Managing false-positive Ebola PCR test results in the post-outbreak era: experience in the EBOVAC vaccine trial in rural Sierra Leone

Frank Baiden*[1,2], David Ishola[1,2], Brett Lowe[3], Brian Kohn[1,2], Tuda Otieno[1,2], Thomas Mooney[2], Kenneth Awuondo[1,2], Augustin Fombah[1,4], Daniela Manno[2], Kwabena Owusu-Kyei[1,2], Muhammed Afolabi[1,2], Mohammed Samai[1,4], Bailah Leigh[1,4], Brian Greenwood[2], Deborah Watson-Jones[2,5]

1 EBOVAC-Salone Project. Kambia, Kambia District, Sierra Leone . 2 London School of Hygiene and Tropical Medicine, London, United Kingdom .3 KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya. 4 College of Medicine and Allied Health Sciences, Freetown, Sierra Leone. 5 Mwanza Intervention Trials Unit, Mwanza, Tanzania.

Facts & Figures

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Contributions	
IMI funding:	58 292 722 €
EFPIA in kind:	33 745 758 €
Other:	1 €
Total Cost:	92 038 481 €

Challenge

• Sierra Leone experienced a severe Ebola outbreak between 2014 & 2016

•. The country was declared EBOLA-free on 17 March 2016. The threat of resurgence of Ebola virus disease (EVD) remains a source of anxiety to health workers, communities and political authorities. Achieving an effective vaccine against Ebola has become a major global challenge

Approach & Methodology

- A phase 2/3 expanded safety and immunogenicity trial of the Ad26.ZEBOV/MVA-BN-Filo prime-boost Ebola vaccine developed and produced by Janssen has been underway in Kambia District in Northern Sierra Leone since Sept 2015.
- The trial enrolls only healthy participants who do not have a history of EVD. Serum samples are shipped for immunogenicity analysis in laboratories in Europe and USA. Laboratory-specific regulations require samples to be tested for Ebola prior to shipment to the US.
- PCR tests for EVD are performed in the Kambia trial laboratory using the Cepheid GeneXpert®Dx system for the detection of Ebola RNA in whole venous blood. **4553** tests have been performed up to March 2018. Three were positive in our lab and then that all were retested and the original result considered false-positive results i.e. Specificity – 99.9%.
- The impact of these positive tests is shown in Table 1

Results

Characteristic	1st episode	2nd episode	3rd episode
Date of event	09 Nov. 2017	21 Feb. 2018	23 Mar. 2018
Participant demographics	7yr, male, Healthy	13yr, male, Healthy	26yr, male, Healthy
Cycle threshold for PCR positivity (GP)	43.7	30.6	43.1
Actions taken			
Recall participant for repeat blood draw	No	No	No
Re-test sample onsite	No	No	Yes
Re-test sample in reference laboratory	Yes	Yes	No
Lab shut down and decontamination	Yes (7 days)	Yes (3 days)	No
Intensified monitoring of community news rumour	Yes	Yes	Yes
Inform trial participant	No	No	No

Table 1. Episodes and impact to false-positive Ebola virus tests

Value of IMI collaboration: How challenges were overcome

- The first 2 results were very disruptive to trial activities, necessitating laboratory shutdown and decontamination, locating a laboratory to re-test the samples etc (Table 1)
- We adapted Standard Operating Procedures for the 3rd result that were more pragmatic and we iintensified monitoring of community news & rumours. Community liaison staff actively monitored concerns and rumours
- *Effective networks*: Quick turnaround for 2nd tests (<4days) in National Reference Labs. This is critical and we relied on networks established in advance of event
- *Transparency with stakeholders: (Weekly team and sponsor meetings):* We briefed national and district MoH stakeholders in the first and second positive PCR episodes. Pros and cons of continuing Ebola testing was openly discussed with sponsors.
- The IMI Collaboration has taught us how best to work with communities in such situations

Impact & take home message

- False-positive EVD results present unique challenges in Ebola trials.
- Balancing duty-to-alert and risk of causing unwarranted fear and panic with a positive PCR result is a particular challenge and systems and networks need to be in place to handle this.
- Community trust, laboratory networks and close stakeholder engagement are very valuable during such events.

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* Author of correspondence : frank.baiden@lshtm.ac.uk

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