Clinical trial results:
A Phase 2, Dose-Finding, Randomized, Parallel-Group, Double-Blind, Placebo-Controlled Study, Evaluating the Safety and Efficacy of Pridopidine 45 mg, 67.5 mg, 90 mg, and 112.5 mg Twice-Daily versus Placebo for Symptomatic Treatment in Patients with Huntington's Disease

Summary

EudraCT number	2013-001888-23
Trial protocol	DE IT NL AT PL DK
Global end of trial date	07 July 2016

Results information

Result version number	v1
This version publication date	09 March 2018
First version publication date	09 March 2018

Trial information

Trial identification

Sponsor protocol code	TV7820-CNS-20002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02006472
WHO universal trial number (UTN)	-
Other trial identifiers	Sponsor study acronym: PRIDE-HD

Notes:

Sponsors

Sponsor organisation name	Teva Branded Pharmaceutical Products R&D, Inc
Sponsor organisation address	41 Moores Road, Frazer, Pennsylvania, United States, 19355
Public contact	Global Head Clinical Development, Neurodegenerative Diseases, Teva Branded Pharmaceuticals Products R&D, Inc., 001 215-591-3000, info.era-clinical@teva.de
Scientific contact	Global Head Clinical Development, Neurodegenerative Diseases, Teva Branded Pharmaceuticals Products R&D, Inc., 001 215-591-3000, info.era-clinical@teva.de

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	08 August 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of pridopidine 67.5 to 112.5 mg twice daily(bid) on motor impairment in patients with Huntington's Disease (HD) after 26 weeks of treatment using the Unified Huntington's Disease Rating Scale Total Motor Score (TMS).

Protection of trial subjects:

This study was conducted in full accordance with the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline (E6) and any applicable national and local laws and regulations (eg, Code of Federal Regulations Title 21, Parts 50, 54, 56, 312, and 314; European Union (EU) Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of
GCP in the conduct of clinical trials on medicinal products for human use).

Written and/or oral information about the study was provided to all patients in a language understandable by the patients. The information included an adequate explanation of the aims, methods, anticipated benefits, potential hazards, and insurance arrangements in force. Written informed consent was obtained from each patient before any study procedures or assessments were done. It was explained to the patients that they were free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment.
Each patient's willingness to participate in the study was documented in writing in a consent form that was signed by the patient with the date of that signature indicated. Each investigator kept the original consent forms, and copies were given to the patients.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	7 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Poland: 50
Country: Number of subjects enrolled	United Kingdom: 39
Country: Number of subjects enrolled	Austria: 27
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 46
Country: Number of subjects enrolled	Italy: 56

Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	United States: 63
Worldwide total number of subjects	408
EEA total number of subjects	262

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)	360
From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 492 patients were screened for enrollment; 408 patients at 53 centers in Australia, Austria, Canada, Denmark, France, Germany, Italy, the Netherlands, Poland, Russia, the United Kingdom, and the US met entry criteria

Period 1

Period 1 title	Treatment Period #1 (Week 26)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Randomization was performed by IRT using dynamic randomization to balance the treatment groups within centers and neuroleptics use or no use. Patients were randomly and equally assigned to the 5 treatment groups of the study (4 active treatment groups and placebo, allocation ratio of 1:1:1:1:1). All of the roles listed were blinded until the database was locked for analysis after the first 26-week study period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients in the Placebo arm were only supplied placebo capsules which were taken from Day 1 to Week 26 in Period 1.

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Arm title	Pridopidine 45 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 26 (Period 1).

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Arm title	Pridopidine 67.5 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 26 (Period 1).

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Arm title	Pridopidine 90 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 26 (Period 1).

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard

Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Arm title	Pridopidine 112.5 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 26 (Period 1).

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Number of subjects in period 1	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid
Started	82	81	82
Completed	70	59	65
Not completed	12	22	17
Consent withdrawn by subject	3	9	3
Adverse event, non-fatal	5	6	11
Not specified	1	5	-
Non-compliance	2	1	1
Protocol deviation	1	1	1
Lack of efficacy	-	-	1

Number of subjects in period 1	Pridopidine 90 mg bid	Pridopidine 112.5 mg bid
Started	81	82
Completed	67	62
Not completed	14	20
Consent withdrawn by subject	-	3

Adverse event, non-fatal	11	14
Not specified	2	3
Non-compliance	-	-
Protocol deviation	1	-
Lack of efficacy	-	-

Period 2

Period 2 title	Treatment Period #2 (Week 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

After the data base was cleaned and locked for the analysis of the first 26-week study period and treatment assignment were revealed, select sponsor personnel had access to treatment assignments. The sponsor study core team were only exposed to data summaries by treatments. Investigators, the patient, and any other personnel involved in patients' assessment, monitoring, analysis and data management were blinded to patient assignment until the database was locked for analysis of week 52 data.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients assigned to the Placebo arm were supplied only placebo capsules which were taken from Day 1 to week 26 in Period 1, and then continued to week 52 in Period 2.

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Arm title	Pridopidine 45 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 26 (Period 1) and then continued to week 52 in Period 2.

Arm type	Experimental

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Arm title	Pridopidine 67.5 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 26 (Period 1), and continued to Week 52 in Period 2.

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Arm title	Pridopidine 90 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 26 (Period 1) and continued up to Week 52 in Period 2.

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Arm title	Pridopidine 112.5 mg bid

Arm description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 26 (Period 1), continuing up to Week 52 in Period 2.

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

Dosage and administration details:

Placebo was presented as white, hard gelatin capsules matching the 22.5 mg or 45 mg pridopidine capsules but containing no active ingredient.

Investigational medicinal product name	pridopidine
Investigational medicinal product code	
Other name	pridopidine hydrochloride, TV-7820
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Pridopidine was presented as white, hard gelatin capsules of 22.5 mg or 45 mg.

Number of subjects in period 2[1]	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid
Started	57	49	54
Completed	52	43	44
Not completed	5	6	10
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	2	1	2
Adverse event, non-fatal	1	4	5
Not specified	-	1	-
Non-compliance	1	-	-
Did not receive study drug	-	-	2
Sponsor decision	-	-	1

Lack of efficacy	1	-	-

Number of subjects in period 2[1]	Pridopidine 90 mg bid	Pridopidine 112.5 mg bid
Started	56	46
Completed	53	44
Not completed	3	2
Adverse event, serious fatal	1	1
Consent withdrawn by subject	-	-
Adverse event, non-fatal	-	-
Not specified	1	-
Non-compliance	-	-
Did not receive study drug	-	-
Sponsor decision	-	-
Lack of efficacy	1	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Sixty-one participants completed treatment period 1 but did not continue into treatment period 2. These patients were lost due to prolonged IRB review periods at certain sites.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients in the Placebo arm were only supplied placebo capsules which were taken from Day 1 to Week 26 in Period 1.	
Reporting group title	Pridopidine 45 mg bid
Reporting group description:	
All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 26 (Period 1).	
Reporting group title	Pridopidine 67.5 mg bid
Reporting group description:	
All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 26 (Period 1).	
Reporting group title	Pridopidine 90 mg bid
Reporting group description:	
All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 26 (Period 1).	
Reporting group title	Pridopidine 112.5 mg bid
Reporting group description:	
All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 26 (Period 1).	

Reporting group values	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid
Number of subjects	82	81	82
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 50.3 ± 11.34	 51.9 ± 11.75	 51.0 ± 11.83
Gender categorical Units: Subjects			
Female	40	40	41

Male	42	41	41

Race Units: Subjects			
White	73	75	78
Black	0	0	1
Asian	1	0	0
Other	0	1	0
Missing	8	5	3
Ethnicity Units: Subjects			
Not Hispanic or Latino	71	73	76
Hispanic or Latino	3	3	3
Unknown	0	0	0
Missing	8	5	3
Use of Neuroleptics			
Antipsychotic drugs to treat psychiatric or behavioral problems associated with HD.			
Units: Subjects			
Neuroleptics use	31	31	32
Neuroleptics no use	51	50	50
CYP2D6 Genotype			
CYP2D6 is an enzyme. An association between CYP2D6 genotypes (genetic make-up) and phenotypes (response to treatment, specifically rate of metabolism of the drug) is believed to exist.			
Units: Subjects			
Poor	1	5	4
Extensive	72	70	70
Intermediate	8	5	8
Ultra-rapid	1	1	0
Weight Units: kg			
arithmetic mean	72.7	69.5	69.9
standard deviation	± 1.36	± 1.55	± 12.76
Height Units: cm			
arithmetic mean	171.2	170.5	168.9
standard deviation	± 9.77	± 9.70	± 9.77
Body Mass Index Units: kg/m^2			
arithmetic mean	24.9	23.8	24.5
standard deviation	± 4.38	± 3.78	± 3.93
Number of Cytosine-Adenosine-Guanine (CAG) Repeats			
The normal huntington protein contains multiple repeats of a sequence of three DNA bases, cytosine-adenine-guanine (CAG), which encodes the amino acid glutamine. When more than 36 repeats are present in the protein, stemming from a mutation in the huntingtin gene, an abnormal protein is produced. This mutant form of the protein is more prone to aggregation than versions of the protein with a normal number of repeats. Individuals with 36–40 CAG repeats may or may not develop symptoms of HD, while people with more than 40 repeats will develop the disorder during a normal lifetime.			
Units: repeats			
arithmetic mean	44.4	44.1	45.0
standard deviation	± 3.23	± 4.12	± 4.73

Reporting group values	Pridopidine 90 mg bid	Pridopidine 112.5 mg bid	Total
Number of subjects	81	82	408
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.3	47.5	
standard deviation	± 12.69	± 11.40	-
Gender categorical Units: Subjects			
Female	43	39	203
Male	38	43	205
Race Units: Subjects			
White	75	77	378
Black	0	0	1
Asian	1	0	2
Other	1	0	2
Missing	4	5	25
Ethnicity Units: Subjects			
Not Hispanic or Latino	76	75	371
Hispanic or Latino	0	2	11
Unknown	1	0	1
Missing	4	5	25
Use of Neuroleptics			
Antipsychotic drugs to treat psychiatric or behavioral problems associated with HD.			
Units: Subjects			
Neuroleptics use	31	32	157
Neuroleptics no use	50	50	251
CYP2D6 Genotype			
CYP2D6 is an enzyme. An association between CYP2D6 genotypes (genetic make-up) and phenotypes (response to treatment, specifically rate of metabolism of the drug) is believed to exist.			
Units: Subjects			
Poor	2	4	16
Extensive	74	69	355
Intermediate	5	9	35
Ultra-rapid	0	0	2
Weight Units: kg			
arithmetic mean	70.5	70.7	
standard deviation	± 11.83	± 14.60	-
Height Units: cm			
arithmetic mean	169.8	170.5	
standard deviation	± 10.03	± 9.22	-
Body Mass Index Units: kg/m^2			
arithmetic mean	24.4	24.2	
standard deviation	± 3.63	± 3.89	-

Number of Cytosine-Adenosine-Guanine (CAG) Repeats			
The normal huntington protein contains multiple repeats of a sequence of three DNA bases, cytosine-adenine-guanine (CAG), which encodes the amino acid glutamine. When more than 36 repeats are present in the protein, stemming from a mutation in the huntingtin gene, an abnormal protein is produced. This mutant form of the protein is more prone to aggregation than versions of the protein with a normal number of repeats. Individuals with 36–40 CAG repeats may or may not develop symptoms of HD, while people with more than 40 repeats will develop the disorder during a normal lifetime.			
Units: repeats			
arithmetic mean	44.5	45.3	
standard deviation	± 4.90	± 3.66	-

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients in the Placebo arm were only supplied placebo capsules which were taken from Day 1 to Week 26 in Period 1.

Reporting group title	Pridopidine 45 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 26 (Period 1).

Reporting group title	Pridopidine 67.5 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 26 (Period 1).

Reporting group title	Pridopidine 90 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 26 (Period 1).

Reporting group title	Pridopidine 112.5 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 26 (Period 1).

Reporting group title	Placebo

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients assigned to the Placebo arm were supplied only placebo capsules which were taken from Day 1 to week 26 in Period 1, and then continued to week 52 in Period 2.

Reporting group title	Pridopidine 45 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 26 (Period 1) and then continued to week 52 in Period 2.

Reporting group title	Pridopidine 67.5 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 26 (Period 1), and continued to Week 52 in Period 2.

Reporting group title	Pridopidine 90 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 26 (Period 1) and continued up to Week 52 in Period 2.

Reporting group title	Pridopidine 112.5 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 26 (Period 1), continuing up to Week 52 in Period 2.

Subject analysis set title	Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients in the Placebo arm were only supplied placebo capsules which were taken from Day 1 to Week 52.

Subject analysis set title	Pridopidine 45 mg bid
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 52.

Subject analysis set title	Pridopidine 67.5 mg bid
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 52.

Subject analysis set title	Pridopidine 90 mg bid
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 52.

Subject analysis set title	Pridopidine 112.5 mg bid
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 52.

Primary: Change from Baseline in Total Motor Score (TMS) at Week 26

End point title	Change from Baseline in Total Motor Score (TMS) at Week 26

End point description:

TMS was defined as the sum of all Unified Huntington's Disease Rating Scale (UHDRS) motor domains ratings. The motor section of the UHDRS assesses
motor features of Huntington's Disease (HD) with standardized ratings of oculo- motor function, dysarthria, chorea, dystonia, gait, and postural stability. Each of 15 assessments is rated on a scale of 0 (normal) to 4 (marked impairment) for a TMS range of 0-60. Negative change from baseline values indicate improvement.

The change from baseline in TMS was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline TMS score, and categorical week in study by baseline TMS interaction.

Baseline was the last observation prior to the first dose of study drug.

End point type	Primary

End point timeframe:

Baseline (Day 0), Weeks 4, 8, 12, 16, 20, and 26 (or endpoint for the first treatment period)

End point values	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid	Pridopidine 90 mg bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81[1]	75[2]	79[3]	81[4]
Units: units on a scale				
least squares mean (standard error)	-4.79 (± 0.99)	-3.37 (± 1.05)	-3.09 (± 1.02)	-4.13 (± 1.00)

Notes:

[1] - Full analysis set - those who received >= 1 dose of study drug and >=1 post-baseline efficacy.

[2] - FAS

[3] - FAS

[4] - FAS

End point values	Pridopidine 112.5 mg bid			
Subject group type	Reporting group			
Number of subjects analysed	81[5]			
Units: units on a scale				
least squares mean (standard error)	-2.74 (± 1.01)			

Notes:

[5] - FAS

Statistical analyses

Statistical analysis title	TMS: Pridopidine 45 mg - Placebo

Statistical analysis description:

The change from baseline in TMS was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline TMS score, and categorical week in study by baseline TMS interaction.

Comparison groups	Pridopidine 45 mg bid v Placebo
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3202
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.39
upper limit	4.23

Statistical analysis title	TMS: Pridopdine 67.5 mg - Placebo

Statistical analysis description:

The change from baseline in TMS was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline TMS score, and categorical week in study by baseline TMS interaction.

Comparison groups	Pridopidine 67.5 mg bid v Placebo
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2266
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.06
upper limit	4.46

Statistical analysis title	TMS: Pridopdine 90 mg - Placebo

Statistical analysis description:

The change from baseline in TMS was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline TMS score, and categorical week in study by baseline TMS interaction.

Comparison groups	Pridopidine 90 mg bid v Placebo

Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6348
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.07
upper limit	3.39

Statistical analysis title	TMS: Pridopdine 112.5 mg - Placebo

Statistical analysis description:

The change from baseline in TMS was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline TMS score, and categorical week in study by baseline TMS interaction.

Comparison groups	Pridopidine 112.5 mg bid v Placebo
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1447
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	2.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.71
upper limit	4.8

Secondary: Change from Baseline in Modified Physical Performance Test (mPPT) at Week 26

End point title	Change from Baseline in Modified Physical Performance Test (mPPT) at Week 26

End point description:

mPPT includes 9 physical challenges, each scored on a 0-4 scale with 0 = unable to perform and 4 = performed well for a total score of 0-36. Positive change from baseline scores indicate improvement.

The change from baseline in mPPT was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline mPPT score, and categorical week in study by baseline mPPT interaction.

End point type	Secondary

End point timeframe:

Baseline (Day 0), Weeks 4, 8, 12, 16, 20, and 26 (or endpoint for the first treatment period)

End point values	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid	Pridopidine 90 mg bid
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	78[6]	75[7]	75[8]	80[9]
Units: units on a scale				
least squares mean (standard error)	0.71 (± 0.41)	0.75 (± 0.42)	0.64 (± 0.41)	0.70 (± 0.40)

Notes:

[6] - FAS

[7] - FAS

[8] - FAS

[9] - FAS

End point values	Pridopidine 112.5 mg bid			
Subject group type	Reporting group			
Number of subjects analysed	81[10]			
Units: units on a scale				
least squares mean (standard error)	1.00 (± 0.40)			

Notes:

[10] - FAS

Statistical analyses

Statistical analysis title	mPPT: Pridopidine 45 mg - Placebo

Statistical analysis description:

The change from baseline in mPPT was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline mPPT score, and categorical week in study by baseline mPPT interaction.

Comparison groups	Placebo v Pridopidine 45 mg bid
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9462
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.09
upper limit	1.17

Statistical analysis title	mPPT: Pridopidine 67.5 mg - Placebo

Statistical analysis description:

The change from baseline in mPPT was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical

week in study by treatment interaction, country, neuroleptic use or no use, baseline mPPT score, and categorical week in study by baseline mPPT interaction.

Comparison groups	Pridopidine 67.5 mg bid v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8968
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.05

Statistical analysis title	mPPT: Pridopidine 90 mg - Placebo

Statistical analysis description:

The change from baseline in mPPT was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline mPPT score, and categorical week in study by baseline mPPT interaction.

Comparison groups	Pridopidine 90 mg bid v Placebo
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9853
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.12
upper limit	1.1

Statistical analysis title	mPPT: Pridopidine 112.5 mg - Placebo

Statistical analysis description:

The change from baseline in mPPT was analyzed using a Repeated Measures model (SAS® MIXED procedure with REPEATED sub-command). The model included the following fixed effects: categorical week in study by treatment interaction, country, neuroleptic use or no use, baseline mPPT score, and categorical week in study by baseline mPPT interaction.

Comparison groups	Pridopidine 112.5 mg bid v Placebo

Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6063
Method	Mixed models analysis
Parameter estimate	LSM difference
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.82
upper limit	1.4

Secondary: Participants with Adverse Events

End point title	Participants with Adverse Events

End point description:

An adverse event was defined as any untoward medical occurrence that develops or worsens in severity during the conduct of a clinical study and does not necessarily have a causal relationship to the study drug. Severity was rated by the investigator on a scale of mild, moderate and severe, with severe= an AE which prevents usual activities. Relationship of AE to treatment was determined by the investigator. Serious AEs include death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, OR an important medical event that jeopardized the patient and required medical intervention to prevent the previously listed serious outcomes.

End point type	Secondary

End point timeframe:

Day 1 to Week 52

End point values	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid	Pridopidine 90 mg bid
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	82[11]	81[12]	82[13]	81[14]
Units: participants				
All AEs	62	63	69	71
AEs leading to discontinuation	6	10	16	12
Serious AEs	0	8	9	9
Severe AEs	5	7	10	12
AEs assessed as related to study drug	27	26	40	38

Notes:

[11] - Safety

[12] - Safety

[13] - Safety

[14] - Safety

End point values	Pridopidine 112.5 mg bid			
Subject group type	Subject analysis set			
Number of subjects analysed	82[15]			
Units: participants				

All AEs	67			
AEs leading to discontinuation	15			
Serious AEs	9			
Severe AEs	11			
AEs assessed as related to study drug	36			

Notes:

[15] - Safety

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Week 52

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned treatment. Patients in the Placebo arm were only supplied placebo capsules which were taken from Day 1 to Week 52.

Reporting group title	Pridopidine 45 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 90mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 90 mg which was taken from Day 28 to Week 52.

Reporting group title	Pridopidine 67.5 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 135 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 135 mg which was taken from Day 28 to Week 52.

Reporting group title	Pridopidine 90 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 180mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 180 mg which was taken from Day 28 to Week 52.

Reporting group title	Pridopidine 112.5 mg bid

Reporting group description:

All patients in this study were administered 3 capsules twice daily (ie, 3 capsules in the morning and 3 capsules in the afternoon). Capsules either contained pridopidine in doses of 22.5 mg or 45 mg or placebo (sized to match the two active doses to assure the blind) and were supplied by the sponsor in medication packs to support the assigned total daily dose of 225 mg. Doses were titrated during the first 4 weeks, starting at a total daily dose of 45 mg, up to the assigned total daily dose of 225 mg which was taken from Day 28 to Week 52.

Serious adverse events	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 82 (0.00%)	8 / 81 (9.88%)	9 / 82 (10.98%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myeloid leukaemia			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			

subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 82 (0.00%)	4 / 81 (4.94%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 82 (0.00%)	2 / 81 (2.47%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face injury			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Akathisia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychomotor hyperactivity			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Duodenal ulcer perforation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			

subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Mood disorder due to a general medical condition			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 82 (0.00%)	1 / 81 (1.23%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Peritonitis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 82 (0.00%)	0 / 81 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pridopidine 90 mg bid	Pridopidine 112.5 mg bid	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 81 (11.11%)	9 / 82 (10.98%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events			
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myeloid leukaemia			

subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Head injury			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Akathisia			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychomotor hyperactivity			

subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer perforation			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Uterine prolapse			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 81 (1.23%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Psychiatric disorders			
Mood disorder due to a general medical condition			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			

subjects affected / exposed	1 / 81 (1.23%)	2 / 82 (2.44%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 81 (1.23%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Peritonitis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Pridopidine 45 mg bid	Pridopidine 67.5 mg bid
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 82 (54.88%)	49 / 81 (60.49%)	63 / 82 (76.83%)
Investigations			
Weight decreased			
subjects affected / exposed	3 / 82 (3.66%)	4 / 81 (4.94%)	3 / 82 (3.66%)
occurrences (all)	3	4	3
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 82 (1.22%)	5 / 81 (6.17%)	2 / 82 (2.44%)
occurrences (all)	1	6	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	17 / 82 (20.73%)	16 / 81 (19.75%)	21 / 82 (25.61%)
occurrences (all)	31	44	31
Contusion			
subjects affected / exposed	3 / 82 (3.66%)	6 / 81 (7.41%)	6 / 82 (7.32%)
occurrences (all)	3	7	8
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 82 (1.22%)	0 / 81 (0.00%)	1 / 82 (1.22%)
occurrences (all)	1	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 82 (9.76%)	7 / 81 (8.64%)	7 / 82 (8.54%)
occurrences (all)	8	18	11
Chorea			
subjects affected / exposed	1 / 82 (1.22%)	4 / 81 (4.94%)	13 / 82 (15.85%)
occurrences (all)	1	4	15
Dizziness			
subjects affected / exposed	2 / 82 (2.44%)	2 / 81 (2.47%)	6 / 82 (7.32%)
occurrences (all)	2	2	12
Balance disorder			
subjects affected / exposed	3 / 82 (3.66%)	2 / 81 (2.47%)	5 / 82 (6.10%)
occurrences (all)	3	3	6

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 82 (8.54%)	3 / 81 (3.70%)	6 / 82 (7.32%)
occurrences (all)	10	3	6
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 82 (10.98%)	9 / 81 (11.11%)	11 / 82 (13.41%)
occurrences (all)	14	11	14
Vomiting			
subjects affected / exposed	4 / 82 (4.88%)	5 / 81 (6.17%)	6 / 82 (7.32%)
occurrences (all)	6	7	7
Nausea			
subjects affected / exposed	4 / 82 (4.88%)	4 / 81 (4.94%)	7 / 82 (8.54%)
occurrences (all)	4	6	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 82 (2.44%)	5 / 81 (6.17%)	2 / 82 (2.44%)
occurrences (all)	2	5	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 82 (2.44%)	6 / 81 (7.41%)	6 / 82 (7.32%)
occurrences (all)	2	6	6
Suicidal ideation			
subjects affected / exposed	0 / 82 (0.00%)	2 / 81 (2.47%)	7 / 82 (8.54%)
occurrences (all)	0	2	8
Insomnia			
subjects affected / exposed	3 / 82 (3.66%)	5 / 81 (6.17%)	11 / 82 (13.41%)
occurrences (all)	5	6	11
Irritability			
subjects affected / exposed	7 / 82 (8.54%)	4 / 81 (4.94%)	6 / 82 (7.32%)
occurrences (all)	8	4	7
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 82 (3.66%)	4 / 81 (4.94%)	3 / 82 (3.66%)
occurrences (all)	3	4	3
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	7 / 82 (8.54%)	14 / 81 (17.28%)	12 / 82 (14.63%)
occurrences (all)	8	21	16
Urinary tract infection			
subjects affected / exposed	4 / 82 (4.88%)	3 / 81 (3.70%)	6 / 82 (7.32%)
occurrences (all)	4	3	6

Non-serious adverse events	Pridopidine 90 mg bid	Pridopidine 112.5 mg bid	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 81 (70.37%)	53 / 82 (64.63%)	
Investigations			
Weight decreased			
subjects affected / exposed	3 / 81 (3.70%)	7 / 82 (8.54%)	
occurrences (all)	3	7	
Creatinine renal clearance decreased			
subjects affected / exposed	3 / 81 (3.70%)	5 / 82 (6.10%)	
occurrences (all)	4	8	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	13 / 81 (16.05%)	16 / 82 (19.51%)	
occurrences (all)	19	42	
Contusion			
subjects affected / exposed	0 / 81 (0.00%)	3 / 82 (3.66%)	
occurrences (all)	0	4	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 81 (6.17%)	2 / 82 (2.44%)	
occurrences (all)	6	2	
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 81 (13.58%)	8 / 82 (9.76%)	
occurrences (all)	19	10	
Chorea			
subjects affected / exposed	3 / 81 (3.70%)	7 / 82 (8.54%)	
occurrences (all)	3	8	
Dizziness			

subjects affected / exposed	5 / 81 (6.17%)	6 / 82 (7.32%)	
occurrences (all)	5	8	
Balance disorder			
subjects affected / exposed	1 / 81 (1.23%)	3 / 82 (3.66%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 81 (8.64%)	1 / 82 (1.22%)	
occurrences (all)	7	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	11 / 81 (13.58%)	10 / 82 (12.20%)	
occurrences (all)	17	15	
Vomiting			
subjects affected / exposed	5 / 81 (6.17%)	4 / 82 (4.88%)	
occurrences (all)	5	4	
Nausea			
subjects affected / exposed	4 / 81 (4.94%)	3 / 82 (3.66%)	
occurrences (all)	6	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 81 (1.23%)	5 / 82 (6.10%)	
occurrences (all)	1	5	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 81 (8.64%)	5 / 82 (6.10%)	
occurrences (all)	8	5	
Suicidal ideation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 82 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	9 / 81 (11.11%)	9 / 82 (10.98%)	
occurrences (all)	10	11	
Irritability			
subjects affected / exposed	5 / 81 (6.17%)	2 / 82 (2.44%)	
occurrences (all)	5	2	

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 81 (7.41%)	5 / 82 (6.10%)	
occurrences (all)	9	6	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 81 (16.05%)	15 / 82 (18.29%)	
occurrences (all)	15	23	
Urinary tract infection			
subjects affected / exposed	4 / 81 (4.94%)	5 / 82 (6.10%)	
occurrences (all)	5	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 September 2013	Amendment 1 to the protocol (dated 24 September 2013) was issued before any patients were enrolled in the study. The following major procedural changes (not all-inclusive) were made to the protocol: - The duration of treatment with study drug was increased from 12 weeks to 26 weeks - The 45 mg dose was removed from the efficacy analyses - The timing of the DSMB meetings was changed - The opportunity to enter the open-label extension study was introduced - Rules for discontinuation of treatment groups were modified
03 February 2014	Amendment 2 to the protocol (dated 03 February 2014) was issued before any patients were enrolled in the study. Clarification that the mPPT will be used as the secondary efficacy endpoint - Increased frequency of DSMB meetings until 100 patients (20 from each treatment group) have completed two weeks of treatment on full dose - Clarification that Patients with a legal guardian should be consented according to local requirements - The EQ-5D-5L scale was added as an assessment - The possibility for patients to continue in the study after study drug discontinuation, due to safety or tolerability reasons, was introduced - Clarification regarding the number of capsules in the dispensed bottles - Change to time points at which exploratory efficacy endpoints (PBA-s, CIBIC-Plus, PDS, CGI-C, Walk-12, and TUG test) are assessed to reduce patient burden
16 September 2014	Amendment 3 to the protocol (dated 16 September 2014) was issued after 24 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 following major procedural changes (not all-inclusive) were made to the protocol: - Extension of the period between screening and baseline visit to 12 weeks, to allow a switch in concomitant drugs if deemed medically justified and for the benefit of the patient by the investigator - Revised text to reflect that the investigator can unblind the treatment code in an emergency situation without prior approval of the sponsor - The ECG on Day 56 would be optional, unless required by local regulations - Clarification regarding the ECG at Week 2 (ie, that it will be performed in triplicate before the afternoon dose of that visit) - Prolonged QTcF deleted from baseline visit as an eligibility criterion. Prolonged QT at baseline will be handled according to the discontinuation rules specified in the protocol - Inclusion criterion was revised to read "IS equal to or less than 90% at the screening visit", to include also patients with a IS of 90% - The protocol was updated to require that all serious adverse events be reported within 24 hours of when the investigator learns of the event, regardless of whether it's a non-working day - Instructions on how to resume study drug after temporary interruption -Prohibited medications timing also changed from 6 weeks prior to screening to 6 weeks prior to baseline (eg, QT-interval prolonging meds, CYP2D6 metabolized meds, and tetrabenazine) - Rescreening of selected patients now permitted if not originally eligible for enrollment - Clarification regarding the time frame for suicide attempts prior to screening (ie, if the attempt or acts were performed within 1 year of screening) - New text regarding required reporting of suicidality as an adverse event

12 January 2015	Amendment 4 to the protocol (dated 12 January 2015) was issued after 133 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 following major procedural changes (not all-inclusive) were made to the protocol: - endpoints modified and/or added to reflect the study extension - days of assessments and procedures modified to reflect changes in time points - clarification to allow only 1 titration during the entire study period - new text added to define the population sets that will be used to analyze the data from the second study period
31 March 2016	Amendment 5 to the protocol (dated 31 March 2016) was issued after 408 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. - Addition of 2 telephone calls for safety evaluation (at Weeks 40 to 44 and Weeks 46 to 51) including C-SSRS and an abbreviated PBA-s assessment - Addition of suicidal ideations and suicide attempts as protocol-defined adverse events for expedited reporting - Addition of discontinuation criteria for individual patients and stopping rules for treatment groups - Clarification of study conduct - Revision of the Study Procedures and Assessments and Overall Study Schema to reflect the amended study design

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported