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A drug-drug interaction study of DNL343 on midazolam in healthy participants

Submission date
12/04/2023

Recruitment status
No longer recruiting

Registration date
21/04/2023

Overall study status
Completed

Last Edited
07/06/2024

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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 DNL343 on the pharmacokinetics (PK) of oral midazolam (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 to 65 years.

What does the Study Involve?
The total duration of each participant’s involvement in the study will be approximately 53 days from screening through follow-up.

What are the Possible Benefits and Risks of Participating?
Healthy volunteers will not receive any health benefit (beyond that of an assessment of their medical status) from participating in the study. The risks of participation are primarily those associated with adverse reactions to the study interventions and procedures. DNL343 has been extensively evaluated in nonclinical studies (ie, animal studies and studies done with cells in a petri dish) and evaluation in clinical studies to characterize its safety profile.

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

When is the study starting and how long is it expected to run for?
November 2022 to June 2023

Who is funding the study?
Denali Therapeutics Inc. (USA)

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

Contact information

Type(s)
Principal Investigator

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Public

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Additional identifiers

EudraCT/CTIS number
2022-003926-38

IRAS number
1007175

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 1007175

Study information

Scientific Title
A drug-drug interaction study of the effect of DNL343 on midazolam pharmacokinetics in healthy participants

Study objectives
To assess the pharmacokinetics (PK) of midazolam (MDZ) in the presence and absence of DNL343

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 10/03/2023, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)2922941119; Wales.REC2@wales.nhs.uk), ref: 23/WA/0041
2. Approved 14/03/2023, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0)20 3080 6000; info@mhra.gov.uk), ref: CTA 50398/0011/001-0001
The HRA approved the deferral of the publication of trial details. Full details were added after the deferral ended.

Study design
Fixed sequence crossover drug-drug interaction study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Pharmaceutical testing facility

Study type(s)
Other

Participant information sheet
Not available in web format

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 DNL343 for 14 days then coadministered with a single dose of MDZ on the 14th day

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I

Drug/device/biological/vaccine name(s)
DNL343, midazolam (MDZ)

Primary outcome measure
MDZ PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples including, but not limited to, the following at multiple timepoints over 25 days:
1. Maximum concentration (Cmax)
2. Time to reach maximum concentration (tmax)
3. Area under the concentration-time curve from time zero to infinity (AUC∞)
4. Terminal elimination half-life (t1/2)

Secondary outcome measures
1. Incidence of treatment-emergent adverse events (TEAEs) and SAEs as reported by the participant continuously over 25 days:
2. MDZ metabolite PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples including, but not limited to, the following at multiple timepoints over 25 days:
2.1 Maximum concentration (Cmax)
2.2 Time to reach maximum concentration (tmax)
2.3 Area under the concentration-time curve from time zero to infinity (AUC∞)
2.4 Terminal elimination half-life (t1/2)
3. DNL343 PK parameters, as measured by laboratory analysis of plasma concentrations from blood samples including, but not limited to, the following at multiple timepoints over 25 days:
3.1 AUC during a dosage interval (tau) (AUCτ)
3.2 Maximum concentration at steady state (Cmax,ss)

Overall study start date
30/11/2022

Completion date
09/06/2023

Eligibility

Key inclusion criteria
1. Healthy female participants of non-childbearing potential or healthy male participants between 18 and 65 years of age, inclusive
2. Body mass index (BMI) between 18.5 and 30 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
65 Years

Sex
Both

Target number of participants
16

Total final enrolment
16

Key exclusion criteria
1. Any history of hepatic, pulmonary, and/or renal disease
2. History of serious adverse reaction or serious hypersensitivity to any drug
3. History of allergy to any component of the study intervention
4. Have any surgical or medical condition affecting drug absorption (eg, gastrectomy)

Date of first enrolment
29/03/2023

Date of final enrolment
15/05/2023

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec-Orion Clinical Pharmacology (AKA Simbec Research Ltd)
Merthyr Tydfil Industrial Park

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Sponsor information

Organisation
Denali Therapeutics Inc.

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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
10/03/2025

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		25/03/2024	09/05/2024	No	No