Clinical trial results:
A Phase I, Open-Label, Single-Dose Study To Investigate The Pharmacokinetics, Safety, And Tolerability Of Dalbavancin In Hospitalized Children Of Age 3 Months To 11 Years Receiving Standard Intravenous Anti-Infective Treatment For Bacterial Infections

Summary

EudraCT number	2013-003227-11
Trial protocol	EE
Global end of trial date	16 April 2015

Results information

Result version number	v1 (current)
This version publication date	22 August 2018
First version publication date	22 August 2018

Trial information

Trial identification

Sponsor protocol code	DUR001-106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01946568
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allergan Pharmaceutical International Ltd
Sponsor organisation address	Clonshaugh Business & Technology Park, Coolock, Dublin, Ireland, D17 E400
Public contact	Clinical Trials Registry Team, Allergan plc, 001 8772778566, IR-CTRegistration@Allergan.com
Scientific contact	Therapeutic Area Head, Allergan plc, 001 862-261-7000, IR-CTRegistration@Allergan.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical trial was to characterize the pharmacokinetics of dalbavancin in pediatric participants of age 3 months to 11 years (inclusive) following the intravenous administration of a single dose of dalbavancin.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 August 2013
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: 36
Worldwide total number of subjects	36
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)	12
Children (2-11 years)	24
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:

Participants were treated and results were evaluated in 3 age cohorts as follows: Cohort 1: Age 6 to 11 years, inclusive Cohort 2: Age 2 to <6 years Cohort 3: Age 3 months to <2 years. To have at least 10 participants in each cohort, approximately 12 participants per cohort were planned to be enrolled.

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 3: 3 Months to <2 Years

Arm description:

Participants of age 3 months to <2 years received dalbavancin at a dose of 10 mg/kg as a 30-minute intravenous (IV) infusion.

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

Dosage and administration details:

Intravenous dalbavancin was administered at a dose of 10 mg/kg as a 30-minute IV infusion to participants to participants 3 months to <2 years of age.

Arm title	Cohort 2: 2 to 6 Years

Arm description:

Participants of age 2 years to <6 years received dalbavancin at a dose of 15-25 mg/kg as a 30-minute IV infusion.

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

Dosage and administration details:

Intravenous dalbavancin was administered at a dose of 15-25 mg/kg as a 30-minute IV infusion to participants between 2 to 6 years of age.

Arm title	Cohort 1: 6 to 11 Years

Arm description:

Participants of age 6 years to 11 years, inclusive received dalbavancin at a dose of 15 mg/kg as a 30-minute IV infusion.

Arm type	Experimental

Investigational medicinal product name	Dalbavancin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous dalbavancin was administered at a dose of 15 mg/kg as a 30-minute IV infusion (not to exceed 1000 mg) to participants between 6 to 11 years of age.

Number of subjects in period 1	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years
Started	12	13	11
Completed	10	12	10
Not completed	2	1	1
Not Treated	1	1	-
Lost to follow-up	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 3: 3 Months to <2 Years
Reporting group description:	
Participants of age 3 months to <2 years received dalbavancin at a dose of 10 mg/kg as a 30-minute intravenous (IV) infusion.	
Reporting group title	Cohort 2: 2 to 6 Years
Reporting group description:	
Participants of age 2 years to <6 years received dalbavancin at a dose of 15-25 mg/kg as a 30-minute IV infusion.	
Reporting group title	Cohort 1: 6 to 11 Years
Reporting group description:	
Participants of age 6 years to 11 years, inclusive received dalbavancin at a dose of 15 mg/kg as a 30-minute IV infusion.	

Reporting group values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years
Number of subjects	12	13	11
Age categorical Units: Subjects			
3 months to <2 Years	12	0	0
2 to <6 Years	0	13	0
6 to 11 Years	0	0	11
Age Continuous			
Here, for Cohort 3, the unit of measurement is 'months' and for cohorts 2 and 1, the unit is 'years'.			
Units: years arithmetic mean standard deviation	 10.71 ± 5.712	 3.53 ± 1.158	 9.35 ± 1.709
Sex: Female, Male Units: Subjects			
Female	2	5	2
Male	10	8	9

Reporting group values	Total		
Number of subjects	36		
Age categorical Units: Subjects			
3 months to <2 Years	12		
2 to <6 Years	13		
6 to 11 Years	11		
Age Continuous			
Here, for Cohort 3, the unit of measurement is 'months' and for cohorts 2 and 1, the unit is 'years'.			
Units: years arithmetic mean standard deviation	 -		
Sex: Female, Male Units: Subjects			
Female	9		
Male	27		

End points

End points reporting groups

Reporting group title	Cohort 3: 3 Months to <2 Years
Reporting group description:	
Participants of age 3 months to <2 years received dalbavancin at a dose of 10 mg/kg as a 30-minute intravenous (IV) infusion.	
Reporting group title	Cohort 2: 2 to 6 Years
Reporting group description:	
Participants of age 2 years to <6 years received dalbavancin at a dose of 15-25 mg/kg as a 30-minute IV infusion.	
Reporting group title	Cohort 1: 6 to 11 Years
Reporting group description:	
Participants of age 6 years to 11 years, inclusive received dalbavancin at a dose of 15 mg/kg as a 30-minute IV infusion.	

Primary: Area Under The Plasma Concentration-Time Curve From Zero To Infinity (AUC0–Inf) of Dalbavancin

End point title	Area Under The Plasma Concentration-Time Curve From Zero To Infinity (AUC0–Inf) of Dalbavancin[1]
End point description:	
Area under the concentration-time curve of the dalbavancin in plasma over the time interval from 0 extrapolated to infinity based on the population pharmacokinetic model. AUC0-inf was calculated as Dose (mg) divided by clearance (CL) in L/hr. AUC is expressed as microgram hours per milliliter (µg*hr/mL). The Pharmacokinetic analysis population comprised all treated participants who had at least 1 evaluable pharmacokinetic sample.	
End point type	Primary
End point timeframe:	
Based on plasma concentrations at 0.5 hours, 4 hours, 12 hours, 24 hours, 144 hours and 648 hours post-dose	
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: The primary objective of this study is to evaluate the safety and tolerability of dalbavancin in children and it is not powered for inferential statistical analysis.	

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: µg*hr/mL				
median (full range (min-max))	7890 (6630 to 11000)	22100 (8670 to 28800)	18200 (11500 to 24000)	

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of Dalbavancin

End point title	Maximum Observed Plasma Concentration (Cmax) of Dalbavancin[2]

End point description:

Maximum measured concentration of the dalbavancin in plasma based on the population pharmacokinetic model. Concentration is expressed as microgram per milliliter (µg/mL). The Pharmacokinetic analysis population comprised all treated participants who had at least 1 evaluable pharmacokinetic sample.

End point type	Primary

End point timeframe:

Based on plasma concentrations at 0.5 hours, 4 hours, 12 hours, 24 hours,144 hours and 648 hours post-dose

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: The primary objective of this study is to evaluate the safety and tolerability of dalbavancin in children and it is not powered for inferential statistical analysis.

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: µg/mL				
median (full range (min-max))	141 (114 to 192)	328 (221 to 443)	247 (183 to 289)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time 0 to 120 Hours Post-dose (AUC0-120) for Dalbavancin

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to 120 Hours Post-dose (AUC0-120) for Dalbavancin[3]

End point description:

Area under the concentration-time curve of the dalbavancin in plasma over the time interval from 0 up to 120 hours based on the population pharmacokinetic model. AUC is expressed as microgram hours per milliliter (µg*hr/mL). The Pharmacokinetic analysis population comprised all treated participants who had at least 1 evaluable pharmacokinetic sample.

End point type	Primary

End point timeframe:

Based on plasma concentrations at 0.5 hours, 4 hours, 12 hours, 24 hours,144 hours and 648 hours post-dose

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: The primary objective of this study is to evaluate the safety and tolerability of dalbavancin in children and it is not powered for inferential statistical analysis.

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: µg*hr/mL				
median (full range (min-max))	5120 (4090 to 6460)	12400 (7060 to 16300)	9000 (6660 to 12100)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-Time Curve From Time 0 to 648 Hours Post-dose (AUC0-648) for Dalbavancin

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to 648 Hours Post-dose (AUC0-648) for Dalbavancin[4]

End point description:

Area under the concentration-time curve of the dalbavancin in plasma from 0 to last measurable concentration. AUC is expressed as microgram hours per milliliter (µg*hr/mL). The Pharmacokinetic analysis population comprised all treated participants who had at least 1 evaluable pharmacokinetic sample.

End point type	Primary

End point timeframe:

Based on plasma concentrations at 0.5 hours, 4 hours, 12 hours, 24 hours,144 hours and 648 hours post-dose

Notes:

[4] - 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: The primary objective of this study is to evaluate the safety and tolerability of dalbavancin in children and it is not powered for inferential statistical analysis.

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: µg*hr/mL				
median (full range (min-max))	7500 (6330 to 10200)	20500 (8520 to 26500)	16300 (10800 to 21400)	

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Observed Plasma Concentration

End point title	Time to Maximum Observed Plasma Concentration[5]

End point description:

Time to Maximum Serum Concentration (Tmax) of dalbavancin based on the population pharmaokinetic model. The Pharmacokinetic analysis population comprised all treated participants who had at least 1 evaluable pharmacokinetic sample.

End point type	Primary

End point timeframe:

Based on plasma concentrations at 0.5 hours, 4 hours, 12 hours, 24 hours,144 hours and 648 hours post-dose

Notes:

[5] - 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: The primary objective of this study is to evaluate the safety and tolerability of dalbavancin in children and it is not powered for inferential statistical analysis.

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: hours				
median (full range (min-max))	0.5 (0.5 to 0.5)	0.5 (0.5 to 0.5)	0.5 (0.5 to 0.5)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Terminal Phase Elimination Half-life (T1/2) for Dalbavancin[6]

End point description:

T1/2 of dalbavancin was derived based on population pharmacokinetic model-derived individual post hoc pharmacokinetic parameters. The Pharmacokinetic analysis population comprised all treated participants who had at least 1 evaluable pharmacokinetic sample.

End point type	Primary

End point timeframe:

Based on plasma concentrations at 0.5 hours, 4 hours, 12 hours, 24 hours,144 hours and 648 hours post-dose

Notes:

[6] - 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: The primary objective of this study is to evaluate the safety and tolerability of dalbavancin in children and it is not powered for inferential statistical analysis.

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	11	11	
Units: hours				
median (full range (min-max))	279 (244 to 298)	315 (271 to 332)	390 (317 to 490)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-emergent Adverse Events

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

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation participant administered a product; the event need not necessarily have a causal relationship with the treatment or usage. An AE is considered treatment emergent if the AE starts during or after study drug administration through the last follow-up visit (Day 28). The safety population consists of participants enrolled in the study who have received any amount of the study drug.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	12	11	
Units: participants	4	9	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Abnormal Hematology and Chemistry Laboratory Values

End point title	Percentage of Participants With Abnormal Hematology and Chemistry Laboratory Values

End point description:

The percentage of participants with abnormal hematology and chemistry laboratory values that occurred in more than 1 participant are reported. Here, Laboratory abnormalities were assessed using local laboratory criteria in which ULN indicates Upper Limit of Normal and LLN is Lower Limit of Normal. The safety population consists of participants enrolled in the study who have received any amount of the study drug and were evaluable for laboratory abnormality.

End point type	Secondary

End point timeframe:

Up to Day 7

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	10	12	11	
Units: percentage of participants				
number (not applicable)				

Basophils (>1.2 x ULN)	0	0	45.5	
Eosinophil (>1.2 x ULN)	30	0	9.1	
Leukocytes (<0.6 x LLN)	0	16.7	0	
Lymphocytes (<0.6 x LLN)	0	16.7	0	
Monocytes (>1.2 x ULN)	50	8.3	9.1	
Neutrophils (<0.6 x LLN)	0	16.7	0	
Carbon dioxide (<0.9 x LLN)	20.0	25.0	9.1	
Carbon dioxide (>1.1 x ULN)	0	0	27.3	
Potassium (<0.9 x LLN)	0	25.0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Change in Vital Signs

End point title	Percentage of Participants with Change in Vital Signs

End point description:

Vital signs included supine blood pressure and pulse rate. Categorical summaries of vital signs data were reported as absolute vital signs, increases in vital signs, and decreases in vital signs. For 3 months to <2 years of age group, criteria for supine systolic BP was <80 mmHg, supine diastolic BP was <55, supine pulse rate was <80 to >120 mmHg. For 2 to <6 years of age group, criteria for supine systolic BP was <95 mmHg, supine diastolic BP was <60, supine pulse rate was <65 to >110 mmHg. For 6 to 11 years of age group, criteria for supine systolic BP was <100 mmHg, supine diastolic BP was <60, supine pulse rate was <60 to >95 mmHg. The criteria for reporting increase and decrease in supine systolic BP was >=30 and supine diastolic BP was >=20 mmHg for all age groups. The safety population consists of participants enrolled in the study who have received any amount of the study drug.

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	Cohort 3: 3 Months to <2 Years	Cohort 2: 2 to 6 Years	Cohort 1: 6 to 11 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	12	11	
Units: percentage of participants				
number (not applicable)				
Absolute Supine Systolic BP	9.1	41.7	45.5	
Absolute Supine Diastolic BP	63.6	83.3	81.8	
Absolute Supine Pulse Rate <80	0	0	0	
Absolute Supine Pulse Rate >120	100.0	91.7	72.7	
Increase in Supine Systolic BP	9.1	0	9.1	
Increase in Supine Diastolic BP	27.3	33.3	9.1	
Decrease in Supine Systolic BP	9.1	8.3	18.2	
Decrease in Supine Diastolic BP	36.4	0	45.5	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 28 days	
Adverse event reporting additional description:	
The safety population consists of participants enrolled in the study who have received any amount of the study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Cohort 3: 3 Months to <2 Years
Reporting group description:	
Participants of age 3 months to <2 years received dalbavancin at a dose of 10 mg/kg as a 30-minute intravenous (IV) infusion.	
Reporting group title	Cohort 1: 6 to 11 Years
Reporting group description:	
Participants of age 6 years to 11 years, inclusive received dalbavancin at a dose of 15 mg/kg as a 30-minute IV infusion.	
Reporting group title	Cohort 2: 2 to 6 Years
Reporting group description:	
Participants of age 2 years to <6 years received dalbavancin at a dose of 15-25 mg/kg as a 30-minute IV infusion.	

Serious adverse events	Cohort 3: 3 Months to <2 Years	Cohort 1: 6 to 11 Years	Cohort 2: 2 to 6 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	2 / 11 (18.18%)	2 / 12 (16.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	0 / 12 (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

Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device-related sepsis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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 3: 3 Months to <2 Years	Cohort 1: 6 to 11 Years	Cohort 2: 2 to 6 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	5 / 11 (45.45%)	9 / 12 (75.00%)
Investigations			
Acoustic stimulation tests abnormal			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Audiogram abnormal			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Blood pressure increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal stoma output increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Heart rate increased			

subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Leukocytosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Infusion site discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			

Hypersensitivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Chapped lips			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oral pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Acute respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Pruritus			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Dermatitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Scab			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 11 (9.09%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 11 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2013	1. 5 participants were enrolled under version 1 of protocol dated 11-April-2013. 2. No participants were enrolled under version 2.1 dated 07-November-2013. 3. Study Design was changed from all participants to be enrolled in parallel to participants in cohort 1 and 2 to be enrolled in parallel, and participants in cohort 3 to be enrolled after safety data from the other 2 cohorts had been reviewed and shared with the FDA to reflect communications from FDA requesting that enrollment in cohort 3 begin after safety data from the older cohorts were reviewed and shared with FDA. 4. Other assessments and analyses stated that interim analysis of PK and safety would be performed in approximately the first 6 evaluable participants. 5. The wording of criterion#1 was clarified in inclusion criteria which reflects that participants with urinary tract infection could be enrolled. 6. Inclusion Criterion#5 was changed to remove "normal" from the audiologic assessment and to change the time within which the audiologic assessment had to be performed from with 3 days before study drug administration to within 7 days before in order to clarify that participant may be enrolled during the 7 days before the first dose of study drug, regardless of the results of audiology assessments. This change reflects the lack of association between dalbavancin treatment and ototoxicity, but audiology assessments would continue to be performed due to previous regulatory commitment. 7. "Half-lives", treatment with an investigational drug within 30 days or 5 half-lives, whichever was longer, were removed from exclusion criterion#1 to make it more clinically relevant.
07 November 2013	8. Exclusion Criteria#2, History of fluctuant hearing; persistent tinnitus; balance disorder; otologic surgery or disease; tumor of the head, neck, or auditory system; head injury; Meniere's disease; autoimmune inner ear disease; perilymphatic fistula; CNS disorder resulting in hearing deficits; or significant noise exposure was removed because audiology assessments would provide necessary data regarding baseline and follow-up hearing for each participant. 9. Exclusion Criteria#3 significant exposure (greater than one week duration of therapy) to aminoglycoside antibiotics or chemotherapy currently or within a week prior to enrollment into the study or current use of loop diuretics was removed because there is no known drug interaction between dalbavancin and the drugs listed. Additionally, audiology assessments would provide necessary data regarding baseline and follow-up hearing for each participant. 10. Exclusion Criteria#4 was modified to clarify that participants currently receiving IV vancomycin should be excluded. The safety of dalbavancin co-administered with other glycopeptides has not been established. However, given the short half-life of vancomycin, and the likely subtherapeutic concentration of vancomycin in children, prior use of intravenous vancomycin should not prohibit the administration of dalbavancin, as long as dalbavancin is administered at least 8 hours after the last dose of vancomycin. 11. Exclusion Criteria#6, "or physical exam evidence of malnutrition" was removed to make it more clinically relevant. 12. New text, "Patients enrolled with an abnormal baseline audiology exam may be replaced if needed" was added to Overall Study Design and Plan to ensure enough evaluable participants were available for analysis.
07 November 2013	13. Table 1 was removed from Treatment Administration and "Reconstituted dalbavancin must be further diluted by addition of 5% Dextrose for Injection, USP and mixed gently (see the Pharmacy Manual)" was added. 14. In Packing and Labeling "by addition to a 250 ml infusion bag of 5% Dextrose Injection, USP" was deleted. 15. In Pharmacokinetic Sampling, proper collection of PK samples was clarified and allowed for collection of extra PK sample if needed. 16. 19 participants were enrolled under version 2.2, also dated 07-November-2013. This amendment was due to a corporate name change, from Durata Therapeutics, Inc. to Durata Therapeutics International B.V.

12 September 2014	1. 12 participants were enrolled under version 3.0. 2. Study Design was changed to add ± 2 minutes to the 30-minute dalbavancin infusion in order to maintain consistency with Pharmacy Manual. 3. Dalbavancin dose was adjusted to 10 mg/kg for participants in Cohort 3 in the study design as based on interim PK analysis, it was inferred that dose of 10 mg/kg in participants 3 months to < 2 years of age expected to provide dalbavancin exposure similar to that previously observed in clinical studies with adults. 4. Results of interim PK analysis were added in study design to support revision to dalbavancin dosing for remaining participants. 5. An exclusion criterion was added for participants diagnosed with cystic fibrosis as PK and audiology rest results more variable in cystic fibrosis participants than in other children. 6. Approximate duration of study was changed from 1.0 years, ending in June 2014, to 2.0 years, ending in October 2015 to reflect recruitment. 7. Storage time was changed for both reconstituted and diluted dalbavancin from 24 hours to 48 hours in Storage and Accountability section to maintain consistency with approved product information for dalbavancin. 8. The language was simplified regarding audiologic testing. 9. Window of ±5 minutes was added to PK sampling within 30 minutes of dalbavancin IV infusion to maintain consistency with windows for other PK sample collections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported