Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, 26-Week, Phase 3 Study of Two Doses of EVP-6124 or Placebo in Subjects with Mild to Moderate Alzheimer?s Disease Currently or Previously Receiving an Acetylcholinesterase Inhibitor Medication

Summary

EudraCT number	2013-002618-10
Trial protocol	IT DE BE ES
Global end of trial date	20 November 2015

Results information

Result version number	v1 (current)
This version publication date	04 January 2017
First version publication date	04 January 2017

Trial information

Trial identification

Sponsor protocol code	EVP-6124-024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01969123
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 102623

Notes:

Sponsors

Sponsor organisation name	FORUM Pharmaceuticals Inc.
Sponsor organisation address	225 Second Avenue, Waltham, MA, United States, 02451
Public contact	Franz Buchholzer, inVentiv Health Clinical UK Ltd, RegOpsEurope@inventivhealth.com
Scientific contact	Franz Buchholzer, inVentiv Health Clinical UK Ltd, RegOpsEurope@inventivhealth.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	24 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objectives are to evaluate the safety and efficacy of 2 fixed doses of EVP-6124 HCl (2 or 3 mg daily) compared to placebo for 26 weeks in subjects with mild to moderate dementia due to AD currently receiving stable treatment or previously treated with an AChEI (donepezil, rivastigmine, or galantamine). The primary efficacy response will be an assessment of the change from baseline in cognitive, (ADAS-Cog-13) and functional/global (CDR-SB) endpoints.

Protection of trial subjects:

There were no invasive or potentially pain-inducing procedures in this study except blood sampling. If patients experience pain, analgesic treatment was allowed per the physician discretion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 15
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Japan: 17
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	South Africa: 52
Country: Number of subjects enrolled	Korea, Republic of: 26
Country: Number of subjects enrolled	United States: 251
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 11
Worldwide total number of subjects	474
EEA total number of subjects	86

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)	61
From 65 to 84 years	395
85 years and over	18

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

On Day -14, eligible subjects will enter a single-blind run-in period to assess compliance with placebo study drug. To qualify for randomization at baseline, subjects must return unused study drug, be ≥75% compliant with study drug, considered capable of completing the study assessments, and meet all eligibility requirements.

Pre-assignment period milestones

Number of subjects started	832[1]
Intermediate milestone: Number of subjects	Run-in: 543
Number of subjects completed	474

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Other: 358

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of randomized subjects (474) per country is indicated in the Trial information section. The number of screened subjects (832) is reported in the pre-assignment period.

Period 1

Period 1 title	Double-blind period (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	Placebo

Arm description:

Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.

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

Dosage and administration details:

Subjects will be instructed to take 1 tablet once daily at the same time each day, preferably between 8 and 10 AM, with or without food, and with an adequate amount of water.

Arm title	EVP-6124, 2 mg

Arm description:

Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.

Arm type	Experimental

Investigational medicinal product name	Encenicline
Investigational medicinal product code	EVP-6124
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects will be instructed to take 1 tablet once daily at the same time each day, preferably between 8 and 10 AM, with or without food, and with an adequate amount of water.

Arm title	EVP-6124, 3 mg

Arm description:

Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.

Arm type	Experimental
Investigational medicinal product name	Encenicline
Investigational medicinal product code	EVP-6124
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects will be instructed to take 1 tablet once daily at the same time each day, preferably between 8 and 10 AM, with or without food, and with an adequate amount of water.

Number of subjects in period 1	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg
Started	156	157	161
Completed	85	78	72
Not completed	71	79	89
Consent withdrawn by subject	2	-	6
Adverse event, non-fatal	3	11	6
Other	-	3	3
Death	-	-	1
Withdrawal by Subject/Caregiver	2	4	7
Due to Clinical hold	64	60	64
Lost to follow-up	-	1	1
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.	
Reporting group title	EVP-6124, 2 mg
Reporting group description:	
Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.	
Reporting group title	EVP-6124, 3 mg
Reporting group description:	
Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.	

Reporting group values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg
Number of subjects	156	157	161
Age categorical Units: Subjects			
Adults (18-64 years)	19	15	27
From 65-84 years	132	131	132
85 years and over	5	11	2
Age continuous Units: years			
arithmetic mean	74.3	74	73.3
full range (min-max)	57 to 85	55 to 85	55 to 85
Gender categorical Units: Subjects			
Female	93	81	99
Male	63	76	62

Reporting group values	Total		
Number of subjects	474		
Age categorical Units: Subjects			
Adults (18-64 years)	61		
From 65-84 years	395		
85 years and over	18		
Age continuous Units: years arithmetic mean full range (min-max)	-		
Gender categorical Units: Subjects			
Female	273		
Male	201		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.	
Reporting group title	EVP-6124, 2 mg
Reporting group description:	
Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.	
Reporting group title	EVP-6124, 3 mg
Reporting group description:	
Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.	

Primary: Cognitive Subscale 13-item (ADAS-Cog-13) (change from baseline)

End point title	Cognitive Subscale 13-item (ADAS-Cog-13) (change from baseline)[1]
End point description:	
End point type	Primary
End point timeframe:	
On Day -14 (run-in), baseline (predose on Day 1) and Days 84, 140, and 182 or early termination.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed. An analysis of the available data at the time of halting the trial was conducted to determine of there was any indication of a clinical response. However, these exploratory analyses were negative.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	150	157	
Units: n/a				
arithmetic mean (full range (min-max))	2.4 (-14 to 29)	1.7 (-15 to 19)	2.5 (-11 to 19)	

Statistical analyses

No statistical analyses for this end point

Primary: Clinical Dementia Rating Sum of the Boxes (CDR-SB) (change from baseline)

End point title	Clinical Dementia Rating Sum of the Boxes (CDR-SB) (change from baseline)[2]
End point description:	
End point type	Primary
End point timeframe:	
At baseline (predose on Day 1) and Days 84, 140, and 182 or early termination.	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	150	157	
Units: n/a				
arithmetic mean (full range (min-max))	0.64 (-3 to 9)	0.81 (-4 to 6)	0.71 (-2.5 to 7)	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of adverse events

End point title	Summary of adverse events[3]

End point description:

End point type	Primary

End point timeframe:

Any time after the subject signs the ICF through the safety follow-up visit (Day 189 or early termination, as applicable)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: Subjects reporting at least one TEAE	101	105	102	

Statistical analyses

No statistical analyses for this end point

Primary: Summary of serious adverse events

End point title	Summary of serious adverse events[4]

End point description:

End point type	Primary

End point timeframe:

Any time after the subject signs the ICF through the safety follow-up visit (Day 189 or early termination,

as applicable)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: subjects reporting any serious TEAE	12	18	16	

Statistical analyses

No statistical analyses for this end point

Primary: Albumin (change from baseline)

End point title	Albumin (change from baseline)[5]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (pre-dose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: g/L				
arithmetic mean (full range (min-max))	-0.4 (-6 to 6)	-0.8 (-7 to 4)	-0.3 (-6 to 6)	

Statistical analyses

No statistical analyses for this end point

Primary: Alkaline phosphatase (change from baseline)

End point title	Alkaline phosphatase (change from baseline)[6]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56,

84, 112, 140, and 182 or early termination.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: U/L				
arithmetic mean (full range (min-max))	-1.2 (-97 to 66)	-2.1 (-24 to 20)	-3.1 (-71 to 33)	

Statistical analyses

No statistical analyses for this end point

Primary: Alanine Aminotransferase (change from baseline)

End point title	Alanine Aminotransferase (change from baseline)[7]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: U/L				
arithmetic mean (full range (min-max))	-1.1 (-18 to 24)	-0.3 (-20 to 47)	-6.8 (-476 to 22)	

Statistical analyses

No statistical analyses for this end point

Primary: Aspartate Aminotransferase (change from baseline)

End point title	Aspartate Aminotransferase (change from baseline)[8]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (pre-dose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: U/L				
arithmetic mean (full range (min-max))	-0.5 (-15 to 11)	-1.1 (-42 to 11)	-3.6 (-281 to 16)	

Statistical analyses

No statistical analyses for this end point

Primary: Bicarbonate (change from baseline)

End point title	Bicarbonate (change from baseline)[9]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.67 (-6.9 to 7.7)	-0.37 (-5.1 to 8)	-0.66 (-9.2 to 7.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Bilirubin (change from baseline)

End point title	Bilirubin (change from baseline)[10]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (pre-dose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: umol/L				
arithmetic mean (full range (min-max))	0.07 (-6.2 to 9.2)	-0.17 (-12 to 7.2)	-1.07 (-75.9 to 9.1)	

Statistical analyses

No statistical analyses for this end point

Primary: Blood Urea Nitrogen (change from baseline)

End point title	Blood Urea Nitrogen (change from baseline)[11]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: MMOL UREA/L				
arithmetic mean (full range (min-max))	0.42 (-3.2 to 7.5)	-0.08 (-4.6 to 4.2)	0.11 (-7.1 to 4.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Calcium (change from baseline)

End point title	Calcium (change from baseline)[12]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.006 (-0.2 to 0.15)	-0.016 (-0.27 to 0.18)	-0.014 (-0.23 to 0.27)	

Statistical analyses

No statistical analyses for this end point

Primary: Creatine kinase (change from baseline)

End point title	Creatine kinase (change from baseline)[13]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: U/L				
arithmetic mean (full range (min-max))	-6.2 (-206 to 125)	-49.7 (-3564 to 185)	14.8 (-143 to 330)	

Statistical analyses

No statistical analyses for this end point

Primary: Chloride (change from baseline)

End point title	Chloride (change from baseline)[14]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (pre-dose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	0 (-6 to 12)	-0.4 (-8 to 5)	0 (-5 to 8)	

Statistical analyses

No statistical analyses for this end point

Primary: Creatinine (change from baseline)

End point title	Creatinine (change from baseline)[15]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: umol/L				
arithmetic mean (full range (min-max))	4.64 (-25.6 to 168.8)	1.59 (-24.7 to 32.7)	2.09 (-28.2 to 21.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Gamma Glutamyl Transferase (change from baseline)

End point title	Gamma Glutamyl Transferase (change from baseline)[16]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: U/L				
arithmetic mean (full range (min-max))	0.3 (-18 to 36)	-0.4 (-18 to 39)	-3.5 (-207 to 23)	

Statistical analyses

No statistical analyses for this end point

Primary: Glucose (change from baseline)

End point title	Glucose (change from baseline)[17]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.29 (-6.1 to 6.72)	0.458 (-2.61 to 4.44)	0.206 (-7.22 to 6.32)	

Statistical analyses

No statistical analyses for this end point

Primary: Potassium (change from baseline)

End point title	Potassium (change from baseline)[18]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.07 (-1 to 1.8)	0.02 (-1.7 to 1.4)	0.11 (-0.9 to 1.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Magnesium (change from baseline)

End point title	Magnesium (change from baseline)[19]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.0024 (-0.139 to 0.103)	-0.0079 (-0.246 to 0.123)	-0.003 (-0.103 to 0.206)	

Statistical analyses

No statistical analyses for this end point

Primary: Inorganic phosphate (change from baseline)

End point title	Inorganic phosphate (change from baseline)[20]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.0012 (-0.33 to 0.281)	0.0069 (-0.41 to 0.381)	0.0076 (-0.465 to 0.578)	

Statistical analyses

No statistical analyses for this end point

Primary: Protein (change from baseline)

End point title	Protein (change from baseline)[21]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: g/L				
arithmetic mean (full range (min-max))	-0.6 (-10 to 7)	-0.3 (-8 to 7)	-0.1 (-8 to 12)	

Statistical analyses

No statistical analyses for this end point

Primary: Sodium (change from baseline)

End point title	Sodium (change from baseline)[22]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.2 (-6 to 11)	-0.4 (-9 to 6)	0.2 (-5 to 8)	

Statistical analyses

No statistical analyses for this end point

Primary: Urate (change from baseline)

End point title	Urate (change from baseline)[23]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56,

84, 112, 140, and 182 or early termination.

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: mmol/l				
arithmetic mean (full range (min-max))	0.006 (-0.09 to 0.14)	0.003 (-0.08 to 0.21)	0.004 (-0.14 to 0.09)	

Statistical analyses

No statistical analyses for this end point

Primary: Leukocytes (change from baseline)

End point title	Leukocytes (change from baseline)[24]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.235 (-4.62 to 7.23)	-0.009 (-4.4 to 3.33)	-0.279 (-4.68 to 5.13)	

Statistical analyses

No statistical analyses for this end point

Primary: Erythrocytes (change from baseline)

End point title	Erythrocytes (change from baseline)[25]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^12/L				
arithmetic mean (full range (min-max))	-0.036 (-0.61 to 0.51)	-0.024 (-0.7 to 0.51)	-0.062 (-2.88 to 0.53)	

Statistical analyses

No statistical analyses for this end point

Primary: Hemoglobin (change from baseline)

End point title	Hemoglobin (change from baseline)[26]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: g/L				
arithmetic mean (full range (min-max))	-1.6 (-27 to 19)	-0.9 (-16 to 29)	-3.2 (-91 to 13)	

Statistical analyses

No statistical analyses for this end point

Primary: Hematocrit (change from baseline)

End point title	Hematocrit (change from baseline)[27]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: %(v/v)				
arithmetic mean (full range (min-max))	0.0038 (-0.093 to 0.066)	0.0032 (-0.06 to 0.088)	0.0026 (-0.108 to 0.068)	

Statistical analyses

No statistical analyses for this end point

Primary: Platelets (change from baseline)

End point title	Platelets (change from baseline)[28]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^9/L				
arithmetic mean (full range (min-max))	3.9 (-122 to 168)	-2.2 (-111 to 87)	8.3 (-105 to 167)	

Statistical analyses

No statistical analyses for this end point

Primary: Basophils (change from baseline)

End point title	Basophils (change from baseline)[29]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.001 (-0.14 to 0.05)	-0.001 (-0.15 to 0.04)	0.001 (-0.08 to 0.14)	

Statistical analyses

No statistical analyses for this end point

Primary: Eosinophils (change from baseline)

End point title	Eosinophils (change from baseline)[30]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.009 (-0.51 to 0.39)	0.012 (-0.24 to 0.7)	-0.008 (-0.34 to 0.61)	

Statistical analyses

No statistical analyses for this end point

Primary: Lymphocytes (change from baseline)

End point title	Lymphocytes (change from baseline)[31]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.03 (-1.48 to 1.41)	0.083 (-0.59 to 1.25)	-0.06 (-2.25 to 0.97)	

Statistical analyses

No statistical analyses for this end point

Primary: Monocytes (change from baseline)

End point title	Monocytes (change from baseline)[32]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.011 (-0.41 to 0.68)	-0.001 (-0.41 to 0.43)	-0.013 (-0.34 to 0.49)	

Statistical analyses

No statistical analyses for this end point

Primary: Neutrophils (change from baseline)

End point title	Neutrophils (change from baseline)[33]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (10^9/L)				
arithmetic mean (full range (min-max))	0.186 (-4.48 to 6.07)	-0.104 (-4.18 to 3.08)	-0.196 (-3.66 to 4.13)	

Statistical analyses

No statistical analyses for this end point

Primary: pH (change from baseline)

End point title	pH (change from baseline)[34]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: n/a				
arithmetic mean (full range (min-max))	-0.1 (-3 to 2)	0.1 (-3 to 3)	0.1 (-2 to 2)	

Statistical analyses

No statistical analyses for this end point

Primary: Specific gravity (change from baseline)

End point title	Specific gravity (change from baseline)[35]

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests performed non-fasting at screening and Days 1 (predose), 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: n/a				
arithmetic mean (full range (min-max))	0.0011 (-0.02 to 0.02)	-0.0006 (-0.025 to 0.02)	0.0007 (-0.025 to 0.025)	

Statistical analyses

No statistical analyses for this end point

Primary: Heart rate (change from baseline)

End point title	Heart rate (change from baseline)[36]

End point description:

End point type	Primary

End point timeframe:

Screening, pre-dose and within 3 hours post-dose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[36] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: beats/min				
arithmetic mean (full range (min-max))	1.5 (-23 to 52)	-0.3 (-25 to 23)	0.1 (-20 to 23)	

Statistical analyses

No statistical analyses for this end point

Primary: QT Duration (change from baseline)

End point title	QT Duration (change from baseline)[37]

End point description:

End point type	Primary

End point timeframe:

Screening, pre-dose and within 3 hours post-dose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[37] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: msec				
arithmetic mean (full range (min-max))	-1.3 (-96 to 92)	1.1 (-60 to 68)	1.3 (-64 to 52)	

Statistical analyses

No statistical analyses for this end point

Primary: QRS Duration (change from baseline)

End point title	QRS Duration (change from baseline)[38]

End point description:

End point type	Primary

End point timeframe:

Screening, predose and within 3 hours, post-dose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination

Notes:

[38] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be

performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: msec				
arithmetic mean (full range (min-max))	0.5 (-26 to 80)	0.1 (-20 to 30)	0.4 (-40 to 48)	

Statistical analyses

No statistical analyses for this end point

Primary: PR Duration (change from baseline)

End point title	PR Duration (change from baseline)[39]

End point description:

End point type	Primary

End point timeframe:

Screening, pre-dose and within 3 hours post-dose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination

Notes:

[39] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: msec				
arithmetic mean (full range (min-max))	0.7 (-76 to 42)	-0.5 (-30 to 36)	-3.3 (-48 to 38)	

Statistical analyses

No statistical analyses for this end point

Primary: QTcF Fridericia's correction formula (change from baseline)

End point title	QTcF Fridericia's correction formula (change from baseline)[40]

End point description:

End point type	Primary

End point timeframe:

At screening, pre-dose and within 3 hours post-dose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination.

Notes:

[40] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: msec				
arithmetic mean (full range (min-max))	1.4 (-45 to 92)	0.3 (-40 to 41)	1.1 (-38 to 46)	

Statistical analyses

No statistical analyses for this end point

Primary: Temperature (change from baseline)

End point title	Temperature (change from baseline)[41]

End point description:

End point type	Primary

End point timeframe:

At each clinic visit, including pre-dose and within 3 hours post-dose on Day 1.

Notes:

[41] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (c)				
arithmetic mean (full range (min-max))	-0.04 (-61.5 to 61.7)	-3.25 (-62.5 to 3)	2.15 (-61.7 to 62.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Systolic Blood Pressure (change from baseline)

End point title	Systolic Blood Pressure (change from baseline)[42]

End point description:

End point type	Primary

End point timeframe:

At each clinic visit, including pre-dose and within 3 hours post-dose on Day 1.

Notes:

[42] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (mmHg)				
arithmetic mean (full range (min-max))	0.2 (-36 to 40)	-2.5 (-53 to 47)	-0.9 (-51 to 48)	

Statistical analyses

No statistical analyses for this end point

Primary: Diastolic Blood Pressure (change from baseline)

End point title	Diastolic Blood Pressure (change from baseline)[43]

End point description:

End point type	Primary

End point timeframe:

At each clinic visit, including pre-dose and within 3 hours post-dose on Day 1.

Notes:

[43] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (mmHg)				
arithmetic mean (full range (min-max))	-1.5 (-27 to 20)	0.1 (-22 to 26)	-1.5 (-24 to 21)	

Statistical analyses

No statistical analyses for this end point

Primary: Heart Rate (change from baseline)

End point title	Heart Rate (change from baseline)[44]

End point description:

End point type	Primary

End point timeframe:

At each clinic visit, including pre-dose and within 3 hours post-dose on Day 1

Notes:

[44] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (bpm)				
arithmetic mean (full range (min-max))	0.9 (-22 to 49)	0.7 (-37 to 25)	0.2 (-19 to 26)	

Statistical analyses

No statistical analyses for this end point

Primary: Respiratory Rate (change from baseline)

End point title	Respiratory Rate (change from baseline)[45]

End point description:

End point type	Primary

End point timeframe:

At each clinic visit, including pre-dose and within 3 hours post-dose on Day 1.

Notes:

[45] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (breaths/min)				
arithmetic mean (full range (min-max))	-0.3 (-8 to 6)	-0.4 (-6 to 7)	0.1 (-9 to 6)	

Statistical analyses

No statistical analyses for this end point

Primary: Weight (change from baseline)

End point title	Weight (change from baseline)[46]

End point description:

End point type	Primary

End point timeframe:

At each clinic visit, including pre-dose and within 3 hours post-dose on Day 1.

Notes:

[46] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: (kg)				
arithmetic mean (full range (min-max))	2.38 (-85.2 to 99.5)	-0.04 (-76.5 to 101.1)	0.16 (-74.8 to 129.2)	

Statistical analyses

No statistical analyses for this end point

Primary: Columbia Suicide Severity Rating Scale (C-SSRS)

End point title	Columbia Suicide Severity Rating Scale (C-SSRS)[47]

End point description:

End point type	Primary

End point timeframe:

At screening (lifetime history version) and Days 1 (predose), 28, 56, 84, 112, 140, 182 or early termination (symptoms since the last study visit)

Notes:

[47] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: Subjects wishing to be dead	3	1	0	

Statistical analyses

No statistical analyses for this end point

Primary: Geriatric Depression Scale (GDS) (change from baseline)

End point title	Geriatric Depression Scale (GDS) (change from baseline)[48]

End point description:

End point type	Primary

End point timeframe:

At screening and Days 1 (predose), 84, and 182 or early termination

Notes:

[48] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the premature termination of the studies, a full statistical analysis could not be performed.

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	156	159	
Units: n/a				
arithmetic mean (full range (min-max))	0.1 (-6 to 7)	0.3 (-4 to 9)	0.1 (-4 to 4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disability assessment for dementia (DAD) (change from baseline)

End point title	Disability assessment for dementia (DAD) (change from baseline)

End point description:

End point type	Secondary

End point timeframe:

At baseline (predose on Day 1), and Days 84, 140, and 182 or early termination

End point values	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	155	150	157	
Units: n/a				
arithmetic mean (full range (min-max))	-3.9 (-64 to 21)	-4.3 (-38 to 30)	-5 (-52 to 35)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events observed at any time after the subject signs the ICF through the safety follow-up visit (Day 189 or early termination, as applicable) are to be recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.

Reporting group title	EVP-6124, 2 mg

Reporting group description:

Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.

Reporting group title	EVP-6124, 3 mg

Reporting group description:

Eligible subjects will be randomized to 1 of 3 groups, 2 or 3 mg EVP-6124 or placebo, for 26 weeks.

Serious adverse events	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 155 (7.74%)	18 / 156 (11.54%)	16 / 159 (10.06%)
number of deaths (all causes)	1	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metastases to liver			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hip fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laceration			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sick sinus syndrome			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	1 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Brain stem infarction			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	1 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	1 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia of the Alzheimer's type, with delusions			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Coagulopathy			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	1 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	1 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer perforation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	1 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	1 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia, obstructive			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Bile duct stone			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	1 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	1 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences causally related to treatment / all	0 / 12	0 / 18	0 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	EVP-6124, 2 mg	EVP-6124, 3 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 155 (65.16%)	105 / 156 (67.31%)	102 / 159 (64.15%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	3 / 155 (1.94%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Lung cancer metastatic			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Squamous cell carcinoma			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Benign ear neoplasm			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Cancer pain			

subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Colon cancer			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Lipoma			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Lung neoplasm malignant			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Metastases to liver			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Oesophageal carcinoma			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Pituitary tumour benign			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Seborrhoeic keratosis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 155 (1.94%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Hypotension			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	3 / 159 (1.89%)
occurrences (all)	101	105	102
Deep vein thrombosis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Aortic arteriosclerosis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Aortic dilatation			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hot flush			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hypertensive crisis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Peripheral vascular disorder			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Varicose vein			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 155 (1.29%)	2 / 156 (1.28%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Irritability			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	3 / 159 (1.89%)
occurrences (all)	101	105	103
Asthenia			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	102	105	101
Non-cardiac chest pain			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Oedema peripheral			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	103
Pain			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Local swelling			

subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Chest discomfort			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Feeling cold			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Inflammation			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Malaise			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Pyrexia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Vessel puncture site bruise			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Contrast media allergy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Vulvovaginal discomfort			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	6 / 155 (3.87%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Dyspnoea			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Pulmonary embolism			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Productive cough			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Pulmonary mass			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Respiratory tract congestion			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Asthma			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Dyspnoea exertional			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Oropharyngeal pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Pneumonia aspiration			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rhinitis allergic			

subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rhinorrhoea			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Sinus congestion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Upper-airway cough syndrome			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Psychiatric disorders			
Agitation			
subjects affected / exposed	4 / 155 (2.58%)	7 / 156 (4.49%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Confusional state			
subjects affected / exposed	4 / 155 (2.58%)	2 / 156 (1.28%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Depression			
subjects affected / exposed	1 / 155 (0.65%)	4 / 156 (2.56%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Anxiety			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Delusion			
subjects affected / exposed	3 / 155 (1.94%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Insomnia			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Aggression			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Delirium			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Depressed mood			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Hallucination			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Nervousness			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Psychotic disorder			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Suicidal ideation			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Abnormal behaviour			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Abnormal dreams			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Apathy			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Hallucination, visual			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Hypersexuality			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Restlessness			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Somnambulism			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Stress			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 155 (0.65%)	3 / 156 (1.92%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
White blood cells urine			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Alanine aminotransferase increased			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Blood urea increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Protein urine			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
White blood cells urine positive			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Blood calcium increased			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Blood creatinine increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Blood glucose increased			

subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Blood phosphorus increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Blood pressure increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Body temperature increased			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Electrocardiogram abnormal			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Glucose urine			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	2
Platelet count decreased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Precancerous cells present			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Specific gravity urine increased			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Transaminases increased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Urinary sediment present			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Urine ketone body present			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Vitamin D decreased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Weight decreased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 155 (3.23%)	2 / 156 (1.28%)	6 / 159 (3.77%)
occurrences (all)	101	105	102
Contusion			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Excoriation			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Laceration			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Animal bite			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Arthropod bite			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Bone contusion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Clavicle fracture			

subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Epicondylitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Femoral neck fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Femur fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Forearm fracture			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hand fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hip fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Injury			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Intentional overdose			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Joint injury			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Limb injury			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Lip injury			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Meniscus injury			

subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Muscle strain			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Pelvic fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Periorbital contusion			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Post procedural haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Procedural complication			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Procedural pain			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Scar			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Spinal compression fracture			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Thermal burn			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Toxicity to various agents			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Wrist fracture			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Atrial fibrillation			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Bradycardia			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Sinus bradycardia			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Atrioventricular block first degree			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Cardiac failure			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Myocardial infarction			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Palpitations			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Bundle branch block left			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Bundle branch block right			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Coronary artery disease			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Diastolic dysfunction			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Mitral valve incompetence			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Myocardial ischaemia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Sick sinus syndrome			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Supraventricular tachycardia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Tachycardia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 155 (4.52%)	6 / 156 (3.85%)	5 / 159 (3.14%)
occurrences (all)	101	105	102
Dizziness			
subjects affected / exposed	4 / 155 (2.58%)	5 / 156 (3.21%)	4 / 159 (2.52%)
occurrences (all)	101	105	102
Dementia Alzheimer's type			
subjects affected / exposed	2 / 155 (1.29%)	2 / 156 (1.28%)	3 / 159 (1.89%)
occurrences (all)	101	105	102
Somnolence			
subjects affected / exposed	4 / 155 (2.58%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Apraxia			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Cognitive disorder			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Sciatica			

subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Syncope			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Transient ischaemic attack			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Tremor			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Amnesia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Aphasia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Ataxia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Balance disorder			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Brain stem infarction			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Convulsion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Decreased vibratory sense			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Dementia of the Alzheimer's type, with delusions			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Dysarthria			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Essential tremor			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hemiparesis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Memory impairment			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Movement disorder			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Myoclonus			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Neuropathy peripheral			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Nystagmus			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Paraesthesia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Presyncope			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Restless legs syndrome			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Sinus headache			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Upper motor neurone lesion			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Coagulopathy			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Eosinophilia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Leukocytosis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Leukopenia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Lymphadenopathy			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Lymphopenia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Thrombocytopenia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Motion sickness			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Vertigo			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Vertigo positional			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Glaucoma			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Cataract			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Conjunctivitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Eye allergy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Eye haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Eye pruritus			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Lacrimation increased			

subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Visual impairment			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	17 / 155 (10.97%)	49 / 156 (31.41%)	50 / 159 (31.45%)
occurrences (all)	101	105	102
Diarrhoea			
subjects affected / exposed	15 / 155 (9.68%)	21 / 156 (13.46%)	20 / 159 (12.58%)
occurrences (all)	101	105	102
Abdominal pain			
subjects affected / exposed	8 / 155 (5.16%)	16 / 156 (10.26%)	15 / 159 (9.43%)
occurrences (all)	101	105	102
Nausea			
subjects affected / exposed	9 / 155 (5.81%)	10 / 156 (6.41%)	6 / 159 (3.77%)
occurrences (all)	101	105	102
Vomiting			
subjects affected / exposed	5 / 155 (3.23%)	4 / 156 (2.56%)	5 / 159 (3.14%)
occurrences (all)	101	105	102
Faeces hard			
subjects affected / exposed	0 / 155 (0.00%)	7 / 156 (4.49%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Haemorrhoids			
subjects affected / exposed	1 / 155 (0.65%)	3 / 156 (1.92%)	3 / 159 (1.89%)
occurrences (all)	101	105	102
Haematochezia			
subjects affected / exposed	0 / 155 (0.00%)	4 / 156 (2.56%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rectal tenesmus			
subjects affected / exposed	0 / 155 (0.00%)	4 / 156 (2.56%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences (all)	101	105	102

Inguinal hernia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	3 / 159 (1.89%)
occurrences (all)	101	105	102
Rectal haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Abdominal distension			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Abdominal pain upper			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Abnormal faeces			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Dyschezia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Dyspepsia			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Faecal incontinence			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Flatulence			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Gastritis			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Abdominal discomfort			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Abdominal tenderness			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Barrett's oesophagus			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Diverticulum			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Dry mouth			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Dysphagia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Faecaloma			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Faeces discoloured			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Food poisoning			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Gastric ulcer perforation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Inguinal hernia, obstructive			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Large intestine perforation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Proctalgia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rectal discharge			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rectal polyp			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rectal ulcer			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Swollen tongue			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Toothache			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Cholelithiasis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Cholecystitis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Jaundice			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	2 / 155 (1.29%)	4 / 156 (2.56%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Actinic keratosis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Dermatitis			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Dermatitis allergic			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Eczema			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Eczema asteatotic			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hyperhidrosis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Night sweats			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Pruritus			
subjects affected / exposed	0 / 155 (0.00%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Acne			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Dermal cyst			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Dry skin			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Ecchymosis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Erythema			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Precancerous skin lesion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Psoriasis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rash maculo-papular			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Rash papular			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rash pruritic			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rash vesicular			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Scar pain			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Skin exfoliation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Skin irritation			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Skin lesion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Skin ulcer			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	103
Stasis dermatitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 155 (1.29%)	8 / 156 (5.13%)	4 / 159 (2.52%)
occurrences (all)	101	105	102
Leukocyturia			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Urinary retention			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Dysuria			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Proteinuria			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Renal impairment			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Urinary incontinence			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Azotaemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Chromaturia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Pollakiuria			

subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Renal failure			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Renal failure acute			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 155 (3.23%)	2 / 156 (1.28%)	4 / 159 (2.52%)
occurrences (all)	101	105	102
Arthralgia			
subjects affected / exposed	1 / 155 (0.65%)	3 / 156 (1.92%)	3 / 159 (1.89%)
occurrences (all)	101	105	103
Muscle spasms			
subjects affected / exposed	1 / 155 (0.65%)	2 / 156 (1.28%)	4 / 159 (2.52%)
occurrences (all)	101	105	102
Musculoskeletal chest pain			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	3 / 159 (1.89%)
occurrences (all)	101	105	103
Pain in extremity			
subjects affected / exposed	2 / 155 (1.29%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	102	105
Musculoskeletal pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Neck pain			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Costochondritis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Groin pain			

subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Joint range of motion decreased			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Myalgia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Osteitis deformans			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Osteoarthritis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Osteoporosis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Rotator cuff syndrome			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Torticollis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Trigger finger			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	9 / 155 (5.81%)	6 / 156 (3.85%)	8 / 159 (5.03%)
occurrences (all)	101	105	102
Nasopharyngitis			
subjects affected / exposed	2 / 155 (1.29%)	4 / 156 (2.56%)	7 / 159 (4.40%)
occurrences (all)	101	105	102

Bronchitis			
subjects affected / exposed	2 / 155 (1.29%)	2 / 156 (1.28%)	3 / 159 (1.89%)
occurrences (all)	101	105	102
Upper respiratory tract infection			
subjects affected / exposed	5 / 155 (3.23%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Gastroenteritis viral			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Pneumonia			
subjects affected / exposed	2 / 155 (1.29%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Bacteriuria			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Pharyngitis			
subjects affected / exposed	1 / 155 (0.65%)	2 / 156 (1.28%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Sinusitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Cellulitis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Cystitis			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Diverticulitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Fungal skin infection			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Herpes zoster			
subjects affected / exposed	1 / 155 (0.65%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Oral herpes			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Periodontitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Tooth infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Abscess			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Acute sinusitis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Clostridium difficile infection			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Gastroenteritis			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Gingivitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Helicobacter infection			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Impetigo			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Influenza			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Oropharyngitis fungal			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102

Respiratory tract infection			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Rhinitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Sinobronchitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Tooth abscess			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Viral infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 155 (1.29%)	2 / 156 (1.28%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Dehydration			
subjects affected / exposed	3 / 155 (1.94%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Hypokalaemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	2 / 159 (1.26%)
occurrences (all)	101	105	102
Diabetes mellitus			
subjects affected / exposed	2 / 155 (1.29%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hypoglycaemia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Diabetes mellitus inadequate control			

subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Gout			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hypercholesterolaemia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hyperglycaemia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 156 (0.64%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Hyperkalaemia			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102
Hypocalcaemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Increased appetite			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 155 (0.65%)	0 / 156 (0.00%)	0 / 159 (0.00%)
occurrences (all)	101	105	102
Vitamin D deficiency			
subjects affected / exposed	0 / 155 (0.00%)	0 / 156 (0.00%)	1 / 159 (0.63%)
occurrences (all)	101	105	102

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2014	Protocol Amendment 1, Version 2.0 (dated 30 June 2014)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
20 November 2015	The Phase 3 Alzheimer's disease studies (EVP-6124-024, EVP-6124-025 and EVP-6124-026) were placed on complete clinical hold by the FDA due to potential gastrointestinal safety concern(s) around September 1st, 2015. Subsequent to this time, they were terminated to analyze the available data around January 1st, 2016.	-

Notes:

Limitations and caveats

None reported