Clinical trial results:
A comparative phase2 study assessing the efficacy of triheptanoin, an anaplerotic therapy in Huntington's Disease (TRIHEP 3)

Summary

EudraCT number	2014-005112-42
Trial protocol	FR NL
Global end of trial date	02 January 2020

Results information

Result version number	v1 (current)
This version publication date	21 April 2022
First version publication date	21 April 2022

Trial information

Trial identification

Sponsor protocol code	C14-62

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	INSERM
Sponsor organisation address	8, rue de la croix Jarry, Paris, France, 75013
Public contact	Sonia GUEGUEN, INSERM, 33 144236041, rqrc.siege@inserm.fr
Scientific contact	Sonia GUEGUEN, INSERM, 33 144236041, rqrc.siege@inserm.fr

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 December 2019
Global end of trial reached?	Yes
Global end of trial date	02 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

the primary objectice is to evaluate the efficacy of triheptanoin in
- increasing the energy response in the metabolic profile of the brain of early affected HD patients , as captured by 31-Phosphorus Magnetic Resonance Spectroscopy
- slowing atrophy in the caudate of early affected HD patients as measured with volumetric resonance imaging

Protection of trial subjects:

Trial was performed as described on the CPP (Committee for people's protection) decision #33-15 .

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 48
Country: Number of subjects enrolled	France: 52
Worldwide total number of subjects	100
EEA total number of subjects	100

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	100
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

TRIHEP 3 is a multi-centre (Paris and Leiden) randomized, double-blind, controlled study recruiting 100 early HD patients. Patients will receive either triheptanoin or a placebo for 6 months followed by a 6 month open-label phase with triheptanoin. At the end of the open-label phase, an extension period of 1 year may be proposed.

Pre-assignment

Screening details:

A screening visit will be conducted in which information about the study will be provided and patients will have the opportunity to ask any questions. Inclusion/non-inclusion criteria including the ability to undergo MRI scanning will be verified to confirm the patient's eligibility for the study.

Period 1

Period 1 title	Full study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

To ensure acceptability for patients, we conducted a 6-month randomized controlled bi-centric trial (Paris and Leiden) called TRIHEP3 (NCT02453061), comparing triheptanoin 1g/kg/day vs placebo in 100 patients (ratio 1/1) at an early stage of HD, followed by a 6-month open label phase. After one year, patients could opt for a one-year extension study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

triheptanoin treated arm

Arm type	Active comparator
Investigational medicinal product name	triheptanoin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid, Oral solution, Oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

triheptanoin 1g/kg/day

Arm title	Comparator arm

Arm description:

To perform a comparative analysis of triheptanoin versus placebo over one year, we used the placebo arm of a one-year randomized controlled trial (NCT02336633), conducted in parallel with identical methods, in HD patients with similar clinical characteristics (age, disease duration, TMS, CAG repeats).

Arm type	Placebo
Investigational medicinal product name	Safflower oil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

1g/kg/dqy

Number of subjects in period 1	Active	Comparator arm
Started	50	50
Completed	50	50

Baseline characteristics

Reporting groups	
Reporting group title	Active
Reporting group description:	
triheptanoin treated arm	
Reporting group title	Comparator arm
Reporting group description:	
To perform a comparative analysis of triheptanoin versus placebo over one year, we used the placebo arm of a one-year randomized controlled trial (NCT02336633), conducted in parallel with identical methods, in HD patients with similar clinical characteristics (age, disease duration, TMS, CAG repeats).	

Reporting group values	Active	Comparator arm	Total
Number of subjects	50	50	100
Age categorical			
Units: Subjects			
Adults (18-64 years)	46	47	93
From 65-84 years	4	3	7
Gender categorical			
Units: Subjects			
Female	32	30	62
Male	18	20	38

Subject analysis sets	
Subject analysis set title	Comparator arm
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
external placebo control group	
Subject analysis set title	Active arm
Subject analysis set type	Full analysis
Subject analysis set description:	
To ensure acceptability for patients, we conducted a 6-month randomized controlled bi-centric trial (Paris and Leiden) called TRIHEP3 (NCT02453061), comparing triheptanoin 1g/kg/day vs placebo in 100 patients (ratio 1/1) at an early stage of HD, followed by a 6-month open label phase. After one year, patients could opt for a one-year extension study.	

Reporting group values	Comparator arm	Active arm	
Number of subjects	50	50	
Age categorical			
Units: Subjects			
Adults (18-64 years)	46	47	
From 65-84 years	4	3	
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	Active
Reporting group description: triheptanoin treated arm	
Reporting group title	Comparator arm
Reporting group description: To perform a comparative analysis of triheptanoin versus placebo over one year, we used the placebo arm of a one-year randomized controlled trial (NCT02336633), conducted in parallel with identical methods, in HD patients with similar clinical characteristics (age, disease duration, TMS, CAG repeats).	
Subject analysis set title	Comparator arm
Subject analysis set type	Sub-group analysis
Subject analysis set description: external placebo control group	
Subject analysis set title	Active arm
Subject analysis set type	Full analysis
Subject analysis set description: To ensure acceptability for patients, we conducted a 6-month randomized controlled bi-centric trial (Paris and Leiden) called TRIHEP3 (NCT02453061), comparing triheptanoin 1g/kg/day vs placebo in 100 patients (ratio 1/1) at an early stage of HD, followed by a 6-month open label phase. After one year, patients could opt for a one-year extension study.	

Primary: rate of caudate atrophy at 6 months

End point title	rate of caudate atrophy at 6 months
End point description: The primary outcome measure was the rate of caudate atrophy at 6 months using cBSI (caudate boundary shift integral).	
End point type	Primary
End point timeframe: 6 months	

End point values	Active	Comparator arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Cubic centimetre				
number (not applicable)	50	50		

Statistical analyses

Statistical analysis title	method
Statistical analysis description: To ensure acceptability for patients, we conducted a 6-month randomized controlled bi-centric trial followed by a 6-month open label phase. After one year, patients could opt for a one-year extension study. To perform a comparative analysis of triheptanoin versus placebo over one year, we used the placebo arm of a one-year randomized controlled trial (NCT02336633), conducted in parallel with identical methods, in HD patients with similar clinical characteristics (age, disease duration, CAG-rep)	

Comparison groups	Comparator arm v Active
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 48 hours	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	1
Reporting groups	
Reporting group title	Active
Reporting group description: triheptanoin treated arm	
Reporting group title	Comparator arm
Reporting group description: To perform a comparative analysis of triheptanoin versus placebo over one year, we used the placebo arm of a one-year randomized controlled trial (NCT02336633), conducted in parallel with identical methods, in HD patients with similar clinical characteristics (age, disease duration, TMS, CAG repeats).	

Serious adverse events	Active	Comparator arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Active	Comparator arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 50 (4.00%)	2 / 50 (4.00%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 50 (4.00%)	2 / 50 (4.00%)	
occurrences (all)	2	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported