Clinical trial results:
A multicenter, Double-blind 58 week Rollover Study to assess the Safety and Tolerability of BMS-820836 in Patients with Treatment Resistant Major Depression.

Summary

EudraCT number	2010-024371-12
Trial protocol	ES SE FI AT GB IT
Global end of trial date	22 October 2013

Results information

Result version number	v1 (current)
This version publication date	16 June 2016
First version publication date	16 June 2016

Trial information

Trial identification

Sponsor protocol code	CN162-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01361555
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Bristol-Myers Squibb International Corporation Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	22 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study was to compare the long term effect of three target doses of BMS-820836 (0.5, 1, and 2 mg/day) through 54 weeks of follow-up in the change from randomization baseline in mean seated blood pressure in subjects with treatment-resistant depression.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Finland: 28
Country: Number of subjects enrolled	France: 71
Country: Number of subjects enrolled	United States: 553
Country: Number of subjects enrolled	South Africa: 30
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Argentina: 33
Country: Number of subjects enrolled	India: 21
Country: Number of subjects enrolled	Puerto Rico: 30
Worldwide total number of subjects	788
EEA total number of subjects	113

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)	775
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 119 centers in 12 countries.

Pre-assignment

Screening details:

A total of 788 subjects were enrolled into the study. Of the 788 subjects enrolled, 321 subjects rolled over from Study CN162-006 (EudraCT Number - 2010-022841-93) and 467 rolled over from Study CN162-007 (EudraCT Number - 2011-000778-71).

Period 1

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

Blinding implementation details:

Subject, Investigator, Assessor and Sponsor remained blinded during the study. Unblinding was performed only in the event of a medical emergency or pregnancy of the individual subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	BMS-820836 0.5 mg

Arm description:

Subjects received BMS-820836 0.5 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.

Arm type	Experimental
Investigational medicinal product name	Liafensine
Investigational medicinal product code	BMS-820836
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

BMS-820836 0.5-mg tablet was administered orally once daily for 54 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 Placebo tablet matching to BMS-820836 0.5 mg and 1 Placebo tablet matching BMS-820836 1 mg were administered once daily for 54 weeks.

Arm title	BMS-820836 1 mg

Arm description:

Subjects received BMS-820836 1 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.

Arm type	Experimental

Investigational medicinal product name	Liafensine
Investigational medicinal product code	BMS--820836
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 BMS-820836 0.5-mg tablets were administered orally once daily for 54 weeks.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 Placebo tablet matching to BMS-820836 1 mg was administered once daily for 54 weeks.

Arm title	BMS-820836 2 mg

Arm description:

Subjects received BMS-820836 2 mg tablets once daily for 54 weeks.

Arm type	Experimental
Investigational medicinal product name	Liafensine
Investigational medicinal product code	BMS-820836
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 BMS-820836 1-mg tablet and 2 BMS-820836 0.5 mg tablets were administered orally once daily for 54 weeks.

Number of subjects in period 1	BMS-820836 0.5 mg	BMS-820836 1 mg	BMS-820836 2 mg
Started	226	265	297
Completed	66	75	84
Not completed	160	190	213
Consent withdrawn by subject	16	15	21
Poor/Non compliance	2	6	8
Adverse event, non-fatal	15	14	25
Subject request to discontinue study treatment	8	17	15
Pregnancy	2	1	2
other	6	5	6
Lost to follow-up	20	14	22
Subject no longer meets study criteria	6	5	8
Administrative reason by sponsor	57	85	79
Lack of efficacy	28	28	27

Baseline characteristics

Reporting groups	
Reporting group title	BMS-820836 0.5 mg
Reporting group description:	
Subjects received BMS-820836 0.5 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.	
Reporting group title	BMS-820836 1 mg
Reporting group description:	
Subjects received BMS-820836 1 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.	
Reporting group title	BMS-820836 2 mg
Reporting group description:	
Subjects received BMS-820836 2 mg tablets once daily for 54 weeks.	

Reporting group values	BMS-820836 0.5 mg	BMS-820836 1 mg	BMS-820836 2 mg
Number of subjects	226	265	297
Age categorical Units: Subjects			
<=50 years	140	156	169
>50 years	86	109	128
Age continuous Units: years			
arithmetic mean	45.71	46.48	46.65
standard deviation	± 11.216	± 11.122	± 11.03
Gender categorical Units: Subjects			
Female	161	177	212
Male	65	88	85

Reporting group values	Total		
Number of subjects	788		
Age categorical Units: Subjects			
<=50 years	465		
>50 years	323		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	550		
Male	238		

End points

End points reporting groups

Reporting group title	BMS-820836 0.5 mg
Reporting group description:	
Subjects received BMS-820836 0.5 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.	
Reporting group title	BMS-820836 1 mg
Reporting group description:	
Subjects received BMS-820836 1 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.	
Reporting group title	BMS-820836 2 mg
Reporting group description:	
Subjects received BMS-820836 2 mg tablets once daily for 54 weeks.	

Primary: Change From Baseline through 54 Weeks in Mean of Seated Systolic and Diastolic Blood Pressure

End point title	Change From Baseline through 54 Weeks in Mean of Seated Systolic and Diastolic Blood Pressure[1]
End point description:	
Blood pressure in seated position was measured using a blood pressure monitor. The subject was first rested for at least 10 minutes in the seated position. Seated blood pressure was determined from the mean of 3 replicated measurements obtained at 2 minutes apart. Mean seated BP was calculated using the following formula for seated mean arterial pressure (MAP): SeatedMAP = (2*SeDBP + SeSBP)/3. The analysis was performed in all subjects who received at least 1 dose of BMS-820836 during the study. Missing data were not imputed. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.	
End point type	Primary
End point timeframe:	
Baseline, Week 12, Week 24, Week 36, Week 48, Week 54	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the study was terminated, all data were summarized descriptively, and no statistical comparisons were performed across dose groups.

End point values	BMS-820836 0.5 mg	BMS-820836 1 mg	BMS-820836 2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	226	265	297	
Units: mmHg				
arithmetic mean (standard deviation)				
Baseline (n=225, 263, 295)	90.37 (± 9.555)	93.06 (± 10.228)	91.55 (± 9.905)	
Change at Week 12 (n=178, 218, 247)	0.15 (± 8.204)	0.96 (± 7.08)	1.51 (± 8.288)	
Change at Week 24 (n=149, 183, 195)	0.59 (± 9.532)	0.97 (± 8.016)	1.14 (± 9.35)	
Change at Week 36 (n=101, 137, 146)	0.81 (± 9.185)	1.2 (± 8.525)	1.56 (± 9.377)	
Change at Week 48 (n=71, 92, 103)	2.64 (± 10.528)	0.44 (± 8.482)	1.57 (± 8.517)	
Change at Week 54 (n=61, 66, 79)	0.96 (± 7.6)	2.93 (± 8.808)	2.56 (± 9.418)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs) and Discontinuation Due to Adverse Events

End point title	Number of Subjects With Adverse Events (AEs), Serious Adverse Events (SAEs) and Discontinuation Due to Adverse Events

End point description:

An AE is any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. An AE can therefore be any unfavorable and unintended sign (example, a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death, initial or prolonged inpatient hospitalization, life-threatening experience (immediate risk of dying), persistent or significant disability/incapacity, or a congenital anomaly, or a medically important event. A treatment-emergent adverse event is defined as an adverse event with an onset that occurs after receiving study drug. The analysis was performed in all subjects who received at least 1 dose of BMS-820836 during the study.

End point type	Secondary

End point timeframe:

Baseline up to 30 days after the last dose of the study drug

End point values	BMS-820836 0.5 mg	BMS-820836 1 mg	BMS-820836 2 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	226	265	297	
Units: Subjects				
AEs	171	185	230	
SAEs	7	13	9	
Discontinuation due to AEs	14	12	24	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline up to 30 days post last dose or till start of Washout Phase, whichever is earlier (approximately 58 weeks).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	BMS-820836 0.5 mg
Reporting group description: Subjects received BMS-820836 0.5 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.	
Reporting group title	BMS-820836 1 mg
Reporting group description: Subjects received BMS-820836 1 mg and matching placebo to BMS-820836 tablets once daily for 54 weeks.	
Reporting group title	BMS-820836 2 mg
Reporting group description: Subjects received BMS-820836 2 mg tablets once daily for 54 weeks.	

Serious adverse events	BMS-820836 0.5 mg	BMS-820836 1 mg	BMS-820836 2 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 226 (3.10%)	13 / 265 (4.91%)	9 / 297 (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)			
Breast cancer stage III			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 226 (0.00%)	2 / 265 (0.75%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary thrombosis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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			
Major depression			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Depression			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression suicidal			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Homicidal ideation			

subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Intentional self-injury			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Self injurious behaviour			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Ankle fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Overdose			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Cardiac disorders			

Coronary artery occlusion			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Loss of consciousness			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Polyneuropathy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Syncope			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Haemorrhoids			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Cholecystitis chronic			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Hepatic steatosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Musculoskeletal and connective tissue disorders			
Spondylitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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			
Appendicitis perforated			

subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Gastroenteritis			
subjects affected / exposed	0 / 226 (0.00%)	0 / 265 (0.00%)	1 / 297 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Wound infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 265 (0.38%)	0 / 297 (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
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 265 (0.00%)	0 / 297 (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

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

Non-serious adverse events	BMS-820836 0.5 mg	BMS-820836 1 mg	BMS-820836 2 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	173 / 226 (76.55%)	199 / 265 (75.09%)	234 / 297 (78.79%)
Investigations			
Weight increased			
subjects affected / exposed	16 / 226 (7.08%)	12 / 265 (4.53%)	9 / 297 (3.03%)
occurrences (all)	16	12	9
Nervous system disorders			
Headache			
subjects affected / exposed	39 / 226 (17.26%)	38 / 265 (14.34%)	31 / 297 (10.44%)
occurrences (all)	63	51	38
Dizziness			

subjects affected / exposed	18 / 226 (7.96%)	11 / 265 (4.15%)	12 / 297 (4.04%)
occurrences (all)	20	13	14
Somnolence			
subjects affected / exposed	6 / 226 (2.65%)	9 / 265 (3.40%)	15 / 297 (5.05%)
occurrences (all)	7	10	17
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 226 (5.31%)	15 / 265 (5.66%)	21 / 297 (7.07%)
occurrences (all)	14	16	21
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	13 / 226 (5.75%)	13 / 265 (4.91%)	23 / 297 (7.74%)
occurrences (all)	15	13	27
Constipation			
subjects affected / exposed	7 / 226 (3.10%)	10 / 265 (3.77%)	24 / 297 (8.08%)
occurrences (all)	7	13	29
Dry mouth			
subjects affected / exposed	8 / 226 (3.54%)	13 / 265 (4.91%)	17 / 297 (5.72%)
occurrences (all)	8	14	17
Psychiatric disorders			
Insomnia			
subjects affected / exposed	10 / 226 (4.42%)	13 / 265 (4.91%)	21 / 297 (7.07%)
occurrences (all)	13	14	21
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	14 / 226 (6.19%)	14 / 265 (5.28%)	7 / 297 (2.36%)
occurrences (all)	16	14	7
Arthralgia			
subjects affected / exposed	10 / 226 (4.42%)	10 / 265 (3.77%)	15 / 297 (5.05%)
occurrences (all)	11	11	15
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	21 / 226 (9.29%)	18 / 265 (6.79%)	16 / 297 (5.39%)
occurrences (all)	25	20	18
Upper respiratory tract infection			

subjects affected / exposed	12 / 226 (5.31%)	14 / 265 (5.28%)	21 / 297 (7.07%)
occurrences (all)	12	16	22
Urinary tract infection			
subjects affected / exposed	13 / 226 (5.75%)	13 / 265 (4.91%)	16 / 297 (5.39%)
occurrences (all)	15	13	17
Influenza			
subjects affected / exposed	12 / 226 (5.31%)	11 / 265 (4.15%)	5 / 297 (1.68%)
occurrences (all)	12	14	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2012	The purpose of this amendment was to re-define the research hypothesis, add exploratory objectives and to include guidance for the pharmacological and non-pharmacological treatment interventions for subjects that develop elevated blood pressure during the study.
16 January 2013	The purpose of this amendment was to revise the dosing recommendations for zolpidem tartrate as per Food and Drug administration recommendation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early when the primary objective in each of the 2 parent studies CN162-006 (EudraCT Number: 2010-022841-93) and CN162-007 (EudraCT Number: 2011-000778-71) was not achieved.

Notes: