



Clinical trial results:

An Open-Label, Non-Comparative Study to Assess the Pharmacokinetics, Safety and Efficacy of Topical Retapamulin (SB-275833) Ointment, 1%, Twice Daily for Five Days in the Treatment of Uncomplicated Skin and Skin Structure Infections in Pediatric Subjects Aged 2 to 24 Months

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-003374-10 |
| Trial protocol | DE NL |
| Global end of trial date | 18 August 2008 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 02 May 2016 |
| First version publication date | 31 January 2015 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | TOC106489 |
|-----------------------|-----------|

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 8664357343, |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 1 8664357343, |

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? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 26 September 2008 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 August 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To characterize the systemic exposure, by using pharmacokinetic (PK) sampling at four to eight hours post-dose, of Retapamulin Ointment, 1%, when applied topically, twice daily for five days, in the treatment of pediatric subjects aged ≥ 2 to ≤ 6 months, > 6 to ≤ 12 months, and > 12 to ≤ 24 months with uncomplicated skin and skin structure infections, including secondarily-infected traumatic lesions (SITL), secondarily-infected dermatoses (SID) and impetigo.

Protection of trial subjects:

Written, dated informed consent required from parent or guardian for all participants, where study procedures and any associated pain or discomfort were described.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 25 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 | Germany: 6 |
| Country: Number of subjects enrolled | Argentina: 5 |
| Country: Number of subjects enrolled | Chile: 10 |
| Country: Number of subjects enrolled | Costa Rica: 11 |
| Country: Number of subjects enrolled | Mexico: 1 |
| Country: Number of subjects enrolled | South Africa: 45 |
| Country: Number of subjects enrolled | United States: 8 |
| Worldwide total number of subjects | 86 |
| EEA total number of subjects | 6 |

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 | 86 |

| | |
|---------------------------|---|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were recruited from 10 sites in 7 countries.

Pre-assignment

Screening details:

Participants eligible for enrollment in the study must have met all inclusion criteria.

Period 1

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

Arms

| | |
|------------------|--------------------------|
| Arm title | Retapamulin Ointment, 1% |
|------------------|--------------------------|

Arm description:

Retapamulin ointment, 1%, administered twice daily for 5 consecutive days

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Retapamulin 1% ointment |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Ointment |
| Routes of administration | Topical use |

Dosage and administration details:

Using a sterile swab, retapamulin ointment was applied, in an approximately 1 millimeter (mm)-thick layer, over the entire cleansed lesion(s). Ointment was applied twice daily at 10-hour to 12-hour intervals for 5 days.

The area to be treated was not to exceed 2% body surface area (BSA).

| Number of subjects in period 1 | Retapamulin Ointment, 1% |
|--------------------------------|--------------------------|
| Started | 86 |
| Completed | 78 |
| Not completed | 8 |
| Consent withdrawn by subject | 2 |
| Adverse event, non-fatal | 3 |
| Lost to follow-up | 2 |
| Protocol deviation | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Retapamulin Ointment, 1% |
|-----------------------|--------------------------|

Reporting group description:

Retapamulin ointment, 1%, administered twice daily for 5 consecutive days

| Reporting group values | Retapamulin Ointment, 1% | Total | |
|--|--------------------------|-------|--|
| Number of subjects | 86 | 86 | |
| 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) | 86 | 86 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 10.6 | | |
| standard deviation | ± 6.89 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 32 | 32 | |
| Male | 54 | 54 | |
| Race, customized | | | |
| Units: Subjects | | | |
| African American/African Heritage | 46 | 46 | |
| White/Caucasian | 36 | 36 | |
| American Indian or Alaska Native | 1 | 1 | |
| Central/South Asian | 1 | 1 | |
| East Asian | 1 | 1 | |
| Missing | 1 | 1 | |

End points

End points reporting groups

| | |
|---|--------------------------|
| Reporting group title | Retapamulin Ointment, 1% |
| Reporting group description: | |
| Retapamulin ointment, 1%, administered twice daily for 5 consecutive days | |

Primary: Number of participants with measurable plasma concentrations, by age group

| | |
|-----------------|---|
| End point title | Number of participants with measurable plasma concentrations, by age group ^[1] |
|-----------------|---|

End point description:

Pharmacokinetic (PK) samples were collected randomly in the window of 4 to 8 hours post-dose (except one at 3 hours and one at 11 hours post-dose) after the first daily dose of treatment on Day 3 or Day 4 . The lower limit of quantification (LLQ) for retapamulin was 0.5 ng/mL. PK Population: all participants who received at least one dose of study medication and who had PK samples taken.

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

End point timeframe:

Days 3 to 4; 4 to 8 hours post-dose of the first dose of the day

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: No statistical analysis was conducted; thus, there are no statistical data to report.

| End point values | Retapamulin Ointment, 1% | | | |
|-----------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 79 ^[2] | | | |
| Units: participants | | | | |
| All ages | 36 | | | |
| ≥2 months to ≤6 months | 17 | | | |
| >6 months to ≤12 months | 10 | | | |
| >12 months to ≤24 months | 9 | | | |

Notes:

[2] - Pharmacokinetic (PK) Population. Seven participants did not have PK samples collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Clinical Success at Follow-up, by Type of Skin Infection and by Age

| | |
|-----------------|---|
| End point title | Number of participants with Clinical Success at Follow-up, by Type of Skin Infection and by Age |
|-----------------|---|

End point description:

SID = Secondarily Infected Dermatoses; SITL = Secondarily Infected Traumatic Lesions. Clinical Success is the number of participants with resolution of signs/symptoms of infection or improvement such that no additional antibiotic therapy was needed. Intent-to-Treat Clinical (ITTC) Population: all participants who received at least one dose of study medication.

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

End point timeframe:
Follow-up, Days 12 to 16

| End point values | Retapamulin Ointment, 1% | | | |
|--|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 86 ^[3] | | | |
| Units: participants | | | | |
| Impetigo, ≥2 months to ≤6 months, n=11 | 10 | | | |
| Impetigo, >6 months to ≤12 months, n=18 | 17 | | | |
| Impetigo, >12 months to ≤24 months, n=18 | 17 | | | |
| SID, ≥2 months to ≤6 months, n=17 | 11 | | | |
| SID, >6 months to ≤12 months, n=9 | 7 | | | |
| SID, >12 months to ≤24 months, n=4 | 4 | | | |
| SITL, ≥2 months to ≤6 months, n=1 | 1 | | | |
| SITL, >6 months to ≤12 months, n=2 | 2 | | | |
| SITL, >12 months to ≤24 months, n=6 | 6 | | | |

Notes:

[3] - ITTC Population. Participants who were clinical successes are shown (n=X in category title).

Statistical analyses

No statistical analyses for this end point

Secondary: Bacteriological Success Rate at Follow-up, by Baseline Pathogen

| | |
|-----------------|---|
| End point title | Bacteriological Success Rate at Follow-up, by Baseline Pathogen |
|-----------------|---|

End point description:

Bacteriological success is defined as: (1) Bacteriological Eradication, elimination of the baseline pathogen via culture results; (2) Presumed Bacteriological Eradication, clinical success plus no culturable material from the wound; or (3) Colonization, new pathogen identified at Follow-up in a non-symptomatic participant who does not require additional antibiotic therapy. The number of pathogens eradicated out of the number isolated (shown as "n" in the category title) for each respective category is shown. ITTB (Intent-to-Treat Bacteriological) Population: participants who had at least one dose of study medication and a clinical diagnosis of infection plus a pathogen isolated at Baseline.

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

End point timeframe:

Follow-up, Days 12 to 16

| End point values | Retapamulin Ointment, 1% | | | |
|---------------------------------------|--------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 61 ^[4] | | | |
| Units: Number of pathogens eradicated | | | | |
| All Pathogens, n=93 | 79 | | | |
| Staphylococcus aureus (SA), n=44 | 40 | | | |

| | | | | |
|-----------------------------------|----|--|--|--|
| Methicillin-resistant SA, n=3 | 3 | | | |
| Methicillin-susceptible SA, n=41 | 37 | | | |
| Mupirocin susceptible SA, n=44 | 40 | | | |
| Fusidic acid-resistant SA, n=2 | 2 | | | |
| Fusidic acid-susceptible SA, n=42 | 38 | | | |
| Streptococcus pyogenes, n=9 | 9 | | | |
| Other Gram (+) pathogens, n=11 | 9 | | | |
| Gram (-) pathogens, n=29 | 21 | | | |

Notes:

[4] - ITTB Population. Participants with >1 pathogen may be represented in the table more than once.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants by age with therapeutic response of success

| | |
|-----------------|--|
| End point title | Number of participants by age with therapeutic response of success |
|-----------------|--|

End point description:

Therapeutic response is a measure of the overall efficacy response; a response of "therapeutic success" was based on both clinical success and bacteriological success in a given participant. ITTB and ITTC Populations. The number analyzed is the number of participants who were clinical successes both in the ITTC Population and the ITTB Population.

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

End point timeframe:

Follow-up, Days 12 to 16

| | | | | |
|---------------------------------|--------------------------|--|--|--|
| End point values | Retapamulin Ointment, 1% | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 61 ^[5] | | | |
| Units: participants | | | | |
| All ages | 51 | | | |
| >2 months to <=6 months, n=21 | 15 | | | |
| >6 months to <=12 months, n=20 | 17 | | | |
| >12 months to <=24 months, n=20 | 19 | | | |

Notes:

[5] - The number of participants who were therapeutic successes is shown (n=X in category titles).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected throughout the course of the study.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|--------------------------|
| Reporting group title | Retapamulin Ointment, 1% |
|-----------------------|--------------------------|

Reporting group description:

Retapamulin ointment, 1%, administered twice daily for 5 consecutive days

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events occurred at or above the specified 5% reporting threshold.

| Serious adverse events | Retapamulin Ointment, 1% | | |
|---|--------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 86 (1.16%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

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

| Non-serious adverse events | Retapamulin Ointment, 1% | | |
|---|--------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 86 (0.00%) | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported