

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

Submission date 12/04/2023	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 21/04/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 07/06/2024	Condition category Other	<input type="checkbox"/> 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

Contact name

Dr Helen Philpott

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Type(s)

Public

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Contact details

Denali Therapeutics

-

United States of America

-

None provided

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Additional identifiers

Clinical Trials Information System (CTIS)

2022-003926-38

Integrated Research Application System (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

Study type(s)

Other

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

Phase

Phase I

Drug/device/biological/vaccine name(s)

DNL343, midazolam (MDZ)

Primary outcome(s)

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 (C_{max})
2. Time to reach maximum concentration (t_{max})
3. Area under the concentration-time curve from time zero to infinity (AUC_∞)
4. Terminal elimination half-life (t_{1/2})

Key secondary outcome(s)

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 (C_{max})
 - 2.2 Time to reach maximum concentration (t_{max})
 - 2.3 Area under the concentration-time curve from time zero to infinity (AUC_∞)
 - 2.4 Terminal elimination half-life (t_{1/2})
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) (AUC_τ)
 - 3.2 Maximum concentration at steady state (C_{max,ss})

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

65 years

Sex

All

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

Cardiff Road

Merthyr Tydfil

United Kingdom

CF48 4DR

Sponsor information**Organisation**

Denali Therapeutics Inc.

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

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