A Clinical Phase II Study Confirming the Safety and Immunogenicity of One or Two Doses IMVAMUNE® *(MVA-BN®)* Smallpox Vaccine in Vaccinia-experienced Elderly Subjects


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**Background**

IMVAMUNE® (MVA-BN®) is a live, highly attenuated Modified Vaccinia Ankara virus vaccine formulated at a dose of 1 x 10⁷ TCID₅₀/0.5 mL IMVAMUNE® and not replicate in human cells and is in clinical development as a 3rd generation smallpox vaccine.

A Phase II study (POX-MVA-024) was conducted to evaluate safety and immunogenicity (using both ELISA and PRNT) of one and two doses of IMVAMUNE® smallpox vaccine in 56-80 year old vaccinia-experienced subjects (n = 120). Subjects received either two injections of 0.5 mL IMVAMUNE® or one injection of 0.5 mL placebo and one injection of IMVAMUNE® four weeks apart.

Vaccinations were well tolerated by all subjects. No serious adverse events related to IMVAMUNE® and no cases of myo- / pericarditis were reported. The overall incidence of unsolicited AEs was similar in both groups. A second dose did not increase reactogenicity. ELISA as well as PRNT results were comparable after one dose for the two groups.

**Objective**

The results indicate that in an emergency situation it is sufficient to vaccinate this population only once.

**Methods**

This randomized, double-blind, placebo-controlled Phase II trial conducted at four sites in the US enrolled 120 subjects divided among two groups. Vaccinia-experienced women and men aged 56 to 80 years were eligible. The study consisted of a screening period of up to four weeks, an active study period of eight to 10 weeks consisting of five visits, and a follow-up period of at least 26 weeks after the last vaccination.

Group 1 (N=61) received two subcutaneous (s.c.) vaccinations with IMVAMUNE® (0.5 mL vaccine containing 1 x 10⁷ tissue culture infectious dose 50% (TCID₅₀)/dose) at 0 and 4 weeks. Group 2 (N=59) received a first s.c. vaccination with placebo (0.5 mL saline), followed by a second s.c. vaccination with IMVAMUNE® four weeks later.

**Safety**

To evaluate safety of the IMVAMUNE® vaccinations, solicited and unsolicited adverse events (AEs) were recorded and safety laboratory tests including troponin I, physical examinations including vital signs and electrocardiograms (ECG) were performed.

**Criteria for evaluation**

- Serious adverse events (SAEs) associated with the study vaccine
- Unsolicited non-serious AEs within 28 days after each vaccination
- Grade 3 or 4 AEs associated with the study vaccine within 28 days after each vaccination
- Any cardiac events and/or any ECG change indicating a case of myo- / pericarditis
- Solicited local adverse reactions within one week (Days 0 to 7) after each vaccination
- Solicited general AEs within one week (Days 0 to 7) after each vaccination

**Immunogenicity**

Immune analyses were performed for each trial visit except for the screening visit. The baseline assessment for immunogenicity parameters was performed prior to the first vaccination. The humoral immune response was tested at each visit using a direct vaccinia-specific ELISA and a vaccinia-specific PRNT.

**Criteria for evaluation of ELISA & PRNT:**

- Percentage of subjects with responses
- Percentage of subjects seroconverting defined as either the appearance of antibody titer for initially seronegative subjects or a doubling or more of the antibody titer compared to the baseline titer for subjects with a pre-existing antibody titer
- Geometric mean titers (GMTs)

**Results**

**Immunogenicity in Vaccinia-naive Subjects**

The two graphs show the ELISA and PRINT GMTs from a vaccinia-naïve population (mean age 25.3 years) after two vaccinations with 1x10⁷ TCID₅₀ IMVAMUNE® at week 0 and week 4. Data are taken from the clinical trial POX-MVA-010.