



Clinical trial results:

A phase II, multi-centre, randomized, double blind, placebo-controlled study to determine the mode of action of omalizumab in patients with chronic idiopathic urticaria (CIU) who remain symptomatic with antihistamine treatment (H1)

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2011-004216-31 |
| Trial protocol | DE |
| Global end of trial date | 10 September 2013 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 26 April 2018 |
| First version publication date | 26 April 2018 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CIGE025E2201 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01599637 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | CH-4002, Basel, Switzerland, |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, |

Notes:

Paediatric regulatory details

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|--|----|
| 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 | 10 September 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 September 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 September 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine whether treatment with omalizumab in patients with CIU results in a reduction of the high affinity IgE receptor (FcεRI) and/or IgE positive skin cells following 12 weeks of treatment (Day 85).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

The use of loratadine as rescue medication was reduced by treatment with omalizumab 300 mg both in terms of the number of days per week and the number of tablets per week.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 17 April 2012 |
| 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 | Germany: 30 |
| Worldwide total number of subjects | 30 |
| EEA total number of subjects | 30 |

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) | 30 |
| From 65 to 84 years | 0 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A planned number of approximately 30 patients with CIU were randomized 2:1 to receive either 300 mg omalizumab or matching placebo s.c.. Study treatment was administered on 3 separate occasions i.e. at Day 1, Day 29 and Day 57.

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, Carer, Data analyst, Assessor |

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | IGE025 |

Arm description:

IGE025 administered subcutaneously every 4 weeks at the study center

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | omalizumab |
| Investigational medicinal product code | IGE025 |
| Other name | omalizumab |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

omalizumab 300 mg s.c. on Day 1, Day 29 and Day 57

| | |
|------------------|-------------------|
| Arm title | Placebo to IGE025 |
|------------------|-------------------|

Arm description:

Placebo administered subcutaneously every 4 weeks at the study center

| | |
|--|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | Placebo to IGE025 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo to IGE025 s.c. on Day 1, Day 29 and Day 57

| Number of subjects in period 1 | IGE025 | Placebo to IGE025 |
|---------------------------------------|--------|-------------------|
| Started | 20 | 10 |
| Completed | 19 | 8 |
| Not completed | 1 | 2 |
| Adverse event, non-fatal | 1 | - |
| administrative problems | - | 2 |

Baseline characteristics

Reporting groups

| | |
|---|-------------------|
| Reporting group title | IGE025 |
| Reporting group description: IGE025 administered subcutaneously every 4 weeks at the study center | |
| Reporting group title | Placebo to IGE025 |
| Reporting group description: Placebo administered subcutaneously every 4 weeks at the study center | |

| Reporting group values | IGE025 | Placebo to IGE025 | Total |
|---|---------|-------------------|-------|
| Number of subjects | 20 | 10 | 30 |
| 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) | 20 | 10 | 30 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 37.5 | 41.1 | |
| standard deviation | ± 11.02 | ± 7.96 | - |
| Gender, Male/Female Units: Participants | | | |
| Female | 18 | 8 | 26 |
| Male | 2 | 2 | 4 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 0 |
| Not Hispanic or Latino | 20 | 10 | 30 |
| Unknown or Not Reported | 0 | 0 | 0 |

Subject analysis sets

| | |
|---|--------------------|
| Subject analysis set title | Urticaria Patients |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All patients for study at baseline | |
| Subject analysis set title | Healthy Subjects |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Baseline Value, healthy volunteers, no treatment applied | |

| Reporting group values | Urticaria Patients | Healthy Subjects | |
|---|--------------------|------------------|--|
| Number of subjects | 30 | 10 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 30 | 10 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | |
| Gender, Male/Female | | | |
| Units: Participants | | | |
| Female | | | |
| Male | | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | | | |
| Not Hispanic or Latino | | | |
| Unknown or Not Reported | | | |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | IGE025 |
| Reporting group description: IGE025 administered subcutaneously every 4 weeks at the study center | |
| Reporting group title | Placebo to IGE025 |
| Reporting group description: Placebo administered subcutaneously every 4 weeks at the study center | |
| Subject analysis set title | Urticaria Patients |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All patients for study at baseline | |
| Subject analysis set title | Healthy Subjects |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Baseline Value, healthy volunteers, no treatment applied | |

Primary: Observed values and absolute change from baseline in FcεRI positive skin cells: Dermis, lesional and non lesional skin

| | |
|---|--|
| End point title | Observed values and absolute change from baseline in FcεRI positive skin cells: Dermis, lesional and non lesional skin |
| End point description: Observed values and absolute change in FcεRI positive skin cells: dermis non-lesional and lesional. The primary variable for this study was the relative change from baseline in the high affinity IgE receptor (FcεRI) positive skin cells, based on skin biopsies collected from patients with CIU after 12 weeks of treatment. The values are average of cell numbers derived from counting 5 consecutive microscopic fields. Area counted is 5x 0.196 mm ² No Statistical analysis was planned for this primary outcome. | |
| End point type | Primary |
| End point timeframe: Baseline through Day 85 post-treatment | |

| End point values | IGE025 | Placebo to IGE025 | | |
|--|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: FcεRI positive skin cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| FcεRI +ve skin cells: dermis lesional D1 (n=19,8) | 18.14 (± 7.08) | 15.17 (± 3.11) | | |
| FcεRI +ve skin cells: dermis lesional d85 (n=10,7) | 13.4 (± 5.88) | 20.19 (± 8.76) | | |
| FcεRI +ve skin cells:dermis lesional Chge(n=10,6) | -5.42 (± 7.42) | 3.69 (± 10.58) | | |
| FcεRI +ve skincells:dermis nonlesional D1(n=19,10) | 18.91 (± 9.42) | 20.48 (± 5.54) | | |
| FcεRI +ve skincells:dermis nonlesional D85(n=18,8) | 14.72 (± 7.56) | 20.81 (± 7.3) | | |
| FcεRI +ve skincells:dermis nonlesional Chg(n=17,8) | -5.4 (± 9.06) | -0.07 (± 9.33) | | |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Primary D1-D85 |
| Comparison groups | IGE025 v Placebo to IGE025 |
| Number of subjects included in analysis | 30 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.82 |
| Method | t-test, 2-sided |

Primary: Observed values and absolute change from baseline in IgE positive skin cells: Dermis, lesional and non lesional skin

| | |
|---|--|
| End point title | Observed values and absolute change from baseline in IgE positive skin cells: Dermis, lesional and non lesional skin |
| End point description: Observed values and absolute change in IgE positive skin cells: dermis non-lesional and lesional The primary variable for this study was the relative change from baseline in IgE positive skin cells, based on skin biopsies collected from patients with CIU after 12 weeks of treatment. The values are average of cell numbers derived from counting 5 consecutive microscopic fields. Area counted is 5x 0.196 mm ² . No Statistical analysis was planned for this primary outcome. | |
| End point type | Primary |
| End point timeframe: Baseline through Day 85 post-treatment | |

| End point values | IGE025 | Placebo to IGE025 | | |
|---|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: IgE positive skin cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| IgE positive cells, lesional D1 (n=19,8) | 12.93 (± 8.61) | 15.23 (± 15.71) | | |
| IgE positive cells, lesional D85 (n=10,7) | 6.73 (± 7.9) | 12.47 (± 6.54) | | |
| IgE positive cells, lesional chg(n=10.6) | -5.69 (± 10.96) | -3.95 (± 20.76) | | |
| IgE positive cells,non-lesional D1 (n=19,10) | 13.82 (± 10.21) | 16.59 (± 9.35) | | |
| IgE positive cells,non-lesional D85 (n=18,8) | 9.8 (± 11.66) | 18.3 (± 7.51) | | |
| IgE positive cells,non-lesional Chng (n=17,8) | -4.87 (± 9.83) | -0.84 (± 6.18) | | |

Statistical analyses

| | |
|---|----------------------------|
| Statistical analysis title | Stats Primary |
| Comparison groups | IGE025 v Placebo to IGE025 |
| Number of subjects included in analysis | 30 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.82 |
| Method | t-test, 2-sided |

Secondary: Correlation of change from baseline in IgE receptor FcεRI with change from baseline in UAS7 at week 12 by treatment, skin layer and lesion status

| | |
|-----------------|---|
| End point title | Correlation of change from baseline in IgE receptor FcεRI with change from baseline in UAS7 at week 12 by treatment, skin layer and lesion status |
|-----------------|---|

End point description:

Correlation of primary endpoint with The UAS7 which is a composite eDiary–recorded score with numeric severity intensity ratings on a scale of 0–3 (0 = none to 3 = intense/severe) for 1) the number of wheals (hives); and 2) the intensity of the itch. The daily UAS is the average of the morning and evening scores and the UAS7 is the sum of the daily UAS scores over 7 days. UAS7 score: The sum of the daily UAS scores over 7 days. Range: 0-42. If fewer than 7 but at least 4 daily values were non-missing, the remaining values were imputed to be the average. This is equivalent to multiplying the average of the non missing values by 7. UAS7 score: The sum of the daily UAS scores over 7 days. Range: 0-42. A higher score indicates worse disease.

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: correlation coefficient | | | | |
| number (not applicable) | | | | |
| Dermis, lesional | 0.3305 | -0.1889 | | |
| Dermis, non-lesional | 0.2785 | 0.5057 | | |
| Epidermis, lesional | 0.0021 | 0.0101 | | |
| Epidermis, non-lesional | 0.0644 | 0.1563 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Correlation of change from baseline in IgE on positive skin cells with change from baseline in UAS7 at week 12 by treatment, skin layer and lesion status

| | |
|-----------------|---|
| End point title | Correlation of change from baseline in IgE on positive skin cells with change from baseline in UAS7 at week 12 by treatment, skin layer and lesion status |
|-----------------|---|

End point description:

Correlation of primary endpoint with The UAS7 which is a composite eDiary–recorded score with numeric severity intensity ratings on a scale of 0–3 (0 = none to 3 = intense/severe) for 1) the number of wheals (hives); and 2) the intensity of the itch. The daily UAS is the average of the morning and evening scores and the UAS7 is the sum of the daily UAS scores over 7 days. UAS7 score: The sum of the daily UAS scores over 7 days. Range: 0-42. If fewer than 7 but at least 4 daily values were non-missing, the remaining values were imputed to be the average. This is equivalent to multiplying the average of the non missing values by 7. UAS7 score: The sum of the daily UAS scores over 7 days. Range: 0-42. A higher score indicates worse disease.

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: correlation coefficient | | | | |
| number (not applicable) | | | | |
| Dermis, lesional | 0.4841 | -0.0952 | | |
| Dermis, non-lesional | 0.2759 | 0.4947 | | |
| Epidermis, lesional | 0.219 | -0.1142 | | |
| Epidermis, non-lesional | 0.1574 | -0.231 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: observed values and absolute change from baseline in skin cell subsets (CD3, CD4, CD8, Eosinophils, DCs, and Mast Cells) by parameter, skin layer, lesion status, treatment and visit

| | |
|-----------------|---|
| End point title | observed values and absolute change from baseline in skin cell subsets (CD3, CD4, CD8, Eosinophils, DCs, and Mast Cells) by parameter, skin layer, lesion status, treatment and visit |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline to Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: # positive cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| CD11c Epidermis Non lesional Baseline (n= 19,10) | 1.06 (± 1.077) | 1.25 (± 0.584) | | |
| CD11c Epidermis Non lesional Day 8 (n=19,10) | 1.41 (± 1.313) | 0.95 (± 0.92) | | |
| CD11c Epidermis Non lesional D 8(n=18,10) Chge | 0.39 (± 1.351) | -0.3 (± 1.255) | | |
| CD11c Epidermis Non lesional D 29(n=4,0) | 1 (± 0) | 0 (± 0) | | |
| CD11c Epidermis Non lesional D 29(n=4,0) Chg | 0.7 (± 0.383) | 0 (± 0) | | |
| CD11c Epidermis Non lesional D 85(n=18,8) | 1.19 (± 0.806) | 0.53 (± 0.544) | | |
| CD11c Epidermis Non lesional D 85(n=17,8) Chge | 0.04 (± 1.216) | -0.84 (± 0.524) | | |
| CD11c Epidermis Non lesional D 140(n=17,7) | 1.25 (± 1.63) | 0.58 (± 0.942) | | |
| CD11c Epidermis Non lesional D 140(n=17,7) Chge | 0.04 (± 1.216) | -0.75 (± 0.939) | | |
| CD11c Epidermis lesional baseline (n=19,8) | 1.17 (± 1.363) | 3.79 (± 8.028) | | |
| CD11c Epidermis lesional D8 (n=11,10) | 1.63 (± 1.425) | 1.19 (± 1.329) | | |
| CD11c Epidermis lesional D8 (n=11,8) Change | 0.39 (± 1.153) | -2.74 (± 8.466) | | |
| CD11c Epidermis lesional D29 (n=5,0) | 1.56 (± 1.609) | 0 (± 0) | | |
| CD11c Epidermis lesional D29 (n=5,0) Change | 0.88 (± 1.677) | 0 (± 0) | | |
| CD11c Epidermis lesional D85 (n=10,7) | 1.18 (± 0.577) | 0.46 (± 0.378) | | |
| CD11c Epidermis lesional D85 (n=10,6) Change | -0.06 (± 1.234) | -4.06 (± 9.384) | | |
| CD11c Epidermis lesional D140 (n=6,5) | 0.53 (± 0.555) | 0.18 (± 0.171) | | |
| CD11c Epidermis lesional D140 (n=6,5) Change | 0.12 (± 0.599) | -6.37 (± 11.503) | | |
| CD11c Dermis non lesional baseline (n=19,10) | 17.86 (± 7.322) | 22.97 (± 12.248) | | |
| CD11c Dermis non lesional D8 (n=19,10) | 18.33 (± 8.971) | 20.22 (± 10.861) | | |
| CD11c Dermis non lesional D8 (n=19,10) Change | 0.42 (± 7.613) | -2.75 (± 6.149) | | |
| CD11c Dermis non lesional D29 (n=4,0) | 15.63 (± 10.636) | 0 (± 0) | | |
| CD11c Dermis non lesional D29 (n=4,0) Change | 0.93 (± 15.472) | 0 (± 0) | | |
| CD11c Dermis non lesional D85 (n=18,8) | 17.05 (± 5.656) | 23.73 (± 19.031) | | |
| CD11c Dermis non lesional D85 (n=17,8) Change | -1.52 (± 7.562) | -1.23 (± 15.514) | | |
| CD11c Dermis non lesional D140 (n=17,7) | 22.85 (± 11.189) | 15.58 (± 9.691) | | |
| CD11c Dermis non lesional D140 (n=16,7) Change | 3.51 (± 11.162) | -11.51 (± 15.849) | | |
| CD11c Dermis lesional baseline(n=19,8) | 27.14 (± 12.552) | 22.46 (± 9.7) | | |
| CD11c Dermis lesional D8(n=11,10) | 28.85 (± 22.24) | 22.12 (± 8.669) | | |

| | | | | |
|---|------------------|------------------|--|--|
| CD11c Dermis lesional D8(n=11,8) Change | 3.56 (± 16.705) | 0.99 (± 8.677) | | |
| CD11c Dermis lesional D29 (n=5,0) | 27.04 (± 11.509) | 0 (± 0) | | |
| CD11c Dermis lesional D29 (n=5,0) Change | -0.28 (± 5.403) | 0 (± 0) | | |
| CD11c Dermis lesional D85 (n=10,7) | 24.82 (± 13.724) | 22.59 (± 16.719) | | |
| CD11c Dermis lesional D85 (n=10,6) Change | -0.09 (± 15) | 4.07 (± 22.288) | | |
| CD11c Dermis lesional D140 (n=6,5) | 37.33 (± 21.229) | 22.59 (± 16.719) | | |
| CD11c Dermis lesional D140 (n=6,4) Change | 11.3 (± 23.485) | 12.43 (± 9.21) | | |
| CD3 Epidermis non lesional Baseline (n=19,10) | 0.37 (± 0.593) | 0.68 (± 1.151) | | |
| CD3 Epidermis non lesional Day 8 (n=19,10) | 0.49 (± 0.754) | 0.34 (± 0.422) | | |
| CD3 Epidermis non lesional Day 8 (n=18,10) Change | 0.14 (± 0.636) | -0.34 (± 1.091) | | |
| CD3 Epidermis non lesional Day 29 (n=4,0) | 0.32 (± 0.367) | 0 (± 0) | | |
| CD3 Epidermis non lesional Day 29 (n=4,0) Change | 0.07 (± 0.094) | 0 (± 0) | | |
| CD3 Epidermis non lesional Day 85 (n=18,8) | 0.47 (± 0.66) | 0.3 (± 0.283) | | |
| CD3 Epidermis non lesional Day 85 (n=17,8) Change | 0.14 (± 0.438) | -0.46 (± 1.249) | | |
| CD3 Epidermis non lesional Day 140 (n=17,7) | 0.36 (± 0.47) | 0.75 (± 1.245) | | |
| CD3 Epidermis non lesional Day 140 (n=16,7) Change | -0.08 (± 0.554) | -0.09 (± 2.092) | | |
| CD3 Epidermis lesional Baseline (n=19,8) | 0.42 (± 0.459) | 0.49 (± 0.892) | | |
| CD3 Epidermis lesional Day 8(n=11,10) | 0.55 (± 0.561) | 0.84 (± 0.913) | | |
| CD3 Epidermis lesional Day 8(n=11,10) Change | 0.14 (± 0.604) | 0.11 (± 1.058) | | |
| CD3 Epidermis lesional Day 29(n=5,0) | 0.28 (± 0.438) | 0 (± 0) | | |
| CD3 Epidermis lesional Day 29(n=5,0) Change | -0.33 (± 0.574) | 0 (± 0) | | |
| CD3 Epidermis lesional Day 85(n=10,7) | 0.46 (± 0.558) | 0.47 (± 0.499) | | |
| CD3 Epidermis lesional Day 85(n=10,6) Change | 0.07 (± 0.672) | -0.09 (± 0.873) | | |
| CD3 Epidermis lesional Day 140(n=7,5) | 0.84 (± 0.983) | 0.94 (± 0.969) | | |
| CD3 Epidermis lesional Day 140(n=7,4) Change | 0.27 (± 0.843) | 0.98 (± 0.642) | | |
| CD3 Dermis non lesional Baseline(n=19,10) | 9.97 (± 4.924) | 12.46 (± 7.954) | | |
| CD3 Dermis non lesional Day 8(n=19,10) | 10.81 (± 5.359) | 8.66 (± 4.495) | | |
| CD3 Dermis non lesional Day 8(n=18,10) Change | 0.72 (± 6.503) | -3.8 (± 5.984) | | |
| CD3 Dermis non lesional Day 29(n=4,0) | 6.87 (± 1.427) | 0 (± 0) | | |
| CD3 Dermis non lesional Day 29(n=4,0) Change | -1.78 (± 3.096) | 0 (± 0) | | |
| CD3 Dermis non lesional Day 85(n=18,8) | 12.71 (± 9.845) | 11.46 (± 7.9) | | |
| CD3 Dermis non lesional Day 85(n=18,8) Change | 2.61 (± 8.287) | -2.09 (± 5.865) | | |
| CD3 Dermis non lesional Day 140(n=17,7) | 11.8 (± 6.96) | 7.22 (± 5.823) | | |

| | | | | |
|---|-----------------|------------------|--|--|
| CD3 Dermis non lesional Day 140(n=16,7) Change | 1.03 (± 5.717) | -6.15 (± 10.618) | | |
| CD3 Dermis lesional Baseline(n=19,8) | 12.75 (± 6.934) | 11.94 (± 6.245) | | |
| CD3 Dermis lesional Day 8 (n=11,10) | 14.93 (± 8.543) | 12.56 (± 8.894) | | |
| CD3 Dermis lesional Day 8 (n=11,10) Change | 2.07 (± 6.576) | 1.58 (± 7.177) | | |
| CD3 Dermis lesional Day 29 (n=5,0) | 13.08 (± 7.275) | 0 (± 0) | | |
| CD3 Dermis lesional day 29 (n=5,0) Change | 0.78 (± 10.054) | 0 (± 0) | | |
| CD3 Dermis lesional Day 85 (n=10,7) | 11.01 (± 3.615) | 14.44 (± 13.122) | | |
| CD3 Dermis lesional Day 85 (n=10,6) Change | 0.46 (± 5.775) | 2.24 (± 13.351) | | |
| CD3 Dermis lesional Day 140 (n=7,5) | 12.42 (± 7.6) | 14.58 (± 19.403) | | |
| CD3 Dermis lesional Day 140(n=7,4) Change | 0.93 (± 10.179) | 6.33 (± 20.884) | | |
| CD4 Epidermis non lesional Baseline (n=19,10) | 0.99 (± 1.4) | 1.07 (± 1.018) | | |
| CD4 Epidermis non lesional Day 8 (n=19,10) | 1.2 (± 1.428) | 1.46 (± 1.639) | | |
| CD4 Epidermis non lesional Day 8 (n=18,10) Change | 0.33 (± 1.287) | 0.39 (± 1.826) | | |
| CD4 Epidermis non lesional Day 29 (n=4,0) | 1.43 (± 1.144) | 0 (± 0) | | |
| CD4 Epidermis non lesional Day 29 (n=4,0) change | -0.13 (± 0.922) | 0 (± 0) | | |
| CD4 Epidermis non lesional Day 85(n=18,8) | 0.69 (± 1.528) | 0.44 (± 0.36) | | |
| CD4 Epidermis non lesional Day 85(n=18,8) Change | -0.31 (± 2.239) | -0.49 (± 0.797) | | |
| CD4 Epidermis non lesional Day 140(n=17,7) | 0.81 (± 0.742) | 0.76 (± 1.355) | | |
| CD4 Epidermis non lesional Day 140(n=16,7) Change | -0.07 (± 1.283) | -0.04 (± 1.802) | | |
| CD4 Epidermis lesional Baseline(n=19,8) | 0.95 (± 1.066) | 0.91 (± 1.204) | | |
| CD4 Epidermis lesional Day 8(n=11,10) | 0.63 (± 0.725) | 0.9 (± 0.92) | | |
| CD4 Epidermis lesional Day 8(n=11,8) Change | -0.46 (± 1.193) | -0.04 (± 0.68) | | |
| CD4 Epidermis lesional Day 29(n=5,0) | 1.52 (± 1.927) | 0 (± 0) | | |
| CD4 Epidermis lesional Day 29(n=5,0) Change | 0.12 (± 1.726) | 0 (± 0) | | |
| CD4 Epidermis lesional Day 85(n=10,7) | 0.68 (± 0.691) | 0.47 (± 0.432) | | |
| CD4 Epidermis lesional Day 85(n=10,6) Change | -0.2 (± 0.847) | -0.78 (± 1.3489) | | |
| CD4 Epidermis lesional Day 140(n=6,5) | 0.03 (± 0.082) | 0.84 (± 0.518) | | |
| CD4 Epidermis lesional Day 140(n=6,4) Change | -0.61 (± 1.281) | -0.73 (± 1.473) | | |
| CD4 Dermis non lesional Baseline(n=19,10) | 16.81 (± 6.868) | 19.39 (± 13.966) | | |
| CD4 Dermis non lesional Day 8(n=19,10) | 17.8 (± 8.144) | 16.04 (± 10.59) | | |
| CD4 Dermis non lesional Day 8(n=18,10) Change | 1.21 (± 9.816) | -3.35 (± 10.063) | | |
| CD4 Dermis non lesional Day 29(n=4,0) | 15.58 (± 5.07) | 0 (± 0) | | |
| CD4 Dermis non lesional Day 29(n=4,0) Change | -0.88 (± 1.928) | 0 (± 0) | | |

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| CD4 Dermis non lesional Day 85(n=18,8) Change | 19.33 (± 7.741) | 19.21 (± 10.316) | | |
| CD4 Dermis non lesional Day 85(n=17,8) Change | 1.94 (± 10.126) | -2.32 (± 9.451) | | |
| CD4 Dermis non lesional Day 140(n=17,7) | 21.14 (± 11.3) | 16.9 (± 10.151) | | |
| CD4 Dermis non lesional Day 140(n=16,7) Change | 3.36 (± 11.994) | -2.01 (± 13.6) | | |
| CD4 Dermis lesional baseline(n=19,8) | 14.28 (± 5.351) | 18.98 (± 9.361) | | |
| CD4 Dermis lesional Day 8(n=11,10) | 17.84 (± 10.403) | 17.74 (± 9.23) | | |
| CD4 Dermis lesional Day 8(n=11,8) Change | 2.86 (± 7.576) | 0.1 (± 10.085) | | |
| CD4 Dermis lesional Day 29(n=5,0) | 17.12 (± 8.146) | 0 (± 0) | | |
| CD4 Dermis lesional Day 29(n=5,0) Change | 3.2 (± 4.25) | 0 (± 0) | | |
| CD4 Dermis lesional Day 85(n=10,7) | 17.2 (± 6.815) | 19.8 (± 12.617) | | |
| CD4 Dermis lesional Day 85(n=10,6) Change | 3.41 (± 7.859) | 0.98 (± 10.706) | | |
| CD4 Dermis lesional Day 140(n=6,5) | 12.81 (± 10.305) | 19.8 (± 12.617) | | |
| CD4 Dermis lesional Day 140(n=6,4) Change | 2.58 (± 11.073) | -0.15 (± 11.3) | | |
| CD8 Epidermis non lesional Baseline(n=19,10) | 0.2 (± 0.306) | 0.24 (± 0.42) | | |
| CD8 Epidermis non lesional Day 8(n=19,10) | 0.4 (± 0.593) | 0.2 (± 0.34) | | |
| CD8 Epidermis non lesional Day 8(n=18,10) Change | 0.24 (± 0.55) | -0.04 (± 0.532) | | |
| CD8 Epidermis non lesional Day 29(n=4,0) | 0.39 (± 0.347) | 0 (± 0) | | |
| CD8 Epidermis non lesional Day 29(n=4,0) Change | -0.21 (± 0.448) | 0 (± 0) | | |
| CD8 Epidermis non lesional Day 85(n=18,8) | 0.22 (± 0.361) | 0.15 (± 0.207) | | |
| CD8 Epidermis non lesional Day 85(n=17,8) Change | 0 (± 0.473) | -0.13 (± 0.354) | | |
| CD8 Epidermis non lesional Day 140(n=17,7) | 0.16 (± 0.215) | 0.28 (± 0.351) | | |
| CD8 Epidermis non lesional Day 140(n=16,7) Change | -0.04 (± 0.344) | -0.01 (± 0.566) | | |
| CD8 Epidermis lesional Baseline(n=19,8) | 0.34 (± 0.644) | 0.14 (± 0.207) | | |
| CD8 Epidermis lesional Day 8(n=11,10) | 0.43 (± 0.568) | 0.08 (± 0.14) | | |
| CD8 Epidermis lesional Day 8(n=11,8) Change | 0.3 (± 0.534) | -0.11 (± 0.236) | | |
| CD8 Epidermis lesional Day 29(n=5,0) | 0.2 (± 0.346) | 0 (± 0) | | |
| CD8 Epidermis lesional Day 29(n=5,0) Change | 0.08 (± 0.363) | 0 (± 0) | | |
| CD8 Epidermis lesional Day 85(n=10,7) | 0.14 (± 0.313) | 0.03 (± 0.076) | | |
| CD8 Epidermis lesional Day 85(n=10,6) Change | -0.01 (± 0.356) | -0.15 (± 0.235) | | |
| CD8 Epidermis lesional Day 140(n=6,5) | 0.03 (± 0.082) | 0.33 (± 0.239) | | |
| CD8 Epidermis lesional Day 140(n=6,4) Change | -0.53 (± 1.129) | 0.18 (± 0.304) | | |
| CD8 Dermis non lesional Baseline(n=19,10) | 5.74 (± 3.278) | 6.59 (± 3.826) | | |

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| CD8 Dermis non lesional Day 8(n=19,10) | 7.1 (± 5.02) | 5.5 (± 3.779) | | |
| CD8 Dermis non lesional Day 8 (n=18,10) Change | 1.19 (± 4.798) | -1.09 (± 1.374) | | |
| CD8 Dermis non lesional Day 29(n=4,0) | 8.45 (± 5.369) | 0 (± 0) | | |
| CD8 Dermis non lesional Day 29(n=4,0) Change | 1.8 (± 1.849) | 0 (± 0) | | |
| CD8 Dermis non lesional Day 85 (n=18,8) Change | 5.51 (± 3.725) | 7.62 (± 4.288) | | |
| CD8 Dermis non lesional Day 85 (n=17,8) Change | -0.46 (± 2.757) | 0.35 (± 3.067) | | |
| CD8 Dermis non lesional Day 140(n=17,7) Change | 4.3 (± 2.357) | 5.09 (± 3.523) | | |
| CD8 Dermis non lesional Day 140(n=16,7) Change | -1.74 (± 2.726) | -2.65 (± 1.686) | | |
| CD8 Dermis lesional Baseline(n=19,8) | 5.67 (± 2.983) | 4.63 (± 2.448) | | |
| CD8 Dermis non lesional Day 8(n=11,10) | 7.55 (± 4.953) | 6.12 (± 3.847) | | |
| CD8 Dermis non lesional Day 8(n=11,8) Change | 1.02 (± 5.174) | 0.88 (± 2.679) | | |
| CD8 Dermis non lesional Day 29(n=5,0) | 10.14 (± 6.133) | 0 (± 0) | | |
| CD8 Dermis non lesional Day 29(n=5,0) Change | 2.48 (± 5.639) | 0 (± 0) | | |
| CD8 Dermis non lesional Day 85(n=10,7) | 7.19 (± 3.022) | 6.7 (± 6.69) | | |
| CD8 Dermis non lesional Day 85(n=10,6) Change | 0.98 (± 3.556) | 1.48 (± 6.628) | | |
| CD8 Dermis non lesional Day 140(n=6,5) | 7.73 (± 6.774) | 6.37 (± 10.549) | | |
| CD8 Dermis non lesional Day 140(n=6,4) | 1.87 (± 7.44) | 3.57 (± 10.671) | | |
| CD117 Epidermis non lesional Baseline (n=19,10) | 9.47 (± 5.07) | 10.99 (± 4.498) | | |
| CD117 Epidermis non lesional Day 8 (n=19,10) | 10.29 (± 4.555) | 9.68 (± 3.057) | | |
| CD117 Epidermis non lesional Day 8 (n=18,10) Chge | 0.99 (± 5.511) | -1.31 (± 2.493) | | |
| CD117 Epidermis non lesional Day 29 (n=4,0) | 12 (± 4.578) | 0 (± 0) | | |
| CD117 Epidermis non lesional Day 29 (n=4,0) Chge | 1.05 (± 2.996) | 0 (± 0) | | |
| CD117 Epidermis non lesional Day 85 (n=18,8) | 8.75 (± 4.492) | 9.17 (± 2.55) | | |
| CD117 Epidermis non lesional Day 85 (n=17,8) Chge | -1.62 (± 5.338) | -1.02 (± 4.166) | | |
| CD117 Epidermis non lesional Day 140 (n=17,7) | 9.89 (± 3.427) | 8.01 (± 2.744) | | |
| CD117 Epidermis non lesional Day 140 (n=16,7) Chge | 0.023 (± 3.866) | -2.43 (± 2.234) | | |
| CD117 Epidermis lesional baseline(n=19,8) | 7.64 (± 3.71) | 10.18 (± 3.804) | | |
| CD117 Epidermis lesional Day 8(n=11,10) | 11.25 (± 5.742) | 10.84 (± 3.865) | | |
| CD117 Epidermis lesional Day 8(n=11,8) Change | 2.58 (± 4.315) | 1.42 (± 5.978) | | |
| CD117 Epidermis lesional Day 29(n=5,0) | 14.06 (± 4.272) | 0 (± 0) | | |
| CD117 Epidermis lesional Day 29(n=5,0) Change | 3.74 (± 4.844) | 0 (± 0) | | |
| CD117 Epidermis lesional Day 85(n=10,7) | 10.68 (± 6.16) | 8.77 (± 2.606) | | |

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| CD117 Epidermis lesional Day 85(n=10,6) Change | 2.1 (± 5.703) | -0.97 (± 3.885) | | |
| CD117 Epidermis lesional Day 140(n=6,5) | 9.88 (± 4.399) | 8.66 (± 2.136) | | |
| CD117 Epidermis lesional Day 140(n=6,4) Change | 2.41 (± 3.792) | -0.98 (± 3.444) | | |
| CD117 Dermis non lesional Baseline (n=19,10) | 10.59 (± 6.616) | 10.11 (± 2.91) | | |
| CD117 Dermis non lesional Day 8 (n=19,10) | 12 (± 6.37) | 9.2 (± 3.319) | | |
| CD117 Dermis non lesional Day 8 (n=18,10) Change | 1.49 (± 5.924) | -0.91 (± 3.078) | | |
| CD117 Dermis non lesional Day 29 (n=4,0) | 10.08 (± 2.062) | 0 (± 0) | | |
| CD117 Dermis non lesional Day 29 (n=4,0) Change | -0.47 (± 2.968) | 0 (± 0) | | |
| CD117 Dermis non lesional Day 85 (n=18,8) | 10.93 (± 6.046) | 11.18 (± 4.568) | | |
| CD117 Dermis non lesional Day 85 (n=17,8) Change | -0.01 (± 5.75) | 0.52 (± 3.239) | | |
| CD117 Dermis non lesional Day 140(n=17,7) | 12.05 (± 4.212) | 7.22 (± 2.1) | | |
| CD117 Dermis non lesional Day 140 (n=16,7) Change | 0.69 (± 5.439) | -3.79 (± 2.284) | | |
| CD117 Dermis lesional Baseline(n=19,8) | 9 (± 4.57) | 7.31 (± 2.468) | | |
| CD117 Dermis lesional Day 8(n=11,10) | 10.15 (± 6.629) | 8.08 (± 2.743) | | |
| CD117 Dermis lesional Day 8(n=11,8) Change | 0.6 (± 4.374) | 1.26 (± 2.89) | | |
| CD117 Dermis lesional Day 29(n=5,0) | 12.42 (± 5.175) | 0 (± 0) | | |
| CD117 Dermis lesional Day 29(n=5,0) Change | 5.39 (± 5.412) | 0 (± 0) | | |
| CD117 Dermis lesional Day 85(n=10,7) | 11.07 (± 6.023) | 9.51 (± 2.891) | | |
| CD117 Dermis lesional Day 85(n=10,6) Change | 2.11 (± 5.917) | 3.03 (± 2.659) | | |
| CD117 Dermis lesional Day 140(n=6,5) | 10.92 (± 6.704) | 8.87 (± 4.017) | | |
| CD117 Dermis lesional Day 140(n=6,4) Change | 5.12 (± 6.41) | 2.88 (± 4.907) | | |
| Giemsa Epidermis non lesional Baseline (n=19,10) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 8 (n=19,10) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 8 (n=18,10) Chge | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 29 (n=4,0) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 29 (n=4,0) Chge | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 85 (n=18,8) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 85 (n=17,8) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 140(n=18,8) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis non lesional Day 140(n=17,8) Chge | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis lesional Baseline (n=19,8) | 0 (± 0) | 0.03 (± 0.071) | | |

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| Giemsa Epidermis lesional Day 8 (n=11,10) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis lesional Day 8 (n=11,8) Chge | 0 (± 0) | -0.03 (± 0.071) | | |
| Giemsa Epidermis lesional Day 29(n=5,0) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis lesional Day 29(n=5,0) Chge | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis lesional Day 85 (n=10,6) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Epidermis lesional Day 85 (n=10,5) Chge | 0 (± 0) | -0.04 (± 0.089) | | |
| Giemsa Epidermis lesional Day 140(n=6,5) | 0 (± 0) | 1 (± 2.236) | | |
| Giemsa Epidermis lesional Day 140(n=6,4) Chge | 0 (± 0) | 1.25 (± 2.5) | | |
| Giemsa Dermis non lesional Baseline (n=19,10) | 6.91 (± 4.751) | 6.8 (± 8.61) | | |
| Giemsa Dermis non lesional Day 8 (n=19,10) | 5.51 (± 4.142) | 4.47 (± 4.529) | | |
| Giemsa Dermis non lesional Day 8 (n=18,10) Chge | -1.33 (± 5.141) | -2.33 (± 4.75) | | |
| Giemsa Dermis non lesional Day 29 (n=4,0) | 3.88 (± 1.876) | 0 (± 0) | | |
| Giemsa Dermis non lesional Day 29 (n=4,0) Chge | -1.62 (± 1.811) | 0 (± 0) | | |
| Giemsa Dermis non lesional Day 85 (n=18,8) | 4.75 (± 3.397) | 5.28 (± 4.906) | | |
| Giemsa Dermis non lesional Day 85 (n=17,8) Chge | -2.34 (± 3.618) | -2.16 (± 6.705) | | |
| Giemsa Dermis non lesional Day 140 (n=18,10) | 6.69 (± 5.409) | 3.12 (± 3.12) | | |
| Giemsa Dermis non lesional Day 140 (n=18,10) Chge | -1.35 (± 5.078) | -4.86 (± 7.348) | | |
| Giemsa Dermis lesional Baseline(n=19,8) | 8.29 (± 5.189) | 4.79 (± 5.931) | | |
| Giemsa Dermis lesional Day 8(n=11,10) | 6.71 (± 4.309) | 4.8 (± 4.512) | | |
| Giemsa Dermis lesional Day 8(n=11,8) Chge | -1.75 (± 6.143) | 0.18 (± 3.394) | | |
| Giemsa Dermis lesional Day 29(n=5,0) | 8.09 (± 11.851) | 0 (± 0) | | |
| Giemsa Dermis lesional Day 29(n=5,0) Chge | 2.57 (± 12.812) | 0 (± 0) | | |
| Giemsa Dermis lesional Day 85(n=10,6) | 5.96 (± 2.589) | 10.3 (± 15.647) | | |
| Giemsa Dermis lesional Day 85 (n=10,5) Chge | -1.56 (± 7.155) | 6.36 (± 9.563) | | |
| Giemsa Dermis lesional Day 140(n=6,5) | 7.57 (± 2.589) | 9.44 (± 10.468) | | |
| Giemsa Dermis lesional Day 140 (n=6,4) Chge | -1.2 (± 7.929) | 4.5 (± 5.073) | | |
| H&E Epidermis non lesional Baseline(n=19,10) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional day 8(n=19,10) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional Day 8(n=18,10) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional Day 29(n=4,0) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional Day 29(n=4,0) Chge | 0 (± 0) | 0 (± 0) | | |

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| H&E Epidermis non lesional Day 85(n=17,8) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional Day 85(n=16,8) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional Day 140 (n=17,7) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis non lesional Day 140 (n=16,7) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Baseline(n=19,8) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 8(n=11,10) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 8(n=11,8) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 29(n=5,0) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 29(n=5,0) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 85(n=10,6) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 85(n=10,5) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 140(n=6,5) | 0 (± 0) | 0 (± 0) | | |
| H&E Epidermis lesional Day 140(n=6,4) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis non lesional Baseline(n=19,10) | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis non lesional Day 8(n=19,10) | 0.01 (± 0.046) | 0.02 (± 0.063) | | |
| H&E Dermis non lesional Day 8(n=18,10) Chge | 0.01 (± 0.047) | 0.02 (± 0.063) | | |
| H&E Dermis non lesional Day 29(n=4,0) | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis non lesional Day 29(n=4,0) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis non lesional Day 85(n=17,8) | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis non lesional Day 85(n=16,8) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis non lesional Day 140(n=17,7) | 0 (± 0) | 0.03 (± 0.076) | | |
| H&E Dermis non lesional Day 140(n=16,7) Chge | 0 (± 0) | 0.03 (± 0.076) | | |
| H&E Dermis lesional Baseline(n=19,8) | 0.02 (± 0.071) | 0.03 (± 0.071) | | |
| H&E Dermis lesional Day 8(n=11,10) | 0.05 (± 0.129) | 0 (± 0) | | |
| H&E Dermis lesional Day 8(n=11,8) Chge | 0.03 (± 0.159) | -0.03 (± 0.071) | | |
| H&E Dermis lesional Day 29(n=5,0) | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis lesional Day 29(n=5,0) Chge | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis lesional Day 85(n=10,6) | 0 (± 0) | 0.03 (± 0.082) | | |
| H&E Dermis lesional Day 85(n=10,5) Chge | 0 (± 0) | 0.04 (± 0.089) | | |
| H&E Dermis lesional Day 140(n=6,5) | 0 (± 0) | 0 (± 0) | | |
| H&E Dermis lesional Day 140(n=6,4) Chge | 0 (± 0) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Baseline (n=19,10) | 0 (± 0) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day 8 (n=19,10) | 0.02 (± 0.092) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day 8(n=18,10) Chg | 0.02 (± 0.094) | 0 (± 0) | | |

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| Tryptase Epidermis non lesional Day 29 (n=4,0) | 0 (± 0) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day 29 (n=4,0) Chg | 0 (± 0) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day 85 (n=18,8) | 0.03 (± 0.103) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day 85(n=17,8) Chg | 0.04 (± 0.1) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day 140 (n=17,7) | 0.02 (± 0.097) | 0 (± 0) | | |
| Tryptase Epidermis non lesional Day140(n=16,7) Chg | 0.03 (± 0.1) | 0 (± 0) | | |
| Tryptase Epidermis lesional Baseline (n=19,8) | 0.01 (± 0.046) | 0.08 (± 0.149) | | |
| Tryptase Epidermis lesional day 8 (n=11,10) | 0.33 (± 1.085) | 0.1 (± 0.316) | | |
| Tryptase Epidermis lesional Day 8 (n=11,8) Chg | 0.31 (± 1.093) | 0.05 (± 0.334) | | |
| Tryptase Epidermis lesional Day 29 (n=5,0) | 0.12 (± 0.268) | 0 (± 0) | | |
| Tryptase Epidermis lesional Day 29 (n=5,0) Chg | 0.08 (± 0.179) | 0 (± 0) | | |
| Tryptase Epidermis lesional Day 85(n=10,7) | 0 (± 0) | 0 (± 0) | | |
| Tryptase Epidermis lesional Day 85(n=10,6) Chg | -0.02 (± 0.063) | -0.1 (± 0.167) | | |
| Tryptase Epidermis lesional Day 140 (n=7,5) | 0 (± 0) | 0 (± 0) | | |
| Tryptase Epidermis lesional Day 140 (n=7,4) Chg | -0.03 (± 0.076) | -0.1 (± 0.2) | | |
| Tryptase Dermis non lesional Baseline (n=19,10) | 6.55 (± 3.988) | 7.2 (± 3.045) | | |
| Tryptase Dermis non lesional Day 8 (n=19,10) | 7.14 (± 4.479) | 8.37 (± 2.305) | | |
| Tryptase Dermis non lesional Day 8 (n=18,10) Chg | 1.14 (± 2.989) | 1.17 (± 3.03) | | |
| Tryptase Dermis non lesional Day 29 (n=4,0) | 8.22 (± 4.981) | 0 (± 0) | | |
| Tryptase Dermis non lesional Day 29 (n=4,0) Chg | 0.67 (± 4.816) | 0 (± 0) | | |
| Tryptase Dermis non lesional Day 85 (n=18,8) | 7.66 (± 4.076) | 8.33 (± 3.547) | | |
| Tryptase Dermis non lesional Day 85 (n=17,8) Chg | 0.54 (± 3.753) | 1.35 (± 3.839) | | |
| Tryptase Dermis non lesional Day 140 (n=17,7) | 7.77 (± 4.296) | 6.95 (± 1.812) | | |
| Tryptase Dermis non lesional Day 140 (n=16,7) Chg | 1.27 (± 3.599) | -0.62 (± 3.002) | | |
| Tryptase Dermis lesional Baseline (n=19,8) | 6.08 (± 3.764) | 6.41 (± 2.658) | | |
| Tryptase Dermis lesional Day 8 (n=11,10) | 7.19 (± 3.618) | 6.99 (± 3.451) | | |
| Tryptase Dermis lesional Day 8 (n=11,8) Chg | 0.71 (± 2.809) | 0.88 (± 2.998) | | |
| Tryptase Dermis lesional Day 29(n=5,0) | 10.2 (± 4.658) | 0 (± 0) | | |
| Tryptase Dermis lesional Day 29(n=5,0) Chg | 3.8 (± 3.023) | 0 (± 0) | | |
| Tryptase Dermis lesional Day 85(n=10,7) | 6.76 (± 3.082) | 6.93 (± 3.135) | | |
| Tryptase Dermis lesional Day 85(n=10,6) Chg | 0.39 (± 4.141) | 1.67 (± 2.047) | | |

| | | | | |
|---|----------------|----------------|--|--|
| Tryptase Dermis lesional Day 140(n=7,5) | 6.59 (± 6.335) | 6.79 (± 1.635) | | |
| Tryptase Dermis lesional Day 140(n=7,4) Chg | 2.68 (± 6.641) | 1.97 (± 2.049) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Observed values from baseline through end of study of serum chemkines or histamine in peripheral blood cells by parameter, treatment and visit

| | |
|-----------------|--|
| End point title | Observed values from baseline through end of study of serum chemkines or histamine in peripheral blood cells by parameter, treatment and visit |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: ug/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Chemokine CCR3 Baseline (n=19,10) | 2.9669 (± 2.31825) | 3.0394 (± 2.38102) | | |
| Chemokine CCR3 Day 2 (n=20, 10) | 2.819 (± 2.94786) | 3.3035 (± 3.52023) | | |
| Chemokine CCR3 Day 8 (n=20,10) | 2.5597 (± 2.22009) | 2.2742 (± 1.58648) | | |
| Chemokine CCR3 Day 15 (n=19,8) | 2.2711 (± 1.98781) | 2.0216 (± 1.46346) | | |
| Chemokine CCR3 Day 29 (n=20,9) | 2.5869 (± 2.31661) | 2.2826 (± 1.56237) | | |
| Chemokine CCR3 Day 85 (n=17,8) | 2.5178 (± 1.93931) | 1.8724 (± 1.16171) | | |
| Chemokine CCR3 Day 140 (n=18,10) | 2.022 (± 2.44218) | 2.406 (± 1.85351) | | |
| Chemokine CXCR3/IP-10 Baseline (n=19,10) | 0.102 (± 0.07807) | 0.0638 (± 0.07208) | | |
| Chemokine CXCR3/IP-10 Day 2 (n=20,9) | 0.0836 (± 0.0663) | 0.0621 (± 0.06496) | | |
| Chemokine CXCR3/IP-10 Day 8 (n=19,8) | 0.091 (± 0.07704) | 0.0772 (± 0.0599) | | |
| Chemokine CXCR3/IP-10 Day 15 (n=19,7) | 0.0883 (± 0.06303) | 0.0546 (± 0.0255) | | |
| Chemokine CXCR3/IP-10 Day 29 (n=20,9) | 0.0881 (± 0.07624) | 0.0601 (± 0.04219) | | |
| Chemokine CXCR3/IP-10 Day 85 (n=17,8) | 0.0714 (± 0.03079) | 0.043 (± 0.0291) | | |

| | | | | |
|--|--------------------|--------------------|--|--|
| Chemokine CXCR3/IP-10 Day 140 (n=18,9) | 0.0864 (± 0.07319) | 0.0859 (± 0.07489) | | |
| Histamine Baseline (n=19,10) | 5.0526 (± 2.06757) | 5.2 (± 1.13529) | | |
| Histamine Day 2 (n=20,10) | 4.15 (± 1.6111) | 5 (± 1.76383) | | |
| Histamine Day 8 (n=20,10) | 4.5 (± 2.01311) | 5.4 (± 2.01108) | | |
| Histamine Day 15 (n=19,8) | 4.5789 (± 1.6437) | 4.75 (± 1.83225) | | |
| Histamine Day 29 (n=20,9) | 5.15 (± 2.20705) | 4.7778 (± 3.38296) | | |
| Histamine Day 85 (n=17,8) | 5.8235 (± 1.50977) | 5 (± 1.30931) | | |
| Histamine Day 140 (n=18,10) | 4.8333 (± 2.64019) | 5.7 (± 1.76698) | | |
| Chemokine ICAM-1 Baseline (n=19,10) | 0.4858 (± 0.09955) | 0.5191 (± 0.14846) | | |
| Chemokine ICAM-1 Day 2 (n=20,10) | 0.4468 (± 0.07872) | 0.4975 (± 0.14406) | | |
| Chemokine ICAM-1 Day 8 (n=20,10) | 0.4967 (± 0.12551) | 0.4728 (± 0.15713) | | |
| Chemokine ICAM-1 Day 15 (n=19,8) | 0.4788 (± 0.12577) | 0.4709 (± 0.11789) | | |
| Chemokine ICAM-1 Day 29 (n=20,9) | 0.4633 (± 0.10172) | 0.4704 (± 0.11356) | | |
| Chemokine ICAM-1 Day 85 (n= 17,8) | 0.4314 (± 0.10424) | 0.4037 (± 0.05599) | | |
| Chemokine ICAM-1 Day 140 (n=15,10) | 0.4314 (± 0.10921) | 0.4918 (± 0.1525) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Observed values and change from baseline in peripheral blood cell subsets (FACS parameters) at Week 12 (Day 85) by treatment (PD analysis set) measured as % out of leukocytes.

| | |
|-----------------|---|
| End point title | Observed values and change from baseline in peripheral blood cell subsets (FACS parameters) at Week 12 (Day 85) by treatment (PD analysis set) measured as % out of leukocytes. |
|-----------------|---|

End point description:

Fluorescence-activated cell sorting (FACS) is a specialized type of flow cytometry that provides a method for sorting a heterogeneous mixture of biological cells into two or more containers, one cell at a time, based upon the specific light scattering and fluorescent characteristics of each cell. (FACS) provides fast, objective and quantitative recording of fluorescent signals from individual cells as well as physical separation of cells of particular interest. A wide range of fluorophores can be used as labels in flow cytometry. Fluorophores are typically attached to an antibody that recognizes a target feature on or in the cell; they may also be attached to a chemical entity with affinity for the cell membrane or another cellular structure. Each fluorophore has a characteristic peak excitation and emission wavelength.

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: % out of leukocytes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Basophils D1 (n=19,10) Units | 0.23 (± 0.132) | 0.36 (± 0.482) | | |
| Basophils D85 (n=7,5) Units | 0.47 (± 0.215) | 0.4 (± 0.451) | | |
| Basophils chge (n=7,5) Units | 0.22 (± 0.268) | -0.06 (± 0.176) | | |
| CD19+ B cells bound IgE D1 (n=8,8) | 4.53 (± 5.001) | 15.19 (± 22.609) | | |
| CD19+ B cells bound IgE D85(n=5,7) | 7.32 (± 7.579) | 25.66 (± 26.485) | | |
| CD19+ B cells bound IgE chge (n=5,7) | 1.46 (± 3.545) | 12.53 (± 21.725) | | |
| CD19+ B cells D1 (n=10,9) | 3.57 (± 2.298) | 2.5 (± 1.247) | | |
| CD19+ B cells D85 (n=7,7) | 3.84 (± 1.595) | 3.25 (± 2.007) | | |
| CD19+ B cells Chge (n=7,7) | 0.31 (± 1.377) | 0.73 (± 0.805) | | |
| Dendritic cells D1 (n=10,7) | 0.37 (± 0.196) | 0.24 (± 0.14) | | |
| Dendritic cells D85 (n=8,5) | 0.37 (± 0.231) | 0.27 (± 0.21) | | |
| Dendritic cells Chge (n=7,5) | 0.02 (± 0.272) | -0.02 (± 0.182) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Observed values and change from baseline in peripheral blood cell subsets (FACS parameters) at Week 12 (Day 85) by treatment (PD analysis set) measured in fluorescence units.

| | |
|-----------------|--|
| End point title | Observed values and change from baseline in peripheral blood cell subsets (FACS parameters) at Week 12 (Day 85) by treatment (PD analysis set) measured in fluorescence units. |
|-----------------|--|

End point description:

Fluorescence-activated cell sorting (FACS) is a specialized type of flow cytometry that provides a method for sorting a heterogeneous mixture of biological cells into two or more containers, one cell at a time, based upon the specific light scattering and fluorescent characteristics of each cell. (FACS) provides fast, objective and quantitative recording of fluorescent signals from individual cells as well as physical separation of cells of particular interest. A wide range of fluorophores can be used as labels in flow cytometry. Fluorophores are typically attached to an antibody that recognizes a target feature on or in the cell; they may also be attached to a chemical entity with affinity for the cell membrane or another cellular structure. Each fluorophore has a characteristic peak excitation and emission wavelength.

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: Flourescence units | | | | |
| arithmetic mean (standard deviation) | | | | |
| Basophils with FcεR1 exp D1 (n=11,8) | 292391 (± 135848) | 312038 (± 147037) | | |
| Basophils with FcεR1 exp D85 (n=7,5) | 79457 (± 29333) | 291000 (± 108028) | | |
| Basophils with FcεR1 expression Chge (n=6,5) | -243700 (± 118883) | -38260 (± 60085) | | |
| Basophils with bound IgE D 1 (n=11,7) | 149656 (± 112936) | 236071 (± 89043) | | |
| Basophils with bound IgE D85 (n=7,5) | 9554 (± 6214) | 212620 (± 109645) | | |
| Basophils with bound IgE Chge (n=6,5) | -178487 (± 103456) | -12680 (± 59998) | | |
| CD19+ B cells with FcεR2 exp D1 (n=10,9) | 59040 (± 42446) | 59700 (± 27171) | | |
| CD19+ B cells with FcεR2 exp D85 (n=7,7) | 59429 (± 55980) | 49243 (± 33460) | | |
| CD19+ B cells with FcεR2 exp chge (n=7,7) | 12814 (± 32631) | 3986 (± 16779) | | |
| Dendritic cells with FcεR1 expr D1 (n=10,7) | 40880 (± 17191) | 43029 (± 12363) | | |
| Dendritic cells with FcεR1 expr D85 (n=6,5) | 38283 (± 5768) | 36962 (± 18562) | | |
| Dendritic cells with FcεR1 expr Chge (n=5,5) | -10100 (± 16887) | -516 (± 5925) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of baseline PD parameters between healthy volunteers and urticaria patients by skin layer Pharmacodynamic analysis set

| | |
|---|---|
| End point title | Comparison of baseline PD parameters between healthy volunteers and urticaria patients by skin layer Pharmacodynamic analysis set |
| End point description: The # positive cell values are average of cell numbers derived from counting 5 consecutive microscopic fields. Area counted is 5x 0.196 mm ² | |
| End point type | Secondary |
| End point timeframe: Baseline | |

| End point values | Healthy Subjects | Urticaria Patients | | |
|---|----------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 10 | 30 | | |
| Units: # positive cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| CD11c Epidermis (n= 10,29) | 1.16 (± 1.13058) | 1.1241 (± 0.92944) | | |
| CD11c Dermis (n=10,29) | 14.64 (± 9.31083) | 19.6207 (± 9.4226) | | |
| CD11c All skin layers (n=20,58) | 7.9 (± 9.45983) | 10.3724 (± 11.44855) | | |
| CD 3 Epidermis (n=10,29) | 0.16 (± 0.26331) | 0.4759 (± 0.82046) | | |
| Cd 3 Dermis (n=10,29) | 10.16 (± 9.00311) | 10.8276 (± 6.11385) | | |
| CD 3 All Skin Layers (n=20,58) | 5.16 (± 8.04634) | 5.6517 (± 6.77879) | | |
| CD 4 Epidermis (n=10,29) | 1.025 (± 1.75804) | 1.0207 (± 1.26297) | | |
| CD 4 Dermis (n=10,29) | 15.775 (± 10.06565) | 17.7 (± 9.72481) | | |
| CD 4 All Skin Layers (n=20,58) | 8.4 (± 10.33004) | 9.3603 (± 10.86324) | | |
| CD 8 Epidermis (n=10,29) | 0.06 (± 0.13499) | 0.2138 (± 0.34197) | | |
| CD 8 Dermis (n=10,29) | 5.9083 (± 4.07998) | 6.0322 (± 3.43255) | | |
| CD 8 All Skin Layers (n=20,58) | 2.9842 (± 4.11029) | 3.123 (± 3.80226) | | |
| CD 117 Epidermis (n=10,29) | 10.16 (± 3.80386) | 9.9931 (± 4.85502) | | |
| CD 117 Dermis (n=10,29) | 8.22 (± 2.44849) | 10.4241 (± 5.56025) | | |
| CD 117 All Skin Layers (n=20,58) | 9.19 (± 3.26865) | 10.2086 (± 5.17814) | | |
| Fc epsilon receptor I Epidermis (n=10,29) | 4.98 (± 2.02309) | 6.0776 (± 3.12906) | | |
| Fc epsilon receptor I Dermis (n=10,29) | 14.2 (± 6.76133) | 19.45 (± 8.21582) | | |
| Fc epsilon receptor I All Skin Layers (n=20,58) | 9.59 (± 6.77968) | 12.7638 (± 9.13548) | | |
| Giemsa Epidermis (n=10,29) | 0 (± 0) | 0 (± 0) | | |
| Giemsa Dermis (n=10,29) | 4.8 (± 5.62929) | 6.869 (± 6.19228) | | |
| Giemsa All Skin Layers (n=20,58) | 2.4 (± 4.59061) | 3.4345 (± 5.55324) | | |
| Haematoxylin + Eosin Epidermis (n=10,29) | 0 (± 0) | 0 (± 0) | | |
| Haematoxylin + Eosin Dermis (n=10,29) | 0 (± 0) | 0 (± 0) | | |
| Haematoxylin + Eosin All Skin Layers (n=20,58) | 0 (± 0) | 0 (± 0) | | |
| IgE Epidermis (n=10,29) | 0.08 (± 0.13984) | 1.0603 (± 2.30385) | | |
| IgE Dermis (n=10,29) | 8.76 (± 5.92231) | 14.7776 (± 9.84503) | | |
| IgE All Skin layers (n=20,58) | 4.42 (± 6.03739) | 7.919 (± 9.9038) | | |
| IgE + CD 11c Epidermis (n=10,28) | 0 (± 0) | 0.0357 (± 0.12237) | | |

| | | | | |
|--|--------------------|--------------------|--|--|
| IgE + CD 11c Dermis (n=10,29) | 0.915 (± 1.29401) | 1.0115 (± 1.0529) | | |
| IgE+CD 11c All Layers (n=20,57) | 0.4575 (± 1.00672) | 0.5322 (± 0.89651) | | |
| IgE + Tryptase Epidermis (n=10,28) | 0 (± 0) | 0 (± 0) | | |
| IgE + Tryptase Dermis (n=10,29) | 1.3 (± 1.01215) | 0.8713 (± 0.79919) | | |
| IgE + Tryptase All Skin Layers (n=20,57) | 0.65 (± 0.96437) | 0.4433 (± 0.71586) | | |
| Tryptase Epidermis (n=10,29) | 0 (± 0) | 0 (± 0) | | |
| Tryptase Dermis (n=10,29) | 6.64 (± 3.53371) | 6.7741 (± 3.64713) | | |
| Tryptase All Skin Layers (n=20,58) | 3.32 (± 4.18539) | 3.3871 (± 4.26704) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of omalizumab

| | |
|---|----------------------------|
| End point title | Serum levels of omalizumab |
| End point description: Serum concentrations (ng/mL) of omalizumab by visit after the administration of omalizumab 300 mg every 4 weeks | |
| End point type | Secondary |
| End point timeframe: Baseline through Day 85 | |

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 0 ^[1] | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 | 0 (± 0) | () | | |
| Day 2 | 13400 (± 4690) | () | | |
| Day 8 | 30100 (± 7800) | () | | |
| Day 29 | 17000 (± 5500) | () | | |
| Day 57 | 25000 (± 8640) | () | | |
| Day 85 | 28800 (± 11400) | () | | |

Notes:

[1] - There was not a serum level in placebo arm

Statistical analyses

No statistical analyses for this end point

Secondary: Mean (SD) serum total IgE concentration from baseline by visit

| | |
|-------------------------|--|
| End point title | Mean (SD) serum total IgE concentration from baseline by visit |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline through Day 85 | |

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 Mean (n=20,10) | 1037 (± 2474) | 442 (± 580.7) | | |
| Day 2 Mean (20,10) | 1152 (± 2539) | 447 (± 587.5) | | |
| Day 8 Mean (n=20,10) | 1970 (± 2992) | 449 (± 593.1) | | |
| Day 29 Mean (n=20,9) | 2160 (± 2688) | 462 (± 628.7) | | |
| Day 57 Mean (n=19,8) | 2430 (± 3343) | 490 (± 648) | | |
| Day 85 Mean (n=17,8) | 2222 (± 2931) | 475 (± 616.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean (SD) serum total IgE % change from baseline by visit

| | |
|-------------------------|---|
| End point title | Mean (SD) serum total IgE % change from baseline by visit |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline through Day 85 | |

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: Percent | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 2 % Change (n=19,10) | 27.1 (± 20.08) | 0.2 (± 5.13) | | |
| Day 8 % Change (n=19,10) | 174.7 (± 84.93) | -1.5 (± 9.13) | | |

| | | | | |
|--------------------------|------------------|----------------|--|--|
| Day 29 % Change (n=19,9) | 247.2 (± 121.81) | -4 (± 12.17) | | |
| Day 57 % Change (n=18,8) | 247.8 (± 134.1) | -4.4 (± 18.59) | | |
| Day 85 % Change (n=16,8) | 244.8 (± 138.28) | -6.9 (± 24.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean (SD) serum free IgE concentration from baseline by visit

| | |
|-----------------|---|
| End point title | Mean (SD) serum free IgE concentration from baseline by visit |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 Mean (n=20,10) | 1037 (± 2474) | 442 (± 580.69) | | |
| Day 2 Mean (n= 20,9) | 26.8 (± 34.27) | 111.5 (± 60.75) | | |
| Day 8 Mean (n=20,10) | 24.306 (± 29.7698) | 112.169 (± 58.6525) | | |
| Day 29 Mean (n=20,9) | 41.506 (± 40.5322) | 107.881 (± 60.1708) | | |
| Day 57 Mean (n=19,8) | 38.502 (± 39.5567) | 122.318 (± 51.1087) | | |
| Day 85 Mean (n=17,8) | 35.776 (± 41.5426) | 120.978 (± 50.6692) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean (SD) serum free IgE % change from baseline by visit

| | |
|-----------------|--|
| End point title | Mean (SD) serum free IgE % change from baseline by visit |
|-----------------|--|

End point description:

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

End point timeframe:
Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|--------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 2 % Change (n=19,9) | -96.166 (± 2.9216) | -60.475 (± 17.933) | | |
| Day 8 % Change (n=20,10) | -96.446 (± 2.0162) | -60.804 (± 15.8379) | | |
| Day 29 % Change (n=19,9) | -93.363 (± 3.5975) | -61.456 (± 17.234) | | |
| Day 57 % Change (n=18,8) | -94.46 (± 3.0681) | -61.27 (± 18.6447) | | |
| Day 85 % Change (n=16,8) | -94.75 (± 3.42) | -61.906 (± 17.7819) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary statistics of observed values and absolute change from baseline in specific IgE against allergens and bacterial antigens by parameter, treatment and visit

| | |
|--|--|
| End point title | Summary statistics of observed values and absolute change from baseline in specific IgE against allergens and bacterial antigens by parameter, treatment and visit |
| End point description: | |
| End point type | Secondary |
| End point timeframe: Baseline through Day 140 | |

| End point values | IGE025 | Placebo to IGE025 | | |
|---|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 10 | | |
| Units: IU/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Alternaria alternata Baseline (n= 0, 1) | 0 (± 0) | 0.136 (± 0) | | |
| Alternaria alternata Day 140 (n= 0,1) | 0 (± 0) | 0.114 (± 0) | | |
| Artemisia vulgaris (Mugwort) Baseline (n=1,1) | 0.273 (± 0) | 1.48 (± 0) | | |

| | | | | |
|--|-----------------------|----------------------|--|--|
| Artemisia vulgaris (Mugwort) Day 140(n=0,1) | 0 (± 0) | 1.91 (± 0) | | |
| Cat dander Baseline (n=3,1) | 17.9677 (± 22.73833) | 0.698 (± 0) | | |
| Cat dander Day 140 (n=2,1) | 21.01 (± 26.14881) | 0.898 (± 0) | | |
| Common silver Birch Baseline (n=6,3) | 12.364 (± 19.48667) | 12.3767 (± 11.22609) | | |
| Common silver Birch Day 140 (n=4,3) | 4.489 (± 6.15938) | 14.86 (± 16.58164) | | |
| Dog dander Baseline (n=2,1) | 26.772 (± 37.09199) | 0.512 (± 0) | | |
| Dog dander Day 140 (n=1,1) | 50.1 (± 0) | 0.669 (± 0) | | |
| Dermatophagoides farinae Baseline (n=3,1) | 3.3333 (± 3.39883) | 0.434 (± 0) | | |
| Dermatophagoides farinae Day 140 (n=2,1) | 5.32 (± 0.89095) | 0.497 (± 0) | | |
| Dermatophagoides pteronyssinus Baseline (n=5,1) | 2.125 (± 1.46791) | 0.455 (± 0) | | |
| Dermatophagoides pteronyssinus Day 140(n=4,1) | 5.2463 (± 3.72052) | 0.517 (± 0) | | |
| Grey Alder (t2) Baseline (n=4,3) | 15.765 (± 20.03961) | 10.9533 (± 10.92027) | | |
| Grey Alder (t2) Day 140(n=3,3) | 4.49 (± 5.16654) | 13.0533 (± 15.24029) | | |
| German Cockroach Baseline (n=4,2) | 0.8605 (± 0.93609) | 0.4425 (± 0.62579) | | |
| German Cockroach Day 140 (n=4,2) | 3.0263 (± 2.8719) | 0.4705 (± 0.66539) | | |
| Hazelnut Baseline (n=3,3) | 8.9627 (± 14.49722) | 7.3267 (± 8.2816) | | |
| Hazelnut Day 140 (n=2,3) | 1.445 (± 1.50977) | 8.9927 (± 10.59244) | | |
| Olive (black, fresh) Baseline (n=4,1) | 0.089 (± 0.178) | 0 (± 0) | | |
| Olive (black, fresh) Day 140 (n=3,1) | 0.1037 (± 0.17956) | 0 (± 0) | | |
| Platanus acerifolia Baseline (n=1,1) | 0.121 (± 0) | 3.71 (± 0) | | |
| Platanus acerifolia Day 140 (n=0,1) | 0 (± 0) | 4.83 (± 0) | | |
| Parietaria judaica Baseline(n=0,1) | 0 (± 0) | 1.49 (± 0) | | |
| Parietaria judaica Day 140 (n=0,1) | 0 (± 0) | 2 (± 0) | | |
| Staphylococcal enterotoxin A Baseline (n=20,10) | 0.7264 (± 3.07821) | 0.0741 (± 0.1358) | | |
| Staphylococcal enterotoxin A Day 140 (n=18,10) | 1.6161 (± 4.39936) | 0.1077 (± 0.15294) | | |
| Staphylococcal enterotoxin C Baseline (n=20,10) | 0.8976 (± 3.02621) | 0.1626 (± 0.27226) | | |
| Staphylococcal enterotoxin C Day 140 (n=18,10) | 2.1089 (± 4.19834) | 0.1922 (± 0.28071) | | |
| Staphylococcal enterotoxin TSST Baseline (n=20,10) | 0.539 (± 1.02581) | 0.1537 (± 0.23902) | | |
| Staphylococcal enterotoxin TSST Day 140 (n=18,10) | 0.8402 (± 1.05356) | 0.1468 (± 0.22155) | | |
| Alternaria alternara Absolute Change (n = 0,1) | 0 (± 0) | -0.022 (± 0) | | |
| Artemisia vulgaris Absolute Change (n = 0,1) | 0 (± 0) | 0.43 (± 0) | | |
| Cat dander Absolute Change (n = 2,1) | -1.1315 (± 4.33951) | 0.2 (± 0) | | |
| Common Silver Birch Absolute Change (n = 4,3) | -10.2145 (± 26.47094) | 2.4833 (± 5.63479) | | |

| | | | | |
|---|---------------------|---------------------|--|--|
| Dog dander Absolute Change (n = 1,1) | -2.9 (± 0) | 0.157 (± 0) | | |
| Dermatophagoides farinae Absolute Change(n=2,1) | 3.935 (± 1.46371) | 0.063 (± 0) | | |
| Dermatophagoides pteronyssinus Abs Chge (n=4,1) | 3.68 (± 3.05938) | 0.062 (± 0) | | |
| Grey Alder Absolute Change(n=3,3) | -12.63 (± 27.47614) | 2.1 (± 4.509) | | |
| German Cockroach Absolute Change(n=4,2) | 2.1658 (± 2.03436) | 0.028 (± 0.0396) | | |
| Hazelnut Absolute Change(n=2,3) | -11.83 (± 18.1585) | 1.666 (± 2.47183) | | |
| Olive (black, fresh) Absolute Change(n=3,1) | -0.015 (± 0.02598) | 0 (± 0) | | |
| Platanus acerifolia Absolute Change(n=0,1) | 0 (± 0) | 1.12 (± 0) | | |
| Parietaria judaica Absolute Change(n=0,1) | 0 (± 0) | 0.51 (± 0) | | |
| Staphylococcal enterotoxin A Abs chge (n=18,10) | 0.809 (± 2.63582) | 0.0336 (± 0.09116) | | |
| Staphylococcal enterotoxin C Abs chge (n=18,10) | 1.1116 (± 2.26524) | 0.0296 (± 0.06545) | | |
| Staphylococcal enterotoxin TSST Abs chge(n=18,10) | 0.2608 (± 0.72963) | -0.0069 (± 0.15669) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Urticaria activity score (UAS7)

| | |
|--|---|
| End point title | Change from baseline in Urticaria activity score (UAS7) |
| End point description: | |
| Efficacy was assessed by the urticaria activity score (UAS). UAS was completed each morning and evening on a daily basis to record patient symptoms of itch and hives via an electronic diary. The UAS is a composite eDiary-recorded score with numeric severity intensity ratings on a scale of 0–3 (0 = none to 3 = intense/severe) for 1) the number of wheals (hives); and 2) the intensity of the itch. The daily UAS is the average of the morning and evening scores and the UAS7 is the sum of the daily UAS scores over 7 days. UAS7 score: The sum of the daily UAS scores over 7 days. Range: 0-42. If fewer than 7 but at least 4 daily values were non-missing, the remaining values were imputed to be the average. This is equivalent to multiplying the average of the non missing values by 7. UAS7 score: The sum of the daily UAS scores over 7 days. Range: 0-42. A higher score indicates worse disease. A negative change score (Week 12 score minus Baseline score) indicates improvement. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Day 85 | |

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 8 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -23.1 (± 12.94) | -8.1 (± 14.45) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Likert scale-Physician's and Patients in-clinic global assessment by treatment

| | |
|-----------------|--|
| End point title | Likert scale-Physician's and Patients in-clinic global assessment by treatment |
|-----------------|--|

End point description:

The investigator or the person he or she designated and the patient provided scoring of the patient's global assessment of symptoms (urticaria lesions (hives) and pruritus) reflective of the patient's condition over the 12 hours prior to the visit (0 = no symptoms, 1 = mild, 2 = moderate 3 = severe

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

End point timeframe:

Baseline, Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|---------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 8 | | |
| Units: score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Physicians Baseline (n=17,9) | 2 (± 0.87) | 2.2 (± 0.83) | | |
| Physicians Week 12, (day 85) (n=17,8) | 0.8 (± 1.01) | 2 (± 1.31) | | |
| Patients Baseline (n=17,9) | 2.4 (± 0.87) | 2.4 (± 0.53) | | |
| Patients Week 12, (day 85) (n=17,8) | 0.9 (± 1.05) | 1.9 (± 0.99) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of angioedema-free days weeks 4 through 12 by treatment

| | |
|-----------------|--|
| End point title | Percentage of angioedema-free days weeks 4 through 12 by treatment |
|-----------------|--|

End point description:

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

End point timeframe:

Day 29 to Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 8 | | |
| Units: Percentage of days | | | | |
| arithmetic mean (standard deviation) | 90.9 (± 22.83) | 70.5 (± 28.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Dermatology Life Quality Index (DLQI) by treatment

| | |
|-----------------|--|
| End point title | Change from baseline in Dermatology Life Quality Index (DLQI) by treatment |
|-----------------|--|

End point description:

The DLQI is a 10-item dermatology-specific health-related quality of life measure. Patients rated their dermatology symptoms as well as the impact of their skin condition on various aspects of their lives. An overall score was calculated as well as for the following domains: Symptoms and Feelings, Daily Activities, Leisure, Work and School, Personal Relationships, Treatment. Negative score shows positive efficacy. Meaning of DLQI Scores 0-1 = no effect at all on patient's life 2-5 = small effect on patient's life 6-10 = moderate effect on patient's life 11-20 = very large effect on patient's life 21-30 = extremely large effect on patient's life. The DLQI is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. The DLQI can also be expressed as a percentage of the maximum possible score of 30.

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

End point timeframe:

Baseline through Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 8 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | -10.19 (± 8.159) | -3.13 (± 7.18) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Skindex-29 by treatment

| | |
|-----------------|-------------------------|
| End point title | Skindex-29 by treatment |
|-----------------|-------------------------|

End point description:

The Skindex-29 is a validated 29-item instrument to measure the effects of skin disease on patients' quality of life. Results are reported as 3 scale scores (functioning, emotions and symptoms) and a composite score (average scale score). The domain scores and the overall score are expressed on a 100-point scale, with higher scores indicating a lower level of quality of life. The cutoff values for each category are noted below. Symptoms; 39 mild, 42 moderate, 52 severe. Emotions; 24 mild, 35 moderate, 39 severe. Functioning: 21 mild, 32 moderate, 37 severe. Overall Score: 25 mild, 32 moderate, 44 severe.

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

End point timeframe:

Baseline and Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 8 | | |
| Units: Score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 16,9) | 17.98 (± 7.807) | 21.67 (± 9.068) | | |
| Day 85 (n=16,8) | 6.17 (± 7.119) | 22.63 (± 10.276) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Chronic Urticaria Quality of Life Questionnaire (Cu-Q2OL) by treatment

| | |
|-----------------|--|
| End point title | Chronic Urticaria Quality of Life Questionnaire (Cu-Q2OL) by treatment |
|-----------------|--|

End point description:

The Cu-Q2OL is a 23-item CIU-specific health-related quality of life questionnaire. Patients rated their CIU symptoms and the impact of their CIU on various aspects of their lives. An overall score was calculated as well for the following domains: pruritus, swelling, impact on life activities, sleep problems, limits, and looks. Zero is the minimum score and 100 the maximum score. The higher score correlates to more disease activity.

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

End point timeframe:

Baseline and Day 85

| End point values | IGE025 | Placebo to IGE025 | | |
|--------------------------------------|------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 9 | | |
| Units: score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=16,8) | 53.71 (± 19.881) | 59.24 (± 15.35) | | |

| | | | | |
|-----------------|---------------------|---------------------|--|--|
| Day 85 (n=17,8) | 14.51 (± 22.319) | 53.53 (± 29.817) | | |
|-----------------|---------------------|---------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse events are reported in this record from First Patient First Treatment until Last Patient Last Visit

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

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

Reporting group description:

Placebo

| | |
|-----------------------|--------------|
| Reporting group title | IGE025 300mg |
|-----------------------|--------------|

Reporting group description:

IGE025 300mg

| Serious adverse events | Placebo | IGE025 300mg | |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 20 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (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 | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (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 | Placebo | IGE025 300mg | |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 7 / 10 (70.00%) | 17 / 20 (85.00%) | |
| Investigations Fungal test positive subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 20 (0.00%) 0 | |
| Injury, poisoning and procedural complications Fractured coccyx subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |
| Vascular disorders Haematoma subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 1 / 20 (5.00%) 2 | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Tongue pruritus subjects affected / exposed occurrences (all) Toothache | 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 20 (0.00%) 0 | |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 1 / 20 (5.00%) 1 | |
| Pleurisy subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |
| Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 3 / 20 (15.00%) 3 | |
| Alopecia areata subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |
| Musculoskeletal and connective tissue disorders Tenosynovitis subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 20 (0.00%) 0 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 10 (40.00%) 5 | 7 / 20 (35.00%) 9 | |
| Influenza subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 2 | 3 / 20 (15.00%) 5 | |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 20 (5.00%) 1 | |

| | | | |
|-----------------------------|-----------------|----------------|--|
| Periodontitis | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 20 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 17 January 2012 | Amendment 1: This amendment was created to address comments raised by the reviewing Ethics Committee and recommendations by the Health Authority. Changes requested that impacted the protocol included: adding additional risk/benefit text concerning the sampling procedure and local anesthesia risks for the biopsies performed during the trial, including text in the statistical analysis section concerning the healthy volunteer control subjects and removing text related to assenting procedures. The lower weight limit for entry into the study was increased, and sample processing details were also updated based on the requirements of the analyzing laboratories. |
| 06 November 2012 | Amendment 2: This amendment was primarily initiated to align Inclusion criteria #2 (assessment of UAS7 score for the determination of patient eligibility) with the intended patient population. Additional changes being made to the protocol were largely administrative and provided greater clarity on study procedures and address earlier inconsistencies in wording. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported