Clinical trial results:
Thiamin against robust IBD fatigue
- The effect of oral thiamin supplement in 4 weeks to patients with inflammatory bowel disease (IBD) in remission and chronic fatigue.
A randomised placebo controlled crossover study

Summary

EudraCT number	2018-002324-17
Trial protocol	DK
Global end of trial date	27 October 2020

Results information

Result version number	v1 (current)
This version publication date	25 September 2021
First version publication date	25 September 2021

Trial information

Trial identification

Sponsor protocol code	TARIF

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03634735
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus N, Denmark, 8230
Public contact	Palle Bager, Aarhus University Hospital, 45 51500697, pallbage@rm.dk
Scientific contact	Christian Lodberg Hvas, Aarhus University Hospital, 45 28351839, christian.hvas@auh.rm.dk

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	01 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 October 2020
Global end of trial reached?	Yes
Global end of trial date	27 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate if the levels of fatigue can be reduced after 4 weeks treatment with Thiamin, among patients with inflammatory bowel disease in remission and chronic fatigue

Protection of trial subjects:

Safety were continuous monitored for all subjects

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	39
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects were included from the outpatient clinic at Aarhus University Hospital, Denmark.

Pre-assignment

Screening details:

A total of 84 patients were screened. 44 were not included, primary due to: low level of fatigue, fatigue duration or disease activity.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Intervention

Arm description:

Thiamine tablets for 4 weeks.
Daily dose 600 -1800 mg, depending of body weight and gender.

Arm type	Experimental
Investigational medicinal product name	Thiamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600 - 1800 mg daily

Arm title	Placebo

Arm description:

Placebo tablets for 4 weeks.
The number of tablet taken was depending of body weight and gender and was equal to the number of tablets taken in the intervention arm.

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

Dosage and administration details:

2 - 6 tablets daily for 4 weeks

Number of subjects in period 1	Intervention	Placebo
Started	40	40
Completion of the blinded part	40	40
Completed	40	40

Period 2	
Period 2 title	Unblinded period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:
300 mg thiamine tablets daily for 12 weeks

Arm type	Experimental
Investigational medicinal product name	Thiamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
300 mg daily for 12 weeks

Arm title	No thiamine

Arm description:
No thiamine supplementation for 12 weeks

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Intervention	No thiamine
Started	20	20
End of open label	20	20
Completed	20	20

Period 3	
Period 3 title	Follow up period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Arm title	Observation
Arm description:	
All subjects were followed for 6 months after the two interventions studies	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Observation
Started	40
End of follow up	38
Completed	38
Not completed	2
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Blinded period

Reporting group description:

40 subjects were enrolled in the intervention trail.
20 subjects were enrolled for one visit only and acted as a control group for the group of 40 subjects

Reporting group values	Blinded period	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	39	39	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	35	35	
Male	5	5	

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description:	
Thiamine tablets for 4 weeks. Daily dose 600 -1800 mg, depending of body weight and gender.	
Reporting group title	Placebo
Reporting group description:	
Placebo tablets for 4 weeks. The number of tablet taken was depending of body weight and gender and was equal to the number of tablets taken in the intervention arm.	
Reporting group title	Intervention
Reporting group description:	
300 mg thiamine tablets daily for 12 weeks	
Reporting group title	No thiamine
Reporting group description:	
No thiamine supplementation for 12 weeks	
Reporting group title	Observation
Reporting group description:	
All subjects were followed for 6 months after the two interventions studies	

Primary: Fatigue improvement

End point title	Fatigue improvement
End point description:	
An improvement ≥ 3 points on the IBD-F, Section I scale was defined as a clinically relevant improvement	
End point type	Primary
End point timeframe:	
After 4 weeks of treatment compared to placebo	

End point values	Intervention	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: Fatigue severity on a scale				
IBD-F, Section I	40	40		

Statistical analyses

Statistical analysis title	Comparison between groups
Statistical analysis description:	
Change in fatigue severity: intervention period compared to placebo period	
Comparison groups	Placebo v Intervention

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001 [1]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	6.2

Notes:

[1] - A reduction of fatigue in the intervention period of 4.5 points compared to an increase in fatigue of 0.75 points in the placebo period.

Primary: Fatigue maintenance

End point title	Fatigue maintenance

End point description:

The 20 subjects who were randomised to thiamine 300 mg daily were compared to the 20 subjects who did not receive thiamine

End point type	Primary

End point timeframe:

After 12 weeks of thiamine treatment vs. no thiamine

End point values	Intervention	No thiamine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Fatigue severity				
IBD.F, Section I	20	20		

Statistical analyses

Statistical analysis title	Comparison between groups
Comparison groups	Intervention v No thiamine
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.75 [3]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	3.5

Variability estimate	Standard deviation
Dispersion value	3.5

Notes:

[2] - Comparison of the fatigue severity between groups after 12 weeks

[3] - The thiamine group had a mean increase of fatigue of 1.4 points vs. the no thiamine group who had an increase of 1.9. point.

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From study start to end of trial	
Adverse event reporting additional description:	
Data on adverse events were collected at every visit. Furthermore, the subjects were able to report adverse events at any time during the study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	2.1

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

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: We found no serious adverse events. The number of adverse events were < 5 %

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/33210299