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

Prof Elizabeth Miller on behalf of the 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 e.g. 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