Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: Dose Ranging Study on the Safety and Immunogenicity of 15 and 30 µg HA of a Prepandemic Monovalent Inactivated Subunit Influenza A/H5N1 (OrniFlu) Vaccine Candidate in Healthy Adults

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

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Participants:
- Research Institute of Influenza RAMS, St. Petersburg, RF
- Mechnikov Research Institute of Vaccines and Sera, Mosco, RF.

Study Design (including the phase of clinical trial): A randomized, placebo-controlled, double-blind, multicenter trial, Phase II. A total of 360 participants were enrolled into three groups (120 participants per group). Participants were vaccinated as follows:
  - Group 1: 15 µg HA OrniFlu Vaccine twice (at Day 0 and at Day 28).
  - Group 2: 30 µg HA OrniFlu Vaccine twice (at Day 0 and at Day 28).
  - Group 3: placebo twice (at Day 0 and at Day 28).

Blood and urine samples for laboratory tests were collected on Day 0, 7, 28, 35 and 56 while sera for HAI and MN - on Day 0 and 56. Totally clinical observation was conducted over 56 days’ period.

Vaccine: OrniFlu H5N1  Manufacturer: Microgen State Scientific Industrial Company, RF
Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector): a monovalent inactivated (formaldehyde) subunit, strain A/Vietnam/1194/2004, egg grown
Adjuvant: aluminum hydroxide
Delivery system/site: intramuscular
Doses (antigen and adjuvant, number of doses, intervals between administrations): 15 µg and 30 µg of HA and 0,5 of Al(OH)₃ in 0,5 ml dose, 2 doses given 28 days apart.

Study population
Number of subjects involved: 360  Age range: 18 to 60
Health status: Health
Special inclusion: Healthy adults (men and women) 18 up to 60, seronegative for Influenza A virus, H5N1 (titre Ab < 1:10 ) , a Volunteer Informed Consent in written
Exclusion criteria: Standard for influenza vaccine clinical trials.

Clinical Endpoints Assessed

Safety assessments: The vaccine safety and reactogenicity were evaluated by the analysis of post-vaccination local and general reactions during a 56 days’ period. The results of laboratory tests (Hgb, WBC, Plts, Cr, Alt; IgE) of blood and urine samples collected on Day 0, 7, 28, 35 and 56 were considered as well while assessment of the vaccine candidate safety.

Immunogenicity assessments:
  immunoassay type
  HI (type of RBC used): horse RBC
  NT (type of neutralization assay): microneutralization test
  SRH
**Results**

**Safety:**

Reactogenicity: The local reactions in the recipients administrated with 15 and 30 µg HA doses were traced not to be dose-dependent. Severe local reactions were reported neither after V1 nor V2. Of all the recipients 6.9% and 7.7% of local slight and moderate reactions were reported in total after V1 and V2 correspondingly. In 5.5% (V1) and 6.9% (V2) of them it was pain in the injection site along with hyperemia, swelling and infiltrate. Hyperemia, swelling and infiltrate without pain in the injection site were registered in 1.4% after V1 and 0.8% after V2.

Temperature reaction in a small number of recipients (6-7) was reported both after the V1 and V2 but among all the cases it was mainly low, ranged from 37.0 to 37.5 °C.

Most cases of general reactions, 33% in total, were traced in the participants received 15 µg HA dose. 30 µg HA dose gave rise to 25.5% general reactions compared to 18.9% cases registered in the recipients received placebo. Most frequently occurred systemic reactions were rhinitis, 15% of all the cases, and headache. Ten point eight percent cases of rhinitis were reported after the first and 10.2% after the second immunization with 15 µg OrniFlu dose. Headache is registered in 5.8% recipients from both 15 µg and 30 µg OrniFlu dosage groups. The second administration of the vaccines did not much influence the character and sharpness of general reactions.

Neither the first not second vaccine administration gave rise to severe systemic reactions.

Biochemical blood parameters as well as clinical urine ones were within the normal range in all the volunteers. Dynamic changes in IgE level were insignificant and within the normal range as well.

**Immunogenicity**

**HAI:**

<table>
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<tr>
<th></th>
<th>OrniFlu (15 µg HA\dose), n=117</th>
<th>Placebo, n=119</th>
<th>OrniFlu (30 µg HA\dose), n=116</th>
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</thead>
<tbody>
<tr>
<td>4-fold SC (%)</td>
<td>48 %</td>
<td>45 %</td>
<td>47 %</td>
</tr>
<tr>
<td>Protective Ab titre ≥ 1:40 (%)</td>
<td>3,2</td>
<td>3 %</td>
<td>46 %</td>
</tr>
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<td>GMT Ratios (post:pre)</td>
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<td>1 %</td>
<td>3,1</td>
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<tr>
<td>4-fold SC (%)</td>
<td>78 %</td>
<td>70 %</td>
<td>78 %</td>
</tr>
<tr>
<td>Protective Ab titre ≥ 1:40 (%)</td>
<td>9,8</td>
<td>3 %</td>
<td>57 %</td>
</tr>
<tr>
<td>GMT Ratios (post:pre)</td>
<td>9,8</td>
<td>1 %</td>
<td>7,3</td>
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</tbody>
</table>

**NT:**

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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:

Planned time schedule for next phase of development: