

Efficacy of Lactobacillus Rhamnosus GG add-on therapy in mild-to-moderate ulcerative colitis

Submission date 30/03/2026	Recruitment status No longer recruiting	☐ Prospectively registered ☒ Protocol
Registration date 08/04/2026	Overall study status Completed	☐ Statistical analysis plan ☐ Results
Last Edited 31/03/2026	Condition category Digestive System	☐ Individual participant data ☒ Record updated in last year

Plain English summary of protocol

Background and study aims

Ulcerative colitis is a chronic inflammatory disease of the intestine that can cause symptoms such as diarrhea, abdominal pain, and fatigue. Recent research suggests that gut bacteria (the microbiome) may play an important role in this condition.

This study aims to evaluate whether adding a probiotic (Lactobacillus rhamnosus GG) to standard treatment can improve quality of life and reduce symptoms in patients with mild-to-moderate ulcerative colitis.

Who can participate?

Adults aged 18 years or older with a diagnosis of mild-to-moderate ulcerative colitis.

What does the study involve?

Participants will first attend a screening visit to check whether they are eligible to take part. This will include signing a consent form, having blood tests, and providing a stool sample.

Those who are eligible will be randomly assigned to receive either the probiotic Lactobacillus rhamnosus GG or a placebo, in addition to their usual mesalazine treatment, for 4 weeks.

Participants who show an improvement after this first phase will continue into a maintenance phase and will again be randomly assigned to receive either the probiotic or placebo for a further 12 weeks.

During the study, participants will provide blood and stool samples and complete questionnaires about their symptoms, fatigue, and quality of life. Their ulcerative colitis activity will also be assessed at regular study visits, some of which may take place by telephone. Each participant will be involved in the study for approximately 24 weeks.

What are the possible benefits and risks of participating?

Participants may benefit from an improvement in symptoms or quality of life, but this cannot be guaranteed.

The probiotic used in this study is generally considered safe. Possible risks are minimal but may include mild digestive symptoms. Blood sampling may cause minor discomfort.

Where is the study run from?

The study is conducted at the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico in Milan, Italy.

When is the study starting and how long is it expected to run for?

The study is expected to start in September 2021 and end in May 2023.

Who is funding the study?

The study is supported by an unconditional grant from Dicofarm S.p.A.

Who is the main contact?

Prof. Maurizio Vecchi, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy,
federica.facciotti@unimib.it

Contact information

Type(s)

Scientific, Principal investigator, Public

Contact name

Prof Maurizio Vecchi

Contact details

Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico
via Francesco Sforza, 28
Milano
Italy
20122
+39 0255053395
chiara.amoroso@policlinico.mi.it

Additional identifiers

Study information

Scientific Title

Efficacy of Lactobacillus Rhamnosus GG add-on therapy in mild-to-moderate Ulcerative Colitis patients

Acronym

LaRhGG-UC

Study objectives

The primary objective of the study is to evaluate the impact of treatment with Lactobacillus rhamnosus GG, in addition to standard therapy, on quality of life in patients with mild-to-moderate ulcerative colitis.

Secondary objectives include the assessment of clinical efficacy in terms of clinical response and remission, improvement of IBS-like symptoms, improvement of disease-related fatigue, changes in fecal calprotectin levels, and changes in the composition of the intestinal microbiota.

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 14/12/2021, Comitato Etico Territoriale Lombardia 2 (Via Ripamonti 435, Milan, 20141, Italy; +39 02 57 48 98 48/47; comitato.etico@ieo.it), ref: 1172_2021

Primary study design

Interventional

Allocation

Randomized controlled trial

Masking

Blinded (masking used)

Control

Placebo

Assignment

Parallel

Purpose

Treatment

Study type(s)**Health condition(s) or problem(s) studied**

Ulcerative colitis

Interventions

At the screening visit (Week -2), patients will sign the informed consent and will be assessed according to the inclusion and exclusion criteria. Blood tests and fecal calprotectin measurements will be performed. Participants are randomised in a 1:1 ratio to receive *Lactobacillus rhamnosus* GG (LGG) or placebo, one sachet twice daily during a 4-week induction treatment period (from Week 0 to Week 4), in addition to conventional therapy with mesalazine-based compounds. Randomisation is performed using a computer-generated randomisation list implemented in REDCap (Research Electronic Data Capture) software. Allocation is concealed using sequentially numbered, identical treatment packs prepared by an independent party. The study is double-blind (participants, investigators, and outcome assessors).

Patients who achieve a clinical response at Week 4 (defined as a reduction of ≥ 2 points in the Partial Mayo Score and a decrease of ≥ 1 point in the rectal bleeding subscore or an absolute rectal bleeding subscore ≤ 1) will enter the maintenance phase and will be re-randomized in a 1:1 ratio to receive LGG or placebo, one sachet once daily for a 12-week maintenance treatment period (from Week 4 to Week 16), in addition to conventional therapy with mesalazine-based compounds.

Stool and blood samples will be collected at Week -2, Week 4, Week 16, and Week 24.

Fecal samples will be analyzed using Whole Metagenome Shotgun (WMS) sequencing to obtain species-level metagenomic data and functional microbiome profiles. Fecal metabolomics will

also be analyzed. Serum levels of pro- and anti-inflammatory cytokines will be measured by ELISA.

Fecal water containing metabolites from patients treated and not treated with *Lactobacillus rhamnosus* GG will be used to modulate in vitro the functional profile of ex vivo isolated LPMCs. Fecal calprotectin will be measured at Weeks -2, 4, 16, and 24.

Clinical activity of ulcerative colitis will be assessed using the Partial Mayo Score at Weeks -2, 0, 4, 8, 12, 16, and 24. Visits at Week 8 and Week 12 may be conducted by telephone.

The IBDQ and SF-36 questionnaires will be administered at Weeks 0, 4, 16, and 24 to assess disease-related quality of life and perceived health status. The IBS-SSS will be administered at Weeks 0, 4, 16, and 24 to assess the severity of functional symptoms. The FACIT-F questionnaire will be administered at Weeks 0, 4, 16, and 24 to assess fatigue.

Intervention Type

Supplement

Primary outcome(s)

1. Health-related quality of life (HRQoL) measured using the Inflammatory Bowel Disease Questionnaire (IBDQ) questionnaire at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

Key secondary outcome(s)

1. Clinical remission rate measured using the Partial Mayo Score < 3 at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

2. Clinical response rate measured using a reduction > 2 points in the Partial Mayo Score and a decrease of at least 1 point in the rectal bleeding subscore or an absolute rectal bleeding subscore ≤ 1 at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

3. IBS severity based on pain, bloating, and quality of life measured using the Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS) at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

4. HRQoL in IBD measured using the Short Form Health Survey (SF-36) score at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

5. Fatigue severity measured using the Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

6. Fecal calprotectin levels measured using particle-enhanced turbidimetric immunoassay at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

7. Gut microbiome composition measured using 16s rRNA sequencing at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

8. Flare rate measured using the Mayo Score >5 at baseline, T1 (4 weeks post treatment), T2 (16 weeks post treatment), T3 (24 weeks post treatment)

Completion date

31/03/2025

Eligibility

Key inclusion criteria

1. Age $\geq$ 18 years at the time of enrollment
2. Ability to understand the study and provide informed consent
3. Diagnosis of ulcerative colitis at least 3 months prior to enrollment
4. Clinically active mild-to-moderate ulcerative colitis, defined as a Partial Mayo Score of 3–7 with a rectal bleeding subscore $\geq$ 1 at baseline
5. Permitted Concomitant Medications
6. Oral and topical mesalazine

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

18 Years

Upper age limit

65 Years

Sex

All

Total final enrolment

36

Key exclusion criteria

1. Clinically active severe ulcerative colitis, defined as a Partial Mayo Score $>$ 7
2. Use of probiotics and/or systemic antibiotic therapy within the previous 4 weeks
3. Pregnancy or breastfeeding
4. History of severe renal, hepatic, cardiac, or metabolic disease
5. Inability to comply with study procedures
6. Prohibited Concomitant Medications
7. Systemic, low-bioavailability oral, or topical corticosteroids
8. Immunosuppressants such as azathioprine, 6-mercaptopurine, methotrexate
9. Biologic therapy for UC (infliximab, adalimumab, golimumab, vedolizumab)
10. Tofacitinib
11. Systemic antibiotic therapy
12. Use of probiotics

Date of first enrolment

16/05/2022

Date of final enrolment

13/11/2024

Locations

Countries of recruitment

Italy

Sponsor information

Organisation

Dicofarm S.p.A.

Funder(s)

Funder type

Funder Name

Dicofarm S.p.A.

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	26/07/2021	31/03/2026	No	Yes
Protocol file	version 1.0	26/07/2021	31/03/2026	No	No