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A study evaluating the effect of itraconazole on DNL343 in healthy participants

Submission date	Recruitment status	[_] Prospectively registered
05/03/2024	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/03/2024	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
31/01/2025	Other	

Plain English summary of protocol

Background and study aims
This is a drug-drug interaction (DDI) study designed to evaluate the pharmacokinetics (PK), safety, and tolerability of a single dose of DNL343 in the absence and presence of itraconazole (ITZ) with a planned enrollment of 16 healthy participants. A DDI study is run to see how 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 - 55 years

What does the study involve?
The total duration of each participant’s involvement in the study will be approximately 73 days from screening through follow-up.

What are the possible benefits and risks of participating?
Healthy participants in this study will not receive any health benefit from participating in the study. The risks of DNL343 treatment are based on extensive evaluation in 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. The potential risks of participation are primarily those associated with adverse reactions to the study interventions (DNL343 and ITZ).

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

When is the study starting and how long is it expected to run for?
December 2021 to July 2022

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

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

Clinical Trials Information System (CTIS)
2021-006382-37

Integrated Research Application System (IRAS)
310753

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
DNLI-F-0005, IRAS 310753

Study information

Scientific Title
A fixed-sequence, drug-drug interaction study evaluating the effect of the cytochrome P450 3A inhibitor itraconazole on DNL343 in healthy participants

Study objectives
To evaluate the pharmacokinetics (PK) safety, and tolerability of a single dose of DNL343 in the absence and presence of itraconazole.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 18/01/2022, Wales Research Ethics Committee 2 (Health and Care Research Wales Castlebridge 4 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0) 2922941119; Wales.REC2@wales.nhs.uk), ref: 22/WA/0009

Study design
Phase 1 single-center open-label fixed-sequence drug-drug interaction study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
Single oral dose of DNL343 without and with repeating oral doses of itraconazole.

The total duration of each participant’s involvement in the study will be approximately 73 days from screening through follow-up.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
DNL343; itraconazole

Primary outcome(s)
DNL343 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)
[Timeframe: Multiple timepoints over 45 days]

Key secondary outcome(s))
Incidence, severity, and seriousness of treatment-emergent adverse events (TEAEs) as reported by the participant (or, when appropriate, by a caregiver, a surrogate, or the participant's legally authorized representative)
[Timeframe: Continuously over 45 days]

Completion date
25/07/2022

Eligibility

Key inclusion criteria
1. Healthy male participants and healthy female participants of non-childbearing potential
2. Aged ≥18 to ≤55 years
3. Body mass index (BMI) of ≥18.5 to ≤30 kg/m²
4. Body weight of ≥50 kg

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
55 years

Sex
All

Total final enrolment
24

Key exclusion criteria
1. History of clinically significant endocrine, pulmonary, cardiovascular, gastrointestinal, hepatic, pancreatic, renal, metabolic, hematologic, immunologic, or allergic disease, or other major disorders
2. History of malignancy, except fully resected basal cell carcinoma
3. History of clinically significant neurological or psychiatric diseases
4. History of serious adverse reaction or serious hypersensitivity to any drug, or history of allergy to any component of the DNL343 or itraconazole products
5. Are pregnant (ie, positive pregnancy test) or breastfeeding

Date of first enrolment
09/02/2022

Date of final enrolment
18/05/2022

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 (United States)

ROR
https://ror.org/00pprn321

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		21/07/2023	31/01/2025	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes