Buccal Apomorphine (APORON) administration

Gepubliceerd: 21-06-2021 Laatst bijgewerkt: 15-05-2024

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

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26898

Bron
NTR

Verkorte titel
CHDR1933

Aandoening

Parkinson's Disease

Ondersteuning

Primaire sponsor: Criceto
Overige ondersteuning: Sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

Up to -31 days till EOS

Onderzoeksproduct en/of interventie

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

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	27-04-2021
Aantal proefpersonen:	46
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting
N.A.

Ethische beoordeling

Positief advies

Datum:	21-06-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 52414
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N.A.