Clinical trial results:
Double-blind, randomised, placebo-controlled, parallel-group phase II study to evaluate the effect of oral ibodutant in irritable bowel syndrome with diarrhoea (IBS-D) - The Iris-2 Study.

Summary

EudraCT number	2010-018300-85
Trial protocol	CZ DE ES SE IT DK BG
Global end of trial date	11 May 2012

Results information

Result version number	v1 (current)
This version publication date	15 November 2018
First version publication date	15 November 2018

Trial information

Trial identification

Sponsor protocol code	NAK-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01303224
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Menarini Ricerche S.p.A.
Sponsor organisation address	Via Sette Santi 1, Florence, Italy, 50131
Public contact	Corporate Director of Clinical Sciences, Corporate Clinical Sciences, +39 05556809990, acapriati@menarini-ricerche.it
Scientific contact	Corporate Director of Clinical Sciences, Corporate Clinical Sciences, +39 05556809990, acapriati@menarini-ricerche.it

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	11 May 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2012
Global end of trial reached?	Yes
Global end of trial date	11 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 3 oral doses of ibodutant on IBS symptoms relief and abdominal pain/discomfort relief as compared to placebo in IBS-D patients following an 8-week oral treatment course.

Protection of trial subjects:

If any event(s) related to the conduct of the study or the development of the IMP which affected the safety of the study participants, the sponsor and the investigator were to take appropriate urgent safety measures to protect the patients against any immediate hazard. The CAs and IRB/ECs were to be informed forthwith about these new events and the measures taken.
For patients participating in the study, Menarini Ricerche S.p.A. had stipulated an insurance policy in accordance with local regulatory requirements.

Background therapy: -

Evidence for comparator:

The choice of placebo as control group also complied with requirements of institutional and academic guidelines and was justified because there was unison agreement that there were no standard therapy for IBS. Moreover, the "placebo effect" in IBS was known to be high with response rates ranging from 0% to 84% (median: 47%) so that demonstration of superiority over placebo was most likely to reflect a true advantage for the patient.

Actual start date of recruitment	06 October 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 188
Country: Number of subjects enrolled	Spain: 23
Country: Number of subjects enrolled	Sweden: 26
Country: Number of subjects enrolled	Bulgaria: 162
Country: Number of subjects enrolled	Czech Republic: 50
Country: Number of subjects enrolled	Denmark: 67
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Italy: 14
Worldwide total number of subjects	565
EEA total number of subjects	565

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)	519
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was screened on 06 Oct 2010 and the first subject was randomised on 22 Oct 2010. The last patient completed the study on 11 May 2012. The study was conducted at 78 investigational sites in 8 European countries.

Pre-assignment

Screening details:

A total of 1054 entered into the 2-week screening period. Of these, 565 patients were eligible for randomisation, indicating a screening failure rate of 53.6%.
A total of 559 patients took at least one dose of study medication and provided at least one primary endpoint assessment (ITT-population)

Period 1

Period 1 title	8-week Double-blind Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

Double-blind conditions were ensured by the identical appearance and weight of the three different strengths of ibodutant tablets as well as the placebo tablets.
In order to preserve the double-blind conditions of the study, persons who were involved in the preparation or the handling of the randomisation list were not involved in the study conduct and statistical analysis. This remained in effect until the database was completed and locked.

Arms

Are arms mutually exclusive?	Yes
Arm title	Ibodutant 1mg

Arm description:

Ibodutant 1mg, oral tablet to be given once daily for 8 weeks of treatment.

Arm type	Experimental
Investigational medicinal product name	Ibodutant
Investigational medicinal product code	MEN 15596
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ibodutant 1 mg oral tablet, to be given once daily in fasting conditions.

Arm title	Ibodutant 3mg

Arm description:

Ibodutant 3mg, oral tablet to be given once daily for 8 weeks of treatment.

Arm type	Experimental
Investigational medicinal product name	Ibodutant
Investigational medicinal product code	MEN 15596
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Ibodutant 3 mg oral tablet, to be given once daily in fasting conditions.

Arm title	Ibodutant 10mg

Arm description:	
Ibodutant 10mg, oral tablet to be given once daily for 8 weeks of treatment.	
Arm type	Experimental
Investigational medicinal product name	Ibodutant
Investigational medicinal product code	MEN 15596
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Other use
Dosage and administration details:	
Ibodutant 10 mg oral tablet, to be given once daily in fasting conditions.	
Arm title	Placebo
Arm description:	
Placebo, oral tablet to be given once daily for 8 weeks of treatment.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Sugar pill
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Placebo oral tablet (identical in appearance and weight to ibodutant tablets) to be given once daily in fasting conditions.	

Number of subjects in period 1	Ibodutant 1mg	Ibodutant 3mg	Ibodutant 10mg
Started	141	142	139
Completed	130	131	133
Not completed	11	11	6
Consent withdrawn by subject	4	8	2
unk	2	1	2
Adverse event, non-fatal	2	1	1
Sponsor request	1	-	-
Lost to follow-up	1	1	1
Protocol deviation	1	-	-

Number of subjects in period 1	Placebo
Started	143
Completed	133
Not completed	10
Consent withdrawn by subject	4
unk	3
Adverse event, non-fatal	-
Sponsor request	-
Lost to follow-up	3

Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Ibodutant 1mg
Reporting group description:	
Ibodutant 1mg, oral tablet to be given once daily for 8 weeks of treatment.	
Reporting group title	Ibodutant 3mg
Reporting group description:	
Ibodutant 3mg, oral tablet to be given once daily for 8 weeks of treatment.	
Reporting group title	Ibodutant 10mg
Reporting group description:	
Ibodutant 10mg, oral tablet to be given once daily for 8 weeks of treatment.	
Reporting group title	Placebo
Reporting group description:	
Placebo, oral tablet to be given once daily for 8 weeks of treatment.	

Reporting group values	Ibodutant 1mg	Ibodutant 3mg	Ibodutant 10mg
Number of subjects	141	142	139
Age categorical Units: Subjects			
Adults (18-70 years)	141	142	139
Age continuous Units: years			
arithmetic mean	46.1	46.8	47.0
standard deviation	± 13.3	± 13.5	± 12.8
Gender categorical Units: Subjects			
Female	89	89	79
Male	52	53	60
Time since onset of IBS symptoms Units: Years			
arithmetic mean			
standard deviation	±	±	±
IBS symptoms at baseline/randomisation: abdominal pain			
Abdominal pain			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	±	±
IBS symptoms at baseline/randomisation: bloating			
Bloating			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	±	±
IBS symptoms at baseline/randomisation: urgency			
Urgency			
Units: Scores on a scale			
arithmetic mean			

standard deviation	±	±	±
IBS symptoms at baseline/randomisation: severity			
IBS symptom severity rate			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	±	±
Stool frequency/day			
Units: Bowel movements/day			
arithmetic mean			
standard deviation	±	±	±
Stool consistency			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	±	±
IBS symptomes severity scale score			
IBS symptomes severity scale score			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	±	±
QoL questionnaire EQ-5D VAS			
Quality of Life questionnaire EQ-5D Visual analog scales			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	Placebo	Total	
Number of subjects	143	565	
Age categorical			
Units: Subjects			
Adults (18-70 years)	143	565	
Age continuous			
Units: years			
arithmetic mean	44.2		
standard deviation	± 14.0	-	
Gender categorical			
Units: Subjects			
Female	79	336	
Male	64	229	
Time since onset of IBS symptoms			
Units: Years			
arithmetic mean			
standard deviation	±	-	
IBS symptoms at baseline/randomisation: abdominal pain			
Abdominal pain			
Units: Scores on a scale			
arithmetic mean			
standard deviation	±	-	
IBS symptoms at baseline/randomisation: bloating			
Bloating			

Units: Scores on a scale arithmetic mean standard deviation	±	-	
IBS symptoms at baseline/randomisation: urgency			
Urgency			
Units: Scores on a scale arithmetic mean standard deviation	±	-	
IBS symptoms at baseline/randomisation: severity			
IBS symptom severity rate			
Units: Scores on a scale arithmetic mean standard deviation	±	-	
Stool frequency/day Units: Bowel movements/day arithmetic mean standard deviation	±	-	
Stool consistency Units: Scores on a scale arithmetic mean standard deviation	±	-	
IBS symptomes severity scale score			
IBS symptomes severity scale score			
Units: Scores on a scale arithmetic mean standard deviation	±	-	
QoL questionnaire EQ-5D VAS			
Quality of Life questionnaire EQ-5D Visual analog scales			
Units: Scores on a scale arithmetic mean standard deviation	±	-	

Subject analysis sets

Subject analysis set title	ITT 1 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients randomised to the 1 mg Ibudutant group who took at least one dose of the study medication and provided at least one primary endpoint assessment.

