Clinical trial results:
A randomized, double-blind, placebo-controlled, multi-center study of the efficacy and safety of STG320 sublingual tablets of house dust mite (HDM) allergen extracts in adults and adolescents with HDM-associated allergic rhinitis

Summary

EudraCT number	2014-004223-46
Trial protocol	BE SK DE CZ BG PL ES IT
Global end of trial date	25 June 2018

Results information

Result version number	v1 (current)
This version publication date	04 October 2019
First version publication date	04 October 2019

Trial information

Trial identification

Sponsor protocol code	SL75.14

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02443805
WHO universal trial number (UTN)	-
Other trial identifiers	16252: IND Number

Notes:

Sponsors

Sponsor organisation name	Stallergenes Greer
Sponsor organisation address	6 rue Alexis de Tocqueville, Antony, France, 92160
Public contact	Director of Clinical Development, Stallergenes Greer, 0033 155592556, martine.legall@stallergenesgreer.com
Scientific contact	Director of Clinical Development, Stallergenes Greer, 0033 155592556, martine.legall@stallergenesgreer.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	12 July 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 June 2018
Global end of trial reached?	Yes
Global end of trial date	25 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to assess the efficacy and safety of 12 months of treatment with 300 IR of STG320 sublingual tablets compared with placebo in adults and adolescents with HDM-associated allergic rhinitis.

Protection of trial subjects:

An independent Data and Safety Monitoring Board was responsible for assuring that study patients were not exposed to unnecessary or unreasonable risks and that the study was being conducted according to high scientific and ethical standards.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 September 2015
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	Belgium: 40
Country: Number of subjects enrolled	Bulgaria: 74
Country: Number of subjects enrolled	Canada: 173
Country: Number of subjects enrolled	Czech Republic: 138
Country: Number of subjects enrolled	France: 37
Country: Number of subjects enrolled	Germany: 88
Country: Number of subjects enrolled	Israel: 50
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Poland: 382
Country: Number of subjects enrolled	Russian Federation: 49
Country: Number of subjects enrolled	Slovakia: 158
Country: Number of subjects enrolled	Spain: 60
Country: Number of subjects enrolled	United States: 342
Worldwide total number of subjects	1607
EEA total number of subjects	993

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)	343
Adults (18-64 years)	1262
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted between 29 September 2015 (first patient, first visit) and 25 June 2018 (last patient, last visit).

Pre-assignment

Screening details:

A total of 4,267 patients were screened and 1,607 patients were randomized.
2 174 (50.9%) and 486 (11.4%) patients were excluded before and during the placebo run-in period, respectively. The main reason for screen failures at these two stages was a failure to meet randomization criteria.

Pre-assignment period milestones

Number of subjects started	1607
Number of subjects completed	1607

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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	300 IR

Arm description:

300 IR tablet of HDM Allergen Extracts

Arm type	Experimental
Investigational medicinal product name	300 IR tablet of HDM Allergen Extracts
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

300 IR tablet of HDM Allergen Extracts
Initiation phase: patients took 1 tablet of 100 IR on Day 1 and 2 tablets of 100 IR on Day 2.
Maintenance phase: from the 3rd day until the end of treatment patients took 1 tablet of 300 IR per day.

Arm title	Placebo

Arm description:

Placebo tablet

Arm type	Placebo
Investigational medicinal product name	Placebo tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sublingual tablet
Routes of administration	Sublingual use

Dosage and administration details:

Placebo tablet

Initiation phase: patients took 1 tablet of placebo on Day 1 and 2 tablets of placebo on Day 2. Maintenance phase: from the 3rd day until the end of treatment patients took 1 tablet of placebo per day.

Number of subjects in period 1	300 IR	Placebo
Started	802	805
Completed	589	678
Not completed	213	127
Consent withdrawn by subject	73	74
Any other reason not above-mentioned	3	2
Adverse event, non-fatal	100	18
Pregnancy	6	5
Non-compliance with study drug	6	4
Lost to follow-up	19	14
Withdrawal by parent/guardian	3	5
Protocol deviation	2	4
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	300 IR
Reporting group description:	
300 IR tablet of HDM Allergen Extracts	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet	

Reporting group values	300 IR	Placebo	Total
Number of subjects	802	805	1607
Age categorical Units: Subjects			
Adolescents (12-17 years)	179	164	343
Adults (18-64 years)	621	641	1262
From 65-84 years	2	0	2
Age continuous Units: years			
arithmetic mean	29.3	29.5	
standard deviation	± 12.89	± 12.56	-
Gender categorical Units: Subjects			
Female	413	416	829
Male	389	389	778
Ethnicity Units: Subjects			
Hispanic or Latino	57	50	107
Not Hispanic or Latino	744	755	1499
Unknown or not reported	1	0	1
Race Units: Subjects			
Black or African American	28	40	68
American Indian or Alaska Native	0	1	1
Asian	23	22	45
Native Hawaiian or Other Pacific Islander	2	0	2
White	746	736	1482
Multiple	2	3	5
Unknown	1	3	4
Region of Enrollment Units: Subjects			
North America	256	259	515
Rest of World	546	546	1092

End points

End points reporting groups	
Reporting group title	300 IR
Reporting group description: 300 IR tablet of HDM Allergen Extracts	
Reporting group title	Placebo
Reporting group description: Placebo tablet	

Primary: Total Combined Score (TCS)	
End point title	Total Combined Score (TCS)
End point description: Average Total Combined Score (TCS), calculated for each patient as the average of the daily TCSs during the primary evaluation period in FAS. The daily TCS (scale 0-15) was the sum of the patient's daily Rhinitis Total Symptom Score (RTSS, scale 0-12) and daily Rescue Medication Score (RMS, scale 0-3). Lower is better.	
End point type	Primary
End point timeframe: 12 months	

End point values	300 IR	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	586	676		
Units: Units on a scale				
least squares mean (confidence interval 95%)	3.62 (3.33 to 3.92)	4.35 (4.06 to 4.66)		

Statistical analyses

Statistical analysis title	LS Means Difference (300 IR vs Placebo)
Comparison groups	300 IR v Placebo
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Secondary: Rhinitis Total Symptom Score (RTSS)	
End point title	Rhinitis Total Symptom Score (RTSS)

End point description:

Average Rhinitis Total Symptom Score (RTSS) during the primary evaluation period in FAS. The daily RTSS was the sum of the 4 rhinitis symptom scores: sneezing, rhinorrhoea, nasal pruritus and nasal congestion, each graded on a 4-point scale (0: absent, 1: mild, 2: moderate, 3: severe).
It ranges from 0 to 12. Lower is better.

End point type	Secondary

End point timeframe:

12 months

End point values	300 IR	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	586	676		
Units: Units on a scale				
least squares mean (confidence interval 95%)	3.16 (2.89 to 3.43)	3.79 (3.53 to 4.07)		

Statistical analyses

Statistical analysis title	LS Means Difference (300 IR vs Placebo)
Comparison groups	300 IR v Placebo
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANCOVA

Secondary: Rescue Medication Score (RMS)

End point title	Rescue Medication Score (RMS)

End point description:

Average Rescue Medication Score (RMS) during the primary evaluation period in FAS. It ranges from 0 to 3. Lower is better.

End point type	Secondary

End point timeframe:

12 months

End point values	300 IR	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	586	676		
Units: Units on a scale				
least squares mean (confidence interval 95%)	0.21 (0.17 to 0.25)	0.30 (0.26 to 0.35)		

Statistical analyses

Statistical analysis title	LS Means Difference (300 IR vs Placebo)
Comparison groups	300 IR v Placebo
Number of subjects included in analysis	1262
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12 months

Adverse event reporting additional description:

Safety variables were adverse events (AEs) monitored throughout the study and data from physical examinations and clinical laboratory assessments.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	300 IR

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	300 IR	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 800 (2.63%)	9 / 801 (1.12%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid neoplasm			

subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic fatigue syndrome			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst ruptured			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pharyngeal disorder			
subjects affected / exposed	2 / 800 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			

subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 800 (0.13%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Intracranial aneurysm			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			

subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	2 / 800 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Chondromalacia			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plica syndrome			

subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	3 / 800 (0.38%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 800 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tick-borne viral encephalitis			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 800 (0.13%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	300 IR	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	424 / 800 (53.00%)	223 / 801 (27.84%)	
Nervous system disorders			
Headache			
subjects affected / exposed	57 / 800 (7.13%)	68 / 801 (8.49%)	
occurrences (all)	158	214	
Ear and labyrinth disorders			

Ear pruritus			
subjects affected / exposed	115 / 800 (14.38%)	13 / 801 (1.62%)	
occurrences (all)	206	17	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	43 / 800 (5.38%)	12 / 801 (1.50%)	
occurrences (all)	64	16	
Dysphagia			
subjects affected / exposed	53 / 800 (6.63%)	2 / 801 (0.25%)	
occurrences (all)	71	2	
Lip oedema			
subjects affected / exposed	61 / 800 (7.63%)	8 / 801 (1.00%)	
occurrences (all)	100	10	
Nausea			
subjects affected / exposed	47 / 800 (5.88%)	8 / 801 (1.00%)	
occurrences (all)	65	8	
Oedema mouth			
subjects affected / exposed	112 / 800 (14.00%)	3 / 801 (0.37%)	
occurrences (all)	186	3	
Oral pruritus			
subjects affected / exposed	189 / 800 (23.63%)	29 / 801 (3.62%)	
occurrences (all)	329	35	
Tongue oedema			
subjects affected / exposed	68 / 800 (8.50%)	3 / 801 (0.37%)	
occurrences (all)	100	3	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	45 / 800 (5.63%)	31 / 801 (3.87%)	
occurrences (all)	67	52	
Pharyngeal oedema			
subjects affected / exposed	46 / 800 (5.75%)	1 / 801 (0.12%)	
occurrences (all)	62	1	
Throat irritation			
subjects affected / exposed	136 / 800 (17.00%)	27 / 801 (3.37%)	
occurrences (all)	233	37	
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	107 / 800 (13.38%) 169	117 / 801 (14.61%) 173	

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