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Safety and effectiveness of MVA-BN vaccination against MPox infection in at-risk individuals in Germany & US

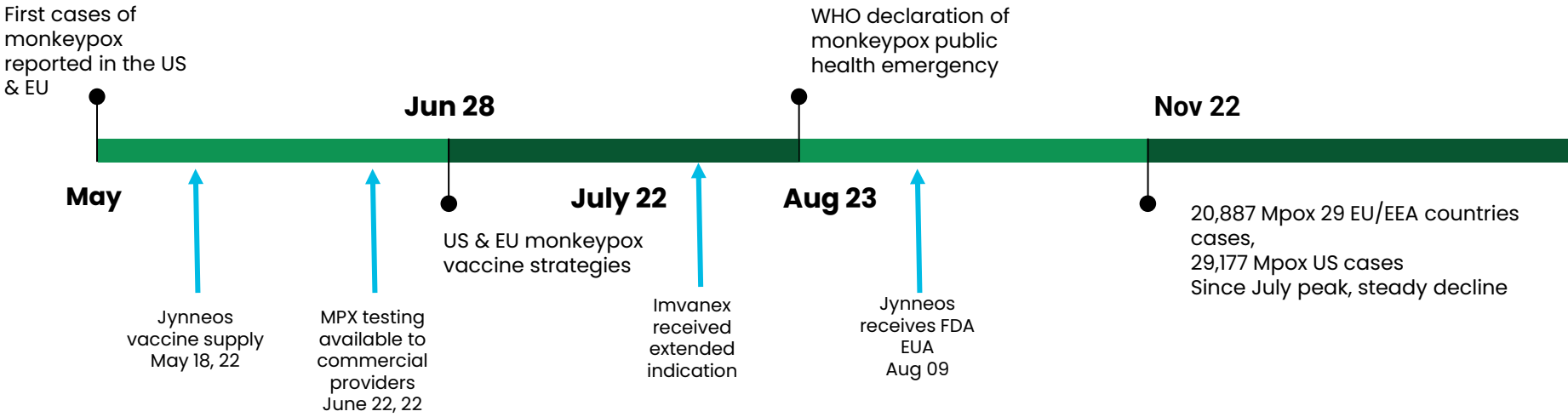
Pierre Engel, ENCePP Plenary, Nov 30, 2022

ENEPP

Disclaimer

- Pierre ENGEL is an employee of Aetion inc. specialized in RWE and currently selected among the EMA framework contractors for pharmacoepidemiology research
- Pierre ENGEL has signed for this study a declaration of interest endorsed by the EMA and has no direct or indirect link with MonkeyPox (Mpox) Vaccine or Drug manufacturers

Monkeypox outbreak & studies context



- EMA and ECDC support pharmacoepidemiological studies to reactively assess its benefit risk of MVA-BN on Mpox
- Aetion has been selected as the scientific coordinator for SEMVAc* (primary data collection) & is conducting USMVac (secondary data collection)

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

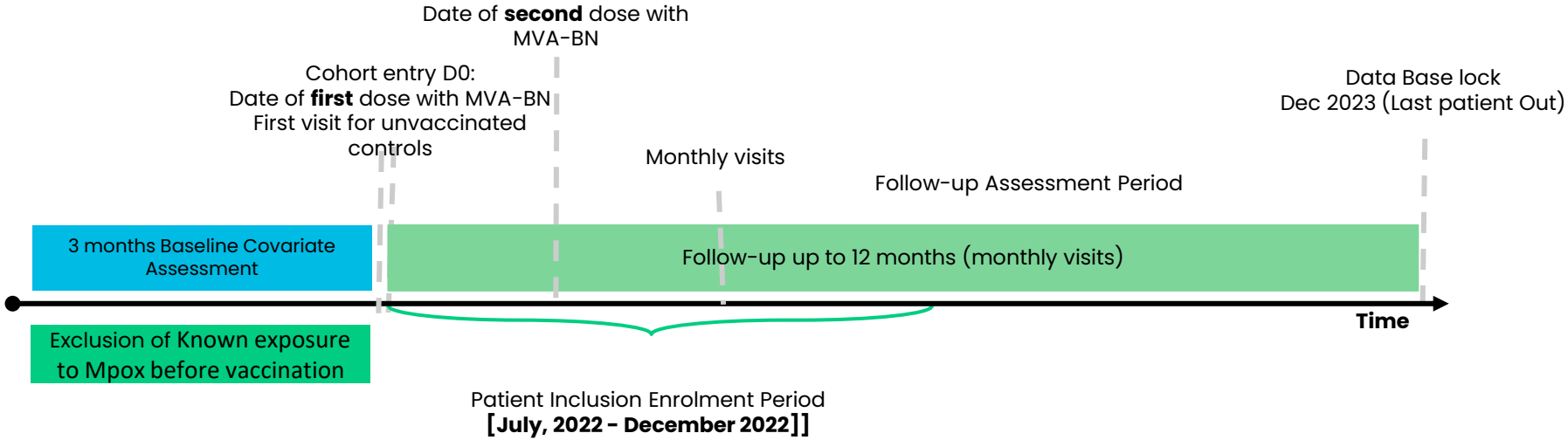
General challenges of MPX vaccines studies

Identification of population at risk	Heterogeneity of disease severity
Measuring vaccine exposure and identifying Mpox cases	The dynamic epidemiology of MonkeyPox
Sample size	Channeling bias
Safety data	Vaccine distribution and administration patterns
Follow-up and attrition of the MPX population	Balancing the challenges of working with near-real-time data with need for timely and relevant data

SEMVAc Study Diagram

Design: Observational, prospective based on multicentre primary data collection cohort

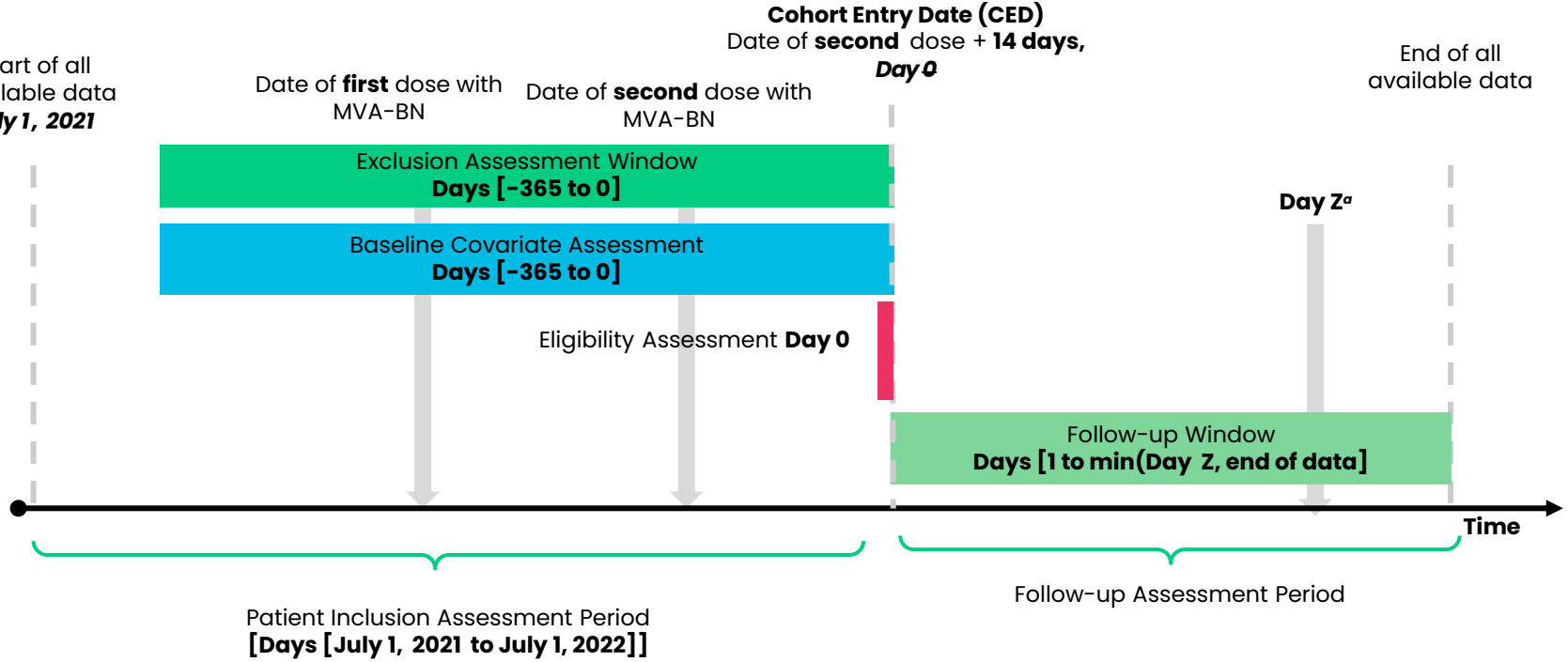
Objective: To Assess the safety & effectiveness of MVA-BN against Monkeypox disease in the vulnerable high-risk MSM population.



USMVAc Study Diagram

Design: Observational cohort study using U.S. secondary healthcare data aggregated from HealthVerity

Objective: Assess the safety & effectiveness of MVA-BN against Monkeypox disease in the vulnerable high-risk MSM population.



[a]**Day Z:** *Patients who develop the outcome of interest depending on the study objective, died*

Trade-offs between data collection methods

SEMVAc (Primary data collection)

Advantages

Patient variables

- Study tailored CRF
- Accuracy of exposure assessment
- Outcome assessments (symptoms, PCR confirmation) & risk behavior)

Benefit Risk analyses

- Timely/on safety monitoring
- Lower probability of misclassification outcome assessment

Limitations

Operations

- Enrolment challenges
- Duration and resources for the study
- (differential) Loss to follow-up

Bias

- Selection bias
- Hawthorne effect
- Reporting/information bias
- Residual confounding

USMVAc (Secondary data collection)

Advantages

Patient variables

- Near-real-time data capture
- Resources (faster and generally cheaper)
- Health care resource use
- Limited information / recall bias for available variables

Benefit Risk analyses

- Sample size
- Good look back period prior vaccination Mpox,
- Data representativeness
- Risk-set sampling strategies
- Resource utilization

Limitations

Operations

- Limited or no PROs information
- Missing data

Bias

- Identification of MPX patients
- Misclassification of vaccination status
- Residual confounding

Complementary approaches

	SEMVAc	USMVAc	Comments
Population	• Pre-Exposure Prophylaxis (PrPEP) MSM populations	• Post-Exposure Prophylaxis (PEP) & Pre-Exposure Prophylaxis (PrPEP) MSM populations • Three other populations are considered	• USMVaC provides further descriptions of MPX populations • US & EU populations with similar vaccination policies
Intervention / Comparison (exposure)	• 15,000 (5,000 vaccination group, 10,000 control group)	• Two doses of MVA-BN administration • Unvaccinated population	• Similar patients • PS matching • SEMVAc is not subject to vaccination misclassification
Outcomes	• Primary Outcome Measure: reduction in risk of disease in vaccinated versus unvaccinated individuals. • Secondary Outcome Measures=Safety and tolerability of MVA-BN vaccination	• Primary Outcome: reduction in MPX infection, Hospitalization for MPX, Death or hospitalization, • Secondary Outcome Measures=Safety and tolerability	• More outcomes are studied in USMVAc however Safety reporting, tolerability and causality assessment is better in SEMVAc

Complementary approaches

	SEMVAc	USMVAc	Comments
Timing	• Follow-up duration : up to 12 months,	• Follow-up from July 2022 till the last available date at the time of cohort extraction but FU may be shorter.	• Broader pre- vaccination exposure observation period in USMVAc
Setting	• Study centers experienced treatment of MSM and HIV patients in Germany (Berlin Area mainly)	• Patients identified through Medical and pharmacy claims along with hospital chargemaster, EMR, and laboratory data (HV)	• German study centers not EU representative • HV greater representativeness in US
Covariates	• Risk of Exposure to Mpox (Risk behavior, Sexual history • Health indicators and underlying medical conditions • Tolerability/reactogenicity of the vaccine • Symptoms indicative of Mpox infection	• Previous infections/vaccinations • Immunocompromised status • Immunosuppressive therapies • Healthcare utilization intensity	• PROs Risk behavior and symptoms (SEMVac) • More covariates to be included for PS matching in USMVAc

Conclusion

1. Both studies are focus on the Benefit Risk of smallpox vaccination against the current Monkeypox pandemic

1. Primary data collection and secondary data use, both have advantages and disadvantages and are of complementary value

1. Given the similarity of vaccination strategies, the use of routine US healthcare data is powerful and timely

1. Beyond the assessment of safety and effectiveness, different impact of potential confounders and subgroup analysis may provide important public health insights

Credits

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