Clinical trial results:
A Multi-Center, Open-Label Study Evaluating the Safety, Tolerability, and Efficacy of Pridopidine in Patients with Huntington's Disease (Open PRIDE-HD) (Open PRIdopidine Dose Evaluation in Huntington's Disease)

Summary

EudraCT number	2015-000904-24
Trial protocol	DE GB AT NL IT
Global end of trial date	12 January 2018

Results information

Result version number	v2 (current)
This version publication date	26 August 2021
First version publication date	11 March 2021
Version creation reason	• Correction of full data set alignment with CT.gov

Trial information

Trial identification

Sponsor protocol code	TV7820-CNS-20016

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02494778
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Prilenia Neurotherapeutics Ltd.
Sponsor organisation address	Hamenofim 10, Herzliya, Israel, 4672561
Public contact	Michal Geva, Prilenia Neurotherapeutics Ltd., clinicaltrialseu@prilenia.com
Scientific contact	Michal Geva, Prilenia Neurotherapeutics Ltd., clinicaltrialseu@prilenia.com

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	10 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 January 2018
Global end of trial reached?	Yes
Global end of trial date	12 January 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate safety and tolerability of pridopidine in patients with Huntington's Disease (HD).

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator:

No comparison drug was used in this open-label study.

Actual start date of recruitment	24 September 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: 9
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Austria: 18
Country: Number of subjects enrolled	France: 18
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	Italy: 34
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Russian Federation: 34
Country: Number of subjects enrolled	United States: 34
Worldwide total number of subjects	248
EEA total number of subjects	167

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)	215
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

248 patients, ≥21 years of age, with a body weight of ≥50 kg, with a diagnosis of HD who completed the double-blind, randomized phase in PRIDE-HD study, including the follow-up period, or who participated in the open-label ACR16C015 (Open-HART) extension study, were scheduled to be included in this study.

Pre-assignment

Screening details:

The study consisted of a screening period/baseline visit of up to 2 weeks.

Period 1

Period 1 title	Overall trial (78 weeks) (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

This was an open-label study with no blinding.

Arms

Arm title	Pridopidine 45 mg bid

Arm description:

Pridopidine (45 mg) was administered as oral capsules, taken twice daily (bid).

Arm type	Experimental
Investigational medicinal product name	Pridopidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine (45 mg) was administered as oral capsules, taken twice a day (bid).

Number of subjects in period 1	Pridopidine 45 mg bid
Started	248
Completed	27
Not completed	221
Consent withdrawn by subject	20
Adverse event, non-fatal	18
Other	173
Death	3
Noncompliance with study drug administration	1
Lost to follow-up	2
Lack of efficacy	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (78 weeks)

Reporting group description: -

Reporting group values	Overall trial (78 weeks)	Total	
Number of subjects	248	248	
Age categorical Units: Subjects			
Adults (18-64 years)	215	215	
From 65-84 years	33	33	
Age continuous Units: years			
arithmetic mean	50.6		
standard deviation	± 11.61	-	
Gender categorical Units: Subjects			
Female	129	129	
Male	119	119	

End points

End points reporting groups

Reporting group title	Pridopidine 45 mg bid
Reporting group description:	
Pridopidine (45 mg) was administered as oral capsules, taken twice daily (bid).	

Primary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events[1]
End point description:	
End point type	Primary
End point timeframe:	
78 weeks	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No statistical analyses have been specified for this primary end point.	

End point values	Pridopidine 45 mg bid			
Subject group type	Reporting group			
Number of subjects analysed	248			
Units: Patients	193			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative Motor (Q-motor) Measurements, Pro-Sup-Inter-Onset-interval-SD-Hand

End point title	Change From Baseline in Quantitative Motor (Q-motor) Measurements, Pro-Sup-Inter-Onset-interval-SD-Hand
End point description:	
Q-motor assessments were based on the application of force transducers and 3-dimensional position sensors. The reported parameter is the Pro-Sup-Inter-Onset-interval-SD-Hand, measured in seconds. Positive change from baseline indicates worsening.	
End point type	Secondary
End point timeframe:	
Week 52, end of treatment (EOT)	

End point values	Pridopidine 45 mg bid			
Subject group type	Reporting group			
Number of subjects analysed	146			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Change from baseline to Week 52	0.0 (± 0.05)			
Change from baseline to EOT	-0.1 (± 0.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Quantitative Motor (Q-motor) Measurements, Pro-Sup-Peak-Force-CV-Hand

End point title	Change From Baseline in Quantitative Motor (Q-motor) Measurements, Pro-Sup-Peak-Force-CV-Hand

End point description:

Q-motor assessments were based on the application of force transducers and 3-dimensional position sensors. The reported parameter is the Pro-Sup-Peak-Force-CV-Hand, measured in %. Positive change from baseline indicates worsening.

End point type	Secondary

End point timeframe:

Week 52, end of treatment (EOT)

End point values	Pridopidine 45 mg bid			
Subject group type	Reporting group			
Number of subjects analysed	146			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Change from baseline to Week 52	-2.9 (± 9.31)			
Change from baseline to EOT	-5.9 (± 8.05)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

78 weeks

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Pridopidine 45 mg bid

Reporting group description: -

Serious adverse events	Pridopidine 45 mg bid		
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 248 (12.50%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma in situ			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 248 (1.21%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Depression			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination, auditory				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paranoia				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Weight decreased				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Fall				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 248 (1.61%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 248 (0.81%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain contusion				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Contusion				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Craniocerebral injury				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Extradural haematoma				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Head injury				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Skull fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skull fractured base				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Huntington’s disease				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Chorea				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 248 (1.21%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Dystonia				

alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral nerve palsy				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Dysphagia				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal polyp haemorrhage				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 248 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
alternative assessment type: Systematic				

subjects affected / exposed	2 / 248 (0.81%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Cachexia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 248 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Pridopidine 45 mg bid		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	191 / 248 (77.02%)		
Investigations			
Weight decreased			
alternative assessment type: Systematic			

subjects affected / exposed	13 / 248 (5.24%)		
occurrences (all)	13		
Injury, poisoning and procedural complications			
Fall			
alternative assessment type: Systematic			
subjects affected / exposed	74 / 248 (29.84%)		
occurrences (all)	163		
Contusion			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 248 (5.24%)		
occurrences (all)	20		
Nervous system disorders			
Chorea			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 248 (9.27%)		
occurrences (all)	30		
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 248 (5.65%)		
occurrences (all)	19		
Psychiatric disorders			
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 248 (8.06%)		
occurrences (all)	27		
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 248 (6.45%)		
occurrences (all)	17		
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 248 (5.65%)		
occurrences (all)	15		
Infections and infestations			

Nasopharyngitis alternative assessment type: Systematic subjects affected / exposed occurrences (all)	29 / 248 (11.69%) 36		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2015	Amendment 1 to the protocol was issued before any patients were enrolled into the study. Following the voluntary harmonization procedure protocol assessment, the primary reasons for this amendment were to limit the duration of treatment with study drug to 52 weeks and to clarify the use of permitted medications and prohibited tricyclic antidepressants. The following major procedural changes were made to the protocol: • Treatment with study drug was limited to 52 weeks. • Butriptyline and mianserin were removed from the list of allowed antidepressants, and trimipramine and mirtazapine were removed to clarify the use of the permitted medications and prohibited tricyclic and tetracyclic antidepressants. • Clarification of the assessment time points following the limitation of the study drug treatment duration to 52 weeks.
31 March 2016	Amendment 2 to the protocol was issued after 94 patients were enrolled into the study. Changes to the protocol were considered to have no negative impact on the safety of patients already enrolled into the study. The primary reason for this global amendment was to implement the following major procedural changes made to the protocol: • The 2 telephone calls for safety evaluation at weeks 18 and 38 were added, including C-SSRS and an abbreviated PBA-s assessment. • The treatment duration in the study was extended by an additional period of 52 weeks (for a total of 104 weeks). • Q-Motor assessments were added to the protocol as an efficacy measure. • Suicidal thoughts and ideations were defined as protocol-defined adverse events for expedited reporting.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
10 November 2017	This was an open-label extension of study TV7820-CNS-20002. It was terminated on 10 Nov 2017, as it was considered by the sponsor to have served its purpose in providing long-term safety data. Study termination was not based on safety concerns.	-

Notes:

Limitations and caveats

None reported