



## Clinical trial results:

### A Multicenter, Open-Label, Uncontrolled, Extension Study of RA101495 in Subjects with Paroxysmal Nocturnal Hemoglobinuria who have Completed a RA101495 Clinical Study

#### Summary

EudraCT number	2016-003523-34
Trial protocol	FI HU DK GB
Global end of trial date	26 October 2021

#### Results information

Result version number	v2 (current)
This version publication date	15 December 2022
First version publication date	23 September 2022
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review.</li></ul>

#### Trial information

##### Trial identification

Sponsor protocol code	RA101495-01.202
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03225287
WHO universal trial number (UTN)	-
Other trial identifiers	UCB Study Id: PNH001

Notes:

#### Sponsors

Sponsor organisation name	Ra Pharmaceuticals, Inc.
Sponsor organisation address	87 Cambridge Park Drive, Cambridge, Massachusetts, United States, 02140
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

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	21 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 September 2021
Global end of trial reached?	Yes
Global end of trial date	26 October 2021
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

- To provide access to RA101495 for participants with PNH who have completed a Ra Pharmaceuticals sponsored study, have demonstrated clinical benefit, and who wish to continue receiving RA101495 for treatment of PNH
- To evaluate the long-term safety and tolerability of RA101495 administered to participants with PNH who have completed a Ra Pharmaceuticals sponsored RA101495 clinical study
- To evaluate the long-term preliminary efficacy of RA101495 administered to participants with PNH who have completed a Ra Pharmaceuticals sponsored RA101495 clinical study
- To obtain periodic PK and PD data to confirm long-term maintenance of steady-state RA101495 plasma levels and sustained inhibition of hemolysis and complement

Protection of trial subjects:

During the conduct of the study all participants were monitored for safety.

Background therapy:

Background therapy as permitted in the protocol at the discretion of each treating physician.

Evidence for comparator:

Not applicable

Actual start date of recruitment	17 July 2017
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	Australia: 3
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	19
EEA total number of subjects	5

Notes:

<b>Subjects enrolled per age group</b>	
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)	13
From 65 to 84 years	6
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study started to enroll participants in July 2017 and concluded in October 2021.

### Pre-assignment

Screening details:

The Participant Flow refers to the All Enrolled Subjects.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Zilucoplan-Cohort A (Eculizumab Naïve)
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Arm description:

Cohort A (Eculizumab Naïve) included all participants from study RA101495-01.201 (NCT03078582) who had not received eculizumab for treatment of paroxysmal nocturnal hemoglobinuria (PNH). Participants received a loading dose of 0.3 milligram/kilogram (mg/kg) zilucoplan administered by subcutaneous (SC) injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.

Arm type	Experimental
Investigational medicinal product name	Zilucoplan
Investigational medicinal product code	RA101495
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received zilucoplan administered by SC injection at pre-defined timepoints.

<b>Arm title</b>	Zilucoplan-Cohort B (Eculizumab Switch)
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Arm description:

Cohort B (Eculizumab Switch) included all participants from study RA101495-01.201 (NCT03078582) who had received eculizumab for treatment of PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.

Arm type	Experimental
Investigational medicinal product name	Zilucoplan
Investigational medicinal product code	RA101495
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received zilucoplan administered by SC injection at pre-defined timepoints.

<b>Arm title</b>	Zilucoplan (Inadequate Responder to Eculizumab)
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Arm description:

Inadequate Responder cohort included participants from qualifying study RA101495-01.203

(NCT03030183) who had an inadequate response to eculizumab treatment for PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.

Arm type	Experimental
Investigational medicinal product name	Zilucoplan
Investigational medicinal product code	RA101495
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received zilucoplan administered by SC injection at pre-defined timepoints.

Number of subjects in period 1	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)
Started	10	6	3
Completed	0	0	0
Not completed	10	6	3
Stem cell transplantation	-	1	-
Protocol non-compliance	-	-	1
Adverse event, non-fatal	-	-	1
Trial drug not effective	-	1	-
Sponsor, regulatory, or EC/IRB request	7	3	1
Subject withdraws consent	3	-	-
Need of transfusions and signs of hemolysis	-	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Zilucoplan-Cohort A (Eculizumab Naïve)
Reporting group description:	
Cohort A (Eculizumab Naïve) included all participants from study RA101495-01.201 (NCT03078582) who had not received eculizumab for treatment of paroxysmal nocturnal hemoglobinuria (PNH). Participants received a loading dose of 0.3 milligram/kilogram (mg/kg) zilucoplan administered by subcutaneous (SC) injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.	
Reporting group title	Zilucoplan-Cohort B (Eculizumab Switch)
Reporting group description:	
Cohort B (Eculizumab Switch) included all participants from study RA101495-01.201 (NCT03078582) who had received eculizumab for treatment of PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.	
Reporting group title	Zilucoplan (Inadequate Responder to Eculizumab)
Reporting group description:	
Inadequate Responder cohort included participants from qualifying study RA101495-01.203 (NCT03030183) who had an inadequate response to eculizumab treatment for PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.	

Reporting group values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)
Number of subjects	10	6	3
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	6	4	3
>=65 years	4	2	0
Age Continuous Units: years			
arithmetic mean	59.6	45.0	35.3
standard deviation	± 14.5	± 23.0	± 16.3
Sex: Female, Male Units: participants			
Female	6	1	1
Male	4	5	2

Reporting group values	Total		
Number of subjects	19		
Age Categorical Units: participants			
<=18 years	0		
Between 18 and 65 years	13		

>=65 years	6		
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Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: participants			
Female	8		
Male	11		

## End points

### End points reporting groups

Reporting group title	Zilucoplan-Cohort A (Eculizumab Naïve)
Reporting group description: Cohort A (Eculizumab Naïve) included all participants from study RA101495-01.201 (NCT03078582) who had not received eculizumab for treatment of paroxysmal nocturnal hemoglobinuria (PNH). Participants received a loading dose of 0.3 milligram/kilogram (mg/kg) zilucoplan administered by subcutaneous (SC) injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.	
Reporting group title	Zilucoplan-Cohort B (Eculizumab Switch)
Reporting group description: Cohort B (Eculizumab Switch) included all participants from study RA101495-01.201 (NCT03078582) who had received eculizumab for treatment of PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.	
Reporting group title	Zilucoplan (Inadequate Responder to Eculizumab)
Reporting group description: Inadequate Responder cohort included participants from qualifying study RA101495-01.203 (NCT03030183) who had an inadequate response to eculizumab treatment for PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.	

### Primary: Percentage of participants with Treatment Emergent Adverse events (TEAEs)

End point title	Percentage of participants with Treatment Emergent Adverse events (TEAEs) <sup>[1]</sup>
End point description: TEAEs were defined as an AE that occurs after a participant's initial treatment zilucoplan start for this study (RA101495-01.202) that was not present at the time of treatment start, or an AE that increases in severity after treatment start in this study, if the event was present at the time of treatment start. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of this extension study.	
End point type	Primary
End point timeframe: From Day 1 until the Final Study Visit (up to Month 49)	

#### 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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	6	3	
Units: percentage of participants				
number (not applicable)	90.0	100	66.7	



## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of participants with Serious TEAEs

End point title	Percentage of participants with Serious TEAEs <sup>[2]</sup>
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End point description:

Serious Adverse event (SAE) was defined as any untoward medical occurrence that: • results in death, • is life-threatening threatening (note that this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it were more severe), • requires hospitalization or prolongation of existing hospitalization, • results in persistent or significant disability/incapacity, and • results in a congenital anomaly/birth defect. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of this extension study.

End point type	Primary
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End point timeframe:

From Day 1 until the Final Study Visit (up to Month 49)

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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	6	3	
Units: percentage of participants				
number (not applicable)	10.0	50.0	66.7	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with anti-drug antibodies (ADA)

End point title	Number of participants with anti-drug antibodies (ADA)
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End point description:

Blood samples collection were planned to analyze for the presence/absence of ADAs to zilucoplan for immunogenicity assessments. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of this extension study. The planned analysis of immunogenicity (ADA) was not performed as the assay was considered not fit for purpose due to an insufficient level of drug tolerance; therefore, no samples were processed.

End point type	Secondary
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End point timeframe:

At Day 1, Month 1, 2, 3, 6, 9, and 12

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[3]</sup>	0 <sup>[4]</sup>	0 <sup>[5]</sup>	
Units: participants				

Notes:

[3] - Due to insufficient level of drug tolerance samples were not processed.

[4] - Due to insufficient level of drug tolerance samples were not processed.

[5] - Due to insufficient level of drug tolerance samples were not processed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Serum Lactate Dehydrogenase (LDH) Levels at each time point

End point title	Change from Baseline in Serum Lactate Dehydrogenase (LDH) Levels at each time point
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End point description:

Serum LDH levels were measure of intravascular hemolysis. As high level of LDH in the blood was indicative of hemolysis in participants with PNH. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of this extension study. Baseline was generally the final visit of the qualifying study (RA101495-01.201 or RA101495-01.203). Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: Units per litre (U/L)				
arithmetic mean (standard deviation)				
Month 1 (n= 9, 6, 3)	-3.7 (± 71.5)	10.0 (± 16.4)	336.7 (± 636.9)	
Month 2 (n= 9, 5, 2)	50.3 (± 156.2)	-2.4 (± 22.2)	676.5 (± 970.9)	
Month 3 (n= 8, 5, 2)	-6.5 (± 58.2)	-1.6 (± 40.5)	39.5 (± 40.3)	
Month 6 (n=8, 5, 2)	32.4 (± 142.5)	-28.4 (± 127.3)	-3.5 (± 12.0)	
Month 9 (n=8, 3, 2 )	-18.1 (± 59.7)	22.7 (± 23.6)	-5.0 (± 35.4)	

Month 12 (n= 7, 3, 2)	-39.7 (± 54.9)	8.7 (± 10.1)	456.0 (± 640.6)	
Month 15 (n= 6, 3, 2)	-24.5 (± 70.8)	4.0 (± 30.4)	174.5 (± 215.7)	
Month 18 (n=7, 3, 1)	-27.9 (± 54.8)	5.7 (± 56.8)	-56.0 (± 99999)	
Month 21 (n= 7, 3, 1)	-12.0 (± 93.9)	-7.3 (± 33.5)	73.0 (± 99999)	
Month 24 (n= 7, 3, 1)	-18.7 (± 53.9)	-27.0 (± 64.1)	-29.0 (± 99999)	
Month 27 (n= 5, 2, 0)	-14.0 (± 99.3)	58.0 (± 8.5)	99999 (± 99999)	
Month 30 (n= 5, 2, 1)	-28.0 (± 36.1)	59.0 (± 140.0)	1817.0 (± 99999)	
Month 33 (n= 5, 3, 0)	-39.0 (± 65.9)	-16.3 (± 66.7)	99999 (± 99999)	
Month 36 (n= 5, 2, 0)	-61.6 (± 47.1)	0.5 (± 4.9)	99999 (± 99999)	
Month 39 (n= 5, 3, 0)	-78.4 (± 80.9)	-29.7 (± 83.5)	99999 (± 99999)	
Month 42 (n= 4, 2, 0)	-42.3 (± 78.3)	35.5 (± 75.7)	99999 (± 99999)	
Month 45 (n= 1, 1, 0)	27.0 (± 99999)	53.0 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 9, 5, 2)	41.6 (± 303.1)	-93.2 (± 139.8)	682.0 (± 548.7)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Total Bilirubin Values at each time point

End point title	Change from Baseline in Total Bilirubin Values at each time point
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End point description:

Total Bilirubin was monitored for signs and symptoms of hepatic or biliary dysfunction. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of the extension study. Baseline was generally the final visit of the qualifying study (RA101495-01.201 or RA101495-01.203). Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' (Number analyzed) signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: micromole per litre (umol/L)				

arithmetic mean (standard deviation)				
Month 1 (n= 9, 6, 3)	-2.1 (± 7.7)	1.7 (± 6.2)	-0.3 (± 4.5)	
Month 2 (n= 9, 5, 2)	0.1 (± 10.7)	2.0 (± 7.2)	6.0 (± 2.8)	
Month 3 (n= 8, 5, 2)	1.4 (± 13.7)	8.2 (± 13.1)	3.5 (± 2.1)	
Month 6 (n= 8, 5, 2)	4.6 (± 14.8)	3.2 (± 7.2)	2.5 (± 0.7)	
Month 9 (n= 8, 3, 2)	-0.3 (± 7.4)	6.0 (± 3.0)	-1.0 (± 1.4)	
Month 12 (n= 8, 3, 2)	3.9 (± 8.4)	3.0 (± 2.0)	2.5 (± 3.5)	
Month 15 (n= 7, 3, 2)	-0.4 (± 6.4)	6.0 (± 9.5)	8.5 (± 9.2)	
Month 18 (n= 6, 3, 1)	2.8 (± 9.5)	2.0 (± 6.2)	3.0 (± 99999)	
Month 21 (n= 7, 3, 1)	3.9 (± 8.3)	2.0 (± 7.8)	7.0 (± 99999)	
Month 24 (n= 7, 3, 1)	5.1 (± 16.0)	-1.3 (± 3.1)	8.0 (± 99999)	
Month 27 (n= 7, 2, 0)	4.3 (± 12.2)	-2.0 (± 5.7)	99999 (± 99999)	
Month 30 (n= 5, 2, 1)	5.8 (± 14.6)	3.0 (± 7.1)	13.0 (± 99999)	
Month 33 (n= 5, 3, 0)	2.6 (± 5.7)	3.0 (± 2.6)	99999 (± 99999)	
Month 36 (n= 5, 2, 0)	-3.8 (± 6.8)	3.0 (± 0.0)	99999 (± 99999)	
Month 39 (n= 5, 3, 0)	0.2 (± 3.1)	0.7 (± 4.6)	99999 (± 99999)	
Month 42 (n= 5, 2, 0)	4.8 (± 15.5)	4.0 (± 15.6)	99999 (± 99999)	
Month 45 (n= 2, 1, 0)	5.0 (± 17.0)	-2.0 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 9, 5, 2)	8.0 (± 17.3)	0.4 (± 3.9)	0.0 (± 9.9)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Total Hemoglobin Values at each time point

End point title	Change from Baseline in Total Hemoglobin Values at each time point
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End point description:

Total Hemoglobin Values were analyzed for hematology assessments. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of the extension study. Baseline was generally the final visit of the qualifying study (RA101495-01.201 or RA101495-01.203). Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' (Number analyzed) signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: grams per litre (g/L)				
arithmetic mean (standard deviation)				
Month 1 (n= 8, 6, 3)	0.0 (± 11.4)	0.0 (± 8.2)	-5.7 (± 3.8)	
Month 2 (n= 9, 5, 2)	1.1 (± 8.3)	-5.0 (± 9.9)	-2.0 (± 11.3)	
Month 3 (n= 7, 5, 2)	6.4 (± 6.4)	3.0 (± 9.1)	-3.5 (± 6.4)	
Month 6 (n= 8, 5, 2)	1.1 (± 11.2)	2.0 (± 17.9)	-5.0 (± 17.0)	
Month 9 (n= 8, 3, 2)	2.9 (± 7.1)	-1.3 (± 4.0)	-9.0 (± 5.7)	
Month 12 (n= 8, 3, 2)	2.9 (± 6.1)	-1.7 (± 6.8)	-5.0 (± 17.0)	
Month 15 (n= 7, 3, 2)	3.9 (± 8.4)	-5.0 (± 5.3)	-9.0 (± 28.3)	
Month 18 (n= 7, 3, 1)	5.0 (± 4.9)	1.7 (± 9.5)	-2.0 (± 99999)	
Month 21 (n= 7, 3, 1)	6.4 (± 6.3)	-6.7 (± 7.6)	-1.0 (± 99999)	
Month 24 (n= 7, 3, 0)	7.9 (± 12.6)	-5.0 (± 2.6)	99999 (± 99999)	
Month 27 (n= 7, 2, 0)	7.0 (± 10.0)	-5.0 (± 11.3)	99999 (± 99999)	
Month 30 (n= 5, 2, 1)	10.8 (± 7.0)	-4.5 (± 12.0)	-8.0 (± 99999)	
Month 33 (n= 5, 3, 0)	10.0 (± 8.8)	-3.0 (± 4.4)	99999 (± 99999)	
Month 36 (n= 5, 2, 0)	8.4 (± 14.2)	-2.0 (± 4.2)	99999 (± 99999)	
Month 39 (n= 5, 3, 0)	7.6 (± 10.1)	4.7 (± 2.9)	99999 (± 99999)	
Month 42 (n= 5, 2, 0)	5.2 (± 11.2)	5.5 (± 0.7)	99999 (± 99999)	
Month 45 (n= 3, 1, 0)	-1.3 (± 23.3)	-4.0 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 9, 4, 1)	1.8 (± 10.6)	-2.0 (± 4.1)	-7.0 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Free Hemoglobin Values at each time point

End point title	Change from Baseline in Free Hemoglobin Values at each time point
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End point description:

Free Hemoglobin Values were analyzed for hematology assessments. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of the extension study. Baseline was generally the final visit of the qualifying study (RA101495-01.201 or RA101495-01.203). Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' (Number analyzed) signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, and Final Study Visit (Month 49)

<b>End point values</b>	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	5	2	
Units: milligrams per decilitre (mg/dL)				
arithmetic mean (standard deviation)				
Month 1 (n= 6, 5, 2)	-0.20 (± 2.78)	2.86 (± 4.30)	0.80 (± 4.38)	
Month 2 (n= 5, 5, 1)	-1.14 (± 3.04)	0.48 (± 1.77)	6.10 (± 99999)	
Month 3 (n= 5, 5, 1)	1.34 (± 0.48)	-0.02 (± 0.95)	0.80 (± 99999)	
Month 6 (n= 6, 4, 1)	-0.43 (± 1.24)	0.55 (± 2.45)	1.20 (± 99999)	
Month 9 (n= 6, 3, 1)	-1.10 (± 2.11)	-1.50 (± 1.57)	0.00 (± 99999)	
Month 12 (n= 7, 2, 1)	-0.56 (± 2.80)	0.80 (± 0.28)	2.10 (± 99999)	
Month 15 (n= 4, 2, 1)	3.93 (± 11.61)	-1.35 (± 2.19)	1.60 (± 99999)	
Month 18 (n= 4, 3, 0)	1.98 (± 3.05)	0.77 (± 1.56)	99999 (± 99999)	
Month 21 (n= 4, 2, 0)	3.15 (± 5.84)	-1.30 (± 0.85)	99999 (± 99999)	
Month 24 (n= 3, 2, 0)	0.27 (± 0.35)	-0.50 (± 0.99)	99999 (± 99999)	
Month 27 (n= 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Month 30 (n= 3, 0, 0)	0.33 (± 2.37)	99999 (± 99999)	99999 (± 99999)	
Month 33 (n= 3, 1, 0)	0.17 (± 2.66)	5.80 (± 99999)	99999 (± 99999)	
Month 36 (n= 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Month 39 (n= 1, 2, 0)	-0.60 (± 99999)	-0.95 (± 0.64)	99999 (± 99999)	
Month 42 (n= 1, 2, 0)	1.30 (± 99999)	0.50 (± 3.68)	99999 (± 99999)	
Month 45 (n= 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 1, 2, 1)	-2.70 (± 99999)	-0.60 (± 1.13)	-3.10 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Haptoglobin Values at each time point

End point title	Change from Baseline in Haptoglobin Values at each time point
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End point description:

Haptoglobin values were analyzed for hematology assessments. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of the extension study. Baseline was generally the final visit of the qualifying study (RA101495-01.201 or RA101495-01.203). Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' (Number analyzed) signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0

participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
End point timeframe:	
Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, and Final Study Visit (Month 49)	

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: g/L				
arithmetic mean (standard deviation)				
Month 1 (n= 9, 6, 3)	0.032 (± 0.097)	0.000 (± 0.000)	0.000 (± 0.000)	
Month 2 (n= 9, 5, 2)	0.053 (± 0.160)	0.000 (± 0.000)	0.000 (± 0.000)	
Month 3 (n= 8, 5, 2)	0.021 (± 0.060)	0.000 (± 0.000)	0.000 (± 0.000)	
Month 6 (n= 8, 5, 2)	0.031 (± 0.088)	0.036 (± 0.080)	0.020 (± 0.028)	
Month 9 (n= 8, 3, 2)	0.008 (± 0.021)	0.000 (± 0.000)	0.000 (± 0.000)	
Month 12 (n= 8, 3, 2)	0.000 (± 0.000)	0.000 (± 0.000)	0.000 (± 0.000)	
Month 15 (n= 7, 3, 2)	0.000 (± 0.000)	0.000 (± 0.000)	0.000 (± 0.000)	
Month 18 (n= 7, 3, 1)	0.000 (± 0.000)	0.000 (± 0.000)	0.000 (± 99999)	
Month 21 (n= 7, 3, 1)	0.030 (± 0.079)	0.000 (± 0.000)	0.000 (± 99999)	
Month 24 (n= 7, 3, 1)	0.030 (± 0.079)	0.000 (± 0.000)	0.000 (± 99999)	
Month 27 (n= 7, 2, 0)	0.000 (± 0.000)	0.000 (± 0.000)	99999 (± 99999)	
Month 30 (n= 5, 2, 1)	0.004 (± 0.009)	0.000 (± 0.000)	0.000 (± 99999)	
Month 33 (n= 5, 3, 0)	0.002 (± 0.004)	0.000 (± 0.000)	99999 (± 99999)	
Month 36 (n= 5, 2, 0)	0.036 (± 0.080)	0.000 (± 0.000)	99999 (± 99999)	
Month 39 (n= 5, 3, 0)	0.020 (± 0.045)	0.000 (± 0.000)	99999 (± 99999)	
Month 42 (n= 5, 2, 0)	0.034 (± 0.076)	0.000 (± 0.000)	99999 (± 99999)	
Month 45 (n= 2, 1, 0)	0.080 (± 0.113)	0.000 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 9, 5, 2)	0.042 (± 0.127)	0.006 (± 0.013)	0.000 (± 0.000)	

## Statistical analyses

**Secondary: Change from Baseline in Reticulocytes Values at each time point**

End point title	Change from Baseline in Reticulocytes Values at each time point
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## End point description:

Reticulocytes values were analyzed for hematology assessments. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of the extension study. Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' (Number analyzed) signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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## End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: 10 <sup>12</sup> reticulocytes (cells)/L				
arithmetic mean (standard deviation)				
Month 1 (n= 8, 6, 3)	0.0104 (± 0.0484)	0.0107 (± 0.0299)	-0.0457 (± 0.0505)	
Month 2 (n= 9, 5, 2)	-0.0046 (± 0.0354)	-0.0046 (± 0.0130)	0.0115 (± 0.0049)	
Month 3 (n= 7, 5, 2)	-0.0249 (± 0.0310)	-0.0112 (± 0.0251)	0.0170 (± 0.0113)	
Month 6 (n= 8, 5, 2)	-0.0006 (± 0.0452)	-0.0042 (± 0.0363)	0.0200 (± 0.0382)	
Month 9 (n= 8, 3, 2)	0.0063 (± 0.0334)	0.0070 (± 0.0171)	0.0640 (± 0.0297)	
Month 12 (n= 8, 3, 2)	-0.0041 (± 0.0427)	-0.0070 (± 0.0346)	0.0240 (± 0.0113)	
Month 15 (n= 7, 3, 2)	-0.0264 (± 0.0601)	-0.0343 (± 0.0191)	0.0285 (± 0.0290)	
Month 18 (n= 7, 3, 1)	-0.0040 (± 0.0382)	0.0027 (± 0.0380)	0.0460 (± 99999)	
Month 21 (n= 7, 3, 0)	-0.0223 (± 0.0554)	-0.0087 (± 0.0380)	99999 (± 99999)	
Month 24 (n= 7, 3, 0)	-0.0123 (± 0.0711)	-0.0093 (± 0.0186)	99999 (± 99999)	
Month 27 (n= 7, 2, 0)	-0.0017 (± 0.0553)	0.0150 (± 0.0127)	99999 (± 99999)	
Month 30 (n= 5, 2, 1)	0.0016 (± 0.0524)	0.0060 (± 0.0594)	0.0300 (± 99999)	
Month 33 (n= 5, 3, 0)	-0.0302 (± 0.0446)	-0.0093 (± 0.0234)	99999 (± 99999)	
Month 36 (n= 5, 2, 0)	-0.0630 (± 0.0621)	-0.0215 (± 0.0078)	99999 (± 99999)	
Month 39 (n= 5, 3, 0)	-0.0340 (± 0.0860)	-0.0133 (± 0.0291)	99999 (± 99999)	



Month 42 (n= 5, 2, 0)	-0.0270 (± 0.0721)	-0.0015 (± 0.0078)	99999 (± 99999)	
Month 45 (n= 3, 1, 0)	-0.0423 (± 0.1189)	-0.0050 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 8, 4, 1)	-0.0433 (± 0.0480)	-0.0333 (± 0.0116)	0.0100 (± 99999)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Hemoglobinuria Values at each time point

End point title	Change from Baseline in Hemoglobinuria Values at each time point
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End point description:

Hemoglobinuria was assessed using a urine colorimetric scoring system with a score of 1 through 10 where 1 represents no hemoglobinuria and 10 represents maximum hemoglobinuria. Safety population included all participants who received at least 1 injection of zilucoplan on or after Day 1 of the extension study. Baseline was generally the final visit of the qualifying study (RA101495-01.201 or RA101495-01.203). Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' (Number analyzed) signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and Standard Deviation (SD) was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48 and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: score on a scale				
arithmetic mean (standard deviation)				
Month 1 (n= 8, 6, 3)	0.1 (± 1.0)	0.2 (± 1.5)	1.7 (± 1.5)	
Month 2 (n= 9, 5, 2)	0.9 (± 1.4)	0.8 (± 1.3)	1.0 (± 1.4)	
Month 3 (n= 8, 5, 1)	0.4 (± 1.2)	0.8 (± 1.3)	0.0 (± 99999)	
Month 6 (n= 8, 5, 1)	0.4 (± 0.9)	0.8 (± 1.3)	0.0 (± 99999)	
Month 9 (n= 8, 2, 1)	0.4 (± 0.9)	1.5 (± 2.1)	0.0 (± 99999)	
Month 12 (n= 8, 3, 2)	0.9 (± 1.4)	1.0 (± 1.7)	1.0 (± 1.4)	
Month 15 (n= 7, 3, 2)	0.9 (± 1.1)	1.0 (± 1.7)	1.0 (± 1.4)	
Month 18 (n= 7, 3, 1)	0.1 (± 0.9)	0.3 (± 0.6)	0.0 (± 99999)	
Month 21 (n= 7, 3, 1)	0.7 (± 1.6)	1.0 (± 1.7)	0.0 (± 99999)	
Month 24 (n= 7, 3, 1)	0.6 (± 1.6)	0.3 (± 0.6)	0.0 (± 99999)	
Month 27 (n= 7, 2, 1)	0.7 (± 1.5)	1.5 (± 2.1)	0.0 (± 99999)	
Month 30 (n= 5, 2, 1)	0.6 (± 1.3)	1.5 (± 2.1)	0.0 (± 99999)	
Month 33 (n= 5, 3, 0)	1.4 (± 0.9)	1.0 (± 1.7)	99999 (± 99999)	

Month 36 (n= 5, 2, 0)	1.4 (± 1.9)	1.5 (± 2.1)	99999 (± 99999)	
Month 39 (n= 5, 3, 0)	0.4 (± 1.7)	1.0 (± 1.7)	99999 (± 99999)	
Month 42 (n= 5, 2, 0)	1.0 (± 1.2)	1.5 (± 2.1)	99999 (± 99999)	
Month 45 (n= 3, 1, 0)	1.0 (± 1.0)	-1.0 (± 99999)	99999 (± 99999)	
Month 48 (n= 0, 0, 0)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	
Final Study Visit (Month 49) (n= 9, 5, 2)	0.4 (± 1.1)	0.6 (± 0.9)	2.5 (± 3.5)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma concentrations of RA101495 and its major metabolite(s)

End point title	Plasma concentrations of RA101495 and its major metabolite(s)
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End point description:

Blood samples of RA101495 (zilucoplan) and its metabolites (RA102758 and RA103488) were collected for Plasma concentration analysis. Pharmacokinetic (PK) population included all participants in the Safety population who had at least 1 plasma sample obtained for PK assessment. Here, 'n' signifies participants who were evaluable at specified time points. '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Predose: At Day 1 (Screening), Month 1, 2, 3, 6, 9, 12, and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	3	
Units: micrograms per litre (ug/L)				
arithmetic mean (standard deviation)				
RA101495- Day 1 (n= 9, 5, 3)	10999.99 (± 2698.29)	13616.08 (± 1490.81)	6976.50 (± 5663.23)	
RA101495- Month 1 (n= 9, 6, 3)	10879.13 (± 2405.19)	12645.38 (± 1620.31)	7630.03 (± 7060.56)	
RA101495- Month 2 (n= 9, 5, 2)	11276.17 (± 2896.98)	12220.10 (± 2188.78)	6865.45 (± 8108.18)	
RA101495- Month 3 (n= 8, 5, 2)	10806.17 (± 3418.92)	12315.28 (± 2515.84)	12430.00 (± 16.55)	
RA101495- Month 6 (n= 6, 5, 1)	9393.42 (± 2224.52)	12218.72 (± 2166.05)	12254.00 (± 99999)	
RA101495- Month 9 (n= 7, 3, 2)	11848.67 (± 2685.92)	12282.83 (± 3064.42)	15193.35 (± 2756.66)	
RA101495- Month 12 (n= 8, 3, 2)	11495.99 (± 2885.81)	13279.97 (± 2148.60)	12038.65 (± 7934.94)	
RA101495-Final Study Visit (Month 49) (n= 0, 0, 1)	99999 (± 99999)	99999 (± 99999)	7174.20 (± 99999)	

RA102758- Day 1 (n= 9, 5, 3)	1883.49 (± 593.93)	2443.62 (± 560.97)	1280.07 (± 1109.03)
RA102758- Month 1 (n= 9, 6, 3)	1865.06 (± 594.31)	2185.00 (± 631.37)	757.30 (± 997.44)
RA102758- Month 2 (n= 9, 5, 2)	1894.86 (± 608.46)	2090.04 (± 831.80)	757.85 (± 1018.59)
RA102758- Month 3 (n= 8, 5, 2)	1758.55 (± 689.03)	1990.54 (± 700.70)	1954.05 (± 160.58)
RA102758- Month 6 (n= 6, 5, 1)	1467.85 (± 563.68)	1819.20 (± 613.14)	1725.50 (± 99999)
RA102758- Month 9 (n= 7, 3, 2)	1686.80 (± 554.87)	1881.73 (± 583.87)	1238.55 (± 166.24)
RA102758- Month 12 (n= 8, 3, 1)	1646.99 (± 536.00)	1954.23 (± 725.54)	10.00 (± 99999)
RA102758- Final Study Visit (Month 49) (n=0,0,1)	99999 (± 99999)	99999 (± 99999)	1094.60 (± 99999)
RA103488- Day 1 (n= 9, 5, 3)	3587.68 (± 1747.12)	4887.98 (± 1969.22)	2084.83 (± 1791.35)
RA103488- Month 1 (n= 9, 6, 3)	4344.99 (± 2319.10)	4400.68 (± 1823.93)	1703.73 (± 1605.96)
RA103488- Month 2 (n= 9, 5, 2)	4799.29 (± 3113.57)	4365.84 (± 1537.67)	1591.35 (± 1552.03)
RA103488- Month 3 (n= 8, 5, 2)	4191.36 (± 2347.65)	4541.78 (± 1706.07)	2715.60 (± 1345.48)
RA103488- Month 6 (n= 6, 5, 1)	4027.53 (± 2730.92)	4436.46 (± 2341.16)	1929.60 (± 99999)
RA103488- Month 9 (n= 7, 3, 2)	3132.54 (± 1320.61)	4217.97 (± 2015.36)	2954.85 (± 1754.97)
RA103488- Month 12 (n= 8, 3, 2)	3903.41 (± 1960.30)	4334.47 (± 1976.47)	2319.20 (± 2534.84)
RA103488- Final Study Visit (Month 49) (n=0,0,1)	99999 (± 99999)	99999 (± 99999)	2210.00 (± 99999)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum plasma concentration (Cmax) of RA101495

End point title	Maximum plasma concentration (Cmax) of RA101495
End point description:	
Cmax is the maximum plasma drug concentration. PK population included all participants in the Safety population who had at least 1 plasma sample obtained for PK assessment. Data was not collected and analyzed for this outcome measure due to change in planned analysis.	
End point type	Secondary
End point timeframe:	
At Day 1, Month 1, 2, 3, 6, 9, and 12	

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[6]</sup>	0 <sup>[7]</sup>	0 <sup>[8]</sup>	
Units: ug/L				
geometric mean (geometric coefficient of variation)	()	()	()	

Notes:

[6] - As per the change in planned analyses, maximum plasma concentration was not collected and analyzed.

[7] - As per the change in planned analyses, maximum plasma concentration was not collected and analyzed.

[8] - As per the change in planned analyses, maximum plasma concentration was not collected and analyzed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time corresponding to Cmax (tmax) of RA101495

End point title	Time corresponding to Cmax (tmax) of RA101495
End point description:	
tmax is the time to corresponding Cmax. PK population included all participants in the Safety population who had at least 1 plasma sample obtained for PK assessment. Data was not collected and analyzed for this outcome measure due to change in planned analysis.	
End point type	Secondary
End point timeframe:	
At Day 1, Month 1, 2, 3, 6, 9, and 12	

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[9]</sup>	0 <sup>[10]</sup>	0 <sup>[11]</sup>	
Units: hours (h)				
median (full range (min-max))	( to )	( to )	( to )	

Notes:

[9] - As per the change in planned analyses, time corresponding to Cmax was not collected and analyzed.

[10] - As per the change in planned analyses, time corresponding to Cmax was not collected and analyzed.

[11] - As per the change in planned analyses, time corresponding to Cmax was not collected and analyzed.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area under the drug concentration-time curve (AUC0-t) of RA101495

End point title	Area under the drug concentration-time curve (AUC0-t) of RA101495
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End point description:

AUC0-t is area under the drug concentration-time curves. PK population included all participants in the Safety population who had at least 1 plasma sample obtained for PK assessment. As per the change in planned analyses, samples/data were not collected, and AUC0-t not calculated.

End point type	Secondary
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End point timeframe:

At Day 1, Month 1, 2, 3, 6, 9, and 12

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[12]</sup>	0 <sup>[13]</sup>	0 <sup>[14]</sup>	
Units: hours*ug/L				
geometric mean (geometric coefficient of variation)	()	()	()	

Notes:

[12] - As per the change in planned analyses, samples/data were not collected, and AUC0-t not calculated.

[13] - As per the change in planned analyses, samples/data were not collected, and AUC0-t not calculated.

[14] - As per the change in planned analyses, samples/data were not collected, and AUC0-t not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Total complement (CH50) Levels

End point title	Total complement (CH50) Levels
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End point description:

Blood samples collection were planned to assess complement (CH50) levels. The planned analysis of CH50 was not performed because the CH50 assay was not able to be validated due to lack of reproducibility of the manufacturer's kits. Pharmacodynamic (PD) population included all participants in the Safety population who had at least 1 plasma sample obtained for PD assessment. Data was not collected and analyzed for this outcome measure due to change in planned analysis.

End point type	Secondary
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End point timeframe:

At Day 1, Month 1, 2, 3, 6, 9, and 12

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[15]</sup>	0 <sup>[16]</sup>	0 <sup>[17]</sup>	
Units: ug/mL				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[15] - As per the change in planned analyses, CH50 levels were not collected and analyzed.

[16] - As per the change in planned analyses, CH50 levels were not collected and analyzed.

[17] - As per the change in planned analyses, CH50 levels were not collected and analyzed.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Sheep Red Blood Cell (sRBC) Values at each time point

End point title	Change from Baseline in Sheep Red Blood Cell (sRBC) Values at each time point
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End point description:

Blood samples were collected for measurement of sRBC lysis for the Classical Complement Pathways. PD population included all participants in the Safety population who had at least 1 plasma sample obtained for PD assessment. Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and SD was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12 and Final Study Visit (Month 49)

End point values	Zilucoplan- Cohort A (Eculizumab Naïve)	Zilucoplan- Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	1	
Units: percent lysis of sheep erythrocytes				
arithmetic mean (standard deviation)				
Month 1 (n= 9, 6,1)	1.378 (± 2.277)	0.523 (± 0.772)	93.870 (± 99999)	
Month 2 (n= 9, 5,1)	1.248 (± 1.789)	-0.308 (± 0.452)	93.870 (± 99999)	
Month 3 (n= 8, 5, 1)	1.256 (± 1.799)	0.576 (± 0.972)	-2.620 (± 99999)	
Month 6 (n= 6, 5, 1)	1.493 (± 2.838)	0.458 (± 1.657)	-2.300 (± 99999)	
Month 9 (n= 7, 3, 1)	0.683 (± 1.055)	0.757 (± 0.673)	-1.410 (± 99999)	
Month 12 (n= 8, 3, 1)	0.759 (± 0.557)	0.773 (± 0.415)	8.390 (± 99999)	
Final Study Visit (Month 49) (n= 0, 2, 0)	99999 (± 99999)	25.230 (± 35.200)	99999 (± 99999)	

## Statistical analyses

**Secondary: Change from Baseline in Wieslab enzyme-linked immunosorbent assay (ELISA) Values for alternative complement pathway at each time point**

End point title	Change from Baseline in Wieslab enzyme-linked immunosorbent assay (ELISA) Values for alternative complement pathway at each time point
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## End point description:

Blood samples were collected for measurement of membrane attack complex (MAC) by Wieslab ELISA for alternative complement pathway. PD population included all participants in the Safety population who had at least 1 plasma sample obtained for PD assessment. Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and SD was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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## End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12 and Final Study Visit (Month 49)

End point values	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan-Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	2	
Units: percentage of activity				
arithmetic mean (standard deviation)				
Month 1 (n= 9, 6, 2)	1.7 (± 5.8)	1.0 (± 1.7)	48.0 (± 67.9)	
Month 2 (n= 9, 5, 2)	0.1 (± 1.9)	-1.0 (± 1.0)	51.5 (± 74.2)	
Month 3 (n= 8, 5, 2)	0.1 (± 2.0)	0.0 (± 0.7)	2.0 (± 1.4)	
Month 6 (n= 6, 5, 1)	1.0 (± 4.5)	-0.2 (± 1.9)	5.0 (± 99999)	
Month 9 (n= 8, 3, 1)	-0.9 (± 0.8)	-0.7 (± 0.6)	-2.0 (± 99999)	
Month 12 (n= 8, 3, 2)	-1.4 (± 1.4)	-1.3 (± 0.6)	4.5 (± 6.4)	
Final Study Visit (Month 49) (n= 0, 2, 0)	99999 (± 99999)	1.0 (± 2.8)	99999 (± 99999)	

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline in Complement Component 5 (C5) Values at each time point**

End point title	Change from Baseline in Complement Component 5 (C5) Values at each time point
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## End point description:

Blood samples were collected for measurement of Complement component 5 (C5) levels. PD population included all participants in the Safety population who had at least 1 plasma sample obtained for PD assessment. Here, Number of participants analyzed included those participants who were evaluable for the assessment and 'n' signifies participants who were evaluable at specified time points. '99999' (n=0) signifies that the Mean and SD was not calculated due to 0 participants and '99999' (n=1) signifies that SD could not be calculated for a single participant.

End point type	Secondary
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End point timeframe:

Baseline, Month 1, 2, 3, 6, 9, 12 and Final Study Visit (Month 49)

<b>End point values</b>	Zilucoplan- Cohort A (Eculizumab Naïve)	Zilucoplan- Cohort B (Eculizumab Switch)	Zilucoplan (Inadequate Responder to Eculizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	2	
Units: ug/mL				
arithmetic mean (standard deviation)				
Month 1 (n= 9, 6, 2)	-11.231 (± 24.960)	20.488 (± 31.024)	-27.505 (± 90.092)	
Month 2 (n= 9, 5, 2)	-15.914 (± 32.737)	17.716 (± 33.125)	16.310 (± 36.077)	
Month 3 (n= 8, 5, 2)	-24.404 (± 50.084)	-2.898 (± 49.747)	22.355 (± 19.764)	
Month 6 (n= 6, 5, 1)	-6.823 (± 44.787)	9.572 (± 24.927)	91.640 (± 99999)	
Month 9 (n= 8, 3, 1)	-0.019 (± 53.475)	1.177 (± 27.654)	89.670 (± 99999)	
Month 12 (n= 7, 3, 2)	-40.591 (± 34.977)	-23.487 (± 30.911)	-24.905 (± 17.685)	
Final Study Visit (Month 49) (n= 3, 3, 0)	-28.663 (± 46.526)	-19.770 (± 74.604)	99999 (± 99999)	

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Day 1 until the Final Study Visit (up to Month 49)

Adverse event reporting additional description:

TEAEs were reported for Safety population. Deaths and TEAEs were monitored together for each cohort regardless of dose administered.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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### Reporting groups

Reporting group title	Zilucoplan-Cohort A (Eculizumab Naïve)
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Reporting group description:

Cohort A (Eculizumab Naïve) included all participants from study RA101495-01.201 (NCT03078582) who had not received eculizumab for treatment of paroxysmal nocturnal hemoglobinuria (PNH). Participants received a loading dose of 0.3 milligram/kilogram (mg/kg) zilucoplan administered by subcutaneous (SC) injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.

Reporting group title	Zilucoplan (Inadequate Responder to Eculizumab)
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Reporting group description:

Inadequate Responder cohort included participants from qualifying study RA101495-01.203 (NCT03030183) who had an inadequate response to eculizumab treatment for PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.

Reporting group title	Zilucoplan-Cohort B (Eculizumab Switch)
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Reporting group description:

Cohort B (Eculizumab Switch) included all participants from study RA101495-01.201 (NCT03078582) who had received eculizumab for treatment of PNH. Participants received a loading dose of 0.3 mg/kg zilucoplan administered by SC injection at Day 1 of this study. Following in-clinic education and training, all participants self-injected 0.1 mg/kg of zilucoplan by SC injection once daily for 12 months. From Week 2 onwards, if a participant had not achieved an adequate response, the zilucoplan dose was escalated to 0.3 mg/kg daily.

Serious adverse events	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan (Inadequate Responder to Eculizumab)	Zilucoplan-Cohort B (Eculizumab Switch)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 10 (10.00%)	2 / 3 (66.67%)	3 / 6 (50.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Tongue haematoma			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Zilucoplan-Cohort A (Eculizumab Naïve)	Zilucoplan (Inadequate Responder to Eculizumab)	Zilucoplan-Cohort B (Eculizumab Switch)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	2 / 3 (66.67%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Lymphoedema			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
General disorders and administration			

site conditions			
Chest discomfort			
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	3 / 10 (30.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Injection site bruising			
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Fatigue			
subjects affected / exposed	4 / 10 (40.00%)	1 / 3 (33.33%)	2 / 6 (33.33%)
occurrences (all)	9	1	3
Chest pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injection site haematoma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Alloimmunisation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			

Oropharyngeal pain subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 4	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0
Laryngospasm subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Pleural effusion subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 3 (33.33%) 2	1 / 6 (16.67%) 1
Insomnia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0
Grip strength decreased			

subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Post vaccination syndrome			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Animal bite			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Bone contusion			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Eye contusion			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Foot fracture			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tooth fracture			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Traumatic haematoma			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)  Headache subjects affected / exposed occurrences (all)  Sensory disturbance subjects affected / exposed occurrences (all)  Amnesia subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 4  2 / 10 (20.00%) 4  1 / 10 (10.00%) 1  0 / 10 (0.00%) 0	0 / 3 (0.00%) 0  1 / 3 (33.33%) 2  0 / 3 (0.00%) 0  1 / 3 (33.33%) 1	0 / 6 (0.00%) 0  2 / 6 (33.33%) 6  0 / 6 (0.00%) 0  0 / 6 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)  Pancytopenia subjects affected / exposed occurrences (all)  Aplastic anaemia subjects affected / exposed occurrences (all)  Haemolysis subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 4  0 / 10 (0.00%) 0  0 / 10 (0.00%) 0  1 / 10 (10.00%) 1	0 / 3 (0.00%) 0  0 / 3 (0.00%) 0  0 / 3 (0.00%) 0  0 / 3 (0.00%) 0	0 / 6 (0.00%) 0  1 / 6 (16.67%) 1  1 / 6 (16.67%) 2  1 / 6 (16.67%) 1
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders			

Lacrimation increased subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	5 / 10 (50.00%) 8	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Abdominal pain subjects affected / exposed occurrences (all)	3 / 10 (30.00%) 7	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	4 / 10 (40.00%) 5	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Large intestine polyp subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Oral discomfort subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Rectal polyp			



subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Retching			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Actinic keratosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Rash			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urticaria			

subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders			
Paroxysmal nocturnal haemoglobinuria			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Chromaturia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 10 (30.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	9	1	0
Muscle spasms			
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Joint swelling			
subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Limb discomfort			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 10 (0.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle tightness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Plantar fasciitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 10 (40.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	10	0	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 10 (40.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	5	0	1
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Viral infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Pharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Rhinitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0

Cystitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin bacterial infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tooth abscess			
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Urinary tract infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Metabolism and nutrition disorders			
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported