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Clinical study to identify factors that affect the immune response to yellow fever and dengue vaccines

Submission date
06/07/2025

Recruitment status
Recruiting

Registration date
23/06/2026

Overall study status
Ongoing

Last Edited
23/06/2026

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Vector-borne orthoflaviviruses, including WNV, DENV, ZIKV, and YFV, represent a growing threat to global public health. Their spread in Europe has been facilitated by environmental and anthropogenic factors, with an increase in WNV cases and autochthonous outbreaks of DENV and ZIKV transmitted by Ae. albopictus. The European vaccine arsenal against orthoflaviviruses is limited, comprising inactivated vaccines for TBE and JE, the live attenuated YF17D vaccine, and the live recombinant QDENGA vaccine. Despite the demonstrated efficacy of YF17D and QDENGA, their immunogenic mechanisms remain unclear. The YELLOW4FLAVI consortium, funded by the Horizon Europe program, aims to elucidate the mechanisms of action of these vaccines and the immune response to orthoflaviviruses. The objective is to characterize the post-vaccination immune response, with particular attention to host factors that influence the response to YF17D and QDENGA vaccines. The study considers pre-exposure to genetically related orthoflaviviruses and the impact of concomitant vaccinations. The expected results could provide crucial insights for the development of personalized vaccines against orthoflaviviruses, optimizing immunological efficacy and practical implementation.

Who can participate?
Healthy volunteers aged between 18 and 60 years old

What does the study involve?
This is an in vitro study on biological samples, aimed at evaluating the immune response to YF17D (yellow fever) and QDENGA (dengue) vaccines in a healthy adult population in the Veneto Region. The primary objective is to determine the influence of pre-existing immunity against orthoflaviviruses on vaccine response, considering both the protective role and the risk of antibody-dependent enhancement (ADE) of infection. The study plans to enroll 200 subjects for each vaccination, to include at least 20 individuals with pre-existing immunity to West Nile virus (WNV) or Usutu virus (USUV). Subject recruitment (provision of information and collection of written informed consent) will take place at the Microbiology and Virology Unit of the Padua University Hospital. Data collection includes a detailed medical history and the collection of biological samples (blood, saliva, and urine) at the time of vaccination (T0), during follow-ups at

days 14 and 28 post-vaccination, and one year after vaccination. Analyses will include serological tests for IgM and IgG against various orthoflaviviruses, with confirmation by viral neutralization assays, evaluation of cell-mediated response, analysis of viral replication kinetics, and study of predictive biomarkers for adaptive immune response efficacy. Data management involves pseudonymized coding of subjects and anonymous treatment of data in flow. This study will provide crucial insights into the dynamics of the immune response to orthoflavivirus vaccines, considering the context of pre-existing immunity, with potential significant implications for the development of optimized and personalized vaccination strategies.

What are the possible benefits and risks of participating?
Participants may benefit from being closely monitored for any side effects of vaccination and receiving appropriate support and advice. Additionally, they can opt to receive free results of antibody dosage tests related to the vaccination. By participating, they will also contribute to improving the understanding of how vaccines work and the factors that influence the immune system's response, thus helping researchers develop better vaccines.

A possible risk associated with participation in the study concerns blood draws, which will be performed at the blood collection clinics of the UOC Microbiology and Virology by qualified personnel. This procedure, although simple, could cause some discomfort, such as pain or swelling at the site where the needle is inserted. However, no special protective measures are necessary beyond those already normally adopted for blood collection. It is important to emphasize that medical and nursing staff will follow all standard procedures to ensure the participant's safety and comfort during this phase of the study.

Where is the study run from?
This clinical study is coordinated by the Department of Molecular Medicine at the University of Padua (Promoting Center) in collaboration with the Microbiology and Virology Unit of the Padua University Hospital.

When is the study starting and how long is it expected to run for?
January 2024 to December 2028

Who is funding the study?
HORIZON EUROPE Framework Programme, European Union.

Who is the main contact?
The PI of the study and main contact is Prof. Luisa Barzon, luisa.barzon@unipd.it

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Study information

Scientific Title
Clinical study for the identification of factors influencing the immune response to yellow fever and dengue vaccines

Study objectives
The primary objective of this study is to assess whether previous immunity to orthoflaviviruses (acquired through natural infection or vaccination), such as West Nile Virus (WNV) and Usutu virus (USUV), influences the innate and adaptive immune response to YF17D and QDENGA vaccination

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 12/06/2025, Comitato Etico Territoriale Area Centro - Est Veneto (USTS CET-ACEV) (Azienda Ospedale Università di Padova, via Giustiniani 2, Padova, 35128, Italy; +39 049 8212342; ce.sperimentazione@aopd.veneto.it), ref: AOP 3778

Primary study design
Observational

Study design
Longitudinal observational study

Study type(s)
Prevention, Efficacy

Health condition(s) or problem(s) studied
Investigation of the immune response to the yellow fever and dengue vaccines in healthy volunteers with or without prior orthoflavivirus immunity

Interventions
This is an investigation of the immune response to the yellow fever (YF17D) and dengue (QDENGA) vaccines in healthy adult volunteers with or without prior orthoflavivirus immunity in the Veneto Region. Biological fluids (blood, saliva and urine) are collected from study subjects at baseline and during follow-up visits.

The study plans to enrol 200 subjects for each vaccination, to include at least 20 individuals with pre-existing immunity to West Nile virus (WNV) or Usutu virus (USUV). Subject recruitment (provision of information and collection of written informed consent) will take place at the Microbiology and Virology Unit of the Padua University Hospital. Data collection includes a detailed medical history and the collection of biological samples (blood, saliva, and urine) at the time of vaccination (T0), during follow-ups at days 14 and 28 post-vaccination, and one year after vaccination.

Analyses will include serological tests for IgM and IgG against various orthoflaviviruses, with confirmation by viral neutralization assays, evaluation of cell-mediated response, analysis of viral replication kinetics, and study of predictive biomarkers for adaptive immune response efficacy. Data management involves pseudonymized coding of subjects and anonymous treatment of data in the flow. This study will provide crucial insights into the dynamics of the immune response to orthoflavivirus vaccines, considering the context of pre-existing immunity, with potential significant implications for the development of optimized and personalized vaccination strategies.

Intervention Type
Other

Primary outcome(s)
YF17D-binding (IgM and IgG) and neutralizing antibody titres measured by enzyme immunoassay (EIA) and microneutralization assays; evaluation of cell-mediated response using flow-cytometry, analysis of viral replication kinetics using quantitative PCR (qPCR), and study of predictive biomarkers for adaptive immune response efficacy by cytokine profiling by multiplex assays on Luminex platform. Analyses will be performed at baseline and during follow-ups at days 14 and 28 post-vaccination, and one year after vaccination.

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Male or female individuals aged between 18 and 60 years
2. Healthy individuals, free from acute infections or chronic diseases
3. Willingness to provide written informed consent after being adequately informed about the risks and benefits of the study
4. Availability to participate in at least two study-scheduled visits

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Hypersensitivity to vaccine components (active ingredients or excipients) for YF17D and QDENGA vaccines, including egg/chicken proteins for YF17D.
2. Severe hypersensitivity reactions to previous yellow fever or dengue vaccines.
3. Immunodeficiency (congenital, idiopathic, or treatment-induced).
4. History of thymic dysfunction.
5. Symptomatic HIV infection or asymptomatic HIV with compromised immune response.
6. Moderate to severe illness or acute disease.
7. Pregnancy or breastfeeding.
8. Body temperature >38°C or acute illness on study entry day.
9. Autoimmune diseases or immunosuppressive therapy within 6 months.
10. Corticosteroid therapy >2 weeks in the past 3 months.
11. Known allergic or anaphylactic reactions.
12. Use of unregistered drugs or participation in other clinical trials.
13. Recent (<3 months) or planned administration of immunoglobulins or blood products.
14. Non-compliance with study objectives or protocol (investigator's opinion).
15. Anticipated absence from the study center during the study period.

Date of first enrolment
01/07/2025

Date of final enrolment
31/12/2028

Locations

Countries of recruitment
Italy

Study participating centre
Azienda Ospedale - Università Padova
Via Giustiniani 2
Padova
Italy
35128

Sponsor information

Organisation
University of Padua

ROR
https://ror.org/00240q980

Funder(s)

Funder type
Government

Funder Name
HORIZON EUROPE Framework Programme

Alternative Name(s)
Horizon Europe, Horizon Europe Programme, Framework Programme, Horizon Europe, EU Framework Programme, Horizon, Horizonte Europa

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Prof. Luisa Barzon, luisa.barzon@unipd.it. Anonymized individual participant data that underlie the results reported in publications (e.g., text, tables, figures, and appendices) will be available beginning 6 months and ending 24 months following article publication, as well as the study protocol. Consent from participants about data sharing was required and obtained.

IPD sharing plan summary
Available on request