

ORIGINAL ARTICLE

Oral Nirmatrelvir–Ritonavir as Postexposure Prophylaxis for Covid-19

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ABSTRACT

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BACKGROUND

Clinical trials of treatments for coronavirus disease 2019 (Covid-19) have not shown a significant benefit of postexposure prophylaxis.

METHODS

We conducted a phase 2–3 double-blind trial to assess the efficacy and safety of nirmatrelvir–ritonavir in asymptomatic, rapid antigen test–negative adults who had been exposed to a household contact with Covid-19 within 96 hours before randomization. The participants were randomly assigned in a 1:1:1 ratio to receive nirmatrelvir–ritonavir (300 mg of nirmatrelvir and 100 mg of ritonavir) every 12 hours for 5 days or for 10 days or matching placebo for 5 or 10 days. The primary end point was the development of symptomatic SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection, confirmed on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) or rapid antigen testing, through 14 days in participants who had a negative RT-PCR test at baseline.

RESULTS

A total of 2736 participants were randomly assigned to a trial group — 921 to the 5-day nirmatrelvir–ritonavir group, 917 to the 10-day nirmatrelvir–ritonavir group, and 898 to the placebo group. Symptomatic, confirmed SARS-CoV-2 infection developed by day 14 in 2.6% of the participants in the 5-day nirmatrelvir–ritonavir group, 2.4% of those in the 10-day nirmatrelvir–ritonavir group, and 3.9% of those in the placebo group. In each nirmatrelvir–ritonavir group, the percentage of participants in whom symptomatic, confirmed SARS-CoV-2 infection developed did not differ significantly from that in the placebo group, with risk reductions relative to placebo of 29.8% (95% confidence interval [CI], –16.7 to 57.8; $P=0.17$) in the 5-day nirmatrelvir–ritonavir group and 35.5% (95% CI, –11.5 to 62.7; $P=0.12$) in the 10-day nirmatrelvir–ritonavir group. The incidence of adverse events was similar across the trial groups, with dysgeusia being the most frequently reported adverse event (in 5.9% and 6.8% of the participants in the 5-day and 10-day nirmatrelvir–ritonavir groups, respectively, and in 0.7% of those in the placebo group).

CONCLUSIONS

In this placebo-controlled trial, postexposure prophylaxis with nirmatrelvir–ritonavir for 5 or 10 days did not significantly reduce the risk of symptomatic SARS-CoV-2 infection. (Funded by Pfizer; ClinicalTrials.gov number, NCT05047601.)