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# Investigating the effects of repeated once-daily administration of the non-hormonal Neurokinin 1,3 receptor antagonist NT-814 on sex hormone levels in healthy women

**Submission date**
14/09/2020

**Recruitment status**
No longer recruiting

**Registration date**
18/09/2020

**Overall study status**
Completed

**Last Edited**
13/08/2021

**Condition category**
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Endometriosis is a condition where small pieces of the womb lining (the endometrium) are found outside the womb. Uterine fibroids are non-cancerous growths that develop in or around the womb. The ideal treatment for endometriosis and uterine fibroids would lower the female sex hormone estrogen, whilst avoiding the menopausal flushing and bone loss associated with current treatments. Substance P and neurokinin B bind to the neurokinin (NK) receptors 1 and 3, respectively, to control reproductive hormone levels. NT-814 is a new, non-hormonal treatment which blocks the NK 1,3 receptors. However, the effects of NT-814 on reproductive hormone levels in healthy women is currently unknown. Current treatments for hormone-driven disorders, such as endometriosis and uterine fibroids, are limited by side effects and effectiveness. The aim of this study is to assess the effectiveness and safety of NT-814 in healthy women.

Who can participate?
Healthy women aged 18-45 with regular menstrual cycles, not taking any medications or hormonal contraception

What does the study involve?
Healthy women attend for two consecutive menstrual cycles. No treatment is given in Cycle 1. During Cycle 2, women are randomly allocated to receive placebo (dummy drug) or NT-814 40 mg, 80 mg or 120 mg for up to 21 days. In each cycle, blood samples are taken on days 3/4, 9/10, 15/16 and 21/22 to measure blood reproductive hormone levels.

What are the possible benefits and risks of participating?
Regular monitoring (using blood samples, clinical observations and ECG) are used throughout to maintain participant safety.

Where is the study run?
Quotient Sciences (USA)

When is the study starting and how long is it expected to run?
February 2019 to September 2019

Who is funding the study?
KaNDy Therapeutics (USA)

Who is the main contact?
Dr Steve Pawsey
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# Contact information

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Public

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# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers
814-1-05

# Study information

### Scientific Title
A randomized, single-blind, placebo-controlled study of the effects of repeat doses of NT-814 on oestradiol and other sex hormone concentrations in healthy pre-menopausal female volunteers

### Study objectives
NT-814 is a dual NK1,3 receptor antagonist and therefore has the theoretical potential to reduce GnRH pulsatility by blocking the endogenous effects of NKB and substance P on the reproductive axis. This would lower LH levels and subsequently estradiol concentrations in healthy pre-menopausal women.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 22/05/2019, Institutional Review Board Advarra (6940 Columbia Gateway Drive, Suite 110, Columbia, MD 21046, USA; +1 (0)410 884 2900; adviser@advarra.com), ref: Pro00034218

### Study design
Single-centre phase 1 randomized single-blind placebo-controlled study

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Other

### Study type(s)
Treatment

### Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

### Health condition(s) or problem(s) studied
Reproductive hormone levels in women with hormone-driven disorders

### Interventions
This is a Phase 1, randomized, single-blind, placebo-controlled study designed to determine the effects of NT-814 (40, 80, 120, 160 mg once daily) on GnRH pathway hormones in healthy female subjects.

Thirty-two healthy women attend for two consecutive menstrual cycles. In each cycle, blood samples are taken on days 3/4, 9/10, 15/16 and 21/22 to measure serum reproductive hormone levels, and plasma NT-814 levels (Cycle 2 only). No treatment is given in Cycle 1 (baseline). During Cycle 2, participants are randomized by block randomization to receive placebo or NT-814 40 mg, 80 mg or 120 mg (n=8 per group) for up to 21 days.

### Intervention Type
Drug

### Phase
Phase I

### Drug/device/biological/vaccine name(s)
NT-814: a novel, non-hormonal NK1,3 antagonist

### Primary outcome measure
GnRH pathway hormones measured using serum LH, FSH, oestradiol and progesterone concentrations on Days 3/4, 9/10, 15/16 and 21/22 in both Cycle 1 (baseline) and Cycle 2 (treatment)

### Secondary outcome measures
1. The safety of NT 814 measured using clinical laboratory assessments (haematology and biochemistry), vital signs (BP and HR), and recording of treatment-emergent adverse events on Days 3/4, 9/10, 15/16 and 21/22 in both Cycle 1 (baseline) and Cycle 2 (treatment)
2. The PK-PD relationship of NT-814 measured using NT-814 plasma concentration levels during Cycle 2 Days 3/4, 9/10, 15/16 and 21/22
3. Menstrual cycle length measured using the difference in cycle length (in days) between Cycle 1 and Cycle 2

### Overall study start date
01/02/2019

### Completion date
30/09/2019

## Eligibility

### Key inclusion criteria
1. Healthy, female, aged 18 to 45 years inclusive (age at time of informed consent)
2. Have regular (approximately) monthly menstrual periods
3. Be able and willing to understand and comply with the requirements of the study and give written informed consent
4. Have a body mass index (BMI) in the range 18.0 to 32.0 kg/m2 and body weight not less than 40.0 kg
5. Be judged to be in good health, based on the results of medical history, physical examination, vital signs, 12-lead ECG, and clinical laboratory findings
6. Not be pregnant and not lactating, with no intention of pregnancy during study treatment
7. Agree to use two acceptable methods of birth control, one of which a barrier method with spermicide for the duration of participation in the study and 30 days after the last dose of study medication

## Participant type(s)
Healthy volunteer

## Age group
Adult

## Lower age limit
18 Years

## Sex
Female

## Target number of participants
32 women

## Total final enrolment
33

## Key exclusion criteria
1. Been previously enrolled in this study or any other study with NT-814
2. Have clinically significant findings on physical examination at screening
3. Have any relevant medical history, in particular: liver or renal insufficiency, cholecystectomy, significant cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, haematologic, rheumatologic, psychiatric, or metabolic disturbances, any inflammatory illness or any other condition that the Investigator considers should exclude the subject
4. Undergone bilateral oophorectomy and/or hysterectomy
5. Have positive serology for any of hepatitis B, hepatitis C, or human immunodeficiency virus (HIV)
6. Have any serum biochemistry and full blood count outside the normal reference ranges and considered by the Investigator to be of clinical significance, assessed at screening and on Cycle 1 Day 21/22. Haemoglobin must not be less than 11.0 g/dL at either screening or Day 21/22
7. Have Stage 2 or higher hypertension (supine/semi-recumbent systolic blood pressure [SBP] >160 mmHg; diastolic blood pressure [DBP] >100 mmHg or Stage 1 hypertension (supine/semi-recumbent SBP 140 160 mmHg; DBP 90 100 mmHg associated with indication for treatment i.e. evidence of end-organ damage, diabetes or a 10 year cardiovascular risk, estimated using a standard calculator, e.g. https://qrisk.org/three/, greater than 20%. Measurements are based on the mean of duplicate values recorded at least 2 minutes apart and are assessed at screening, on Cycle 1 Day 21 or 22 and pre-dose on Cycle 2 Day 1 or 2
8. Have clinically relevant abnormal 12 lead ECG, including QTcF >450 msec, QRS interval >120 msec, PR interval >220 msec, assessed at screening, on Cycle 1 Day 21 or 22 and pre-dose on Cycle 2 Day 1 or 2; if any value are out of range, two repeated assessments are permitted at that time point and the value based on the mean of the triplicate measure
9. Have a history of any grade of drug or alcohol use disorder according to Diagnostic and Statistical Manual of Mental Disorders 5 criteria (or later edition if applicable) within 6 months before Screening or have a positive test result(s) for drugs of abuse (opiates including methadone, cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates, and benzodiazepines) at screening, Cycle 1 Day 21 or 22, or Cycle 2 Day 1 or 2
10. Have a clinically significant acute illness within 7 days before first study drug administration
11. Been drinking, on average, more than 6 cups of coffee or other caffeinated beverages daily (where each cup of coffee or beverage contained approximately 120 mg caffeine)

12. Been smoking more than an average of 5 cigarettes (or equivalent) per day
13. Use any non-permitted prior prescription, over-the-counter or herbal medication
14. Have a history of clinically significant drug and/or food allergies, particularly known allergy to any of the excipients used in the study medications
15. Receive an investigational drug (including vaccines) or use an investigational medical device within 3 calendar months before the first dose of study medication or currently enrolled in an investigational study
16. Have major surgery within 2 calendar months before first dose of study medication, or surgery planned during the time the subject is expected to participate in the study
17. Donate blood or experienced acute loss of a significant amount of blood within 3 calendar months before first dose of study medication
18. Have psychological and/or emotional problems that would render the informed consent invalid or limited the ability of the subject to comply with the study requirements
19. Have any condition for which, in the opinion of the Investigator, participation would not have be in the best interest of the subject or that could prevent, limit, or confound the protocol-specified assessments

### Date of first enrolment
06/06/2019

### Date of final enrolment
16/07/2019

## Locations

### Countries of recruitment
United States of America

### Study participating centre
**Quotient Sciences**
3898 NW 7th St
Miami
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FL 33126

## Sponsor information

### Organisation
KaNDy Therapeutics

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### Sponsor type
Industry

# Funder(s)

### Funder type
Industry

### Funder Name
KaNDy Therapeutics

# Results and Publications

### Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

### Intention to publish date
01/12/2020

### Individual participant data (IPD) sharing plan
Based on the sponsor's data transparency policy (https://www.clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Bayer.aspx), individual patient-level data will not be published for this type of study (single centre, small patient number) in order to avoid the risk for re-identification of participants.

### IPD sharing plan summary
Not expected to be made available

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol file | version V1.0 | 10/05/2019 | 08/10/2020 | No | No |
| Results article | | 13/07/2021 | 13/08/2021 | Yes | No |