Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Determine the Efficacy and Safety of BIIB122/DNL151 in Participants with Parkinson's Disease and Pathogenic LRRK2 Variants

Summary

EudraCT number	2022-000747-77
Trial protocol	DE ES FR IT BE
Global end of trial date	27 July 2023

Results information

Result version number	v2 (current)
This version publication date	28 July 2024
First version publication date	14 March 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	283PD302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05418673
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 Binney Street, Cambridge, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy of BIIB122 225 milligrams (mg) compared with placebo, based on the time to confirmed worsening in Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts II and III combined score.

Protection of trial subjects:

Written informed consent was obtained from each subject or subject's legally authorised representative (e.g., parent or legal guardian), as applicable, prior to evaluations performed for eligibility. Subjects or the subject's legally authorised representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	United Kingdom: 1
Worldwide total number of subjects	7
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2
From 65 to 84 years	5

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at multiple investigative sites in the United States and the United Kingdom from 26 Aug 2022 to 27 Jul 2023.

Pre-assignment

Screening details:

A total of 7 participants were enrolled and treated in the study, but none of the participants completed it.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received BIIB122-matching placebo tablets, orally, once daily (QD) for up to 290 days.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered as specified in the treatment arm.

Arm title	BIIB122 225 mg

Arm description:

Participants received BIIB122 225 milligrams (mg) tablets, orally, QD for up to 290 days.

Arm type	Experimental
Investigational medicinal product name	BIIB122
Investigational medicinal product code	
Other name	DNL151
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered as specified in the treatment arm.

Number of subjects in period 1	Placebo	BIIB122 225 mg
Started	3	4
Completed	0	0
Not completed	3	4
Study Terminated by Sponsor	2	4
Lost to follow-up	1	-

Baseline characteristics

Subject analysis sets	
Subject analysis set title	BIIB 122 or matching-placebo (Pooled)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants either received BIIB122 225 mg or BIIB122-matching placebo tablets, orally, QD for up to 290 days. To maintain blinding, pooled data are reported for baseline characteristics.

Reporting group values	BIIB 122 or matching-placebo (Pooled)		
Number of subjects	7		
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	66.9		
standard deviation	± 10.70		
Gender categorical Units: Subjects			
Male	5		
Female	2		
Ethnicity Units: Subjects			
Not Hispanic or Latino	7		
Race Units: Subjects			
White	7		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received BIIB122-matching placebo tablets, orally, once daily (QD) for up to 290 days.	
Reporting group title	BIIB122 225 mg
Reporting group description:	
Participants received BIIB122 225 milligrams (mg) tablets, orally, QD for up to 290 days.	
Subject analysis set title	BIIB 122 or matching-placebo (Pooled)
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants either received BIIB122 225 mg or BIIB122-matching placebo tablets, orally, QD for up to 290 days. To maintain blinding, pooled data are reported for baseline characteristics.	

Primary: Time to Confirmed Worsening in Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts II and III

End point title	Time to Confirmed Worsening in Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Parts II and III[1]
End point description:	
Time to confirmed worsening is defined as a worsening event sustained over 2 consecutive assessments. MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assesses motor experiences of daily living (range 0-52). It contains 13 questions which are to be completed by the participant. Part III assesses the motor signs of PD and is administered by the rater (range 0-132). Part III contains 33 scores based on 18 items. For each question, a numeric score is assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. MDS-UPDRS Part II and III combined score equals the sum of Parts II and III (range 0-184). A higher score indicates more severe symptoms of PD. Based on the low enrolment number and to protect and maintain participant privacy/confidentiality, no data is reported, as only 1 participant completed post-baseline visit for clinical efficacy outcomes.	
End point type	Primary
End point timeframe:	
From Week 96 to Week 180	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analysis is planned to be analysed.

End point values	Placebo	BIIB122 225 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Days				
median (full range (min-max))	(to)	(to)		

Notes:

[2] - Data were not reported for this endpoint as no participants were analyzed.

[3] - Data were not reported for this endpoint as no participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose results in death; in the view of the investigator, places the participant at immediate risk of death (a life-threatening event); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect or is a medically important event. Safety analysis set.

End point type	Secondary

End point timeframe:

From the first dose (Day 1) of study drug up to end of follow-up (up to 336 days)

End point values	Placebo	BIIB122 225 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	4		
Units: participants				
AEs	2	3		
SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Confirmed Worsening in Modified Schwab and England Activities of Daily Living Scale (mSE-ADL) Score

End point title	Time to Confirmed Worsening in Modified Schwab and England Activities of Daily Living Scale (mSE-ADL) Score

End point description:

Time to confirmed worsening is defined as a worsening event sustained over 2 consecutive assessments. The mSE-ADL scale reflects the speed, ease, and independence with which an individual performs daily activities or personal chores with 100% indicating total independence, falling to 0%, which indicates a state of complete dependence. The individual is asked to rate his or her function using an 11-point scale (10% increments), from 100% (completely independent; able to do all chores without slowness, difficulty, or impairment; essentially normal; unaware of any difficulty) to 0% (vegetative functions such as swallowing, bladder and bowels are not functioning; bedridden). The lower the score, the worse the functional status. Based on the low enrolment number and to protect and maintain participant privacy/confidentiality, no data is reported, as only 1 participant completed post-baseline visit for clinical efficacy outcomes.

End point type	Secondary

End point timeframe:

From Week 96 to Week 180

End point values	Placebo	BIIB122 225 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Days				
median (full range (min-max))	(to)	(to)		

Notes:

[4] - Data were not reported for this endpoint as no participants were analyzed.

[5] - Data were not reported for this endpoint as no participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Confirmed Worsening in MDS-UPDRS Part II Score

End point title	Time to Confirmed Worsening in MDS-UPDRS Part II Score

End point description:

Time to confirmed worsening is defined as a worsening event sustained over 2 consecutive assessments. MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assesses motor experiences of daily living (range 0-52). It contains 13 questions which are to be completed by the participant. Part III assesses the motor signs of PD and is administered by the rater (range 0-132). Part III contains 33 scores based on 18 items. For each question, a numeric score is assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. MDS-UPDRS Part II and III combined score equals the sum of Parts II and III (range 0-184). A higher score indicates more severe symptoms of PD. Based on the low enrolment number and to protect and maintain participant privacy/confidentiality, no data is reported, as only 1 participant completed post-baseline visit for clinical efficacy outcomes.

End point type	Secondary

End point timeframe:

From Week 96 to Week 180

End point values	Placebo	BIIB122 225 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: Days				
median (full range (min-max))	(to)	(to)		

Notes:

[6] - Data were not reported for this endpoint as no participants were analyzed.

[7] - Data were not reported for this endpoint as no participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MDS-UPDRS Parts II and III Combined Score at Week 96

End point title	Change From Baseline in MDS-UPDRS Parts II and III Combined Score at Week 96

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assesses motor experiences of daily living (range 0-52). It contains 13 questions which are to be completed by the participant. Part III assesses the motor signs of PD and is administered by the rater (range 0-132). Part III contains 33 scores based on 18 items. For each question, a numeric score is

assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. MDS-UPDRS Part II and III combined score equals the sum of Parts II and III (range 0-184). A higher score indicates more severe symptoms of PD. Due to the early termination of the study (at week 48), sufficient data were not collected for the outcome measure analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	Placebo	BIIB122 225 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[8] - Data were not reported for this endpoint as no participants were analyzed.

[9] - Data were not reported for this endpoint as no participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MDS-UPDRS Parts I, II, and III Combined Score at Week 96

End point title	Change From Baseline in MDS-UPDRS Parts I, II, and III Combined Score at Week 96

End point description:

The MDS-UPDRS is a multimodal scale consisting of four parts. Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contains 6 questions and are assessed by the examiner (Range 0-24). Part IB contains 7 questions on non-motor experiences of daily living which was completed by the participant (Range 0-28). Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the participant. Part III assessed the motor signs of PD and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score is assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. The MDS-UPDRS Total Score equals the sum of Parts I,II, and III (Range: 0-236). A higher score indicated more severe symptoms of PD. Due to the early termination of the study (at week 48), sufficient data were not collected for the outcome measure analysis.

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	Placebo	BIIB122 225 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: Score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[10] - Data were not reported for this endpoint as no participants were analyzed.

[11] - Data were not reported for this endpoint as no participants were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose (Day 1) of the study drug up to the end of follow-up (up to 336 days)

Adverse event reporting additional description:

SAS included all randomised subjects who received atleast 1 dose of study treatment. Low number of subjects were enrolled in study& some subjects have been rolled over to283PD201(NCT05348785),data was reported as pooled group & preferred terms are reported as system organ class to avoid identification of individual subjects & to maintain blinding.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	BIIB 122 or matching-placebo (Pooled)

Reporting group description:

Participants either received BIIB122 225 mg or BIIB122-matching placebo tablets, orally, QD for up to 290 days.

Serious adverse events	BIIB 122 or matching-placebo (Pooled)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	BIIB 122 or matching-placebo (Pooled)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 7 (71.43%)		
Injury, poisoning and procedural complications			
Injury, Poisoning and Procedural Complications			
subjects affected / exposed	2 / 7 (28.57%)		
occurrences (all)	2		
Nervous system disorders			

Nervous System Disorders subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Ear and labyrinth disorders Ear and Labyrinth Disorders subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders Skin and Subcutaneous Tissue Disorders subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Psychiatric disorders Psychiatric Disorders subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Musculoskeletal and connective tissue disorders Musculoskeletal and Connective Tissue Disorders subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Infections and infestations Infections and Infestations subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 April 2023	A category of medications was added to be used with caution and corresponding updates to exclusionary medications and disallowed concomitant medications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Sponsor decided to stop study based on operational & strategic considerations & not for reasons related to efficacy/safety.Due to early cessation of study before subjects reached timewindow for efficacy assessments,efficacy analysis was not possible.

Notes: