Safety and Effectiveness of MVA-BN vaccination against MPXV infection in at-risk individuals in Germany (SEMVAc)

A prospective, non-interventional, multicentric cohort study

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Outline

» Current MPXV situation in Germany
» Study design
   – Hypotheses
   – Study outcomes
» Visit plan
» eCRF and questionnaires
Background

Current MPX outbreak with >21,000 confirmed cases worldwide (July 28, 2022)

- Germany: 2677 confirmed cases (Aug 1, 2022, RKI)
- Berlin: 1377 confirmed cases (Aug 1, 2022, LaGeSo)

https://ourworldindata.org/monkeypox
Vaccine – Current recommendation in Germany

» **Post-exposure prophylaxis (PEP)**

» **Indication vaccination (Prophylactic)**
  – Men who have sex with men (MSM) with changing sexual contacts
  – Staff in special laboratories with contact to MPXV

» **Estimates of eligible / at risk population**
  – Approx. 1.5 million persons identify as MSM in GER
  – Approx. 130-180,000 persons with high-risk / frequently changing sexual contacts

Prioritisation strategy due to vaccine shortage:

„Since the vaccine is currently only available in limited quantities, PEP should be offered to exposed individuals as a matter of priority. In addition, individuals with an increased risk of a severe disease course (e.g. individuals with immunodeficiency) should be vaccinated with priority both for the PEP and for the indication vaccination. “
Vaccine distribution in specialised outpatient clinics for infectious diseases / HIV:

Due to vaccine shortage doctors are advised to assess patients into two risk groups:

**Group A:** Individuals at high risk, who should receive vaccination with high priority (according to the official recommendation, patients with an increased risk of a severe disease course, e.g. patients with immunodeficiency).

**Group B:** Individuals at risk. Persons that are eligible for vaccination according to the recommendation, but for whom a severe course of disease is not expected and for whom it is acceptable to receive vaccination at a later time point. These individuals receive closer monitoring as part of routine medical care, in addition to detailed information about the risk of MPX infection, especially in the case of anonymous and changing sexual contacts.

→ As long as vaccine supply is limited, not all individuals are able to receive vaccination.
→ Care givers will need to allocate vaccines within risk group B.
→ opportunity for „randomized“ allocation of vaccine among individuals with similar risk of infection.
Hypotheses

1. Vaccination with MVA-BN reduces the likelihood of infection with MPXV and symptomatic monkeypox disease compared to non-vaccinated individuals.

2. Pre-existing conditions and medication may influence the risk of contracting monkeypox as a vaccinated person.

3. MVA-BN induces specific antibodies against MPXV. This is influenced by pre-existing conditions and medication.
**Outcome Measures**

» **Primary Outcome Measure**
   - Vaccine effectiveness of MVA-BN against symptomatic PCR-confirmed monkeypox disease, defined as reduction in risk of disease in vaccinated versus unvaccinated individuals.

\[
\text{Vaccine effectiveness} = \frac{\text{Attack rate of unvaccinated people} - \text{Attack rate of vaccinated people}}{\text{Attack rate of unvaccinated people}}
\]

» **Secondary Outcome Measures**
   - For study participants who have received at least one dose of MVA-BN vaccination:
     • Safety and tolerability of MVA-BN vaccination, assessed by questionnaires
     • Influence of pre-existing (co-) infections (e.g. HIV) and co-medication (e.g. HIV pre-exposure prophylaxis [PrEP]) on the tolerability of the vaccination.

» **Exploratory Outcome Measures (excerpt)**
   - In a subgroup of 1.000 vaccinated and 1.000 unvaccinated individuals:
     • Immunogenicity before and after vaccination, measured by MPXV specific antibodies, i.e. reactivity in a serological assay
Outcome Measures

» Exploratory Outcome Measures

– In a subgroup of 1,000 vaccinated and 1,000 unvaccinated individuals:
  • Pre-existing immunity before first vaccination, measured by MPXV specific antibodies, i.e. reactivity in a serological assay.
  • Immunogenicity 4 weeks after 1st vaccination or before 2nd vaccination, measured by MPXV specific antibodies, i.e. reactivity in a serological assay.
  • Immunogenicity 3, 6, 9 and 12 months after first vaccination, measured by MPXV specific antibodies, i.e. reactivity in a serological assay.
  • Influence of pre-existing immunity after immunisation against Variola major on immunogenicity of MVA-BN vaccination
  • Influence of HIV PrEP on immunogenicity of MVA-BN vaccination
  • Influence of previous diseases (e.g. HIV, STIs, atopic dermatitis) and medication on immunogenicity
  • Influence of immunity against other infectious diseases, measured by specific antibodies, e.g. against Treponema pallidum, on immunogenicity
  • Changes in the humoral immune response over time in vaccinated and unvaccinated individuals
Study design

15,000 Participants
Individual observation for 12 months

5,000 Vaccine group
- Inclusion study visit
- 1 or 2 MVA-BN vaccinations (in regards to smallpox vaccination status)
- Monthly questionnaire and 2 weeks after (each) vaccination

10,000 Control group
- Inclusion study visit
- No vaccination
- Monthly questionnaire

Expected cross-over to vaccination group.

Immunogenicity: 1,000 people
- Existing medical indication for quarterly blood samples

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- Existing medical indication for quarterly blood samples
Study design

Inclusion criteria:
MSM (>18y) eligible for MVA-BN vaccination (according to STIKO criteria)

Exclusion criteria:
Previous exposure to MPXV
Inability or unwillingness to consent

Recruitment goal n=15,000
» Compensation for: Loss-to-follow up, expected cross-over to vaccination group
» Aim: 7,500 individuals / group

Recruitment strategy:
Multicenter study involving specialized ID clinics (private practices, approx. 50 sites) across Germany (requires ethics in each state)
## Visit plan

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<thead>
<tr>
<th>Group</th>
<th>Measure</th>
<th>Time Schedule (W= Week)</th>
<th>Up to 1 year</th>
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<td>Control group, no blood sample</td>
<td>Study Visit for inclusion</td>
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<td>Questionnaire</td>
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<td>Additional to above serology</td>
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<td>quarterly (3, 6, 9, 12 months)</td>
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<td>1st MVA-BN Vaccination*</td>
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<td>2nd MVA-BN Vaccination*</td>
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* Vaccination with MVA-BN is carried out independently from this study.
eCRF and questionnaires

» Combined reporting by study physician on-site and participants via digital surveys with personalized links

» Physician
  – Baseline variables (e.g., age, relevant past medical history, STDs, immunosuppression, HIV therapy, HIV PrEP, previous smallpox vaccination)
  – Safety and (S)AE reporting
  – MPX infection
  – MVA-BN vaccination

» Participant
  – Sexual behaviour (e.g., number of sexual partners, sexual practices, possible exposure)
  – Reactogenicity after 1st and 2nd vaccination with MVA-BN via modified FDA toxicity scale
  – MPX infection: clinical course and outcome (e.g., location of skin lesions, assessment of pain, concomitant general symptoms)
Thank you for your attention!

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