CORRESPONDENCE

Changes from the pre-specified primary outcome in the ring vaccination trial of an rVSV-vectored vaccine for Ebola

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Dear Editor

We read with interest the ring vaccination trial of an rVSV-vectored vaccine for Ebola virus disease.[1] This trial represents a fantastic effort in a very short space of time, in challenging circumstances. The World Health Organization sponsored the trial, offering the opportunity to demonstrate best practices in the design, conduct and reporting of trials.[2]

The authors published their study protocol in the British Medical Journal in July 2015.[3] In Figure 2 of that report, the primary analysis for vaccine efficacy was described as a comparison of outcomes in the individuals randomized to immediate vaccination compared to the individuals randomized to delayed vaccination. According to intention-to-treat principles, all randomized individuals should be included.

In the preliminary report in the Lancet, the primary analysis differed from this pre-specified plan. Specifically, the pre-specified plan for the primary analysis would have been a comparison of the 4123 individuals randomized to immediate vaccination with the 3528 individuals randomized to delayed vaccination (the fourth column in Table 2 of the Lancet paper[1]), whereas the preliminary report described the primary analysis as a comparison of 2014 individuals who actually received immediate vaccination with 2380 who were eligible for delayed vaccination regardless of whether or not they received it. The pre-specified primary analysis was not statistically significant with a p-value of 0.3351, while the new primary analysis appeared to be statistically significant with a p-value of 0.0036 although actually this did not meet the O'Brien Fleming threshold for the interim analysis of $p<0.0027$.[4]

REFERENCES

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