



Clinical trial results:

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study in Cat-Allergic Patients with Asthma to Evaluate the Efficacy of a Single Dose of REGN1908-1909 to Reduce Bronchoconstriction Upon Cat Allergen Challenge

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-002477-22 |
| Trial protocol | FR |
| Global end of trial date | 06 April 2020 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v2 (current) |
| This version publication date | 16 September 2021 |
| First version publication date | 17 April 2021 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|---------------------|
| Sponsor protocol code | R1908-1909-ALG-1703 |
|-----------------------|---------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03838731 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Regeneron Pharmaceuticals, Inc. |
| Sponsor organisation address | 777 Old Saw Mill River Rd., Tarrytown, NY, United States, 10591 |
| Public contact | Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.com |
| Scientific contact | Clinical Trials Administrator, Regeneron Pharmaceuticals, Inc., 001 844-734-6643, clinicaltrials@regeneron.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 | 06 April 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 April 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the prophylactic efficacy of REGN1908-1909 (anti-Fel d 1) administered as a single dose on day 1 in cat-allergic asthmatic subjects not living with a cat in the prevention of a Controlled Cat Allergen Challenge-induced early asthmatic response (EAR) assessed by measures of lung function (forced expiratory volume in 1 second [FEV1]) compared to placebo-treated subjects on day 8.

Protection of trial subjects:

This clinical study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with the International Council for Harmonisation (ICH) guidelines for Good Clinical Practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 12 February 2019 |
| 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 | France: 56 |
| Worldwide total number of subjects | 56 |
| EEA total number of subjects | 56 |

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) | 56 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 130 subjects were screened for study eligibility. Screen failures were mostly attributed to eligibility criteria not being met. The study was conducted at one site in France.

Pre-assignment

Screening details:

A total of 56 subjects were randomized in a 1:1 ratio to receive a single dose of either 600 milligrams (mg) of REGN1908-1909 or matching placebo.

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, Monitor, Data analyst, Assessor, Carer |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Subjects received a single dose of matching placebo

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

Dosage and administration details:

Single subcutaneous (SC) dose of matching placebo

| | |
|------------------|----------------------|
| Arm title | REGN1908-1909 600 mg |
|------------------|----------------------|

Arm description:

Subjects received a single 600 mg dose of REGN1908-1909

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | REGN1908-1909 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Single subcutaneous (SC) dose of REGN1908 and REGN1909

| Number of subjects in period 1 | Placebo | REGN1908-1909 600 mg |
|---------------------------------------|---------|----------------------|
| Started | 27 | 29 |
| Completed | 26 | 28 |
| Not completed | 1 | 1 |
| Pregnancy | - | 1 |
| Withdrawal of consent | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|----------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received a single dose of matching placebo | |
| Reporting group title | REGN1908-1909 600 mg |
| Reporting group description: | |
| Subjects received a single 600 mg dose of REGN1908-1909 | |

| Reporting group values | Placebo | REGN1908-1909 600 mg | Total |
|--|---------|----------------------|-------|
| Number of subjects | 27 | 29 | 56 |
| 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) | 27 | 29 | 56 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 30.2 | 28.4 | |
| standard deviation | ± 8.8 | ± 7.1 | - |
| Sex: Female, Male Units: Subjects | | | |
| Female | 17 | 18 | 35 |
| Male | 10 | 11 | 21 |
| Race, Customized Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 3 | 0 | 3 |
| White | 24 | 27 | 51 |
| Other | 0 | 1 | 1 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | 2 |
| Not Hispanic or Latino | 26 | 28 | 54 |
| Unknown or Not Reported | 0 | 0 | 0 |

End points

End points reporting groups

| | |
|---|----------------------|
| Reporting group title | Placebo |
| Reporting group description: | |
| Subjects received a single dose of matching placebo | |
| Reporting group title | REGN1908-1909 600 mg |
| Reporting group description: | |
| Subjects received a single 600 mg dose of REGN1908-1909 | |

Primary: Time to Early Asthmatic Response (EAR) upon Controlled Cat Allergen Challenge in an Environmental Exposure Unit (EEU) on Day 8

| | |
|---|--|
| End point title | Time to Early Asthmatic Response (EAR) upon Controlled Cat Allergen Challenge in an Environmental Exposure Unit (EEU) on Day 8 |
| End point description: | |
| Time to EAR was defined as the time to a $\geq 20\%$ reduction in FEV1 or when the subject voluntarily departed the EEU due to clinically significant allergic and/or asthmatic symptoms. | |
| End point type | Primary |
| End point timeframe: | |
| Day 8 | |

| End point values | Placebo | REGN1908-1909 600 mg | | |
|----------------------------------|---------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Minutes | | | | |
| median (confidence interval 95%) | 51 (33.92 to 70.70) | 99999 (130.87 to 99999) | | |

Statistical analyses

| | |
|---|----------------------------------|
| Statistical analysis title | Placebo vs. REGN1908-1909 600 mg |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0083 |
| Method | Cox Hazard Proportional |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.36 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.17 |
| upper limit | 0.77 |

Secondary: Time to EAR upon Controlled Cat Allergen Challenge in an EEU on Days 29, 57, and 85

| | |
|--|---|
| End point title | Time to EAR upon Controlled Cat Allergen Challenge in an EEU on Days 29, 57, and 85 |
| End point description: | |
| Time to EAR was defined as the time to a $\geq 20\%$ reduction in FEV1 or when the subject voluntarily departed the EEU due to clinically significant allergic and/or asthmatic symptoms | |
| End point type | Secondary |
| End point timeframe: | |
| Days 29, 57 and 85 | |

| End point values | Placebo | REGN1908-1909 600 mg | | |
|----------------------------------|---------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Minutes | | | | |
| median (confidence interval 95%) | | | | |
| Day 29 | 41 (31.38 to 61.13) | 99999 (131.22 to 99999) | | |
| Day 57 | 56 (40.52 to 80.63) | 232 (81.05 to 99999) | | |
| Day 85 | 41 (31.03 to 60.93) | 99999 (90.97 to 99999) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | < 0.0001 |
| Method | Cox Hazard Model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.12 |
| upper limit | 0.48 |

Notes:

[1] - Day 29

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 85 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0003 |
| Method | Cox Hazard Model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.13 |
| upper limit | 0.56 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 57 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0222 |
| Method | Cox Hazard Model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.45 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.22 |
| upper limit | 0.89 |

Secondary: Percent Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

| | |
|-----------------|---|
| End point title | Percent Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85 |
|-----------------|---|

End point description:

The AUC was analyzed by mixed-effect model repeated measures (MMRM) with the treatment, time, treatment-by-time interaction, and day of challenge as factors and baseline FEV1 as a continuous covariate. Full analysis set; Here 'n' = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if the patients remained in EEU for less than 2 hours. The AUCs were calculated using the trapezoidal rule and were normalized by dividing by the length of time (2 hours).

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

End point timeframe:

Days 8, 29, 57, and 85

| End point values | Placebo | REGN1908-1909 600 mg | | |
|-------------------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Percentage of change | | | | |
| least squares mean (standard error) | | | | |
| Day 8 | 1.59 (± 2.58) | 15.15 (± 2.50) | | |
| Day 29 | 0.46 (± 3.60) | 16.67 (± 3.43) | | |
| Day 57 | 1.77 (± 3.55) | 14.07 (± 3.43) | | |
| Day 85 | 0.20 (± 3.28) | 12.73 (± 3.14) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | < 0.001 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 13.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.35 |
| upper limit | 20.77 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 3.59 |

Notes:

[2] - Day 8

| | |
|-----------------------------------|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Comparison groups | Placebo v REGN1908-1909 600 mg |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.002 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 16.21 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.18 |
| upper limit | 26.24 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.97 |

Notes:

[3] - Day 29

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | = 0.016 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 12.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.4 |
| upper limit | 22.2 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.94 |

Notes:

[4] - Day 57

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | = 0.008 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 12.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.43 |
| upper limit | 21.65 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
| Dispersion value | 4.54 |

Notes:

[5] - Day 85

Secondary: Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

| | |
|-----------------|---|
| End point title | Change in Normalized Area Under the Curve (AUC) of the Forced Expiratory Volume in 1 Second (FEV1) Induced by a Controlled Cat Allergen Challenge over Exposure Interval from Baseline to Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85 |
|-----------------|---|

End point description:

The AUC was analyzed by mixed-effect model repeated measures (MMRM) with the treatment, time, treatment-by-time interaction, and day of challenge as factors and baseline FEV1 as a continuous covariate. Full analysis set; Here "n" = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if the patients remained in EEU for less than 2 hours. The AUCs were calculated using the trapezoidal rule and were normalized by dividing by the length of time (2 hours).

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

End point timeframe:

Days 8, 29, 57 and 85

| End point values | Placebo | REGN1908-1909 600 mg | | |
|-------------------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Liters (L) | | | | |
| least squares mean (standard error) | | | | |
| Day 8 | 0.01 (± 0.06) | 0.38 (± 0.06) | | |
| Day 29 | -0.03 (± 0.08) | 0.43 (± 0.08) | | |
| Day 57 | 0.00 (± 0.08) | 0.34 (± 0.07) | | |
| Day 85 | -0.05 (± 0.08) | 0.32 (± 0.08) | | |

Statistical analyses

| | |
|----------------------------|-------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
|----------------------------|-------------------------------|

Statistical analysis description:

Day 8

| | |
|---|--------------------------------|
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.37 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.21 |
| upper limit | 0.53 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.08 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 29 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.23 |
| upper limit | 0.68 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.11 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 57 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.13 |
| upper limit | 0.55 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.11 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 85 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.002 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.15 |
| upper limit | 0.47 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.11 |

Secondary: Change from Baseline in the Normalized AUC of Patient-Assessed Nasal Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

| | |
|-----------------|--|
| End point title | Change from Baseline in the Normalized AUC of Patient-Assessed Nasal Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85 |
|-----------------|--|

End point description:

Individual nasal symptoms, including rhinorrhea, nasal congestion, nasal itching, and sneezing were evaluated on a 4-point Likert scale (0, none; 1, mild; 2, moderate; and 3, severe) and combined to give the Total Nasal Symptom Score (TNSS) with a maximum score of 12. Scale range is 0-12. The higher the total, the more severe the symptoms. Full analysis set; Here 'n' = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if participants remained in EEU for less than 2 hours. AUCs were calculated using trapezoidal rule and were normalized by dividing by the length of time (2 hours).

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

End point timeframe:

Days 8, 29, 57 and 85

| | | | | |
|-------------------------------------|-----------------|----------------------|--|--|
| End point values | Placebo | REGN1908-1909 600 mg | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Day 8 | -0.71 (± 0.38) | -0.49 (± 0.38) | | |

| | | | | |
|--------|---------------------|---------------------|--|--|
| Day 29 | -0.70 (\pm 0.37) | -1.39 (\pm 0.34) | | |
| Day 57 | -0.93 (\pm 0.43) | -0.83 (\pm 0.43) | | |
| Day 85 | -0.49 (\pm 0.43) | -1.37 (\pm 0.41) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 8 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.675 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.85 |
| upper limit | 1.29 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.53 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 29 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.182 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.33 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.51 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 57 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.866 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.12 |
| upper limit | 1.32 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.61 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 85 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.146 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.08 |
| upper limit | 0.32 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.6 |

Secondary: Change from Baseline in the Normalized AUC in Patient-Assessed Ocular Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85

| | |
|-----------------|---|
| End point title | Change from Baseline in the Normalized AUC in Patient-Assessed Ocular Symptoms Induced by a Controlled Cat Allergen Challenge over the Exposure Interval to the Controlled Cat Allergen Challenge on Days 8, 29, 57, and 85 |
|-----------------|---|

End point description:

Individual ocular symptoms for itching/burning, redness, swelling/puffiness, and tearing/watery eyes were evaluated on a 4-point Likert scale (0, none; 1, mild; 2, moderate; and 3, severe) and combined

to give the TOSS, with a maximum score of 12. Scale range is 0-12. The higher the score, the more severe the symptoms. Full analysis set; Here 'n' = number of evaluable participants analyzed at each time point. For each participant at each controlled cat allergen challenge, AUC was calculated over the time period of 0 to 2 hours, with last observation carried forward used to impute values out to 2 hours if participants remained in EEU for less than 2 hours. AUCs were calculated using trapezoidal rule and were normalized by dividing by the length of time (2 hours).

| | |
|-----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Days 8, 29, 57 and 85 | |

| End point values | Placebo | REGN1908-1909 600 mg | | |
|-------------------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Scores on a scale | | | | |
| least squares mean (standard error) | | | | |
| Day 8 | -0.37 (± 0.17) | -0.23 (± 0.17) | | |
| Day 29 | -0.43 (± 0.15) | -0.43 (± 0.14) | | |
| Day 57 | -0.40 (± 0.15) | -0.34 (± 0.15) | | |
| Day 85 | -0.36 (± 0.11) | -0.51 (± 0.10) | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 8 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.572 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.35 |
| upper limit | 0.63 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.24 |

| | |
|-----------------------------------|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 29 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.997 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.41 |
| upper limit | 0.41 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.2 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 57 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.756 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 0.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.36 |
| upper limit | 0.49 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.21 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 85 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.333 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.15 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.46 |
| upper limit | 0.16 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.15 |

Secondary: Mean Change from Baseline in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85 |
|-----------------|---|

End point description:

Cat Allergen Exposure Tolerated in ng = Minute Ventilation (L/min) x Allergen Concentration (ng/m³) x Time in EEU (minutes), where 1 L/min = 0.001 m³/min. The change in cat allergen quantity (tolerated exposure) from the baseline Cat Allergen Challenge, will be analyzed using a similar MMRM model with treatment, visit and treatment by-visit interaction as factors and the cat allergen quantity tolerated in the baseline Controlled Cat Allergen Challenge as a covariate.

Full analysis set: included all randomized participants who received any investigational product and had completed the Day 8 Cat Allergen Challenge; Here 'n' = number of evaluable participants analyzed at each time point

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

End point timeframe:

Days 8, 29, 57 and 85

| End point values | Placebo | REGN1908-1909 600 mg | | |
|-------------------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Nanograms (ng) | | | | |
| least squares mean (standard error) | | | | |
| Day 8 | 19.55 (± 8.93) | 59.05 (± 8.70) | | |
| Day 29 | 14.14 (± 8.67) | 68.21 (± 8.21) | | |
| Day 57 | 21.94 (± 10.23) | 55.38 (± 9.93) | | |
| Day 85 | 12.93 (± 9.29) | 54.03 (± 8.94) | | |

Statistical analyses

| | |
|----------------------------|-------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
|----------------------------|-------------------------------|

Statistical analysis description:

Day 8

| | |
|-------------------|--------------------------------|
| Comparison groups | Placebo v REGN1908-1909 600 mg |
|-------------------|--------------------------------|

| | |
|---|----------------------------|
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 39.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 14.36 |
| upper limit | 64.65 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 12.5 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 29 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 39.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 14.36 |
| upper limit | 64.65 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 12.5 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: | |
| Day 57 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.023 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 33.44 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.79 |
| upper limit | 62.08 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 14.28 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: Day 85 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.003 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 41.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 15.1 |
| upper limit | 67.09 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 12.92 |

Secondary: Percent Change in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85

| | |
|---|--|
| End point title | Percent Change in Cat Allergen Quantity as Experienced by Subjects During Exposure on Days 8, 29, 57, and 85 |
| End point description: Cat Allergen Exposure Tolerated in ng = Minute Ventilation (L/min) x Allergen Concentration (ng/m3) x Time in EEU (minutes), where 1 L/min = 0.001 m3/min. The change in cat allergen quantity (tolerated exposure) from the baseline Cat Allergen Challenge, will be analyzed using a similar MMRM model with treatment, visit and treatment by-visit interaction as factors and the cat allergen quantity tolerated in the baseline Controlled Cat Allergen Challenge as a covariate. Full analysis set: included all randomized participants who received any investigational product and had completed the Day 8 Cat Allergen Challenge; Here 'n' = number of evaluable participants analyzed at each time point | |
| End point type | Secondary |
| End point timeframe: Days 8, 29, 57 and 85 | |

| End point values | Placebo | REGN1908-1909 600 mg | | |
|-------------------------------------|------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Percentage of change | | | | |
| least squares mean (standard error) | | | | |
| Day 8 | 119.86 (± 73.22) | 325.29 (± 70.79) | | |
| Day 29 | 93.62 (± 71.48) | 338.22 (± 68.26) | | |
| Day 57 | 118.08 (± 69.58) | 301.11 (± 67.11) | | |
| Day 85 | 76.75 (± 82.08) | 317.76 (± 78.84) | | |

Statistical analyses

| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
|---|--------------------------------|
| Statistical analysis description: | |
| Day 8 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.049 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 205.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 410.17 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 102.09 |

| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
|---|--------------------------------|
| Statistical analysis description: | |
| Day 29 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 244.6 |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 45.6 |
| upper limit | 443.59 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 99.05 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: Day 57 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.064 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 183.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.29 |
| upper limit | 377.35 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 96.91 |

| | |
|---|--------------------------------|
| Statistical analysis title | Placebo, REGN1908-1909 600 mg |
| Statistical analysis description: Day 85 | |
| Comparison groups | Placebo v REGN1908-1909 600 mg |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.039 |
| Method | MMRM |
| Parameter estimate | LS Mean Difference |
| Point estimate | 241.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 12.44 |
| upper limit | 469.57 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 114 |

Secondary: Number of Non-Serious and Serious Treatment-Emergent Adverse Events (TEAEs) through End of Study

| | |
|-----------------|--|
| End point title | Number of Non-Serious and Serious Treatment-Emergent Adverse Events (TEAEs) through End of Study |
|-----------------|--|

End point description:

Adverse events and serious adverse events were collected from the time of informed consent signature and then at each visit until the end of the study with the exception of symptoms that occurred in response to the EEU within 24 hours following the EEU. Safety Analysis Set (SAF): included all subjects who received any investigational product and were analyzed as treated.

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

End point timeframe:

Baseline to 16 weeks

| End point values | Placebo | REGN1908-1909 600 mg | | |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 27 | 29 | | |
| Units: Events | | | | |
| number (not applicable) | | | | |
| Non-serious TEAEs | 66 | 76 | | |
| Serious TEAEs | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline (day 1) to the end of study (week 16)

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | REGN1908-1909 600mg |
|-----------------------|---------------------|

Reporting group description:

Subjects received single 600 mg dose of REGN1908-1909

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

Reporting group description:

Subjects received a single dose of matching placebo

| Serious adverse events | REGN1908-1909 600mg | Placebo | |
|---|------------------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 27 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | REGN1908-1909 600mg | Placebo | |
|---|------------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 22 / 29 (75.86%) | 19 / 27 (70.37%) | |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 27 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 5 / 29 (17.24%) | 2 / 27 (7.41%) | |
| occurrences (all) | 5 | 2 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|------------------------|------------------------|--|
| Influenza like illness subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 4 / 27 (14.81%) 4 | |
| Injection site pain subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 1 / 27 (3.70%) 1 | |
| Eye disorders Conjunctivitis allergic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 0 / 27 (0.00%) 0 | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 27 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) | 11 / 29 (37.93%) 19 | 16 / 27 (59.26%) 35 | |
| Asthma exercise induced subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 3 / 27 (11.11%) 3 | |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 5 | 2 / 27 (7.41%) 2 | |
| Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 2 / 27 (7.41%) 2 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 2 / 27 (7.41%) 2 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 18 December 2018 | Added exploratory objective information; clarification of several sections and study exit parameters, addition of Independent Data Monitoring Committee (IDMC) section; updates to inclusion and exclusion criteria; editorial changes |
| 20 May 2019 | Clarified language in adverse events; clarified inclusion and exclusion criteria information; clarified timing of analysis; procedural clarifications of timing of events, tests and measurements; added clarification on concomitant medications; other administrative updates |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported