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

Published: 25-10-2021
Last updated: 15-05-2024

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 3-dose PrEP to revaccination five years later.

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

Summary

ID

NL-OMON22516

Source
Nationaal Trial Register

Brief title
SIRAVA

Condition

- Viral infectious disorders

Health condition

Rabies

Research involving
Human

Sponsors and support

Primary sponsor: Leiden University Medical Center (LUMC), Department of

	Infectious Diseases
Secondary sponsors:	Bavarian Nordic
Source(s) of monetary or material Support:	Bavarian Nordic A/S

Intervention

Explanation

Outcome measures

Primary outcome

Rate of increase of GMC of RVNA between day 1 and day 8 after simulated PEP.

Secondary outcome

Percentage of subjects with RVNA titer >0.5 IU/mL at D1, D57 or D78, 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 D78, Y1, Y2 and Y5 after primary vaccination, and at D1, D8 and D15 after the simulated post-exposure vaccination.

Study description

Background summary

Rationale: 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, three-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. 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 3-dose PrEP to revaccination five years later. Study design: Randomized controlled non-inferiority trial. Study population: Healthy

adult volunteers. Intervention: Participants will be randomized between standard 3-dose intramuscular PrEP (D1, D8, D22) or single-dose PrEP (standard intramuscular dose). After 5 years, all subjects will 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/D78 (depending on study group), year 1, year 2 and year 5; and at D1, D8 and D15 after simulated PEP vaccination. Main study parameters/endpoints: The primary endpoint is the rate of increase of geometric mean concentrations (GMC) of neutralizing antibodies between day 1 and day 8 after revaccination. Nature and extent of the burden and risks associated with participation, benefit and group relatedness: In total, 3 or 5 injections will be given with a registered rabies vaccine. A maximum of 98 mL of blood will be collected during 7 sampling moments. Depending on the study arm eight to ten visits are required for the study. Participants are asked to complete a diary for safety evaluation during the study. The standard 3-dose PrEP (D1, D8, D22) 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.

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 3-dose PrEP to revaccination five years later.

Study design

D1 (baseline), D57 or D78, Y1, Y2, and Y5 D1 (day of first dose of simulated rabies PEP), Y5 D8 and Y5 D15.

Intervention

- Study group A – one single intramuscular dose (1 mL) of rabies vaccine (D1) - Study group B – standard three-dose (1 mL) intramuscular PrEP vaccination (D1, D8, D22)

Contacts

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Eligibility criteria

Age
Adults (18-64 years)
Adults (18-64 years)
Elderly (65 years and older)
Elderly (65 years and older)

Inclusion criteria

• Age ≥18 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 or breastfeeding • 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:	Recruitment stopped
Start date (anticipated):	10-01-2022
Enrollment:	200
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO

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

Study registrations

Followed up by the following (possibly more current) registration

ID: 51662
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL9827
CCMO	NL79547.058.21
OMON	NL-OMON51662

Study results