Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial.

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Summary

Background

A recombinant, replication-competent vesicular stomatitis virus-based vaccine expressing a surface glycoprotein of Zaire Ebolavirus (rVSV-ZEBOV) is a promising Ebola vaccine candidate. We report the results of an interim analysis of a trial of rVSV-ZEBOV in Guinea, west Africa.

Methods
For this open-label, cluster-randomised ring vaccination trial, suspected cases of Ebola virus disease in Basse-Guinée (Guinea, west Africa) were independently ascertained by Ebola response teams as part of a national surveillance system. After laboratory confirmation of a new case, clusters of all contacts and contacts of contacts were defined and randomly allocated 1:1 to immediate vaccination or delayed (21 days later) vaccination with rVSV-ZEBOV (one dose of $2 \times 10^7$ plaque-forming units, administered intramuscularly in the deltoid muscle). Adults (age ≥18 years) who were not pregnant or breastfeeding were eligible for vaccination. Block randomisation was used, with randomly varying blocks, stratified by location (urban vs rural) and size of rings (≤20 vs >20 individuals). The study is open label and masking of participants and field teams to the time of vaccination is not possible, but Ebola response teams and laboratory workers were unaware of allocation to immediate or delayed vaccination. Taking into account the incubation period of the virus of about 10 days, the prespecified primary outcome was laboratory-confirmed Ebola virus disease with onset of symptoms at least 10 days after randomisation. The primary analysis was per protocol and compared the incidence of Ebola virus disease in eligible and vaccinated individuals in immediate vaccination clusters with the incidence in eligible individuals in delayed vaccination clusters. This trial is registered with the Pan African Clinical Trials Registry, number PACTR201503001057193.

Findings

Between April 1, 2015, and July 20, 2015, 90 clusters, with a total population of 7651 people were included in the planned interim analysis. 48 of these clusters (4123 people) were randomly assigned to immediate vaccination with rVSV-ZEBOV, and 42 clusters (3528 people) were randomly assigned to delayed vaccination with rVSV-ZEBOV. In the immediate vaccination group, there were no cases of Ebola virus disease with symptom onset at least 10 days after randomisation, whereas in the delayed vaccination group there were 16 cases of Ebola virus disease from seven clusters, showing a vaccine efficacy of 100% (95% CI 74–100; p=0.0036). No new cases of Ebola virus disease were diagnosed in vaccinees from the immediate or delayed groups from 6 days post-vaccination. At the cluster level, with the inclusion of all eligible adults, vaccine effectiveness was 75% (95% CI 71 to 80; p=0.1791), and 76% (95% CI 71 to 81; p=0.3351) with the inclusion of everyone (eligible or not eligible for vaccination). 43 serious adverse events were reported; one serious adverse event was judged to be causally related to vaccination (a febrile episode in a vaccinated participant, which resolved without sequelae). Assessment of serious adverse events is ongoing.
Interpretation

The results of this interim analysis indicate that rVSV-ZEBOV might be highly efficacious and safe in preventing Ebola virus disease, and is most likely effective at the population level when delivered during an Ebola virus disease outbreak via a ring vaccination strategy.

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