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Efficacy and safety of the new recombinant subunit vaccine for varicella zoster virus in people living with HIV

Submission date
13/02/2024

Recruitment status
No longer recruiting

Registration date
05/03/2024

Overall study status
Ongoing

Last Edited
05/03/2024

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Herpes zoster (HZ) is a common result of Varicella-Zoster virus reactivation, occurring as a painful rash. Long-lasting neuropathic pain (post-herpetic neuralgia [PHN]) can persist after rash resolution in up to 20% of patients. As cell-mediated immunity is the main defence against herpes zoster, any condition associated with its impairment, including HIV infection, can lead to a higher risk of VZV reactivation. A live attenuated vaccine showed only modest effectiveness and could not be used in immunosuppressed patients.
A new vaccine (HZ/su) named Shingrix achieved outstanding results in preventing both HZ and PHN in diverse immunocompromised categories. To date data regarding HZ/su vaccine use in people living with HIV (PLWHIV) are very limited but still promising. This study will investigate the immunologic response and safety of the HZ/su vaccine in PLWHIV on effective antiretroviral treatment.

Who can participate?
People living with HIV (PLWHIV) aged 18 years and over who are virally suppressed on antiretroviral treatment

What does the study involve?
Participation in the study involves two additional blood samples before the first vaccine dose and 1 month after the second vaccine dose. Moreover, 1 week after both the first and the second dose patients will be given a questionnaire investigating their symptoms (via a phone call). Finally, a follow-up visit assessing possible further adverse events and/or Herpes Zoster episodes will be scheduled 6 months after the second vaccine dose.

What are the possible benefits and risks of participating?
The main benefit will be the understanding of Herpes Zoster recombinant subunit vaccine immunogenicity in people living with HIV. Blood sampling procedures can cause bleeding, bruises, and superficial vein thrombosis (blood clots).

Where is the study run from?
Policlinico Tor Vergata of Rome, Policlinico Umberto I of Rome and San Paolo Hospital of Milan (Italy)

When is the study starting and how long is it expected to run for?
April 2023 to December 2026

Who is funding the study?
1. Società Italiana di Malattie Infettive e Tropicali (SIMIT) (Italy)
2. GlaxoSmithKline (GSK) (UK)

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Additional identifiers

Protocol serial number
AIFA_RSO: 697

Study information

Scientific Title
Varicella zoster recombinant HZ/su vaccine: immunogenicity and safety in people living with HIV according to LTCD4 count strata

Acronym

HZ/su_PLWHIV

Study objectives
1. The HZ/su recombinant vaccine is immunogenic in people living with HIV (PLWHIV) eliciting both humoral and cell-mediated specific immunity with a high vaccine response rate (VRR) in the group of patients on-ART with high LTCD4 cell count, but poorer in those with lower LTCD4.
2. The HZ/su recombinant vaccine is safe and has an acceptable reactogenicity profile in PLWHIV in a real-life scenario, with a potential different grading according to LTCD4 count.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 26/05/2023, Comitato Etico indipendente Fondazione PTV Policlinico Tor Vergata (Viale Oxford 81, Rome, 00133, Italy; +39 (0)620900035; comitatoetico.lazioarea2@ptvonline.it), ref: 115.23

Primary study design
Observational

Study design
Multicentric observational prospective study

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Prevention of herpes zoster in people living with HIV

Interventions
The present study will investigate the immunologic response and safety of the HZ/su vaccine in PLWHIV on effective antiretroviral treatment, according to the immunological situation.

Three infectious disease centers in Italy will participate in the study, prospectively enrolling a total of 500 PLWHIV (250 with current CD4+ T-lymphocyte (LTCD4) counts <350 cell/mm3 and 250 with current LTCD4 ≥350 cells/mm3).

A two-dose schedule of Shingrix will be administered to adult PLWHIV (2 months apart), as recommended by national guidelines. Blood samples will be collected at baseline and 1 month after schedule completion.

The primary objective of the study is the evaluation of immunogenicity assessed in terms of vaccine response rates (VRR) as in pivotal trials, according to LTCD4 count strata. For humoral response, VRR is defined as a four-fold increase in anti-gE antibodies compared to baseline by ELISA. In a subgroup of 100 patients (50 for each LTCD4 stratum), cell-mediated immunity will be investigated at baseline (M0) and one month (+/- 14 days) after the second HZ/su vaccine dose (M2 +1).

Intervention Type
Biological/Vaccine

Phase
Not Applicable

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

Primary outcome(s)
HZ/su vaccine immunogenicity will be evaluated through the analysis of humoral immunity and vaccine response rate (VRR) in PLWHIV according to the current LTCD4 absolute count (cells /mm3). To this purpose, anti-glycoprotein E (gE) antibodies concentration will be assessed for the whole population at baseline (M0) and 1 month (± 14 days) after the second Hz/su vaccine dose (M2+1). Humoral vaccine response rate (VRR) is defined as a fourfold increase over baseline (prior to vaccination) anti-gE concentration (mUI/ml).

Key secondary outcome(s)
1. HZ/su reactogenicity and safety profile verified after each of the two scheduled doses in PLWHIV according to current LTCD4 absolute count (cells/mm3), using a semi-structured questionnaire investigating local and systemic symptoms, 1 week after both the first and the second dose. A follow-up visit assessing possible further adverse events and/or HZ episodes will be scheduled 6 months (±1 month) after HZ/su vaccine dose 2 (M2 +6).
2. HZ/su vaccine immunogenicity evaluated through analysis of cell-mediated immunity and vaccine response rate (VRR) in PLWHIV according to current LTCD4 absolute count (cells/mm3) In a subgroup of 100 patients (50 for each LTCD4 stratum), cell-mediated immunity will be investigated at baseline (M0) and 1 month (+/- 14 days) after the second HZ/su vaccine dose (M2 +1), using an intracellular cytokine staining (ICS) assay for Interferon-gamma, IL-2, TNF-alpha, and an IFN-gamma release assay (IGRA). Cell-mediated vaccine response rate (VRR) is defined as a twofold increase over baseline (prior to vaccination) of gE-specific polypositive LTCD4 (for ICS) and a twofold increase over baseline (prior to vaccination) of gE-specific IFN-gamma production (for IGRA).
3. HZ/su vaccine immunogenicity verified through analysis of humoral and cell-mediated immunity and vaccine response rate (VRR) in PLWHIV according to the current LTCD4/CD8 ratio. In a subgroup of 100 patients (50 for each LTCD4 stratum), cell-mediated immunity will be investigated at baseline (M0) and one month (+/- 14 days) after the second HZ/su vaccine dose (M2 +1), using an intracellular cytokine staining (ICS) assay for Interferon-gamma, IL-2, TNF-alpha, and an IFN-gamma release assay (IGRA). Cell-mediated vaccine response rate (VRR) is defined as a twofold increase over baseline (prior to vaccination) of gE-specific polypositive LTCD4 (for ICS) and a twofold increase over baseline (prior to vaccination) of gE-specific IFN-gamma production (for IGRA).

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. People living with HIV (PLWHIV) ≥18 years old, on antiretroviral treatment, virally suppressed (HIVRNA <50 copies/ml in the last 6 months)
2. Able to provide informed consent
3. Available CD4 cell count in the last 6 months

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Key exclusion criteria
1. Age <18 years old
2. Active herpes zoster episode at enrollment
3. Acute disease/fever at enrollment
4. Known allergy to vaccine component
5. Other than HIV immunosuppressive condition or treatment. Prednisone <20 mg/day, or equivalent, is allowed. Inhaled and topical steroids are allowed
6. Pregnancy
7. Lactation
8. Women planning to become pregnant or planning to discontinue contraceptive methods

Date of first enrolment
15/02/2024

Date of final enrolment
15/05/2026

Locations

Countries of recruitment
Italy

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Sponsor information

Organisation
University of Rome Tor Vergata

ROR
https://ror.org/02p77k626

Funder(s)

Funder type
Research organisation

Funder Name
Società Italiana di Malattie Infettive e Tropicali (SIMIT)

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			14/02/2024	No	No