

SEEK

FLU-v: Universal Influenza Vaccine Clinical Development

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PIONEERING SCIENCE, COMMERCIALY DELIVERED

FLU-v composition

An equimolar admixture of four individual synthetic polypeptides (20 to 32 aa long) covering conserved immunogenic regions in M1, M2 and NP.

Criteria for selection of immunogenic sequences:

- **LENGTH:** Short Regions (<40 aa)
- **CONSERVATION:** Present in >70% of all animal and human influenza strains.
- **IMMUNOREACTIVITY:** Each region contains >5 potential T cell epitopes.
- **UNIVERSALITY:** Absence of all epitopes in any Flu strain: $p < 10^{-10}$



Previous clinical data

- Phase I
 - FLU-v was safe and well tolerated with no vaccine associated severe adverse events.
 - Dose-dependent IFN-gamma responses >2-fold the pre-vaccination level were detected in 80% and 100% of volunteers receiving, respectively, the low (250ug) and high dose (500ug) adjuvanted FLU-v formulations.
- Challenge study
 - FLU-v was safe and well tolerated.
 - Day-19 post-vaccination, the FLU-v group, but not the Placebo, developed FLU-v specific IFN-g responses (8.2 ± 3.9 vs 1.3 ± 0.1 fold increase, respectively).
 - FLU-v specific cellular responses correlated with reductions in both viral titre ($p=0.01$) and symptom score ($p=0.02$) post-challenge.



UNISEC Clinical trial protocol

- **Single centre double-blind randomised trial**
- **4 arms:**
 - **Single dose adjuvanted FLUv (500ug) n=74**
 - **Two doses non-adjuvanted FLUv (500ug) n=74**
 - **Placebo: single dose adjuvanted water for injection n=37**
 - **Placebo: two doses saline n=37**
- **Visits:**
 - **Screening /Inclusion/ Exclusion criteria / Blood chemistry (approx day -7)**
 - **Randomisation/ Blood sample/ first dose (day 0)**
 - **Second dose (day 21)**
 - **Blood sample (day 42)**
 - **Blood sample (day 180)**



Study end points

- **Immunogenicity:** Measured at prevaccination, post vaccination (day 42) and long term (day 180)
 - **Cellular**
 - **CMI studies: multiparametric FACS analysis CD4+/CD8+ cells and cytokines (IFN γ , TNF) (Primary Endpoint)**
 - **Additional assays (Granzyme B secretion)(Exploratory)**
 - **Humoral**
 - **Isotyping of antibody responses to FLUv**
 - **ADCC/ADC assays**



Study end points

- **Efficacy:**
 - Reduction in influenza symptom scores (daily diary score during influenza season)
 - Reduction in the number of RT-PCR –confirmed influenza infections (nasal and throat swab when predefined symptom scores persist for 24h)
- **Safety:**
 - Solicited Adverse effects until 21 days post -vaccination
 - Unsolicited Adverse Effects and Severe Adverse effects during the entire duration of the study.



Trial progress

- **Study Protocol in the final stages.**
- **Peptide GMP Manufacturing: American Peptide, San Diego, US. Ready to sign contract.**
- **Sterile vialling company and Analytical & Stability studies: Symbiosis, Scotland. Ready to sign contract.**
- **Trial centre: Isala Clinics, Zwolle, The Netherlands. Negotiations to start immediately.**
- **Ethics & Regulatory: Information on manufacturing (CMC) required in order to update IMP Dossier to add to Clinical Trial Application and submit to Ethics and Regulatory boards.**
- **Support to WP5 in protocol development (PBMC isolation and flow cytometry assays)**

