Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: A Multi-Center, Open-Label, Randomized Phase I Study of an Investigational Influenza DNA Vaccine Followed by 2009/2010 Seasonal Influenza Trivalent Inactivated Vaccine (TIV) Compared to Two Injections of TIV in Adults 45-70 Years

Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov): NCT00995982

Objectives:
- To test the safety and immune response of an experimental DNA vaccine for seasonal influenza, compared to the standard vaccine for seasonal influenza.

Authors/sponsors: National institute of Health, USA

Study Design:
- Participants will have six planned clinic visits (Weeks 0, 1, 3, 4, 6, and 27) and two telephone follow-up contacts (within 2 days after each injection) during this study.
- Participants will be divided into two groups: one group will receive two standard (TIV) flu vaccine injections given using a needle and syringe, while the other will receive the DNA flu vaccine using a needleless injection system followed by the TIV vaccine.
  - The vaccine injections for both groups will be given approximately 3 weeks apart,
  - Clinic staff will observe participants for at least 30 minutes after each vaccination. One to two days after each injection, participants must telephone the clinic staff, and for 7 days after the vaccination participants will keep a diary card to report on possible side effects.
  - During study visits, blood samples will be collected for research purposes to test for responses to vaccine.

Vaccine:
- Manufacturer: National institute of Health, USA

   Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector): DNA vaccine

   It is composed of 3 closed-circular DNA plasmids, each with a CMV/R promoter, that encode for H1, H3, and influenza B hemagglutinin (HA) proteins from the same 2009-2010 influenza vaccine strains. DNA vaccine vials will be supplied at 4 mg/mL with each dose administered in a 1 mL volume.

   The TIV is the subunit inactivated vaccine for the 2009-2010 season. Each dose is composed of 45 microg hemagglutinin (HA) in 0.5 mL; with the recommended ratio of 15 microg HA of each of the following 3 strains: A/Brisbane/59/2007-like (H1N1); A/Brisbane/10/2007-like (H3N2); and B/Brisbane/60/2008-like. All injections will be administered intramuscularly (IM) in the deltoid muscle. The DNA injections will be administered by Biojector[Registered Trademark] 2000 Needle-Free Injection Management System and the TIV by needle and syringe.

   Adjuvant:

   Delivery system/site: IM by Biojector for DNA vaccine and needles/syringe for inactivated vaccine

   Doses (antigen and adjuvant): 4000 - in DNA vaccine; 15- each strain in TIV

   Study population: Healthy individuals between ages 45 and 70 who have not yet received the seasonal influenza vaccine.

   Age range: Health status: healthy volunteers

   Inclusion criteria:
   1. 45 to 70 years old.
2. Available for clinical follow-up through Week 27.
3. Able to provide proof of identity to the satisfaction of the study clinician completing the enrollment process.
4. Complete an AoU prior to enrollment and verbalize understanding of all questions answered incorrectly.
5. Able and willing to complete the informed consent process.
6. Willing to donate blood for sample storage to be used for future research.
7. No evidence of previously undiagnosed clinically significant chronic diseases.
8. Physical examination and laboratory results without clinically significant findings and a Body Mass Index (BMI) < 42 within the 56 days prior to enrollment.

LABORATORY CRITERIA WITHIN 56 DAYS PRIOR TO ENROLLMENT:

9. Hemoglobin greater than or equal to 11.5 g/dL for women; greater than or equal to 13.5 g/dL for men
10. White blood cells (WBC) equal to 3,300-12,000 cells/mm(3)
11. Differential either within institutional normal range or accompanied by site physician approval as a differential that is consistent with healthy volunteer status
12. Total lymphocyte count greater than or equal to 800 cells/mm(3)
13. Platelets equal to 125,000 - 500,000/mm(3)
14. Alanine aminotransferase (ALT) less than or equal to 2.5 times upper limit of normal (ULN)
15. Serum creatinine less than or equal to 1 times ULN (less than or equal to 1.3 mg/dL for females; less than or equal to 1.4 mg/dL for males).
16. Negative FDA-approved HIV blood test. [Note: Results of HIV enzyme-linked immunosorbent assay (ELISA) will be documented, but a negative HIV polymerase chain reaction (PCR) test result will be sufficient for eligibility screening of subjects with positive HIV ELISA that is due to prior participation in an HIV vaccine study].

FEMALE-SPECIFIC CRITERIA:

17. Negative human chorionic gonadotropin (Beta-HCG) pregnancy test (urine or serum) for women presumed to be of reproductive potential on the day of enrollment.
18. A female subject must meet one of the following criteria:
   • No reproductive potential because of menopause [one year without menses] or because of a hysterectomy, bilateral oophorectomy, or tubal ligation,
   OR
   - Agrees to be heterosexually inactive at least 21 days prior to enrollment and through the last study visit,
   OR
   • Agrees to consistently practice contraception at least 21 days prior to enrollment and through the last study visit by one of the following methods:
     • condoms, male or female, with or without a spermicide;
     • diaphragm or cervical cap with spermicide;
     • intrauterine device;
     • contraceptive pills, patch, implant or any other FDA-approved contraceptive method;
     • male partner has previously undergone a vasectomy.

Specific inclusion/exclusion criteria:
Clinical Endpoints Assessed:

Safety assessments:

Immunogenicity assessments:

Results:

Safety:

Immunogenicity

GMTs:

GMT Ratios (post:pre):

Per cent responding (4 fold or greater rise and definition for reporting):

Per cent responders at specified tite:

Others assays:

Status of trial (ongoing/completed): Completed: 2009-2010