



Clinical trial results:

Effacité du Rituximab au cours du syndrome néphrotique idiopathique ciclosporinodépendant de l'enfant.

Summary

EudraCT number	2009-018266-35
Trial protocol	FR BE
Global end of trial date	23 June 2014

Results information

Result version number	v1 (current)
This version publication date	03 June 2021
First version publication date	03 June 2021
Summary attachment (see zip file)	RRF Nephurutix (Résumé rapport final signé.pdf) Statistical report (Rapport statistique NEPHRUTIX V1.pdf)

Trial information

Trial identification

Sponsor protocol code	I08013
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01268033
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CHU de Limoges
Sponsor organisation address	2 avenue Martin Luther King, Limoges, France,
Public contact	Pr Vincent GUIGONIS, CHU de Limoges, +33 55556358, vincent.guigonis@unilim.fr
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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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 August 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 June 2014
Global end of trial reached?	Yes
Global end of trial date	23 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluer l'efficacité, en terme de prévention des rechutes lors d'une stratégie d'épargne des autres traitements immunosuppresseurs, du Rituximab dans le traitement des patients présentant un syndrome néphrotique ciclosporinodépendant, dans la population en intention de traiter.

Protection of trial subjects:

Premedication administered to patients should be completed 30 minutes before the infusion:

For patients weighing less than 40 kg:

- Paracetamol 20mg / kg (maximum 1g per infusion).
- Antihistamine: intravenous or oral:
 - * Dexchlorpheniramine: 1 ampoule of 5 mg IV (if weight greater than 20 kg) and ½ bulb if weight less than 20 kg).
 - *Or Ceterizine (oral route): <6 years: 2.5 mg; <12 years: 5 mg; ≥12 years: 10mg.
- Methylprednisolone: 0.5 mg / kg (maximum 20 mg IV).

For patients weighing 40 kg and over:

- Paracetamol (1g IV).
- Antihistamine: intravenous or oral:
 - *Dexchlorpheniramine: 1 ampoule of 5 mg IV.
 - *Or Ceterizine (oral route): 10mg.
- Methylprednisolone: 100mg IV.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 March 2011
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: 26
Worldwide total number of subjects	26
EEA total number of subjects	26

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	15
Adolescents (12-17 years)	11
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No pre-assignment period

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	Placebo
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Glucose 5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

in a bag of 250 ml for intravenous drip use

Investigational medicinal product name	Sodium chloride 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

use only for diabetic patient in a bag of 250 ml for intravenous drip use

Arm title	Mabthera
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Rituximab 100mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

750 mg/m² per day diluted in a bag of 250 ml for intravenous drip use

375mg/m² maximum per perfusion

Investigational medicinal product name	Rituximab 500mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous drip use

Dosage and administration details:

750 mg/m² per day diluted in a bag of 250 ml for intravenous drip use

375mg/m² maximum per perfusion

Number of subjects in period 1	Placebo	Mabthera
Started	14	12
Completed	13	12
Not completed	1	0
lack of inclusion criteria	1	-

Baseline characteristics

Reporting groups

Reporting group title	overall study
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Reporting group description: -

Reporting group values	overall study	Total	
Number of subjects	26	26	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	12		
full range (min-max)	5.34 to 17.34	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	19	19	

Subject analysis sets

Subject analysis set title	Treated patients
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

all patient treated

Reporting group values	Treated patients		
Number of subjects	25		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			

From 65-84 years 85 years and over			
Age continuous Units: years median full range (min-max)	12,16 5.34 to 17.34		
Gender categorical Units: Subjects			
Female Male	6 19		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Mabthera
Reporting group description: -	
Subject analysis set title	Treated patients
Subject analysis set type	Intention-to-treat
Subject analysis set description: all patient treated	

Primary: Number of patients having relapsed within 5 months

End point title	Number of patients having relapsed within 5 months ^[1]
End point description:	
End point type	Primary
End point timeframe: 5 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: see statistical report

End point values	Placebo	Mabthera		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: number	13	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	All patients
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Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 25 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Venous thrombosis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug ineffective for unapproved indication			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal pain			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 25 (8.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
gastrointestinal trouble			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Tracheobronchitis			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
eating intolerance			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 25 (72.00%)		
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	9 / 25 (36.00%) 14		
Gastrointestinal disorders Gastrointestinal pain subjects affected / exposed occurrences (all)	9 / 25 (36.00%) 9		
Vomiting subjects affected / exposed occurrences (all)	4 / 25 (16.00%) 8		
Infections and infestations nasopharyngitis subjects affected / exposed occurrences (all)	10 / 25 (40.00%) 15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2010	Addition of the PedsQL quality of life scale.
10 February 2011	Decrease in the period of use of anticalcineurins from 3 years to 1 year
21 March 2012	Clarification on the treatment methods in the event of a relapse. Addition of an investigation center. Update of the remedication modalities.
21 March 2013	Extension of the inclusion period by one year. Addition of investigator. Provision of details concerning the methods of decreasing immunosuppressive treatments Update of the side effects of Rituximab in the information leaflet following the letter of modifications from the ROCHE laboratory.
12 July 2013	Increased number of subjects required

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/29056249>