World Health Organization

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novel Coronavirus

An international randomised trial of candidat vaccines against COVID-19

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Powering research
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OUTLINE OF SOLIDARITY VACCINE TRIAL

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Summary

Recognizing the critical importance to world health of the rapid availability and deployment of effective vaccines against COVID-19, this large, international, multi-site, individually randomized controlled clinical trial will enable the concurrent evaluation of the benefits and risks of each promising candidate vaccine within 3-6 months of it being made available for the trial.

Goal of the trial

Coordinate evaluation of the many preventive candidate SARS-CoV-2 vaccines under development, to evaluate promptly, efficiently and reliably their safety and efficacy, enabling assessment of whether any are appropriate for deployment to influence the course of the pandemic.

Adaptive design

Candidate vaccines may be added to the trial as they become available if they meet prioritization criteria (to be defined via the WHO vaccine prioritization group). Expected high enrollment rates, together with adaptive vaccine success criteria will allow the study to achieve reliable results within a defined time frame (within 3-6 months of receiving sufficient supplies from the vaccine developer). To target resources on vaccines more likely to be successful, other vaccines may be eliminated if evidence emerges that they can have no benefit relative to placebo or to other vaccines. Participants will be centrally randomized such that they have the same chance of receiving a placebo/control as they have of receiving each individual vaccine. The study will enroll continuously.

Features and Advantages

A large international multicenter trial to test vaccines is consistent with the collaborative spirit underlying COVID vaccine development and will foster international deployment with equity of access. As compared with conducting separate trials for each candidate vaccine, the trial design, which evaluates candidate vaccines in parallel with a common placebo group:

1. increases the likelihood that participants receive one of the candidate vaccines while improving the efficiency of the clinical trial, promoting efficient allocation of world-wide clinical trial resources, and increasing the likelihood that effective vaccines will be quickly, efficiently and reliably evaluated;
2. reduces uncertainties in endpoint acquisition rates, further increasing the likelihood of enrolling enough trial participants to rapidly assess efficacy of each vaccine;
3. provides all trial participants a fair chance at receiving ultimately successful vaccines;
4. rapidly identifies the most successful vaccines by eliminating inadequately performing candidate vaccines, which will speed the evaluation and further deployment of vaccines that have the needed clinical benefit;
5. allows candidate vaccines to rapidly progress through clinical development and be entered into the trial as soon as they are ready, eliminating inefficiency of designing and conducting separate trials and decreasing costs to developers; and
6. increases the consistency of the evaluation process across vaccines by standardizing the populations enrolled, study screening and follow-up procedures, and endpoint determination, avoiding the scenario where any one of these factors impacts disease rates across vaccines studied in separate protocols.

Participating sites

All sites with sufficient transmission rates at the time of entering the trial can participate. Participating sites must be able to determine whether trial participants develop COVID-19, perform safety follow-up, and assure multiple ways to contact participants to assure follow-up and retention. Some sites may not evaluate all vaccines (due to local regulatory constraints, product availability or other limiting factors).

Participating populations

Adults in locations considered at high risk for exposure to SARS-CoV-2. After supportive safety data are available for a given vaccine, enrollment in some sites will be extended to include immunocompromised, pregnant, or lactating individuals.

Major outcome

The primary outcome will be virologically confirmed COVID-19 disease, regardless of severity. Disease rates for each vaccine will be compared with disease rates for all concurrently randomized placebo/control recipients.

Secondary outcomes

Sites will participate in evaluating some or all secondary endpoints, which may include infection with SARS—CoV-2 (e.g., as determined by serology) and severe disease including death. Additional supportive outcomes could include 1) immunogenicity, 2) immunological correlates of risk, 3) other potential correlates of risk, 4) viral shedding, 5) patterns of transmission within the household or other transmission group, 6) for two-dose vaccines, efficacy after the first dose and 7) storage of serum/cells, with consent for unlimited research on them explicitly obtained.

Safety

All sites will monitor vaccine safety, including the possibility of enhanced disease in vaccine recipients.

Blinding

Previous experience shows that blinding can be maintained in trials of similar design. All possible measures will be taken to assure that study blinding is maintained.

Follow up

Efficacy follow-up will include weekly contacts to reduce loss of trial participants and to increase likelihood of detecting COVID-19 disease. Blinded study follow-up, including for adverse events, will be planned for at least one year, although for vaccines found to be substantially protective, vaccine and placebo recipients may be unblinded sooner.

Study governance

There will be a single steering committee (SC) and a single data monitoring committee (DMC). Adaptive aspects of the study, to the extent not predefined in the protocol, will be governed by the SC, which will not have access to unblinded study data. The role of the DMC will be to apply pre- (or SC-) defined efficacy and lack of benefit criteria to the vaccines, and to address potential safety issues. Once one or more vaccines meet definite success criteria, new efficacy/lack of benefit criteria will be introduced.