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TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

Ritonavir-boosted nirmatrelvir (Paxlovid®): And you thought we were done with COVID!

CLINICAL QUESTION

Is ritonavir-boosted nirmatrelvir (Paxlovid®) a safe and effective oral therapy for the treatment of COVID-19?

BOTTOM LINE

In unvaccinated patients at risk of severe outcomes, oral ritonavir-boosted nirmatrelvir (Paxlovid®) reduces the risk of hospitalization due to COVID-19 from 6.2% to 0.8% and all-cause mortality from 1.2% to 0%. Real-world evidence suggests effectiveness in Omicron-infected. Adverse events include taste disturbances and potentially serious drug interactions exist.

EVIDENCE

- Outcomes statistically significant unless noted.
- Manufacturer funded, randomized, placebo-controlled trial of 2246 unvaccinated COVID-19 outpatients [median age 46, ≥1 risk factor like BMI ≥25 (81%), smoking (39%) or hypertension (33%)]. Randomized to 5-day course of ritonavir-boosted nirmatrelvir or placebo within 5 days of symptom onset. Patients enrolled prior to Omicron dominance.[1] Outcomes at 28 days:
    - COVID-19 hospitalization: 8/1039 (0.8%) versus 65/1046 (6.2%) placebo; number needed to treat (NNT)=19.
    - All-cause death: 0/1039 (0%) versus 12/1046 (1.2%; placebo); NNT=88.
    - Stopping due to adverse event: No difference (<1%).

    - Taste disturbances: ~6% versus 0.3% (placebo).
        - Real-world evidence finds higher rates of taste disturbances (~60%) and gastrointestinal upset (10-30%).[2]
- Cohort studies:
    - Israel: 109,254 COVID-positive patients aged 40 years or older at high risk of severe outcomes during Omicron wave.[2] COVID-19 related hospitalization:
        - Aged 65+: 75% relative risk reduction.
            - From 59 to 15 cases per 100,000 person-years. Relative risk reductions did not change based on previous infection or vaccination status.
            - Aged 40-64: No statistically significant difference.
    - Similar (>50% relative risk reduction in hospitalization or death,[3, 4] or hospitalization alone[5]) found in other North American cohort studies (Ontario & Colorado) of adults >17 years old performed during Omicron wave.
        - Benefit was seen for both unvaccinated and vaccinated patients.[3-5]

CONTEXT

- COVID-19 hospitalizations significantly lower, ~50%, with Omicron versus Delta.[6]
- Prescribing recommendations vary by jurisdictions: British Columbia,[7] Alberta.[8]
    - Generally, jurisdictions direct eligibility toward those with higher age and more comorbidities, fewer vaccine doses, and immunocompromised patients.
- Drug interactions with medications common: Drug interactions resource.[9]
    - Renal dosing adjustment required.
- Post-Paxlovid® "rebound" possible:
    - Revert to testing positive, mild symptoms return, but <1% return to hospital within 15 days of treatment.[10]

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