Design of Randomized, Double-blind, Controlled, Multi-center Phase II Trials as Part of the EU-funded UNISEC Project to Assess the Safety and Immunogenicity of Cross-seasonal Universal Influenza Vaccines With or Without Pandemic Influenza Vaccine in Healthy Adults

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Background

Each year during seasonal epidemics, influenza infects 5-10% of the adult population and 20-30% of all children, resulting in 3 to 5 million cases of severe illness and 250,000 to 500,000 deaths worldwide. Current seasonal influenza vaccines mainly induce immune responses against viral membrane glycoproteins, which undergo continuous mutations by a process called antigenic drift. To prevent immune escape, annual vaccination with the latest predicted viral strains is adopted. Such vaccination strategy not only poses inconvenience and cost-inefficiency, but also results in poor protective effectiveness when the vaccinated strains are mismatched with the actual circulating strains. The latter point is especially of concern during a pandemic outbreak, when a large geographical area is affected and the general population is naïve to the newly reassorted viral strain due to antigenic shift.

Objective

As part of the EU-funded Universal Influenza Vaccines Secured (UNISEC) project (http:// www.unisecconsortium.eu), we designed phase II studies to evaluate the safety and immunogenicity of two influenza vaccine candidates targeting conserved and immunogenic regions of influenza A and B viruses.

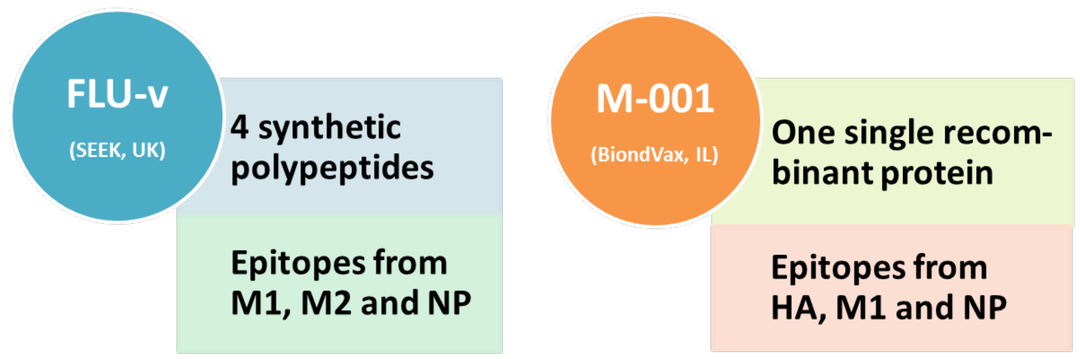

Fig.1 Study vaccines

Methods

Healthy volunteers aged 18-60 in Hungary and the Netherlands will be recruited for the M-001 trial (for the 2015-2016 influenza season) and the FLU-v trial (for the 2016-2017 influenza season), respectively. Subjects will be recruited and randomized to receive the study treatments outlined in Fig. 2 through a double-blind procedure. Pandemic H5N1 influenza vaccine will be given in the M-001 trial to evaluate the effect of the study vaccine on antibody responses to pandemic influenza strains.

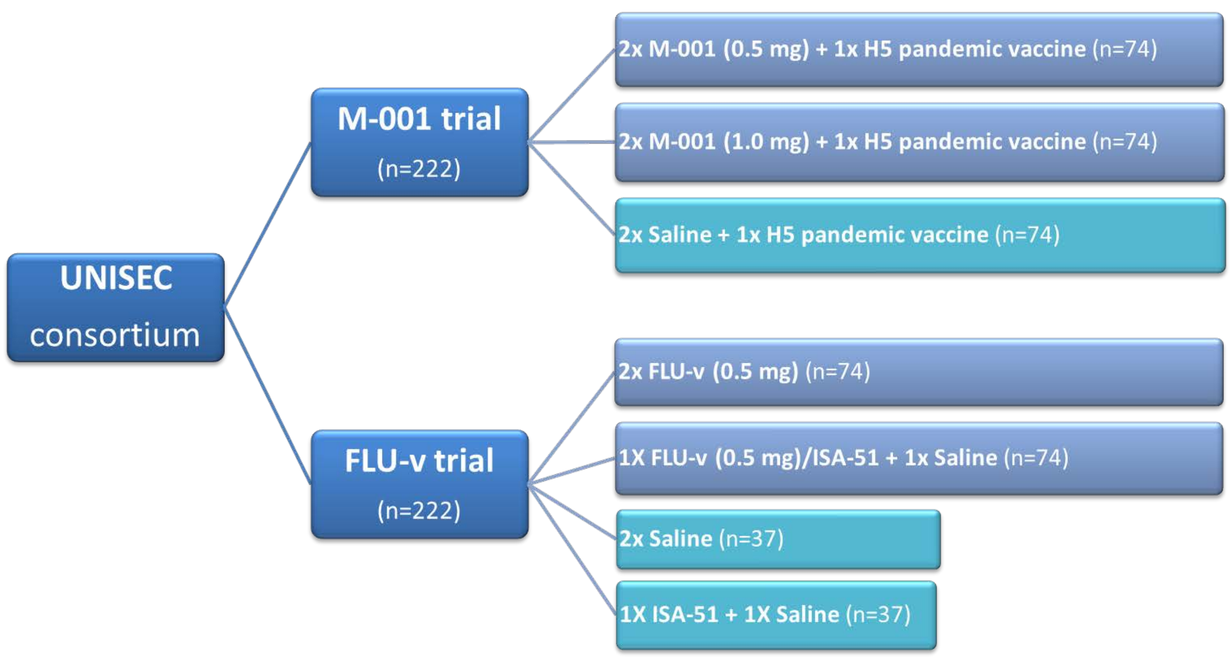

Fig.2 Study design

All vaccinations are to be given by parenteral route with a 21 day interval. For both trials, adverse events and immune responses will be monitored and evaluated as outlined in Fig 3. Scientifically validated assays for cellular medicated immunity and non–neutralizing antibody responses will be used to evaluate the vaccine efficacy and cross-reactivity. In addition, as an exploratory endpoint, the FLU-v trial will explore clinical efficacy of the study vaccine.

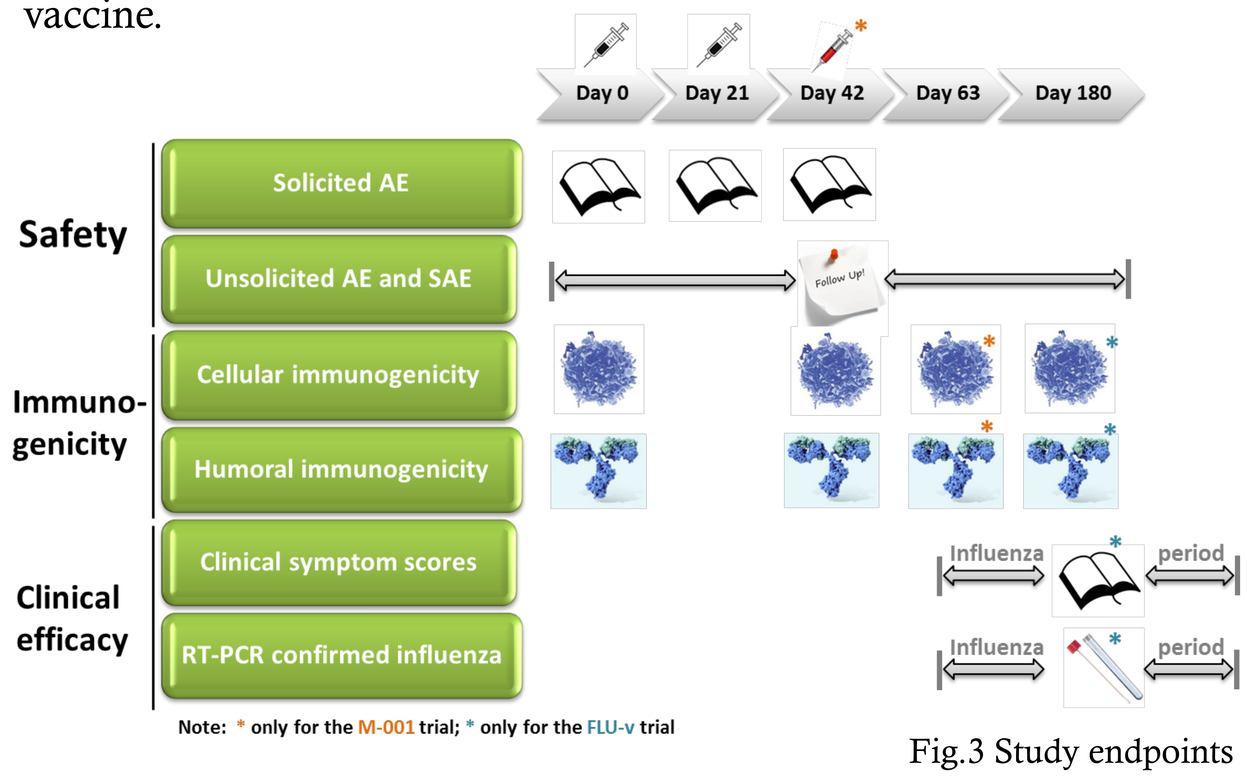

Fig.3 Study endpoints

Conclusions

Broad range influenza vaccines targeting highly conserved regions of influenza viruses are urgently needed. Here we describe the experimental setup for Phase II studies with two promising influenza vaccine candidates, Flu-v and M-001.

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