Please use your first name and health center name when you join the session.

Use the “chat” feature to let us know if you have a question.

Please remember to mute your microphone unless speaking.

If you can’t connect audio via computer or lose computer audio at anytime, you can call in to session at (669) 900-6833, Meeting ID 958-5486-4417##
Disclosures

• No one in a position to control the education content of the activity has any relevant financial disclosures with ineligible companies to disclose.

• What gets said here today may change based on new data and recommendations
  – Knowledge is shared more rapidly through ECHO
Agenda

• Prevention and treatment of SARS-CoV-2
  • Monoclonal antibodies
  • Drugs
• COVID Update
  • BA-2
  • Vaccine effectiveness
  • Urban vs rural vaccination rates
Prevention Options

- Vaccination
  - Not the focus today but the best prevention available for those who can get it!
- Monoclonal antibody
Tixagevimab and Cilgavimab (Evusheld)

- Given intramuscularly in outpatient setting
- Child/adolescent ≥12 years of age and weighing ≥40 kg, and
- No SARS-CoV-2 infection or exposure and not currently infected with SARS-CoV-2 and
- Moderately or severely immunocompromised from an underlying condition or medication that does not allow for an adequate immune response to COVID-19 vaccination
  - Known underlying primary immunodeficiency (i.e., DiGeorge syndrome, Wiskott-Aldrich syndrome)
  - Untreated or advanced HIV infection
  - Hematopoietic cell transplantation in the previous 2 years and lack of immune reconstitution or taking immunosuppressive medications
  - Receipt of a solid organ transplant within the last 3 months and receiving immunosuppressive medications leading to moderate/severe immunocompromise
  - Receipt of chimeric antigen receptor (CAR) T-cell therapies in the previous 2 years
  - Receiving active chemotherapy for malignancies
  - Actively receiving treatment with immunosuppressive medications leading to moderate/severe immunocompromised (e.g. high dose steroids, TNF blockers, rituximab or other B-cell directed therapies)

- The duration of protection against variants is being evaluated and may not be as long as initial described in clinical trials (i.e., 6 months)
  - There are no recommendations for optimal timing for repeated doses due to uncertainty about variant formation

Treatment
Treatment of Non-hospitalized

- Supportive/symptomatic care with NSAID’s or acetaminophen
  - For most people that is enough to get by
- Insufficient evidence for or against zinc or vitamins C or D
- Recommend against oral steroids, azithromycin, ivermectin, chloroquine/hydroxychloroquine, colchicine, ASA/anticoagulants
- For those with mild-moderate disease consider
  - Monoclonal antibodies
  - Oral or iv antivirals

Outpatient Treatment Options

• Monoclonal antibodies
  • Sotrovimab
  • Bebtelovimab

• Parenteral products
  • Remdesivir

• Oral antivirals
  • Paxlovid (nirmatrelvir and ritonavir)

Monoclonal Antibodies
**Sotrovimab**

- Nonhospitalized patient ≥12 years of age and weighing ≥40 kg, **and**
- Laboratory-confirmed SARS-CoV-2 infection, **and**
- Mild to moderate COVID-19, **and**
- Within 10 days of symptom onset, **and**
- High risk for progressing to severe COVID-19 and/or hospitalization
  - **Not for use in**
    - Patients hospitalized for COVID-19; **or**
    - Patients who require oxygen therapy for COVID-19; or who require an increase in oxygen in those already receiving it for other, non–COVID-19 related, underlying conditions

**Bebtelovimab**

- Nonhospitalized patient ≥12 years of age and weighing ≥40 kg, **and**
- Laboratory-confirmed SARS-CoV-2 infection, **and**
- Mild to moderate COVID-19, **and**
- Within 7 days of symptom onset, **and**
- High risk for progressing to severe COVID-19 and/or hospitalization

Who Should Get Treated with a Monoclonal Ab

- Limited by drug availability so will change based on supplies and space
- FDA EUA allows use children ≥12 years of age, weighing ≥40 kg who are high risk
  - BMI ≥85th percentile for age and gender
  - Immunosuppressive disease or receipt of immunosuppressive therapies
  - Neurodevelopmental or psychiatric disorders (i.e., cerebral palsy, trisomy 21, severe mood disorder, substance use disorder)
  - Technological dependence that is not related to COVID-19 (i.e., tracheostomy, positive pressure ventilation, gastrostomy)
  - Sickle cell disease
  - Congenital or acquired functional heart disease
  - Chronic lung disease that requires daily medication for control
  - Diabetes
  - Chronic kidney disease
  - Chronic liver disease (i.e., cirrhosis, autoimmune hepatitis)
  - Pregnancy
- Age <1 year with admission to the ICU or mechanical ventilation, and has prematurity (gestational age <37 weeks) as a risk factor for severe COVID-19

Remember this list as it applies to all the treatment options

Monoclonal Antibody Use and Side Effects

• Administration
  • IV infusion: one hour infusion, then one hour observation
  • Be able to manage anaphylaxis so usually given in infusion center (exception is Evusheld which is an injection and can be given in office setting)

• Side effects
  • Local injection site reactions (4%-12%)
  • Infusion-related reactions (rare)
    • Fever, chills, SOB, dizziness, abdominal pain, nausea, vomiting, flushing, pruritus, and anaphylaxis like any antibody product

Oral Agents
Paxlovid (Nirmatrelvir and Ritonavir)

• Protease inhibitor
  • In vitro data confirm that nirmatrelvir is a potent inhibitor of the Omicron

• High-risk patients ≥12 years old enrolled in EPIC-HR study (n= 2,246), compared to placebo:
  • 89% reduced risk of hospitalization or death if given within three days of symptom onset
  • 88% reduced risk of hospitalization or death if given within five days of symptom onset
  • 70% reduction in hospitalization and no deaths in the treated population in EPIC-SR trial

• For mild to moderate COVID
  • Not for hospitalized patients

• For patients at high risk for severe disease
• Use for people ≥12yo and ≥40kg
Paxlovid

• 3 pills (2 are nirmatrelvir and 1 is ritonavir) BID for 5 days
• Start within 5 days of symptom onset
• Side effects
  • Diarrhea, hypertension, myalgia, altered sense of taste
  • All <3% which was less than placebo
• Pregnancy is not a contraindication
• Do not use for those with:
  • Chronic kidney GFR < 30 (reduce dose if GFR 30-59)
  • Severe hepatic impairment (Child-Pugh Class C)
    • Caution if any liver disease or LFT abnormality
  • Uncontrolled HIV
• Getting easier to find
• Huge number of drug-drug interaction

Paxlovid

• Many drug-drug interactions; before dispensing, check:
  • Liverpool COVID-19 Drug Interactions: [www.covid19-druginteractions.org](http://www.covid19-druginteractions.org)
  • EUA Fact Sheet for Providers for Paxlovid: [www.fda.gov/media/155050/download](http://www.fda.gov/media/155050/download)

Paxlovid Drug-drug Interactions – examples

• Preclude use: many anticonvulsants; clopidogrel, clozapine, rifampin, salmeterol, St. John’s wort
• If possible, might be held while taking Paxlovid: some benzodiazepines, opioids, statins; sildenafil, tamsulosin
• Consider lower dose or careful monitoring: calcium channel blockers, clarithromycin, warfarin, HIV meds
• Some systemic corticosteroids may have increase risk for Cushing’s and adrenal suppression – consider change to beclomethasone or prednisolone
• Oral contraceptives – may decrease efficacy, use backup contraception
• HIV, cancer, immunosuppressive meds: consider consult with patient’s specialist

Modified slide from Paul Lunning of PCC Wellness
Molnupiravir Mechanism

• Generally increases the frequency of viral RNA mutations and impairs Sars-CoV-2 replication

• When the RdRp within the virus allows this to happen, the active metabolite gets incorporated and causes mutated RNA products

