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	2013-002653-30
Trial protocol	IT GB DE ES CZ NL
Global end of trial date	11 November 2015

Results information

Result version number	v1 (current)
This version publication date	28 December 2016
First version publication date	28 December 2016

Trial information

Trial identification

Sponsor protocol code	EVP-6124-025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01969136
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	26 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 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	23 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: 11
Country: Number of subjects enrolled	Argentina: 2
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Japan: 27
Country: Number of subjects enrolled	Mexico: 5
Country: Number of subjects enrolled	South Africa: 25
Country: Number of subjects enrolled	Korea, Republic of: 26
Country: Number of subjects enrolled	United States: 184
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	Czech Republic: 40
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Italy: 6
Worldwide total number of subjects	403
EEA total number of subjects	115

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)	75
From 65 to 84 years	316
85 years and over	12

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	661[1]
Intermediate milestone: Number of subjects	Run-in: 445
Number of subjects completed	403

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Other: 258

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 (403) per country is indicated in the Trial information section. The number of screened subjects (661) 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, Monitor, 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	134	134	135
Completed	55	55	55
Not completed	79	79	80
Withdrawal by subject/caregiver	4	4	4
Due to Clinical Hold	59	60	63
Consent withdrawn by subject	2	-	1
Medication prohibited by protocol	1	-	-
Adverse event, non-fatal	10	10	7
Death	1	-	1
Administrative reasons	-	1	-
Other	-	3	3
Lost to follow-up	2	1	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	134	134	135
Age categorical Units: Subjects			
Adults (18-64 years)	23	26	26
From 65-84 years	105	105	106
85 years and over	6	3	3
Age continuous Units: years			
arithmetic mean	73.8	73.1	71.9
full range (min-max)	55 to 85	55 to 85	55 to 85
Gender categorical Units: Subjects			
Female	86	67	80
Male	48	67	55

Reporting group values	Total		
Number of subjects	403		
Age categorical Units: Subjects			
Adults (18-64 years)	75		
From 65-84 years	316		
85 years and over	12		
Age continuous Units: years arithmetic mean full range (min-max)	-		
Gender categorical Units: Subjects			
Female	233		
Male	170		

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	133	133	132	
Units: n/a				
arithmetic mean (full range (min-max))	-0.1 (-13 to 20)	0.4 (-19 to 19)	0.9 (-18 to 18)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Clinical Dementia Rating Sum of the Boxes (CDR-SB) Score (change from baseline)[2]
End point description:	
End point type	Primary

End point timeframe:

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	133	133	132	
Units: n/a				
arithmetic mean (full range (min-max))	0.11 (-6 to 7)	0.06 (-6 to 3)	0.19 (-6 to 9)	

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	134	134	135	
Units: Subjects reporting at least one TEAE	79	79	79	

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:

Observed at 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	134	134	135	
Units: Subjects reporting any serious TEAE	8	9	7	

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 will be performed non-fasting at screening and Days 1 (predose), 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	134	134	135	
Units: g/L				
arithmetic mean (full range (min-max))	0.1 (-6 to 7)	0.2 (-5 to 6)	-0.6 (-7 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:

Routine clinical laboratory tests will be 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	134	134	135	
Units: U/L				
arithmetic mean (full range (min-max))	0.4 (-42 to 53)	-2.9 (-33 to 32)	-2.4 (-34 to 41)	

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 will be 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	134	134	135	
Units: U/L				
arithmetic mean (full range (min-max))	-1.9 (-48 to 18)	-1.5 (-22 to 18)	-1.1 (-48 to 18)	

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 will be performed non-fasting at screening and Days 1 (predose), 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	134	134	135	
Units: U/L				
arithmetic mean (full range (min-max))	-0.9 (-31 to 13)	-0.4 (-13 to 42)	0 (-42 to 24)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.36 (-7.1 to 7.1)	-0.17 (-6.1 to 7)	-0.43 (-7.7 to 5)	

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 will be performed non-fasting at screening and Days 1 (predose), 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	134	134	135	
Units: umol/L				
arithmetic mean (full range (min-max))	0.05 (-3.9 to 11.3)	0.44 (-5.2 to 8.7)	-0.56 (-12 to 4.6)	

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 will be 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	134	134	135	
Units: MMOL UREA/L				
arithmetic mean (full range (min-max))	-0.06 (-7.1 to 3.2)	0.04 (-6 to 3.5)	0.54 (-3.6 to 13.3)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.004 (-0.27 to 0.2)	0.001 (-0.25 to 0.22)	-0.01 (-0.25 to 0.17)	

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 will be 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	134	134	135	
Units: U/L				
arithmetic mean (full range (min-max))	1 (-532 to 192)	2 (-357 to 315)	24.6 (-133 to 1541)	

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 will be performed non-fasting at screening and Days 1 (predose), 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.1 (-8 to 7)	-0.6 (-8 to 3)	-0.2 (-11 to 5)	

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 will be 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	134	134	135	
Units: umol/L				
arithmetic mean (full range (min-max))	1.24 (-25.6 to 24.7)	1.84 (-31 to 23)	8 (-15 to 295.3)	

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 will be 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	134	134	135	
Units: U/L				
arithmetic mean (full range (min-max))	-2.2 (-52 to 26)	-2.4 (-46 to 21)	-0.4 (-39 to 25)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.066 (-6.66 to 3.28)	0.264 (-3.66 to 7.6)	0.09 (-5.28 to 3.83)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.05 (-1.9 to 1.5)	0.1 (-1.3 to 1.3)	0.08 (-1 to 0.7)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.0079 (-0.136 to 0.132)	-0.0041 (-0.123 to 0.127)	0.0024 (-0.14 to 0.124)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.0047 (-0.375 to 0.4)	0.0277 (-0.452 to 0.798)	0.0395 (-0.352 to 0.649)	

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 will be 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	134	134	135	
Units: g/L				
arithmetic mean (full range (min-max))	0.5 (-9 to 12)	0.1 (-6 to 12)	0.2 (-10 to 8)	

Statistical analyses

No statistical analyses for this end point

Primary: Sodium (change fron baseline)

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

End point description:

End point type	Primary

End point timeframe:

The routine clinical laboratory tests will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	0.7 (-5 to 7)	0.3 (-6 to 7)	0.2 (-9 to 7)	

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 will be 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	134	134	135	
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.005 (-0.15 to 0.16)	0.001 (-0.26 to 0.11)	0.019 (-0.08 to 0.35)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.255 (-3.76 to 9.74)	-0.002 (-4.1 to 2.78)	0.388 (-2.77 to 11.58)	

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 will be 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	134	134	135	
Units: 10^12/L				
arithmetic mean (full range (min-max))	0.022 (-0.52 to 1.42)	0.029 (-0.41 to 0.6)	-0.047 (-0.87 to 0.66)	

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 will be 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	134	134	135	
Units: g/L				
arithmetic mean (full range (min-max))	-0.8 (-23 to 30)	0.1 (-16 to 20)	-1.7 (-24 to 21)	

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 will be 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	134	134	135	
Units: %(v/v)				
arithmetic mean (full range (min-max))	0.0029 (-0.068 to 0.118)	0.0078 (-0.07 to 0.09)	0.0015 (-0.078 to 0.061)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0 (-153 to 60)	6 (-56 to 62)	8.7 (-72 to 302)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.002 (-0.05 to 0.03)	0.002 (-0.04 to 0.04)	0.001 (-0.07 to 0.06)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.015 (-0.57 to 0.22)	-0.009 (-0.91 to 0.26)	0.039 (-0.19 to 0.55)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.009 (-1.2 to 0.63)	-0.024 (-1.12 to 0.68)	0.051 (-0.87 to 0.73)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.013 (-0.61 to 0.61)	-0.01 (-0.4 to 0.3)	0.052 (-0.27 to 0.9)	

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 will be 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	134	134	135	
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.301 (-3.62 to 9.14)	0.037 (-4.6 to 2.68)	0.245 (-3.42 to 11.31)	

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 will be 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	134	134	135	
Units: n/a				
arithmetic mean (full range (min-max))	-0.2 (-2 to 3)	0.1 (-2 to 3)	0 (-2 to 3)	

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 will be 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	134	134	135	
Units: n/a				
arithmetic mean (full range (min-max))	0.0012 (-0.03 to 0.03)	0.0008 (-0.015 to 0.02)	-0.0003 (-0.02 to 0.02)	

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:

Standard 12-lead ECG tracings will be obtained at screening, predose and within 3 hours postdose 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	134	134	134	
Units: beats/min				
arithmetic mean (full range (min-max))	0.1 (-16 to 20)	-0.4 (-34 to 27)	1.8 (-17 to 16)	

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:

Standard 12-lead ECG tracings will be obtained at screening, predose and within 3 hours postdose 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	134	134	135	
Units: msec				
arithmetic mean (full range (min-max))	1.8 (-68 to 54)	5.3 (-74 to 78)	-4.8 (-72 to 38)	

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:

Standard 12-lead ECG tracings will be obtained at screening, predose and within 3 hours postdose 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	134	134	135	
Units: msec				
arithmetic mean (full range (min-max))	0.5 (-16 to 14)	1.2 (-14 to 40)	-0.3 (-18 to 16)	

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:

Standard 12-lead ECG tracings will be obtained at screening, predose and within 3 hours postdose 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	134	134	135	
Units: msec				
arithmetic mean (full range (min-max))	-3.7 (-62 to 24)	1.9 (-28 to 34)	0.4 (-40 to 28)	

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

End point description:

End point type	Primary

End point timeframe:

Standard 12-lead ECG tracings will be obtained at screening, predose and within 3 hours postdose 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	134	134	135	
Units: msec				
arithmetic mean (full range (min-max))	2.2 (-41 to 40)	4 (-45 to 49)	-1 (-42 to 30)	

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:

Recorded at each clinic visit, including predose and within 3 hours postdose 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	134	134	135	
Units: (c)				
arithmetic mean (full range (min-max))	-1.8 (-61 to 62)	2.7 (-62 to 61)	-0.8 (-62 to 62)	

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:

Recorded at each clinic visit, including predose and within 3 hours postdose 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	134	134	135	
Units: mmHg				
arithmetic mean (full range (min-max))	-2.7 (-35 to 33)	0.3 (-38 to 42)	1.2 (-38 to 45)	

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:

Recorded at each clinic visit, including predose and within 3 hours postdose 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	134	134	135	
Units: mmHg				
arithmetic mean (full range (min-max))	-0.6 (-25 to 38)	0.4 (-32 to 27)	-2.3 (-26 to 24)	

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:

Standard 12-lead ECG tracings will be obtained at screening, predose and within 3 hours postdose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination.

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	134	134	134	
Units: bpm				
arithmetic mean (full range (min-max))	-1.7 (-16 to 18)	1.5 (-21 to 37)	1.3 (-10 to 16)	

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:

Recorded at each clinic visit, including predose and within 3 hours postdose 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	134	134	135	
Units: breaths/min				
arithmetic mean (full range (min-max))	-0.3 (-6 to 4)	-0.2 (-7 to 4)	0.4 (-5 to 9)	

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 screening, predose on Day 1, and Days 28, 56, 84, 112, 140, and 182 or early termination.

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	134	134	134	
Units: kg				
arithmetic mean (full range (min-max))	-0.2 (-88 to 92)	2.2 (-78 to 91)	-3.2 (-113 to 18)	

Statistical analyses

No statistical analyses for this end point

Primary: Columbia Suicide Severity Rating Scale (C-SSRS) (Day 182)

End point title	Columbia Suicide Severity Rating Scale (C-SSRS) (Day 182)[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	134	134	135	
Units: Subjects wishing to be dead	0	0	1	

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	134	134	135	
Units: n/a				
arithmetic mean (full range (min-max))	0.2 (-3 to 9)	-0.1 (-5 to 5)	0.4 (-2 to 9)	

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:

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	133	133	132	
Units: n/a				
arithmetic mean (full range (min-max))	-1 (-28 to 36)	-1.7 (-35 to 33)	-3.4 (-50 to 32)	

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	8 / 134 (5.97%)	9 / 134 (6.72%)	7 / 135 (5.19%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	1 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Fall			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	1 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Large intestine perforation			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Peptic ulcer			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary arterial hypertension			

subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar I disorder			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	1 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder leukoplakia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 9	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 8	0 / 9	1 / 7
deaths causally related to treatment / all	0 / 1	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	79 / 134 (58.96%)	79 / 134 (58.96%)	79 / 135 (58.52%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Malignant pleural effusion			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Mucinous breast carcinoma			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Myelodysplastic syndrome			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Prostate cancer			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 134 (2.24%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Haemorrhage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hypertension			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Malaise			

subjects affected / exposed	0 / 134 (0.00%)	3 / 134 (2.24%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Fatigue			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Pyrexia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Asthenia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Chest discomfort			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Chest pain			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Device breakage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Temperature intolerance			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Prostatitis			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 134 (2.24%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Bronchiectasis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Dyspnoea			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Dyspnoea exertional			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Epistaxis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Hiccups			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Nasal congestion			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Oropharyngeal pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Respiratory failure			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Rhinorrhoea			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Rhonchi			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Wheezing			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Psychiatric disorders			
Agitation			
subjects affected / exposed	2 / 134 (1.49%)	3 / 134 (2.24%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Anxiety			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	3 / 135 (2.22%)
occurrences (all)	79	79	79
Depression			
subjects affected / exposed	2 / 134 (1.49%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Insomnia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Nervousness			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Abnormal dreams			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Aggression			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Bipolar I disorder			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Confusional state			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Delirium			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Depressed mood			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Emotional disorder			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hallucination			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hallucination, auditory			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hallucination, visual			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hyposomnia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Libido decreased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Mania			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Paranoia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Restlessness			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Sleep disorder			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Investigations			
Blood urea increased			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Blood creatinine increased			
subjects affected / exposed	0 / 134 (0.00%)	2 / 134 (1.49%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Alanine aminotransferase increased			
subjects affected / exposed	2 / 134 (1.49%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood pressure increased			
subjects affected / exposed	2 / 134 (1.49%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Weight decreased			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Weight increased			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
White blood cells urine			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood alkaline phosphatase increased			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood glucose increased			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Electrocardiogram abnormal			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Eosinophil count increased			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood albumin decreased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood bicarbonate decreased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood magnesium decreased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood phosphorus increased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Blood pressure decreased			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Blood uric acid increased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Crystal urine present			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
ECG signs of myocardial ischaemia			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Platelet count decreased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Protein total decreased			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Protein urine present			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 134 (1.49%)	4 / 134 (2.99%)	4 / 135 (2.96%)
occurrences (all)	79	79	79
Laceration			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Rib fracture			
subjects affected / exposed	0 / 134 (0.00%)	2 / 134 (1.49%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Contusion			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Subdural haematoma			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Accidental overdose			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Ankle fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Arthropod bite			

subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Arthropod sting			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Back injury			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Excoriation			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Face injury			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Femur fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Foot fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hand fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Heat stroke			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hip fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Humerus fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Limb injury			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Lumbar vertebral fracture			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Muscle strain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Post procedural complication			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Procedural pain			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Radius fracture			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Scapula fracture			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Scratch			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Tibia fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Tooth fracture			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Toxicity to various agents			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Wound haemorrhage			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 134 (0.00%)	2 / 134 (1.49%)	0 / 135 (0.00%)
occurrences (all)	79	79	79

Angina pectoris			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Bradycardia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Cardiac failure			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Myocardial infarction			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Palpitations			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Ventricular extrasystoles			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 134 (3.73%)	3 / 134 (2.24%)	3 / 135 (2.22%)
occurrences (all)	79	79	79
Headache			
subjects affected / exposed	4 / 134 (2.99%)	1 / 134 (0.75%)	6 / 135 (4.44%)
occurrences (all)	79	79	79
Syncope			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Somnolence			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Tremor			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Amnesia			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Ataxia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Cerebrovascular accident			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Cognitive disorder			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Convulsion			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Dementia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Dementia Alzheimer's type			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Parkinsonism			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Psychomotor hyperactivity			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Sciatica			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Anaemia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79

Haemolysis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Lymphadenopathy			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Deafness unilateral			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Tinnitus			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Tympanic membrane perforation			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Vertigo			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Vertigo positional			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Eye disorders			
Cataract			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Dry eye			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Ocular hyperaemia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Visual impairment			

subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 134 (6.72%)	37 / 134 (27.61%)	34 / 135 (25.19%)
occurrences (all)	79	79	79
Diarrhoea			
subjects affected / exposed	9 / 134 (6.72%)	17 / 134 (12.69%)	8 / 135 (5.93%)
occurrences (all)	79	79	79
Abdominal pain			
subjects affected / exposed	3 / 134 (2.24%)	18 / 134 (13.43%)	6 / 135 (4.44%)
occurrences (all)	79	79	79
Nausea			
subjects affected / exposed	9 / 134 (6.72%)	8 / 134 (5.97%)	5 / 135 (3.70%)
occurrences (all)	79	79	79
Vomiting			
subjects affected / exposed	3 / 134 (2.24%)	4 / 134 (2.99%)	6 / 135 (4.44%)
occurrences (all)	79	79	79
Faeces hard			
subjects affected / exposed	1 / 134 (0.75%)	2 / 134 (1.49%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Dyspepsia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Haemorrhoids			
subjects affected / exposed	2 / 134 (1.49%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Toothache			
subjects affected / exposed	3 / 134 (2.24%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Abdominal distension			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Dental caries			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79

Faecal incontinence			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Rectal haemorrhage			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Abdominal tenderness			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Cheilitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Colitis ulcerative			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Diverticulum intestinal			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Dry mouth			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Dyschezia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Eructation			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Flatulence			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Gastric ulcer			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79

Gastritis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Haematochezia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Large intestine perforation			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Pancreatitis acute			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Peptic ulcer			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Rectal prolapse			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Rectal tenesmus			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 134 (1.49%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Rash			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Acne			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Drug eruption			

subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Dry skin			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Ecchymosis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Night sweats			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Skin lesion			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Skin ulcer			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Vascular skin disorder			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	3 / 134 (2.24%)	3 / 134 (2.24%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Dysuria			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Renal failure			
subjects affected / exposed	0 / 134 (0.00%)	2 / 134 (1.49%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Renal failure acute			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Urinary incontinence			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79

Bladder leukoplakia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Micturition urgency			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Proteinuria			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 134 (3.73%)	1 / 134 (0.75%)	3 / 135 (2.22%)
occurrences (all)	79	79	79
Arthralgia			
subjects affected / exposed	3 / 134 (2.24%)	0 / 134 (0.00%)	3 / 135 (2.22%)
occurrences (all)	79	79	79
Muscle spasms			
subjects affected / exposed	2 / 134 (1.49%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Musculoskeletal chest pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Osteoarthritis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Pain in extremity			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Bursitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Fracture pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Intervertebral disc degeneration			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Muscular weakness			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Myalgia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Neck pain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Spinal pain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Vertebral wedging			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 134 (3.73%)	3 / 134 (2.24%)	6 / 135 (4.44%)
occurrences (all)	79	79	79
Nasopharyngitis			
subjects affected / exposed	8 / 134 (5.97%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Upper respiratory tract infection			
subjects affected / exposed	2 / 134 (1.49%)	3 / 134 (2.24%)	3 / 135 (2.22%)
occurrences (all)	79	79	79
Influenza			
subjects affected / exposed	2 / 134 (1.49%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Bronchitis			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Cystitis			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79

Herpes zoster			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	2 / 135 (1.48%)
occurrences (all)	79	79	79
Tinea pedis			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Gastroenteritis			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Gastroenteritis viral			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Pneumonia			
subjects affected / exposed	0 / 134 (0.00%)	2 / 134 (1.49%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Rhinitis			
subjects affected / exposed	2 / 134 (1.49%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Tooth abscess			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Bacteriuria			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Bronchopneumonia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Otitis media acute			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Paronychia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Periodontitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79

Sinusitis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Soft tissue infection			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Tooth infection			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Tracheitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Viral infection			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 134 (0.00%)	2 / 134 (1.49%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Decreased appetite			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Gout			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	79	79	79
Hypokalaemia			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Dyslipidaemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Folate deficiency			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hyperlipidaemia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hyperuricaemia			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Hypovitaminosis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Vitamin B12 deficiency			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79
Vitamin D deficiency			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	79	79	79

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
11 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