Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

Title of Trial: Safety, Tolerability, and Immunogenicity Of Bivalent Influenza Peptide Conjugate Vaccine (BIPCV) In Healthy Adults
Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov)

Saint-Louis University, University of Rochester, University of Virginia, and Merck Research Laboratories

Study Design (including the phase of clinical trial): Phase I placebo-controlled clinical trial evaluating the safety and immunogenicity of several combinations of three different dose levels of antigen and three different concentrations of the proprietary adjuvant in healthy adults.

Vaccine subtype: Manufacturer: Merck
Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector): Bivalent peptide OMPC conjugate vaccine (BIPCV) containing: A/M2- peptide from the external portion of M2 protein from Influenza type A and B/ HA0 - peptide from the cleavage region of HA from Influenza type B

Adjuvant: Vaccine formulated on Merck Aluminum (BIPCV/MAA) only or Merck Aluinium and proprietary adjuvant (BIPCV/MAA + Adj)

Delivery system/site: needle/syringe for IM injection
Doses (antigen and adjuvant, number of doses, intervals between administrations): 3-dose regimen given at 0, 2, and 6 months; A/M2 anf B/HA antigens: in the phase 1a: 05, 5, 40 µg; in the phse 1b: 20, 60 and 100µg

Study population: Number of subjects involved: 370 Age range: 18 to 35 years
Health status: healthy volunteers
Special inclusion/exclusion criteria

Clinical Endpoints Assessed

Safety assessments: Injection site and systemic adverse experiences with emphasis on influenza-like symptoms (fever, myalgia, headache, nausea)
Immunogenicity assessments:
immunoassay type: Multi-platform Luminex Assay (beads coated with peptides of interest) used for the evaluation of vaccine-induced immune responses
HI (type of RBC used): Not Applicable
NT (type of neutralization assay): Not Applicable
SRH: Not Applicable

Results
Safety:
These preliminary summary results should be taken with caution given the small number of subjects enrolled in the different treatment groups.

**Reactogenicity:**
Approximately 90% of subjects reporting pain at the injection site and approximately 5% to 30% reporting injection site redness and/or swelling. Reactions were mostly mild to moderate in intensity but highest dose of antigen combined with medium to high concentration of proprietary adjuvant were associated with more moderate to severe local pain, with approximately 10% of subjects reporting severe pain.

**AEs:**
Solicited systemic adverse experiences included flu-like symptoms (headache, myalgia, nausea, and headache) and were reported by 18% to 60% of subjects; Symptoms were generally mild to moderate. More subjects vaccinated with study vaccine composed of the highest dose of antigen combined with medium to high concentration of proprietary adjuvant reported flu-like symptoms than their counterparts immunized with study vaccine composed of low to medium dose of antigen combined with low to medium concentration of the proprietary adjuvant. Moreover, no correlation was found between the incidence of solicited and unsolicited adverse experiences and the number of vaccine doses received.

**SAEs**
No vaccine-related serious adverse experiences were reported during the course of the study.

**Immunogenicity**

**HI or NT:** Not applicable

**GMTs**
**GMT Ratios (post:pre)**
**Per cent responding (4 fold or greater rise and definition for reporting)**
**Per cent responders at specified titer**

**SRH:** Not applicable

**Per cent with titre (in mm²)**

**A/M2- and B/HA₀-specific immune responses by Multi-platform Luminex Assay**
Vaccine-induced responses were evaluated by measuring serum antibodies directed to A/M2 and B/HA₀ peptides using Multi-platform Luminex Assay (beads coated with peptides of interest).

A modest dose response effect was observed when comparing Bivalent Influenza Peptide Conjugate Vaccine formulated on Merck Amorphous Aluminum only (BIPCV/MAA) containing low dose and medium dose of each peptide. No difference was observed when comparing GMTs between subjects receiving BIPCV/MAA at medium and high doses of each peptide. Contrary to preclinical findings, vaccine-induced antibodies do not return to baseline at Month 12 (6 months Post-dose 3) BIPCV formulated on MAA + Proprietary Adjuvant is significantly more immunogenic than BIPCV formulated on MAA only.
• **Post dose 1:** No impact on the magnitude of A/M2-specific antibody titers was observed after initial dose while modest increase (~2-fold) was observed for B/HA0-specific antibody titers

• **Post dose 2:** Significant increase (~1 Log) was observed for both A/M2- and B/HA0-specific antibodies even at the lowest concentration of Adjuvant

Proprietary Adjuvant displays an antigen-sparing effect as lower dose of peptide combined with different concentrations of the proprietary adjuvant elicits antibody levels similar to higher dose of peptides administered without the proprietary adjuvant. Also, a trend towards a dose-response effect was observed. At the same dose level of peptide, increase in the concentration of the proprietary adjuvant was associated with higher antibody titers for both A/M2 and B/HA0-specific antibodies. Finally, a trend towards a dose-response effect was also observed with increasing concentration of peptides for a given amount of the proprietary adjuvant.

Results shown in the 2 figures below represent A/M2- and B/HA0-specific antibodies measured in subjects immunized with BIPCV/MAA containing the medium dose of each peptide and BIPCV/MAA + Proprietary adjuvant containing the medium dose of each peptide combined with different concentrations (low, medium, and high) of the proprietary adjuvant. Similar trends were observed with study vaccine containing low and high peptide dose combined with different concentrations of the proprietary adjuvant.
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: