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A trial to determine bexarotene's safety and tolerability and its ability to promote brain repair in patients with multiple sclerosis

Submission date
14/10/2015

Recruitment status
No longer recruiting

Registration date
14/10/2015

Overall study status
Completed

Last Edited
07/11/2023

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Multiple sclerosis (MS) is one of the most common diseases of the central nervous system (brain and spinal cord). Healthy nerves are coated in a fatty casing (myelin sheath) which helps messages to travel quickly and smoothly along nerves. When a person is suffering from MS, the immune system, which normally helps to protect against infection, attacks the myelin sheath, stripping it from the nerves (demyelination). This demyelination means that messages cannot travel along the nerves effectively, causing a range of disturbances including loss of vision, problems with balance and coordination and weakness in the arms or legs. At first, the body is able to rebuild the myelin sheath (remyelination) but as the disease progresses to the secondary phase (secondary progressive MS), this process fails and the nerves themselves break down (neurodegeneration), ultimately leading to paralysis and death. One of the most important parts of treatment is delaying the onset of secondary progressive MS as long as possible. Around 85% of MS sufferers are diagnosed with the relapsing remitting type. This is where the sufferer has sudden flare-ups of symptoms (relapses) followed by periods where the symptoms are very mild or disappear completely. The anti-cancer drug bexarotene has shown that it can actually help to encourage remyelination in animal studies. The aim of this study is to find out whether treatment with bexarotene can help to promote remyelination in humans suffering from relapsing remitting MS.

Who can participate?
Adults between 30 and 50 years old who are suffering from relapsing remitting MS.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are given bexarotene capsules to take for nine months. Those in the second group are given a placebo (dummy pill) to take for the same length of time. During the nine month study period, participants in both groups will attend the clinic regularly to assess the any remyelination that has occurred.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Addenbrookes Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2015 to November 2019

Who is funding the study?
Multiple Sclerosis Society (UK)

Who is the main contact?
Mrs Arti Gulati

Contact information

Type(s)
Public

Contact name
Mrs Arti Gulati

Contact details
Addenbrookes Hospital
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Additional identifiers

Clinical Trials Information System (CTIS)
2014-003145-99

Central Portfolio Management System (CPMS)
19281

Study information

Scientific Title
A randomised placebo-controlled study of the safety and tolerability of a retinoid-X receptor agonist's ability to promote remyelination in people with relapsing-remitting multiple sclerosis already on interferon-beta therapy: a phase 2a trial

Study objectives
The aim of this study is to establish the safety and tolerability of bexarotene in the treatment of relapsing remitting multiple sclerosis.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Westminster Research Ethics Committee, 19/03/2015, ref: 15/LO/0108

Primary study design
Interventional

Study design
Randomized placebo-controlled phase 2a trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Neurological disorders; Subtopic: Neurological (all Subtopics); Disease: Multiple Sclerosis

Interventions
Participants are randomly allocated into two groups who receive a different medication for a period of nine months. Those in the first group are given Bexarotene and those in the second group are given a placebo. During the nine month study period, participants in both groups will have regular assessments.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Bexarotene

Primary outcome(s)
Number of adverse events and withdrawals attributable to bexarotene are determined at 9 months.

Key secondary outcome(s)
Change in mean lesional MTR between month 0 and month 6 for lesions selected for each patient.

Completion date
15/11/2019

Eligibility

Key inclusion criteria
1. Aged between 30 and 50 years inclusive
2. Able to provide informed consent
3. Relapsing remitting multiple sclerosis as per the McDonald 2010 criteria, including an MRI satisfying the radiological criteria

4. At least five T2 lesions, attributable to MS, on baseline MRI brain scan
5. Kurtzke Expanded Disability Status Scale (EDSS) 3.0-6.0
6. At least one relapse in the two years prior to screening
7. At the time of screening (and for at least the last 6 months) being treated with interferon-beta (any preparation)
8. Able and willing to comply with all study requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
30 Years

Upper age limit
50 Years

Sex
All

Total final enrolment
52

Key exclusion criteria
1. Pregnant, lactating or planning pregnancy during course of trial
2. Female and male participants unwilling or unable to use two reliable non-hormonal methods of contraception during the course of the trial and for one month thereafter
3. Taking gemfibrozil
4. Taking disease-modifying therapy for multiple sclerosis, other than interferon-beta within the previous six months
5. Significant renal or hepatic impairment (Grade III or worse)
6. Known hypersensitivity to bexarotene or to any of the excipients of the product
7. Unwillingness to take a product containing gelatin
8. Known reaction to gadolinium (within the contrast agent used for MRI scans)
9. History of pancreatitis
10. Fasting triglycerides over 2.3 mmol/L or baseline dyslipidaemia requiring treatment
11. Known hypervitaminosis A
12. Uncontrolled thyroid disease
13. Excessive alcohol consumption (>24units/week for men, >14 units/week for women)
14. Uncontrolled diabetes mellitus
15. Biliary tract disease
16. Hereditary fructose intolerance
17. Use of CYP3A4-substrates (ketoconazole, itraconazole, protease inhibitors, clarithromycin and erythromycin) or CYP3A4-inducers (rifampicin, phenytoin, dexamethasone or phenobarbital), unless patients are willing to stop these (and it is safe to do so)
18. Any other significant disease, disability or investigation result which in the opinion of the

Investigator may either put the participant at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study

Date of first enrolment
17/01/2017

Date of final enrolment
17/05/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation trust & University of Cambridge (Comprehensive)

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Multiple Sclerosis Society

Alternative Name(s)

mssocietyuk, MS Society UK, Multiple Sclerosis Society UK, Multiple Sclerosis Society of Great Britain and Northern Ireland, The MS Society, MS Society

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

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

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		23/08/2021	23/08/2021	Yes	No
Results article		17/09/2022	07/11/2023	Yes	No
HRA research summary			28/06/2023	No	No
Other publications		19/05/2022	07/11/2023	Yes	No