Clinical trial results:
Double-Blind, Randomized, Placebo-Controlled, Parallel-Group, Multicenter/Multinational, Efficacy and Safety Study of Desloratadine 5 mg in the Treatment of Subjects With Allergic Rhinitis Who Meet the Criteria for Persistent Allergic Rhinitis (PER)

Summary

EudraCT number	2005-005450-45
Trial protocol	FI PT ES DE HU SE GR DK IT BE NL Outside EU/EEA
Global end of trial date	03 April 2008

Results information

Result version number	v1 (current)
This version publication date	10 February 2016
First version publication date	15 July 2015

Trial information

Trial identification

Sponsor protocol code	P04684

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00405964
WHO universal trial number (UTN)	-
Other trial identifiers	Protocol number: MK-4117-175

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Sponsor organisation name	Merck Sharp & Dohme Corp.
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Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 April 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2008
Global end of trial reached?	Yes
Global end of trial date	03 April 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to compare the efficacy and safety of desloratadine with placebo in the symptomatic treatment of participants 12 years and older with persistent allergic rhinitis (PER) .

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 August 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	Sweden: 31
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Finland: 21
Country: Number of subjects enrolled	France: 111
Country: Number of subjects enrolled	Germany: 86
Country: Number of subjects enrolled	Hungary: 48
Country: Number of subjects enrolled	Italy: 87
Country: Number of subjects enrolled	Canada: 194
Country: Number of subjects enrolled	Russian Federation: 101
Country: Number of subjects enrolled	Turkey: 2
Worldwide total number of subjects	716
EEA total number of subjects	419

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)	18
Adults (18-64 years)	689
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled from 12 countries in Europe.

Pre-assignment

Screening details:

Approximately 10 participants were to be enrolled at each site, but up to approximately 30 participants could be enrolled at each site with the sponsor’s approval.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Desloratadine 5 mg

Arm description:

5-mg Desloratadine tablet, oral, once daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Desloratadine
Investigational medicinal product code	
Other name	SCH 34117, Aerius
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5-mg Desloratadine tablet, oral, once daily for 12 weeks

Arm title	Placebo

Arm description:

Placebo tablet to desloratadine 5 mg, oral, once daily for 12 weeks

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to desloratadine, tablet, oral, once daily for 12 weeks

Number of subjects in period 1	Desloratadine 5 mg	Placebo
Started	360	356
Completed	301	261
Not completed	59	95
Consent withdrawn by subject	19	23
Adverse event, non-fatal	7	16
Lost to follow-up	5	5
Lack of efficacy	17	45
Protocol deviation	11	6

Baseline characteristics

Reporting groups	
Reporting group title	Desloratadine 5 mg
Reporting group description:	
5-mg Desloratadine tablet, oral, once daily for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet to desloratadine 5 mg, oral, once daily for 12 weeks	

Reporting group values	Desloratadine 5 mg	Placebo	Total
Number of subjects	360	356	716
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)	9	9	18
Adults (18-64 years)	348	341	689
From 65-84 years	3	6	9
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	34	33.9	
standard deviation	± 12.1	± 12.3	-
Gender categorical Units: Subjects			
Female	208	198	406
Male	152	158	310

End points

End points reporting groups

Reporting group title	Desloratadine 5 mg
Reporting group description:	
5-mg Desloratadine tablet, oral, once daily for 12 weeks	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet to desloratadine 5 mg, oral, once daily for 12 weeks	

Primary: Change From Baseline in Participant's AM/PM PRIOR (Reflective) Total 5 Symptom Score (T5SS) Over Days 1 to 29 of Treatment

End point title	Change From Baseline in Participant's AM/PM PRIOR (Reflective) Total 5 Symptom Score (T5SS) Over Days 1 to 29 of Treatment
End point description:	
AM/PM PRIOR (the participant's status over previous 12 hours [reflective]) T5SS from the participant's daily diary averaged over treatment Days 1 to 29. AM/PM is the average of separate morning (AM) and evening (PM) evaluations. Scores were defined for T5SS as 0: no symptoms to 15: all severe symptoms. A two-way analysis of variance (ANOVA) model with treatment and site effects was used to examine the treatment difference.	
End point type	Primary
End point timeframe:	
Baseline and Days 1-29	

End point values	Desloratadine 5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	355[1]	351[2]		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	9.63 (± 0.13)	9.55 (± 0.12)		
Days 1-29	-3.76 (± 0.22)	-2.87 (± 0.21)		

Notes:

[1] - All randomized participants with non-missing baseline and at least some postbaseline data.

[2] - All randomized participants with non-missing baseline and at least some postbaseline data.

Statistical analyses

Statistical analysis title	Treatment Difference
Statistical analysis description:	
Difference in the least squares means between change from baseline in AM/PM PRIOR T5SS for participants taking desloratadine over Day 1 to Day 29 of treatment vs. change from baseline in AM/PM PRIOR (Reflective) T5SS for participants taking placebo over Day 1 to Day 29 of treatment. Negative differences are in favor of the desloratadine treatment group in the comparison.	
Comparison groups	Desloratadine 5 mg v Placebo

Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.33
upper limit	-0.46

Notes:

[3] - Analyses were performed using an ANOVA, extracting sources of variation due to treatment and site.

Secondary: Change From Baseline in the Total Rhinoconjunctivitis Quality of Life Questionnaire-Standarized Version (RQLQ-S) After 29 Days

End point title	Change From Baseline in the Total Rhinoconjunctivitis Quality of Life Questionnaire-Standarized Version (RQLQ-S) After 29 Days

End point description:

The RQLQ-S was only completed for participants above 18 years of age. The RQLQ-S was not available for participants 12 to 17 years of age. This questionnaire asked questions pertaining to daily activities, sleep, non-nose eye symptoms, practical problems, nasal symptoms, eye symptoms, and emotions. The scale went from 0 (not troubled) to 6 (extremely troubled). A two-way analysis of variance (ANOVA) model with treatment and site effects was used to examine the treatment difference.

End point type	Secondary

End point timeframe:

Baseline and Day 29

End point values	Desloratadine 5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[4]	289[5]		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	3.3 (± 0.08)	3.15 (± 0.08)		
Day 29	-1.35 (± 0.1)	-0.95 (± 0.1)		

Notes:

[4] - All randomized participants with non-missing baseline and at least some postbaseline data.

[5] - All randomized participants with non-missing baseline and at least some postbaseline data.

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

Difference in the least squares means between change from baseline in RQLQ-S for participants taking desloratadine at Day 29 of treatment vs. change from baseline in RQLQ-S for participants taking placebo at Day 29 of treatment. Negative differences are in favor of the desloratadine treatment group in the comparison.

Comparison groups	Desloratadine 5 mg v Placebo

Number of subjects included in analysis	602
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	-0.2

Notes:

[6] - Analyses were performed using an ANOVA, extracting sources of variation due to treatment and site.

Secondary: Change From Baseline in Participant's AM/PM PRIOR (Reflective) T5SS Over Days 1 to 85 of Treatment

End point title	Change From Baseline in Participant's AM/PM PRIOR (Reflective) T5SS Over Days 1 to 85 of Treatment

End point description:

AM/PM PRIOR (the participant’s status over previous 12 hours [reflective]) T5SS from the participant's daily diary averaged over treatment Days 1 to 85. AM/PM is the average of separate morning (AM) and evening (PM) evaluations. Scores were defined for T5SS as 0: no symptoms to 15: all severe symptoms. A two-way analysis of variance (ANOVA) model with treatment and site effects was used to examine the treatment difference.

End point type	Secondary

End point timeframe:

Baseline and Days 1-85

End point values	Desloratadine 5 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	355[7]	351[8]		
Units: Units on a scale				
least squares mean (standard error)				
Baseline	9.63 (± 0.13)	9.55 (± 0.12)		
Days 1-85	-4.5 (± 0.23)	-3.61 (± 0.23)		

Notes:

[7] - All randomized participants with non-missing baseline and at least some postbaseline data.

[8] - All randomized participants with non-missing baseline and at least some postbaseline data.

Statistical analyses

Statistical analysis title	Treatment Difference

Statistical analysis description:

Difference in the least squares means between change from baseline in AM/PM PRIOR T5SS for participants taking desloratadine over Day 1 to Day 85 of treatment vs. change from baseline in AM/PM PRIOR (Reflective) T5SS for participants taking placebo over Day 1 to Day 85 of treatment. Negative differences are in favor of the desloratadine treatment group in the comparison.

Comparison groups	Desloratadine 5 mg v Placebo

Number of subjects included in analysis	706
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.001
Method	ANOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	-0.43

Notes:

[9] - Analyses were performed using an ANOVA, extracting sources of variation due to treatment and site.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Week 12	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.0
Reporting groups	
Reporting group title	Desloratadine 5 mg
Reporting group description: All randomized participants who received at least one dose of study drug.	
Reporting group title	Placebo
Reporting group description: All randomized participants who received at least one dose of study drug.	

Serious adverse events	Desloratadine 5 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 360 (0.28%)	2 / 356 (0.56%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 360 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diverticulum intestinal			
subjects affected / exposed	0 / 360 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Bronchospasm			
subjects affected / exposed	0 / 360 (0.00%)	1 / 356 (0.28%)	
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 %

Non-serious adverse events	Desloratadine 5 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 360 (16.67%)	48 / 356 (13.48%)	
Nervous system disorders			
Headache			
subjects affected / exposed	25 / 360 (6.94%)	37 / 356 (10.39%)	
occurrences (all)	45	63	
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	38 / 360 (10.56%)	17 / 356 (4.78%)	
occurrences (all)	44	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 June 2006	This amendment included an updated version of a study questionnaire.
05 June 2007	This amendment includes changes to study evaluations, criteria for subject discontinuation, and prohibited medications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported