Clinical trial results:
Peripheral Histamine 1 receptor blockage in Irritable Bowel Syndrome: multicentric trial

Summary

EudraCT number	2013-001199-39
Trial protocol	BE
Global end of trial date	02 November 2022

Results information

Result version number	v1 (current)
This version publication date	27 April 2025
First version publication date	27 April 2025
Summary attachment (see zip file)	Article ebastine vs. placebo (FINAL-PUBLISHED_artikel Lisse Decraecker.pdf)

Trial information

Trial identification

Sponsor protocol code	MulticenterEbastineIBS

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01908465
WHO universal trial number (UTN)	-
Other trial identifiers	EC UZ Leuven S-number: S55485

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium,
Public contact	TARGID, KU Leuven, guy.boeckxstaens@kuleuven.be
Scientific contact	TARGID, KU Leuven, guy.boeckxstaens@kuleuven.be

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	07 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Relief of global symptoms of Irritable Bowel Syndrome (IBS), as well as abdominal pain in IBS

Protection of trial subjects:

In case of troublesome side effects of an allergic reaction to the medicine used, the treatment was stopped immediately.
Every adverse event was reported in the eCRF.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2014
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	Netherlands: 22
Country: Number of subjects enrolled	Belgium: 181
Worldwide total number of subjects	203
EEA total number of subjects	203

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)	203
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from the outpatient clinic of the participating centers.

Pre-assignment

Screening details:

Inclusion criteria:
- Rome III criteria
- No organic cause of symptoms
- Age 18-65

Exclusion criteria:
- IBS constipation predominant
- history of coeliakie, lactose-intolerance, ...
- medication: anti-histaminics, antidepressants, antipsychotics
- symptoms started after operation in abdominal cavity

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ebastine

Arm description:

20 mg ebastine, once daily

Arm type	Experimental
Investigational medicinal product name	ebastine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

1 tablet/day (around the same time every day), 20mg

Arm title	Placebo

Arm description:

Placebo, once daily

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

Dosage and administration details:

1 tablet per day, around the same time every day

Number of subjects in period 1[1]	Ebastine	Placebo
Started	101	101
Completed	90	87
Not completed	11	14
Consent withdrawn by subject	3	3
Adverse event, non-fatal	2	2
Lost to follow-up	6	8
Lack of efficacy	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One patient was excluded from the baseline period full analysis set because of a diagnosis of bile acid diarrhea (= exclusion) after enrollment.

Baseline characteristics

Reporting groups	
Reporting group title	Ebastine
Reporting group description:	
20 mg ebastine, once daily	
Reporting group title	Placebo
Reporting group description:	
Placebo, once daily	

Reporting group values	Ebastine	Placebo	Total
Number of subjects	101	101	202
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	32	32	
standard deviation	± 12	± 11	-
Gender categorical			
Units: Subjects			
Female	68	70	138
Male	33	31	64

End points

End points reporting groups

Reporting group title	Ebastine
Reporting group description:	
20 mg ebastine, once daily	
Reporting group title	Placebo
Reporting group description:	
Placebo, once daily	

Subject analysis set title	IBS-D/ebastine
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients with IBS subtype diarrhea were evaluated for the effect of ebastine on stool consistency	
Subject analysis set title	IBS-D/placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients with IBS subtype diarrhea were evaluated for the effect of ebastine on stool consistency	

Primary: Responder rates for clinical response

End point title	Responder rates for clinical response

End point description:

1. Abdominal pain intensity (API): API was assessed daily using a 10-point Visual Analogue Scale. For each week, an average pain score of the worst abdominal pain per day was calcualated. Then, the change in weekly pain score was calculated from the average pain score recorded during the screening phase (baseline). An API weekly responder is defined as a subject who had a decrease of≥30% compared with baseline.
2. Global Relief of Symptoms (GRS): GRS was assessed weekly using a 6-point scale for 12 weeks during treatment and runout. A subject is considered as a GRS weekly responder if he/ she scores total or considerable relief of symptoms compared with baseline.
A study subject is considered as a weekly clinical responder for a particular week if the subject was both an API and GRS responder. Using this definition, a study subject will be defined as a 'clinical responder' if he/she is a weekly Clinical Responder for at least 6 of the 12 weeks of treatment.

End point type	Primary

End point timeframe:

API was assessed daily, for 12 weeks of treatment and run-out period.
GRS was assessed weekly, for 12 weeks of treatment and run-out period.

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	86		
Units: Subjects	22	13		

Statistical analyses

Statistical analysis title	RD - Clinical response rate FAS

Statistical analysis description:

Response rates and p values were determined using multiple imputation with 100 imputations to account for missing data.
FAS = full analysis set

Comparison groups	Ebastine v Placebo
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0471
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	15.2

Primary: Responder rate for GRS

End point title	Responder rate for GRS

End point description:

A subject was defined as a GRS responder if he/she reported total or obvious relief of symptoms compared with baseline for at least 6 of the 12 weeks of treatment.

End point type	Primary

End point timeframe:

GRS was assessed weekly, for 12 weeks of treatment and run-out period.

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	85		
Units: Subjects	22	17		

Statistical analyses

Statistical analysis title	RD -Global relief of symptoms response rate FAS

Statistical analysis description:

Response rates and p values were determined using multiple imputation with 100 imputations to account for missing data.
FAS = full analysis set

Comparison groups	Ebastine v Placebo

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0715
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	17.1

Primary: Responder rate for API

End point title	Responder rate for API

End point description:

An API-responder was defined as a patient who experienced an improvement in weekly average API of ≥30% compared with baseline for at least 6 of the 12 treatment weeks.

End point type	Primary

End point timeframe:

API was assessed daily, for 12 weeks of treatment and run-out period.

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	86		
Units: Subjects	48	32		

Statistical analyses

Statistical analysis title	RD Abdominal pain intensity response rate FAS
Comparison groups	Ebastine v Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0813
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	22.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	24.9

Secondary: IBS-D clinical responders

End point title	IBS-D clinical responders

End point description:

In line with the primary endpoint, IBS-D clinical responders are defined as subjects that were weekly responders for both stool consistency and API during at least 6 of the 12 treatment weeks.
A subject is considered a weekly responder for stool consistency if he/she experiences a ≥50% reduction in the number of days per week with at least one stool of type 6 or 7 on the BSFS compared with baseline.

End point type	Secondary

End point timeframe:

Stool consistency was assessed daily for 12 weeks of treatment and run-out period.

End point values	IBS-D/ebastine	IBS-D/placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	60		
Units: Subjects	10	4		

Statistical analyses

Statistical analysis title	Stool consistency and API response (IBS-D)
Comparison groups	IBS-D/placebo v IBS-D/ebastine
Number of subjects included in analysis	121
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1309
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	19

Secondary: IBS-D Stool consistency responder

End point title	IBS-D Stool consistency responder

End point description:

A subject is considered a weekly responder for stool consistency if he/she experiences a ≥50% reduction in the number of days per week with at least one stool of type 6 or 7 on the BSFS compared with baseline. A subject was a stool consistency responder if the subject was a weekly responder during at least 6 of the 12 treatment weeks.

End point type	Secondary

End point timeframe:

Stool consistency was assessed daily for 12 weeks of treatment and run-out.

End point values	IBS-D/ebastine	IBS-D/placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	59	60		
Units: Subjects	18	17		

Statistical analyses

Statistical analysis title	Stool consistency response (IBS-D) last 4 weeks
Comparison groups	IBS-D/ebastine v IBS-D/placebo
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8046
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	17.1

Secondary: HADS anxiety score

End point title	HADS anxiety score

End point description:

Mental health and health-related quality of life questionnaire scores were compared between treatment groups and adjusted for baseline values

End point type	Secondary

End point timeframe:

Filled out before and after treatment period (on visit 1 and visit 4)

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	85		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	0.00 (-2.00 to 2.00)	0.00 (-3.00 to 1.00)		

Statistical analyses

Statistical analysis title	Interaction clinical responder and HADS anxiety
Statistical analysis description:	
responder rates for 6 or more of the 12 treatment weeks for clinical response	
Comparison groups	Ebastine v Placebo
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7114
Method	Regression, Logistic

Secondary: HADS depression score

End point title	HADS depression score
End point description:	
Mental health and health-related quality of life questionnaire scores were compared between treatment groups and adjusted for baseline values	
End point type	Secondary
End point timeframe:	
Filled out before and after treatment period (on visit 1 and visit 4)	

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	86		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	0.00 (-2.00 to 1.00)	-1.00 (-2.00 to 0.00)		

Statistical analyses

Statistical analysis title	Interaction clinical responder - HADS depression
Statistical analysis description:	
responder rates for 6 or more of the 12 treatment weeks for clinical response	
Comparison groups	Placebo v Ebastine

Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.9146
Method	Regression, Logistic

Secondary: SF-36 General Health

End point title	SF-36 General Health

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	40 (30 to 63)	45 (30 to 60)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Bodily pain

End point title	SF-36 Bodily pain

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	45 (24 to 63)	48 (35 to 58)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Social functioning

End point title	SF-36 Social functioning

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	63 (38 to 75)	63 (50 to 75)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Mental health

End point title	SF-36 Mental health

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	66 (44 to 76)	64 (52 to 76)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Vitality

End point title	SF-36 Vitality

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	43 (30 to 60)	45 (30 to 55)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Role-emotional

End point title	SF-36 Role-emotional

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	100 (33 to 100)	100 (33 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Role-physical

End point title	SF-36 Role-physical

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	25 (0 to 100)	50 (0 to 75)		

Statistical analyses

No statistical analyses for this end point

Secondary: SF-36 Physical functioning

End point title	SF-36 Physical functioning

End point description:

End point type	Secondary

End point timeframe:

Median change between baseline and week 12

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: relative unit(s)				
median (inter-quartile range (Q1-Q3))	89 (78 to 95)	90 (75 to 95)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Responder rate for clinical response (3/6)

End point title	Responder rate for clinical response (3/6)

End point description:

3/6 refers to at least 3 out of the last 6 weeks of the treatment period

End point type	Post-hoc

End point timeframe:

API was assessed daily, for 12 weeks of treatment and run-out period.
GRS was assessed weekly, for 12 weeks of treatment and run-out period.

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	87		
Units: Subjects	18	8		

Statistical analyses

Statistical analysis title	RD - clinical responder (3/6)
Comparison groups	Ebastine v Placebo
Number of subjects included in analysis	176
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	= 0.0386
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	10.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	19.8

Post-hoc: Responder rate GRS (3/6)

End point title	Responder rate GRS (3/6)

End point description:

3/6 refers to at least 3 out of the last 6 weeks of the treatment period

End point type	Post-hoc

End point timeframe:

GRS was assessed weekly, for 12 weeks of treatment and run-out period

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	87		
Units: Subjects	18	11		

Statistical analyses

Statistical analysis title	GRS clinical responder (3/6)
Comparison groups	Placebo v Ebastine
Number of subjects included in analysis	174
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	= 0.1748
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	18.2

Post-hoc: Responder rate API (3/6)

End point title	Responder rate API (3/6)

End point description:

3/6 refers to at least 3 out of the last 6 weeks of the treatment period

End point type	Post-hoc

End point timeframe:

API was assessed daily, for 12 weeks of treatment and run-out period.

End point values	Ebastine	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	85		
Units: Subjects	46	28		

Statistical analyses

Statistical analysis title	RD - API responder (3/6)
Comparison groups	Ebastine v Placebo
Number of subjects included in analysis	177
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	= 0.0378
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	29

Post-hoc: Responder rate stool consistency (3/6)

End point title	Responder rate stool consistency (3/6)
End point description:	
3/6 refers to at least 3 out of the last 6 weeks of the treatment period	
End point type	Post-hoc
End point timeframe:	
Stool consistency was assessed daily for 12 weeks of treatment and run-out period.	

End point values	IBS-D/ebastine	IBS-D/placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	59	60		
Units: Subjects	23	21		

Statistical analyses

Statistical analysis title	RD - stool consistency responder (3/6)
Comparison groups	IBS-D/ebastine v IBS-D/placebo

Number of subjects included in analysis	119
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	= 0.651
Method	Chi-squared
Parameter estimate	Risk difference (RD)
Point estimate	3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.7
upper limit	20.1

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Every adverse event was reported in the eCRF in a timely manner. In case of a serious adverse event, the coördinating center was informed. In case of AEs leading to death, the ethical committee was also informed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Ebastine
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Ebastine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 101 (0.00%)	0 / 101 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Ebastine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 101 (12.87%)	21 / 101 (20.79%)	
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 101 (2.97%)	7 / 101 (6.93%)	
occurrences (all)	3	7	
Immune system disorders			
Allergic reaction	Additional description: Allergic reaction included skin rash, itching skin or eyes, sneezing and swelling of the throat.		
subjects affected / exposed	4 / 101 (3.96%)	5 / 101 (4.95%)	
occurrences (all)	4	5	
Respiratory, thoracic and mediastinal disorders			

Upper respiratory infection subjects affected / exposed occurrences (all)	6 / 101 (5.94%) 6	9 / 101 (8.91%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2014	Adding an advertisement to share on intranet and the notice boards of KULeuven en UZ Leuven.
30 October 2015	Informing regional general practitioners and recruiting patients from referral by general practitioners.
09 December 2016	To evaluate whether inflammatory mediators and/or metabolites in urine have a predictive value regarding therapeutic response, a urine sample was taken before and after treatment with the study medication.
01 May 2017	Open-label follow up with treatment of patients with 2x20mg of ebastine. After 8 and 12 weeks of treatment, patients were evaluated.
22 January 2020	Addition of site: ZNA Middelheim Antwerpen
22 January 2020	Addition of site: AZ Sint-Maarten

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/38191268