Clinical trial results:
A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy, Safety and Tolerability of a Single Infusion of MK-6072 (Human Monoclonal Antibody to Clostridium difficile toxin B), and MK-3415A (Human Monoclonal Antibodies to Clostridium difficile toxin A and B) in Patients Receiving Antibiotic Therapy for Clostridium difficile Infection (MODIFY II)

Summary

EudraCT number	2011-004994-94
Trial protocol	SE ES DE CZ FI PL GR
Global end of trial date	22 May 2015

Results information

Result version number	v2
This version publication date	06 January 2018
First version publication date	12 May 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	3415A-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01513239
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	22 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2015
Global end of trial reached?	Yes
Global end of trial date	22 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

MK-3415A is the combination of monoclonal antibodies to Clostridium (C.) difficile toxin A (MK-3415) and toxin B (MK-6072). This study will investigate whether: 1) treatment with MK-6072 or MK-3415A in addition to standard of care (SOC) antibiotic therapy will decrease Clostridium Difficile Infection (CDI) recurrence compared with placebo; and 2) MK-6072 and MK-3415A will be generally well tolerated in participants receiving SOC therapy for CDI compared with placebo.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy:

Standard of Care (SOC) for CDI will be prescribed for 10 to 14 days and can begin on the day of study drug infusion; but the first dose must have been administered prior to or within a few hours following study drug infusion. SOC is defined as the receipt of oral metronidazole, oral vancomycin, intravenous (IV) metronidazole concurrent with oral vancomycin, oral fidaxomicin, or oral fidaxomicin concurrent with IV metronidazole.

Evidence for comparator: -

Actual start date of recruitment	01 February 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	9 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 17
Country: Number of subjects enrolled	Canada: 74
Country: Number of subjects enrolled	Czech Republic: 57
Country: Number of subjects enrolled	Finland: 20
Country: Number of subjects enrolled	France: 68
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	Israel: 18
Country: Number of subjects enrolled	Japan: 95
Country: Number of subjects enrolled	Korea, Republic of: 66
Country: Number of subjects enrolled	Poland: 90
Country: Number of subjects enrolled	Russian Federation: 33
Country: Number of subjects enrolled	Spain: 94

Country: Number of subjects enrolled	Sweden: 56
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Taiwan: 22
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	United States: 410
Worldwide total number of subjects	1203
EEA total number of subjects	437

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)	531
From 65 to 84 years	559
85 years and over	113

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male and female participants 18 years of age or older, diagnosed with CDI and receiving SOC therapy were recruited for this trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MK-3415A + Standard Of Care (SOC)

Arm description:

Single intravenous (IV) infusion of 10 mg/kg MK-3415A + SOC for CDI

Arm type	Experimental
Investigational medicinal product name	MK-3415A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of MK-3415A (10 mg/kg of monoclonal antibody to C. difficile Toxin A and 10 mg/kg of monoclonal antibody to C. difficile Toxin B)

Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Standard of Care (SOC) for CDI will be prescribed for 10 to 14 days and can begin on the day of study drug infusion; but the first dose must have been administered prior to or within a few hours following study drug infusion. SOC is defined as the receipt of oral metronidazole, oral vancomycin, intravenous (IV) metronidazole concurrent with oral vancomycin, oral fidaxomicin, or oral fidaxomicin concurrent with IV metronidazole

Arm title	MK-6072 + Standard Of Care (SOC)

Arm description:

Single intravenous (IV) infusion of 10 mg/kg MK-6072 + SOC for CDI

Arm type	Experimental
Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Standard of Care (SOC) for CDI will be prescribed for 10 to 14 days and can begin on the day of study drug infusion; but the first dose must have been administered prior to or within a few hours following

study drug infusion. SOC is defined as the receipt of oral metronidazole, oral vancomycin, intravenous (IV) metronidazole concurrent with oral vancomycin, oral fidaxomicin, or oral fidaxomicin concurrent with IV metronidazole

Investigational medicinal product name	MK-6072
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single IV infusion of MK-6072 (10 mg/kg of monoclonal antibody to C. difficile Toxin B)

Arm title	Placebo + Standard Of Care (SOC)

Arm description:

Normal saline IV infusion (0.9% sodium chloride) + SOC for CDI

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

Dosage and administration details:

Single IV infusion of normal saline (0.9% sodium chloride)

Investigational medicinal product name	SOC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

Standard of Care (SOC) for CDI will be prescribed for 10 to 14 days and can begin on the day of study drug infusion; but the first dose must have been administered prior to or within a few hours following study drug infusion. SOC is defined as the receipt of oral metronidazole, oral vancomycin, intravenous (IV) metronidazole concurrent with oral vancomycin, oral fidaxomicin, or oral fidaxomicin concurrent with IV metronidazole

Number of subjects in period 1	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)
Started	397	407	399
Treated	391	396	381
All Participants as Treated	390	396	381
Completed	322	337	311
Not completed	75	70	88
Physician decision	4	4	4
Consent withdrawn by subject	27	29	42
Adverse event, non-fatal	1	1	2
Death	29	22	32
Technical Problems	1	2	-
Lost to follow-up	11	10	6
Protocol deviation	2	2	2

Baseline characteristics

Reporting groups	
Reporting group title	MK-3415A + Standard Of Care (SOC)
Reporting group description:	
Single intravenous (IV) infusion of 10 mg/kg MK-3415A + SOC for CDI	
Reporting group title	MK-6072 + Standard Of Care (SOC)
Reporting group description:	
Single intravenous (IV) infusion of 10 mg/kg MK-6072 + SOC for CDI	
Reporting group title	Placebo + Standard Of Care (SOC)
Reporting group description:	
Normal saline IV infusion (0.9% sodium chloride) + SOC for CDI	

Reporting group values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)
Number of subjects	397	407	399
Age Categorical Units: Subjects			
Adults (18-64 years)	150	198	183
From 65-84 years	203	177	179
85 years and over	44	32	37
Age Continuous Units: years			
arithmetic mean	65.9	62.6	64.3
standard deviation	± 17.3	± 17.5	± 16.4
Gender Categorical Units: Subjects			
Female	216	220	239
Male	181	187	160

Reporting group values	Total		
Number of subjects	1203		
Age Categorical Units: Subjects			
Adults (18-64 years)	531		
From 65-84 years	559		
85 years and over	113		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Subjects			
Female	675		
Male	528		

End points

End points reporting groups

Reporting group title	MK-3415A + Standard Of Care (SOC)
Reporting group description:	
Single intravenous (IV) infusion of 10 mg/kg MK-3415A + SOC for CDI	
Reporting group title	MK-6072 + Standard Of Care (SOC)
Reporting group description:	
Single intravenous (IV) infusion of 10 mg/kg MK-6072 + SOC for CDI	
Reporting group title	Placebo + Standard Of Care (SOC)
Reporting group description:	
Normal saline IV infusion (0.9% sodium chloride) + SOC for CDI	

Primary: Percentage of participants with CDI recurrence

End point title	Percentage of participants with CDI recurrence
End point description:	
CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile after clinical cure of the initial CDI episode. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. The Full Analysis Set (FAS) population is analyzed consisting of all randomized participants with participants excluded for the failure to receive infusion of study medication; for lack of a positive local stool test for toxigenic C. difficile; or for failure to receive protocol defined standard of care therapy within a 1 day window of the infusion.	
End point type	Primary
End point timeframe:	
12 weeks	

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	395	378	
Units: Percentage of participants				
number (not applicable)	14.9	15.7	25.7	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	Placebo + Standard Of Care (SOC) v MK-3415A + Standard Of Care (SOC)

Number of subjects included in analysis	768
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	-10.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	-5.1

Notes:

[1] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	773
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003 [2]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.5
upper limit	-4.3

Notes:

[2] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Statistical analysis title	Comparison of MK-3415A + SOC versus MK-6072 + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v MK-6072 + Standard Of Care (SOC)
Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3718 [3]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	4.2

Notes:

[3] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Primary: Percentage of participants with one or more adverse events during 4 weeks following infusion treatment	
End point title	Percentage of participants with one or more adverse events during 4 weeks following infusion treatment
End point description:	
An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the medicinal product, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition which is temporally associated with the use of the medicinal product, is also an adverse event. The population analyzed is all participants as treated (APaT), based on the treatment actually received. One participant randomized to the MK-3415A + SOC arm who was treated with MK-3415, but was not treated with MK-6072, was not analyzed.	
End point type	Primary
End point timeframe:	
Up to 4 weeks	

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	396	381	
Units: Percentage of participants				
number (not applicable)	57.4	58.1	60.4	

Statistical analyses

Statistical analysis title	Comparison of 6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.517
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.2
upper limit	4.6

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC

Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	771
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.408
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.8
upper limit	4

Primary: Percentage of participants with one or more drug-related adverse events during 4 weeks following infusion treatment

End point title	Percentage of participants with one or more drug-related adverse events during 4 weeks following infusion treatment

End point description:

An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the medicinal product, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition which is temporally associated with the use of the medicinal product, is also an adverse event. A drug-related adverse event is determined by the investigator to be related to the drug. The population analyzed is APaT, based on the treatment actually received. One participant randomized to the MK-3415A + SOC arm who was treated with MK-3415, but was not treated with MK-6072, was not analyzed.

End point type	Primary

End point timeframe:

Up to 4 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	396	381	
Units: Percentage of Participants				
number (not applicable)	6.7	6.8	6.8	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)

Number of subjects included in analysis	771
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.931
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	3.5

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.997
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	3.6

Primary: Percentage of participants with one or more serious drug-related adverse events during 4 weeks following infusion treatment

End point title	Percentage of participants with one or more serious drug-related adverse events during 4 weeks following infusion treatment

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of the medicinal product that results in death; or is life threatening; or results in a persistent or significant disability/incapacity; or results in or prolongs an existing inpatient hospitalization; or is a congenital anomaly/birth defect; or other important medical events. A serious drug-related adverse event is determined by the investigator to be related to the drug. The population analyzed is APaT, based on the treatment actually received. One participant randomized to the MK-3415A + SOC arm who was treated with MK-3415, but was not treated with MK-6072, was not analyzed.

End point type	Primary

End point timeframe:

Up to 4 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	396	381	
Units: Percentage of participants				
number (not applicable)	0.8	0.0	0.3	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	771
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.328
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	2

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.308
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.7

Primary: Percentage of participants who discontinued study medication due to an adverse event during 4 weeks following infusion treatment

End point title	Percentage of participants who discontinued study medication due to an adverse event during 4 weeks following infusion

	treatment

End point description:

An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the medicinal product, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition which is temporally associated with the use of the medicinal product, is also an adverse event. The population analyzed is APaT, based on the treatment actually received. One participant randomized to the MK-3415A + SOC arm who was treated with MK-3415, but was not treated with MK-6072, was not analyzed.

End point type	Primary

End point timeframe:

Up to 4 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	396	381	
Units: Percentage of participants				
number (not applicable)	0	0	0	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	771
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)

Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Miettinen and Nurminen
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1

Primary: Percentage of participants with one or more infusion-specific adverse events on the day of infusion or the day after infusion

End point title	Percentage of participants with one or more infusion-specific adverse events on the day of infusion or the day after infusion

End point description:

An AE is any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the medicinal product, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition which is temporally associated with the use of the medicinal product, is also an adverse event. The population analyzed is APaT, based on the treatment actually received. One participant randomized to the MK-3415A + SOC arm who was treated with MK-3415, but was not treated with MK-6072, was not analyzed.

End point type	Primary

End point timeframe:

Up to 24 hours

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	396	381	
Units: Percentage of participants				
number (not applicable)	7.2	8.8	7.6	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)

Number of subjects included in analysis	771
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Percentage Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3.3

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	777
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Percentage Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	5.2

Secondary: Percentage of participants with Global Cure

End point title	Percentage of participants with Global Cure

End point description:

Global cure is defined as the clinical cure of the initial CDI episode with no CDI recurrence through Week 12. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. The FAS population is analyzed consisting of all randomized participants with participants excluded for the failure to receive infusion of study medication; for lack of a positive local stool test for toxigenic C. difficile; or for failure to receive protocol defined standard of care therapy within a 1 day window of the infusion.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	395	378	
Units: Percentage of participants				
number (not applicable)	57.4	66.8	52.1	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	768
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0722 [4]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	12.2

Notes:

[4] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	773
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	21.4

Notes:

[5] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Statistical analysis title	Comparison of MK-3415A + SOC versus MK-6072 + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v MK-6072 + Standard Of Care (SOC)

Number of subjects included in analysis	785
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9969 [6]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	-9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.1
upper limit	-2.7

Notes:

[6] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Secondary: Percentage of participants with CDI recurrence in those with clinical cure of the initial CDI episode

End point title	Percentage of participants with CDI recurrence in those with clinical cure of the initial CDI episode

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. The population analyzed is treated participants who achieved a clinical cure of the initial CDI episode.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	282	326	294	
Units: Percentage of participants				
number (not applicable)	20.6	19.0	33.0	

Statistical analyses

Statistical analysis title	Comparison of MK-3415A + SOC versus Placebo + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)

Number of subjects included in analysis	576
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006 [7]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	-11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19
upper limit	-4.7

Notes:

[7] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Statistical analysis title	Comparison of MK-6072 + SOC versus Placebo + SOC
Comparison groups	MK-6072 + Standard Of Care (SOC) v Placebo + Standard Of Care (SOC)
Number of subjects included in analysis	620
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	-13.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.4
upper limit	-6.9

Notes:

[8] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Statistical analysis title	Comparison of MK-3415A + SOC versus MK-6072 + SOC
Comparison groups	MK-3415A + Standard Of Care (SOC) v MK-6072 + Standard Of Care (SOC)
Number of subjects included in analysis	608
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6962 [9]
Method	Miettinen and Nurminen
Parameter estimate	Adjusted Difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	8

Notes:

[9] - One sided p-value based on the Miettinen and Nurminen method stratified by SOC therapy (metronidazole vs. vancomycin vs. fidaxomicin) and hospitalization status (inpatient vs. outpatient)

Secondary: Percentage of participants with CDI recurrence in those with a history of CDI in the 6 months prior to enrollment

End point title	Percentage of participants with CDI recurrence in those with a history of CDI in the 6 months prior to enrollment

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. The population analyzed consists of treated participants with a history of CDI in the past 6 months.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	104	113	110	
Units: Percentage of participants				
number (not applicable)	20.2	23.9	42.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDI recurrence in those with the 027 ribotype

End point title	Percentage of participants with CDI recurrence in those with the 027 ribotype

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. The 027 ribotype is a more virulent, epidemic strain responsible for several outbreaks of disease associated with an increased risk of severity and mortality. The population analyzed consists of treated participants with the 027 ribotype.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	43	64	
Units: Percentage of participants				
number (not applicable)	12.8	20.9	32.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDI recurrence in those with an epidemic strain

End point title	Percentage of participants with CDI recurrence in those with an epidemic strain

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. An epidemic strain includes ribotypes 027, 014, 002, 001, 106 or 020. The population analyzed consists of treated participants with an epidemic strain.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	102	127	
Units: Percentage of participants				
number (not applicable)	14.7	18.6	29.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDI recurrence in those with clinically severe CDI

End point title	Percentage of participants with CDI recurrence in those with clinically severe CDI

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen.

Participants with clinically severe CDI have a Zar Score greater than or equal to 2 points based on the presence of 1 or more of the following: 1) age >60 years old (1 point); 2) body temperature >38.3°C (>100°F) (1 point); 3) albumin level 2.5 mg/dl (1 point); 4) peripheral white blood cell count >15,000 cells/mm^3 within 48 hours (1 point); 5) endoscopic evidence of pseudomembranous colitis (2 points); and 6) treatment in Intensive Care Unit (2 points). The population analyzed consists of treated participants with clinically severe CDI.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	80	55	65	
Units: Percentage of participants				
number (not applicable)	11.3	10.9	20.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDI recurrence in those 65 years and older

End point title	Percentage of participants with CDI recurrence in those 65 years and older

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. The population analyzed consists of treated participants 65 years and older.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	241	205	206	
Units: Percentage of participants				
number (not applicable)	17.4	15.6	29.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with CDI recurrence in those with compromised immunity

End point title	Percentage of participants with CDI recurrence in those with compromised immunity

End point description:

CDI recurrence is defined as the development of a new episode of diarrhea (3 or more loose stools in 24 or fewer hours) and a positive lab stool test (local or central) for toxigenic C. difficile. Clinical cure is defined as no diarrhea [2 or fewer loose stools per 24 hours] for 2 consecutive days following completion of SOC therapy for the initial CDI episode in participants who received =< 14 day regimen. Compromised immunity is an active hematological malignancy (including leukemia, lymphoma, multiple myeloma), an active malignancy requiring recent cytotoxic chemotherapy, receipt of a prior hematopoietic stem cell transplant, receipt of a prior solid organ transplant, asplenia, or neutropenia/pancytopenia due to other conditions. The population analyzed consists of treated participants with compromised immunity.

End point type	Secondary

End point timeframe:

12 weeks

End point values	MK-3415A + Standard Of Care (SOC)	MK-6072 + Standard Of Care (SOC)	Placebo + Standard Of Care (SOC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	91	61	
Units: Percentage of participants				
number (not applicable)	16.5	12.1	26.2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events collected systematically up to Day 28; serious adverse events collected systematically up to Day 90

Adverse event reporting additional description:

APaT, based on the treatment actually received. One participant randomized to the MK-3415A + SOC arm who was treated with MK-3415, but was not treated with MK-6072, is placed in his own arm for MK-3415 (not a randomized arm for this study).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	MK-3415A + SOC

Reporting group description:

Single IV infusion of 10 mg/kg MK-3415A + SOC for CDI

Reporting group title	Placebo + SOC

Reporting group description:

Normal saline IV infusion (0.9% sodium chloride) + SOC for CDI

Reporting group title	MK-3415 + SOC

Reporting group description:

Single intravenous (IV) infusion of 10 mg/kg MK-3415 + SOC for CDI

Reporting group title	MK-6072 + SOC

Reporting group description:

Single IV infusion of 10 mg/kg MK-6072 + SOC for CDI

Serious adverse events	MK-3415A + SOC	Placebo + SOC	MK-3415 + SOC
Total subjects affected by serious adverse events			
subjects affected / exposed	118 / 390 (30.26%)	129 / 381 (33.86%)	1 / 1 (100.00%)
number of deaths (all causes)	31	33	1
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute myeloid leukaemia recurrent			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Adenocarcinoma gastric			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Bile duct cancer			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Bone cancer			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone cancer metastatic			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Breast cancer metastatic			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Colon cancer			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal cancer metastatic			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Glioblastoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hodgkin's disease			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Leiomyosarcoma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Lung adenocarcinoma			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lymphocytic leukaemia			

subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Malignant melanoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Medulloblastoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metastatic renal cell carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Metastatic squamous cell carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myeloid leukaemia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Pancreatic carcinoma			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peripheral T-cell lymphoma unspecified			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Prostate cancer			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer metastatic			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Deep vein thrombosis			
subjects affected / exposed	1 / 390 (0.26%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry gangrene			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Hypertension			

subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 390 (0.51%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Phlebitis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Thrombophlebitis			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 390 (0.77%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chest pain			
subjects affected / exposed	2 / 390 (0.51%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 390 (0.26%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Device breakage			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Device malfunction			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disuse syndrome			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Drug withdrawal syndrome			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Fatigue			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Generalised oedema			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Impaired healing			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Influenza like illness			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 390 (0.26%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Pelvic mass			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 390 (0.51%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suprapubic pain			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Asthma			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 390 (0.77%)	3 / 381 (0.79%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal stenosis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Lung disorder			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pneumonia aspiration			
subjects affected / exposed	3 / 390 (0.77%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Pulmonary embolism			

subjects affected / exposed	0 / 390 (0.00%)	3 / 381 (0.79%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (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
Pulmonary oedema			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory depression			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	4 / 390 (1.03%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Psychiatric disorders			
Agitation			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety disorder			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Confusional state			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Mental status changes			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactic acid increased			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood pressure decreased			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Escherichia test positive			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
International normalised ratio increased			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Injury, poisoning and procedural complications			
Arteriovenous fistula site haematoma			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Concussion			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Femur fracture			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Frostbite			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Hip fracture			
subjects affected / exposed	0 / 390 (0.00%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Post procedural inflammation			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Arrhythmia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial fibrillation			

subjects affected / exposed	1 / 390 (0.26%)	3 / 381 (0.79%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Bradycardia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Cardiac arrest			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorder			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	5 / 390 (1.28%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 0
Cardiac failure acute			
subjects affected / exposed	2 / 390 (0.51%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			

subjects affected / exposed	5 / 390 (1.28%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Prinzmetal angina			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Aphasia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Cerebellar haemorrhage			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral haemorrhage			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	2 / 390 (0.51%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dementia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Encephalopathy			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Hemiparesis			

subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Loss of consciousness			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	2 / 390 (0.51%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 390 (0.26%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Senile dementia			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	2 / 390 (0.51%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wernicke's encephalopathy			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 390 (0.51%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia of malignant disease			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Coagulopathy			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Febrile neutropenia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Haemorrhagic anaemia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 390 (0.51%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sickle cell anaemia with crisis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Eye disorders			
Blindness unilateral			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 390 (0.51%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Anal fistula			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Colitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Diarrhoea			
subjects affected / exposed	4 / 390 (1.03%)	6 / 381 (1.57%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Dysphagia			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 390 (0.26%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic erosive gastritis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Haemorrhoids			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			

subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Intestinal haemorrhage			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Large intestinal haemorrhage			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Oesophageal ulcer			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Pancreatitis acute			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			

subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Vomiting			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Cholecystitis acute			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cirrhosis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Decubitus ulcer			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis allergic			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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 ulcer			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 390 (0.26%)	4 / 381 (1.05%)	1 / 1 (100.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Calculus ureteric			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Chronic kidney disease			
subjects affected / exposed	1 / 390 (0.26%)	4 / 381 (1.05%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dysuria			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Haematuria			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Nephritic syndrome			

subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Urinary retention			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Muscular weakness			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Musculoskeletal chest pain			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue necrosis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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			
Abdominal abscess			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Anal abscess			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Arthritis infective			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Bacteraemia			
subjects affected / exposed	3 / 390 (0.77%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective staphylococcal			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 390 (0.51%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	13 / 390 (3.33%)	28 / 381 (7.35%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 13	0 / 34	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Device related infection			

subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Diabetic foot infection			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Endocarditis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Erysipelas			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungaemia			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Gastroenteritis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
HIV infection			

subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Infective spondylitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Influenza			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 390 (0.00%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Lung abscess			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis tuberculous			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Necrotising fasciitis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Pelvic abscess			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Periodontitis			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Peritonitis bacterial			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	9 / 390 (2.31%)	9 / 381 (2.36%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (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
Pyelonephritis acute			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			

subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Sepsis			
subjects affected / exposed	3 / 390 (0.77%)	13 / 381 (3.41%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 14	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 5	0 / 0
Septic shock			
subjects affected / exposed	3 / 390 (0.77%)	6 / 381 (1.57%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 5	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 390 (0.26%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	7 / 390 (1.79%)	4 / 381 (1.05%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	4 / 390 (1.03%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Viraemia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			
subjects affected / exposed	1 / 390 (0.26%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercreatininaemia			
subjects affected / exposed	0 / 390 (0.00%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 390 (0.00%)	2 / 381 (0.52%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Hyponatraemia			
subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (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
Shock hypoglycaemic			

subjects affected / exposed	0 / 390 (0.00%)	0 / 381 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MK-6072 + SOC		
Total subjects affected by serious adverse events			
subjects affected / exposed	111 / 396 (28.03%)		
number of deaths (all causes)	25		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myeloid leukaemia recurrent			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Adenocarcinoma gastric			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct cancer			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bone cancer				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone cancer metastatic				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer metastatic				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal cancer metastatic				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Glioblastoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatocellular carcinoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hodgkin's disease				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Leiomyosarcoma				

subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Lung adenocarcinoma				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Lung neoplasm				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphocytic leukaemia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medulloblastoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic renal cell carcinoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic squamous cell carcinoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myeloid leukaemia				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal carcinoma				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pancreatic carcinoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral T-cell lymphoma unspecified				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cell myeloma				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal cancer metastatic				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Circulatory collapse				

subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Deep vein thrombosis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dry gangrene				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phlebitis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Shock				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombophlebitis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device breakage				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device malfunction				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disuse syndrome				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug withdrawal syndrome				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Generalised oedema				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Impaired healing				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza like illness				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				

subjects affected / exposed	2 / 396 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Non-cardiac chest pain			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	2 / 396 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pelvic mass			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suprapubic pain			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Asthma			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 396 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngeal stenosis			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia aspiration				
subjects affected / exposed	5 / 396 (1.26%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 3			
Pneumothorax				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary embolism				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory arrest				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory depression				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				

subjects affected / exposed	3 / 396 (0.76%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Upper respiratory tract inflammation				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Agitation				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anxiety disorder				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Blood lactic acid increased				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood pressure decreased				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia test positive				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
International normalised ratio increased				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Arteriovenous fistula site haematoma				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Frostbite				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Hip fracture				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intentional overdose				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural inflammation				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				

subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Arteriosclerosis coronary artery				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Cardiac disorder				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	3 / 396 (0.76%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Cardiac failure acute				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	3 / 396 (0.76%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Cardiac failure congestive				
subjects affected / exposed	5 / 396 (1.26%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prinzmetal angina				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Altered state of consciousness				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aphasia				

subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebellar haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	2 / 396 (0.51%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cerebral ischaemia			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dementia			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			

subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolic encephalopathy			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			

subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Senile dementia			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wernicke's encephalopathy			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	3 / 396 (0.76%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Anaemia of malignant disease				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coagulopathy				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemolytic anaemia				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Haemorrhagic anaemia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sickle cell anaemia with crisis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blindness unilateral				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	4 / 396 (1.01%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Diarrhoea				
subjects affected / exposed	7 / 396 (1.77%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	4 / 396 (1.01%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal inflammation				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic erosive gastritis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				

subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Impaired gastric emptying			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestinal haemorrhage			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophageal ulcer			

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholangitis				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cholangitis acute				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic cirrhosis				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Decubitus ulcer				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis allergic				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Calculus ureteric				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Dysuria				

subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephritic syndrome			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperparathyroidism			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal chest pain				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue necrosis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis infective				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bursitis infective staphylococcal				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				

subjects affected / exposed	14 / 396 (3.54%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic foot infection			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocarditis			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Erysipelas			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fungaemia			
subjects affected / exposed	0 / 396 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gangrene			

subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
HIV infection				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective spondylitis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Kidney infection				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection viral				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis tuberculous				

subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising fasciitis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periodontitis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis bacterial				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	5 / 396 (1.26%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 2			
Pseudomembranous colitis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				

subjects affected / exposed	2 / 396 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhinitis				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	6 / 396 (1.52%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Septic shock				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	9 / 396 (2.27%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viraemia				

subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fluid overload				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercreatininaemia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	0 / 396 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	1 / 396 (0.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				

subjects affected / exposed	2 / 396 (0.51%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock hypoglycaemic			
subjects affected / exposed	1 / 396 (0.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MK-3415A + SOC	Placebo + SOC	MK-3415 + SOC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 390 (9.49%)	37 / 381 (9.71%)	1 / 1 (100.00%)
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	1 / 390 (0.26%)	1 / 381 (0.26%)	1 / 1 (100.00%)
occurrences (all)	1	1	1
Neutrophil count increased			
subjects affected / exposed	1 / 390 (0.26%)	3 / 381 (0.79%)	1 / 1 (100.00%)
occurrences (all)	1	3	1
White blood cell count increased			
subjects affected / exposed	0 / 390 (0.00%)	1 / 381 (0.26%)	1 / 1 (100.00%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 390 (4.36%)	21 / 381 (5.51%)	0 / 1 (0.00%)
occurrences (all)	19	23	0
Nausea			
subjects affected / exposed	17 / 390 (4.36%)	12 / 381 (3.15%)	0 / 1 (0.00%)
occurrences (all)	17	12	0
Infections and infestations			

Clostridium difficile infection subjects affected / exposed occurrences (all)	4 / 390 (1.03%) 5	2 / 381 (0.52%) 2	1 / 1 (100.00%) 1

Non-serious adverse events	MK-6072 + SOC		
Total subjects affected by non-serious adverse events subjects affected / exposed	44 / 396 (11.11%)		
Investigations Lymphocyte count decreased subjects affected / exposed occurrences (all) Neutrophil count increased subjects affected / exposed occurrences (all) White blood cell count increased subjects affected / exposed occurrences (all)	 0 / 396 (0.00%) 0 2 / 396 (0.51%) 3 1 / 396 (0.25%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 17 / 396 (4.29%) 18 23 / 396 (5.81%) 23		
Infections and infestations Clostridium difficile infection subjects affected / exposed occurrences (all)	 3 / 396 (0.76%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 May 2013	Amendment 1 was implemented after enrollment of participants had commenced and before database lock and unblinding. Major changes included: increased infusion set filter pore size to 5 micron or smaller from 0.2 microns or smaller; report serious adverse experiences that either had an outcome of death or were considered to be related to study medication during the 9-month extension period; updated eligibility criteria to exclude subjects who had received an experimental C. difficile vaccine or other experimental monoclonal antibody against C. difficile toxin A or B, or subjects who planned to receive during the follow-up period fecal transplantation therapy or any other therapies that had been demonstrated to decrease CDI recurrence; modified the definition of the clinical cure endpoint with regard to the duration of standard of care medication: a 14 day regimen was defined as treatment spanning no more than 16 calendar days.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported