



Clinical trial results:

A randomised, double blind, placebo-controlled phase I study investigating the safety of ALK HDM tablet in children

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-000402-67 |
| Trial protocol | ES |
| Global end of trial date | 01 April 2008 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 16 February 2016 |
| First version publication date | 26 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------|
| Sponsor protocol code | MT-03 |
|-----------------------|-------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | ALK-Abelló S.A. |
| Sponsor organisation address | Miguel Fleta, 19, Madrid, Spain, E-28037 |
| Public contact | Clinical Development, ALK, +45 45 74 75 76, ClinicalTrials@alk.net |
| Scientific contact | Clinical Development, ALK, +45 45 74 75 76, ClinicalTrials@alk.net |

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 | 01 April 2008 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 April 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 April 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To identify a dose range of the ALK house dust mite tablet (SQ HDM SLIT-tablet) that has a safety profile that will allow once-daily intake (as self-medication) by 5-14 year old children with allergic asthma (with or without rhinitis) due to house dust mites.

Protection of trial subjects:

Dose groups were treated in a staggered manner at intervals of approximately 2 weeks. A safety committee reviewed the initial safety data of the previous dose (-s), and only by their approval did the trial enter the next (higher) level of dose strength.

Background therapy:

Subjects being treated for asthma continued the prescribed asthma medication during the trial.

Evidence for comparator:

Placebo comparator

| | |
|---|-------------------|
| Actual start date of recruitment | 13 September 2007 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 72 |
| Worldwide total number of subjects | 72 |
| EEA total number of subjects | 72 |

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) | 59 |
| Adolescents (12-17 years) | 13 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |

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

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 4 clinical groups in Spain

Pre-assignment

Screening details:

A total of 78 subjects were screened for this trial. Six subjects failed screening.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

The IMPs were produced so that all tablets were identical in appearance, smell and taste. In order to maintain the blinding, subjects within each dose group received the same number of tablets, whether they received tablet containing active ingredient or not.

Dose groups 0.5, 1, 3 and 6 SQ-HDM received one tablet daily and dose groups 9 and 12 SQ-HDM received two tablets daily to obtain a daily-dose.

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 0.5 SQ-HDM |

Arm description:

active treatment

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | SQ HDM SLIT-tablet |
| Investigational medicinal product code | |
| Other name | ALK HDM tablet |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake of the tablet was performed at home (self-medicating).

| | |
|------------------|----------|
| Arm title | 1 SQ-HDM |
|------------------|----------|

Arm description:

active treatment

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | SQ HDM SLIT-tablet |
| Investigational medicinal product code | |
| Other name | ALK HDM tablet |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake of the tablet was performed at home (self-medicating).

| | |
|--|--------------------|
| Arm title | 3 SQ-HDM |
| Arm description: active treatment | |
| Arm type | Experimental |
| Investigational medicinal product name | SQ HDM SLIT-tablet |
| Investigational medicinal product code | |
| Other name | ALK HDM tablet |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake of the tablet was performed at home (self-medicating).

| | |
|--|--------------------|
| Arm title | 6 SQ-HDM |
| Arm description: active treatment | |
| Arm type | Experimental |
| Investigational medicinal product name | SQ HDM SLIT-tablet |
| Investigational medicinal product code | |
| Other name | ALK HDM tablet |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake of the tablet was performed at home (self-medicating).

| | |
|--|--------------------|
| Arm title | 9 SQ-HDM |
| Arm description: active treatment | |
| Arm type | Experimental |
| Investigational medicinal product name | SQ HDM SLIT-tablet |
| Investigational medicinal product code | |
| Other name | ALK HDM tablet |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake

of the tablet was performed at home (self-medicating).

| | |
|--|--------------------|
| Arm title | 12 SQ-HDM |
| Arm description: active treatment | |
| Arm type | Experimental |
| Investigational medicinal product name | SQ HDM SLIT-tablet |
| Investigational medicinal product code | |
| Other name | ALK HDM tablet |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake of the tablet was performed at home (self-medicating).

| | |
|--|-------------------|
| Arm title | Placebo |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sublingual tablet |
| Routes of administration | Sublingual use |

Dosage and administration details:

The tablet (-s) were to be taken out of the blister pack with dry fingers and placed under the tongue (at the same time in the case of two tablets). After 1 minute the saliva was to be swallowed. Subjects were not to eat or drink for 5 minutes after administration of IMP.

Administration was to take place at a time of the day when children were under observation. At days 1, 2, 8, 15 and 22, medication was performed at the trial site. At days 3-7, 9-14, 16-21 and 23-28, intake of the tablet was performed at home (self-medicating).

| Number of subjects in period 1 | 0.5 SQ-HDM | 1 SQ-HDM | 3 SQ-HDM |
|---------------------------------------|------------|----------|----------|
| Started | 9 | 9 | 9 |
| Completed | 9 | 9 | 9 |

| Number of subjects in period 1 | 6 SQ-HDM | 9 SQ-HDM | 12 SQ-HDM |
|---------------------------------------|----------|----------|-----------|
| Started | 9 | 9 | 9 |
| Completed | 9 | 9 | 9 |

| Number of subjects in period 1 | Placebo |
|---------------------------------------|---------|
| Started | 18 |
| Completed | 18 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|------------|
| Reporting group title | 0.5 SQ-HDM |
| Reporting group description: | |
| active treatment | |
| Reporting group title | 1 SQ-HDM |
| Reporting group description: | |
| active treatment | |
| Reporting group title | 3 SQ-HDM |
| Reporting group description: | |
| active treatment | |
| Reporting group title | 6 SQ-HDM |
| Reporting group description: | |
| active treatment | |
| Reporting group title | 9 SQ-HDM |
| Reporting group description: | |
| active treatment | |
| Reporting group title | 12 SQ-HDM |
| Reporting group description: | |
| active treatment | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Reporting group values | 0.5 SQ-HDM | 1 SQ-HDM | 3 SQ-HDM |
|---------------------------|------------|----------|----------|
| Number of subjects | 9 | 9 | 9 |
| Age categorical | | | |
| Units: Subjects | | | |
| Children (2-11 years) | 7 | 8 | 8 |
| Adolescents (12-17 years) | 2 | 1 | 1 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 7.9 | 8.2 | 8.6 |
| standard deviation | ± 2.9 | ± 2.2 | ± 2.6 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 4 | 2 |
| Male | 5 | 5 | 7 |

| Reporting group values | 6 SQ-HDM | 9 SQ-HDM | 12 SQ-HDM |
|---------------------------|----------|----------|-----------|
| Number of subjects | 9 | 9 | 9 |
| Age categorical | | | |
| Units: Subjects | | | |
| Children (2-11 years) | 7 | 8 | 6 |
| Adolescents (12-17 years) | 2 | 1 | 3 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 9.4 | 9.1 | 10.6 |
| standard deviation | ± 2.4 | ± 2 | ± 2.7 |

| | | | |
|---------------------------------------|---|---|---|
| Gender categorical Units: Subjects | | | |
| Female | 3 | 3 | 2 |
| Male | 6 | 6 | 7 |

| | | | |
|---------------------------------------|---------|-------|--|
| Reporting group values | Placebo | Total | |
| Number of subjects | 18 | 72 | |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 15 | 59 | |
| Adolescents (12-17 years) | 3 | 13 | |
| Age continuous Units: years | | | |
| arithmetic mean | 9.6 | | |
| standard deviation | ± 2.3 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 4 | 22 | |
| Male | 14 | 50 | |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | 0.5 SQ-HDM |
| Reporting group description: active treatment | |
| Reporting group title | 1 SQ-HDM |
| Reporting group description: active treatment | |
| Reporting group title | 3 SQ-HDM |
| Reporting group description: active treatment | |
| Reporting group title | 6 SQ-HDM |
| Reporting group description: active treatment | |
| Reporting group title | 9 SQ-HDM |
| Reporting group description: active treatment | |
| Reporting group title | 12 SQ-HDM |
| Reporting group description: active treatment | |
| Reporting group title | Placebo |
| Reporting group description: - | |

