Clinical trial results:
Pharmacokinetics of a Single-dose of Dalbavancin in Preterm Neonates to Infants Ages 3 Months with Suspected or Confirmed Bacterial Infection

Summary

EudraCT number	2022-000415-32
Trial protocol	Outside EU/EEA
Global end of trial date	03 April 2019

Results information

Result version number	v1 (current)
This version publication date	21 July 2022
First version publication date	21 July 2022

Trial information

Trial identification

Sponsor protocol code	DAL-PK-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02688790
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan
Sponsor organisation address	2525 Dupont Dr., Irvine, CA, United States, 92612
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000016-PIP01-07
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	03 April 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 April 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study were:
• To evaluate the pharmacokinetic (PK) profile of a single intravenous (IV) infusion dose of dalbavancin.
• To evaluate the safety and tolerability of a single dalbavancin IV infusion.

Protection of trial subjects:

This study was conducted in conformance with the International Conference on Harmonisation (ICH) E6 guideline for good clinical practice (GCP) and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research was conducted, whichever afforded the greater protection to the individual.
At the first study visit, the study was discussed with each parent, legal guardian, or legally authorized representative (LAR), and written informed consent and privacy-related documentation were obtained in accordance with applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2016
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: 8
Worldwide total number of subjects	8
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	1
Newborns (0-27 days)	1
Infants and toddlers (28 days-23 months)	6
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: -

Pre-assignment

Screening details:

This study enrolled pediatric patients with known or suspected bacterial infection. No more than 20% of these evaluable patients were to have urinary tract infections due to Gram-positive organisms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Infants older than 28 days and less than 3 months old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.

Arm type	Experimental
Investigational medicinal product name	Dalbavancin
Investigational medicinal product code	DUR001
Other name	Dalvance for Injection
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as a single dose in a 30 minute intravenous infusion on Day 1.

Arm title	Cohort 2

Arm description:

Term neonates (gestational age ≥ 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.

Arm type	Experimental
Investigational medicinal product name	Dalbavancin
Investigational medicinal product code	DUR001
Other name	Dalvance for Injection
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered as a single dose in a 30 minute intravenous infusion on Day 1.

Arm title	Cohort 3

Arm description:

Preterm neonates (gestational age ≥ 32 to < 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.

Arm type	Experimental
Investigational medicinal product name	Dalbavancin
Investigational medicinal product code	DUR001
Other name	Dalvance for Injection
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Administered as a single dose in a 30 minute intravenous infusion on Day 1.

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	6	1	1
Completed	6	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Infants older than 28 days and less than 3 months old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	
Reporting group title	Cohort 2
Reporting group description:	
Term neonates (gestational age ≥ 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	
Reporting group title	Cohort 3
Reporting group description:	
Preterm neonates (gestational age ≥ 32 to < 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	6	1	1
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	1
Newborns (0-27 days)	0	1	0
Infants and toddlers (28 days-23 months)	6	0	0
Children (2-11 years)	0	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			
"99999" indicates not applicable			
Units: days			
arithmetic mean	49.3	6.0	23.0
standard deviation	± 15.02	± 99999	± 99999
Gender categorical Units: Subjects			
Female	4	1	1
Male	2	0	0
Race Units: Subjects			
White	5	1	1
Multiple	1	0	0

Reporting group values	Total		
Number of subjects	8		
Age categorical Units: Subjects			
In utero	0		

Preterm newborn infants (gestational age < 37 wks)	1		
Newborns (0-27 days)	1		
Infants and toddlers (28 days-23 months)	6		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
"99999" indicates not applicable			
Units: days			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	6		
Male	2		
Race			
Units: Subjects			
White	7		
Multiple	1		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Infants older than 28 days and less than 3 months old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	
Reporting group title	Cohort 2
Reporting group description:	
Term neonates (gestational age ≥ 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	
Reporting group title	Cohort 3
Reporting group description:	
Preterm neonates (gestational age ≥ 32 to < 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	

Primary: Dalbavancin Plasma Concentrations Following Single Dose Administration

End point title	Dalbavancin Plasma Concentrations Following Single Dose Administration[1]
End point description:	
End point type	Primary
End point timeframe:	
Day 1 at the end of infusion (0-5 minutes) and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion	

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: Statistical analyses were not conducted in this exploratory study.

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	1	1	
Units: µg/mL				
median (full range (min-max))				
0-5 minutes post dose	197.42 (133.82 to 236.60)	250.85 (250.85 to 250.85)	198.66 (198.66 to 198.66)	
2-6 hours post dose	106.10 (86.87 to 128.60)	120.39 (120.39 to 120.39)	130.94 (130.94 to 130.94)	
10-14 hours post dose	75.09 (61.76 to 103.74)	88.38 (88.38 to 88.38)	100.19 (100.19 to 100.19)	
20-28 hours post dose	63.89 (50.75 to 100.15)	84.45 (84.45 to 84.45)	76.87 (76.87 to 76.87)	
96-192 hours post dose	19.76 (10.98 to 29.33)	17.50 (17.50 to 17.50)	20.59 (20.59 to 20.59)	
552-744 hours post dose	1.00 (0.00 to 1.94)	2.05 (2.05 to 2.05)	1.29 (1.29 to 1.29)	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Treatment-emergent Adverse Events

End point title	Number of Participants with Treatment-emergent Adverse Events[2]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation patient administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.
A serious AE is any untoward medical occurrence that at any dose
- Resulted in death;
- Was life threatening;
- Required inpatient hospitalization or prolongation of existing hospitalization;
- Resulted in persistent or significant disability/incapacity;
- Was a congenital anomaly or birth defect.

End point type	Primary

End point timeframe:

Up to 35 days

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: Statistical analyses were not conducted in this exploratory study.

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	1	1	
Units: participants				
Treatment-emergent adverse events (TEAE)	6	0	0	
Treatment-emergent serious adverse events (TESAE)	1	0	0	
TEAE Leading to Treatment Discontinuation	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Maximum Plasma Concentration (Tmax) of Dalbavancin

End point title	Time to Maximum Plasma Concentration (Tmax) of Dalbavancin

End point description:

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion (EOI) and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	1	1	
Units: hours				
median (full range (min-max))	0.60 (0.57 to 0.67)	0.58 (0.58 to 0.58)	0.57 (0.57 to 0.57)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Dalbavancin

End point title	Maximum Plasma Concentration (Cmax) of Dalbavancin

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	1	1	
Units: µg/mL				
arithmetic mean (standard deviation)	191.58 (± 39.96)	250.85 (± 99999)	198.66 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve from Time 0 to t (AUC0-t) for Dalbavancin

End point title	Area Under the Plasma Concentration Versus Time Curve from Time 0 to t (AUC0-t) for Dalbavancin

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	1	1	
Units: h*µg/mL				
arithmetic mean (standard deviation)	9412.32 (± 2941.69)	13016.77 (± 99999)	10329.65 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Versus Time Curve from Time 0 to Infinity (AUC0-inf) for Dalbavancin

End point title	Area Under the Plasma Concentration Versus Time Curve from Time 0 to Infinity (AUC0-inf) for Dalbavancin

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	1	1	
Units: h*µg/mL				
arithmetic mean (standard deviation)	10353.37 (± 2582.47)	13380.93 (± 99999)	10536.28 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-time Curve from Time Zero to 120 Hours (AUC0-120) for Dalbavancin

End point title	Area Under the Plasma Concentration-time Curve from Time Zero to 120 Hours (AUC0-120) for Dalbavancin

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	1	1	
Units: h*µg/mL				
arithmetic mean (standard deviation)	6247.891 (± 1493.993)	7758.40 (± 99999)	6512.44 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-life (T1/2) for Dalbavancin

End point title	Terminal Elimination Half-life (T1/2) for Dalbavancin

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	1	1	
Units: hours				
arithmetic mean (standard deviation)	103.26 (± 9.14)	122.89 (± 99999)	111.20 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Total Body Clearance of Dalbavancin from Plasma (CL)

End point title	Apparent Total Body Clearance of Dalbavancin from Plasma (CL)

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	1	1	
Units: mL/h				
arithmetic mean (standard deviation)	7.74 (± 1.85)	5.04 (± 99999)	5.77 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution of Dalbavancin at Steady-state (Vss)

End point title	Volume of Distribution of Dalbavancin at Steady-state (Vss)

End point description:

"99999" indicates values that could not be calculated due to a sample size of 1.

End point type	Secondary

End point timeframe:

Day 1 at the end of infusion and between 2-6, 10-14, 20-28, 96-192, and 552-744 hours after start of infusion

End point values	Cohort 1	Cohort 2	Cohort 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	1	1	
Units: mL				
arithmetic mean (standard deviation)	1031.29 (± 156.83)	819.34 (± 99999)	831.52 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 35 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Cohort 1
Reporting group description: Infants older than 28 days and less than 3 months old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	
Reporting group title	Cohort 2
Reporting group description: Term neonates (gestational age ≥ 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	
Reporting group title	Cohort 3
Reporting group description: Preterm neonates (gestational age ≥ 32 to < 37 weeks) up to and including 28 days old received a single intravenous infusion of 22.5 mg/kg dalbavancin on Day 1.	

Serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Hydrocephalus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Necrotising colitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Fungal test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
Brachiocephalic vein thrombosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial thrombosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Left ventricular dysfunction			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Paroxysmal sympathetic hyperactivity			

subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	3	0	0
Hypothermia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Withdrawal syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			

subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bacterial tracheitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Oral hairy leukoplakia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Stoma site cellulitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Feeding intolerance			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Hypovolaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 1 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 March 2016	(1) revise the amount of blood to be collected for safety laboratory assessments; (2) correct the PK blood sampling windows for samples collected on Day 7 (± 2 days) and Day 28 (± 4 days) in terms of time in hours; (3) specify that those participants who have had laboratory evaluations conducted as part of standard of care within 72 hours of Day 1 will not be required to have an additional blood sample collected at screening for eligibility; (4) clarify that audiology ABR testing will be optional; (5) update the information to be recorded for concomitant medications in the eCRF; (6) clarify the number of participants with urinary tract infection due to Gram-positive organisms that may be enrolled; (7) clarify laboratory data will not be transferred electronically; (8) clarify the timing of the IP infusion and flushing.
09 August 2016	(1) allowing PK blood collection from the peripheral IV line (PIV), central venous catheter (CVC) or peripherally inserted central catheter (PICC) line; and (2) to clarify how dalbavancin is administered.
17 April 2018	(1) update the sponsor information; (2) reduce the required number of participants from 24 to approximately 22; (3) allow Cohorts 2 and 3 to be enrolled in parallel after 4 participants are enrolled in Cohort 1; (4) remove the hospitalization requirement; (5) clarify that urine output, and not creatinine clearance, should be used at screening to assess renal function;(6) add the email address for SAE submission; (7) add criteria for Potential Hy's law; and (8) confirm the dose of 22.5 mg/kg for Cohorts 2 and 3, based on interim population PK analysis results and safety review from 4 participants in Cohort 1.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported