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Evaluation of a prototype vaccine against enterotoxigenic Escherichia coli diarrhoea

Submission date	Recruitment status	[_] Prospectively registered
03/03/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/03/2011	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
18/03/2011	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-015741-23

Protocol serial number
EudraCT number: , OEV-120

Study information

Scientific Title
Evaluation of the safety and immunogenicity of a prototype enterotoxigenic Escherichia coli (ETEC) vaccine: a three-armed, double-blinded, randomised, single-centre study

Study objectives
Enterotoxigenic E. coli (ETEC) bacteria are known to be a primary cause of traveller's diarrhoea and diarrhoea in children in developing countries. ETEC bacteria produce heat-labile toxin (LT), heat stable toxin (ST) or both toxins and colonise the intestine by means of so called colonisation factors (CFs).

The aim of this study is to determine if a new potentially improved prototype ETEC vaccine, consisting of bacteria over-expressing the colonisation factor CFA/I and administered together with a hybrid of the binding subunits of LT and cholera toxin (LTB/CTB), is safe and gives rise to stronger immune responses than a previously tested ETEC vaccine, consisting of a natural CFA/I expressing ETEC strain + CTB.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Independent Ethics Committee in the Gothenburg region (IECGR) in Sweden approved on 26 /10/2009, amendment approved 13/03/2010, ref no 570-09
2. Western Institutional Review Board (WIRB) Olympia, Washington, USA approved on 11/05 /2010, ref no 20100565

Study design
Three-armed double-blinded randomised single-centre study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Enterotoxigenic E. coli (ETEC) diarrhoea

Interventions
Healthy adult volunteers will be immunised with two consecutive doses of two different ETEC vaccines (Vaccine A and Vaccine B) with 12-16 days interval. Vaccine A consists of ETEC bacteria that over-express the colonisation factor CFA/I + LTB/CTB hybrid protein. Vaccine B consists of a previously tested CFA/I expressing ETEC strain + CTB protein. The vaccines will be mixed with a bicarbonate buffer and administered orally.

The volunteers will be randomised into three different study arms:
First arm: Subjects immunised with 2 doses of Vaccine A
Second arm: Subject immunised with 2 doses of Vaccine B
Third arm: Subjects immunised with 2 doses of Vaccine B; each dose containing 4 times higher numbers of bacteria and 4 times more LTB/CTB protein compared to the second arm

Intervention Type

Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Enterotoxigenic E. coli (ETEC) vaccine

Primary outcome(s)
1. To evaluate the safety of a new prototype ETEC vaccine (Vaccine A) and to compare the immunogenicity, i.e. intestinal or intestine-derived IgA antibody responses, against CFA/I and LTB, of the new prototype ETEC vaccine with that of a previously tested ETEC strain in combination with CTB (Vaccine B)
1.1. The safety of the vaccines will be determined by evaluation of study diaries throughout the study period, by clinical chemistry and haematology tests (at screening and 7 days after each immunisation) and by physical examination (at screening and on day 42)
1.2. Intestinal antibody responses are based on enzyme-linked immunosorbent assay (ELISA) measurements of specific antibodies in stool extracts (day 0, 7 and 21)
1.3. Intestine-derived antibody responses are based on ELISA measurements of specific antibodies secreted from cultured peripheral blood cells (using the ALS method) or on ELISPOT assay determinations of the numbers of specific antibody secreting cells (ASC) among peripheral blood mononuclear cells (day 0, 7 and 21)

Key secondary outcome(s))
1. To evaluate IgA and IgG antibody responses against CFA/I, LTB and CTB in serum as well as specific IgA in those mucosal samples that are not used as primary endpoints
1.1. Serum and intestinal antibody responses are based on enzyme-linked immunosorbent assay (ELISA) measurements of specific antibodies in sera (day 0, 7, 14, 21 and 42) and stool (day 0, 7 and 21), respectively
1.2. Intestine-derived antibody responses are based on ELISA measurements of specific antibodies secreted from cultured peripheral blood cells (using the ALS method) or on enzyme-linked immunosorbent spot (ELISPOT) assay determinations of the numbers of specific antibody secreting cells (ASC) among peripheral blood mononuclear cells

Completion date
01/06/2011

Eligibility

Key inclusion criteria
1. Males or females aged 18-55 years
2. Healthy constitution as established by medical history, medical examination and clinical chemistry and haematology testing
3. Give written informed consent to participate
4. Willing and able to communicate with the investigators and understand the requirements of the study
5. Sexually active females should unless being menopausal agree to use reliable contraception as assessed by the investigator, during 1 month prior to inclusion and one month after the last intake of study vaccine and should have a negative pregnancy test before each vaccination

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex
All

Key exclusion criteria
1. Has received the oral cholera vaccine Dukoral® in the last 5 years
2. Travelled to ETEC-endemic area within the last 2 years
3. Concomitant intake of immunomodulating drugs during the study period or less than four weeks prior to the first immunisation
4. Vaccination with some other vaccine during the study period or within two weeks prior to trial vaccination
5. Any condition which would limit the subjects ability to complete the study in the opinion of the investigator
6. History of drug or chemical abuse in the year before the study
7. Receipt of any other investigational product in the month before study entry
8. Concomitant participation in any other clinical study
9. Donation of blood 6 weeks before study entry or at any time during the study
10. Females who are pregnant
11. Females who are nursing
12. History of gastrointestinal or systemic inflammatory or autoimmune disease
13. Any known hypersensitivity to any ingredient in the vaccines
14. Gastroenteritis within two weeks prior to vaccination
15. Antibiotic therapy within six weeks prior to the vaccination

Date of first enrolment
12/05/2010

Date of final enrolment
01/06/2011

Locations

Countries of recruitment
Sweden

Study participating centre

Dept. of microbiology and immunology
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Sponsor information

Organisation
Gothenburg University Vaccine Research Institute (GUVAX) (Sweden)

ROR
https://ror.org/01tm6cn81

Funder(s)

Funder type
Other

Funder Name
PATH (USA)

Alternative Name(s)
Program for Appropriate Technology in Health, Program for the Introduction and Adaptation of Contraceptive Technology

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location
United States of America

Funder Name
Sahlgrenska University Hospital (Sweden) (ref: LUA/ALF)

Funder Name
Swedish Research Council (Sweden)

Alternative Name(s)
Swedish Research Council, VR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Sweden

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration