

# Prospective Cohort Study and Emulated Target Trial to Estimate the Safety and Effectiveness of MVA-BN vaccination against MPXV infection in at-risk individuals in Germany (SEMVAc/TEMVAc)

**First published:** 15/12/2022

**Last updated:** 20/09/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS50093

---

### Study ID

50282

---

### DARWIN EU® study

No

---

### Study countries

 Germany

---

## Study description

The SEMVAc study is a prospective, non-interventional, multicentric cohort study of the safety and effectiveness of the MVA-BN vaccine in a population of MSM and transgender persons. SEMVAc aimed to assess effectiveness of the MVA-BN vaccine and to describe the incidence of safety events (SAR, AR, AESIs) and reactogenicity (tolerability) of mpox vaccination. It also aimed to describe the influence of sexual behaviour, HIV status, PrEP use, and history of smallpox vaccination (HSMV) on the safety and effectiveness of mpox vaccination. The additional analysis, TEMVAc, used a retrospective, target trial emulation approach only for the primary objective of vaccine effectiveness.

---

## Study status

Finalised

# Research institutions and networks

## Institutions

### Charité-Universitätsmedizin

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

### Aetion



Spain

**First published:** 24/11/2022

Last updated: 16/07/2024

Institution

Other

ENCePP partner

## Contact details

### Study institution contact

Leif Erik Sander [infektiologie@charite.de](mailto:infektiologie@charite.de)

Study contact

[infektiologie@charite.de](mailto:infektiologie@charite.de)

### Primary lead investigator

Leif Erik Sander

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 30/12/2022

---

### Study start date

Planned: 01/07/2022

---

### Data analysis start date

Planned: 09/01/2023

---

### Date of interim report, if expected

Planned: 07/02/2023

Actual: 30/04/2024

---

### **Date of final study report**

Planned: 08/01/2024

Actual: 19/08/2024

## Sources of funding

- Other

## More details on funding

EMA, Intramural funds of the Charité - Universitätsmedizin Berlin and Berlin Institute of Health (BIH)

## Study protocol

[20221202\\_SEMVAc\\_V1.3 final\\_shared version.docx.pdf](#) (534.65 KB)

## Regulatory

### **Was the study required by a regulatory body?**

Yes

---

### **Is the study required by a Risk Management Plan (RMP)?**

EU RMP category 3 (required)

## Other study registration identification numbers and links

## Methodological aspects

### Study type

#### Study type list

**Study topic:**

Disease /health condition  
Human medicinal product

---

**Study type:**

Non-interventional study

---

**Scope of the study:**

Disease epidemiology  
Effectiveness study (incl. comparative)  
Safety study (incl. comparative)

**Study design:**

Primary data collection: Prospective patient-based data collection in infectious disease clinics (SEMVAc) and retrospective data abstraction from EHRs in a subset of the SEMVAc clinics (TEMVAc)

**Main study objective:**

SEMVAc aimed to assess effectiveness of the MVA-BN vaccine and to describe the incidence of safety events (SAR, AR, AESIs) and reactogenicity (tolerability) of mpox vaccination. It also aimed to describe the influence of sexual

behaviour, HIV status, PrEP use, and history of smallpox vaccination (HSMV) on the safety and effectiveness of mpox vaccination. The additional analysis, TEMVAc, was conducted only for the primary objective of vaccine effectiveness.

## Study Design

### **Non-interventional study design**

Cohort

## Study drug and medical condition

### **Medicinal product name**

IMVANEX

---

### **Study drug International non-proprietary name (INN) or common name**

MODIFIED VACCINIA ANKARA – BAVARIAN NORDIC LIVE VIRUS

---

### **Anatomical Therapeutic Chemical (ATC) code**

(J07BX01) smallpox and monkeypox vaccines

smallpox and monkeypox vaccines

---

### **Medical condition to be studied**

Monkeypox

Monkeypox immunisation

## Population studied

## **Age groups**

- **Adult and elderly population ( $\geq 18$  years)**
- 

## **Special population of interest**

Other

---

## **Special population of interest, other**

MSM and transgender persons

---

## **Estimated number of subjects**

15000

# Study design details

## **Outcomes**

In SEMVAc and TEMVAc, the primary outcome of vaccine effectiveness was mpox, defined as the confirmation of a positive Polymerase chain reaction (PCR) laboratory test result indicating mpox virus (MPXV) infection and reported by the study centre physician on the electronic case report form (eCRF). In SEMVAc, The safety outcomes included any event that classifies as adverse reaction, severe adverse reaction, or specified AESI's myo- and pericarditis and encephalitis. Moreover, in SEMVAc, participants completed reactogenicity questionnaires regarding symptoms experienced within 7 days of receiving the vaccination and sexual behaviour questionnaires were collected on a monthly basis for the entire cohort, and after each vaccination in participants who were vaccinated during the study period.

---

## **Data analysis plan**

In SEMVAc, vaccine effectiveness was estimated by comparing the occurrence of the outcome, mpox confirmed by positive PCR, in vaccinated versus unvaccinated participants. Initially, the analysis of the primary endpoint VE was defined as reduction in risk of infection/disease in vaccinated versus unvaccinated participants by  $VE = 1 - RR$  defined using cumulative incidences or hazard ratios. Propensity score matching was planned at a ratio of 1:2 for vaccinated and unvaccinated, using a caliper of 0.1, to reduce bias in results and ensure comparability and balance in baseline characteristics across groups. However, no mpox cases were observed in the unvaccinated group at the time of the SEMVAc final analyses, thereby requiring TEMVAc to calculate VE. For TEMVAc, matching was performed based on a rolling cohort, thereby, beginning on 1 July 2022 and advancing daily, eligible persons receiving the first MVA-BN vaccination on that day were matched to controls that were not previously recruited at a ratio 1:1. Exact matching was performed based on variables such as age, HIV infection, PrEP intake or history of smallpox vaccination, among others. If exact matching was not feasible, matching rules for each variable were adapted accordingly or variables were excluded from the matching algorithm. VE was calculated as  $(1 - RR) * 100$ . VE was reported for both groups, those with one dose and two doses of MVA-BN.

In SEMVAc, safety endpoints SARs and ARs were described via absolute frequencies of participants. Time-to-event analysis was used for time to first AR/SAR for each safety endpoint via cumulative incidences using the Kaplan-Meier estimator. In the presence of competing events (e.g. death), cumulative incidences would be estimated via Aalen-Johansen estimator. Each AR was counted once for a given participant and graded using the highest intensity and relationship to MVA-BN vaccination.

## Documents

## Study report

[SEMVAc and TEMVAc\\_Extended Study Report.pdf](#) (4.69 MB)

## Study, other information

[Annex 2\\_Supplementary Material\\_SEMVAc and TEMVAc extended study report.pdf](#) (1.69 MB)

# Data management

## ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### Data source(s)

Other data source

---

### Data sources (types)

[Other](#)

---

### Data sources (types), other

Prospective patient-based data collection in infectious disease clinics (SEMVAc) and retrospective data abstraction from EHRs in a subset of the SEMVAc clinics (TEMVAc)

## Use of a Common Data Model (CDM)

## **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

---

### **Check completeness**

Yes

---

### **Check stability**

Unknown

---

### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

Not applicable