Buccal Apomorphine (APORON) administration

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26898

Source
Nationaal Trial Register

Brief title
CHDR1933

Health condition

Parkinson's Disease

Sponsors and support

Primary sponsor: Criceto
Source(s) of monetary or material Support: Sponsor

Intervention

Outcome measures

Primary outcome

Primary part A
-Apomorphine plasma concentrations
o Derived parameters including but not limited to Cmax, Tmax, Tlag, T1/2, AUC, relative bioavailability
o Dose-normalized AUC and Cmax

o Ratio of buccal to subcutaneous AUC and Cmax

Primary part B
- Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III
o Change from baseline in MDS-UPDRS part III of apomorphine compared to placebo
o 90% confidence interval of the estimated difference in change from baseline MDS-UPDRS part III between buccal and subcutaneous apomorphine
o Number of responders based on ≥ 7 points improvement of MDS-UPDRS part III
- Disease State Assessment by physician (5 categories: 'on' with disabling dyskinesia, 'on' with non-disabling dyskinesia, 'on' state with no dyskinesia and normal motor function, partial 'on' state and 'off' state).
o Number and percentage of patients turning ON
o Number and percentage of patients ON at each time point
- Patient ON/OFF assessment (3 categories: OFF, partial ON, full ON)
o Number and percentage of patients who achieved a full on response within 30 min post-dose
- Apomorphine plasma concentrations (parameters as above for Part A)
- Treatment-emergent (serious) adverse events ((S)AEs).
- Concomitant medication
- Clinical laboratory tests
o Haematology
o Chemistry
o Coagulation
o Urinalysis
- Vital signs
o Pulse Rate (bpm)
o Systolic blood pressure (mmHg)
o Diastolic blood pressure (mmHg)
o Orthostatic hypotension (delta mmHg sit-sta)
o Respiratory rate (breaths/min)
o Pulse oximetry (SpO2) (%)
- ECG
o Heart Rate (HR) (bpm), PR, QRS, QT, QTcF

Primary part C
- Treatment-emergent (S)AEs
- Concomitant medication
- Clinical laboratory tests (as above)
- Vital signs (as above)
- ECG (as above)
- C-SSRS

Secondary outcome

Secondary Part A
- Treatment-emergent (S)AEs
- Concomitant medication

- Clinical laboratory tests (as above)
- Vital signs (as above)
- ECG (as above)

Secondary part C
- Percentage of patients in each response category (no improvement/ slight improvement /moderate improvement/ full ON response
within 30 minutes after administration of buccal apomorphine) as based on interview by phone and on patient diaries.
- Question during phone call which determines patient preference for buccal or subcutaneous administration.
- Average buccal dose used in Part C of the study
- Daily used subcutaneous dose in clinical practice before entering the study

Study description

Background summary

APORON is a novel formulation of apomorphine. Apomorphine is a registered drug indicated for the treatment of off-periods in patients
with Parkinson's disease. Currently, apomorphine is often administered via subcutaneous injections, which can cause pain, local injection site reactions and may be difficult to use for patients when they are experiencing an off-period. APORON is a highly concentrated apomorphine buccal spray formulation which is expected to be easy and painless to self-administer and has the same efficacy as the subcutaneous injection.

Study objective

To determine the pharmacokinetics, (local) tolerability and efficacy of a buccal apomorphine spray (APORON) and compare it with a subcutaneous apomorphine injection (and placebo).

Study design

Up to -31 days till EOS

Intervention

subcutaneous apomorphine (APO-go® 5 ml ampoules 10 mg/ml)
buccal apomorphine (APORON)
saline placebo injection
buccal apomorphine placebo spray (APORON formulation without apomorphine)

Contacts

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Eligibility criteria

Inclusion criteria

Part A
1) Male or female, 30-85 years of age, inclusive at screening.
4) Clinical diagnosis (confirmed by a neurologist) of Parkinson’s disease and classified by the investigator as Hoehn and Yahr stage I to IV in the ON state.
5) Having clear, self-described motor fluctuations as assessed by the 9-symptom Wearing-off Questionnaire (WOQ-9): at least one motor symptom (Question 1, 2, 4, 6, 9) indicated to improve after the subject’s next antiParkinson medication dose.
6) Mini-Mental State Examination (MMSE) score ≥ 20 and assessed by the investigator or qualified designee as able to provide informed consent.

Part B and C
1) Male or female, 30-85 years of age, inclusive at screening.
4) Clinical diagnosis (confirmed by a neurologist) of Parkinson’s disease and classified by the investigator as Hoehn and Yahr stage I to III in the ON state.
5) Mini-Mental State Examination (MMSE) score ≥ 20 and assessed by the investigator or qualified designee as able to provide informed consent.
8) On a stable dose of 1 to 4 mg subcutaneous apomorphine (APO-GO PEN) for the management of OFF episodes for at least 4 weeks prior to first study drug administration.
9) Subject’s at-home subcutaneous apomorphine injection location is the abdomen.
11) Subjects who experience motor fluctuations (as assessed by the 9-symptom Wearing-off Questionnaire (WOQ-9): at least one motor symptom (Question 1, 2, 4, 6, 9) indicated to improve after the subject’s next antiParkinson medication dose) with recognizable OFF periods at least once per day.

Exclusion criteria

Part A:
1) Atypical or secondary parkinsonism e.g., multiple-system atrophy or progressive supranuclear palsy, or evidence of drug-induced parkinsonism.
2) Subjects with a borderline QT interval corrected for heart rate according to Fridericia's formula (QTcF) of >450 ms for male and >470 ms for female, PR interval > 220 msec or QRS duration > 120 msec at screening or history
of long QT syndrome.
6) Currently taking medication that can influence the efficacy of apomorphine in the opinion of the investigator, such as dopamine antagonists and dopamine depleting drugs, with the exception of domperidone.

Part B and C:
1) Atypical or secondary parkinsonism e.g., multiple-system atrophy or progressive supranuclear palsy, or evidence of drug-induced parkinsonism.
2) Subjects with a borderline QT interval corrected for heart rate according to Fridericia's formula (QTcF) of >450 ms for male and >470 ms for female, PR interval > 220 msec or QRS duration > 120 msec at screening or history
of long QT syndrome.
4) Use of apomorphine formulations other than subcutaneous injections in the 4 weeks prior to first dosing.
7) Currently taking medication that can influence the efficacy of apomorphine in the opinion of the investigator, such as dopamine antagonists and dopamine depleting drugs, with the exception of domperidone.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-04-2021

Enrollment:	46
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
N.A.

Ethics review

Positive opinion
Date:	21-06-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 52414
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9540
CCMO	NL71179.056.20
OMON	NL-OMON52414

Study results

Summary results

N.A.