Clinical trial results:
A Phase III, multi-center, randomized, 24 week, double-blind, parallel-group, placebo-controlled study to evaluate efficacy and safety of RO4917838 in stable patients with persistent, predominant negative symptoms of schizophrenia treated with antipsychotics followed by a 28 week double-blind treatment period.

Summary

EudraCT number	2010-020467-21
Trial protocol	ES DE LT LV SK NL
Global end of trial date	09 June 2014

Results information

Result version number	v1 (current)
This version publication date	22 April 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	WN25309

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01192906
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG , 41 61 6878333, global.trial_information@roche.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	09 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 June 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives of this study are :

• To evaluate the efficacy of 24 weeks treatment with bitopertin in the Positive and Negative Syndrome Scale (PANSS) Negative Symptom Factor Score (NSFS) in patients with persistent, predominant negative symptoms of schizophrenia treated with antipsychotics
• To evaluate the safety and tolerability of 24 weeks of treatment with bitopertin in patients with persistent, predominant negative symptoms of schizophrenia treated with antipsychotics

Protection of trial subjects:

Signed written informed consent after the scope and nature of the investigation had been explained to them before screening evaluations and willingness to comply with the study restrictions.

Background therapy:

This is an add-on therapy to selected typical and atypical antipsychotics treatment.

Evidence for comparator: -

Actual start date of recruitment	27 October 2010
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	Netherlands: 3
Country: Number of subjects enrolled	Poland: 85
Country: Number of subjects enrolled	Slovakia: 10
Country: Number of subjects enrolled	Spain: 38
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Latvia: 12
Country: Number of subjects enrolled	Lithuania: 40
Country: Number of subjects enrolled	Turkey: 25
Country: Number of subjects enrolled	Ukraine: 58
Country: Number of subjects enrolled	Canada: 51
Country: Number of subjects enrolled	United States: 73
Country: Number of subjects enrolled	Brazil: 155
Country: Number of subjects enrolled	Chile: 26
Country: Number of subjects enrolled	Taiwan: 27
Worldwide total number of subjects	621
EEA total number of subjects	206

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)	609
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study enrolled outpatients aged 18 and above with a Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) diagnosis of schizophrenia with persistent, predominant negative symptoms and on current stable antipsychotic treatment.

Period 1

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

Blinding implementation details:

Subjects and investigators remained blinded to the treatment they received throughout the study. In the Follow-up, subjects did not receive drug but they remained blinded to the treatment they had received previously.

Arms

Are arms mutually exclusive?	No
Arm title	Placebo - Treatment Period 1

Arm description:

Participants received placebo orally once daily for 24 weeks

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

Dosage and administration details:

Matching dose of 5 or 10 mg tablet taken once daily in the morning, with or without food

Arm title	Bitopertin 5 mg - Treatment Period 1

Arm description:

Participants received bitopertin 5 mg orally once daily for 24 weeks

Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg taken orally once daily in the morning, with or without food

Arm title	Bitopertin 10 mg - Treatment Period 1

Arm description:

Participants received bitopertin 10 mg orally once daily for 24 weeks

Arm type	Experimental

Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg taken orally once daily in the morning, with or without food

Arm title	Placebo - Treatment Period 2

Arm description:

Participants received placebo orally once daily for 28 weeks

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

Dosage and administration details:

Matching dose of 5 or 10 mg tablet taken once daily in the morning, with or without food

Arm title	Bitopertin 5 mg - Treatment Period 2

Arm description:

Participants received bitopertin 5 mg orally once daily for 28 weeks

Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg taken orally once daily in the morning, with or without food

Arm title	Bitopertin 10 mg - Treatment Period 2

Arm description:

Participants received bitopertin 10 mg orally once daily for 28 weeks

Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg taken orally once daily in the morning, with or without food

Arm title	Placebo - Washout Period

Arm description:

Participants received placebo orally once daily for 4 weeks

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

Dosage and administration details: Matching dose of 5 or 10 mg tablet taken once daily in the morning, with or without food	

Arm title	Bitopertin 5 mg - Washout Period
Arm description: Participants received bitopertin 5 mg orally once daily for 4 weeks	
Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 5 mg taken orally once daily in the morning, with or without food	
Arm title	Bitopertin 5 mg to placebo - Washout Period
Arm description: Participants received placebo orally once daily for 4 weeks	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Matching dose of 5 or 10 mg tablet taken once daily in the morning, with or without food	
Arm title	Bitopertin 10 mg - Washout Period
Arm description: Participants received bitopertin 10 mg orally once daily for 4 weeks	
Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 10 mg taken orally once daily in the morning, with or without food	
Arm title	Bitopertin 10 mg to placebo - Washout Period
Arm description: Participants received placebo orally once daily for 4 weeks	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Matching dose of 10 mg tablet taken once daily in the morning, with or without food	
Arm title	Placebo to Bitopertin 10 mg - Long-Term Extension

Arm description:	
Participants received bitopertin 10 mg orally once daily for up to 3 years	
Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 mg taken orally once daily in the morning, with or without food	
Arm title	Bitopertin 5 mg to Bitopertin 10 mg - Long-Term Extension
Arm description:	
Participants received bitopertin 10 mg orally once daily for up to 3 years	
Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 mg taken orally once daily in the morning, with or without food	
Arm title	Bitopertin 10 mg - Long-Term Extension
Arm description:	
Participants received bitopertin 10 mg orally once daily for up to 3 years	
Arm type	Experimental
Investigational medicinal product name	Bitopertin
Investigational medicinal product code	RO4917838
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 mg taken orally once daily in the morning, with or without food	
Arm title	Placebo - Safety Follow-Up Period
Arm description:	
Participants were not treated during the follow-up period	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Bitopertin 5 mg - Safety Follow-Up Period
Arm description:	
Participants were not treated during the follow-up period	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Bitopertin 10 mg - Safety Follow-Up Period
Arm description:	
Participants were not treated during the follow-up period	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Placebo - Treatment Period 1	Bitopertin 5 mg - Treatment Period 1	Bitopertin 10 mg - Treatment Period 1
Started	209	211	201
Completed	181	185	166
Not completed	28	26	35
Adverse event, non-fatal	20	12	10
Protocol violation	-	2	2
Death	-	-	-
Non-compliance	2	1	7
Administrative/Other	-	3	1
Lost to follow-up	2	-	1
Withdrawal by subject	3	6	12
Lack of efficacy	1	2	2

Number of subjects in period 1	Placebo - Treatment Period 2	Bitopertin 5 mg - Treatment Period 2	Bitopertin 10 mg - Treatment Period 2
Started	178	181	165
Completed	134	136	127
Not completed	44	45	38
Adverse event, non-fatal	6	7	5
Protocol violation	1	1	-
Death	1	-	-
Non-compliance	4	-	2
Administrative/Other	28	28	23
Lost to follow-up	1	1	5
Withdrawal by subject	3	6	1
Lack of efficacy	-	2	2

Number of subjects in period 1	Placebo - Washout Period	Bitopertin 5 mg - Washout Period	Bitopertin 5 mg to placebo - Washout Period
Started	133	66	66
Completed	129	62	66
Not completed	4	4	0
Adverse event, non-fatal	1	1	-
Protocol violation	-	-	-
Death	-	-	-
Non-compliance	-	1	-
Administrative/Other	2	2	-
Lost to follow-up	-	-	-
Withdrawal by subject	-	-	-
Lack of efficacy	1	-	-

Number of subjects in period 1	Bitopertin 10 mg - Washout Period	Bitopertin 10 mg to placebo - Washout Period	Placebo to Bitopertin 10 mg - Long-Term Extension
Started	63	63	121
Completed	61	61	0
Not completed	2	2	121
Adverse event, non-fatal	-	1	1
Protocol violation	-	-	1
Death	-	-	-
Non-compliance	-	-	2
Administrative/Other	2	-	112
Lost to follow-up	-	-	-
Withdrawal by subject	-	1	2
Lack of efficacy	-	-	3

Number of subjects in period 1	Bitopertin 5 mg to Bitopertin 10 mg - Long-Term Extension	Bitopertin 10 mg - Long-Term Extension	Placebo - Safety Follow-Up Period
Started	116	114	88
Completed	0	0	53
Not completed	116	114	35
Adverse event, non-fatal	4	7	5
Protocol violation	-	-	-
Death	-	-	2
Non-compliance	1	1	-
Administrative/Other	100	100	5
Lost to follow-up	1	-	8
Withdrawal by subject	8	4	15
Lack of efficacy	2	2	-

Number of subjects in period 1	Bitopertin 5 mg - Safety Follow-Up Period	Bitopertin 10 mg - Safety Follow-Up Period
Started	95	438
Completed	60	370
Not completed	35	68
Adverse event, non-fatal	4	4
Protocol violation	-	-
Death	1	-
Non-compliance	-	-
Administrative/Other	14	13
Lost to follow-up	7	22
Withdrawal by subject	9	29
Lack of efficacy	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall period (overall period)

Reporting group description: -

Reporting group values	Overall period (overall period)	Total	
Number of subjects	621	621	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 41.4 ± 11.7	 -	
Gender categorical Units: Subjects			
Female	191	191	
Male	430	430	

End points

End points reporting groups

Reporting group title	Placebo - Treatment Period 1
Reporting group description:	
Participants received placebo orally once daily for 24 weeks	
Reporting group title	Bitopertin 5 mg - Treatment Period 1
Reporting group description:	
Participants received bitopertin 5 mg orally once daily for 24 weeks	
Reporting group title	Bitopertin 10 mg - Treatment Period 1
Reporting group description:	
Participants received bitopertin 10 mg orally once daily for 24 weeks	
Reporting group title	Placebo - Treatment Period 2
Reporting group description:	
Participants received placebo orally once daily for 28 weeks	
Reporting group title	Bitopertin 5 mg - Treatment Period 2
Reporting group description:	
Participants received bitopertin 5 mg orally once daily for 28 weeks	
Reporting group title	Bitopertin 10 mg - Treatment Period 2
Reporting group description:	
Participants received bitopertin 10 mg orally once daily for 28 weeks	
Reporting group title	Placebo - Washout Period
Reporting group description:	
Participants received placebo orally once daily for 4 weeks	
Reporting group title	Bitopertin 5 mg - Washout Period
Reporting group description:	
Participants received bitopertin 5 mg orally once daily for 4 weeks	
Reporting group title	Bitopertin 5 mg to placebo - Washout Period
Reporting group description:	
Participants received placebo orally once daily for 4 weeks	
Reporting group title	Bitopertin 10 mg - Washout Period
Reporting group description:	
Participants received bitopertin 10 mg orally once daily for 4 weeks	
Reporting group title	Bitopertin 10 mg to placebo - Washout Period
Reporting group description:	
Participants received placebo orally once daily for 4 weeks	
Reporting group title	Placebo to Bitopertin 10 mg - Long-Term Extension
Reporting group description:	
Participants received bitopertin 10 mg orally once daily for up to 3 years	
Reporting group title	Bitopertin 5 mg to Bitopertin 10 mg - Long-Term Extension
Reporting group description:	
Participants received bitopertin 10 mg orally once daily for up to 3 years	
Reporting group title	Bitopertin 10 mg - Long-Term Extension
Reporting group description:	
Participants received bitopertin 10 mg orally once daily for up to 3 years	
Reporting group title	Placebo - Safety Follow-Up Period
Reporting group description:	
Participants were not treated during the follow-up period	
Reporting group title	Bitopertin 5 mg - Safety Follow-Up Period

Reporting group description:

Participants were not treated during the follow-up period

Reporting group title	Bitopertin 10 mg - Safety Follow-Up Period

Reporting group description:

Participants were not treated during the follow-up period

Primary: Mean Change from Baseline in the PANSS Negative Symptom Factor Score at Week 24

End point title	Mean Change from Baseline in the PANSS Negative Symptom Factor Score at Week 24[1]

End point description:

The PANSS is a 30-item scale designed to capture the degree of severity for many symptoms in schizophrenia. Each of the 30 items is rated on a 7-point scale, from 1 to 7 (absence of to extreme psychopathology). The negative symptom subscale is composed of 7 items: Blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, stereotyped thinking. The score on the negative symptom subscale can range from 0 to 49, with a higher score indicating more negative symptom psychopathology. A negative change score indicates improvement.

Intent-to-treat population: All randomized participants who received at least 1 dose of double-blind study drug and had at least one post-baseline assessment of the primary efficacy variable.

For all analyses of PANSS data, the scores were transformed into 0-6 points to express "absent" as 0.

End point type	Primary

End point timeframe:

Baseline to Week 24

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This final abbreviated Clinical Study Report (CSR) presents the data at Week 24 for the key primary endpoint, Positive and Negative Syndrome Scale (PANSS) Negative Symptom Factor Score (NSFS), and the key secondary endpoint, Personal and Social Performance (PSP) total score. The study did not meet its primary endpoint.

End point values	Placebo - Treatment Period 1	Bitopertin 5 mg - Treatment Period 1	Bitopertin 10 mg - Treatment Period 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	205	197	
Units: number				
arithmetic mean (standard error)	-5.25 (± 0.365)	-5.53 (± 0.33)	-5.87 (± 0.366)	

Statistical analyses

Statistical analysis title	Placebo vs. Bitopertin 5 mg - PANSS at Week 24

Statistical analysis description:

Primary analysis population was ITT population. For all analyses of PANSS data, scores were transformed into 0-6 points to express "absent" as 0. Mean change from baseline in PANSS NSFS and PSP at Week 24 was analyzed using an MMRM incorporating data collected up to 24 weeks of treatment to assess all data collected over time with consideration of the variance−covariance matrix of repeated measures. No imputation for missing data were used in primary analyses.

Comparison groups	Placebo - Treatment Period 1 v Bitopertin 5 mg - Treatment Period 1

Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4742
Method	Mixed Models Repeated Measures Analysis

Statistical analysis title	Placebo vs. Bitopertin 10 mg - PANSS at Week 24

Statistical analysis description:

Primary analysis population was ITT population. For all analyses of PANSS data, scores were transformed into 0-6 points to express "absent" as 0. Mean change from baseline in PANSS NSFS and PSP at Week 24 was analyzed using an MMRM incorporating data collected up to 24 weeks of treatment to assess all data collected over time with consideration of the variance−covariance matrix of repeated measures. No imputation for missing data was used in primary analyses.

Comparison groups	Placebo - Treatment Period 1 v Bitopertin 10 mg - Treatment Period 1
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0989
Method	Mixed Models Repeated Measures Analysis

Secondary: Mean Change from Baseline in the Personal and Social Performance (PSP) Total Score at Week 24

End point title	Mean Change from Baseline in the Personal and Social Performance (PSP) Total Score at Week 24[2]

End point description:

The PSP is a clinician-rated 100-point rating scale subdivided into 10 equal intervals, enabling the determination of small changes in levels of functioning. The ratings are based upon assessment of the patient's functioning in 4 areas: 1) Socially useful activities; 2) personal and social relationships; 3) self-care; and 4) disturbing and aggressive behaviors. Each of the 4 areas is rated in 6 degrees of severity (absent, mild, manifest, marked, severe, very severe). Higher scores represent better personal and social functioning, with ratings from 91-100 referring to more than adequate functioning, while scores under 30 refer to poor functioning that intensive supervision is required. A higher score indicates better functioning. A positive change score indicates improvement.

