



Clinical trial results:

Rifaximin-treatment of Collagenous colitis: A prospective, double-blind, placebo-controlled study

Summary

EudraCT number	2018-001891-39
Trial protocol	DK
Global end of trial date	01 December 2021

Results information

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

Trial information

Trial identification

Sponsor protocol code	version4.6,29082018
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03658993
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Sabine Becker, Senior Physician Clinic of Gastrointestinal- and Infectious Diseases, Diagnostic Center Silkeborg Regional Hospital,
Sponsor organisation address	Falkevej 1-3,, Silkeborg, Denmark, 8600
Public contact	XiCoCo study group, sabbec@rm.dk, XiCoCo study group, sabbec@rm.dk, sabbec@rm.dk
Scientific contact	XiCoCo study group, sabbec@rm.dk, XiCoCo study group, sabbec@rm.dk, sabbec@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	16 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2021
Global end of trial reached?	Yes
Global end of trial date	01 December 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to assess if 4 weeks treatment with Rifaximin as a supplement to a standard course of Budesonide against active Collagenous Colitis can reduce the risk of relapse after treatment cessation.

Protection of trial subjects:

All procedures were standard procedures.

Background therapy: -

Evidence for comparator:

The hypothesis of this study is that an altered gut microbiota is a contributory factor in initiating an inflammatory process in the colonic mucosa leading to CC. We suggest that treatment with Budesonide reduces the inflammation without treating the underlying cause. In this trial we will try to remodel gut microbiota by adding Rifaximin and see whether we can reduce the risk of relapse after Budesonide-cessation.

Actual start date of recruitment	03 September 2018
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	Denmark: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	11
From 65 to 84 years	5

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Patients with biopsy-verified CC and active disease. Patients were invited to participate in the study independently of age and disease duration.

Pre-assignment

Screening details:

Patients with known and new diagnosed collagenous colitis was considered for participation in the study. 39 pt were screened. 14 patients did not fulfil inclusion criteria and were excluded. 25 patients were included in the study and 16 patients fulfil the criteria for randomisation.

Pre-assignment period milestones

Number of subjects started	39 ^[1]
Number of subjects completed	16

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 23
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: This is a single center study

Period 1

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

Blinding implementation details:

Computer-generated block randomisation was performed by local pharmacy in blocks of eight. Study drug and placebo were packed and provided by Norgine. Data analysis was performed before treatment-group allocation was disclosed

Arms

Are arms mutually exclusive?	Yes
Arm title	Rifaxamine

Arm description:

Patients in clinical remission after 4 weeks of open-label budesonide-therapy will randomly be assigned to receive oral rifaximin 550 mg TID for 4 weeks. Study drugs were commenced during budesonide treatment and continued 2 weeks after cessation of budesonide treatment.

Arm type	Active comparator
Investigational medicinal product name	Rifaxamine
Investigational medicinal product code	A07AA11
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

oral rifaximin 550 mg TID for 4 weeks

Arm title	placeboo
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Arm description:

Patients in clinical remission after 4 weeks of open-label budesonide-therapy will randomly be assigned to receive either: oral placebo TID for 4 weeks. Study drugs were commenced during budesonide treatment and continued 2 weeks after cessation of budesonide treatment.

Arm type	placebo
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Rifaxamine	placeboo
Started	8	8
Completed	7	8
Not completed	1	0
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	Randomised
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Reporting group description: -

Reporting group values	Randomised	Total	
Number of subjects	16	16	
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)	11	11	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	13	13	
Male	3	3	

End points

End points reporting groups

Reporting group title	Rifaxamine
Reporting group description: Patients in clinical remission after 4 weeks of open-label budesonide-therapy will randomly be assigned to receive oral rifaximin 550 mg TID for 4 weeks . Study drugs were commenced during budesonide treatment and continued 2 weeks after cessation of budesonide treatment.	
Reporting group title	placebo
Reporting group description: Patients in clinical remission after 4 weeks of open-label budesonide-therapy will randomly be assigned to receive either: oral placebo TID for 4 weeks. Study drugs were commenced during budesonide treatment and continued 2 weeks after cessation of budesonide treatment.	

Primary: Clinical remission

End point title	Clinical remission
End point description: Remission defined as < 3 daily bowel movements or < 1 watery stool per day measured as a mean during the last week.	
End point type	Primary
End point timeframe: Number of patients in clinical remission 12 weeks after cessation of Budesonide in the Rifaximin group compared to the placebo group.	

End point values	Rifaxamine	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7 ^[1]	8		
Units: subjects	7	8		

Notes:

[1] - One patient was excluded because of protocol violation

Statistical analyses

Statistical analysis title	Final- clinical data
Comparison groups	Rifaxamine v placebo
Number of subjects included in analysis	15
Analysis specification	Pre-specified
Analysis type	superiority ^[2]
P-value	< 0.05 ^[3]
Method	Logrank
Parameter estimate	Median difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Notes:

[2] - All statistical tests were two-sided with the level of statistical significance set at P-value < 0.05

[3] - All statistical tests were two-sided with the level of statistical significance set at P-value < 0.05

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse effect were reported at each control-visit

Assessment type	Systematic
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Dictionary used

Dictionary name	SNOMED CT
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Dictionary version	2022-08-31
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Reporting groups

Reporting group title	Rifaxamine group
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Reporting group description: -

Reporting group title	placebo
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Reporting group description: -

Serious adverse events	Rifaxamine group	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Rifaxamine group	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	2 / 8 (25.00%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 8 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Pain	Additional description: Muscular pain		

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1	0 / 8 (0.00%) 1	
Infections and infestations Herpes dermatitis subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 1	1 / 8 (12.50%) 1	

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