Primary: Specific IgE-blocking antibodies against D. farinae

| | |
|--|---|
| End point title | Specific IgE-blocking antibodies against D. farinae |
| End point description: IgE-blocking factor: the inhibitory capacity of competing components to specific IgE-allergen binding. IgE-blocking factor is a dimensionless number which varies theoretically from 0 (no presence of IgE-blocking components) to 1 (all allergen-specific IgE antibodies are blocked from binding to allergen). The primary objective of the trial was tolerability (descriptive statistics of adverse events only). In order to comply with system requirements of a primary endpoint, this endpoint has been promoted as the primary endpoint. | |
| End point type | Primary |
| End point timeframe: change from baseline to end of trial | |

| End point values | 0.5 SQ-HDM | 1 SQ-HDM | 3 SQ-HDM | 6 SQ-HDM |
|--------------------------------------|-----------------|-----------------|-----------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 9 | 9 | 8 ^[1] |
| Units: dimensionless | | | | |
| arithmetic mean (standard deviation) | 0.02 (± 0.08) | 0.02 (± 0.08) | 0.08 (± 0.1) | 0.11 (± 0.1) |

Notes:

[1] - 1 sample was invalid

| End point values | 9 SQ-HDM | 12 SQ-HDM | Placebo | |
|------------------|----------|-----------|---------|--|
|------------------|----------|-----------|---------|--|

| | | | | |
|--------------------------------------|--------------------|--------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 9 | 18 | |
| Units: dimensionless | | | | |
| arithmetic mean (standard deviation) | 0.09 (\pm 0.14) | 0.09 (\pm 0.08) | -0.01 (\pm 0.07) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | IgE-blocking factor, 12 SQ-HDM vs placebo |
| Statistical analysis description: | |
| Analysis of difference (active vs. placebo) in change from baseline in IgE-blocking factor against D. farinae | |
| Comparison groups | 12 SQ-HDM v Placebo |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0048 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.035 |
| upper limit | 0.185 |
| Variability estimate | Standard deviation |

| | |
|---|--|
| Statistical analysis title | IgE-blocking factor, 9 SQ-HDM vs placebo |
| Statistical analysis description: | |
| Analysis of difference (active vs. placebo) in change from baseline in IgE-blocking factor against D. farinae | |
| Comparison groups | Placebo v 9 SQ-HDM |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0174 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.094 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.017 |
| upper limit | 0.171 |
| Variability estimate | Standard deviation |

| | |
|---|--|
| Statistical analysis title | IgE-blocking factor, 6 SQ-HDM vs placebo |
| Statistical analysis description: | |
| Analysis of difference (active vs. placebo) in change from baseline in IgE-blocking factor against D. farinae | |
| Comparison groups | Placebo v 6 SQ-HDM |
| Number of subjects included in analysis | 26 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0029 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.115 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.041 |
| upper limit | 0.19 |
| Variability estimate | Standard deviation |

| | |
|---|--|
| Statistical analysis title | IgE-blocking factor, 3 SQ-HDM vs placebo |
| Statistical analysis description: | |
| Analysis of difference (active vs. placebo) in change from baseline in IgE-blocking factor against D. farinae | |
| Comparison groups | Placebo v 3 SQ-HDM |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0184 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.016 |
| upper limit | 0.164 |
| Variability estimate | Standard deviation |

| | |
|---|--|
| Statistical analysis title | IgE-blocking factor, 1 SQ-HDM vs placebo |
| Statistical analysis description: | |
| Analysis of difference (active vs. placebo) in change from baseline in IgE-blocking factor against D. farinae | |
| Comparison groups | Placebo v 1 SQ-HDM |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3453 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.036 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.039 |
| upper limit | 0.111 |
| Variability estimate | Standard deviation |

| | |
|---|--|
| Statistical analysis title | IgE-blocking factor, 0.5 SQ-HDM vs placebo |
| Statistical analysis description: | |
| Analysis of difference (active vs. placebo) in change from baseline in IgE-blocking factor against D. farinae | |
| Comparison groups | Placebo v 0.5 SQ-HDM |
| Number of subjects included in analysis | 27 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.3861 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.034 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.043 |
| upper limit | 0.11 |
| Variability estimate | Standard deviation |

Adverse events

Adverse events information

Timeframe for reporting adverse events:
from signing informed consent to end of trial

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 11.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | 0.5 SQ-HDM |
|-----------------------|------------|

Reporting group description:
active treatment

| | |
|-----------------------|----------|
| Reporting group title | 1 SQ-HDM |
|-----------------------|----------|

Reporting group description:
active treatment

| | |
|-----------------------|----------|
| Reporting group title | 3 SQ-HDM |
|-----------------------|----------|

Reporting group description:
active treatment

| | |
|-----------------------|----------|
| Reporting group title | 6 SQ-HDM |
|-----------------------|----------|

Reporting group description:
active treatment

| | |
|-----------------------|----------|
| Reporting group title | 9 SQ-HDM |
|-----------------------|----------|

Reporting group description:
active treatment

| | |
|-----------------------|-----------|
| Reporting group title | 12 SQ-HDM |
|-----------------------|-----------|

Reporting group description:
active treatment

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

Reporting group description: -

| Serious adverse events | 0.5 SQ-HDM | 1 SQ-HDM | 3 SQ-HDM |
|---|---------------|---------------|---------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | 6 SQ-HDM | 9 SQ-HDM | 12 SQ-HDM |
|---|---------------|---------------|---------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | Placebo | | |
|---|----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

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

| Non-serious adverse events | 0.5 SQ-HDM | 1 SQ-HDM | 3 SQ-HDM |
|---|----------------|-----------------|----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 9 (88.89%) | 9 / 9 (100.00%) | 8 / 9 (88.89%) |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| chest discomfort | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| oedema mucosal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |

| | | | |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 9 (33.33%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 3 | 1 |
| Asthma exercise induced | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 9 (22.22%) | 4 / 9 (44.44%) |
| occurrences (all) | 1 | 4 | 11 |
| Dry throat | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| hoarseness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal passage irritation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 19 |
| Pharyngolaryngeal irritation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 1 | 6 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 3 / 9 (33.33%) |
| occurrences (all) | 0 | 2 | 23 |
| throat secretion increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 2 | 1 |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| aphonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 2 |
| Headache | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Syncope vasovagal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Ear pruritus subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 3 | 1 / 9 (11.11%) 1 |
| Eye disorders | | | |
| Conjunctival hyperaemia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Conjunctival irritation subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Conjunctivitis allergic subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Eye pruritus subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 3 |
| eye redness subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Eyelid oedema subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Lacrimation increased subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 6 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Aphthous stomatitis | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 3 |
| Glossodynia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| loose stools | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema mouth | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all) | 0 | 0 | 8 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral pruritus | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 1 / 9 (11.11%) | 8 / 9 (88.89%) |
| occurrences (all) | 5 | 5 | 59 |
| Swollen tongue | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 15 |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 6 |
| Tongue eruption | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Vomiting | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| mucosal inflammation subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Hepatobiliary disorders Sensation of foreign body subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 | 1 / 9 (11.11%) 1 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 36 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 10 |
| Face oedema subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Skin lesion subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Swelling face subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 9 (0.00%) 0 |
| Renal and urinary disorders Enuresis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| neck pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis viral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Influenza | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 9 (22.22%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 7 | 2 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Increased appetite | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Non-serious adverse events | 6 SQ-HDM | 9 SQ-HDM | 12 SQ-HDM |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 9 (100.00%) | 8 / 9 (88.89%) | 9 / 9 (100.00%) |

| | | | |
|--|----------------|----------------|----------------|
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 4 | 2 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 4 | 2 |
| Malaise | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema mucosal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 9 (22.22%) | 3 / 9 (33.33%) |
| occurrences (all) | 0 | 2 | 4 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Asthma exercise induced | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Cough | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 9 (33.33%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 3 | 2 |
| Dry throat | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| hoarseness | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasal passage irritation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 2 |
| Pharyngolaryngeal irritation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Throat irritation | | | |
| subjects affected / exposed | 7 / 9 (77.78%) | 4 / 9 (44.44%) | 4 / 9 (44.44%) |
| occurrences (all) | 40 | 52 | 37 |
| throat secretion increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Injury, poisoning and procedural | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| aphonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 9 (22.22%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 3 | 1 |
| Syncope vasovagal | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear pruritus | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 5 | 0 | 26 |
| Eye disorders | | | |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Conjunctival irritation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Eye pruritus | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| eye redness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Eyelid oedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 9 (11.11%) | 3 / 9 (33.33%) |
| occurrences (all) | 9 | 1 | 3 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glossodynia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| loose stools | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema mouth | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 5 / 9 (55.56%) | 1 / 9 (11.11%) | 6 / 9 (66.67%) |
| occurrences (all) | 48 | 4 | 36 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 9 (22.22%) | 2 / 9 (22.22%) |
| occurrences (all) | 6 | 2 | 3 |
| Oral pruritus | | | |
| subjects affected / exposed | 6 / 9 (66.67%) | 6 / 9 (66.67%) | 6 / 9 (66.67%) |
| occurrences (all) | 75 | 51 | 69 |
| Swollen tongue | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue eruption | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| mucosal inflammation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Sensation of foreign body | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 3 |
| Face oedema | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 3 | 2 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 3 | 1 |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 5 | 1 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Enuresis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| neck pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchitis viral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 9 (11.11%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 9 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 9 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Placebo | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 17 / 18 (94.44%) | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| oedema mucosal | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | | |
| occurrences (all) | 6 | | |
| Asthma exercise induced | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cough | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | | |
| occurrences (all) | 7 | | |
| Dry throat | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| hoarseness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal passage irritation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pharyngolaryngeal irritation | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | | |
| occurrences (all) | 2 | | |
| Rhinitis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | | |
| occurrences (all) | 2 | | |
| Sneezing | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Throat irritation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| throat secretion increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Wheezing | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| aphonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 2 | | |
| Headache | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 5 / 18 (27.78%) | | |
| occurrences (all) | 11 | | |
| Syncope vasovagal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear and labyrinth disorders | | | |
| Ear pruritus | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Conjunctival irritation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | | |
| occurrences (all) | 3 | | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Eye pruritus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 4 | | |
| eye redness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eyelid oedema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | | |
| occurrences (all) | 17 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Glossodynia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| loose stools | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema mouth | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral pruritus | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | | |
| occurrences (all) | 6 | | |
| Swollen tongue | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|---------------------|--|--|
| Tongue eruption subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Toothache subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 2 | | |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| mucosal inflammation subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Hepatobiliary disorders Sensation of foreign body subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Erythema subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Face oedema subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Skin lesion subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Swelling face subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Urticaria | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed occurrences (all) | 1 / 18 (5.56%) 1 | | |
| Renal and urinary disorders Enuresis subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders neck pain subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Bronchitis viral subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Viral infection subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 2 / 18 (11.11%) 2 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 1 / 18 (5.56%) 1 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|--|---------------------|--|--|
| Increased appetite subjects affected / exposed occurrences (all) | 0 / 18 (0.00%) 0 | | |
|--|---------------------|--|--|

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 23 October 2007 | The amendment was proposed after the evaluation of subjects included in the 2nd cohort (dose group 1 SQ-HDM).Inclusion of two additional dose groups: 9 SQ-HDM and 12 SQ-HDM. Both doses were below the maximum tolerable dose found in adults in the MT-01 trial |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|----------------|
| Not applicable |
|----------------|

Notes: