Clinical trial results:
A Phase 3 Randomized, Active-comparator-controlled Clinical Trial to Study the Safety and Efficacy of MK-1986 (Tedizolid Phosphate) and Comparator in Subjects from Birth to less than 12 Years of Age with Acute Bacterial Skin and Skin Structure Infections (ABSSSI)

Summary

EudraCT number	2016-003884-20
Trial protocol	Outside EU/EEA DE PL BG LT LV
Global end of trial date	13 September 2023

Results information

Result version number	v1 (current)
This version publication date	13 March 2024
First version publication date	13 March 2024

Trial information

Trial identification

Sponsor protocol code	MK-1986-018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03176134
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001379-PIP01-12
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	06 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2023
Global end of trial reached?	Yes
Global end of trial date	13 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the safety, tolerability, and efficacy of tedizolid phosphate (MK-1986) compared with comparator antibacterial agent in participants from birth to less than 12 years of age with acute bacterial skin and skin structure infections (ABSSSI).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 42
Country: Number of subjects enrolled	Georgia: 11
Country: Number of subjects enrolled	Guatemala: 12
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Lithuania: 2
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	South Africa: 11
Country: Number of subjects enrolled	Türkiye: 1
Country: Number of subjects enrolled	Ukraine: 14
Worldwide total number of subjects	100
EEA total number of subjects	45

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)	20
Children (2-11 years)	80
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:

This study was conducted at 20 centers in 14 countries. No participants were enrolled for Cohort 4: Tedizolid phosphate (Birth to <28 Days Neonates) and Cohort 4: Comparator (Birth to <28 Days Term & preterm neonates).

Pre-assignment

Screening details:

101 participants were screened and 100 received treatment. Subjects were randomized in a 3:1 ratio to tedizolid phosphate (intravenous [IV] and/or oral suspension) or comparator (IV and/or oral dosage form). Subjects are stratified by age group, with dose level determined by weight.

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Tedizolid phosphate 6 to <12 Years

Arm description:

Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.

Arm type	Experimental
Investigational medicinal product name	Tedizolid Phosphate IV solution or oral suspension
Investigational medicinal product code	
Other name	MK-1986, TR-701 FA
Pharmaceutical forms	Powder for oral suspension, Powder for injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Once-daily, single 200-mg dose (subjects with body weight ≥50 kg), for 6 to 10 days OR twice-daily (q12h) 2 mg /kg doses (subjects with body weight ≥30 to <50 kg), for 6 to 10 days OR twice-daily (q12h) 2.5 mg /kg doses (subjects with body weight 3.2 to <30 kg), for 6 to 10 days.

Arm title	Cohort 1: Comparator 6 to <12 Years

Arm description:

Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.

Arm type	Active comparator
Investigational medicinal product name	Vancomycin IV, linezolid IV or oral (outside European Union only), clindamycin IV or oral, flucloxacillin IV or oral, cefazolin IV, or cephalexin oral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Powder for injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Vancomycin: 10 mg/kg with goal trough level of 10 to 15 mcg/mL every 6 to 8 hours, for 10 to 14 days OR

Cephazolin (Cefazolin): 50 or 100 mg/kg/day (up to 1,000 mg/dose) OR

Linezolid: 10 mg/kg/dose (up to maximum dose 600 mg) OR

Clindamycin: IV: 30 mg/kg/day (up to 600 mg/dose), Oral: 30 mg/kg/day (up to 450 mg/dose) OR

Flucloxacillin: IV: 125 to 250 mg (2 to 10 years) or 62.5 to 125 mg (<2 years), Oral: 125 mg (2 to 10 years) or 62.5 mg (<2 years) OR

Cephalexin (Cefalexin): 25 to 50 mg/kg/day (up to 500 mg/dose).

Arm title	Cohort 2: Tedizolid phosphate 2 to <6 Years

Arm description:

Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.

Arm type	Experimental
Investigational medicinal product name	Tedizolid phosphate IV solution or oral suspension
Investigational medicinal product code	
Other name	MK-1986, TR-701 FA
Pharmaceutical forms	Powder for oral suspension, Powder for injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Once-daily, single 200-mg dose (subjects with body weight ≥50 kg), for 6 to 10 days OR twice-daily (q12h) 2 mg /kg doses (subjects with body weight ≥30 to <50 kg), for 6 to 10 days OR twice-daily (q12h) 2.5 mg /kg doses (subjects with body weight 3.2 to <30 kg), for 6 to 10 days.

Arm title	Cohort 2: Comparator 2 to <6 Years

Arm description:

Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.

Arm type	Active comparator
Investigational medicinal product name	Vancomycin IV, linezolid IV or oral (outside European Union only), clindamycin IV or oral, flucloxacillin IV or oral, cefazolin IV, or cephalexin oral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Powder for injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Vancomycin: 10 mg/kg with goal trough level of 10 to 15 mcg/mL every 6 to 8 hours, for 10 to 14 days OR Cephazolin (Cefazolin): 50 or 100 mg/kg/day (up to 1,000 mg/dose) OR Linezolid: 10 mg/kg/dose (up to maximum dose 600 mg) OR Clindamycin: IV: 30 mg/kg/day (up to 600 mg/dose), Oral: 30 mg/kg/day (up to 450 mg/dose) OR Flucloxacillin: IV: 125 to 250 mg (2 to 10 years) or 62.5 to 125 mg (<2 years), Oral: 125 mg (2 to 10 years) or 62.5 mg (<2 years) OR Cephalexin (Cefalexin): 25 to 50 mg/kg/day (up to 500 mg/dose).

Arm title	Cohort 3: Tedizolid phosphate 28 Days to <2 Years

Arm description:

Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.

Arm type	Experimental
Investigational medicinal product name	Tedizolid phosphate IV solution or oral suspension
Investigational medicinal product code	
Other name	MK-1986, TR-701 FA
Pharmaceutical forms	Powder for oral suspension, Powder for injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Once-daily, single 200-mg dose (subjects with body weight ≥50 kg), for 6 to 10 days OR twice-daily (q12h) 2 mg /kg doses (subjects with body weight ≥30 to <50 kg), for 6 to 10 days OR twice-daily (q12h) 2.5 mg /kg doses (subjects with body weight 3.2 to <30 kg), for 6 to 10 days.

Arm title	Cohort 3: Comparator 28 Days to <2 Years

Arm description:

Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.

Arm type	Active comparator
Investigational medicinal product name	Vancomycin IV, linezolid IV or oral (outside European Union only), clindamycin IV or oral, flucloxacillin IV or oral, cefazolin IV, or cephalexin oral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral suspension, Powder for injection
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Vancomycin: 10 mg/kg with goal trough level of 10 to 15 mcg/mL every 6 to 8 hours, for 10 to 14 days OR Cephazolin (Cefazolin): 50 or 100 mg/kg/day (up to 1,000 mg/dose) OR Linezolid: 10 mg/kg/dose (up to maximum dose 600 mg) OR Clindamycin: IV: 30 mg/kg/day (up to 600 mg/dose), Oral: 30 mg/kg/day (up to 450 mg/dose) OR Flucloxacillin: IV: 125 to 250 mg (2 to 10 years) or 62.5 to 125 mg (<2 years), Oral: 125 mg (2 to 10 years) or 62.5 mg (<2 years) OR Cephalexin (Cefalexin): 25 to 50 mg/kg/day (up to 500 mg/dose).

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Per protocol, the only role blinded in this study was the assessor.

Number of subjects in period 1	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years
Started	44	15	16
Completed	42	13	14
Not completed	2	2	2
Withdrawal by Parent/Guardian	2	-	2
Lost to follow-up	-	2	-

Number of subjects in period 1	Cohort 2: Comparator 2 to <6 Years	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years
Started	5	15	5
Completed	5	15	5
Not completed	0	0	0
Withdrawal by Parent/Guardian	-	-	-
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Tedizolid phosphate 6 to <12 Years
Reporting group description:	
Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.	
Reporting group title	Cohort 1: Comparator 6 to <12 Years
Reporting group description:	
Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.	
Reporting group title	Cohort 2: Tedizolid phosphate 2 to <6 Years
Reporting group description:	
Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.	
Reporting group title	Cohort 2: Comparator 2 to <6 Years
Reporting group description:	
Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.	
Reporting group title	Cohort 3: Tedizolid phosphate 28 Days to <2 Years
Reporting group description:	
Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.	
Reporting group title	Cohort 3: Comparator 28 Days to <2 Years
Reporting group description:	
Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.	

Reporting group values	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years
Number of subjects	44	15	16
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	44	15	16
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	8.5	9.2	3.1
standard deviation	± 1.7	± 1.4	± 1.1
Gender Categorical Units: Participants			
Female	16	8	8

Male	28	7	8

Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Black or African American	0	0	1
Multiple	3	0	2
White	41	15	13
Ethnicity Units: Subjects			
Hispanic or Latino	6	2	5
Not Hispanic or Latino	38	13	11

Reporting group values	Cohort 2: Comparator 2 to <6 Years	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years
Number of subjects	5	15	5
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	15	5
Children (2-11 years)	5	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	3.4	0.9	1.0
standard deviation	± 1.1	± 0.2	± 0.1
Gender Categorical Units: Participants			
Female	2	11	2
Male	3	4	3
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Black or African American	0	9	1
Multiple	1	1	1
White	4	4	3
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	1
Not Hispanic or Latino	4	13	4

Reporting group values	Total		
Number of subjects	100		

Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	20		
Children (2-11 years)	80		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Participants			
Female	47		
Male	53		
Race Units: Subjects			
American Indian or Alaska Native	1		
Black or African American	11		
Multiple	8		
White	80		
Ethnicity Units: Subjects			
Hispanic or Latino	17		
Not Hispanic or Latino	83		

End points

End points reporting groups

Reporting group title	Cohort 1: Tedizolid phosphate 6 to <12 Years
Reporting group description:	
Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.	
Reporting group title	Cohort 1: Comparator 6 to <12 Years
Reporting group description:	
Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.	
Reporting group title	Cohort 2: Tedizolid phosphate 2 to <6 Years
Reporting group description:	
Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.	
Reporting group title	Cohort 2: Comparator 2 to <6 Years
Reporting group description:	
Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.	
Reporting group title	Cohort 3: Tedizolid phosphate 28 Days to <2 Years
Reporting group description:	
Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.	
Reporting group title	Cohort 3: Comparator 28 Days to <2 Years
Reporting group description:	
Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.	

Primary: Number of participants with ≥1 adverse events (AEs)

End point title	Number of participants with ≥1 adverse events (AEs)[1]
End point description:	
An AE was any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an adverse event. The number of participants with one or more AEs were reported. All randomized participants who received at least 1 dose of study intervention according to the study intervention they received were assessed.	
End point type	Primary
End point timeframe:	
Up to approximately day 35	

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 between-arm statistical comparisons were planned for this endpoint.

End point values	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years	Cohort 2: Comparator 2 to <6 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	15	16	5
Units: Number of participants	7	2	7	2

End point values	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	5		
Units: Number of participants	7	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants discontinuing from study therapy due to AEs

End point title	Number of participants discontinuing from study therapy due to AEs[2]

End point description:

An AE was any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The number of participants discontinued from the study due to an AE were reported. All randomized participants who received at least 1 dose of study intervention according to the study intervention they received were assessed.

End point type	Primary

End point timeframe:

Up to approximately day 15

Notes:

[2] - 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 between-arm statistical comparisons were planned for this endpoint.

End point values	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years	Cohort 2: Comparator 2 to <6 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	15	16	5
Units: Number of participants	0	0	0	0

End point values	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	5		
Units: Number of participants	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with hematopoietic cytopenias

End point title	Number of participants with hematopoietic cytopenias[3]

End point description:

A standardized MedDRA query for hematopoietic cytopenia was conducted. The number of participants with a hematopoietic cytopenia were reported. All randomized participants who received at least 1 dose of study intervention according to the study intervention they received were assessed.

End point type	Primary

End point timeframe:

Up to approximately day 35

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: No between-arm statistical comparisons were planned for this endpoint.

End point values	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years	Cohort 2: Comparator 2 to <6 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	15	16	5
Units: Number of participants	0	0	1	0

End point values	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	5		
Units: Number of participants	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical success

End point title	Number of participants with clinical success

End point description:

The investigator's assessment of clinical response were conducted at the Test of Cure (TOC) visit,

approximately 25 days after the first infusion. Clinical success was defined as 1) resolution or near-resolution of most signs and symptoms, 2) absence or near-resolution of signs of infection, and 3) no new signs, symptoms, or complications attributable to the infections (no further antibiotic therapy required for the primary lesion). The number of participants with clinical success were reported. All randomized participants were assessed.

End point type	Secondary

End point timeframe:

Up to approximately day 25

End point values	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years	Cohort 2: Comparator 2 to <6 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	15	16	5
Units: Number of participants				
Clinical success	41	13	14	5
Clinical failure/indeterminate	3	2	2	0

End point values	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	5		
Units: Number of participants				
Clinical success	15	5		
Clinical failure/indeterminate	0	0		

Statistical analyses

Statistical analysis title	Estimated Difference (%)

Statistical analysis description:

The estimated difference (Tedizolid minus Comparator group) in the clinical success rate and 95% confidence interval were calculated using the unstratified method of Miettinen and Nurminen.

Comparison groups	Cohort 1: Tedizolid phosphate 6 to <12 Years v Cohort 1: Comparator 6 to <12 Years
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Estimated Difference (%)
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	25.3

Statistical analysis title	Estimated Difference (%)
Statistical analysis description:	
The estimated difference (Tedizolid minus Comparator group) in the clinical success rate and 95% confidence interval were calculated using the unstratified method of Miettinen and Nurminen.	
Comparison groups	Cohort 2: Tedizolid phosphate 2 to <6 Years v Cohort 2: Comparator 2 to <6 Years
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Estimated Difference (%)
Point estimate	-12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.7
upper limit	3.7

Statistical analysis title	Estimated Difference (%)
Statistical analysis description:	
The estimated difference (Tedizolid minus Comparator group) in the clinical success rate and 95% confidence interval were calculated using the unstratified method of Miettinen and Nurminen.	
Comparison groups	Cohort 3: Tedizolid phosphate 28 Days to <2 Years v Cohort 3: Comparator 28 Days to <2 Years
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Estimated Difference (%)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 35 days

Adverse event reporting additional description:

All-cause mortality: all randomized participants who received at least one dose of study treatment; Safety: all randomized participants who received at least one dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Cohort 1: Tedizolid phosphate 6 to <12 Years

Reporting group description:

Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.

Reporting group title	Cohort 1: Comparator 6 to <12 Years

Reporting group description:

Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.

Reporting group title	Cohort 2: Tedizolid phosphate 2 to <6 Years

Reporting group description:

Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.

Reporting group title	Cohort 2: Comparator 2 to <6 Years

Reporting group description:

Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.

Reporting group title	Cohort 3: Tedizolid phosphate 28 Days to <2 Years

Reporting group description:

Participants received tedizolid phosphate once-daily single 200-mg dose (body weight ≥50 kg) or twice-daily 2-mg/kg doses (body weight ≥30 kg to <50 kg); or twice-daily 2.5-mg/kg doses (body weight 3.2 kg to <30 kg), by IV and/or oral suspension for 6 to 10 days.

Reporting group title	Cohort 3: Comparator 28 Days to <2 Years

Reporting group description:

Participants received comparator IV and/or oral per local standard of care for 10 to 14 days.

Serious adverse events	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Cohort 2: Comparator 2 to <6	Cohort 3: Tedizolid phosphate 28 Days	Cohort 3: Comparator 28 Days

	Years	to <2 Years	to <2 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Cohort 1: Tedizolid phosphate 6 to <12 Years	Cohort 1: Comparator 6 to <12 Years	Cohort 2: Tedizolid phosphate 2 to <6 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 44 (9.09%)	2 / 15 (13.33%)	7 / 16 (43.75%)
Investigations			
White blood cell count increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Catheter site pain			

subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Infusion site extravasation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Thrombocytosis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 44 (4.55%)	1 / 15 (6.67%)	1 / 16 (6.25%)
occurrences (all)	2	1	1
Diarrhoea			
subjects affected / exposed	1 / 44 (2.27%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 44 (2.27%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 44 (2.27%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Miliaria			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dermatitis diaper			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Nightmare			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Impetigo			

subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 44 (2.27%)	1 / 15 (6.67%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Viral diarrhoea			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 44 (0.00%)	0 / 15 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 2: Comparator 2 to <6 Years	Cohort 3: Tedizolid phosphate 28 Days to <2 Years	Cohort 3: Comparator 28 Days to <2 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	7 / 15 (46.67%)	2 / 5 (40.00%)
Investigations			
White blood cell count increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural			

complications			
Thermal burn			
subjects affected / exposed	1 / 5 (20.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Pallor			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	1 / 5 (20.00%)	0 / 15 (0.00%)	2 / 5 (40.00%)
occurrences (all)	1	0	3
Constipation			
subjects affected / exposed	1 / 5 (20.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Miliaria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Dermatitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Alopecia			

subjects affected / exposed	1 / 5 (20.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Nightmare			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 15 (6.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	0 / 5 (0.00%)	3 / 15 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 5 (20.00%)	2 / 15 (13.33%)	0 / 5 (0.00%)
occurrences (all)	2	2	0
Viral infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 15 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Viral diarrhoea			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 15 (6.67%) 1	0 / 5 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 1 / 5 (20.00%) 1	 1 / 15 (6.67%) 1	 1 / 5 (20.00%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 October 2017	AM1: Reduced minimum age to birth; clarification of minimum sample sizes in each age group.
04 July 2018	AM2: Dose adjustment, addition of excluded medications, modification of inclusion criteria (IC)/exclusion criteria (EC).
19 November 2018	AM3: Dose adjustment including modification to q12h dosing; modified extension of treatment to allow 1- 4 days of extension (not fixed at 4 days' extension); added recommendations for comparator dosing; modification of IC/EC; modification of procedures e.g. pharmacokinetic (PK) sampling to account for twice-daily dosing regimen.
12 November 2019	AM4: Dosing adjustment due to a preplanned analysis.
21 October 2020	AM5: Preplanned addition of dose levels for children 28 days to <2 years of age (Cohort 3) based on updated modeling and simulation using newly available data from ongoing studies; addition of country specific eligibility requirements; and addition of study termination criteria and data protection policies.
19 July 2021	AM6: Eliminated certain eligibility constraints and reduced the number of required in-person visits in order to improve feasibility to enroll outpatients.
05 August 2022	AM7: Added a potential interim analysis for the 2 Cohorts spanning 2 to <12 years of age in order to support a possible regulatory filing for this age group in light of the slower enrollment of children <2 years of age; reduced the sample size from 120 to 100; and revised eligibility criterion regarding allowed duration of prior antibiotic treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported