Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: A Phase I-II, Randomized, Controlled, Dose-Ranging Study of the Safety, Reactogenicity, and Immunogenicity of Intramuscular Inactivated Influenza A/H5N1 Vaccine Given Alone or with Aluminum Hydroxide to Healthy Elderly Adults, DMID Protocol Number 05-0141

Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov)
Authors/sponsors: Rebecca C. Brady, /supported by NIH USA

Study Design: Two doses on days 0 and 28
Vaccine: H5N1, strain A/Vietnam/1203/2004 Manufacturer: Sanofi pasteur
Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector): Inactivated split virus
Adjuvant: Some groups were vaccinated with vaccine containing Al(OH)₃
Delivery system/site: intramuscularly
Doses (antigen and adjuvant): 3.75µg, 7.5µg, 15µg, 45µg of hemagglutinin

Study population
Age range: ≥65 years old
Health status: 600 healthy volunteers

Special inclusion/exclusion criteria:

Inclusion Criteria
- Ambulatory and community dwelling
- Vital signs, especially blood pressure, in the acceptable range
- Stable medical conditions

Exclusion Criteria
- Immunosuppression
- Diagnosis of dementia or associated concomitant medications used for treating dementia
- Major psychiatric diagnosis
- Receipt of certain psychiatric medications
- Planned travel outside of the United States during certain time periods while enrolled in the study

Clinical Endpoints Assessed
Safety assessments: Information on adverse events or serious adverse events.
Immunogenicity assessments
    immunoassay type
    HI (type of RBC used): horse RBC
    Neutralization (type of neutralization assay): microneutralization

Results
Safety:
Reactogenicity: Tenderness at the injection site was the most common solicited adverse event. Most injection site symptoms were mild and peaked on day 0 or day 1. No severe local reactions were reported following either dose. Tenderness was significantly higher in the groups receiving vaccine containing Al(OH)₃ as compared to the non-adjuvanted groups.

AEs: Malaise was the most prevalent systemic symptom reported across all treatment groups. No severe systemic reactogenicity symptoms were reported following either dose. For the groups with or
without Al(OH)$_3$ after dose 1 or dose 2, no dose-related increases in systemic symptoms were observed.

SAEs: No serious adverse events related to vaccination were reported.

Immunogenicity

GMTs

GMR Ratios (post/pre)

Per cent responding (4 fold or greater rise)

Per cent responders at specified titer $\geq$ 40

The table shows the HAI antibody responses for the 545 subjects who received both doses.

<table>
<thead>
<tr>
<th>Dosage (µg HA)</th>
<th>Al(OH)$_3$ adjuvant</th>
<th>N</th>
<th>GMT (95% CI)</th>
<th>% $\geq$ 4-fold rise (95% CI)</th>
<th>% Titer $\geq$ 40 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.75</td>
<td>-</td>
<td>52</td>
<td>6.6 (5.3-8.1)</td>
<td>6% (1-16%)</td>
<td>6% (1-16%)</td>
</tr>
<tr>
<td>3.75</td>
<td>+</td>
<td>51</td>
<td>8.9 (6.3-12.7)</td>
<td>8% (2-19%)</td>
<td>16% (7-29%)</td>
</tr>
<tr>
<td>7.5</td>
<td>-</td>
<td>59</td>
<td>11.0 (7.5-16.1)</td>
<td>15% (7-27%)</td>
<td>22% (12-35%)</td>
</tr>
<tr>
<td>7.5</td>
<td>+</td>
<td>58</td>
<td>9.8 (7.2-13.2)</td>
<td>12% (5-23%)</td>
<td>19% (10-31%)</td>
</tr>
<tr>
<td>15</td>
<td>-</td>
<td>56</td>
<td>13.0 (9.1-18.8)</td>
<td>21% (12-34%)</td>
<td>29% (17-42%)</td>
</tr>
<tr>
<td>15</td>
<td>+</td>
<td>52</td>
<td>10.1 (7.2-14.3)</td>
<td>13% (6-26%)</td>
<td>16% (7-28%)</td>
</tr>
<tr>
<td>45</td>
<td>-</td>
<td>106</td>
<td>19.2 (14.1-26.0)</td>
<td>34% (25-44%)</td>
<td>36% (27-46%)</td>
</tr>
<tr>
<td>45</td>
<td>+</td>
<td>111</td>
<td>19.6 (14.5-26.4)</td>
<td>33% (25-43%)</td>
<td>37% (28-47%)</td>
</tr>
</tbody>
</table>

The best immune responses were in the 45 µg and 45 µg with Al(OH)$_3$ after the second dose of vaccine. Antibody responses to the vaccine at a given dosage level were similar with or without Al(OH)$_3$.

The safety and immunogenicity observations from this study were similar to those from other studies of this vaccine with and without Al(OH)$_3$ in healthy adults. The healthy, carefully selected elderly subjects in this study have similar immune responses to this H5N1 vaccine compared to younger adult subjects.

Current status of the clinical trial (completed, ongoing, in preparation): **Completed**

Date envisaged for availability of results, if not yet available: **Manuscript in preparation**

Planned time schedule for next phase of development: **Not applicable**