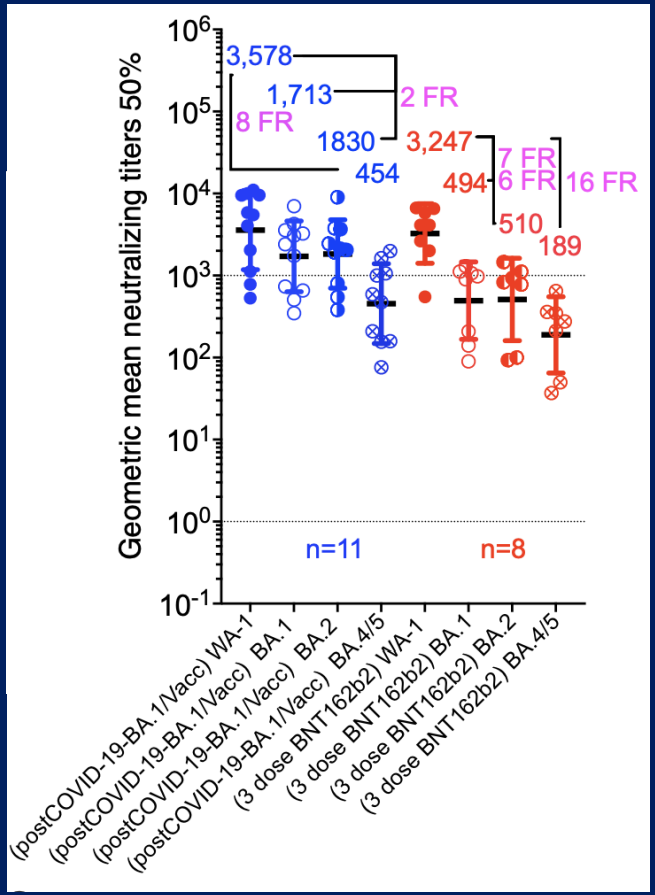
- Sildena
- Tadala
- Varden

Miscellan

- Bosent
- Certain chemo agents
- Ergot d
- Lumac
- St. John
- Tolvapt

Other EUA Therapies: Convalescent Plasma

- Complicated history → EUA for high-titer CP, treat immunocompromised persons (*inpt or outpt*)
- Polyclonal, possibly lower variant evasion risk than mAbs, especially if donors with hybrid immunity (vaccine+infection)
- Complement to other antiviral medications



Sullivan et al., NEJM, 2022
Sullivan et al., Nat Comm, 2022

Summary

- Loss of active mAb due to Omicron subvariants requires alternate treatment approach for complex patients

- Antiviral drugs expected to maintain activity vs subvariants
  - Polyclonal plasma might be more preserved than mAb, data lacking

- Determine risk for severe COVID-19 → tailor antiviral selection
  - Make a plan now for high-risk patients
  - Remdesivir may be best option for complex patient e.g., SOTR
  - Nuanced decision-making in other drug selection (e.g., Paxlovid™ drug-drug interactions versus lower Molnupiravir effectiveness)

Closing Recommendation

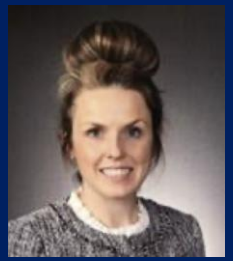
- Maximize vaccination, bivalent boosters, and ring protection of vulnerable
- Masking, physical distancing, testing before gatherings
- Ensure easy access to COVID-19 therapeutics for high-risk patients; make a plan now

Therapeutic Horizons

- Multiple companies developing "pan-Omicron" mAb for treatment and/or prevention

- Combination antiviral therapy may serve role, needs dedicated study

Johns Hopkins Transplant Research Center








Tao Liang
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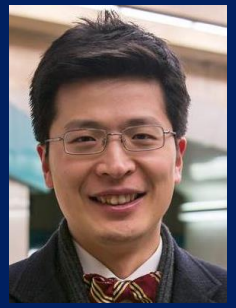



Antibody Susceptibility Testing

Robert Shafer, MD
Division of Infectious Diseases, Department of Medicine
Stanford University

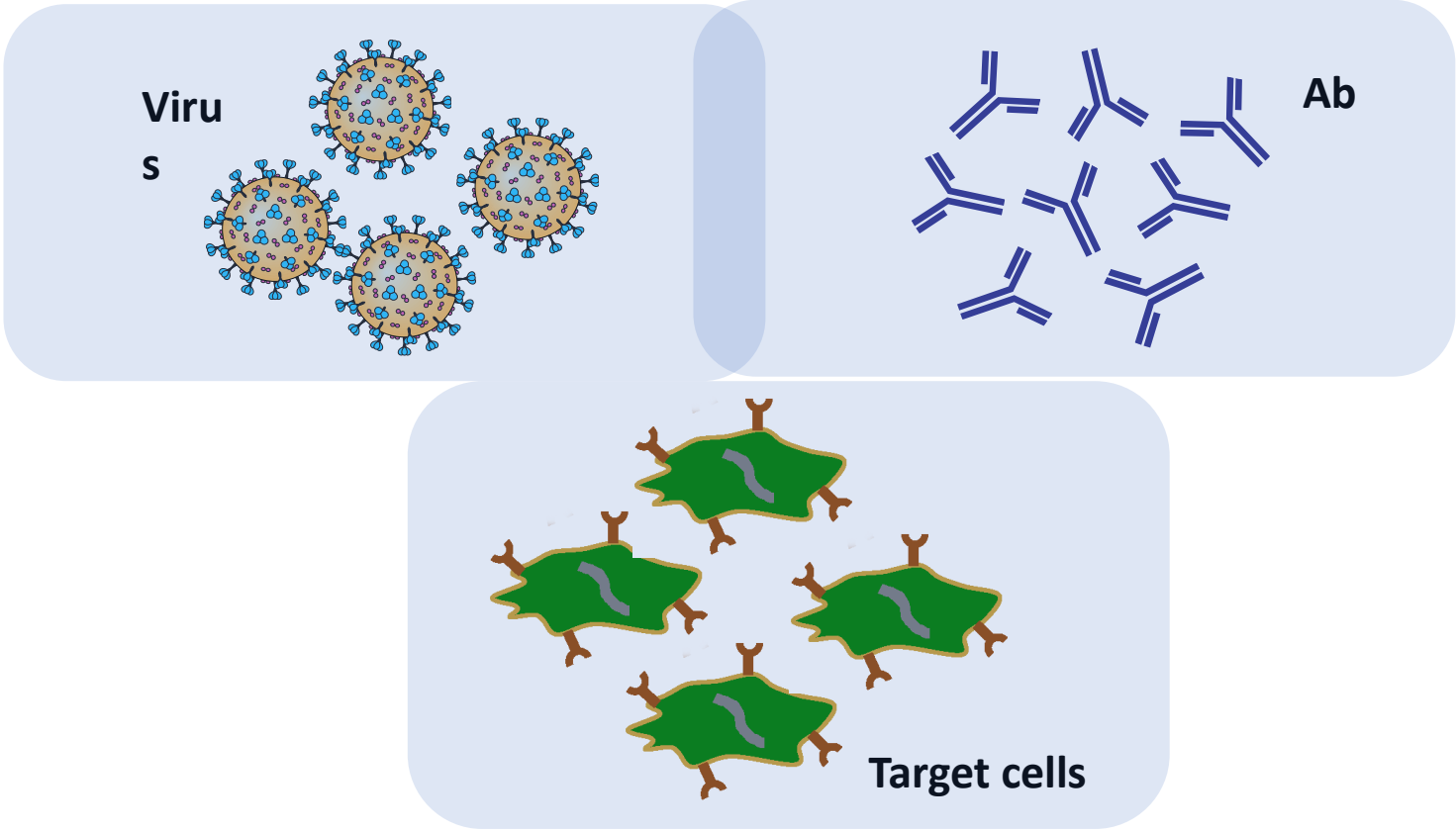
Member, NIH & Infectious Diseases Society of America COVID-19 Treatment Guidelines Panels

Disclosures

Gilead Sciences - Advisory Board Meetings, Scientific Talk

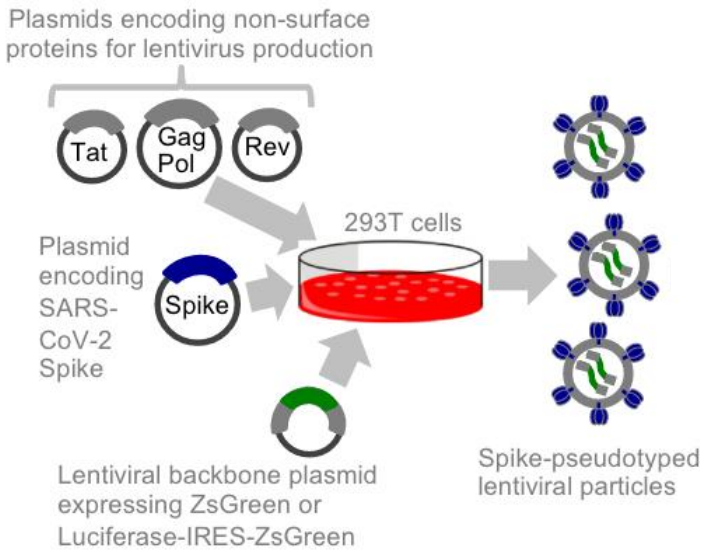
GlaxoSmithKline/Vir - Advisory Board Meetings

Antibody Susceptibility Testing

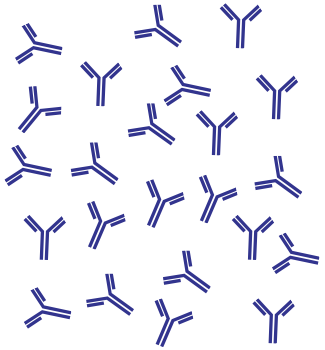


Pseudotyped Virus

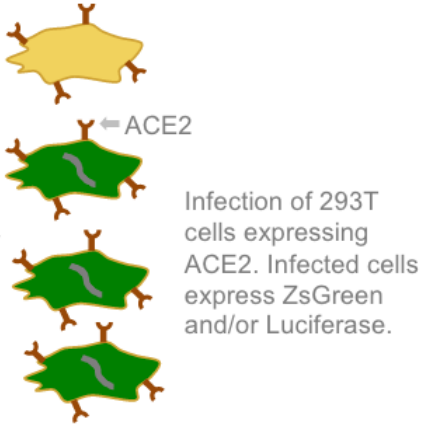
Virus preparation



mAb



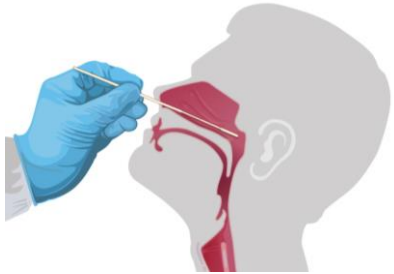
Target cells



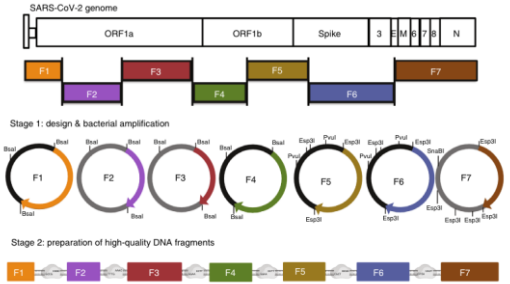
Crawford K. Protocol and Reagents for Pseudotyping Lentiviral Particles with SARS-CoV-2 Spike Protein for Neutralization Assays. Viruses 2020
Schmidt F. Measuring SARS-CoV-2 neutralizing antibody activity using pseudotyped and chimeric viruses. J Exp Med 2020

Infectious Virus

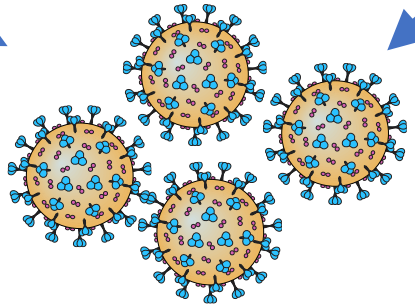
Clinical isolate



Recombinant virus



Plaque purification
Confirmatory sequencing
Titration



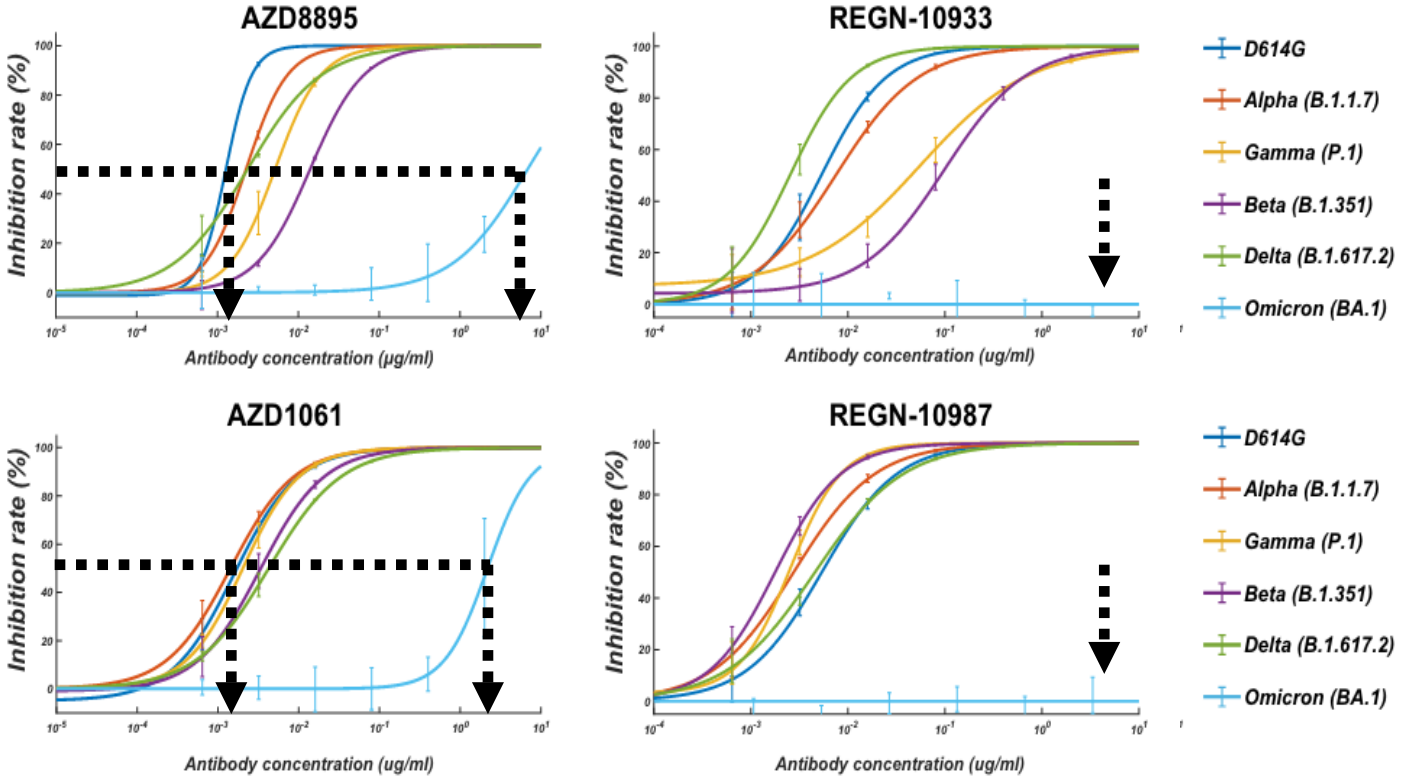
Confirmatory sequencing
Titration

Xie X. Engineering SARS-CoV-2 using a reverse genetic system. Nat Protocol 2021

Assay Conditions

Virus inoculum	• 50% tissue culture infectious dose ($TCID_{50}$) • Multiplicity of infection (MOI) • Relative light units (RLU)
Target cells	• Vero cells, 293T cells • Expression level of ACE2 and TMPRSS2
Measurement	• Cytopathic effect (CPE) • Light or fluorescence

Dose-Response Curves and IC50s

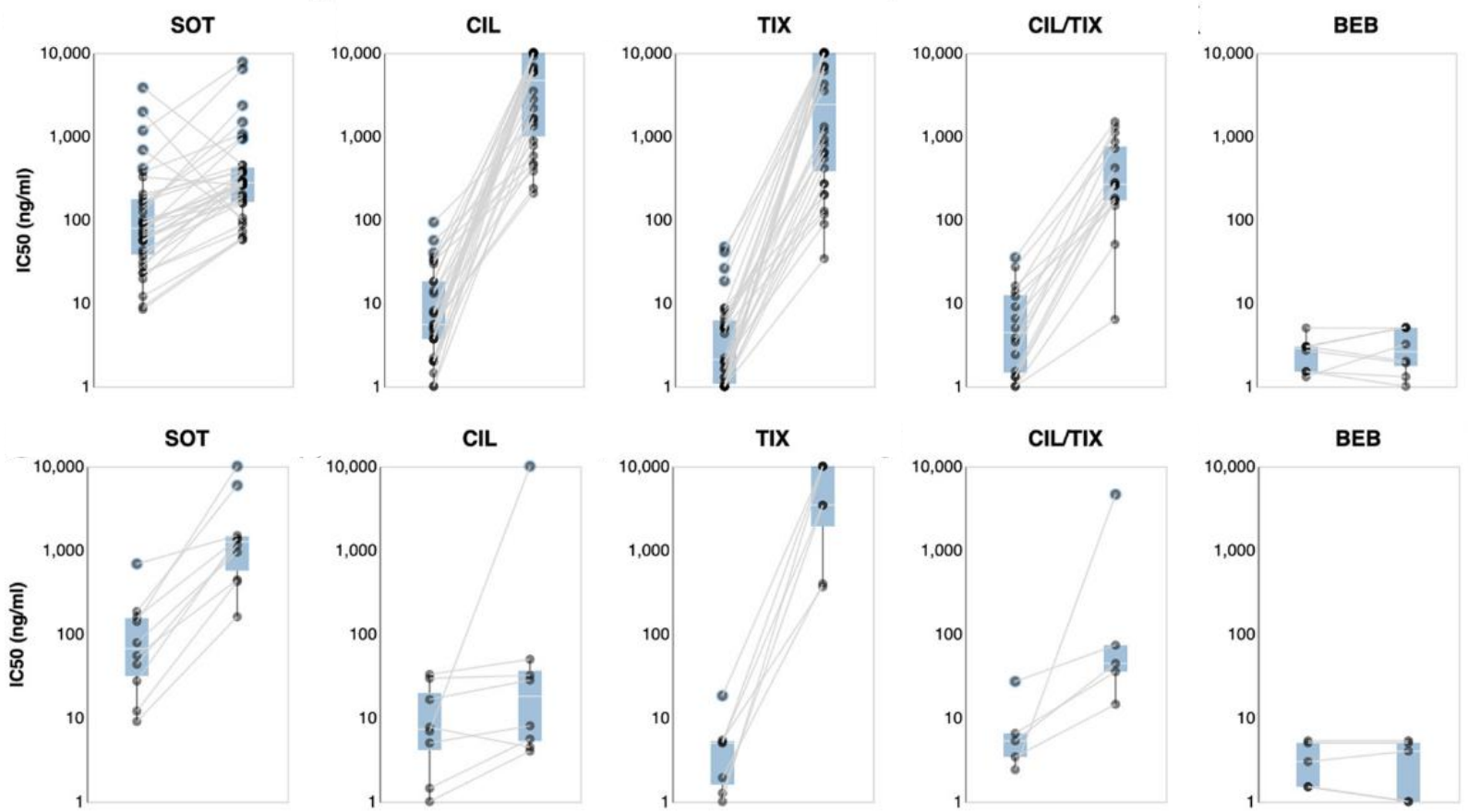


Cao Y. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. Nature 2021

Fold-Reductions in Susceptibility: Reproducibility

BA.1

BA.2



Tao K. Susceptibility of SARS-CoV-2 Omicron Variants to Therapeutic Monoclonal Antibodies: Systematic Review and Meta-analysis. Microbiol Spectrum 2022

Conclusions

Neutralizing Ab susceptibility results are influenced by multiple aspects of assays design.

Results obtained using different approaches are usually concordant.

mAbs achieve extremely high levels in vivo; Substantial losses in activity may be required to completely compromise their activity.

Neutralizing antibody tests do not assess potential non-neutralizing activities which may be relevant for some mAbs.

U.S. Department of Health and Human Services

ASPR Administration for Strategic Preparedness & Response

COVID-19 Therapeutics Update

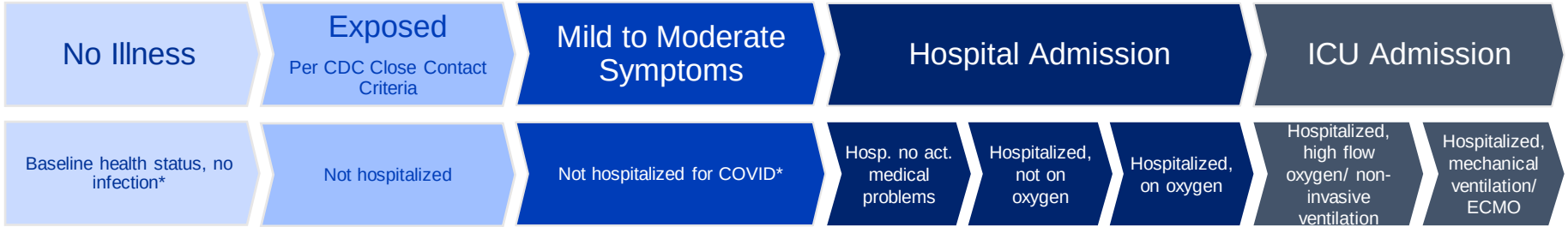
Meghan Pennini, PhD
Chief Therapeutics Officer
HHS Coordination Operations and Response Element (H-CORE)/ASPR

November 12, 2022

https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx

Unclassified/For Public Distribution

Summary of COVID-19 Preventative Agents & Outpatient Treatments



COVID-19 Vaccines

Monoclonal Antibodies for PrEP

- Evusheld (tixagevimab + cilgavimab, AZ)

None currently authorized for use in any US state or territory.

Oral Antivirals

- **Paxlovid (nirmatrelvir + ritonavir, Pfizer)**
- Lagevrio (molnupiravir, Merck) – **Alternative**

Monoclonal Antibodies

- Bebtelovimab (Lilly) – **Alternative**

IV Antiviral

- **Veklury® (remdesivir, Gilead)**

Please see NIH Current Inpatient Therapies
(https://www.covid19treatmentguidelines.nih.gov/therapies/)

There is currently **ample supply** of all authorized and approved therapeutics – every eligible patient should have access to these medications

HHS distribution

Commercially available

*refer to individual product Fact Sheets for authorization details

Therapeutic Management of Nonhospitalized Adults With COVID-19

Therapeutic Management of Hospitalized Adults With COVID-19

Related Resources

Helpful Information and Resources

- HHS Therapeutics Homepage
- Product Expiration Date Extensions
- Test to Treat Initiative webpage and Fact Sheet
- Test to Treat Site Locator and Digital Tool Kit
- General Therapeutics Locator
- HHS Clinical Implementation Guide
- Outpatient Therapeutics Decision Aid
- Side-by-Side Overview of Outpatient Therapeutics
- ASPR Regional Emergency Coordinators
- CMS reimbursement information for mAbs
- CMS reimbursement information for oral antivirals

Latest COVID-19 Therapeutics Updates Found at aspr.hhs.gov

Q&A/
Discussion

Selected Resources

Monkeypox Update – Dr. Cope:

- https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html
- https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html
- Treatment Information for Healthcare Professionals | Monkeypox | Poxvirus | CDC
- Kirk Chan-Tak, MD, U.S. Food and Drug Administration
  https://societycentral.zoom.us/rec/share/lwGP3XMUCXcF4bxqVrBWz2EeO2M9lLSmNgGng3-2RukWUUML2t2gKoNsjkDU7_jV.FRGPMimWRP_NtzAJ?startTime=1668026706000

  Passcode: pFvdP4%^

Update on Emerging SARS-CoV-2 Subvariants – Dr. Thornburg

- https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-omicron-subvariants

Impact of SARS-CoV-2 Subvariants on Therapeutic Effectiveness

Dr. Gandhi

- https://twitter.com/abrahamlabhms
- Iketani Nature 2022; Arora Cell Host Microbe 2022; Dougan medRxiV 2022; NIH Treatment Guidelines; Westendorf Cell Rep 2022
- https://www.fda.gov/media/154701/download
- https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#immunocompromised
- https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Dr. Werbel

- https://www.idsociety.org/globalassets/covid-19-real-time-learning-network/outpatientroadmap-v10.pdf

Selected Resources

Dr. Pennini:

- https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx
- https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-adults/nonhospitalized-adults--therapeutic-management/
- https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/expiration-dating-extension#COVIDtherapeutics
- https://covid-19-test-to-treat-locator-dhhs.hub.arcgis.com/ and https://aspr.hhs.gov/TestToTreat/Pages/digital-toolkit.aspx
- https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/
- https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/USG-COVID19-Tx-Playbook.pdf
- https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/side-by-side-overview.pdf
- https://aspr.hhs.gov/REC/Pages/default.aspx
- https://www.cms.gov/medicare/medicare-part-b-drug-average-sales-price/covid-19-vaccines-and-monoclonal-antibodies
- https://www.cms.gov/files/document/hpms-memo-oral-antiviral-guidance.pdf

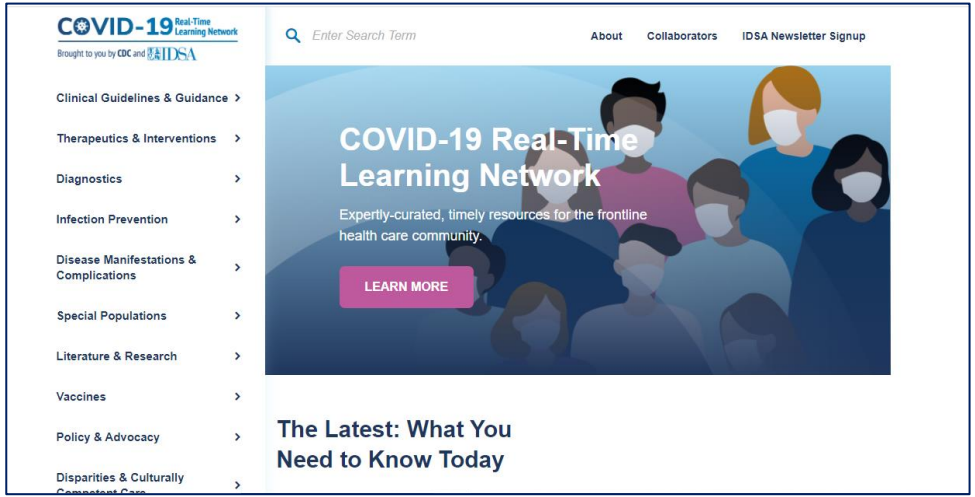
Program Links:

- This webinar is being recorded and can be found with the slides online at https://www.idsociety.org/cliniciancalls
- COVID-19 Real-Time Learning Network: https://www.idsociety.org/covid-19-real-time-learning-network/
- Vaccine FAQ: https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines-information--faq/

COVID-19 Real-Time Learning Network

Brought to you by CDC and IDSA

An online community bringing together information and opportunities for discussion on latest research, guidelines, tools and resources from a variety of medical subspecialties around the world.



Specialty Society Collaborators

American Academy of Family Physicians
American Academy of Pediatrics
American College of Emergency Physicians
American College of Obstetricians & Gynecologists
American College of Physicians
American Geriatrics Society
American Thoracic Society
Pediatric Infectious Diseases Society
Society for Critical Care Medicine
Society for Healthcare Epidemiology of America
Society of Hospital Medicine
Society of Infectious Diseases Pharmacists

www.COVID19LearningNetwork.org
@RealTimeCOVID19
#RealTimeCOVID19

CDC-IDSA Partnership: Clinical Management Call Support

FOR WHOM?

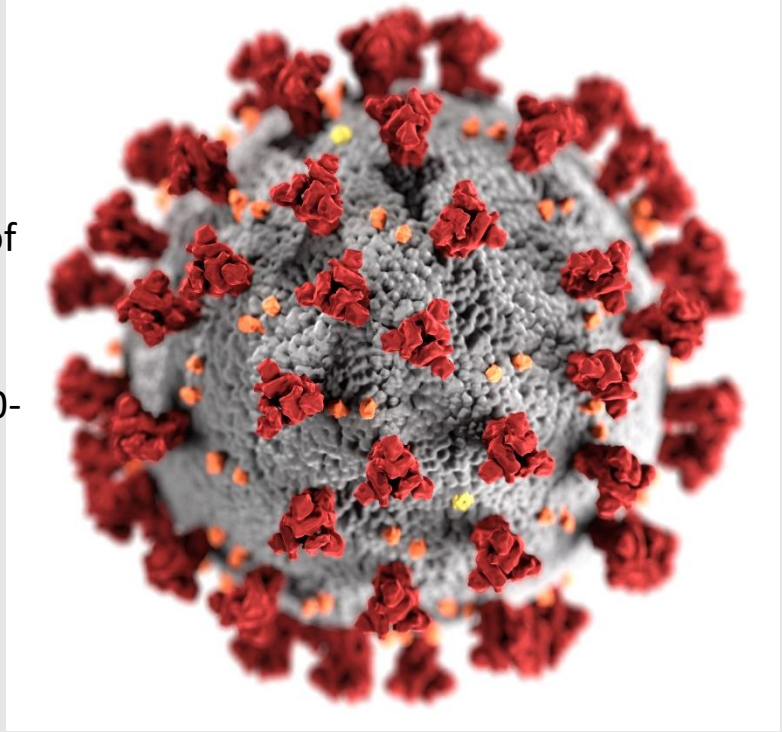
- Clinicians who have questions about the clinical management of COVID-19

WHAT?

- Calls from clinicians will be triaged by CDC to a group of IDSA volunteer clinicians for peer-to-peer support

HOW?

- Clinicians may call the main CDC information line at 800-CDC-INFO (800-232-4636)
- To submit your question in writing, go to www.cdc.gov/cdc-info and click on Contact Form



IDSA
Infectious Diseases Society of America

cdc.gov/coronavirus

THANK YOU

We want to hear from you!

Please complete the post-call survey.

A recording of this call, slides and the answered Q&A will be posted at
www.idsociety.org/cliniciancalls

-- library of all past calls available --

Contact Us:

Dana Wollins (dwollins@idsociety.org)
Deirdre Lewis (dlewis@idsociety.org)