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Chikungunya Vaccine Trial: Exploring the Results

Dr. Birnholz:
Welcome to Audio Abstracts on ReachMD. This episode is sponsored by Valneva. I'm Dr. Matt Birnholz and today, I'm going overview an article, titled Safety and immunogenicity of a single-shot live attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase three trial, which was published by The Lancet in 2023.

Chikungunya is a mosquito-transmitted viral disease that threatens global health with potential life-altering consequences. It's regarded as one of the viruses most likely to spread globally due to unpredictable outbreaks, which can be exacerbated by global travel and the spread of potential vectors. Symptoms can include a high fever, severe joint pain, recurring mild joint pain, viremia, maculopapular rash, and disabling polyarthritis.

More than five million chikungunya infections have been reported in the last 15 years, with cases identified in over 100 countries. But, no vaccine or treatment against the chikungunya virus is available despite an increasingly globalized world. This makes developing prophylactic strategies against chikungunya critical to prevent further spread of this virus and curb infection.

In this study, the authors presented results from a phase three clinical trial of a live attenuated, single-dose vaccine candidate against the chikungunya virus, called VLA1553. The vaccine was attenuated from the La Reunion strain of east central South African genotype, and it was designed to provide broad coverage against chikungunya viral strains. The trial tested the safety and immunogenicity of VLA1553 for active immunization and disease prevention against the chikungunya virus across 43 professional vaccine trial sites in the U.S.

Within this three-to-one randomized, double-blind study, a total of 4,115 healthy adults received the intramuscular VLA1553 vaccine or a placebo. Participants were excluded if they had:

- a history of chikungunya virus infection,
- immune-mediated or chronic arthritis or arthralgia,
- known or suspected immune system defect,
- or if they had received any inactivated or activated vaccine within two or four weeks, respectively, before the trial.

Safety was assessed in all participants who received the vaccine or placebo, but, the immunogenicity analysis was performed on a preselected subset of the first 501 participants.

In terms of methods, immunogenicity was measured using a micro plaque reduction neutralization test. Seroprotection was defined as chikungunya virus neutralization antibody levels that result in a 50 percent plaque reduction at a titer of at least 150. The primary immunogenicity endpoint was described as the percentage of participants who initially had no seroprotection at baseline and subsequently developed seroprotection four weeks post-vaccination. The secondary endpoint similarly measured neutralization antibody titers in baseline negative participants at one and four weeks, and three and six months after vaccination. Additionally, the seroconversion rate was measured in participants who were baseline negative at the start of the trial, as well as in those who started with some immunity and exhibited at least a four-fold increase in target antibody titer from their baseline.

After accounting for participant exclusion or discontinuation, 362 participants remained in the per-protocol immunogenicity analysis at four weeks after trial vaccination. For the primary endpoint, results showed that 28 days after the remaining 266 participants received the VLA1553 vaccine, almost 99 percent demonstrated neutralizing antibody levels predictive of protection against the chikungunya virus. And no significant difference in seroprotection was seen between participants aged 18 to 64 versus those aged 65 years and above.

Also, six months after vaccination, a single dose of VLA1553 still induced a protective neutralizing antibody response to the chikungunya virus in about 96 percent of the immunogenicity analysis participants. Seroconversion also remained high at around 98 percent with a mean antibody titer 107-fold above baseline at the six-month mark. As the authors mentioned, antibody persistence is important for a prophylactic approach against chikungunya infection due to the sporadic and unpredictable epidemiology of the disease.

As for safety, VLA1553 was considered generally safe and well-tolerated. Adverse events potentially related to the vaccine were reported in 51.1 and 31.2 percent of the VLA1553 and placebo trial arms, respectively. Serious adverse events occurred in 1.5 percent of participants in the VLA1553 group verses eight percent of those who received the placebo. Among these, two serious adverse events were thought to be due to the candidate vaccine, including a syndrome of inappropriate antidiuretic hormone secretion and mild myalgia. Both resulted in full recovery.

Overall, the safety and immunogenicity data reported after a single shot of live-attenuated VLA1553 in this phase three trial show promise against the chikungunya virus for at least six months. The authors claim this candidate vaccine could be used prophylactically against chikungunya infection for residents of regions where the disease is endemic or at risk of outbreak, as well as people planning to travel to such places. Of note, the strong immune response observed in older patients becomes relevant given age is a risk factor for severity and mortality in chikungunya infection. In addition, the utilization of a single-dose vaccine can potentially increase immunization compliance without the need for boosters.

However, the authors acknowledge that a live attenuated vaccine presents challenges with severely immunocompromised individuals and pregnant women. Future research also needs to include data on vaccine efficacy and safety in children, as well as people with pre-existing immunity against the chikungunya virus in endemic regions. But, an ongoing five-year long-term assessment of VLA1553 vaccine protection against the chikungunya virus offers hope in these regards.

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