Intent-to-treat population: All randomized participants who received at least 1 dose of double-blind study drug and had at least one post-baseline assessment of the primary efficacy variable.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This final abbreviated Clinical Study Report (CSR) presents the data at Week 24 for the key primary endpoint, Positive and Negative Syndrome Scale (PANSS) Negative Symptom Factor Score (NSFS), and the key secondary endpoint, Personal and Social Performance (PSP) total score. The study did not meet its primary endpoint.

End point values	Placebo - Treatment Period 1	Bitopertin 5 mg - Treatment Period 1	Bitopertin 10 mg - Treatment Period 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	203	205	197	
Units: number				
arithmetic mean (standard error)	8.64 (± 0.752)	6.64 (± 0.712)	8.24 (± 0.733)	

Statistical analyses

Statistical analysis title	Placebo vs. Bitopertin 5 mg - PSP at Week 24

Statistical analysis description:

Primary analysis population was ITT population. For all analyses of PANSS data, scores were transformed into 0-6 points to express "absent" as 0. Mean change from baseline in PSP at Week 24 was analyzed using an MMRM incorporating data collected up to 24 weeks of treatment to assess all data collected over time with consideration of the variance−covariance matrix of repeated measures. No imputation for missing data were used in primary analyses.

Comparison groups	Placebo - Treatment Period 1 v Bitopertin 5 mg - Treatment Period 1
Number of subjects included in analysis	408
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1288
Method	Mixed Models Repeated Measures Analysis

Statistical analysis title	Placebo vs. Bitopertin 10 mg - PSP at Week 24

Statistical analysis description:

Primary analysis population was ITT population. For all analyses of PANSS data, scores were transformed into 0-6 points to express "absent" as 0. Mean change from baseline in PSP at Week 24 was analyzed using an MMRM incorporating data collected up to 24 weeks of treatment to assess all data collected over time with consideration of the variance−covariance matrix of repeated measures. No imputation for missing data were used in primary analyses.

Comparison groups	Placebo - Treatment Period 1 v Bitopertin 10 mg - Treatment Period 1
Number of subjects included in analysis	400
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6471
Method	Mixed Models Repeated Measures Analysis

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From randomization to the end of the study (up to 4 years, 2 months).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	Placebo through Week 52
Reporting group description: -	
Reporting group title	Bitopertin 5 mg through Week 52
Reporting group description: -	
Reporting group title	Bitopertin 10 mg through Week 52
Reporting group description: -	
Reporting group title	Placebo during washout period
Reporting group description: -	
Reporting group title	Bitopertin 5 mg during washout period
Reporting group description: -	
Reporting group title	Bitopertin 5 mg to Placebo during washout period
Reporting group description: -	
Reporting group title	Bitopertin 10 mg during washout period
Reporting group description: -	
Reporting group title	Bitopertin 10 mg to placebo during washout period
Reporting group description: -	
Reporting group title	Placebo to bitopertin 10 mg during long-term extension
Reporting group description: -	
Reporting group title	Bitopertin 5 mg to bitopertin 10 mg during long-term extension
Reporting group description: -	
Reporting group title	Bitopertin 10 mg during long-term extension
Reporting group description: -	
Reporting group title	Placebo during follow-up period
Reporting group description: -	
Reporting group title	Bitopertin 5 mg during follow-up period
Reporting group description: -	
Reporting group title	Bitopertin 10 mg during follow-up period
Reporting group description: -	

Serious adverse events	Placebo through Week 52	Bitopertin 5 mg through Week 52	Bitopertin 10 mg through Week 52
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 209 (7.18%)	11 / 211 (5.21%)	16 / 201 (7.96%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Mass			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Social circumstances			
Victim of homicide			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	3 / 201 (1.49%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	5 / 209 (2.39%)	3 / 211 (1.42%)	3 / 201 (1.49%)
occurrences causally related to treatment / all	2 / 5	0 / 3	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety disorder			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Thinking abnormal			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Wound			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbon monoxide poisoning			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Dermoid Cyst			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Altered state of consciousness			

subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw cyst			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	2 / 201 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	1 / 201 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ehinococciasis			

subjects affected / exposed	1 / 209 (0.48%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 209 (0.00%)	1 / 211 (0.47%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 209 (0.00%)	0 / 211 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo during washout period	Bitopertin 5 mg during washout period	Bitopertin 5 mg to Placebo during washout period
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 133 (0.75%)	0 / 66 (0.00%)	2 / 66 (3.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			

subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Mass			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Victim of homicide			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 133 (0.75%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety disorder			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thinking abnormal			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			

subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbon monoxide poisoning			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			

subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Dermoid Cyst			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw cyst			

subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ehinococciasis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			

subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	1 / 66 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Bitopertin 10 mg during washout period	Bitopertin 10 mg to placebo during washout period	Placebo to bitopertin 10 mg during long-term extension
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	1 / 63 (1.59%)	2 / 121 (1.65%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	1 / 121 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Mass			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	1 / 121 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			

subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Victim of homicide			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	0 / 63 (0.00%)	1 / 63 (1.59%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			

subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety disorder			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thinking abnormal			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			

subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	1 / 121 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbon monoxide poisoning			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Dermoid Cyst			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiomyopathy			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			

subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw cyst			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			

subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ehinococciasis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	1 / 121 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Bitopertin 5 mg to bitopertin 10 mg during long-term extension	Bitopertin 10 mg during long-term extension	Placebo during follow-up period
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 116 (2.59%)	5 / 114 (4.39%)	5 / 88 (5.68%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	1 / 116 (0.86%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Mass			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Victim of homicide			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 116 (0.86%)	1 / 114 (0.88%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Schizophrenia			
subjects affected / exposed	0 / 116 (0.00%)	2 / 114 (1.75%)	3 / 88 (3.41%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety disorder			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Thinking abnormal			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal Ideation			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 116 (0.86%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 116 (0.00%)	1 / 114 (0.88%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	0 / 116 (0.00%)	1 / 114 (0.88%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Wound			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carbon monoxide poisoning			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Dermoid Cyst			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Altered state of consciousness			

subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw cyst			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ehinococciasis			

subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Bitopertin 5 mg during follow-up period	Bitopertin 10 mg during follow-up period	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 95 (4.21%)	9 / 438 (2.05%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign ovarian tumour			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			

subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 95 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Mass			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Victim of homicide			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 95 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 95 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 95 (1.05%)	2 / 438 (0.46%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	2 / 95 (2.11%)	3 / 438 (0.68%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol abuse			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thinking abnormal			
subjects affected / exposed	0 / 95 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			

subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			

subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Dermoid Cyst			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 95 (1.05%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw cyst			

subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 438 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ehinococciasis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 95 (2.11%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			

subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo through Week 52	Bitopertin 5 mg through Week 52	Bitopertin 10 mg through Week 52
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 209 (73.21%)	138 / 211 (65.40%)	122 / 201 (60.70%)
Investigations			
Weight increased			
subjects affected / exposed	12 / 209 (5.74%)	9 / 211 (4.27%)	8 / 201 (3.98%)
occurrences (all)	14	10	10
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 209 (10.53%)	18 / 211 (8.53%)	13 / 201 (6.47%)
occurrences (all)	32	39	24
Somnolence			
subjects affected / exposed	11 / 209 (5.26%)	9 / 211 (4.27%)	10 / 201 (4.98%)
occurrences (all)	11	10	11
Dizziness			
subjects affected / exposed	11 / 209 (5.26%)	5 / 211 (2.37%)	8 / 201 (3.98%)
occurrences (all)	11	6	8
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	11 / 209 (5.26%)	11 / 211 (5.21%)	3 / 201 (1.49%)
occurrences (all)	13	12	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	10 / 209 (4.78%)	11 / 211 (5.21%)	10 / 201 (4.98%)
occurrences (all)	13	18	16
Insomnia			
subjects affected / exposed	11 / 209 (5.26%)	10 / 211 (4.74%)	6 / 201 (2.99%)
occurrences (all)	14	12	6
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	20 / 209 (9.57%)	17 / 211 (8.06%)	13 / 201 (6.47%)
occurrences (all)	23	19	19

Non-serious adverse events	Placebo during washout period	Bitopertin 5 mg during washout period	Bitopertin 5 mg to Placebo during washout period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
Investigations			
Weight increased			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 133 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	0	0	0

	Bitopertin 10 mg	Bitopertin 10 mg to	Placebo to bitopertin

Non-serious adverse events	during washout period	placebo during washout period	10 mg during long-term extension
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	47 / 121 (38.84%)
Investigations			
Weight increased			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	7 / 121 (5.79%)
occurrences (all)	0	0	7
Somnolence			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	0 / 121 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 63 (0.00%)	0 / 63 (0.00%)	7 / 121 (5.79%)
occurrences (all)	0	0	8

Non-serious adverse events	Bitopertin 5 mg to bitopertin 10 mg during long-term extension	Bitopertin 10 mg during long-term extension	Placebo during follow-up period
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 116 (42.24%)	40 / 114 (35.09%)	0 / 88 (0.00%)

Investigations			
Weight increased			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 116 (3.45%)	3 / 114 (2.63%)	0 / 88 (0.00%)
occurrences (all)	4	3	0
Somnolence			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 116 (2.59%)	6 / 114 (5.26%)	0 / 88 (0.00%)
occurrences (all)	3	6	0
Insomnia			
subjects affected / exposed	0 / 116 (0.00%)	0 / 114 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 116 (4.31%)	2 / 114 (1.75%)	0 / 88 (0.00%)
occurrences (all)	6	3	0

Non-serious adverse events	Bitopertin 5 mg during follow-up period	Bitopertin 10 mg during follow-up period	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
Investigations			
Weight increased			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 95 (0.00%)	0 / 438 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2010	Version A: Staggered start approach was removed, increased safety monitoring per Special Protocol Assessment (SPA) feedback, various sections of the protocol were clarified.
15 September 2010	Version B: Clarification for dosing during Long-term Extension Period, addition of criteria to exclude patients who may have pre-existing potentially clinically significant hepatic dysfunction, addition of creatinine phosphokinase (was not listed in the standard laboratory list by error), clarification on procedures for Roche Clinical Repository (RCR), Work Readiness Questionnaire included as exploratory efficacy endpoint, corrected errors in the schedule of assessments and procedures.
21 April 2011	Version C: Inclusion of FDA's requirements for analysis of iron inclusion bodies, changes to safety reporting of adverse events, clarification of screening/rescreening procedures, minor changes to study design (permission of psychosocial/rehabilitative therapies, addition of questionnaire to ensure exclusion of treatment resistant patients, minor changes to schedule of assessments and procedures), description of the VERIFIED™ system (Video Enhancement of Rater Interviewing for Independent Evaluation of Data) part of the rater quality assurance program.
30 May 2012	Version D: Addition of biomarker defined subpopulations as a secondary objective, clarification of hemoglobin exclusion criterion, additional follow-up for treatment withdrawal and at Week 52 initiation of washout, and clarification of withdrawal process, clarification of timing of screening and prospective stabilization period
25 January 2013	Version E: Inclusion of futility analysis, addition of biomarker defined subpopulation analysis as a key secondary objective, change in Data Safety Monitoring Board (DSMB) to Independent Data Monitoring Committee (IDMC), modification of body mass index (BMI) criterion, changes in serious adverse event (SAE) reporting timeframe, and other changes (addition of electrocardiogram [ECG] at Week 58, clarification of safety population, clarification of length of study, removal of analysis of the per protocol population)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 November 2013	While bitopertin was generally well tolerated and its overall safety profile was similar to that seen in the previously reported phase II trial (NN20372), the study failed to meet its primary endpoint at week 24 (treatment period 1). These results do not support continuation of patients' treatment (treatment period 2, until week 56 and long-term extension), and the decision was made to terminate this study early.	-

Notes:

Limitations and caveats

None reported