NIRMATRELVIR/RITONAVIR

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- **Pharmacologic Category:** antiviral agent
- **Mechanism of Action**
  - Peptidomimetic inhibitor
  - Inhibits protease rendering protein incapable of processing polyprotein precursors, prevents viral replication
- **Preclinical studies**
  - Antiviral activity against SARS-CoV-2 (alpha, beta, gamma, delta, lambda variants)
    - Beta variant least susceptible
- **Dosing**
  - 300mg nirmatrelvir plus 100mg ritonavir PO Q 12 hours x 5 days
  - Dose reduction in patients with moderate renal impairment (eGFR $\geq$ 30mL/min to <60 mL/min)

EPIC-HR STUDY

Summary of findings 1. Nirmatrelvir/ritonavir for treating COVID-19 in outpatient settings with asymptomatic or mild disease

Patient or population: unvaccinated, nonhospitalized people with mild symptomatic disease (WHO scale 2 to 3) at high risk for progression to severe disease

Setting: outpatient N = 2224

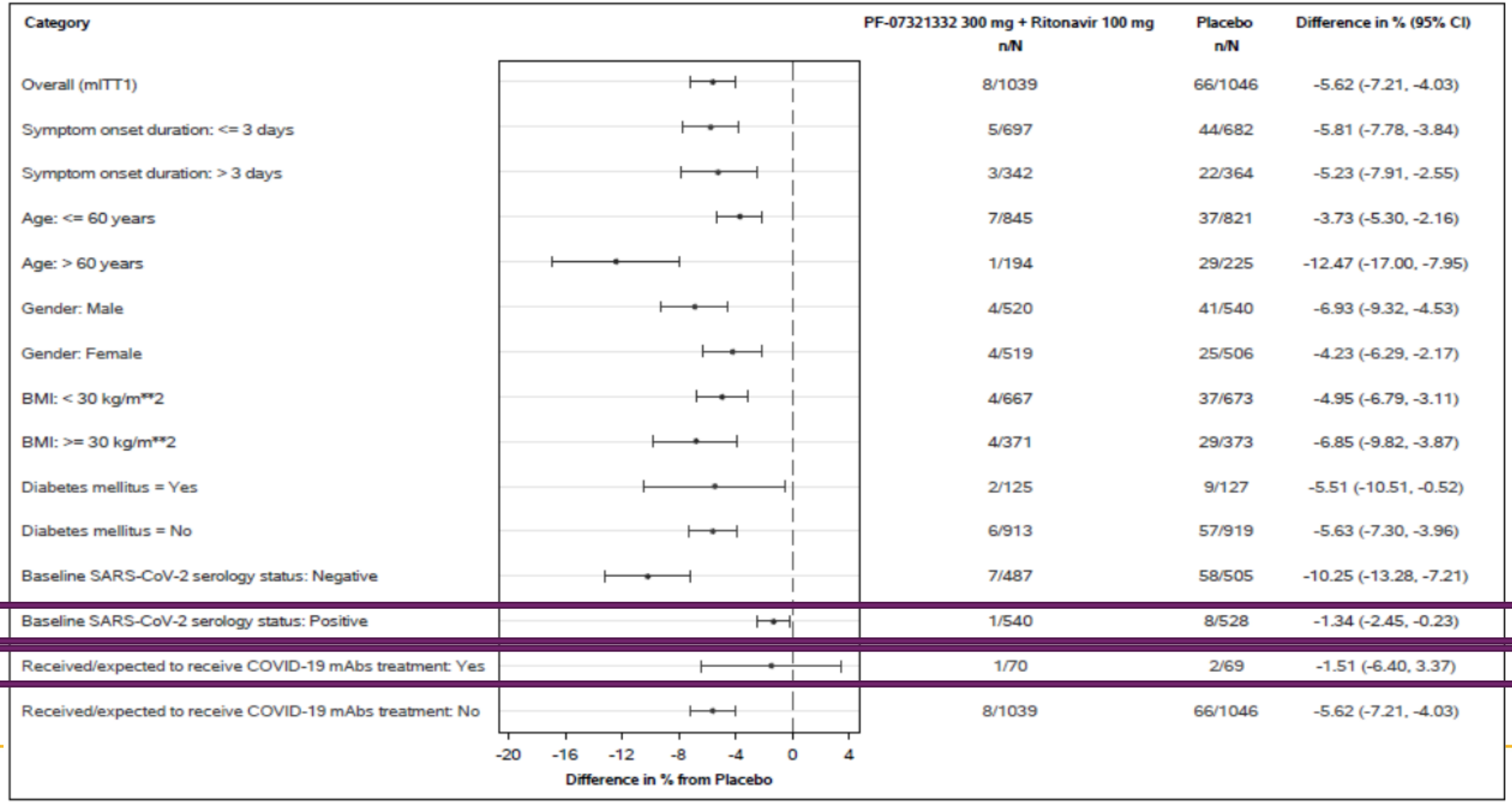
Intervention: nirmatrelvir/ritonavir (plus standard of care)

Comparison: placebo (plus standard of care)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comment
	Risk with placebo	Risk with nirmatrelvir/ritonavir				
All-cause mortality at day 28	**11** per 1000	**0** per 1000	**RR 0.04** (0.00 to 0.68)	2224 (1 RCT)	⨁⨁◯◯ Low[a]	Nirmatrelvir/ritonavir may reduce all-cause mortality[1]
	Difference: **11 fewer per 1000** (11 fewer to 4 fewer)					
Worsening of clinical status						
Admission to hospital or death within 28 days	**61** per 1000	**8** per 1000	**RR 0.13** (0.07 to 0.27)	2224 (1 RCT)	⨁⨁◯◯ Low[b]	Nirmatrelvir/ritonavir may reduce (COVID-19-related) hospitalization or death[2]
	Difference: **53 fewer per 1000** (57 fewer to 45 fewer)					

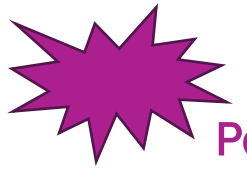
Low certainty of evidence

EPIC-HR STUDY



EUA

- Not authorized for initiation in hospitalized patients
  - If a patient were to become hospitalized after starting treatment, completion of the 5-day course could be considered pending healthcare provider's discretion
- Not authorized for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19
- Not authorized for use for longer than 5 consecutive days



Potential for severe drug-drug interactions

CDC HAN ALERT – COVID-19 REBOUND

- "Paxlovid continues to be recommended for early-stage treatment of mild to moderate COVID-19 among persons at high risk for progression to severe disease"

- "A brief return of symptoms may be part of the natural history of SARS-CoV-2 (the virus that causes COVID-19) infection in some persons, independent of treatment with Paxlovid and regardless of vaccination status."
  - Limited information currently available from case reports
    - Mild illness
    - No reports of severe disease
    - No evidence that additional antiviral treatment is needed

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