



WP6 (Lead Partner RUG)

Clinical Trial Program

Eelko Hak, Work Package leader

**Groningen Research Institute of Pharmacy &
Epidemiology, University of Groningen**





Double-Blind Randomized Controlled Phase IIb Vaccine Trials



➤ Aim:

To evaluate the safety and immunogenicity of two universal influenza vaccines targeting different conserved immunogenic regions of influenza A and B viruses.



- ❖ *FLU-v (SEEK, UK) and M-001 (BiondVax, Israel) are both peptide based vaccines containing epitopes identified from the viral internal (structural) proteins.*
- ❖ *M-001 contains also epitopes from the viral surface glycoproteins.*
- ❖ *While FLU-v is composed of synthetic polypeptides, M-001 is composed of a single recombinant protein.*



Double-Blind Randomized Controlled Phase IIb Vaccine Trials (cont.)



➤ **Trial participants:**

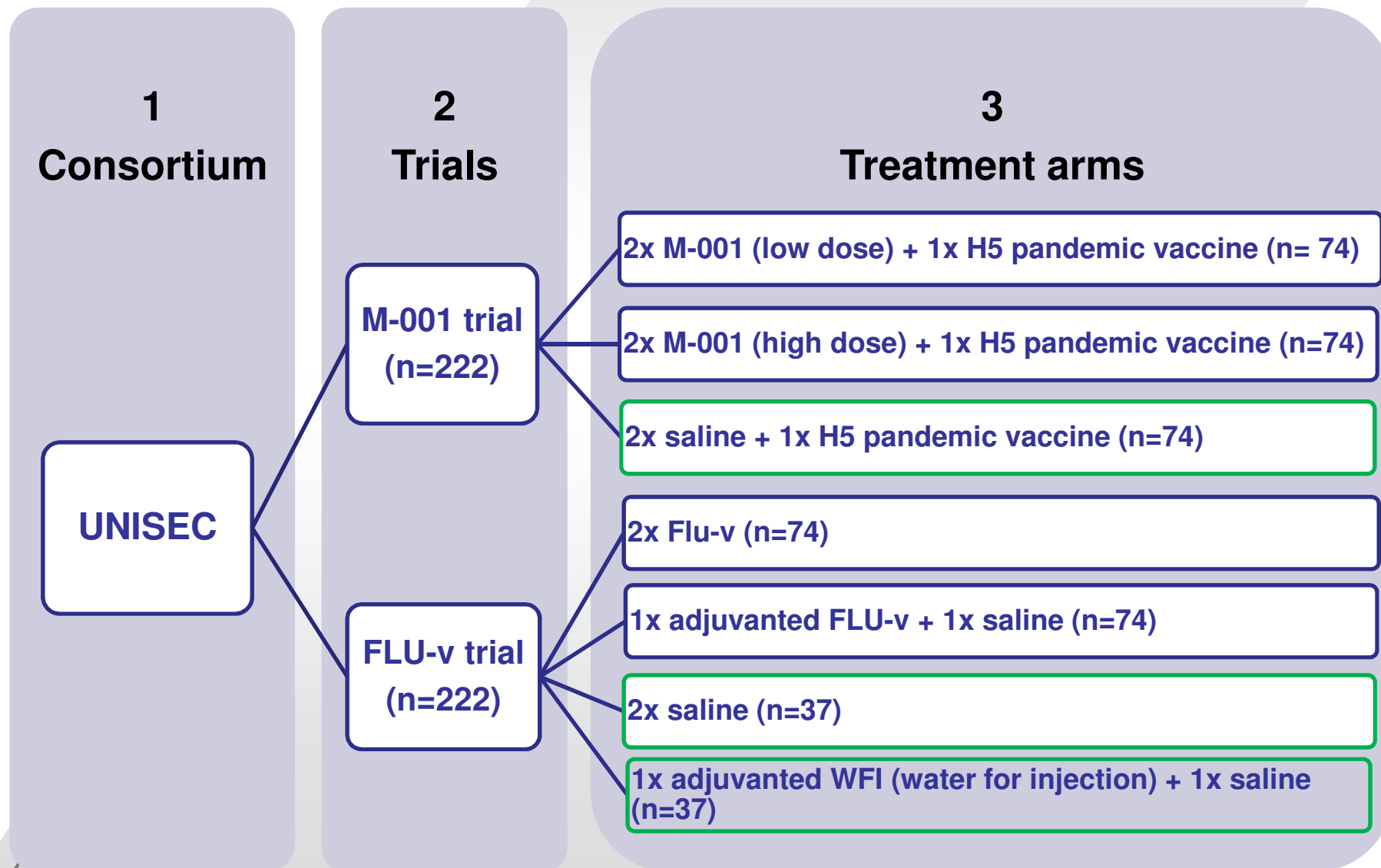
Healthy adults aged 18-60 years, not among the target groups for influenza vaccination.

➤ **Sample size estimation:**

- ❖ Determined on the basis of influenza-specific interferon- γ responses observed from their earlier trials.
 - ❖ FLU-v study: fold increase of influenza-specific interferon- γ responses measured by ELISA.
 - ❖ M-001 study: fold increase of influenza-specific interferon- γ secreting CD8+ T cells measured by FACS analysis.
- ❖ Two-sided α of 5%, power of 80% with continuity correction.
- ❖ Taking a loss to follow up into account, we will include 222 subjects in total (74 subjects per experimental arm).



Study Layout





Study endpoints



Safety

- AE diary cards and questionnaires will be collected until 180 days after the first dosing.

Immune Correlates of Protection

- Cellular immunity will be assessed on day 42 (21 days after the second administration).
- For FLU-v study, cellular immunity on day 180 (159 days after the second administration) will also be assessed. Antibody responses on day 42 and 180 will be evaluated.
- For M-001 study, cellular and humoral immunity (HI) will be assessed 21 days after the H5 pandemic vaccination.

- A maximum of 187 days (from screening to study conclusion) study participation, covering one influenza season.



Exploratory endpoints



➤ **M-001 trial**

- ❖ Additional CMI measures (qRT-PCR assay).
- ❖ Humoral immunity (HI) against drifted H5N1 strains.
- ❖ Association between CMI markers and antibody responses measured in the study.

➤ **FLU-v trial**

- ❖ Clinical efficacy
 - Clinical symptom score (to be collected during the influenza epidemic season (December-March)).
 - RT-PCR –confirmed influenza infections
- ❖ Additional CMI measures.
- ❖ Antibody responses.
 - Isotyping of antibody responses to FLUv
 - ADCC/ADC assays



Trial Logistics



➤ Clinical trial sites:

- ❖ St Istvan St Laszlo Hospital (Hungary) will perform the M-001 study.
- ❖ Isala (Zwolle, NL) is the potential site for the FLU-v study.

➤ PBMC processing sites:

- ❖ National Center of Epidemiology (Hungary) will process clinical samples for the M-001 study.
- ❖ Isala is able to process clinical samples for the FLU-v study.

➤ Laboratories for clinical sample analysis:

- ❖ Robert Koch Institute is the central analytic center for clinical studies run under the UNISEC consortium (WP5 leader). Perform multi-parametric intracellular cytokine FACS analysis and IFN- γ ELISA (primary CMI endpoint).
- ❖ National Center of Epidemiology will analyze HAI assay and additional (exploratory) CMI endpoints for the M-001 study.
- ❖ National Institute Public Health (Norway) is able to measure additional (exploratory) CMI endpoints for the FLU-v study.



Data Management



- Will be performed by UMCG Trial Coordination Center (Iso-certified);
- Project manager Denise Maily, part of WP6-team;
- In close collaboration with sponsors and WP partners;
- Case report forms on secured website;
- Check of data consistency and reliability;
- Pseudo-anonymization;
- Data Safety and Monitoring Board not required.



Action points BVX



- Submission BVX dossier to Hungarian authorities.
- Development of recruitment strategies in Hungary.
- GMP vaccine manufacturing.
- Development and testing IT tool data management.
- Statistical Analysis Plan.



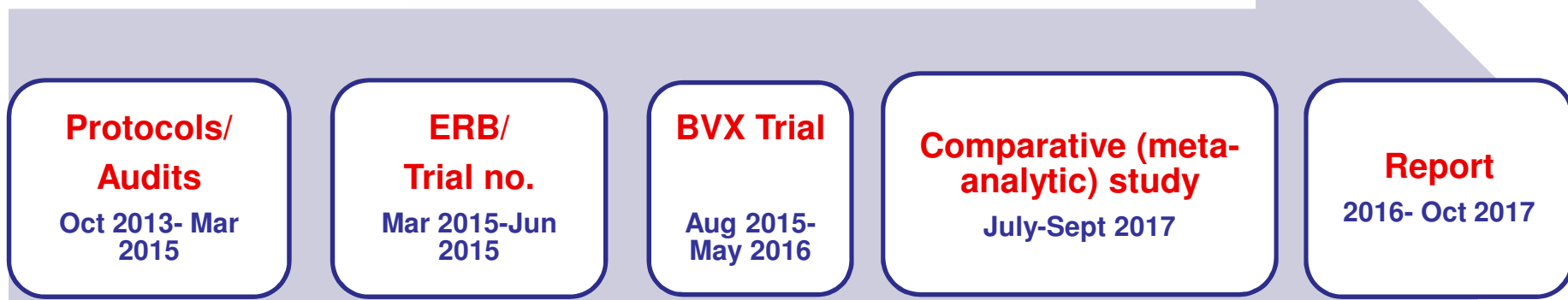
Action points SEEK



- Further tendering GMP manufacturers.
- Tendering CRO.
- Meeting with Zwolle Isala Clinics.
- Meeting with National Institute Public Health.
- Submission SEEK dossier to NL authorities.
- Development of recruitment strategies in Zwolle.
- GMP vaccine manufacturing.
- Development and testing IT tool datamanagement.
- Statistical Analysis Plan.



Timelines



**Batch
information
needed from
GMP producer**

**SEEK trial
possibly delayed
with 6-12 months**