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ABSTRACT BOOK

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(y) were recruited from randomly selected households in study clusters. Each participant completed an interview and provided a blood specimen, which was tested by anti-ZIKV IgM MAC-ELISA assay and anti-CHIKV IgG ELISA assay. We assessed individual, household, and community factors associated with a positive result for CHIKV or ZIKV after adjusting for confounders. Preliminary results are presented. During 2018-2019, 3,422 participants were enrolled; 59% were female and median age was 30y (IQR: 18-42). Among 3,176 participants tested for ZIKV, 462 (15%) had evidence of recent infection. Infection risk increased with older age, from 7% among 1-10y olds up to 18% among 41-50y olds (OR 3.1; 95% CI 1.9-5.1). Males had an increased risk of Zika infection compared with females (OR 1.4; 95% CI 1.1- 1.7). Participants with home screens (OR 0.6; 95% CI 0.5-0.8) and air conditioning (OR 0.6; 95% CI 0.6-0.9) were at lower risk for ZIKV infection compared to those without. ZIKV infection also decreased with higher income and later recruitment dates. Among 1,542 participants tested for CHIKV, 491 (32%) had evidence of previous infection. CHIKV infection did not differ by age or sex. Lower CHIKV infection was associated with home screens (OR 0.5; 95% CI 0.3-0.6) and air conditioning (OR 0.5; 95% CI 0.4-0.6). CHIKV infection also varied by study cluster of residence, employment status, and insurance type. Different infection patterns were observed for recent ZIKV infection and previous CHIKV infection by age, sex, time of specimen collection, and study cluster. However, the presence of screens and air conditioners in the home decreased infection risk from both viruses by as much as 50%.

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SAFETY AND IMMUNOGENICITY OF A REPLICATION DEFICIENT SIMIAN ADENOVIRAL VECTORED CHIKUNGUNYA VACCINE: A PHASE I, FIRST-IN-HUMAN, DOSE ESCALATION TRIAL

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Chikungunya virus (CHIKV) is an alphavirus, transmitted by *Aedes* mosquitoes. The disease consists of an acute illness characterized by fever, rash, myalgia and generally symmetrical, peripheral, and often incapacitating polyarthralgia and/or polyarthritis, which lasts weeks to months. The most cost-effective means of controlling the spread of CHIKV is by vaccination. There is currently no licensed vaccine against CHIKV and although there are several candidates in pre-clinical development, only a few have entered clinical trials. Replication deficient vectors, as opposed to recombinant replication competent live attenuated viruses, avoid the risks of disseminated disease in immunocompromised hosts while maintaining the advantages of native antigen presentation, elicitation of T cell immunity and the ability to express multiple antigens. We developed a chimpanzee adenoviral vector expressing the structural polyprotein cassette of CHIKV (ChAdOx1 Chik) and conducted a Phase I, first-in-human, clinical trial. Twenty-four participants received a single intramuscular injection at 3 escalating doses in Oxford, UK. The trial is now fully recruited and is expected to be completed within 6 months. Preliminary data shows that ChAdOx1 Chik was well tolerated at all doses with no serious adverse events related to the vaccine reported to date. All local and systemic adverse events were self-limiting and short-lived, although higher reactogenicity has been observed at the top dose. A single unadjuvanted dose of ChAdOx1 Chik was immunogenic, eliciting high neutralising antibody titres and an increase in antibody levels was seen at D28 and D56 post vaccination compared to D0 in all groups. Responses against the structural CHIKV antigens show significant increases in IFN-γ levels, peaking at D14 post vaccination and there were no significant differences in ELISpot responses between dosage groups. The safety, cellular and humoral immunogenicity results up to 6 months post vaccination will be presented at the meeting. The results of this trial support a subsequent Phase Ib clinical trial of ChAdOx1 Chik in an endemic region.

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ROBUST IMMUNOGENICITY OF 1- AND 2-DOSE SERIES OF AN ADJUVANTED VLP-BASED CHIKUNGUNYA VACCINE

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Rapid and durable protection against Chikungunya is highly desired, but currently no licensed vaccine exists. An unadjuvanted Chikungunya virus-like particle (CHKV-VLP) candidate vaccine has previously demonstrated a good safety profile and robust immunogenicity in phase 1 and 2 trials in both CHKV-naive and CHKV-exposed adults. Here we report interim results of a phase 2 trial of alum-adjuvanted CHKV-VLP. Healthy US adults 18 to 45 years of age (n=415) were given a 1- or 2-dose series at doses of 6 to 40 mcg over a 2- or 4-week period. Serum neutralizing antibody (SNA) was assessed by a luciferase-based assay and 80% neutralization titers (NT80s) were calculated. All regimens were well-tolerated, with mostly mild or moderate injection site pain in 21% to 49% of subjects, and no vaccine-related severe (Grade 3 or higher) or serious adverse events or discontinuations. Seroconversion occurred in 74% to 98% of subjects by 7 days after 1 dose, and in all subjects by 28 days after the last dose (the primary endpoint). Peak NT80s were similar to those seen after natural CHKV infection. The immune response was persistent, with mean NT80s of 196 to 457 through 6 months. Long-term follow-up is ongoing. These findings strongly support the potential utility and continued development of an alum-adjuvanted VLP-based vaccine for the prevention of CHKV infection, including future studies in a wider age range.

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CHIKUNGUNYA: PHASE 1 CLINICAL DEVELOPMENT OF A SINGLE-SHOT LIVE-ATTENUATED VACCINE

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VLA1553 is a live-attenuated Chikungunya virus (CHIKV) vaccine candidate designed for active immunization of the general population living in endemic regions, as well as serving as a prophylactic measure for travelers to endemic areas or areas at risk for an upcoming outbreak. The replicating CHIKV vaccine comprises a deletion of 60 amino acids in the nsP3 gene encoding the non-structural replicase complex protein leading to attenuation of the virus *in vivo*. VLA1553 is based on the La Reunion strain of the East Central South African genotype, is produced in Vero cells and purified by centrifugation, ultrafiltration, batch-chromatography and sucrose gradient centrifugation. In preclinical models of CHIKV disease (mice and non-human primates) the vaccine candidate demonstrated to be highly attenuated as evidenced by the absence of clinical manifestations typically associated with wild-type CHIKV infections in addition to strongly reduced viremia and inflammatory cytokine levels. Moreover, VLA1553 was highly immunogenic, induced a strong and long-lasting as well as protective neutralizing antibody response against a high dose wild-type CHIKV challenge. A blinded, randomized phase 1 clinical study investigating the safety and immunogenicity of three dose levels administered intramuscularly as a single-shot immunization designed to elicit long-term immunological memory is currently ongoing (NCT: NCT03382964). Initial blinded data across all dose groups up to Day 28 after a single immunization showed an excellent immunogenicity profile with 100% seroconversion rates (proportion of subjects achieving a CHIKV-specific neutralizing antibody titer of NT50≥20) and a high GMT of 648. The safety profile is acceptable supporting further development: no serious adverse events or adverse events of special interest occurred