Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: Safety and Immunogenicity of H5N1 Adjuvanted, Inactivated, Split-Virion Pandemic Influenza Vaccine in Healthy Adults

Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov): NCT00457509

Authors/sponsors: Sanofi Pasteur

Purpose:
To test different adjuvanted vaccine formulations as a two-dose schedule in immunologically naïve adults against one vaccine formulation without adjuvant in terms of tolerance and immunogenicity

Study Design: The Phase I, randomized, single-blinded

Vaccine: H5N1
   Manufacturer: Sanofi Pasteur
   Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector): Inactivated split-virion vaccine based on the strain A/Indonesia/05/2005
   Adjuvant: AF03: 0.5%, 1%, 2.5%
   Delivery system/site: Intramuscular injection

Doses (antigen and adjuvant): 2.5 and 6µg per dose, Two doses

Study population:

   Age range: 18 Years to 40 Years   Health status: Health volunteers

Specific inclusion/exclusion criteria:
Inclusion Criteria :
• Aged 18 to 40 years on day of inclusion
• Informed consent form signed
• Able to attend all scheduled visits and to comply with all trial procedures
• For a woman, inability to bear a child or negative urine pregnancy test.

Exclusion Criteria :
• Participation in another clinical trial in the 4 weeks preceding the first trial vaccination.
• Planned participation in another clinical trial during the present trial period.
• Previous participation in a clinical trial involving an investigational flu pandemic vaccine.
• Vaccination with an influenza vaccine during the past 6 months
• Any vaccination in the 4 weeks preceding the first trial vaccination
• Vaccination planned in the 4 weeks following any trial vaccination
• Breast-feeding.
• For a woman of child-bearing potential, the absence of an effective method of contraception or abstinence non observed for at least 4 weeks prior to the first vaccination and at least 4 weeks after the last vaccination.
• Congenital or acquired immunodeficiency, immunosuppressive therapy such as anti-cancer chemotherapy or radiation therapy within the preceding 6 months, or long-term systemic corticosteroid therapy.
• Known human immunodeficiency virus (HIV), hepatitis B (AgHBs) or hepatitis C seropositivity.
• Known systemic hypersensitivity to egg proteins, chick proteins, or to any of the vaccine components, or history of a life-threatening reaction to the trial vaccine or a vaccine containing the same substances.
• Thrombocytopenia or bleeding disorder contraindicating intramuscular vaccination.
• Chronic illness at a stage that could interfere with trial conduct or completion.
• Current abuse of alcohol or drug addiction that may interfere with the subject's ability to comply with trial procedures.
• Subject deprived of freedom by an administrative or court order, or in an emergency setting, or hospitalized without his/her consent.
• Blood or blood-derived products received in the past 3 months.
• Febrile illness (temperature ≥ 37.5°C) on the day of inclusion.
• Laboratory abnormalities considered clinically significant upon the Investigator's judgment in blood sample taken at screening (for Step 1 only)

Clinical Endpoints Assessed:

Safety assessments:

Immunogenicity assessments: Hemagglutination inhibition and neutralization assays

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: After two doses:

<table>
<thead>
<tr>
<th></th>
<th>HI≥40</th>
<th>NT≥40</th>
</tr>
</thead>
<tbody>
<tr>
<td>82%</td>
<td>96%</td>
<td>(6µg+2.5% AF03)</td>
</tr>
<tr>
<td>75%</td>
<td>90%</td>
<td>(6µg+1% AF03)</td>
</tr>
<tr>
<td>58%</td>
<td>78%</td>
<td>(6µg+0.5% AF03)</td>
</tr>
<tr>
<td>80%</td>
<td>80%</td>
<td>(2.5µg+2.5%AF03)</td>
</tr>
<tr>
<td>55%</td>
<td>81%</td>
<td>(2.5µg+0.5%AF03)</td>
</tr>
<tr>
<td>54%</td>
<td>78%</td>
<td>(2.5µg+0.5%AF03)</td>
</tr>
<tr>
<td>20%</td>
<td></td>
<td>(6µg no AF03)</td>
</tr>
<tr>
<td>5%</td>
<td></td>
<td>(2.5µg no AF03)</td>
</tr>
</tbody>
</table>

Others assays:

Status of trial (ongoing/completed): Completed in 2007 - 2010