Clinical trial results:
A 26-Week Extension Study of the Safety and Clinical Effects of EVP-6124 in Subjects with Alzheimer's Disease Currently or Previously Receiving an Acetylcholinesterase Inhibitor Medication

Summary

EudraCT number	2013-002654-75
Trial protocol	DE BE GB ES IT NL CZ
Global end of trial date	23 December 2015

Results information

Result version number	v1 (current)
This version publication date	05 February 2017
First version publication date	05 February 2017

Trial information

Trial identification

Sponsor protocol code	EVP-6124-026

Additional study identifiers

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

Global end of trial reached?	Yes
Global end of trial date	23 December 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of 2 fixed doses of EVP-6124 (2 or 3 mg daily) for up to 52 weeks in subjects with Alzheimer's disease (AD) who complete (Day 182) studies EVP-6124-024 or EVP-6124-025

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	05 June 2014
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	Spain: 6
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Czech Republic: 8
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Canada: 14
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	South Africa: 43
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	United States: 204
Worldwide total number of subjects	348
EEA total number of subjects	52

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)	60
From 65 to 84 years	274
85 years and over	14

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In this extension study, subjects who complete study EVP-6124-024 or EVP-6124-025 (Day 182) and fulfill all entry criteria will be randomized. Assessments performed at the final double-blind study visit (Day 182) will serve as the baseline for this extension study for all subjects.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EVP-6124, 2 mg

Arm description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

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:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

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	Pbo-EVP-6124, 2 mg

Arm description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

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	Pbo-EVP-6124, 3 mg

Arm description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg
Started	111	114	61
Completed	37	36	20
Not completed	74	78	41
Consent withdrawn by subject	2	1	1
Adverse event, non-fatal	5	5	4
Other	3	2	5
Withdrawal by Subject/Caregiver	2	2	-
Due to Clinical hold	60	67	31
Lost to follow-up	2	1	-

Number of subjects in period 1	Pbo-EVP-6124, 3 mg
Started	62
Completed	12
Not completed	50
Consent withdrawn by subject	3
Adverse event, non-fatal	3
Other	3
Withdrawal by Subject/Caregiver	2
Due to Clinical hold	39
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	EVP-6124, 2 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	
Reporting group title	EVP-6124, 3 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	
Reporting group title	Pbo-EVP-6124, 2 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	
Reporting group title	Pbo-EVP-6124, 3 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	

Reporting group values	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg
Number of subjects	111	114	61
Age categorical Units: Subjects			
Adults (18-64 years)	21	26	7
From 65-84 years	85	86	51
85 years and over	5	2	3
Age continuous Units: years			
arithmetic mean	72.8	71.7	74.3
full range (min-max)	57 to 85	55 to 85	55 to 85
Gender categorical Units: Subjects			
Female	49	62	40
Male	62	52	21

Reporting group values	Pbo-EVP-6124, 3 mg	Total	
Number of subjects	62	348	
Age categorical Units: Subjects			
Adults (18-64 years)	6	60	
From 65-84 years	52	274	
85 years and over	4	14	
Age continuous Units: years			
arithmetic mean	75.4		
full range (min-max)	57 to 85	-	

Gender categorical Units: Subjects			
Female	37	188	
Male	25	160	

End points

End points reporting groups

Reporting group title	EVP-6124, 2 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	
Reporting group title	EVP-6124, 3 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	
Reporting group title	Pbo-EVP-6124, 2 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	
Reporting group title	Pbo-EVP-6124, 3 mg
Reporting group description:	
Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).	

Primary: Albumin (Change from baseline)

End point title	Albumin (Change from baseline)[1]
End point description:	
End point type	Primary
End point timeframe:	
Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.	
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.	

End point values	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: (g/L)				
arithmetic mean (full range (min-max))	-1 (-7 to 2)	-0.7 (-7 to 3)	-0.3 (-6 to 6)	-1.2 (-6 to 3)

Statistical analyses

No statistical analyses for this end point

Primary: Alkaline Phosphatase (Change from baseline)

End point title	Alkaline Phosphatase (Change from baseline)[2]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: U/L				
arithmetic mean (full range (min-max))	-1.1 (-29 to 12)	2.6 (-25 to 29)	-2.9 (-31 to 19)	9.1 (-15 to 104)

Statistical analyses

No statistical analyses for this end point

Primary: Alanine Aminotransferase (Change from baseline)

End point title	Alanine Aminotransferase (Change from baseline)[3]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: U/L				
arithmetic mean (full range (min-max))	-2.5 (-18 to 7)	-1.7 (-17 to 16)	1.2 (-7 to 12)	0.2 (-5 to 17)

Statistical analyses

No statistical analyses for this end point

Primary: Aspartate Aminotransferase (Change from baseline)

End point title	Aspartate Aminotransferase (Change from baseline)[4]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: U/L				
arithmetic mean (full range (min-max))	-2.9 (-35 to 3)	-1.7 (-18 to 10)	0.7 (-5 to 8)	0 (-15 to 10)

Statistical analyses

No statistical analyses for this end point

Primary: Bicarbonate (Change from baseline)

End point title	Bicarbonate (Change from baseline)[5]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.75 (-5.7 to 3.6)	-0.22 (-8.1 to 8.2)	0.29 (-4.4 to 5.2)	0.59 (-2.4 to 7.9)

Statistical analyses

No statistical analyses for this end point

Primary: Bilirubin (Change from baseline)

End point title	Bilirubin (Change from baseline)[6]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: umol/L				
arithmetic mean (full range (min-max))	0.77 (-3.9 to 9.4)	0 (-8 to 7.1)	-0.07 (-6.9 to 8)	0.03 (-3.4 to 4.4)

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)[7]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: MMOL UREA/L				
arithmetic mean (full range (min-max))	-0.29 (-5 to 2.5)	-0.09 (-4.7 to 2.1)	-0.31 (-5 to 2.5)	0.38 (-5.4 to 5.4)

Statistical analyses

No statistical analyses for this end point

Primary: Calcium (Change from baseline)

End point title	Calcium (Change from baseline)[8]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.024 (-0.22 to 0.16)	-0.023 (-0.28 to 0.13)	0.006 (-0.15 to 0.16)	-0.028 (-0.23 to 0.14)

Statistical analyses

No statistical analyses for this end point

Primary: Creatine Kinase (Change from baseline)

End point title	Creatine Kinase (Change from baseline)[9]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: U/L				
arithmetic mean (full range (min-max))	-26.8 (-344 to 61)	-11.6 (-210 to 106)	10.2 (-36 to 123)	-4.6 (-142 to 257)

Statistical analyses

No statistical analyses for this end point

Primary: Chloride (Change from baseline)

End point title	Chloride (Change from baseline)[10]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	0.5 (-5 to 6)	-0.2 (-5 to 6)	0.5 (-6 to 8)	-0.4 (-12 to 6)

Statistical analyses

No statistical analyses for this end point

Primary: Creatinine (Change from baseline)

End point title	Creatinine (Change from baseline)[11]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: umol/L				
arithmetic mean (full range (min-max))	2.51 (-15.9 to 19.5)	2.08 (-15.9 to 23.9)	2.98 (-124.6 to 41.5)	0.52 (-23.9 to 31.8)

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)[12]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: U/L				
arithmetic mean (full range (min-max))	-0.7 (-14 to 12)	0.9 (-17 to 24)	1 (-4 to 11)	8.6 (-12 to 129)

Statistical analyses

No statistical analyses for this end point

Primary: Glucose (Change from baseline)

End point title	Glucose (Change from baseline)[13]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.27 (-9.04 to 2.94)	0.408 (-5.94 to 13.77)	0.309 (-1.5 to 3.44)	-0.382 (-4.11 to 4.49)

Statistical analyses

No statistical analyses for this end point

Primary: Potassium (Change from baseline)

End point title	Potassium (Change from baseline)[14]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	0.06 (-1.6 to 1.1)	-0.07 (-0.8 to 1)	0.16 (-0.5 to 1.6)	0.15 (-0.7 to 0.9)

Statistical analyses

No statistical analyses for this end point

Primary: Magnesium (Change from baseline)

End point title	Magnesium (Change from baseline)[15]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.0079 (-0.123 to 0.164)	-0.0253 (-0.124 to 0.083)	-0.0057 (-0.214 to 0.205)	-0.0213 (-0.164 to 0.185)

Statistical analyses

No statistical analyses for this end point

Primary: Inorganic Phosphate (Change from baseline)

End point title	Inorganic Phosphate (Change from baseline)[16]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.0291 (-0.394 to 0.339)	-0.017 (-0.419 to 0.368)	0.0025 (-0.362 to 0.649)	0.0199 (-0.294 to 0.62)

Statistical analyses

No statistical analyses for this end point

Primary: Protein (Change from baseline)

End point title	Protein (Change from baseline)[17]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: g/L				
arithmetic mean (full range (min-max))	-1.5 (-12 to 4)	-0.9 (-10 to 6)	-0.4 (-6 to 6)	-0.2 (-5 to 8)

Statistical analyses

No statistical analyses for this end point

Primary: Sodium (Change from baseline)

End point title	Sodium (Change from baseline)[18]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	0.8 (-4 to 8)	0.1 (-8 to 5)	1 (-4 to 6)	0.2 (-11 to 9)

Statistical analyses

No statistical analyses for this end point

Primary: Urate (Change from baseline)

End point title	Urate (Change from baseline)[19]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmol/L				
arithmetic mean (full range (min-max))	-0.004 (-0.12 to 0.13)	0 (-0.08 to 0.1)	0.008 (-0.08 to 0.12)	0.014 (-0.1 to 0.1)

Statistical analyses

No statistical analyses for this end point

Primary: Leukocytes (Change from baseline)

End point title	Leukocytes (Change from baseline)[20]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.016 (-2.28 to 8.25)	-0.219 (-3.58 to 1.74)	-0.245 (-5.27 to 2.66)	-0.013 (-10.64 to 4.29)

Statistical analyses

No statistical analyses for this end point

Primary: Erythrocytes (Change from baseline)

End point title	Erythrocytes (Change from baseline)[21]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^12/L				
arithmetic mean (full range (min-max))	-0.054 (-0.63 to 0.75)	-0.085 (-0.65 to 0.42)	-0.065 (-1.74 to 0.45)	-0.075 (-0.51 to 0.55)

Statistical analyses

No statistical analyses for this end point

Primary: Hemoglobin (Change from baseline)

End point title	Hemoglobin (Change from baseline)[22]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: g/L				
arithmetic mean (full range (min-max))	-2.1 (-35 to 13)	-1.7 (-20 to 11)	-1.1 (-42 to 23)	-2.7 (-21 to 11)

Statistical analyses

No statistical analyses for this end point

Primary: Hematocrit (change from baseline)

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

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: %(v/v)				
arithmetic mean (full range (min-max))	0.004 (-0.091 to 0.074)	-0.0038 (-0.058 to 0.061)	0.0006 (-0.144 to 0.059)	-0.0023 (-0.073 to 0.049)

Statistical analyses

No statistical analyses for this end point

Primary: Platelets (Change from baseline)

End point title	Platelets (Change from baseline)[24]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	-13.1 (-84 to 47)	-6.3 (-65 to 135)	2.7 (-71 to 236)	9.7 (-141 to 329)

Statistical analyses

No statistical analyses for this end point

Primary: Basophils (Change from baseline)

End point title	Basophils (Change from baseline)[25]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.001 (-0.06 to 0.05)	0 (-0.03 to 0.08)	0.003 (-0.11 to 0.11)	0.001 (-0.02 to 0.03)

Statistical analyses

No statistical analyses for this end point

Primary: Eosinophils (Change from baseline)

End point title	Eosinophils (Change from baseline)[26]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.01 (-0.31 to 0.25)	-0.017 (-0.6 to 0.28)	-0.009 (-0.38 to 0.32)	0.04 (-0.15 to 0.44)

Statistical analyses

No statistical analyses for this end point

Primary: Lymphocytes (Change from baseline)

End point title	Lymphocytes (Change from baseline)[27]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	2.116 (0.64 to 19.97)	1.725 (0.58 to 3.97)	2.364 (0.81 to 19.09)	1.502 (0.7 to 3.33)

Statistical analyses

No statistical analyses for this end point

Primary: Monocytes (Change from baseline)

End point title	Monocytes (Change from baseline)[28]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	-0.006 (-0.39 to 0.45)	-0.002 (-0.64 to 1.03)	-0.002 (-0.62 to 0.76)	0.034 (-0.59 to 0.5)

Statistical analyses

No statistical analyses for this end point

Primary: Neutrophils (Change from baseline)

End point title	Neutrophils (Change from baseline)[29]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: 10^9/L				
arithmetic mean (full range (min-max))	0.011 (-2.05 to 5.16)	-0.012 (-3.07 to 2.3)	-0.418 (-5.57 to 2.47)	-0.015 (-9.83 to 3.26)

Statistical analyses

No statistical analyses for this end point

Primary: Urinalysis - pH

End point title	Urinalysis - pH[30]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: N/A				
arithmetic mean (full range (min-max))	-0.1 (-3 to 2)	-0.5 (-3 to 1)	0.1 (-2 to 2)	-0.3 (-3 to 1)

Statistical analyses

No statistical analyses for this end point

Primary: Urinalysis - Specific Gravity

End point title	Urinalysis - Specific Gravity[31]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182. Performed non-fasting at each clinic visit.

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: N/A				
arithmetic mean (full range (min-max))	0.001 (-0.025 to 0.02)	0.0019 (-0.02 to 0.025)	0 (-0.02 to 0.015)	0 (-0.015 to 0.01)

Statistical analyses

No statistical analyses for this end point

Primary: Heart Rate (Change from baseline)

End point title	Heart Rate (Change from baseline)[32]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: beats/min				
arithmetic mean (full range (min-max))	1.5 (-22 to 26)	2.5 (-17 to 27)	-0.6 (-40 to 13)	2.5 (-19 to 19)

Statistical analyses

No statistical analyses for this end point

Primary: QT Duration (Change from baseline)

End point title	QT Duration (Change from baseline)[33]

End point description:

End point type	Primary

End point timeframe:

12-lead electrocardiogram (ECG): Days 28, 56, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: msec				
arithmetic mean (full range (min-max))	-6 (-50 to 52)	-4.9 (-86 to 42)	-1.8 (-40 to 126)	-7.3 (-64 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)[34]

End point description:

End point type	Primary

End point timeframe:

12-lead electrocardiogram (ECG): Days 28, 56, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: msec				
arithmetic mean (full range (min-max))	-1.8 (-12 to 8)	0.5 (-14 to 46)	1.2 (-12 to 14)	-0.7 (-12 to 6)

Statistical analyses

No statistical analyses for this end point

Primary: PR Duration (Change from baseline)

End point title	PR Duration (Change from baseline)[35]

End point description:

End point type	Primary

End point timeframe:

12-lead electrocardiogram (ECG): Days 28, 56, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: msec				
arithmetic mean (full range (min-max))	2 (-22 to 24)	2 (-50 to 44)	0.3 (-28 to 24)	-3 (-30 to 18)

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:

12-lead electrocardiogram (ECG): Days 28, 56, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: msec				
arithmetic mean (full range (min-max))	-2.9 (-37 to 23)	0.7 (-25 to 29)	-4.4 (-30 to 31)	-1.5 (-34 to 58)

Statistical analyses

No statistical analyses for this end point

Primary: Temperature (Change from baseline)

End point title	Temperature (Change from baseline)[37]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: celsius				
arithmetic mean (full range (min-max))	4 (-60 to 62)	6.9 (-2 to 62)	2.3 (-57 to 61)	-0.1 (-2 to 1)

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)[38]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmHg				
arithmetic mean (full range (min-max))	-1 (-25 to 40)	-8.2 (-63 to 30)	-4.8 (-37 to 19)	-2.7 (-46 to 38)

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)[39]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: mmHg				
arithmetic mean (full range (min-max))	-0.7 (-26 to 47)	-1.9 (-22 to 28)	0.7 (-20 to 19)	-3.1 (-22 to 30)

Statistical analyses

No statistical analyses for this end point

Primary: Heart Rate (Change from baseline)

End point title	Heart Rate (Change from baseline)[40]

End point description:

End point type	Primary

End point timeframe:

12-lead electrocardiogram (ECG): Days 28, 56, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: bpm				
arithmetic mean (full range (min-max))	0.8 (-22 to 19)	1.3 (-21 to 26)	-0.7 (-20 to 15)	1.4 (-18 to 17)

Statistical analyses

No statistical analyses for this end point

Primary: Respiratory Rate (Change from baseline)

End point title	Respiratory Rate (Change from baseline)[41]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: breaths/min				
arithmetic mean (full range (min-max))	0.7 (-6 to 8)	-0.1 (-7 to 6)	0.1 (-4 to 6)	-0.1 (-5 to 2)

Statistical analyses

No statistical analyses for this end point

Primary: Weight (Change from baseline)

End point title	Weight (Change from baseline)[42]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: kg				
arithmetic mean (full range (min-max))	8.1 (-11 to 101)	7.3 (-91 to 103)	7.7 (-3 to 107)	-0.7 (-18 to 8)

Statistical analyses

No statistical analyses for this end point

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

End point title	Columbia Suicide Severity Rating Scale (C-SSRS) (Change from baseline)[43]

End point description:

End point type	Primary

End point timeframe:

Days 28, 56, 84, 112, 140, and 182

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	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg	Pbo-EVP-6124, 3 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	106	110	61	59
Units: Subjects wishing to be dead	0	1	0	0

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 ICF is signed through the safety follow-up telephone contact (Day 189 or early termination, as applicable) will be recorded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	EVP-6124, 2 mg

Reporting group description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

Reporting group title	EVP-6124, 3 mg

Reporting group description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

Reporting group title	Pbo-EVP-6124, 2 mg

Reporting group description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

Reporting group title	Pbo-EVP-6124, 3 mg

Reporting group description:

Previously treated with EVP-6124 will receive the same dose during this study as received in the previous study and subjects previously treated with placebo will be randomized to EVP-6124 2 or 3 mg daily (1:1 ratio).

Serious adverse events	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 106 (3.77%)	7 / 110 (6.36%)	4 / 61 (6.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer recurrent			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer recurrent			

subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sick sinus syndrome			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia Alzheimer's type			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric occlusion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			

subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences causally related to treatment / all	0 / 4	0 / 7	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pbo-EVP-6124, 3 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 59 (6.78%)		
number of deaths (all causes)	2		

number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastric cancer recurrent			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Bladder cancer recurrent			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Ovarian cancer			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sick sinus syndrome			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			

subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Dementia Alzheimer's type				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Colitis ulcerative				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Mesenteric occlusion				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal				

disorders			
Asthma			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Dehydration			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	EVP-6124, 2 mg	EVP-6124, 3 mg	Pbo-EVP-6124, 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 106 (39.62%)	42 / 110 (38.18%)	23 / 61 (37.70%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer recurrent			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Gastric cancer recurrent			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Ovarian cancer			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Thyroid neoplasm			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Hypotension			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Oedema peripheral			

subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Asthenia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Fatigue			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Irritability			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Non-cardiac chest pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Rhinorrhoea			
subjects affected / exposed	2 / 106 (1.89%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Asthma			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Confusional state			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Delirium			

subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	2 / 61 (3.28%)
occurrences (all)	42	42	23
Hallucination			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Insomnia			
subjects affected / exposed	2 / 106 (1.89%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Abnormal behaviour			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Anxiety			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Depression			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Depressive symptom			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Hypersexuality			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Panic attack			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Investigations			
Specific gravity urine increased			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Blood pressure decreased			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Blood urine present			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23

Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Eosinophil count increased			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Heart rate irregular			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Protein urine			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Specific gravity urine abnormal			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Weight decreased			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Weight increased			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
White blood cells urine			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	2 / 61 (3.28%)
occurrences (all)	42	42	23
Laceration			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Contusion			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Ankle fracture			

subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Arthropod bite			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Confusion postoperative			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Excoriation			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Femoral neck fracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Procedural pain			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Spinal fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Thoracic vertebral fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Acute myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Angina pectoris			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Bradyarrhythmia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23

Bundle branch block left			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Cardiac failure			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Palpitations			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Sick sinus syndrome			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	2 / 61 (3.28%)
occurrences (all)	42	42	23
Syncope			
subjects affected / exposed	1 / 106 (0.94%)	2 / 110 (1.82%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Cognitive disorder			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Headache			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Altered state of consciousness			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Cerebral haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Dementia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Dementia Alzheimer's type			

subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Migraine			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Neuralgia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Parkinsonism			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Postural reflex impairment			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Presyncope			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Psychomotor skills impaired			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Eosinophilia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Lymphopenia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Neutrophilia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Eye disorders			
Cataract			

subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Conjunctivitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Retinal detachment			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 106 (8.49%)	12 / 110 (10.91%)	11 / 61 (18.03%)
occurrences (all)	42	42	23
Diarrhoea			
subjects affected / exposed	9 / 106 (8.49%)	7 / 110 (6.36%)	4 / 61 (6.56%)
occurrences (all)	42	42	23
Nausea			
subjects affected / exposed	5 / 106 (4.72%)	5 / 110 (4.55%)	4 / 61 (6.56%)
occurrences (all)	42	42	23
Abdominal pain			
subjects affected / exposed	3 / 106 (2.83%)	1 / 110 (0.91%)	3 / 61 (4.92%)
occurrences (all)	42	42	23
Vomiting			
subjects affected / exposed	3 / 106 (2.83%)	2 / 110 (1.82%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Faecal incontinence			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Faeces hard			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Haematochezia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Rectal tenesmus			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23

Toothache			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Colitis ulcerative			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Diverticular perforation			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Dyschezia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Gastrointestinal motility disorder			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Mesenteric occlusion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Oesophagitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Periodontal disease			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Salivary gland mass			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Psoriasis			

subjects affected / exposed	2 / 106 (1.89%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Dermatitis contact			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Pruritus			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Rash pruritic			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Skin lesion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Urinary incontinence			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Enuresis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Glycosuria			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Proteinuria			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Renal colic			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Renal failure			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23

Renal failure acute			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Renal impairment			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Urinary retention			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	3 / 61 (4.92%)
occurrences (all)	42	42	23
Arthralgia			
subjects affected / exposed	3 / 106 (2.83%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Musculoskeletal stiffness			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Arthritis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Costochondritis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Foot deformity			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Osteoarthritis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Pain in extremity			

subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Rotator cuff syndrome			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 106 (1.89%)	2 / 110 (1.82%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Upper respiratory tract infection			
subjects affected / exposed	2 / 106 (1.89%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Nasopharyngitis			
subjects affected / exposed	0 / 106 (0.00%)	3 / 110 (2.73%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Bacteriuria			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Cellulitis			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Diverticulitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Herpes zoster			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Pharyngitis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Pneumonia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23

Sepsis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Staphylococcal infection			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Tonsillitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Wound sepsis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 106 (0.94%)	1 / 110 (0.91%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Hypokalaemia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 110 (0.91%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Dehydration			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Gout			
subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23
Hypernatraemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Hyponatraemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 110 (0.00%)	1 / 61 (1.64%)
occurrences (all)	42	42	23
Type 2 diabetes mellitus			

subjects affected / exposed	1 / 106 (0.94%)	0 / 110 (0.00%)	0 / 61 (0.00%)
occurrences (all)	42	42	23

Non-serious adverse events	Pbo-EVP-6124, 3 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 59 (50.85%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer recurrent			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Gastric cancer recurrent			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Ovarian cancer			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Thyroid neoplasm			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Hypotension			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
General disorders and administration site conditions			
Gait disturbance			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Oedema peripheral			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Asthenia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		

Fatigue subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Irritability subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Pain subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 30		
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Asthma subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Confusional state subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Delirium subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Hallucination subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Insomnia			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Abnormal behaviour			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Anxiety			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Depression			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Depressive symptom			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Hypersexuality			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Panic attack			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Investigations			
Specific gravity urine increased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Blood pressure decreased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Blood urine present			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Eosinophil count increased			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		

Heart rate irregular			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Protein urine			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Specific gravity urine abnormal			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Weight decreased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Weight increased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
White blood cells urine			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	30		
Laceration			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Contusion			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Ankle fracture			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Arthropod bite			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Confusion postoperative			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Excoriation			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Femoral neck fracture			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Procedural pain			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Spinal fracture			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Thoracic vertebral fracture			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Acute myocardial infarction			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Angina pectoris			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Bradyarrhythmia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Bundle branch block left			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Cardiac failure			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		

Palpitations			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Sick sinus syndrome			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Syncope			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Cognitive disorder			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Headache			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Altered state of consciousness			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Cerebral haemorrhage			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Dementia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Dementia Alzheimer's type			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Migraine			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Neuralgia			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Parkinsonism			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Postural reflex impairment			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Presyncope			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Psychomotor skills impaired			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Eosinophilia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Lymphopenia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Neutrophilia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Conjunctivitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Retinal detachment			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	9 / 59 (15.25%)		
occurrences (all)	30		
Diarrhoea			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	30		
Nausea			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Abdominal pain			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	30		
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Faecal incontinence			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Faeces hard			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Haematochezia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Rectal tenesmus			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Toothache			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Colitis ulcerative			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		

Diverticular perforation subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Dyschezia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Gastrointestinal motility disorder subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Haemorrhoidal haemorrhage subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Mesenteric occlusion subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 30		
Oesophagitis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 30		
Periodontal disease subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Salivary gland mass subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 30		
Psoriasis subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Pruritus			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Rash pruritic			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Skin lesion			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	30		
Urinary incontinence			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Enuresis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Glycosuria			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Proteinuria			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Renal colic			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Renal failure			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Renal failure acute			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Renal impairment			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		

Urinary retention			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Arthralgia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Arthritis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Costochondritis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Foot deformity			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Osteoarthritis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Pain in extremity			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Rotator cuff syndrome			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Temporomandibular joint syndrome			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Upper respiratory tract infection			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	30		
Nasopharyngitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Bacteriuria			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Cellulitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Diverticulitis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Herpes zoster			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Pharyngitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Pneumonia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		
Sepsis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	30		
Staphylococcal infection			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	30		

Tonsillitis subjects affected / exposed occurrences (all)	1 / 59 (1.69%) 30		
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Wound sepsis subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Dehydration subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Gout subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Hypernatraemia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 59 (0.00%) 30		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
23 December 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