Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: A Phase I Study of the Safety and Immunogenicity of a Recombinant DNA Plasmid Vaccine (VRC-AVIDNA036-00-VP), Encoding for the Influenza Virus H5 Hemagglutinin Protein in Healthy Adults

Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov): NCT00408109

Authors/sponsors: Dr. Julie Ledgerwood, Dr. Barney Graham, Dr. Gary Nabel, VRC/NIAID/NIH USA

Study Design (including the phase of clinical trial): VRC 304 is a Phase I double-blind, placebo-controlled study to evaluate safety, tolerability, and immunogenicity of a recombinant DNA vaccine against the influenza virus hemagglutinin H5. The hypothesis is that this vaccine will be safe for human administration and will elicit antibody and T cell responses against the H5 protein. The primary objectives are to evaluate the safety and tolerability of the investigational vaccine at a 1 mg and 4 mg dose in healthy adults. Secondary and exploratory objectives are related to the immunogenicity of the study vaccine.

Vaccine subtype: H5
Virus: DNA plasmid encoding H5, Indonesian strain
Manufacturer: NIH USA
Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector): DNA vaccine
Adjuvant: None
Delivery system/site: IM by Biojector
Doses (antigen and adjuvant, number of doses, intervals between administrations): 1000; 4000µg. Three injections at days 0, 28 and 56 (at least 21 days in between).

Study population: Adults
Number of subjects involved: 45
Age range: 18-60 years old
Health status: Healthy volunteers
Special inclusion/exclusion criteria: None

Clinical Endpoints Assessed: The primary endpoint is safety and tolerability of the regimen. The secondary study endpoints are related to the vaccine immunogenicity.

Safety assessments:
- Local reactogenicity signs and symptoms
- Systemic reactogenicity signs and symptoms
- Laboratory measures of safety
- Adverse and serious adverse experiences

Immunogenicity assessments:
- immunoassay type
- HI (type of RBC used): hemagglutination inhibition (HAI) assay at Study Week 12-Horse erythrocytes
- NT (type of neutralization assay): Pseudotyped lentivirus reported assay
- SRH: not done
- ELISpot: to determine frequency of T cells producing IFNγ in response to pools of overlapping peptides representing H5 antigens
- ICS: to determine frequency of CD4+ and CD8+ cells that produce IL-2 or IFNγ in response to pools of overlapping peptides representing H5 antigens

Results being analyzed now
Safety: The vaccine was well tolerated by all routws of administration with no vaccine related SAEs.
Reactogenicity:
AEs:
SAEs:

**Immunogenicity:** not yet available

**HI or NT:**

<table>
<thead>
<tr>
<th>GMTs</th>
<th>GMT Ratios (post:pre)</th>
<th>Per cent responding (4 fold increase)</th>
<th>Per cent responders at specified titer</th>
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The placebo group had no subjects with positive HAI responses after two doses, 2 out of 15 in the 1 mg group had titers ≥ 1:40, and 3 subjects out of 15 in the 4 mg group had titers ≥ 1:40.

**SRH:**

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<th>Per cent with titre (in mm²)</th>
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**Current status of the clinical trial (completed, ongoing, in preparation):** Completed

**Date envisaged for availability of results, if not yet available:** 3Q2009

**Planned time schedule for next phase of development:** Evaluation of DNA prime-split product boost in 2009.