Title of Trial: Effect of Administration of Licensed TIV Vaccine on the Safety and Immunogenicity of an Unadjuvanted Sanofi Pasteur H1N1 Influenza Vaccine in Healthy Adult and Elderly Populations

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

Authors/sponsors: Sharon Frey, MD/DMID, National Institute of Health, USA

Study Design (including the phase of clinical trial): randomized, blinded, placebo-controlled, phase II study

Vaccine subtype: H1N1 Virus: influenza Manufacturer: sanofi pasteur

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

Adjuvant: none

Delivery system/site: intramuscular

Doses (antigen and adjuvant, number of doses, intervals between administrations): Adults were stratified into 2 age groups and randomized equally into the following four arms: 1) Two sequential doses of H1N1 followed by TIV; 2) TIV followed by two sequential doses of H1N1; 3) H1N1 followed by H1N1 co-administered with TIV and 4) H1N1 co-administered with TIV followed by H1N1. All vaccination timepoints were placebo (saline) controlled; two injections were administered at the first and second vaccinat timepoint and one injection was administered at the third vaccination time point. The second and third vaccination timepoints occurred 21 days after the previous timepoint.

The vaccine dose was 15mcg as measured by HPLC and 24mcg as measured by SRID.

Study population Number of subjects involved: 805 Age range: 18-65 years and ≥65 years of age

Health status: Healthy volunteers

Special inclusion/exclusion criteria: pregnancy and conditions that would interfere with the evaluation of responses

Clinical Endpoints Assessed

Safety assessments: Immunogenicity assessments:

immunoassay type
HI (type of RBC used):
NT (type of neutralization assay):
SRH

Results

Safety:

Reactogenicity: Local reactogenicity at the vaccination site was predominantly graded by volunteers as mild and there were no severe events. Most systemic reactogenicity events post vaccination were graded as mild; there were few severe events.
AEs:
SAEs:

Immunogenicity

H1 or NT:
GMTs:
GMT Ratios (post:pre):
Per cent responding (4 fold increase):

H1 HA1 Antibody Responses [% 4-Fold Rise (GMT)] in Adult/Elderly to 2009 H1 and/or TIV Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>18–64 Yr</th>
<th>≥65 Yr</th>
<th>18-64 Yr</th>
<th>≥65 Yr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2009 H1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009 H1</td>
<td>89</td>
<td>74</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(332.8)</td>
<td>(186.2)</td>
<td>(40.6)</td>
<td>(38.4)</td>
</tr>
<tr>
<td>Brisbane H1 (as TIV)</td>
<td>19</td>
<td>12</td>
<td>28</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>(13.5)</td>
<td>(15.5)</td>
<td>(85.7)</td>
<td>(60.7)</td>
</tr>
<tr>
<td>Both</td>
<td>84</td>
<td>76</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>(262.3)</td>
<td>(183.3)</td>
<td>(93.7)</td>
<td>(52.5)</td>
</tr>
</tbody>
</table>

Conclusion: 1 dose of 2009 H1N1 is sufficient to induce protective level of antibodies in adults ages 18-64 years. 2009 H1N1 is safe when co-administered with TIV.

Per cent responders at specified titer:

SRH:
Per cent with titre (in mm$^2$)

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

Date envisaged for availability of results, if not yet available: 2Q2010

Planned time schedule for next phase of development: