



## Clinical trial results:

### A Phase 3, Multicenter, Randomized, Double Blind, Placebo-Controlled Study to Confirm the Safety, Tolerability, and Efficacy of Zilucoplan in Subjects with Generalized Myasthenia Gravis

#### Summary

EudraCT number	2019-001564-30
Trial protocol	DE NO GB ES IT
Global end of trial date	30 December 2021

#### Results information

Result version number	v1 (current)
This version publication date	04 January 2023
First version publication date	04 January 2023

#### Trial information

##### Trial identification

Sponsor protocol code	RA101495-02.301
-----------------------	-----------------

##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04115293
WHO universal trial number (UTN)	-

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	18 January 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 December 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To confirm the efficacy, safety and tolerability of zilucoplan in subjects with gMG.

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	17 September 2019
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	Canada: 3
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Japan: 16
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 88
Worldwide total number of subjects	174
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)	126
From 65 to 84 years	48
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study started to enroll participants in September 2019 and concluded in December 2021.

### Pre-assignment

Screening details:

The Participant flow refers to the Randomized Set.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo

Arm description:

Participants self-administered zilucoplan (RA101495) matching placebo as subcutaneous (SC) injection during 12-week Treatment Period.

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

Dosage and administration details:

Participants self-administered zilucoplan matching placebo as SC injection during 12-week Treatment Period or at pre-specified timepoints.

<b>Arm title</b>	Zilucoplan 0.3 mg/kg
------------------	----------------------

Arm description:

Participants self-administered zilucoplan (RA101495) 0.3 milligrams/kilogram/day (mg/kg/day) SC injection during 12-week Treatment Period.

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

Dosage and administration details:

Participants self-administered zilucoplan 0.3 mg/kg SC injection during 12-week Treatment Period or at pre-specified timepoints.

<b>Number of subjects in period 1</b>	Placebo	Zilucoplan 0.3 mg/kg
Started	88	86
Completed	84	82
Not completed	4	4
Adverse event, serious fatal	1	1
Consent withdrawn by subject	2	1
Physician decision	1	-
Adverse event, non-fatal	-	2

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description: Participants self-administered zilucoplan (RA101495) matching placebo as subcutaneous (SC) injection during 12-week Treatment Period.	
Reporting group title	Zilucoplan 0.3 mg/kg
Reporting group description: Participants self-administered zilucoplan (RA101495) 0.3 milligrams/kilogram/day (mg/kg/day) SC injection during 12-week Treatment Period.	

Reporting group values	Placebo	Zilucoplan 0.3 mg/kg	Total
Number of subjects	88	86	174
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	62	64	126
>=65 years	26	22	48
Age Continuous Units: years			
arithmetic mean	53.3	52.6	
standard deviation	± 15.7	± 14.6	-
Sex: Female, Male Units: participants			
Female	47	52	99
Male	41	34	75

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants self-administered zilucoplan (RA101495) matching placebo as subcutaneous (SC) injection during 12-week Treatment Period.	
Reporting group title	Zilucoplan 0.3 mg/kg
Reporting group description: Participants self-administered zilucoplan (RA101495) 0.3 milligrams/kilogram/day (mg/kg/day) SC injection during 12-week Treatment Period.	

### Primary: Change from Baseline (CFB) to Week 12 in Myasthenia Gravis-Activities of Daily Living (MG-ADL) Total Score

End point title	Change from Baseline (CFB) to Week 12 in Myasthenia Gravis-Activities of Daily Living (MG-ADL) Total Score
End point description: The MG-ADL is an 8-item patient-reported outcome measure assessing MG symptoms and their effects on daily activities. Each item in the scale scored 0 to 3 (0=None, 3=severe disease) point scale. The total score was the sum of all individual item scores and ranged from 0 to 24. Higher scores indicated more severe disability due to MG. A decrease from Baseline score indicated improvement. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.	
End point type	Primary
End point timeframe: From Baseline to End of Treatment (Week 12)	

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: score on a scale				
least squares mean (confidence interval 95%)	-2.30 (-3.17 to -1.43)	-4.39 (-5.28 to -3.50)		

### Statistical analyses

Statistical analysis title	RA101495 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.24
upper limit	-0.95

## Secondary: Change from Baseline to Week 12 in the Quantitative Myasthenia Gravis (QMG) Total Score

End point title	Change from Baseline to Week 12 in the Quantitative Myasthenia Gravis (QMG) Total Score
End point description:	
The QMG is a standardized and validated quantitative strength scoring system that was developed specifically for MG. The scale consisted of 13 items. Each item in the scale scored on a 0 to 3-point scale, ranging from 0 (no weakness) to 3 (severe weakness), summing up to the overall score range from 0 to 39. Higher scores indicated more severe impairment. A decrease from Baseline score indicated improvement. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.	
End point type	Secondary
End point timeframe:	
From Baseline to End of Treatment (Week 12)	

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: score on a scale				
least squares mean (confidence interval 95%)	-3.25 (-4.32 to -2.17)	-6.19 (-7.29 to -5.08)		

## Statistical analyses

Statistical analysis title	RA101495 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	MMRM ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.39
upper limit	-1.49



---

**Secondary: Change from Baseline to Week 12 in the Myasthenia Gravis Composite (MGC) Scale Total Score**

---

End point title	Change from Baseline to Week 12 in the Myasthenia Gravis Composite (MGC) Scale Total Score
-----------------	--

**End point description:**

The total MGC score was sum of responses to 10 individual items : 1. Ptosis upward gaze (0 to 3), 2. Double vision on lateral gaze, left or right (0, to 4), 3. Eye closure (0 to 2), 4. Talking (0 to 6), 5. Chewing (0 to 6), 6. Swallowing [0 to 6], 7. Breathing (0 to 9), 8. Neck flexion or extension (0 to 4), 9. Shoulder abduction (0 to 5), 10. Hip flexion (0 to 5). The higher score for each item indicated severity. The total score ranged 0 to 50 with higher score indicative of severe disease activity). A decrease from Baseline score showed improvement. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.

End point type	Secondary
----------------	-----------

**End point timeframe:**

From Baseline to End of Treatment (Week 12)

---

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: score on a scale				
least squares mean (confidence interval 95%)	-5.42 (-6.98 to -3.86)	-8.62 (-10.22 to -7.01)		

**Statistical analyses**

<b>Statistical analysis title</b>	RA101495 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0023
Method	MMRM ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.24
upper limit	-1.16

---

**Secondary: Change from Baseline to Week 12 in the Myasthenia Gravis - Quality of**

---

**Life revised (MG-QoL15r) Scale Total Score**

End point title	Change from Baseline to Week 12 in the Myasthenia Gravis - Quality of Life revised (MG-QoL15r) Scale Total Score
-----------------	--

## End point description:

The MG-QoL15r is a 15-item patient-reported outcome measure designed to assess quality of life in patients with MG. Each item in the scale scored on a 0 to 2-point scale (0=Not much at all, 1=Somewhat, 2=Very much). The total score was the sum of the 15 individual item scores, ranging from 0 to 30. Higher scores indicated more severe impact of the disease on aspects of the patient's life. A decrease from Baseline score indicated improvement. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.

End point type	Secondary
----------------	-----------

## End point timeframe:

From Baseline to End of Treatment (Week 12)

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: score on a scale				
least squares mean (confidence interval 95%)	-3.16 (-4.65 to -1.67)	-5.65 (-7.17 to -4.12)		

**Statistical analyses**

<b>Statistical analysis title</b>	RA101495 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0128
Method	MMRM ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.45
upper limit	-0.54

**Secondary: Time to first receipt of rescue therapy over the 12-week Treatment Period**

End point title	Time to first receipt of rescue therapy over the 12-week Treatment Period
-----------------	---

## End point description:

Time to first receipt of rescue therapy over the 12-week treatment period (in days) was defined as the date of first rescue therapy use minus date of first Investigational Medicinal Product (IMP) + 1. The

modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.

End point type	Secondary
End point timeframe:	
From Baseline to End of Treatment (Week 12)	

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88 <sup>[1]</sup>	86 <sup>[2]</sup>		
Units: Days				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[1] - 99999: Time to first receipt of rescue therapy was not estimated due to less number of events.

[2] - 99999: Time to first receipt of rescue therapy was not estimated due to less number of events.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants achieving Minimal Symptom Expression (MSE) at Week 12 without rescue therapy

End point title	Percentage of participants achieving Minimal Symptom Expression (MSE) at Week 12 without rescue therapy
-----------------	---

End point description:

Percentage of Participants achieving MSE was defined as achieving a MG-ADL value of a 0 (No MG symptoms) or 1 (Mild MG symptoms) at Week 12 and not having taken rescue therapy. Any participant with an event of death, myasthenic crisis or rescue therapy was considered as non-responders. Any other missing data was imputed using the Missing at Random (MAR) assumption. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.

End point type	Secondary
End point timeframe:	
End of Treatment (Week 12)	

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: percentage of participants				
number (not applicable)	5.8	14.0		

## Statistical analyses

Statistical analysis title	Zilucoplan 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0885
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.608
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.866
upper limit	7.86

### Secondary: Percentage of participants achieving a $\geq 3$ -point reduction in MG-ADL Score at Week 12 without rescue therapy

End point title	Percentage of participants achieving a $\geq 3$ -point reduction in MG-ADL Score at Week 12 without rescue therapy
End point description:	Percentage of participants achieving a $\geq 3$ -point reduction in MG-ADL Score at Week 12 without rescue therapy were reported. The MG-ADL is an 8-item patient-reported outcome measure assessing MG symptoms and their effects on daily activities. Each item in the scale scored on a 0 to 3 (0=None, 3=severe disease) point scale. The total score was the sum of all individual item scores and ranged from 0 to 24. Higher scores indicated more severe disability due to MG. Any participant with an event of death, myasthenic crisis or rescue therapy was considered as non-responders. Any other missing data was imputed using the MAR assumption. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.
End point type	Secondary
End point timeframe:	
End of Treatment (Week 12)	

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: percentage of participants				
number (not applicable)	46.1	73.1		

### Statistical analyses

Statistical analysis title	Zilucoplan 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.184
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.662
upper limit	6.101

## Secondary: Percentage of participants achieving a $\geq 5$ -point reduction in QMG Score without rescue therapy at Week 12

End point title	Percentage of participants achieving a $\geq 5$ -point reduction in QMG Score without rescue therapy at Week 12
End point description:	Percentage of participants achieving a $\geq 5$ -point reduction in QMG Score without rescue therapy at Week 12 were reported. The QMG is a standardized and validated quantitative strength scoring system that was developed specifically for MG. The scale consisted of 13 items. Each item in the scale scored on a 0 to 3-point scale, ranging from 0 (no weakness) to 3 (severe weakness), summing up to the overall score range from 0 to 39. Higher scores indicated more severe impairment. Any participant with an event of death, myasthenic crisis or rescue therapy was considered as non-responders. Any other missing data was imputed using the MAR assumption. The modified Intention-to-Treat (mITT) population included all randomized participants who received at least 1 dose of study drug and had at least 1 post-dosing MG-ADL score.
End point type	Secondary
End point timeframe:	
End of Treatment (Week 12)	

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: percentage of participants				
number (not applicable)	33.0	58.0		

## Statistical analyses

Statistical analysis title	Zilucoplan 0.3 mg/kg vs Placebo
Comparison groups	Placebo v Zilucoplan 0.3 mg/kg

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0012
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.865
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.518
upper limit	5.409

### Secondary: Percentage of participants with treatment-emergent adverse events (TEAEs)

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs)
-----------------	---

End point description:

A TEAE is defined as an AE starting on or after the time of first administration of IMP and up to and including 40 days after the final dose (or last contact depending on which occurs first). Adverse events starting before the date of the first administration of IMP were not considered TEAEs. The Safety Set (SS) included all participants who received at least 1 dose of study drug based on the actual study treatment received.

End point type	Secondary
----------------	-----------

End point timeframe:

From Baseline (Day 1) to Safety Follow-up visit (19 Weeks [12 weeks Treatment Period plus up to 7 weeks Follow-up])

End point values	Placebo	Zilucoplan 0.3 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: percentage of participants				
number (not applicable)	70.5	76.7		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) to Safety Follow-up visit (19 Weeks [12 weeks Treatment Period plus up to 7 weeks Follow-up])

Adverse event reporting additional description:

A TEAE is defined as an AE starting on or after the time of first administration of IMP and up to and including 40 days after the final dose (or last contact depending on which occurs first). Adverse events starting before the date of the first administration of IMP were not considered TEAEs.

Assessment type	Non-systematic
-----------------	----------------

### Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	24
--------------------	----

### Reporting groups

Reporting group title	Placebo
-----------------------	---------

Reporting group description:

Participants self-administered zilucoplan (RA101495) matching placebo as subcutaneous (SC) injection during 12-week Treatment Period.

Reporting group title	RA101495 0.3 mg/kg
-----------------------	--------------------

Reporting group description:

Participants self-administered zilucoplan (RA101495) 0.3 mg/kg/day SC injection during 12-week Treatment Period.

Serious adverse events	Placebo	RA101495 0.3 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 88 (14.77%)	11 / 86 (12.79%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Investigations			
Lipase increased			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			

subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	5 / 88 (5.68%)	2 / 86 (2.33%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Hyperemesis gravidarum			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphthous ulcer			



subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Oesophageal candidiasis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 88 (2.27%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	2 / 88 (2.27%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex meningoencephalitis			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Placebo	RA101495 0.3 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 88 (38.64%)	41 / 86 (47.67%)	
Investigations			
Lipase increased			
subjects affected / exposed	1 / 88 (1.14%)	6 / 86 (6.98%)	
occurrences (all)	1	6	
Amylase increased			
subjects affected / exposed	2 / 88 (2.27%)	5 / 86 (5.81%)	
occurrences (all)	2	5	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	3 / 88 (3.41%)	7 / 86 (8.14%)	
occurrences (all)	3	8	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	14 / 88 (15.91%) 19	13 / 86 (15.12%) 16	
Myasthenia gravis subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 6	8 / 86 (9.30%) 10	
General disorders and administration site conditions			
Injection site bruising subjects affected / exposed occurrences (all)	8 / 88 (9.09%) 11	14 / 86 (16.28%) 18	
Injection site pain subjects affected / exposed occurrences (all)	3 / 88 (3.41%) 3	8 / 86 (9.30%) 9	
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	2 / 88 (2.27%) 2	9 / 86 (10.47%) 9	
Vomiting subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 5	3 / 86 (3.49%) 3	
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	5 / 88 (5.68%) 9	3 / 86 (3.49%) 3	
Infections and infestations			
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 88 (4.55%) 4	7 / 86 (8.14%) 7	
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 88 (3.41%) 3	5 / 86 (5.81%) 5	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2020	<p>Protocol Amendment Version 2.0 was dated 18 Dec 2020 and had incorporated all the country-specific amendments into single protocol amendment:</p> <ul style="list-style-type: none"><li>• The total sample size was increased from 130 study participants (65 study participants per treatment group) to 156 study participants (78 study participants per treatment group). This increase was made to account for higher variability in the primary endpoint than originally assumed, and to maintain the power of the study.</li><li>• An unblinded interim analysis was added to be performed after the final study participant had completed the Week 12 Visit, or after the final study participant had prematurely discontinued prior to reaching Week 12. The purpose of this interim analysis was to perform a comprehensive evaluation of all available double-blind data to prepare regulatory submissions for approval of the gMG target indication.</li><li>• Changes made in earlier country-specific protocol amendments (France, Germany, Italy, Japan, Norway, United Kingdom) were consolidated into a single global protocol.</li><li>• The objectives and endpoints were revised to reflect current UCB practices for the categorization and description of study objectives, estimands, and endpoints.</li></ul>
18 December 2020	<p>Protocol amendment version 2.0 Continued:</p> <ul style="list-style-type: none"><li>• The following provisions for the coronavirus disease 2019; disease caused by severe acute respiratory syndrome coronavirus 2 (COVID-19) pandemic were included: – In situations when the study participant could not return to the study site, the Investigator assessed the study participant's safety by telephone/video contact. If the study participant was suitable for IMP continuation, the Investigator or designee assessed if the study participant agreed to provide name, address, telephone number, and email to the appointed courier. If the shipment was agreed, the Investigator or designee clearly explained to the study participant everything needed regarding the handling (in case of inconsistencies at delivery) and administration of the IMP and how to return all unused IMP to the study site at the next on-site visit. Additional details regarding the shipment of IMP and deviations to data collection are provided in the protocol.</li><li>– Ad hoc study participant contact may have been warranted to understand the current health status of the study participants, to follow up on AEs, and to inform them of any protective measures taken by the clinical site as a result of the COVID-19 pandemic.</li><li>– If a study participant needed to be discontinued from the study and could not come into the clinic, a visit was scheduled to perform final safety assessments as soon as possible.</li><li>– If a study participant visited another facility for a medical issue, the Investigator was to request contact with the physician providing care to provide a detailed explanation of the study participant's condition and his/her participation in the clinical study. Study participants and/or caregivers were reminded to completely collect and keep records of this visit.</li></ul> <ul style="list-style-type: none"><li>• Administrative updates.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

