

RESEARCH SUMMARY

Nirmatrelvir for Vaccinated or Unvaccinated Adult Outpatients with Covid-19

Hammond J et al. DOI: 10.1056/NEJMoa2309003

CLINICAL PROBLEM

Effective oral treatments for Covid-19 are needed that can shorten the time to symptom resolution and reduce the risk of progression to severe illness. The oral antiviral nirmatrelvir, in combination with ritonavir, has been shown to reduce the risk of Covid-19–related hospitalization or death from any cause in unvaccinated adults at high risk for severe Covid-19, but whether it can reduce the duration of symptoms in a broader group is unknown.

CLINICAL TRIAL

Design: A phase 2–3, double-blind, randomized, controlled trial assessed the efficacy and safety of nirmatrelvir–ritonavir in adult outpatients (either unvaccinated or not vaccinated within the previous year) without risk factors for severe Covid-19 and fully vaccinated adults with at least one risk factor for severe disease.

Intervention: 1296 adults with confirmed Covid-19 and symptom onset within the previous 5 days were assigned to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir or placebo every 12 hours for 5 days. The primary end point was the time to sustained alleviation of all targeted signs and symptoms of Covid-19.

RESULTS

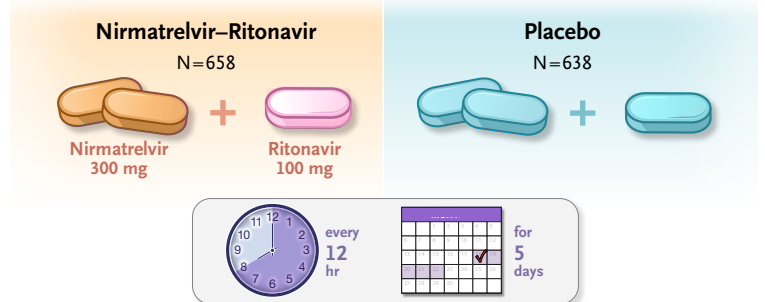
Efficacy: The time to sustained alleviation of symptoms did not differ significantly between the two groups.

Safety: The percentages of participants with adverse events through day 34 were similar in the two groups; the most common adverse events in the nirmatrelvir–ritonavir group were dysgeusia, diarrhea, and nausea.

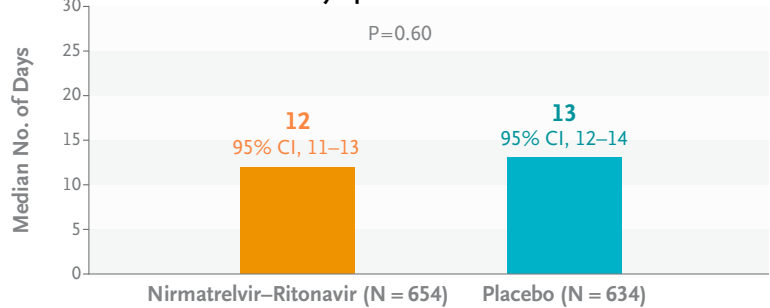
LIMITATIONS AND REMAINING QUESTIONS

- The participants in the vaccinated high-risk subgroup were enrolled regardless of the time since their last administered vaccine dose.
- Nirmatrelvir–ritonavir has a distinctive taste, so participants may have suspected that they were taking that medication.
- The trial was started during the period of delta-variant predominance, and therefore the efficacy of the treatment against other variants is unknown.

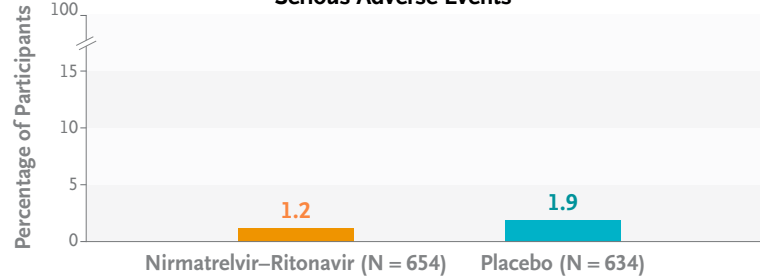
Links: [Full Article](#) | [NEJM Quick Take](#) | [Editorial](#)



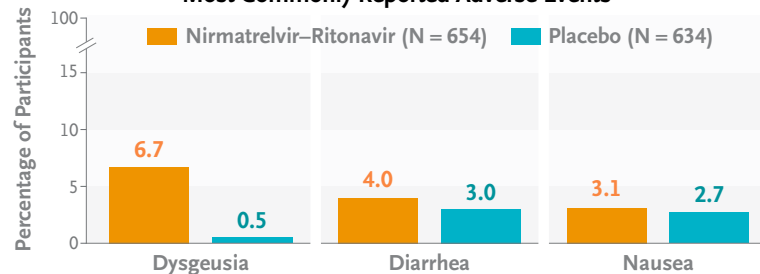
Time to Sustained Alleviation of All Targeted Signs and Symptoms of Covid-19



Serious Adverse Events



Most Commonly Reported Adverse Events



CONCLUSIONS

Among outpatients with Covid-19 who were at standard risk or high risk for progression to severe Covid-19, nirmatrelvir and ritonavir did not significantly shorten the time to symptom alleviation.