



## Clinical trial results:

### Crise Rénale sclérodermique : amélioration du pronostic par adjonction de Bosentan au traitement de référence de la maladie.

#### Summary

EudraCT number	2010-021452-26
Trial protocol	FR
Global end of trial date	20 April 2015

#### Results information

Result version number	v1 (current)
This version publication date	29 June 2022
First version publication date	29 June 2022

#### Trial information

##### Trial identification

Sponsor protocol code	P081217
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01241383
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	ASSISTANCE PUBLIQUE - HOPITAUX DE PARIS (AP-HP)
Sponsor organisation address	4 Avenue Victoria, PARIS, France, 75004
Public contact	Investigateur Coordonnateur, Dr Alice BEREZNE, aberezne@ch-annecygenevois.fr
Scientific contact	Investigateur Coordonnateur, Dr Alice BEREZNE , aberezne@ch-annecygenevois.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 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 April 2015
Global end of trial reached?	Yes
Global end of trial date	20 April 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

L'objectif principal est de déterminer l'efficacité à un an du bosentan, prescrit durant 6 mois, chez des patients présentant une crise rénale sclérodermique venant d'être diagnostiquée. En l'absence de toute étude et de possibilité de réaliser à ce stade de nos connaissances une étude randomisée contre placebo, nous nous donnons l'objectif d'obtenir au cours de cette étude, au moins la même efficacité en terme de survie et de taux d'insuffisance rénale que ce qui est observé dans les études les plus récentes de la littérature.

Protection of trial subjects:

Présence d'un DSMB

Remise au patient d'un carnet de suivi de l'observance (recueil des doses de Tracleer®, d'IEC, de notifier les éventuels EI).

Questionnaires SF36 et HAQ pour le patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	France: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	8

From 65 to 84 years	8
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

number of patients screened=44 28 patients not included:

- 20 with non inclusion criteria (other disease or delay for inclusion)
- 7 not included because of organisation problems (non declared centers)
- 1 no reason known

### Period 1

Period 1 title	Etude "SCS REINBO" overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	one arm
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Arm description:

Bosentan en association du traitement conventionnel incluant un IEC

Arm type	one arm
Investigational medicinal product name	Tracleer
Investigational medicinal product code	
Other name	Bosentan
Pharmaceutical forms	Buccal tablet
Routes of administration	Oral use

Dosage and administration details:

Les médicaments utilisés dans le cadre de cette étude seront le Tracleer® 62,5 et 125 mg.

Le traitement sera débuté à 62,5 mg deux fois par jour pendant 28 jours et en l'absence d'intolérance, augmenté à 125 mg deux fois par jours pendant 5 mois (5 fois 28 jours de traitement).

<b>Number of subjects in period 1</b>	one arm
Started	16
Etude ScS REINBO	16
Completed	16

## Baseline characteristics

### Reporting groups

Reporting group title	Etude "SCS REINBO" overall trial
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Reporting group description:

Bras unique\_ Bosentan en association avec le traitement conventionnel incluant un IEC

Reporting group values	Etude "SCS REINBO" overall trial	Total	
Number of subjects	16	16	
Age categorical			
Age supérieur ou égal à 18 ans. Adultes (18-64 ans) et de de 65 à 84 ans.			
Units: Subjects			
supérieur ou égal à 18 ans	16	16	
Gender categorical			
Units: Subjects			
Female	10	10	
Male	6	6	

## End points

### End points reporting groups

Reporting group title	one arm
Reporting group description: Bosentan en association du traitement conventionnel incluant un IEC	
Subject analysis set title	workaround needs
Subject analysis set type	Sub-group analysis
Subject analysis set description: We reported the same number of subjects declared in the single arm for the workaround to work (note that no subjects were included in this subgroup).	

### Primary: Renal survival at one year defined as increase of two-fold of creatine level

End point title	Renal survival at one year defined as increase of two-fold of creatine level
End point description:	
End point type	Primary
End point timeframe: Le critère de jugement principal sera l'évolution de la fonction rénale à 6 mois et 1 an du début de la crise rénale	

End point values	one arm	workaround needs		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	16 <sup>[1]</sup>	16 <sup>[2]</sup>		
Units: countable	16	16		

Notes:

[1] - One arm

[2] - workaround needs

### Statistical analyses

Statistical analysis title	Analyse descriptive
Statistical analysis description: Single-arm descriptive analysis of 16 subjects only.	
Comparison groups	one arm v workaround needs
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other <sup>[3]</sup>
P-value	< 0.05
Method	Analyse descriptive
Parameter estimate	renal survival at M6 and M12
Variability estimate	Standard deviation

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Notes:

[3] - We reported the same number of subjects declared in the single arm for the workaround to work (note that no subjects were included in the subgroup workarounds needs).

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

12 months

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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### Reporting groups

Reporting group title	Etude ScS REINBO
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Reporting group description: -

Serious adverse events	Etude ScS REINBO		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events			
Vascular disorders			
Arterial Hypotension			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
General disorders and administration site conditions			
Reduced general Condition	Additional description: Reduced general Condition Edema Lower Limb		
subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Hepatobiliary disorders			
Hepatitis	Additional description: Hepatitis acute Hepatic Cytolysis		



subjects affected / exposed	2 / 16 (12.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		

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

<b>Non-serious adverse events</b>	Etude ScS REINBO		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)		
General disorders and administration site conditions			
Epigastralgies, Diarrhée	Additional description: Epigastralgies Diarrhée		
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2011	MS1 - ajout de prélèvements aux visites M6 et M12 ; - ajout de la liste investigateur (inchangée) au niveau du protocole
16 December 2011	MS2 : ajout de nouveaux centres
10 January 2012	MS3 : interruption des inclusions
06 April 2012	MS4 : Description du renforcement des mesures de surveillances des patients traités par le Bosentan suite à la demande de l'afssaps.
05 June 2012	MS5: - demande d'autorisation pour la reprise des inclusions dans l'étude SCS-Reinbo suite aux conclusions du rapport des membres du Comité de surveillance indépendant  - pour pallier à l'absence des inclusions depuis la première réunion du CSI en date du 05/01/2012, nous souhaitons prolonger la période des inclusions de 6 mois, soit fin de la recherche au 02/05/2014.
23 February 2013	MS6 : - Allongement du délai autorisé entre le diagnostic de la crise rénale sclérodermique et l'inclusion dans le protocole. - Suppression du test grossesse Béta HCG sanguin à la visite M6. - Ajout de l'interdiction de prescrire du Tacleer pendant les 6 mois de suivi des patients. - Ajout de 3 nouveaux centres investigateurs
11 October 2013	MS7 : Prolongation de la durée des inclusions de 1 an avec une fin d'étude au 09/09/2015 afin d'atteindre les objectifs en termes d'inclusions
07 March 2014	MS8 : Mise à jour de la liste des centres investigateurs.
20 April 2015	MS9 : - Mise à jour des coordonnées des personnes en charge de l'étude chez le promoteur et de l'investigatrice coordinatrice qui exerce maintenant à Pringy. - Ajout d'une précision dans le protocole sur le nombre de patients à inclure. - Mise à jour de la liste des investigateurs.

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
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10 January 2012	Suite à la réunion du Comité de Surveillance Indépendant, il est décidé : - d'interrompre les inclusions de cet essai, - de renforcer la surveillance de manière plus rapprochée des patients 4 et 5 jusqu'à la fin de leur participation à l'étude, avant d'envisager la reprise des inclusions	10 July 2012
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Notes:

## Limitations and caveats

None reported