Subject analysis set title	ITT 3 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients randomised to the 3 mg Ibudutant group who took at least one dose of the study medication and provided at least one primary endpoint assessment.

Subject analysis set title	ITT 10 mg
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients randomised to the 10 mg Ibudutant group who took at least one dose of the study medication and provided at least one primary endpoint assessment.

Subject analysis set title	ITT placebo
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients randomised to the placebo group who took at least one dose of the study medication and provided at least one primary endpoint assessment.

Reporting group values	ITT 1 mg	ITT 3 mg	ITT 10 mg
Number of subjects	140	138	139
Age categorical			
Units: Subjects			
Adults (18-70 years)	140	138	139
Age continuous			
Units: years			
arithmetic mean	45.9	47.1	47.0
standard deviation	± 13.7	± 13.4	± 12.8
Gender categorical			
Units: Subjects			
Female	89	87	79
Male	51	51	60
Time since onset of IBS symptoms			
Units: Years			
arithmetic mean	6.2	6.3	6.3
standard deviation	± 7.3	± 7.5	± 6.9
IBS symptoms at baseline/randomisation: abdominal pain			
Abdominal pain			
Units: Scores on a scale			
arithmetic mean	2.5	2.3	2.3
standard deviation	± 0.6	± 0.5	± 0.5
IBS symptoms at baseline/randomisation: bloating			
Bloating			
Units: Scores on a scale			
arithmetic mean	2.4	2.2	2.2
standard deviation	± 0.8	± 0.7	± 0.7
IBS symptoms at baseline/randomisation: urgency			
Urgency			
Units: Scores on a scale			
arithmetic mean	2.5	2.5	2.4
standard deviation	± 0.7	± 0.6	± 0.6
IBS symptoms at baseline/randomisation: severity			
IBS symptom severity rate			
Units: Scores on a scale			
arithmetic mean	2.7	2.6	2.6
standard deviation	± 0.7	± 0.6	± 0.6
Stool frequency/day			
Units: Bowel movements/day			
arithmetic mean	4.6	4.4	4.4
standard deviation	± 1.5	± 1.3	± 1.5
Stool consistency			
Units: Scores on a scale			
arithmetic mean	5.7	5.7	5.7
standard deviation	± 0.6	± 0.5	± 0.6

IBS symptomes severity scale score			
IBS symptomes severity scale score			
Units: Scores on a scale			
arithmetic mean	343.4	333.3	332.6
standard deviation	± 68.8	± 78.3	± 74.3
QoL questionnaire EQ-5D VAS			
Quality of Life questionnaire EQ-5D Visual analog scales			
Units: Scores on a scale			
arithmetic mean	54.5	55.5	58.1
standard deviation	± 22.9	± 21.9	± 22.9

Reporting group values	ITT placebo		
Number of subjects	142		
Age categorical			
Units: Subjects			
Adults (18-70 years)	142		
Age continuous			
Units: years			
arithmetic mean	44.1		
standard deviation	± 14.0		
Gender categorical			
Units: Subjects			
Female	78		
Male	64		
Time since onset of IBS symptoms			
Units: Years			
arithmetic mean	4.6		
standard deviation	± 6.2		
IBS symptoms at baseline/randomisation: abdominal pain			
Abdominal pain			
Units: Scores on a scale			
arithmetic mean	2.3		
standard deviation	± 0.6		
IBS symptoms at baseline/randomisation: bloating			
Bloating			
Units: Scores on a scale			
arithmetic mean	2.2		
standard deviation	± 0.6		
IBS symptoms at baseline/randomisation: urgency			
Urgency			
Units: Scores on a scale			
arithmetic mean	2.4		
standard deviation	± 0.6		
IBS symptoms at baseline/randomisation: severity			
IBS symptom severity rate			
Units: Scores on a scale			
arithmetic mean	2.6		
standard deviation	± 0.6		
Stool frequency/day			

Units: Bowel movements/day			
arithmetic mean	4.4		
standard deviation	± 1.2		
Stool consistency			
Units: Scores on a scale			
arithmetic mean	5.7		
standard deviation	± 0.6		
IBS symptomes severity scale score			
IBS symptomes severity scale score			
Units: Scores on a scale			
arithmetic mean	335.7		
standard deviation	± 69.4		
QoL questionnaire EQ-5D VAS			
Quality of Life questionnaire EQ-5D Visual analog scales			
Units: Scores on a scale			
arithmetic mean	55.3		
standard deviation	± 22.3		

End points

End points reporting groups

Reporting group title	Ibodutant 1mg
Reporting group description:	
Ibodutant 1mg, oral tablet to be given once daily for 8 weeks of treatment.	
Reporting group title	Ibodutant 3mg
Reporting group description:	
Ibodutant 3mg, oral tablet to be given once daily for 8 weeks of treatment.	
Reporting group title	Ibodutant 10mg
Reporting group description:	
Ibodutant 10mg, oral tablet to be given once daily for 8 weeks of treatment.	
Reporting group title	Placebo
Reporting group description:	
Placebo, oral tablet to be given once daily for 8 weeks of treatment.	
Subject analysis set title	ITT 1 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to the 1 mg Ibudutant group who took at least one dose of the study medication and provided at least one primary endpoint assessment.	
Subject analysis set title	ITT 3 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to the 3 mg Ibudutant group who took at least one dose of the study medication and provided at least one primary endpoint assessment.	
Subject analysis set title	ITT 10 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to the 10 mg Ibudutant group who took at least one dose of the study medication and provided at least one primary endpoint assessment.	
Subject analysis set title	ITT placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised to the placebo group who took at least one dose of the study medication and provided at least one primary endpoint assessment.	

Primary: Response for Relief of Overall IBS Symptoms and of Abdominal Pain/Discomfort at the End of 8 Weeks of Treatment, Where the Response is Defined as at Least 6 Weeks With Satisfactory Relief During 8 Weeks of Treatment (75% Rule)

End point title	Response for Relief of Overall IBS Symptoms and of Abdominal Pain/Discomfort at the End of 8 Weeks of Treatment, Where the Response is Defined as at Least 6 Weeks With Satisfactory Relief During 8 Weeks of Treatment (75% Rule)
End point description:	
Weekly binary questions (yes/no) from Interactive Voice/Web Response (IV/WRS) diary records: "Did you have satisfactory relief of your overall IBS symptoms during the last week?" and "Did you have satisfactory relief of your abdominal pain or discomfort during the last week?" Responder: Report of satisfactory overall IBS symptom relief ="Yes" and of satisfactory abdominal pain/discomfort relief = "Yes" 6/8 weeks (75% rule)	
End point type	Primary
End point timeframe:	
Eight weeks	

End point values	ITT 1 mg	ITT 3 mg	ITT 10 mg	ITT placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	140	138	139	142
Units: Number of Responders				
Responder	45	46	55	39
Non Responder	95	92	84	103

Statistical analyses

Statistical analysis title	Cochran-Mantel-Haenszel Test

Statistical analysis description:

Mantel-Haenszel-Test was used to compare separately each of the 3 active treatment groups with placebo using a two-sided overall significance level of 5%. The proportion of responders was tested with the following hypotheses: H0 (placebo) vs H1(Ibodutant:1mg/3mg/10mg). Approximately 80% power based on the assumptions: rate placebo 40%, expected mean therapeutic gain over placebo 15% for at least one dose of Ibodutant.

Comparison groups	ITT 3 mg v ITT 1 mg v ITT 10 mg v ITT placebo
Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [1]
Method	t-test, 2-sided

Notes:

[1] - Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
Multiplicity was adjusted by using the Hochberg Procedure.

Secondary: Response of satisfactory relief of overall IBS symptoms AND abdominal pain/discomfort during 8 weeks of treatment according to the 50% rule

End point title	Response of satisfactory relief of overall IBS symptoms AND abdominal pain/discomfort during 8 weeks of treatment according to the 50% rule

End point description:

Weekly binary questions (yes/no) from IV/WRS diary records: "Did you have satisfactory relief of your overall IBS symptoms during the last week?" and "Did you have satisfactory relief of your abdominal pain or discomfort during the last week?"

Responder: Report of satisfactory overall IBS symptom relief ="Yes" and of satisfactory abdominal pain/discomfort relief = "Yes" 4/8 weeks with at least 2 consecutive weeks of satisfactory relief during Week 5 to Week 8(50% rule)

End point type	Secondary

End point timeframe:

Eight weeks

End point values	ITT 1 mg	ITT 3 mg	ITT 10 mg	ITT placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	140	138	139	142
Units: Number of responders				
Responder	72	61	74	55
Non-Responder	68	77	65	87

Statistical analyses

Statistical analysis title	Mantel Haenszel
Comparison groups	ITT 1 mg v ITT 3 mg v ITT 10 mg v ITT placebo
Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [2]
Method	Mantel-Haenszel

Notes:

[2] - Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:
Multiplicity was adjusted using the Hochberg procedure.

Secondary: Quality of Life Changes

End point title	Quality of Life Changes

End point description:

Change in EQ-5D Quality of Life (visual analogue scale) score at the end of 8 weeks of treatment versus baseline (at randomisation). EQ-5D quality of life visual analogue scale ranges from "0"= worst imaginable health state to "100"=best imaginable health state.

all ITT patients who provided EQ-5D data at Visit 2 (start of treatment) and Visit 4 (end of treatment).

No statistical analysis provided for Quality of Life Changes (Using EuroQoL EQ-5D Questionnaire).

End point type	Secondary

End point timeframe:

Eight weeks

End point values	ITT 1 mg	ITT 3 mg	ITT 10 mg	ITT placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	131	133	133	131
Units: VAS				
arithmetic mean (standard deviation)				
Baseline	56.4 (± 20.6)	58.2 (± 22.0)	57.2 (± 22.0)	58.7 (± 21.5)
Visit 4	71.3 (± 17.2)	72.1 (± 18.7)	66.7 (± 20.7)	72.2 (± 17.0)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subgroup Analysis: Response for Relief of Overall IBS Symptoms and of Abdominal Pain/Discomfort According to the 75% Rule in the Female ITT Population

End point title	Subgroup Analysis: Response for Relief of Overall IBS Symptoms and of Abdominal Pain/Discomfort According to the 75% Rule in the Female ITT Population

End point description:

Weekly binary questions (yes/no) from IV/WRS diary records: "Did you have satisfactory relief of your overall IBS symptoms during the last week?" and "Did you have satisfactory relief of your abdominal pain or discomfort during the last week?"
Responder: Report of satisfactory overall IBS symptom relief ="Yes" and of satisfactory abdominal pain/discomfort relief = "Yes" 6/8 weeks (75% rule)

Population: Female ITT Population
No statistical analysis provided for Subgroup Analysis

End point type	Other pre-specified

End point timeframe:

Eight weeks

End point values	ITT 1 mg	ITT 3 mg	ITT 10 mg	ITT placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	89	87	79	78
Units: Participants				
Responders	32	35	37	19
Non-Responders	57	52	42	59

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Subgroup Analysis: Response for Relief of Overall IBS Symptoms and of Abdominal Pain/Discomfort According to the 75% Rule in the Male ITT Population

End point title	Subgroup Analysis: Response for Relief of Overall IBS Symptoms and of Abdominal Pain/Discomfort According to the 75% Rule in the Male ITT Population

End point description:

Weekly binary questions (yes/no) from IV/WRS diary records: "Did you have satisfactory relief of your overall IBS symptoms during the last week?" and "Did you have satisfactory relief of your abdominal pain or discomfort during the last week?"
Responder: Report of satisfactory overall IBS symptom relief ="Yes" and of satisfactory abdominal pain/discomfort relief = "Yes" 6/8 weeks (75% rule)

Population: Intention-to-Treat in the male population
No statistical analysis provided for Subgroup Analysis.

End point type	Other pre-specified

End point timeframe:

Eight weeks

End point values	ITT 1 mg	ITT 3 mg	ITT 10 mg	ITT placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	51	51	60	64
Units: Participants				
Responders	13	11	18	20
Non-Responders	38	40	42	44

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) for 12 weeks
Treatment Emergent Signs and Symptoms (TESS) for 8 weeks

Adverse event reporting additional description:

TESS (collected from first drug intake at Visit 2 (randomisation) during the treatment period of 8 weeks) were analysed for the Safety Population (all patients who took at least one dose of study medication, N = 565).

Generally, Adverse Events were reported/patient for a period of 12 weeks (during the total individual study period).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Ibodutant 1mg

Reporting group description:

Ibodutant 1mg, oral tablet to be given once daily for 8 weeks of treatment.

Reporting group title	Ibodutant 3mg

Reporting group description:

Ibodutant 3mg, oral tablet to be given once daily for 8 weeks of treatment.

Reporting group title	Ibodutant 10mg

Reporting group description:

Ibodutant 10mg, oral tablet to be given once daily for 8 weeks of treatment.

Reporting group title	Placebo

Reporting group description:

Placebo, oral tablet to be given once daily for 8 weeks of treatment.

Serious adverse events	Ibodutant 1mg	Ibodutant 3mg	Ibodutant 10mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 141 (0.00%)	1 / 142 (0.70%)	1 / 139 (0.72%)
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)			
Uterus myomatosus			
subjects affected / exposed	0 / 141 (0.00%)	0 / 142 (0.00%)	0 / 139 (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			
Mydriasis			

subjects affected / exposed	0 / 141 (0.00%)	0 / 142 (0.00%)	0 / 139 (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			
Worsened abdominal pain			
subjects affected / exposed	0 / 141 (0.00%)	0 / 142 (0.00%)	0 / 139 (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			
Acute appendicitis			
subjects affected / exposed	0 / 141 (0.00%)	1 / 142 (0.70%)	0 / 139 (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 type II			
subjects affected / exposed	0 / 141 (0.00%)	0 / 142 (0.00%)	1 / 139 (0.72%)
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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 143 (2.10%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterus myomatosus			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Mydriasis			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Worsened abdominal pain			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acute appendicitis			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes Mellitus type II			
subjects affected / exposed	0 / 143 (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: 2 %

Non-serious adverse events	Ibodutant 1mg	Ibodutant 3mg	Ibodutant 10mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 141 (29.79%)	40 / 142 (28.17%)	42 / 139 (30.22%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 141 (2.13%)	0 / 142 (0.00%)	1 / 139 (0.72%)
occurrences (all)	3	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 141 (2.13%)	2 / 142 (1.41%)	1 / 139 (0.72%)
occurrences (all)	3	2	1
Headache			
subjects affected / exposed	7 / 141 (4.96%)	3 / 142 (2.11%)	8 / 139 (5.76%)
occurrences (all)	7	3	11
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 141 (0.71%)	2 / 142 (1.41%)	0 / 139 (0.00%)
occurrences (all)	1	2	0
Nausea			

subjects affected / exposed	1 / 141 (0.71%)	4 / 142 (2.82%)	5 / 139 (3.60%)
occurrences (all)	1	4	5
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 141 (0.00%)	2 / 142 (1.41%)	3 / 139 (2.16%)
occurrences (all)	0	2	3
Influenza			
subjects affected / exposed	0 / 141 (0.00%)	2 / 142 (1.41%)	3 / 139 (2.16%)
occurrences (all)	0	2	3
Nasopharyngitis			
subjects affected / exposed	5 / 141 (3.55%)	4 / 142 (2.82%)	5 / 139 (3.60%)
occurrences (all)	6	4	5
Upper respiratory tract infection			
subjects affected / exposed	0 / 141 (0.00%)	0 / 142 (0.00%)	3 / 139 (2.16%)
occurrences (all)	0	0	3

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 143 (20.28%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	4 / 143 (2.80%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 143 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	5 / 143 (3.50%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	3 / 143 (2.10%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	1 / 143 (0.70%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2010	substantial; effective in the Czech Republic modified inclusion criterion no 2 in such a way that all patients older than 50 years OR patients with positive family history of colorectal cancer had to have normal results from a colonoscopy or flexible sigmoidoscopy that has been performed after onset of IBS symptoms and within one year before Screening. Moreover, amendment required all Czech patients to have a documented negative IgA antibodies against tissue transglutaminase and endomysium within the last 24 months in order to ascertain the absence of gluten enteropathy
06 July 2010	substantial; effective in Germany modified inclusion criterion no 2 in such a way that all study participants, irrespective of their age, had to have normal results from colonoscopy or flexible sigmoidoscopy performed within the last 5 years and after the onset of IBS symptoms, and completed before Screening
12 July 2011	non-substantial, administrative became necessary because of the changes in responsibilities resulting from the fact that on July 12, 2011 INC Research, LLC, a therapeutically focused Contract Research Organization (CRO) privately held by Avista Capital Partners and Ontario Teachers' Pension Plan, announced its completed acquisition of Kendle International Inc.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27196574