ORIGINAL ARTICLE

Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant

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ABSTRACT

BACKGROUND

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants threatens progress toward control of the coronavirus disease 2019 (Covid-19) pandemic. In a phase 1–2 trial involving healthy adults, the NVX-CoV2373 nanoparticle vaccine had an acceptable safety profile and was associated with strong neutralizing-antibody and antigen-specific polyfunctional CD4+ T-cell responses. Evaluation of vaccine efficacy was needed in a setting of ongoing SARS-CoV-2 transmission.

METHODS

In this phase 2a–b trial in South Africa, we randomly assigned human immunodeficiency virus (HIV)–negative adults between the ages of 18 and 84 years or medically stable HIV-positive participants between the ages of 18 and 64 years in a 1:1 ratio to receive two doses of either the NVX-CoV2373 vaccine (5 μg of recombinant spike protein with 50 μg of Matrix-M1 adjuvant) or placebo. The primary end points were safety and vaccine efficacy against laboratory-confirmed symptomatic Covid-19 at 7 days or more after the second dose among participants without previous SARS-CoV-2 infection.

RESULTS

Of 6324 participants who underwent screening, 4387 received at least one injection of vaccine or placebo. Approximately 30% of the participants were seropositive for SARS-CoV-2 at baseline. Among 2684 baseline seronegative participants (94% HIV-negative and 6% HIV-positive), predominantly mild-to-moderate Covid-19 developed in 15 participants in the vaccine group and in 29 in the placebo group (vaccine efficacy, 49.4%; 95% confidence interval [CI], 6.1 to 72.8). Vaccine efficacy among HIV-negative participants was 60.1% (95% CI, 19.9 to 80.1). Of 41 sequenced isolates, 38 (92.7%) were the B.1.351 variant. Post hoc vaccine efficacy against B.1.351 was 51.0% (95% CI, −0.6 to 76.2) among the HIV-negative participants. Preliminary local and systemic reactogenicity events were more common in the vaccine group; serious adverse events were rare in both groups.

CONCLUSIONS

The NVX-CoV2373 vaccine was efficacious in preventing Covid-19, with higher vaccine efficacy observed among HIV-negative participants. Most infections were caused by the B.1.351 variant. (Funded by Novavax and the Bill and Melinda Gates Foundation; ClinicalTrials.gov number, NCT04533399.)

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*The members of the 2019nCoV-501 Study Group are listed in the Supplementary Appendix, available at NEJM.org.

This article was published on May 5, 2021, at NEJM.org.

This is the *New England Journal of Medicine* version of record, which includes all *Journal* editing and enhancements. The Author Final Manuscript, which is the author's version after external peer review and before publication in the *Journal*, is available under a CC BY license at PMC8091623.

N Engl J Med 2021;384:1899-909.
DOI: 10.1056/NEJMoa2103055

the trial design, conduct, oversight, and analyses are provided in the Supplementary Appendix and the protocol (which includes the statistical analysis plan), available at NEJM.org.

OVERSIGHT

The NVX-CoV2373 vaccine was developed by Novavax, which sponsored the trial and was responsible for the overall design (with input from the lead investigator), site selection, monitoring, and analysis. Trial investigators were responsible for data collection. The protocol was approved by the South African Health Products Regulatory Authority and by the institutional review board at each trial center. Oversight of safety, which included monitoring for specific vaccination-pause rules, was performed by an independent safety monitoring committee.

The first author wrote the first draft of the manuscript with assistance from a medical writer who is an author and an employee of Novavax. All the authors made the decision to submit the manuscript for publication and vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

TRIAL PROCEDURES

Participants were randomly assigned in a 1:1 ratio to receive two intramuscular injections, 21 days apart, of either NVX-CoV2373 (5 μg of recombinant spike protein with 50 μg of Matrix-M1 adjuvant) or saline placebo (injection volume, 0.5 ml), administered by staff members who were aware of trial-group assignments but were not otherwise involved with other trial procedures or data collection. All other staff members and trial participants remained unaware of trial-group assignments. Participants were scheduled for in-person follow-up visits on days 7, 21, and 35 and at 3 months and 6 months to collect vital signs, review any adverse events, discuss changes in concomitant medications, and obtain blood samples for immunogenicity analyses. A follow-up telephone visit was scheduled for 12 months after vaccination.

SAFETY ASSESSMENTS

The primary safety end points were the occurrence of all unsolicited adverse events, including those that were medically attended, serious, or of special interest, through day 35 (Tables S2 and S3) and solicited local and systemic adverse events that were evaluated by means of a reactogenicity diary for 7 days after each vaccination (Tables S4 and S5). Safety follow-up was ongoing through month 12.

EFFICACY ASSESSMENTS

The primary efficacy end point was confirmed symptomatic Covid-19 that was categorized as mild, moderate, or severe (hereafter called symptomatic Covid-19) and that occurred within 7 days after receipt of the second injection (i.e., after day 28) (Table S6). Starting on day 8 and continuing through 12 months, we performed active surveillance (telephone calls every 2 weeks from trial sites to participants) and passive surveillance (telephone contact at any time from participants to trial sites) for symptoms of suspected Covid-19 (Table S7 and Fig. S1). A new onset of suspected symptoms of Covid-19 triggered initial in-person and follow-up surveillance visits to perform clinical assessments (vital signs, including pulse oximetry, and a lung examination) and for collection of nasal swabs (Fig. S2). In addition, suspected Covid-19 symptoms were also assessed and nasal swabs collected at all scheduled trial visits. Nasal-swab samples were tested for the presence of SARS-CoV-2 by NAAT with the use of the BD MAX system (Becton Dickinson). We used the InFLUenza Patient-Reported Outcome (FLU-PRO) questionnaire to comprehensively assess symptoms for the first 10 days of a suspected episode of Covid-19.

WHOLE-GENOME SEQUENCING

In a blinded fashion, we performed post hoc whole-genome sequencing of nasal samples obtained from all the participants who had symptomatic Covid-19. Details regarding the whole-genome sequencing methods and phylogenetic analysis are provided in Fig. S3.

STATISTICAL ANALYSIS

The safety analysis population included all the participants who had received at least one injection of NVX-CoV2373 or placebo; regardless of group assignment, participants were evaluated according to the intervention they had actually received. Safety analyses were presented as numbers and percentages of participants who had solicited local and systemic adverse events through day 7 after each vaccination and who had unsolicited adverse events through day 35.