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			
Fuscidic acid-resistant SA, n=2	2			
Fuscidic 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