A transparent framework for selecting vaccines to be evaluated in Phase 2b/Phase 3 trials – experience from COVID vaccines

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WHO Working Group on COVID vaccine prioritization
for the SOLIDARITY TRIALS VACCINE (STV)
Solidarity Trial Vaccines (who.int)

What is the Solidarity Trial Vaccines (STV)?

- an international RCT to rapidly evaluate promising new vaccines for COVID-19
- led by WHO and co-sponsored by WHO and Ministries of Health
- flexible to work across countries, settings and populations
- aim to expand current portfolio of vaccines and access to them in settings with limited vaccine availability
- focus now on 2nd generation vaccines which offer advantages over current vaccine platforms
  - ease of administration eg nasal or oral inhalation
  - wider coverage of variants
  - more durable protection
  - protection against infection and transmission

Stage 1: development of criteria against which candidate COVID-19 vaccines can be evaluated

- safety and potential for effectiveness
- stability of the vaccine
- demonstration that they can be stored and transported easily under normal conditions
- availability - whether they can be produced quickly for global distribution
- the ease with which they can be given to individuals (how the vaccines are given, the number of doses etc)

Stage 2: establishing a process to select candidate vaccines for inclusion in the STV

- Process should be transparent, independent, thorough and provide a basis for comparison between candidate vaccines eg scoring system
- Working group of independent experts formed with broad range of expertise:
  - Pharmacovigilance; vaccine safety
  - Clinical immunology, antibody assays
  - Vaccine trials
  - Microbiology/virology
  - Regulatory science
  - Vaccine manufacturing, vaccine formulations
  - EPI, cold chain management
  - Animal models
- Evaluation template developed with scores allocated to the different criteria

How the process works

- STV and its aims publicised by WHO and expressions of interest from candidate vaccine manufacturers elicited
- Interested manufacturers sent spreadsheet to complete for initial evaluation by Chair, secretariat and rapporteur
- Template summarises available data on
    1. safety
    2. potential for efficacy
    3. stability
    4. implementation
    5. vaccine availability

- Candidates with sufficient data to evaluate for entry to STV Phase 3 or Phase 2b invited to present to WG
    - meeting arranged when minimum quorum of 5 of the 8 voting members can attend
    - for Phase 3 entry safety data base of “several hundred” and some information on responses by age
    - for Phase 2b entry more limited clinical trial data but SVT used to expand immunogenicity/safety database prior to approving progression to Phase 3
    - manufacturers asked to submit relevant material for review before presentation eg investigator’s brochure, study reports and published papers

Scoring against the five evaluation criteria

1. Safety profile: (20 points)
   - studies to evaluate potential for disease enhancement (COVID vaccine specific)
   - method of collection of safety data in clinical trials (eg via diary cards, solicited vs unsolicited, duration of FU, haematology and chemical pathology measurements etc,)
   - characteristic of trial population studied (age, co-morbidities, pregnancy, immune compromised)
   - DART studies in animals

2. Potential for efficacy: (20 points)
   - Serological and CMI responses in human and animals e.g. neutralisation, ELISA IgG, ELISpot, ICS)
   - Challenge studies in animals (or humans)
   - Robustness of evidence for selected schedule and dosage

3. Stability (10 points); 4. Implementation (15 points); 5. Availability (20 points); plus BONUS points up to 15 for 2nd generation attributes

Process for reporting outcome of WG's evaluation

- Scoring system supplemented by vote of Yes/No by WG members
  - scoring against criteria and sub-criteria provides a structure for the WG's evaluation
  - but scores can be unreliable eg WG members may score differently and not all members present at each meeting
- Summaries produced by rapporteur of pre-clinical and clinical data reviewed by WG under the five criteria using a standard format
- Questions asked by WG of manufacturer at meeting or in follow up correspondence summarised together with responses
- Follow up meeting of WG with or without manufacturer arranged if necessary
- Presentation of WG's deliberations and data summaries, scores and consensus recommendation made by Chair and rapporteur to SVT Steering Committee

Evaluation process easily applied to other vaccines

- WG recently asked to extend its remit to select candidate ebolavirus vaccines
- Urgent response needed in face of outbreak of Sudan strain in Uganda
- Rapid RCT planned by WHO and Ugandan MoH
- Limited number of candidates available
- WG asked to review pre-clinical and clinical dossiers for the candidate vaccines and attend presentations from manufacturers
- No time to develop scoring system but WG members used the framework of safety, efficacy, stability, implementation and availability as a basis for their review
- WG able to rapidly arrive at a Yes/No recommendation
- Summary produced of WGs questions to manufacturer and its response, plus rationale supporting the consensus recommendation

Lessons learned from COVID-19 prioritisation committee

- Important to develop formal evaluation criteria that reflect:
  - the context in which the vaccine is to be applied e.g are long term supply volumes important (COVID) or having a product as soon as possible (Ebola)
  - any vaccine-specific issues eg safety or potential efficacy issues relating to vaccines against this pathogen, or with a specific vaccine platform
- Scoring is a useful device for ensuring a thorough and transparent evaluation process but
  - Scoring not an “exact science”
  - Go/No decisions useful to arrive at a consensus view
- Evaluation process will need to evolve as scientific landscape changes