



Clinical trial results:

Essai multicentrique de traitement de la maladie de Huntington par la cystéamine

Summary

EudraCT number	2010-019444-39
Trial protocol	FR
Global end of trial date	31 August 2017

Results information

Result version number	v1 (current)
This version publication date	09 September 2020
First version publication date	09 September 2020
Summary attachment (see zip file)	résumé RF CYST-HD (résumé rapport final signé.pdf)

Trial information

Trial identification

Sponsor protocol code	PHRC2004-03bis
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03296176
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU Angers
Sponsor organisation address	4 rue Larrey, Angers, France,
Public contact	Pr Dominique Bonneau, CHU Angers, dobonneau@chu-angers.fr
Scientific contact	Pr Dominique Bonneau, CHU Angers, dobonneau@chu-angers.fr

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2017
Global end of trial reached?	Yes
Global end of trial date	31 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluer l'effet de la cystéamine chez des patients symptomatiques atteints de la maladie de Huntington en comparant les deux groupes de patients (cystéamine versus placebo) sur les résultats de l'Unified Huntington Disease Rating Scale (UHDRS, Huntington Study Group 1996). Le critère principal de l'étude sera la progression du score moteur de l'UHDRS en comparant les valeurs obtenues dans le groupe traité aux valeurs obtenues dans le groupe contrôle à 18 mois.

Protection of trial subjects:

Une comparaison de l'évolution sera effectuée sur 18 mois avant/après traitement sur l'ensemble des patients

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 October 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	72 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 96
Worldwide total number of subjects	96
EEA total number of subjects	96

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)	96

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Il s'agit d'un essai thérapeutique de phase II-III national, multicentrique, randomisé contrôlé cystéamine versus placebo en double aveugle

Les sujets sont sélectionnés par les investigateurs et parmi les patients atteints de la maladie de Huntington, volontaires, pris en charge par les services de neurologie et de génétique de chacun des centres

Pre-assignment

Screening details:

La phase d'inclusion des patients est prévue sur 2 visites à 1 mois d'intervalle : M-1 et M0. Ce n'est qu'à l'issue de cette deuxième visite que la décision d'inclusion pourra être prise après avoir vérifié les différents critères et avoir fait signer le consentement au moins en 2 exemplaires par les différentes parties.

Period 1

Period 1 title	double aveugle
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	traitement

Arm description: -

Arm type	Experimental
Investigational medicinal product name	RP103
Investigational medicinal product code	cysteamine
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Le traitement à l'étude est le RP103 dosé à 75mg. Le principe actif est le bitartrate de cystéamine. Le traitement se présente sous la forme de gélules à libération retardée de cystéamine, de taille 0.

Les excipients sont les suivants : cellulose microcristalline, hypromellose, sodium laurylsulfate et eau purifiée. L'enrobage gastro-résistant est constitué par l'Eudragit L30D55, du citrate triéthyle et du talc.

Les traitements sont administrés par voie orale deux fois par jour à 12 heures d'intervalle

Arm title	placebo
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Arm description: -

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

Dosage and administration details:

Les traitements sont administrés par voie orale deux fois par jour à 12 heures d'intervalle. Le traitement comparateur est représenté par des gélules de placebo de même taille et de même aspect. Les gélules de placebo sont des gélules composées de microsphères de sucrose et d'amidon associés à du talc comme lubrifiant.

Number of subjects in period 1	traitement	placebo
Started	51	45
Completed	45	44
Not completed	6	1
Lost to follow-up	6	1

Period 2

Period 2 title	traitement compassionnel
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	traitement
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	RP103
Investigational medicinal product code	cysteamine
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Le traitement à l'étude est le RP103 dosé à 75mg. Le principe actif est le bitartrate de cystéamine. Le traitement se présente sous la forme de gélules à libération retardée de cystéamine, de taille 0. Les excipients sont les suivants : cellulose microcristalline, hypromellose, sodium laurylsulfate et eau purifiée. L'enrobage gastro-résistant est constitué par l'Eudragit L30D55, du citrate triéthyle et du talc. Les traitements sont administrés par voie orale deux fois par jour à 12 heures d'intervalle

Number of subjects in period 2 ^[1]	traitement
Started	86
Completed	66
Not completed	20
Adverse event, serious fatal	8
Consent withdrawn by subject	5
Adverse event, non-fatal	5
Lost to follow-up	1
Protocol deviation	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: 10 patients n'ont pas souhaité participer aux différentes phases de l'étude

Period 3

Period 3 title	prolongation de l'étude
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	prolongation de l'étude
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	RP103
Investigational medicinal product code	cysteamine
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Le traitement à l'étude est le RP103 dosé à 75mg. Le principe actif est le bitartrate de cystéamine. Le traitement se présente sous la forme de gélules à libération retardée de cystéamine, de taille 0. Les excipients sont les suivants : cellulose microcristalline, hypromellose, sodium laurylsulfate et eau purifiée. L'enrobage gastro-résistant est constitué par l'Eudragit L30D55, du citrate triéthyle et du talc. Les traitements sont administrés par voie orale deux fois par jour à 12 heures d'intervalle

Number of subjects in period 3	prolongation de l'étude
Started	66
Completed	14
Not completed	52
Adverse event, serious fatal	4
Physician decision	2
Consent withdrawn by subject	2
discontinuation of treatment by the laboratory	37
Adverse event, non-fatal	1
Pregnancy	1
Lack of efficacy	1
Protocol deviation	4

Baseline characteristics

Reporting groups

Reporting group title	traitement
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Reporting group values	traitement	placebo	Total
Number of subjects	51	45	96
Age categorical			
Units: Subjects			
Adults (18-64 years)	51	45	96
Age continuous			
Age compris entre 18 et 65 ans.			
Units: years			
median	45.5	50.4	
standard deviation	± 8.9	± 9.7	-
Gender categorical			
Units: Subjects			
Female	21	25	46
Male	30	20	50

Subject analysis sets

Subject analysis set title	Phase primaire : M0 à M18 placebo versus traitement
Subject analysis set type	Full analysis

Subject analysis set description:

L'effet de la cystéamine sur le fonctionnement moteur, négativement impactée dans le cas de la maladie de Huntington, a été étudié en opposant une population traitée et une population témoin choisies de manière randomisée en double-aveugle parmi les 96 patients de l'étude. Trois mesures de score moteur ont été effectuées à 0, 12 et 18 mois.

Après 18 mois de traitement vs placebo, nous n'avons pas mis en évidence un effet significatif du traitement sur l'évolution du score moteur (SMD = -1.5 ± 1.71 , $P=0.385$).

Subject analysis set title	Etude M0 à M72 (sans placebo)
Subject analysis set type	Full analysis

Subject analysis set description:

Nous avons effectué une deuxième phase d'analyse en incorporant les données de la phase de prolongation. Nous voyons qu'un nombre important de patients a choisi de poursuivre le traitement à l'issu des 36 mois de l'étude (plus que 4 visites). Les patients avec 9 visites ont complété l'intégralité de la phase de prolongation.

Reporting group values	Phase primaire : M0 à M18 placebo versus traitement	Etude M0 à M72 (sans placebo)	
Number of subjects	96	86	
Age categorical			
Units: Subjects			
Adults (18-64 years)	96	86	

Age continuous			
Age compris entre 18 et 65 ans.			
Units: years			
median	46.9	46.9	
standard deviation	± 9.4	± 9.4	
Gender categorical			
Units: Subjects			
Female	46	41	
Male	50	45	

End points

End points reporting groups

Reporting group title	traitement
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	
Reporting group title	traitement
Reporting group description: -	
Reporting group title	prolongation de l'étude
Reporting group description: -	
Subject analysis set title	Phase primaire : M0 à M18 placebo versus traitement
Subject analysis set type	Full analysis
Subject analysis set description:	
L'effet de la cystéamine sur le fonctionnement moteur, négativement impactée dans le cas de la maladie de Huntington, a été étudié en opposant une population traitée et une population témoin choisies de manière randomisée en double-aveugle parmi les 96 patients de l'étude. Trois mesures de score moteur ont été effectuées à 0, 12 et 18 mois. Après 18 mois de traitement vs placebo, nous n'avons pas mis en évidence un effet significatif du traitement sur l'évolution du score moteur (SMD = -1.5 ± 1.71 , $P=0.385$).	
Subject analysis set title	Etude M0 à M72 (sans placebo)
Subject analysis set type	Full analysis
Subject analysis set description:	
Nous avons effectué une deuxième phase d'analyse en incorporant les données de la phase de prolongation. Nous voyons qu'un nombre important de patients a choisi de poursuivre le traitement à l'issue des 36 mois de l'étude (plus que 4 visites). Les patients avec 9 visites ont complété l'intégralité de la phase de prolongation.	

Primary: phase primaire

End point title	phase primaire
End point description:	
End point type	Primary
End point timeframe:	
Trois mesures de score moteur ont été effectuées à 0, 12 et 18 mois	

End point values	traitement	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	44		
Units: SMD = -1.5 ± 1.71	1	1		

Statistical analyses

Statistical analysis title	phase primaire
Comparison groups	traitement v placebo

Number of subjects included in analysis	89
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.385
Method	score moteur

Primary: phase deux

End point title	phase deux
End point description:	
End point type	Primary
End point timeframe:	
M0 à M72	

End point values	traitement	placebo	traitement	prolongation de l'étude
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	45	86	66
Units: score moteur	51	45	86	66

Statistical analyses

Statistical analysis title	Phase primaire : M0 à M18 placebo vs traitement
Comparison groups	traitement v placebo
Number of subjects included in analysis	96
Analysis specification	Post-hoc
Analysis type	other ^[1]
P-value	= 0.385
Method	motor score
Parameter estimate	Mean difference (final values)
Point estimate	1.5
Confidence interval	
level	90 %
sides	1-sided
upper limit	2
Variability estimate	Standard deviation
Dispersion value	1.71

Notes:

[1] - évaluer l'effet de la cystéamine chez les patients symptomatiques

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Les événements indésirables ont été recueillis pendant toute la durée de l'étude de M0 à M72.

Adverse event reporting additional description:

Les événements indésirables non graves sont décrits par bras pendant la phase en double aveugle de M0 à M18.

Les événements indésirables graves sont décrits sur la totalité de l'étude de M0 à M72 sans mention de bras de traitement étant donné que l'aveugle n'a été levé que pour les suspicions d'effets indésirables graves.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18
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Reporting groups

Reporting group title	M0-M72
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Reporting group description: -

Serious adverse events	M0-M72		
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 96 (36.46%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	5		
Vascular disorders			
Haemorrhage intracranial			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Pilonidal sinus repair			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aborted pregnancy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Consciousness fluctuating			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Death	Additional description: unknown cause of death (at home)		
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	2 / 2		
Respiratory, thoracic and mediastinal disorders			
Foreign body aspiration			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Anxiety disorder			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Depressive symptom				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 96 (2.08%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
alternative assessment type: Non-systematic				
subjects affected / exposed	7 / 96 (7.29%)			
occurrences causally related to treatment / all	3 / 7			
deaths causally related to treatment / all	3 / 3			
Delusional disorder, unspecified type				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Disorientation				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination, auditory				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 96 (1.04%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Panic attack				

alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	2 / 2		
Violence-related symptom			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Weight decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 96 (3.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Alcohol abuse			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 96 (3.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 96 (3.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Fracture			
alternative assessment type: Non-systematic			

subjects affected / exposed	3 / 96 (3.13%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Tachyarrhythmia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hypotonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Confusional state			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Language disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphopenia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Enzyme activity increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Peritonitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural infection bacterial			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bursitis infective			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Feeding disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 96 (2.08%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	M0-M72		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 96 (12.50%)		
Investigations			
Alanine aminotransferase increased	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Blood creatine phosphokinase increased	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Aspartate aminotransferase increased	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Nervous system disorders			
Headache	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Nausea	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Breath odour	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Vomiting	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Abdominal pain	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Infections and infestations			
Gastroenteritis	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Possibly related-treatment adverse event in M0-M18 phase		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 96 (1.04%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2011	Modification d'un critère de non-inclusion
20 September 2011	Prolongation de la durée de recrutement avec modification de la durée d'essai clinique
19 June 2012	Changement d'investigateur principal dans un lieu de recherche déjà déclaré
17 September 2013	changement de statisticien et Modification de la période de traitement
10 July 2014	Ajout des co-investigateurs et Modification de la période de traitement
03 February 2015	Modification de la période de traitement
07 July 2015	Ajout d'une IRM durant la troisième période de prolongation de l'étude (visite M63). Suppression du dosage du BDNF aux visites M63 et M72. Ajout d'un co-investigateur. Changement d'investigateur principal dans un lieu de recherche déjà déclaré
26 May 2016	Ajout d'une étude ancillaire PK-CYST-HD et Changement du nom/coordonnées du représentant légal du promoteur
20 September 2016	Modification du suivi des patients suite à l'arrêt prématuré ou non du traitement

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28436572>