• These RNA products form stable base pairs resulting in chain termination and a decrease in RNA synthesis

• reduced the risk of hospitalization or death from 9.7% in the placebo group (68/699) to 6.8% (48/709) in the molnupiravir group, for an absolute risk reduction of 3.0% (95% confidence interval [CI]: 0.1, 5.9; nominal p-value=0.0218) and a relative risk reduction of 30%”

  • Not clear if worth the risk given uncertainty about the side effect profile, vote by FDA after more data was 13 in favor 10 against
Molnupiravir

- Not for <18 years old
- 800 mg twice daily PO regimen x 5 days
- Give within 5 days symptom onset
- Only if other therapies are unavailable or not feasible
- Risk for mutagenesis,
  - contraindicated in pregnant patients,
  - Only for use in those >18 years old
  - Female patients of child-bearing age should be on effective
  - Contraception during therapy and for 4 days after
  - Male patients who are sexually active with females should use contraception during
    treatment and for 3 months after

- Efficacy: 30% reduction in hospitalizations/death, not clear it is worth the risk
Parenteral Agents
Remdesivir

• Only drug approved by the FDA for the treatment of COVID-19 (≥12 years)
  • EUA includes treatment of high-risk children who weigh at least 3.5 kg with
  • laboratory-confirmed SARS-CoV-2, and
  • are within 7 days of symptom onset, and
  • are at high risk for progression to severe COVID-19, and
  • not hospitalized for COVID-19

• In a randomized, double-blind, placebo-controlled trial of non-hospitalized patients ≥12 years of age and having at least one high-risk factor for COVID-19 disease progression showed 87% reduction in risk of hospitalization, little data in those under 12 years old

• Dosage depends on age and weight as follows:
  • 3.5 kg to 40 kg: remdesivir 5 mg/kg on day 1 (loading dose), followed by 2.5 mg/kg once daily on
day 2 and 3
  • ≥12 years and ≥40 kg: remdesivir 200 mg on day 1 (loading dose), followed by 100 mg IV daily on
days 2 and 3
  • The dose is given once daily on 3 consecutive days; the intravenous infusion is administered over
30 to 120 minutes and monitor for nausea, headache, and cough during and for at least 1 hour
after the dose
  • Adverse events were infrequent (0.7% vs 5.3% compared with placebo)

Treatment Options for High-Risk Nonhospitalized Patients With Mild to Moderate COVID-19

**Sotrovimab IV**
- 500mg IV dose x 1
- Give within 7-10 days symptom onset
- Well tolerated, no significant drug-drug interaction
- IV infusion over 60 min + 60 min clinical monitoring
- Efficacy: 85% reduction hospitalizations/death
- Age 12 years and ≥ 40 kg

**Remdesivir IV**
- 200mg IV x 1, then 100mg q24hrs x 2 IV (3 total days)
- Give within 7 days symptom onset
- Well tolerated, no significant drug-drug interaction
- IV infusion over 60 min
- Contraindicated if ALT > 10xULN
- Efficacy: 87% reduction hospitalizations
- Approved for ≥12 yrs and ≥40 kg; also authorized for <12 years and ≥3.5 kg

**Nirmatrelvir/ritonaviravir (Paxlovid) PO**
- 300mg/100mg twice daily PO regimen x 5 days, dose reduce for GFR
- Give within 5 days of symptom onset
- Significant risk for drug-drug interactions (potent CYP3A4 inhibitor)
- Efficacy: 88% reduction hospitalizations/death
- Age >12 years and ≥40 kg

**Molnupiravir PO (not for <18 years old)**
- 800mg twice daily PO regimen x 5 days
- Give within 5 days symptom onset
- Only if other therapies are unavailable or not feasible
- Risk for mutagenesis, contraindicated in pregnant patients,
  - Only for use in those >18 yrs old
  - Female patients of child-bearing age should be on effective contraception during therapy and for 4 days after
  - Male patients who are sexually active with females should use contraception during treatment and for 3 months after
- Efficacy: 30% reduction in hospitalizations/death, not clear it is worth the risk

### Comparison of Recommended Outpatient Therapies*

<table>
<thead>
<tr>
<th></th>
<th>Paxlovid™ (1)</th>
<th>Sotrovimab (2)</th>
<th>Remdesivir (3)</th>
<th>Molnupiravir (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age allowed for use</strong></td>
<td>≥12 yr</td>
<td>≥12 yr</td>
<td>All ages, ≥3.5kg</td>
<td>≥18 yr</td>
</tr>
<tr>
<td><strong>Initiate within # of days of symptom onset</strong></td>
<td>5 days</td>
<td>10 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
<tr>
<td><strong>Route of Administration</strong></td>
<td>PO</td>
<td>IV</td>
<td>IV</td>
<td>PO</td>
</tr>
<tr>
<td><strong>Duration of Therapy</strong></td>
<td>5 days</td>
<td>1 time infusion</td>
<td>3 days</td>
<td>5 days</td>
</tr>
<tr>
<td><strong>Pros</strong></td>
<td>-High efficacy -Oral</td>
<td>-High efficacy -Single IV infusion</td>
<td>-High efficacy -Greater experience</td>
<td>-Oral -No drug-drug interaction concerns</td>
</tr>
<tr>
<td><strong>Cons</strong></td>
<td>-Ritonavir-related drug-drug interactions</td>
<td>-Requires IV infusion</td>
<td>-Requires 3 days of IV infusion -FDA approved for ≥12yr, weighing at least 40kg. -EUA for all other pediatric patients weighing at least 3.5kg</td>
<td>-low efficacy -Not authorized for age 12-17 years -Not approved for pregnancy -Concerns for mutagenicity</td>
</tr>
<tr>
<td><strong>Supply Availability</strong></td>
<td>Limited supply</td>
<td>Limited supply</td>
<td>Commercially available</td>
<td>More supply than Paxlovid™ &amp; Sotrovimab</td>
</tr>
<tr>
<td><strong>Efficacy (prevention of hospitalization or death)</strong></td>
<td>Relative risk reduction: 88%</td>
<td>Relative risk reduction: 85%</td>
<td>Relative risk reduction: 87%</td>
<td>Relative risk reduction: 30%</td>
</tr>
</tbody>
</table>
COVID-19 Update
The BA.2 Omicron sublineage has displaced the original strain and is driving new surges in cases across Europe, with Denmark and the Netherlands now past their BA.2 peaks.

7-day average of new confirmed cases per 100k people, by variant*

*Each variant's share of all cases estimated using method from Tom Wenseleers / @TWenseleers, then applied to case rates
Source: FT analysis of data from Johns Hopkins CSSE, World Health Organization and Gisaid
FT graphic: John Burn-Murdoch / @burnmurdoch
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Vaccine Effectiveness Over Time and Number of Doses: US Data August 2021- January 2022

VE against Omicron ED/UC Encounter

VE against Omicron Hospitalization

[Graphs showing vaccine effectiveness over time and number of doses for ED/UC encounters and hospitalization for Omicron cases, with lines indicating the percentage of vaccine effectiveness declining over time for both 2 doses and 3 doses.]
COVID-19 vaccination coverage of a 1st dose of vaccine was lower in rural (58.5%) than in urban counties (75.4%).

Receipt of booster or additional doses was similar.
Questions?
Implementation Support

• Peer support from a clinician in your geographical region.
• Available in each of the 11 COVID-19 regions of the state.
• Support throughout the process – no question is too small!

Fill out a form at:
• illinoisvaccinates.com under implementation support
OR
• Email facts@illinoisvaccinates.com

REQUEST SUPPORT FROM A REGIONAL ADVISOR

Please fill out the form below to connect with a regional I-VAC advisor. Please allow one to three business days for their response.

Name
First
Last
Number
Role
Email
Next Session: Tuesday, April 12th

For any questions, email us at pgower@peds.bsd.uchicago.edu