Clinical trial results:
CHARACTERIZATION OF RITUXIMAB PHARMACOKINETICS IN PATIENTS WITH KIDNEY DISEASES WITH PRIMARY GLOMERULAR AFFECTATION

Summary

EudraCT number	2020-000484-23
Trial protocol	ES
Global end of trial date	16 May 2024

Results information

Result version number	v1 (current)
This version publication date	27 October 2024
First version publication date	27 October 2024

Trial information

Trial identification

Sponsor protocol code	NEFRTX1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Vall d'Hebron Institute of Research
Sponsor organisation address	Paseo del Valle de Hebrón, 119-129 , Barcelona, Spain, 08035
Public contact	Maria Larrosa Garcia, Vall d'Hebron Institute of Research, 0034 934 89 30 00, maria.larrosa@vallhebron.cat
Scientific contact	Maria Larrosa Garcia, Vall d'Hebron Institute of Research, 0034 934 89 30 00, maria.larrosa@vallhebron.cat

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	16 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2024
Global end of trial reached?	Yes
Global end of trial date	16 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objetive of this study is to characterize the rituximab pharmacokinetic profile in patients with kidney disease with primary glomerular involvement; as well as evaluating the influence of proteinuria, FCGRT polymorphism and the presence of anti-drug antibodies on rituximab clearance.

Protection of trial subjects:

Blood and urine sampling was minimized in order to reduce patients charge and disconfort.

Background therapy:

This is a open-label, uncontrolled trial. All patients received rituximab according to clinical protocols and regular premedication including acetaminophen, methylprednisolone and dexchlorfeniramine, in order to avoid infusion reaction.

Evidence for comparator:

This is an uncontrolled trial.

Actual start date of recruitment	07 September 2020
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	Spain: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	21
From 65 to 84 years	27

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was done in the Vall d'Hebron University Hospital from September 2020 to May 2023.

Pre-assignment

Screening details:

Sixty-five patients went through screening, seventeen where not enrrolled due to refusal to participate in the clinical trial (16) and languaje barrier (1). Since patients received standard treatment in all cases in the context of an open-label, uncontrolled, low-intervention clinical trial there was not treatment assingment.

Period 1

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

Arms

Arm title	RItuximab

Arm description:

There was only one arm. All patients received rituximab according to clinical decision based on international clinical guidelines as a standard treatment.

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Patients received 500mg or 1000mg of rituximab according to clinical criteria, a second dose could be administered on day 14.
Medication was prepared in the Hospital Pharmacy Service, following the good manufacturing practice (GMP) guidelines.
Infusion was done accorging to standard clinical practice by trained nurses; measures to prevent infusion reaction included low rate infusion, post-infusion monitoring and premedication with acetaminophen, methylprednisolone and dexchlorfeniramine.

Number of subjects in period 1	RItuximab
Started	48
Pharmacokinetic analysis	35
Completed	35
Not completed	13
Samples degradation during conservation	7
Protocol deviation	6

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	48	48	
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			
Patients included were 62 (17) years old at the time at the enrollment. All of them were adults.			
Units: years			
arithmetic mean	62.3		
standard deviation	± 16.8	-	
Gender categorical			
Gender was obtained from the electronic medical record, where only male or female options are considered.			
Units: Subjects			
Female	22	22	
Male	26	26	
Diagnosis			
Patients could receive rituximab due to glomerular damage having differnet diseases.			
Units: Subjects			
ANCA-associated vasculitis	16	16	
Membranous neprhopathy	20	20	
Minimal change disease	11	11	
Focal segmental glomerulosclerosis	1	1	
Previous exposure to rituximab			
Patients that received rituximab previous to study enrollment. Rituximab was administered at least 6 months prioir to enrolment following inclusion criteria.			
Units: Subjects			
Previously exposed	35	35	
Not previously exposed	13	13	
Newly diagnosed			
Patients were considered newly diagnosed in case they received rituximab less than 3 months after diagnosis.			
Units: Subjects			
Yes	7	7	

No	41	41	

End points

End points reporting groups

Reporting group title	RItuximab

Reporting group description:

There was only one arm. All patients received rituximab according to clinical decision based on international clinical guidelines as a standard treatment.

Subject analysis set title	Patients included
Subject analysis set type	Per protocol

Subject analysis set description:

Patients that received rituximab and have the minimum blood and urine samples available for analysis and pharmacokinetic evaluation.

Subject analysis set title	Patients enrolled
Subject analysis set type	Full analysis

Subject analysis set description:

All patients included.

Primary: Maximum rituximab concentration

End point title	Maximum rituximab concentration[1]

End point description:

End point type	Primary

End point timeframe:

Day 1 after rituximab admisnitration.

