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 Major Surgery

Summary

EudraCT number	2012-005710-19
Trial protocol	DK
Global end of trial date	08 April 2014

Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	25 July 2015

Trial information

Trial identification

Sponsor protocol code	M13-958

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01897519
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	08 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To determine the safety and pharmacokinetics of 800 mcg/kg intravenous (IV) infusions of ABT-719 in the first 6 subjects enrolled who are at risk of acute kidney injury (AKI) and undergoing high risk major surgery.
-To compare the safety and efficacy of doses of 800 mcg/kg, 1600 mcg/kg and 2100 mcg/kg IV infusions of ABT-719 to placebo in subjects who are at risk of AKI and undergoing high risk major surgery.

Protection of trial subjects:

Participant 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	21 May 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: 7
Country: Number of subjects enrolled	United States: 49
Worldwide total number of subjects	56
EEA total number of subjects	7

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)	14
From 65 to 84 years	40

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This subject population was selected for having a high-risk for developing AKI while undergoing high risk major surgery.

Pre-assignment

Screening details:

Part 1 was an open-label, multiple-center study to evaluate the safety and pharmacokinetics of 800 mcg/kg of ABT-719 in 6 subjects. Part 2 was a placebo-controlled, double-blind, parallel group, randomized, multiple-center study to evaluate the safety and efficacy of ABT-719.
Subjects had a screening visit 5 to 28 days prior to surgery.

Period 1

Period 1 title	Part 1 and Part 2 (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: 800 mcg/kg ABT-719

Arm description:

Subjects received 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg, 400 mcg/kg, and 200 mcg/kg on Day 0 (the day of surgery).

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:

10 mg/mL solution for intravenous injection

Arm title	Part 2: Placebo

Arm description:

Subjects received 6 infusions of placebo beginning on Day 0 (the day of surgery) and at 2 hours after the first dose and 6, 12, 24 and 48 hours after the second dose.

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:

Normal saline solution for intravenous injection

Arm title	Part 2: 800 mcg/kg ABT-719

Arm description:

Subjects received up to 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg on Day 0 at the start of surgery, 200–400 mcg/kg 2 hours after the first dose and 200 mcg/kg 6 hours after the second dose and placebo injections at 12, 24 and 48 hours after the second dose.

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:

10 mg/mL solution for intravenous injection

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:

Normal saline solution for intravenous injection

Arm title	Part 2: 1600 mcg/kg ABT-719

Arm description:

Subjects received up to 1600 mcg/kg ABT-719 divided in 5 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose, 300 mcg/kg 6 hours after the second dose, 200 mcg/kg at 12 and 24 hours after the second dose and placebo at 48 hours after the second dose.

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:

10 mg/mL solution for intravenous injection

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:

Normal saline solution for intravenous injection

Arm title	Part 2: 2100 mcg/kg ABT-719

Arm description:

Subjects received up to 2100 mcg/kg ABT-719 divided in 6 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose and 300 mcg/kg 6, 12, 24, and 48 hours after the second dose.

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:

10 mg/mL solution for intravenous injection

Number of subjects in period 1	Part 1: 800 mcg/kg ABT-719	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719
Started	6	13	12
Received treatment	4	7	9
Completed	4	7	7
Not completed	2	6	5
Other	-	-	1
Adverse event	-	-	1
Discontinued prior to receiving treatment	2	6	3

Number of subjects in period 1	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Started	12	13
Received treatment	10	10
Completed	10	8
Not completed	2	5
Other	-	-
Adverse event	-	2
Discontinued prior to receiving treatment	2	3

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: 800 mcg/kg ABT-719
Reporting group description:	
Subjects received 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg, 400 mcg/kg, and 200 mcg/kg on Day 0 (the day of surgery).	
Reporting group title	Part 2: Placebo
Reporting group description:	
Subjects received 6 infusions of placebo beginning on Day 0 (the day of surgery) and at 2 hours after the first dose and 6, 12, 24 and 48 hours after the second dose.	
Reporting group title	Part 2: 800 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg on Day 0 at the start of surgery, 200–400 mcg/kg 2 hours after the first dose and 200 mcg/kg 6 hours after the second dose and placebo injections at 12, 24 and 48 hours after the second dose.	
Reporting group title	Part 2: 1600 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 1600 mcg/kg ABT-719 divided in 5 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose, 300 mcg/kg 6 hours after the second dose, 200 mcg/kg at 12 and 24 hours after the second dose and placebo at 48 hours after the second dose.	
Reporting group title	Part 2: 2100 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 2100 mcg/kg ABT-719 divided in 6 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose and 300 mcg/kg 6, 12, 24, and 48 hours after the second dose.	

Reporting group values	Part 1: 800 mcg/kg ABT-719	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719
Number of subjects	6	13	12
Age categorical Units: Subjects			
< 65 years	1	3	5
>= 65 years	5	10	7
Age continuous Units: years			
arithmetic mean	73.2	70.5	66.2
standard deviation	± 11.86	± 7.75	± 13.22
Gender categorical Units: Subjects			
Female	4	3	3
Male	2	10	9

Reporting group values	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719	Total
Number of subjects	12	13	56
Age categorical Units: Subjects			
< 65 years	3	2	14
>= 65 years	9	11	42

Age continuous Units: years			
arithmetic mean	71.3	71.2	
standard deviation	± 8.72	± 7.72	-
Gender categorical Units: Subjects			
Female	4	4	18
Male	8	9	38

End points

End points reporting groups

Reporting group title	Part 1: 800 mcg/kg ABT-719
Reporting group description:	
Subjects received 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg, 400 mcg/kg, and 200 mcg/kg on Day 0 (the day of surgery).	
Reporting group title	Part 2: Placebo
Reporting group description:	
Subjects received 6 infusions of placebo beginning on Day 0 (the day of surgery) and at 2 hours after the first dose and 6, 12, 24 and 48 hours after the second dose.	
Reporting group title	Part 2: 800 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg on Day 0 at the start of surgery, 200–400 mcg/kg 2 hours after the first dose and 200 mcg/kg 6 hours after the second dose and placebo injections at 12, 24 and 48 hours after the second dose.	
Reporting group title	Part 2: 1600 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 1600 mcg/kg ABT-719 divided in 5 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose, 300 mcg/kg 6 hours after the second dose, 200 mcg/kg at 12 and 24 hours after the second dose and placebo at 48 hours after the second dose.	
Reporting group title	Part 2: 2100 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 2100 mcg/kg ABT-719 divided in 6 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose and 300 mcg/kg 6, 12, 24, and 48 hours after the second dose.	

Primary: Maximal change from Baseline in urine neutrophil gelatinase-associated lipocalin (NGAL) until Day 7 or discharge

End point title	Maximal change from Baseline in urine neutrophil gelatinase-associated lipocalin (NGAL) until Day 7 or discharge[1]
End point description:	
Raw urine NGAL data were log transformed for analysis of change from Baseline. The Full Analysis Set (FAS) was defined as the set of all randomized subjects who received at least 1 infusion of study drug. Subjects with a negative maximal change were removed from the analysis.	
End point type	Primary
End point timeframe:	
Baseline to Day 7	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	9	10	8
Units: ng/mL				
least squares mean (standard error)	118.9 (± 1.7)	207.3 (± 1.6)	411.3 (± 1.6)	196.6 (± 1.7)

Statistical analyses

Statistical analysis title	Primary efficacy analysis

Statistical analysis description:

The primary efficacy analysis of each ABT-719 dose group versus placebo in the mean maximal change from baseline in urine NGAL (on log scale) until Day 7 or discharge was performed using an analysis of covariance (ANCOVA) model with fixed factors of treatment group and randomization stratification as fixed factors and baseline urine NGAL as a covariate.
Comparisons versus placebo were based on a 1-sided significance level of 0.050.

Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.7

Statistical analysis title	Primary efficacy analysis

Statistical analysis description:

The primary efficacy analysis of each ABT-719 dose group versus placebo in the mean maximal change from baseline in urine NGAL (on log scale) until Day 7 or discharge was performed using an analysis of covariance (ANCOVA) model with fixed factors of treatment group and randomization stratification as fixed factors and baseline urine NGAL as a covariate.
Comparisons versus placebo were based on a 1-sided significance level of 0.050.

Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.081
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	2.6

Variability estimate	Standard error of the mean
Dispersion value	0.7

Statistical analysis title	Primary efficacy analysis

Statistical analysis description:

The primary efficacy analysis of each ABT-719 dose group versus placebo in the mean maximal change from baseline in urine NGAL (on log scale) until Day 7 or discharge was performed using an analysis of covariance (ANCOVA) model with fixed factors of treatment group and randomization stratification as fixed factors and baseline urine NGAL as a covariate.
Comparisons versus placebo were based on a 1-sided significance level of 0.050.

Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.499
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.7

Secondary: Maximal change from Baseline in serum NGAL until Day 7 or discharge

End point title	Maximal change from Baseline in serum NGAL until Day 7 or discharge[2]

End point description:

Raw serum NGAL data were log transformed for analysis of change from Baseline. The per-protocol analysis set was defined as the set of all randomized subjects who received all 6 infusions of study drug and underwent the pre-defined surgery. Subjects with a negative maximal change were removed from the analysis.

End point type	Secondary

End point timeframe:

Baseline to Day 7

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	10	6
Units: ng/mL				
least squares mean (standard error)	360.3 (± 1.3)	477.7 (± 1.4)	619.6 (± 1.3)	436.3 (± 1.4)

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.54 [3]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.5

Notes:

[3] - ANCOVA model with treatment group as the factor and baseline as a covariate .

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.15 [4]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[4] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719

Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.656 [5]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.4

Notes:

[5] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Secondary: Maximal change from baseline in urine interleukin-18 until Day 7 or discharge

End point title	Maximal change from baseline in urine interleukin-18 until Day 7 or discharge[6]

End point description:

Raw urine interleukin-18 data were log transformed for analysis of change from Baseline. The per-protocol analysis set was defined as the set of all randomized subjects who received all 6 infusions of study drug and underwent the pre-defined surgery. Subjects with a negative maximal change were removed from the analysis.

End point type	Secondary

End point timeframe:

Baseline to Day 7

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	5	9	6
Units: pg/mL				
least squares mean (standard error)	43.7 (± 1.7)	41.6 (± 1.7)	53.5 (± 1.6)	48.8 (± 1.6)

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719

Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.948 [7]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:

[7] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.752 [8]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:

[8] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.879 [9]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.6

Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[9] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Secondary: Maximal change from Baseline in urine kidney injury molecule (KIM-1) until Day 7 or discharge

End point title	Maximal change from Baseline in urine kidney injury molecule (KIM-1) until Day 7 or discharge[10]

End point description:

Raw urine KIM-1 data were log transformed for analysis of change from Baseline. The per-protocol analysis set was defined as the set of all randomized subjects who received all 6 infusions of study drug and underwent the pre-defined surgery. Subjects with a negative maximal change were removed from the analysis.

End point type	Secondary

End point timeframe:

Baseline to Day 7

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	4	10	6
Units: ng/mL				
least squares mean (standard error)	0.9 (± 1.6)	2.8 (± 2)	1.1 (± 1.5)	1.1 (± 1.7)

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.179 [11]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	2.9
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:
[11] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.731 [12]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.6

Notes:
[12] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.739 [13]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.8

Notes:
[13] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Secondary: Number of subjects developing acute kidney injury (AKI) as defined by the AKIN scoring criteria

End point title	Number of subjects developing acute kidney injury (AKI) as defined by the AKIN scoring criteria[14]

End point description:

the Acute Kidney Injury Network (AKIN) classification/staging system of acute kidney injury:
Stage 1: Increased serum creatinine ≥ 26.5 µmol/L (≥ 0.3 mg/dL) or an increase ≥ 1.5 x Baseline; urine output < 0.5 mL/kg/hr for more than 6 hours.
Stage 2: Increased serum creatinine 2 x Baseline; urine output < 0.5 mL/kg/hr for more than 12 hours.
Stage 3: Increased serum creatinine 3 x Baseline or if Baseline creatinine ≥ 353.6 µmol/L (≥ 4 mg/dL) an increase of ≥ 44.2 µmol/L (≥ 0.5 mg/dL); urine output < 0.3 mL/kg/hr for 24 hours or anuria for 12

hours.

End point type	Secondary

End point timeframe:

90 days

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[15]	5[16]	10[17]	8[18]
Units: subjects				
Stage 1	2	0	2	2
Stage 2	1	1	3	2
Stage 3	1	0	3	2

Notes:

[15] - Per protocol analysis set

[16] - Per protocol analysis set

[17] - Per protocol analysis set

[18] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293
Method	Fisher exact

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	Fisher exact

Statistical analysis title	Comparison 3
Comparison groups	Part 2: 2100 mcg/kg ABT-719 v Part 2: Placebo

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.608
Method	Fisher exact

Secondary: Number of subjects developing one of the composite events: death, renal replacement therapy (RRT), or ≥ 25% reduction in serum creatinine based estimated glomerular filtration rate (eGFR) at Day 90

End point title	Number of subjects developing one of the composite events: death, renal replacement therapy (RRT), or ≥ 25% reduction in serum creatinine based estimated glomerular filtration rate (eGFR) at Day 90[19]

End point description:

The number of subjects developing at least one of the composite events:
- death,
- needing RRT during the 90-day post-operative period, or
- a ≥ 25% reduction in serum creatinine (SCr) based estimated glomerular filtration rate (eGFR) at the Day 90 post-surgery visit.

End point type	Secondary

End point timeframe:

90 days

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[20]	5[21]	10[22]	8
Units: subjects	0	0	2	3

Notes:

[20] - Per protocol analysis set

[21] - Per protocol analysis set

[22] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.485
Method	Fisher exact

Statistical analysis title	Comparison 2

Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Fisher exact

Secondary: Number of subjects developing one of the composite events: death, RRT or ≥ 25% reduction in SCr based GFR at Day 60

End point title	Number of subjects developing one of the composite events: death, RRT or ≥ 25% reduction in SCr based GFR at Day 60[23]

End point description:

The number of subjects developing at least one of the composite events:
- death,
- needing RRT during the 60-day post-operative period, or
- having a ≥ 25% reduction in SCr based eGFR or measured GFR at Day 60 post-surgery visit.

End point type	Secondary

End point timeframe:

60 days

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[24]	5[25]	10[26]	8[27]
Units: subjects	0	0	4	4

Notes:

[24] - Per protocol analysis set

[25] - Per protocol analysis set

[26] - Per protocol analysis set

[27] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.103
Method	Fisher exact

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.077
Method	Fisher exact

Secondary: Number of subjects developing one of the composite events: death, RRT, or ≥ 25% reduction in S-Cystatin C based eGFR at Day 90

End point title	Number of subjects developing one of the composite events: death, RRT, or ≥ 25% reduction in S-Cystatin C based eGFR at Day 90[28]

End point description:

Number of subjects developing at least one of the composite events:
- death,
- needing RRT during the 90-day post-operative period, or
- having a ≥ 25% reduction in S-Cystatin C based eGFR or measured GFR at Day 90 post surgery visit

End point type	Secondary

End point timeframe:

90 days

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[29]	5[30]	10[31]	8[32]
Units: subjects	0	0	5	2

Notes:

[29] - Per protocol analysis set

[30] - Per protocol analysis set

[31] - Per protocol analysis set

[32] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044
Method	Fisher exact

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.467
Method	Fisher exact

Secondary: Number of subjects developing one of the composite events: death, or ≥ 25% reduction in S-Cystatin C based eGFR at Day 60

End point title	Number of subjects developing one of the composite events: death, or ≥ 25% reduction in S-Cystatin C based eGFR at Day 60[33]

End point description:

Number of subjects developing at least one of the composite events:
- death,
- needing RRT during the 60-day post-operative period, or
- having a ≥ 25% reduction in S-Cystatin C based eGFR or measured GFR at Day 60 post surgery visit.

End point type	Secondary

End point timeframe:

60 days

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[34]	5[35]	10[36]	8[37]
Units: subjects	0	0	6	2

Notes:

[34] - Per protocol analysis set

[35] - Per protocol analysis set

[36] - Per protocol analysis set

[37] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035
Method	Fisher exact

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.467
Method	Fisher exact

Secondary: Number of subjects developing AKI as defined by the RIFLE scoring criteria

End point title	Number of subjects developing AKI as defined by the RIFLE scoring criteria[38]

End point description:

The RIFLE classification defines three grades of severity of AKI (Risk, Injury and Failure) based on changes to serum creatinine, urine output and two clinical outcomes (Loss and End-stage). The 3 severity grades are defined on the basis of the changes in serum creatinine or urine output where the worst of each criterion is used. The 2 outcome criteria, Loss and End Stage Kidney Disease, are defined by the duration of loss of kidney function.
Stage 1 (Risk): Increased serum creatinine × 1.5 or decreased GFR > 25%; urine output < 0.5 mL/kg/hr for more than 6 hours.
Stage 2 (Injury): Increased serum creatinine × 2 or a decrease in GFR > 50%; urine output < 0.5 mL/kg/hr for more than 12 hours.
Stage 3 (Failure): Increased serum creatinine × 3 or a decrease in GFR >75% or if baseline SCr ≥ 353.6 µmol/L (≥ 4 mg/dL), increased SCr > 44.2 µmol/L (> 0.5 mg/dL); urine output < 0.3 mL/kg/hr for 24 hours or anuria for 12 hours.

End point type	Secondary

End point timeframe:

90 days

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[39]	5[40]	10[41]	8[42]
Units: subjects				
Stage 1	1	0	2	2
Stage 2	2	1	3	2
Stage 3	1	0	3	2

Notes:

[39] - Per protocol analysis set

[40] - Per protocol analysis set

[41] - Per protocol analysis set

[42] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293
Method	Fisher exact

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	Fisher exact

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.608
Method	Fisher exact

Secondary: Number of subjects who developed AKI as determined by the Kidney Disease Improving Global Outcomes (KDIGO) Scoring criteria

End point title	Number of subjects who developed AKI as determined by the Kidney Disease Improving Global Outcomes (KDIGO) Scoring criteria[43]

End point description:

Kidney Disease Improving Global Outcomes (KDIGO) defined AKI as: increase in serum creatinine (SCr) by ≥ 0.3 mg/dl (≥ 26.5 µmol/l) within 48 hours; or 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.
Stage 1: Serum creatinine 1.5 – 1.9 x Baseline OR ≥ 0.3 mg/dl (≥ 26.5 µmol/l) increase; urine output < 0.5 mL/kg/hr for 6 – 12 hours.
Stage 2: Serum creatinine 2.0 – 2.9 x Baseline; urine output < 0.5 mL/kg/hr for ≥ 12 hours.
Stage 3: Serum creatinine 3.0 x Baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 µmol/l) OR Initiation of renal replacement therapy OR In patients < 18 years, decrease in eGFR to < 35 mL/min per 1.73 m²; urine output < 0.3 mL/kg/hr for ≥ 24 hours OR Anuria for ≥ 12 hours.

End point type	Secondary

End point timeframe:

90 days

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[44]	5[45]	10[46]	8[47]
Units: subjects				
Stage 1	2	0	2	2
Stage 2	1	1	3	2
Stage 3	1	0	3	2

Notes:

[44] - Per protocol analysis set

[45] - Per protocol analysis set

[46] - Per protocol analysis set

[47] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.293
Method	Fisher exact

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.593
Method	Fisher exact

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.608
Method	Fisher exact

Secondary: Changes from Baseline in serum creatinine (SCr) and S-Cystatin C at all study visits from Day 0 to Day 90

End point title	Changes from Baseline in serum creatinine (SCr) and S-Cystatin C at all study visits from Day 0 to Day 90[48]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Day 90

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[49]	0[50]	0[51]	0[52]
Units: mg/dL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[49] - Not analyzed due to study termination

[50] - Not analyzed due to study termination

[51] - Not analyzed due to study termination

[52] - Not analyzed due to study termination

Statistical analyses

No statistical analyses for this end point

Secondary: Maximal change from Baseline in serum creatinine until Day 7 or until discharge from the hospital

End point title	Maximal change from Baseline in serum creatinine until Day 7 or until discharge from the hospital[53]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Day 7

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[54]	5[55]	10[56]	8[57]
Units: mg/dL				
least squares mean (standard error)	14.1 (± 22.9)	9.2 (± 28.7)	61.5 (± 19.6)	22.4 (± 21.8)

Notes:

[54] - Per protocol analysis set

[55] - Per protocol analysis set

[56] - Per protocol analysis set

[57] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.894 [58]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-78.8
upper limit	69
Variability estimate	Standard error of the mean
Dispersion value	36.6

Notes:

[58] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.119 [59]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	47.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.8
upper limit	107.5
Variability estimate	Standard error of the mean
Dispersion value	29.8

Notes:

[59] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719

Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.793 [60]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55
upper limit	71.6
Variability estimate	Standard error of the mean
Dispersion value	31.4

Notes:

[60] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Secondary: Maximal change from Baseline in S-Cystatin C until Day 7 or until discharge from the hospital

End point title	Maximal change from Baseline in S-Cystatin C until Day 7 or until discharge from the hospital[61]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Day 7

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[62]	5[63]	10[64]	8[65]
Units: mg/L				
least squares mean (standard error)	2 (± 13.4)	5.7 (± 16.1)	38.1 (± 11.3)	25.1 (± 12.8)

Notes:

[62] - Per protocol analysis set

[63] - Per protocol analysis set

[64] - Per protocol analysis set

[65] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.863 [66]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-38.5
upper limit	45.8
Variability estimate	Standard error of the mean
Dispersion value	20.9

Notes:

[66] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.044 [67]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	36.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	71.1
Variability estimate	Standard error of the mean
Dispersion value	17.4

Notes:

[67] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.211 [68]
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	23.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	59.8

Variability estimate	Standard error of the mean
Dispersion value	18.2

Notes:

[68] - ANCOVA model with treatment group as the factor and baseline as a covariate.

Secondary: Change from Baseline in SCr based eGFR, S-Cystatin C based eGFR and measured GFR at all study visits from Day 0 to Day 90

End point title	Change from Baseline in SCr based eGFR, S-Cystatin C based eGFR and measured GFR at all study visits from Day 0 to Day 90[69]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Day 90

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[70]	0[71]	0[72]	0[73]
Units: mL/min/1.73 m²				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[70] - Not analyzed due to study termination

[71] - Not analyzed due to study termination

[72] - Not analyzed due to study termination

[73] - Not analyzed due to study termination

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in AKI Biomarkers (urine and serum) at all study visits from Day 0 to Day 90

End point title	Changes from Baseline in AKI Biomarkers (urine and serum) at all study visits from Day 0 to Day 90[74]

End point description:

End point type	Secondary

End point timeframe:

Baseline to Day 90

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[75]	0[76]	0[77]	0[78]
Units: mg/dL				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[75] - Not analyzed due to study termination

[76] - Not analyzed due to study termination

[77] - Not analyzed due to study termination

[78] - Not analyzed due to study termination

Statistical analyses

No statistical analyses for this end point

Secondary: Number of days hospitalized during the 90-day post-operative period

End point title	Number of days hospitalized during the 90-day post-operative period[79]

End point description:

End point type	Secondary

End point timeframe:

90 days

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[80]	5[81]	10[82]	8[83]
Units: days				
least squares mean (standard error)	53.3 (± 12)	36.4 (± 14.2)	50.5 (± 10.1)	43.4 (± 11.2)

Notes:

[80] - Per protocol analysis set

[81] - Per protocol analysis set

[82] - Per protocol analysis set

[83] - Per protocol analysis set

Statistical analyses

Statistical analysis title	Comparison 1
Comparison groups	Part 2: Placebo v Part 2: 800 mcg/kg ABT-719

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.369 [84]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-16.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-48.1
upper limit	14.3
Variability estimate	Standard error of the mean
Dispersion value	18.6

Notes:

[84] - ANOVA model with treatment as the factor.

Statistical analysis title	Comparison 2
Comparison groups	Part 2: Placebo v Part 2: 1600 mcg/kg ABT-719
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86 [85]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-2.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-29.1
upper limit	23.5
Variability estimate	Standard error of the mean
Dispersion value	15.7

Notes:

[85] - ANOVA model with treatment as the factor.

Statistical analysis title	Comparison 3
Comparison groups	Part 2: Placebo v Part 2: 2100 mcg/kg ABT-719
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55 [86]
Method	ANOVA
Parameter estimate	LS Mean Difference
Point estimate	-9.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-37.5
upper limit	17.7

Variability estimate	Standard error of the mean
Dispersion value	16.5

Notes:

[86] - ANOVA model with treatment as the factor.

Secondary: Change from Baseline in Euroqol 5 Dimensions (EQ-5D) index score

End point title	Change from Baseline in Euroqol 5 Dimensions (EQ-5D) index score[87]

End point description:

The EQ-5D consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. There are 3 levels to each dimension: no problems, some problems, and extreme problems. The scores of the 5 dimensions were converted into a single summary index by utilizing country specific value sets, from 0 to 1 where 1 represents perfect health.

End point type	Secondary

End point timeframe:

Baseline, day of discharge and 90 days post surgery

Notes:

[87] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[88]	5[89]	10[90]	8[91]
Units: units on a scale				
arithmetic mean (standard deviation)				
Change to Day of Discharge (n=4, 2, 3, 2)	-0.017 (± 0.051)	0.021 (± 0.03)	-0.055 (± 0.056)	-0.065 (± 0.067)
Change to Day 90 (n=2, 2, 3, 3)	-0.031 (± 0.065)	0.156 (± 0.025)	-0.078 (± 0.071)	0.07 (± 0.132)

Notes:

[88] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

[89] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

[90] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

[91] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in for EQ-5D visual analog scale (VAS) Score

End point title	Change from Baseline in for EQ-5D visual analog scale (VAS) Score[92]

End point description:

The EQ-5D is a patient-completed, multidimensional measure of health related quality of life. The EQ-5D VAS records the respondent's self-rated health status on a vertical graduated (0-100) visual analogue scale. Higher EQ-5D VAS scores represent better health status.

End point type	Secondary

End point timeframe:

Baseline, day of discharge and 90 days post-surgery

Notes:

[92] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7[93]	5[94]	10[95]	8[96]
Units: units on a scale				
arithmetic mean (standard deviation)				
Change to Day of Discharge (n=4, 2, 3, 2)	7.5 (± 17.08)	7.5 (± 3.54)	-6 (± 10.39)	9 (± 1.41)
Change to Day 90 (n=2, 2, 3, 3)	15 (± 21.21)	-42.5 (± 67.18)	13 (± 12.12)	40.7 (± 22.9)

Notes:

[93] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

[94] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

[95] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

[96] - Per protocol analysis set; subjects with available data at each time point is indicated by "n".

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with 'no problem' and 'problems' in 5 dimensions of EQ-5D

End point title	Number of subjects with 'no problem' and 'problems' in 5 dimensions of EQ-5D[97]

End point description:

Number of subjects who experience 'no problem' (level 1) and 'problems' (level 2 and 3) in 5 dimensions of EQ-5D. The EQ-5D-3L consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. There are 3 levels to each dimension: no problems (level 1), some problems (level 2), and extreme problems (level 3).

End point type	Secondary

End point timeframe:

Day of discharge

Notes:

[97] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Efficacy endpoints were only assessed in Part 2 subjects

End point values	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[98]	2[99]	3[100]	2[101]
Units: subjects				
Mobility - No Problems	1	2	0	1
Mobility - Problems	3	0	3	1
Self-care - No Problems	4	2	0	1
Self-care - Problems	0	0	3	1
Usual Activities - No Problems	0	2	1	0

Usual Activities - Problems	4	0	2	2
Pain/Discomfort - No problems	1	0	0	1
Pain/Discomfort - Problems	3	2	3	1
Anxiety/Depression - No Problems	4	2	1	2
Anxiety/Depression - Problems	0	0	2	0

Notes:

[98] - Per protocol analysis set with available data

[99] - Per protocol analysis set with available data

[100] - Per protocol analysis set with available data

[101] - Per protocol analysis set with available data

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first dose of study drug until 30 days after last dose.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Part 1: 800 mcg/kg ABT-719
Reporting group description:	
Subjects received 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg, 400 mcg/kg, and 200 mcg/kg on Day 0 (the day of surgery).	
Reporting group title	Part 2: Placebo
Reporting group description:	
Subjects received 6 infusions of placebo beginning on Day 0 (the day of surgery) and at 2 hours after the first dose and 6, 12, 24 and 48 hours after the second dose.	
Reporting group title	Part 2: 800 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 800 mcg/kg ABT-719 divided in 3 doses given as 10 minute infusions of 200 mcg/kg on Day 0 at the start of surgery, 200–400 mcg/kg 2 hours after the first dose and 200 mcg/kg 6 hours after the second dose and placebo injections at 12, 24 and 48 hours after the second dose.	
Reporting group title	Part 2: 1600 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 1600 mcg/kg ABT-719 divided in 5 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose, 300 mcg/kg 6 hours after the second dose, 200 mcg/kg at 12 and 24 hours after the second dose and placebo at 48 hours after the second dose.	
Reporting group title	Part 2: 2100 mcg/kg ABT-719
Reporting group description:	
Subjects received up to 2100 mcg/kg ABT-719 divided in 6 doses given as 10 minute infusions of 300 mcg/kg on Day 0 at the start of surgery, 300–600 mcg/kg 2 hours after the first dose and 300 mcg/kg 6, 12, 24, and 48 hours after the second dose.	

Serious adverse events	Part 1: 800 mcg/kg ABT-719	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	3 / 7 (42.86%)	3 / 9 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Oxygen Saturation Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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
Nervous system disorders			

Cerebrovascular Accident			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diplegia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
Gastrointestinal disorders			
Diaphragmatic Hernia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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
Gastric Ulcer			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 9 (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
Gastritis Erosive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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
Intestinal Perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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
Mechanical Ileus			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (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
Skin and subcutaneous tissue disorders			
Diabetic Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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 Ischaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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
Infections and infestations			
Septic Shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (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	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 9 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (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

Serious adverse events	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	

number of deaths (all causes) number of deaths resulting from adverse events	1	0	
Investigations			
Oxygen Saturation Decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplegia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diaphragmatic Hernia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric Ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis Erosive			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Ischaemia			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Perforation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical Ileus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic Ulcer			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal Ischaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Septic Shock			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wound Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: 800 mcg/kg ABT-719	Part 2: Placebo	Part 2: 800 mcg/kg ABT-719
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	5 / 7 (71.43%)	8 / 9 (88.89%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Pallor			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Prophylaxis Against Gastrointestinal Ulcer			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Medical Device Complication			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pleural Effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Pneumothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory Acidosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory Failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Wheezing			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Mental Status Changes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated Partial Thromboplastin Time Prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood Bilirubin Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood Pressure Systolic Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Body Temperature Increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cystatin C Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Haemoglobin Decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
International Normalised Ratio Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Red Blood Cells Urine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Troponin Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary Sediment Present			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urine Albumin/Creatinine Ratio Increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urine Analysis Abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urine Output Decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
White Blood Cells Urine Positive			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Arterial Injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Incision Site Pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Laceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Post Procedural Constipation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Postoperative Ileus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Procedural Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Procedural Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Procedural Pain			
subjects affected / exposed	2 / 4 (50.00%)	2 / 7 (28.57%)	7 / 9 (77.78%)
occurrences (all)	2	2	7
Procedural Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Scrotal Haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Wound Complication			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Neuropathy Peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Eye disorders			
Visual Impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Colitis Ischaemic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	3 / 9 (33.33%)
occurrences (all)	0	1	3
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Haematemesis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Ileus			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Vomiting			
subjects affected / exposed	3 / 4 (75.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	3	0	1
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Renal and urinary disorders			

Renal Failure Acute			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Renal Impairment			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary Retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Groin Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Muscle Spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscular Weakness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Pain In Extremity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Eye Infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gangrene			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Lung Infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Fluid Overload			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 7 (14.29%)	1 / 9 (11.11%)
occurrences (all)	1	1	1
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	2 / 4 (50.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	3	1	0

Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Malnutrition			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolic Acidosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vitamin D Deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part 2: 1600 mcg/kg ABT-719	Part 2: 2100 mcg/kg ABT-719	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	9 / 10 (90.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	
occurrences (all)	1	3	
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Pallor			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
Prophylaxis Against Gastrointestinal Ulcer			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Medical Device Complication			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal Pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pleural Effusion			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	

Pneumothorax			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Respiratory Acidosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Respiratory Failure			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Confusional State			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Delirium			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Mental Status Changes			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Investigations			
Activated Partial Thromboplastin Time Prolonged			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Blood Bilirubin Increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Blood Creatinine Increased			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Blood Pressure Increased				
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)		
occurrences (all)	0	0		
Blood Pressure Systolic Increased				
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Body Temperature Increased				
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)		
occurrences (all)	0	0		
Cystatin C Increased				
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Haemoglobin Decreased				
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)		
occurrences (all)	0	0		
International Normalised Ratio Increased				
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Red Blood Cells Urine				
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Troponin Increased				
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)		
occurrences (all)	1	0		
Urinary Sediment Present				
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Urine Albumin/Creatinine Ratio Increased				
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)		
occurrences (all)	0	1		
Urine Analysis Abnormal				

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Urine Output Decreased			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
White Blood Cells Urine Positive			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Arterial Injury			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Incision Site Pain			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Laceration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Post Procedural Constipation			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Postoperative Ileus			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Procedural Hypotension			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Procedural Nausea			
subjects affected / exposed	3 / 10 (30.00%)	0 / 10 (0.00%)	
occurrences (all)	3	0	
Procedural Pain			
subjects affected / exposed	3 / 10 (30.00%)	5 / 10 (50.00%)	
occurrences (all)	3	5	
Procedural Vomiting			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Scrotal Haematoma			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Wound Complication			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Bradycardia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Neuropathy Peripheral			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	4 / 10 (40.00%)	3 / 10 (30.00%)	
occurrences (all)	4	3	
Leukocytosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	
occurrences (all)	0	2	
Eye disorders			
Visual Impairment			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Colitis Ischaemic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Haematemesis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Ileus			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	2 / 10 (20.00%)	4 / 10 (40.00%)	
occurrences (all)	2	4	
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			

Hypertransaminasaemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Ecchymosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	
occurrences (all)	0	3	
Rash			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal Failure Acute			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Renal Impairment			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Urinary Retention			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Groin Pain			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Muscle Spasms			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Muscular Weakness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal Stiffness			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	

Pain In Extremity			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Eye Infection			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Gangrene			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Lung Infection			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Urinary Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Fluid Overload			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	
occurrences (all)	2	1	
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hypernatraemia			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	
occurrences (all)	1	2	
Hypoglycaemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Hypomagnesaemia			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	
occurrences (all)	2	2	
Hyponatraemia			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Metabolic Acidosis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Vitamin D Deficiency			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2013	The purpose of this amendment was to: ● Revise benefits and risks section to clarify the proper medical terminology of gastric fundus rather than ventricular fundus. ● Revise study procedures sections to note that a urine pregnancy test was to be performed rather than a serum pregnancy test at Baseline for Part 1 and Part 2 to meet exclusion criterion number 15. ● Revise throughout that the unblinded pharmacist could designate pharmacy procedures to an unblinded non-pharmacist staff member. ● Revise exclusion criteria section to add that subjects who required intravascular (IV) iodinated contrast within 5 days of the day of surgery (Day 0) and experienced a known SCr change of ≥ 0.3 mg on repeat testing 24 hours apart post-contrast were to be excluded. ● Revise exclusion criteria section to add that subjects who were scheduled to have a total or partial nephrectomy were to be excluded. ● Revise study procedures table to clarify that study drug administration was to only take place on Day 0 (Surgery Day) for Part 1 and that study drug administration was not to take place on Day 3 for Part 2. ● Clarify that blood pressure (BP) was to be taken in the sitting position when possible, as it cannot be taken while the subject is in surgery on Day 0 (Surgery Day). ● Clarify that pregnancy tests were to be conducted only on females of childbearing potential. ● Clarify the stratification variables for surgical procedures from 'Vascular or Other' to 'Endovascular or Other.' ● Revise Independent Data Monitoring Committee (IDMC) sections to remove external Data Monitoring Committee (DMC) members and add that unblinded AbbVie statisticians and medical doctors(s) not associated with the conduct of the study were to be part of the DMC. Rationale for Change: An external IDMC committee was no longer included in the protocol. ● Clarify randomization methods section to differentiate between low, mid and high doses of ABT-719.
15 January 2014	The purpose of this amendment was to: ● Revise definition for High Risk Major Surgery. ● Clarify the patient population was to include subjects that were undergoing high risk major surgeries including: cardiac (non-CPB), TAVR, endovascular surgery or vascular surgery. ● Clarify that subjects who failed Screening on laboratory criteria at this visit, or had their surgery delayed for > 28 days could be re-screened once, at the discretion of the principal investigator and study designated physician. ● Clarify that up to approximately 180 additional subjects may have been randomized to placebo and/or to the ABT-719 dose groups selected for further study based on the results of the interim analysis, as appropriate. ● Remove requirement for a Day 7 visit if subject was discharged prior to Day 5. ● Revisions to exclusion criteria ● Revise prior and concomitant therapy section to add the following: Nephrotoxic medications such as non-steroidal anti-inflammatory drugs (daily prophylactic aspirin use was acceptable) and aminoglycosides were to be minimized or avoided. ● Clarify that subjects who were discontinued from study drug after receiving at least 1 dose were to be followed for safety for 30 days. For subjects who were randomized but never received study drug or did not undergo surgery, additional enrollment may have occurred to maintain the power of the study. ● Revise randomization sections to delete: and ≤ 59 mL/min/1.73 m² from eGFR stratification arm and clarify that subjects were to be stratified in the IVRS based on screening eGFR (between 16 – 45 mL/min/1.73 m², and eGFR greater than 45 mL/min/1.73 m²).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported