ISRCTN94357046 https://doi.org/10.1186/ISRCTN94357046

A pharmacokinetic and safety study of BIIB132 in adults with spinocerebellar ataxia 3

Submission date
19/02/2022

Recruitment status
No longer recruiting

Registration date
05/05/2022

Overall study status
Completed

Last Edited
07/06/2022

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Spinocerebellar ataxia 3 (SCA3) is a rare, autosomal mainly inherited (a condition can be passed down from parent to child) neurodegenerative disorder, and currently no specific approved therapy is available to slow clinical progression.
This is a Phase I, first in human, blinded (participant and doctor will not know which medication will be given) study where participants will be randomly assigned to either the study drug, i.e. BIIB132, or placebo (looks like the study drug but contains no active ingredient). This study is being carried out to find out more about the study drug, BIIB067 as a potential treatment for people with SCA3.

Who can participate?
Adult participants (aged 18 years and over) diagnosed with spinocerebellar ataxia 3 (SCA3)

What does the study involve?
Potential participants will be screened to assess their eligibility to enter the study within 6 weeks before the dose administration. If a potential participant is eligible to take part in the study, he/she will enter the treatment period for that group, also called “cohort”, to which participants will be assigned randomly (by chance).
This study will have five cohorts, and each cohort will test a different dose of the study drug. The frequency of study treatment administration is projected to be every 4 weeks (total of 4 doses) for participants in Cohorts 1 to 4 and every 4 weeks (total of 4 doses), every 8 weeks (total of 2 doses), or every 12 weeks (total of 2 doses) for participants in Cohort 5. However, dose levels and frequency of administration may be revised based on the safety data from previous cohorts. The study medication is given intrathecally (by an injection into the spinal canal). The total study duration for each participant will be up to 44 weeks.

What are the possible benefits and risks of participating?
There might be no direct benefit from taking part in the study. Since BIIB132 has not yet been tested in humans, the possible side effects are not known; however, as with other medicines, it is possible that BIIB132 may cause adverse reactions.

Where is the study run from?
The study sites are all hospital-based specialist ataxia centres

When is the study starting and how long is it expected to run for?
February 2022 to March 2025

Who is funding the study?
Biogen Idec Research Limited (UK)

Who is the main contact?
clinicaltrials@biogen.com

Contact information

Type(s)
Principal Investigator

Contact name
Dr Paola Giunti

Contact details
250 Euston Road
London
United Kingdom
WC1 2PG
+44 (0)203 448 3141
p.giunti@ucl.ac.uk

Additional identifiers

EudraCT/CTIS number
2021-002223-37

IRAS number
1004052

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
260SA101, IRAS 1004052, CPMS 50391

Study information

Scientific Title
A Phase I, blinded, randomized, placebo-controlled study to investigate the safety, tolerability, and pharmacokinetics of multiple ascending doses of BIIB132 administered intrathecally to adults with spinocerebellar ataxia 3

Study objectives

1. To evaluate the safety and tolerability of multiple ascending doses of BIIB132 administered via intrathecal (IT) injection to participants with spinocerebellar ataxia 3 (SCA3)
2. To characterize the multiple-dose pharmacokinetics (PK) of BIIB132 administered via IT injection to participants with SCA3

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/04/2022, East of England - Cambridgeshire and Hertfordshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)20 710 48096; cambsandherts.rec@hra.nhs.uk), ref: 22/EE/0059

Study design
Randomized double-blind placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Spinocerebellar ataxia 3

Interventions
Randomisation process:
Interactive Response Technology (IRT)

Study arms:

Experimental: BIIB132: Dose 1
Participants will receive BIIB132, Dose 1, intrathecally (IT), every 4 weeks (Q4W), up to Day 85.

Experimental: BIIB132: Dose 2
Participants will receive BIIB132, Dose 2, IT, Q4W, up to Day 85.

Experimental: BIIB132: Dose 3
Participants will receive BIIB132, Dose 3, IT, Q4W, up to Day 85.

Experimental: BIIB132: Dose 4
Participants will receive BIIB132, Dose 4, IT, Q4W, up to Day 85.

Experimental: BIIB132: Dose 5
Participants will receive BIIB132, Dose 5, IT, either Q4W or every 12 weeks (Q12W), up to Day 85 or every 8 weeks (Q8W) up to Day 57.

Placebo Comparator: BIIB132-Matching Placebo: Doses 1 to 5
Participants will receive a BIIB132-matching placebo of Doses 1 to 4, IT, Q4W, up to Day 85 and a BIIB132-matching placebo of Dose 5, IT, either Q4W or Q12W, up to Day 85 or Q8W, up to Day 57.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
BIIB132

Primary outcome measure
1. Number of participants with adverse events (AEs) assessed using National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE, Version 5) from Day 1 to Day 267
2. Number of participants with serious adverse events (SAEs) assessed using National Cancer Institute CTCAE, Version 5 from Screening to Day 267

Secondary outcome measures
1. Area under the concentration-time curve (AUC) of BIIB132 measured using serum samples at pre-dose and multiple timepoints post-dose on Day 1 up to Day 85
2. Area under the concentration versus time curve, from time of dosing (time = 0) to infinity (AUCinf) of BIIB132 measured using serum samples at pre-dose and multiple timepoints post-dose on Day 1 up to Day 85
3. Area under the concentration versus time curve, from time of dosing (time = 0) to time of the last measurable effect (AUClast) of BIIB132 measured using serum samples at pre-dose and multiple timepoints post-dose on Day 1 up to Day 85
4. Maximum observed concentration (Cmax) of BIIB132 measured using serum samples at pre-dose and multiple timepoints post-dose on Day 1 up to Day 85
5. Time to reach maximum observed concentration (Tmax) of BIIB132 measured using serum samples at pre-dose and multiple timepoints post-dose on Day 1 up to Day 85
6. Elimination half-life (t½) of BIIB132 measured using serum samples at pre-dose and multiple timepoints post-dose on Day 1 up to Day 85

Overall study start date
16/02/2022

Completion date
31/03/2025

Eligibility

Key inclusion criteria

1. Diagnosis of SCA3 with CAG repeats ≥60 in ATXN3 gene
2. Symptomatic ataxia with a screening Scale for Assessment and Rating of Ataxia (SARA) score 3 to 15 (still ambulatory) and a minimum SARA gait subscore of 1
3. Able to ambulate 8 m independently without any assistive device
4. Treatment naïve or on a stable dose of symptomatic therapy for a minimum of 4 weeks prior to screening

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
48

Key exclusion criteria
1. Unstable psychiatric illness or untreated major depression within 90 days before screening
2. History or screening magnetic resonance imaging (MRI) results show evidence of structural abnormalities that couldcontribute to the participant's clinical state other than findings typical of SCA3 or any finding that might pose a risk to the participant
3. MRI brain findings of prior cerebellar stroke or clinical stroke within 12 months before screening
4. History of brain surgery regardless of purpose
5. Any contraindications to undergoing brain MRI
6. History of, or ongoing, malignant disease, (with the exception of basal cell carcinomas and squamous cell carcinomas that have been completely excised and considered cured at least 12 months prior to screening). Participants with cancers in remission for longer than 5 years may be included
7. History of epilepsy or the occurrence of seizures within 3 years prior to screening
8. Evidence of untreated/unstable thyroid disease
9. Poorly controlled diabetes mellitus
10. History of alcohol or substance abuse within the past year prior to screening
11. Use of off-label drugs for ataxia within 4 weeks prior to screening
12. Prior enrollment in any interventional clinical study in which an investigational treatment or approved therapy forinvestigational use is administered within 5 half-lives or 3 months, whichever is longer, prior to the screening visit
13. Any antiplatelet (except for aspirin up to 100 mg/day) or anticoagulant medication that cannot be safely interrupted for a lumbar puncture (LP) procedure
14. Any contraindications to LP procedures
15. Participants who are pregnant or currently breastfeeding and those intending to become pregnant during the study
16. Prior enrollment in any interventional clinical study in which an investigational treatment or approved therapy for investigational use is administered within 3 months prior to screening visit

Note: other protocol-defined inclusion/exclusion criteria may apply

Date of first enrolment
17/12/2021

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
England

France

Germany

Israel

Netherlands

Portugal

United Kingdom

Study participating centre
National Hospital for Neurology & Neurosurgery
Queen Square
London
United Kingdom
WC1N 3BG

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
Biogen Idec Research Limited

Sponsor details

Innovation House
70 Norden Road
Maidenhead
England
United Kingdom
SL6 4AY
-
clinicaltrials@biogen.com

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Biogen Idec

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Submission to regulatory authorities
4. Other

Throughout the study, subject data will be identified only by a subject identification number. Personal data will be blinded in all clinical data analyses. Authorised Sponsor personnel, including study monitors, auditors, other relevant parties and health regulatory agencies will have access to personal medical data to ensure a high-quality standard for the study.

Intention to publish date

31/12/2025

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request. For general enquiries, please contact DataSharing@Biogen.com. The data to be shared is the individual participant data collected during the trial, which supports the research proposal, after anonymization and upon approval of the research proposal, along with Study Protocols and Clinical Study Reports. Data will be available 18 months after study completion and post US and EU marketing approvals, with no end date. The data will be shared with qualified scientific researchers who provide a methodologically sound proposal to achieve the objectives in the approved proposal. Proposals should be submitted through Vivli (https://vivli.org). To gain access, data requestors will need to sign a data-sharing agreement. Data are made available for 1 year on a secure platform.
Exceptions to Biogen's Data Sharing Policy:
1. Clinical trials where there is a reasonable likelihood that the study participant could be re-identified, such as with trials of rare diseases and single-center studies.
2. Clinical trials where data sharing is prohibited by the informed consent; or where regulatory, legal, contractual, or other limitations exist.
3. Clinical trials where data/documents are not in English.
4. Clinical trials where there are ongoing regulatory activities or publication plans.
Imaging data (e.g. DICOM files of images from x-rays, ultrasounds, MRI scans, etc) is not generally shared and genomic data is only shared with explicit consent.

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?
HRA research summary			28/06/2023	No	No