Clinical trial results:
A Phase 2a, Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled Trial of IBD98-M Delayed-release Capsules to Induce Remission in Patients with Active, Mild to Moderate Ulcerative Colitis

Summary

EudraCT number	2015-001022-42
Trial protocol	IT
Global end of trial date	02 July 2018

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021
Summary attachment (see zip file)	holystone-ibd98-m-2002-synopsis (holystone-ibd98-m-2002-synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	IBD98-M-2002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02196662
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Holy Stone Healthcare Co., Ltd
Sponsor organisation address	Neihu road, Taipei, Taiwan,
Public contact	Clinical Trials Information, Holy Stone Biotech Co., Ltd., +41 22 704 0545, info@hsbiotech.co.uk
Scientific contact	Clinical Trials Information, Holy Stone Biotech Co., Ltd., +41 22 704 0545, info@hsbiotech.co.uk

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	27 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2018
Global end of trial reached?	Yes
Global end of trial date	02 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the percentage of patients in UC remission at Week 6 for each of the 2 IBD98-M dose groups versus placebo (remission defined as the modified Ulcerative Colitis Disease Activity Index [UCDAI] score of ≤1, with a score of 0 for rectal bleeding and stool frequency, no mucosal friability, and sigmoidoscopy score not exceeding 1)

Protection of trial subjects:

In case of injury or disease further to your participation in this study, you will receive appropriate medical care. The Holy Stone Healthcare is committed to cover all medical costs not covered by the provincial health plan or your private medical insurance (if any).

If you suffer a serious or lasting injury as a result of participation in this study, it may affect your ability to obtain private health insurance, your employability, and/or quality of life. No compensation other than that mentioned in this Informed Consent Form will routinely be offered.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2015
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	Italy: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	41
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients having a score of ≥ 4 and ≤ 10 on the modified UCDAI and a score of ≥ 1 on the endoscopy mucosal appearance subscore were enrolled in the study.

Pre-assignment

Screening details:

During the screening period, patients will be evaluated by conducting laboratory tests, physical examination, and sigmoidoscopy. To be eligible, patients are to have a score of ≥4 and ≤10 on the modified UCDAI, and a score of ≥1 on the modified UCDAI endoscopy subscore. In addition, the diagnosis of UC must be confirmed by endoscopic and histolog

Pre-assignment period milestones

Number of subjects started	51
Number of subjects completed	51

Period 1

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

Blinding implementation details:

double dummy techniques

Arms

Are arms mutually exclusive?	Yes
Arm title	High dose arm of IBD98-M

Arm description:

1.2 g/day

Arm type	Experimental
Investigational medicinal product name	IBD98-M
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1.2 g/day, 6 capsules/day

Arm title	Lower dose arm of IBD98-M

Arm description:

0.8 g/day

Arm type	Experimental
Investigational medicinal product name	IBD98-M low dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.8 g/day, total 4 capsules/day

Arm title	Placebo

Arm description:

No HA and mesalamine enteric coated pellets filled in a capsule

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

Dosage and administration details:

6 capsules/day

Number of subjects in period 1	High dose arm of IBD98-M	Lower dose arm of IBD98-M	Placebo
Started	16	17	18
Completed	14	11	12
Not completed	2	6	6
Consent withdrawn by subject	1	2	-
Physician decision	-	-	1
Lost to follow-up	1	-	-
Lack of efficacy	-	3	5
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	High dose arm of IBD98-M
Reporting group description:	
1.2 g/day	
Reporting group title	Lower dose arm of IBD98-M
Reporting group description:	
0.8 g/day	
Reporting group title	Placebo
Reporting group description:	
No HA and mesalamine enteric coated pellets filled in a capsule	

Reporting group values	High dose arm of IBD98-M	Lower dose arm of IBD98-M	Placebo
Number of subjects	16	17	18
Age categorical			
Demographic and baseline characteristics will be summarized using descriptive statistics for each treatment group and overall for the safety population.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	17	17
From 65-84 years	1	0	1
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	9	5	9
Male	7	12	9

Reporting group values	Total		
Number of subjects	51		
Age categorical			
Demographic and baseline characteristics will be summarized using descriptive statistics for each treatment group and overall for the safety population.			
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)	49		

From 65-84 years	2		
85 years and over	0		

Gender categorical Units: Subjects			
Female	23		
Male	28		

Subject analysis sets

Subject analysis set title	Subject enroll_ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The safety population will include all randomized patients who receive at least 1 dose of study drug. The treatment group assignment in this population will be defined by the treatment actually received. This population will be used for the analysis of safety.

Reporting group values	Subject enroll_ITT		
Number of subjects	51		
Age categorical			
Demographic and baseline characteristics will be summarized using descriptive statistics for each treatment group and overall for the safety population.			
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)	49		
From 65-84 years	2		
85 years and over	0		
Gender categorical Units: Subjects			
Female	23		
Male	28		

End points

End points reporting groups

Reporting group title	High dose arm of IBD98-M
Reporting group description:	
1.2 g/day	
Reporting group title	Lower dose arm of IBD98-M
Reporting group description:	
0.8 g/day	
Reporting group title	Placebo
Reporting group description:	
No HA and mesalamine enteric coated pellets filled in a capsule	
Subject analysis set title	Subject enroll_ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The safety population will include all randomized patients who receive at least 1 dose of study drug. The treatment group assignment in this population will be defined by the treatment actually received. This population will be used for the analysis of safety.	

Primary: The percentage of patients in remission at Week 6.

End point title	The percentage of patients in remission at Week 6.
End point description:	
To compare the percentage of patients in ulcerative colitis (UC) remission at Week 6 for each of the 2 IBD98-M dose groups versus placebo (remission defined as the modified Ulcerative Colitis Disease Activity Index [UCDAI] score of ≤1, with a score of 0 for rectal bleeding and stool frequency, no mucosal friability, and sigmoidoscopy score not exceeding 1)	
End point type	Primary
End point timeframe:	
6 weeks	

End point values	High dose arm of IBD98-M	Lower dose arm of IBD98-M	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	18	
Units: percentage	13	6	11	

Statistical analyses

Statistical analysis title	Primary Efficacy Analysis:
Statistical analysis description:	
The percentage of patients in remission at Week 6 is summarized for the ITT population	
Comparison groups	Lower dose arm of IBD98-M v High dose arm of IBD98-M v Placebo

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Fisher exact

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

6 weeks

Adverse event reporting additional description:

The safety endpoints include:
Treatment-Emergent Adverse Events (TEAEs)
Serious Adverse Events (SAEs)
Physical examination findings
Vital signs
Clinical laboratory parameters (including chemistry, hematology, coagulation, and urinalysis)
Electrocardiograms (ECGs).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	IBD98-M 1.2 g/day

Reporting group description:

1.2 g/day

Reporting group title	IBD98-M 0.8 g/day

Reporting group description:

0.8 g/day

Reporting group title	Placebo

Reporting group description:

No HA and Mesalamine enteric coated pellets filled in a capsule

Serious adverse events	IBD98-M 1.2 g/day	IBD98-M 0.8 g/day	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	IBD98-M 1.2 g/day	IBD98-M 0.8 g/day	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There are no non-serious adverse events recorded for these results as the disease of patient is not considered as severe.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2017	the Substantial Amendment to the IBD98-M-2002 Protocol Amendment 3 dated 09 May 2017 (Amendment Code 201500102242-003), according to the Law Decree n. 211 dated 24 June 2003, the Law Decree n. 200 dated 6 November 2007 and the Law n. 189 dated 8 November 2012.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported