Clinical trial results:
A Randomised Dose-Optimisation Study to Evaluate the Efficacy and Safety of Cobitolimod in Moderate to Severe Active left-sided Ulcerative Colitis Patients- CONDUCT

Summary

EudraCT number	2016-004217-26
Trial protocol	DE HU SE ES CZ FR IT
Global end of trial date	30 August 2019

Results information

Result version number	v1 (current)
This version publication date	30 November 2020
First version publication date	30 November 2020

Trial information

Trial identification

Sponsor protocol code	CSUC-01/16

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03178669
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	InDex Pharmaceuticals AB
Sponsor organisation address	Berzeliusväg 13, Solna, Sweden, 171 65
Public contact	Karin Arnesson, InDex Pharmaceuticals AB, +46 8 122 038 57, karin.arnesson@indexpharma.com
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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	30 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 August 2019
Global end of trial reached?	Yes
Global end of trial date	30 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of cobitolimod treatment at different dose levels and frequencies compared to placebo with regard to clinical remission 6 weeks after first treatment, in patients with moderate to severe active left-sided ulcerative colitis (UC).

Protection of trial subjects:

The protocol, Informed Consent Form and recruitment material were approved by Independent Ethics Committee before study initiation. The study was conducted according to international scientific and ethical standards.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 April 2017
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	Poland: 31
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 13
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Romania: 6
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	Ukraine: 47
Worldwide total number of subjects	211
EEA total number of subjects	99

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)	177
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 91 sites in Czech Republic (2), France (9), Germany (10), Hungary (6), Italy (6), Poland (15), Romania (4), Russian Federation (15), Serbia (4), Spain (5), Sweden (1) and Ukraine (14). First Patient Randomized June 30, 2017 and Last Patient Randomized June 26, 2019

Pre-assignment

Screening details:

A total of 383 participants were screened, of these 213 participants were randomized in a 1:1:1:1:1 ratio and 211 patients received either cobitolimod 2 x 31 mg, 2 x 125 mg , 2 x 250 mg, 4 x 125 or placebo. In the treatment arms with 2 treatment occasions of cobitolimod, placebo was also given at 2 times to ensure the blindness of the study.

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, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Cobitolimod 2x31 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cobitolimod 2x31 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Participants were treated with an enema containing 31 mg cobitolimod at Week 0 and 3 and with an enema containing placebo at Week 1 and 2, to ensure the blindness of the study.

Arm title	Cobitolimod 2x125 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cobitolimod 2 x 125 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Participants were treated with an enema containing 125 mg cobitolimod at Week 0 and 3 and with an enema containing placebo at Week 1 and 2, to ensure the blindness of the study.

Arm title	Cobitolimod 2x250 mg

Arm description: -

Arm type	Experimental

Investigational medicinal product name	Cobitolimod 2 x 250 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Participants were treated with an enema containing 250 mg cobitolimod at Week 0 and 3 and with an enema containing placebo at Week 1 and 2, to ensure the blindness of the study.

Arm title	Cobitolimod 4x125 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cobitolimod 4 x 125 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Participants were treated with an enema containing 125 mg cobitolimod at Week 0, 1, 2 and 3.

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Rectal solution
Routes of administration	Rectal use

Dosage and administration details:

Participants were treated with an enema containing placebo at Week 0,1,2 and 3.

Number of subjects in period 1	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg
Started	40	43	42
Completed	35	42	35
Not completed	5	1	7
Adverse event, serious fatal	-	-	-
Physician decision	-	-	-
Participant decision to withdraw	1	-	-
Adverse event, non-fatal	4	1	4
Patients decision to withdraw from study	-	-	1
Lack of efficacy	-	-	2

Number of subjects in period 1	Cobitolimod 4x125 mg	Placebo
Started	42	44
Completed	38	40
Not completed	4	4

Adverse event, serious fatal	-	1
Physician decision	-	1
Participant decision to withdraw	-	-
Adverse event, non-fatal	3	1
Patients decision to withdraw from study	1	-
Lack of efficacy	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cobitolimod 2x31 mg
Reporting group description: -	
Reporting group title	Cobitolimod 2x125 mg
Reporting group description: -	
Reporting group title	Cobitolimod 2x250 mg
Reporting group description: -	
Reporting group title	Cobitolimod 4x125 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg
Number of subjects	40	43	42
Age categorical Units: Subjects			
Adults (18-64 years)	32	35	37
From 65-84 years	8	8	5
85 years and over	0	0	0
Age continuous Units: years			
median	46.5	51.0	44.0
standard deviation	± 16.38	± 16.87	± 14.94
Gender categorical Units: Subjects			
Female	14	23	16
Male	26	20	26
Race Units: Subjects			
Asian	0	1	1
White	39	42	40
Other	1	0	1
BMI Units: kg/m2			
median	24.7	24.9	24.7
standard deviation	± 4.54	± 4.65	± 3.70

Reporting group values	Cobitolimod 4x125 mg	Placebo	Total
Number of subjects	42	44	211
Age categorical Units: Subjects			
Adults (18-64 years)	35	38	177
From 65-84 years	7	6	34
85 years and over	0	0	0

Age continuous Units: years			
median	44.5	45.0	
standard deviation	± 14.94	± 15.38	-
Gender categorical Units: Subjects			
Female	18	11	82
Male	24	33	129
Race Units: Subjects			
Asian	2	2	6
White	39	42	202
Other	1	0	3
BMI Units: kg/m2			
median	23.8	26.0	
standard deviation	± 5.06	± 4.80	-

End points

End points reporting groups	
Reporting group title	Cobitolimod 2x31 mg
Reporting group description: -	
Reporting group title	Cobitolimod 2x125 mg
Reporting group description: -	
Reporting group title	Cobitolimod 2x250 mg
Reporting group description: -	
Reporting group title	Cobitolimod 4x125 mg
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Clinical Remission	
End point title	Clinical Remission
End point description:	
Proportion of patients with clinical remission at Week 6, defined by Modified Mayo sub scores, i) rectal bleeding of 0, ii) stool frequency of 0 or 1 (with at least one point decrease from Baseline, Week 0), and iii) endoscopy score of 0 or 1 (excluding friability).	
End point type	Primary
End point timeframe:	
Week 6	

End point values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg	Cobitolimod 4x125 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	42
Units: Frequency				
Yes	5	2	9	4
No	35	41	33	38

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Frequency				
Yes	3			
No	41			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Non Responder Imputation (NRI)

Comparison groups	Cobitolimod 2x31 mg v Placebo
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1806 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.75
upper limit	5.47
Variability estimate	Standard deviation

Notes:

[1] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Non Responder Imputation (NRI)

Comparison groups	Placebo v Cobitolimod 2x125 mg
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6649 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.2
upper limit	2.24
Variability estimate	Standard deviation

Notes:

[2] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Non Responder Imputation (NRI)

Comparison groups	Placebo v Cobitolimod 2x250 mg

Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0247 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.53
upper limit	9.47
Variability estimate	Standard deviation

Notes:

[3] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Non Responder Imputation (NRI)

Comparison groups	Placebo v Cobitolimod 4x125 mg
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3279 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.52
upper limit	3.88
Variability estimate	Standard deviation

Notes:

[4] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Secondary: Symptomatic Remission

End point title	Symptomatic Remission

End point description:

Proportion of patients with symptomatic remission at Week 6, defined by the Mayo sub scores, i) rectal bleeding of 0, ii) stool frequency of 0 or 1 (with at least one point decrease from Baseline, Week 0), (patient reported outcome) [PRO2]

End point type	Secondary

End point timeframe:

Week 6

End point values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg	Cobitolimod 4x125 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	42	37	40
Units: Frequency				
Yes	10	11	13	10
No	27	31	24	30

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Frequency				
Yes	9			
No	34			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Cobitolimod 2x31 mg v Placebo
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2335 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.74
upper limit	2.94
Variability estimate	Standard deviation

Notes:

[5] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x125 mg

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2511 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.73
upper limit	2.69
Variability estimate	Standard deviation

Notes:

[6] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x250 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1162 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.96
upper limit	3.52
Variability estimate	Standard deviation

Notes:

[7] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 4x125 mg

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3467 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.63
upper limit	2.4
Variability estimate	Standard deviation

Notes:

[8] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Secondary: Endoscopic Remission

End point title	Endoscopic Remission

End point description:

Proportion of patients with endoscopic remission at Week 6, defined by the Modified Mayo endoscopic sub score of 0 or 1 (excluding friability)

End point type	Secondary

End point timeframe:

Week 6

End point values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg	Cobitolimod 4x125 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	41	37	39
Units: Frequency				
Yes	7	5	15	10
No	27	36	22	29

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Frequency				
Yes	12			
No	28			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Cobitolimod 2x31 mg v Placebo
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7994 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.32
upper limit	1.27
Variability estimate	Standard deviation

Notes:

[9] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x125 mg
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9665 [10]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.16
upper limit	0.72
Variability estimate	Standard deviation

Notes:

[10] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x250 mg

Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2049 [11]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.8
upper limit	2.82
Variability estimate	Standard deviation

Notes:

[11] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 4x125 mg
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6504 [12]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.42
upper limit	1.6
Variability estimate	Standard deviation

Notes:

[12] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Secondary: Modified Clinical Remission

End point title	Modified Clinical Remission

End point description:

Proportion of patients with modified clinical remission at Week 6, defined by the Modified Mayo score ≤ 2 and sub scores, i) rectal bleeding of 0, ii) stool frequency of 0 or 1 (with at least one point decrease from Baseline, Week 0), iii) endoscopy score of 0 or 1 (excluding friability) and iiii) physician´s global assessment (PGA) of 0 or 1

End point type	Secondary

End point timeframe:

Week 6

End point values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg	Cobitolimod 4x125 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	41	35	39
Units: Frequency				
Yes	5	1	7	3
No	28	40	28	36

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Frequency				
Yes	3			
No	36			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Cobitolimod 2x31 mg v Placebo
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2115 [13]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.69
upper limit	4.99
Variability estimate	Standard deviation

Notes:

[13] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all

randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x125 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8498 [14]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.06
upper limit	1.34
Variability estimate	Standard deviation

Notes:

[14] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x250 mg
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0977 [15]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.01
upper limit	6.62
Variability estimate	Standard deviation

Notes:

[15] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 4x125 mg

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.522 [16]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.32
upper limit	2.84
Variability estimate	Standard deviation

Notes:

[16] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Secondary: Histological Remission

End point title	Histological Remission

End point description:

Proportion of patients with histological remission at Week 6, defined by the Nancy histological index of grade 0 or 1

End point type	Secondary

End point timeframe:

Week 6

End point values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg	Cobitolimod 4x125 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	41	37	39
Units: Frequency				
Yes	4	5	8	7
No	11	36	29	32

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Frequency				
Yes	10			
No	31			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Cobitolimod 2x31 mg v Placebo
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9207 [17]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.18
upper limit	0.93

Notes:

[17] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x125 mg
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9228 [18]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.4
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.19
upper limit	0.92

Notes:

[18] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x250 mg

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6636 [19]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.39
upper limit	1.61

Notes:

[19] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 4x125 mg
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7449 [20]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.7
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.34
upper limit	1.41

Notes:

[20] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Secondary: Clinical Response

End point title	Clinical Response

End point description:

Proportion of patients with clinical response at Week 6, defined as clinical remission or a three point and ≥30 % decrease from Baseline, Week 0 in the sum of the Modified Mayo score, i) rectal bleeding, ii) stool frequency and iii) endoscopy score (excluding friability), iiii) physicians global assessment (PGA)

End point type	Secondary

End point timeframe:

Week 6

End point values	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg	Cobitolimod 4x125 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	41	35	39
Units: Frequency				
Yes	17	18	20	15
No	16	23	15	24

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Frequency				
Yes	20			
No	19			

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x31 mg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6326 [21]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.5
upper limit	1.5

Notes:

[21] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x125 mg

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7127 [22]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.45
upper limit	1.37

Notes:

[22] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 2x250 mg
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2658 [23]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.75
upper limit	2.34

Notes:

[23] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

The full analysis set (FAS), will be based on the intention-to-treat (ITT) principles, which consists of all randomised patients who meet the inclusion criteria (as assessed by the investigator on the inclusion/exclusion criteria form), and receive at least one dose of the study drug (active or placebo). Missing data was replaced using Placebo Multiple Imputation (PMI)

Comparison groups	Placebo v Cobitolimod 4x125 mg
Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8301 [24]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.6

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.36
upper limit	1.16

Notes:

[24] - one-sided and adjusted for stratification factors, p values of less than 0.10 were regarded as statistically significant.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Collection of AEs started directly after the Informed Consent Form was signed. During the screening period only AEs related to study procedure was reported. Patient was asked at each visits if any AEs had occurred.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Cobitolimod 2x31 mg

Reporting group description:

Participants were treated with 31 mg cobitolimod at Week 0 and 3 and with placebo at Week 1 and 2 to ensure the blindness of the study.

Reporting group title	Cobitolimod 2x125 mg

Reporting group description:

Participants were treated with 125 mg cobitolimod at Week 0 and 3 and with placebo at Week 1 and 2 to ensure the blindness of the study.

Reporting group title	Cobitolimod 2x250 mg

Reporting group description:

Participants were treated with 250 mg cobitolimod at Week 0 and 3 and with placebo at Week 1 and 2 to ensure the blindness of the study.

Reporting group title	Cobitolimod 4x125 mg

Reporting group description:

Participants were treated with 125 mg cobitolimod at Week 0, 1, 2 and 3.

Reporting group title	Placebo

Reporting group description:

Participants were treated with placebo at Week 0, 1, 2 and 3.

Serious adverse events	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 40 (5.00%)	0 / 43 (0.00%)	4 / 42 (9.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Wound dehiscence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Deep vein thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 40 (5.00%)	0 / 43 (0.00%)	3 / 42 (7.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (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
Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cobitolimod 4x125 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 42 (4.76%)	2 / 44 (4.55%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			

Wound dehiscence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 42 (0.00%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 42 (2.38%)	2 / 44 (4.55%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin and subcutaneous tissue disorders			
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 42 (2.38%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cobitolimod 2x31 mg	Cobitolimod 2x125 mg	Cobitolimod 2x250 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 40 (12.50%)	12 / 43 (27.91%)	8 / 42 (19.05%)
Investigations			
Faecal calprotectin increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 40 (5.00%)	0 / 43 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	5 / 43 (11.63%)	2 / 42 (4.76%)
occurrences (all)	0	5	2
General disorders and administration site conditions			
Colitis ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 40 (10.00%)	5 / 43 (11.63%)	7 / 42 (16.67%)
occurrences (all)	5	5	8
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 40 (2.50%)	1 / 43 (2.33%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Infections and infestations			
Viral upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 40 (0.00%)	1 / 43 (2.33%)	2 / 42 (4.76%)
occurrences (all)	0	1	2

Non-serious adverse events	Cobitolimod 4x125 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 42 (23.81%)	11 / 44 (25.00%)	
Investigations			
Faecal calprotectin increased			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 42 (2.38%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 42 (4.76%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Colitis ulcerative			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 42 (7.14%)	5 / 44 (11.36%)	
occurrences (all)	4	6	
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 42 (4.76%)	3 / 44 (6.82%)	
occurrences (all)	2	4	
Infections and infestations			
Viral upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 42 (4.76%)	4 / 44 (9.09%)	
occurrences (all)	2	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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/33031757