Clinical trial results:
A Randomized, Double-Blind, Placebo- and Active-Controlled Study of DS-5565 in Subjects with Pain Associated with Fibromyalgia

Summary

EudraCT number	2013-005163-10
Trial protocol	GB SK EE LT HU LV BG
Global end of trial date	07 July 2016

Results information

Result version number	v2 (current)
This version publication date	04 November 2017
First version publication date	25 August 2017
Version creation reason	• Correction of full data set The actual end of trial date was 07-July-2016, so the record is updated accordingly.

Trial information

Trial identification

Sponsor protocol code	DS5565-A-E311

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02187159
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo, Inc.
Sponsor organisation address	211 Mt. Airy Road, Basking Ridge, United States, 07920
Public contact	Clinical Trial Application, Daiichi Sankyo Development Ltd, +44 1753482800, euregaffairs@dsd-eu.com
Scientific contact	Clinical Trial Application, Daiichi Sankyo Development Ltd, +44 1753482800, euregaffairs@dsd-eu.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	02 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare change in weekly average daily pain score (ADPS) from baseline to Week 13 in subjects receiving either dose of DS-5565 versus placebo.
Weekly ADPS is based on daily pain scores reported by the subject that best describes his or her worst pain over the previous 24 hours.

Protection of trial subjects:

This trial was conducted under ICH E6 Good Clinical Practices, which has it's foundation in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 41
Country: Number of subjects enrolled	United Kingdom: 153
Country: Number of subjects enrolled	Romania: 31
Country: Number of subjects enrolled	Bulgaria: 74
Country: Number of subjects enrolled	Estonia: 21
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Latvia: 32
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	India: 44
Country: Number of subjects enrolled	New Zealand: 33
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	United States: 752
Worldwide total number of subjects	1270
EEA total number of subjects	382

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)	1146
From 65 to 84 years	124
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of 2280 patients screened, 1270 from 13 countries were randomized into study groups.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Patients take one each of placebo tablet and capsule, twice daily (BID)

Arm type	Placebo
Investigational medicinal product name	Placebo tablet and/or capsule
Investigational medicinal product code	
Other name	Matching Placebo
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo for oral administration matching tablet for DS-5565 and matching capsule for pregabalin

Arm title	Pregabalin

Arm description:

Patients take one pregabalin capsule and one placebo tablet BID

Arm type	Active comparator
Investigational medicinal product name	Pregabalin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pregabalin 150 mg capsule for oral administration

Investigational medicinal product name	Placebo tablet and/or capsule
Investigational medicinal product code	
Other name	Matching Placebo
Pharmaceutical forms	Tablet, Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo for oral administration matching tablet for DS-5565 and matching capsule for pregabalin

Arm title	DS-5565 QD

Arm description:

Patients take one each of placebo tablet and capsule in the morning and one DS-5565 tablet once daily (QD) with a placebo capsule in the evening

Arm type	Active comparator
Investigational medicinal product name	DS-5565
Investigational medicinal product code	
Other name	mirogabalin
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DS-5565 15 mg tablet for oral administration

Investigational medicinal product name	Placebo tablet and/or capsule
Investigational medicinal product code	
Other name	Matching Placebo
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo for oral administration matching tablet for DS-5565 and matching capsule for pregabalin

Arm title	DS-5565 BID

Arm description:

Patients take one DS-5565 tablet and one placebo capsule BID

Arm type	Experimental
Investigational medicinal product name	DS-5565
Investigational medicinal product code	
Other name	mirogabalin
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

DS-5565 15 mg tablet for oral administration

Investigational medicinal product name	Placebo tablet and/or capsule
Investigational medicinal product code	
Other name	Matching Placebo
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo for oral administration matching tablet for DS-5565 and matching capsule for pregabalin

Number of subjects in period 1	Placebo	Pregabalin	DS-5565 QD
Started	318	317	318
Safety analysis set	315	312	315
Modified intent to treat set (mITT)	315	312	315
Completed double-blind treatment	249	238	241
Completed	249	238	241
Not completed	69	79	77
Consent withdrawn by subject	24	28	25
Adverse event, non-fatal	28	33	42
Reason missing or not reported	3	7	3
Lack of efficacy	10	5	4

Protocol deviation	4	6	3

Number of subjects in period 1	DS-5565 BID
Started	317
Safety analysis set	313
Modified intent to treat set (mITT)	313
Completed double-blind treatment	221
Completed	221
Not completed	96
Consent withdrawn by subject	26
Adverse event, non-fatal	50
Reason missing or not reported	9
Lack of efficacy	7
Protocol deviation	4

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Patients take one each of placebo tablet and capsule, twice daily (BID)	
Reporting group title	Pregabalin
Reporting group description:	
Patients take one pregabalin capsule and one placebo tablet BID	
Reporting group title	DS-5565 QD
Reporting group description:	
Patients take one each of placebo tablet and capsule in the morning and one DS-5565 tablet once daily (QD) with a placebo capsule in the evening	
Reporting group title	DS-5565 BID
Reporting group description:	
Patients take one DS-5565 tablet and one placebo capsule BID	

Reporting group values	Placebo	Pregabalin	DS-5565 QD
Number of subjects	318	317	318
Age categorical Units: Subjects			
Adults (18-64 years)	289	287	286
From 65-84 years	29	30	32
Age continuous Units: years			
arithmetic mean	50.2	50.9	50.2
standard deviation	± 11.43	± 11.58	± 11.85
Gender categorical Units: Subjects			
Female	290	288	295
Male	28	29	23

Reporting group values	DS-5565 BID	Total	
Number of subjects	317	1270	
Age categorical Units: Subjects			
Adults (18-64 years)	284	1146	
From 65-84 years	33	124	
Age continuous Units: years			
arithmetic mean	50.6		
standard deviation	± 11.46	-	
Gender categorical Units: Subjects			
Female	287	1160	
Male	30	110	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Patients take one each of placebo tablet and capsule, twice daily (BID)	
Reporting group title	Pregabalin
Reporting group description:	
Patients take one pregabalin capsule and one placebo tablet BID	
Reporting group title	DS-5565 QD
Reporting group description:	
Patients take one each of placebo tablet and capsule in the morning and one DS-5565 tablet once daily (QD) with a placebo capsule in the evening	
Reporting group title	DS-5565 BID
Reporting group description:	
Patients take one DS-5565 tablet and one placebo capsule BID	

Primary: Average daily pain score (ADPS) for either dose of DS-5565 versus placebo

End point title	Average daily pain score (ADPS) for either dose of DS-5565 versus placebo[1][2]
End point description:	
Average daily pain scores reported by the patient that best describes his or her worst pain over the previous 24 hours. A daily pain score has a scale of 0 = no pain to 10 = worst possible pain.	
End point type	Primary
End point timeframe:	
Baseline, Week 13	

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: No statistical analyses were performed to arrive at this aggregate summary data.

[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: Pregabalin was not included in this outcome measure

End point values	Placebo	DS-5565 QD	DS-5565 BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	315	313	
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline	7.04 (± 1.282)	7.08 (± 1.209)	7.13 (± 1.301)	
Week 13 (MI)	5.21 (± 0.13)	4.83 (± 0.133)	4.98 (± 0.134)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients who answered "much improved or better" in PGIC at

Week 13 receiving either dose of DS-5565 versus placebo

End point title	Number of patients who answered "much improved or better" in PGIC at Week 13 receiving either dose of DS-5565 versus placebo[3]

End point description:

Patients rated global impression of change (PGIC) on a categorical scale from 1 = very much improved to 7 = very much worse

End point type	Secondary

End point timeframe:

Baseline, Week 13

Notes:

[3] - 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: Pregabalin was not included in this outcome measure.

End point values	Placebo	DS-5565 QD	DS-5565 BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	315	313	
Units: Patients	84	106	104	

Statistical analyses

No statistical analyses for this end point

Secondary: Average score on the fibromyalgia index questionnaire (FIQ) in patients receiving either dose of DS-5565 or placebo

End point title	Average score on the fibromyalgia index questionnaire (FIQ) in patients receiving either dose of DS-5565 or placebo[4]

End point description:

The FIQ is composed of 10 items. The first item contains 11 questions related to physical functioning - each question is rated on a 4-point Likert-type scale. Items 2 and 3 ask the patient to mark the number of days that they feel well and the number of days they were unable to work (including housework) because of fibromyalgia (FM) symptoms. Items 4 through 10 are horizontal linear scales marked in 10 increments on which the patient rates work difficulty, pain, fatigue, morning tiredness, stiffness, anxiety, and depression. A higher score indicates a greater impact of the syndrome on the patient. Scores were collected from patients who completed the assessment at the given time point.

End point type	Secondary

End point timeframe:

Baseline, Week 13

Notes:

[4] - 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: Pregabalin was not included in this outcome measure

End point values	Placebo	DS-5565 QD	DS-5565 BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	315	313	
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=313,312,312)	62.87 (± 13.399)	63.96 (± 12.953)	63.28 (± 13.304)	

Week 13 (MI; n=246,238,220)	48.78 (± 20.171)	46.59 (± 21.065)	45.17 (± 19.378)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients receiving either dose of DS-5565 or placebo classified as responders at Week 13

End point title	Number of patients receiving either dose of DS-5565 or placebo classified as responders at Week 13[5]

End point description:

Patients classified as responders are those with a substantial reduction in ADPS in Week 13 compared to baseline.

End point type	Secondary

End point timeframe:

Baseline, Week 13

Notes:

[5] - 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: Pregabalin was not included in this outcome measure

End point values	Placebo	DS-5565 QD	DS-5565 BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	315	313	
Units: Patients				
30% Responders	113	123	118	
50% Responders	61	79	68	

Statistical analyses

No statistical analyses for this end point

Secondary: Average daily pain score (ADPS) for pregabalin

End point title	Average daily pain score (ADPS) for pregabalin[6]

End point description:

Average daily pain scores reported by the patient that best describes his or her worst pain over the previous 24 hours. A daily pain score has a scale of 0 = no pain to 10 = worst possible pain.

End point type	Secondary

End point timeframe:

Baseline, Week 13

Notes:

[6] - 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: Pregabalin was reported separately

End point values	Pregabalin			
Subject group type	Reporting group			
Number of subjects analysed	312			
Units: scores on a scale				
arithmetic mean (standard deviation)				
Baseline (n=311) Week 13 (MI; n=312)	7.03 (± 1.392) 4.6 (± 0.133)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Events that emerge or get worse on or after the first dosing of double blind study medication and during study treatment up to 4 weeks after the last dose of double blind study medication

Adverse event reporting additional description:

Total number of treatment-emergent adverse events (TEAEs) counts all occurrences in all subjects. In the system organ class and preferred term summarization, a patient was counted only once when one or more events were reported, so the occurrences mirror the number of patients.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Patients take one each of placebo tablet and capsule, twice daily (BID)

Reporting group title	Pregabalin

Reporting group description:

Patients take one pregabalin capsule and one placebo tablet BID

Reporting group title	DS-5565 QD

Reporting group description:

Patients take one each of placebo tablet and capsule in the morning and one DS-5565 tablet once daily (QD) with a placebo capsule in the evening

Reporting group title	DS-5565 BID

Reporting group description:

Patients take one DS-5565 tablet and one placebo capsule BID

Serious adverse events	Placebo	Pregabalin	DS-5565 QD
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 315 (1.90%)	5 / 312 (1.60%)	7 / 315 (2.22%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lip squamous cell carcinoma			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	0 / 315 (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			
Haematoma			

subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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			
Asthma			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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
Alveolitis allergic			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	0 / 315 (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
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			

subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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
Suicide attempt			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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
Transaminases increased			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	0 / 315 (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
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	0 / 315 (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
Ankle fracture			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	0 / 315 (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			
Cardiomegaly			

subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Supraventricular tachycardia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	0 / 315 (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
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	0 / 315 (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			
Papilloedema			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	0 / 315 (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 disorders			
Abdominal hernia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	0 / 315 (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
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	0 / 315 (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			
Osteoarthritis			

subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	0 / 315 (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
Fibromyalgia			
subjects affected / exposed	1 / 315 (0.32%)	0 / 312 (0.00%)	0 / 315 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 315 (0.00%)	1 / 312 (0.32%)	0 / 315 (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			
Diabetes mellitus			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 315 (0.00%)	0 / 312 (0.00%)	1 / 315 (0.32%)
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	DS-5565 BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 313 (3.51%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lip squamous cell carcinoma			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Haematoma			

subjects affected / exposed	1 / 313 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 313 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 313 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 313 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Alveolitis allergic			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	2 / 313 (0.64%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Mania			

subjects affected / exposed	1 / 313 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 313 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 313 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	1 / 313 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 313 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Upper limb fracture				
subjects affected / exposed	1 / 313 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 313 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardiomegaly				

subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Papilloedema			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver injury			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	1 / 313 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fibromyalgia			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 313 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Pregabalin	DS-5565 QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	212 / 315 (67.30%)	221 / 312 (70.83%)	233 / 315 (73.97%)
Investigations			
Weight increased			
subjects affected / exposed	9 / 315 (2.86%)	39 / 312 (12.50%)	17 / 315 (5.40%)
occurrences (all)	9	39	17
Nervous system disorders			
Headache			
subjects affected / exposed	39 / 315 (12.38%)	37 / 312 (11.86%)	44 / 315 (13.97%)
occurrences (all)	39	37	44

Dizziness			
subjects affected / exposed	23 / 315 (7.30%)	47 / 312 (15.06%)	44 / 315 (13.97%)
occurrences (all)	23	47	44
Somnolence			
subjects affected / exposed	10 / 315 (3.17%)	29 / 312 (9.29%)	23 / 315 (7.30%)
occurrences (all)	10	29	23
General disorders and administration site conditions			
Drug withdrawal syndrome			
subjects affected / exposed	20 / 315 (6.35%)	32 / 312 (10.26%)	32 / 315 (10.16%)
occurrences (all)	20	32	32
Fatigue			
subjects affected / exposed	9 / 315 (2.86%)	11 / 312 (3.53%)	17 / 315 (5.40%)
occurrences (all)	9	11	17
Oedema peripheral			
subjects affected / exposed	4 / 315 (1.27%)	10 / 312 (3.21%)	9 / 315 (2.86%)
occurrences (all)	4	10	9
Eye disorders			
Vision blurred			
subjects affected / exposed	5 / 315 (1.59%)	14 / 312 (4.49%)	16 / 315 (5.08%)
occurrences (all)	5	14	16
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	14 / 315 (4.44%)	10 / 312 (3.21%)	18 / 315 (5.71%)
occurrences (all)	14	10	18
Diarrhoea			
subjects affected / exposed	15 / 315 (4.76%)	15 / 312 (4.81%)	20 / 315 (6.35%)
occurrences (all)	15	15	20
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	16 / 315 (5.08%)	15 / 312 (4.81%)	10 / 315 (3.17%)
occurrences (all)	16	15	10
Back pain			
subjects affected / exposed	17 / 315 (5.40%)	8 / 312 (2.56%)	12 / 315 (3.81%)
occurrences (all)	17	8	12
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	17 / 315 (5.40%)	19 / 312 (6.09%)	17 / 315 (5.40%)
occurrences (all)	17	19	17
Urinary tract infection			
subjects affected / exposed	6 / 315 (1.90%)	13 / 312 (4.17%)	11 / 315 (3.49%)
occurrences (all)	6	13	11

Non-serious adverse events	DS-5565 BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	238 / 313 (76.04%)		
Investigations			
Weight increased			
subjects affected / exposed	33 / 313 (10.54%)		
occurrences (all)	33		
Nervous system disorders			
Headache			
subjects affected / exposed	45 / 313 (14.38%)		
occurrences (all)	45		
Dizziness			
subjects affected / exposed	41 / 313 (13.10%)		
occurrences (all)	41		
Somnolence			
subjects affected / exposed	29 / 313 (9.27%)		
occurrences (all)	29		
General disorders and administration site conditions			
Drug withdrawal syndrome			
subjects affected / exposed	28 / 313 (8.95%)		
occurrences (all)	28		
Fatigue			
subjects affected / exposed	11 / 313 (3.51%)		
occurrences (all)	11		
Oedema peripheral			
subjects affected / exposed	16 / 313 (5.11%)		
occurrences (all)	16		
Eye disorders			
Vision blurred			

subjects affected / exposed	13 / 313 (4.15%)		
occurrences (all)	13		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	28 / 313 (8.95%)		
occurrences (all)	28		
Diarrhoea			
subjects affected / exposed	14 / 313 (4.47%)		
occurrences (all)	14		
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	16 / 313 (5.11%)		
occurrences (all)	16		
Back pain			
subjects affected / exposed	11 / 313 (3.51%)		
occurrences (all)	11		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	20 / 313 (6.39%)		
occurrences (all)	20		
Urinary tract infection			
subjects affected / exposed	17 / 313 (5.43%)		
occurrences (all)	17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2015	Update and clarify screening procedures and duration. Update and provide further direction on how to deal with borderline pregnancy results.
29 July 2015	Clarify study objectives, endpoints, pain assessment and study procedures
06 April 2016	Modify and clarify discontinuation criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported