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POSTER PRESENTER
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A SINGLE DOSE OF THE MVA-BN SMALLPOX VACCINE INDUCES AN EARLY PROTECTIVE ANTIBODY RESPONSE SIMILAR TO A TRADITIONAL REPLICATING VACCINE AND IS A VACCINE FOR MONKEYPOX

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BAVARIAN NORDIC

BACKGROUND

- More than 100 monkeypox (MPX) cases reported in Nigeria since 2017
- Travelers from Nigeria to the UK, Israel, and Singapore becoming ill; incidents of secondary transmission; no approved MPX vaccine at that time
- Vaccination with MVA-BN® post-exposure to MPX and for MPX prevention in ongoing trials:
  - Healthcare workers in England during the outbreak in 2018 (NCT03745131)
  - CDC sponsored trial in Africa (Democratic Republic of the Congo) (NCT02977715)
- Approval of MVA-BN (JYNNEOS™) for prevention of MPX and smallpox (SPX) in September 2019 by FDA

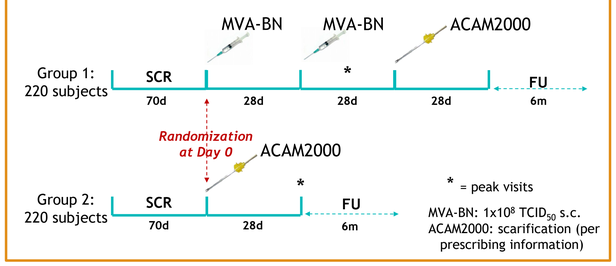
SMALLPOX

POX-MVA-006 - Phase 3 Pivotal Clinical Trial (NCT01913353)

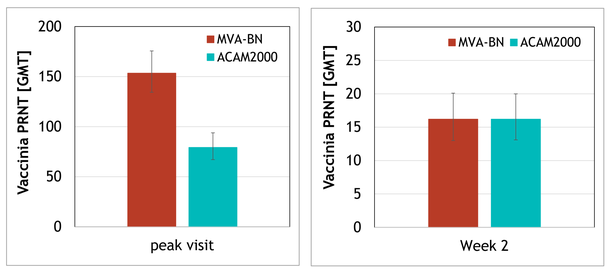
Immunogenicity
Non-inferiority of MVA-BN compared to ACAM2000® in terms of vaccinia specific neutralizing antibody response at the peak visits (Day 42 for Group 1 and Day 28 for Group 2)
→ ***Endpoint: PRNT GMT at the peak visits***

Efficacy
Showing that vaccination with MVA-BN prior to administration of ACAM2000 results in an attenuation of take in terms of Maximum Lesion Area (MLA)
→ ***Endpoint: MLA in mm² after scarification with ACAM2000***

POX-MVA-006 Vaccination Schedule



Immune Response Data – Neutralizing Antibodies



- (Co-)Primary immunogenicity endpoint met
- PRNT GMTs at peak visits were significantly higher for MVA-BN group compared to ACAM group, 153.5 vs. 79.3 (ratio of 1.935; 95% CI: 1.562, 2.397), demonstrating non-inferiority of MVA-BN compared to ACAM2000
- PRNT GMTs at Week 2 (after 1 vaccination) were 16.2 in both groups

Lesion Area Attenuation

	Group 1 (MVA-BN) (N=165)		Group 2 (ACAM2000) (N=161)		Attenuation Ratio (95% CI)	
	Median	(Min, Max)	Median	(Min, Max)		
Lesion Area [mm²]						
Day 6-8	0.0	(0.0, 96.0)	37.0	(0.0, 133.0)	95.2%	(93.8, 96.2)
Day 13-15	0.0	(0.0, 99.0)	75.0	(0.0, 368.0)	98.2%	(97.7, 98.4)
Maximum	0.0	(0.0, 99.0)	76.0	(0.0, 368.0)	97.9%	(96.6, 98.3)

- (Co-)Primary endpoint of take attenuation met
- Significant reduction in MLA with MVA-BN priming prior to ACAM2000 scarification compared to ACAM2000 only: Area Attenuation Ratio for MLA: 97.9% (pre-specified threshold for clinical relevance: 40%)

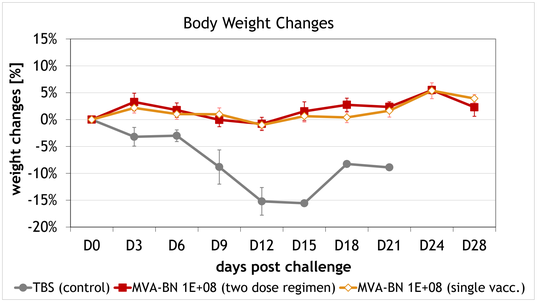
Conclusions - Smallpox

- **Peak visit neutralizing antibodies** induced by MVA-BN were **two-fold higher** compared to ACAM2000.
- Immune responses were shown to be **non-inferior after a single dose** of MVA-BN vaccination – at a time when ACAM2000 is reported to have induced a protective response.
- The attenuated take and an accelerated healing time observed in subjects who received MVA-BN prior to scarification with ACAM2000 shows that MVA-BN is able to suppress the viral replication induced by ACAM2000, providing **evidence of the efficacy** afforded by MVA-BN to protect against smallpox.
- MVA-BN shows **significantly better tolerability** compared to ACAM2000. No SAEs related to MVA-BN were reported, and the frequency of Grade 3 or higher related AEs was less for MVA-BN (1.2%) in comparison to ACAM2000 (10.3%) (data not shown).

MONKEYPOX

Protection Studies

NHP Monkeypox Challenge Study



Vaccination of cynomolgus macaques with TBS (N=5), 1 standard MVA-BN dose (N=6), or 2 standard MVA-BN doses 4 weeks apart (N=6) followed by intravenous (i.v.) challenge with monkeypox virus (5 weeks after last vaccination).

- Both single and two dose vaccination regimen with MVA-BN were 100% protective in the monkeypox i.v. challenge model
- TBS group significantly differed from vaccinated groups: all monkeys died by day 21
- MVA-BN induced neutralizing antibodies as measured by PRNT (data not shown)

Summary - Overall Survival in NHP Challenge Studies

Vaccination	% Survival (Survivor NHP / Total NHP)		
	Intravenous ($5x10^7$ pfu MPX virus)	Intratracheal ($1x10^6$-$5x10^6$ pfu MPX virus)	Aerosol ($3x10^5$ pfu MPX virus)
MVA-BN $1x10^8$ $TCID_{50}$ Single vaccination	100% (6/6)	88% (14/16)	-
MVA-BN $1x10^8$ $TCID_{50}$ Two dose regimen	100% (19/19)	89% (24/27)	100% (18/18)
Control (TBS)	31% (4/13)	13% (3/23)	6% (1/16)

Data in table are from combined challenge studies: intravenous (2 studies), intratracheal (3 studies), aerosol (2 studies)

Conclusions - Monkeypox

- Overall survival in pooled NHP challenge studies was 88-100% of MVA-BN-vaccinated animals compared to 6-31% of control animals
- Single dose of MVA-BN provided similar protection from MPX challenge compared to two dose regimen
- MVA-BN was effective to reduce morbidity (e.g. body weight, viral load, lesion counts, respiratory symptoms)

OVERALL CONCLUSIONS

- A single dose of MVA-BN provides an early protective vaccinia-specific antibody response similar to a replicating smallpox vaccine
- MVA-BN provides protection from lethal monkeypox virus challenge in cynomolgus macaques
- Nonclinical and clinical evidence support safety and efficacy for prevention of both smallpox and monkeypox

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