Clinical trial results:
Multicentric, double-blind, placebo controlled clinical trial with 5-hydroxytryptophan (5-HTP) in patients with inflammatory bowel disease in clinical and biologic remission: effect on fatigue scores

Summary

EudraCT number	2017-005059-10
Trial protocol	BE
Global end of trial date	03 March 2021

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	Trp-IBD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03574948
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospital of Ghent
Sponsor organisation address	C. Heymanslaan 10, Ghent, Belgium, 9000
Public contact	Bimetra Clinics, Ghent University Hospital, +32 9332 0500, anneleen.peeters@uzgent.be
Scientific contact	Bimetra Clinics, Ghent University Hospital, 093321073 9332 0500, anneleen.peeters@uzgent.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	06 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 March 2021
Global end of trial reached?	Yes
Global end of trial date	03 March 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the effect of oral 5-HTP on the global fatigue score self-reported by patient (VAS)

Protection of trial subjects:

Ethics review and approval, informed consent, supportive care and routine monitoring.

Background therapy:

The subject is treated with biologicals and/or immunosuppressiva since at least 6 months with stable dose over last 3 months

Evidence for comparator: -

Actual start date of recruitment	01 August 2018
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	Belgium: 166
Worldwide total number of subjects	166
EEA total number of subjects	166

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)	166
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrollment occurred between December 2018 and November 2020 at 13 sites across Belgium

Pre-assignment

Screening details:

The subject is male or female and aged 18 to 60 yrs (inclusive), has CD or CU, is in clinical remission at day 0 based on validated scores (SCCAI ≤ 2 for CU or Harvey Bradshaw index ≤ 4 for CD), reports fatigue on a quantified scale (visual analogue scale 0 – 10) of 5 or more, treated with biologicals and/or immunosuppressiva since at least 6 month

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, Data analyst, Carer, Assessor

Blinding implementation details:

Subjects, researchers & statisticians were blinded to allocation to Investigational Medicinal Product (IMP). Placebo and active medication comparator were designed and manufactured to be visually indistinguishable.

Arms

Are arms mutually exclusive?	Yes
Arm title	5-HTP first then placebo

Arm description:

Subjects were randomised to 5-HTP for the first 8 weeks and Placebo in the following 8 weeks in a cross over study.

Arm type	experimental and placebo
Investigational medicinal product name	5-HTP
Investigational medicinal product code	
Other name	L-5-hydroxytryptophan (5-HTP) (Levotonine R)
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

100MG twice daily for the first 8 weeks

Investigational medicinal product name	placebo for 5-HTP
Investigational medicinal product code	
Other name	Lactose monohydrate 100 mg
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

100mg twice daily dor the following 8 weeks

Arm title	placebo first, then 5HTP

Arm description:

Subjects were randomised to placebo for the first 8 weeks and 5-HTP in the following 8 weeks in a cross over study.

Arm type	experimental and placebo

Investigational medicinal product name	5-HTP
Investigational medicinal product code	
Other name	L-5-hydroxytryptophan (5-HTP) (Levotonine R)
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

100MG twice daily for the following 8 weeks in cross over study

Investigational medicinal product name	placebo for 5-HTP
Investigational medicinal product code	
Other name	Lactose monohydrate 100 mg
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

100mg twice daily for the first 8 weeks

Number of subjects in period 1	5-HTP first then placebo	placebo first, then 5HTP
Started	82	84
period 1	82	84
Period 2	78	78
Completed	75	74
Not completed	7	10
drug toxicity	2	4
patient's wish	-	4
patient wish	3	-
poor compliance	1	2
no longer meets study criteria	1	-

Baseline characteristics

Reporting groups	
Reporting group title	5-HTP first then placebo
Reporting group description:	
Subjects were randomised to 5-HTP for the first 8 weeks and Placebo in the following 8 weeks in a cross over study.	
Reporting group title	placebo first, then 5HTP
Reporting group description:	
Subjects were randomised to placebo for the first 8 weeks and 5-HTP in the following 8 weeks in a cross over study.	

Reporting group values	5-HTP first then placebo	placebo first, then 5HTP	Total
Number of subjects	82	84	166
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			
median	38.5	39.0	
inter-quartile range (Q1-Q3)	29.8 to 45.0	29.3 to 48.0	-
Gender categorical			
Units: Subjects			
Female	45	49	94
Male	37	35	72

End points

End points reporting groups

Reporting group title	5-HTP first then placebo
Reporting group description:	
Subjects were randomised to 5-HTP for the first 8 weeks and Placebo in the following 8 weeks in a cross over study.	
Reporting group title	placebo first, then 5HTP
Reporting group description:	
Subjects were randomised to placebo for the first 8 weeks and 5-HTP in the following 8 weeks in a cross over study.	
Subject analysis set title	after 5-HTP treatment
Subject analysis set type	Per protocol
Subject analysis set description:	
subject analysis set after 8 weeks of 5-HTP	
Subject analysis set title	after placebo
Subject analysis set type	Per protocol
Subject analysis set description:	
subject analysis set after 8 weeks of placebo	

Primary: Percentage of patients reaching >=20% reduction in fVAS

End point title	Percentage of patients reaching >=20% reduction in fVAS
End point description:	
End point type	Primary
End point timeframe:	
At end of Treatment Periods 1 and 2	

End point values	after 5-HTP treatment	after placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	149	149		
Units: patients	53	56		

Statistical analyses

Statistical analysis title	McNemar’s test
Comparison groups	after placebo v after 5-HTP treatment
Number of subjects included in analysis	298
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.83
Method	Mcnemar

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were reported from the first drug administration until the end of study (week 16)

Adverse event reporting additional description:

AEs were assessed at each study visit and were defined as serious if they resulted in death (or were life-threatening), required hospitalization, or resulted in significant disability.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	gastrointestinal

Reporting group description: -

Reporting group title	surgical and medical procedures

Reporting group description: -

Serious adverse events	gastrointestinal	surgical and medical procedures	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 161 (0.62%)	2 / 161 (1.24%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Hospitalisation for polysomnography	Additional description: Hospitalisation for polysomnography		
subjects affected / exposed	0 / 161 (0.00%)	1 / 161 (0.62%)	
occurrences causally related to treatment / all	0 / 161	0 / 161	
deaths causally related to treatment / all	0 / 0	0 / 0	
knee replacement			
subjects affected / exposed	0 / 161 (0.00%)	1 / 161 (0.62%)	
occurrences causally related to treatment / all	0 / 161	0 / 161	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain and diarhea requiring hospitalisation		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 161 (0.62%)	0 / 161 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	gastrointestinal	surgical and medical procedures	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 161 (11.18%)	0 / 161 (0.00%)	
Gastrointestinal disorders			
gastrointestinal			
subjects affected / exposed	18 / 161 (11.18%)	0 / 161 (0.00%)	
occurrences (all)	18	0	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Mainly patients with Crohn’s disease were included

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35940251