



Clinical trial results:

A Phase 2b, Randomized, Double-Blind, Placebo-Controlled, Safety and Efficacy Trial of Multiple Dosing Regimens of ABT-719 for the Prevention of Acute Kidney Injury in Subjects Undergoing High Risk Cardiac Surgery

Summary

EudraCT number	2012-003942-33
Trial protocol	DK
Global end of trial date	07 March 2014

Results information

Result version number	v2 (current)
This version publication date	18 May 2016
First version publication date	25 July 2015
Version creation reason	• Correction of full data set potential category issues

Trial information

Trial identification

Sponsor protocol code	M13-796
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01777165
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	Abbott House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire , United Kingdom, SL6 4XE
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Ann Eldred, MD, AbbVie, ann.eldred@abbvie.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	07 March 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study objective is to compare the safety and efficacy of doses of 800 mcg/kg, 1600 mcg/kg and 2100 mcg/kg intravenous (IV) infusions of ABT-719 to placebo in subjects who are at risk of acute kidney injury (AKI) and undergoing pre-defined on-pump cardiac surgery.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2013
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	Denmark: 49
Country: Number of subjects enrolled	United States: 191
Worldwide total number of subjects	240
EEA total number of subjects	49

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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	66
From 65 to 84 years	162
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 39 investigative sites in Denmark and the United States.

Pre-assignment

Screening details:

Screening visit occurred between Day -28 and Day -5 prior to surgery.

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	Placebo

Arm description:

A total of 6, 10-minute infusions administered 1) prior to skin incision; 2) before clamp release but at least 1 hour after the first dose 3) 6 hours (\pm 30 minutes) after clamp release; 4) 12 hours (\pm 30 minutes) after clamp release; 5) 24 hours (\pm 60 minutes) after clamp release; and 6) 48 hours (\pm 60 minutes) after clamp release.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Placebo administered by intravenous infusion

Arm title	ABT-719 800 mcg/kg
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Arm description:

Six 10-minute infusions with a total dose of 800 mcg/kg ABT-719, administered 1) prior to skin incision (200 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (400 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (0 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (0 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).

Arm type	Experimental
Investigational medicinal product name	ABT-719
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

ABT-719 administered by intravenous infusion

Arm title	ABT-719 1600 mcg/kg
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Arm description:

Six 10-minute infusions with a total dose of 1600 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (200 mcg/kg); and 6) 48 hours (\pm 60

minutes) after clamp release (0 mcg/kg).

Arm type	Experimental
Investigational medicinal product name	ABT-719
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
ABT-719 administered by intravenous infusion	
Arm title	ABT-719 2100 mcg/kg

Arm description:

Six 10-minute infusions with a total dose of 2100 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (300 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (300 mcg/kg).

Arm type	Experimental
Investigational medicinal product name	ABT-719
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

ABT-719 administered by intravenous infusion

Number of subjects in period 1^[1]	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg
Started	59	57	59
Completed	51	54	55
Not completed	8	3	4
Other, not specified	8	3	4

Number of subjects in period 1^[1]	ABT-719 2100 mcg/kg
Started	56
Completed	49
Not completed	7
Other, not specified	7

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 240 subjects were enrolled; 9 subjects discontinued before receiving any study drug; and 231 subjects are included in the full analysis set (FAS).

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

A total of 6, 10-minute infusions administered 1) prior to skin incision; 2) before clamp release but at least 1 hour after the first dose 3) 6 hours (\pm 30 minutes) after clamp release; 4) 12 hours (\pm 30 minutes) after clamp release; 5) 24 hours (\pm 60 minutes) after clamp release; and 6) 48 hours (\pm 60 minutes) after clamp release.

Reporting group title	ABT-719 800 mcg/kg
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Reporting group description:

Six 10-minute infusions with a total dose of 800 mcg/kg ABT-719, administered 1) prior to skin incision (200 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (400 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (0 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (0 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).

Reporting group title	ABT-719 1600 mcg/kg
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Reporting group description:

Six 10-minute infusions with a total dose of 1600 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (200 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).

Reporting group title	ABT-719 2100 mcg/kg
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Reporting group description:

Six 10-minute infusions with a total dose of 2100 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (300 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (300 mcg/kg).

Reporting group values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg
Number of subjects	59	57	59
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	71.1 \pm 9.39	68.9 \pm 10.23	67.7 \pm 12.54
Gender categorical Units: Subjects			
Female	13	17	16
Male	46	40	43

Reporting group values	ABT-719 2100 mcg/kg	Total	
Number of subjects	56	231	
Age categorical Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	68.6		
standard deviation	± 10.6	-	
Gender categorical			
Units: Subjects			
Female	20	66	
Male	36	165	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: A total of 6, 10-minute infusions administered 1) prior to skin incision; 2) before clamp release but at least 1 hour after the first dose 3) 6 hours (\pm 30 minutes) after clamp release; 4) 12 hours (\pm 30 minutes) after clamp release; 5) 24 hours (\pm 60 minutes) after clamp release; and 6) 48 hours (\pm 60 minutes) after clamp release.	
Reporting group title	ABT-719 800 mcg/kg
Reporting group description: Six 10-minute infusions with a total dose of 800 mcg/kg ABT-719, administered 1) prior to skin incision (200 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (400 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (0 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (0 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).	
Reporting group title	ABT-719 1600 mcg/kg
Reporting group description: Six 10-minute infusions with a total dose of 1600 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (200 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).	
Reporting group title	ABT-719 2100 mcg/kg
Reporting group description: Six 10-minute infusions with a total dose of 2100 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (300 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (300 mcg/kg).	
Subject analysis set title	Placebo
Subject analysis set type	Per protocol
Subject analysis set description: All randomized subjects who received all 6 infusions of study drug and underwent the pre-defined on-pump cardiac surgery.	
Subject analysis set title	ABT-719 800 mcg/kg
Subject analysis set type	Per protocol
Subject analysis set description: All randomized subjects who received all 6 infusions of study drug and underwent the pre-defined on-pump cardiac surgery.	
Subject analysis set title	ABT-719 1600 mcg/kg
Subject analysis set type	Per protocol
Subject analysis set description: All randomized subjects who received all 6 infusions of study drug and underwent the pre-defined on-pump cardiac surgery.	
Subject analysis set title	ABT-719 2100 mcg/kg
Subject analysis set type	Per protocol
Subject analysis set description: All randomized subjects who received all 6 infusions of study drug and underwent the pre-defined on-pump cardiac surgery.	

Primary: Percentage of Subjects Developing Acute Kidney Injury (AKI) as Defined by the Acute Kidney Injury Network (AKIN) Scoring Criteria

End point title	Percentage of Subjects Developing Acute Kidney Injury (AKI) as Defined by the Acute Kidney Injury Network (AKIN) Scoring Criteria
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End point description:

The AKIN is an evidence-based definition for AKI based on changes to serum creatinine (SCr), urine output (UO), and renal replacement therapy (RRT). The 3 severity grades are defined on the basis of the changes in SCr or UO where the worst of each criterion is used: Stage 1 (increased Cr x 1.5 or ≥ 0.3 mg/dL; UO < 0.5 mL/kg/hr x 6 hr), Stage 2 (increased Cr x 2; UO < 0.5 mL/kg/hr x 12 hr), and Stage 3 (increased Cr x 3 Cr ≥ 4 mg/dL with acute rise of ≥ 0.5 mg/dL; UO < 0.3 mL/kg/hr x 24 hr or anuria x 12 hr). A change in SCr of ≥ 26.2 μ mol/L defines the presence of AKI. The AKIN scoring criteria includes a time limit of 48 hours for diagnosis of AKI, and any patients receiving RRT are classified as Stage 3 AKI, regardless of the stage that the patient is in at the time of commencement of RRT. The number of subjects analyzed = all subjects in the full analysis set with available data.

End point type	Primary
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End point timeframe:

Day 0 (Surgery) to Day 7

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58	55	59	56
Units: percentage of subjects				
number (not applicable)				
No	29.31	27.27	35.59	28.57
Stage 1	10.34	18.18	6.78	14.29
Stage 2	48.28	49.09	50.85	51.79
Stage 3	12.07	5.45	6.78	5.36
Any stage	70.69	72.73	64.41	71.43

Statistical analyses

Statistical analysis title	Statistical analysis 1
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Statistical analysis description:

P-value from pairwise comparisons between each ABT-719 dose group and placebo using 2-sided Cochran-Mantel-Haenszel test after adjustment for type of surgery and SCr-based estimated glomerular filtration rate (eGFR).

Comparison groups	Placebo v ABT-719 800 mcg/kg
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Number of subjects included in analysis	113
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Analysis specification	Pre-specified
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Analysis type	other
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P-value	= 0.848
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Method	Cochran-Mantel-Haenszel
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Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

P-value from pairwise comparisons between each ABT-719 dose group and placebo using 2-sided Cochran-Mantel-Haenszel test after adjustment for type of surgery and SCr-based estimated glomerular filtration rate (eGFR).

Comparison groups	Placebo v ABT-719 1600 mcg/kg
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Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.469
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Statistical analysis 3
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Statistical analysis description:

P-value from pairwise comparisons between each ABT-719 dose group and placebo using 2-sided Cochran-Mantel-Haenszel test after adjustment for type of surgery and SCr-based estimated glomerular filtration rate (eGFR).

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.906
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 25% Reduction in Serum Creatinine Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90

End point title	Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 25% Reduction in Serum Creatinine Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90
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End point description:

The percentage of subjects developing at least 1 of the composite events: death, needing RRT during the 90 day post-operative period, or having a $\geq 25\%$ reduction in SCr eGFR at the Day 90 post-surgery visit. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
End point timeframe:	
Day 0 (Surgery) to Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	54	55	42
Units: percentage of subjects				
number (not applicable)	19.23	12.96	10.91	20.41

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 50% Reduction in Serum Creatinine Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90

End point title	Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 50% Reduction in Serum Creatinine Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90
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End point description:

The percentage of subjects developing at least 1 of the composite events: death, needing RRT during the 90 day post-operative period, or having a $\geq 50\%$ reduction in SCr eGFR at the Day 90 post-surgery visit. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 90

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	54	55	49
Units: percentage of subjects				
number (not applicable)	11.54	5.56	3.64	8.16

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 25% Reduction in S-Cystatin C Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90

End point title	Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 25% Reduction in S-Cystatin C Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90
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End point description:

The percentage of subjects developing at least 1 of the composite events: death, needing RRT during the 90 day post-operative period, or having a $\geq 25\%$ reduction in S-Cystatin C eGFR at the Day 90 post-surgery visit. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 90

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	54	55	49
Units: percentage of subjects				
number (not applicable)	13.46	7.41	7.27	10.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 50% Reduction in S-Cystatin C Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90

End point title	Percentage of Subjects Developing a Composite Event (Death, Renal Replacement Therapy [RRT], or 50% Reduction in S-Cystatin C Based Estimated Glomerular Filtration Rate [SCr eGFR]) – Day 90
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End point description:

The percentage of subjects developing at least 1 of the composite events: death, needing RRT during the 90 day post-operative period, or having a $\geq 50\%$ reduction in S-Cystatin C eGFR at the Day 90 post-surgery visit. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 90

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	52	52	46
Units: percentage of subjects				
number (not applicable)	11.54	7.41	1.82	8.16

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Neutrophil Gelatinase Associated Lipocalin (NGAL): Change from Baseline to Day 90

End point title	Serum Neutrophil Gelatinase Associated Lipocalin (NGAL): Change from Baseline to Day 90
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End point description:

From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in serum NGAL (ng/mL). Lower measures for NGAL are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 90

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	47	44	36
Units: ng/mL				
least squares mean (standard error)	120.4 (± 38.6)	78.5 (± 36.7)	113.1 (± 37.8)	113.7 (± 41.6)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-41.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-146.3
upper limit	62.5
Variability estimate	Standard error of the mean
Dispersion value	53.2

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	ABT-719 1600 mcg/kg v Placebo
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-7.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-113.3
upper limit	62.5
Variability estimate	Standard error of the mean
Dispersion value	54

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-118
upper limit	104.5
Variability estimate	Standard error of the mean
Dispersion value	56.7

Secondary: Urine Interleukin-18 (IL-18): Change from Baseline to Day 90

End point title	Urine Interleukin-18 (IL-18): Change from Baseline to Day 90
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End point description:

From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in urine IL-18 (pg/mL). Lower measures for IL-18 are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 90

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	43	47	44	36
Units: pg/mL				
least squares mean (standard error)	1.7 (± 16.7)	1.1 (± 15.9)	6.3 (± 16.5)	-2.7 (± 18.2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.9
upper limit	44.6
Variability estimate	Standard error of the mean
Dispersion value	23.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.7
upper limit	50.8
Variability estimate	Standard error of the mean
Dispersion value	23.6

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53
upper limit	44.2
Variability estimate	Standard error of the mean
Dispersion value	24.8

Secondary: Urine Kidney Injury Molecule (KIM-1): Change from Baseline to Day 90

End point title	Urine Kidney Injury Molecule (KIM-1): Change from Baseline to Day 90
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End point description:

From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in urine KIM-1 (ng/mL). Lower measures for urine KIM-1 are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
End point timeframe:	
Day 0 (Surgery) to Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	43	47	44	36
Units: ng/mL				
least squares mean (standard error)	0.17 (± 0.27)	0.2 (± 0.25)	-0.02 (± 0.26)	0.36 (± 0.29)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.

Comparison groups	Placebo v ABT-719 800 mcg/kg
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Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.69
upper limit	0.74
Variability estimate	Standard error of the mean
Dispersion value	0.37

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.

Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.38

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.96

Variability estimate	Standard error of the mean
Dispersion value	0.4

Secondary: Urine Neutrophil Gelatinase Associated Lipocalin (NGAL): Change from Baseline to Day 90

End point title	Urine Neutrophil Gelatinase Associated Lipocalin (NGAL): Change from Baseline to Day 90
End point description: From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in NGAL (ng/mL). Lower measures for NGAL are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.	
End point type	Secondary
End point timeframe: Day 0 (Surgery) to Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	43	47	44	36
Units: ng/mL				
least squares mean (standard error)	399 (\pm 107.3)	47 (\pm 103.7)	18 (\pm 106.9)	1 (\pm 118.2)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-352.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-645
upper limit	-60
Variability estimate	Standard error of the mean
Dispersion value	149.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-381.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-679
upper limit	-84
Variability estimate	Standard error of the mean
Dispersion value	151.54

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; the autoregressive variance-covariance structure is used.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-389.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-711
upper limit	-86
Variability estimate	Standard error of the mean
Dispersion value	159.4

Secondary: Hospitalization Days Within 90 Days after Surgery	
End point title	Hospitalization Days Within 90 Days after Surgery
End point description:	
From ANOVA model. The LS mean number of days that subjects spent hospitalized, up to 90 days after surgery. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.	
End point type	Secondary
End point timeframe:	
Day 0 (Surgery) to Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	51	54	55	49
Units: days				
least squares mean (standard error)	19 (\pm 3.4)	16.5 (\pm 3.3)	12.2 (\pm 3.3)	26.4 (\pm 3.5)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: ANOVA model with treatment as the factor.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	5.3
Variability estimate	Standard error of the mean
Dispersion value	4.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: ANOVA model with treatment as the factor.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.5
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	4.7

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: ANOVA model with treatment as the factor.	
Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	15.4
Variability estimate	Standard error of the mean
Dispersion value	4.8

Secondary: Percentage of Subjects Developing Acute Kidney Injury (AKI) as Defined by the Risk, Injury and Failure (RIFLE) Scoring Criteria

End point title	Percentage of Subjects Developing Acute Kidney Injury (AKI) as Defined by the Risk, Injury and Failure (RIFLE) Scoring Criteria
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End point description:

The RIFLE is an evidence-based definition for AKI based on changes to serum creatinine (SCr), urine output (UO), and two clinical outcomes (Loss [acute kidney failure for > 4 weeks] and End-stage renal disease). The 3 severity grades are defined on the basis of the changes in SCr or UO where the worst of each criterion is used: Risk (increased Cr x 1.5 or GFR decreased < 25%; UO < 0.5 mL/kg/hr x 6 hr), Injury (increased Cr x 2 or GFR decreased < 50%; UO < 0.5 mL/kg/hr x 12 hr), and Failure (increased Cr x 3 or GFR decreased < 25% or Cr ≥ 4 mg/dL with acute rise of ≥ 0.5 mg/dL; UO < 0.3 mL/kg/hr x 24 hr or anuria x 12 hr). The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 7

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	54	55	49
Units: percentage of subjects				
number (not applicable)				
No	26.92	25.93	32.73	22.45
Risk	11.54	14.81	9.09	18.37
Injury	51.92	53.7	52.73	53.06
Failure	9.62	5.56	5.45	6.12
Any stage	73.08	74.07	67.27	77.55

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Developing Acute Kidney Injury (AKI) as Defined by the Kidney Disease: Improving Global Outcomes (KDIGO) Scoring Criteria

End point title	Percentage of Subjects Developing Acute Kidney Injury (AKI) as Defined by the Kidney Disease: Improving Global Outcomes (KDIGO) Scoring Criteria
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End point description:

The KDIGO is based on the RIFLE and the AKIN criteria and risk relationships. AKI is defined as increase in SCr by ≥ 3 mg/dl (≥ 26.5 $\mu\text{mol/L}$) within 48 hours; increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume < 0.5 mL/kg/h for 6 hours. The 3 severity grades are defined as: Stage 1 (increased Cr x 1.5-1.9 x baseline or ≥ 3 mg/dl [≥ 26.5 $\mu\text{mol/L}$] UO < 0.5 mL/kg/hr x 6-12 hr), Stage 2 (increased Cr x 2.0-2.9; UO < 0.5 mL/kg/hr x 12 hr), and Stage 3 (increased Cr x 3.0 OR increase Cr to ≥ 4.0 mg/dL (≥ 353.6 $\mu\text{mol/L}$) OR initiation of renal replacement therapy OR, in patients < 18 years, decrease in eGFR to < 35 mL/min per 1.73 m^2 ; UO < 0.3 mL/kg/hr for ≥ 24 hr or anuria for ≥ 12 hr). The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 7

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	52	54	55	49
Units: percentage of subjects				
number (not applicable)				
No	26.92	25.93	34.55	26.53
Stage 1	11.54	18.52	7.27	14.29
Stage 2	51.92	50	52.73	53.06
Stage 3	9.62	5.56	5.45	6.12
Any stage	73.08	74.07	65.45	73.47

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Creatinine (SCr): Change from Baseline to Day 90

End point title	Serum Creatinine (SCr): Change from Baseline to Day 90
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End point description:

From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit

in SCr ($\mu\text{mol/L}$). Lower measures for SCr are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
End point timeframe:	
Baseline (Day 0) through Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	47	48	35
Units: $\mu\text{mol/L}$				
least squares mean (standard error)	10.9 (\pm 3.54)	9.3 (\pm 3.37)	3.4 (\pm 3.38)	6.5 (\pm 3.85)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.2
upper limit	8
Variability estimate	Standard error of the mean
Dispersion value	4.89

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg

Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.2
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	4.9

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.6
upper limit	6
Variability estimate	Standard error of the mean
Dispersion value	5.25

Secondary: Serum Creatinine (SCr): Maximal Change from Baseline Over All Study Visits up to Day 7 (or Hospital Discharge)

End point title	Serum Creatinine (SCr): Maximal Change from Baseline Over All Study Visits up to Day 7 (or Hospital Discharge)
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End point description:

From ANCOVA model. The least squares mean (LS mean) maximal change from baseline to each visit up to Day 7 in SCr ($\mu\text{mol/L}$). Lower measures for SCr are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) through Day 7

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	51	54	50	48
Units: $\mu\text{mol/L}$				
least squares mean (standard error)	30.2 (\pm 6.08)	32.8 (\pm 5.9)	26.3 (\pm 6.14)	28.4 (\pm 6.26)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: ANCOVA model with treatment group as the factor and baseline as a covariate.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	19.3
Variability estimate	Standard error of the mean
Dispersion value	8.47

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: ANCOVA model with treatment group as the factor and baseline as a covariate.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.9
upper limit	13.1
Variability estimate	Standard error of the mean
Dispersion value	8.64

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

ANCOVA model with treatment group as the factor and baseline as a covariate.

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19
upper limit	15.4
Variability estimate	Standard error of the mean
Dispersion value	8.73

Secondary: S-Cystatin C: Change from Baseline to Day 90

End point title	S-Cystatin C: Change from Baseline to Day 90
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End point description:

From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in S-Cystatin C (nmol/L). Lower measures for S-Cystatin C are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Day 0 (Surgery) to Day 90

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	40	47	46	35
Units: nmol/L				
least squares mean (standard error)	16.1 (± 3.13)	11.3 (± 2.96)	11.6 (± 3.03)	12.8 (± 3.34)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 800 mcg/kg
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Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-4.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.2
upper limit	3.7
Variability estimate	Standard error of the mean
Dispersion value	4.31

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.1
upper limit	4.1
Variability estimate	Standard error of the mean
Dispersion value	4.36

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.3
upper limit	5.7

Variability estimate	Standard error of the mean
Dispersion value	4.58

Secondary: S-Cystatin C: Maximal Change from Baseline Over All Study Visits up to Day 7 (or Hospital Discharge)

End point title	S-Cystatin C: Maximal Change from Baseline Over All Study Visits up to Day 7 (or Hospital Discharge)
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End point description:

From ANCOVA model. The least squares mean (LS mean) maximal change from baseline to each visit up to Day 7 in S-Cystatin C (nmol/L). Lower measures for S-Cystatin C are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) through Day 7

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	51	54	50	48
Units: µmol/L				
least squares mean (standard error)	22.6 (± 4.04)	23 (± 3.92)	18.4 (± 4.08)	20.6 (± 4.16)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

ANCOVA model with treatment group as the factor and baseline as a covariate.

Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	11.5
Variability estimate	Standard error of the mean
Dispersion value	5.63

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

ANCOVA model with treatment group as the factor and baseline as a covariate.

Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	7.2
Variability estimate	Standard error of the mean
Dispersion value	5.74

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

ANCOVA model with treatment group as the factor and baseline as a covariate.

Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	9.4
Variability estimate	Standard error of the mean
Dispersion value	5.8

Secondary: Measured Glomerular Filtration Rate (GFR): Change from Baseline to Day 90

End point title	Measured Glomerular Filtration Rate (GFR): Change from Baseline to Day 90
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End point description:

From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in GFR (L/min/1.73m²). Higher measures for GFR are desirable. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.

End point type	Secondary
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End point timeframe:

Baseline (Day 0) through Day 7

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	45	48	35
Units: mL/min/1.73m ²				
least squares mean (standard error)	-4 (± 1.72)	-4.9 (± 1.67)	-1.2 (± 1.67)	-5.9 (± 1.86)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	3.8
Variability estimate	Standard error of the mean
Dispersion value	2.41

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	7.5
Variability estimate	Standard error of the mean
Dispersion value	2.4

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.	
Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	3.1
Variability estimate	Standard error of the mean
Dispersion value	2.54

Secondary: Estimated Glomerular Filtration Rate (eGFR): Change from Baseline to Day 90

End point title	Estimated Glomerular Filtration Rate (eGFR): Change from Baseline to Day 90
End point description: From repeated measures analysis. The least squares mean (LS mean) change from baseline to each visit in eGFR (L/min/1.73m ²). Higher measures for eGFR are desirable. All subjects in the per protocol analysis set with available data are included in the analysis.	
End point type	Secondary
End point timeframe: Baseline (Day 0) through Day 7	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	6	7	4
Units: mL/min/1.73m ²				
least squares mean (standard error)	-11.1 (± 5.04)	-6.6 (± 5.13)	2.3 (± 4.9)	2.7 (± 6.46)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	19.2
Variability estimate	Standard error of the mean
Dispersion value	7.27

Statistical analysis title

Statistical Analysis 2

Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	27.8
Variability estimate	Standard error of the mean
Dispersion value	7.11

Statistical analysis title

Statistical Analysis 3

Statistical analysis description:

A mixed effects, repeated measures model including fixed, categorical effects of treatment, visit, and treatment-by-visit interaction, as well as fixed, continuous effects of baseline measurements and subject effects; covariance structure is unstructured.

Comparison groups	Placebo v ABT-719 1600 mcg/kg
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Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	13.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	30.3
Variability estimate	Standard error of the mean
Dispersion value	8.15

Secondary: Intensive Care Unit (ICU) Days Within 90 Days after Surgery

End point title	Intensive Care Unit (ICU) Days Within 90 Days after Surgery
End point description:	
From ANOVA model. The LS mean number of days that subjects spent in ICU, up to 90 days after surgery. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.	
End point type	Secondary
End point timeframe:	
Day 0 (Surgery) to Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	49	51	54	49
Units: days				
least squares mean (standard error)	5.4 (± 0.8)	4.6 (± 0.8)	3.5 (± 0.8)	6.3 (± 0.8)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
ANOVA model with treatment as the factor.	
Comparison groups	Placebo v ABT-719 800 mcg/kg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	1.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: ANOVA model with treatment as the factor.	
Comparison groups	Placebo v ABT-719 1600 mcg/kg
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	1.1

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: ANOVA model with treatment as the factor.	
Comparison groups	Placebo v ABT-719 2100 mcg/kg
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	LS mean of difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.7
Variability estimate	Standard error of the mean
Dispersion value	1.2

Other pre-specified: Euroqol 5 Dimensions Questionnaire (EQ-5D) Index: Change from Baseline to Day 90

End point title	Euroqol 5 Dimensions Questionnaire (EQ-5D) Index: Change from Baseline to Day 90
End point description: The EQ-5D-3L consists of 5 dimensions: 1) mobility, 2) self-care, 3) usual activities, 4) pain/discomfort, and 5) anxiety/depression. There are 3 levels to each dimension; Level 1 = no problem, Level 2 = some problem, and Level 3 = extreme problem. The scores of the 5 dimensions were converted into a single summary index by utilizing country specific value sets. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.	
End point type	Other pre-specified
End point timeframe: Day 0 (Surgery) and Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	46	49	52	38
Units: units on a scale				
arithmetic mean (standard deviation)	0.034 (± 0.092)	0.072 (± 0.1)	0.017 (± 0.093)	0.017 (± 0.102)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage of Subjects Who Experienced "No Problem" (Level 1) and "Problems" (Levels 2 and 3) in the 5 Dimensions of the Euroqol 5 Dimensions (EQ-5D) Questionnaire on Day 90

End point title	Percentage of Subjects Who Experienced "No Problem" (Level 1) and "Problems" (Levels 2 and 3) in the 5 Dimensions of the Euroqol 5 Dimensions (EQ-5D) Questionnaire on Day 90
End point description: The EQ-5D-3L consists of 5 dimensions: 1) mobility, 2) self-care, 3) usual activities, 4) pain/discomfort, and 5) anxiety/depression. There are 3 levels to each dimension; Level 1 = no problem, Level 2 = some problem, and Level 3 = extreme problem. All subjects in the per protocol analysis set with available data are included in the analysis. The number of subjects analyzed = all subjects in the per protocol analysis set with available data.	
End point type	Other pre-specified
End point timeframe: Day 90	

End point values	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg	ABT-719 2100 mcg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	46	49	53	38
Units: percentage of subjects				
number (not applicable)				
Mobility - no problem	73.91	85.71	69.81	76.32
Mobility - some problem	26.09	14.29	30.19	23.68

Mobility - extreme problem	0	0	0	0
Self-care - no problem	93.48	95.92	90.57	94.74
Self-care - some problem	6.52	4.08	9.43	5.26
Self-care - extreme problem	0	0	0	0
Usual activities - no problem	63.04	83.67	60.38	71.05
Usual activities - some problem	34.78	16.33	35.85	28.95
Usual activities - extreme problem	2.17	0	3.77	0
Pain/discomfort - no problem	71.74	77.55	67.92	73.68
Pain/discomfort - some problem	23.91	22.45	26.42	26.32
Pain/discomfort - extreme problem	4.35	0	5.66	0
Anxiety/depression - no problem	84.78	91.84	77.36	84.21
Anxiety/depression - some problem	15.22	8.16	22.64	10.53
Anxiety/depression - extreme problem	0	0	0	5.26

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from study drug administration until 30 days after last dose (32 days); serious adverse events (SAEs) were collected from the time that informed consent was obtained (60 days).

Adverse event reporting additional description:

AEs were collected whether solicited or spontaneously reported by the subject until 30 days after last dose; after 30 days, only AEs that were spontaneously reported were collected.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

A total of 6, 10-minute infusions administered 1) prior to skin incision; 2) before clamp release but at least 1 hour after the first dose 3) 6 hours (\pm 30 minutes) after clamp release; 4) 12 hours (\pm 30 minutes) after clamp release; 5) 24 hours (\pm 60 minutes) after clamp release; and 6) 48 hours (\pm 60 minutes) after clamp release.

Reporting group title	ABT-719 800 mcg/kg
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Reporting group description:

Six 10-minute infusions with a total dose of 800 mcg/kg ABT-719, administered 1) prior to skin incision (200 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (400 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (0 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (0 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).

Reporting group title	ABT-719 1600 mcg/kg
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Reporting group description:

Six 10-minute infusions with a total dose of 1600 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (200 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (200 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (0 mcg/kg).

Reporting group title	ABT-719 2100 mcg/kg
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Reporting group description:

Six 10-minute infusions with a total dose of 2100 mcg/kg ABT-719, administered 1) prior to skin incision (300 mcg/kg); 2) before clamp release but at least 1 hour after the first dose (600 mcg/kg); 3) 6 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 4) 12 hours (\pm 30 minutes) after clamp release (300 mcg/kg); 5) 24 hours (\pm 60 minutes) after clamp release (300 mcg/kg); and 6) 48 hours (\pm 60 minutes) after clamp release (300 mcg/kg).

Serious adverse events	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 59 (44.07%)	12 / 57 (21.05%)	13 / 59 (22.03%)
number of deaths (all causes)	3	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Lung neoplasm malignant subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Vascular disorders			
Deep vein thrombosis subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage subjects affected / exposed	2 / 59 (3.39%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypoperfusion subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Hypotension subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
General disorders and administration site conditions			
Multi-organ failure subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 59 (1.69%)	1 / 57 (1.75%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Pulmonary hypertension			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	2 / 59 (3.39%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	3 / 59 (5.08%)	1 / 57 (1.75%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Mental status changes			

subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Investigations			
Escherichia test positive			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart rate decreased			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Pulse absent			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Injury, poisoning and procedural complications			
Cardiac valve rupture			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Postoperative thoracic procedure complication			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous injury			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	5 / 59 (8.47%)	1 / 57 (1.75%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrioventricular block			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 59 (1.69%)	1 / 57 (1.75%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular dissociation			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 59 (3.39%)	2 / 57 (3.51%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			

subjects affected / exposed	3 / 59 (5.08%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Myocardial haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Pulseless electrical activity			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricle rupture			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ventricular fibrillation			

subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Ventricular tachycardia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 59 (3.39%)	1 / 57 (1.75%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Dizziness			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Encephalopathy			
subjects affected / exposed	1 / 59 (1.69%)	1 / 57 (1.75%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			

subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heparin-induced thrombocytopenia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal compartment syndrome			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Ileus			

subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic ischaemia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decubitus ulcer			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Renal failure			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	3 / 59 (5.08%)	1 / 57 (1.75%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal failure chronic			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Critical illness myopathy			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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			
Diverticulitis			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	0 / 59 (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
Mediastinitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 59 (1.69%)	0 / 57 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Fluid overload			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Hypercalcaemia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	0 / 59 (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
Hyponatraemia			
subjects affected / exposed	0 / 59 (0.00%)	0 / 57 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ABT-719 2100 mcg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 56 (48.21%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			

subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoperfusion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subclavian vein thrombosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea paroxysmal nocturnal			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory arrest			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Escherichia test positive			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Heart rate decreased			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hepatic enzyme increased subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulse absent subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Cardiac valve rupture subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Fall subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Postoperative thoracic procedure complication			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Procedural haemorrhage subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous injury subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Wound dehiscence			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrioventricular dissociation			

subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 56 (1.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				
subjects affected / exposed	2 / 56 (3.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Myocardial haemorrhage				
subjects affected / exposed	0 / 56 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulseless electrical activity			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Supraventricular tachycardia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricle rupture			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular fibrillation			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic encephalopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Heparin-induced thrombocytopenia			

subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal compartment syndrome			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Duodenal ulcer haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic ischaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Angioedema			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Decubitus ulcer			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal disorder			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure chronic			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Critical illness myopathy			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mediastinitis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia klebsiella			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fluid overload			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hyponatraemia			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	ABT-719 800 mcg/kg	ABT-719 1600 mcg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 59 (91.53%)	42 / 57 (73.68%)	54 / 59 (91.53%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 59 (0.00%)	3 / 57 (5.26%)	0 / 59 (0.00%)
occurrences (all)	0	3	0
Hypertension			
subjects affected / exposed	2 / 59 (3.39%)	6 / 57 (10.53%)	2 / 59 (3.39%)
occurrences (all)	2	6	2
Hypotension			
subjects affected / exposed	8 / 59 (13.56%)	7 / 57 (12.28%)	11 / 59 (18.64%)
occurrences (all)	9	8	11
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 59 (0.00%)	1 / 57 (1.75%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Oedema			
subjects affected / exposed	2 / 59 (3.39%)	3 / 57 (5.26%)	2 / 59 (3.39%)
occurrences (all)	2	3	2
Oedema peripheral			
subjects affected / exposed	3 / 59 (5.08%)	3 / 57 (5.26%)	3 / 59 (5.08%)
occurrences (all)	3	3	3
Pain			
subjects affected / exposed	6 / 59 (10.17%)	3 / 57 (5.26%)	7 / 59 (11.86%)
occurrences (all)	7	3	7
Pyrexia			

subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	3 / 57 (5.26%) 3	5 / 59 (8.47%) 6
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	3 / 57 (5.26%) 3	2 / 59 (3.39%) 2
Atelectasis subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6	9 / 57 (15.79%) 9	10 / 59 (16.95%) 10
Dyspnoea subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	2 / 57 (3.51%) 2	1 / 59 (1.69%) 1
Pleural effusion subjects affected / exposed occurrences (all)	18 / 59 (30.51%) 19	10 / 57 (17.54%) 11	13 / 59 (22.03%) 13
Pneumothorax subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	3 / 57 (5.26%) 3	2 / 59 (3.39%) 2
Respiratory failure subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	3 / 57 (5.26%) 3	4 / 59 (6.78%) 4
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	2 / 57 (3.51%) 2	3 / 59 (5.08%) 3
Confusional state subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	1 / 57 (1.75%) 1	2 / 59 (3.39%) 2
Delirium subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	3 / 57 (5.26%) 3	1 / 59 (1.69%) 1
Insomnia subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4	2 / 57 (3.51%) 2	2 / 59 (3.39%) 2
Mental status changes			

subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	3 / 57 (5.26%) 3	0 / 59 (0.00%) 0
Investigations			
Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4	0 / 57 (0.00%) 0	2 / 59 (3.39%) 2
Cardiac index decreased subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	3 / 57 (5.26%) 3	0 / 59 (0.00%) 0
Urine output decreased subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	1 / 57 (1.75%) 1	7 / 59 (11.86%) 7
Injury, poisoning and procedural complications			
Anaemia postoperative subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	1 / 57 (1.75%) 1	1 / 59 (1.69%) 1
Incision site pain subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 7	5 / 57 (8.77%) 5	5 / 59 (8.47%) 5
Procedural haemorrhage subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	0 / 57 (0.00%) 0	3 / 59 (5.08%) 3
Procedural nausea subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6	8 / 57 (14.04%) 8	6 / 59 (10.17%) 6
Procedural pain subjects affected / exposed occurrences (all)	22 / 59 (37.29%) 22	19 / 57 (33.33%) 19	20 / 59 (33.90%) 20
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	25 / 59 (42.37%) 27	17 / 57 (29.82%) 17	13 / 59 (22.03%) 14
Atrial flutter subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	1 / 57 (1.75%) 1	0 / 59 (0.00%) 0
Sinus tachycardia			

subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	0 / 57 (0.00%) 0	4 / 59 (6.78%) 4
Tachycardia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	2 / 57 (3.51%) 2	1 / 59 (1.69%) 1
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	16 / 59 (27.12%) 16	12 / 57 (21.05%) 12	20 / 59 (33.90%) 20
Haemorrhagic anaemia subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	0 / 57 (0.00%) 0	8 / 59 (13.56%) 8
Leukocytosis subjects affected / exposed occurrences (all)	4 / 59 (6.78%) 4	3 / 57 (5.26%) 3	2 / 59 (3.39%) 3
Thrombocytopenia subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6	8 / 57 (14.04%) 8	9 / 59 (15.25%) 9
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	16 / 59 (27.12%) 17	10 / 57 (17.54%) 10	14 / 59 (23.73%) 14
Diarrhoea subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	0 / 57 (0.00%) 0	2 / 59 (3.39%) 2
Dysphagia subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	3 / 57 (5.26%) 3	1 / 59 (1.69%) 1
Nausea subjects affected / exposed occurrences (all)	19 / 59 (32.20%) 21	13 / 57 (22.81%) 13	22 / 59 (37.29%) 23
Vomiting subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 4	3 / 57 (5.26%) 3	1 / 59 (1.69%) 1
Renal and urinary disorders			

Renal failure subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 1	1 / 57 (1.75%) 1	1 / 59 (1.69%) 1
Renal failure acute subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	2 / 57 (3.51%) 2	2 / 59 (3.39%) 2
Musculoskeletal and connective tissue disorders Musculoskeletal pain subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	1 / 57 (1.75%) 1	1 / 59 (1.69%) 1
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	2 / 57 (3.51%) 2	0 / 59 (0.00%) 0
Metabolism and nutrition disorders Acidosis subjects affected / exposed occurrences (all)	3 / 59 (5.08%) 3	2 / 57 (3.51%) 2	5 / 59 (8.47%) 5
Electrolyte imbalance subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	0 / 57 (0.00%) 0	3 / 59 (5.08%) 3
Fluid overload subjects affected / exposed occurrences (all)	10 / 59 (16.95%) 10	10 / 57 (17.54%) 10	19 / 59 (32.20%) 20
Fluid retention subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2	3 / 57 (5.26%) 3	2 / 59 (3.39%) 2
Hyperglycaemia subjects affected / exposed occurrences (all)	15 / 59 (25.42%) 15	10 / 57 (17.54%) 10	15 / 59 (25.42%) 15
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 0	1 / 57 (1.75%) 1	2 / 59 (3.39%) 2
Hypocalcaemia subjects affected / exposed occurrences (all)	6 / 59 (10.17%) 6	5 / 57 (8.77%) 5	12 / 59 (20.34%) 12

Hypokalaemia			
subjects affected / exposed	14 / 59 (23.73%)	14 / 57 (24.56%)	16 / 59 (27.12%)
occurrences (all)	16	14	16
Hypomagnesaemia			
subjects affected / exposed	6 / 59 (10.17%)	4 / 57 (7.02%)	9 / 59 (15.25%)
occurrences (all)	6	4	9
Hyponatraemia			
subjects affected / exposed	2 / 59 (3.39%)	2 / 57 (3.51%)	3 / 59 (5.08%)
occurrences (all)	2	2	3
Hypovolaemia			
subjects affected / exposed	3 / 59 (5.08%)	2 / 57 (3.51%)	3 / 59 (5.08%)
occurrences (all)	3	2	3
Metabolic acidosis			
subjects affected / exposed	5 / 59 (8.47%)	2 / 57 (3.51%)	3 / 59 (5.08%)
occurrences (all)	5	2	3

Non-serious adverse events	ABT-719 2100 mcg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 56 (87.50%)		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	6 / 56 (10.71%)		
occurrences (all)	6		
Hypotension			
subjects affected / exposed	11 / 56 (19.64%)		
occurrences (all)	12		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Oedema			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		

Oedema peripheral subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Pain subjects affected / exposed occurrences (all)	7 / 56 (12.50%) 7		
Pyrexia subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 4		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure subjects affected / exposed occurrences (all)	0 / 56 (0.00%) 0		
Atelectasis subjects affected / exposed occurrences (all)	6 / 56 (10.71%) 8		
Dyspnoea subjects affected / exposed occurrences (all)	2 / 56 (3.57%) 2		
Pleural effusion subjects affected / exposed occurrences (all)	13 / 56 (23.21%) 15		
Pneumothorax subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Respiratory failure subjects affected / exposed occurrences (all)	5 / 56 (8.93%) 5		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	4 / 56 (7.14%) 4		
Confusional state subjects affected / exposed occurrences (all)	3 / 56 (5.36%) 3		
Delirium			

subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Mental status changes			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Investigations			
Blood creatinine increased			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Cardiac index decreased			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Urine output decreased			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	4 / 56 (7.14%)		
occurrences (all)	4		
Incision site pain			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	5		
Procedural haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Procedural nausea			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	9		
Procedural pain			
subjects affected / exposed	23 / 56 (41.07%)		
occurrences (all)	23		
Cardiac disorders			

Atrial fibrillation subjects affected / exposed occurrences (all) Atrial flutter subjects affected / exposed occurrences (all) Sinus tachycardia subjects affected / exposed occurrences (all) Tachycardia subjects affected / exposed occurrences (all)	21 / 56 (37.50%) 21		
	4 / 56 (7.14%) 4		
	0 / 56 (0.00%) 0		
	3 / 56 (5.36%) 3		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Haemorrhagic anaemia subjects affected / exposed occurrences (all) Leukocytosis subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	12 / 56 (21.43%) 12		
	0 / 56 (0.00%) 0		
	5 / 56 (8.93%) 5		
	4 / 56 (7.14%) 5		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dysphagia subjects affected / exposed occurrences (all) Nausea	15 / 56 (26.79%) 15		
	3 / 56 (5.36%) 3		
	1 / 56 (1.79%) 1		

subjects affected / exposed	19 / 56 (33.93%)		
occurrences (all)	19		
Vomiting			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Renal failure acute			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Electrolyte imbalance			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Fluid overload			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	9		
Fluid retention			
subjects affected / exposed	1 / 56 (1.79%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	17 / 56 (30.36%)		
occurrences (all)	17		

Hypoalbuminaemia			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Hypocalcaemia			
subjects affected / exposed	9 / 56 (16.07%)		
occurrences (all)	10		
Hypokalaemia			
subjects affected / exposed	14 / 56 (25.00%)		
occurrences (all)	14		
Hypomagnesaemia			
subjects affected / exposed	5 / 56 (8.93%)		
occurrences (all)	5		
Hyponatraemia			
subjects affected / exposed	2 / 56 (3.57%)		
occurrences (all)	2		
Hypovolaemia			
subjects affected / exposed	3 / 56 (5.36%)		
occurrences (all)	3		
Metabolic acidosis			
subjects affected / exposed	0 / 56 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2012	To remove both 1200 mcg/kg groups and add the 1600 mcg/kg and 2100 mcg/kg groups and update procedures and statistical analyses; for doses given outside the operating room, allow principal investigator to write an order for study drug to be administered by hospital personnel; permit an additional 20 subjects per treatment group if appropriate based on results from interim analysis; add that some of the study visits may be conducted in the home or in a non-hospital setting and that subjects may use a home trial support service with agreement of the investigatory; modify inclusion criteria to clarify the definition of stable renal function, that patients with intravascular iodinated contrast within 48 hours of the day of surgery could be included if no known serum creatinine change ≥ 0.3 mg; modify exclusion criteria to clarify definition of active peptic ulcer, exclude patients with known or document RIFLE 'R' or AKIN 'Stage 1' results within the previous 4 weeks; specify timing of urine output collection; add must specify need for RRT; clarify measurements and procedures; add secondary endpoints to evaluate composite events utilizing cystatin-C based eGFR in addition to SCr based eGFR; change number of infusions from 5 to 6 and, if study drug is administered through a central line, then it should be administered through a separate port; add 2 interim analyses; revise total of number of subjects to up to 240.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported