ISRCTN71619711 https://doi.org/10.1186/ISRCTN71619711

BK-SE36 two-stage phase 1b vaccine trial for falciparum malaria

Submission date	Recruitment status	[X] Prospectively registered
18/03/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/04/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
13/01/2014	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
BK-SE36/002

Study information

Scientific Title
Single-blind randomised controlled phase 1b trial of the safety and immunogenicity of lyophilised recombinant precipitated tropical malaria vaccine (BK-SE36) in Uganda

Study objectives
Combating malaria is a complex proposition. No vaccine exists today against malaria. Research identified SE36 protein based from the N-terminal domain of serine repeat antigen (SERA5) of Plasmodium falciparum, as a vaccine candidate with strong potential. Immunoepidemiological data underscores the uniqueness of SERA versus other candidates, showing a semi-perfect correlation of the naturally induced antibody response to SE36 protein with increased protective immunity in adults and children. GMP-grade SE36 was formulated adsorbed to aluminum hydroxide gel as BKSE36. The pre-clinical toxicity, safety and reactogenicity studies demonstrate that BK-SE36 was immunogenic and well tolerated. In a small clinical trial in malaria-naïve adults in Japan, BK-SE36 was proven safe and immunogenic. This will be the first trial in an endemic area and will evaluate the safety and immunogenicity of BK-SE36 in malaria-exposed individuals aged 6 - 40 years old.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Japan:
1. Osaka University Research Ethical Review Board, approved on 03/09/2008 (ref: 20-3)
2. Institutional Review Board of the Research Foundation for Microbial Diseases of Osaka University, approved on 09/02/2009

Uganda:
3. Med Biotech Laboratories, Institutional Review Committee, approved on 11/03/2009 (ref: IRB-00003990)

Study design
Phase 1b single-blind randomised placebo-controlled staggered two-stage single centre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet
Patient information sheet can be found at: http://www.biken.or.jp/english/document/bk_se36.pdf

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

Interventions
BK-SE36 versus placebo.

Route of administration: subcutaneous
Frequency of administration: twice with 21 day interval
Dose of administration:
Stage 1: each administration contains full dose of BK-SE36
Stage 2: each administration will contain either full or half dose of BK-SE36

The total duration of follow-up is 84 days: 43 days active surveillance (this includes two administrations in a period of 21 days, and four visits after each administration - 1, 7, 14 and 21 days after administration); plus 40 days passive surveillance (additional follow-up visits whenever subject is ill).

Please note that as of 29/07/09 the start and end dates of this trial were changed. The previously anticipated duration of the trial was from 23/04/09 to 21/11/09

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
BK-SE36 malaria vaccine

Primary outcome measure
The safety of BK-SE36 will be assessed by the presence or absence of adverse events. This information will be gathered from patient symptoms, vital signs and laboratory test results obtained 1 hour after administration and 1, 7, 14 and 21 ±1 days after each administration.

Secondary outcome measures
Changes in the anti-SE36 protein antibody titre at each time point: screening, before each administration and 21 +/- 1 day post-administration (final visit).

Overall study start date
22/09/2009

Completion date
21/04/2010

Eligibility

Key inclusion criteria
1. Inclusion criteria for Stage 1: 21 to 40 years old
Healthy subjects are specified, and the inclusion criteria of malnutrition index and laboratory test values were included to reduce individual variation.
1.1. Healthy adults; Ugandan males and females aged 21 to 40 years (age on informed consent)
1.2. Those who do not suffer from severe malnutrition (defined as an adult whose weight-for-height is below -3 standard deviation or less than 70% of the median of the National Center for

Health Statistics [NCHS]/World Health Organization [WHO] normalised reference values)
1.3. Those who are able to agree, comply with matters to be observed during participation in the trial, undergo consultation/examination, as described in this protocol, and report symptoms
1.4. Those who are considered to be eligible to participate in this trial based on screening:
1.4.1. Vital signs and physical examination are within baseline range
1.4.2. Haematology within 25% deviations from the upper and lower limits of the baseline range. The differential white blood count is not questioned when the white blood cell count is within the baseline range.
1.4.3. Blood chemistry:
i. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and creatinine within the baseline range
ii. Total bilirubin within 50% deviation from the upper limit
iii. Serum electrolytes within the baseline range
iv. Other blood chemistry items within 25% deviation from the upper and lower limits of the baseline range
1.4.4. Urinalysis within the normal range

2. Inclusion criteria for Stage 2: 6 to 20 years old
2.1. Healthy volunteers, irrespective of gender, aged 6 to 20 years (age on informed consent)
2.2. Those who do not suffer from severe malnutrition (defined as a child or adult whose weight-for-height is below -3 standard deviation or less than 70% of the median of the NCHS/WHO normalised reference values)
2.3. Those who can give affirmative agreement to participate in the trial. For children between 8 to 17 years, the child's assent takes precedence over the parent(s)/guardian(s) consent
2.4. Those who are able to agree, comply with matters to be observed during participation in the trial, undergo consultation/examination, as described in this protocol and report symptoms
2.5. Those who are considered to be eligible to participate in this trial based on screening:
2.5.1. Vital signs and physical examination are within baseline range
2.5.2. Hematology within 25% deviations from the upper and lower limits of the baseline range. The differential white blood count is not questioned when the white blood cell count is within the baseline range.
2.5.3. Blood chemistry:
i. AST, ALT, and creatinine within the baseline range
ii. Total bilirubin within 50% deviation from the upper limit
iii. Serum electrolytes within the baseline range
iv. Other blood chemistry items within 25% deviation from the upper and lower limits of the baseline range
2.5.4. Urinalysis within the normal range

Participant type(s)
Healthy volunteer

Age group
Other

Sex
Both

Target number of participants
140 (Stage 1: 56; Stage 2: 84)

Key exclusion criteria
Exclusion criteria for Stages 1 and 2:
1. Persons with fever (37.5°C or higher) on administration of the test vaccine
2. Persons with a clear history of food/drug-related anaphylaxis
3. Females (adolescents/adults) who are pregnant or have a positive urine beta-human chorionic gonadotrophin [beta-hCG] on the day of, or prior to, administration
4. Females currently lactating or breast-feeding
5. Persons with acute or chronic cardiovascular, pulmonary, hepatic, renal, or neurological condition, which in the opinion of the investigator may increase the risk of the subject from participating in the trial
6. Persons with a history of fever within 2 days after preventive administration with other types of vaccine, or those in whom symptoms have suggested systemic allergy
7. Persons with a history of convulsion
8. Persons with any confirmed or suspected immunosuppressive or immunodeficient condition, including human immunodeficiency virus (HIV) infection. (No infectious disease testing will be conducted. HIV testing will not be done. Severe, suspected infectious diseases will be ruled out by investigators during physical examination/consultation, blood haematology/chemistry tests; although not conclusive of the causative agent). Additional oral confirmation: Subject informed the investigator that he/she has been tested positive for HIV/acquired immune deficiency virus (AIDS).
9. Persons with a history or tentative diagnosis of drug allergy
10. Persons with a history of or present drug/alcohol dependency
11. Persons who took any medication within 1 week before administration of this test vaccine (except for artemether/lumefantrine and dihydroartemisinin-piperaquine)
12. Persons to whom any live vaccine was administered within 4 weeks before administration of this test vaccine, or inactivated vaccine/toxoid was administered within 1 week
13. Persons who participated in another trial within 4 months before administration of this test vaccine
14. Persons in whom 200 ml of blood was collected (donation) within 1 month before administration of this test vaccine, or more than 400 ml of blood was collected within 3 months
15. Others who are not considered to be eligible by the investigator or those whose medical condition would, in the opinion of the investigator, make the subject unsuitable for the trial

Date of first enrolment
22/09/2009

Date of final enrolment
21/04/2010

Locations

Countries of recruitment
Japan

Uganda

Study participating centre
The Research Foundation for Microbial Diseases of Osaka University
Osaka

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565-0871

Sponsor information

Organisation
The Research Foundation for Microbial Diseases of Osaka University (BIKEN) (Japan)

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Sponsor type
University/education

Website
http://www.biken.or.jp/index.html

ROR
https://ror.org/035t8zc32

Funder(s)

Funder type
University/education

Funder Name
The Research Foundation for Microbial Diseases of Osaka University (BIKEN) (Japan)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	28/05/2013		Yes	No