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Trial of the functional food Biobran in patients with persistent symptoms attributed to Lyme borreliosis

Submission date
25/06/2017

Recruitment status
No longer recruiting

Registration date
28/06/2017

Overall study status
Completed

Last Edited
09/09/2024

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Lyme disease is a bacterial infection spread to humans by infected ticks. This study focuses on boosting the immune system of Lyme disease patients using a food supplement called Biobran - a water-soluble rice bran extract. The aim of this study is to investigate whether daily supplementation with Biobran over three months improves immune system functioning in patients with persistent symptoms due to Lyme disease.

Who can participate?
Patients aged 18 or over with Lyme disease

What does the study involve?
Patients undergo an assessment which includes a clinical history, questionnaires, a physical examination and a blood test. This takes a morning or afternoon. The patients are randomly allocated to be given either Biobran or a placebo (dummy supplement) to take daily for three months. At the end of three months, another assessment takes place, which will be similar to the first one.

What are the possible benefits and risks of participating?
Possible benefits include undergoing an assessment, including history, which might indicate the presence of a previously unknown or unsuspected clinically relevant finding. There are no anticipated possible risks.

Where is the study run from?
The TBD Clinic (UK)

When is the study starting and how long is it expected to run for?
August 2016 to December 2023

Who is funding the study?
Daiwa (Japan)

Who is the main contact?
Prof. B Puri, bpuri@cantab.net

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
V2

Study information

Scientific Title
Randomised, double-blind, placebo-controlled three-month trial of Biobran MGN-3 in patients with persistent symptoms attributed to Lyme borreliosis

Study objectives
There is good evidence that the functional food Biobran MGN-3 is a safe immunomodulator which enhances NK cell activity, enhances human T lymphocyte and human B lymphocyte proliferation, enhances phagocytosis of bacteria, enhances the oxidative burst in human neutrophils and monocytes, and enhances the production of the cytokines TNF-α, IL-6, IL-8 and

IL-10. It is therefore hypothesised that regular daily intake of this functional food will be associated with improved immune system functioning in patients with persistent symptoms attributed to Lyme borreliosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
AONMREC (The Academy of Nutritional Medicine Research Ethics Committee), 22/02/2017, ref: 0217

Study design
Single-centre randomized double-blind placebo-controlled three-month trial (the baseline data [patients versus controls] will constitute an initial cross-sectional cohort study)

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Persistent symptoms attributed to Lyme borreliosis

Interventions
Current interventions as of 18/08/2022:
Following baseline assessment, each patient will be randomly allocated to either the active group or the placebo group, in a one-to-one allocation ratio. This randomisation will be computerised and balanced by minimisation for age, sex and duration of symptoms. The researchers directly involved in the study and the participants will be blinded to group allocation.

1. Active: Biobran MGN-3 at a dose of 3 grams daily for three months. Administration: oral
2. Placebo: of identical appearance and taste to the active intervention, and isocaloric with the active intervention. Administration: oral
Measurements will be made at two time-points, namely at baseline and at three-month follow-up

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Previous interventions:
Following the baseline assessment of the patients and controls, each patient will be randomly allocated to either the active group or the placebo group, in a one-to-one allocation ratio. This

randomisation will be computerised and balanced by minimisation for age, sex and duration of symptoms. The researchers directly involved in the study and the participants will be blinded to group allocation.

1. Active: Biobran MGN-3 at a dose of 3 grams daily for three months. Administration: oral
2. Placebo: of identical appearance and taste to the active intervention, and isocaloric with the active intervention. Administration: oral

Measurements will be made at two timepoints, namely at baseline and at three-month follow-up.

Intervention Type
Supplement

Primary outcome measure
Current primary outcome measure as of 18/08/2022:
Immune system functioning measured using RNA-seq and flow cytometry at baseline and three-month follow-up

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Previous primary outcome measure:
Immune system functioning, assessed using flow cytometry at baseline and three-month follow-up

Secondary outcome measures
Current secondary outcome measure as of 18/08/2022:
1. The following questionnaires will be administered at baseline and three-month follow-up:
1.1. Epworth Sleepiness Scale (Johns, 1991)
1.2. Overactive Bladder Symptom and Health-Related Quality of Life Questionnaire (OAB-q) (Coyne et al., 2002)
1.3. Refined and Abbreviated Composite Autonomic Symptom Score (COMPASS 31) (Sletten et al., 2012)
1.4. Modified Chalder Fatigue Scale (CFQ) (Chalder et al., 1993)
1.5. Fatigue Severity Scale (FSS) (Krupp et al., 1989)
1.6. Pain Visual Analogue Scale (VAS) (Portenoy and Kanner, 1996)
1.7. McGill Pain Questionnaire (MPQ) (Melzack, 1975)
1.8. Tinnitus Handicap Inventory (THI) (Newman et al., 1996)
2. Course of Lyme disease symptomatology, assessed by history taking, clinical examination and the use of questionnaires at baseline and three-month follow-up

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Previous secondary outcome measure:
1. Electrocardiographic function, assessed using electrocardiography
2. Neuropsychological outcome, assessed using the Cambridge Neuropsychological Test Automated Battery. The questionnaires will be as follows:
2.1. Rheumatoid Arthritis Severity Scale (RASS) (Bardwell et al., 2002)
2.2. Epworth Sleepiness Scale (Johns, 1991)
2.3. Overactive Bladder Symptom and Health-Related Quality of Life Questionnaire (OAB-q) (Coyne et al., 2002)
2.4. Refined and Abbreviated Composite Autonomic Symptom Score (COMPASS 31) (Sletten et

al., 2012)
2.5. Modified Chalder Fatigue Scale (CFQ) (Chalder et al., 1993)
2.6. Fatigue Severity Scale (FSS) (Krupp et al., 1989)
2.7. Pain Visual Analogue Scale (VAS) (Portenoy and Kanner, 1996)
2.8. McGill Pain Questionnaire (MPQ) (Melzack, 1975)
2.9. Tinnitus Handicap Inventory (THI) (Newman et al., 1996)
3. Course of Lyme disease symptomatology, assessed by history taking, clinical examination and the use of questionnaires
Assessments made at baseline and three-month follow-up

Overall study start date
29/08/2016

Completion date
31/12/2023

Eligibility

Key inclusion criteria
For the patients, the inclusion criteria will be as follows:
1. Meeting the diagnostic criteria for the syndrome of Borrelia-associated persistent symptoms used by the Persistent Lyme Empiric Antibiotic Study Europe (PLEASE); PLEASE criterion 2B will be extended to include other appropriate laboratory tests including the Elispot. PLEASE criterion #1 specifies that the subjects must be males or non-pregnant, non-lactating females who are 18 years of age or older

For the controls, the inclusion criteria will be as follows:
1. Healthy males or non-pregnant, non-lactating females who are 18 years of age or older

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
52 patients

Total final enrolment
20

Key exclusion criteria
Current participant exclusion criteria as of 18/08/2022:
1. A history of hypersensitivity to Biobran MGN-3

2. Having received > 5 days' antimicrobial therapy during the previous four weeks
3. Regularly taking Biobran MGN-3 during the previous four weeks
4. Current enrolment in another clinical trial
5. Currently receiving other antimicrobial therapy
6. An inability to give full informed consent
7. Currently pregnant or breastfeeding

Previous participant exclusion criteria:
For the patients, the exclusion criteria will be as follows.
1. A history of hypersensitivity to Biobran MGN-3
2. Having received > 5 days' antimicrobial therapy during the previous four weeks
3. Regularly taking Biobran MGN-3 during the previous four weeks
4. Current enrolment in another clinical trial
5. Currently receiving other antimicrobial therapy
6. An inability to give full informed consent

For the controls, the exclusion criteria will be as follows.
1. Suffering from Lyme disease or a major neuropsychiatric disorder
2. Being the child of a known Lyme disease affected mother
3. Being in a non-platonic relationship with a known Lyme disease patient

Date of first enrolment
30/06/2017

Date of final enrolment
10/10/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
The TBD Clinic
United Kingdom
BN3 4EE

Sponsor information

Organisation
Daiwa

Sponsor details

1-16-19 Sangenjaya
Setagaya-ku
Tokyo
Japan
#154-0024

Sponsor type
Industry

ROR
https://ror.org/007pxvx88

Funder(s)

Funder type
Industry

Funder Name
Daiwa

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 18/08/2022:
The findings of the study will be communicated to colleagues and the public in lectures, academic journals and public talks. The trial results will not be available until the group allocation coding is broken, which will be at the end of the final assessment of the final patient; the corresponding results will be submitted for publication after this date.

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Previous publication and dissemination plan:
The findings of the study will be communicated to colleagues and the public in lectures, academic journals and public talks. The baseline data, from baseline assessments of the patients and controls, will be analysed first; it is intended that these results be submitted for publication from the last quarter of 2017 onwards. The overall trial results will not be available until the group allocation coding is broken, which will be at the end of the final assessment of the final patient; the corresponding results will be submitted for publication after this date.

Intention to publish date
31/03/2025

Individual participant data (IPD) sharing plan
The datasets will not be made available in order fully to ensure patient confidentiality. Consent forms, questionnaires and identifying information will be kept in a locked filing cabinet and only the investigators involved in the study will have a key. All data will be rendered anonymous on

entry into spreadsheets and statistical analysis software and held in password-protected hardware. Hard copies of data will be kept in locked filing cabinets and only the investigators involved in the study will have a key.

IPD sharing plan summary

Not expected to be made available