Clinical trial results:
Evaluation of tolerability and efficacy of subcutaneous cluster-immunotherapy in patients with allergic rhinitis / rhino-conjunctivitis due to grass pollen

Summary

EudraCT number	2010-022083-12
Trial protocol	DE
Global end of trial date	30 June 2016

Results information

Result version number	v1 (current)
This version publication date	16 September 2021
First version publication date	16 September 2021

Trial information

Trial identification

Sponsor protocol code	SC-11A

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ROXALL Medizin GmbH
Sponsor organisation address	Carl-Petersen-Str. 4, Hamburg, Germany, 20535
Public contact	ROXALL Medizin GmbH, ROXALL Medizin GmbH, 0049 408972520,
Scientific contact	ROXALL Medizin GmbH, ROXALL Medizin GmbH, 0049 408972520,

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	28 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2016
Global end of trial reached?	Yes
Global end of trial date	30 June 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective: to assess the efficacy of four different concentrations for subcutaneous immunotherapy with cluster-allergoid CLUSTOID® Wiesenlieschgras by means of the threshold concentration that is needed to provoke an allergic response after titrated nasal provocation with increasing concentrations of an allergen extract of Phleum pratense.

Protection of trial subjects:

Before each injection the eligibility of the patient was checked.
After each injection the patient was to stay at the trial site for a 30 minutes follow-up observation by the physician.
To reduce any risk for trial participants stopping rules were established for the clinical trial.
In general, any complications or severe AEs related to the study medication which are not tolerable for the patient are considered as individual reasons for stopping the participation in the study. A serious systemic reaction (Grade IV according to Ring J. 2007) requiring intensive treatment such as cardiopulmonary reanimation, was defined as stopping rule for the individual patient, independently of the dosing group and the treatment phase. If in the investigator´s opinion, continuation in the study would be detrimental to the patient´s wellbeing, the patient should be withdrawn from the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

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)	81
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	103[1]
Number of subjects completed	81

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening failure: 22

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Overall, 103 patients were screened for the trial and 83 were randomized, of these 81 patients received study medication. Altogether, 22 patients were screening failures.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	CLUSTOID Wiesenlieschgras 2000 TU/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Maintenance dose 0.5 mL in monthly intervals.

Arm title	Group 2

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	CLUSTOID Wiesenlieschgras 10000 TU/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Maintenance dose 0.5 mL in monthly intervals.

Arm title	Group 3

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	CLUSTOID Wiesenlieschgras 30000 TU/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Maintenance dose 0.5 mL in monthly intervals.

Arm title	Group 4

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	CLUSTOID Wiesenlieschgras 50000 TU/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Maintenance dose 0.5 mL in monthly intervals.

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	21	20	20
Completed	20	19	20
Not completed	1	1	0
Lost to follow-up	1	1	-

Number of subjects in period 1	Group 4
Started	20
Completed	18
Not completed	2
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2
Reporting group description: -	
Reporting group title	Group 3
Reporting group description: -	
Reporting group title	Group 4
Reporting group description: -	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	21	20	20
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	21	20	20
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	9	9	7
Male	12	11	13

Reporting group values	Group 4	Total	
Number of subjects	20	81	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	81	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	10	35	

Male	10	46	

Subject analysis sets

Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

All randomized patients for which the primary study outcome parameter (pre- and post-treatment tNPT) was available

Reporting group values	mITT		
Number of subjects	77		
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	77		
From 65-84 years			
85 years and over			
Gender categorical Units: Subjects			
Female	32		
Male	45		

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2
Reporting group description: -	
Reporting group title	Group 3
Reporting group description: -	
Reporting group title	Group 4
Reporting group description: -	
Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized patients for which the primary study outcome parameter (pre- and post-treatment tNPT) was available	

Primary: tNPT change

End point title	tNPT change
End point description:	
End point type	Primary
End point timeframe:	
Visit 1 to Visit 8	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	20	18
Units: steps				
arithmetic mean (standard deviation)	1.08 (± 1.553)	2.27 (± 1.191)	1.64 (± 1.008)	1.64 (± 0.745)

Statistical analyses

Statistical analysis title	tNPT change
Statistical analysis description:	
Group 1 vs. Group 2 comparison, mITT set	
Comparison groups	Group 1 v Group 2
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.027
Method	2-sided Wilcoxon, Bonferroni adjusted

Notes:

[1] - inter-group comparison

Statistical analysis title	tNPT change
Statistical analysis description:	
Group 1 vs. Group 3 comparison, mITT set	
Comparison groups	Group 1 v Group 3
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.1458
Method	2-sided Wilcoxon, Bonferroni adjusted

Notes:

[2] - inter-group comparison

Statistical analysis title	tNPT change
Statistical analysis description:	
Group 1 vs. Group 4 comparison, mITT set	
Comparison groups	Group 1 v Group 4
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.0108
Method	2-sided Wilcoxon, Bonferroni adjusted

Notes:

[3] - inter-group comparison

Statistical analysis title	tNPT change
Statistical analysis description:	
Group 2 vs. Group 3 comparison, mITT set	
Comparison groups	Group 2 v Group 3
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.2556
Method	2-sided Wilcoxon, Bonferroni adjusted

Notes:

[4] - inter-group comparison

Statistical analysis title	tNPT change
Statistical analysis description:	
Group 2 vs. Group 4 comparison, mITT set	
Comparison groups	Group 2 v Group 4
Number of subjects included in analysis	37
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 1
Method	2-sided Wilcoxon, Bonferroni adjusted

Notes:

[5] - inter-group comparison

Statistical analysis title	tNPT change

Statistical analysis description:

Group 3 vs. Group 4 comparison, mITT set

Comparison groups	Group 3 v Group 4
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.954
Method	2-sided Wilcoxon, Bonferroni adjusted

Notes:

[6] - inter-group comparison

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Visit 1 to Visit 8	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2
Reporting group description: -	
Reporting group title	Group 3
Reporting group description: -	
Reporting group title	Group 4
Reporting group description: -	

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Group 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 21 (47.62%)	16 / 20 (80.00%)	18 / 20 (90.00%)
Investigations			

C-reactive protein increased			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	2	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	8 / 21 (38.10%)	13 / 20 (65.00%)	16 / 20 (80.00%)
occurrences (all)	15	34	115
Eye disorders			
Eye pruritus			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 21 (0.00%)	3 / 20 (15.00%)	2 / 20 (10.00%)
occurrences (all)	0	3	3
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 21 (0.00%)	2 / 20 (10.00%)	0 / 20 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Group 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)		
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 3		
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all)	 17 / 20 (85.00%) 126		
Eye disorders Eye pruritus subjects affected / exposed occurrences (all)	 2 / 20 (10.00%) 2		
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0		
Infections and infestations Acute sinusitis subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2015	A substantial amendment (protocol version 7.1) was made to extend the overall duration of the study due to low recruitment status of all study centres. Duration of study participation did not change for the individual study participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported