Indian Academy of Pediatrics (IAP)

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Newer **R**esearch and recommendations **I**n **C**hild **H**ealth

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UNDER THE AUSPICES OF THE IAP ACTION PLAN 2023

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Dear fellow IAPans,

nRICH

Newer **R**esearch and recommendations **I**n **C**hild **H**ealth-aims to bring you the abstracts of some of the breakthrough developments in pediatrics, carefully selected from reputed journals published worldwide.

Expert commentaries will evaluate the importance and relevance of the article and discuss its application in Indian settings. nRICH will cover all the different subspecialities of pediatrics from neonatology, gastroenterology, hematology, adolescent medicine, allergy and immunology, to urology, neurology,vaccinology etc. Each issue will begin with a concise abstract and will represent the main points and ideas found in the originals. It will then be followed by the thoughtful and erudite commentary of Indian experts from various subspecialties who will give an insight on way to read and analyze these articles.

I'm sure students, practitioners and all those interested in knowing about the latest research and recommendations in child health will be immensely benefitted by this endeavor which will be published online on every Monday.

Happy reading!

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Safety And Immunogenicity Of A Single-shot Live-attenuated Chikungunya Vaccine: A Double-blind, Multicentre, Randomised, Placebo-controlled, Phase 3 Trial

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BASED ON ARTICLE

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SUMMARY

Background: VLA1553 is a live-attenuated vaccine candidate for active immunisation and prevention of disease caused by chikungunya virus. Safety and immunogenicity data up to day 180 after vaccination with VLA1553 is presented in this paper.

Methods: This double-blind, multicentre, randomised, phase 3 trial was done in 43 professional vaccine trial sites in the USA. Eligible participants were healthy volunteers aged 18 years and older. Patients were excluded if they had history of chikungunya virus infection or immune-mediated or chronic arthritis or arthralgia, known or suspected defect of the immune system, any inactivated vaccine received within 2 weeks before vaccination with VLA1553, or any live vaccine received within 4 weeks before vaccination with VLA1553. Participants were randomised (3:1) to receive VLA1553 or placebo. The primary endpoint was the proportion of baseline negative participants with a seroprotective chikungunya virus antibody level defined as 50% plaque reduction in a micro plaque reduction neutralisation test (μPRNT) with a $\mu PRNT_{50}$ titre of at least 150, 28 days after vaccination. The safety analysis included all individuals who received vaccination. Immunogenicity analyses were done in a subset of participants at 12 pre-selected study sites. These participants were required to have no major protocol deviations to be included in the per-protocol population for immunogenicity analyses.

Findings: Between Sept 17, 2020 and April 10, 2021, 6100 people were screened for eligibility. 1972 people were excluded and 4128 participants were enrolled and randomised (3093 to VLA1553 and 1035 to placebo). 358 participants in the VLA1553 group and 133 participants in the placebo group discontinued before trial end. The per-protocol population for immunogenicity analysis comprised 362 participants (266 in the VLA1553 group and 96 in the placebo group). After a single vaccination, VLA1553 induced seroprotective chikungunya virus neutralising antibody levels in 263 (98·9%) of 266 participants in the VLA1553 group (95% CI 96·7–99·8; p<0·0001) 28 days post-vaccination, independent of age. VLA1553 was generally safe with an adverse event profile similar to other licensed vaccines and equally well tolerated in younger and older adults. Serious adverse events were

reported in 46 (1·5%) of 3082 participants exposed to VLA1553 and eight (0·8%) of 1033 participants in the placebo arm. Only two serious adverse events were considered related to VLA1553 treatment (one mild myalgia and one syndrome of inappropriate antidiuretic hormone secretion). Both participants recovered fully.

Interpretation: The strong immune response and the generation of seroprotective titres in almost all vaccinated participants suggests that VLA1553 is an excellent candidate for the prevention of disease caused by chikungunya virus.

Comment: Chikungunya is a viral infection caused by chikungunya virus which belongs to the family Togaviridae, genus alphavirus. Chikungunya virus has a single stranded, positive sense RNA genome. The virus particles are enveloped icosahedral capsid with diameter of 60-70nm.

Chikungunya virus is transmitted to human being by bite of an infected mosquito mainly Ades aegyptus and Ades albopictus. Human are the primary host of the chikungunya virus during epidemic period. Mosquitoes become infected when they feed on an infected person. Blood borne transmission of chikungunya virus is reported in laboratory personnel and health care personnel while drawing the blood sample from an infected person or handling the infected blood sample. In-utero transmission is rare but can occur during 2nd trimester and intrapartum transmission has been reported if mother is infected with viremia.

Chukungunya symptoms begin 3-7 days after the infected mosquito bite. Most common symptoms are fever, joint pains, headache, rash. Death due to chikungunya is rare but can lead to persist rheumatological problems. Chikungunya is diagnosed by detecting viral nucleic acid from plasma or blood or by virus specific IgM neutralising antibodies. There is no specific treatment. Symptomatic treatment with paracetamol, rest and fluids

The above study is a double blind randomised multicentre safety and immunogenicity study. A live attenuated vaccine VLA1553 was used as single intramuscular injection in the deltoid muscle on day one. The study met its primary endpoint. 28-day post-vaccination, VLA1553 induced seroprotective levels of antibodies in 98·9% of participants, and high seroprotection rates were sustained up to 180 days after vaccination, with GMT indicating high immunogenicity in adults of all age groups. The generation of protective titres in virtually all vaccinated participants independent of age positions VLA1553 as an excellent candidate for protection against chikungunya.

As there is no specific treatment or vaccine available against chikungunya virusbinduces debilitating disease, and its various symptoms, or long-term sequelae. This live-attenuated vaccine is intended to be used for active immunisation to protect against chikungunya for the people above the age of 18 years. As age is a risk factor for severity and mortality after chikungunya virus infection, the strong immune response and favourable safety profile observed in older adults could be of relevance. Safety profile is comparable to the existing vaccines. Being live attenuated vaccine it cannot be advised to immunocompromised individuals and pregnant women

Though the vaccine is not licenced yet but it can be promising vaccine for prevention of chikungunya.

REFERENCES

1. http//www.cdc.gov. chikungunya
2. http//www.who.int/news-room/fact-sheets/details/ chikungunya
3. http//www.paho.org /en/topic/chikungunya
4. https:/ncvbdc.mohfw.gov.in/index4