# ACENT 1

15/12/2025 07:23:31

## Main Information

**Primary registry identifying number**
LBCTR2024015480

**Protocol number**
NN7533-4470

**MOH registration number**

**Study registered at the country of origin**
Yes

**Study registered at the country of origin: Specify**

**Type of registration**
Prospective

**Type of registration: Justify**
N/A

**Date of registration in national regulatory agency**
15/01/2024

**Primary sponsor**
Novo Nordisk

**Primary sponsor: Country of origin**
Denmark

**Date of registration in primary registry**
26/03/2024

**Date of registration in national regulatory agency**
15/01/2024

**Public title**
ACENT 1

**Acronym**

**Scientific title**
A multicentre trial evaluating the efficacy and safety of oral decitabine-tetrahydrouridine (NDec) in patients with sickle cell disease

**Acronym**

**Brief summary of the study: English**

Sickle cell disease (SCD) pathophysiology is driven by the polymerisation of mutated sickle cell haemoglobin (HbS) in red blood cells. Foetal haemoglobin (HbF) decreases polymerisation of HbS but is epigenetically silenced in early infancy and onward by DNA methyltransferase 1 (DNMT1). A mechanism to re-induce HbF expression is via epigenetic therapy by inhibiting DNMT1 activity. NDec is an oral formulation of a combination of decitabine and tetrahydrouridine. Decitabine depletes DNMT1 while tetrahydrouridine inhibits cytidine deaminase, the enzyme that otherwise rapidly deaminates/inactivates decitabine.

The primary purpose of this trial is to investigate two dosing regimens of oral decitabinetetrahydrouridine (NDec) in terms of treatment-related effects on total haemoglobin and HbF as well as clinical efficacy and safety parameters compared with placebo in patients with SCD who are not receiving hydroxyurea (HU) treatment at screening (HU-non-eligible patients). An active comparator HU treatment arm is included to allow exploratory comparisons between NDec and HU in patients receiving HU treatment at screening (HU-active patients).

**Brief summary of the study: Arabic**

في خلايا الدم الحمراء. يقلل (HbS) مدفوعة ببلمرة الهيموغلوبين المنجلي المتحور (SCD) الفيزيولوجيا المرضية لمرض فقر الدم المنجلي ولكن يتم إسكاته وراثيا في مرحلة الطفولة المبكرة وما بعدها بواسطة HbS من بلمرة (HbF) الهيموغلوبين الجنيني DNA methyltransferase 1 (DNMT1). هي عن طريق العلاج اللاجيني عن طريق تثبيط نشاط HbF آلية إعادة تحفيز تعبير DNMT1. بينما يثبط رباعي هيدروووريدين DNMT1عبارة عن تركيبة فموية لمزيج من ديسيتابين وتتراهيدرويوريدين. يستنفد ديسيتابين ال NDec الديأميناز السيتيدين، وهو الإنزيم الذي يزيل / يعطل ديسيتابين بسرعة.

من حيث التأثيرات (NDec) الغرض الأساسي من هذه التجربة هو التحقيق في نظامين لجرعات ديسيتابينيتتراهيدروريدين عن طريق الفم بالإضافة إلى الفعالية السريرية ومعايير السلامة مقارنة بالدواء الوهمي في المرضى الذين HbF المرتبطة بالعلاج على إجمالي الهيموغلوبين و HU). يتم تضمين ذراع علاج HU المرضى غير المؤهلين ل) عند الفحص (HU) الذين لا يتلقون علاج هيدروكسي يوريا SCD يعانون من عند الفحص (المرضى النشطين في HU في المرضى الذين يتلقون علاج HU و NDec للمقارنة النشطة للسماح بإجراء مقارنات استكشافية بين HU).

**Health conditions/problem studied: Specify**

Patients with Sickle Cell Disease.

**Interventions: Specify**

Patients will be receiving a new medication oral decitabinetetrahydrouridine (NDec).

**Key inclusion and exclusion criteria: Inclusion criteria**

Key inclusion criteria:
- Age above or equal to 18 years at the time of signing informed consent
- Confirmed diagnosis of SCD (including HbSS, HbSC, HbSβ0 thalassaemia and HbSβ+ thalassaemia or other Sickle Cell disease variants)
- 2–10 episodes of documented VOCs within the last 12 months prior to the screening visit
- Haemoglobin ≥5.0 g/dL and ≤10.5 g/dL at visit 1
- Absolute reticulocyte (absolute) count above ULN at visit 1
- Body weight 40 to 125 kg (inclusive)

**Key inclusion and exclusion criteria: Gender**

Both

**Key inclusion and exclusion criteria: Specify gender**

**Key inclusion and exclusion criteria: Age minimum**

18

**Key inclusion and exclusion criteria: Age maximum**

75

**Key inclusion and exclusion criteria: Exclusion criteria**

Key exclusion criteria:
- Patient is on chronic transfusion therapy as defined by receiving scheduled (pre-planned) series of blood transfusion (simple or exchange) for prophylactic purposes, or the patient is likely to begin chronic transfusion therapy during the course of the trial, or has received RBC or whole blood transfusion for any reason within 28 days of visit 1
- Receipt of erythropoietin or other haematopoietic growth factor treatment within 28 days of signing ICF, or planned treatment with these agents during the trial
- Receipt of voxelotor, crizanlizumab or L-glutamine treatment within 12 weeks of signing the informed consent form, or planned treatment with such agents during the trial
- Platelet count >800 x 109/L at visit 1
- Absolute neutrophil count ≤1.5 x 109/L at visit 1
- Any condition/concurrent chronic disease involving the stomach or small intestine which may affect drug absorption, as per investigator's judgement
- Female who is:
    - pregnant, breast-feeding or intends to become pregnant within 6 months after the final trial product administration or
    - child-bearing potential and not using highly effective methods of contraception and whose male partner is not using effective contraception, at screening and until 6 months after the last dose of trial product
- Male with female partner of childbearing potential who does not agree to use condom and whose female partner of childbearing potential is not using a highly effective contraceptive measure from trial start to:
    - Six (6) months after the last dose of trial product for patients on NDec/Placebo
    - Six (6) months after the last dose of trial product for patients outside US and CA randomised to HU
    - Twelve (12) months after the last dose of trial product for patients randomised to HU in US and CA

**Type of study**

Interventional

**Type of intervention**

Pharmaceutical

**Type of intervention: Specify type**

N/A

**Trial scope**

Other

**Trial scope: Specify scope**

**Study design: Allocation**

**Study design: Masking**

Randomized controlled trial

Blinded (masking used)

**Study design: Control**

Placebo

**Study phase**

2

**Study design: Purpose**

Treatment

**Study design: Specify purpose**

N/A

**Study design: Assignment**

Parallel

**Study design: Specify assignment**

N/A

**IMP has market authorization**

No

**IMP has market authorization: Specify**

**Name of IMP**

Oral decitabine-tetrahydrouridine

**Year of authorization**

**Month of authorization**

**Type of IMP**

Others

**Pharmaceutical class**

Haemoglobin F inducer

**Therapeutic indication**

Patients with sickle cell disease

**Therapeutic benefit**

NDec is being investigated for efficacy and safety for use as a disease-modifying treatment to prevent complications associated with SCD. NDec specifically targets the root cause of the disease (polymerization of haemoglobin S (HbS)), and treatment might therefore provide therapeutic benefits and improve outcomes. Among clinical benefits, patients may have fewer and/or less severe VOCs and a reduced need for blood transfusion when treated with NDec. They may also experience fewer hospital visits/admissions into hospital, and fewer days spent in hospital. Patients treated with NDec might also experience improvements in laboratory parameters predicting clinical benefits in laboratory parameters, including, but not limited to, an increase in total Hb and HbF levels and decreases in measures of haemolysis. HbF decreases erythrocyte sickling and subsequent haemolysis. Clinical observations and standard clinical practice indicate that an increase in total haemoglobin by decreasing haemolytic anaemia is clinically meaningful (improvement in an established surrogate for clinical benefit).

**Study model**

N/A

**Study model: Explain model**

N/A

**Study model: Specify model**

N/A

**Time perspective**

N/A

**Time perspective: Explain time perspective**

N/A

**Time perspective: Specify perspective**

N/A

**Target follow-up duration**

**Target follow-up duration: Unit**

**Number of groups/cohorts**

**Biospecimen retention**

Samples with DNA**

**Biospecimen description**

Genetic variation may impact a patient's response to trial treatment, susceptibility to, and severity and progression of disease. Variable response to trial treatment may be due to genetic determinants that impact drug absorption, distribution, metabolism and excretion, mechanism of action of the drug, disease aetiology, and/or molecular subtype of the disease being treated. Therefore, where local regulations and IRB/IEC allow, samples will be collected for DNA analysis from consenting patients. DNA samples will be used for research related to NDec and SCD and other heamatological diseases. Genetic research may consist of the analysis of one or more candidate genes, or the analysis of genetic markers throughout the genome or analysis of the entire genome as appropriate.

**Target sample size**

87

**Actual enrollment target size**

**Date of first enrollment: Type**

Anticipated

**Date of first enrollment: Date**

26/02/2024

**Date of study closure: Type**

Anticipated

**Date of study closure: Date**

31/08/2025

**Recruitment status**

Pending

**Recruitment status: Specify**

**Date of completion**

**IPD sharing statement plan**

No

**IPD sharing statement description**

Not applicable

**Additional data URL**

**Admin comments**

**Trial status**

Approved

## Secondary Identifying Numbers

No Numbers

## Sources of Monetary or Material Support

| Name |
|---|
| Novo Nordisk A/S |

## Secondary Sponsors

No Sponsors

## Contact for Public/Scientific Queries

| Contact type | Contact full name | Address | Country | Telephone | Email | Affiliation |
|---|---|---|---|---|---|---|
| Public | Badiaa Masri | Sin el Fil, Azar building | Lebanon | 009613003245 | bams@novonordisk.com | Novo Nordisk Pharma SARL |
| Scientific | Antoine Gebrayel | Sin el Fil, Azar Building | Lebanon | 0096176586409 | aogb@novonordisk.com | Novo Nordisk Pharma SARL |

## Centers/Hospitals Involved in the Study

| Center/Hospital name | Name of principles investigator | Principles investigator speciality | Ethical approval |
|---|---|---|---|
| Nini Hospital | Dr. Adlette Inati | Paediatric Haematologist Oncologist | Approved |

## Ethics Review

| Ethics approval obtained | Approval date | Contact name | Contact email | Contact phone |
|---|---|---|---|---|
| Nini Hospital | 11/12/2023 | Elias Bitar | NA | 00961 6 431 400 Ext: 3164 |

## Countries of Recruitment

| Name |
|---|
| Lebanon |
| Turkey |
| United States of America |
| France |
| Spain |
| Italy |
| South Africa |
| Canada |
| Greece |
| India |
| United Kingdom |

## Health Conditions or Problems Studied

| Condition | Code | Keyword |
|---|---|---|
| Sickel Cell | Sickle-cell disorders (D57) | Sickle cell disease (SCD) Foetal haemoglobin (HbF) mutated sickle cell haemoglobin (HbS) |

## Interventions

| Intervention | Description | Keyword |
|---|---|---|
| HU-non-eligible block | NDec once weekly: 1 dose of active treatment and 1 dose of placebo on 2 consecutive days  NDec twice weekly: 1 dose of active treatment on each of 2 consecutive days  Placebo: 1 dose of placebo on each of 2 consecutive days | decitabine-tetrahydrouridine (NDec) Placebo |
| HU-active block | HU | hydroxyurea HU |

## Primary Outcomes

| Name | Time Points | Measure |
|---|---|---|
| Change in total haemoglobin | From baseline (week 0) to week 24 | g/dL |

## Key Secondary Outcomes

| Name | Time Points | Measure |
|---|---|---|
| Cmax for decitabine from pharmacokinetic assessment | At week 24 | ng/mL |
| Cmax for tetrahydrouridine from pharmacokinetic assessment | At week 24 | ng/mL |
| Change in DNMT1 activity | From baseline (week 0) to week 24 | MFI |
| Change in CDA activity | From baseline (week 0) to week 24 | µmol/L/min |
| Change in foetal haemoglobin (g/dL) | From baseline (week 0) to week 24 | g/dL |
| Number of adverse events of grade 3b or higher | From baseline (week 0) to week 52 | Number of events |

## Trial Results

**Summary results**

**Study results globally**

**Date of posting of results summaries**

**Date of first journal publication of results**

**Results URL link**

**Baseline characteristics**

**Participant flow**

**Adverse events**

**Outcome measures**

**URL to protocol files**