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: This is a low-intervention study to characterize rituximab pharmacokinetics in a population. The goal of this study was to describe pharmacokinetic parameters in this population; therefore, our results are descriptive and there is no statistical analysis of the endpoints.

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: µg/ml				
arithmetic mean (standard deviation)	179.4 (± 71.8)	179.4 (± 71.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Distribution volume

End point title	Distribution volume[2]

End point description:

End point type	Primary

End point timeframe:

This value was calculated at the time of pharmacockinetic analysis, when rituximab plasma concentrations measured from d1 to d45 were determined.

Notes:

[2] - 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: This is a low-intervention study to characterize rituximab pharmacokinetics in a population. The goal of this study was to describe pharmacokinetic parameters in this population; therefore, our results are descriptive and there is no statistical analysis of the endpoints.

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: ml/kg				
arithmetic mean (standard deviation)	78.9 (± 31.4)	78.9 (± 31.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Clearance

End point title	Clearance[3]

End point description:

End point type	Primary

End point timeframe:

This value was calculated at the time of pharmacockinetic analysis, when rituximab plasma concentrations measured from d1 to d45 were determined.

Notes:

[3] - 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: This is a low-intervention study to characterize rituximab pharmacokinetics in a population. The goal of this study was to describe pharmacokinetic parameters in this population; therefore, our results are descriptive and there is no statistical analysis of the endpoints.

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: ml/h/kg				
arithmetic mean (standard deviation)	0.30 (± 0.27)	0.30 (± 0.27)		

Statistical analyses

No statistical analyses for this end point

Primary: Half-life

End point title	Half-life[4]

End point description:

End point type	Primary

End point timeframe:

This value was calculated at the time of pharmacockinetic analysis, when rituximab plasma concentrations measured from d1 to d45 were determined.

Notes:

[4] - 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: This is a low-intervention study to characterize rituximab pharmacokinetics in a population. The goal of this study was to describe pharmacokinetic parameters in this population; therefore, our results are descriptive and there is no statistical analysis of the endpoints.

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: days				
arithmetic mean (standard deviation)	11.6 (± 5.8)	11.6 (± 5.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Elimination constant (Kel)

End point title	Elimination constant (Kel)[5]

End point description:

End point type	Primary

End point timeframe:

This value was calculated at the time of pharmacockinetic analysis, when rituximab plasma concentrations measured from d1 to d45 were determined.

Notes:

[5] - 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: This is a low-intervention study to characterize rituximab pharmacokinetics in a population. The goal of this study was to describe pharmacokinetic parameters in this population; therefore, our results are descriptive and there is no statistical analysis of the endpoints.

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: h-1				
arithmetic mean (standard deviation)	0.0036 (± 0.0030)	0.0036 (± 0.0030)		

Statistical analyses

No statistical analyses for this end point

Primary: Area under the curve

End point title	Area under the curve[6]

End point description:

End point type	Primary

End point timeframe:

This value was calculated at the time of pharmacockinetic analysis, when rituximab plasma concentrations measured from d1 to d45 were determined.

Notes:

[6] - 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: This is a low-intervention study to characterize rituximab pharmacokinetics in a population. The goal of this study was to describe pharmacokinetic parameters in this population; therefore, our results are descriptive and there is no statistical analysis of the endpoints.

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: µg·h/ml				
arithmetic mean (standard deviation)	117756.1 (± 88228.1)	117756.1 (± 88228.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete response

End point title	Complete response

End point description:

Complete response was evaluated according to Kidney Glomerular Diseases Guidelines 2021.

End point type	Secondary

End point timeframe:

Clinical response was evaluated 1 year after rituximab administration (day 1).

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: patients	14	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Partial response

End point title	Partial response

End point description:

Complete response was evaluated according to Kidney Glomerular Diseases Guidelines 2021.

End point type	Secondary

End point timeframe:

Clinical response was evaluated 1 year after rituximab administration (day 1).

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: patients	12	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse

End point title	Relapse

End point description:

Relapse was evaluated according to Kidney Glomerular Diseases Guidelines 2021.

End point type	Secondary

End point timeframe:

Clinical response was evaluated 1 year after rituximab administration (day 1).

End point values	RItuximab	Patients included		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	35	35		
Units: patients	4	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were recorded during the time of the study, one year after rituximab admisnitration.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups	
Reporting group title	Patients enrolled
Reporting group description:	
All the 48 patients enrolled were included in the safety analysis.	

Serious adverse events	Patients enrolled		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Patients enrolled		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 48 (2.08%)		
Immune system disorders			
Infusion related hypersensitivity reaction	Additional description: A patient experienced an infusion reaction with throat itching and redness of the ears. The adverse reaction was controlled with medication, and rituximab could continue to be administered minutes later at a slower rate under medical supervision.		
subjects affected / exposed	1 / 48 (2.08%)		
occurrences (all)	1		

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