



## Clinical trial results:

### Clinical assessment of GW815SF Salmeterol/fluticasone propionate (HFA MDI) in pediatric patients with bronchial asthma -A long term (24-week) study

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-004881-27   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 24 November 2007 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 14 January 2017 |
| First version publication date | 14 January 2017 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 110101 |
|-----------------------|--------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline  |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |

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:

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**Results analysis stage**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 18 February 2008 |
| Is this the analysis of the primary completion data? | No               |

|                                  |                  |
|----------------------------------|------------------|
| Global end of trial reached?     | Yes              |
| Global end of trial date         | 24 November 2007 |
| Was the trial ended prematurely? | No               |

Notes:

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**General information about the trial**

Main objective of the trial:

TBD

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 30 March 2007 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Japan: 40 |
| Worldwide total number of subjects   | 40        |
| EEA total number of subjects         | 0         |

Notes:

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**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)                     | 35 |
| Adolescents (12-17 years)                 | 5  |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

|                              |    |
|------------------------------|----|
| Number of subjects started   | 40 |
| Number of subjects completed | 40 |

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Salmeterol/fluticasone propionate |
|------------------|-----------------------------------|

Arm description:

Salmeterol/fluticasone propionate patients received 2 inhalations twice daily each inhalation was 25/50mcg for 24 weeks(Total daily dose was 100/200mcg)

|  |                                   |
|--|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | Salmeterol/fluticasone propionate |
| Investigational medicinal product code |                                   |
| Other name                             |                                   |
| Pharmaceutical forms                   | Inhalation powder                 |
| Routes of administration               | Oral use                          |

Dosage and administration details:

Two inhalations twice daily

|                                       |                                   |
|---------------------------------------|-----------------------------------|
| <b>Number of subjects in period 1</b> | Salmeterol/fluticasone propionate |
| Started                               | 40                                |
| Completed                             | 40                                |

## Baseline characteristics

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Salmeterol/fluticasone propionate |
|-----------------------|-----------------------------------|

Reporting group description:

Salmeterol/fluticasone propionate patients received 2 inhalations twice daily each inhalation was 25/50mcg for 24 weeks(Total daily dose was 100/200mcg)

| Reporting group values                                      | Salmeterol/fluticasone propionate | Total |  |
|---|-----------------------------------|-------|--|
| Number of subjects  | 40                                | 40    |  |
| Age categorical<br>Units: Subjects                          |                                   |       |  |
| Age continuous  |                                   |       |  |
| Age continuous description                                  |                                   |       |  |
| Units: years<br>arithmetic mean<br>standard deviation       | 8.7<br>± 2.5                      | -     |  |
| Gender categorical  |                                   |       |  |
| Gender categorical description                              |                                   |       |  |
| Units: Subjects   |                                   |       |  |
| Female  | 16                                | 16    |  |
| Male  | 24                                | 24    |  |
| Race/Ethnicity, Customized                                  |                                   |       |  |
| One participant counted twice due to having multiple races. |                                   |       |  |
| Units: Subjects   |                                   |       |  |
| Asian   | 40                                | 40    |  |

## End points

### End points reporting groups

|  |                                   |
|--|-----------------------------------|
| Reporting group title  | Salmeterol/fluticasone propionate |
| Reporting group description:<br>Salmeterol/fluticasone propionate patients received 2 inhalations twice daily each inhalation was 25/50mcg for 24 weeks(Total daily dose was 100/200mcg) |                                   |

### Primary: Most Frequent Adverse Events - On Therapy

|   |  |
|---|--|
| End point title   | Most Frequent Adverse Events - On Therapy <sup>[1]</sup> |
| End point description:<br>Adverse events, Clinical laboratory tests, Adrenocortical function test, Physical examinations, 12-lead electrocardiogram (ECG), Oropharyngeal examination were included. |  |
| End point type  | Primary  |
| End point timeframe:<br>Baseline to Week 24   |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

| End point values            | Salmeterol/fluticasone propionate |  |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type          | Reporting group                   |  |  |  |
| Number of subjects analysed | 40 <sup>[2]</sup>                 |  |  |  |
| Units: Participants         |                                   |  |  |  |
| Laryngopharyngitis          | 8                                 |  |  |  |
| Bronchitis                  | 8                                 |  |  |  |
| Nasopharyngitis             | 8                                 |  |  |  |
| Asthma                      | 8                                 |  |  |  |
| Pharyngitis                 | 6                                 |  |  |  |
| Pyrexia                     | 5                                 |  |  |  |
| Otitis media                | 4                                 |  |  |  |
| Pharyngotonsillitis         | 3                                 |  |  |  |
| Laryngotracheo bronchitis   | 3                                 |  |  |  |
| Molluscum contagiosum       | 3                                 |  |  |  |
| Stomatitis                  | 3                                 |  |  |  |

Notes:

[2] - Safety analysis was performed on the primary outcome measures, adverse events and safety population

### Statistical analyses

No statistical analyses for this end point

### Primary: Serious Adverse Events (SAEs) - On Therapy

|   |   |
|---|---|
| End point title   | Serious Adverse Events (SAEs) - On Therapy <sup>[3]</sup> |
| End point description:<br>Number of participants considered by the investigator to be related to study medication. Adverse events, Clinical laboratory tests, Adrenocortical function test, Physical examinations, 12-lead ECG, |   |

Oropharyngeal examination were included. Frequency threshold of reported SAE's is 0%(100% reported)

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to Week 24

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical data to report.

|                             |                                   |  |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>     | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type          | Reporting group                   |  |  |  |
| Number of subjects analysed | 40 <sup>[4]</sup>                 |  |  |  |
| Units: Participants         | 1                                 |  |  |  |

Notes:

[4] - Safety population, all who entered treatment period and received at least 1 dose of study med

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Morning Peak Expiratory Flow (PEF) During Weeks 1-24

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Morning Peak Expiratory Flow (PEF) During Weeks 1-24 |
|-----------------|--|

End point description:

PEF taken daily and average used for week 1-24 value. The peak expiratory flow rate measures how fast a person can (exhale) air. Then, compares it to normal flow rates to predict obstruction and disease. The average PEF for a child or adolescent whose height is 43" is 147 L/min, whose height is 66" is 454 L/min.

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

End point timeframe:

Baseline and during Weeks 1-24

|                                      |                                   |  |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>              | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type                   | Reporting group                   |  |  |  |
| Number of subjects analysed          | 40 <sup>[5]</sup>                 |  |  |  |
| Units: L/min                         |                                   |  |  |  |
| arithmetic mean (standard deviation) | 32.9 (± 34.48)                    |  |  |  |

Notes:

[5] - Efficacy analyses were performed on the secondary outcome measures and Full analysis set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Percent Predicted Morning Peak Expiratory

### Flow (PEF) During Weeks 1-24

|  |  |
|--|--|
| End point title  | Change from Baseline in Percent Predicted Morning Peak Expiratory Flow (PEF) During Weeks 1-24 |
| End point description:<br>Percent Predicted Morning Peak Expiratory flow were the percent of patients that were predicted to have their Peak expiratory flow in the morning. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Baseline and during Weeks 1-24   |  |

|                                      |                                   |  |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>              | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type                   | Reporting group                   |  |  |  |
| Number of subjects analysed          | 40 <sup>[6]</sup>                 |  |  |  |
| Units: Percent Change                |                                   |  |  |  |
| arithmetic mean (standard deviation) | 12.5 (± 11.294)                   |  |  |  |

Notes:

[6] - Efficacy analyses were performed on the secondary outcome measures and Full analysis set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Evening Peak Expiratory Flow (PEF) During Weeks 1-24

|  |  |
|--|--|
| End point title  | Change from Baseline in Evening Peak Expiratory Flow (PEF) During Weeks 1-24 |
| End point description:<br>The peak expiratory flow rate measures how fast a person can (exhale) air. Then compares it to normal flow rates to predict obstruction and disease. The average PEF for a child or adolescent whose height is 43" is 147 L/min, whose height is 66" is 454 L/min. |  |
| End point type   | Secondary  |
| End point timeframe:<br>Baseline and during Weeks 1-24   |  |

|                                      |                                   |  |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>              | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type                   | Reporting group                   |  |  |  |
| Number of subjects analysed          | 40 <sup>[7]</sup>                 |  |  |  |
| Units: L/min                         |                                   |  |  |  |
| arithmetic mean (standard deviation) | 31.2 (± 29.28)                    |  |  |  |

Notes:

[7] - Efficacy analyses were performed on the secondary outcome measures and Full analysis set

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Circadian Variation in Peak Expiratory Flow (PEF) During Weeks 1-24

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Circadian Variation in Peak Expiratory Flow (PEF) During Weeks 1-24 |
|-----------------|---|

End point description:

Circadian Variation means the various changes in a day. The peak expiratory flow rate measures how fast a person can (exhale) air using a mini-Wright peak flow meter. The average PEF for a child or adolescent whose height is 43" is 147 L/min, whose height is 66" is 454 L/min.

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

End point timeframe:

Baseline and during Weeks 1-24

|                                      |                                   |  |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>              | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type                   | Reporting group                   |  |  |  |
| Number of subjects analysed          | 40 <sup>[8]</sup>                 |  |  |  |
| Units: Percent Change                |                                   |  |  |  |
| arithmetic mean (standard deviation) | -1.62 (± 3.583)                   |  |  |  |

Notes:

[8] - Efficacy analyses were performed on the secondary outcome measures and Full analysis set

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Symptom-Free Nights and Days

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Symptom-Free Nights and Days |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline and Week 24

|                             |                                   |  |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>     | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type          | Reporting group                   |  |  |  |
| Number of subjects analysed | 40 <sup>[9]</sup>                 |  |  |  |
| Units: Participants         |                                   |  |  |  |
| Baseline                    | 29                                |  |  |  |
| Week 24                     | 31                                |  |  |  |



Notes:

[9] - Efficacy analyses were performed on the secondary outcome measures and Full analysis set

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Rescue Medication-Free Nights and Days

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Rescue Medication-Free Nights and Days |
|-----------------|--|

End point description:

Rescue free means without the use of other medication.

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

End point timeframe:

Baseline and Week 24

|                             |                                   |  |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>     | Salmeterol/fluticasone propionate |  |  |  |
| Subject group type          | Reporting group                   |  |  |  |
| Number of subjects analysed | 40 <sup>[10]</sup>                |  |  |  |
| Units: Participants         |                                   |  |  |  |
| Baseline                    | 33                                |  |  |  |
| Week 24                     | 32                                |  |  |  |

Notes:

[10] - Efficacy analyses were performed on the secondary outcome measures and Full analysis set

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were monitored throughout the 24 weeks of treatment

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 10.0 |
|--------------------|------|

### Reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Salmeterol/fluticasone propionate |
|-----------------------|-----------------------------------|

Reporting group description:

Salmeterol/fluticasone propionate patients received 2 inhalations twice daily each inhalation was 25/50mcg for 24 weeks(Total daily dose was 100/200mcg)

| Serious adverse events                            | Salmeterol/fluticasone propionate |  |  |
|---|-----------------------------------|--|--|
| Total subjects affected by serious adverse events |                                   |  |  |
| subjects affected / exposed                       | 1 / 40 (2.50%)                    |  |  |
| number of deaths (all causes)                     | 0                                 |  |  |
| number of deaths resulting from adverse events    | 0                                 |  |  |
| Respiratory, thoracic and mediastinal disorders   |                                   |  |  |
| Asthma  |                                   |  |  |
| alternative dictionary used: MedDRA 10.0          |                                   |  |  |
| subjects affected / exposed                       | 1 / 40 (2.50%)                    |  |  |
| occurrences causally related to treatment / all   | 0 / 1                             |  |  |
| deaths causally related to treatment / all        | 0 / 0                             |  |  |

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

| Non-serious adverse events                            | Salmeterol/fluticasone propionate |  |  |
|---|-----------------------------------|--|--|
| Total subjects affected by non-serious adverse events |                                   |  |  |
| subjects affected / exposed                           | 35 / 40 (87.50%)                  |  |  |
| General disorders and administration site conditions  |                                   |  |  |
| Pyrexia   |                                   |  |  |
| alternative dictionary used: MedDRA 10.0              |                                   |  |  |
| subjects affected / exposed                           | 5 / 40 (12.50%)                   |  |  |
| occurrences (all)                                     | 5                                 |  |  |

|  |  |  |  |
|--|--|--|--|
| <p>Gastrointestinal disorders</p> <p>Abdominal pain</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 40 (5.00%)</p> <p>2</p> <p>Acetonaemic vomiting</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 40 (5.00%)</p> <p>2</p> <p>Stomatitis</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>3 / 40 (7.50%)</p> <p>3</p> |  |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Asthma</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>8 / 40 (20.00%)</p> <p>13</p>  |  |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Eczema</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 40 (5.00%)</p> <p>2</p> <p>Heat Rash</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>2 / 40 (5.00%)</p> <p>2</p>   |  |  |  |
| <p>Infections and infestations</p> <p>Bronchitis</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>8 / 40 (20.00%)</p> <p>8</p> <p>Gastroenteritis</p> <p>alternative dictionary used:<br/>MedDRA 10.0</p>  |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                 | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                           | 3               |  |  |
| Laryngopharyngitis                          |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 8 / 40 (20.00%) |  |  |
| occurrences (all)                           | 17              |  |  |
| Laryngotracheo bronchitis                   |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                           | 4               |  |  |
| Molluscum contagiosum                       |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                           | 4               |  |  |
| Nasopharyngitis                             |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 8 / 40 (20.00%) |  |  |
| occurrences (all)                           | 14              |  |  |
| Otitis Media                                |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 4 / 40 (10.00%) |  |  |
| occurrences (all)                           | 4               |  |  |
| Pharyngitis                                 |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 6 / 40 (15.00%) |  |  |
| occurrences (all)                           | 7               |  |  |
| Pharyngotonsillitis                         |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                           | 3               |  |  |
| Sinusitis                                   |                 |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                 |  |  |
| subjects affected / exposed                 | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                           | 2               |  |  |

|   |                |  |  |
|---|----------------|--|--|
| tonsillitis                                 |                |  |  |
| alternative dictionary used:<br>MedDRA 10.0 |                |  |  |
| subjects affected / exposed                 | 2 / 40 (5.00%) |  |  |
| occurrences (all)                           | 2              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported