Clinical trial results:
Pilot study of the effects of desipramine on neurovegetative parameters in children with Rett's syndrome

Summary

EudraCT number	2007-006739-30
Trial protocol	FR
Global end of trial date	11 August 2014

Results information

Result version number	v1 (current)
This version publication date	11 August 2018
First version publication date	11 August 2018
Summary attachment (see zip file)	Summary (Summary.docx)

Trial information

Trial identification

Sponsor protocol code	2007-37

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00990691
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ASSISTANCE PUBLIQUE DES HOPITAUX DE MARSEILLE
Sponsor organisation address	DRCI, 80 RUE BROCHIER, MARSEILLE, France, 13354
Public contact	Me GARRIDO PRADALIE, DIRECTION DE LA RECHERCHE CLINIQUE ET DE L'INNOVATION, +33 491382870, drci@ap-hm.fr
Scientific contact	Pr Josette MANCINI, Service de Santé Publique Information médicale, Hôpital de la Timone, 147 Bd baille, 13005 M, +33 491382870, alexandra.giuliani@ap-hm.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 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2014
Global end of trial reached?	Yes
Global end of trial date	11 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to study the efficacy of desipramine on cardiorespiratory variability and tolerance of desipramine in 36 patients with Rett Syndrome aged 4 to 18 years weighing up to 60 kg and presenting respiratory rate disorders

Protection of trial subjects:

no protection was needed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	7 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	24
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients are recruited in 5 French centers . It is a randomized, double-blind, placebo-controlled study in 3 parallel groups in subjects with Rett Syndrome (high dose of Desipramine, low dose and placebo).
Patient with Rett Syndrome diagnosed clinically and genotyped MECP2 (Xq28), aged 6 to 17 and weighing up to 60 kg

Pre-assignment

Screening details:

The screening visit verifies that the patient meets the inclusion criteria.
the subject and the holders of parental authority or guardianship give their consent for written participation after presentation by the investigator of the study, reading of the informed consent form and response of the investigator to his questions.

Period 1

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

Blinding implementation details:

The randomization will be balanced by block of 12 patients and stratified per center in order to maintain sufficient power when a center effect is highlighted.
The sealed decoding envelopes will be kept at the pharmacy of each site and in the investigative file of each site. The randomization list will be kept in a sealed envelope in the UPCET biometrics department. The code will only be opened after a process of blind review of the data and freezing of the database.

Arms

Are arms mutually exclusive?	Yes
Arm title	High desipramine

Arm description:

Daily single oral dose of "strong" dose desipramine.
The dose delivered to each patient will depend on their initial weight (15-25kg: 50mg, 26-35kg: 75mg, 36-45kg: 100mg,> 46kg: 150mg)

Arm type	Experimental
Investigational medicinal product name	DESIPRAMINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cachet
Routes of administration	Oral use

Dosage and administration details:

Weight of patient

15-25 kg	26-35 kg		36-45 kg		>46kg
Groupe 1	50 mg	75 mg	100 mg	150 mg	
Groupe 2	25 mg	50 mg	75 mg	100 mg	
Groupe 3	placebo	placebo	placebo	placebo	

Arm title	Low desipramine

Arm description:

Daily single oral intake of low dose desipramine.
The dose delivered to each patient will depend on their initial weight (15-25kg: 25mg, 26-35kg: 50mg, 36-45kg: 75mg,> 46kg: 100mg)

Arm type	Experimental

Investigational medicinal product name	DESIPRAMINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cachet
Routes of administration	Oral use

Dosage and administration details:

Weight of patient
15-25 kg 26-35 kg 36-45 kg >46kg
25 mg 50 mg 75 mg 100 mg

Arm title	placebo

Arm description:

Daily single oral intake of placebo.

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

Dosage and administration details:

25 mg

Number of subjects in period 1	High desipramine	Low desipramine	placebo
Started	12	12	12
Completed	11	12	11
Not completed	1	0	1
Consent withdrawn by subject	1	-	1

Period 2

Period 2 title	TREATMENT PERIOD
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

The randomization will be balanced by block of 12 patients and stratified per center in order to maintain sufficient power when a center effect is highlighted.
The sealed decoding envelopes will be kept at the pharmacy of each site and in the investigative file of each site. The randomization list will be kept in a sealed envelope in the UPCET biometrics department. The code will only be opened after a process of blind review of the data and freezing of the database.

Arms

Are arms mutually exclusive?	Yes

Arm title	High desipramine
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	DESIPRAMINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cachet
Routes of administration	Oral use

Dosage and administration details:

Weight of patient

	15-25 kg	26-35 kg	36-45 kg	>46kg
Groupe 1	50 mg	75 mg	100 mg	150 mg
Groupe 2	25 mg	50 mg	75 mg	100 mg
Groupe 3	placebo	placebo	placebo	placebo

Arm title	Low desipramine
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	DESIPRAMINE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Weight of patient

15-25 kg	26-35 kg	36-45 kg	>46kg
25 mg 50 mg	75 mg 100 mg		

Arm title	placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	lactose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cachet
Routes of administration	Oral use

Dosage and administration details:

Weight of patient

	15-25 kg	26-35 kg	36-45 kg	>46kg
Groupe 1	50 mg	75 mg	100 mg	150 mg
Groupe 2	25 mg	50 mg	75 mg	100 mg
Groupe 3	placebo	placebo	placebo	placebo

Number of subjects in period 2	High desipramine	Low desipramine	placebo
Started	11	12	11
Completed	7	8	11
Not completed	4	4	0
Adverse event, non-fatal	3	4	-
Lost to follow-up	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	baseline

Reporting group description: -

Reporting group values	baseline	Total	
Number of subjects	36	36	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	24	24	
Adolescents (12-17 years)	12	12	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	10		
standard deviation	± 1	-	
Gender categorical Units: Subjects			
Female	36	36	
Male	0	0	

End points

End points reporting groups

Reporting group title	High desipramine
Reporting group description:	
Daily single oral dose of "strong" dose desipramine. The dose delivered to each patient will depend on their initial weight (15-25kg: 50mg, 26-35kg: 75mg, 36-45kg: 100mg,> 46kg: 150mg)	
Reporting group title	Low desipramine
Reporting group description:	
Daily single oral intake of low dose desipramine. The dose delivered to each patient will depend on their initial weight (15-25kg: 25mg, 26-35kg: 50mg, 36-45kg: 75mg,> 46kg: 100mg)	
Reporting group title	placebo
Reporting group description:	
Daily single oral intake of placebo.	
Reporting group title	High desipramine
Reporting group description: -	
Reporting group title	Low desipramine
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Primary: Apnea-hypopnea index

End point title	Apnea-hypopnea index
End point description:	
End point type	Primary
End point timeframe:	
1h of monitoring	

End point values	High desipramine	Low desipramine	placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	8	11	
Units: number by hour	7	25	11	

Statistical analyses

Statistical analysis title	respiratory assessment
Comparison groups	High desipramine v Low desipramine v placebo

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.05
Method	Kruskal-wallis
Parameter estimate	Mean difference (net)

Secondary: plasma concentration of DMI

End point title	plasma concentration of DMI

End point description:

End point type	Secondary

End point timeframe:

6 months of treatment

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 6 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	2
Reporting groups	
Reporting group title	low desipramine
Reporting group description: -	
Reporting group title	high despiramine
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Serious adverse events	low desipramine	high despiramine	placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	1 / 11 (9.09%)	1 / 11 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Nervous system disorders			
Status epilepticus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Motor dysfunction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (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
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
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			
INSOMNIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3.9 %

Non-serious adverse events	low desipramine	high despiramine	placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	9 / 11 (81.82%)	11 / 11 (100.00%)
Vascular disorders			
Peripheral coldness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
ECG QTc interval prolonged			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
EPILEPSY			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	5	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	1 / 11 (9.09%)
occurrences (all)	0	1	0
dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
rectal hemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Obstructive airways disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
ABNORMAL BEHAVIOR			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Affective disorder			

subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	0 / 12 (0.00%)	2 / 11 (18.18%)	1 / 11 (9.09%)
occurrences (all)	0	2	3
Mood altered			
subjects affected / exposed	1 / 12 (8.33%)	0 / 11 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 11 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 11 (9.09%)	0 / 11 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29468173