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LEISH2a: Assessing the safety and immunogenicity of a new Leishmania vaccine candidate ChAd63-KH

Submission date
25/01/2016

Recruitment status
No longer recruiting

Registration date
28/01/2016

Overall study status
Completed

Last Edited
11/08/2022

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Leishmaniasis is a parasitic disease that is spread from an infected animal or person to another by bites from a sand fly. It mostly affects the world's poorest people in India, Bangladesh, Nepal, the Sudan and Brazil. Approximately 20-40,000 people, mostly children and young adults, die of leishmaniasis each year, and hundreds of thousands develop skin ulcers that cause unsightly or disfiguring scars. In its most severe form, leishmaniasis affects internal organs such as the liver and spleen and it is this form that is usually fatal if not treated. Although drugs for the treatment of leishmaniasis are available they are extremely costly, have side effects and often need to be taken for a long time. In addition, resistance to these drugs is beginning to develop. There is also no effective preventative vaccine currently available. However, the vaccine tested here is not designed to prevent people from getting leishmaniasis but to lower the numbers of the parasite within the body, either so that other treatments can work more effectively or to help the immune system to remove all the parasites without the need for drugs. This is known as a therapeutic vaccine. A recent study has demonstrated that this vaccine was safe and triggered the right type of immune response in healthy UK volunteers. In this study, the safety of this vaccine will now be assessed in patients with one form of leishmaniasis called post kala azar dermal leishmaniasis (PKDL). This is a long lasting and disfiguring disease, but is not life threatening. Researchers will also look at how well the immune system in these patients responds to this vaccine by testing blood in the laboratory.

Who can participate?
Adults aged between 18-50 and adolescents aged between 12-17, diagnosed with PKDL but in otherwise good health.

What does the study involve?
Each participant is given a single injection of the test vaccine. The first 8 volunteers are given a lower dose than the other 8 volunteers. This is to compare the difference in side effects and responses to the vaccine depending on how much of the vaccine given to people. Blood samples

are taken from each participant before vaccination and then again at 1, 3, 7, 21 42 and 90 days after the vaccination for routine blood chemistry tests. Photographs are also taken to see if the PKDL symptoms have improved.

What are the possible benefits and risks of participating?
Patients may gain a direct health benefit from taking part in this study. They may also, however, experience some side effects. These side effects are expected to be similar to the side effects that occur after other immunisations, including fevers, chills, general muscle aches (like flu), feeling unusually tired, headache, nausea, or discomfort, redness or swelling at the injection site (upper arm).Because this vaccine has not been used before in patients, the side effects listed above could be worse than expected and there may be other side effects that are not yet known about. It is possible if the vaccine is given to a pregnant woman it will harm the unborn child. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her study doctor. Blood sampling can sometimes cause bruising and soreness of the arms or very rarely a blockage of the vein or a small nerve injury which can cause numbness and pain. Normally these problems resolve with time. Some people may faint while blood is being taken. Rarely some people experience a reaction to receiving a vaccine which can be serious. If this occurs it is likely to happen shortly after they receive the vaccine. Each participant is required to stay in the hospital for seven days after the vaccination and there will be a doctor and a nurse present with them during this time.

Where is the study run from?
Institute of Endemic Diseases, Khartoum and Professor El-Hassan Centre for Tropical Diseases (Sudan)

When is the study starting and how long is it expected to run for?
February 2016 to September 2017

Who is funding the study?
Wellcome Trust (grant code WT108518MA)

Who is the main contact?
Professor Paul Kaye

Contact information

Type(s)
Scientific

Contact name
Prof Paul Kaye

ORCID ID
https://orcid.org/0000-0002-8796-4755

Contact details
Centre for Immunology and Infection
University of York
York
United Kingdom
YO10 5DD

Additional identifiers

ClinicalTrials.gov (NCT)
NCT02894008

Clinical Trials Information System (CTIS)
2016-000369-22

Protocol serial number
LEISH2a

Study information

Scientific Title
LEISH2a: A phase IIa safety study to assess the safety and immunogenicity of a new Leishmania vaccine candidate ChAd63-KH

Acronym
LEISH2a

Study objectives
LEISH2a is a study to assess the safety and effects of a new Leishmaniasis vaccine in patients with post kala-azar dermal leishmaniasis (PKDL). PKDL is a parasitic disease that is spread from an infected animal or person to another by bites from a sand fly and develops most commonly after a patient has previously recovered from visceral leishmaniasis. The aim of this study is to assess the safety of a new therapeutic vaccine in patients with persistent PKDL, and to look at how well the immune system responds to it. The study involves giving adult patients either a low dose or a higher dose of the vaccine. This is to compare the difference in side effects and responses to the vaccine depending on how much of the vaccine is given. One dose of the vaccine will then be selected to be given to adolescents, as adolescents are commonly affected by PKDL.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Primary study design
Interventional

Study design
Non randomised intervention trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Leishmaniasis

Interventions
The study involves patient volunteers receiving a single intramuscular injection of a recombinant adenovirus vaccine encoding two proteins derived from the Leishmania parasite. The first 8 adult volunteers will receive 1x10(10)vp; the subsequent 8 adult volunteers will receive 7.5x10 (10)vp; the 8 adolescents will receive one of these doses. Doses will be administered at a single time point to patients with persistent PKDL. Prior to therapeutic vaccination, on the day of vaccination and at days 1, 3, 7, 21, 42 and 90 post vaccination (+/- 1-3 days), blood samples will be taken for routine blood chemistry and to study immune responses generated by the vaccine. Clinical evaluation of vaccine response is non-invasive and requires observation only (including photographing of lesions). Patients with significant remaining PKDL 42 days post vaccination will be treated with liposomal amphotericin B (as standard of care).

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
ChAd63-KH

Primary outcome(s)
Safety, as measured by clinical assessment of local and systemic effects (e.g. injection site pain, headache, vomiting) following vaccination.

To be assessed immediately after vaccination and at days 1, 3, 7, 21, 42 and 90 post vaccination.

Key secondary outcome(s)
1. Changes to PKDL lesions, via photographing them
2. Measures of immune response (measured by analysis of blood samples using ELISA, ELISPOT, RNASeq or other techniques)

To be assessed immediately after vaccination and at days 1, 3, 7, 21, 42 and 90 post vaccination.

Completion date
31/03/2019

Eligibility

Key inclusion criteria
Adults:
1. Aged 18 to 50 years on the day of screening
2. Females must be unmarried, single, or widowed
3. Willing and able to give written informed consent

Adolescents:
1. Aged 12 to 17 years on the day of screening
2. Female adolescents must be unmarried
3. Written informed consent must be obtained from a parent

All Participants:
1. Uncomplicated PKDL of > 6 months duration
2. Available for the duration of the study
3. In otherwise good health as determined by medical history, physical examination, results of screening tests and the clinical judgment of a medically qualified Clinical Investigator
4. Judged, in the opinion of a medically qualified Clinical Investigator, to be able and likely to comply with all study requirements as set out in the protocol
5. Willing to undergo screening for HIV, Hepatitis B and Hepatitis C
6. For females only, willing to undergo urinary pregnancy tests on the day of screening, on the day of vaccination (prior to vaccination) and 28 and 90 days after vaccination

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Total final enrolment
24

Key exclusion criteria
The volunteer may not enter the study if any of the following apply:
1. Has mucosal or conjunctival PKDL
2. Has had treatment for PKDL within 21 days
3. Is negative for antibodies in the RK39 strip test
4. Receipt of a live attenuated vaccine within 60 days or other vaccine within 14 days of screening
5. Administration of immunoglobulins and/or any blood products within the three months preceding the planned administration of the vaccine candidate
6. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine or a history of severe or multiple allergies to drugs or pharmaceutical agents
7. Any history of severe local or general reaction to vaccination as defined as:
7.1. Local : extensive, indurated redness and swelling involving most of the antero-lateral thigh or the major circumference of the arm, not resolving within 72 hours
7.2. General : fever ≥ 39.5°C within 48 hours, anaphylaxis, bronchospasm, laryngeal oedema, collapse, convulsions or encephalopathy within 48 hours
8. Females – pregnancy, less than 12 weeks postpartum, lactating or willingness/intention to become pregnant during the study and for 3 months following vaccination.
9. Seropositive for hepatitis B surface antigen (HBsAg) or Hepatitis C (antibodies to HCV)
10. Any clinically significant abnormal finding on screening biochemistry or haematology blood tests or urinalysis
11. Any confirmed or suspected immunosuppressive or immunodeficient state, including HIV infection; asplenia; recurrent, severe infections and chronic (more than 14 days) immunosuppressant medication within the past 6 months
12. Tuberculosis, leprosy, or malnutrition
13. Any other significant disease, disorder or finding, which, in the opinion of a medically

qualified Clinical Investigator, may either put the volunteer at risk because of participation in the study, or may influence the result of the study, or the volunteer's ability to participate in the study
14. Unlikely to comply with the study protocol

Date of first enrolment
01/04/2016

Date of final enrolment
01/02/2017

Locations

Countries of recruitment
Sudan

Study participating centre
Institute of Endemic Diseases, Khartoum and Professor El-Hassan Centre for Tropical Diseases
Dooka
Sudan
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Sponsor information

Organisation
University of York

ROR
https://ror.org/04m01e293

Funder(s)

Funder type
Research organisation

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/07/2021	10/06/2022	Yes	No
Protocol file	version 1.55	01/05/2018	11/08/2022	No	No