2014. Budesonide dose

RCT/Budesonide/ CD/ Induction

Once versus three times daily dosing of oral budesonide for active Crohn's disease: A double-blind, double-dummy, randomised trial

Multicentre, double-blind, double-dummy, phase III trial.
Patients with mild-moderately active ileocolonic CD (CDAI >200-<400) were randomized to 9mg budesónida OD or 3mg three-times daily (TID).

Primary endpoint: Clinical remission defined as CDAI <150 at week 8 (last observation carried forward)

Results: N=471

- At week 8: 71.3% 9mg budesonide vs 75.1% 3mg TID, a difference of -3.9% p=0.020 for non-inferiority.
- Mean time to remission was 21.9 days vs 21.4 days in 9 mg vs 3 mg TID.
- No differences in adverse events

Conclusion:
Budesonide at the recommended dose of 9 mg/day can be administered OD without impaired efficacy and safety compared to 3 mg TID dosing in mild-to-moderately active Crohn's disease.

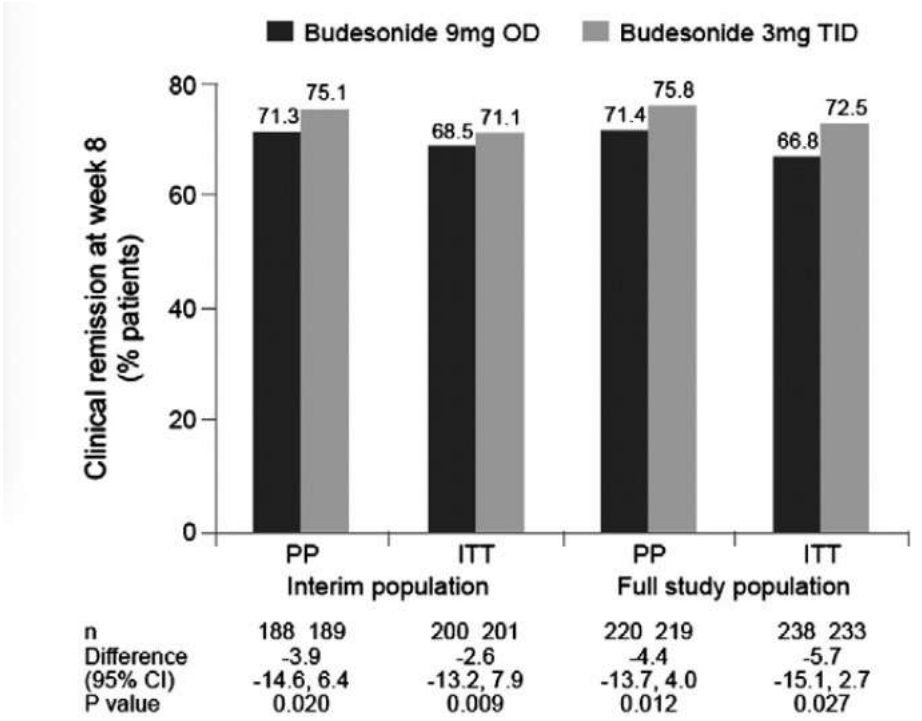


Figure 2 Clinical remission at week 8 (LOCF). Results are shown for the interim population (confirmative analysis) and the full study population (explorative analysis).

Dignass A et al. J Crohns Colitis. 2014; 8: 970-980

2017. Iron IV/PO

RCT/Iron / IV or PO/ IBD

Oral versus intravenous iron replacement therapy distinctly alters the gut microbiota and metabolome in patients with IBD

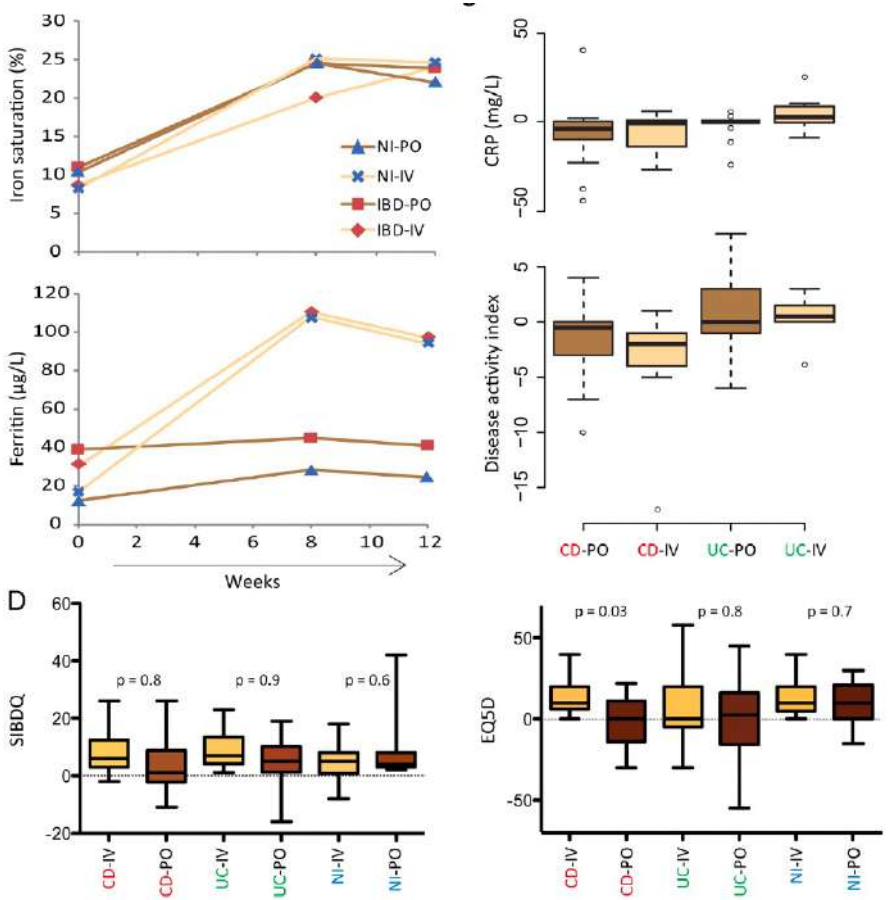
Open-label clinical trial.
Patients with CD, UC and non-IBD iron deficient were randomized to receive iron sulfate orally (PO) or iron sucrose (IV) over 3 months.

Primary endpoint: Clinical parameters, faecal bacterial communities and metabolomes were assessed before and after.

Results: N=72

- Both IV and PO ameliorated iron deficiency but higher ferritin levels were observed with IV. No differences in haemoglobin.
- Changes in disease activity were independent of iron type.
- Major shifts in bacterial diversity occurred in most patients but patients with CD were most susceptible.
- PO treatment was associated with decreased abundances of F. prausnitzii, Ruminococcus bromii, Dorea sp and Collinsella aerofaciens.
- No differences in quality of life and CRP observed between PO/IV

Conclusion:
Shifts in gut bacterial diversity and composition associated with iron treatment are pronounced in IBD participants. Despite similar clinical outcome, oral administration differentially affects bacterial phylotypes and faecal metabolites compared with IV therapy.



Lee T et al. Gut 2017;66:863–871.

2017. Cannabidiol

RCT/Cannabidiol / CD/ Induction

Low-Dose Cannabidiol Is Safe but Not Effective in the Treatment for Crohn's Disease, a Randomized Controlled Trial

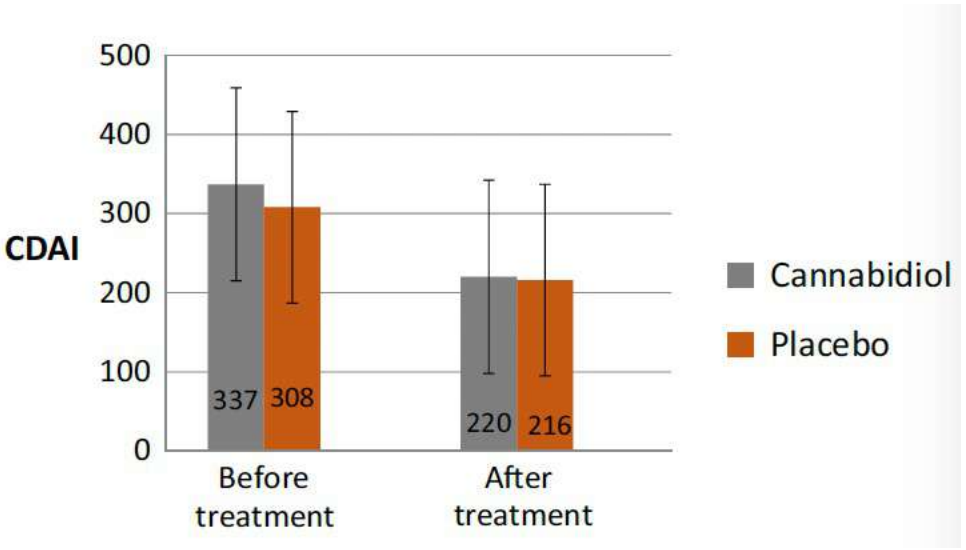
Patients with active CD (CDAI >200-<450) were randomized to receive 10 mg CBD or placebo twice daily.
Steroids, 5ASA, antiTNF, thiopurine, methotrexate allowed at stable dose.

Primary endpoint: Reduction of 70 points in CDAI at week 8.

Results: N=19

- At week 8: CDAI was 2020 cannabidiol vs 216 placebo, p=0.6
- No differences in the number of patients achieving clinical remission between groups.
- No differences in blood tests.
- No differences in adverse events.

Conclusion:
In this study of moderately active Crohn's disease, CBD was safe but had no beneficial effects.



Naftali T et al. Dig Dis Sci. 2017; 62:1615–1620

2011. L-Carnitine

RCT/L-Carnitine / UC/ Induction

Randomised clinical trial: the efficacy and safety of propionyl-L-carnitine therapy in patients with ulcerative colitis receiving stable oral treatment

Multicentre, pase II, double-blind, parallel-group trial.
Patients with UC with disease activity index >2-<11 under stable doce of 5ASA or thiopurine were randomized to propionyl-L-carnitine (PLC) 1g/day, 2 g/day for 4 weeks or placebo.

Primary endpoint: Clinical/endoscopic response defined as a decrease in DAI of >or equal 3 points or remission DAI <3a

Results: N=121

- Clinical response 72% PLC (combined 1 and 2 g) vs 50% placebo, p=0.02.
- Clinical/endoscopic response PLC1 75% vs PLC2 69% vs 50% placebo.
- Rates of remission 55% PLC1, 49% PLC2 and 35% placebo.
- No differences in safety profile were found with placebo

Conclusion:
Propionyl-L-carnitine 1 g / day should be investigated further as a co-treatment for mild-to-moderate ulcerative colitis

Table 2 | Clinical/endoscopic response and remission findings (ITT population, *n* = 119)*

Patient group	Placebo *n/N* (%) (1)	Combined PLC cohort *n/N* (%) (2)	PLC 1 g/day *n/N* (%) (3)	PLC 2 g/day *n/N* (%) (4)	Difference (95% CI)† Based on (2)-(1), (3)-(1) and (4)-(1)	*P* value†
Clinical/endoscopic responses						
All (*n* = 119)	20/40 (50)	57/79 (72)			22 (4-41)	0.02
			30/40 (75)		25 (5-46)	0.02
				27/39 (69)	19 (−2-41)	0.08
Mild disease (*n* = 96)‡	15/32 (47)	46/64 (72)			25 (5-46)	0.02
			24/32 (75)		28 (5-51)	0.02
				22/32 (69)	22 (−2-45)	0.08
Moderate disease (*n* = 23)‡	5/8 (63)	11/15 (73)			11 (−39-61)	0.59
			6/8 (75)		13 (−33-58)	0.59
				5/7 (71)	9 (−38-56)	0.71
Clinical/endoscopic remissions						
All (*n* = 119)	14/40 (35)	41/79 (52)			17 (−2-35)	0.08
			22/40 (55)		20 (−13-41)	0.06
				19/39 (49)	14 (−8-35)	0.23
Mild disease (*n* = 96)‡	13/32 (41)	36/64 (56)			16 (−13-37)	0.15
			21/32 (66)		25 (1-49)	0.05
				15/32 (47)	6 (−18-31)	0.61
Moderate disease (*n* = 23)‡	1/8 (13)	5/15 (33)			21 (−12-54)	0.28
			1/8 (13)		0 (−32-32)	1.00
				4/7 (57)	44 (1-88)	0.07

CI, confidence interval; DAI, disease activity index; LOCF, last observation carried forward; PLC, propionyl-L-carnitine.

Milkhailova TL et al. Aliment Pharmacol Ther. 2011; 34: 1088–1097

2017. Golimumab-Japan

RCT/Golimumab / UC/ Maintenance

Efficacy and safety of golimumab 52-week maintenance therapy in Japanese patients with moderate to severely active ulcerative colitis: a phase 3, double-blind, randomized, placebo-controlled study-(PURSUIT-J study)

Phase 3, double-blind, placebo-controlled, parallel group, randomized withdrawal study.
Patients with moderately-severe active UC received 200mg GOLI SC at week 0 and 100mg at week 2 durnig the 6-week open-label induction. Patients who responded entered maintenance and were randomized to 100mg q4w or placebo for 52 w.

Primary endpoint: Maintenance of clinical response through the end of maintenance at w54.

Results: N=144

- Of the 144, 123 (85.4%) completed the induction phase and 63 (43.8%) were randomized.
- Clinical response was maintained at w54 in 56.3% (18/32) GOLI vs 19.4% (6/31) placebo, p<0.05.
- Clinical remission at w30 and w54 GOLI 50% vs 6.5%placebo, p<0.05.
- Mucosal healing at w54 was 59.4% GOLI vs 16.1% placebo.

Conclusion:
Golimumab SC treatment maintained clinical efficacy through week 54 among induction responders, and no new safety signals were observed in the patients with moderate to severely active UC.

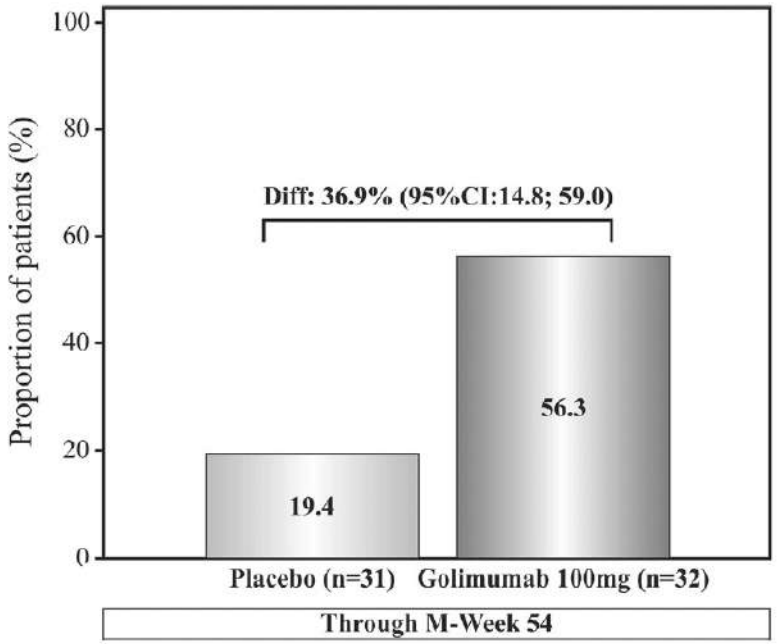


Fig. 2 Proportion of patients with clinical response through M-week 54, Full analysis set-DB. *CI* confidence interval, *DB* double-blind, *M-week* maintenance week

Hibi T et al. J Gastroenterol. 2017; 52: 1101-1111

RCT/5ASA / UC/ Maintenance

Randomised clinical trial: a comparative dose-finding study of three arms of dual release mesalazine for maintaining remission in ulcerative colitis

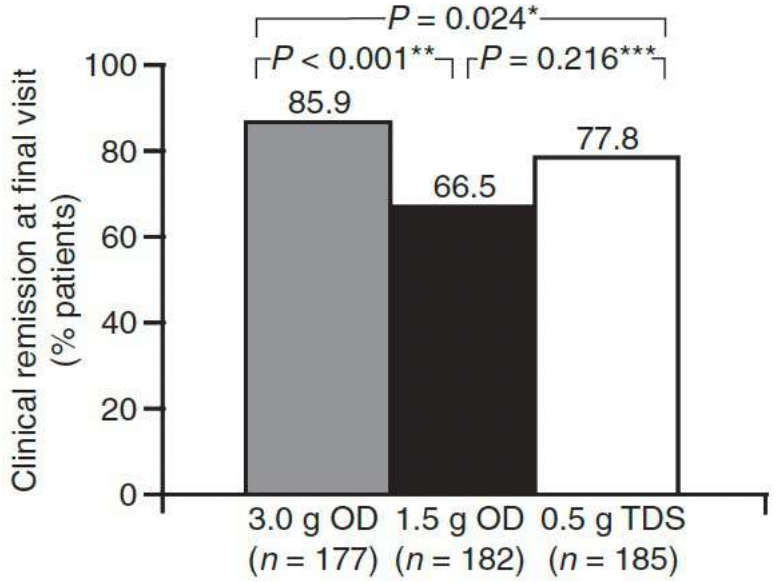
Multicentre, double-blind, double-dummy, 1 year trial.
Patients with endoscopically and histologically confirmed UC in remission were randomized to oral mesalazine 3g OD, 1.5 g OD or 0.5g three times per day (TDS).

Primary endpoint: Clinical remission at 1 year

Results: N=647

- Clinical remission at 1 year was 75% 3gOD vs 61% 1.5gOD and 69% 0.5TID.
- Superiority testing showed higher rate of primary efficacy endpoint in the 3g group vs 1.5g and vs 0.5gTID

Conclusion:
Mesalazine 3.0 g once daily was the most effective dose for maintenance of remission in ulcerative colitis of the three regimens assessed, with no penalty in terms of safety.



Kruis W et al. Alim Pharmacol Ther. 2011; 33: 313–322

Submucosal Injection of the RNA Oligonucleotide GUT-1 in Active Ulcerative Colitis Patients: A Randomized, Double-Blind, Placebo-Controlled Phase 2a Induction Trial

Phase IIa, randomized, double-blind, placebo-controlled trial. Endoscopically active UC patients, refractory to convencional therapy were randomized to a single dosing of 25 nM GUT-1, 250 nM GUT-1, or placebo by endoscopic submucosal injections.

Primary endpoint: Improvement of endoscopic lessions at week 2 or 4 using mayo endoscopic score, improvement was considered Mayo 0-1.

Results: N=24

- Endoscopic improvement at w2 or 4 was achieved in 71.4% GUT-1 250nM, 0% in GUT-1 25nM and 28.6% in placebo.
- Clinical remission was 57.1% GUT-1 250, 0% GUT-1 25 and 14.3% placebo.
- Histological improvement was shown by 42.9% GUT-1 250, 0% GUT-125 and 0% placebo.
- GUT-1 application was well tolerated.

Conclusion:
Single dosing by submucosal injection of GUT-1 repressed CHST15 mucosal expression and may represent a novel induction therapy by modulating tissue remodelling in UC

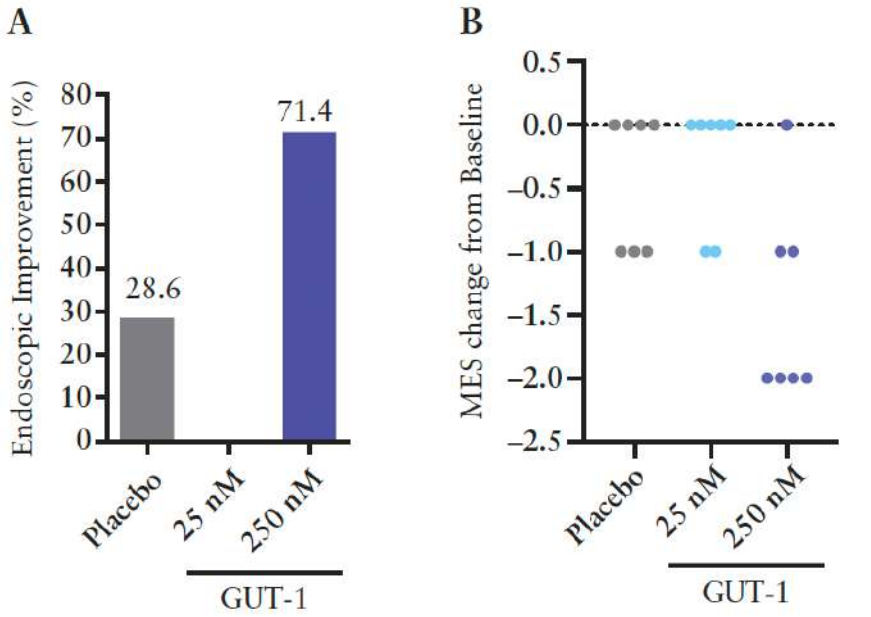


Figure 2. Induction of endoscopic improvement by GUT-1. [A] Rates of endoscopic improvement at week 2 or 4. [B] Changes in the mean Mayo Endoscopic Subscore [MES] at the end of the induction study [weeks 2 or 4] in the GUT1 250 nM [dotted purple], GUT-1 25 nM [dotted light blue], and placebo [dotted grey] groups.

Atreya R et al. J Crohns Colitis. 2024; 18: 406-415

2013. Naltrexone

RCT/Naltrexone/ pCD/ Induction

Safety and Tolerability of Low-dose Naltrexone Therapy in Children With Moderate to Severe Crohn's Disease A Pilot Study

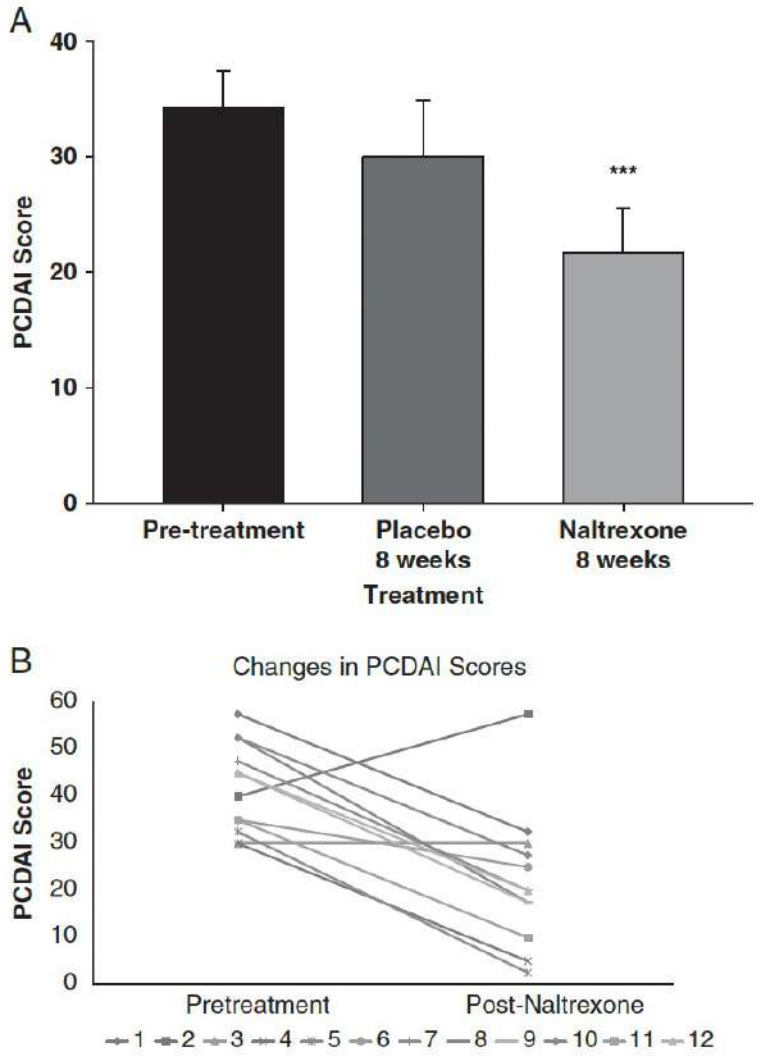
Pilot clinical trial.
Children with mod-severe CD were randomized to naltrexone (0.1mg/kg) orally or placebo for 8 weeks, followed by open-label treatment with additional 8 weeks of naltrexone.

Primary endpoint: Safety and toxicity of administering naltrexone in children by measuring laboratory parameters and recording any potential side effects

Results: N=14

- Oral naltrexone was well tolerated.
- PCDAI scores at w8 decreased (34.2+/-3.3) with an 8-week course of naltrexone therapy (21.7+/-3.9), p=0.005
- Clinical remission w8 25% naltrexone a
- Systemic and social quality of life improved with naltrexone treatment (P=0.035).

Conclusion:
Naltrexone therapy seems safe with limited toxicity when given to children with Crohn's disease and may reduce disease activity.



Smith JP et al. *J Clin Gastroenterol 2013;47:339–345*

2014. Mindfulness-UC

RCT/Mindfulness/UC/ Stress reduct

A Randomized Controlled Trial of Mindfulness- Based Stress Reduction to Prevent Flare-Up in Patients with Inactive Ulcerative Colitis

Randomized controlled trial.
Patients with mod-severe UC who were in clinical remission were randomized to MBSR (minduflness-based stress reduction) or time/attention control.

Primary endpoint: Disease status (absence of flares, time to flare and severity of flares) at year 1.

Results: N=55

- Absence of flares, time to flare and severity of flare over 1 year were similar between groups.
- Post hoc analysis showed that MBSR decreased the % of participants with at least one flare-up among those with top tertile urinary cortisol and baseline perceived stress 30% vs 70%, p<0.0001.
- MBSR prevented a drop in the IBD-QoL during flare p>0.01

Conclusion:
MBSR did not affect the rate or severity of flare-ups in UC patients in remission. However, MBSR might be effective for those with high stress reactivity (high perceived stress and urinary cortisol) during remission. MBSR appears to improve QOL in UC patients by minimizing the negative impact of flare-ups on QOL.

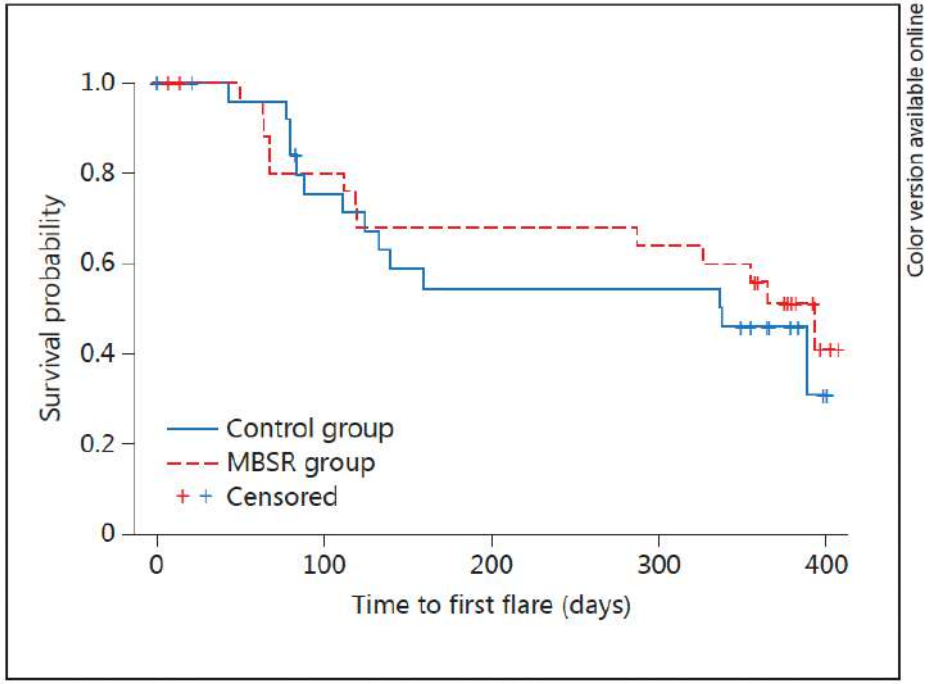


Fig. 2. Kaplan-Meier survival analysis. Comparison of time to flare from baseline to last visit (flare-up). Time to first flare: as measured in number of days from baseline visit to flare-up.

Jedel S et al. *Digestion 2014;89:142–155*

2012. RIFAXIMIN-CD

RCT/Rifaximin/CD/ Induction

Rifaximin-Extended Intestinal Release Induces Remission in Patients With Moderately Active Crohn's Disease

Multicentre, randomized, double-blind trial.
Patients with moderately active CD were randomized to 400, 800 or 1200mg twice daily rifaximin-extended intestinal reléase or placebo for 12 weeks.

Primary endpoint: CDAI <150at week 12

Results: N=55

- W12 CDAI<150 was 62% RIFAX800 vs 43% placebo, p=0.005. RIFAX400 54% and RIFAX1200 47% did not differ from placebo.
- RIFAX400 and RIFAX800 doses had low rates of withdrawal, howeer RIFAX1200 had significantly higher 16%.

Conclusion:
Administration of 800 mg rifaximin-EIR twice daily for 12 weeks induced remission with few adverse events in patients with moderately active CD.

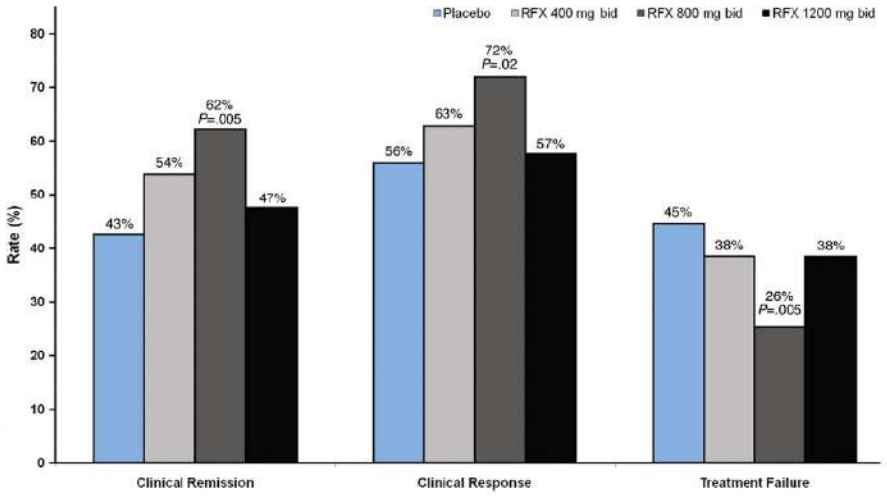


Figure 2. Efficacy of the 3 different doses of rifaximin-EIR 400 mg tablet, as compared with placebo (FA dataset). As evaluated on the CDAI, percentages of patients with a clinical remission (CDAI < 150 points), clinical response (reduction of at least 100 points) and treatment failure rates are shown. RFX, rifaximin-EIR.

Prantera C et al. Gastroenterology. 2012; 142:473-481