



Clinical trial results:

The ReSScue trial. Aiming to Reduce disease-related gastro-intestinal symptoms in patients with Systemic Sclerosis by repeat intestinal infusions of Anaerobic Cultivated Human Intestinal Microbiome (ACHIM); a Phase II, randomized, double-blinded placebo-controlled 12 week followed by a 8 week open-label extension period

Summary

EudraCT number	2019-004400-35
Trial protocol	NO
Global end of trial date	27 June 2022

Results information

Result version number	v1 (current)
This version publication date	10 April 2025
First version publication date	10 April 2025

Trial information

Trial identification

Sponsor protocol code	2016/1529
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oslo University Hospital
Sponsor organisation address	Sognsvannveien 20, Oslo, Norway,
Public contact	Department of Rheumatology, Oslo University Hospital, resscue@ous-hf.no
Scientific contact	Department of Rheumatology, Oslo University Hospital, resscue@ous-hf.no

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	02 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2022
Global end of trial reached?	Yes
Global end of trial date	27 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary and secondary endpoints of the ReSScue trial will be estimated at week 12, which represents the end of study period 1, while safety and tolerability will be assessed throughout the 26 week study period. In addition, a number of explorative clinical endpoints will be assessed at weeks 12 and 26. The study is designed with repeat scheduled samplings of biological materials, allowing for explorative endpoints on biomarkers during study periods 1 and 2, and later development of research studies at molecular level (see Section 8).

- Estimate efficacy of ACHIM compared to placebo on lower GIT symptoms

Protection of trial subjects:

Strict exclusion-criteria prior to study entry, close monitoring before-during-and after all interventions and during the whole study. Blood-samples and other vital measures were monitored closely. Data monitoring committee has reviewed recruitment, data quality (protocol deviations) and monitored evidence for treatment harm (AEs, SAEs, SUSARs, deaths) twice during the trial.

Background therapy:

No modifications were implemented to the background-therapies. Specific medications were established as exclusion criteria, as delineated in the study protocol.

Evidence for comparator: -

Actual start date of recruitment	26 May 2020
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	Norway: 67
Worldwide total number of subjects	67
EEA total number of subjects	67

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	44
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment period started in September 2020 and the last patient entered the study in February 2022.

Pre-assignment

Screening details:

Participants found to be eligible for the ReSScue study at the first screening visit will be instructed to fill out the UCLA-GIT score form and a fecal incontinence assessment form at home once every week, for a minimum period of four weeks before they can come to the baseline visit.

Period 1

Period 1 title	Inclusion period (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:

Randomised, Placebo-controlled, double blind.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Intervention with Undiluted culture medium with no bacteria.

Arm type	Placebo
Investigational medicinal product name	ACHIM
Investigational medicinal product code	
Other name	Anaerobically cultivated human intestinal microbiota
Pharmaceutical forms	Gastroenteral solution
Routes of administration	Solution for infusion

Dosage and administration details:

30 ml (109 bacteria /ml culture solution) given as infusion by endoscopy

Investigational medicinal product name	Undiluted culture medium with no bacteria
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Gastroenteral solution
Routes of administration	Gastroenteral use

Dosage and administration details:

Duodenal infusions of 30 ml undiluted culture medium with no bacteria.

Arm title	ACHIM
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Arm description:

Intervention with undiluted anaerobic bacteria culture

Arm type	Experimental
Investigational medicinal product name	ACHIM
Investigational medicinal product code	
Other name	Anaerobically cultivated human intestinal microbiota
Pharmaceutical forms	Gastroenteral solution
Routes of administration	Solution for infusion

Dosage and administration details:

30 ml (109 bacteria /ml culture solution) given as infusion by endoscopy

Number of subjects in period 1	Placebo	ACHIM
Started	34	33
Completed	34	31
Not completed	0	2
Adverse event, non-fatal	-	2

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Intervention with Undiluted culture medium with no bacteria.	
Reporting group title	ACHIM
Reporting group description:	
Intervention with undiluted anaerobic bacteria culture	

Reporting group values	Placebo	ACHIM	Total
Number of subjects	34	33	67
Age categorical			
ACHIM -group			
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)	22	25	47
From 65-84 years	12	8	20
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	60.1	57.9	
standard deviation	± 11.7	± 11.5	-
Gender categorical			
Gender description			
Units: Subjects			
Female	29	33	62
Male	5	0	5
Severity of Baseline symptoms			
Severity of Baseline symptoms measured at Baseline-visit			
Units: Subjects			
Moderate	7	6	13
Severe	27	27	54

Subject analysis sets

Subject analysis set title	Per protocol analysis of ACHIM/placebo from week 0 to week 12.
Subject analysis set type	Per protocol
Subject analysis set description:	
Change from baseline to week 12 in UCLA GIT score item diarrhea or bloating, depending which was the worst symptom at the baseline evaluated separately for each patient	

Reporting group values	Per protocol analysis of ACHIM/placebo from week 0 to week 12.		
Number of subjects	63		
Age categorical			
ACHIM -group			
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)	47		
From 65-84 years	20		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	58.91		
standard deviation	± 11.59		
Gender categorical			
Gender description			
Units: Subjects			
Female	62		
Male	5		
Severity of Baseline symptoms			
Severity of Baseline symptoms measured at Baseline-visit			
Units: Subjects			
Moderate	13		
Severe	54		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Intervention with Undiluted culture medium with no bacteria.	
Reporting group title	ACHIM
Reporting group description: Intervention with undiluted anaerobic bacteria culture	
Subject analysis set title	Per protocol analysis of ACHIM/placebo from week 0 to week 12.
Subject analysis set type	Per protocol
Subject analysis set description: Change from baseline to week 12 in UCLA GIT score item diarrhea or bloating, depending which was the worst symptom at the baseline evaluated separately for each patient 12 weeks	

Primary: Primary endpoint

End point title	Primary endpoint
End point description: The model has fixed effects for stratification factor worst symptom, time, treatment and an interaction term between time and treatment. Time is a categorical variable, with levels corresponding to different weeks. Model is adjusted for the baseline worst symptom GIT score. Random intercepts are included. The primary estimate is the treatment effect at change between baseline and 12 weeks and is presented with two-sided 95% confidence intervals.	
End point type	Primary
End point timeframe: The change between baseline and week 12 in the worst symptom GIT score after 12 weeks is analysed here using a linear mixed model, including the worst symptom GIT score value at baseline, 2, 4, 6, and 12 weeks as longitudinal outcome.	

End point values	Placebo	ACHIM	Per protocol analysis of ACHIM/placebo from week 0 to week 12.	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	33	30	63	
Units: UCLA GIT score	33	30	63	

Statistical analyses

Statistical analysis title	Primary endpoint
Statistical analysis description: The change between baseline and week 12 in the worst symptom GIT score after 12 weeks is analysed here using a linear mixed model, including the worst symptom GIT score value at baseline, 2, 4, 6, and 12 weeks as longitudinal outcome. The model has fixed effects for stratification factor worst symptom, time, treatment and an interaction term between time and treatment. Time is a categorical variable, with levels corresponding to different weeks.	

Comparison groups	ACHIM v Placebo
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.25 ^[2]
Method	Mixed models analysis
Parameter estimate	AME
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.47
Variability estimate	Standard deviation

Notes:

[1] - Continuous primary endpoint “worst symptom derived from UCLA GIT score items diarrhea and bloating” is assessed four times during the screening period and five times during the study Part A1 (at weeks 0, 2, 4, 6, and 12), and will be analyzed using a linear mixed model accounting for the correlations between repeated measurements within each participants by random intercept and slope.

[2] - Estimates will be presented with two-sided

95% confidence intervals, and p-values smaller than 0.05 will be considered significant. The primary estimate will be the treatment effect (average marginal effect) at 12 weeks.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AE will be collected from the start of intervention until the follow-up visit at the time points specified in the SoA.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	ACHIM
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	ACHIM	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)	1 / 19 (5.26%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Myelitis transverse	Additional description: Myelitis transverse		
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Acute abdomen	Additional description: Acute abdomen		
subjects affected / exposed	2 / 16 (12.50%)	1 / 19 (5.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	ACHIM	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	19 / 19 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm skin			
subjects affected / exposed	2 / 16 (12.50%)	0 / 19 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Raynaud's phenomenon			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Calcinosis	Additional description: Calcinosis		
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Chest discomfort	Additional description: Chest discomfort		
subjects affected / exposed	0 / 16 (0.00%)	11 / 19 (57.89%)	
occurrences (all)	0	1	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	5 / 16 (31.25%)	5 / 19 (26.32%)	
occurrences (all)	5	5	
Reproductive system and breast disorders			
Menopausal symptoms			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Pneumonia aspiration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Psychiatric disorders			
Emotional disorder			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Sleep disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Fine motor skill dysfunction			
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 16 (6.25%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Anemia	Additional description: Anemia		
subjects affected / exposed	1 / 16 (6.25%)	1 / 19 (5.26%)	
occurrences (all)	1	1	
Iron deficiency anemia	Additional description: Iron deficiency anemia		
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Eye disorders			

Dry eye subjects affected / exposed occurrences (all)	Additional description: Dry eye		
	0 / 16 (0.00%)	1 / 19 (5.26%)	
	0	1	
Gastrointestinal disorders			
	Additional description: Abdominal discomfort		
	1 / 16 (6.25%)	2 / 19 (10.53%)	
Abdominal discomfort subjects affected / exposed occurrences (all)	1	2	
Abdominal distension subjects affected / exposed occurrences (all)	Additional description: Abdominal distension		
	1 / 16 (6.25%)	1 / 19 (5.26%)	
	1	1	
Abdominal pain subjects affected / exposed occurrences (all)	Additional description: Abdominal pain		
	5 / 16 (31.25%)	2 / 19 (10.53%)	
	5	2	
Abdominal pain upper subjects affected / exposed occurrences (all)	Additional description: Abdominal pain upper		
	2 / 16 (12.50%)	1 / 19 (5.26%)	
	2	1	
Anal Incontinence subjects affected / exposed occurrences (all)	Additional description: Anal Incontinence		
	1 / 16 (6.25%)	0 / 19 (0.00%)	
	1	0	
anal prolaps subjects affected / exposed occurrences (all)	Additional description: anal prolaps		
	1 / 16 (6.25%)	0 / 19 (0.00%)	
	1	0	
Diarrhoea subjects affected / exposed occurrences (all)	Additional description: Diarrhoea		
	2 / 16 (12.50%)	2 / 19 (10.53%)	
	2	2	
Dry mouth subjects affected / exposed occurrences (all)	Additional description: Dry mouth		
	0 / 16 (0.00%)	1 / 19 (5.26%)	
	0	1	
Eructation subjects affected / exposed occurrences (all)	Additional description: Eructation		
	1 / 16 (6.25%)	0 / 19 (0.00%)	
	1	0	
Flatulence subjects affected / exposed occurrences (all)	Additional description: Flatulence		
	1 / 16 (6.25%)	0 / 19 (0.00%)	
	1	0	
Nausea	Additional description: Nausea		

subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	4 / 19 (21.05%) 4	
Oesophagitis	Additional description: Oesophagitis		
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0	
Vomiting	Additional description: Vomiting		
subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2	1 / 19 (5.26%) 1	
Hepatobiliary disorders			
Hepatitis	Additional description: Hepatitis		
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	2 / 19 (10.53%) 2	
Cutaneous calcification			
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0	
Dry skin			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1	
Pruritus			
subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1	
skin ulcer			
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0	
Renal and urinary disorders			
Urge incontinence			
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0	
Urinary incontinence			
subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Arthralgia subjects affected / exposed occurrences (all)	Additional description: Arthralgia	
	5 / 16 (31.25%) 5	3 / 19 (15.79%) 3
Back pain subjects affected / exposed occurrences (all)	Additional description: Back pain	
	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Joint stiffness subjects affected / exposed occurrences (all)	Additional description: Joint stiffness	
	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Joint swelling subjects affected / exposed occurrences (all)	Additional description: Joint swelling	
	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Limb discomfort subjects affected / exposed occurrences (all)	Additional description: Limb discomfort	
	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Muscle spasms subjects affected / exposed occurrences (all)	Additional description: Muscle spasms	
	1 / 16 (6.25%) 1	1 / 19 (5.26%) 1
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	Additional description: Musculoskeletal stiffness	
	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Myalgia subjects affected / exposed occurrences (all)	Additional description: Myalgia	
	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)		
	1 / 16 (6.25%) 1	0 / 19 (0.00%) 0
Tendonitis subjects affected / exposed occurrences (all)		
	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Infections and infestations Candida infection subjects affected / exposed occurrences (all) Erythema migrans		
	Additional description: Candida infection	
	0 / 16 (0.00%) 0	1 / 19 (5.26%) 1
Additional description: Erythema migrans		

subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Staphylococcal infection	Additional description: Staphylococcal infection		
subjects affected / exposed	1 / 16 (6.25%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Tooth infection	Additional description: Tooth infection		
subjects affected / exposed	0 / 16 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	0 / 16 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	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? Yes

Date	Interruption	Restart date
19 March 2021	Stop in new inclusions due to ongoing Covid-19 pandemic	10 May 2021

Notes:

Limitations and caveats

None reported