Five-year boostability after single-visit single-dose intramuscular rabies pre-exposure prophylaxis.

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The aim of this study is to demonstrate that a single dose of rabies vaccine can induce an equally rapid and adequate anamnestic antibody response as 2-dose PrEP to revaccination five years later.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON51662

Source
ToetsingOnline

Brief title
SIRAVA

Condition

- Viral infectious disorders

Synonym
Rabies

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Bavarian Nordic A/S

Intervention

Keyword: rabies, vaccination

Outcome measures

Primary outcome

The primary endpoint is the rate of increase of geometric mean concentrations (GMC) of rabies virus neutralizing antibodies between day 1 and day 8 after revaccination.

Secondary outcome

Percentage of subjects with RVNA titer >0.5 IU/mL at D1, D57 or D64, Y1, Y2 and Y5 after primary vaccination.

Percentage of subjects with RVNA titers>0.5 IU/mL at D1, D8 and D15, after the simulated post-exposure vaccination.

Percentage of subjects with RVNA titers>3 IU/mL, and percentage of subjects with RVNA titers >5 IU/mL at day 8 after simulated PEP.

GMCs at D1, D57 or D64, Y1, Y2 and Y5 after primary vaccination, and at D1, D8 and D15 after the simulated post-exposure vaccination.

Study description

Background summary

The main purpose of prophylactic rabies pre-exposure immunization (PrEP) is to induce an effective and rapid anamnestic antibody response after revaccination that obviates the need for human rabies immunoglobulins (RIG) and simplifies post-exposure immunization (PEP) to just 2 doses of rabies vaccine (D1, D4) in case of high-risk bite wounds. Many travellers decline pre-travel PrEP because of costs and insufficient time between visit at the travel clinic and departure. If a single dose of rabies vaccine would be equally effective in inducing a rapid and adequate anamnestic antibody response, guidelines on

pre-travel PrEP could be simplified. In particular, the induction of long-term immunological memory might be an issue in the case of single-visit PrEP. To evaluate if single-visit PrEP is a reasonable alternative for one of the approved current standards, two-visit PrEP, we aim to study whether single-visit priming results in non-inferior long-term immunological memory, that is boostable by simulated post-exposure prophylaxis (PEP) after five years.

Study objective

The aim of this study is to demonstrate that a single dose of rabies vaccine can induce an equally rapid and adequate anamnestic antibody response as 2-dose PrEP to revaccination five years later.

Study design

Randomized controlled non-inferiority trial.

Intervention

Participants will be randomized between standard 2-dose intramuscular PrEP (D1, D8) or single-dose PrEP (standard intramuscular dose). After 5 years, all subjects receive a simulated 2-dose post-exposure intramuscular vaccination schedule (D1 and D4). Serum (all participants) and blood samples (50 participants) are collected after PrEP at D1, D57/D64 (depending on study group), year 1, year 2 and year 5; and at D1, D8 and D15 after simulated PEP vaccination. Some timepoints contain a margin in which it is acceptable that the study visit takes place. For D57/D64, this margin is -2 days and +7 days. For year 1, year 2 and year 5, this margin is -7 days and +7 days.

Study burden and risks

In total, 3 or 4 injections will be given with registered rabies vaccine Rabipur. A maximum of 238 mL of blood will be collected during 7 sampling moments. Depending on the study arm eight to nine visits are required for the study. Participants are asked to complete a diary for safety evaluation during the study, up to 7 days after each vaccination. The standard 2-dose PrEP (D1, D8) has been endorsed by the WHO. No risks are associated with participation in this study other than those of routine vaccination and minimal to moderate physical discomfort that can be experienced after vaccination or the collection of blood. Participants will receive financial compensation for their participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Age >=18 years and <=40 years
• Good health according to investigator
• Willingness and ability to adhere to the study regimen
• Able to provide informed consent
• Naïve to rabies exposure or vaccination
• Willing to comply to a follow-up of 5 years
• Unlikely to require rabies PrEP in next 5 years

Exclusion criteria

• History of previous rabies vaccination
• Suspected previous vaccination against rabies

• Known or suspected severe allergy against egg protein
• Known or suspected allergy against any of the other vaccine components
• History of unusual or severe reactions to any previous vaccination
• History of (pre)syncope associated with medical procedures involving needles
• Immunocompromized state due to illness or medication
• Administration of plasma or blood products three months prior to inclusion
• (hydroxy)chloroquine or mefloquine use
• History of any neurological disorder including epilepsy
• Pregnancy during study visits in which the participant is vaccinated
• Breastfeeding during and up to 4 weeks after study visits in which the participant is vaccinated
• Any current infectious disease other than seasonal cold
• Bleeding disorders or use of anticoagulants

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-11-2022
Enrollment:	240
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rabipur

Ethics review

Approved WMO Date:	09-11-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-12-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	07-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	24-09-2022
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	24-10-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22516
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2021-005564-21-NL
CCMO	NL79547.058.21
OMON	NL-OMON22516