Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: Phase 1 double-blind study in healthy adults to assess safety, reactogenicity and dose-related immunogenicity of the inactivated virosomal split influenza vaccine

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

Authors/sponsors: Dr I. Krasilnikov, Dr A.Katlinsky, Dr S. Korovkin, Dr S. Melnikov, Dr A.Mironov/Microgen, Russia

Study Design (including the phase of clinical trial): Phase I double-blind study.

Vaccine subtype: H5N2  Virus: A/17/duck/Potsdam/88/92 (H5N2) x Len 17 (H2N2)
Manufacturer: Microgen State Scientific Industrial Company, Russia

Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector):
Inactivated virosomal split
Adjuvant: AL(OH)3
Delivery system/site: IM
Doses (antigen and adjuvant, number of doses, intervals between administrations): 15 µg of viral protein per dose, two doses on days 0 and 28

Study population
Number of subjects involved: 20  Age range: 18-50
Health status: Healthy volunteers

Inclusion criteria
- Healthy adults (men and women) 18 up to 60 years of age
- Seronegative for Influenza A virus, H5 (titre Ab < 1:10), a Volunteer Informed Consent in written

Exclusion criteria
• Allergy to chicken egg protein or prior flu immunization
• Bronchial asthma, chronic lung disease (CLD), chronic rhinitis, primary immunodeficit, immunosuppression, acute infection and non-infection disease
• Leucosis, cancer, hepatitis B and C, positive reaction to HIV
• Volunteers received immunoglobulins or blood transfusion during the last three months’ period
• Pregnancy and lactation period
• Participation in any other clinical trials

Clinical Endpoints Assessed

Safety assessments:
Safety:

Reactogenicity:

Frequency (%) of post-vaccination local and systemic reactions

<table>
<thead>
<tr>
<th>Post-vaccination reactions</th>
<th>Systemic reaction (temperature)</th>
<th>Local reactions (hyperemia, swelling, infiltrate)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low (t 37,0-37,5°C)</td>
<td>Middle (t 37,6 - 38,5°C)</td>
</tr>
<tr>
<td>V 1</td>
<td>AviFlu (Duck H5N2 15 µg HA/dose)</td>
<td>-</td>
</tr>
<tr>
<td>V 2</td>
<td>AviFlu (Duck H5N2 15 µg HA/dose)</td>
<td>-</td>
</tr>
</tbody>
</table>

Immunogenicity assessments:

<table>
<thead>
<tr>
<th>immunoassay type</th>
<th>type of RBC used</th>
<th>type of neutralization assay</th>
<th>SRH</th>
</tr>
</thead>
<tbody>
<tr>
<td>HI</td>
<td>HI with horse erytrocites</td>
<td>Microneutralization</td>
<td>No</td>
</tr>
</tbody>
</table>

Results
After vaccination with all the series of AviFlu vaccine candidate there were no detections of undue reactions in post-vaccination period. Slightly shaped local reactions were a short period (1-3 days) and did not much influence a good state of health of the vaccine recipients.

**Immunogenicity**

**HI or NT:**

**GMTs:**

**GMT Ratios (post:pre):** Fold increase in HI: 20.4 \((15\mu g+Alum)\)

**Per cent responding (4 fold increase):**

HI≥4 fold increase after 2 doses: 100% \((15\mu g+Alum)\)

**Per cent responders at specified titer:**

HI≥40 after 2 doses: 90% \((15\mu g+Alum)\)

Two-fold immunization with the inactivated avian influenza split adjuvanted vaccine candidates has induced a strong antibody response with the antibody titres above the seroprotection level (HAI and MN titre ≥40) to the homologous vaccine strains. In addition the mock-up vaccines promoted broad and persistent cross-clade immunity which is a pre-requisite for a pre-pandemic vaccine.

**SRH:**

**Per cent with titre (in mm²):** Not used

**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:**