Multiple dose study of YTX-7739

Gepubliceerd: 05-01-2021 Laatst bijgewerkt: 15-05-2024

To investigate the safety, tolerability and pharmacokinetics after multiple daily doses of YTX-7739

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

Samenvatting

ID

NL-OMON20317

Bron
Nationaal Trial Register

Verkorte titel
CHDR1916 / 7739-01-002

Aandoening

Parkinson's Disease

Ondersteuning

Primaire sponsor: Yumanity Therapeutics
Overige ondersteuning: Sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- Safety:
o Safety and tolerability of YTX-7739 will be measured by assessing the severity and incidence of treatment-emergent adverse events (TEAEs), clinical laboratory tests, ECGs, vital signs and physical examinations.
- Pharmacokinetic:

o The non-compartmental PK parameters of YTX-7739 will be estimated including AUC, C(max), T(max), elimination half-life (t1/2) and elimination rate constant (Ke).

Toelichting onderzoek

Achtergrond van het onderzoek

There are currently no disease-modifying drugs available for the major age-related neurodegenerative diseases, including Parkinson’s disease (PD). The lack of therapies results from a poor understanding of disease biology, unproven predictive value of animal models, challenges in translating pharmacology from animals to man and difficulties in patient stratification and assessment of clinical response. These challenges are exacerbated by a lack of novel drug targets and drug molecules. Yumanity Therapeutics uses a proprietary discovery platform that seeks to identify novel drug targets and drug molecules that protect cells from toxicity
caused by the accumulation of misfolded proteins. Using this platform, the Yumanity team determined that elevated cellular levels of monounsaturated fatty acids regulates toxicity caused by alpha-synuclein, the major protein component of Lewy body pathology and a key genetic risk factor for Parkinson’s disease. In a variety of cellular assay systems, inhibitors of the enzyme stearoyl-CoAdesaturase (SCD) reduce levels of monounsaturated fatty acids and also reduce alpha-synuclein toxicity. YTX-7739 is a novel, orally active inhibitor of SCD enzymatic activity.Here, we aim to explore the safety, tolerability and pharmacokinetic properties of YTX-7739, as well as the pharmacodynamic response to YTX-7739, following 14-28 daily doses in healthy adult volunteers and individuals with Parkinson’s Disease.

Doel van het onderzoek

To investigate the safety, tolerability and pharmacokinetics after multiple daily doses of YTX-7739

Onderzoeksopzet

-56 Days - EOS

Onderzoeksproduct en/of interventie

YTX-7739
Placebo

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Part A
1. Adult male or female subjects 18-55 years of age, inclusive.
Part B
2. Male or female subjects 40-75 years of age, inclusive, with a confirmed diagnosis of Parkinson’s disease (Hoehn and Yahr grade 1-3.

Part A + B
3. Healthy status as defined by absence of evidence of any significant active acute or chronic disease or illness following a detailed medical and surgical history, a complete physical examination including vital signs, 12-lead ECG, hematology, blood chemistry and urinalysis, as judged by the investigator;
4. Body mass index (BMI) between 18-32 kg/m2, inclusive, and with a minimum weight of 50kg and maximum weight of 120kg
5. If subject is a female, she agrees to report onset and duration of menses if it occurs anytime during participation in the study (screening to end of study)
6. Evidence of a personally signed and witnessed informed consent document indicating that the subject has been informed of all pertinent aspects of the study;

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Part A:
1. Clinically significant findings as determined by medical history taking, physical

examination, , fundoscopy, ECG, laboratory findings (including lipid or hormone profiles) and vital signs;
2. Hemodynamic status at screening: systolic blood pressure <100 or >160 mmHg, diastolic blood pressure <50 or >95 mmHg, heart rate <45 or >100 bpm;

