

Fractional dose yellow fever vaccines for outbreak response

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Background

Yellow fever (YF) vaccine supply for outbreak response is limited. In 2016, large urban YF outbreaks occurring concurrently in different parts of Africa and the risk of further spread led WHO to develop recommendations for use of fractional dose vaccination as a dose-sparing strategy. We are conducting a trial in Mbarara, Uganda and Kilifi, Kenya, to assess the applicability of fractional dose of all four WHO-prequalified YF vaccines and the performance of fractional dose in young children and populations with HIV.

Methods

This is a double blinded, randomized, non-inferiority trial. Fractional dose was defined as 1/5th of a standard dose. Unvaccinated adults were randomly assigned to vaccine manufacturer and dosage (standard or 1/5th) and seen 10 days, 28 days and 1 year post-vaccination for immunogenicity and safety assessment. The primary objective is non-inferiority in seroconversion, with a 10% margin, of a fractional dose compared to standard dose for each pre-qualified vaccine at 28 days post-vaccination, measured by PRNT50. Sub-studies on children and HIV+ adults are ongoing with one vaccine.

Results

A total of 1029 adult participants were screened and 960 vaccinated (240 per manufacturer and 120 per dose). Overall, 55.1% of participants were female and mean age at enrollment was 35.7 years.

At baseline, 5.1% participants were positive for yellow fever by PRNT50. Baseline characteristics were not significantly different between standard and fractional dose groups for each manufacturer. At 28 days post-vaccination 99.4% participants seroconverted. The maximum difference between fractional and standard dose group was -6.1%.

Conclusions

Fractional dose of YF vaccine meets non-inferiority criteria for all pre-qualified manufacturers 28 days after vaccination. There were no safety concerns of the reduced dose. Results are pending to evaluate the rapidity of protection (10 days follow-up) and the persistence of antibodies at 1 year post-vaccination.

The stockpile of yellow fever vaccines has been shown to be insufficient to respond to large outbreaks. Fractional doses could be used in emergency situations when there are insufficient standard doses to protect the population at risk.