



Clinical trial results:

Effect of Beclometasone dipropionate (BDP) on faecal Calprotectin levels in patients with clinically inactive Ulcerative Colitis at risk of relapse. BeCalCU study

Summary

EudraCT number	2017-000330-61
Trial protocol	ES
Global end of trial date	01 June 2021

Results information

Result version number	v1 (current)
This version publication date	19 October 2022
First version publication date	19 October 2022

Trial information

Trial identification

Sponsor protocol code	CHI-DIP-2016-01
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Chiesi España S.A.U.
Sponsor organisation address	Torre Realia BCN - Plaça d'Europa, 41-43, planta 10, Barcelona, Spain, 08908
Public contact	Chiesi España, Chiesi España S.A.U., 0034 934 94 80 00,
Scientific contact	Medical Advisor - Special Care, Marta López Sanromà , 0034 934 948 000,

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	15 September 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the superiority of oral BDP over placebo in reducing FCP levels below 100 µg/g after 4 weeks of treatment in patients with clinical remission and at risk of relapse* who are receiving 5-ASA therapy.)

Protection of trial subjects:

This clinical trial was conducted in accordance with the protocol, the principles established in the revised version of the Declaration of Helsinki regarding medical research in humans (64 General Assembly, Fortaleza, Brazil, 2013), and the Harmonized Tripartite Guidelines of the International Conference on Harmonisation (ICH) for Good Clinical Practice 1996. Likewise, it was carried out in accordance with the applicable regulatory requirements, in particular Royal Decree 1090/2015 and Regulation (EU) 536/2014, regulating clinical trials with medicinal products in Spain and the European Union, respectively, and Law 14/2007, on biomedical research. The study started once approval was available from the CREC, as well as from the Spanish Agency for Medicinal Products and Medical Devices (AEMPS). Each patient invited to participate in the study was given a written document called the "Patient Information Sheet", which contained the relevant and necessary information about the nature of the study, its objectives and procedures, the potential benefits and risks for the patient, as well as the guarantee of personal data protection. This document reflected the voluntary nature of patient participation in the study, and fully and unequivocally indicated the possibility of refusing to participate and of withdrawing consent at any time and for any reason, without having to justify the decision, and without the decision affecting his/her subsequent medical treatment and follow-up, or his/her relationship with the treating physician.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2017
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	Spain: 43
Worldwide total number of subjects	43
EEA total number of subjects	43

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)	37
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

91 patients recruited from 12 Spanish sites since 15 July 2017

Pre-assignment

Screening details:

Patients with 18 years old diagnosed with left-side or extended ulcerative colitis at least one year before, in clinical remission at the screening visit, with central laboratory confirmed FCP levels > 250 ug/g and treated with 5-ASA for at least 4 weeks prior to the screening visit. Patients without presence of a stoma or prior colon resection.

Period 1

Period 1 title	Part I
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Patients were treated for 4 weeks with 5 mg/day of BDP orally.

Arm type	Experimental
Investigational medicinal product name	Beclomethasone dipropionate (BDP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

BDP dose is 5 mg/day and it was administrated orally.

Arm title	Group B
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Arm description:

Patients will be treated for 4 weeks with placebo orally.

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:

Placebo dose is 5 mg/day and was administrated orally.

Number of subjects in period 1	Group A	Group B
Started	22	21
Completed	22	17
Not completed	0	4
premature withdrawal	-	4

Period 2

Period 2 title	Part II
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Single arm (group A)

Arm description:

During part II, patients were also treated for 4 weeks with 5 mg/day of BDP, administered orally. Patients with fecal calprotectin values > 100 ug/g after 4 weeks of treatment who came from group A of part I (BDP treated) of the study.

Arm type	Experimental
Investigational medicinal product name	Beclomethasone dipropionate (BDP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

BDP dose is 5 mg/day and it was administrated orally.

Arm title	Single arm (group B)
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Arm description:

During part II, patients were also treated for 4 weeks with 5 mg/day of BDP, administered orally. Patients with fecal calprotectin values > 100 ug/g after 4 weeks of treatment who came from group B of part I (placebo treated) of the study.

Arm type	Experimental
Investigational medicinal product name	Beclomethasone dipropionate (BDP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

BDP dose is 5 mg/day and it was administrated orally.

Number of subjects in period 2 ^[1]	Single arm (group A)	Single arm (group B)
Started	9	14
Completed	9	14

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: According to the protocol, 16 patients obtained fecal calprotectin values < 100 ug/g after 4 weeks of treatment and therefore completed the study and did not initiate part II.

Baseline characteristics

Reporting groups

Reporting group title	Group A
Reporting group description:	
Patients were treated for 4 weeks with 5 mg/day of BDP orally.	
Reporting group title	Group B
Reporting group description:	
Patients will be treated for 4 weeks with placebo orally.	

Reporting group values	Group A	Group B	Total
Number of subjects	22	21	43
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	49.6	48.4	
standard deviation	± 12.4	± 12.9	-
Gender categorical			
Units: Subjects			
Female	6	7	13
Male	16	14	30
Cormobilities			
Patients may have more than one cormobility at the same time.			
Units: Subjects			
Infectious disease	1	0	1
Cardiovascular disease	1	3	4
Musculoskeletal disorders	0	1	1
Gastrointestinal disorder	1	3	4
Neurological/psychiatric disorder	3	1	4
Haematological disorder	1	0	1
Respiratory disease	1	2	3
Renal impairment	0	1	1
Endocrine disorder	1	3	4
Other comorbidities	3	4	7
None	10	3	13
Extent of ulcerative colitis			
Units: Subjects			
Left side	7	16	23
Extensive	15	5	20
Number of patients currently being treated for ulcerative colitis			
Units: Subjects			
No	0	0	0
Yes	22	21	43
Number of patients who received oral 5-ASA			
Units: Subjects			

No	0	2	2
Yes	22	19	41
Number of patients who received topical 5-ASA Units: Subjects			
No	8	13	21
Yes	14	8	22
Number of patients who received oral corticosteroids Units: Subjects			
No	14	11	25
Yes	8	9	17
Unknown	0	1	1
Number of patients who received azathioprine Units: Subjects			
No	19	18	37
Yes	3	2	5
Unknown	0	1	1
Partial Mayo Score, Item 1. Stool frequency Units: Subjects			
Normal	19	17	36
1-2 more than usual	3	4	7
Partial Mayor Score, Item 2. Rectal bleeding Units: Subjects			
No	22	21	43
Yes	0	0	0
Partial Mayo Score, Item 3. Physician's global assessment Units: Subjects			
Normal	19	19	38
Mild disease	3	2	5
Time from diagnosis of ulcerative colitis Units: years arithmetic mean standard deviation	10.6 ± 8.6	7.6 ± 8.7	-
Time from last relapse to signing of informed consent Units: years arithmetic mean standard deviation	1.7 ± 1.7	1.7 ± 2.1	-
Time from last colonoscopy to signing of informed consent Units: Years arithmetic mean standard deviation	2.0 ± 1.9	1.2 ± 1.8	-
Number of relapses in the last two years Units: Years arithmetic mean standard deviation	1.0 ± 0.8	1.2 ± 0.4	-
Faecal calprotectin in last 60 days Units: mg/kg			

arithmetic mean standard deviation	899.9 ± 699.0	1255.5 ± 788.1	-
Systolic blood pressure Units: mmHg arithmetic mean standard deviation	133.2 ± 21.1	130.6 ± 17.9	-
Diastolic blood pressure Units: mmHg arithmetic mean standard deviation	83.2 ± 11.3	76.5 ± 9.8	-
Pulse Units: Pulse/ min arithmetic mean standard deviation	80.6 ± 14.6	72.0 ± 10.9	-
Mean Partial Mayo Score Units: score arithmetic mean standard deviation	0.3 ± 0.6	0.3 ± 0.6	-

End points

End points reporting groups

Reporting group title	Group A
Reporting group description: Patients were treated for 4 weeks with 5 mg/day of BDP orally.	
Reporting group title	Group B
Reporting group description: Patients will be treated for 4 weeks with placebo orally.	
Reporting group title	Single arm (group A)
Reporting group description: During part II, patients were also treated for 4 weeks with 5 mg/day of BDP, administered orally. Patients with fecal calprotectin values > 100 ug/g after 4 weeks of treatment who came from group A of part I (BDP treated) of the study.	
Reporting group title	Single arm (group B)
Reporting group description: During part II, patients were also treated for 4 weeks with 5 mg/day of BDP, administered orally. Patients with fecal calprotectin values > 100 ug/g after 4 weeks of treatment who came from group B of part I (placebo treated) of the study.	

Primary: Patients with FCP levels < 100 µg/g after 4 weeks

End point title	Patients with FCP levels < 100 µg/g after 4 weeks
End point description: To evaluate the superiority of oral BDP over placebo in reducing FCP levels below 100 µg/g after 4 weeks of treatment in patients with clinical remission and at risk of relapse* who are receiving 5-ASA therapy.	
End point type	Primary
End point timeframe: After 4 weeks of treatment (at week 5)	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[1]		
Units: patients	13	3		

Notes:

[1] - 4 patients were prematurely withdrawn

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Group A v Group B

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Fisher exact

Primary: FCP values at week 5

End point title	FCP values at week 5
End point description: To evaluate the superiority of oral BDP over placebo in reducing FCP levels below 100 µg/g after 4 weeks of treatment in patients with clinical remission and at risk of relapse* who are receiving 5-ASA therapy.	
End point type	Primary
End point timeframe: After 4 weeks of treatment (at week 5)	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[2]		
Units: ug/g				
arithmetic mean (standard deviation)	150 (± 158)	512 (± 497)		

Notes:

[2] - 4 patients were prematurely withdrawn

Statistical analyses

Statistical analysis title	Wilcoxon rank-sum test
Comparison groups	Group A v Group B
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Wilcoxon (Mann-Whitney)

Secondary: Patients with FCP levels < 100 µg/g after 8 weeks

End point title	Patients with FCP levels < 100 µg/g after 8 weeks
End point description: To evaluate the effect of oral BDP on the reduction of FCP levels to below 100 µg/g after 8 weeks of treatment.	
End point type	Secondary
End point timeframe: After 8 weeks of treatment (at week 9)	

End point values	Single arm (group A)	Single arm (group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8 ^[3]	13 ^[4]		
Units: patients	2	5		

Notes:

[3] - One missing data

[4] - One missing data

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Single arm (group A) v Single arm (group B)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.656
Method	Fisher exact

Secondary: FCP values at week 9

End point title	FCP values at week 9
End point description:	To evaluate the effect of oral BDP on the reduction of FCP levels to below 100 µg/g after 8 weeks of treatment.
End point type	Secondary
End point timeframe:	After 8 weeks of treatment (week 9)

End point values	Single arm (group A)	Single arm (group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	13		
Units: ug/g				
arithmetic mean (standard deviation)	426 (± 501)	214 (± 212)		

Statistical analyses

Statistical analysis title	Wilcoxon rank-sum test
Comparison groups	Single arm (group A) v Single arm (group B)

Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.491
Method	Wilcoxon (Mann-Whitney)

Secondary: FCP values at week 9 (LOFCP)

End point title	FCP values at week 9 (LOFCP)
End point description: To evaluate the effect of oral BDP on the reduction of FCP levels to below 100 µg/g after 8 weeks of treatment. Data referred to the last observation of FCP (LOFCP) values for each patient.	
End point type	Secondary
End point timeframe: After 8 weeks of treatment (at week 9)	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[5]		
Units: ug/g				
arithmetic mean (standard deviation)	195 (± 344)	244 (± 318)		

Notes:

[5] - 4 patients were prematurely withdrawal

Statistical analyses

Statistical analysis title	Wilcoxon rank-sum test
Comparison groups	Group B v Group A
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.327
Method	Wilcoxon (Mann-Whitney)

Secondary: Patients with FCP levels < 100 µg/g after 8 weeks (LOFCP)

End point title	Patients with FCP levels < 100 µg/g after 8 weeks (LOFCP)
End point description:	
End point type	Secondary
End point timeframe: After 8 weeks of treatment (at week 9)	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[6]		
Units: patients	15	8		

Notes:

[6] - 4 patients prematurely withdrawn

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Group B v Group A
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.209
Method	Fisher exact

Secondary: Patients with FCP levels < 150 µg/g after 4 weeks

End point title	Patients with FCP levels < 150 µg/g after 4 weeks
End point description:	Effect of BPD in reducing FCP levels below 150 µg/g versus placebo.
End point type	Secondary
End point timeframe:	After 4 weeks of treatment (week 5)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[7]		
Units: patients	14	4		

Notes:

[7] - 4 patients prematurely withdrawn

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Group A v Group B

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Fisher exact

Secondary: Patients with FCP levels < 150 µg/g after 8 weeks

End point title	Patients with FCP levels < 150 µg/g after 8 weeks
End point description:	
End point type	Secondary
End point timeframe:	
After 8 weeks of treatment (week 9)	

End point values	Single arm (group A)	Single arm (group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8 ^[8]	13 ^[9]		
Units: patients	3	6		

Notes:

[8] - One missing data

[9] - One missing data

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Single arm (group A) v Single arm (group B)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Fisher exact

Secondary: Patients with FCP levels < 150 µg/g after 8 weeks (LOFCP)

End point title	Patients with FCP levels < 150 µg/g after 8 weeks (LOFCP)
End point description:	
Data referred to the last observation of FCP (LOFCP) values for each patient	
End point type	Secondary
End point timeframe:	
After 8 weeks of treatment (week 9)	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: patients	16	9		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Group A v Group B
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.314
Method	Fisher exact

Secondary: Patients with FCP levels < 50 µg/g after 4 weeks

End point title	Patients with FCP levels < 50 µg/g after 4 weeks
End point description:	Effect of BPD in reducing FCP levels to below 50µg/g versus placebo was studied.
End point type	Secondary
End point timeframe:	After 4 weeks of treatment (week 5)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[10]		
Units: patients	6	2		

Notes:

[10] - 4 patients prematurely withdrawn

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Group A v Group B
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.426
Method	Fisher exact

Secondary: Patients with FCP levels < 50 µg/g after 8 weeks

End point title	Patients with FCP levels < 50 µg/g after 8 weeks
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End point description:

End point type	Secondary
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End point timeframe:

After 8 weeks of treatment (week 9)

End point values	Single arm (group A)	Single arm (group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8 ^[11]	13 ^[12]		
Units: patients	1	3		

Notes:

[11] - One missing data

[12] - One missing data

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Single arm (group B) v Single arm (group A)
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Fisher exact

Secondary: Patients with FCP levels < 50 µg/g after 8 weeks (LOFCP)

End point title	Patients with FCP levels < 50 µg/g after 8 weeks (LOFCP)
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End point description:

Data referred to the last observation of FCP (LOFCP) values for each patient

End point type	Secondary
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End point timeframe:

After 8 weeks of treatment (week 9)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: patients	7	5		

Statistical analyses

Statistical analysis title	Fisher's exact test
Comparison groups	Group A v Group B
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999
Method	Fisher exact

Secondary: FCP reduction

End point title	FCP reduction
End point description: Differences between treatment groups in FCP reduction between week 5 and baseline and between week 9 and baseline. Na and Nb are the number of patients analyse in groups A and B, respectively.	
End point type	Secondary
End point timeframe: Different timepoints	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[13]	17 ^[14]		
Units: ug/g				
arithmetic mean (standard deviation)				
W5-baseline (Na=22; Nb=17)	472 (± 396)	119 (± 505)		
W9-baseline (Na=8; Nb=13)	168 (± 512)	497 (± 420)		
W9-baseline (LOFCP) (Na=22; Nb=17)	426 (± 499)	387 (± 468)		

Notes:

[13] - Na y Nb indicates number of patients analyse in group A and group B, respectively.

[14] - Na y Nb indicates number of patients analyse in group A and group B, respectively.

Statistical analyses

Statistical analysis title	Wilcoxon rank-sum test
Comparison groups	Group A v Group B
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Wilcoxon (Mann-Whitney)

Secondary: Partial Mayo Score at week 5

End point title	Partial Mayo Score at week 5
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End point description:

Categorised score (< 4 and ≥ 4 points) obtained from the Partial Mayo Score after 5 weeks of treatment.

End point type	Secondary
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End point timeframe:

After 4 weeks of treatment

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17 ^[15]		
Units: patients				
< 4	22	17		
≥ 4	0	0		

Notes:

[15] - 4 patients prematurely withdrawn

Statistical analyses

No statistical analyses for this end point

Secondary: Partial Mayo Score at week 9

End point title	Partial Mayo Score at week 9
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End point description:

Categorised score (< 4 and ≥ 4 points) obtained from the Partial Mayo Score after 9 weeks of treatment.

End point type	Secondary
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End point timeframe:

After 8 weeks of treatment

End point values	Single arm (group A)	Single arm (group B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	13 ^[16]		
Units: patients				
< 4	9	13		
≥ 4	0	0		

Notes:

[16] - One missing data

Statistical analyses

No statistical analyses for this end point

Secondary: Partial Mayo Score at week 16 or 21

End point title	Partial Mayo Score at week 16 or 21
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End point description:

Categorised score (< 4 and ≥ 4 points) obtained from the Partial Mayo Score 3 months after the end of treatment (week 16 or week 21).

End point type	Secondary
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End point timeframe:

3 month after the end of treatment

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	15		
Units: patients				
< 4	20	15		
≥ 4	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: FCP reduction three months after the end of the treatment

End point title	FCP reduction three months after the end of the treatment
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End point description:

Effect of BDP in modifying the FCP levels three months after the end of the treatment.

End point type	Secondary
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End point timeframe:

3 months after the end of the treatment (weeks 16 or 21)

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 ^[17]	17 ^[18]		
Units: ug/g				
arithmetic mean (standard deviation)				
Original population (Na=19; Nb=15)	253 (± 588)	182 (± 527)		
LOFCP population (Na=22; Nb=17)	254 (± 591)	137 (± 539)		

Notes:

[17] - Na and Nb indicates patients analysed in groups A and B respectively in each population

[18] - Na and Nb indicates patients analysed in groups A and B respectively in each population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Parts I and II of the study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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Reporting groups

Reporting group title	Safety population: group A
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Reporting group description: -

Reporting group title	Safety population: group B
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Reporting group description: -

Serious adverse events	Safety population: group A	Safety population: group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Ulcerative gastritis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 21 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Safety population: group A	Safety population: group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 22 (31.82%)	10 / 21 (47.62%)	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 22 (4.55%)	1 / 21 (4.76%)	
occurrences (all)	2	1	
General disorders and administration site conditions			

Influenza-like illness subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Gastrointestinal disorders			
Ulcerative colitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 21 (9.52%) 2	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 21 (4.76%) 1	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Abdominal pain subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 21 (4.76%) 1	
Toothache subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 21 (4.76%) 1	
Constipation subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Anal fissure subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Flatulence subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Haematochezia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	1 / 21 (4.76%) 1	
Rectal haemorrhage subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 21 (4.76%) 1	
Nausea			

subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 21 (4.76%) 1	
Respiratory, thoracic and mediastinal disorders Common cold subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 21 (4.76%) 1	
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	2 / 21 (9.52%) 2	
Cough subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 21 (4.76%) 1	
Productive cough subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 21 (4.76%) 1	
Skin and subcutaneous tissue disorders Dermatitis acneiform subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	
Infections and infestations Influenza subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1	0 / 21 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2017	Extension of 3 months in the follow-up of patients in order to assess whether the clinical benefit is maintained over time, as well as to determine disease relapses (if any).
12 February 2018	In order to facilitate patient recruitment, the decision is made to: - Remove inclusion criterion 4. - Extend the time period between Visits 1 and 2, adjusting more realistically to the times required to obtain the results of the FCP test. - Modify inclusion criterion 5 by extending the time period in which an available FCP value is required in the patient clinical history to 60 days.
19 November 2018	Addition of 4 sites: - Hospital Universitario Josep Trueta de Girona - Complejo Hospitalario de Ferrol - Hospital Clínico Universitario de Valencia - Hospital Parc Taulí
03 March 2020	The following modifications are made to facilitate recruitment and to better adapt to clinical practice at the sites: - Only the FCP levels of the central laboratory are considered. - Patients receiving thiopurines (azathioprine and mercaptopurine) are accepted. - Addition of sites. In addition, corrections of errata and administrative changes are made

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported