Single dose rabies PRE-exposure Priming induces a rapid and effective anamnestic Antibody REsponse

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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 six months later.

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

Summary

ID

NL-OMON45358

Source
ToetsingOnline

Brief title
PREPARE

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: zonmw

Intervention

Keyword: memory response, pre-exposure prophylaxis, rabies vaccine, rabies virus neutralizing antibodies

Outcome measures

Primary outcome

The primary endpoint is the rate of increase of geometric mean concentrations (GMC) of neutralizing antibodies between day 0 and day 7 after revaccination for the different study groups.

Secondary outcome

Risk perception, knowledge and health beliefs concerning animal bites, animal associated injuries and rabies

Attitudes towards rabies vaccination

Percentage of travellers with RVNA titer >0.5 IU/mL at day 0, 2 months, and six months after primary vaccination. Percentage of travellers with RVNA titers>0.5 IU/mL at day 3, after the simulated post-exposure vaccination. Percentage of travellers with RVNA titers>3 IU/mL, and percentage of travellers with RVNA titers >5 IU/mL at day 7 after simulated PEP.

Which cellular and humoral immune responses are associated with an adequate anamnestic response after simulated post-exposure vaccination?

1. Is there a difference in cellular and humoral immune responses induced by the two immunization regimes?

2. Is there a difference in kinetics of the immune response during immunization?

3. Is adaptive and innate immune activation/ modulation during immunization

related to a differential degree of antigen exposure during immunization and

booster response after simulated PEP?

Is there a set of biomarkers on transcriptional level that predicts an adequate

anamnestic response?

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 (D0, D3) in case of high risk bite wound.
Many travellers decline pre-travel 3-dose 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. Pre-travel rabies PrEP would come within reach of most travellers.

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 six months later.

Study design

randomized controlled non-inferiority study

Intervention

Travellers will be randomized between standard 2-dose PrEP (D0, D7), single dose PrEP (standard intramuscular dose or one-fifth fractional intradermal dose) or no PrEP before travel. After 6 months, all subjects receive a simulated 2-dose post-exposure vaccination schedule (D0 and D3). Serum samples are collected at 0, 2, and 6 months after PrEP, and at 0, 3, 7 and 21 days

after the simulated post-exposure vaccinations

Study burden and risks

In total, 3 to 4 injections will be given with a registered rabies vaccine. A maximum of 416 mL of blood will be collected during 8 sampling moments. Up to eight visits are required for the study. Participants are asked to complete a diary for safety evaluation during the study. Participants will be interviewed on risk perception and health beliefs concerning bite wounds and rabies. In the Netherlands intradermal administration of rabies vaccine is off-label use. However, intradermal administration is safe and effective. The intradermal route of administration is endorsed by the WHO for pre- and post-exposure rabies vaccination. 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. Participants will have documented adequate levels of rabies virus neutralizing antibodies (RVNA) after completing the study

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Travellers visiting the travel clinics of AMC, "Tropen Advies Centrum - Travel Clinic Harbour Hospital" and LUMC will be invited to participate in this study. In order to be eligible to participate in this study, a subject must meet all of the following criteria:
Age >=18 years
Travelling for less than 8 weeks
Expected time of departure >1 weeks
Good health according to investigator
Willingness and ability to adhere to the study regimen
Able to provide informed consent

Exclusion criteria

Previous vaccination against rabies vaccine
Requirement for standard rabies PrEP according to the national guidelines
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
Temporary exclusion criterion for vaccination: body temperature >= 38.5°C or acute illness will lead to postponement of participation and vaccination. Screening may continue when the temperature has normalized.

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):	17-05-2018
Enrollment:	368
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	rabipur

Ethics review

Approved WMO Date:	27-07-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2017
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-12-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-03-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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: 24881
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-000089-31-NL
CCMO	NL60550.056.17
OMON	NL-OMON24881