Q-VaxCelerate: Development of a T Cell-Based Vaccine for Q Fever

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Identification of T cell epitopes that will serve as the basis for a novel Q fever vaccine with fewer side effects. This will be done by determining ex vivo the effect of Cb-derived T cell epitopes on IFN-γ production in blood of healthy…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON47795

Source
ToetsingOnline

Brief title
Q-VaxCelerate

Condition

- Bacterial infectious disorders

Synonym
Q fever; Coxiellosis

Research involving
Human

Sponsors and support

Primary sponsor: Massachusetts General Hospital
Source(s) of monetary or material Support: Defense Threat Reduction Agency (onderdeel van het ministerie van defensie van de VS. Innatoss is subcontractor van Massachussetts General Hospital

Intervention

Keyword: Coxiella burnetii, Immune response, T cell epitopes, Vaccine

Outcome measures

Primary outcome

Determining ex vivo the effect of Cb-derived T cell epitopes on IFN-γ production in blood of healthy volunteers, subjects with active or resolved (chronic) Q fever infection, and subjects vaccinated with Q-VAX.

Secondary outcome

• Comparison of T cell responses in subjects with and without acute disease.

• Biomarker discovery to differentiate protective, non-protective, and reactogenic epitopes and responses.

• Determine the role of anti-Coxiella antibody formation on T cell responses.

Study description

Background summary

Coxiella burnetii is a highly infectious and stable pathogen that can cause acute and severe chronic Q fever in humans. Q fever outbreaks have occurred in Australia and the Netherlands and have been of concern to the Department of Defense (USA). Although C. burnetii infection can be treated with antibiotics, a vaccine is considered to be critical to control this disease. There is a clear mandate and a medical need to develop an efficacious and less reactogenic vaccine for occupational and biodefense purposes, which is addressed by our proposal. As CD4+ T cell immunity plays a much more critical role in protective immunity against the pathogen than antibodies, the Q-VaxCelerate proposal sets out to develop a T-cell based Q fever vaccine candidate. Innatoss has developed a T cell based Q fever test, that will be used to identify protective T cell epitopes in humans that have been exposed to Cb.

Study objective

Identification of T cell epitopes that will serve as the basis for a novel Q

fever vaccine with fewer side effects. This will be done by determining ex vivo the effect of Cb-derived T cell epitopes on IFN-γ production in blood of healthy volunteers, subjects with active or resolved Q fever infection (acute or chronic), and subjects previously vaccinated with Q-VAX. All participants will be HLA-typed and T cell responses and antibody formation will be characterized prior to testing selected peptides.
In addition, comparison of T cell responses in subject with and without acute disease will be done for biomarker discovery to differentiate protective, non-protective and reactogenic epitopes. Also, the role of anti-Coxiella antibody formation on T cell responses will be determined.

Study design

T cell responses will be determined in former acute Q fever patients, subjects exposed to Cb who did not develop disease, healthy controls, chronic Q fever patients, and vaccinees. In a selection of volunteers with good T cell responses, cell markers and cytokines in response to Cb will be investigated using different technologies in search of markers for non-protective, protective and reactogenic responses. Subsequently, blood samples from these subjects will be used to screen up 200 potential protective T cell epitopes.

Study burden and risks

The risks associated with standard blood drawing are negligible. Blood drawing posts will assist participants and when needed, in particular during the intake, an Innatoss employee will be present to coordinate blood drawing and assist participants.
Risks associated with testing for Q fever are that a control subject may be positive in Q-detect indicating recent exposure to C. burnetii since all subjects were tested previously. If results during the study suggest possible acute or chronic Q fever, a microbiologist will be consulted and subjects and their GP will be informed. Considering the consequence of lack of treatment, it is not possible to participate without consent on this point.
This research can only be done with blood of coxiella exposed (or vaccinated) subjects, as only these people have Cb and Cb derived peptide specific T cel responses. These responses are required to select for potentially protective T cel epitopes to develop a Q fever vaccine.

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

Participants in this study have been exposed to Coxiella burnetii resulting in chronic Q fever, resolved acute Q fever, or have a strong T cell mediated immune response to Coxiella without having any clinical symptoms. A control group consisting of people without a Cb immune response will be recruited. In addition, a group that was vaccinated with Q-VAX in 2011 in the RIVM/GGD campaign for people with an increased risk of chronic Q fever will be included.

Exclusion criteria

blood-transmissable infectious disease
known immune disease
use of immune suppressives

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2015
Enrollment:	252
Type:	Actual

Ethics review

Approved WMO Date:	15-06-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-01-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-01-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-12-2019

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL51305.028.15

Study results

Date completed:	03-07-2018
Results posted:	28-10-2020
Actual enrolment:	173

Summary results
Trial is onging in other countries

First publication
01-01-1900

URL result
URL
Type
ext
Naam
iai.asm.org
URL
Type
ext

Naam
www.frontiersin.org
URL