Part B:
3. Clinically significant findings as determined by medical history taking, MRI, physical examination, fundoscopy, ECG and vital signs, other that Parkinson's disease;
4. Any current, clinically significant, known medical condition other than Parkinson's disease. Patients with a diagnosis of neurological diseases, other than Parkinson's disease, including Alzheimer's disease, Huntington's disease, vascular dementia, progressive supranuclear gaze palsy, multiple system atrophy, drug-induced parkinsonism, essential tremor, primary dystonia, epilepsy, etc., that are considered clinically relevant by the investigator.
5. Dementia indicated by MMSE <18 at Screening;
6. Use of drugs known to prolong QT interval;
7. Hemodynamic status at screening: results that are considered clinically relevant by the investigator;
8. Any contra-indication to performing a MRI (including (an history of) a cardiac pacemaker, implanted cardiac defibrillator, neurostimulator, hydrocephalus pomp, drug pump, stents or clips in vessels, non-removable hearing aid, non-removable implants containing a magnet in the jaw, tissue expander in the breast, IUD, metal splinters of fragments in the body, non-removable medication patch, tattoo or permanent make-up applied less than 6 weeks ago, non-removable piercing, non-removable hair extensions containing metal);
9. An history of claustrophobia, tinnitus or hyperacusis;
10. An history of allergic reaction during previous MRI examination;
11. History of repeated head injury; history of epilepsy or seizure disorder other than febrile seizures as a child
12. Reside in a nursing home or assisted care facility
13. Concomitant disease or condition that could interfere with, or treatment of which might interfere with, the conduct of the study, or that would, in the opinion of the Investigator, pose an unacceptable risk to the participant in this study or interfere with the participant's ability to comply with study procedures or abide by study restrictions, or with the ability to interpret safety data
14. Prior lack of response to dopaminergic medication (for example, levodopa or a dopaminergic agonist)
15. Continuous use of any of the following within 30 days prior to baseline: antipsychotics (including clozapine and olanzapine), metoclopramide, alpha methyldopa, clozapine, olanzapine, flunarizine, amoxapine, amphetamine derivatives, reserpine, bupropion, buspirone, cocaine, mazindol, methamphetamine, methylphenidate, norephedrine, phentermine, phenylpropanolamine, and modafinil. Single use up to 7 days prior to the start of the study is allowed for metoclopramide.

Part A + B
16. Legal incapacity or inability to understand or comply with the requirements of the study;
17. Subjects with a QTcF of > 450 ms for males and > 470 ms for females at screening or a history of long QT syndrome;
18. Any current, clinically significant, known medical condition;

19. Pregnant, lactating or breast-feeding women
20. Have a urine drug screen detecting illicit drug(s) of abuse (morphine, benzodiazepines, cocaine, amphetamine, THC) or positive alcohol breath test at screening. For part B, a positive urine drug screen for prescribed medication is allowed at the discretion of the investigator;
21. Consume, on average, >8 units/day of (methyl)xanthines (e.g., coffee, tea, cola, chocolate) and not able to refrain from use during each stay at the CHDR clinic;
22. History or clinical evidence of alcoholism or drug abuse;
23. Smoking of >5 cigarettes/day or equivalent and not being able to refrain from smoking cigarettes for the duration of the study. For Parkinson's disease patients, smoking up to 5 cigarettes/day is allowed during the study;
24. Being on a diet composed of relevantly altered amounts of fat, protein or carbohydrates that may affect triglyceride and fatty acid levels (such as high-fat, gluten-free, carbohydrate-free, protein rich diets);
25. Gastrointestinal disease (such as irritable bowel syndrome, inflammatory bowel disease, chronic gastritis, peptic ulcer disease, etc.) that could affect absorption of the study drug;
26. History of gastric surgery, including Roux-en-Y gastric bypass surgery, an antrectomy with vagotomy, or gastrectomy;

27. Use of prescription, illicit or herbal medication within 7 days or 5 half-lives of study initiation, except for contraception; For part B, use of concomitant medication for treatment of Parkinson's disease and comorbidities is allowed.
28. Participation in a clinical trial with an investigational drug or device within 90 days of first dosing or more than 4 times in the previous year;
29. Loss of blood ≥ 500 ml within 3 months before screening;
30. Not willing to practice effective contraception during the study and not willing and able to continue contraception for at least 3 months after their last dose of study treatment;
31. Positive blood screen for human immunodeficiency virus (HIV antibody), hepatitis B virus surface antigen, or hepatitis C virus antibody at screening
32. History of spinal cord compression, any other current abnormalities in the lumbar region (skin infection, structural abnormalities in lower spine, etc.), or any other issue that, in the opinion of the investigator, would make CSF collection unsafe.
33. Contact lens wearer who does not agree to use glasses instead of lenses starting at least 7 days prior to study initiation and during the study.
34. History of eye dryness or diagnosis of dry eye.
35. History of cultivating plants or crops using rotenone or paraquat or MPTP containing pesticides during a period of over 10 years
36. Allergy to any component of YTX-7739

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	13-09-2020
Aantal proefpersonen:	48
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:	05-01-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 55131
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9172
CCMO	NL72549.056.20
OMON	NL-OMON55131

Resultaten

Samenvatting resultaten
N.A.