JN 20es Journées Nationales d'Infectiologie
Lyon et la région Auvergne-Rhône-Alpes
du mercredi 5 juin 2019 au vendredi 7 juin 2019

Emergences : Maladie à Virus Ebola : Actualités

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HCL – GHN – Hôpital de la Croix Rousse

Liens d'Intérêts

Au cours des 3 dernières années,
avec les sociétés Pharmaceutiques suivantes

- **Recherche clinique** : participation aux protocoles académiques et industriels du service
- **Advisory Boards :** néant
- **Interventions ponctuelles :** Pfizer, ViiV Healthcare, MSD, Teva, Gilead
- **Aides pour des recherches** : néant

Situation Report WHO june 10, 2016

- 28 616 cas
- 11 310 décès
- 10 000 survivants
- Derniers clusters :
  - 7 cas confirmés, 3 probables en guinée
  - 3 cas au Libéria
- 42 j de délai après le dernier cas pour déclarer la fin d'une épidémie (2 x durée d'incubation)

http://apps.who.int/iris/bitstream/10665/208883/1/ebolasitrep_10Jun2016_eng.pdf?ua=1

Ebola hits 2,000 cases as vaccine OK'd in some pregnant, lactating women

Filed Under: Ebola; VHF

Stephanie Soucheray | News Reporter | CIDRAP News | Jun 03, 2019

Today the Ebola case count in the Democratic Republic of the Congo (DRC) will likely surpass 2,000 cases, a new milestone ushered in by heavy transmission in May, by a good measure the most active month in this outbreak.

World Bank, Vincent Tremeau / Flickr cc

Over the weekend, the ministry of health in the DRC recorded 20 new cases of the virus, and reports on Twitter suggest the ministry will announce 14 more cases today. If confirmed, the cases will raise the outbreak total to 2,008 cases.

The cases over the weekend originated in Mabalako, Katwa, Beni, Butembo, and Mangurujipa, all villages and cities in North Kivu province. Sixteen deaths were also recorded over the weekend, bringing the fatality total to 1,339 as of yesterday.

This outbreak, in its 11th month, is the world's second largest after West Africa's 2014-2016 Ebola outbreak, which involved more than 28,600 cases and more than 11,300 deaths.

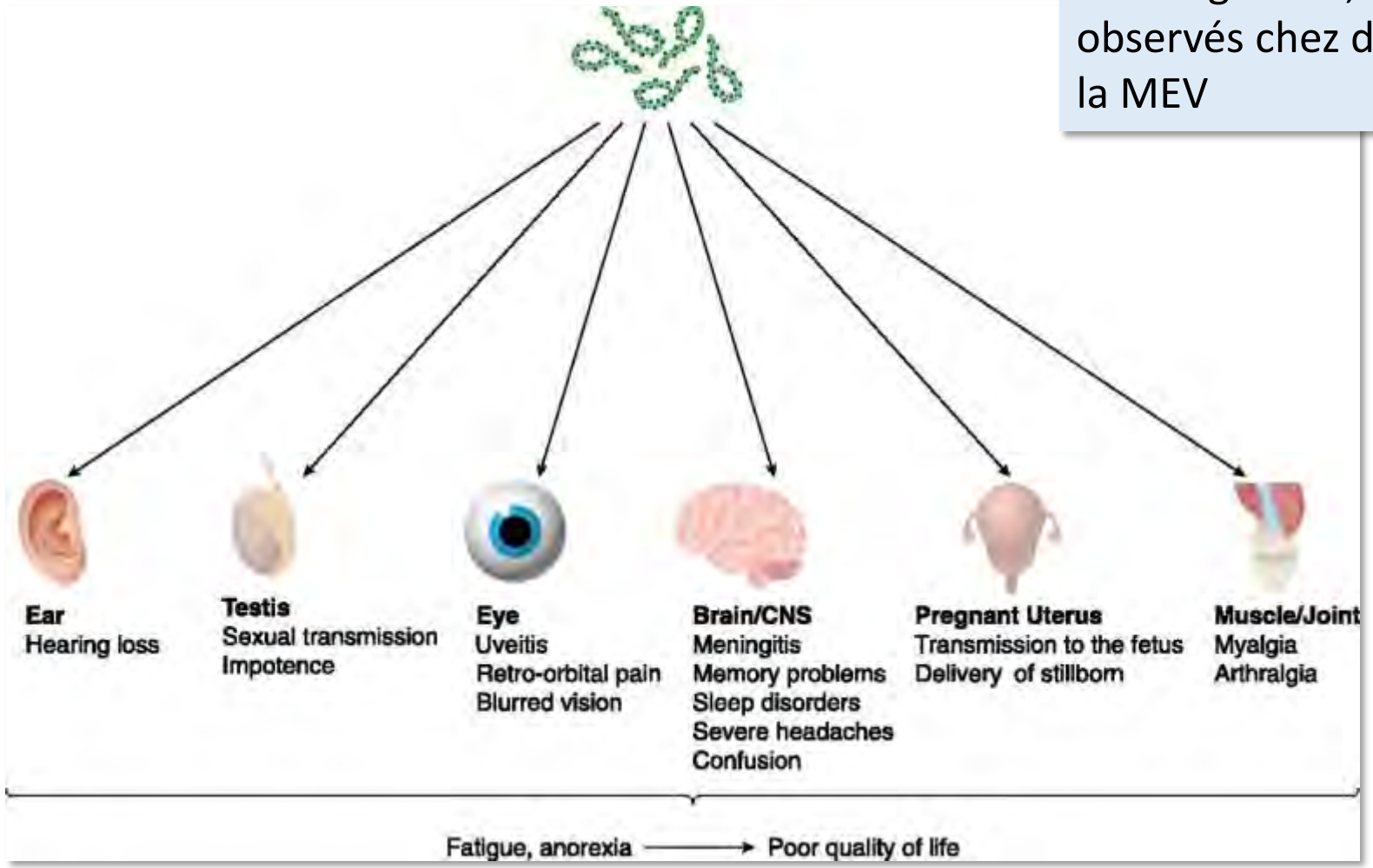
The DRC topped 1,000 cases on Mar 24—8 months into the outbreak. It added its second 1,000 cases in only 71 days, or just a little over 2 months later, data that demonstrate how the outbreak has accelerated.

Vaccine for pregnant, lactating women

Yesterday the ministry of health confirmed that an ethics committee at the School of Public Health at the University of Kinshasa had approved an amendment to the vaccination protocol dictating the use of Merck's rVSV-ZEBOV vaccine.

Long-Term Post-EBOV Consequences

Entrée et persistance d'EBOV dans les « sanctuaires » : oreilles, testicules, yeux, SNC, utérus gravide, tissus musculaires, ont été observés chez des survivants, avec séquelles de la MEV



Riviera A J Leukoc Biol 2016;100:889-904

Sequelles de la Maladie à Virus Ebola

Cohorte Postebogui[1]

- 375 survivants (15 dec 2015)
- 1 081 évènements; 296 (79 %) survivants :
  - Signes généraux (39 %) : asthénie, fièvre, anoréxie.
  - Signes neurologiques (32 %): fièvre.
  - Signes rhumatologiques (46 %).
  - Symptômes oculaires (16 %): conjonctivites, iridocyclites, atteinte vision.
  - Signes infectieux (22 %).
  - Douleurs pelviennes (21 %).
  - Anémie (13 %).

Cohorte Sierra Leone[2]

- 277 survivants (114 males), âge médian 29 ans (IQR 20-36), délai médian de sortie du centre de traitement 121 jours (82-151)
  - Arthralgies (210, 76 %),
  - Nouveaux symptôimes oculaires (167, 60 %), uvéites (50, 18 %),
  - Symptômes auditifs (67, 24 %).
- Charge virale EBOV élevée à la phase aigue de la MVE indépendamment associée :
  - Uvéites (OR ajusté : 3,33, 95% IC 1,97-5,91).
  - Nouveau symptômes oculaire (OR ajusté 3,04, 95% IC 1,87-4,94).

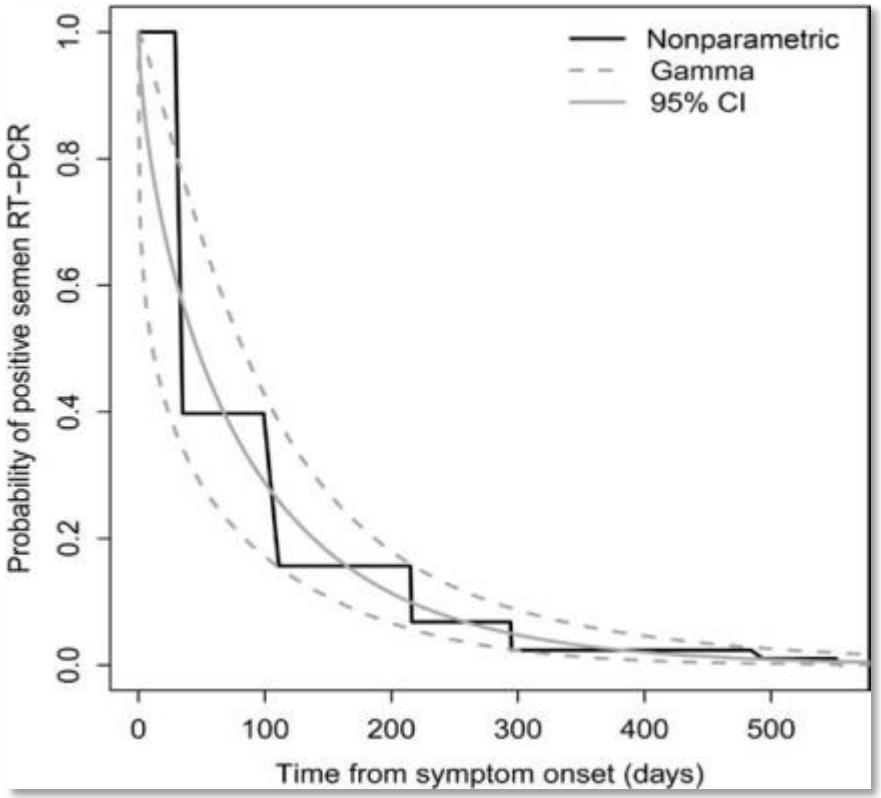
1 : Etard JF. CROI 2016, Boston 22-25 février 2016 Abstract 73LB 2 : Mattia JG Lancet Infect Dis 2015 doi: 10.1016/S1473-3099(15)00489-2

Dynamics of Ebola RNA Persistence in Semen : A Report From the Postebogui Cohort in Guinea

- Postebogui study includes Ebola survivors from 4 study centers in Guinea.
- Follow-up visits scheduled :
  - at inclusion.
  - and 1, 3, 6, 9, 12, 18, and 24 months after inclusion.
- Semen samples :
  - Collected from men ≥ 15 years of age at each visit.
  - Tested by RT-PCR for the presence of EBOV RNA.
- 315 men included at the time of data extraction:
  - 188 provided at least 1 semen sample.
  - with a total of 409 samples.

Estimated probability of remaining positive for EBOV RNA in semen :

- 31.6% (95% CI, 18.6%–46.0%) at 3 months
- 13.5% (95% CI, 7.8%–21.0%) at 6 months
- 2.9% (95% CI, 1.1%–5.7%) at 12 months
- 0.7% (95% CI, 0.1%–2.0%) at 18 months



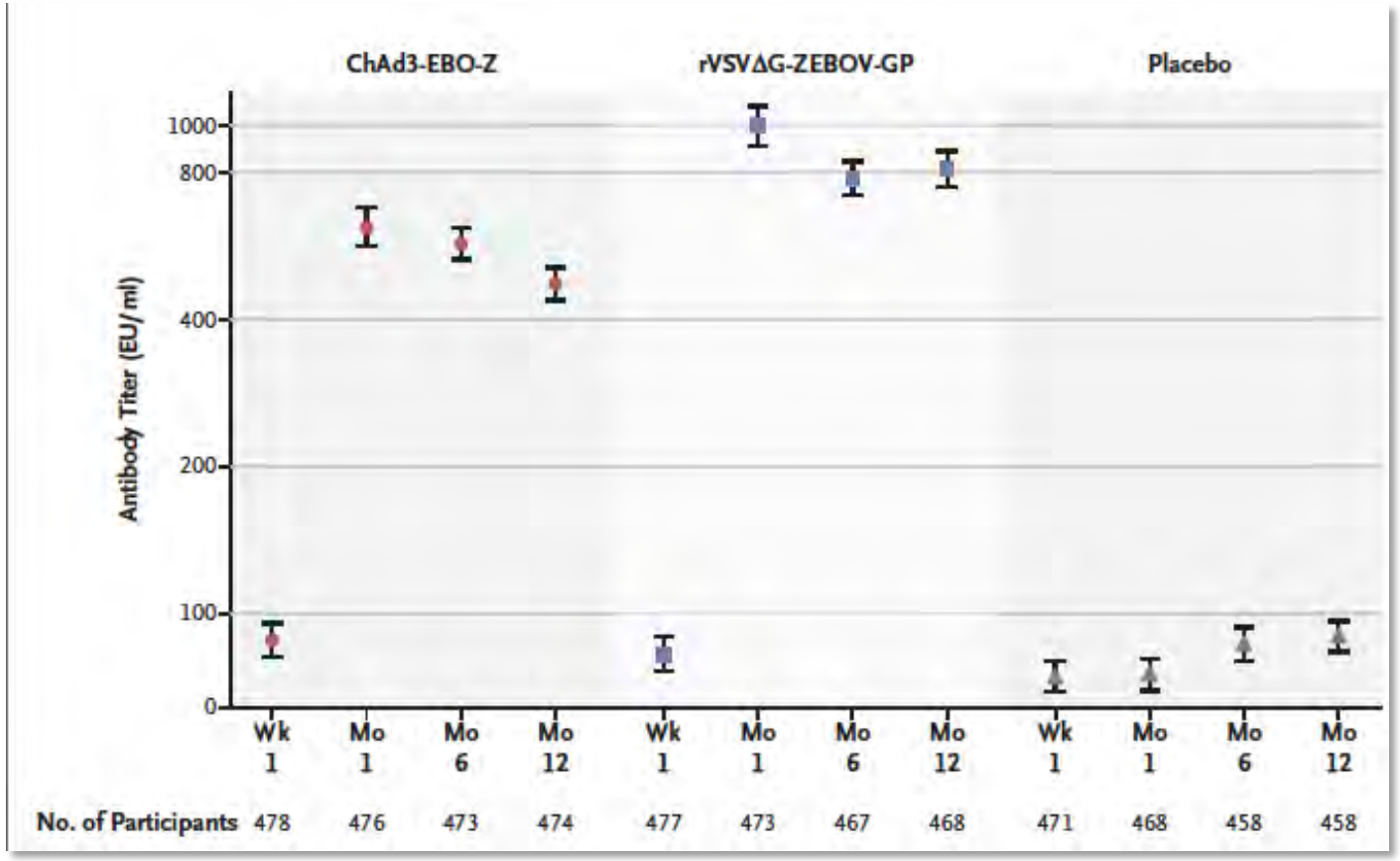
Probability for Ebola virus disease survivors' semen to test positive for Ebola virus

Parametric survival models adjusted to estimate the probability of positive RT-PCR result over time, using exponential, Weibull, Gompertz, log-logistic, log-normal, gamma, and inverse Gaussian distributions

