



Clinical trial results:

An Individualized treatment approach for older patients: A randomized, controlled study in type 2 diabetes Mellitus (IMPERIUM)

Summary

EudraCT number	2013-001473-24
Trial protocol	GB DE AT
Global end of trial date	14 October 2015

Results information

Result version number	v1 (current)
This version publication date	20 October 2016
First version publication date	20 October 2016

Trial information

Trial identification

Sponsor protocol code	14842
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02072096
WHO universal trial number (UTN)	-
Other trial identifiers	Trial ID: 14842, Trial Alias: F3Z-MC-IOQL

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

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	14 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	14 October 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to compare the benefits and risks associated with the use of 2 treatment strategies to lower blood sugar in participants aged 65 and older with type 2 diabetes Mellitus (T2DM). One strategy is based on the use of oral and injectable medications that only reduce blood sugar (glucose) when it is high. The other strategy is based on non-glucose dependent agents. The trial will last up to 72 weeks for each participant.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 February 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Germany: 36
Country: Number of subjects enrolled	Austria: 32
Country: Number of subjects enrolled	Puerto Rico: 39
Country: Number of subjects enrolled	United States: 64
Worldwide total number of subjects	192
EEA total number of subjects	89

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)	0
From 65 to 84 years	189
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All participants completed the first 24 weeks of the study at which time interim analysis was triggered to assess feasibility. The study was terminated after the interim analysis. Some participants continued into the Core study but discontinued at the next office study visit. Data was assessed from Baseline to last participant visit, up to 72 week

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Strategy A (Glucose-Dependent)

Arm description:

Participants may receive oral and injectable therapies (glucagon-like peptide-1 receptor agonists [GLP-1 RA]) that exert a glucose-dependent mode of action. Medications allowed in this arm include: metformin, pioglitazone, acarbose, linagliptin, sitagliptin, liraglutide, exenatide once weekly (QW), and exenatide twice daily (BID). Choice of therapy is based on investigator's discretion. Treatment used in label. Treatment may last up to 72 weeks.

Metformin: Administered orally

Pioglitazone: Administered orally

Acarbose: Administered orally

Linagliptin: Administered orally

Sitagliptin: Administered orally

Liraglutide: Administered subcutaneous (SC)

Exenatide once weekly (QW): Administered SC

Exenatide twice daily (BID): Administered SC

Arm type	Experimental
Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Metformin Administered orally every day.

Investigational medicinal product name	Pioglitazone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pioglitazone administered orally every day.

Investigational medicinal product name	Acarbose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Acarbose administered orally every day	
Investigational medicinal product name	Linagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Linagliptin administered orally every day.	
Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Sitagliptin administered orally daily.	
Investigational medicinal product name	Liraglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Liraglutide administered subcutaneous (SC) daily.	
Investigational medicinal product name	Exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Exenatide once weekly administered SC.	
Investigational medicinal product name	Exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Exenatide twice daily administered SC.	
Arm title	Strategy B (Reference)

Arm description:

Participants will receive glimepiride and may receive basal insulin glargine as a first line injectable therapy. Medications allowed in this arm include: glimepiride, metformin, pioglitazone, acarbose, linagliptin, sitagliptin and basal insulin glargine. Choice of therapy is based on investigator's discretion. Treatment used in label. Dose titrated by treatment algorithm. Treatment may last up to 72 weeks.

Glimepiride: Administered orally

Metformin: Administered orally

Pioglitazone: Administered orally

Acarbose: Administered orally

Linagliptin: Administered orally

Sitagliptin: Administered orally

Insulin Glargine: Administered SC

Arm type	Active comparator
Investigational medicinal product name	Glimepiride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Glimepiride administered orally every day.

Investigational medicinal product name	Metformin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Metformin administered orally every day.

Investigational medicinal product name	Pioglitazone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pioglitazone administered orally every day.

Investigational medicinal product name	Acarbose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Acarbose administered orally every day.

Investigational medicinal product name	Linagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Linagliptin administered orally every day.

Investigational medicinal product name	Sitagliptin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Sitagliptin administered orally every day.

Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin Glargine administered subcutaneous every day.

Number of subjects in period 1	Strategy A (Glucose-Dependent)	Strategy B (Reference)
Started	99	93
Received at least one dose of study drug	98	93
Completed	14	15
Not completed	85	78
Adverse event, serious fatal	2	-
Consent withdrawn by subject	5	7
Physician decision	-	1
Adverse event, non-fatal	5	2
No Reason Provided	4	2
Study Terminated by Sponsor	43	30
Lost to follow-up	1	-
Lack of efficacy	18	29
Protocol deviation	7	7

Baseline characteristics

Reporting groups

Reporting group title	Strategy A (Glucose-Dependent)
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Reporting group description:

Participants may receive oral and injectable therapies (glucagon-like peptide-1 receptor agonists [GLP-1 RA]) that exert a glucose-dependent mode of action. Medications allowed in this arm include: metformin, pioglitazone, acarbose, linagliptin, sitagliptin, liraglutide, exenatide once weekly (QW), and exenatide twice daily (BID). Choice of therapy is based on investigator's discretion. Treatment used in label. Treatment may last up to 72 weeks.

Metformin: Administered orally

Pioglitazone: Administered orally

Acarbose: Administered orally

Linagliptin: Administered orally

Sitagliptin: Administered orally

Liraglutide: Administered subcutaneous (SC)

Exenatide once weekly (QW): Administered SC

Exenatide twice daily (BID): Administered SC

Reporting group title	Strategy B (Reference)
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Reporting group description:

Participants will receive glimepiride and may receive basal insulin glargine as a first line injectable therapy. Medications allowed in this arm include: glimepiride, metformin, pioglitazone, acarbose, linagliptin, sitagliptin and basal insulin glargine. Choice of therapy is based on investigator's discretion. Treatment used in label. Dose titrated by treatment algorithm. Treatment may last up to 72 weeks.

Glimepiride: Administered orally

Metformin: Administered orally

Pioglitazone: Administered orally

Acarbose: Administered orally

Linagliptin: Administered orally

Sitagliptin: Administered orally

Insulin Glargine: Administered SC

Reporting group values	Strategy A (Glucose-Dependent)	Strategy B (Reference)	Total
Number of subjects	99	93	192
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	0	0	0
From 65-84 years	96	93	189
85 years and over	3	0	3
Age Continuous			
Units: years			
arithmetic mean	70.7	70.7	
standard deviation	± 5.3	± 4.4	-
Gender, Male/Female			
Units: participants			
Female	43	34	77
Male	56	59	115
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	35	32	67
Not Hispanic or Latino	63	59	122
Unknown or Not Reported	1	2	3
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	10	16
White	93	81	174
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Region of Enrollment			
Units: Subjects			
Austria	18	14	32
Puerto Rico	23	16	39
United States	29	35	64
United Kingdom	10	11	21
Germany	19	17	36

End points

End points reporting groups

Reporting group title	Strategy A (Glucose-Dependent)
Reporting group description:	
Participants may receive oral and injectable therapies (glucagon-like peptide-1 receptor agonists [GLP-1 RA]) that exert a glucose-dependent mode of action. Medications allowed in this arm include: metformin, pioglitazone, acarbose, linagliptin, sitagliptin, liraglutide, exenatide once weekly (QW), and exenatide twice daily (BID). Choice of therapy is based on investigator's discretion. Treatment used in label. Treatment may last up to 72 weeks.	
Metformin: Administered orally	
Pioglitazone: Administered orally	
Acarbose: Administered orally	
Linagliptin: Administered orally	
Sitagliptin: Administered orally	
Liraglutide: Administered subcutaneous (SC)	
Exenatide once weekly (QW): Administered SC	
Exenatide twice daily (BID): Administered SC	
Reporting group title	Strategy B (Reference)
Reporting group description:	
Participants will receive glimepiride and may receive basal insulin glargine as a first line injectable therapy. Medications allowed in this arm include: glimepiride, metformin, pioglitazone, acarbose, linagliptin, sitagliptin and basal insulin glargine. Choice of therapy is based on investigator's discretion. Treatment used in label. Dose titrated by treatment algorithm. Treatment may last up to 72 weeks.	
Glimepiride: Administered orally	
Metformin: Administered orally	
Pioglitazone: Administered orally	
Acarbose: Administered orally	
Linagliptin: Administered orally	
Sitagliptin: Administered orally	
Insulin Glargine: Administered SC	

Primary: Percentage of Participants Achieving and Maintaining Individualized Glycated Hemoglobin A1c (HbA1c) Targets Without Clinically Significant Hypoglycemia

End point title	Percentage of Participants Achieving and Maintaining Individualized Glycated Hemoglobin A1c (HbA1c) Targets Without Clinically Significant Hypoglycemia
End point description:	
Failed to reach and maintain HbA1c target, without clinically significant hypoglycemia, is defined as having 2 consecutive HbA1c > upper limit of HbA1c target over 12 weeks starting from Week 24 for participants with HbA1c data beyond Week 24, or Week 24 HbA1c > upper limit of HbA1c target for participants without HbA1c data beyond Week 24. Clinically significant hypoglycemia is defined as any severe hypoglycemia or repeated hypoglycemia interrupting participants activities or sleep and associated with blood glucose ≤ 3.9 millimole per liter (mmol/L), or repeated asymptomatic hypoglycemia associated with blood glucose <3.0 mmol/L. Success is defined as lacking of failure.	

End point type	Primary
End point timeframe:	
Baseline to last participant visit (up to 72 weeks)	

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98 ^[1]	93 ^[2]		
Units: percentage of participants				
number (confidence interval 95%)	64.5 (54.4 to 73.4)	54.9 (44.6 to 64.9)		

Notes:

[1] - All participants who received at least one dose of study drug.

[2] - All participants who received at least one dose of study drug.

Statistical analyses

Statistical analysis title	Achieving and Maintaining Individualized HbA1c
Comparison groups	Strategy A (Glucose-Dependent) v Strategy B (Reference)
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Logistic
Parameter estimate	Adjusted Proportion
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	23.2

Secondary: Percentage of Participants Requiring Alternative Treatment Due to Glycemic Failure of First Line Injectable Therapy

End point title	Percentage of Participants Requiring Alternative Treatment Due to Glycemic Failure of First Line Injectable Therapy
End point description:	
End point type	Secondary
End point timeframe:	
Baseline to last participant visit (up to 72 weeks)	

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98 ^[3]	93 ^[4]		
Units: percentage of participants				
number (not applicable)	21	13		

Notes:

[3] - All participants who received at least one dose of study drug.

[4] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Total Hypoglycemia and Other Categories of Hypoglycemia

End point title	Number of Participants with Total Hypoglycemia and Other Categories of Hypoglycemia
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End point description:

End point type	Secondary
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End point timeframe:

Baseline to last participant visit (up to 72 weeks)

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98 ^[5]	93		
Units: Participants				
number (not applicable)				
Total Hypoglycemia	10	50		
Severe Hypoglycemia	0	0		
Clinically Significant Hypoglycemia	0	1		
Symptomatic Hypoglycemia	5	34		
Asymptomatic Hypoglycemia	8	30		
Probable Symptomatic Hypoglycemia	0	7		
Unspecified Hypoglycemia	2	7		
Relative Hypoglycemia	1	6		
Nocturnal Hypoglycemia	4	10		

Notes:

[5] - All participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline of Urinary Albumin to Creatinine Ratio

End point title	Change from Baseline of Urinary Albumin to Creatinine Ratio
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End point description:

The Urinary Albumin to Creatinine Ratio is used in addition to Estimated Glomerular Filtration Rate (eGFR) to measure the incidence and progression of diabetic kidney disease.

End point type	Secondary
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End point timeframe:

Baseline, Week 72

End point values	Strategy A (Glucose- Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80 ^[6]	83 ^[7]		
Units: milligram per millimole (mg/mmol)				
arithmetic mean (standard deviation)	1.85 (± 22.99)	1.85 (± 16.46)		

Notes:

[6] - Received 1 dose of study drug with baseline & post-baseline urinary albumin/creatinine ratio data.

[7] - Received 1 dose of study drug with baseline & post-baseline urinary albumin/creatinine ratio data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Mass Index (BMI)

End point title	Change from Baseline in Body Mass Index (BMI)
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End point description:

End point type	Secondary
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End point timeframe:

Baseline, Week 72

End point values	Strategy A (Glucose- Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98 ^[8]	93		
Units: kilogram per square meter (kg/m ²)				
arithmetic mean (standard deviation)	-0.47 (± 1.56)	0.2 (± 2.91)		

Notes:

[8] - Participants who received 1 dose of study drug & had evaluable baseline & post-baseline BMI data.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline of Estimated Glomerular Filtration Rate (eGFR)

End point title	Change From Baseline of Estimated Glomerular Filtration Rate
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End point description:

The eGFR is used in addition to the Urinary Albumin to Creatinine Ratio to measure the incidence and progression of diabetic kidney disease.

End point type Secondary

End point timeframe:

Baseline, Week 72

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85 ^[9]	85 ^[10]		
Units: milliliter per minute/1.73 square meter				
arithmetic mean (standard deviation)	-5 (± 13.64)	-5.88 (± 10.95)		

Notes:

[9] - Participants who received 1 dose of study drug and had evaluable baseline & post-baseline eGFR data.

[10] - Participants who received 1 dose of study drug and had evaluable baseline & post-baseline eGFR data.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Adult Low Blood Sugar Survey (ALBSS) Score

End point title Change from Baseline in Adult Low Blood Sugar Survey (ALBSS) Score

End point description:

End point type Other pre-specified

End point timeframe:

Baseline, Week 72

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[11]	0 ^[12]		
Units: number				
number (not applicable)				

Notes:

[11] - Unable to conduct change from baseline analysis due to study closure and lack of endpoint data.

[12] - Unable to conduct change from baseline analysis due to study closure and lack of endpoint data.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in European Quality of Life-5 Dimensions 5 Levels (EQ-5D-5L) Score

End point title	Change from Baseline in European Quality of Life-5 Dimensions 5 Levels (EQ-5D-5L) Score
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End point description:

End point type	Other pre-specified
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End point timeframe:

Baseline, Week 72

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[13]	0 ^[14]		
Units: number				
number (not applicable)				

Notes:

[13] - Unable to conduct change from baseline analysis due to study closure and lack of endpoint data.

[14] - Unable to conduct change from baseline analysis due to study closure and lack of endpoint data.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change from Baseline in Mini-mental State Examination (MMSE) Score

End point title	Change from Baseline in Mini-mental State Examination (MMSE) Score
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End point description:

End point type	Other pre-specified
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End point timeframe:

Baseline, Week 72

End point values	Strategy A (Glucose-Dependent)	Strategy B (Reference)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[15]	0 ^[16]		
Units: number				
number (not applicable)				

Notes:

[15] - Unable to conduct change from baseline analysis due to study closure and lack of endpoint data.

[16] - Unable to conduct change from baseline analysis due to study closure and lack of endpoint data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Final

Adverse event reporting additional description:

F3Z-MC-IOQL

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	Strategy A
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Reporting group description: -

Reporting group title	Strategy B
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Reporting group description: -

Serious adverse events	Strategy A	Strategy B	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 98 (15.31%)	14 / 93 (15.05%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
benign neoplasm of spinal cord			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
benign ovarian tumour			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed ^[1]	0 / 98 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostatic adenoma			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed ^[2]	0 / 98 (0.00%)	1 / 59 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
squamous cell carcinoma of lung			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
asthma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory failure			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
hepatic enzyme increased			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
muscle rupture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rib fracture			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
road traffic accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 18.1			

subjects affected / exposed	0 / 98 (0.00%)	2 / 93 (2.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac failure congestive			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
microvascular coronary artery disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	2 / 93 (2.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
carotid artery stenosis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrovascular accident			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
syncope			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
retinal vascular thrombosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
gastritis			
alternative dictionary used: MedDRA 18.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
cholecystitis chronic			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
intervertebral disc protrusion			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteoarthritis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
appendicitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory tract infection			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Strategy A	Strategy B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 98 (83.67%)	74 / 93 (79.57%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acrochordon			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
basal cell carcinoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
benign neoplasm of adrenal gland			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
colon adenoma			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
seborrhoeic keratosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
squamous cell carcinoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
thyroid neoplasm			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
Vascular disorders			
arteriosclerosis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	1	
essential hypertension			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	3	
hypertension			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	5 / 98 (5.10%)	4 / 93 (4.30%)	
occurrences (all)	5	5	
hypotension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
peripheral vascular disorder			
alternative dictionary used: MedDRA 18.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>peripheral venous disease</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>2 / 93 (2.15%)</p> <p>2</p>	
<p>subclavian artery stenosis</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>Surgical and medical procedures</p> <p>cataract operation</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 98 (3.06%)</p> <p>3</p>	<p>2 / 93 (2.15%)</p> <p>4</p>	
<p>coronary angioplasty</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>inguinal hernia repair</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>large intestinal polypectomy</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>lens extraction</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>ptosis repair</p> <p>alternative dictionary used: MedDRA 17.1</p>			

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>tendon sheath lesion excision</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>tooth extraction</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>General disorders and administration site conditions</p> <p>asthenia</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>chest pain</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>3 / 98 (3.06%)</p> <p>3</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>fatigue</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>influenza like illness</p> <p>alternative dictionary used: MedDRA 18.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 98 (2.04%)</p> <p>3</p>	<p>2 / 93 (2.15%)</p> <p>2</p>	
<p>injection site nodule</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>malaise</p> <p>alternative dictionary used: MedDRA 18.0</p>			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>oedema</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>oedema peripheral</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>peripheral swelling</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pyrexia</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p> <p>6 / 98 (6.12%)</p> <p>7</p> <p>1 / 98 (1.02%)</p> <p>1</p> <p>1 / 98 (1.02%)</p> <p>1</p> <p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p> <p>0 / 93 (0.00%)</p> <p>0</p> <p>6 / 93 (6.45%)</p> <p>6</p> <p>2 / 93 (2.15%)</p> <p>2</p> <p>1 / 93 (1.08%)</p> <p>1</p>	
<p>Immune system disorders</p> <p>hypersensitivity</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>seasonal allergy</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p> <p>1 / 98 (1.02%)</p> <p>1</p>	<p>1 / 93 (1.08%)</p> <p>1</p> <p>1 / 93 (1.08%)</p> <p>2</p>	
<p>Reproductive system and breast disorders</p> <p>benign prostatic hyperplasia</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>breast mass</p> <p>alternative dictionary used: MedDRA 18.0</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>3 / 93 (3.23%)</p> <p>3</p>	

<p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>prostatitis</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>prostatomegaly</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 98 (2.04%)</p> <p>2</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>Respiratory, thoracic and mediastinal disorders</p> <p>asthma</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>1 / 93 (1.08%)</p> <p>1</p>	
<p>chronic obstructive pulmonary disease</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>1 / 93 (1.08%)</p> <p>2</p>	
<p>cough</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 98 (4.08%)</p> <p>4</p>	<p>3 / 93 (3.23%)</p> <p>5</p>	
<p>dry throat</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>dysphonia</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>dyspnoea</p> <p>alternative dictionary used: MedDRA 17.1</p>			

subjects affected / exposed	3 / 98 (3.06%)	0 / 93 (0.00%)
occurrences (all)	3	0
dyspnoea exertional		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
emphysema		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
epistaxis		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
nasal congestion		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
oropharyngeal pain		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
respiratory tract congestion		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
rhinitis allergic		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
sleep apnoea syndrome		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0

<p>Psychiatric disorders</p> <p>anxiety</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>confusional state</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>depression</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>food aversion</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>insomnia</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>sleep disorder</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>Investigations</p> <p>arteriogram coronary</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>2</p>	
<p>arthroscopy</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 98 (2.04%)</p> <p>2</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>aspiration pleural cavity</p>			

alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
blood creatinine increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
blood glucose abnormal			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
blood glucose increased			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 98 (2.04%)	1 / 93 (1.08%)	
occurrences (all)	2	1	
blood pressure diastolic decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
blood pressure diastolic increased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	1	
blood pressure systolic decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
blood pressure systolic increased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	1	
blood urea increased			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
blood uric acid		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
cardiac imaging procedure		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
catheterisation cardiac		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
gamma-glutamyltransferase increased		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
glomerular filtration rate decreased		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
heart rate increased		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)
occurrences (all)	1	1
prostatic specific antigen increased		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
urine analysis abnormal		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1

weight decreased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	5 / 98 (5.10%) 5	0 / 93 (0.00%) 0	
weight increased alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
Injury, poisoning and procedural complications			
arthropod bite alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
arthropod sting alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 2	0 / 93 (0.00%) 0	
contusion alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 3	4 / 93 (4.30%) 5	
eye contusion alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
fall alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 3	2 / 93 (2.15%) 2	
foot fracture alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
joint dislocation alternative dictionary used:			

MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	2 / 93 (2.15%)	
occurrences (all)	0	2	
laceration			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	4 / 93 (4.30%)	
occurrences (all)	2	5	
ligament sprain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
limb injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
meniscus injury			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)	
occurrences (all)	2	0	
post procedural haematoma			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
radius fracture			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
scratch			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
skin abrasion			
alternative dictionary used: MedDRA 18.0			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>spinal compression fracture</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p> <p>1 / 93 (1.08%)</p> <p>1</p>	
<p>Congenital, familial and genetic disorders</p> <p>type v hyperlipidaemia</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>1 / 98 (1.02%)</p> <p>1</p>	<p>0 / 93 (0.00%)</p> <p>0</p>	
<p>Cardiac disorders</p> <p>aortic valve stenosis</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>atrial fibrillation</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>cardiac failure</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>left ventricular hypertrophy</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>mitral valve incompetence</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>palpitations</p> <p>alternative dictionary used: MedDRA 18.0</p>	<p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p>	<p>1 / 93 (1.08%)</p> <p>1</p> <p>1 / 93 (1.08%)</p> <p>1</p> <p>1 / 93 (1.08%)</p> <p>1</p> <p>1 / 93 (1.08%)</p> <p>1</p>	

subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)	
occurrences (all)	2	0	
tachycardia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
amnesia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
autonomic neuropathy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
carotid artery stenosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
cerebral haemorrhage			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
dizziness			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 98 (4.08%)	1 / 93 (1.08%)	
occurrences (all)	4	1	
headache			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	7 / 98 (7.14%)	1 / 93 (1.08%)	
occurrences (all)	14	1	
paraesthesia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
parkinson's disease			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
polyneuropathy			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	1	
restless legs syndrome			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
sciatica			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	1	
transient ischaemic attack			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
tremor			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
vascular encephalopathy			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.1			

<p>subjects affected / exposed</p> <p>1 / 98 (1.02%)</p> <p>2 / 93 (2.15%)</p> <p>occurrences (all)</p> <p>1</p> <p>2</p>			
<p>iron deficiency anaemia</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>0 / 98 (0.00%)</p> <p>1 / 93 (1.08%)</p> <p>occurrences (all)</p> <p>0</p> <p>1</p>			
<p>lymphadenopathy</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>1 / 98 (1.02%)</p> <p>0 / 93 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p>			
<p>nephrogenic anaemia</p> <p>alternative dictionary used: MedDRA 17.1</p> <p>subjects affected / exposed</p> <p>1 / 98 (1.02%)</p> <p>0 / 93 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p>			
<p>Ear and labyrinth disorders</p> <p>cerumen impaction</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>1 / 98 (1.02%)</p> <p>0 / 93 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p> <p>sudden hearing loss</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>1 / 98 (1.02%)</p> <p>0 / 93 (0.00%)</p> <p>occurrences (all)</p> <p>1</p> <p>0</p>			
<p>Eye disorders</p> <p>diplopia</p> <p>alternative dictionary used: MedDRA 17.0</p> <p>subjects affected / exposed</p> <p>0 / 98 (0.00%)</p> <p>1 / 93 (1.08%)</p> <p>occurrences (all)</p> <p>0</p> <p>1</p> <p>lacrimation increased</p> <p>alternative dictionary used: MedDRA 18.0</p> <p>subjects affected / exposed</p> <p>0 / 98 (0.00%)</p> <p>1 / 93 (1.08%)</p> <p>occurrences (all)</p> <p>0</p> <p>1</p> <p>vision blurred</p> <p>alternative dictionary used: MedDRA 17.0</p>			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
abdominal discomfort			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
abdominal distension			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 98 (4.08%)	0 / 93 (0.00%)	
occurrences (all)	4	0	
abdominal pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	2 / 98 (2.04%)	2 / 93 (2.15%)	
occurrences (all)	2	2	
abdominal pain lower			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
abdominal pain upper			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 98 (3.06%)	2 / 93 (2.15%)	
occurrences (all)	3	2	
anal pruritus			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
barrett's oesophagus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
constipation			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)
occurrences (all)	2	0
dental caries		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
diarrhoea		
alternative dictionary used: MedDRA 18.1		
subjects affected / exposed	12 / 98 (12.24%)	6 / 93 (6.45%)
occurrences (all)	18	6
dyspepsia		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
flatulence		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	3 / 98 (3.06%)	1 / 93 (1.08%)
occurrences (all)	4	1
food poisoning		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
gastritis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)
occurrences (all)	1	1
gastrointestinal disorder		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
gastrooesophageal reflux disease		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	2 / 98 (2.04%)	2 / 93 (2.15%)
occurrences (all)	2	2

haemorrhoids			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
hiatus hernia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
impaired gastric emptying			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
large intestine polyp			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
loose tooth			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
nausea			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	7 / 98 (7.14%)	3 / 93 (3.23%)	
occurrences (all)	8	3	
toothache			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 98 (3.06%)	1 / 93 (1.08%)	
occurrences (all)	3	2	
vomiting			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	3 / 98 (3.06%)	0 / 93 (0.00%)	
occurrences (all)	5	0	
Skin and subcutaneous tissue disorders			

dermatitis contact alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	2 / 93 (2.15%) 2	
eczema alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
nail bed inflammation alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
pruritus generalised alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
urticaria contact alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
Renal and urinary disorders chronic kidney disease alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 2	0 / 93 (0.00%) 0	
hydronephrosis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
hypertonic bladder alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
microalbuminuria alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 98 (0.00%)	2 / 93 (2.15%)	
occurrences (all)	0	2	
nephrolithiasis			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	2	0	
nocturia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
urinary incontinence			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
goitre			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 98 (2.04%)	3 / 93 (3.23%)	
occurrences (all)	2	3	
hyperparathyroidism secondary			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)	
occurrences (all)	1	1	
hyperthyroidism			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
hypothyroidism			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	2 / 93 (2.15%)	
occurrences (all)	1	2	
primary hypothyroidism			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 98 (4.08%)	4 / 93 (4.30%)	
occurrences (all)	4	4	
back pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	9 / 98 (9.18%)	11 / 93 (11.83%)	
occurrences (all)	9	11	
bursitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
fibromyalgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
muscle spasms			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)	
occurrences (all)	3	0	
muscular weakness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
musculoskeletal chest pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
musculoskeletal pain			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	2 / 98 (2.04%)	1 / 93 (1.08%)
occurrences (all)	2	1
myalgia		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
neck pain		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
osteoarthritis		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	2 / 93 (2.15%)
occurrences (all)	0	2
osteopenia		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
pain in extremity		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	2 / 98 (2.04%)	1 / 93 (1.08%)
occurrences (all)	2	1
sjogren's syndrome		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
spinal osteoarthritis		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
torticollis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0

Infections and infestations abscess alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
acarodermatitis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
bronchitis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 6	2 / 93 (2.15%) 2	
cellulitis alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 93 (0.00%) 0	
chikungunya virus infection alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 4	5 / 93 (5.38%) 5	
colon gangrene alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
conjunctivitis alternative dictionary used: MedDRA 17.1 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 93 (1.08%) 1	
cystitis alternative dictionary used: MedDRA 18.0 subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	1 / 93 (1.08%) 1	
dermatitis infected alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
ear infection		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
erysipelas		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
fungus infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
fungus skin infection		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
gastroenteritis		
alternative dictionary used: MedDRA 17.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
gastroenteritis viral		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	2 / 93 (2.15%)
occurrences (all)	1	2
gastrointestinal infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)
occurrences (all)	2	0
gingivitis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)
occurrences (all)	3	0

helicobacter infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
herpes zoster		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)
occurrences (all)	1	1
influenza		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	4 / 98 (4.08%)	3 / 93 (3.23%)
occurrences (all)	4	3
laryngitis		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
lower respiratory tract infection		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
lung infection		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
nasopharyngitis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	10 / 98 (10.20%)	16 / 93 (17.20%)
occurrences (all)	17	18
onychomycosis		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	0 / 98 (0.00%)	2 / 93 (2.15%)
occurrences (all)	0	2
rhinitis		
alternative dictionary used: MedDRA 18.0		

subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)
occurrences (all)	1	1
sinusitis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	3 / 98 (3.06%)	2 / 93 (2.15%)
occurrences (all)	3	2
staphylococcal abscess		
alternative dictionary used: MedDRA 17.1		
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)
occurrences (all)	1	0
tonsillitis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	1 / 98 (1.02%)	1 / 93 (1.08%)
occurrences (all)	1	1
tooth infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1
upper respiratory tract infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	3 / 98 (3.06%)	7 / 93 (7.53%)
occurrences (all)	3	7
urinary tract infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	3 / 98 (3.06%)	8 / 93 (8.60%)
occurrences (all)	3	9
viral infection		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	2 / 98 (2.04%)	2 / 93 (2.15%)
occurrences (all)	2	2
vulvitis		
alternative dictionary used: MedDRA 18.0		
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)
occurrences (all)	0	1

Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)	
occurrences (all)	3	0	
dehydration			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	2 / 98 (2.04%)	0 / 93 (0.00%)	
occurrences (all)	2	0	
fructose intolerance			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
gout			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	0 / 98 (0.00%)	3 / 93 (3.23%)	
occurrences (all)	0	3	
hypercholesterolaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	1	0	
hyperglycaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	4 / 98 (4.08%)	0 / 93 (0.00%)	
occurrences (all)	4	0	
hyperlipidaemia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	3 / 98 (3.06%)	1 / 93 (1.08%)	
occurrences (all)	3	1	
hyperuricaemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
hypoglycaemia			
alternative dictionary used: MedDRA 18.0			

subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	8	
hyponatraemia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 98 (0.00%)	1 / 93 (1.08%)	
occurrences (all)	0	1	
obesity			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	1 / 98 (1.02%)	0 / 93 (0.00%)	
occurrences (all)	2	0	
vitamin d deficiency			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	9 / 98 (9.18%)	3 / 93 (3.23%)	
occurrences (all)	9	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported