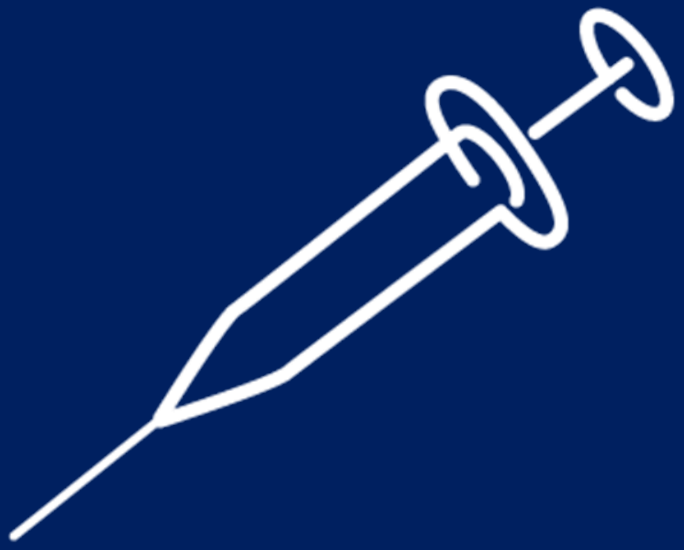


Vakzin-Entwicklung heute – die Ebola-Impfstoffkandidaten

Dr. Michael Saeftel für MSD, Janssen und GSK, 20.04.2015

MSD

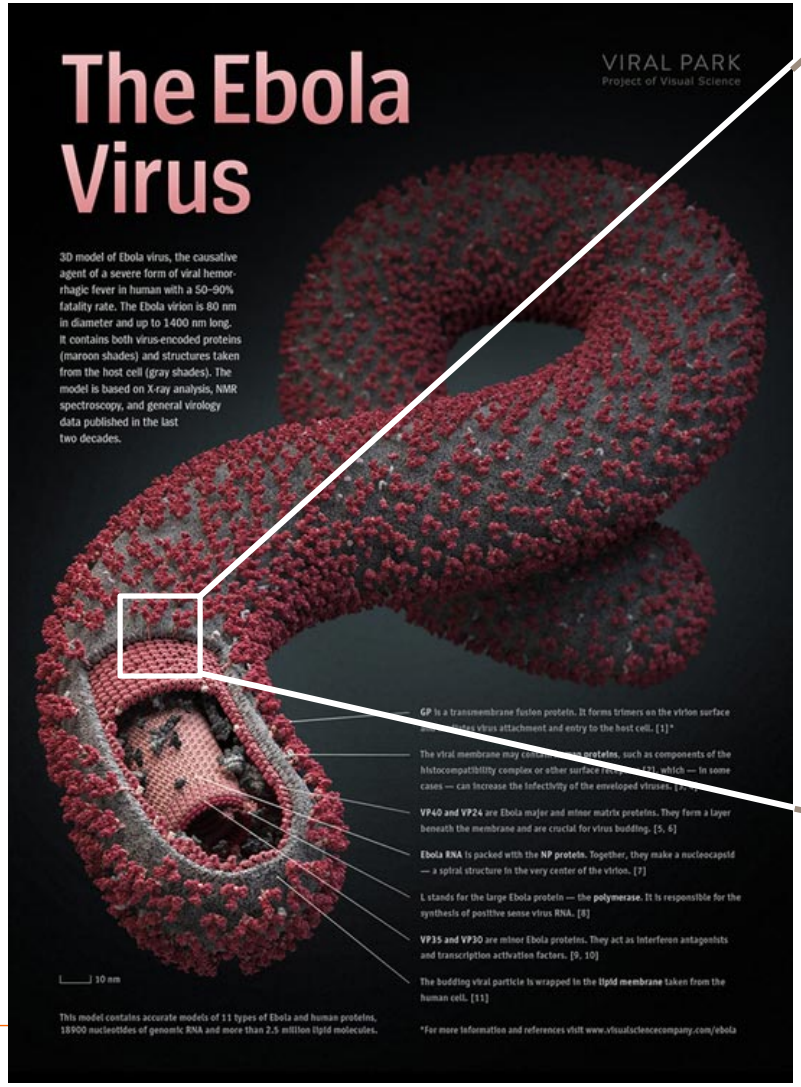
Janssen
PHARMACEUTICAL COMPANIES OF Johnson&Johnson

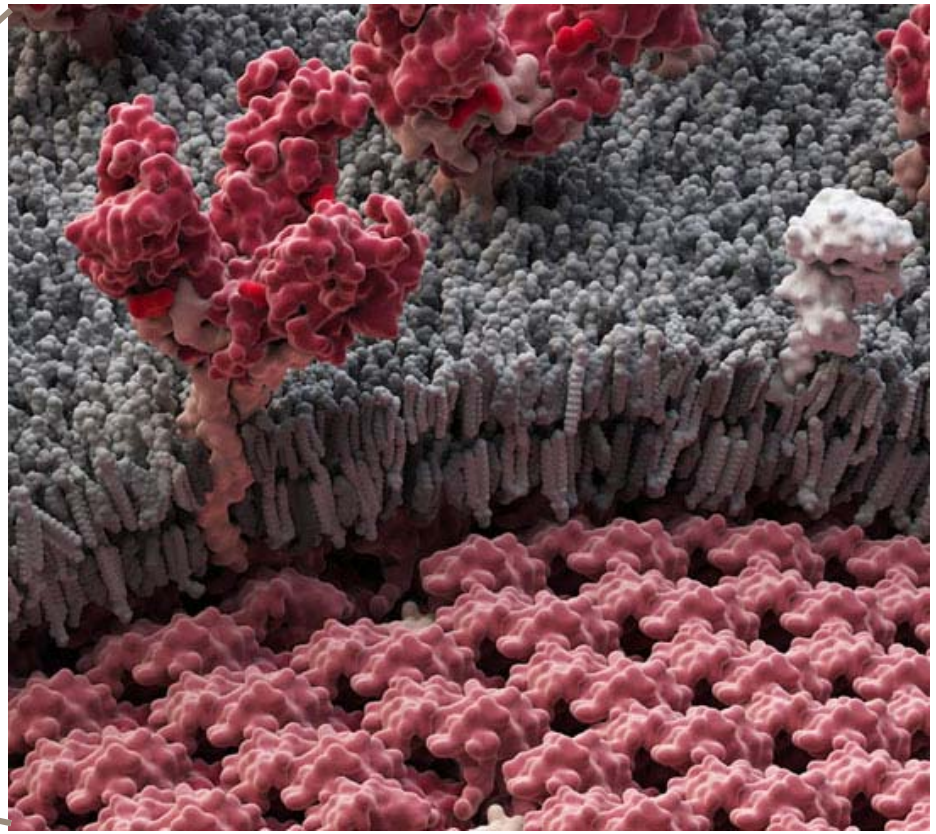
gsk

vfa. Die forschenden Pharma-Unternehmen

DE/VAC/156/15

Oberflächen-Glykoprotein ist das Ziel bei der Entwicklung von Impfstoffen





Immunological goal is induction of effective antibody and CD8 T cell responses for both acute and durable protection

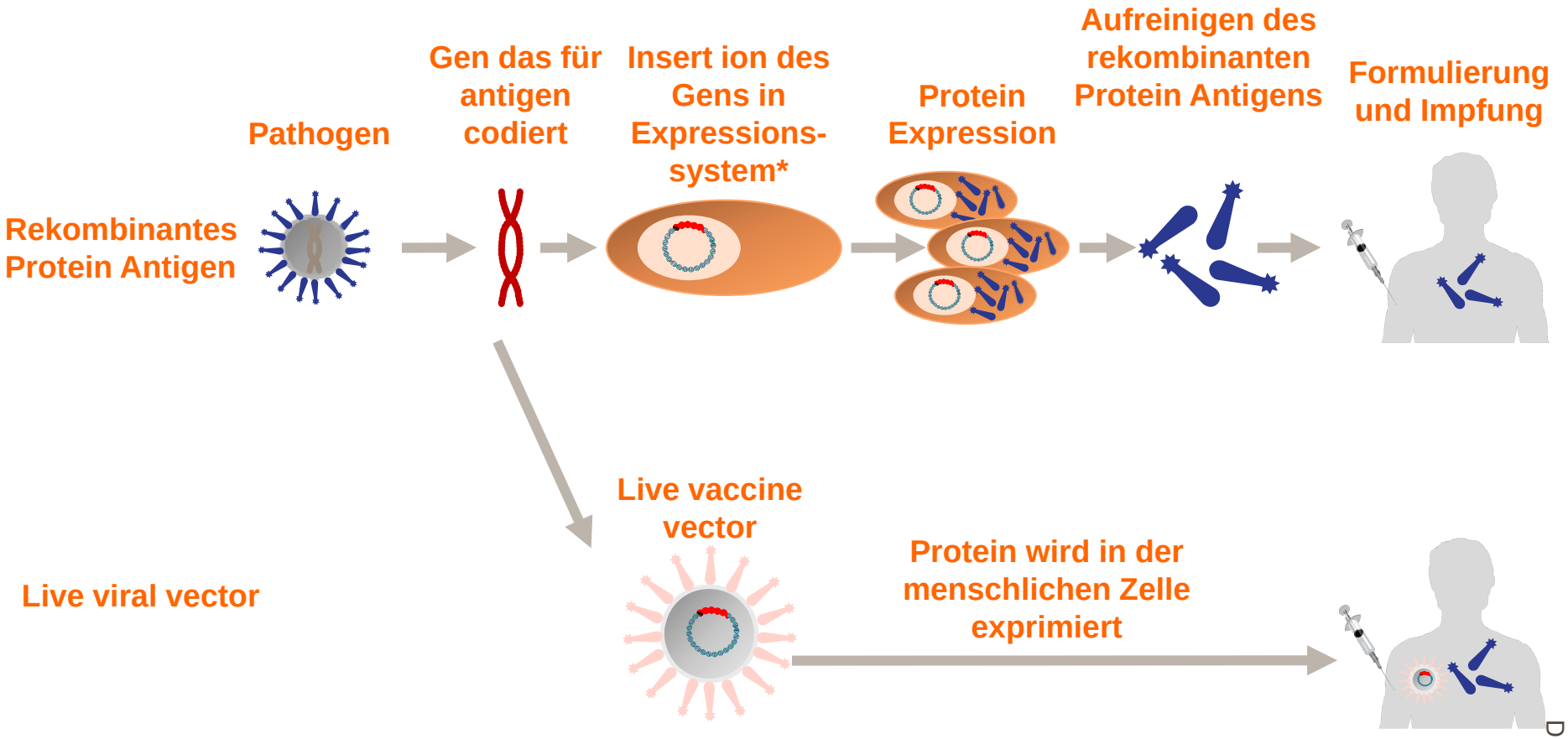
Visualscience.ru

Die am weitesten entwickelten Ebola-Impfstoffkandidaten

ChAd3-ZEBOV	rVSV-ZEBOV	Ad26-EBOV and MVA-EBOV (the two vaccines are injected sequentially)
GSK	MSD / NewLink Genetics	Janssen (Crucell) and Bavarian Nordic
US National Institute of Allergy and Infectious Diseases, Department of Defence, Biomedical Advanced Research and Development Authority	Public Health Agency of Canada, NIH, Department of Defence, BARDA	US National Institute of Allergy and Infectious Diseases
Phase II & Phase III, started	**Phase II & Phase III, started**	Phase I trial began in January 2015.

http://www.biopharma-reporter.com/Bio-Developments/Ebola-which-are-the-leading-vaccine-candidates

Wie funktioniert ein viraler Vektor bei einem Impfstoff?



*yeast or insect cell

Strugnell *et al.* Chapter 3 in: Garçon *et al.* Understanding Modern Vaccines, Perspectives in vaccinology, Vol 1, Amsterdam. Elsevier 2011;p61–88

Phase 1 und 2 Programme für die Impfstoffe ChAd3-EBOV und rVSV-ZEBOV

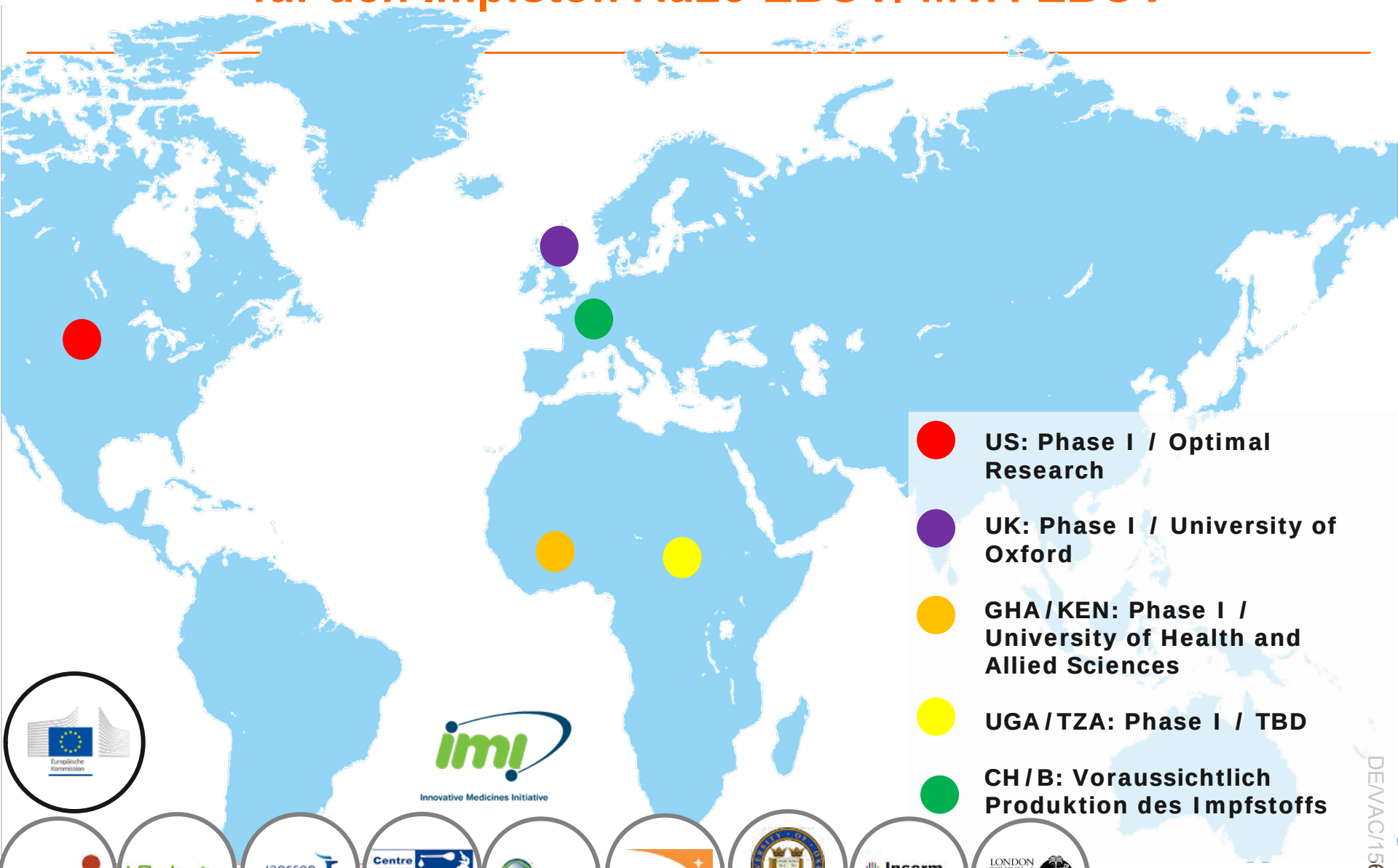
Vaccine platform	Trial type	Start date [b]	Location	Enrollment [c]	Sponsor
Chimpanzee adenovirus vector (ChAd3-ZEBOV-GP)	Phase I a/b dose escalating	2014 Aug	USA (Georgia and Maryland)	26	National Institute of Allergy and Infectious Diseases (NIAID), USA
	Phase Ia dose escalating	2014 Sept	United Kingdom	60	University of Oxford, UK
	Phase I/II	2014 Oct	Lausanne, Switzerland	120	University of Lausanne Hospitals, Switzerland
	Phase Ib dose escalating	2014 Nov	Mali; Africa	40	University of Maryland, USA
Vesicular stomatitis virus vector (VSVΔG-ZEBOV-GP) [9,10]	Phase Ia dose escalating	2014 Aug	USA (National Institutes of Health, Maryland)	120	NewLink Genetics, USA
	Phase Ia dose escalating	2014 Oct	USA (Walter Reed Army Institute of Research, Maryland)	117	NewLink Genetics, USA
	Phase I/II	2014 Nov	Geneva, Switzerland	115	University Hospital, Geneva, Switzerland
	Phase I	2014 Nov	Germany	30	Hamburg-Eppendorf, Germany

A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of the BPSC1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Volunteers in Kilifi, Kenya. (Start: November 2014)

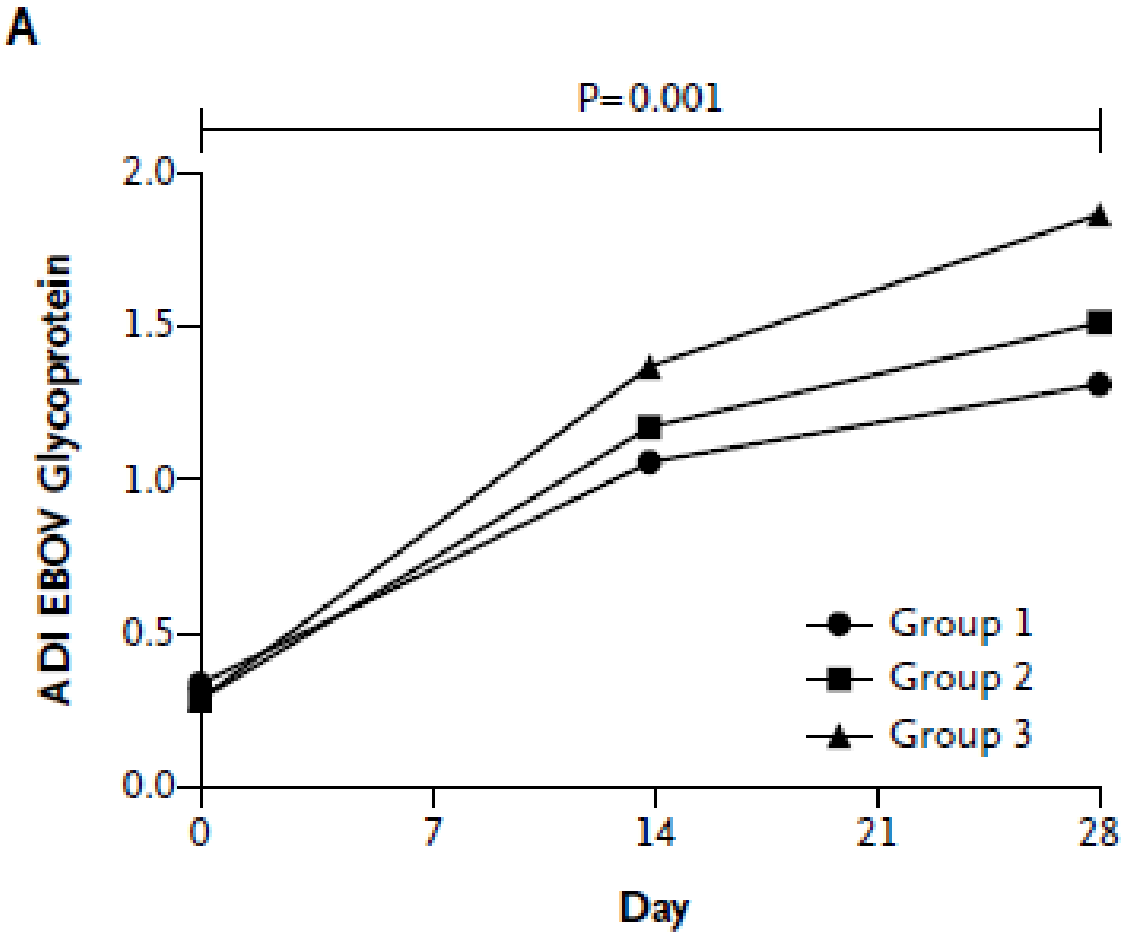
A Phase 1, Open-Label, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of the BPSC1001 (VSVΔG-ZEBOV) Ebola Virus Vaccine Candidate in Healthy Adult Volunteers in Lambarene, Gabon. (Start: November 2014)

Cooper & Bavari, Trends in Microbiology February 2015, Vol. 23, No. 2

Phase 1 Programme und Kooperationen für den Impfstoff Ad26-EBOV/ MVA-EBOV



Phase I: ChAd3-EBOV induziert eine Immunantwort

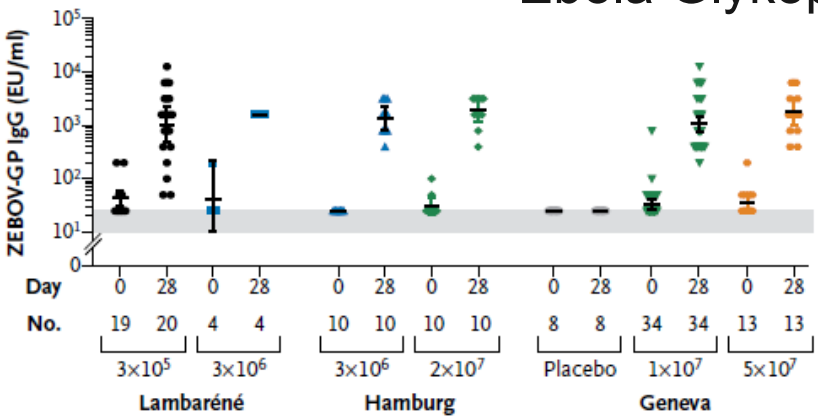


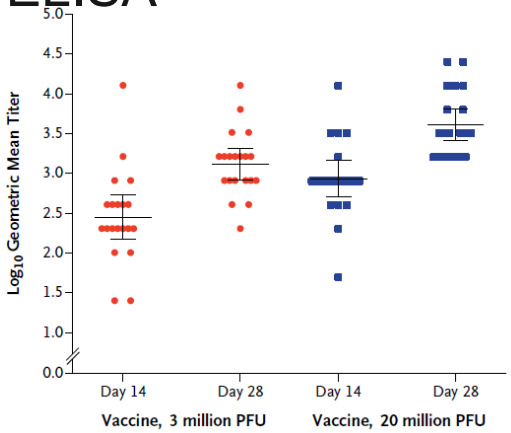
60 healthy adult volunteers in Oxford, United Kingdom, received a single dose of the ChAd3 vaccine at one of three dose levels: 1×10^{10} viral particles, 2.5×10^{10} viral particles, and 5×10^{10} viral particles (with 20 participants per group)

Rampling et al., 2015; The New England Journal of Medicine DOI: 10.1056/NEJMoa1411627

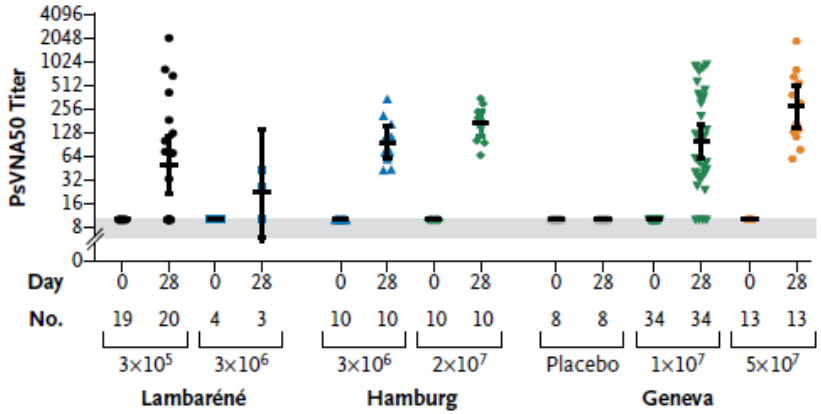
Phase I: VSV-ZEBOV induziert eine Immunantwort

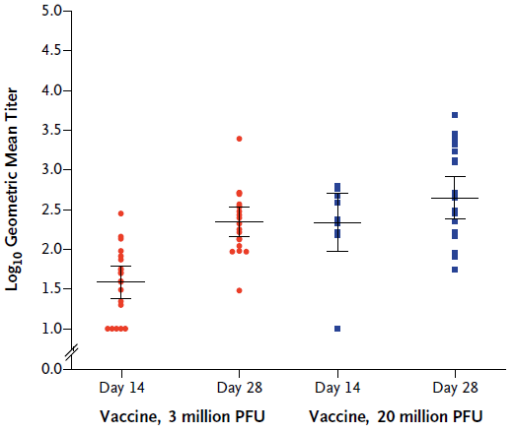
Ebola Glykoprotein ELISA





Pseudovirion Neutralization Assay



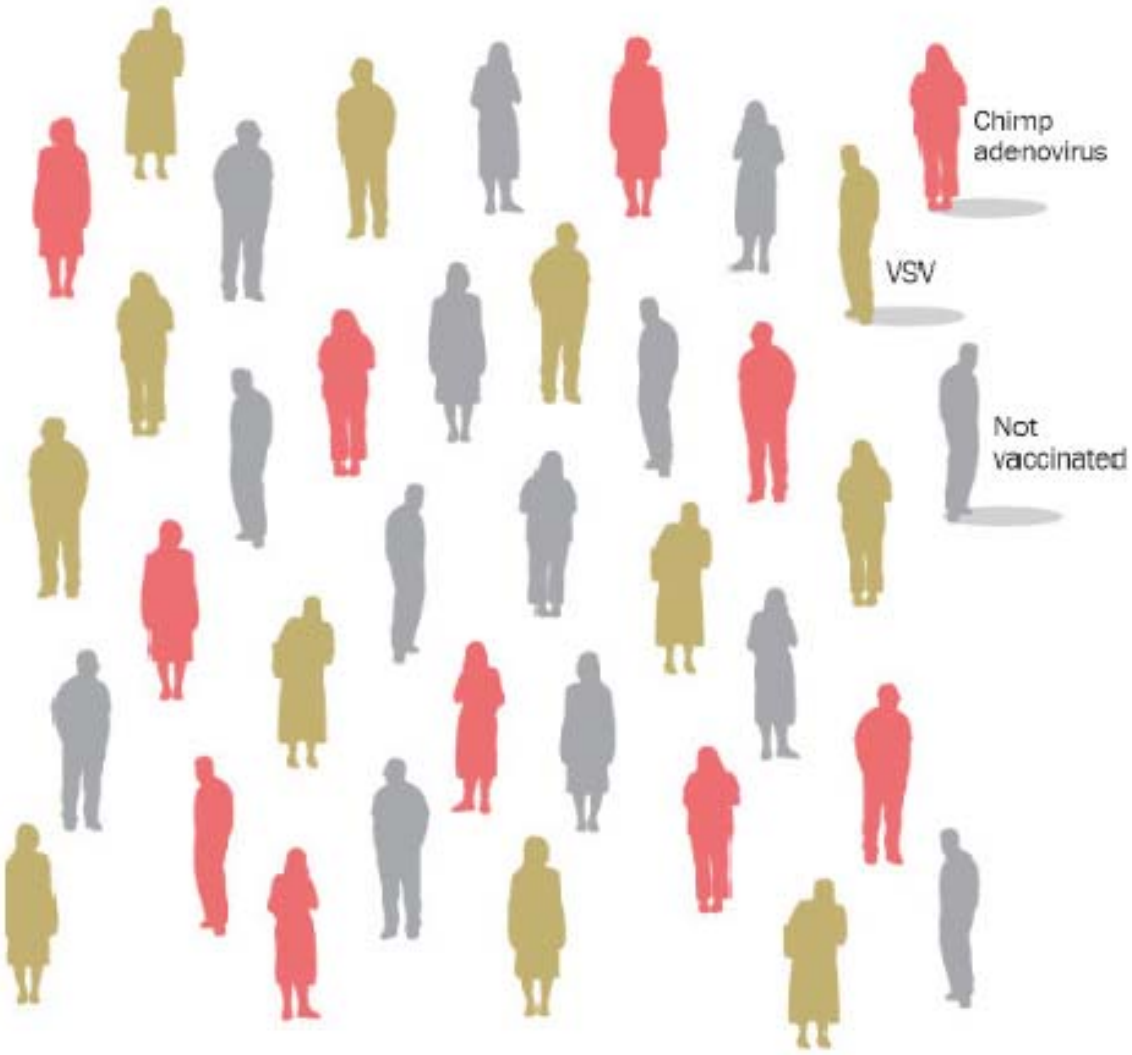


Agnandji ST et al., N Engl J Med. 2015 Apr 1. [Epub ahead of print]
Regules JA et al., N Engl J Med. 2015 Apr 1. [Epub ahead of print]

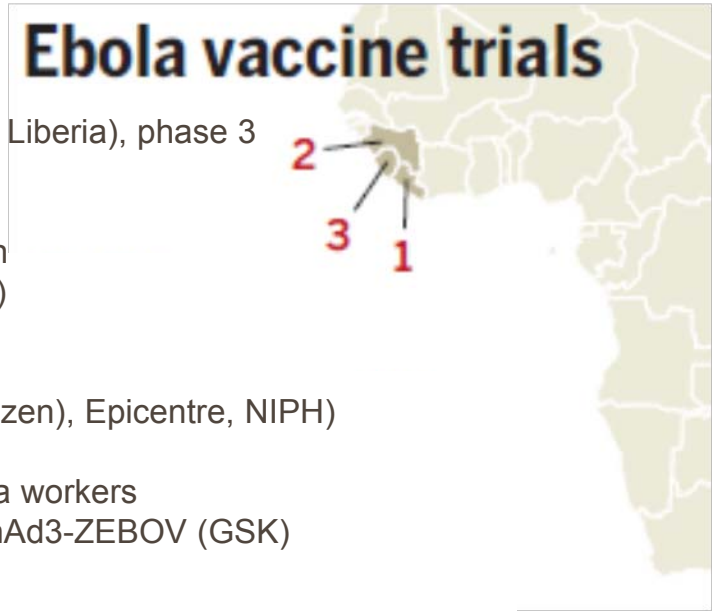
Phase 3 Studien – Gewichtung der Studien

- **Zulassungsbehörden und WHO haben folgende Gewichtung:**
  - ✓ Evidenz-Level 1: Randomisierte Studie
  - ✓ Evidenz-Level 2: Prospektive Studie
  - ✓ Evidenz-Level 3: Beobachtungsstudie
- **Studien mit Evidenz-Level 1 haben die größte Aussagekraft.**
- **Im Fall von Ebola würden aber auch Studien mit Level 2 zur Zulassung akzeptiert werden**
- **Studien mit Level 3 sind für Analysen nach Zulassung gedacht**

Randomisierte Studie



Studien-Programme
für die Impfstoffe in Afrika



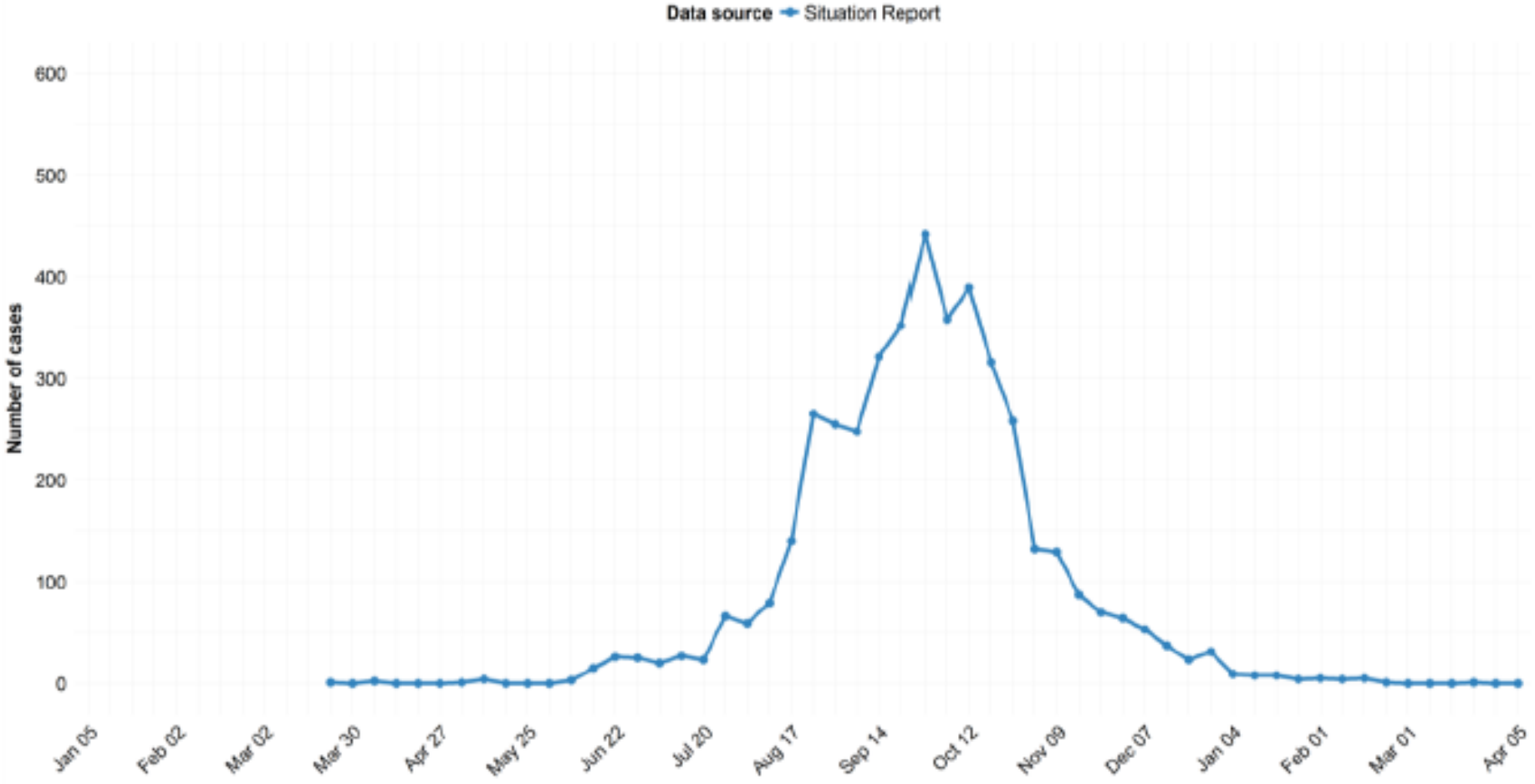
1. Liberia
PREVAIL Study (Partnership for Research on Ebola Vaccines in Liberia), phase 3
Led by: NIH (National Institutes of Health, USA)
Participants: 30.000
Design: Randomized Trial with control arm in general population
Vaccines: rVSV-ZEBOV (MSD/NewLink), ChAd3-ZEBOV (GSK)

2. Guinea
Led by: International Consortium (WHO, MSF (Ärzte ohne Grenzen), Epicentre, NIPH)
Participants: 9.000
Design: 1. Ring vaccination trial; 2. Observational study in Ebola workers
Vaccines: Phase 1: rVSV-ZEBOV (MSD/NewLink), Phase 2: ChAd3-ZEBOV (GSK)

3. Sierra Leone
STRIVE Study (Sierra Leone Trial to Introduce a Vaccine against Ebola), phase 3
Led by: CDC (Centers for Disease Control, USA)
Participants: 6.000
Design: Stepped-wedge trial in Ebola workers
Vaccine: rVSV-ZEBOV (MSD/NewLink)

4. Tanzania, Uganda, Ghana, Kenya
3 studies, phase 1
Participants: N/A
Design: Placebo controlled randomized trials
Vaccine: Ad26.ZEBOV (Janssen) + MVA-BN-Filo (Bavarian Nordic)

Figure 4: Confirmed weekly Ebola virus disease cases reported nationally and by district from Liberia



Letzter Ebolafall in Liberia am 27.03.15

WHO Situation Report 8. April 2015

DE/VAC/156/15

Zusammenfassung

- **Beschleunigtes Entwicklungsprogramm der Impfstoffe für West-Afrika**
- **Drei Schutzimpfungen in fortgeschrittener Entwicklung. (von MSD/NewLink Genetics, GSK, Janssen + Bavarian Nordic)**
- **Mit abnehmenden Fallzahlen werden, Phase 3 Studien schwieriger**
- **Zugang zu den Impfstoffen in den betroffenen Ländern könnte z.B. durch GAVI und einen Non Profit Preis erfolgen (MSD hat hier bereits eine Zusage gegeben)**

Herzlichen Dank für Ihre Aufmerksamkeit

Quelle: Mathias Grade, Quakenbrück