

ZIKAVAC: a first-in-person trial of a novel vaccine to prevent Zika virus disease

Submission date 04/05/2022	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 13/07/2022	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 04/12/2024	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Zika virus is a mosquito-transmitted virus with some cases causing serious damage to the unborn child of a mother that is infected in the first 3 months of pregnancy. More rarely, Zika virus can cause problems with nerves, called Guillain Barré syndrome, or inflammation of the brain, called encephalitis. There are currently no treatments for any of the illnesses, which can cause lasting brain damage. Therefore researchers want to develop a vaccine to prevent these illnesses from occurring. MVAZIKB001 is a new vaccine that has not yet been tested in people but has in animals to show that it can create an immune response against the Zika virus. The aim of this study is to test the safety of the vaccine and to determine the right dose that can be given safely.

Who can participate?

Healthy volunteers aged 18 to 59 years

What does the study involve?

The study is designed to be undertaken in two seamless stages including Stage 1, a dose-escalation study to assess the safety of the vaccine, followed by Stage 2, which is the dose-expansion stage to evaluate vaccine activity. Participants will receive two vaccinations in total at the Liverpool Clinical Research Facility based within the Liverpool University Hospitals Royal Site. Blood and urine samples will be taken to confirm eligibility before receiving the study vaccine. On dosing days, volunteers will be required to remain on the unit for 1-hour post-dose administration for observation and will then be discharged from the facility. There will be nine outpatient appointments lasting a duration of 56 days.

What are the possible benefits and risks of participating?

Because the vaccine has not been tested in people before, there is a small chance that there will be side effects that we cannot predict. Zika vaccines made using different technology to this one have been tested before without any serious side effects. One effect of Zika virus infection could be due to the immune response to the virus. This is a form of temporary nerve damage called Guillain Barré syndrome. This is very unlikely to occur with this vaccine and has not occurred with any other Zika vaccine. However, it does remain a remote possibility. The side effects are the same as those for any other vaccination against infectious diseases. The most common are due to local inflammation at the injection site(s), such as redness, swelling, mild

pain or itching. Very occasionally a small blister may form. In a few cases participants may also experience mild flu-like symptoms such as fever or feeling unwell, aches and pains, or headache for a day or two. As with any new drug that is being tested for the first time in humans there could be some unknown side effects. Risks are mitigated by the clinical team observing the patient after administration and physicians confirming the patient is fit for discharge. The nursing team administering the vaccine are trained and experienced in vaccine administration. Patients will be required to give blood samples at specified timepoints. The possible risks associated with blood drawing are pain, bleeding, fainting, bruising, infection and/or hematoma (blood clot under the skin) at the injection site.

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
April 2022 to December 2024

Who is funding the study?
Innovate UK

Who is the main contact?
Prof. Neil French
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Scientific

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Additional identifiers

EudraCT/CTIS number

2021-005868-21

IRAS number

1005626

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

UoL001695, IRAS 1005626

Study information

Scientific Title

A first-in-person trial of a modified Vaccina Ankara vectored anti-Zika vaccine MVAZIKB administered on two occasions 28 days apart at dose levels of 5×10^7 and 1×10^8 plaque-forming units in healthy adults

Acronym

MVAZIKB001

Study objectives

1. The primary objective is to confirm the safety of escalating doses of MVAZIKAB (5×10^7 to 5×10^8 pfu) in healthy 18-59-year-old healthy adults.
2. To assess the immunogenicity of escalating doses (5×10^7 to 5×10^8 pfu) of MVAZIKAB in healthy 18-49-year-old healthy adults
3. To measure antibody concentrations by their ability to inhibit the growth of the virus in the labs
4. To measure how the immune cells in the body respond to the virus

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approval pending, Central Manchester REC then North West 7 REC - GM Central, ref: 22/NW/0154

Study design

Interventional non-randomized study

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Hospital

Study type(s)

Prevention

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Zika virus

Interventions

The IMP is a vaccine administered intramuscularly in clinic. Participants will receive two doses of the IMP. The trial will begin with 5×10^7 pfu. Following satisfactory safety reporting and Independent Data and Safety Monitoring Board authorisation the dose will be increased to 1×10^8 pfu to complete the trial.

Intervention Type

Biological/Vaccine

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

MVAZIKB

Primary outcome measure

Occurrence of serious adverse events (SAEs) relating to the IMP recorded using reported adverse events from source data up to Day 56

Secondary outcome measures

1. The safety, tolerability and reactogenicity of MVAZIKB at up to 1×10^8 pfu, measured using blood draws at baseline, days 3, 7, 14 and 28 post each dose of vaccine
2. Solicited systemic AEs post-vaccination, recorded using reported adverse events from source data from 0-7 days
3. Unsolicited systemic AEs by vaccine dose, recorded using reported adverse events from source data from 0-56 days
4. Laboratory measures at baseline, days 3, 7, 14 and 28 post each dose of vaccine, including:
 - 4.1. Spot-forming cells per million over the lower level of quantitation in antigen-stimulated versus negative control wells at 2 and 4 weeks post vaccine doses, measured by interferon-gamma ELISpot
 - 4.2. Number and % of participants with interferon-gamma ELISpot responses above the cut off for a positive assay in antigen-stimulated versus negative control wells at 2 and 4 weeks post vaccine doses
 - 4.3. Neutralising antibody titre, expressed as reciprocal titre to neutralise 50% of infectious virus quantified by 50% tissue culture infectious dose
5. Adverse events of special interest (ascending polyneuropathy) recorded using reported adverse events from source data from 0-7 days
6. Immunogenicity of escalating doses (5×10^7 to 1×10^8 pfu) of MVAZIKAB in healthy 18-49-year-old adults measured using T cell ELISPOT and neutralising antibody to envelope and non-

structural proteins by ELISpot assay at baseline, days 1, 7, 14, 28, 56

7. Neutralising capacity of antibody measured using plaque reduction neutralisation assay at baseline, days 28 and 56

8. T cell-directed response to envelope and non-structural proteins measured using ELISpot assay at baseline, days 1, 7, 14, 28, 56

Overall study start date

29/04/2022

Completion date

31/07/2025

Eligibility

Key inclusion criteria

Patients eligible for the trial must comply with all of the following at screening. Inclusion criteria as per protocol provided in brackets:

1. A male or female adult between 18 and 59 years of age at consent
4. No planned re-location or foreign travel during the study period
7. If female, negative pregnancy test at the point of screening and dosing
8. If female, prepared to use an efficacious method of contraception during the study from screening and until 28 days after the last vaccine dose for women of childbearing potential

Participant type(s)

Healthy volunteer

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

18

Key exclusion criteria

Any patient meeting any of the criteria listed below at baseline will be excluded from study participation. Exclusion criteria as per protocol provided in brackets:

1. Use of any investigational or non-registered drug within 5 half-lives of the drug, or 30 days preceding administration of study vaccine, whichever is longer
3. Receipt of any biologic agents with mechanisms of action that might affect the immune system, at the discretion of the CI and local PI
4. Administration of immunosuppressants or other immune-modifying drugs within a period of six months before vaccination or at any time during the study period; participants who have received these agents may also be excluded at the discretion of the CI and local PI.
5. Any confirmed or suspected immunosuppressive or immunodeficient condition.
6. A family history of congenital or hereditary immunodeficiency.

7. Any antiviral drug therapy within a period of 5 drug half-lives or 30 days before vaccination, whichever is longer,
8. History of significant allergic reactions likely to be exacerbated by any component of the study vaccine, especially allergic disease or reactions to any previous dose of any vaccine.
9. Any history of anaphylaxis
10. Residence of >6 continuous weeks or 3 months in total in any country where Zika or dengue virus infection is plausible or likely.
11. History of proven or strongly suspected flavivirus infection.
12. Acute disease (for example acute infection) at the time of enrolment or vaccination, if symptoms are rated as anything more significant than a mild adverse event. Entry into the study and/or vaccination may be deferred until the illness has resolved for at least one week.
13. Acute or chronic, clinically significant in the opinion of the investigator, disease in any organ system, as determined by history, physical examination or laboratory testing.
14. Presence of any inflammatory condition that might require immunomodulatory therapy.
15. Recent blood donation (inclusion can be delayed under these circumstances; the participant should be enrolled 16 weeks after their last blood donation. Each participant should give no more than 470 ml per 16 weeks, so regular blood donation should be suspended during the study and can re-commence 1 month after the last study sample).
16. Prior receipt of a vaccinia based vaccine at any time
17. Administration of immunoglobulins or other blood products containing immunoglobulin within the three months preceding the planned administration of vaccine
18. Administration of any other vaccine (e.g. COVID vaccine) within 30 days of vaccination with MVAZIKZB. In this event, screening can be carried out, and dosing can be delayed until 30 days have elapsed.
19. Any autoimmune condition except mild dermatological problems including psoriasis, vitiligo, and mild eczema, asthma, hay fever.
20. History of allergic disease or reactions to vaccine or egg allergy.
21. Any history of angioedema
22. History of cancer
23. History of serious psychiatric condition likely to affect participation in the study.
24. Bleeding disorder or prior history of significant bleeding or bruising following intramuscular injection.
25. Extreme body mass index greater than 40KG per metre squared or less than 18 kilogrammes per metre squared
26. Suspected or known current alcohol abuse defined by greater than 42 units per week.
27. Suspected or known injecting drug use

Date of first enrolment

31/05/2022

Date of final enrolment

15/08/2022

Locations

Countries of recruitment

England

United Kingdom

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Sponsor type

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Funder(s)

Funder type

Government

Funder Name

Innovate UK

Alternative Name(s)

innovateuk

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

- 1. Peer-reviewed scientific journals
- 2. Internal report
- 3. Publication on website
- 4. Submission to regulatory authorities

Intention to publish date
31/12/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Neil French (N.French@liverpool.ac.uk). Access to raw data and the right to publish freely by all investigators in study or by the Independent Steering Committee on behalf of all investigators. Data will be made available by application via the University of Liverpool systems subject to a suitable data sharing agreement. Participants will be made aware of this when signing consent at the screening visit and all data shared will be anonymised.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No