I-VAC Pediatric Learning Collaborative for COVID-19 Vaccination

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I-VAC ILLINOIS VACCINATES AGAINST COVID-19

THE UNIVERSITY OF CHICAGO Department of Pediatrics Established 1930

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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
- COVID Update
  - Schools

References

https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/outpatient-covid-19-management-strategies-in-children-and-adolescents/

https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-children/clinical-management-of-children-summary/?utm_source=site&utm_medium=home&utm_campaign=highlights

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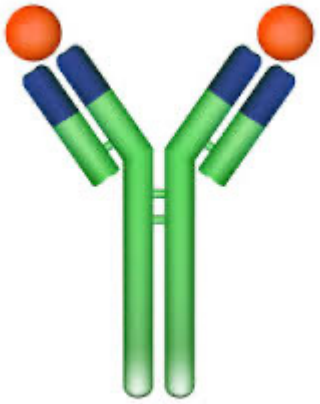
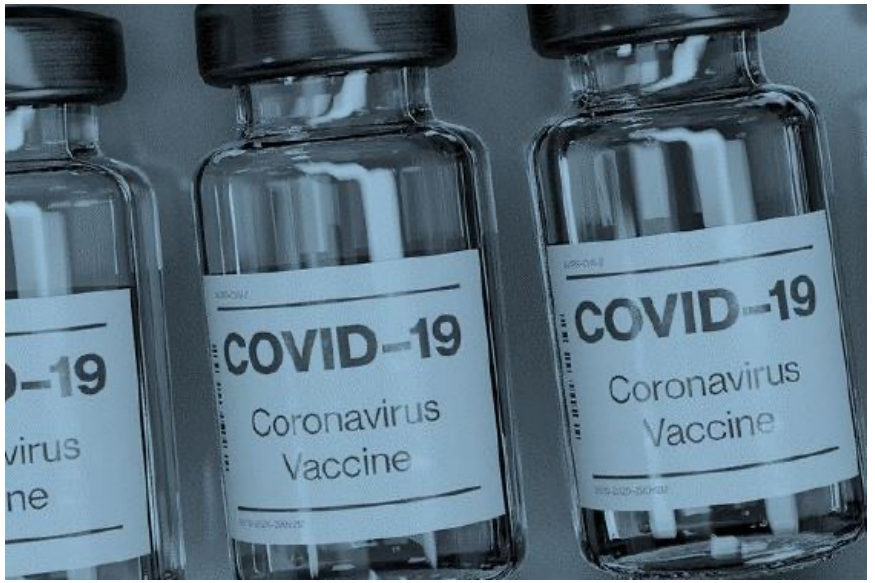
Prevention

Prevention Options

- Vaccination
  - Not the focus today but the best prevention available for a few months after completing the series
- Monoclonal antibody





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Tixagevimab and Cilgavimab (Evusheld)

- Pre-exposure prophylaxis only
- 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, Bruton's, Wiskott-Aldrich syndrome)
  - Untreated or advanced HIV infection
  - Hematopoietic cell transplantation in the previous 2 years and lack of immune reconstitution or on immunosuppressives
  - Receipt of a solid organ transplant within the last 3 months and receiving immunosuppressive medications
  - Receipt of chimeric antigen receptor (CAR) T-cell therapies in the previous 2 years
  - Receiving active chemotherapy for malignancies
  - On treatment with medications leading to moderate/severe immunocompromised (e.g. high dose steroids, TNF blockers, rituximab or other B-cell directed therapies)
- Protection and duration of protection against new variants is always a question but so far so good
- 300 mg of tixagevimab and 300 mg of cilgavimab as two separate IM injections

https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/outpatient-covid-19-management-strategies-in-children-and-adolescents/

Treatment for Non-Hospitalized People

Treatment of Non-hospitalized Patient with No Change or Need for Oxygen

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

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When to Considered Drug Treatment for Kids

- 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 including asthma that requires ≥2 inhaled or ≥1 systemic medications daily
- Diabetes
- Chronic kidney disease
- Chronic liver disease (i.e., cirrhosis, autoimmune hepatitis)
- Pregnancy
- Children < 1 years old who were premature (<37 weeks gestation)?

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Outpatient Treatment Options

- Oral antivirals
  - Paxlovid (nirmatrelvir and ritonavir)
- Parenteral products
  - Remdesivir
- Monoclonal antibodies
  - Bebtelovimab

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Oral Agents

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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 (Delta variant):
  - 88% - 89% reduced risk of hospitalization or death if given within 5 days of symptom onset
- For mild to moderate COVID
  - Not recommended for patients hospitalized due to COVID
- For patients at high risk for severe disease as previously stated
- Use for people ≥12yo and ≥40kg

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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, <3% which was less than placebo
  - Altered sense of taste (6%)
  - Rebound once stopped of 1-5%
- 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
- Huge number of drug-drug interaction

https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/outpatient-covid-19-management-strategies-in-children-and-adolescents/

Paxlovid

- Many drug-drug interactions; before dispensing, check:
  - Liverpool COVID-19 Drug Interactions: www.covid19-druginteractions.org
  - NIH: www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions
  - EUA Fact Sheet for Providers for Paxlovid: www.fda.gov/media/155050/download

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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

Molnupiravir

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

- Only if other therapies are unavailable or not feasible
- Only for ≥18 years old
- 800 mg twice daily PO x 5 days
- Give within 5 days symptom onset
- 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

Parenteral Agents for Outpatient Treatment

Remdesivir

- Approved by the FDA for the treatment of COVID-19 (≥28 days old and who weigh at least 3 kg)
- 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 with 3 days of remdesivir
  - Little data in those under 12 years old but safety and efficacy in CARAVAN trial for children >3 kg documented (n= 53)
- Treatment to be considered for children 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
- 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 - 120 minutes and monitor for nausea, headache, and cough for at least 1 hour after the dose
- Adverse events were infrequent (0.7% placebo vs 5.3% remdesivir)

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Monoclonal Antibodies

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
- Dose is 175 mg administered as a single intravenous injection over at least 30 seconds
- 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

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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
- 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

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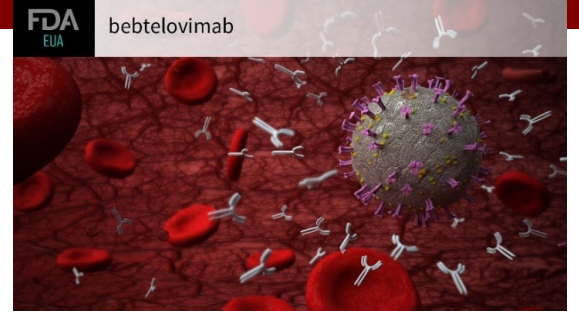
Bebtelovimab is Transitioning to the Commercial Marketplace



- Medicaid will pay for the cost of the bebtelovimab and its administration without the requirement for cost sharing through the last day of the first calendar quarter that begins one year after the last day of the Public Health Emergency
- No cost sharing (no copayment/coinsurance or deductible) for monoclonal antibody therapies to treat COVID-19 for people with Medicare fee-for-service and Medicare Advantage beneficiaries for the duration of the calendar year in which the COVID-19 public health emergency ends
- Lilly and the US government are developing a path to ensure access of bebtelovimab for the under- and uninsured populations during the transition to commercialization
- Clinical sites with an excess of bebtelovimab starting the week of August 15, 2022, should prioritize the US government-supplied drug for the under- and uninsured patients at their sites and use the commercially available supply for those with Medicare, Medicaid and private insurance
- Most recent cost cited is around $2500 per dose plus infusion cost
- For any questions regarding product access, please contact c19therapies@amerisourcebergen.com

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https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-11August2022.aspx

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Summary Table

	ANTIBODIES		ANTIVIRALS		
	Bebtelovimab	**Evusheld**	**Paxlovid**	**Remdesivir**	**Molnupiravir**
COVID-19 indication	Treatment	Preexposure prophylaxis	Treatment	Treatment	Treatment
Approved age (y), weight (kg)	≥12 y	≥12 y	≥12 y	28 days and ≥3.5 kg	≥18 y
Route	IV	IM	PO	IV	PO
Symptom onset, in days	≤7	n/a	≤5	≤7	≤5
Duration of therapy, in days	One time	n/a	5	3	5
Other considerations	• Requires IV infusion x1	• Intramuscular administration at 2 sites (larger muscle groups preferred, e.g., gluteal) • Little pediatric data	• Drug-drug interactions • Little pediatric data • No liquid formulation	• Requires IV infusion on 3 consecutive days and post-infusion monitoring • Operational and reimbursement challenges	• Not recommended in pregnancy and children • Lower efficacy, thus use only when other treatment agents cannot be used • Little pediatric data • Concerns for mutagenicity (low, based on animal studies)

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COVID-19 Update

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School Year is About to Start

- Vaccination, vaccination, vaccination
- If an employee or student is sick, stay home and test
  - One rapid test doesn't exclude SARS-CoV-2 infection – at least 2 tests 24-48 hours apart
- Encourage kids to wear a mask in the classroom, especially if living with someone high risk
- Encourage schools to maximize ventilation
  - Open windows and doors where possible
  - Keep fans running to maximize air exchanges
  - Clean air filters
  - Support with hepa-filters if poor air movement
- Use of hand sanitizers
- Transmission is less about schools and more about steps outside of schools

Masking and Vaccination Makes a Difference

- Dates were pre-Omicron
- Boston University
- No physical distancing

August 5, 2022

Examination of SARS-CoV-2 In-Class Transmission at a Large Urban University With Public Health Mandates Using Epidemiological and Genomic Methodology

Kayla Kuhfeldt, MPH[1]; Jacquelyn Turcinovic, BS[2,3,4]; Madison Sullivan, MPH[1]; et al

» Author Affiliations | Article Information

JAMA Netw Open. 2022;5(8):e2225430. doi:10.1001/jamanetworkopen.2022.25430

Key Points

Question Is there evidence of in-class transmission of SARS-CoV-2 on a university campus that had mandated vaccination and masking?

Findings In this cohort study of 140 000 class meetings at a large US university, there were over 850 cases of SARS-CoV-2 infection identified through weekly surveillance testing of all students and faculty on campus during the fall 2021 semester. There were 9 instances of potential in-class transmission identified as identical lineages confirmed by SARS-CoV-2 genome sequencing, and none of these instances were confirmed to be in-class transmission.

Meaning These results suggest that in-class transmission of SAR-CoV-2 in an urban university with masking and vaccine protocols in-place was negligible.

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Questions?

CME credits

You can claim CME credits for all IVAC Pediatric Learning Collaborative sessions between May-August 2022 together. Attendance will be sent out next week.

Next Session: Tuesday, October 11th

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

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