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Podcast Contributor Show Notes

New Outpatient Treatment Options for Covid-19

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Sample Tweet: There are so many NEW outpatient treatments for #COVID19 that it can be hard to keep up, especially with the omicron variant! Which med is best for which patient? How do we find it or prescribe it? What about PrEP? Listen to this FREE bonus piece, as Academic ID expert @pateldevangm breaks it all down for us in this timely conversation. Then, download the free quick reference table! [Insert hyperlink to bonus on the PC RAP page and for the image, use the designed covid medication table]

Title: New Outpatient Treatment Options for Covid-19

Objectives:
- Explore how the landscape of covid treatment options has changed since the start of the pandemic
- Review the indications, administration modalities, and outcomes of multiple newer covid-19 therapeutics, including nirmatrelvir/ritonavir, sotrovimab, and molnupiravir
- Describe the pre-exposure prophylaxis option that is available for high-risk patients

Summary:
So much has changed since the start of the Covid-19 pandemic, including all the new treatment options for outpatients with SARS-CoV-2 infection. From oral medications to IV infusions, the range of options can feel overwhelming. Which treatment should we prescribe when? And for which patients? How does the omicron variant surge affect our choices? What's even available? In this Hippo Education bonus, academic Infectious Diseases expert and medical educator Dr. Devang Patel joins host Dr. Neda Frayha to break it all down for us. As an added bonus, download and share our free quick reference medication table!

Resources:
- **Hippo Education's Quick Reference Table for Outpatient Treatment and Pre-Exposure Prophylaxis Options for SARS-CoV-2 Infection**

- Department of Health and Human Services (HHS) Covid-19 Therapeutics Locator
- HHS Protect Public Data Hub – Therapeutics Distribution
- National Infusion Center Association (NICA)
- State and Territorial Health Department Websites

References:

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Tags:
Infectious Disease, ID, Public Health

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Neda Intro: So much has changed since the start of the Covid-19 pandemic, including all the new treatment options for outpatients with SARS-CoV-2 infection. From oral medications to IV infusions, the range of brand new treatment options can feel overwhelming. Which medication should we prescribe when? For which patients? How does the omicron surge affect our choices? What's even available?

I'm Dr. Neda Frayha, a primary care internist and host of Hippo Education's Primary Care Reviews and Perspectives podcast. Today we're excited to bring you a conversation with academic infectious diseases expert Dr. Devang Patel, so we can share the most practical information front-line clinicians need to know about outpatient treatments for covid-19.

Main Talking Points:
Broadly, how has the landscape of covid-19 treatment options changed since the start of the pandemic?
[Answer]

For many of our healthy outpatients, treatment will still consist of supportive care - rest, fluids, symptom management. Who counts as "high-risk" and should receive the covid-19 treatments we're about to discuss?

- Very broad list as defined by the CDC and NIH
- Over age 65
- Medical conditions such as cancer, CKD, chronic liver or lung disease, DM, heart disease
- Immune compromise from HIV, chemotherapy, organ transplant

With such limited doses available for so many of the treatment options, how can we prioritize who's REALLY high-risk? E.g., active chemotherapy, solid organ transplant, etc.

- NIH addressed this exact question
- Essentially, immunocompromised individuals who can't mount an adequate immune response to either the vaccine or infection
- People over the age of 75, or over the age of 65 with risk factors for severe disease
- In limited supply, prioritize TREATMENT over post-exposure prophylaxis
- NIH guidelines also say to prioritize unvaccinated over vaccinated *(interesting ethical issue IMO)*

For the purposes of this conversation, we're going to focus on outpatient treatments that are available for people over the age of 12. Let's go through the main options, in order of what we should consider first and foremost based on NIH and FDA guidance.

SEE TABLE HERE.

- Nirmatrelvir/ritonavir (Paxlovid) - oral antiviral
    - Protease inhibitor plus booster
    - Effective against delta AND omicron
    - 300mg/100mg PO BID for 5 days
    - Meant for age 12+ and weight 40kg+, with risk of severe illness
    - Need to have a positive covid test
    - Best if given within 5 days of symptom onset
    - In a study of 2246 participants, RRR of 88% for hospitalization or death compared to placebo, ARR 6.3% to 0.8%
    - Main SEs: impaired taste, diarrhea, myalgias
    - Dose adjustment for eGFR between 30 and 60: nirmatrelvir dose cut in half
    - Avoid if eGFR <30, also in liver failure
    - CYP3A inhibitor, so there's a huge list of drug-drug interactions
    - Some of the most commonly prescribed drugs that would be a contraindication to Paxlovid:
        - HMG-CoA reductase inhibitors: lovastatin, simvastatin
        - Anti-gout: colchicine
        - Antiarrhythmics: amiodarone, flecainide
        - Antipsychotics: clozapine
        - Herbal products: St. John's Wort

- Sotrovimab - monoclonal antibody
    - 500mg IV one time infusion
    - Also effective against delta and omicron
    - Same intended patient population as Paxlovid
    - Can be given within 10 days of symptom onset – so a little more wiggle room
    - In a study of 583 participants, 85% RRR of hospitalization or death compared to placebo (NEJM), ARR 7% to 1%

    - SE: mainly infusion related reactions (F/C, BP changes, dizziness, rash), but placebo group had higher incidence of severe AE

- What about remdesivir? This used to be only for inpatients, but now it seems to have a role in the outpatient setting.
    - (Answer)
    - Nucleoside analog
    - A lot of the same specifications as before - age 12+, weight 40+ kg, within 7 days of symptom onset, for people at increased risk of severe illness
    - 200mg IV on day 1, 100mg IV on days 2 and 3
    - 87% RRR hospitalization or death compared to placebo in a NEJM study of 562 participants, ARR 5.3% to 0.7%

- Molnupiravir - oral antiviral
    - Ribonucleoside analog
    - Also effective against delta and omicron (though overall less so than the previous two options)
    - 800mg PO BID x 5 days
    - Meant for people ages 18 and older, so this is different from most of our other treatments which are for 12 and up
    - Needs to have a positive covid test and be given within 5 days of symptom onset
    - Study of 1433 participants, only 30% RRR hospitalization or death compared to placebo, ARR 9.7% to 6.5%
    - NOT intended for pregnant patients and actually needs post-use contraception! Found to be potentially mutagenic in pregnant animals. Not studied in pregnant humans. FDA says patients need to use contraception during molnupiravir regimen AND for 4 days afterwards.
    - SE: diarrhea, nausea, dizziness

Now, there are two other monoclonal antibody treatments that the FDA recently stopped authorizing for the treatment of covid given their lack of effectiveness against the omicron variant. Let's mention them but not spend too much time on them, given we won't be prescribing them anymore.

- *Casirivimab/imdevimab (REGEN-COV) - monoclonal antibody*
    - *One time infusion, dose 600mg/600mg either SC or IV*
    - *NOT effective against omicron*
    - *In a study of 2696 participants, RRR of 71% for hospitalization or death compared to placebo*
    - *Median time to resolution of symptoms was 4 days shorter compared to placebo*
    - *SE: infusion related reactions, with a higher incidence of severe AE in placebo group*

- *Bamlanivimab/etesevimab - monoclonal antibody*

    - *One time infusion of 700mg/1400mg IV*
    - *NOT effective against omicron*
    - *In a study of 1035 participants, RRR of 70% for hospitalization or death compared to placebo*
    - *16 fold reduction in viral load in 7 days compared to placebo*
    - *SE: nausea, rash, dizziness; incidence comparable to placebo*

(Here I'll want to lift up and summarize major take-aways so far and/or illuminate nuance as to which options we should prioritize when)

- TWO oral options - nirmatrelvir/ritonavir (Paxlovid) and molnupiravir. Both antivirals. Both effective against omicron and delta. Paxlovid has much better RRR and ARR when it comes to hospitalization and death compared to molnupiravir.
- Important to keep in mind the drug-drug interactions with Paxlovid, and that we can't use it if eGFR < 30 or in liver failure.
- We can also remember that molnupiravir is NOT for children (only option we're discussing for 18+ as opposed to 12+) OR pregnant patients and actually needs post-use contraception!
- When it comes to mAb, sotrovimab is the option that is effective against omicron and delta.
- And the IV antiviral remdesivir is entering the outpatient space as well.

Now let's explore some of the logistics of finding these medications and prescribing them. This can be so overwhelming in real-world, daily practice.

- HOW do we prescribe these meds?
    - For the two oral medications, Paxlovid and molnupiravir, the Department of Health and Human Services has Covid-19 Therapeutics Locator website with a list of dedicated pharmacies that have these meds in supply
        - https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com
    - For the monoclonal antibodies, state departments should have lists of facilities where you can refer your patients for infusion.
    - Covid.infusioncenter.org – national infusion center locator

- Cost to the patient?
    - Federal government is paying for monoclonal antibodies and oral antivirals (for now) → no cost to patient other than possible delivery fees from pharmacies

~~Before we leave the realm of outpatient treatment options that have been authorized by the FDA, there's been some buzz surrounding fluvoxamine. What do we need to know about this medication in relation to Covid-19?~~

- ~~October 2021 Lancet RCT of ~1500 adults in Brazil~~
- ~~Most unvaccinated~~
- ~~Had early, confirmed, symptomatic covid infection plus risk factor(s) for severe disease~~

- ~~SSRI fluvoxamine 100mg PO BID x 10 days compared to placebo~~
- ~~Reduced risk of hospitalization - 11% vs 16% in placebo group~~
- ~~Not authorized by FDA~~
- ~~More research needed~~

Moving away from treatment, there's the concept of pre-exposure prophylaxis that we haven't yet touched on. What about tixagevimab plus cilgavimab (Evusheld) for PrEP?

- (Any general thoughts on PrEP for covid)
- Monoclonal antibody authorized by the FDA in 12/21
- Two consecutive IM injections, good for six months
- Patient population?
    - Age 12+, weight 40+ kg
    - Moderate to severe immunocompromise
    - Unable to take the vaccine due to allergy
- In the PROVENT study of 5172 participants, they saw relative risk reduction of 77% of developing Covid-19 compared to placebo
- Important to know that in the ongoing STORM CHASER trial comparing Evusheld to placebo, they haven't yet seen a statistically significant reduction in developing covid-19, so overall the data is mixed
- Main SE: hypersensitivity reaction to the injection, headache, fatigue
- I'll admit I have yet to prescribe this. Are you seeing this prescribed in clinical practice? Any pearls for us to be aware of?

Until recently, we also had two post-exposure prophylaxis options: the same two monoclonal antibodies that the FDA has recently pulled given their lack of activity against omicron. So, for right now, no PEP options for us to pursue, but as a concept we should be aware of it.

- (Any general thoughts on PEP for covid)

Big picture, most important take-home points: