Outpatient COVID Management, Spring 2022

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Pearls:

- **For patients at high risk of progression to severe COVID illness, the 1st choice treatment recommendation is the antiviral nirmatrelvir / ritonavir (Paxlovid®).**
- **The dose of nirmatrelvir / ritonavir needs to be reduced for those with eGFR ≥30 to <60 mL/min. If eGFR <30 mL/min or hepatic failure, choose a different agent.**
- **The 2nd choice antiviral is the IV-only drug remdesivir.**
- **Consider antivirals in those who are UNVACCINATED, OLDER, and with COMORBIDITIES.**
- **Dexamethasone is recommended for outpatients only if needing home O_2.**
- **Consider the monoclonal antibody bebtelovimab if Paxlovid® or remdesivir not available or contraindicated.**

- **Symptomatic treatment for ALL:**
  - Ibuprofen / acetaminophen for fever and pain
  - Fluids to replace evaporative losses
  - Rest
  - Antitussives –Not a lot of evidence to support OTC or prescription antitussives. Honey can be beneficial.
- **For patients at High Risk of Progression to Severe Illness**
  - **1st choice: <u>Nirmatrelvir / Ritonavir (Paxlovid®)</u> PO**
    - Currently widely available
    - Use if ≤ 5 days from symptom onset (symptom onset = day of first symptoms regardless of test date - OR- for asymptomatic patients the day of the test)
    - How they work:
      - **<u>Ritonavir (RTV)</u>**
        - Antiretroviral drug used in many HIV drug combinations.
        - Some activity against SARS-CoV-2 but more importantly interferes with metabolism of other drugs.
        - Main role is to boost the level of nirmatrelvir.
      - **<u>Nirmatrelvir</u>**
        - Inhibits viral replication of SARS-CoV-2
    - If normal renal function:
      - Nirmatrelvir 300mg (2x 150 mg tabs) + RTV 100mg PO bid x 5 days

        - IF eGFR ≥30 to <60 mL/min:
            - Nirmatrelvir 150mg + RTV 100mg PO bid
        - NOT recommended If:
            - eGFR <30 mL/min:
            - Severe Hepatic Impairment (Child-Pugh Class C)
        - Watch for drug interactions:
            - Warfarin, anticonvulsants, antiarrhythmics … many more
            - Many drug interaction checker options, here's one.
            - NIH Drug Interaction Guidelines
    - **2nd choice: Remdesivir**
        - Inhibits viral replication
        - Use if ≤ 7 days since symptom onset
        - 200 mg IV on Day 1, followed by 100 mg IV daily on Days 2 and 3
        - Administer over 30–120 minutes (common to run it over 60 min)
        - Patients should be observed for ≥1 hour after infusion
- **Who's at Risk of Progression to Severe Illness?**
    - **Tier 1 Priority:**
        - Unvaccinated AND > 75 or > 65 with comorbidities
        - Immunocompromised – Regardless of vaccine status
            - B cell-depleting therapies (rituximab, ocrelizumab, ofatumumab, alemtuzumab)
            - Hematologic malignancy in treatment
            - Transplant recipients
            - Untreated HIV with CD4 <50
    - **Tier 2 Priority:**
        - Unvaccinated, not in Tier 1, and
            - ≥65 years
            - <65 years with clinical risk factors
    - **Tier 3 Priority:**
        - Vaccinated and
            - ≥ 75 years
            - ≥ 65 years with clinical risk factors
    - **Tier 4 Priority:**
        - Vaccinated and
            - ≥65
            - <65 with clinical risk factors
        - Vaccinated but not Boosted

- **Bottom line:** Since supply is not currently a significant issue, consider antiviral drugs in those who are UNVACCINATED, OLDER, and with COMORBIDITIES.

- **Alternative Therapies (if Paxlovid® or Remdesivir not available)**
  - **Monoclonal Antibodies**
    - **Bebtelovimab** 175mg IV once; given over ≥30 seconds.
      - For Symptoms ≤ 7d
      - Observe for ≥1 hour after injection
    - Sotrovimab 500mg IV once; given over 30 minutes.
      - Recently REMOVED from NIH recommendations due to much less activity vs. BA.2
      - For Symptoms < 7d
      - Observe for ≥1 hour after injection
  - **Other Antivirals Options**
    - Molnupiravir 800 mg PO twice daily for 5 days
      - For Symptoms ≤ 5d
      - Lower efficacy than preferred antiviral options
      - Theoretical risk of mutagenesis
      - NOT recommended for pregnant women
  - **Dexamethasone**
    - Recommended for those discharged from ED on home O_2
      - 6mg po daily
      - Continue as long as O_2 needed; max 10 days
    - NOT recommended for other outpatients
- **Relative Risk Reduction for Hospitalization or Death**
  - Paxlovid® 88%
  - Remdesivir 87%
  - Sotrovimab 85%
  - Molnupiravir 30%
  - Bebtelovimab ?
- **NIH Panel Recommends AGAINST**
  - Hydroxychloroquine – There is very good evidence that it does not work.
  - Antibiotics – Bacterial superinfection with COVID is extremely rare.
  - Anticoagulants / Antiplatelet – Not routinely recommended for outpatients.
  - Ivermectin – Recent trial found no difference in admissions. There is now good evidence that it does not work.
- **VACCINATION - Still Most Effective Intervention Against COVID!**

References:

1. https://www.covid19treatmentguidelines.nih.gov
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7. Pilishvili T, et al; Vaccine Effectiveness among Healthcare Personnel Study Team. Effectiveness of mRNA Covid-19 Vaccine among U.S. Health Care Personnel. N Engl J Med. 2021 Dec 16;385(25):e90. PMID: 34551224.