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A study of the effect of BIIB122/DNL151 on midazolam in healthy participants

Submission date 01/04/2024	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 15/04/2024	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 09/05/2024	**Condition category** Other	[_] Individual participant data

Plain English summary of protocol

Background and study aims
This is a drug-drug interaction (DDI) study to investigate the effect of BIIB122/DNL151 on the pharmacokinetics (PK) of oral MDZ and the safety and tolerability of BIIB122/DNL151 when administered alone and along with a single dose of MDZ. A DDI study is conducted to see how the two drugs interact in the body; evaluating PK is figuring out how participants' bodies handle a drug or drugs in combination.

Who can participate?
Healthy volunteers aged 18 - 50 years old

What does the study involve?
The total duration of each participant’s involvement in the study will be approximately 7 weeks. At Visit 1, potential participants will be screened; at Visit 2, participants will be confined in a clinical research unit for 13 days; at Visit 3, participants will have an outpatient visit at the clinical research unit.

What are the possible benefits and risks of participating?
Healthy volunteers will not receive any health benefit from participating in the study. The risks of participation are primarily those associated with adverse reactions to the study treatments and procedures; the risks of DNL151 treatment are based on extensive evaluation of nonclinical studies (ie, animal studies and studies done with cells in a petri dish) and evaluation in clinical studies in healthy participants to characterize the safety profile of BIIB122/DNL151.

Where is the study run from?
Denali Therapeutics (USA)

When is the study starting and how long is it expected to run for?
July 2021 to November 2021

Who is funding the study?
Denali Therapeutics (USA)

Who is the main contact?
Clinical Trials Disclosures Group at Denali Therapeutics, clinical-trials-disclosures@dnli.com

Contact information

Type(s)
Principal Investigator

Contact name
Dr Helen Philpott

Contact details
Simbec-Orion Clinical Pharmacology
Merthyr Tydfil Industrial Park
Cardiff Road
Merthyr Tydfil
United Kingdom
CF48 4DR
+44 (0)1443694315
helen.philpott@simbecorion.com

Type(s)
Public, Scientific

Contact name
Ms Gabrielle Brill

Contact details
Simbec-Orion Clinical Pharmacology
Merthyr Tydfil Industrial Park
Cardiff Road
Merthyr Tydfil
United Kingdom
CF48 4DR
+44 (0)1443 694319
gabrielle.brill@simbecorion.com

Type(s)
Public

Contact name
Dr Clinical Trials Disclosures Group -

Contact details
Denali Therapeutics
-
United States of America
-
None provided
clinical-trials-disclosures@dnli.com

Additional identifiers

EudraCT/CTIS number
2021-002708-10

IRAS number
303787

ClinicalTrials.gov number
NIl known

Secondary identifying numbers
DNLI-C-0008

Study information

Scientific Title
A drug-dr interaction study of the effect of BIIB122/DNL151 on midazolam pharmacokinetics in healthy participants

Study objectives
To assess the pharmacokinetics (PK) of midazolam (MDZ) in the presence and absence of BIIB122 /DNL151

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 13/09/2021, Wales Research Ethics Committee 1 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0) 2922941119; Wales.REC1@wales.nhs.uk), ref: 21/WA/0261

Study design
A fixed sequence crossover drug-drug interaction study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

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
Healthy volunteers

Interventions
Treatment Period 1: Single oral dose of MDZ
Treatment Period 2: Once daily oral dose of BIIB122/DNL151 for 10 consecutive days, coadministered with a single dose of MDZ on the 10th day

The total duration of each participant's involvement in the study will be approximately 7 weeks. At Visit 1, potential participants will be screened; at Visit 2, participants will be confined in a clinical research unit for 13 days; at Visit 3, participants will have an outpatient visit at the clinical research unit.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I

Drug/device/biological/vaccine name(s)
BIIB122/DNL151; midazolam (MDZ)

Primary outcome measure
BIIB122/DNL151 and MDZ PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples, including, but not limited to, the following:
1. Maximum concentration (Cmax)
2. Area under the concentration-time curve from time zero to infinity (AUC∞)
3. Area under the concentration-time curve from time zero to time of last measurable concentration (AUClast)
4. AUC during a dosage interval (tau) (AUCτ)
[Timeframe: Multiple timepoints over 15 days]

Secondary outcome measures
1. BIIB122/DNL151 and MDZ PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples, including, but not limited to, the following:
1.1. Time to maximum concentration (tmax)
1.2. Terminal elimination half-life (t1/2)
[Timeframe: Multiple timepoints over 15 days]

2.Safety assessment including:
2.1. Incidence of treatment-emergent adverse events (TEAEs) and SAEs as reported by the participant [Timeframe: Continuously over 15 days]
2.2. Laboratory assessments of blood and urine samples (including hematology, serum clinical chemistry, and urinalysis) [Timeframe: Multiple timepoints over 15 days]
2.3. 12-lead electrocardiograms (ECGs) [Timeframe: Multiple timepoints over 15 days]

2.4. Vital sign abnormalities [Timeframe: Multiple timepoints over 15 days]
2.5. Physical examinations [Timeframe: Multiple timepoints over 15 days]
2.6. Suicidal ideation and behavior as assessed by the Columbia-Suicide Severity Rating Scale (C-SSRS) [Timeframe: Multiple timepoints over 15 days]

Overall study start date
22/07/2021

Completion date
19/11/2021

Eligibility

Key inclusion criteria
1. Healthy female participants of non-childbearing potential or healthy male participants between 18 and 50 years of age, inclusive
2. Body mass index (BMI) between 18.5 and 31.0 kg/m² and a body weight of at least 50 kg

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
Both

Target number of participants
16

Total final enrolment
14

Key exclusion criteria
1. Take any concomitant medication at the time of screening or during the study, unless deemed acceptable by the investigator (or designee) and Sponsor
2. Any history of hepatic, pulmonary, and/or renal disease
3. History of serious adverse reaction or serious hypersensitivity to any drug
4. History of allergy to any component of the study intervention
5. Have any surgical or medical condition affecting drug absorption (eg, gastrectomy)

Date of first enrolment
27/09/2021

Date of final enrolment
04/11/2021

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec-Orion Clinical Pharmacology (AKA Simbec Research Ltd)
Merthyr Tydfil Industrial Park
Cardiff Road
Merthyr Tydfil
United Kingdom
CF48 4DR

Sponsor information

Organisation
Denali Therapeutics Inc.

Sponsor details
161 Oyster Point Boulevard
South San Francisco
United States of America
94080
+1 (0)650 866 8548
clinical-trials@dnli.com

Sponsor type
Industry

Website
https://www.denalitherapeutics.com/

Funder(s)

Funder type
Industry

Funder Name
Denali Therapeutics

Alternative Name(s)
DENALI, Denali Therapeutics Inc.

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Results summary posted to registry

Intention to publish date
19/04/2024

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are not expected to be made available because of their high commercial sensitivity and the negligible benefit to the public of publication of results of non-therapeutic clinical trials.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		19/04/2024	22/04/2024	No	No