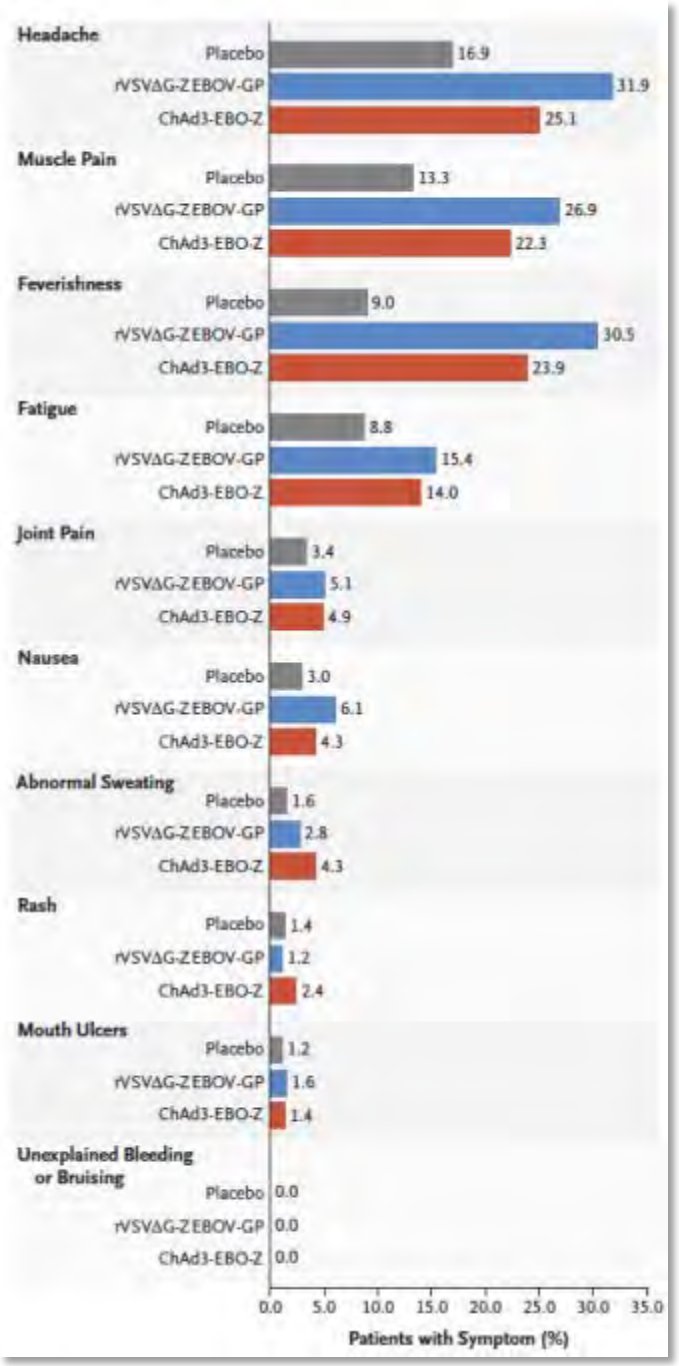
Subtil F Clin Infect Dis 2017 DOI: 10.1093/cid/cix210

Vaccins

Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia



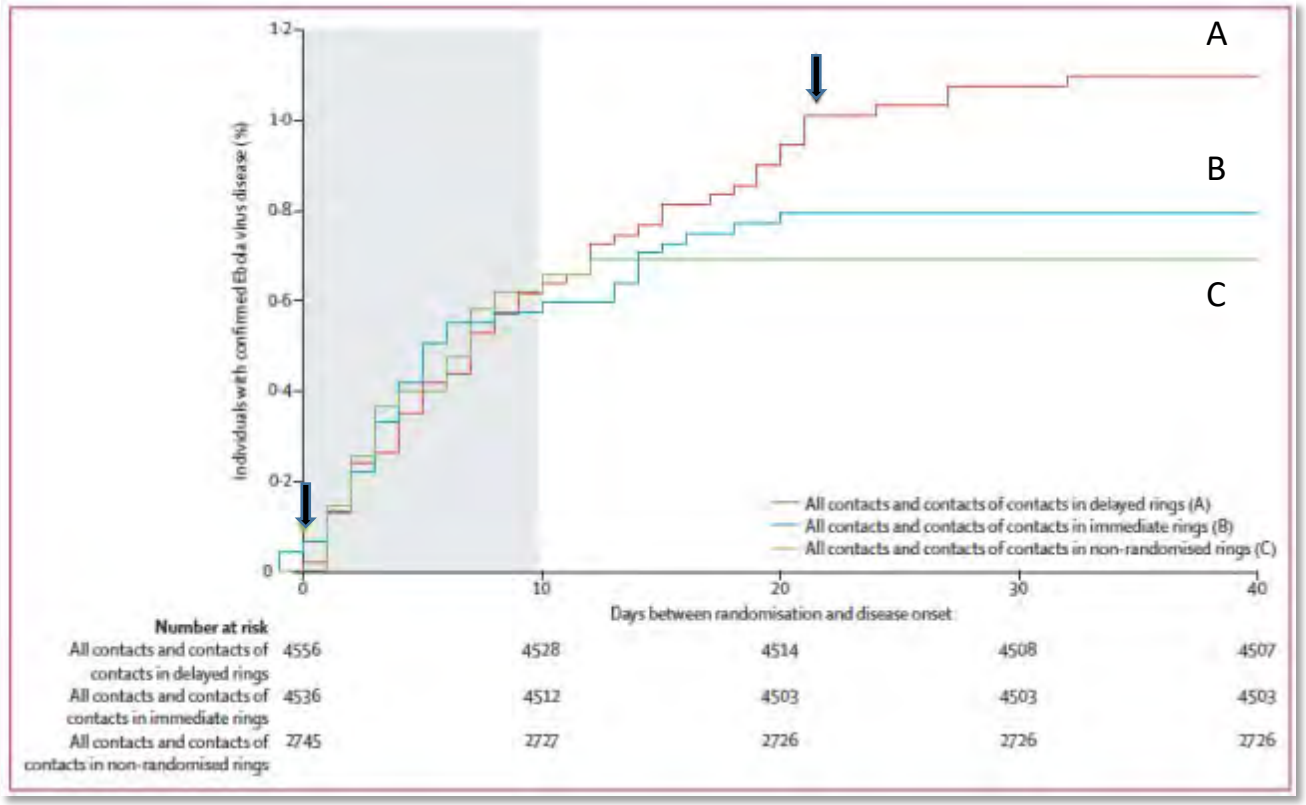
Geometric Mean Titers after Randomization



Kennedy SB N Engl J Med 2017;377:1438-47. DOI: 10.1056/NEJMoa1614067

Efficacy and Effectiveness of an rVSV-Vectored Vaccine in Preventing Ebola Virus Disease: Final Results from the Guinea Ring Vaccination, Open-Label, Cluster-Randomised Trial. (Ebola Ça Suffit!)

- Conakry, 8 préfectures en basse Guinée, Sierra Leone (Tomkolili et Bombali)
- Étude ouverte, randomisée par cluster, en anneau
- En cas de MEV confirmée :
  - Liste nominative des contacts (cluster) et des contacts des contacts
  - Randomisation des clusters 1:1
  - Vaccination immédiate *vs* différée (21 jours) des personnes éligibles
  - Injection unique rVSV-ZEBOV ($2x10^7$ ufp)
- Critère principal :
  - Survenue d'une MVE documentée
  - Tout décès par MVE probable documentée (pvt post mortem)
- Critères secondaires:
  - Effectiveness globale : prévention de la MVE chez tous les contacts et les contacts des contacts dans les clusters randomisés
  - Efficacité sur la mortalité par MVE
  - Effets indésirables graves



Kaplan-Meier plots for all confirmed cases of EVD among all contacts and contacts of contacts in immediate, delayed, and non-randomised clusters
Arrows show time of vaccination (at day 0 or day 21).

Henao-Restrepo AM Lancet 2017; 389: 505–18 http://dx.doi.org/10.1016/S0140-6736(16)32621-6

Efficacy and Effectiveness of an rVSV-Vectored Vaccine in Preventing Ebola Virus Disease: Final Results from the Guinea Ring Vaccination, Open-Label, Cluster-Randomised Trial. (Ebola Ça Suffit!)

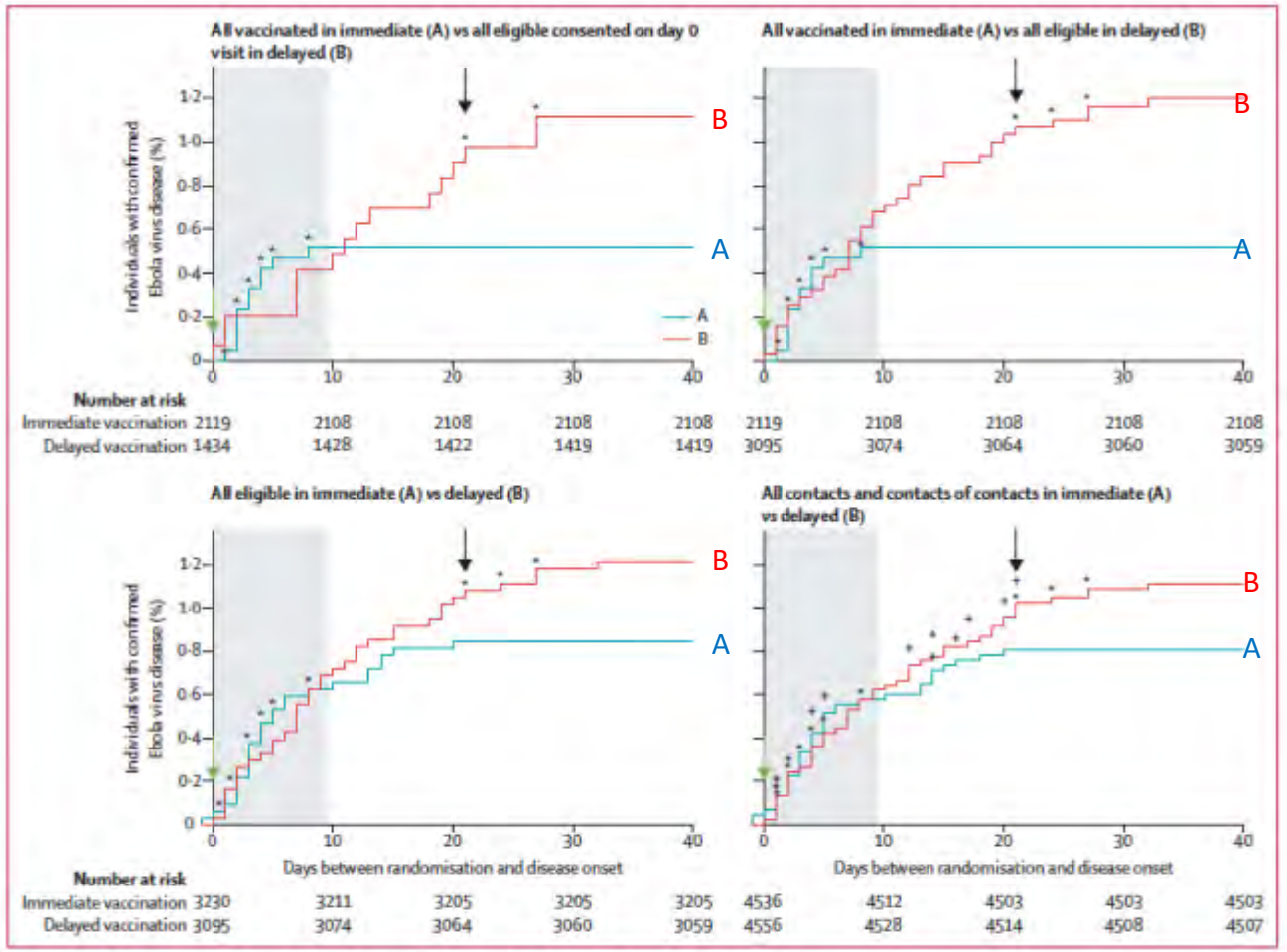


***Figure 3*: Kaplan-Meier plots for confirmed cases of Ebola virus disease in different study populations**
Arrows show time of vaccination (at day 0 or day 21); the plus signs denote cases among non-eligible children and the stars denote cases among vaccinated individuals; the shaded area denotes the a priori defined lag time of 0–9 days.

- Efficacité vaccinale clusters randomisés :
  - Clusters vaccination immédiate (n = 51) : aucun cas de MVE ≥ 10 j après randomisation chez les contacts et contacts des contacts
  - Clusters vaccination différée (n = 47) : 16 cas (7 clusters)
  - **EV = 100%** (IC 95% : 68,9–100, P=0,0045)
- Efficacité vaccinale globale sur 177 clusters (incluant 19 clusters non randomisés)
  - Vaccination immédiate : aucun cas de MVE ≥ 10 j chez les contacts et contacts des contacts
  - Vaccination différée + individus non vaccinés (clusters immédiats) : 23 MVE (11 clusters) chez les contacts et contacts des contacts
  - **EV : 100%** (IC 95% CI 79,3–100,0, P=0·0033).

Henao-Restrepo AM Lancet 2017; 389: 505–18 http://dx.doi.org/10.1016/S0140-6736(16)32621-6

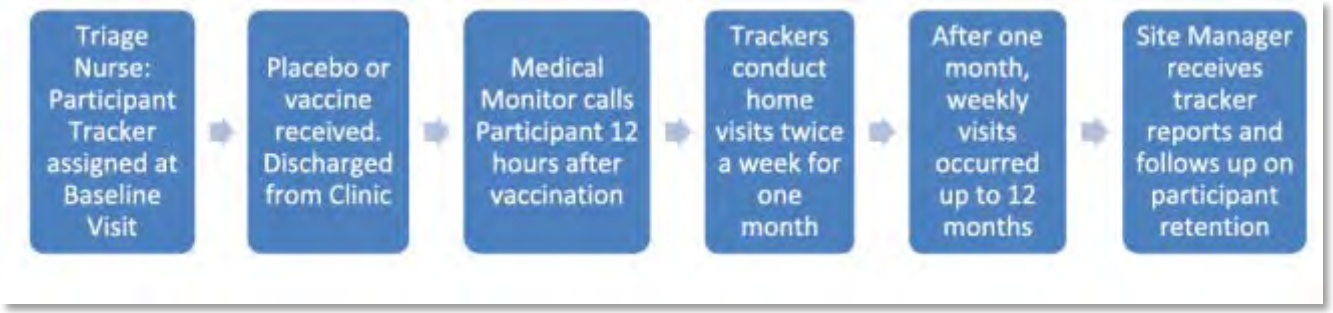
A Review of Strategies Used to Retain Participants in Clinical Research During an Infectious Disease Outbreak: The PREVAIL I Ebola Vaccine Trial Experience

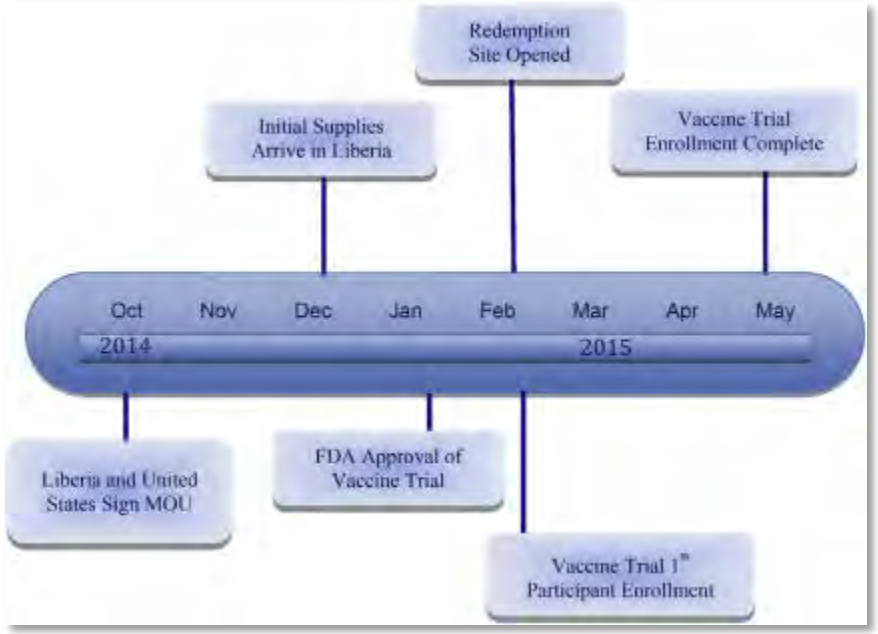
Myths about Ebola, vaccines, and clinical research prevalent in the community in Monrovia, Liberia	
Ebola-Related Myths	**Vaccine-Related Myths**
Ebola is a man-made virus	Ebola vaccines were used to transmit Ebola to more Africans
Ebola was brought to West Africa by Westerners to make money	Ebola vaccine trials were scams invented to infect Africans with the end aim of reducing the African population
Ebola was a conspiracy by the Liberian government to receive funds from the international community	Plasma collected from participants was used for commercial purposes
Health workers were the ones responsible for spreading Ebola	Clinic or hospital visitors would be given an injection meant to accelerate death
Health workers were using Ebola to collect organs and blood	Vaccine trial participants would contract Ebola during the rainy season
Those who drink alcohol are immune from Ebola	The vaccine trial was just a money-making scheme for government, NGOs, and pharmaceutical companies
Ebola normally spreads during the rainy season	Vaccines will kill participants during the rainy season
The Ebola virus can be eliminated by taking a saltwater bath	Participants will experience sudden deaths after six months
Ebola is a death sentence–nobody survives Ebola	The vaccine will turn participants into monsters
Ebola can be cured by traditional herbs alone	The vaccine is made for animals and not human beings

Brown S. Contemporary Clinical Trials Communications 2018 ;11: 50–54 https://doi.org/10.1016/j.conctc.2018.06.004

A Review of Strategies Used to Retain Participants in Clinical Research During an Infectious Disease Outbreak: The PREVAIL I Ebola Vaccine Trial Experience

Participant Flow Process in PREVAIL I Ebola vaccine trial





Trial Visit Attendance for PREVAIL I Ebola vaccine trial

Trial visit	# expected	# attended	%	Sample collected	%
Week- 1	1500	1487	99.1	1487	100%
Month −1	1499	1477	98.5%	1476	99.9%
Month-2	1496	1460	97.6%	–	–
Month-4	1495	1455	97.3	–	–
Month-6	1494	1459	97.7%	1457	99.9%
Month-8	1491	1444	96.8	–	–
Month-10	1488	1436	96.4%	–	–
Month-12	1488	1463	98.3	1460	99.8
Over all	11951	11681	97.77%	5880	99.9%

Brown S. Contemporary Clinical Trials Communications 2018 ;11: 50–54 https://doi.org/10.1016/j.conctc.2018.06.004

Six-Month Safety Data of Recombinant Vesicular Stomatitis Virus–Zaire Ebola Virus Envelope Glycoprotein Vaccine in a Phase 3 Double-Blind, Placebo-Controlled Randomized Study in Healthy Adults and Vaccine Safety Report

- Étude randomisée, double insu, *vs* placebo, volontaires sains
- USA : 40 sites, Espagne : 1 site, Canada : 1 site
- 1197 sujets randomisés & 1194 : vaccinés
- Monitorage effets indésirables : J 1 - 42

- 1 dose de rVSVΔG- ZEBOV-GP (2×10^7 pfu), n = 797
- 1 dose de rVSVΔG-ZEBOV-GP (1×10^8 pfu), n = 264 (high-dose group)
- Placebo, n = 133
- Monitorage effets indésirables : J 1 - 42

Adverse Event	rVSVΔG-ZEBOV-GP Combined Lots		rVSVΔG-ZEBOV-GP High Dose		Placebo	
Subjects in population, No.	790		260		133	
Arthralgia, No. (%)	135	(17.1); **P < .001**	53	(20.4); **P < .001**	4	(3.0)
Day of onset, median (range)	2.0	(1–39)	2.0	(1–25)	5.5	(2–37)
Duration (d), median (range)	3.0	(0.0–113.0)	3.0	(0.1–37.0)	3.0	(2.0–26.0)
Arthritis, No. (%)	40	(5.1); **P = .008**	11	(4.2); **P = .016**	0	(0.0)
Day of onset, median (range)	11.0	(1–25)	10.0	(2–14)	0	(0)
Duration (d), median (range)	7.0	(0.4–44.0)	5.0	(1.0–156.0)	0	(0)
Rash, No. (%)	30	(3.8); P = .181	10	(3.8); P = .202	2	(1.5)
Day of onset, median (range)	7.5	(2–25)	10.5	(2–22)	3.5	(2–5)
Duration (d), median (range)	6.0	(0.4–50.0)	16.0	(4.0–29.0)	14.0	(7.0–21.0)

Halperin SA J Infect Dis 2017;215:1789-98 DOI: 10.1093/infdis/jix189

Antiviraux

Favipiravir et MVE : Impact sur la Mortalité

Auteurs, Pays	Étude	Traitement	Mortalité
Sissoko D, 2016, Guinée (1)	JIKI, Phase II, multicentrique, non randomisée, *vs* cohorte historique	Favipiravir 6000 mg, puis 1200 mg bid, 9j	20% CT ≥ 20 (IC95%, 11,6-32,4%), vs 30% 91% CT < 20 (IC95%, 78,8-91,1%), vs 85%
Bai CQ, 2016, Sierra Leone (2)	Rétrospective comparative *vs* groupe contrôle	Favipiravir 800 mg bid, puis 600 mg bid, au moins 5 j	Taux de survie : 56,4% *vs* 35,3%; *P* = 0,027
Kerber R, 2019, Guinée (3)	Rétrospective, observationnelle, compassionnelle	Favipiravir monothérapie : 87/286 (30%) pts ; Favipiravir + Zmapp : 12/286 (4%) pts IFN-β1a : 9/286 (3%) pts	Mortalité : Univariée : 42,5% (31/73) vs 57,8% (52/90); *P* = 0,053 Multivariée : NS Kaplan-Meier : survie prolongée dans le groupe traité (*P* = 0,015)

1 : PLOS Medicine DOI:10.1371/journal.pmed.1001967 2 : Clin Infect Dis 2016;63:1288–94 DOI: 10.1093/cid/ciw571 3 : J Infect Dis 2019, DOI: 10.1093/infdis/jiz078

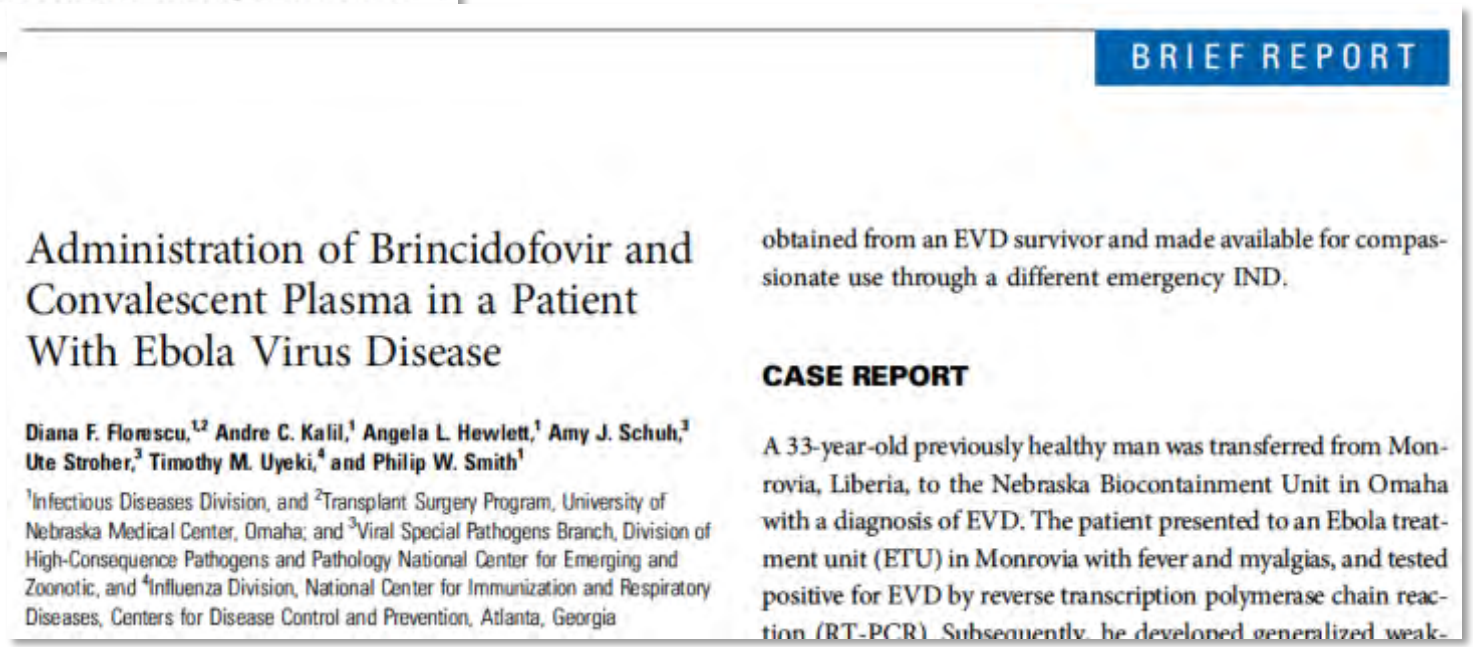
Brincidofovir et MVE : des Données Très Limitées

PLOS ONE

RESEARCH ARTICLE

Experimental Treatment of Ebola Virus Disease with Brincidofovir

Jake Dunning[1‡], Stephen B. Kennedy[2‡], Annick Antierens[3], John Whitehead[4], Iza Ciglenecki[5], Gail Carson[1], Rupa Kanapathipillai[3], Lyndsey Castle[1], Rebecca Howell-Jones[1], Raul Pardinaz-Solis[1], Jennifer Grove[1], Janet Scott[6], Trudie Lang[1], Piero Olliaro[1,7], Peter W. Horby[1]*, for the RAPIDE-BCV trial team[¶]



BRIEF REPORT

Administration of Brincidofovir and Convalescent Plasma in a Patient With Ebola Virus Disease

Diana F. Florescu,[1,2] Andre C. Kalil,[1] Angela L. Hewlett,[1] Amy J. Schuh,[3] Ute Stroher,[3] Timothy M. Uyeki,[4] and Philip W. Smith[1]

[1]Infectious Diseases Division, and [2]Transplant Surgery Program, University of Nebraska Medical Center, Omaha; and [3]Viral Special Pathogens Branch, Division of High-Consequence Pathogens and Pathology National Center for Emerging and Zoonotic, and [4]Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

obtained from an EVD survivor and made available for compassionate use through a different emergency IND.

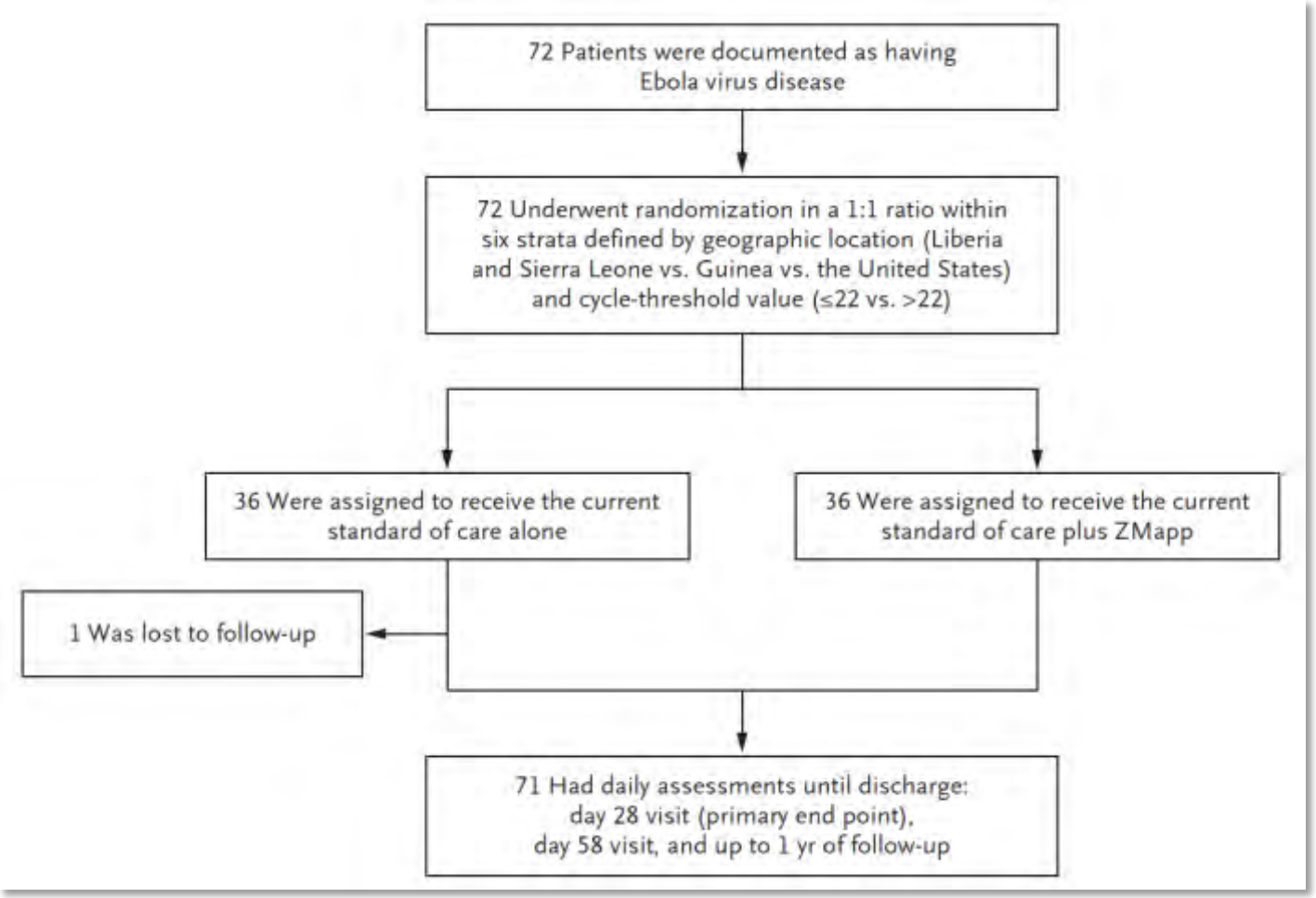
CASE REPORT

A 33-year-old previously healthy man was transferred from Monrovia, Liberia, to the Nebraska Biocontainment Unit in Omaha with a diagnosis of EVD. The patient presented to an Ebola treatment unit (ETU) in Monrovia with fever and myalgias, and tested positive for EVD by reverse transcription polymerase chain reaction (RT-PCR). Subsequently, he developed generalized weak-

1 : Dunning J PLoS ONE 11(9): e0162199.doi:10.1371/journal.pone.0162199 2 : Florescu DF Clin Infect Dis 2015;61:969-73

Ac Monoclonaux, Plasma Convalescents

A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection



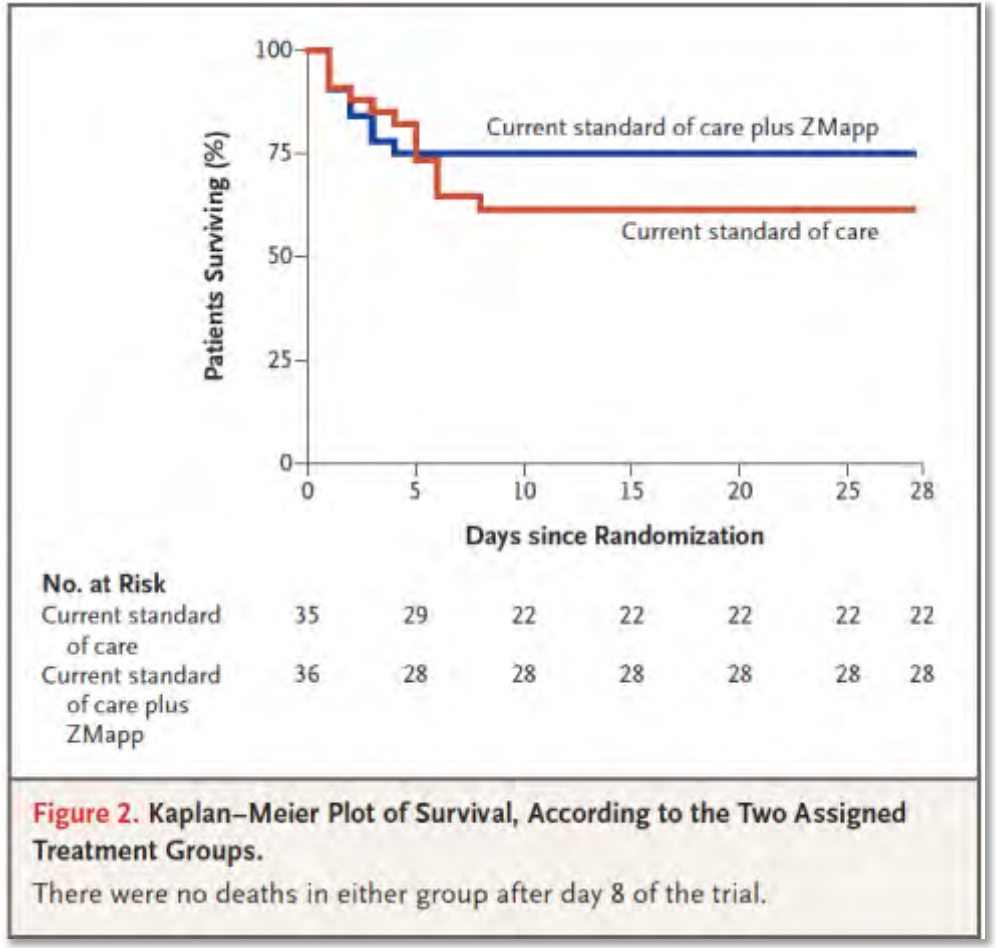
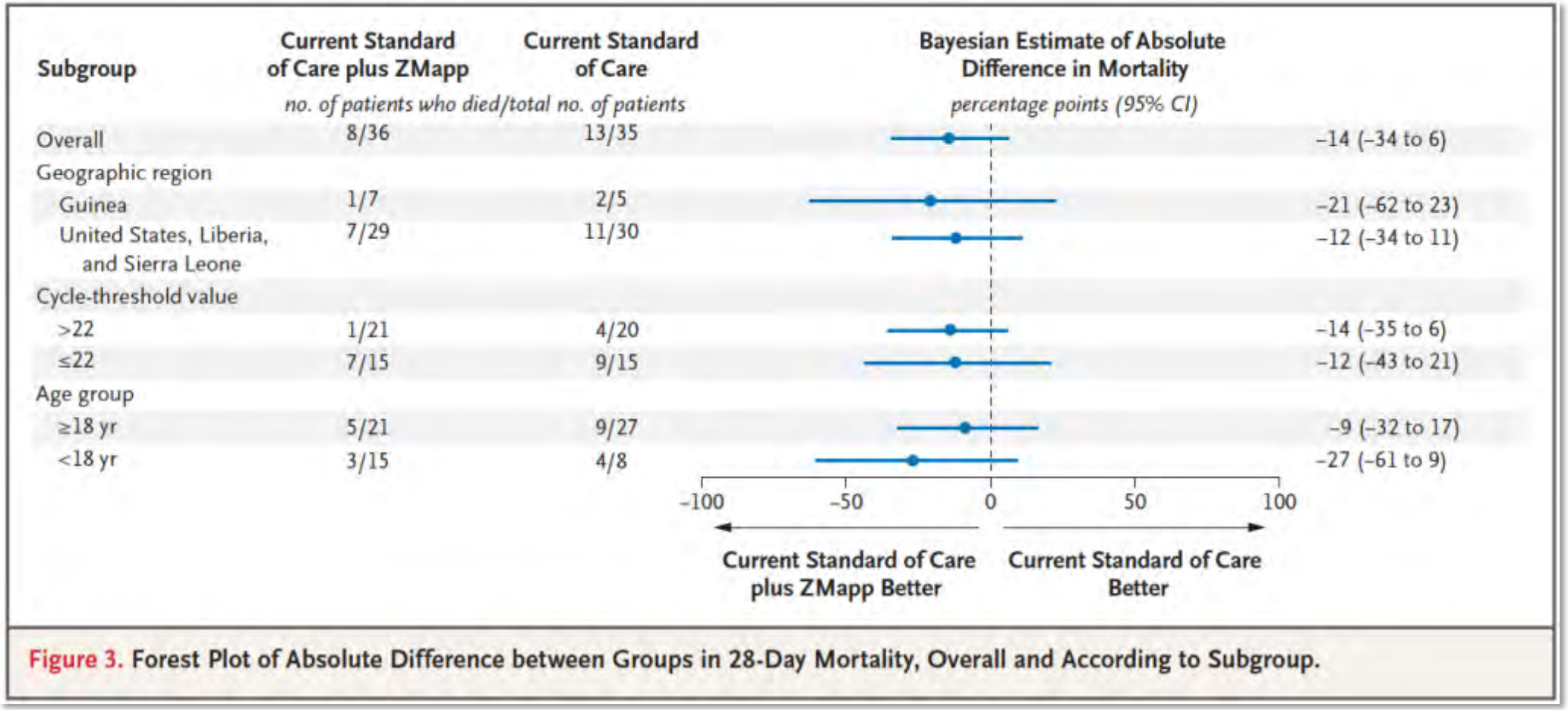


Figure 2. Kaplan–Meier Plot of Survival, According to the Two Assigned Treatment Groups.

There were no deaths in either group after day 8 of the trial.

The PREVAIL II Writing Group N Engl J Med 2016;375:1448-56. DOI: 10.1056/NEJMoa1604330

A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection



Subgroup	Current Standard of Care plus ZMapp	Current Standard of Care	Bayesian Estimate of Absolute Difference in Mortality
	no. of patients who died/total no. of patients		*percentage points (95% CI)*
Overall	8/36	13/35	−14 (−34 to 6)
Geographic region			
Guinea	1/7	2/5	−21 (−62 to 23)
United States, Liberia, and Sierra Leone	7/29	11/30	−12 (−34 to 11)
Cycle-threshold value			
>22	1/21	4/20	−14 (−35 to 6)
≤22	7/15	9/15	−12 (−43 to 21)
Age group			
≥18 yr	5/21	9/27	−9 (−32 to 17)
<18 yr	3/15	4/8	−27 (−61 to 9)

Figure 3. Forest Plot of Absolute Difference between Groups in 28-Day Mortality, Overall and According to Subgroup.

- ZMapp :
  - 50 mg/kg
  - 3 perfusions
  - 1 jour/3
  - Anti histaminiques et antipyrétiques

- Mortalité globale à 28 j :
  - ZMapp + SOC : 8/36 pts (22%)
  - SOC : 13/35 pts (37%)
  - RR 0,62%, [IC95% 0,29-1,24] **NS**

The PREVAIL II Writing Group N Engl J Med 2016;375:1448-56. DOI: 10.1056/NEJMoa1604330

Plasma de Convalescent et MVE

Auteurs, Pays	Étude	Traitement (plasma)	Efficacité
Van Griesven J, 2016 Guinée, Sierra Leone, Libéria (1)	Études comparatives non-randomisées Ebola-Tx, Conakry, Guinée Ebola-CP, Freetown, Sierra Leone EVD001, Monrovia, Liberia	 2 unités 1 unité 2 unités	Absence de données d'efficacité Points positifs : sécurité, acceptabilité, faisabilité
Sahr F, 2017 Feetown, Sierra Leone (2)	Étude non randomisée deux sites	1 unité	Réduction de la CV 24h après transfusion, $P < 0,01$ Mortalité : 27,9% vs 44% OR 2,3 [IC95% 2,3; 0,8-6,5]

1 : Van Griesven J Clin Infect Dis 2016;62(1):69–74 DOI: 10.1093/cid/civ680 2 : Sahr F J Inf 2017;74:302-309 http://dx.doi.org/10.1016/j.jinf.2016.11.009

Evaluation of Convalescent Whole Blood for Treating Ebola Virus Disease in Freetown, Sierra Leone

- Étude non randomisée, deux sites, 2014-2015
- Hôpital militaire Wilberforce
- 69 pts; 44 transfusés 1 unité sang total de convalescent ABO compatible; 25 refus

Réduction mortalité, mais NS

	CWB-group			Non CWB-group					Fischer exact probability
Age, y	**Survived**	**Died**	**CFR**	**Survived**	**Died**	**CFR**	**OR**	**95% CI**	***P* -Value**
0-17	06	4	40.0%	01	03	75.0%	4.5	0.3-60.0	0.28
18-39	20	04	16.7%	09	04	30.8%	2.2	0.5-10.9	0.28
> 40	06	03	33.3%	04	04	50.0%	2.0	0.28-14.2	0.42
Total	32	11	25.6%	14	11	44.0%	2.3	0.8-6.5	0.09
Sex									
Male	14	05	26.3%	07	06	46.2%	2.4	0.5-10.7	0.22
Female	18	06	25%	07	05	41.7%	2.1	0.5-9.3	0.26

Sahr F J Inf 2017;74:302-309 http://dx.doi.org/10.1016/j.jinf.2016.11.009

Clinical Infectious Diseases
VIEWPOINTS

The Use of Ebola Convalescent Plasma to Treat Ebola Virus Disease in Resource-Constrained Settings: A Perspective From the Field

Johan van Griensven,[1] Anja De Weiggheleire,[1] Alexandre Delamou,[2] Peter G. Smith,[3] Tansy Edwards,[3] Philippe Vandekerckhove,[4] Elhadj Ibrahima Bah,[5] Robert Colebunders,[1,6] Isola Herve,[7] Catherine Lazaygues,[7] Nyankoye Haba,[8] and Lutgarde Lynen[1]

Safety, tolerability, pharmacokinetics, and immunogenicity of the therapeutic monoclonal antibody mAb114 targeting Ebola virus glycoprotein (VRC 608): an open-label phase 1 study

Martin R Gaudinski, Emily E Coates, Laura Novik, Alicia Widge, Katherine V Houser, Eugeania Burch, LaSonji A Holman, Ingelise J Gordon, Grace L Chen, Cristina Carter, Martha Nason, Sandra Sitar, Galina Yamshchikov, Nina Berkowitz, Charla Andrews, Sandra Vazquez, Carolyn Laurencot, John Misasi, Frank Arnold, Kevin Carlton, Heather Lawlor, Jason Gall, Robert T Bailer, Adrian McDermott, Edmund Capparelli, Richard A Koup, John R Mascola, Barney S Graham, Nancy J Sullivan, Julie E Ledgerwood, on behalf of the VRC 608 Study team*

- Évaluation priorisée par l'OMS sept 2014
- Guinée, Sierra Leone, Libéria
- Études comparatives non-randomisées
  - Ebola-Tx, Conakry, Guinée
  - Ebola-CP, Freetown, Sierra Leone
  - EVD001, Monrovia, Liberia
- Absence de données d'efficacité
- Points positifs :
  - Sécurité, acceptabilité, faisabilité

- US National Institutes of Health (NIH) Clinical Center (Bethesda, MD, USA),
- Volontaires sains 18–60 ans
  - 3 posologies (mAb114) : 5 mg/kg, 25 mg/kg, 50 mg/kg.
  - Voie IV 30 min
  - Suivi 24 semaines
- Bonne tolérance, PK linéaire, ½ vie 24,2 j
- Administration aisée, perfusion rapide,
- Option thérapeutique attractive

Van Griesven J Clin Infect Dis 2016;62(1):69–74 DOI: 10.1093/cid/civ680 Gaudinski MR Lancet 2019; 393: 889–98 http://dx.doi.org/10.1016/S0140-6736(19)30036-4

Safety, Pharmacokinetics, Immunogenicity of a Co-formulated Cocktail of Three Human Monoclonal Antibodies Targeting Ebola Virus Glycoprotein in Healthy Adults: A Randomised, First-in-human Phase 1 Study

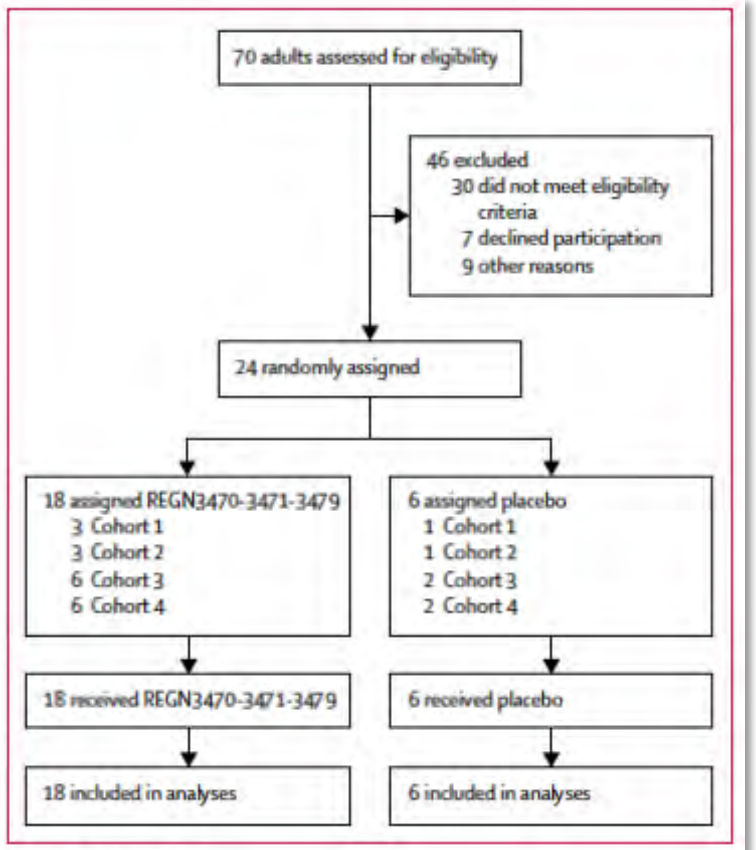


Figure 1: **Trial profile**
Cohort 1: REGN3470-3471-3479 3 mg/kg IV or placebo IV infused over 2 h.
Cohort 2: REGN3470-3471-3479 15 mg/kg IV or placebo IV infused over 2 h.
Cohort 3: REGN3470-3471-3479 60 mg/kg IV or placebo IV infused over 4 h.
Cohort 4: REGN3470-3471-3479 150 mg/kg IV or placebo IV infused over 4 h.
IV=intravenous.

- REGN3470-3471-3479
- Bonne tolérance,
- T ½ : 21,7–27,3 j
- Sans réaction immune quand administré en une seule dose IV.
- Résultats en faveur de la poursuite du développement de REGN3470-3471-3479 pour le traitement de la MVE lors de futures épidémies.

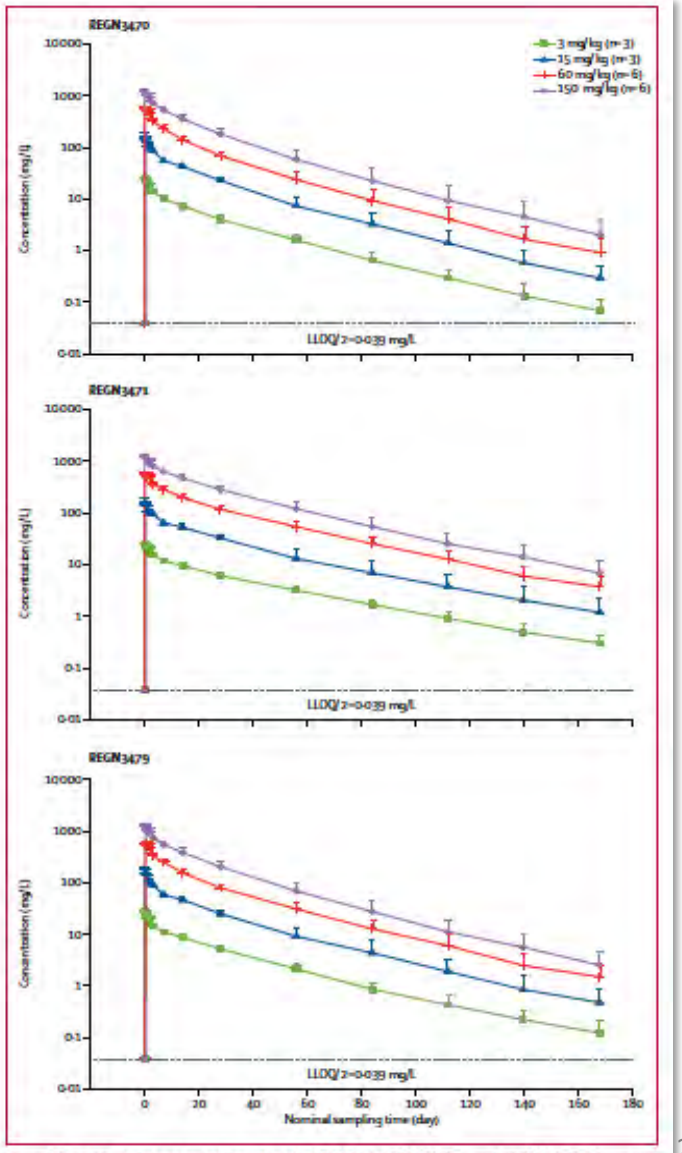
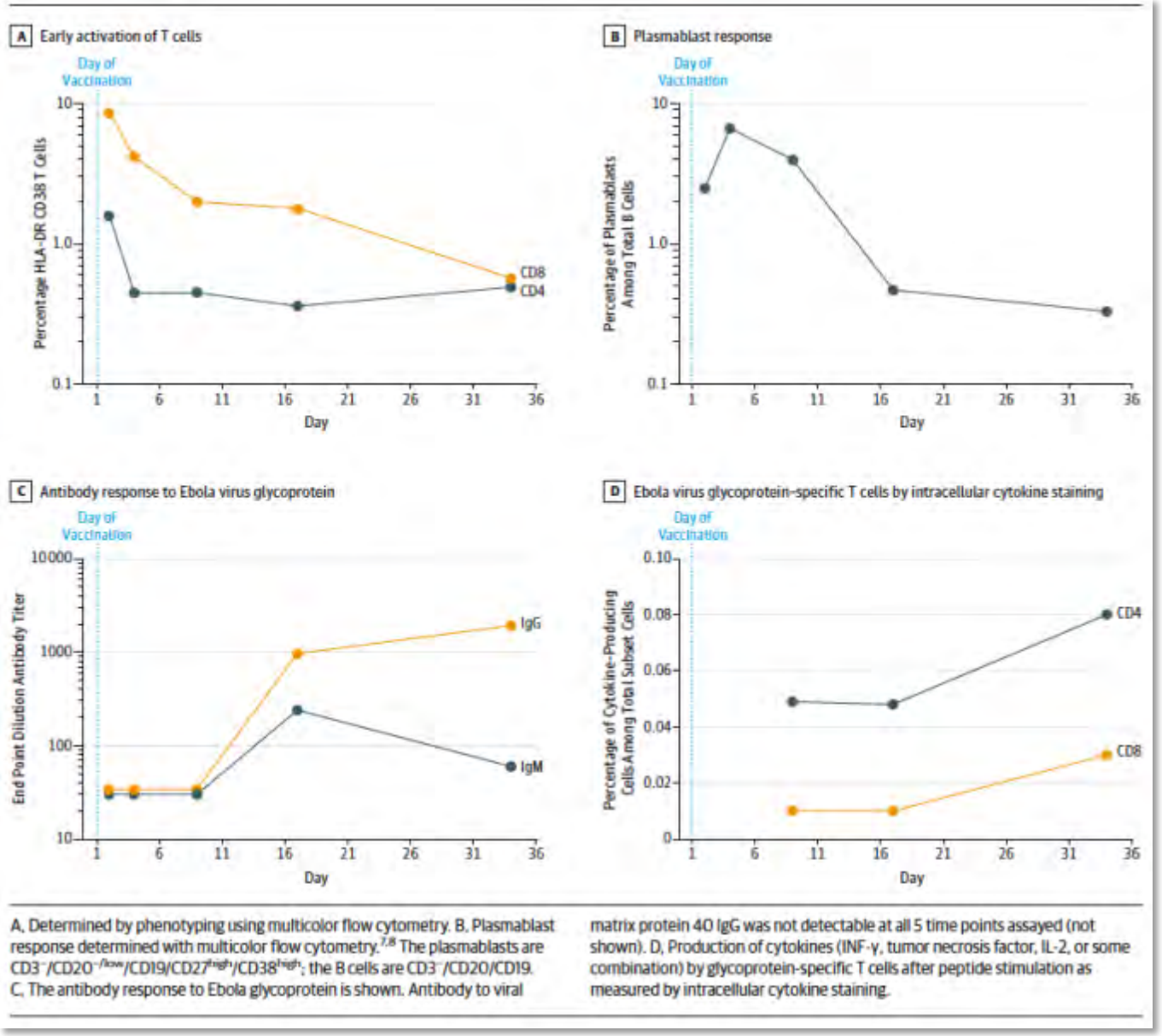


Figure 2: **Mean log-scaled concentrations of total REGN3470, total REGN3471, and total REGN3479 in serum from healthy adults, by nominal time and treatment group**
Error bars show the SD of each mean. LLOQ=lower limit of quantification.

Postexposition

Emergency Postexposure Vaccination With Vesicular Stomatitis Virus–Vectored Ebola Vaccine After Needlestick

- Sécurite d'utilisation et efficacité du rVSV-ZEBOV en post exposition : inconnues après AEV à risque élevé.
- Dans ce cas :
  - Syndrome fébrile modéré
  - Détection transitoire du rVSV dans le sang périphérique
  - Forte réponse immune innée et adaptative anti EBOLA observée après vaccination.
  - Absence d'infection à ZEBOV



A, Determined by phenotyping using multicolor flow cytometry. B, Plasmablast response determined with multicolor flow cytometry.[7,8] The plasmablasts are $CD3^-/CD20^{-/low}/CD19/CD27^{high}/CD38^{high}$; the B cells are $CD3^-/CD20/CD19$. C, The antibody response to Ebola glycoprotein is shown. Antibody to viral matrix protein 40 IgG was not detectable at all 5 time points assayed (not shown). D, Production of cytokines (INF-γ, tumor necrosis factor, IL-2, or some combination) by glycoprotein-specific T cells after peptide stimulation as measured by intracellular cytokine staining.

Lai L JAMA. 2015;313(12):1249-1255. doi:10.1001/jama.2015.1995

Use of Postexposure Prophylaxis After Occupational Exposure to Zaire Ebolavirus

- AEV ZEBOV sept 2014-avril 2015
- 6 pts :
  - 3 IDE, 2 médecins, 1 non soignant
- Évacuation sanitaire USA
- Médicaments utilisés
  - Tous en investigation :
    - 5 pts : vaccin rVSV-ZEBOV (10^8 UFP)
    - 1 pts : TKM-100802 (0,3-0,5 mg/kg/j)
- Délai de PPE : 1-3 j
- TPE VIH : 4 pts
- 6/6 : symptômes post PPE limités
- Aucune infection à ZEBOV

Table 3. Systemic and Local Reactions in 6 Patients Receiving Postexposure Prophylaxis for Potential High-Risk Ebola Virus Exposures

	Type of PEP Received	
Reaction	rVSV-ZEBOV (n = 5)[a]	TKM-100802 (n = 1)
Systemic		
Fever	4	Yes
Highest fever, °C	37.3–39.1	38.1
Myalgias	3	Unknown
Chills/rigors	3	No
Diaphoresis	3	No
Hypotension	1	Yes[b]
Malaise	2	No
Fatigue	3	Unknown
Headache	4	Yes
Dizziness	1	No
Arthralgia	1	No
Arthritis	0	No
Rash	1	No
Chest pain	1	No
Dyspnea	1	No
Hypoxia	1	No
Nausea	4	No
Vomiting	1	No
Diarrhea	2	No
Local		
Redness	0	Yes
Swelling	0	Yes
Pain	3	Yes
Thrombophlebitis	0	Yes

Abbreviation: PEP, postexposure prophylaxis.

[a] Data in this column represent number of patients, unless otherwise specified.

[b] This patient's lowest blood pressure was 90/56 mm Hg while asleep; hypotension resolved without intervention.

Wong K K Clin Infect Dis 2016;63(3):376–9 DOI: 10.1093/cid/ciw256

Ebola Virus Disease: an Update on Post-Exposure Prophylaxis

Caractéristiques d'un agent idéal pour la PPE contre la MVE

- Efficacité prouvée, de préférence chez l'homme, au minimum chez les primates non humains
- Début rapide de la protection et de l'efficacité pendant la plus longue durée possible après l'exposition au virus Ebola
- Efficacité sur les différentes espèces du virus Ebola
- Bonne tolérance toléré, sans effets indésirables graves
- Administration facile, de préférence par voie orale
- Stable, stockage et transport faciles
- Faible coût
- Facilement disponible

	Avantages	inconvénients	Administration
Vaccin			
rVSV-ZEBOV	Immunogénicité Efficacité prouvée Safety à court terme	Délai d'acquisition de l'immunité ? Réactogénicité; Risque faux positif Dg MEV Spécificité souche Zaïre ? Chaine du froid +++	1 injection unique 2 x 10^7 UFP
Anticorps monoclonaux			
ZMapp	Prometteur mais études non conclusives tolérance	Expérience très limitée en postexposition Spécificité souche Zaïre; Chaine du froid	IV lente, tous les 3 jours, 2-3 doses
MIL77	Prometteur	Expérience humaine extrêmement limitée Spécificité Zaïre ;Administration complexe Chaine du froid	IV lente, tous les 3 jours, 2-3 doses
Antiviraux			
Favipiravir	Safety OK à faible dose (grippe) Posologies pour ZEBOV ? Stabilité, voie orale	Activité anti Ebola faible ; Expérience très limitée en post exposition tératogène chez l'animal à posologies élevées	Voie orale
GS-5734	Large spectre Filovirus Prometteur : in vitro, primates non-humain, phase précoce MEV	Expérience très limitée chez l'homme, aucune en postexposition	Voie IV, durée inconnue
BCX4430	Large spectre Filovirus Prometteur : in vitro, primates non-humain, phase précoce MEV	Jamais utilisé en curatif ni en prophylaxie	Voie et posologies inconnues

Fischer WA Lancet Infect Dis 2018;18: e183–92 http://dx.doi.org/10.1016/S1473-3099(17)30677-1

Avis du HCSP

Avis Relatif aux **Mesures Préventives par la Vaccination** contre le Virus Ebola des Personnes Susceptibles d'Être en Contact avec des Patients à Risque de Transmission (29 juin et 10 juillet 2018)

- Balance bénéfices/risques pour une vaccination :
  - Favorable pour les personnels déployés en zone d'épidémie de MVE avant le départ
  - Plus difficile à établir, en préexposition, pour les personnels en France
- Recommande la vaccination
  - Pour tous les professionnels se rendant dans la zone épidémique, en fonction du niveau d'exposition attendu, après analyse des tâches futures
  - Pour les professionnels des ESR susceptibles de prendre en charge un cas de MVE en France, notamment ceux qui seraient en contact direct avec le patient ou leurs produits biologiques
    - Vaccination non systématique, mais rendue accessible aux volontaires
    - Vaccination réactive, si cas rapatrié dans un ESR ;
    - Vaccination immédiatement après un AEV un sujet n'ayant pas été vacciné (post-exposition) ;
    - Capacité d'approvisionnement de vaccins en urgence

Avis Relatif aux Indications en **Prophylaxie et en Curatif** des Antiviraux et des Anticorps Monoclonaux chez les Professionnels de Santé Exposés au Virus Ebola (07 septembre 2018) I

- Deux options thérapeutiques, seules ou en association, à privilégier dans un contexte de prise en charge de MVE :
  - Zmapp
  - Remdesivir (antiviral Gilead Sciences)
- Favipiravir : alternative (voie orale)
  - JIKI : inefficacité
  - Schéma posologique suboptimal
- Zmapp (Prevail II)
  - Effectif non atteint
  - Tendance en faveur de l'efficacité du ZMapp observée dans cet essai
  - Utilisation compassionnelle 9 pts
  - Principaux effets indésirables, de type allergique, gérables en ESR

- Balance bénéfices-risques :
  - En traitement **curatif** : le bénéfice prévaut sur le risque (traitement à titre compassionnel)
  - En situation de **PPE** : la contamination est **hypothétique** et les données de **sécurité d'emploi** sont **prépondérantes** dans la décision
- Balance bénéfices/risques et niveau des connaissances actuelles et l'existence d'un vaccin :
  - Ne permettent pas de recommander l'utilisation des AV en PPE
  - Permettent d'envisager de recourir aux AV et aux anticorps Ac monoclonaux
    - En PPE et en curatif,
    - Sur le terrain et en ESR,
    - Selon des modalités à définir

Avis Relatif aux Indications en **Prophylaxie et en Curatif** des Antiviraux et des Anticorps Monoclonaux chez les Professionnels de Santé Exposés au Virus Ebola (07 septembre 2018) II

En ESR : en traitement curatif MVE

- Ac monoclonaux (Zmapp) et un antiviral d'action directe tel que le remdesivir, seuls ou en association.
- En cas d'indisponibilité immédiate de ces molécules, l'utilisation du favipiravir pourrait être envisagée sous réserve de la détermination d'une posologie appropriée, efficace et bien tolérée
- Décision guidée par avis collégial multidisciplinaire

En ESR : traitement post exposition

- Vaccin rVSV Ebola
- Si traitement AV requis : respecter un délai de l'ordre de 5 à 7 jours
- En l'absence de disponibilité du vaccin
  - En première intention : association ZMapp et remdesivir, voire ZMapp et favipiravir sous réserve qu'une posologie appropriée de favipiravir ait été déterminée.
  - Décision sur avis collégial pluridisciplinaire

Avis Relatif aux Indications en **Prophylaxie et en Curatif** des Antiviraux et des Anticorps Monoclonaux chez les Professionnels de Santé Exposés au Virus Ebola (07 septembre 2018) III

Sur le terrain : traitement curatif MVE

- La stratégie thérapeutique sur le terrain devrait être celle soutenue par les experts internationaux.
- L'utilisation d'une bithérapie associant deux classes thérapeutiques différentes (remdesivir et ZMapp) dans le cadre d'études cliniques randomisées et comparatives menées durant l'épidémie est la stratégie actuellement envisagée

Sur le terrain : traitement post exposition

- La stratégie thérapeutique sur le terrain devrait être celle soutenue par les experts internationaux et locaux.
- Pour la prise en charge d'un soignant, les possibilités de traitement pourraient reposer sur
  - Le remdesivir
  - Et le favipiravir sous réserve qu'une posologie appropriée ait été déterminée.

Take Home Message

- Énormément d'incertitudes
- ZMapp, mAb 114 et REGN-EB3
  - Voie IV
  - Zmapp : spécifique souche Zaïre, 3 perfusions nécessaires, conservation congélateur, données cliniques, mais NS par manque de puissance
- Remdesivir (GS-5734) et favipiravir
  - Favipiravir : essai JIKI non concluant (posologie inadéquate, restant à déterminer), mais seul tt per os
  - Remdesevir : pas de données cliniques
- Vaccin rVSV-ZEBOV
  - Données efficacité en prévention
  - Post exposition ?
- Modalités d'utilisation
  - Antiviraux et vaccins : procédures OMS exceptionnelles
  - En dehors des essais : avis collégial multidisciplinaire

Merci

Séquelles de la MVE

- Musculo-squelettiques
  - Arthralgies (50-75%), ténosynovites, chondrite costale
- Ophtalmologiques :
  - Douleurs, érythème, sécheresse, sensibilité à la lumière, vision floue
  - Uvéite cataracte, atteintes rétiniennes et du nerf optique
- Auditives : 25%
- Perte d'audition, labyrinthite, otite,
- Douleurs abdominales

- Neurologiques
  - Céphalées, troubles de la mémoire, de l'attention, neuropathie périphérique,…
- Santé mentale
- Santé sexuelle
  - Dysfonction erectile, douleur testiculaire, dyspareunie, douleur pelvienne, ménmetrorragies, aménorrhée
- Persistance virale
  - Sites protégés : oeil SNC, testicules, glandes mammaires,
- Risque de résurgence

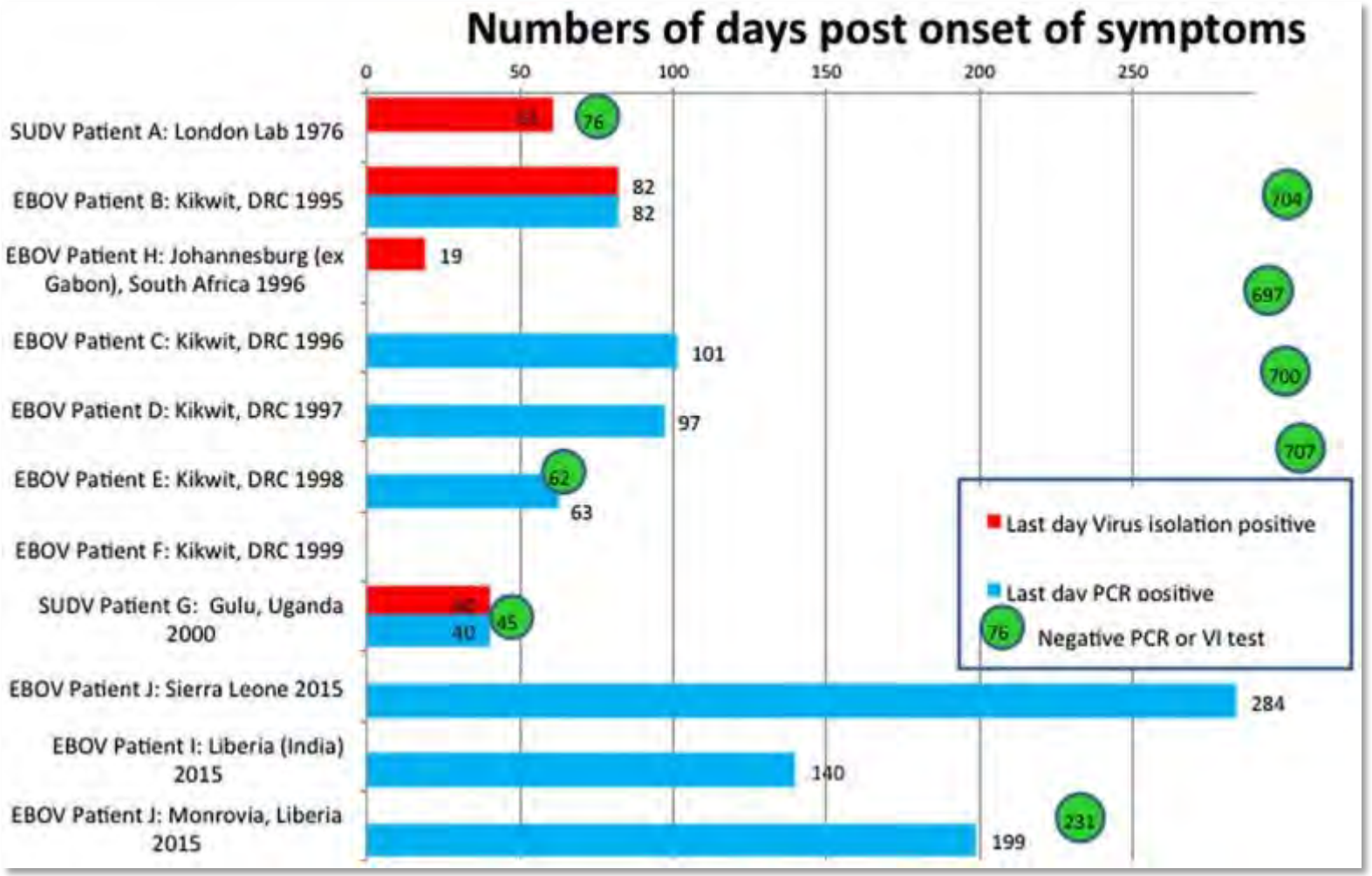
http://www.who.int/csr/disease/ebola/response/infographic/fr/

Virus Isolation and RT-PCR Findings in Other Body Fluids in Recovered Patients

EBOV	Faeces or rectal swabs	Throat swabs or saliva	Sweat	Urine	
Patient 1, London, 1976	EBOV	−VI days 14–27	−VI days 14–27	NA	−VI days 14–27
29 Recovered patients, Kikwit, DRC, 1995	EBOV	−VI days 11–57	−VI days 11–57	NA	−VI days 11–57
8 Recovered patients, Kikwit, DRC, 1995	EBOV	−RT-PCR days 11–33 (total 18 specimens) + RT-PCR days 22 and 29 (total 2 specimens, same woman−RT-PCR days 25 and 33)	−RT-PCR days 11–33 (total 20 specimens)	NA	−RT-PCR days 11–33 (total 19 specimen)
4 Patients, Gulu, Uganda, 2000	SUDV	NA	−RT-PCR days 12–23	NA	−RT-PCR days 12–23
Patient 1, Sierra Leone, 2014	EBOV	−VI after day 17 (negative blood test day 17)	−VI after day 17 (negative blood test day 17)	−VI + RT-PCR until day 40	+ VI repeatedly until day 26 + RT-PCR until day 30

Thorson A BMJ Open2016;6:e008859 doi:10.1136/bmjopen-2015-008859

Persistance du Virus Ebola et de l'ARN Viral dans le Sperme



Thorson A BMJ Open2016;6:e008859 doi:10.1136/bmjopen-2015-008859

Phases Initiales des Vaccins Ebola : rVSVΔG-ZEBOV-GP & ChAd3-EBO-Z

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Recombinant Vesicular Stomatitis Virus Ebola Vaccine

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 1 Trials of rVSV Ebola Vaccine in Africa and Europe

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 2 Placebo-Controlled Trial of Two Vaccines to Prevent Ebola in Liberia

CONCLUSIONS

This Ebola vaccine candidate elicited anti-Ebola antibody responses. After vaccination, rVSV viremia occurred frequently but was transient. These results support further evaluation of the vaccine dose of 20 million PFU for preexposure prophylaxis and suggest that a second dose may boost antibody responses. (Funded by the National Institutes of Health and others; rVSVΔG-ZEBOV-GP ClinicalTrials.gov numbers, NCT02269423 and NCT02280408.)

CONCLUSIONS

In these studies, rVSV-ZEBOV was reactogenic but immunogenic after a single dose and warrants further evaluation for safety and efficacy. (Funded by the Wellcome Trust and others; ClinicalTrials.gov numbers, NCT02283099, NCT02287480, and NCT02296983; Pan African Clinical Trials Registry number, PACTR201411000919191.)

CONCLUSIONS

A randomized, placebo-controlled phase 2 trial of two vaccines that was rapidly initiated and completed in Liberia showed the capability of conducting rigorous research during an outbreak. By 1 month after vaccination, the vaccines had elicited immune responses that were largely maintained through 12 months. (Funded by the National Institutes of Allergy and Infectious Diseases and the Liberian Ministry of Health; PREVAIL I ClinicalTrials.gov number, NCT02344407.)

Regules JA N Engl J Med 2017;376:330-41. DOI: 10.1056/NEJMoa1414216 Agnandji ST N Engl J Med 2016;374:1647-60. DOI: 10.1056/NEJMoa1502924
Kennedy SB N Engl J Med 2017;377:1438-47. DOI: 10.1056/NEJMoa1614067

Efficacy and Effectiveness of an rVSV-Vectored Vaccine in Preventing Ebola Virus Disease: Final Results from the Guinea Ring Vaccination, Open-Label, Cluster-Randomised Trial. (Ebola Ça Suffit!)

	All clusters*				Randomised clusters†			
	1	2	3	4	5	6	7	8
	All vaccinated in immediate (group A) vs all contacts and contacts of contacts in delayed plus all never-vaccinated in immediate or non-randomised (group B)	All vaccinated in immediate (group A) vs all eligible in delayed plus all eligible never-vaccinated in immediate (group B)	All contacts and contacts of contacts in immediate (group A) vs delayed (group B)	All vaccinated in immediate (group A) vs all eligible never vaccinated in immediate (group B)	All vaccinated in immediate (group A) vs all eligible and consented on day 0 visit in delayed (group B)	All vaccinated in immediate (group A) vs all eligible in delayed (group B)	All eligible in immediate (group A) vs all eligible delayed (group B)	All contacts and contacts of contacts in immediate (group A) vs all contacts and contacts of contacts in delayed (group B)
Group A								
Number of individuals (clusters)	3775 (70)	3775 (70)	7241 (70)	3775 (70)	2108 (51)	2108 (51)	3212 (51)	4513 (51)
Cases of Ebola virus disease (clusters affected)	0 (0)	0 (0)	12 (7)	0 (0)	0 (0)	0 (0)	7 (4)	10 (5)
Attack rate	0%	0%	0·17%	0%	0%	0%	0·22%	0·22%
Group B								
Number of individuals (clusters)	7995 (116)	4507 (104)	4529 (47)	1432 (57)	1429 (46)	3075 (47)	3075 (47)	4529 (47)
Cases of Ebola virus disease (clusters affected)	34 (15)	23 (11)	22 (8)	7 (4)	10 (4)	16 (7)	16 (7)	22 (8)
Attack rate	0·43%	0·51%	0·49%	0·49%	0·7%	0·52%	0·52%	0·49%
Vaccine effect								
Vaccine efficacy/effectiveness‡ (%, 95% CI)	100% (77·0 to 100·0)	100% (79·3 to 100·0)	70·1% (−4·9 to 91·5)	100% (−51·5 to 100·0)	100% (63·5 to 100·0)	100% (68·9 to 100·0)	64·6% (−46·5 to 91·4)	64·6% (−44·2 to 91·3)
p value§	0·0012	0·0033	0·2759	0·125	0·0471	0·0045	0·344	0·3761

*Randomly assigned and non-randomly assigned individuals who were allocated to immediate vaccination were combined. †Non-randomised immediate clusters are excluded from this analysis. ‡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 (columns 1, 2, 5, and 6); from a Cox proportional hazards model (column 3, 7, and 8); from signed test (two-sided): probability of observing endpoints in control groups among treatment-control mismatched pairs and under the null hypothesis that the vaccine has no efficacy (column 4). §From Fisher's exact test (two-sided), which is approximate for columns 1 and 2. From signed test (two-sided): probability of observing endpoints in control groups among treatment-control mismatched pairs and under the null hypothesis that the vaccine has no efficacy (column 4).

Table 3: Effect of vaccine on cases of Ebola virus disease in different study populations

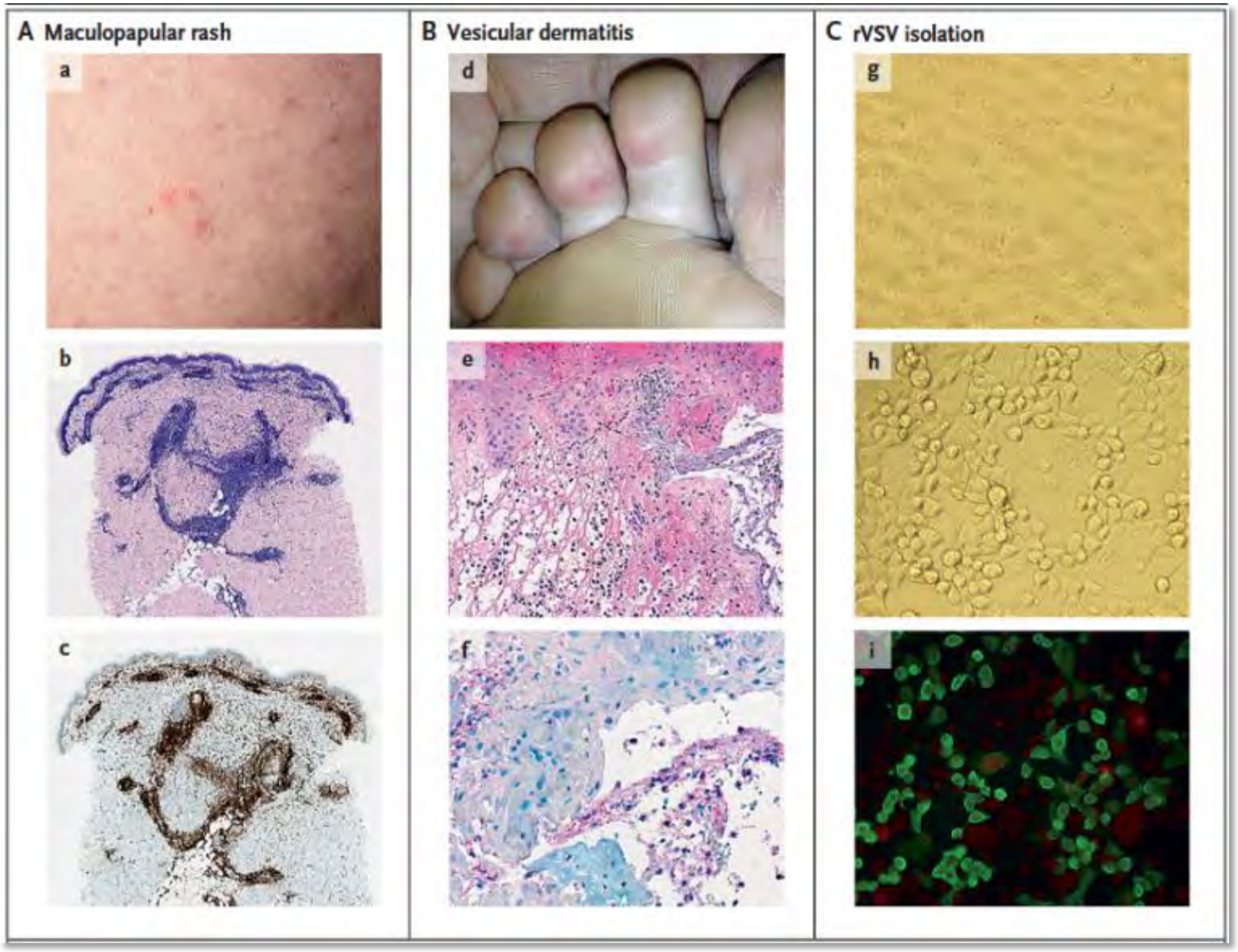
	0–30 min	31 min to 3 days	4–14 days
Children aged between 6–<18 years (n=194)			
Arthralgia	0	3 (3·5%)	1 (9·1%)
Diarrhoea	0	0	1 (9·1%)
Fatigue	0	10 (11·6%)	1 (9·1%)
Fever	0	1 (1·2%)	1 (9·1%)
Headache	0	47 (54·7%)	4 (36·4%)
Induration	0	0	0
Injection pain	0	9 (10·5%)	0
Muscle pain	0	4 (4·7%)	1 (9·1%)
Myalgia	0	4 (4·7%)	1 (9·1%)
Vomiting	0	1 (1·2%)	0
Other adverse events	0	7 (8·1%)	1 (9·1%)
Total	0	86 (100·0%)	11 (100·0%)
Adults aged 18 years and older (n=5643)			
Arthralgia	3 (2%)	851 (13·5%)	79 (12·3%)
Diarrhoea	0	53 (0·8%)	15 (2·3%)
Fatigue	5 (3·3%)	1233 (19·5%)	112 (17·4%)
Fever	2 (1·3%)	8 (0·1%)	2 (0·3%)
Headache	41 (27·3%)	1563 (24·7%)	177 (27·5%)
Induration	0	1 (<1%)	0
Injection pain	70 (46·7%)	362 (5·7%)	8 (1·2%)
Muscle pain	7 (4·7%)	875 (13·8%)	55 (8·5%)
Myalgia	6 (4·0%)	816 (12·9%)	47 (7·3%)
Vomiting	0	21 (0·3%)	4 (0·6%)
Other adverse events	16 (10·7%)	537 (8·5%)	145 (22·5%)
Total	150 (100·0%)	6320 (100·0%)	644 (100·0%)

Data are n (%); individuals might have had more than one adverse event.

Table 5: Frequency of solicited adverse events by time since vaccination in children and adults

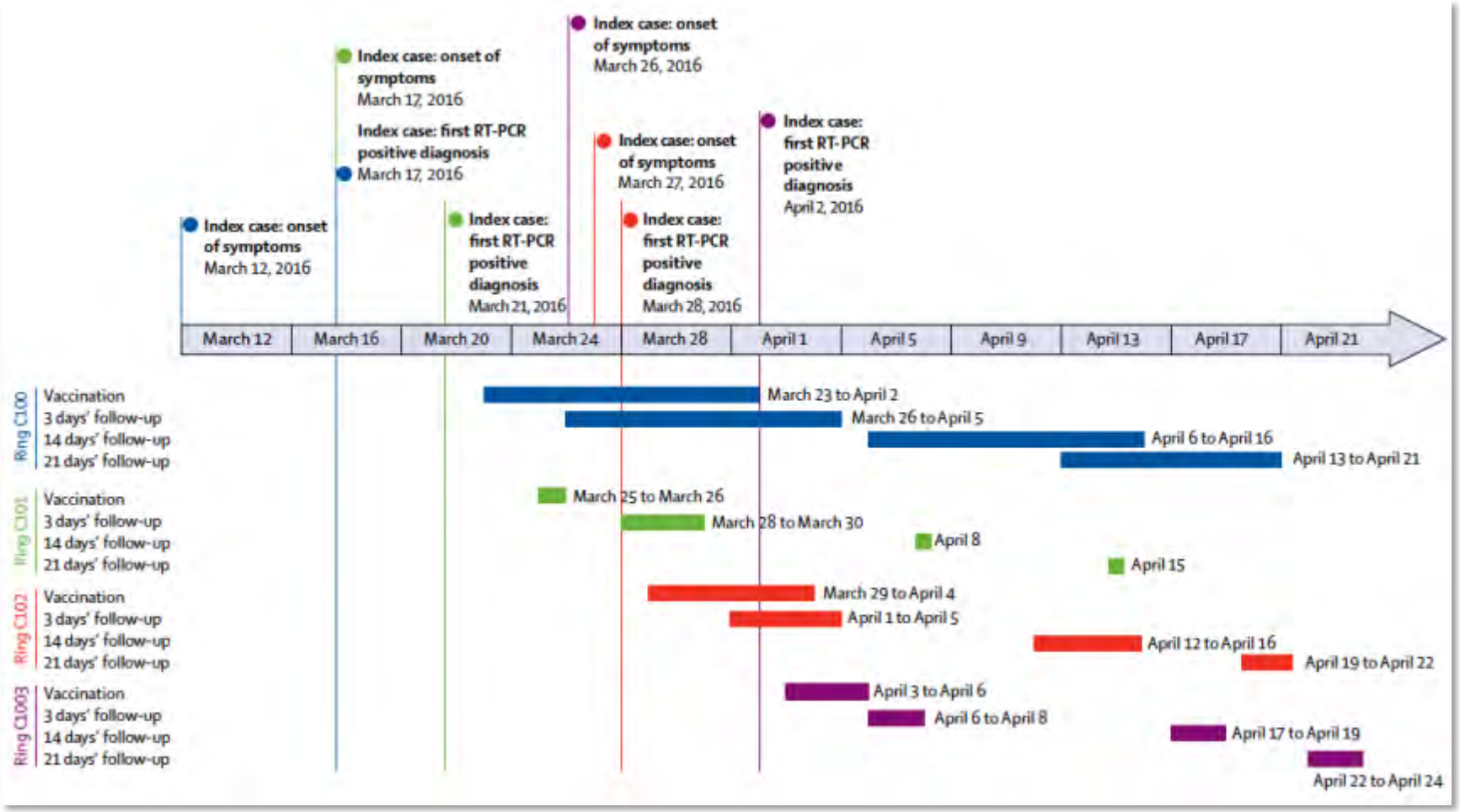
Henao-Restrepo AM Lancet 2017; 389: 505–18 http://dx.doi.org/10.1016/S0140-6736(16)32621-6

Vaccine-Induced Maculopapular and Vesicular Dermatitis



Agnandji ST N Engl J Med 2016;374:1647-60. DOI: 10.1056/NEJMoa1502924

Ring Vaccination with rVSV-ZEBOV under Expanded Access in Response to an Outbreak of EVD In Guinea, 2016: an Operational and Vaccine Safety Report

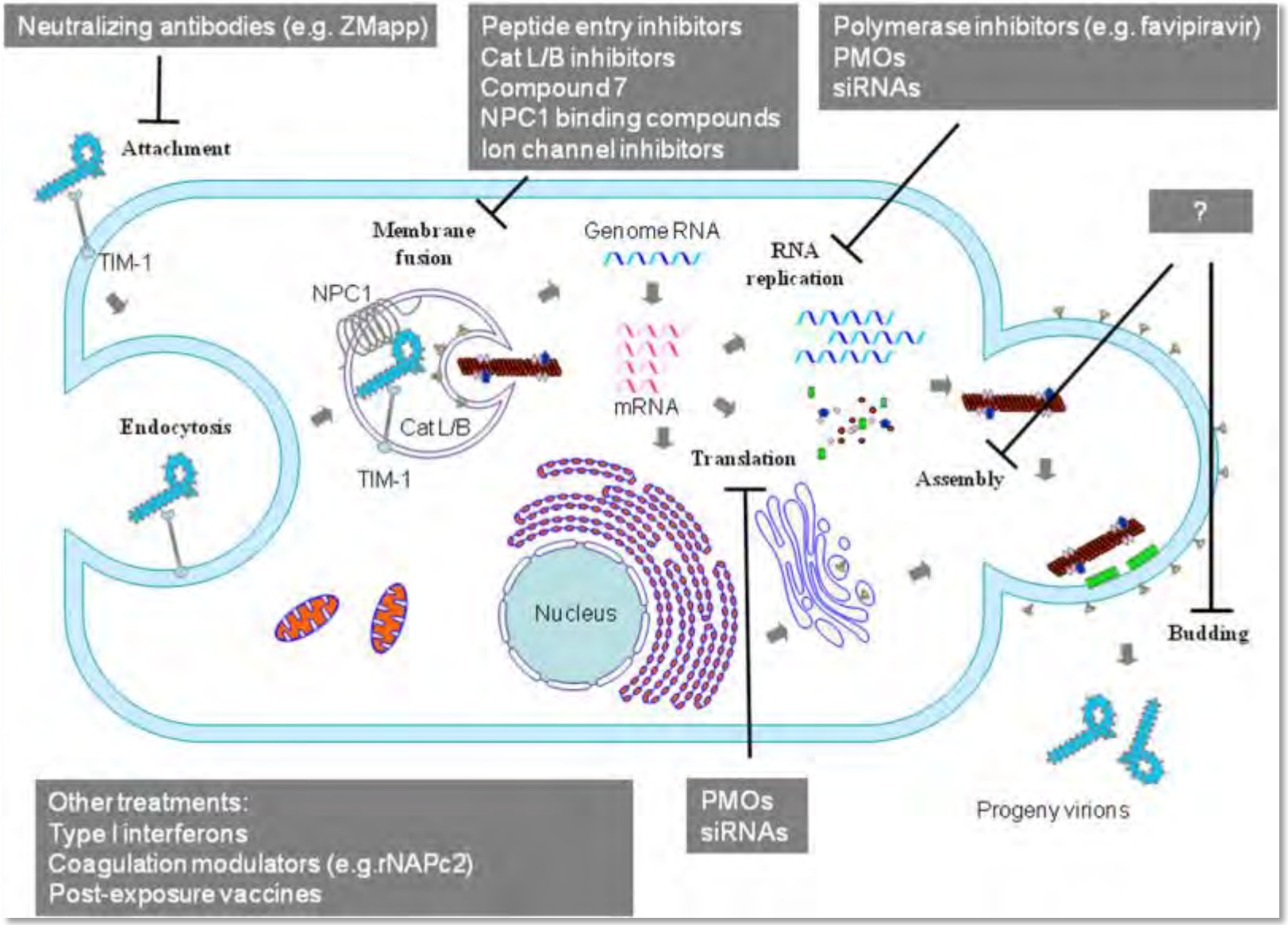


Timeline of operations in the four rings in Guinea

	Overall (0–14 days)	
	Response rate	Frequency
Adults (≥18 years, n=1207)		
Arthralgia	93%	81 (7%)
Diarrhoea	93%	3 (<1%)
Fatigue	94%	119 (10%)
Fever	93%	1 (<1%)
Headache	94%	180 (16%)
Induration	93%	1 (<1%)
Injection pain	93%	38 (3%)
Muscle pain	94%	157 (14%)
Myalgia	94%	149 (13%)
Vomiting	93%	2 (<1%)
Other adverse events	93%	33 (3%)
Any adverse events*	94%	412 (36%)
Children (6–17 years, n=303)		
Arthralgia	93%	1 (<1%)
Diarrhoea	93%	2 (1%)
Fatigue	93%	3 (1%)
Fever	93%	0
Headache	93%	34 (12%)
Induration	93%	0
Injection pain	93%	0
Muscle pain	94%	10 (4%)
Myalgia	94%	9 (3%)
Vomiting	93%	0
Other adverse events	93%	4 (1%)
Any adverse events*	94%	47 (17%)

Gsell PS. Lancet Infect Dis 2017; 17: 1276–1284

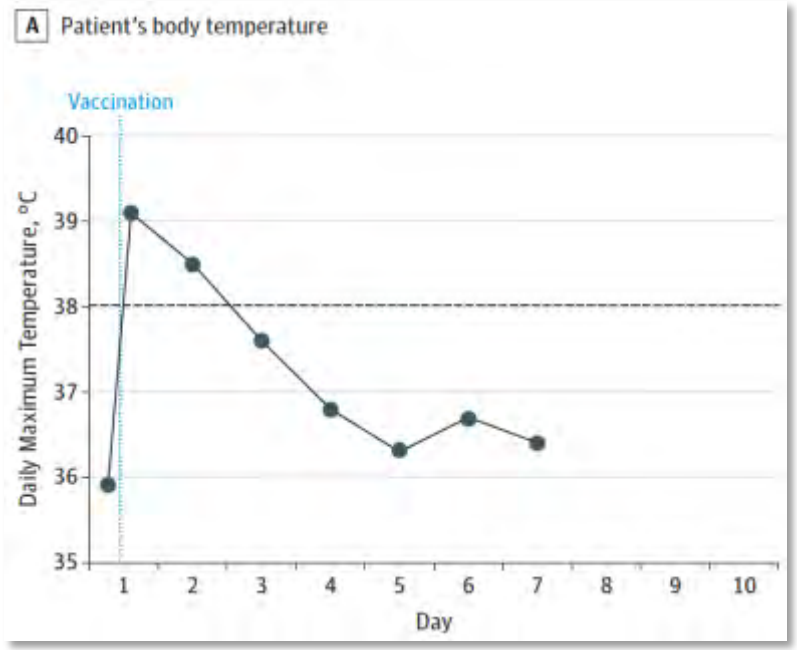
Cycle du Virus EBOLA, Cibles & Antiviraux

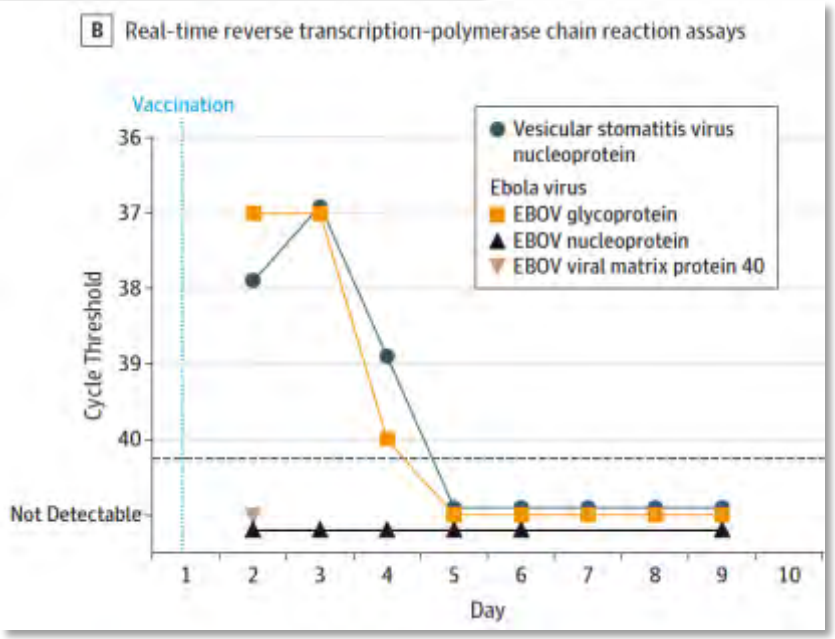


Li H Microbes and Infection 17 (2015) 109e117 http://dx.doi.org/10.1016/j.micinf.2014.11.012

Emergency Postexposure Vaccination With Vesicular Stomatitis Virus–Vectored Ebola Vaccine After Needlestick

- Soignant Sierra Leone, centre de traitement
- Accident d'exposition au sang piqûre accidentelle le 26/09/2014
- Évacuation sanitaire USA
- Vaccination le 28/09/2014 VSVΔG-ZEBOV (1 x 10^8 pfu)
- Syndrome fébrile modéré transitoire
- Virémie transitoire du rVSV
- Réponse Ac anti glycoprotéine ZEBOV
- Réponse cellulaire T





Lai L JAMA. 2015;313(12):1249-1255. doi:10.1001/jama.2015.19

Advantages and Disadvantages of Different Sources of Ab Against EVD

Characteristic/Feature	Convalescent Whole Blood	Convalescent Plasma	Hyperimmune Globulins[a]	Recombinant Monoclonal Antibodies
Availability	Survivors in affected countries can act as source	Survivors in affected countries can act as source	Currently not available, requires high amounts of CP or production in animals	Limited; potential for more efficient production methods
Accessibility in affected low-income countries	Produced within and by the affected countries	Produced within and by the affected countries	Not clear how it will be marketed and how prioritization will be decided	Not clear how it will be marketed and how prioritization will be decided
Collection/production	1 donation/3–4 mo (10 mL/kg)	1 donation/2 wk (10 mL/kg)	One production plant in Africa	US (1) and Chinese (1) company
Storage	>1 mo (2°C–6°C)	3 y (–30°C)	2–3 y (4°C)	Long-term (–20°C)
Administration	IV (4 h)	IV (20–40 min)	IV (variable, usually <1 hour) or IM	IV (6–12 h) or subcutaneous
Potential side effects	+++(+)[b]	+(+)[b]	+[b]	+++(?)[b]
Risk with ABO incompatibility	++++[b]	+[b]	NA	NA
Costs/affordability	+[b]	++[b]	+++[b]	++++[b]
Acceptability in EVD context	Well-known procedure Current data suggest reasonable donor acceptability	New procedure; Current data suggest reasonable donor acceptability	Presumably good	Presumably good
Activity against circulating virus	CWB produced during outbreak likely effective	CP produced during outbreak likely effective	Activity to be shown against viruses causing new outbreaks	Activity to be shown against viruses causing new outbreaks
Production time	Short (<1 d) once donors identified	Short (days) once donors identified	Months	Months

Abbreviations: CP, convalescent plasma; CWB, convalescent whole blood; EVD, Ebola virus disease; IM, intramuscular; IV, intravenous; NA, not applicable.

[a] Most efforts currently focused on human sources of antibodies, but animal production is under exploration as well.

[b] +: Very low; ++: Low; +++: Moderate; +++(+): Moderate to high; ++++: High; (?): Substantial uncertainty given limited clinical experience.

Van Griesven J Clin Infect Dis 2016;62(1):69–74 DOI: 10.1093/cid/civ680

Post-Exposure Prophylaxis against Ebola Virus Disease with Experimental Antiviral Agents: a Case-Series of Health-Care Workers

- Janvier à mars 2015
- 8 soignants
- Centre de traitement en Sierra Leone
- Victimes AEV
- 4 piqures accidentelles
- Évacuation de Royal Free Hospital
- PEC selon le niveau d'exposition

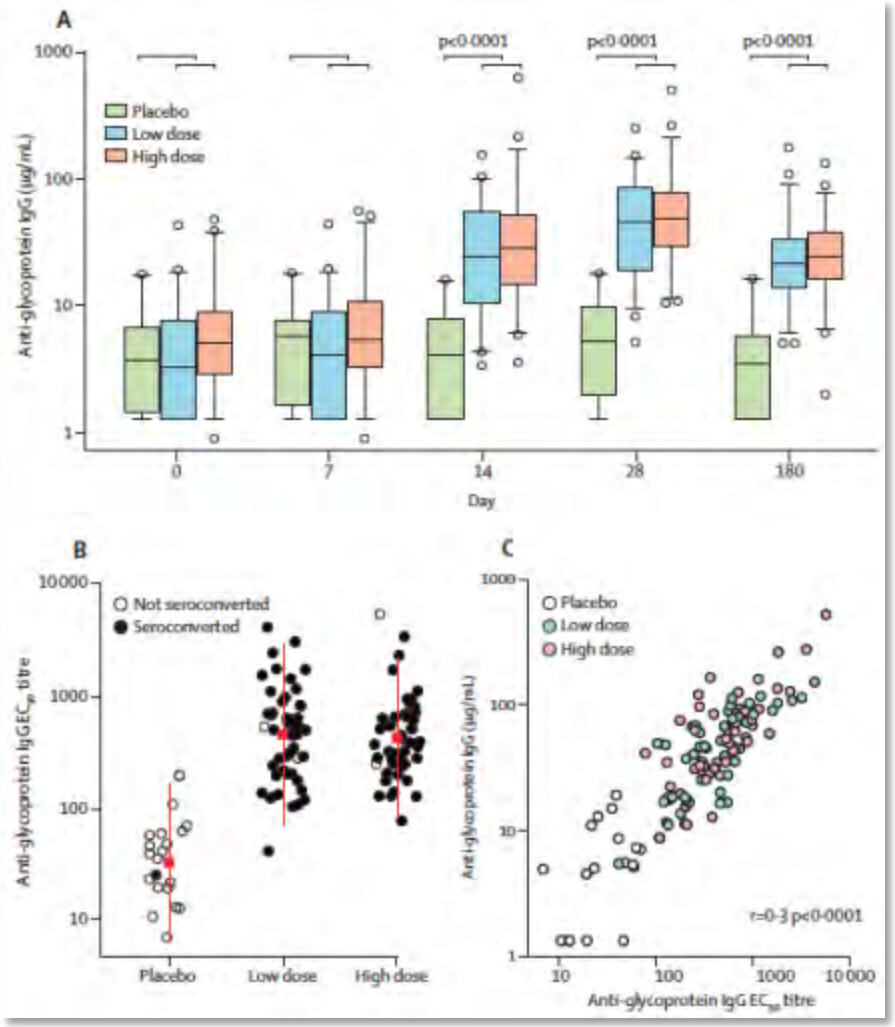
	Role	Date of potential exposure	Type of potential exposure to Ebola virus	Risk categorisation	Management
Case 1	Nurse	Jan 29, 2015	Penetrating injury through gloves from hollow-bore needle freshly used to draw blood from a patient with Ebola virus disease	Maximum	Favipiravir for 10 days, started 10 h after exposure (loading doses of 2400 mg, 2400 mg, and 1200 mg every 8 h on treatment day 1, followed by a maintenance dose of 1200 mg twice a day, orally) ZMAb on day 2 after exposure (total dose 50 mg/kg, intravenously) MIL77 on day 5 after exposure (total dose 50 mg/kg, intravenously)
Case 2	Nurse	Jan 31, 2015	Penetrating injury through potentially but not visibly contaminated gloves from hollow-bore needle on floor of Ebola-treatment unit red zone; not known when or what needle had been used for	Intermediate	Favipiravir for 10 days, started 6 h after exposure (loading doses 2400 mg, 2400 mg, and 1200 mg every 8 h on treatment day 1, followed by a maintenance dose of 1200 mg twice a day, orally)
Case 3	Doctor	Feb 14, 2015	Eye splash while removing personal protective equipment after working in the red zone of the Ebola-treatment unit; no known or visible contamination of personal protective equipment with body fluids, personal protective equipment had been chlorine sprayed	Low	Watchful waiting
Case 4	Nurse	Feb 18, 2015	Trip and fall in suspect zone of Ebola-treatment unit, resulting in tear to personal protective equipment and bleeding skin graze; no known or visible contamination of personal protective equipment or environment	Low	Watchful waiting
Case 5	Doctor	Feb 23, 2015	Penetrating injury through gloves from peripheral intravenous catheter insertion needle freshly used in patient with Ebola virus disease	Maximum	Favipiravir for 10 days, started 6 h after exposure (loading doses 2400 mg, 2400 mg, and 1200 mg every 8 h on treatment day 1, followed by a maintenance dose of 1200 mg twice a day, orally) MIL77 on days 2 and 5 after exposure (total 50 mg/kg per dose, intravenously)
Case 6	Doctor	March 9, 2015	Clinically assessed a patient with early Ebola virus disease before confirmed diagnosis without personal protective equipment; skin contact only, no body fluid exposure	Low	Watchful waiting
Case 7	Doctor	March 10, 2015	Obtained nasopharyngeal swab from a patient with early Ebola virus disease before confirmed diagnosis without mucosal protection; no body fluid exposure	Low	Watchful waiting
Case 8	Doctor	March 12, 2015	Penetrating injury from unused peripheral intravenous catheter insertion needle in red zone of Ebola-treatment unit through potentially but not visibly contaminated gloves	Intermediate	Favipiravir for 10 days, started 7 h after exposure (loading doses 2400 mg, 2400 mg, and 1200 mg every 8 h on treatment day 1, followed by a maintenance dose of 1200 mg twice a day, orally)

Red zone=area where laboratory-confirmed cases of Ebola virus disease are managed.

Table: Summary information about eight consecutive health-care workers medically evacuated to the Royal Free Hospital, London, UK following potential exposure to Ebola virus

Jacobs M Lancet Infect Dis 2015;15: 1300–04 http://dx.doi.org/10.1016/S1473-3099(15)00228-5

Safety and immunogenicity of a chimpanzee adenovirus-vectored Ebola vaccine in healthy adults: a randomised, double-blind, placebo-controlled, dose-finding, phase 1/2a study

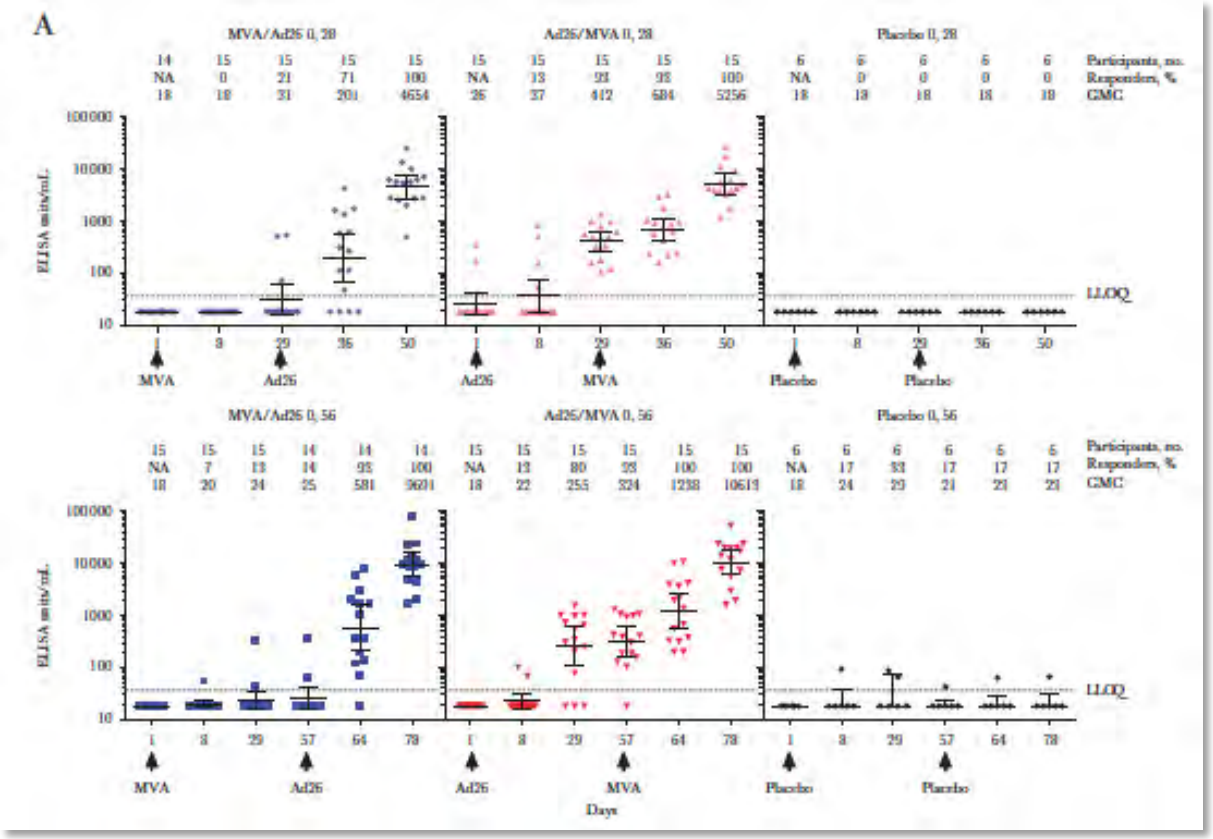


Antibody responses to the Ebola Zaire glycoprotein

The Journal of Infectious Diseases

MAJOR ARTICLE

Safety and Immunogenicity of a 2-Dose Heterologous Vaccination Regimen With Ad26.ZEBOV and MVA-BN-Filo Ebola Vaccines: 12-Month Data From a Phase 1 Randomized Clinical Trial in Uganda and Tanzania



Anti–Ebola virus glycoprotein immunoglobulin G binding Ab responses