Phase 1 Dose Escalation Study Assessing the Safety and Pharmacokinetics of PTC518 in Healthy Subjects

Published: 27-08-2020
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Primary ObjectivesPart 1:To characterize the safety and tolerability of single ascending doses of PTC518 in healthy subjects.Part 2:To characterize the safety and tolerability of PTC518 administered for 14 or up to 21 days in healthy subjects.Part 3...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Interventional

Summary

ID

NL-OMON54972

Source
ToetsingOnline

Brief title
CS0349-200101 PTC518

Condition

- Congenital and hereditary disorders NEC

Synonym
Huntington's Disease

Research involving
Human

Sponsors and support

Primary sponsor: PTC Therapeutics, Inc.
Source(s) of monetary or material Support: PTC Therapeutics;Inc.

Intervention

Keyword: Pharmacokinetics, Safety

Outcome measures

Primary outcome

Part 1 - Single Ascending Dose:

Type, frequency, severity, timing, and relationship to study treatment of any adverse events (AEs), laboratory abnormalities, vital signs abnormalities, physical examination abnormalities or ECG abnormalities when PTC518 is administered as a single dose.

Part 2 - Multiple Ascending Dose:

Type, frequency, severity, timing, and relationship to study treatment of any AEs, laboratory abnormalities, vital signs abnormalities, physical examination abnormalities, ECG abnormalities, and C-SSRS scores when PTC518 is administered as multiple doses.

Part 3 - CSF

PTC518 concentrations in blood and CSF when PTC518 is administered for 7 days.

Part 4 - Food Effect:

PK parameters, eg, Tmax, Cmax, AUC, elimination half-life (t1/2), apparent total body clearance (CL/F), and apparent volume of distribution (Vd/F) when PTC518 is administered in fed (Part 4) and fasted (Part 1) states.

Part 5 (MD28D):

Type, frequency, severity, timing, and relationship to study treatment of any AEs, laboratory abnormalities, vital signs abnormalities, physical examination abnormalities, ECG abnormalities, and C-SSRS scores when PTC518 is administered

as multiple doses.

Secondary outcome

Part 1 - Single Ascending Dose:

PK parameters, eg, Tmax, Cmax, AUC, elimination half-life (t1/2), apparent total body clearance (CL/F), and apparent volume of distribution (Vz/F) when PTC518 is administered as a single dose.

Part 2 - Multiple Ascending Dose:

PK parameters, eg, Tmax, Cmax, AUC, elimination half-life (t1/2), apparent total body clearance (CL/F), and apparent volume of distribution (Vz/F) when PTC518 is administered as multiple doses.

QT, and the corrected QT interval by Fridericia*s formula (QTcF) extracted from Holter monitoring and PTC518 plasma concentration-QTc effects.

Part 3 - CSF

Type, frequency, severity, timing, and relationship to study treatment of any AEs, laboratory abnormalities, vital signs abnormalities, physical examination abnormalities, ECG abnormalities and C-SSRS scores when PTC518 is administered for 7 days.

Part 4 - Food Effect:

Type, frequency, severity, timing, and relationship to study treatment of any AEs, laboratory abnormalities, vital signs abnormalities, physical examination abnormalities or ECG abnormalities when PTC518 is administered in fed state and compare with those in part 1 (fasted).

Part 5 (MD28D):

PK parameters, eg, Tmax, Cmax, AUC, T1/2, CL/F, and V z/F when PTC518 is

administered as multiple doses.

QT, and the corrected QT interval by Fridericia*s formula (QTcF) extracted from

Holter monitoring and PTC518 plasma concentration-QTc effects.

Study description

Background summary

PTC518 is an orally bioavailable, selective Huntingtin (HTT) pre-mRNA splicing modifier designed to distribute uniformly and decrease the levels of HTT protein in the central nervous system (CNS) and periphery. This small molecule modulates splicing of the HTT pre-mRNA, resulting in the inclusion of a novel pseudoexon (located within an intron) carrying a premature translation termination codon. This leads to the degradation of HTT mRNA, and a reduction in HTT protein levels.For further details see the IB.

Study objective

Primary Objectives
Part 1:
To characterize the safety and tolerability of single ascending doses of PTC518 in healthy subjects.
Part 2:
To characterize the safety and tolerability of PTC518 administered for 14 or up to 21 days in healthy subjects.
Part 3:
To characterize the pharmacokinetics in plasma and cerebrospinal fluid (CSF) after administration of PTC518 for 7 days in healthy subjects.
Part 4:
To characterize the food effect on the PK in plasma of PTC518 after administration of a single dose of PTC518 in healthy subjects.
Part 5:
To characterize the safety and tolerability of PTC518 administered for up to 28 days in healthy subjects.

Secondary Objectives
Part 1:
To characterize the pharmacokinetics of single doses of PTC518 in healthy subjects.
Part 2:
• To characterize the pharmacokinetics of PTC518 administered for 14 or up to

21 days in healthy subjects.
• To assess the QTc and drug concentration effect of PTC518 after repeated ascending doses.
Part 3:
To assess safety and tolerability of PTC518 after administration for 7 days in healthy subjects.
Part 4:
To characterize the safety and tolerability of single doses of PTC518 administered in the fed state in healthy subjects.
Part 5:
To characterize the pharmacokinetics of PTC518 administered for up to 28 days in healthy subjects

Study design

This is a 5 part, single-center, randomized SAD, MAD, and FE study.

Intervention

PTC518 as 5 mg and 50 mg tablets.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IB for further information.

Contacts

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PTC Therapeutics, Inc.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. For Part 1, Part 2, Part 4, and Part 5: Healthy male or female subjects aged from 18 to 65 years old, inclusive, at Screening. For Part 3: healthy male of female subjects aged 50 to 65 years old, inclusive, at Screening.
2. Subjects must understand the nature of the study and must provide signed and dated written informed consent before the conduct of any study-related procedures.
3. Body Mass Index (BMI) of >=18.5 kg/m2 and <=30.0 kg/m2 with a body weight >=50.0 kg for male subjects and a body weight >=45.0 kg for female subjects at Screening.
4. Healthy as determined by the Investigator, based upon a medical evaluation including medical history, physical examination, laboratory test results, ECG recording (e.g. QTcF <= 450 msec for males and QTcF <= 470 ms for females) and vital signs. Out of range values can be repeated once.
5. Male subjects and female subjects of childbearing potential must be willing to use 2 methods of birth control for the duration of the study and for 30 days after the last dosing.

Exclusion criteria

1. Subjects that participated in any drug or device clinical investigation within 60 days prior to Screening or who anticipate participating in any drug or device clinical investigation within the duration of this study.
2. Prior or ongoing medical condition (e.g., concomitant illness, psychiatric condition), medical history, physical findings that, in the Investigator*s opinion, could adversely affect the safety of the subject or could impair the assessment of study results.
3. An abnormal general neurological examination.
4. Presence of any clinically significant abnormality during Screening.

5. Any psychological, emotional problems, any disorders or resultant therapy that is likely to invalidate informed consent or limit the ability of the subject to comply with the protocol requirements.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-11-2020
Enrollment:	136
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap
Generic name:	Nap

Ethics review

Approved WMO

Date:	27-08-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO

Date:	15-10-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-02-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-03-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-04-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-05-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-06-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	21-06-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	26-07-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-09-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-003439-33-NL
CCMO	NL74780.000.20

Study results

Results posted: 30-11-2022

Summary results
Trial ended prematurely

First publication
01-07-2022

URL result
Type
int
Naam
M2.1 Wetenschappelijke samenvatting M2 - Synopsis CSR PTC518, dated 01 July 2022
URL