



Clinical trial results:

A Randomized, Double-Blind, Double Dummy, Comparative , Multicenter Study to Assess the Safety and Efficacy of Topical Retapamulin Ointment, 1%, versus Oral Linezolid in the Treatment of Secondarily-Infected Traumatic Lesions and Impetigo Due to Methicillin Resistant Staphylococcus aureus

Summary

EudraCT number	2015-004886-98
Trial protocol	Outside EU/EEA
Global end of trial date	27 September 2010

Results information

Result version number	v1 (current)
This version publication date	12 February 2017
First version publication date	12 February 2017

Trial information

Trial identification

Sponsor protocol code	110978
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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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 December 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 September 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the clinical and bacteriological efficacy of topical retapamulin ointment, 1%, versus oral linezolid, in the treatment of subjects with secondarily-infected traumatic lesions (SITL: excluding abscesses) or impetigo due to methicillin-resistant *Staphylococcus aureus* (MRSA).

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2009
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	United States: 404
Worldwide total number of subjects	404
EEA total number of subjects	0

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)	14
Children (2-11 years)	68
Adolescents (12-17 years)	38
Adults (18-64 years)	256
From 65 to 84 years	24
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

In total, 410 participants were enrolled in the study, 267 received at least 1 dose of retapamulin arm and 137 received at least 1 dose of linezolid. Of these participants, 234 retapamulin participants and 122 linezolid participants completed the study.

Pre-assignment

Screening details:

One participant was randomized to retapamulin but received linezolid. This participant is summarized in the linezolid group for all baseline and safety tables, but is summarized in the retapamulin group for all efficacy tables.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Retapamulin ointment, 1% (weight/weight) plus oral placebo

Arm description:

Retapamulin ointment was administered topically twice daily (BID) for 5 days. The ointment formulation was to be applied to the infected lesion(s) at a dose of approximately 10 milligrams (mg) per centimeter squared (cm²). Placebo was to be dosed, depending on participant age, either BID or three times a day (TID) for 10 days. Placebo oral suspension and oral tablet were formulated to appear identical to the linezolid formulations. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg placebo tablets, pediatric participants 5 to 11 years of age were dosed with oral suspension at 0.5 milliliters (ml)/kilogram (kg) BID, and pediatric participants less than 5 years of age were dosed with oral suspension at 0.5 ml/kg TID.

Arm type	Experimental
Investigational medicinal product name	Retapamulin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

1% (w/w) ointment, twice daily for 5 days

Arm title	Linezolid plus placebo ointment
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Arm description:

Linezolid was to be dosed, depending on participant age, either BID or TID for 10 days. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg tablets for 10 days. Pediatric participants who were 5-11 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg BID for 10 days. Pediatric participants who were < 5 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg TID for 10 days. Placebo ointment was administered topically BID for 5 days.

Arm type	Active comparator
Investigational medicinal product name	Linezolid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension, Tablet
Routes of administration	Oral use

Dosage and administration details:

600mg tablet, q12h for 10 days (≥ 12 years of age) 100 mg/5 mL oral suspension; 10 mg/kg q12h for 10 days (5-11 years of age) 100 mg/5 mL oral suspension; 10 mg/kg q8h for 10 days (<5 years of age)

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment, Oral suspension, Tablet
Routes of administration	Oral use, Topical use

Dosage and administration details:

Topical ointment, twice daily for 5 days. Tablet BID for 10 days (≥ 12 years of age). Suspension BID for 10 days (5-11 years of age). Suspension TID for 10 days (<5 years of age).

Number of subjects in period 1	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment
Started	267	137
Completed	234	122
Not completed	33	15
Consent withdrawn by subject	3	1
Adverse event, non-fatal	10	3
Investigator Discretion	2	3
Lost to follow-up	2	3
Lack of efficacy	15	3
Protocol deviation	1	2

Baseline characteristics

Reporting groups

Reporting group title	Retapamulin ointment, 1% (weight/weight) plus oral placebo
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Reporting group description:

Retapamulin ointment was administered topically twice daily (BID) for 5 days. The ointment formulation was to be applied to the infected lesion(s) at a dose of approximately 10 milligrams (mg) per centimeter squared (cm²). Placebo was to be dosed, depending on participant age, either BID or three times a day (TID) for 10 days. Placebo oral suspension and oral tablet were formulated to appear identical to the linezolid formulations. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg placebo tablets, pediatric participants 5 to 11 years of age were dosed with oral suspension at 0.5 milliliters (ml)/kilogram (kg) BID, and pediatric participants less than 5 years of age were dosed with oral suspension at 0.5 ml/kg TID.

Reporting group title	Linezolid plus placebo ointment
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Reporting group description:

Linezolid was to be dosed, depending on participant age, either BID or TID for 10 days. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg tablets for 10 days. Pediatric participants who were 5-11 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg BID for 10 days. Pediatric participants who were < 5 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg TID for 10 days. Placebo ointment was administered topically BID for 5 days.

Reporting group values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment	Total
Number of subjects	267	137	404
Age categorical			
Units: Subjects			

Age continuous			
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Baseline characteristics were collected in all participants in the Intent-to-Treat Clinical (ITTC) Population, comprised of all randomized participants who took at least one dose of study medication. Three participants in both treatment groups were randomized but did not receive study medication.

Units: years			
arithmetic mean	34.6	33.8	
standard deviation	± 21.37	± 22.38	-

Gender categorical			
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Baseline characteristics were collected in all participants in the Intent-to-Treat Clinical (ITTC) Population, comprised of all randomized participants who took at least one dose of study medication. Three participants in both treatment groups were randomized but did not receive study medication.

Units: Subjects			
Female	108	49	157
Male	159	88	247

Race/Ethnicity, Customized			
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Baseline characteristics were collected in all participants in the Intent-to-Treat Clinical (ITTC) Population, comprised of all randomized participants who took at least one dose of study medication. Three participants in both treatment groups were randomized but did not receive study medication.

Units: Subjects			
African American/African Heritage	16	10	26
American Indian or Alaska Native	5	0	5
Central/South Asian Heritage	1	1	2
East Asian Heritage	0	1	1
Japanese Heritage	5	2	7

South East Asian Heritage	3	0	3
Native Hawaiian or other Pacific Islander	5	1	6
Arabic/North African Heritage	0	3	3
White/Caucasian/European	222	118	340
White - Mixed Race	10	1	11

End points

End points reporting groups

Reporting group title	Retapamulin ointment, 1% (weight/weight) plus oral placebo
Reporting group description:	
Retapamulin ointment was administered topically twice daily (BID) for 5 days. The ointment formulation was to be applied to the infected lesion(s) at a dose of approximately 10 milligrams (mg) per centimeter squared (cm ²). Placebo was to be dosed, depending on participant age, either BID or three times a day (TID) for 10 days. Placebo oral suspension and oral tablet were formulated to appear identical to the linezolid formulations. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg placebo tablets, pediatric participants 5 to 11 years of age were dosed with oral suspension at 0.5 milliliters (ml)/kilogram (kg) BID, and pediatric participants less than 5 years of age were dosed with oral suspension at 0.5 ml/kg TID.	
Reporting group title	Linezolid plus placebo ointment
Reporting group description:	
Linezolid was to be dosed, depending on participant age, either BID or TID for 10 days. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg tablets for 10 days. Pediatric participants who were 5-11 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg BID for 10 days. Pediatric participants who were < 5 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg TID for 10 days. Placebo ointment was administered topically BID for 5 days.	

Primary: Number of participants achieving clinical response at follow-up who had methicillin-resistant Staphylococcus aureus (MRSA) as a baseline pathogen

End point title	Number of participants achieving clinical response at follow-up who had methicillin-resistant Staphylococcus aureus (MRSA) as a baseline pathogen
End point description:	
Follow-up is defined as 7-9 days post-therapy: Day 12-14 for retapamulin; Day 17-19 for linezolid. Clinical success at follow-up was defined as the resolution of clinically meaningful signs and symptoms of infection recorded at baseline, including a pus/exudate skin infection rating scale (SIRS) score of "0." The SIRS is used by the investigator to evaluate infected lesions. Scores on the SIRS range from 0 (absent) to 6 (severe). Intent-to-Treat MRSA (ITTMRSA) Population: all randomized participants who took at least one dose of study medication and who had an MRSA isolated at baseline.	
End point type	Primary
End point timeframe:	
7-9 days post-therapy; Day 12-14 for retapamulin and Day 17-19 for linezolid	

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72 ^[1]	38 ^[2]		
Units: participants	41	32		

Notes:

[1] - Intent-to-Treat MRSA (ITTMRSA) Population.

[2] - Intent-to-Treat MRSA (ITTMRSA) Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Linezolid plus placebo ointment v Retapamulin ointment, 1% (weight/weight) plus oral placebo
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	percentage of participants
Point estimate	56.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	45.5
upper limit	68.4

Statistical analysis title	Statistical analysis 2
Comparison groups	Retapamulin ointment, 1% (weight/weight) plus oral placebo v Linezolid plus placebo ointment
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percentage of participants
Point estimate	84.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	72.6
upper limit	95.8

Secondary: Number of participants achieving microbiological response (MR) at follow-up (FU) who had MRSA as a baseline pathogen (BP)

End point title	Number of participants achieving microbiological response (MR) at follow-up (FU) who had MRSA as a baseline pathogen (BP)
End point description:	
MR was defined as microbiological success if, (1) for participants (par.) whose clinical outcome at end of therapy (EOT) was "clinical success (CS)/improvement," the BP was eradicated/presumed to be eradicated at EOT, or the BP was present at EOT and absent at FU, or the BP was eradicated/presumed to be eradicated at EOT, or the BP was present at EOT and par. was a "CS" such that no culture was obtained due to lack of culturable material secondary to adequate clinical response; or (2) a pathogen not previously identified at baseline was isolated at FU in a par. identified at FU as a "CS." Intent-to-Treat MRSA (ITTMRSA) Population: all randomized participants who took at least one dose of study medication and who had an MRSA isolated at baseline.	
End point type	Secondary
End point timeframe:	
7-9 days post-therapy; Day 12-14 for retapamulin and Day 17-19 for linezolid	

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72 ^[3]	38 ^[4]		
Units: participants	41	32		

Notes:

[3] - Intent-to-Treat MRSA (ITTMRSA) Population.

[4] - Intent-to-Treat MRSA (ITTMRSA) Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical response at follow-up

End point title	Number of participants with clinical response at follow-up
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End point description:

Follow-up is defined as 7-9 days post-therapy: Day 12-14 for retapamulin; Day 17-19 for linezolid. Clinical success at follow-up was defined as the resolution of clinically meaningful signs and symptoms of infection recorded at baseline, including a pus/exudate skin infection rating scale (SIRS) score of "0." The SIRS is used by the investigator to evaluate infected lesions. Scores on the SIRS range from 0 (absent) to 6 (severe). Intent-to-Treat Clinical (ITTC) Population: all randomized participants (par.) who took at least one dose of study medication. One par. was randomized to retapamulin but received linezolid. This par. is summarized in the linezolid group for all baseline and safety tables, but is summarized in the retapamulin group for all efficacy tables.

End point type	Secondary
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End point timeframe:

7-9 days post-therapy; Day 12-14 for retapamulin and Day 17-19 for linezolid

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267 ^[5]	137 ^[6]		
Units: participants	161	112		

Notes:

[5] - One par. was randomized to retapamulin but received linezolid; therefore, n=268.

[6] - One par. was randomized to retapamulin but received linezolid; therefore, n=136.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who achieved microbiological response (MR) at follow-up (FU) who had a baseline pathogen (BP)

End point title	Number of participants who achieved microbiological response (MR) at follow-up (FU) who had a baseline pathogen (BP)
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End point description:

MR was defined as microbiological success if, (1) for participants (par.) whose clinical outcome at end of therapy (EOT) was "clinical success (CS)/improvement," the BP was eradicated/presumed to be

eradicated at EOT, or the BP was present at EOT and absent at FU, or the BP was eradicated/presumed to be eradicated at EOT, or the BP was present at EOT and par. was a "CS" such that no culture was obtained due to lack of culturable material secondary to adequate clinical response; or (2) a pathogen not previously identified at baseline was isolated at FU in a par. identified at FU as a "CS." Intent-to-Treat Bacteriology (ITTb) Population: all randomized participants who took at least one dose of study medication and who had a pathogen isolated at base line .

End point type	Secondary
End point timeframe:	
7-9 days post-therapy; Day 12-14 for retapamulin and Day 17-19 for linezolid	

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177 ^[7]	78 ^[8]		
Units: participants	100	65		

Notes:

[7] - Intent-to-Treat Bacteriology (ITTb) Population.

[8] - Intent-to-Treat Bacteriology (ITTb) Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated clinical (clin.) outcome at the end of therapy (EOT) who had MRSA as a baseline (BL) pathogen

End point title	Number of participants with the indicated clinical (clin.) outcome at the end of therapy (EOT) who had MRSA as a baseline (BL) pathogen
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End point description:

Clin. improvement (imp.)=imp. of signs/symptoms (S/S) of infection recorded at BL to such an extent that no further antimicrobial therapy is necessary. Clin. failure (CF)=insufficient imp./deterioration of S/S of the infection recorded at BL, such that additional antibiotic therapy is required. Clin. success at follow-up (FU)=resolution of clinically meaningful S/S of infection recorded at BL, including a pus/exudate SIRS score of "0." Unable to determine (UTD)=refusal to consent to a clin. examination, lost to FU. Participants who are "CF"/"UTD" at EOT are considered such at FU as well.

End point type	Secondary
End point timeframe:	
2-4 days post-therapy; Day 7-9 for retapamulin and Day 12-14 for linezolid	

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72 ^[9]	38 ^[10]		
Units: participants				
Clinical success	20	28		

Clinical improvement	42	9		
Clinical failure	8	1		
Unable to determine	2	0		

Notes:

[9] - ITTMRSA Population

[10] - ITTMRSA Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated microbiological outcome at the end of therapy who had MRSA as a baseline (BL) pathogen

End point title	Number of participants with the indicated microbiological outcome at the end of therapy who had MRSA as a baseline (BL) pathogen
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End point description:

Eradication is the elimination of BL pathogens. Presumed eradication and presumed improvement are clinical outcomes of success or improvement, respectively, such that no culture was obtained due to lack of culturable material, secondary to adequate clinical response, and is documented in the electronic Case Report Form. Persistence is defined as BL pathogens still being present. Presumed persistence is defined as a participant that is a clinical failure with no obtained culture. "Unable to determine" was used if no determination of BL pathogen microbiological response could be made.

End point type	Secondary
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End point timeframe:

2-4 days post-therapy; Day 7-9 for retapamulin and Day 12-14 for linezolid

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72 ^[11]	38 ^[12]		
Units: participants				
Eradication	1	0		
Presumed eradication	20	28		
Presumed improvement	42	9		
Persistence	4	1		
Presumed persistence	4	0		
Unable to determine	1	0		

Notes:

[11] - ITTMRSA Population

[12] - ITTMRSA Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated clinical (clin.) outcome at the end of therapy (EOT)

End point title	Number of participants with the indicated clinical (clin.) outcome at the end of therapy (EOT)
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End point description:

Clin. improvement (imp.)=imp. of signs/symptoms (S/S) of infection recorded at BL to such an extent that no further antimicrobial therapy is necessary. Clin. failure (CF)=insufficient imp./deterioration of S/S of the infection recorded at BL, such that additional antibiotic therapy is required. Clin. success at follow-up (FU)=resolution of clinically meaningful S/S of infection recorded at BL, including a pus/exudate SIRS score of "0." Unable to determine (UTD)=refusal to consent to a clin. examination, lost to FU. Participants who are "CF"/"UTD" at EOT are considered such at FU as well. ITTC Population. One par. was randomized to retapamulin but received linezolid. This par. is summarized in the linezolid group for all baseline and safety tables, but is summarized in the retapamulin group for all efficacy tables.

End point type	Secondary
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End point timeframe:

2-4 days post-therapy; Day 7-9 for retapamulin and Day 12-14 for linezolid

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267 ^[13]	137 ^[14]		
Units: participants				
Clinical success	92	96		
Clinical improvement	155	34		
Clinical failure	16	4		
Unable to determine	5	2		

Notes:

[13] - One par. was randomized to retapamulin but received linezolid; therefore, n=268.

[14] - One par. was randomized to retapamulin but received linezolid; therefore, n=136.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of baseline pathogens with the indicated microbiological outcome at the end of therapy

End point title	Number of baseline pathogens with the indicated microbiological outcome at the end of therapy
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End point description:

Eradication is the elimination of BL pathogens. Presumed eradication and presumed improvement are clinical outcomes of success or improvement, respectively, such that no culture was obtained due to lack of culturable material, secondary to adequate clinical response, and is documented in the electronic Case Report Form. Persistence is defined as BL pathogens still being present. Presumed persistence is defined as a participant that is a clinical failure with no obtained culture. "Unable to determine" was used if no determination of BL pathogen microbiological response could be made.

End point type	Secondary
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End point timeframe:

2-4 days post-therapy; Day 7-9 for retapamulin and Day 12-14 for linezolid

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177 ^[15]	78 ^[16]		
Units: pathogens				
Eradication	2	1		
Presumed eradication	63	70		
Presumed improvement	120	21		
Persistence	7	1		
Presumed persistence	9	1		
Unable to determine	1	0		

Notes:

[15] - ITTB Population

[16] - ITTB Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with therapeutic response at follow-up

End point title	Number of participants with therapeutic response at follow-up
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End point description:

Therapeutic response is defined as the combined clinical and microbiological response. Therapeutic response is a measure of the overall efficacy response, and a therapeutic success refers to participants who had been deemed both a "clinical success" and a "microbiological success." All other combinations (other than "clinical success" + "microbiological success") were deemed failures for therapeutic response.

End point type	Secondary
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End point timeframe:

7-9 days post-therapy; Day 12-14 for retapamulin and Day 17-19 for linezolid

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177 ^[17]	78 ^[18]		
Units: participants	100	65		

Notes:

[17] - ITTB Population

[18] - ITTB Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean scores on the Skin Infection Rating Scale at Visits 1, 2, 3, 4, and 5

End point title	Mean scores on the Skin Infection Rating Scale at Visits 1, 2, 3, 4, and 5
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End point description:

The investigator evaluated skin infections by grading the infected lesion for exudate (a fluid that leaks out of blood vessels into surrounding tissue)/pus, crusting, erythema (redness of the skin)/inflammation (E/I), tissue warmth, tissue edema (swelling), itching, and pain, according to the Skin Infection Rating Scale. All parameters were graded on a scale of 0 (absent) to 6 (severe). The total score is calculated by summing the individual scores from the 7 parameters; the total score ranges from 0 to 42. ITTC Population. Only participants with non-missing Skin Infection Rating Scale scores were included in this analysis. One par. was randomized to retapamulin but received linezolid. This par. is summarized in the linezolid group for all baseline and safety tables, but is summarized in the retapamulin group for all efficacy tables.

End point type	Secondary
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End point timeframe:

Visits 1 (Day 1), 2 (Day 3-4), 3 (Day 7-9), 4 (Day 12-14), and 5 (Day 17-19)

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267 ^[19]	137 ^[20]		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Pus/exudate, Visit 1, n=268, 136	3.6 (± 0.82)	3.6 (± 0.8)		
Pus/exudate, Visit 2, n=265, 135	1.7 (± 1.37)	1.4 (± 1.25)		
Pus/exudate, Visit 3, n=255, 130	0.6 (± 1.05)	0.4 (± 0.74)		
Pus/exudate, Visit 4, n=237, 125	0.2 (± 0.59)	0.1 (± 0.34)		
Pus/exudate, Visit 5, n=238, 122	0.1 (± 0.39)	0 (± 0.29)		
Crusting, Visit 1, n=268, 136	2.2 (± 1.48)	2.1 (± 1.49)		
Crusting, Visit 2, n=265, 135	1.3 (± 1.21)	1.2 (± 1.15)		
Crusting, Visit 3, n=255, 130	0.9 (± 1.08)	0.8 (± 0.91)		
Crusting, Visit 4, n=237, 125	0.6 (± 0.95)	0.5 (± 0.83)		
Crusting, Visit 5, n=238, 122	0.3 (± 0.59)	0.3 (± 0.73)		
E/I, Visit 1, n=268, 136	3.4 (± 1.09)	3.4 (± 1.08)		
E/I, Visit 2, n=265, 135	2.2 (± 1.19)	2.2 (± 1.26)		
E/I, Visit 3, n=255, 130	1.1 (± 1.15)	1 (± 0.93)		
E/I, Visit 4, n=237, 125	0.5 (± 0.69)	0.5 (± 0.73)		
E/I, Visit 5, n=238, 122	0.2 (± 0.54)	0.2 (± 0.54)		
Tissue warmth, Visit 1, n=268, 136	2.8 (± 1.33)	2.6 (± 1.29)		
Tissue warmth, Visit 2, n=265, 135	1.4 (± 1.22)	1.3 (± 1.22)		
Tissue warmth, Visit 3, n=255, 130	0.6 (± 0.97)	0.4 (± 0.69)		
Tissue warmth, Visit 4, n=237, 125	0.1 (± 0.41)	0.1 (± 0.34)		
Tissue warmth, Visit 5, n=238, 122	0.1 (± 0.38)	0 (± 0.2)		
Tissue edema, Visit 1, n=268, 136	2.8 (± 1.24)	2.7 (± 1.3)		
Tissue edema, Visit 2, n=265, 135	1.6 (± 1.23)	1.5 (± 1.19)		
Tissue edema, Visit 3, n=255, 130	0.7 (± 1.02)	0.7 (± 0.86)		
Tissue edema, Visit 4, n=237, 125	0.3 (± 0.6)	0.2 (± 0.55)		
Tissue edema, Visit 5, n=238, 122	0.1 (± 0.35)	0.1 (± 0.36)		
Itching, Visit 1, n=268, 136	1.6 (± 1.51)	1.8 (± 1.51)		
Itching, Visit 2, n=265, 135	1 (± 1.27)	0.9 (± 1.11)		
Itching, Visit 3, n=255, 130	0.7 (± 1.24)	0.6 (± 1.08)		
Itching, Visit 4, n=237, 125	0.3 (± 0.79)	0.4 (± 0.76)		

Itching, Visit 5, n=238, 122	0.1 (± 0.42)	0.2 (± 0.66)		
Pain, Visit 1, n=268, 136	3.2 (± 1.57)	3 (± 1.65)		
Pain, Visit 2, n=265, 135	1.5 (± 1.56)	1.2 (± 1.39)		
Pain, Visit 3, n=255, 130	0.6 (± 1.14)	0.4 (± 0.96)		
Pain, Visit 4, n=237, 125	0.2 (± 0.6)	0.1 (± 0.56)		
Pain, Visit 5, n=238, 122	0.1 (± 0.39)	0.1 (± 0.45)		
Total score, Visit 1, n=268, 136	19.5 (± 5.69)	19.2 (± 5.56)		
Total score, Visit 2, n=265, 135	10.7 (± 6.78)	9.7 (± 6.32)		
Total score, Visit 3, n=255, 130	5.2 (± 5.83)	4.1 (± 4.16)		
Total score, Visit 4, n=237, 125	3.6 (± 6.13)	2.5 (± 4.13)		
Total score, Visit 5, n=238, 122	2.5 (± 6.14)	1.6 (± 3.92)		

Notes:

[19] - One par. was randomized to retapamulin but received linezolid; therefore, n=268.

[20] - One par. was randomized to retapamulin but received linezolid; therefore, n=136.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean wound size at Visits 1, 2, 3, 4, and 5

End point title	Mean wound size at Visits 1, 2, 3, 4, and 5
End point description:	
Lesion sized was measured in centimeters squared at Visits 1, 2, 3, 4, and 5. ITTC Population. Only participants with non-missing data were included in this analysis. One par. was randomized to retapamulin but received linezolid. This par. is summarized in the linezolid group for all baseline and safety tables, but is summarized in the retapamulin group for all efficacy tables.	
End point type	Secondary
End point timeframe:	
Visits 1 (Day 1), 2 (Day 3-4), 3 (Day 7-9), 4 (Day 12-14), and 5 (Day 17-19)	

End point values	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267 ^[21]	137 ^[22]		
Units: centimeters squared (cm ²)				
arithmetic mean (standard deviation)				
Visit 1, n=268, 136	7.942 (± 13.3124)	5.62 (± 9.6215)		
Visit 2, n=265, 135	4.963 (± 8.5492)	4.115 (± 9.4305)		
Visit 3, n=255, 130	3.27 (± 10.8663)	1.776 (± 6.7537)		
Visit 4, n=237, 125	1.556 (± 5.2201)	0.812 (± 3.4217)		
Visit 5, n=237, 122	0.741 (± 3.5977)	0.588 (± 3.3623)		

Notes:

[21] - One par. was randomized to retapamulin but received linezolid; therefore, n=268.

[22] - One par. was randomized to retapamulin but received linezolid; therefore, n=136

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All on-treatment serious adverse events (SAEs) and non-serious AEs were collected from the start of study treatment day 1 and until the follow-up visit day 19.

Adverse event reporting additional description:

Serious adverse events and non-serious adverse events were collected in the Intent-to-Treat Clinical (ITTC) Population, comprised of all randomized participants who took at least one dose of study medication.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Retapamulin ointment, 1% (weight/weight) plus oral placebo
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Reporting group description:

Retapamulin ointment was administered topically twice daily (BID) for 5 days. The ointment formulation was to be applied to the infected lesion(s) at a dose of approximately 10 milligrams (mg) per centimeter squared (cm²). Placebo was to be dosed, depending on participant age, either BID or three times a day (TID) for 10 days. Placebo oral suspension and oral tablet were formulated to appear identical to the linezolid formulations. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg placebo tablets, pediatric participants 5 to 11 years of age were dosed with oral suspension at 0.5 milliliters (ml)/kilogram (kg) BID, and pediatric participants less than 5 years of age were dosed with oral suspension at 0.5 ml/kg TID.

Reporting group title	Linezolid plus placebo ointment
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Reporting group description:

Linezolid was to be dosed, depending on participant age, either BID or TID for 10 days. Adolescent and adult participants (≥ 12 years of age) were dosed BID with 600 mg tablets for 10 days. Pediatric participants who were 5-11 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg BID for 10 days. Pediatric participants who were < 5 years of age were dosed with a 100 mg/5 ml oral suspension at a dose of 10 mg/kg TID for 10 days. Placebo ointment was administered topically BID for 5 days.

Serious adverse events	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 267 (1.12%)	3 / 137 (2.19%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 267 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Cellulitis			
subjects affected / exposed	2 / 267 (0.75%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 267 (0.37%)	0 / 137 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 267 (0.00%)	1 / 137 (0.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Retapamulin ointment, 1% (weight/weight) plus oral placebo	Linezolid plus placebo ointment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 267 (4.87%)	22 / 137 (16.06%)	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	8 / 267 (3.00%)	16 / 137 (11.68%)	
occurrences (all)	8	16	
Nausea			
subjects affected / exposed	6 / 267 (2.25%)	10 / 137 (7.30%)	
occurrences (all)	6	10	

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