Clinical trial results:
A Phase 3b, Double-Blind, Multicenter, Randomised Study to Compare the Efficacy and Safety of Single Dose Dalbavancin to a Two Dose Regimen of Dalbavancin for the Treatment of Acute Bacterial Skin and Skin Structure Infections

Summary

EudraCT number	2014-000419-15
Trial protocol	LV EE HU BG HR
Global end of trial date	11 March 2015

Results information

Result version number	v1 (current)
This version publication date	19 October 2018
First version publication date	19 October 2018

Trial information

Trial identification

Sponsor protocol code	DUR001-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02127970
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 March 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the efficacy of treatment with a single dose of dalbavancin 1500 mg to treatment with a two-dose regimen of dalbavancin (1000 mg on Day 1 followed by 500 mg on Day 8) in participants with known or suspected Gram-positive acute bacterial skin and skin structure infections (ABSSSI) at 48 to 72 hours after the initiation of treatment.

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	18 April 2014
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	United States: 318
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Estonia: 13
Country: Number of subjects enrolled	Georgia: 31
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Latvia: 63
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	Russian Federation: 54
Country: Number of subjects enrolled	Serbia: 26
Country: Number of subjects enrolled	South Africa: 40
Country: Number of subjects enrolled	Ukraine: 136
Worldwide total number of subjects	698
EEA total number of subjects	93

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	608
From 65 to 84 years	88
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 698 participants were randomly assigned in a 1:1 ratio to the following treatment groups: • Single-dose dalbavancin group, received a single dose of dalbavancin intravenous (IV) on Day 1, and a matching placebo IV on Day 8. • Two-dose dalbavancin group, received dalbavancin IV on Day 1 and Day 8.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Single-Dose Dalbavancin

Arm description:

Single-dose of dalbavancin 1500 mg intravenous (IV) infusion over 30 minutes on Day 1 followed by dalbavancin-matching placebo IV infusion over 30 minutes on Day 8 for participants with creatinine clearance (CrCl) ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin dose was 1000 mg.

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

Dosage and administration details:

Participants randomised to the single-dose dalbavancin group were to receive a single dose of dalbavancin IV on Day 1 over 30 minutes as follows: 1500 mg for participants with CrCl ≥30 mL/min or with creatinine clearance (CrCl) <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin dose was 1000 mg.

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

Dosage and administration details:

Participants randomised to the single-dose dalbavancin group were to receive dalbavancin-matching placebo IV on Day 8 over 30 minutes.

Arm title	Two-Dose Dalbavancin

Arm description:

Two-dose regimen of dalbavancin 1000 mg IV infusion over 30 minutes on Day 1 followed by 500 mg IV infusion over 30 minutes on Day 8 for participants with CrCl ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin doses were 750 mg on Day 1 and 375 mg on Day 8.

Arm type	Experimental

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

Dosage and administration details:

Participants randomised to the two-dose dalbavancin group were to receive dalbavancin IV over 30 minutes as follows: 1000 mg on Day 1 and 500 mg on Day 8 for participants with CrCl ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin doses were 750 mg on Day 1 and 375 mg on Day 8.

Number of subjects in period 1	Single-Dose Dalbavancin	Two-Dose Dalbavancin
Started	349	349
Completed	323	322
Not completed	26	27
Adverse event, non-fatal	2	1
Death	1	1
Pregnancy	-	1
Lost to follow-up	14	14
Participant Withdrew Consent	5	3
Reason not Specified	4	7

Baseline characteristics

Reporting groups	
Reporting group title	Single-Dose Dalbavancin

Reporting group description:

Single-dose of dalbavancin 1500 mg intravenous (IV) infusion over 30 minutes on Day 1 followed by dalbavancin-matching placebo IV infusion over 30 minutes on Day 8 for participants with creatinine clearance (CrCl) ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin dose was 1000 mg.

Reporting group title	Two-Dose Dalbavancin

Reporting group description:

Two-dose regimen of dalbavancin 1000 mg IV infusion over 30 minutes on Day 1 followed by 500 mg IV infusion over 30 minutes on Day 8 for participants with CrCl ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin doses were 750 mg on Day 1 and 375 mg on Day 8.

Reporting group values	Single-Dose Dalbavancin	Two-Dose Dalbavancin	Total
Number of subjects	349	349	698
Age categorical Units: Subjects			
18 to 64 years	308	300	608
65 to 84 years	39	49	88
85 years and over	2	0	2
Age Continuous Units: years			
arithmetic mean	48.0	48.3	
standard deviation	± 14.83	± 14.74	-
Sex: Female, Male Units: Subjects			
Female	145	146	291
Male	204	203	407

End points

End points reporting groups

Reporting group title	Single-Dose Dalbavancin

Reporting group description:

Single-dose of dalbavancin 1500 mg intravenous (IV) infusion over 30 minutes on Day 1 followed by dalbavancin-matching placebo IV infusion over 30 minutes on Day 8 for participants with creatinine clearance (CrCl) ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin dose was 1000 mg.

Reporting group title	Two-Dose Dalbavancin

Reporting group description:

Two-dose regimen of dalbavancin 1000 mg IV infusion over 30 minutes on Day 1 followed by 500 mg IV infusion over 30 minutes on Day 8 for participants with CrCl ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin doses were 750 mg on Day 1 and 375 mg on Day 8.

Primary: Percentage of Participants Who were Clinical Responders 48-72 Hours After the Initiation of Study Drug

End point title	Percentage of Participants Who were Clinical Responders 48-72 Hours After the Initiation of Study Drug

End point description:

Clinical responder was defined as a participant who was alive and had received no rescue therapy for acute bacterial skin and skin structure infection (ABSSSI) prior to the 48-72 hour infection site assessment (if an antibiotic has been given for another reason, the participant will not be considered a non-responder for this reason); and examination of the participant's ABSSSI lesion demonstrates a decrease of ≥ 20% in lesion area (calculated as the longest length multiplied by the longest perpendicular width) relative to the baseline measurement. ITT Population included all randomized participants regardless of whether or not they received study drug.

End point type	Primary

End point timeframe:

Up to 48-72 hours after the initiation of study drug

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	349		
Units: percentage of participants				
number (not applicable)	81.4	84.2		

Statistical analyses

Statistical analysis title	Single Dose Dalbavancin vs Two Dose Dalbavancin

Statistical analysis description:

For the difference in clinical responder rates (single-dose group minus two-dose group), the 95% CI was calculated using the Miettinen and Nurminen method without adjustment.

Comparison groups	Single-Dose Dalbavancin v Two-Dose Dalbavancin

Number of subjects included in analysis	698
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.5
upper limit	2.8

Notes:

[1] - The non-inferiority hypothesis test was to be a one-sided hypothesis test performed at the 2.5% level of significance. If the lower limit of the 95% CI for the difference in responder rates is greater than -10%, then the single-dose dalbavancin regimen was to be declared non-inferior to the two dose dalbavancin regimen.

Secondary: Percentage of Participants by Clinical Status at End of Treatment (EOT) and Final Visit (FV)

End point title	Percentage of Participants by Clinical Status at End of Treatment (EOT) and Final Visit (FV)

End point description:

Clinical Success was defined as follows: For evaluation at EOT visit, lesion area must be decreased by ≥80% from baseline and at FV lesion area must be decreased by ≥90% from baseline; Temperature is ≤37.6°C; Local signs of tenderness to palpation and swelling/induration are no worse than mild; For evaluation at EOT visit, local signs of fluctuance and localized heat/warmth must be improved from baseline and no worse than mild, and at FV local signs of fluctuance and localized heat/warmth must be absent; for participants with a wound infection the severity of purulent drainage is improved and no worse than mild relative to baseline. Clinical Failure was defined as the opposite to success or if the participant died during the study period up to visit or received study therapy for ABSSSI beyond the protocol treatment period. Clinical status was Indeterminate if any of the data needed to determine clinical success or clinical failure were missing. ITT Population.

End point type	Secondary

End point timeframe:

End of Treatment (Day 14-15 after the initiation of study drug) and Final Visit (28 ±2 days after the initiation of study drug)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	349		
Units: percentage of participants				
number (not applicable)				
EOT; Clinical Success	84.0	84.8		
EOT; Clinical Failure	12.0	10.3		
EOT; Indeterminate	4.0	4.9		
FV; Clinical Success	84.5	85.1		
FV; Clinical Failure	8.0	7.2		
FV; Indeterminate	7.4	7.3		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants by Clinical Status Based on Localized Fluctuance and Heat/Warmth at End of Treatment (EOT)

End point title	Percentage of Participants by Clinical Status Based on Localized Fluctuance and Heat/Warmth at End of Treatment (EOT)

End point description:

Clinical Success was defined as localized fluctuance and heat/warmth that if present at Baseline must be improved and no worse than mild. Clinical Failure was defined as the opposite to success. Clinical status was Indeterminate if any of the data needed to determine clinical success or clinical failure were missing. ITT Population included all randomized participants regardless of whether or not they received study drug.

End point type	Other pre-specified

End point timeframe:

EOT (Day 14-15)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	349		
Units: percentage of participants				
number (not applicable)				
Clinical Success	84.8	85.4		
Clinical Failure	7.7	6.9		
Indeterminate	7.4	7.7		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants by Investigator Assessment of Clinical Outcome

End point title	Percentage of Participants by Investigator Assessment of Clinical Outcome

End point description:

A successful outcome was based on resolution or improvement of all signs and symptoms of the infection to such an extent that no further antibacterial treatment was given. An unsuccessful outcome was the opposite of successful. An Indeterminate outcome was defined as any of the data needed to determine a successful or unsuccessful outcome were missing. ITT Population included all randomized participants regardless of whether or not they received study drug. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Other pre-specified

End point timeframe:

Day 3-4, Day 8, EOT (Day 14-15) and Final Visit (Day 28 +/- 2 days)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	344		
Units: percentage of participants				
number (not applicable)				
Successful Outcome (Day 3-4)	93.4	93.0		
Unsuccessful Outcome (Day 3-4)	0.3	0.9		
Indeterminate (Day 3-4)	6.3	6.1		
Successful Outcome (Day 8)	92.2	93.3		
Unsuccessful Outcome (Day 8)	0.6	0.3		
Indeterminate (Day 8)	7.2	6.4		
Successful Outcome (EOT)	92.5	92.7		
Unsuccessful Outcome (EOT)	2.9	1.5		
Indeterminate (EOT)	4.6	5.8		
Successful Outcome (Final Visit)	90.2	91.0		
Unsuccessful Outcome (Final Visit)	2.6	1.7		
Indeterminate (Final Visit)	7.2	7.3		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants Achieving Clinical Outcome of Success Based on Key Target Pathogen at Baseline

End point title	Percentage of Participants Achieving Clinical Outcome of Success Based on Key Target Pathogen at Baseline

End point description:

A successful outcome was based on resolution or improvement of all signs and symptoms of the infection to such an extent that no further antibacterial treatment was given. Microbiological Intent-to-treat (MicroITT) Population included all ITT participants who had at least 1 Gram-positive bacterial pathogen isolated at Baseline. Here, "n" is the number of participants with data available for analysis at the given time-point.

End point type	Other pre-specified

End point timeframe:

Day 3-4 and EOT (Day 14-15)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	220		
Units: percentage of participants				
number (not applicable)				
Staphylococcus aureus (Day 3-4) (n=139, 156)	88.5	85.3		
Streptococcus agalactiae (Day 3-4) (n=6, 6)	100.0	66.7		
Streptococcus anginosus group (Day 3-4) (n=33,19)	93.9	100.0		

Streptococcus dysgalactiae (Day 3-4) (n=4,3)	100.0	100.0		
Streptococcus pyogenes (Day 3-4) (n=14, 22)	100.0	81.8		
Enterococcus faecalis (Day 3-4) (n=4,10)	100.0	80.0		
Staphylococcus aureus (EOT) (n=139,156)	87.8	91.7		
Streptococcus agalactiae (EOT) (n=6,6)	83.3	83.3		
Streptococcus anginosus group (EOT) (n=33,19)	81.8	89.5		
Streptococcus dysgalactiae (EOT) (n=4,3)	100.0	100.0		
Streptococcus pyogenes (EOT) (n=14, 22)	92.9	81.8		
Enterococcus faecalis (EOT) (n=4, 10)	100.0	100.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants With Complete Resolution of Local Signs of Infection

End point title	Percentage of Participants With Complete Resolution of Local Signs of Infection

End point description:

Resolution of Local Signs of Infection that include absence of purulence/drainage, erythema, heat/localized warmth, pain/tenderness to palpation, fluctuance, and swelling/induration. ITT Population included all randomized participants regardless of whether or not they received study drug. Here, "n" is the number of participants with data available for analysis at the given time-point.

End point type	Other pre-specified

End point timeframe:

Day 3-4, Day 8, EOT (Day 14-15) and Final Visit (Day 28 +/- 2 days)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	349		
Units: percentage of participants				
number (not applicable)				
Day 3-4 (n= 321, 324)	1.9	1.5		
Day 8 (n= 328, 329)	22.3	21.1		
EOT Visit (n= 334, 338)	56.3	56.2		
Final Visit (n= 295, 295)	85.8	89.8		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change From Baseline in Participant's Assessment of Pain

End point title	Change From Baseline in Participant's Assessment of Pain

End point description:

Using the Brief Pain Inventory Scale, participants rated their pain “right now” on a scale where: 0=no pain to 10=pain as bad as you can imagine. A negative change from Baseline indicated improvement. ITT Population included all randomized participants regardless of whether or not they received study drug. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Other pre-specified

End point timeframe:

Baseline (Day 0) to Day 3-4, Day 8, EOT (Day 14-15) and Final Visit (Day 28 + /- 2 days)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349	349		
Units: pain score				
arithmetic mean (standard deviation)				
Baseline	7.7 (± 2.09)	7.8 (± 2.12)		
Change from Baseline to Day 3-4	-3.9 (± 2.46)	-3.8 (± 2.43)		
Change from Baseline to Day 8	-5.9 (± 2.53)	-5.8 (± 2.68)		
Change from Baseline to EOT Visit	-6.9 (± 2.37)	-6.9 (± 2.53)		
Change from Baseline to Final Visit	-7.5 (± 2.19)	-7.4 (± 2.40)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants by Resource Utilization Categories

End point title	Percentage of Participants by Resource Utilization Categories

End point description:

Resource Utilization Categories included: Any additional visits (including urgent care), Any additional procedures, Any additional tests, Any home visits or nursing care and Any ER Visits. The percentage of participants in each category is reported. ITT Population included all randomized participants regardless of whether or not they received study drug. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Other pre-specified

End point timeframe:

Final Visit (Day 28 +/- 2 days)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	323	322		
Units: percentage of participants				
number (not applicable)				
Any Additional Visits (including Urgent Care)	1.2	0.6		
Any Additional Procedures	1.5	1.6		
Any Additional Tests	1.9	2.8		
Any Home Visits or Home Nursing Care	1.5	1.2		
Any ER Visits	0.3	0.9		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Participants by Skin and Soft Tissue Infection-Convenience (SSTI-C) Questionnaire: Overall Satisfaction Response

End point title	Percentage of Participants by Skin and Soft Tissue Infection-Convenience (SSTI-C) Questionnaire: Overall Satisfaction Response

End point description:

The SSTI-C Questionnaire is an 11-item self-reported questionnaire that measures subjective experiences of the participant. One of the items assessed was overall satisfaction with treatment. Participants answered the question: "Overall, how satisfied were you with your antibiotic treatment?" using one of the following responses: Extremely satisfied, Moderately satisfied, Not at all satisfied, Slightly satisfied and Very satisfied. The percentage of participants in each category is reported. ITT Population included all randomized participants regardless of whether or not they received study drug. Number analysed is the number of participants with data available for analysis at the given time-point.

End point type	Other pre-specified

End point timeframe:

EOT (Day 14-15)

End point values	Single-Dose Dalbavancin	Two-Dose Dalbavancin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	338	332		
Units: percentage of participants				
number (not applicable)				
Extremely Satisfied	53.6	56.9		
Moderately Satisfied	9.5	7.2		
Not at all Satisfied	0.9	0.9		
Slightly Satisfied	0.3	0.9		
Very Satisfied	35.8	33.7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Up to 28 Days

Adverse event reporting additional description:

The number of participants at risk for Serious Adverse Events and Adverse Events was based on the Safety Population that included all participants who received at least 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Two-Dose Dalbavancin

Reporting group description:

Two-dose regimen of dalbavancin 1000 mg IV infusion over 30 minutes on Day 1 followed by 500 mg IV infusion over 30 minutes on Day 8 for participants with CrCl ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin doses were 750 mg on Day 1 and 375 mg on Day 8.

Reporting group title	Single-Dose Dalbavancin

Reporting group description:

Single-dose of dalbavancin 1500 mg intravenous (IV) infusion over 30 minutes on Day 1 followed by dalbavancin-matching placebo IV infusion over 30 minutes on Day 8 for participants with creatinine clearance (CrCl) ≥30 mL/min or with CrCl <30 mL/min who were receiving regular hemodialysis or peritoneal dialysis. For participants with CrCl <30 mL/min who were not receiving regular hemodialysis or peritoneal dialysis, the dalbavancin dose was 1000 mg.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events occurred at a frequency of 5% or greater.

Serious adverse events	Two-Dose Dalbavancin	Single-Dose Dalbavancin	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 346 (1.45%)	7 / 349 (2.01%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Peripheral ischaemia			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vitreous haemorrhage			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 346 (0.29%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 346 (0.29%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 346 (0.29%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 346 (0.29%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			

subjects affected / exposed	1 / 346 (0.29%)	0 / 349 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin bacterial infection			
subjects affected / exposed	0 / 346 (0.00%)	2 / 349 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 346 (0.00%)	1 / 349 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Two-Dose Dalbavancin	Single-Dose Dalbavancin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 346 (0.00%)	0 / 349 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2014	1. A secondary objective was added to introduce a population PK study in order to compare the population PK profiles of a single dose of dalbavancin 1500 mg versus the two-dose regimen of dalbavancin (1000 mg on Day 1 followed by 500 mg on Day 8) in participants with ABSSSI and to estimate and compare the PK/PD relationship of each dose regimen. 2. Clinical laboratory tests were to be obtained at Baseline, Day 3-4 and at Day 14-15 or premature withdrawal instead of just baseline and Day 28. 3. Minor changes to the protocol included the option to dilute dalbavancin in glucose as well as dextrose, contact information for medical monitoring and safety purposes as well as clarification of statistical methodology.
24 November 2014	1. Clarification was made to the definition of rescue antibacterial therapy as related to the primary endpoint. 2. Clarification was provided related to the analysis populations for the secondary analyses. 3. The protocol sample size was changed from 410 participants to 698 based on the observed response rate at the interim analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported