



Ebola Ça Suffit: What we know and what we don't know about rVSV-ZEBOV

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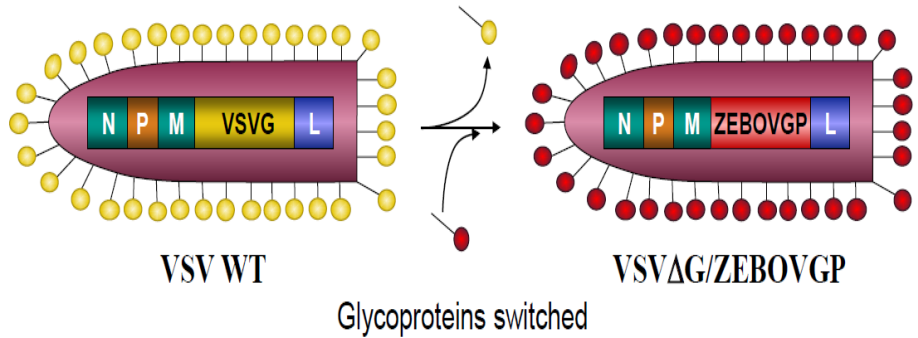


Outline

1. An overview of rVSV vaccine
2. Key aspects of the ring trial (Ebola Ça Suffit)
3. What we know from Ebola Ça Suffit
4. What we don't know from Ebola Ça Suffit
5. Moving forward

1. Vaccine candidate: rVSV Δ G-ZEBOV-GP

- Merck
- Vaccine targets Ebola Zaire (ZEBOV) glycoprotein (GP)
 - Delivered through a live vector (rVSV)
 - rVSV GP replaced with Ebola-Zaire GP
- Replication competence facilitates use as a single-dose

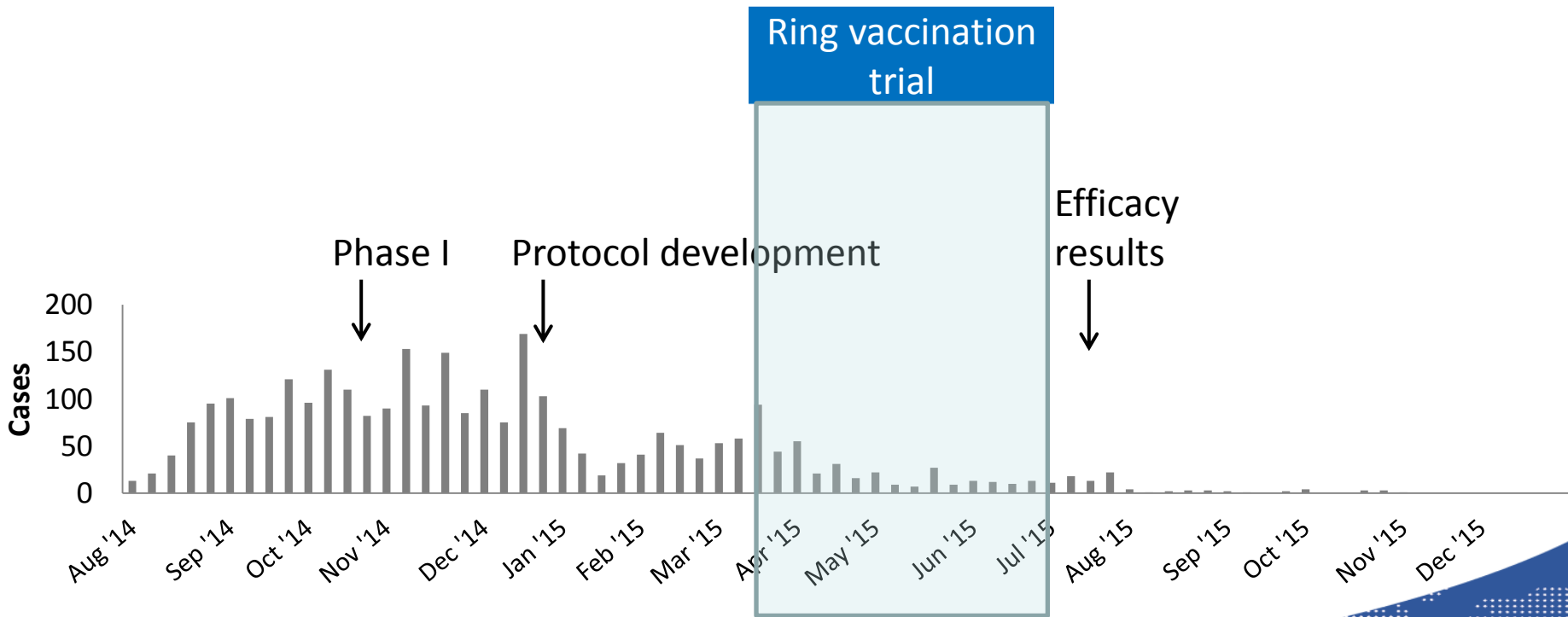


1. Use of the vaccine up to now

- 8 phase I trials
 - 800 adults
- 1 phase II trial
 - ~1,000 adults
- 2 (or 3) phase III trials
 - ~ 15,000 persons

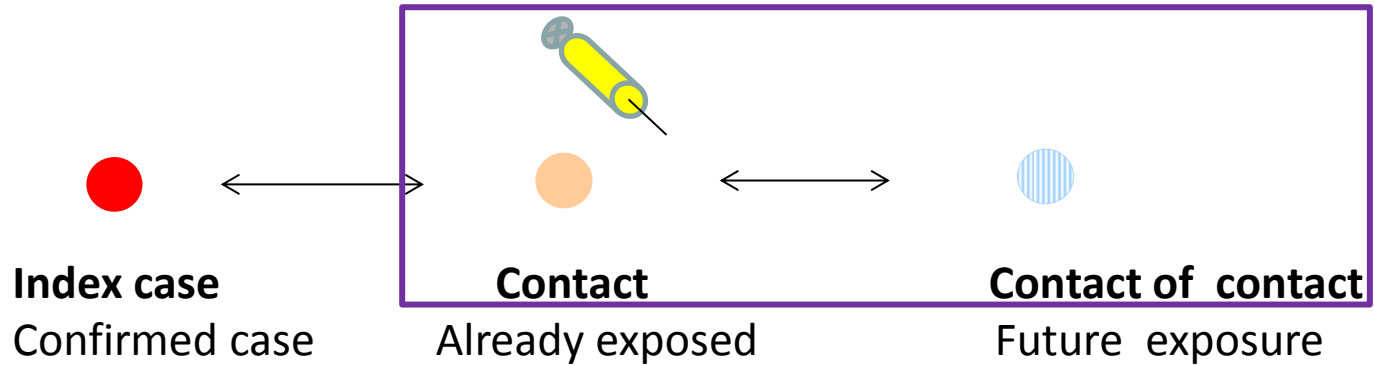
Germany, Kenya, Gabon, Sierra Leone, Guinea, Liberia, USA, Canada, Spain, Switzerland

2. A Timeline Reminder for Guinea



Data source: WHO Ebola Data and Statistics, <http://apps.who.int/gho/data/view.ebola-sitrep.ebola-summary-latest?lang=en>

2. What is ring vaccination?



- **Persons who since onset of fever:**
 - Lived with the case in the same household
 - Visited the case at home or at a health facility
 - Have been visited by the case (including health staff)
- **Had contact with the corpse of a confirmed case**
- **Health personnel in the catchment area**

2. Key points of Ebola Ça Suffit design

- “Rings” randomized to immediate or delayed vaccination (21 days)
- Primary analysis:
 - Incidence of confirmed Ebola infection ≥ 10 days post-randomization
- Results from 90 rings
 - 48 immediate rings (2,014 vaccinate)
 - 42 delayed rings (1,498 vaccinated)

3. What we know from Ebola Ça Suffit

- Intention-to-treat (inconclusive)
 - 7 of 3,212 in immediate vs. 16 of 3,075 in delayed
 - 65% (95% CI: -47–91%)
- Per protocol analysis:
 - 0 of 2,108 in immediate clusters vs 16 of 3,075 in delayed
 - 100% (95% CI, 69–100%)
- Vaccine likely provides protection, protection might even be high, but we cannot say that the vaccine is 100% protective

	All vaccinated in immediate versus all eligible in delayed (primary analysis)	All eligible and consented	All eligible (eligible adults, contacts and contacts of contacts)	All (all contacts and contacts of contacts)
Number of individuals (clusters)				
Immediate	2014 (48)	2048 (48)	3035 (48)	4123 (48)
Delayed	2380 (42)	1930 (42)	2380 (42)	3528 (42)
Number of cases at <10 days (affected clusters)				
Immediate	9 (4)	10 (5)	18 (9)	21 (9)
Delayed	16 (12)	6 (5)	16 (12)	25 (13)
Number of cases at ≥10 days (affected clusters)				
Immediate	0 (0)	0 (0)	6* (3)	8* (4)
Delayed	16† (7)	11† (5)	16† (7)	21† (7)
Vaccine efficacy/ effectiveness‡ (%)	100% (74.7 to 100)	100% (70.8 to 100)	75.1% (-7.1 to 94.2)	76.3% (-15.5 to 95.1)
p value§	0.0036	0.0194	0.1791	0.3351

*All cases occurred in unvaccinated individuals. †Four cases were vaccinated and developed symptoms on day 0, 2, 6, or 6 after vaccination. ‡From fitting a β -binomial distribution to the cluster-level numerators and denominators and using an inverted likelihood ratio test to identify the lower bound for vaccine efficacy (first two columns); from Cox proportional hazards model to estimate vaccine effectiveness (last two columns). §From Fisher's exact test (two-sided).

Table 2: Calculations of vaccine efficacy and vaccine effectiveness based on different study populations

Henao Restrepo et al, Lancet 2016, 2017

3. What we know from Ebola Ça Suffit

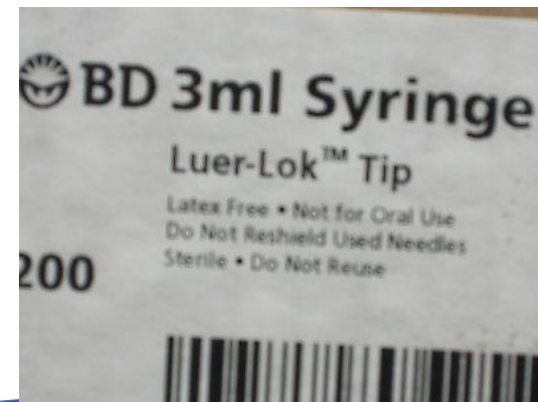
- Safety
 - Similar to other live attenuated vaccines in adults
 - Self-limiting fever, myalgia, arthralgia in ~ 30%
 - Available data suggest similar profile in children (older than 6 years), adolescents and HIV+
 - Few data on pregnant women
- Immunogenicity
 - Depending on the laboratory and assay, between 10 et 40% séropositive at D0
 - No correlate of protection
 - Variable, but appears “acceptable”

4. What we don't know from Ebola Ça Suffit

- Safety and efficacy in pregnant women
- No efficacy in children
- No data on preventive (pre-exposure) use in humans
- Not much on drug interactions
- No correlate of protection
- Not registered by FDA or other regulatory authority, no WHO EUAL provision

5. A Note on the cold-chain

- 10-dose or single dose vials
 - Store at $\leq -60^{\circ}\text{C}$
- Conditions more flexible after thawing:
 - 27 days at $2-8^{\circ}\text{C}$.
 - 15 minutes at $9-25^{\circ}\text{C}$
 - If used with a 3ml « Leur Lock » (8hs at $2-8^{\circ}\text{C}$ in the syringe)





5. Moving Forward

- Adds another tool into the toolbox, but a ways to go
- MSF Sponsored protocol in 12 countries (diverse acceptance)
- Combating mixed messages about what the vaccine does and does not do
- No magic bullet

Study Partners



World Health Organization