Immunogenicity of fractional dose Yellow Fever vaccine in children and HIV+ adults

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Background

Current supply shortages constrain vaccination activities and particularly outbreak response. We showed that fractional doses of all 4 WHO-prequalified yellow fever vaccines were non-inferior to the standard dose in inducing seroconversion 28 days after vaccination in an adult population with no major safety concerns. Following this, we assessed the immunogenicity and safety of fractional doses compared with standard doses of the WHO-prequalified Chumakov Institute of Poliomyelitis and Viral Encephalitides yellow fever vaccine in children and HIV positive adults.

Methods

The children sub-study was conducted at Epicentre Mbarara, Uganda and the HIV sub-study was conducted at KEMRI, Kilifi, Kenya. Children aged 9 months - 5 years or HIV positive adults without contraindications for vaccination were randomly assigned to standard or fractional dose ($1/5^{th}$) at each site. Investigators, participants, and laboratory personnel were blinded to group allocation. Participants were followed up at day 10, day 28 and 1 year post-vaccination. The primary outcome was non-inferiority in seroconversion (-10% margin) 28 days post-vaccination measured by $PRNT_{50}$.

Findings

A total of 433 children and 303 HIV+ adults were assessed and 420 and 250 recruited respectively and randomized to standard dose or to fractional dose. At 28 days post-vaccination, >95% of participants in each study group seroconverted and fractional doses met the non-inferiority criterion. The absolute difference in seroconversion in the per-protocol population between fractional and standard dose groups was -2.42 (95%CI: -4.82, 0.7) in children and -2.56 (95%CI: -6.92 to 1.79) in HIV+ adults. There was no observed difference in occurrence of adverse events and serious adverse events in both arms.

Conclusion

The fractional dose met the non-inferiority criterion in children 9 months – 5 years and non-immunocompromised HIV+ adults. These results will support extending the current WHO recommendation for fractional dosing in the event of a shortage for children and HIV+ adults.

Although YF vaccine is highly effective, the current supply shortages constrain vaccination activities, and particularly outbreak response. These results will support extending the current WHO recommendation for fractional dosing in the event of a shortage for children and HIV+ adults.