ISRCTN13726895 https://doi.org/10.1186/ISRCTN13726895

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

Registration date
13/07/2022

Overall study status
Completed

Last Edited
04/12/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] 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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Clinical Trials Information System (CTIS)
2021-005868-21

Integrated Research Application System (IRAS)
1005626

Protocol serial number
UoL001695

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 5x10e7 and 1x10e8 plaque-forming units in healthy adults

Acronym
MVAZIKB001

Study objectives
1. The primary objective is to confirm the safety of escalating doses of MVAZIKAB (5x10(7) to 5x10(8)pfu) in healthy 18-59-year-old healthy adults.
2. To assess the immunogenicity of escalating doses (5x10(7) to 5x10(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

Primary study design
Interventional

Study design
Interventional non-randomized study

Study type(s)
Prevention

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 x 10e7 pfu. Following satisfactory safety reporting and Independent Data and Safety Monitoring Board authorisation the dose will be increased to 1 x 10e8 pfu to complete the trial.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
MVAZIKB

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

Key secondary outcome(s)
1. The safety, tolerability and reactogenicity of MVAZIKB at up to 1 x 10e8 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 x 10e7 to 1 x 10e8 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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

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 by 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
United Kingdom

England

Study participating centre
Royal Liverpool University Hospital
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Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
Technology Strategy Board

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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