

IBUS HYBRID module 1

7-8TH
NOVEMBER, 2025
MILAN, ITALY

Treat to target and optimization of mesalazine therapy in mild to moderate ulcerative colitis

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Disclosures



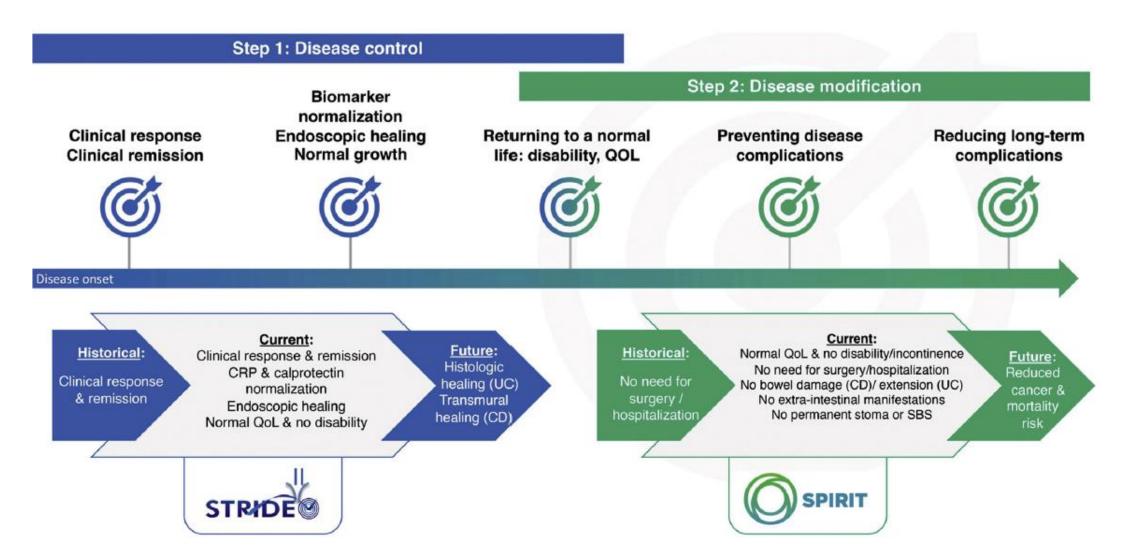
 speaker fees from Alfasigma, Eli Lilly, Ferring, Johnson & Johnson, Lionhealth, Novartis, Pfizer, and Takeda

 advisory board for AbbVie, Celltrion Healthcare, Eli Lilly, Johnson & Johnson and Pfizer

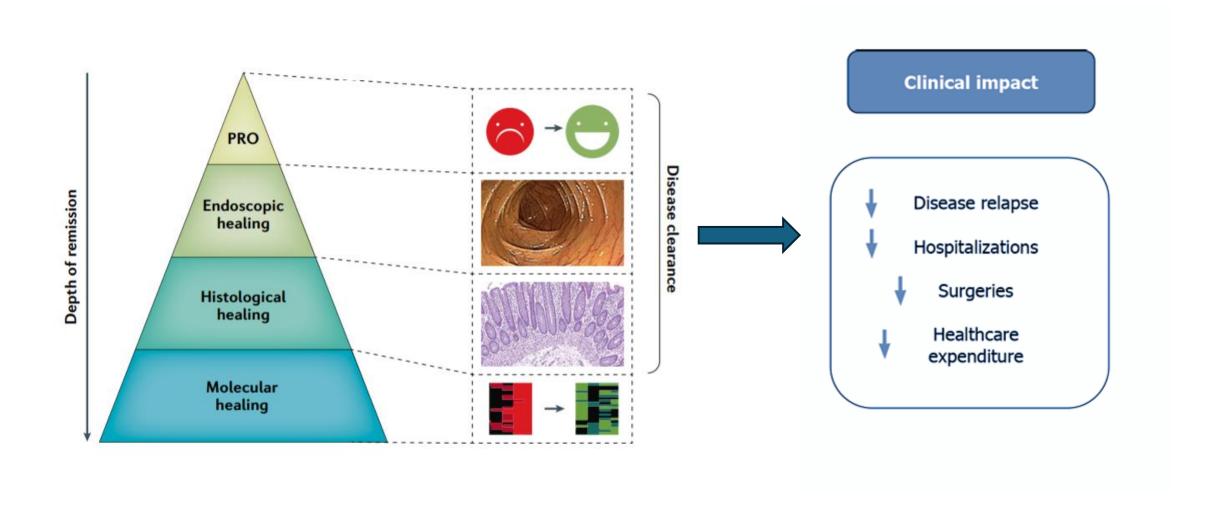


Why treat to target in UC?





The concept of DISEASE CLEARANCE: a new composite desirable outcome



Where mesalazine (5-ASA) fits





Recommendation 1

We recommend 5-aminosalicylates at a dose of ≥2 g/day [d] to induce remission in patients with mildly-to-moderately active UC [strong recommendation; quality of evidence low]

Recommendation 2

We recommend topical [rectal] 5-ASA at a dose of ≥1 g/d for the induction of remission in active distal colitis [strong recommendation, low-quality evidence]

Recommendation 3

We suggest the use of oral 5-ASA [≥2 g/d] combined with topical [rectal] 5-ASA over oral 5-ASA monotherapy for induction of remission in adult patients with active UC of at least rectosigmoid extent [weak recommendation; very low-quality evidence]

Recommendation 8

We recommend the use of oral 5-ASA at a dose ≥2 g/day for maintenance of remission in UC patients [strong recommendation; very low quality of evidence]

Recommendation 9

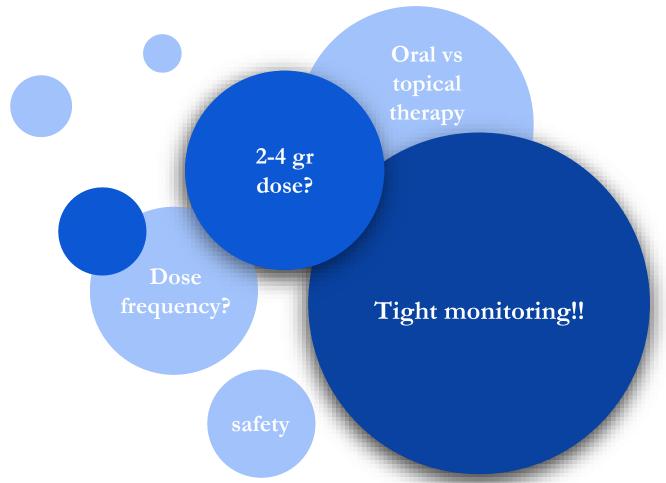
We suggest the use of topical [rectal] 5-ASA for the maintenance of remission in patients with distal UC [weak recommendation, very low-quality evidence]



Principles of optimizing 5-ASA

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Optimization of treatment aims to ensure that the best outcomes for patients are achieved while avoiding the use of systemic steroids whenever possible





Is there an optimal dosage of 5ASA in induction of remission?

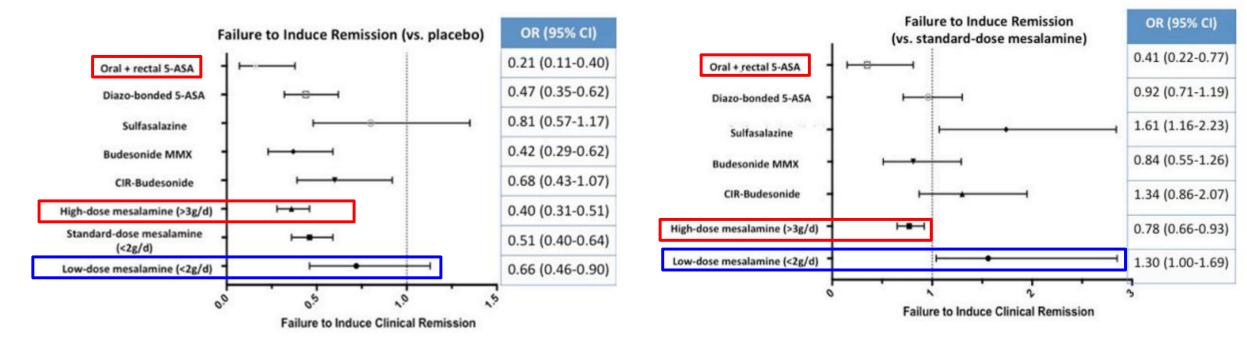
ARTICLES · Volume 3, Issue 11, P742-753, November 2018



Comparative efficacy and tolerability of pharmacological agents for management of mild to moderate ulcerative colitis: a systematic review and network meta-analyses

Nghia H Nguyen, MD ^{a,†} · Mathurin Fumery, MD ^{a,b,†} · Parambir S Dulai, MD ^a · Larry J Prokop, MLS ^c · Prof William J Sandborn, MD ^a · Prof Mohammad Hassan Murad, MD ^d · et al. Show more

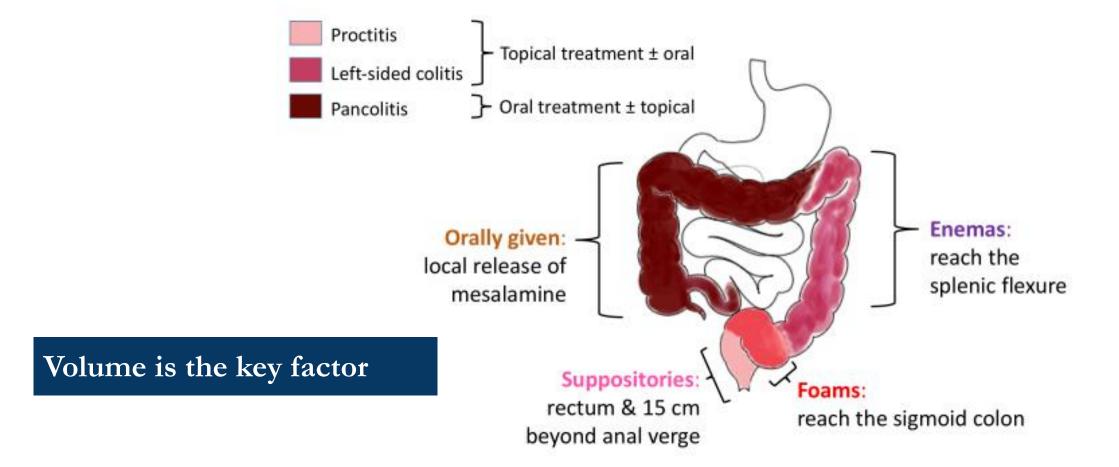
48 induction randomised trials (**8020** participants)



In patients with **mildly to moderately active** left-sided or extensive ulcerative colitis, combined oral and topical mesalazine therapy and high-dose mesalazine are superior to standard-dose mesalazine for induction of remission

Role of topical 5-ASA?

• Possibility to administer high doses of active ingredient directly to the superficially inflamed mucosa







The power of combined therapy: 1+1 = 3!

Efficacy of Oral vs. Topical, or Combined Oral and Topical 5-Aminosalicylates, in Ulcerative Colitis: Systematic Review and Meta-Analysis

Alexander C. Ford, MBChB, MD, MRCP^{1,2}, Khurram J. Khan, MD, FRCPC³, Jean-Paul Achkar, MD⁴ and Paul Moayyedi, BSc, MBChB, PhD, MPH, FRCP, FRCPC³

	Oral and topi	cal 5-ASA	Oral 5-	ASA		Risk ratio		Risk ratio				
Study or subgroup	Events	Total	Events	Total	Weight	M-H, random, 95% CI	Year		M-H, randor	n, 95% CI		
Fruhmorgen and Demling (1980)	2	12	7	11	5.7%	0.26 (0.07, 1.00)	1980	-				
Safdi et al. (1997)	4	20	12	22	10.5%	0.37 (0.14, 0.95)	1997					
Vecchi et al. (2001)	22	63	31	67	35.4%	0.75 (0.49, 1.15)	2001			-		
Marteau et al. (2005)	34	71	36	56	48.4%	0.74 (0.55, 1.02)	2005		-			
Total (95% CI)		166		156	100.0%	0.65 (0.47, 0.91)			•			
Total events	62		86									
Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 4.24$, df = 3 ($P = 0.24$); $I^2 = 29\%$								\vdash		-	$\overline{}$	-
Test for overall effect:	Z=251 (P=0)	11)						0.1 0.2	0.5 1	2	5	10
1031 101 0401dil 011001. Z=2.31 (F=0.01)								Favors oral	Favors oral 5-ASA			

Combined 5-ASA therapy appeared superior to oral 5-ASAs for induction of remission of mildly to moderately active UC. *Intermittent topical 5-ASAs* (3 gr/week) appeared superior to oral 5-ASAs for preventing relapse of quiescent UC.





Analysis 3.1. Comparison 3: Once daily dosing versus conventional dosing, Outcome 1: Failure to induce global/clinical remission

	OD de	OD dosing		Conventional dosing		Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
3.1.1 MMX once daily	(OD) versu	s twice dai	ily (BID)						
Lichtenstein 2007	65	94	60	93	11.2%	1.07 [0.88, 1.31]			
Subtotal (95% CI)		94		93	11.2%	1.07 [0.88, 1.31]			
Total events:	65		60						
Heterogeneity: Not app	licable								
Test for overall effect: 2	Z = 0.67 (P =	0.50)							
3.1.2 Salofalk granule	s once daily	(OD) versi	us three times	daily (TID))				
Kruis 2009	40	191	46	189	8.6%	0.86 [0.59, 1.25]			
Subtotal (95% CI)		191		189	8.6%	0.86 [0.59, 1.25]			
Total events:	40		46						
Heterogeneity: Not app	licable								
Test for overall effect:	Z = 0.79 (P =	0.43)							
3.1.3 MMX once daily	(OD) versu	s Asacol th	ree times daily	(TID)					
Kamm 2007	50	85	57	86	10.5%	0.89 [0.70, 1.12]			
Subtotal (95% CI)		85		86	10.5%	0.89 [0.70, 1.12]			
Total events:	50		57				$\overline{}$		
Heterogeneity: Not app	licable								
Test for overall effect: 2	Z = 1.00 (P =	0.32)							
3.1.4 Pentasa once dai	ily (OD) vers	sus twice d	aily (BID)						
Flourié 2013	56	102	62	104	11.4%	0.92 [0.73, 1.17]			
Subtotal (95% CI)		102		104	11.4%	0.92 [0.73, 1.17]			
Total events:	56		62				$\overline{}$		
Heterogeneity: Not app	licable								
Test for overall effect:	Z = 0.68 (P =	0.49)							
.1.5 Mesalazine once	daily (OD)	versus twic	ce daily (BID)						
O'Haens 2017	322	409	313	408	58.2%	1.03 [0.95, 1.10]	+		
Subtotal (95% CI)		409		408	58.2%	1.03 [0.95, 1.10]	-		
Total events:	322		313				ľ		
leterogeneity: Not app	licable								
Test for overall effect: 2	Z = 0.69 (P =	0.49)							
Total (95% CI)		881		880	100.0%	0.99 [0.93 , 1.06]	•		
Total events:	533		538				T		
Heterogeneity: Chi ² = 3	3.24, df = 4 (1	P = 0.52); I	2 = 0%				0.5 0.7 1 1.5 2		
est for overall effect: 2	Z = 0.28 (P =	0.78)					Favours OD Favours convent		

Test for subgroup differences: Chi2 = 2.98, df = 4 (P = 0.56), I2 = 0%





Once daily?



Analysis 4.1. Comparison 4: 5-ASA versus comparator 5-ASA, Outcome 1: Failure to induce global/clinical remission

	5-ASA form	nulations	5-ASA con	parator		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
4.1.1 Asacol comparate	or						
Forbes 2005	34	46	30	42	6.2%	1.03 [0.80, 1.34]	+
Ito 2010	47	65	46	66	9.0%	1.04 [0.83, 1.29]	<u> </u>
Kamm 2007	49	84	57	86	11.1%	0.88 [0.70, 1.11]	<u>-</u>
Levine 2002	41	49	43	49	8.5%	0.95 [0.81, 1.12]	4
Pruitt 2002	45	84	51	89	9.7%	0.93 [0.72, 1.22]	
Tursi 2004	9	30	14	30	2.8%	0.64 [0.33, 1.25]	
Subtotal (95% CI)		358		362	47.2%	0.94 [0.85, 1.04]	4
Total events:	225		241				٦
Heterogeneity: Chi ² = 2	.88, df = 5 (P =	0.72); I ² = 0	1%				
Test for overall effect: 2	Z = 1.14 (P = 0.2)	25)					
4.1.2 Claversal compa	rator						
Kruis 1998	48	88	41	80	8.4%	1.06 [0.80, 1.42]	-
Raedler 2004	61	181	69	181	13.6%	0.88 [0.67, 1.17]	
Subtotal (95% CI)		269		261	22.0%	0.95 [0.78, 1.17]	•
Total events:	109		110				Ť
Heterogeneity: Chi2 = 0	.85, df = 1 (P =	0.36); $I^2 = 0$	196				
Test for overall effect: 2	Z = 0.47 (P = 0.6)	64)					
4.1.3 Salofalk compara	ator						
Gibson 2006	43	127	48	131	9.3%	0.92 [0.66, 1.29]	<u></u>
Marakhouski 2005	37	118	39	115	7.8%	0.92 [0.64, 1.34]	
Subtotal (95% CI)		245		246	17.1%	0.92 [0.72 , 1.18]	•
Total events:	80		87				ĭ
Heterogeneity: Chi ² = 0	.00, df = 1 (P =	1.00); $I^2 = 0$	1%				
Test for overall effect: 2	Z = 0.63 (P = 0.5	53)					
4.1.4 Pentasa compara	tor						
Farup 2001	93	150	53	77	13.8%	0.90 [0.74, 1.10]	
Subtotal (95% CI)		150		77	13.8%	0.90 [0.74, 1.10]	▲
Total events:	93		53				٦
Heterogeneity: Not appl	licable						
Test for overall effect: 2	Z = 1.05 (P = 0.3)	30)					
Total (95% CI)		1022		946	100.0%	0.94 [0.86 , 1.02]	•
Total events:	507		491				1
Heterogeneity: Chi ² = 4	.07, df = 10 (P	= 0.94); I ² =	0%				0.2 0.5 1 2 5
Test for overall effect: 2	z = 1.58 (P = 0.1)	11)				Fav 5-AS	A formulations Comparator formu

Test for subgroup differences: Chi2 = 0.20, df = 3 (P = 0.98), I2 = 0%







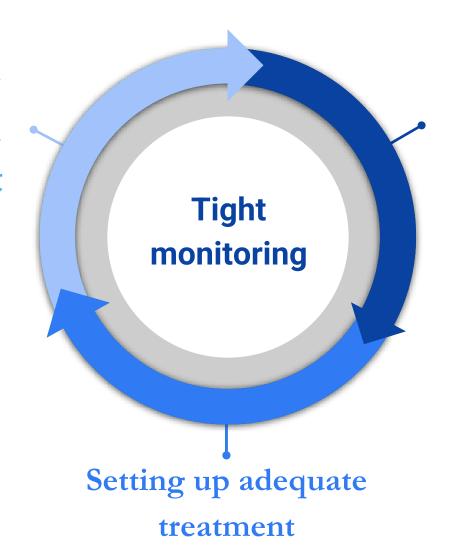


TIGHT MONITORING to reach targets in mild to moderate UC

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Cyclic assessment of treatment response.

Steroid sparing



Prevention and
early identification
of disease relapses



Patient reported outcome (PRO2)

Patient-Reported Outcomes and Endoscopic Appearance of Ulcerative Colitis: A Systematic Review and Meta-analysis

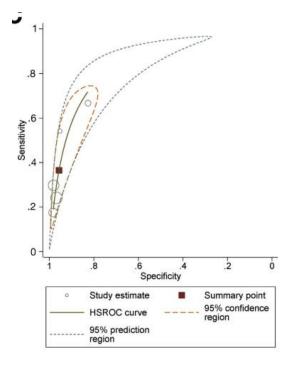
→ PROs correlate closely with overall well-being and should be evaluated regularly throughout the disease course.

→ In UC, PRO2 (including stool frequency and rectal bleeding) has emerged as the standard for

symptom assessment.

However, the correlation between PROs and histological and endoscopic outcomes is poor.

Combined rectal bleeding and stool frequency subscore of 0 identified patients in endoscopic remission with a pooled sensitivity value of 36% and a specificity value of 96%



Prognostic Value of Fecal Calprotectin to Inform Treat-to-Target Monitoring in Ulcerative Colitis



Adult patients with moderately to severely active UC treated with a biologic



Post hoc analysis of data from GEMINI 1/LTS and VARSITY



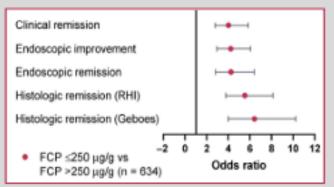
- Cross-sectional accuracy of FCP concentration for the identification of endoscopic activity and histologic inflammation
- Evaluate associations between FCP concentration and week 52 outcomes and long-term complications

Despite modest cross-sectional accuracy, FCP concentration of ≤250 μg/g vs >250 μg/g was associated with increased probability of achieving week 52 outcomes and lower risk of long-term complications

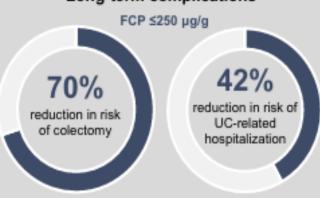
Cross-sectional accuracy

FCP >250 μg/g	GEMINI 1	VARSITY
Moderate-to-severe endoscopic activity	66%	77%
Active endoscopic disease	63%	70%
Histologic inflammation (RHI)	-	72%
Histologic inflammation (Geboes)	-	68%

Week 52 outcomes



Long-term complications



FCP, fecal calprotectin; LTS, long-term safety; RHI, Robarts Histopathology Index; UC, ulcerative colitis. ClinicalTrials.gov: NCT00783718, NCT00790933, NCT02497469 Clinical Gastroenterology and Hepatology

Role of endoscopy

The timing of endoscopic procedures should vary based on clinical activity and fecal calprotectin levels

- → In case of clinical remission with normalization of inflammatory markers it could reasonably be performed WITHIN 12 MONTHS.
- → In case of persistent activity, endoscopy should be performed much **SOONER**

SIGMOIDOSCOPY OR FULL COLONOSCOPY??

Role of endoscopy

Efficacy of sigmoidoscopy for evaluating disease activity in patients with ulcerative colitis

Su Bum Park^{1†}, Seong-Jung Kim^{2†}, Jun Lee^{2*}, Yoo Jin Lee³, Dong Hoon Baek⁴, Geom Seog Seo⁵, Eun Soo Kim⁶, Sang-Wook Kim⁷ and So Yeong Kim⁸

ADEQUACY OF SIGMOIDOSCOPY IN COMPARISION TO COLONOSCOPY TO ASSESS DISEASE ACTIVITY DURING FOLLOW UP IN PATIENTS WITH ULCERATIVE COLITIS

Sameet Patel · Shubham Jain · Sanjay Chandnani · ... · Seemily Kahmei · Rima Kamat · Pravin Rathi ... Show more

Effectiveness of sigmoidoscopy for assessing ulcerative colitis disease activity and therapeutic response

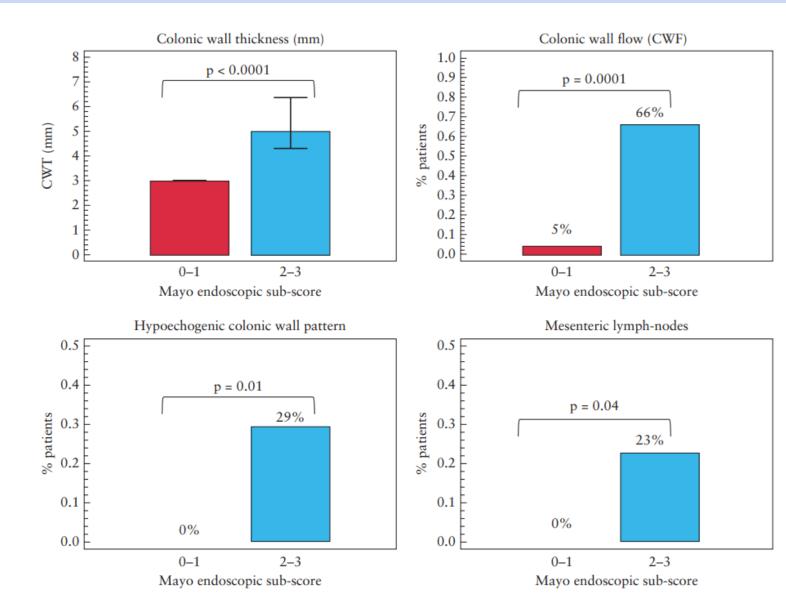
Wei-Chen Lin a,*, Chen-Wang Chang a, Ming-Jen Chen a, Tzu-Chi Hsu b, Horng-Yuan Wang a

Accuracy of Humanitas Ultrasound Criteria in Assessing Disease Activity and Severity in Ulcerative Colitis: A Prospective Study

Mariangela Allocca, a,b Gionata Fiorino, a,b Stefanos Bonovas, a,b,o Federica Furfaro, a Daniela Gilardi, a Marjorie Argollo, c Paola Magnoni, d Laurent Peyrin-Biroulet, e Silvio Danese a,b

$$n = 53$$

- → Colonic wall thickness, colonic wall flow, hypoechogenic wall pattern and the presence of lymph nodes significantly correlated with endoscopic activity.
- → CWT and CWF were independent predictors for endoscopic activity



ECCO-ESGAR-ESP-IBUS Guideline on Diagnostics and Monitoring of Patients with Inflammatory Bowel Disease: Part 1

Recommendation 8 In patients with UC requiring treatment initiation or optimization, we recommend early (within 12 weeks) clinical (EL1), biochemical (EL1), and endoscopic (EL1) or ultrasonographic (EL2) response assessment. Results should be interpreted based on prior baseline assessment. (92% agreement)

Recommendation 9 In patients with UC in stable remission, we suggest using PROs, biomarkers (such as FC and CRP), IUS, or combinations thereof to monitor for disease relapse based on risk stratification. (EL3) (94% agreement)

Baseline assessment

Ulcerative Colitis

Early response assessment within 12 weeks

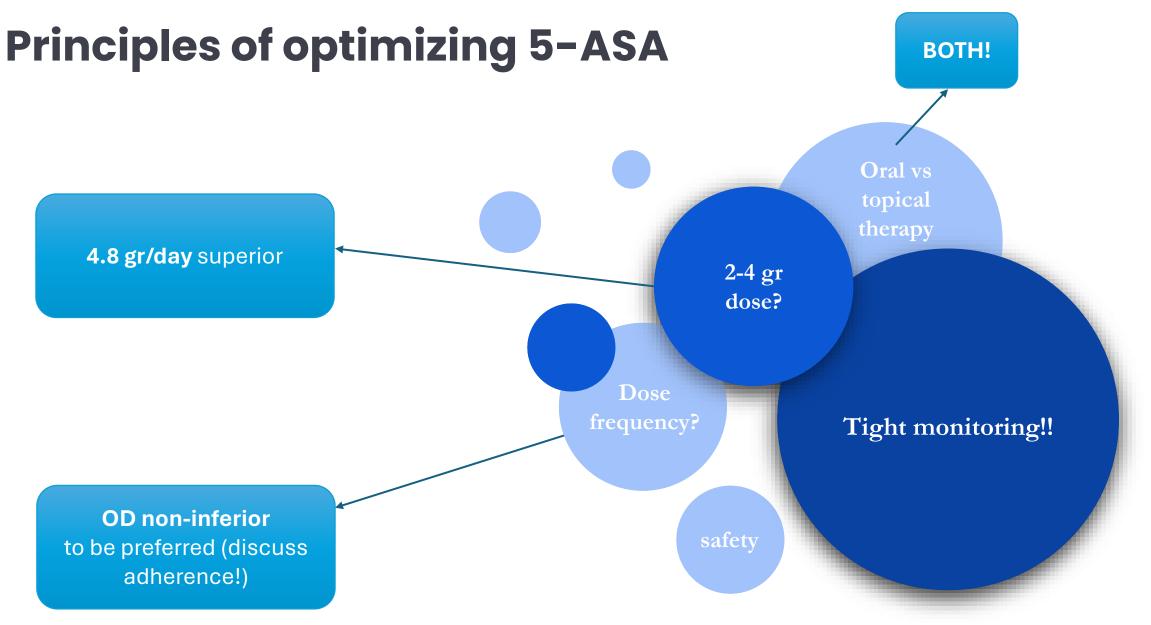
Clinic (PRO) Biomarkers (CRP and/or fCalprotectin)



Endoscopy + histology or IUS





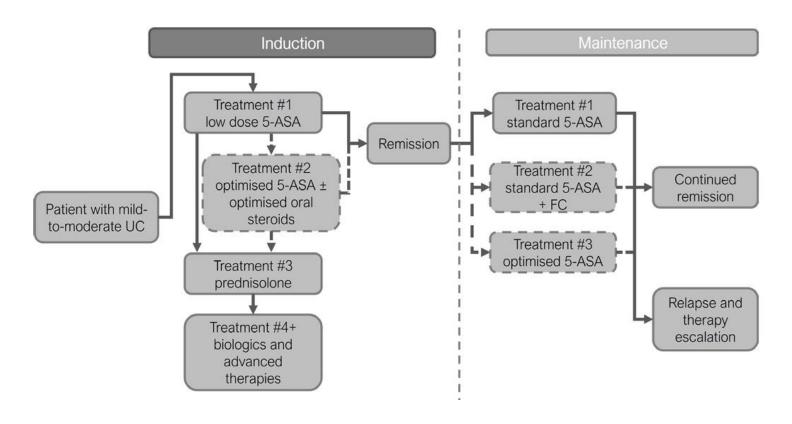






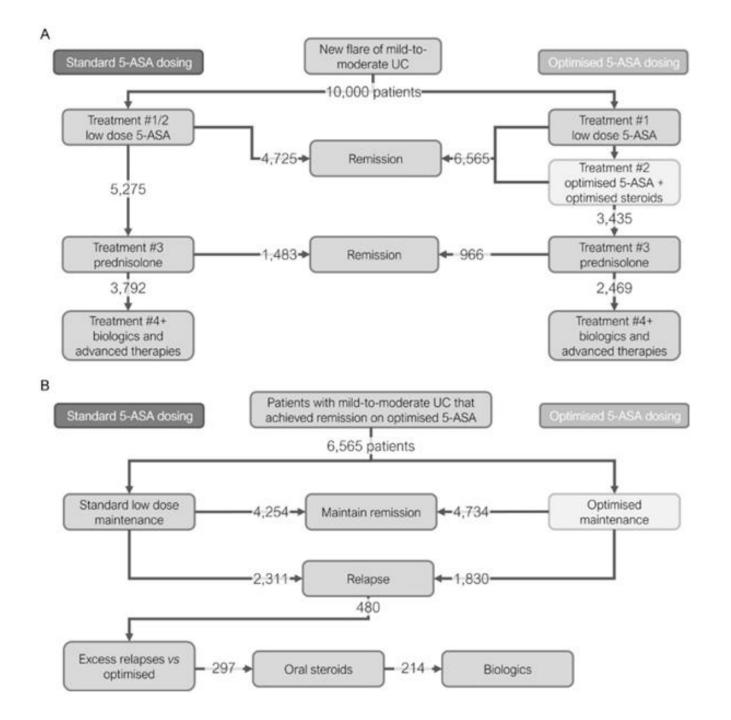


Modelling the benefits of an optimised treatment strategy for 5-ASA in mild-to-moderate ulcerative colitis



A decision tree model followed 10.000 newly diagnosed patients with mild-to-moderate UC through induction and 1 year of maintenance treatment

Optimised treatment (maximising dose of 5-ASA and use of combined oral and rectal therapy before treatment escalation) was compared with standard treatment (standard doses of 5-ASA without optimisation). Modelled data were derived from published meta-analyses.



- 47% achieved remission on standard dose 5ASA compared with 66% on optimised 5ASA (relative increase of 39%)
- 18% of patients avoided systemic steroids due to the use of optimised 5ASA regimen
- The modelling conducted in this study indicates that <u>an optimised treatment</u> <u>pathway for mild- to- moderate UC has clear benefits for patients.</u>



Take-home messages



- T2T strategy is essential (clinical + biomarker + endoscopic)
- IUS is a useful monitoring tool to be used as P.o.C. also in UC.
- <u>Mesalazine is first-line</u> for mild-to-moderate UC; optimize dose (OD!) and route before escalation.
- Monitor early and objectively; adherence and rectal therapy are high-yield interventions.



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Thankyou