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Study to evaluate the immune responses against Salmonella Typhi after vaccination with Vivotif®

Submission date
27/05/2015

Recruitment status
No longer recruiting

Registration date
13/08/2015

Overall study status
Completed

Last Edited
05/09/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Salmonella species are the most common bacterial cause of gastrointestinal infection worldwide and represent a considerable burden in both developing and developed countries. Although Salmonella is an intracellular pathogen (that is, a bacterium that lives inside the body cells), a number of studies have shown that B cells play a crucial role in the control and generation of immunity against this bacterium. Likewise, the main mechanism of protection after vaccination in humans is mediated by antibodies. Outer membrane proteins (Omps), also known as porins, represent important targets of the protective antibody response against Salmonella in humans. Highly purified S. Typhi porins OmpC and F induce long-lasting IgM and IgG bactericidal antibody responses in mice and exhibit intrinsic adjuvant activity. Notably, patients recovering from typhoid fever present both IgG and IgM circulating antibodies against porins and a porin-based vaccine candidate based on S. Typhi porins has been tested in humans resulting to be safe and immunogenic following subcutaneous application. The induction of porin-specific immune responses after vaccination with live attenuated Salmonella vaccine Vivotif® has not been tested. Moreover, the specific antigenic targets that mediate protection during vaccination have not been identified. In this study, healthy volunteers will be vaccinated with Vivotif® commercial Salmonella vaccine and immune responses against S. Typhi porins assessed.

Who can participate?
Healthy adults aged between 18-50 years.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given the Vivotif® vaccine, to be taken orally, on alternative days (1, 3 and 5). Those in group 2 are not vaccinated. Blood and stool samples are collected before treatment begins and then at days 7, 21 and 56 after treatment ends. Immune responses against S. Typhi porins are then assessed.

What are the possible benefits and risks of participating?
Vaccination with Vivotif can protect against typhoid fever. The time of protection lasts approximately 5 years and therefore participants may benefit from vaccination if they attend all

study visits. However, not all recipients of Vivotif will be fully protected against typhoid fever and travellers should take all necessary precautions to avoid contact or ingestion of potentially contaminated food or water. Importantly, since this is a randomised study, participants may be assigned to the control group that will not receive the vaccine. Vivotif is a safe vaccine, but for safety reasons participants should consider not taking some drugs during vaccination (indicated by the investigator) and follow the instructions of medical personnel. Adverse reactions are infrequent and mild, but some people may experience: diarrhea, abdominal pain, nausea, fever, headache, skin rash, vomiting, or urticaria (hives) in the trunk (body) and/or extremities (for example, fingers, toes).

Where is the study run from?
Kantonsspital St.Gallen Hospital (Switzerland)

When is the study starting and how long is it expected to run for?
October 2014 to October 2015

Who is funding the study?
Kantonsspital St.Gallen Hospital (Switzerland)

Who is the main contact?
1. Prof. Burkhard Ludewig (scientific)
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2. Dr Werner Albrich (public)
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Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14/039

Study information

Scientific Title
Open, controlled monocentric clinical study to evaluate the specific immune responses against Salmonella Typhi porins after vaccination with the commercial live oral typhoid vaccine Ty21a Vivotif®

Acronym
PORIMTIF

Study objectives
Specific immune responses against porins are generated after the administration of Vivotif® to healthy volunteers.
H1: The median difference of specific immune responses after and before immunization is not zero.
H0: The median difference of specific immune responses after and before immunization is zero.

Ethics approval required
Old ethics approval format

Ethics approval(s)
the Ethikkommission des Kantons St. Gallen, 06/07/2015, ref: EKSG 15/085

Study design
Open interventional study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Typhoid fever caused by Salmonella Typhi

Interventions
1. Vaccinated group (n=15): Vivotif® (Typhoid Vaccine Live Oral Ty21a) is a live attenuated vaccine for oral administration only. The vaccine contains the attenuated strain Salmonella Typhi Ty21a. Three doses of the vaccine are to be administered in alternate days (1, 3 and 5)
2. Untreated group (n=5): No vaccine/treatment/placebo will be administered to this group

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Not provided at time of registration

Primary outcome measure
1. Antibody levels of IgM and IgG specific against porins in serum (during visits 2, 5, 6 and 7) and IgA in stool (during visits 2, 5, 6 and 7) via enzyme-linked immunosorbent assay (ELISA)
2. Number of porins-specific T cells from blood (during visits 2, 5, 6 and 7) via flow cytometry
3. Amount of porins-specific B cells in blood (during visits 2, 5, 6 and 7) via ELISPot

Secondary outcome measures
Bacteria bearing mutations in their DNA sequences in comparison with bacteria from the original inoculum administered during vaccination

Overall study start date
01/10/2014

Completion date
01/10/2015

Eligibility

Key inclusion criteria
1. Ability to understand the experimental nature of the vaccine evaluation and the participant informed consent form
2. Written informed consent documented by date and signature to be obtained prior to any study specific procedure

3. Age 18-50 years old
4. Regular bowel movement (1+ defecation per day)
5. Willingness to adhere to the strict timing schedule for the study evaluation
6. Willingness to provide stool and blood samples in the indicated visits

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Both

Target number of participants
20

Key exclusion criteria
1. Previous use of an oral vaccine against Salmonella in the past three years
2. Gastrointestinal infection caused by any Salmonella species during the past 3 years
3. Positive HIV serology or any known immune deficiency
4. Current or planned pregnancy during the course of the study
5. Unwillingness to use at least one method of birth control in women of childbearing age during the course of the study
6. Are breastfeeding
7. Suffer from obstipation
8. Suffer from hypersensitivity to any component of the vaccine or the enteric-coated capsule
9. Use of an immune modulator in the past year
10. Use of systemic corticosteroid treatment in the past 30 days
11. Use of antibiotics within 1 week preceding and during the present study
12. Current use of proton-pump inhibitors
13. Participation in another study with investigational drug within the 30 days preceding and during the present study

Date of first enrolment
15/06/2015

Date of final enrolment
15/09/2015

Locations

Countries of recruitment
Switzerland

Study participating centre
Kantonsspital St Gallen
Rorschacherstrasse 95
St Gallen
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Sponsor information

Organisation
Kantonsspital St.Gallen Hospital

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Sponsor type
Hospital/treatment centre

Website
http://www.kssg.ch/

ROR
https://ror.org/00gpmb873

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Kantonsspital St Gallen (Switzerland)

Funder Name

Gottfried und Julia Bangerter-Rhyner-Stiftung

Alternative Name(s)
Gottfried & Julia Bangerter-Rhyner-Stiftung, Bangerter-Stiftung, Gottfried and Julia Bangerter-Rhyner Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2017		Yes	No
Protocol (other)			05/09/2023	No	No