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

Study contact

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 (≥18 years)**

Special population of interest

Other

Special population of interest, other

MSM and transgender persons

Estimated number of subjects

15.000

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

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