



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 objective 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 discomfort.

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 enrolled due to refusal to participate in the clinical trial (16) and language 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 different diseases. | | | |
| Units: Subjects | | | |
| ANCA-associated vasculitis | 16 | 16 | |
| Membranous nephropathy | 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 prior 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 | RIItuximab |
| 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 admisnitation. | |
| 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 | RIItuximab | 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 pharmacokinetic 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 | RIituximab | 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 pharmacokinetic 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 | RIituximab | 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 pharmacokinetic 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 | RIituximab | 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 pharmacokinetic 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 | RIituximab | 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 pharmacokinetic 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 | RIrituximab | 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 | RIrituximab | 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 | RIItuximab | 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 | RIItuximab | 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 administration.

| | |
|-----------------|------------|
| 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