Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

**Title of Trial:** Phase I-II evaluation of the Safety and Immunogenicity of a Replication competent Adenovirus Serotype 4-vectored H5N1 Influenza Candidate Vaccine – Ad4-H5-Vtn

**Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov):** ClinicalTrials.gov number, NCT01006798

**Objective:** Proof of Concept of replicating orally administered Ad4 vector vaccine “platform”

**Authors/sponsors:** M. Gurwith, K. Kelley

**Study Design:** Double blinded, placebo controlled, ascending dosage cohort study. Five sequential dosage cohorts: \(10^7\), \(10^8\), \(10^9\), \(10^{10}\), \(10^{11}\) vp. Post-randomization stratification by pre-existing immunity to Ad4 (neutralizing antibody). All HHCs enrolled and monitored for transmission (Ad4-H5-Vtn infection)

**Vaccine:** H5N1, strain Vietnam/1194  **Manufacturer:** PaxVax, Inc. USA

  - **Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector):** Replication-competent vector virus
  - **Adjuvant:** None
  - **Delivery system/site:** 4 (Ad4) vector, oral application
  - **Booster vaccine:** Inactivated subvirion H5N1
  - **Delivery system (booster vaccine):** intramuscular

**Doses (antigen and adjuvant):** Three Ad4-H5-Vtn vaccinations: Day 0, Day 56, and Day 114, 3 to 12 months after last Ad4-H5-Vtn immunization. Dosage was \(10^7\), \(10^8\), \(10^9\), \(10^{10}\), or \(10^{11}\) vp Protocol subsequently amended to add inactivated H5N1 boost (90 µg HA per dose)

**Study population:** 166 Vaccinees/Placebo Recipients  **Age range:** Adults

  - **Health status:** healthy volunteers

**Specific inclusion/exclusion criteria:** **Exclusion:** Living with more than 2 Healthy Household Coutacts (HHCs); HHC <18 years, or >64 years. HHC unwilling to participate. HHC

**Clinical Endpoints Assessed:**

  - **Safety assessments:** Adverse events; 7 day reactogenicity diaries; clinical laboratory; PCR of blood and throat swabs for evidence of systemic spread of Ad4 vaccine virus
Immunogenicity assessments: HAI, microneutralization, HA-specific ELISPOT, HA-ELISA in serum and mucosal secretions. Ad4 neutralization

Virological assessments: PCR of rectal swabs for shedding of vaccine virus

Results:

Safety: No dose limiting toxicity & no dropouts due to toxicity. Most frequent symptoms were tiredness, headache, nasal congestion/runny nose, and sore throat – similar to placebo
No trend for increase with dosage or number of doses
Ad4-H5-Vtn detected in rectal swabs by PCR in 50-80% of Vaccinees at days 7 and/or 14 post vaccination. Ad4-H5-Vtn not detected in blood; only once (Day 7) in throat swab-asymptomatic Vaccinee
No PCR-based evidence of transmission by rectal or throat swabs

Conclusion: Safety and lack of transmission confirmed at all dosages

Immunogenicity

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<thead>
<tr>
<th>GMTs</th>
<th>10^7vp</th>
<th>10^8vp</th>
<th>10^9vp</th>
<th>10^10vp</th>
<th>10^11vp</th>
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</thead>
<tbody>
<tr>
<td>Pre-boost</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Post-boost</td>
<td>28</td>
<td>48</td>
<td>34</td>
<td>77</td>
<td>135</td>
</tr>
<tr>
<td>GMT Ratios (post:pre):</td>
<td>5.6</td>
<td>6</td>
<td>5.7</td>
<td>15.4</td>
<td>19.3</td>
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Per cent responders at specified tite:

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<tr>
<th>10^7vp</th>
<th>10^8vp</th>
<th>10^9vp</th>
<th>10^10vp</th>
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<tbody>
<tr>
<td>62%</td>
<td>67%</td>
<td>61%</td>
<td>80%</td>
<td>94%</td>
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Per cent responding (4 fold or greater rise and definition for reporting):

<table>
<thead>
<tr>
<th>10^7vp</th>
<th>10^8vp</th>
<th>10^9vp</th>
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<tbody>
<tr>
<td>Pre booster:</td>
<td>4%</td>
<td>12%</td>
<td>19%</td>
<td>4%</td>
</tr>
<tr>
<td>Post booster:</td>
<td>69%</td>
<td>78%</td>
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Conclusion: Robust H5 HA specific antibody responses following parenteral protein boost was shown. Based on vaccine take and cellular response, single administration seems to be sufficient for priming.

Others assays:

Status of trial (ongoing/completed): Completed