WHO-Enterprise

Group 4: Science and Vaccine Development

Recommendations to the MOPH on the RV 144 HIV Phase III Vaccine Trial

Dr. Wai Lin Htun

Mahidol University

WHO-Enterprise

Recommendation 1: Durability of Vaccine Effect

- The protection from infection observed in RV 144 appeared to diminish after the first year following vaccination.
- Some of the immune responses measured in RV 144 declined within the first year following immunization. This decline may have been responsible for the short duration observed in protection from infection.
- An intensive effort is underway to determine the correlate(s) of protection for RV 144.
- An important future question is whether this efficacy could be extended with additional vaccine boosts.

WHO-Enterprise

Recommendation 1 (continued): Durability of Vaccine Effect

- To begin to address this question, we recommend re-vaccinating a small subset of HIV uninfected RV 144 vaccine recipients with ALVAC, AIDSVAX, and the combination of the two. This study should comprehensively assess the effect of such late boosting on immune responses.
- If the vaccines are immediately available, this proposed study provides the opportunity to rapidly follow-up on the immunogenicity results of RV 144.

WHO-Enterprise

Recommendation 2
Characterization of Immune Responses

- RV 144 trial evaluated a limited set of of immune responses.
- Since the demonstration of modest protective efficacy seen in RV 144, there is now considerable scientific interest in a more comprehensive characterization of the immune responses induced by the RV 144 regimen.
- Some of the outstanding scientific questions include:
  - a fuller evaluation of immune responses in blood, genital, and gastrointestinal compartments.
  - the relative contribution of the individual prime-boost vaccine components to these immune responses
  - the impact of additional vaccine boosts.

WHO-Enterprise

Recommendation 2 (continued) Characterization of Immune Responses

- We recommend that an immunogenicity study of HIV uninfected subjects be conducted to further characterize the immune responses to the RV 144 regimen as described above.
- This study will require large volume and multiple blood draws and invasive mucosal sampling.
- This intensive study will inform the design of improved vaccine regimens for future HIV efficacy trials in Thailand and globally.

WHO-Enterprise

Recommendation 3:

Immunogenicity studies with related vaccine products

- The RV 144 vaccine trial was the first demonstration of any degree of protection. The RV 144 vaccine regimen included a poxvirus vector prime (ALVAC) and a recombinant protein subunit boost (AIDSVAX).
- Other vaccine products could improve upon the modest level of protective efficacy observed in RV 144.
- Consideration is being given to the use of related poxvirus as vectors (e.g., NYVAC), in combination with a recombinant protein subunit boost, in future HIV vaccine efficacy trials in multiple parts of the world.
- Alignment of vaccine development in Thailand with activities performed in other parts of the world will accelerate the development of a globally effective HIV vaccine.

WHO-Enterprise

Recommendation 3 (continued):
Immunogenicity studies with related vaccine products

- We recommend that consideration be given to comparing the RV 144 regime with related vaccine products in an intensive immunogenicity study.
- If vaccine products are available, we recommend performing a comparative trial within the intensive immunogenicity trial described in Recommendation 2.

WHO-Enterprise

Recommendation 4:
Future Efficacy Studies

- The RV 144 vaccine trial was the first demonstration of any degree of protection. However, there is an imperative to improve upon the modest level of protective efficacy observed.
- Recommendations 1-3 are a roadmap leading up to future efficacy studies in Thailand to develop a highly effective preventive vaccine for public health use.
- Issues to improve and extend the results seen in RV 144:
  - Confirm the protective efficacy
  - Verify the apparent early protection from infection
  - Determine if the duration of protective efficacy seen in RV 144 be extended with additional boosts
  - Discover, or confirm, a correlate of protection.
  - Extend the evaluation of efficacy to other risk groups (e.g. MSM)

WHO-Enterprise

Recommendation 4:
Future Efficacy Studies

- Thailand is uniquely positioned to extend the results of the RV 144 trial.
- The time line for initiating efficacy studies is long and includes multiple stakeholders. Thus, we recommend that discussions for future HIV vaccine efficacy trials should begin within the global context of HIV vaccine development.