

**Clinical trial results:**

A double-blind, randomised, placebo-controlled, crossover, allergen challenge study, evaluating the safety, tolerability and effects of intranasal administration of recombinant human Clara Cell 10 kDa (rhCC10) protein in subjects with allergic rhinitis.

Summary

EudraCT number	2006-005420-17
Trial protocol	SE
Global end of trial date	02 May 2007

Results information

Result version number	v1 (current)
This version publication date	01 March 2017
First version publication date	01 March 2017

Trial information**Trial identification**

Sponsor protocol code	CC10-200601
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Therabron Therapeutics, Inc.
Sponsor organisation address	9430 Key West Ave. Suite 150, Rockville, United States, MD 20850
Public contact	Anita Fauchier, VP Regulatory Affairs & Quality Assurance, Therabron Therapeutics, Inc., anita.fauchier@therabron.com
Scientific contact	Alan Cohen, Senior Vice President & Chief Medical Officer, Therabron Therapeutics, Inc., alan.cohen@therabron.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	25 September 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 May 2007
Global end of trial reached?	Yes
Global end of trial date	02 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study is a proof-of-concept study with the objective to investigate whether intranasal administration of rhCC10 can affect symptoms from nasal allergen challenge.

Primary:

To evaluate the effect of repeated doses of intranasal rhCC10 administration on nasal symptoms in subjects with allergic rhinitis. In addition, the onset of action of the study drug will be evaluated.

Secondary:

To evaluate the safety and tolerability of repeated doses of intranasal rhCC10 in subjects with allergic rhinitis.

To characterise the effects of rhCC10 treatment on individual nasal symptom scores, peak nasal inspiratory flow (PNIF), and laboratory analyses of nasal lavage fluid.

To evaluate the effects of rhCC10 after histamine challenge.

Protection of trial subjects:

The study received prior CTA from the MPA, Sweden and IERC approval from the local ERC in Lund, Sweden.

Subjects were recruited who were capable of understanding and signing an Informed Consent Form. The subjects were informed about the study, the treatments and methodologies used, and they were informed about their right to withdraw from the study at any time.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2007
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	Sweden: 39
Worldwide total number of subjects	39
EEA total number of subjects	39

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)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 39 subjects (35 completed) were screened and randomised to rhCC10 or placebo for a 7-day treatment period followed by cross-over 7 day treatment period, with a wash-out period of 2 to 3 weeks in between treatment periods. The study was conducted at a single site in Sweden.

Pre-assignment

Screening details:

At the screening visit a nasal allergen test was conducted for each subject. This was to enable an estimate of a symptom-producing, tolerable, and repeatable allergen dose for the nasal challenge series. A subject was randomised to treatment when laboratory results from this titration procedure were available.

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, Subject

Blinding implementation details:

To maintain the double blind design of the study, all study drugs were provided to the clinic in identical 10 mL glass vial reservoirs with Aptar 100 mcl nasal spray pumps. Labels were designed such that no information which would reveal the blind was included. Labels were numbered sequentially and a key was retained in the hospital pharmacy.

Arms

Are arms mutually exclusive?	No
Arm title	rhCC10/placebo arm

Arm description:

Each subject received treatment of 0.56 mg (100 µl) rhCC10 (intranasally into each nostril) daily for 7 days, followed by a wash-out period of 2 to 3 weeks, then 100 µl placebo (intranasally into each nostril) daily for 7 days. The daily dose was 1.1 mg rhCC10 or corresponding placebo (volume 200 µL).

Arm type	Experimental
Investigational medicinal product name	recombinant human Clara Cell 10 kDa (rhCC10)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Intranasal use

Dosage and administration details:

rhCC10 5.6 mg/mL ($\pm 5\%$) solution in sterile, unbuffered normal saline (0.9 % NaCl). A dose of 0.56 mg rhCC10 was administered intranasally with a nasal spray into each nostril for 7 consecutive days. The daily dose was 1.1 mg rhCC10.

Arm title	Placebo/rhCC10 arm
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Arm description:

Each subject received treatment 100 µl placebo (intranasally into each nostril) daily for 7 days, followed by a wash-out period of 2 to 3 weeks, then 0.56 mg (100 µl) rhCC10 (intranasally into each nostril) daily for 7 days. The daily dose was 1.1 mg rhCC10 or corresponding placebo (volume 200 µL).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Intranasal use

Dosage and administration details:

A dose of placebo volume 100 µL was administered intranasally with a nasal spray into each nostril for 7 consecutive days. The daily dose of placebo was volume 200 µL.

Number of subjects in period 1	rhCC10/placebo arm	Placebo/rhCC10 arm
Started	39	39
Completed	35	35
Not completed	4	4
Consent withdrawn by subject	3	3
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
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Reporting group description:

This reporting group is all subject in the clinical trial and therefore consists of the 39 subjects randomised to both arms of the trial.

Reporting group values	Overall trial	Total	
Number of subjects	39	39	
Age categorical			
Male subjects, aged 18-50 years, Body Mass Index between 18 and 28 kg/m2.			
Units: Subjects			
Adults (18-64 years)	39	39	
Gender categorical			
Units: Subjects			
Male	39	39	
Race			
Units: Subjects			
Caucasian	39	39	

Subject analysis sets

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set includes all randomised patients who took study medication. The analysis of all safety and tolerability variables was performed using the safety analysis set.

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) for efficacy analysis is defined as all randomised subjects who received at least two doses of rhCC10, two doses of placebo and for whom at least one observation was recorded for the primary efficacy variable at each treatment period. The analysis of all efficacy variables was performed using the FAS.

Subject analysis set title	Per protocol analysis set
Subject analysis set type	Per protocol

Subject analysis set description:

The per protocol analysis set includes patients that had no major protocol violation and had at least two valid readings of primary outcome variables from the three last days of each allergen challenge period. Moreover the patients had to take at least 4 doses of medication at both treatment periods. The analysis of the primary efficacy variable was performed using the per protocol analysis.

Reporting group values	Safety analysis set	Full analysis set	Per protocol analysis set
Number of subjects	39	37	35
Age categorical			
Male subjects, aged 18-50 years, Body Mass Index between 18 and 28 kg/m2.			
Units: Subjects			
Adults (18-64 years)	39	37	35

Gender categorical			
Units: Subjects			
Male	39	37	35
Race			
Units: Subjects			
Caucasian	39	37	35

End points

End points reporting groups

Reporting group title	rhCC10/placebo arm
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Reporting group description:

Each subject received treatment of 0.56 mg (100 µl) rhCC10 (intranasally into each nostril) daily for 7 days, followed by a wash-out period of 2 to 3 weeks, then 100 µl placebo (intranasally into each nostril) daily for 7 days. The daily dose was 1.1 mg rhCC10 or corresponding placebo (volume 200 µL).

Reporting group title	Placebo/rhCC10 arm
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Reporting group description:

Each subject received treatment 100 µl placebo (intranasally into each nostril) daily for 7 days, followed by a wash-out period of 2 to 3 weeks, then 0.56 mg (100 µl) rhCC10 (intranasally into each nostril) daily for 7 days. The daily dose was 1.1 mg rhCC10 or corresponding placebo (volume 200 µL).

Subject analysis set title	Safety analysis set
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Subject analysis set type	Safety analysis
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Subject analysis set description:

The safety analysis set includes all randomised patients who took study medication. The analysis of all safety and tolerability variables was performed using the safety analysis set.

Subject analysis set title	Full analysis set
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Subject analysis set type	Full analysis
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Subject analysis set description:

The full analysis set (FAS) for efficacy analysis is defined as all randomised subjects who received at least two doses of rhCC10, two doses of placebo and for whom at least one observation was recorded for the primary efficacy variable at each treatment period. The analysis of all efficacy variables was performed using the FAS.

Subject analysis set title	Per protocol analysis set
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Subject analysis set type	Per protocol
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Subject analysis set description:

The per protocol analysis set includes patients that had no major protocol violation and had at least two valid readings of primary outcome variables from the three last days of each allergen challenge period. Moreover the patients had to take at least 4 doses of medication at both treatment periods. The analysis of the primary efficacy variable was performed using the per protocol analysis.

Primary: Means of total nasal symptom scores (TNSS)

End point title	Means of total nasal symptom scores (TNSS)
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End point description:

Means of total nasal symptom scores (TNSS) during the last 3 days of each challenge period of 7 days. The TNSS was recorded 10 minutes after each allergen challenge and daily in the morning and in the evening; the difference in TNSS values between rhCC10 treatment and placebo treatment was calculated.

End point type	Primary
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End point timeframe:

During the last 3 days of each challenge period of 7 days.

End point values	Full analysis set	Per protocol analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	37	37		
Units: total nasal symptom scores	37	37		

Statistical analyses

Statistical analysis title	Primary objective - full analysis set
Statistical analysis description:	
The primary objective of the study was to evaluate the effect of repeated doses of intranasal rhCC10 administration in subjects with allergic rhinitis.	
The primary hypothesis was:	
RhCC10 is superior to placebo in preventing total nasal symptom score (TNSS) recorded 10 minutes after allergen challenge during the last three days of each allergen challenge period.	
Comparison groups	Full analysis set v Per protocol analysis set
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1127 ^[1]
Method	ANOVA
Parameter estimate	Total nasal symptom score

Notes:

[1] - The difference between placebo and rhCC10 by means of total nasal symptom scores (TNSS) during the last 3 days of the challenge period of 7 days was in favour of placebo (p=0.0932, per protocol analysis set; p=0.1127, full analysis set).

Statistical analysis title	Primary objective - per protocol analysis set
Statistical analysis description:	
The primary objective of the study was to evaluate the effect of repeated doses of intranasal rhCC10 administration in subjects with allergic rhinitis.	
The primary hypothesis was:	
RhCC10 is superior to placebo in preventing total nasal symptom score (TNSS) recorded 10 minutes after allergen challenge during the last three days of each allergen challenge period.	
Comparison groups	Per protocol analysis set v Full analysis set
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0932 ^[2]
Method	ANOVA
Parameter estimate	Total nasal symptom score

Notes:

[2] - The difference between placebo and rhCC10 by means of total nasal symptom scores (TNSS) during the last 3 days of the challenge period of 7 days was in favour of placebo (p=0.0932, per protocol analysis set; p=0.1127, full analysis set).

Secondary: Type and incidence of adverse events (AEs)

End point title	Type and incidence of adverse events (AEs)
End point description:	
Type and incidence of adverse events (AEs).	
End point type	Secondary
End point timeframe:	
Duration of trial.	

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: Adverse Event				
number (not applicable)	39			

Statistical analyses

No statistical analyses for this end point

Secondary: To characterise the effects of rhCC10 treatment on individual nasal symptom scores, peak nasal inspiratory flow (PNIF), and laboratory analyses of nasal lavage fluid.

End point title	To characterise the effects of rhCC10 treatment on individual nasal symptom scores, peak nasal inspiratory flow (PNIF), and laboratory analyses of nasal lavage fluid.
End point description:	
Difference between rhCC10 treatment and placebo on individual nasal symptoms :	
1. Nasal congestion	
2. Rhinorrea	
3. Sneezy/itchy nose	
Difference between rhCC10 treatment and placebo on PNIF,	
Difference in nasal lavage content of eosinophilic cationic protein (ECP), tryptase, and myeloperoxidase between rhCC10 treatment and placebo.	
End point type	Secondary
End point timeframe:	
Duration of trial.	

End point values	rhCC10/placebo arm	Placebo/rhCC10 arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	39		
Units: peak nasal inspiratory flow (PNIF)				
number (not applicable)	39	39		

Statistical analyses

Statistical analysis title	1. Treatment of nasal congestion
Statistical analysis description:	
Difference between rhCC10 treatment and placebo on individual nasal symptoms.	
Comparison groups	rhCC10/placebo arm v Placebo/rhCC10 arm

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.886 [3]
Method	ANOVA

Notes:

[3] - Difference between placebo and rhCC10 treatment by mean of nasal congestion was in favour of placebo (p=0.8860).

Statistical analysis title	2. Treatment of rhinorrea
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Statistical analysis description:

Difference between rhCC10 treatment and placebo on individual nasal symptoms.

Comparison groups	rhCC10/placebo arm v Placebo/rhCC10 arm
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0493 [4]
Method	ANOVA

Notes:

[4] - Difference between placebo and rhCC10 treatment by mean of rhinorrea was statistically significantly better with placebo (p=0.0493)

Statistical analysis title	3. Treatment of itchy nose
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Statistical analysis description:

Difference between rhCC10 treatment and placebo on individual nasal symptoms.

Comparison groups	rhCC10/placebo arm v Placebo/rhCC10 arm
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1784 [5]
Method	ANOVA

Notes:

[5] - Difference between placebo and rhCC10 treatment by mean of sneezy/itchy was in favour of placebo (p= 0.1784).

Statistical analysis title	Difference in rhCC10 and placebo on PNIF
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Statistical analysis description:

To characterise the effects of rhCC10 treatment on individual nasal symptom scores, peak nasal inspiratory flow (PNIF), and laboratory analyses of nasal lavage fluid.

Comparison groups	rhCC10/placebo arm v Placebo/rhCC10 arm
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0363 [6]
Method	ANOVA

Notes:

[6] - Difference between placebo and rhCC10 treatment of peak nasal inspiratory flow (PNIF) was statistically significant better of rhCC10 (p=0.0363).

Secondary: Difference in α2-macroglobulin response between rhCC10 treatment and placebo after histamine challenge test.

End point title	Difference in α2-macroglobulin response between rhCC10 treatment and placebo after histamine challenge test.
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End point description:

Difference in α 2-macroglobulin response between rhCC10 treatment and placebo after histamine challenge test.

End point type Secondary

End point timeframe:

Duration of trial.

End point values	Safety analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: α 2-macroglobulin response				
number (not applicable)	39			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The Adverse Event reporting period for began upon receiving the first dose of investigational medication and ended at the 2-week post discontinuation of investigational medication visit (follow-up visit).

Adverse event reporting additional description:

During the study when there was a safety evaluation, the investigator or site staff was responsible for detecting, documenting and reporting AEs and SAEs.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	9.1
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Reporting groups

Reporting group title	rhCC10/placebo arm
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Reporting group description:

rhCC10/placebo arm

Reporting group title	Placebo/rhCC10 arm
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Reporting group description:

Placebo/rhCC10 arm

Serious adverse events	rhCC10/placebo arm	Placebo/rhCC10 arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 39 (0.00%)	0 / 39 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	rhCC10/placebo arm	Placebo/rhCC10 arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 39 (38.46%)	15 / 39 (38.46%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 39 (7.69%)	3 / 39 (7.69%)	
occurrences (all)	3	3	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed occurrences (all)	3 / 39 (7.69%) 3	1 / 39 (2.56%) 1	
Tiredness subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2	0 / 39 (0.00%) 0	
Fever subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 39 (5.13%) 2	
Gastrointestinal disorders Stomach ache subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	
Respiratory, thoracic and mediastinal disorders Sore throat subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	2 / 39 (5.13%) 2	
Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	1 / 39 (2.56%) 1	
Infections and infestations Common cold subjects affected / exposed occurrences (all)	5 / 39 (12.82%) 5	2 / 39 (5.13%) 2	
Mild cold subjects affected / exposed occurrences (all)	1 / 39 (2.56%) 1	0 / 39 (0.00%) 0	
Gastric Influenza subjects affected / exposed occurrences (all)	0 / 39 (0.00%) 0	2 / 39 (5.13%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported