



Clinical trial results:

Evaluation de l'intérêt d'un traitement par hydroquinidine pour la prise en charge des patients atteints d'un syndrome de Brugada à risque rythmique élevé et implantés d'un défibrillateur

Summary

EudraCT number	2008-000994-39
Trial protocol	FR
Global end of trial date	20 October 2014

Results information

Result version number	v1 (current)
This version publication date	20 July 2023
First version publication date	20 July 2023
Summary attachment (see zip file)	Summary final report (résumé de rapport final Quidam signé.pdf)

Trial information

Trial identification

Sponsor protocol code	BRD 06/2-D
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00927732
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Centre Hospitalier et Universitaire de Nantes
Sponsor organisation address	1 place Alexis Ricordeau, Nantes, France, 44093
Public contact	Mme Monique MARGUERITE, Centre Hospitalier et Universitaire de Nantes, +33 253482832, monique.marguerite@chu-nantes.fr
Scientific contact	Mme Monique MARGUERITE, Centre Hospitalier et Universitaire de Nantes, +33 253482832, monique.marguerite@chu-nantes.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	18 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2014
Global end of trial reached?	Yes
Global end of trial date	20 October 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare for patients with Brugada syndrome having an Implantable Automatic Defibrillator (IAD) the time length before the happening of an appropriate electric shock registered on the IAD when they are under hydroquinidine treatment or when they are under placebo (double-blinded cross-over study design)

Protection of trial subjects:

During and after each injection, patients were carefully monitored.

Background therapy:

Patients receive background therapy in the form of a cardiac defibrillator in connection with their pathology (Brugada syndrome)

Evidence for comparator: -

Actual start date of recruitment	06 February 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	45
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

With the inclusion criteria we have adopted, fifty evaluable patients will therefore be required.

Total duration : 6 years

Recruitment period : 3 years

Duration of treatment per patient : 18 months

Follow-up time per patient : 3 years

Pre-assignment

Screening details:

Patient interview

Clinical examination of the patient

Collection of an ECG with an appearance of spontaneous type I Brugada syndrome recorded during the consultation or during a previous consultation. A copy of this ECG will be promptly sent to the experts on the scientific committee for confirmation of Brugada syndrome. Patients enrolled in the

Period 1

Period 1 title	Phase I
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	Hydroquinidine

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Serecor
Investigational medicinal product code	
Other name	HYDROQUINIDINE
Pharmaceutical forms	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

300 mg

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	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

the placebo has the same shape as the treatment capsule, but contains only sugar (sucrose and corn starch)

Number of subjects in period 1	Hydroquinidine	Placebo
Started	26	24
Completed	16	21
Not completed	10	3
Consent withdrawn by subject	1	2
death not caused by the study (accident)	1	-
Adverse event, non-fatal	8	1

Period 2

Period 2 title	Phase II
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Hydroquinidine

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Serecor
Investigational medicinal product code	
Other name	HYDROQUINIDINE
Pharmaceutical forms	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

300 mg

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	Buccal tablet
Routes of administration	Buccal use

Dosage and administration details:

the placebo has the same shape as the treatment capsule, but contains only sugar (sucrose and corn starch)

Number of subjects in period 2	Hydroquinidine	Placebo
Started	21	16
Completed	13	13
Not completed	8	3
Adverse event, non-fatal	6	-
symptoms not related to treatment	2	2
death not rythmic	-	1

Baseline characteristics

Reporting groups

Reporting group title	Hydroquinidine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Hydroquinidine	Placebo	Total
Number of subjects	26	24	50
Age categorical			
Units: Subjects			
Adults (18-64 years)	23	22	45
From 65-84 years	3	2	5
Age continuous			
Units: years			
arithmetic mean	52.5	52.4	
full range (min-max)	22 to 75	25 to 73	-
Gender categorical			
Sex of patients is not done			
Units: Subjects			
Female	4	5	9
Male	22	19	41

Subject analysis sets

Subject analysis set title	patient with complete data
Subject analysis set type	Per protocol
Subject analysis set description:	
It's all patients with their data entire completed	

Reporting group values	patient with complete data		
Number of subjects	26		
Age categorical			
Units: Subjects			
Adults (18-64 years)	45		
From 65-84 years	5		
Age continuous			
Units: years			
arithmetic mean	52.5		
full range (min-max)	22 to 75		
Gender categorical			
Sex of patients is not done			
Units: Subjects			
Female	4		
Male	22		

End points

End points reporting groups

Reporting group title	Hydroquinidine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Hydroquinidine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	patient with complete data
Subject analysis set type	Per protocol
Subject analysis set description:	
It's all patients with their data entire completed	

Primary: evaluation of the extension of pre-shock follow-up time by quinidine therapy in patients with Brugada syndrome and defibrillator therapy.

End point title	evaluation of the extension of pre-shock follow-up time by quinidine therapy in patients with Brugada syndrome and defibrillator therapy. ^[1]
End point description:	
End point type	Primary
End point timeframe:	
The primary endpoint of the study will be the delay in the occurrence of an appropriate electric shock authenticated on the defibrillator's memory.	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: I confirm this answer

End point values	Hydroquinidine	Placebo	patient with complete data	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	26	16	26	
Units: Time				
number (not applicable)	26	16	26	

Statistical analyses

Statistical analysis title	Test Jung
Statistical analysis description:	
To assess the primary endpoint, we will use the Jung test.	
Comparison groups	Hydroquinidine v Placebo

Number of subjects included in analysis	42
Analysis specification	Post-hoc
Analysis type	superiority
P-value	> 1
Method	Test JUNG
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

These serious unexpected adverse events will be reported to the competent authorities within 7 or 15 days of the sponsor becoming aware of them.

Adverse event reporting additional description:

All adverse effects or events encountered during the study, which are observed by the physician or reported by the patient, will be recorded in the observation book in the section provided for this purpose.

All serious adverse effects or events will be reported by the sponsor to the competent authorities in accordance with current regulations.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	7

Reporting groups

Reporting group title	Hydroquinidine
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Serious adverse events	Hydroquinidine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 26 (26.92%)	6 / 24 (25.00%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Ventricular probe change			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
chest pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Discomfort on exertion with mediosternal pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute coronary syndrome			
subjects affected / exposed	0 / 26 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
DAI change			
subjects affected / exposed	1 / 26 (3.85%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic brain injury/bleeding			
subjects affected / exposed	0 / 26 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Oesophageal tumor recurrence			
subjects affected / exposed	0 / 26 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash erythematous			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Intolerance to treatment	Additional description: Case change		
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate endocavity electric shock			

subjects affected / exposed	1 / 26 (3.85%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Hydroquinidine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 26 (15.38%)	1 / 24 (4.17%)	
Investigations			
Probe malfunction			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences (all)	0	0	
VD probe rupture			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Hip prosthesis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences (all)	0	0	
Low back pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 24 (0.00%)	
occurrences (all)	0	0	
knee tunnel surgery			
subjects affected / exposed	0 / 26 (0.00%)	1 / 24 (4.17%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2008	Modify the study design before starting double-blind treatment Add a non-inclusion criterion Add the possibility for patients presenting digestive AEs after randomization to remain in the study Modify the organization of treatment delivery from the Hôtel-Dieu pharmacy (Nantes) to the pharmacies of the associated centers Addition of a 17th center Addition and deletion of certain mentions in the protocol
21 February 2011	Extension of recruitment period from 2 to 3 years (end February 2012)
27 September 2011	Possibility of changing dosage Modification of non-inclusion criteria

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 October 2011	Enormous recruitment difficulties Expected number of events overestimated Numerous premature study withdrawals Short validity of treatment Its/ logistical and financial burden	-

Notes:

Limitations and caveats

None reported