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Chikungunya Virus Control: Is a Vaccine on the Horizon?

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Vector-borne diseases such as malaria and dengue are among the most prevalent and significant infectious diseases on a global scale. For example, the World Health Organization has estimated that 40% of the world's population is at risk of dengue infection and up to 100 million infections may occur annually. In the United States alone, West Nile virus and Lyme disease are prominent examples of vector-borne diseases with over 5,600 and 31,000 human cases estimated, respectively, in 2012.[1, 2] Now, another arthropod-borne virus, chikungunya virus, which has caused over 2.5 million infections worldwide over the past decade, has been found spreading throughout the Americas and has just recently been reported in the United States.[3] Ideally, for both public health and economic reasons, there would be options available for control of these agents before they caused large outbreaks. For chikungunya, on the single island of La Reunion, approximately 300,000 cases were reported during the course of the outbreak with an estimated economic impact of $43.9 million euros (in 2006 values).[4, 5] Studies have demonstrated that the cost of a delayed response to the introduction of a novel arboviral disease could be as much as 346 times as high as the cost of preparedness through surveillance for the outbreak event.[6] Additional preparedness efforts, including the availability of effective and safe vaccines, could further reduce the scope and impact of an eventual outbreak.

A single chikungunya virus vaccine candidate was developed in the US prior to the large outbreaks that started in 2004 in coastal Kenya. Phase 2 clinical trials were conducted on the live-attenuated vaccine candidate before further development was discontinued due to lack of funding and questions regarding the eventual use of the vaccine.[7, 8] However, with the continued expansion of the chikungunya epidemic, Lee-Jah Chang and Vaccine Research Center (VRC) colleagues at the NIH have reinvigorated chikungunya virus vaccine development with the completion of a Phase 1 clinical trial on the VRC virus-like particle (VLP) vaccine candidate, VRC-CHKVLP059-00-VP. The dose-escalation, open-label clinical trial included 25 participants to evaluate the safety, tolerability, and immunogenicity of the candidate vaccine. This VLP vaccine, which had previously been shown to protect non-human primates against virus infection,[9] was shown in a study in this issue of The Lancet, to elicit antibody development in all participants. Significantly, the authors demonstrated that the neutralizing antibodies persisted for at least 6 months in all subjects in all dose groups which indicates the vaccine could provide long-term protection against the virus.

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The development of a VLP vaccine is a novel approach in vaccine technology; one that should result in a safer option than with many more traditional approaches such as killed vaccines or live-attenuated candidates. A VLP contains the outer structural proteins of the virus – the ones that would typically be seen by the immune system. The important safety feature of this approach is that none of the viral genetic material is present so no live virus could ever be generated. The lack of any live virus also provides a manufacturing advantage as no high-containment facilities would be needed for production. The safety profile of the VRC VLP was evaluated in this study in the test subjects with no serious adverse events reported and tenderness at the injection site being the only localized symptom (present in 9 of 25 participants). Mild systemic reactions including headache, malaise, myalgia, and nausea were reported in 10 of the subjects. Overall, the safety data reported suggest the vaccine would indeed be well-tolerated.

In addition to the safety profile shown, the authors also demonstrated increasing levels of antibodies after booster doses. The study design included three doses of vaccine administered at weeks 0, 4, and 20. All subjects were antibody positive after the second dose with the antibody levels reaching a peak after the third dose. While multiple doses can be a challenge in developing countries, alternate formulations of the VLP might increase the immunogenicity. For example, the inclusion of an adjuvant may lead to equally high levels of antibody in fewer doses. Importantly, the levels of antibodies detected in these subjects after just the initial dose appear to be similar to those found in patients who had recovered from wild type infections. Another important aspect of the study was the inclusion of multiple genotypes, or variants, in the antibody analysis. The study showed that the VLP vaccine generated antibodies against these distinct variants suggesting the vaccine would be effective against any strain of the virus, including the type circulating in the Americas.

While this VLP vaccine candidate exhibits a range of properties suggesting that it would be a good vaccine option, there is always concern over whether a vaccine for a vector-borne virus would be licensed. Development of vaccines for “orphan” agents is certainly a challenging endeavor as the market may not be great enough to justify the investment. The cost of development of a vaccine beginning with preclinical studies to vaccine registration is estimated to be $200-500 million (US dollars).[10] Yet even with this tremendous funding requirement, vaccines are still the most cost-effective strategy for disease prevention.[11] In spite of the limitations, there is optimism for vaccine development with the findings that a vaccine for another vector-borne disease, dengue, could be made available at an affordable price[12] and that policymakers in the affected countries expressed interest in the public sector use of a dengue vaccine.[13] Given the known burden of chikungunya outbreaks which have impacted up to 63% of local populations in a matter of months,[14] the continued development of this VLP vaccine candidate, along with other vaccine options, should be encouraged.

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