MEETING OF THE MINDS

WESTIN HARBOUR CASTLE, TORONTO

SATURDAY, November 15, 2025

Canada Future Directions in IBD

Co-Chairs: **Remo Panaccione**, MD FRCPC and **A. Hillary Steinhart**, MD MSc FRCPC

crohn's colitis canada | crohn colite canada | University of Alberta | University of Calgary Medicine | McGill University | McMaster University | University of Toronto Faculty of Medicine

Workshop 3.3
Advanced Sequencing of Biologics and Small Molecules in Pediatrics

Anne Griffiths & Sally Lawrence

Objectives

- Compare available biologics and small molecules for pediatric IBD and their positioning within treatment algorithms
- Apply principles of therapeutic sequencing to optimize in pediatric patients with complex or refractory IBD

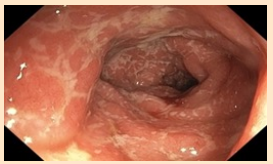
Index patient in late 2016

- As an 8 ½ year old girl, presented with bloody diarrhea, escalating over three month period; up to 7 bloody stools/day + 1/night. Denied abdominal pain. Remaining systemically well. Weight loss 4 lbs.
- Hemoglobin 87 (down from 107 three weeks earlier); CRP 10.9; albumin 38
- Colonoscopy: pancolitis; normal terminal ileum. Normal upper endoscopy.
- Good response to IV steroids with transition to oral prednisone

Questions

- If this were now, what treatment options would you consider to maintain remission?
- What would your monitoring plan be?

New onset paediatric UC: multicentre prospective study



PROTECT
Predicting Response to Standardized Pediatric Colitis Therapy

- Aim: to define rates of week 52 steroid-free remission with 5-ASA maintenance after standardized induction therapy with 5-ASA (if mild) or corticosteroids (if moderate or severe)
- N=423 patients with new onset UC; 33% mild (5-ASA induction); 67% moderate/severe (corticosteroids for induction)

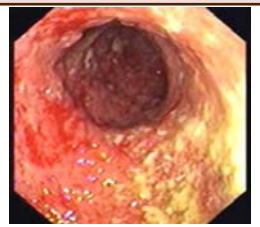
12 month outcomes according to PUCAI at presentation

Baseline disease activity	Mild	Mod/Severe
CS Free Remission on 5-ASA only	49%	30%

Hyams JS et al Lancet Gastroenterol Hepatol 2017; 2: 855-68
Hyams JS et al, Lancet 2019: 1708-1720

CIDsCANN

105 children hospitalized with new onset ASUC (PUCAI≥65) IV Corticosteroid treatment



Steroid refractory N=54

INFLIXIMAB induction n=54 (intensified)

Steroid responsive n=51

Non-biologic maintenance therapy 5-ASA n=45 THIOPURINE n=6 *Steroids tapered*

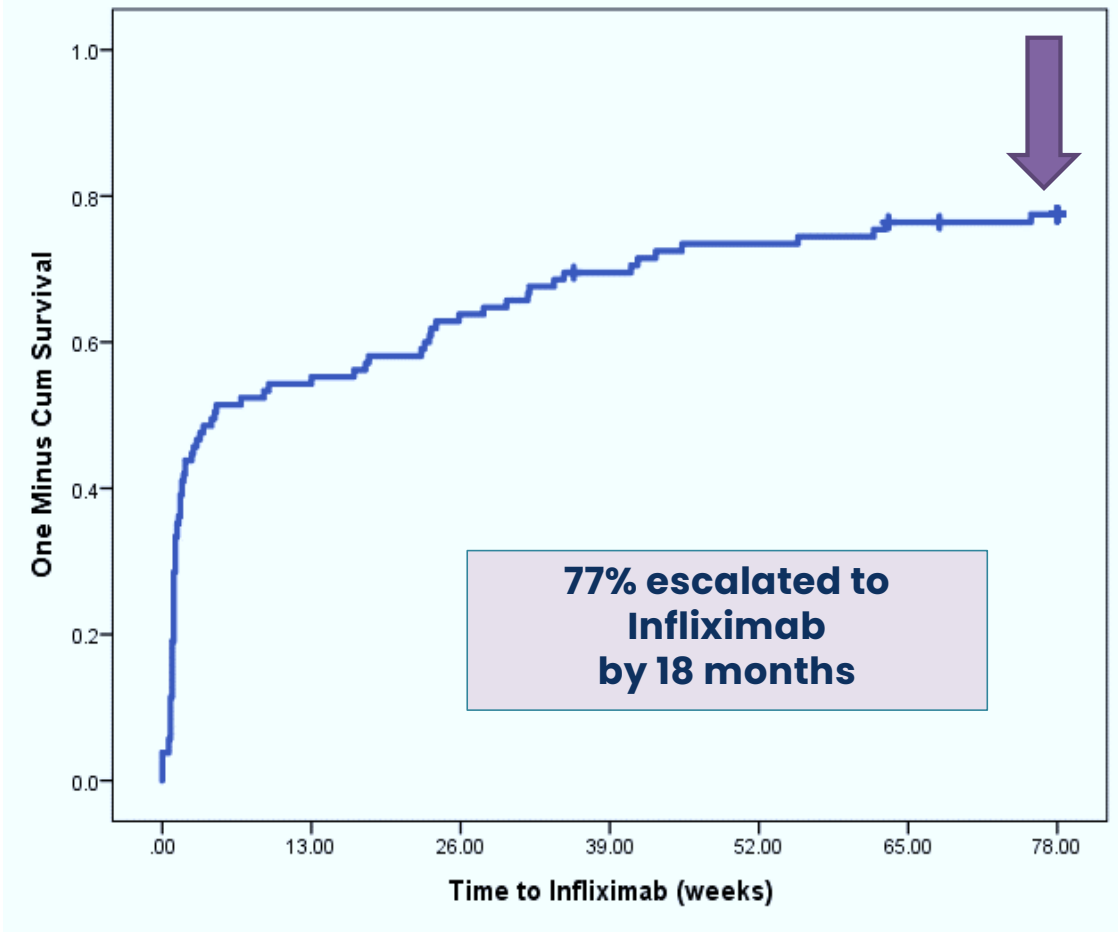
Overall 61% steroid-free clinical remission at 1 year

63% of initially steroid-refractory All on biologics (33 IFX, 1 vedo)

54% of initially steroid responsive 13 5-ASA; 5 thiopurines; 7 IFX, 2 vedo; 1 ADA

Dhaliwal J et al, J Crohn Colitis 2024;18(2):233-245

Time to infliximab: children with ASUC at first presentation with UC



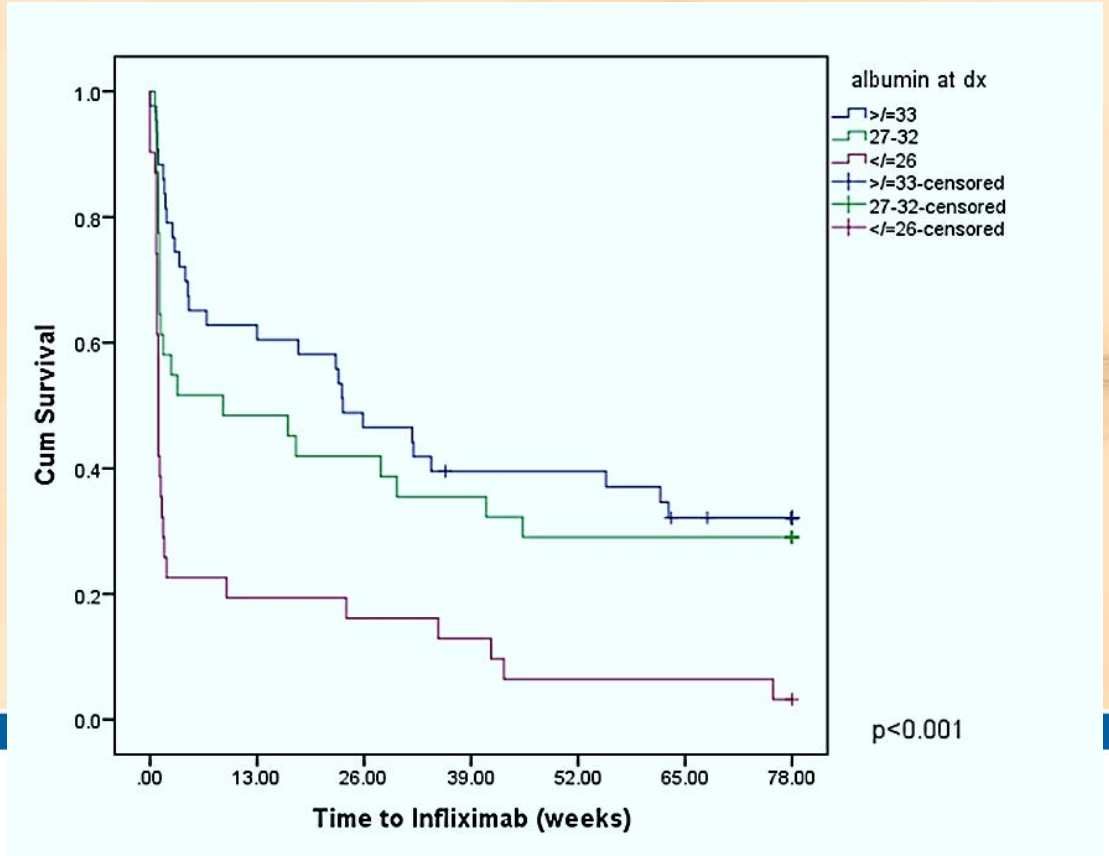
- **Steroid refractory: 54 (67%)**
- **Steroid dependent: 27 (33%)**
- **Median (IQR) time to Infliximab 1.57 (0.93-20.3) weeks**

	2wk	4wk	3mo	6mo	9mo	12mo	18mo
N	46	5	7	9	6	4	4
Cum %	44%	49%	55%	64%	70%	73%	77%

~ equal use of Infliximab monotherapy versus + Ifx + IM (usually MTX)

Dhaliwal J et al, J Crohn Colitis 2024;18(2):233-245

Acute severe colitis (ASUC) at first presentation



Albumin g/L	Hazard ratio (95%CI)	p-value
≤36	1.89 (1.01-3.53)	0.045
≤32	2.00 (1.25-3.18)	0.004
≤26	2.57 (1.60-4.11)	<0.001

Adjusted for PUCAI, gender and age

Reflections on management of acute severe UC at first presentation

- Intensification of infliximab regimen during induction and as needed during maintenance has reduced need for colectomy

- Merits reconsideration of optimal first maintenance for children with ASUC who achieving clinical remission with steroids
  - Thiopurines?
  - “advanced therapy”: Vedolizumab?

Index patient in late 2016

- Following prompt response to steroids, started oral 5-ASA
- Suboptimal follow-up; remained “well” off steroids on oral 5-ASA
- By one year post diagnosis: clear recurrence of loose, bloody stools settling with oral prednisone

Question

- If this was now, how would you manage a patient with known UC pancolitis, who is steroid-dependent despite oral 5-ASA?

Positioning “advanced therapies” in steroid-dependent UC: choices to make (excluding steroid-refractory)

TIMEPOINT	NOW
Choosing FIRST “advanced therapy”	**When to start**? -After 5-ASA (**and/or thiopurine**) failure? **Which** biologic or targeted oral small molecule?

Choice is not just about efficacy

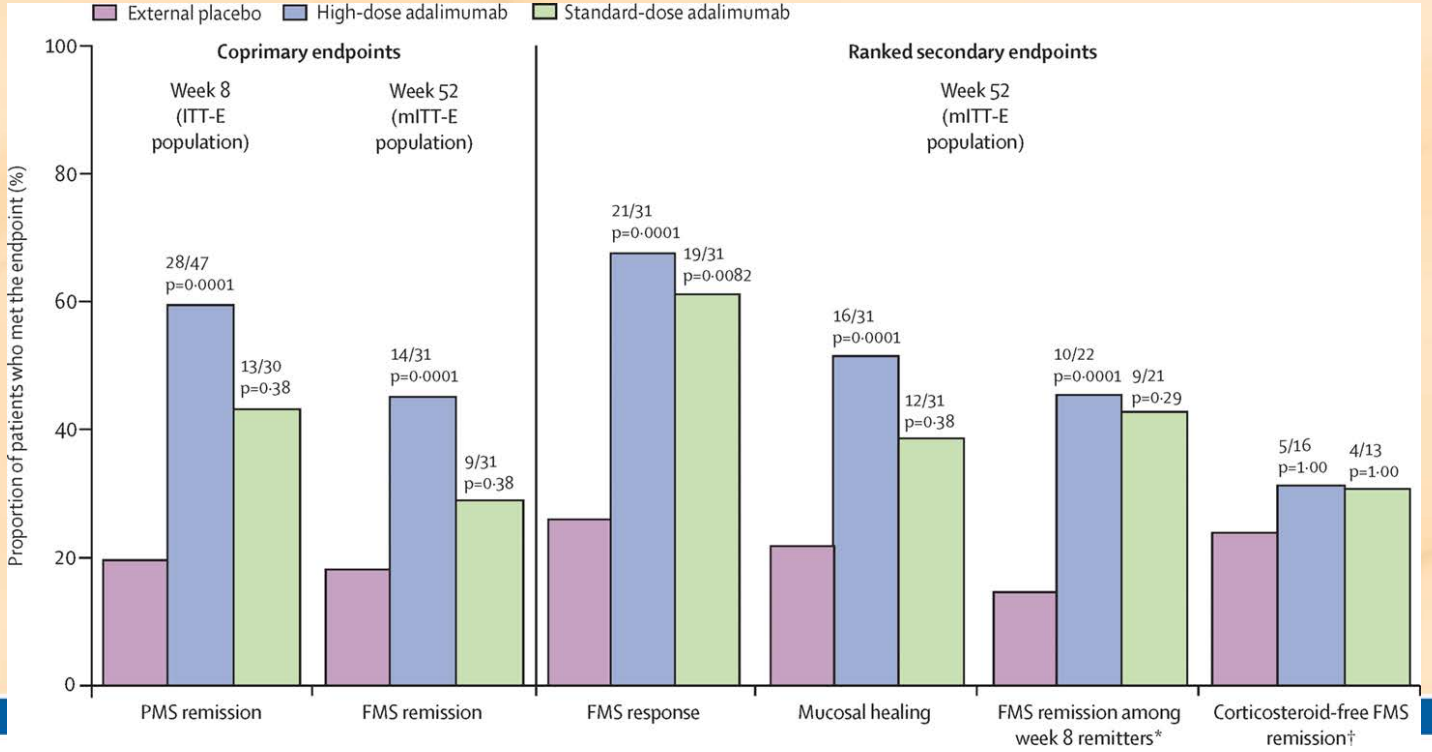
CLINICIAN AND PATIENT / PARENTS CONSIDERATIONS	
Reliable induction of **steroid-free clinical remission**	**Does it work?**
Efficacy in **achieving mucosal healing**	
Favorable safety profile	**Is it safe?**
Knowledge of how optimize efficacy (dosing, TDM)	
Durability of remission (including Immunogenicity)	**Will it keep working?**
Rapidity of onset	**How quickly will my child feel better?**
Patient preference for mode of administration	
Efficacy in special situations (e.g. perianal fistulizing disease; inflammatory co-morbidities)	
Cost	

Positioning advanced therapies in ulcerative colitis (excluding steroid-refractory hospitalized patients)

TIMEPOINT	UNTIL RECENTLY	NOW (*in the near future?)*
FIRST	Infliximab (or adalimumab)	Vedolizumab Infliximab (or adalimumab) Ustekinumab (*or anti-IL23?*) *(Ozanimod?) (etrasimod?)* *(Upadacitinib?)*

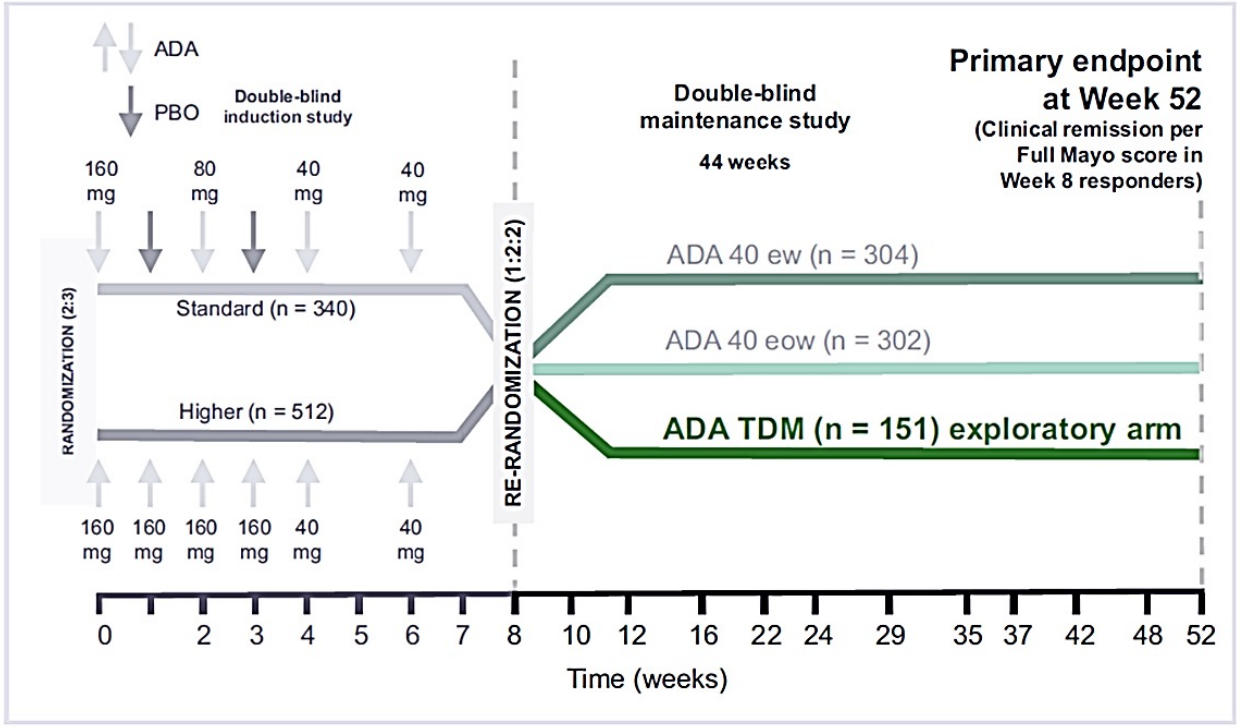
Is adalimumab an alternate first anti-TNF in ambulatory UC?

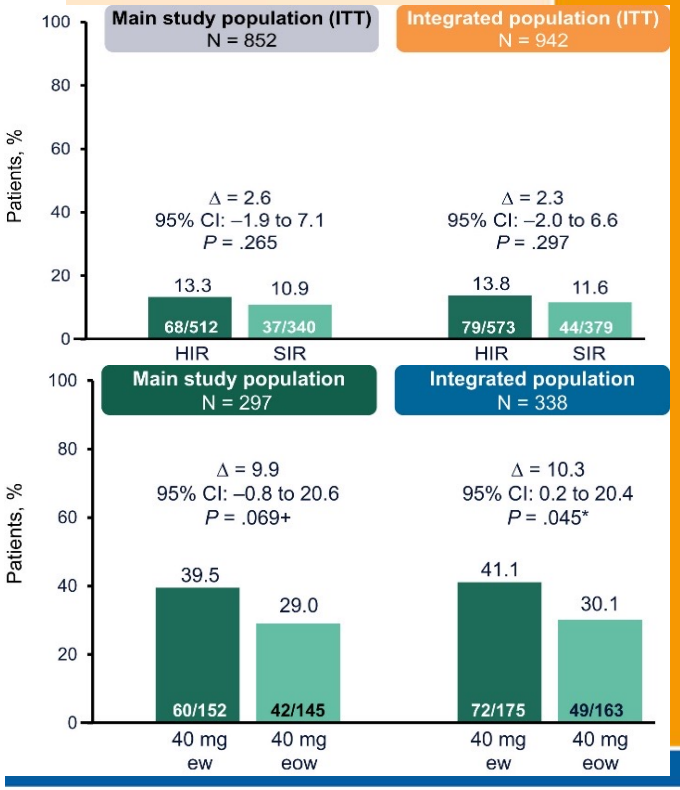
ENVISION paediatric UC trial



Higher vs Standard Adalimumab Induction and Maintenance Dosing Regimens for Treatment of Ulcerative Colitis: SERENE UC Trial Results

Julián Panés,[1] Jean-Frederic Colombel,[2] Geert R. D'Haens,[3] Stefan Schreiber,[4]



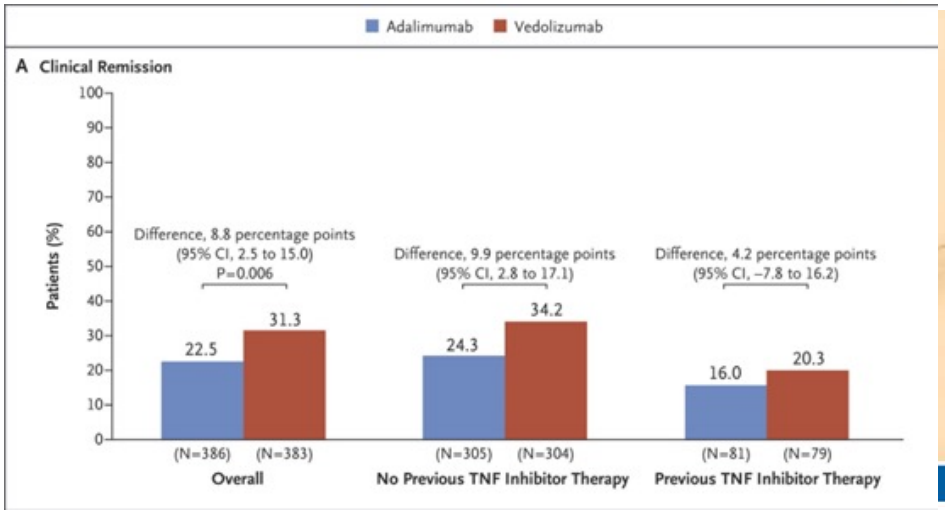


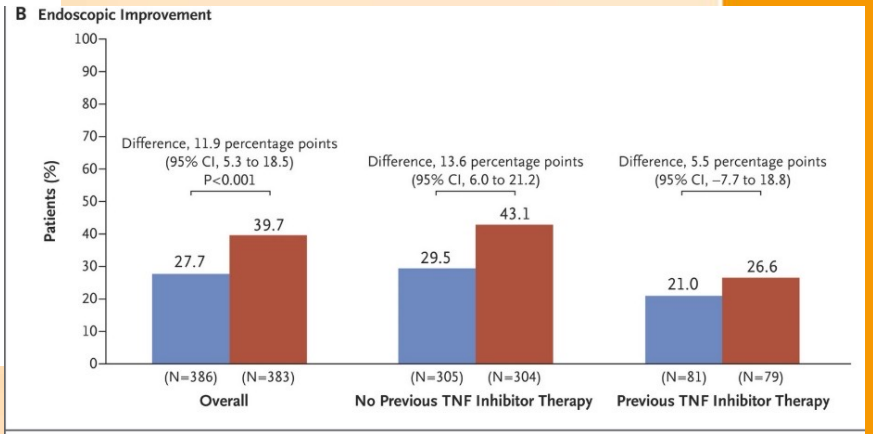
ADA, adalimumab; ew, every week; eow, every other week; PBO, placebo; TDM, therapeutic drug monitoring.

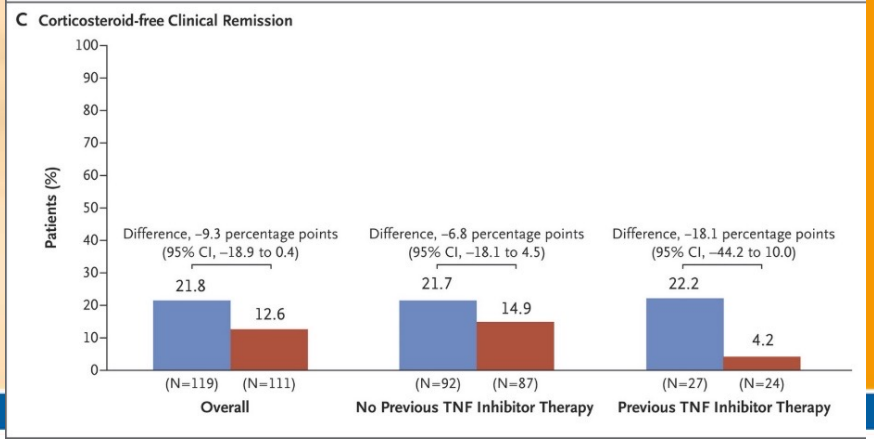
ORIGINAL ARTICLE

Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis

Bruce E. Sands, M.D., Laurent Peyrin-Biroulet, M.D., Ph.D., Edward V. Loftus, Jr., M.D., Silvio Danese, M.D., Jean-Frédéric Colombel, M.D., Murat Törüner, M.D., Laimas Jonaitis, M.D., Ph.D., Brihad Abhyankar, F.R.C.S., Jingjing Chen, Ph.D., Raquel Rogers, M.D., Richard A. Lirio, M.D., Jeffrey D. Bornstein, M.D., and Stefan Schreiber, M.D., Ph.D., for the VARSITY Study Group*







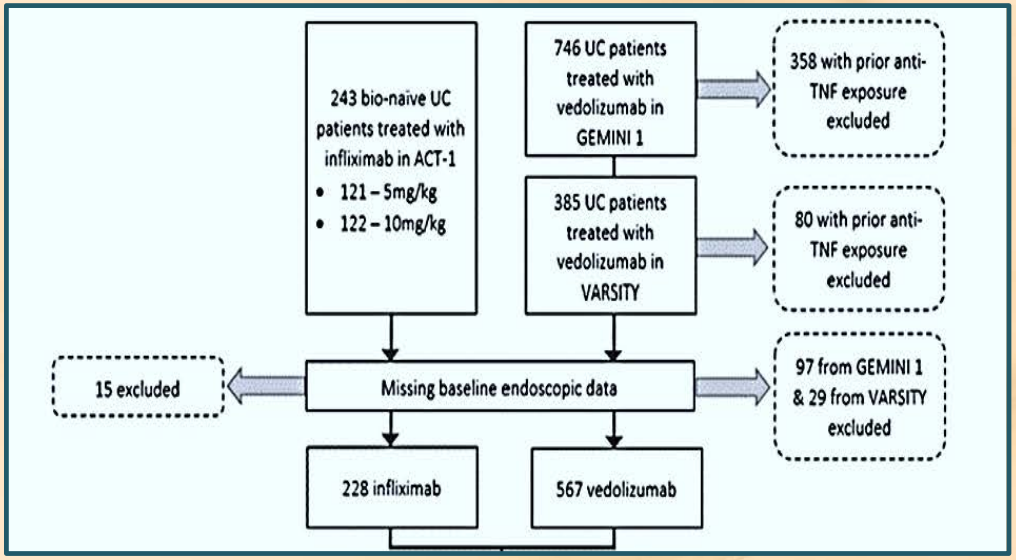
New Eng J Med2019;381:1215-26.

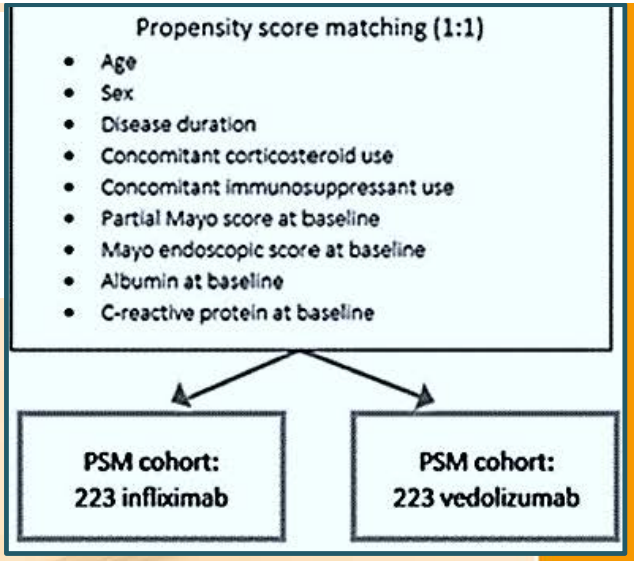
Canada Future Directions in IBD

Comparative Efficacy for Infliximab Vs Vedolizumab in Biologic Naive Ulcerative Colitis

Neeraj Narula,* Emily C. L. Wong,* John K. Marshall,* Jean-Frederic Colombel,‡ Parambir S. Dulai,§,b and Walter Reinisch||,b

Clin Gastro Hepatol 2021





- Comparable week 6 and 1 year clinical remission (~40%)
- With infliximab higher endoscopic remission (36% vs 28%) (aOR, 1.55; 95% CI, 1.08–2.22).
- Higher 1 year steroid-free clinical remission (30% vs 15%) (aOR, 2.36; 95% CI, 1.27–4.39)

Index patient in 2017

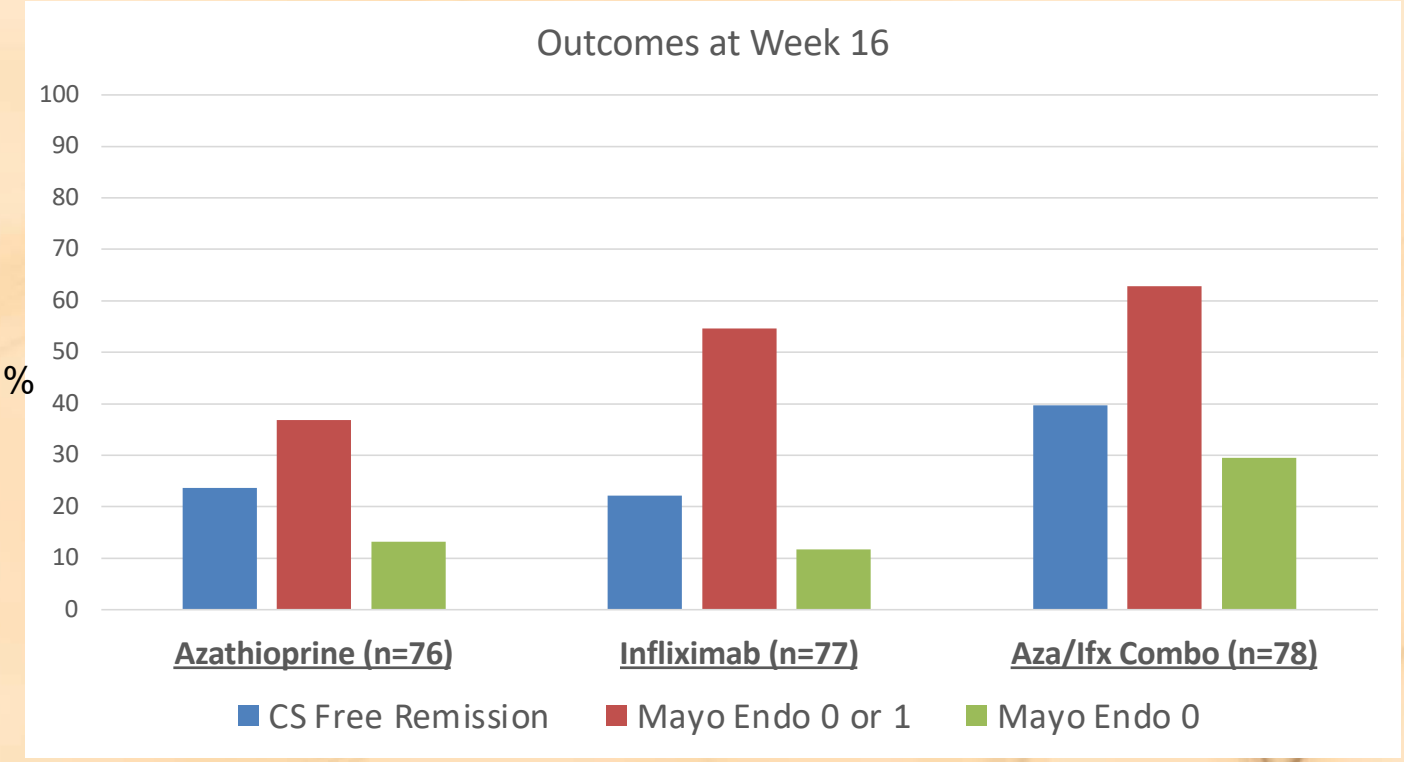
- Symptoms escalated as steroids tapered; hospitalized with active colitis (6-8 stools per 24 hours including 1/night; blood in all stools; some abdominal discomfort prior to stooling; feels weak; Hb 76; CRP 30; albumin 32)

- Hospitalized, given IV steroids; started infliximab

Questions

- How do you initiate infliximab?
  - For ambulatory steroid-dependent UC?
  - For acute severe UC?
- Do you use infliximab monotherapy?
- Do you use combination therapy?
- Do you use proactive therapeutic drug monitoring?

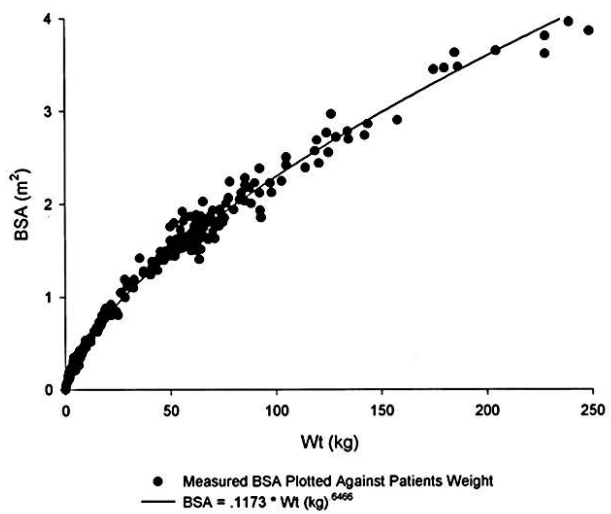
"UC Success" trial



Panaccione et al *Gastro* 2014; 146: 392-400

Pharmacokinetics of biologics in smaller children: lesson learned

Figure A1 Nonlinear regression of estimated body surface area (BSA) and body weight, reproduced with permission from Livingston et al.



70kg older teenager or adult
body surface area 1.8 m2
Dose of 5mg/kg = 350 mg
~200mg/m2

The relationship between weight and body surface area is not linear

30kg child;
body surface area 1.0m2
Dose of 5mg/kg = 150 mg
~150mg/m2

Weight-based dosing of infliximab systematically underdoses lighter (younger) children

Stallard L et al, Gastro Hep Advances. 2024;3(2):215-220

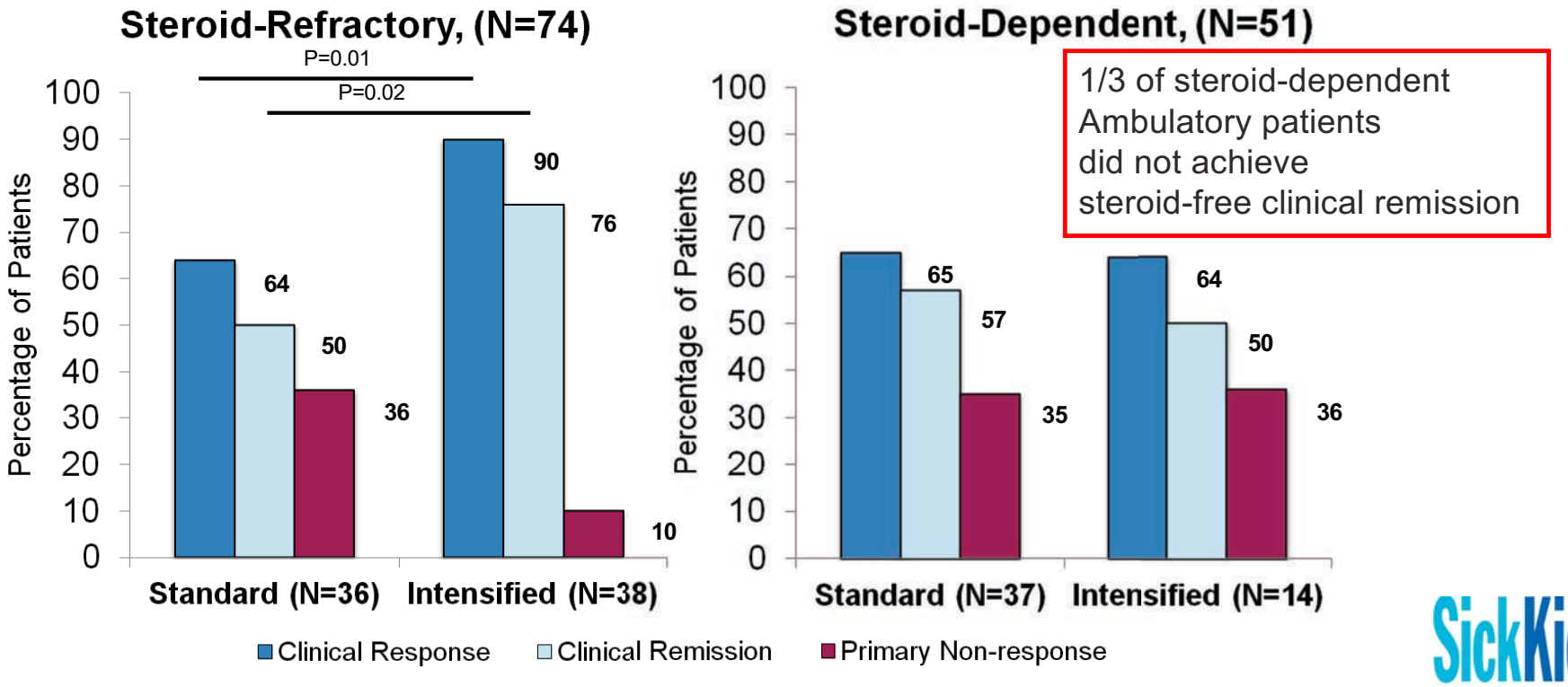
Index patient in 2017

- Infliximab 5 mg/kg at weeks 0, 1, then 11 mg/kg at week 4 and continuing q 4 weekly
- in combination with once weekly oral methotrexate
- Pre-dose 3 infliximab level 21.3 ug/ml; pre-dose 4: 13 ug/ml; pre-dose 7: 20.5 ug/ml
- Symptoms recurred as steroids tapered

Questions

- Is this primary non-response to infliximab? Pharmacokinetic or pharmacodynamic?
- Is this common?
- What are options for management of UC with primary non-response to infliximab?

Our single centre outcomes with anti-TNF (infliximab) in UC



1/3 of steroid-dependent Ambulatory patients did not achieve steroid-free clinical remission

Intensification of infliximab induction regimen was associated with higher response rate in steroid-refractory patients, but did not improve outcomes when used in steroid-dependent patients

Church P et al, JCC 2019; 13: 982-989

Causes of primary anti-TNF failure (or incomplete response) in paediatric UC

- Pharmacokinetic: inadequate drug exposure
- Pharmacodynamic: mechanistic
- Remember also possibility of refractory distal disease

Positioning “advanced therapies” in steroid-dependent UC: choices to make (excluding steroid-refractory)

TIMEPOINT	NOW
Choosing SUBSEQUENT advanced therapy	Which biologic or targeted oral small molecule when first (to date usually infliximab) has failed?
Types of “failure”	Primary non-response or unsatisfactory response (PD failure) Intolerance Secondary loss of response related to anti-drug antibodies? Secondary loss of response not related to anti-drug antibodies

Positioning advanced therapies in ulcerative colitis (excluding steroid-refractory hospitalized patients)

TIMEPOINT	UNTIL RECENTLY	NOW (*in the near future?*)
SUBSEQUENT	When anti-TNF has failed?	

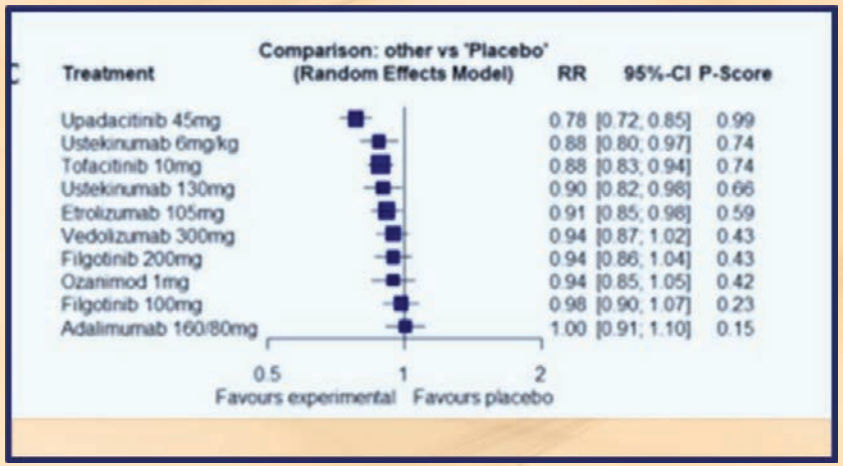
Primary non-response or unsatisfactory response (PD failure) or intolerance:
Ustekinumab or anti-IL23s or JAK inhibitor (upadacitinib > tofacitinib)

Secondary loss of response related to anti-drug antibodies? 2nd anti-TNF

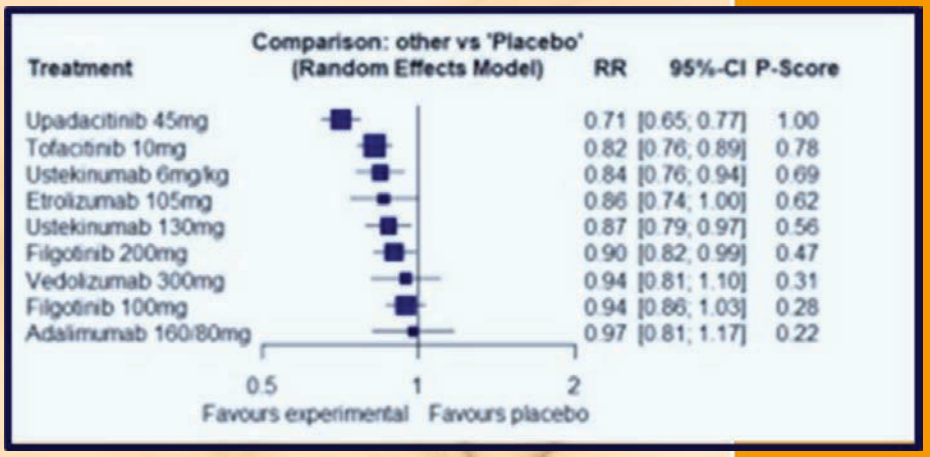
Advanced therapy following anti-TNF failure in UC?

Prior Anti-TNF exposure

Achievement of clinical remission



Achievement of endoscopic improvement



Differential Efficacy of Advanced Therapies in Inducing Remission in Ulcerative Colitis Based on Prior Exposure to TNF Antagonists

Han Hee Lee [1], Virginia Solitano [2], Sujay Singh [3], Ashwin N Ananthakrishnan [4], Vipul Jairath [5], Gaurav Syal [6], Brigid S Boland [6], Pradipta Ghosh [7], John T Chang [8], Siddharth Singh [9]

Prior exposure to TNF antagonists may potentiate JAK inhibitors and attenuate lymphocyte trafficking inhibitors patients with ulcerative colitis

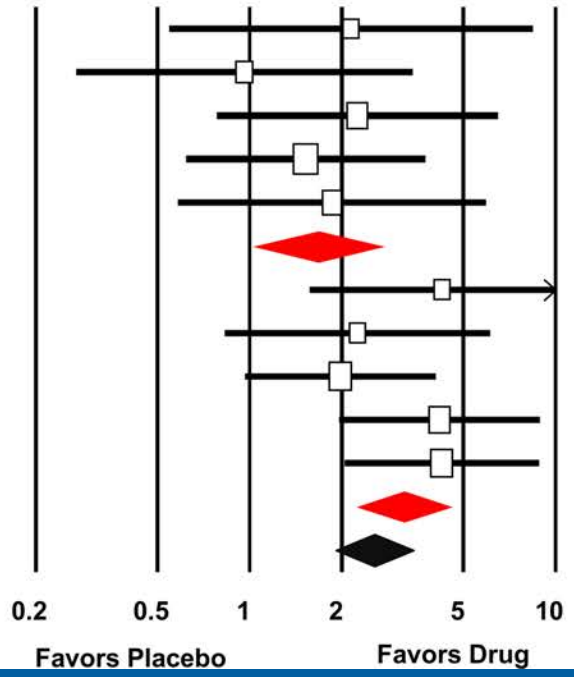
Induction of clinical remission	TNF antagonist-naïve (drug vs. placebo)	TNF antagonist-exposed (drug vs. placebo)	TNF antagonist-naïve vs. TNF antagonist-exposed patients
Lymphocyte trafficking inhibitors (vedolizumab, ozanimod, etrasimod)	**OR, 3.20** [95% CI, 2.23-4.60]	**OR, 1.68** [95% CI, 1.02-2.76]	**Ratio of OR: 1.88** [95% CI, 1.02-3.49]
Interleukin-12/23 or interleukin-23 antagonists (ustekinumab, mirikizumab, risankizumab, guselkumab)	**OR, 2.98** [95% CI, 2.13-4.18]	**OR, 3.23** [95% CI, 2.15-4.84]	**Ratio of OR: 1.07** [95% CI, 0.64-1.80]
Janus kinase inhibitors (tofacitinib, upadacitinib, filgotinib)	**OR, 3.56** [95% CI, 1.92-6.58]	**OR, 8.53** [95% CI, 3.49-20.83]	**Ratio of OR: 0.47** [95% CI, 0.22-1.01]

Lee HH et al CGH 2025 Nov;23(12):2102-2114

Clinical Gastroenterology and Hepatology

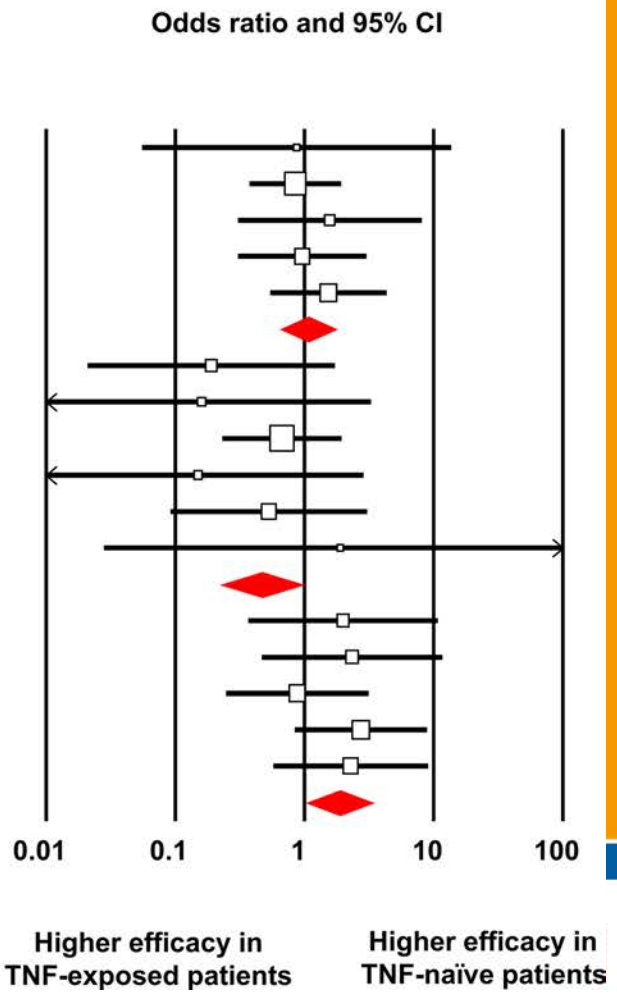
Lymphocyte trafficking inhibitors vs. placebo, by prior TNF antagonist exposure

Study name	Intervention	Odds ratio	Lower limit	Upper limit	Events / Total: Drug	Events / Total: Placebo
GEMINI 1	VDZ	2.15	0.55	8.39	8 / 95	3 / 73
Motoya 2019	VDZ	0.96	0.27	3.40	8 / 85	4 / 41
ELEVATE 12	ETRA	2.25	0.79	6.46	21 / 90	5 / 42
ELEVATE 52	ETRA	1.53	0.62	3.74	21 / 95	8 / 51
TRUE NORTH	OZA	1.86	0.58	5.91	13 / 139	4 / 76
TNF Exposed		**1.68**	**1.02**	**2.76**	**71 / 504**	**24 / 283**
GEMINI 1	VDZ	4.26	1.58	11.52	30 / 130	5 / 76
Motoya 2019	VDZ	2.25	0.83	6.10	22 / 79	6 / 41
ELEVATE 12	ETRA	1.98	0.97	4.05	41 / 148	12 / 74
ELEVATE 52	ETRA	4.18	1.97	8.86	60 / 194	9 / 93
TRUE NORTH	OZA	4.25	2.05	8.81	66 / 287	9 / 137
TNF Naive		**3.20**	**2.23**	**4.60**	**219 / 838**	**41 / 421**
Overall		**2.56**	**1.91**	**3.43**	**290 / 1342**	**65 / 704**



Ratio of Treatment Effect (Drug vs. Placebo), in TNF antagonist-naive vs. TNF antagonist-exposed patients in trials of different advanced therapies for moderate-severe ulcerative colitis

Group by Subgroup within study	Study name	Odds ratio	Lower limit	Upper limit
	AMAC Ph2	0.87	0.06	13.55
	LUCENT	0.85	0.38	1.91
	QUASAR 2B	1.57	0.31	8.00
	QUASAR 3	0.96	0.31	2.99
	INSPIRE	1.53	0.55	4.28
IL23 antagonists		**1.07**	**0.64**	**1.80**
	OCTAVE 1	0.19	0.02	1.71
	OCTAVE 2	0.16	0.01	3.24
	SELECTION	0.67	0.23	1.93
	U-ACHIEVE	0.15	0.01	2.85
	U-ACCOMPLISH	0.53	0.09	3.04
	UPA Ph2	1.89	0.03	126.59
JAK inhibitors		**0.47**	**0.22**	**1.01**
	GEMINI 1	1.99	0.37	10.72
	Motoya	2.34	0.47	11.58
	ELEVATE 12	0.88	0.25	3.12
	ELEVATE 52	2.73	0.85	8.79
	TRUE NORTH	2.28	0.58	8.98
Lymphocyte trafficking inhibitors		**1.88**	**1.02**	**3.49**



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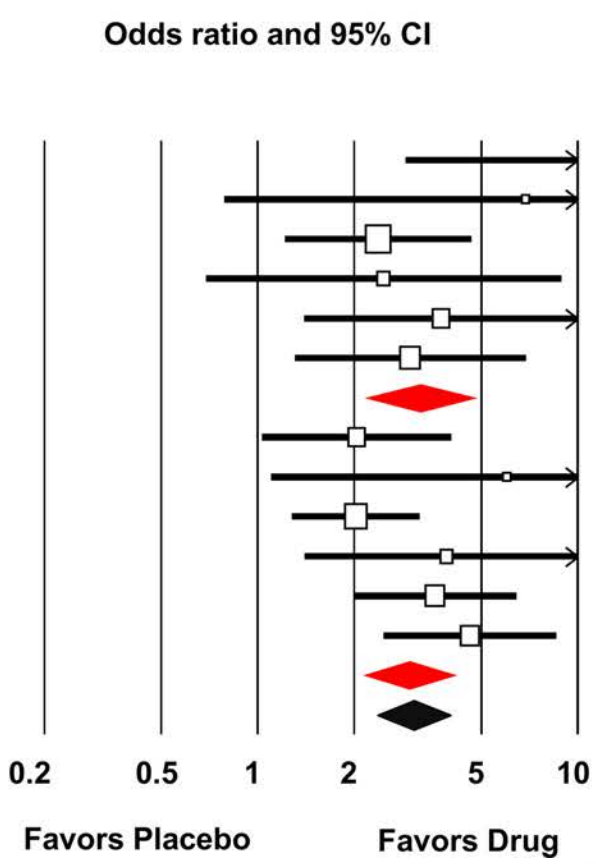
Anti-interleukins vs. placebo, by prior TNF antagonist exposure

Study name	Intervention	Odds ratio	Lower limit	Upper limit	Events / Total: Drug	Events / Total: Placebo
UNIFI	UST	12.56	2.91	54.16	23 / 175	2 / 168
AMAC Ph2	MIRI	6.88	0.79	60.06	6 / 40	1 / 40
LUCENT	MIRI	2.38	1.22	4.64	71 / 418	11 / 139
QUASAR 2B	GUS	2.47	0.69	8.84	8 / 46	4 / 51
QUASAR 3	GUS	3.74	1.40	10.00	26 / 208	5 / 136
INSPIRE	RISA	3.00	1.31	6.87	38 / 333	7 / 170
Exposed		**3.23**	**2.15**	**4.84**	**172 / 1220**	**30 / 704**
UNIFI	UST	2.04	1.04	4.02	27 / 147	15 / 151
AMAC Ph2	MIRI	6.00	1.11	32.54	8 / 22	2 / 23
LUCENT	MIRI	2.03	1.29	3.20	139 / 450	28 / 155
QUASAR 2B	GUS	3.89	1.41	10.78	18 / 55	6 / 54
QUASAR 3	GUS	3.58	2.00	6.41	69 / 213	17 / 144
INSPIRE	RISA	4.60	2.48	8.53	94 / 317	13 / 155
Naive		**2.98**	**2.13**	**4.18**	**355 / 1204**	**81 / 682**
Overall		**3.08**	**2.37**	**3.99**	**527 / 2424**	**111 / 1386**



GEMINI I: Vedolizumab in ulcerative colitis: Week 6 responders (47% overall) re-randomized

	Clinical Remission w6	Clinical Remission W52 with q 8 weekly dosing	Mucosal Healing w52
Anti-TNF naive	23%	47%	60%
Placebo	6.6%	19%	24%
Delta	15.5 (5.1-25.9)	28 (14.9-41.1)	36 (22.3-49.5)
Anti-TNF failure	9.8%	36.1%	44.6%
Placebo	3.2%	5.3%	7.9%
Delta	11.5% (-1.3-15.2)	29.5% (12.8-46.1)	34.9% (17.1-52.8)

Feagan BG, et al Clin Gastro Hepatol 2017; 15: 229-239

Outcomes, dosing, and predictors of vedolizumab treatment in children with inflammatory bowel disease (VEDOKIDS): a prospective, multicentre cohort study

Ohad Atia, Zivia Shavit-Brunschwig*, Diane R Mould, Ronen Stein, Manar Matar, Marina Aloi, Oren Ledder, Gili Focht, Darja Urlep, Jeffrey Hyams, Efrat Broide, Batia Weiss, Jeremiah Levine. Richard K Russell. Dan Turner*

Lancet Gastro Hepatol 2023; 8: 31–42

Under 30 kg
200 mg/m2

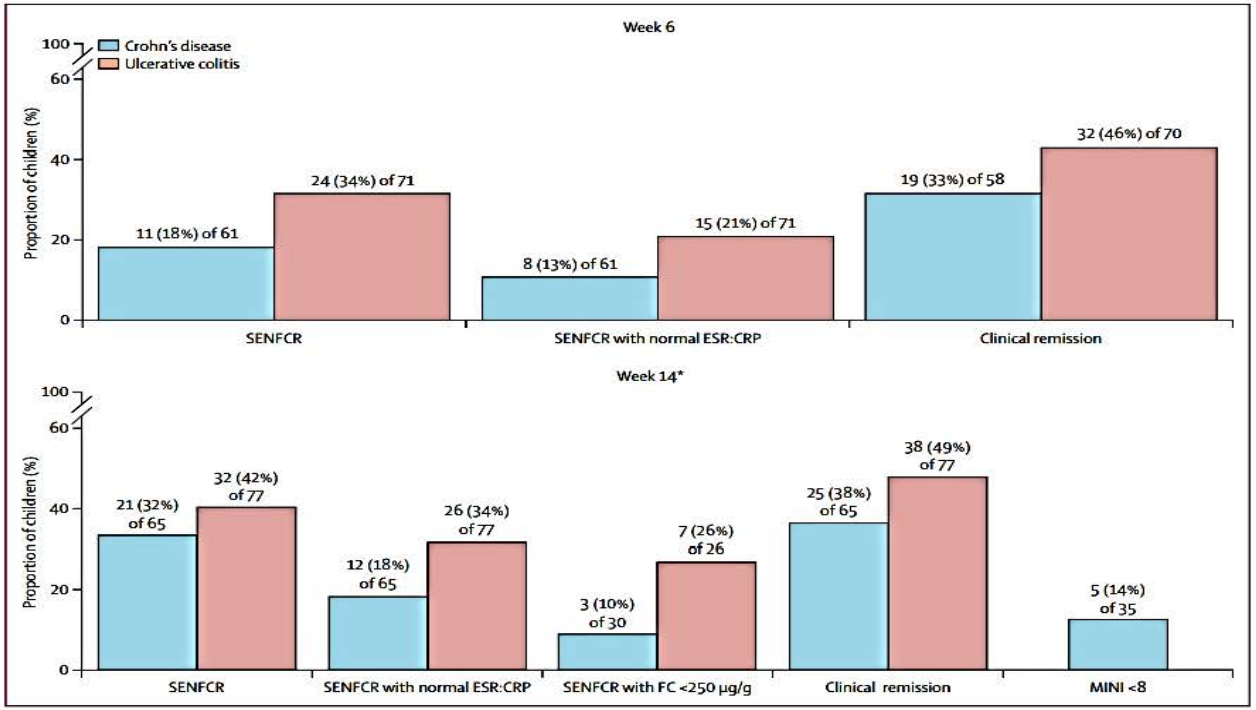
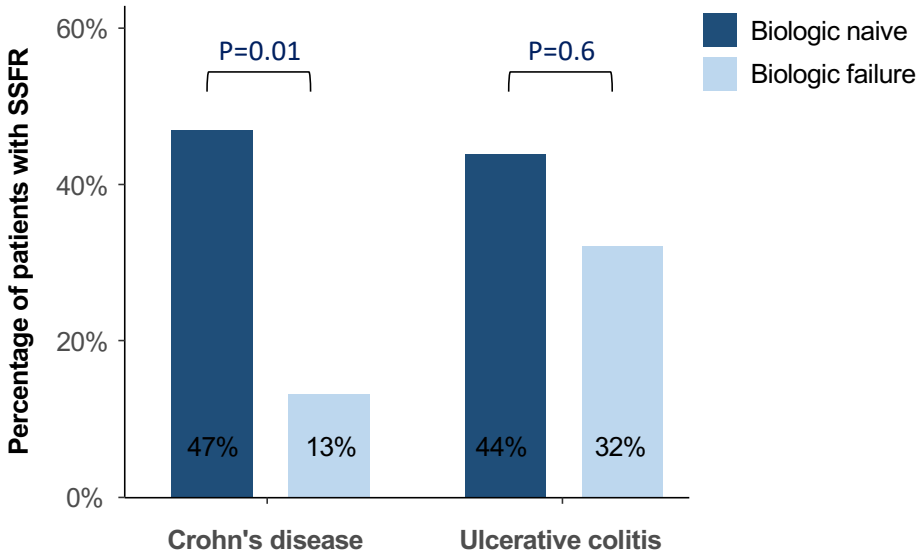


Figure 1: **Disease outcomes at weeks 6 and 14**
Clinical remission defined as Pediatric Ulcerative Colitis Activity Index less than 10 or weighted Pediatric Crohn's Disease Activity Index less than 12·5. Normal ESR:CRP=CRP less than 0·5 mg/dL and ESR less than 25 mm/h. CRP=C-reactive protein. ESR=erythrocyte sedimentation rate. FC=faecal calprotectin. MINI=Mucosal Inflammation Non-Invasive index. SENFCR=steroid-free and exclusive enteral nutrition-free clinical remission. *Primary outcome.

1/3 bio-naive

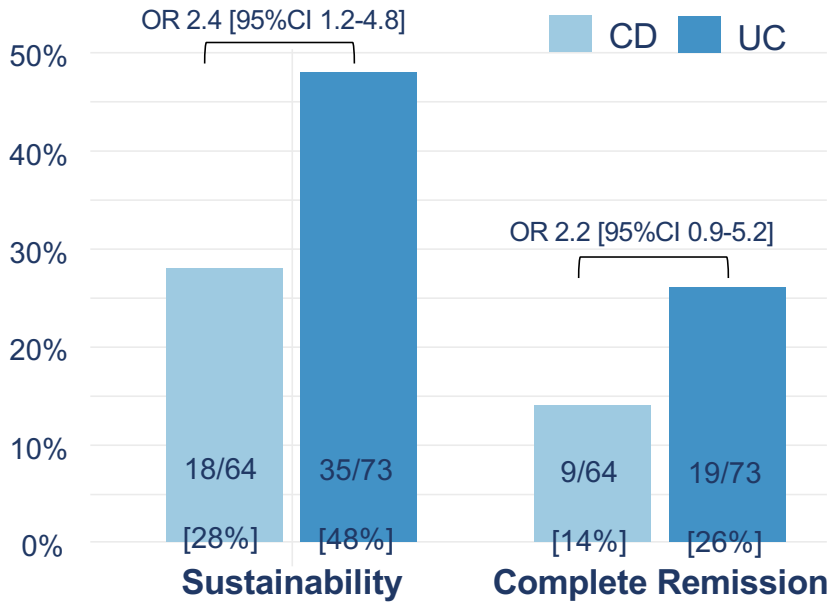
VEDOKIDS study:
Remission rates at 54 weeks: prior exposure to biologics



The biologic-naïve CD patients had milder disease at baseline and shorter disease duration which confounded this analysis; in a multivariable modelling- there was no difference in sequence of treatment

Turner D et al; ESPGHAN annual meeting 2024

The prospective VEDOKIDS study: effectiveness at 3 years



***Complete remission**: steroid-free clinical remission + normal ESR/CRP with sustained vedolizumab treatment*

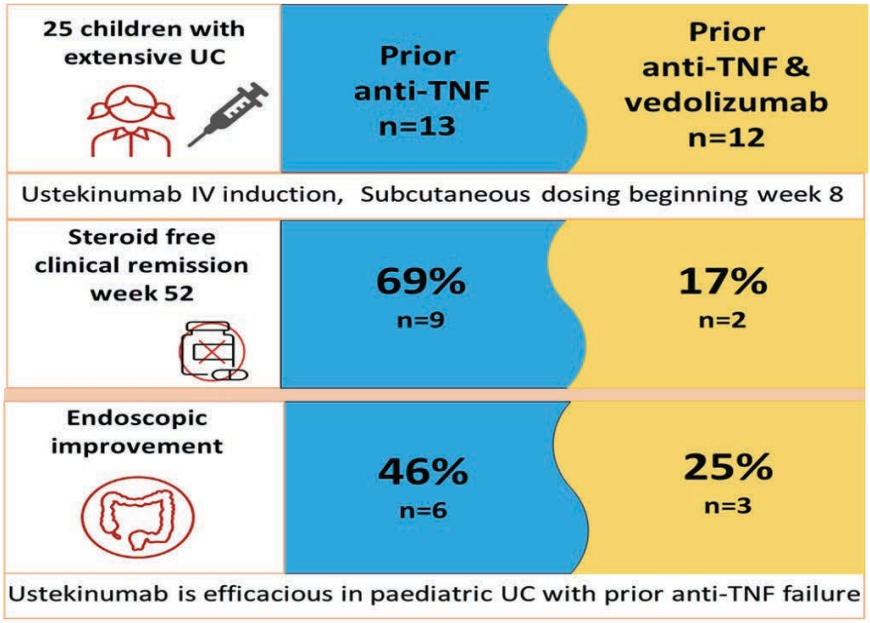
Complete remission rate was 2.6 times higher in isolated colonic Crohn's (L2; 25%) compared to ileal disease (L1 or L3; 13%; OR 2.6 [0.5-12.2]), almost comparable to UC

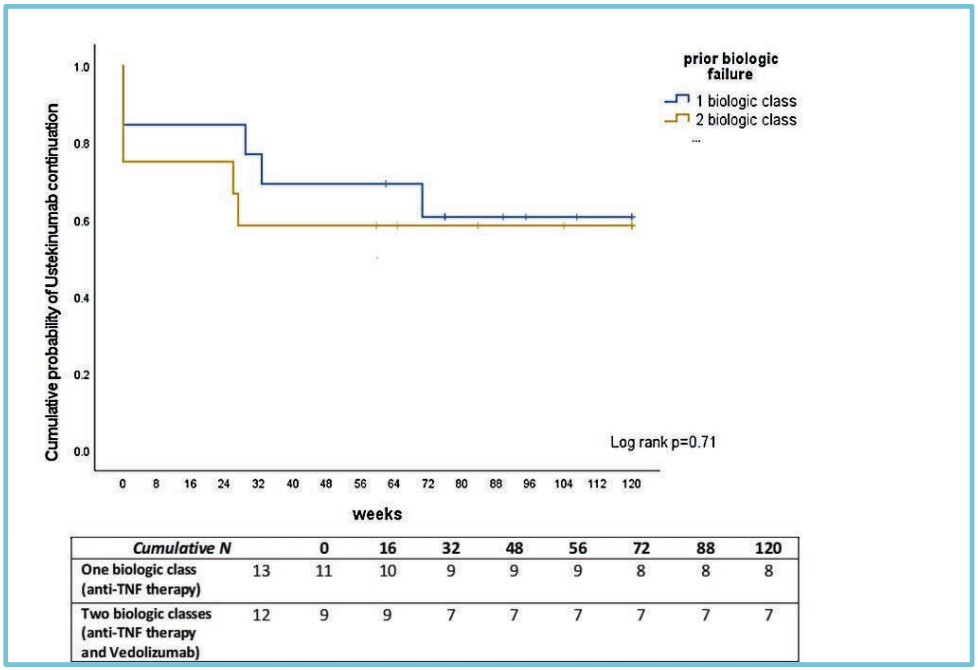
Turner D et al; ESPGHAN annual meeting 2025

Index patient in 2018

- Colonoscopic assessment: persistent extensive continuous colitis mid-ascending to rectum, worse distally (Mayo 2-3 throughout), normal terminal ileum.
- Accessed vedolizumab. Given prednisone at start with symptomatic response. Active symptoms when prednisone finished.
- Accessed ustekinumab

Ustekinumab following anti-TNF failure in paediatric UC





Cumulative N	0	16	32	48	56	72	88	120
One biologic class (anti-TNF therapy)	13	11	10	9	9	9	8	8	8
Two biologic classes (anti-TNF therapy and Vedolizumab)	12	9	9	7	7	7	7	7	7

CIDsCANN

Dhaliwal J, McKay H, Deslandres C, et al Aliment Pharm Therapeutics 2021 on-line

Index patient in 2018

- 2 ½ years of steroid-free clinical remission while receiving ustekinumab 90 mg q 4 weekly; normalization of fecal calprotectin
- Then….return of pattern of steroid-dependency…prompt symptom resolution with oral prednisone…prompt return of symptoms when stopped.
- Failed screening for tofacitinib trial (while on low dose prednisone)

Question now

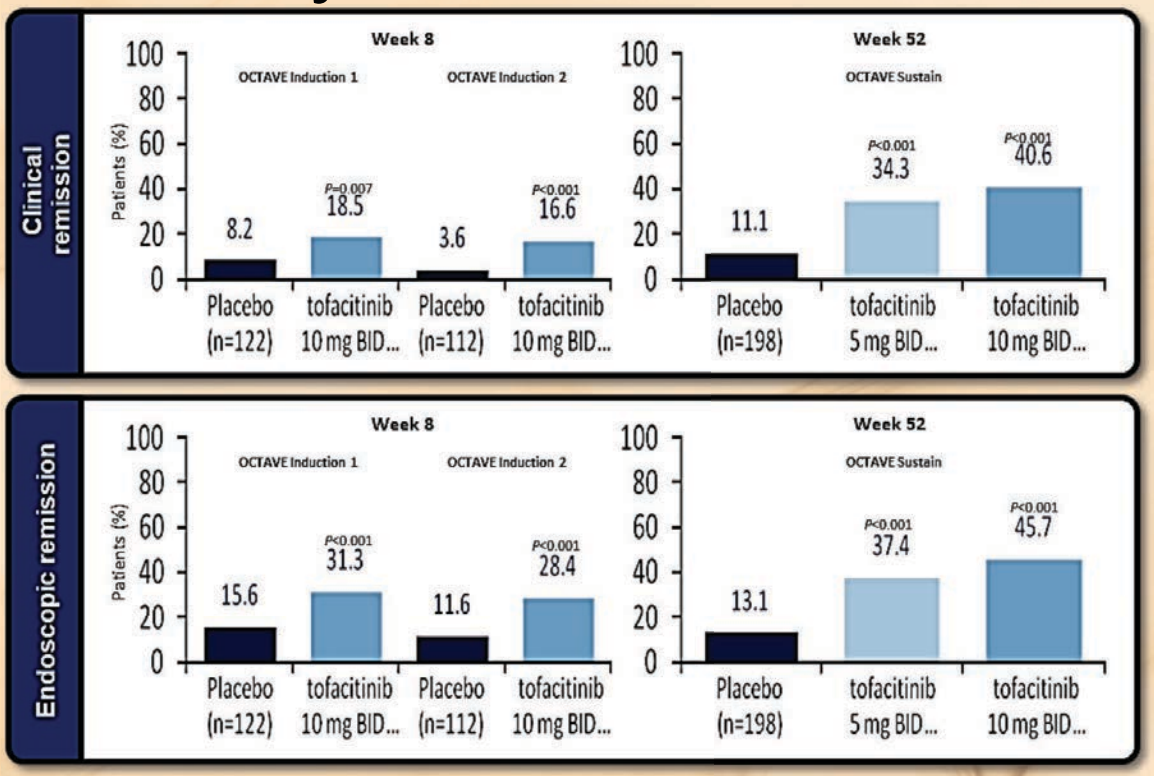
- Secondary loss of response to ustekinumab with prior primary non-response to infliximab and to vedolizumab

- What would you consider?

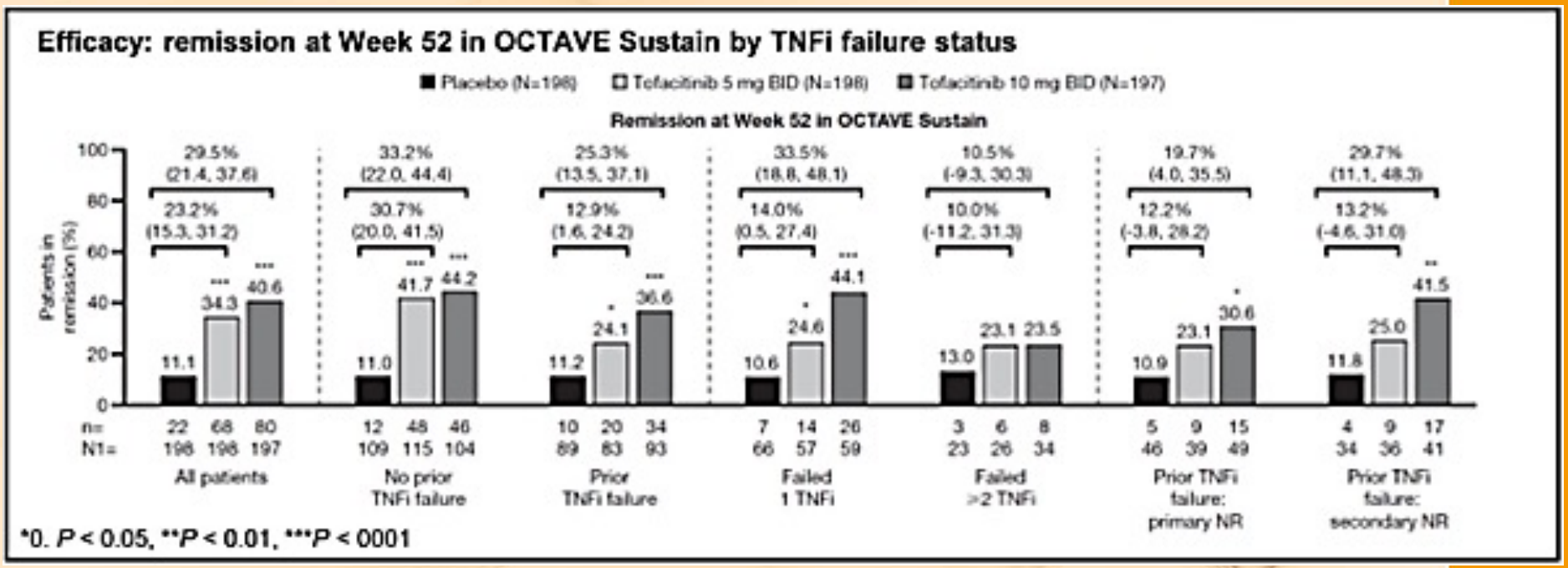
Tofacitinib efficacy data in adults with UC

Phase 3 OCTAVE placebo-controlled induction RCTs (n=1124) (583 with prior anti-TNF failure)

“Responders” to induction were re-randomized for maintenance phase



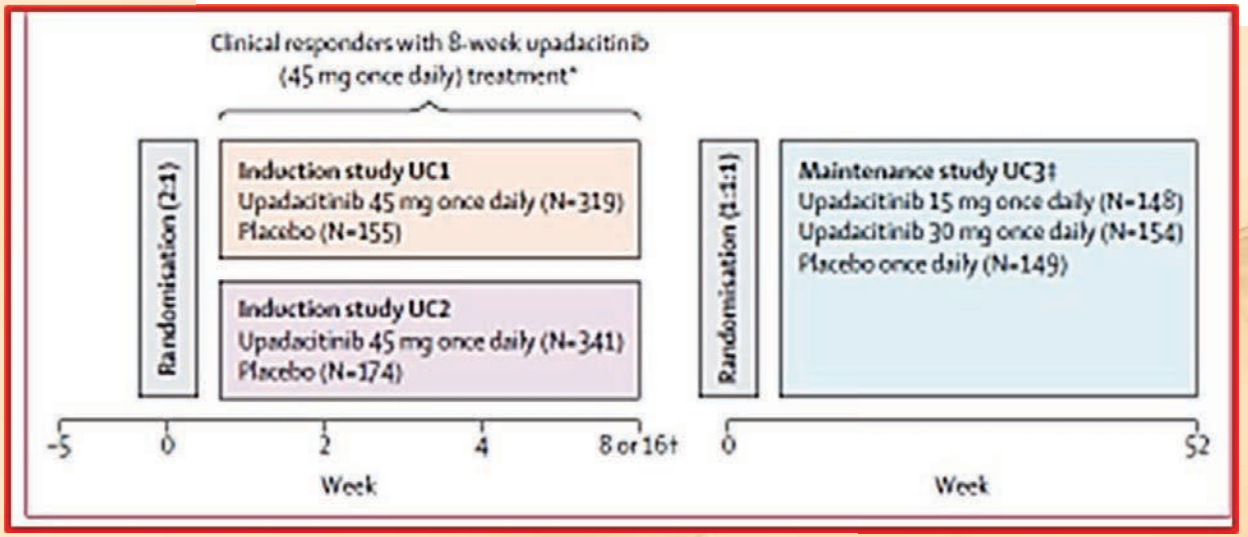
Tofacitinib efficacy in setting of prior anti-TNF failure



Sandborn WJ Clin Gastro Hepatol 2022; 20: 591-601

Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials

Silvio Danese, Séverine Vermeire*, Wen Zhou, Aileen L Pangan, Jesse Siffledeen, Susan Greenbloom, Xavier Hébuterne, Geert D'Haens, Hiroshi Nakase, Julian Panés, Peter D R Higgins, Pascal Juillerat, James O Lindsay, Edward V Loftus Jr, William J Sandborn, Walter Reinisch, Min-Hu Chen, Yuri Sanchez Gonzalez, Bidan Huang, Wangang Xie, John Liu, Michael A Weinreich, Remo Panaccione*



50% Left-sided UC; 50% extensive/pancolitis

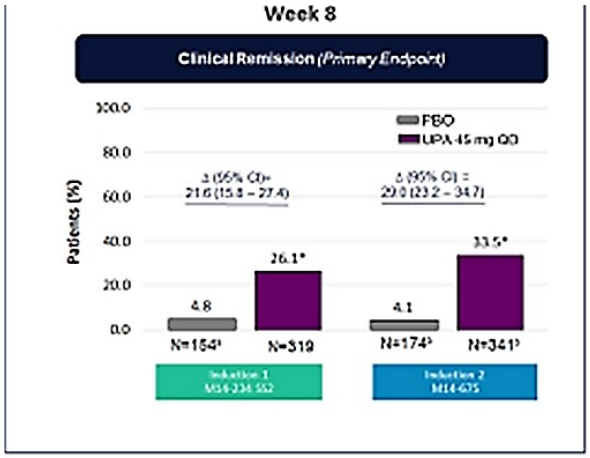
70% Mayo 3

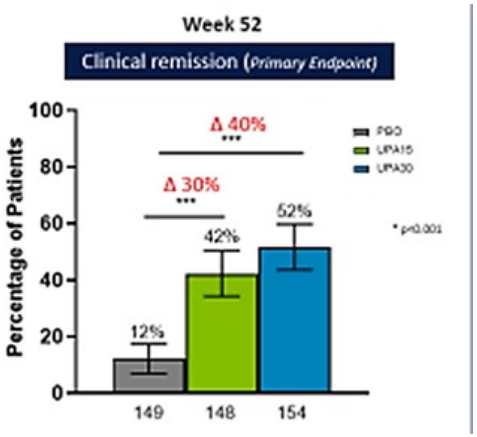
50% prior biologic failure; 40% on steroids

	INDUCTION	MAINTENANCE among responders to induction
PRIMARY ENDPOINT	Week 8 clinical remission per adapted Mayo score	Week 52 clinical remission per adapted Mayo score

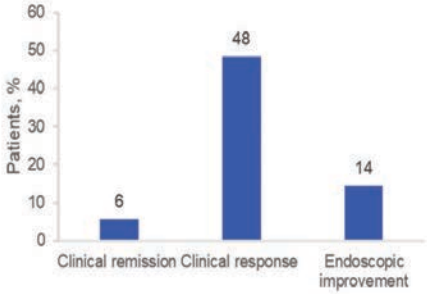
Lancet. 2022 Jun 4;399(10341):2113-2128

Results: Upadacitinib induction and maintenance in UC

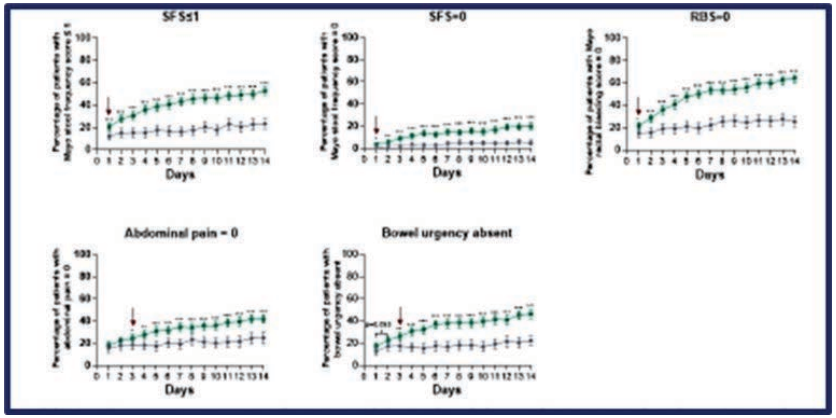


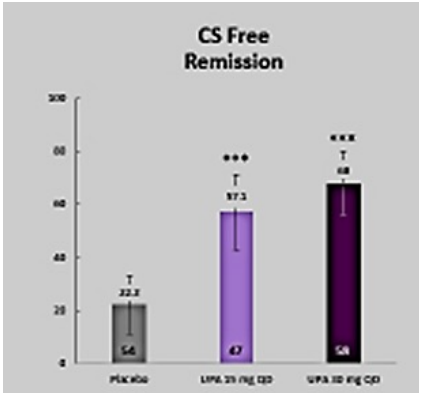


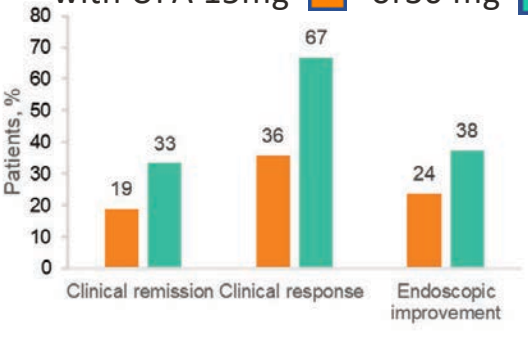
16 weeks (extended induction) among week 8 non-responders



Maintenance treatment once daily with UPA 15mg or30 mg



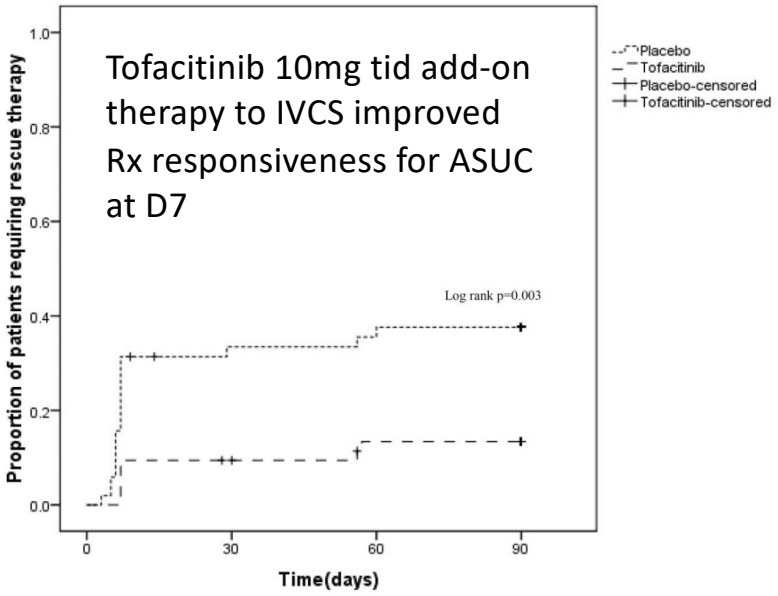




Danese S et al, Lancet. 2022;399(10341):2113-2128

JAKS for Acute Severe UC

TACOs; Tofacitinib n=104; Need for rescue therapy



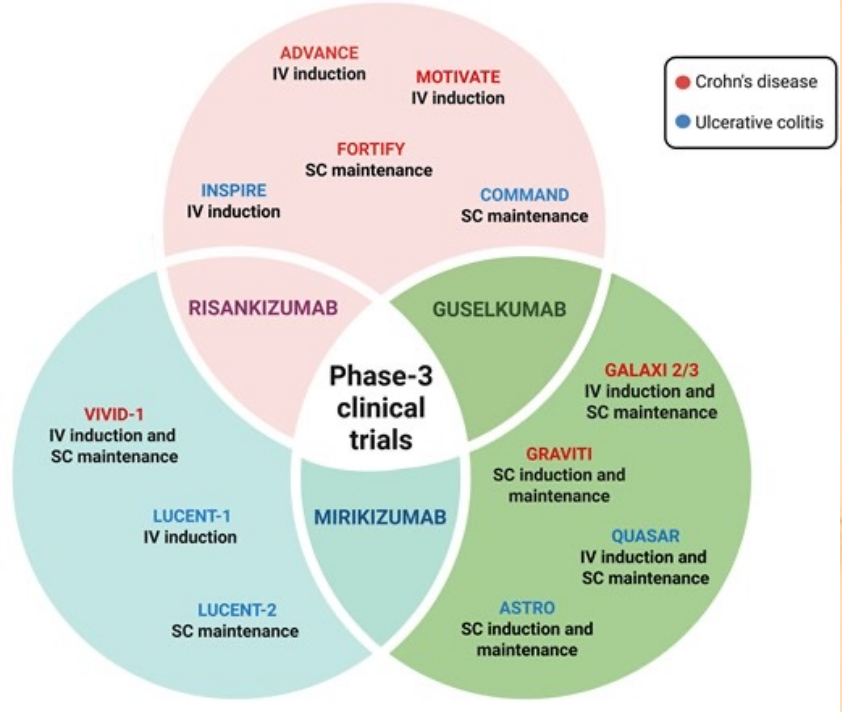
Tofacitinib systematic review ASUC
N=148 ASUC IFX failures
90-day colectomy-free survival was 86%

Upadacitinib systematic review ASUC
N=55 ASUC advanced therapy failures
90 day colectomy-free survival was 83.7%

Oral small molecules may circumvent accelerated protein clearance

Singh A et al Am J Gastroenterol 2024;119:1365-72
Steenholdt C et al J Crohns Colitis 2023;17:1354-63
Damianos J et al Inflamm Bowel Dis 2024

IL23p19 therapy in UC



- IL23p19 antagonists have demonstrated superiority over PBO in UC for clinical, endoscopic, histologic and PRO outcomes in moderate to severely active UC
- They are most effective in advanced therapy naïve patients but do maintain efficacy even in advanced treatment exposed populations
- Safety profile was favorable with no clear signal for malignancy or serious infections
- No comparative trials between IL23p19 and Ustekinumab in UC

Ahmed N et al Expert opinion on biological agents, 2025:25:363-78

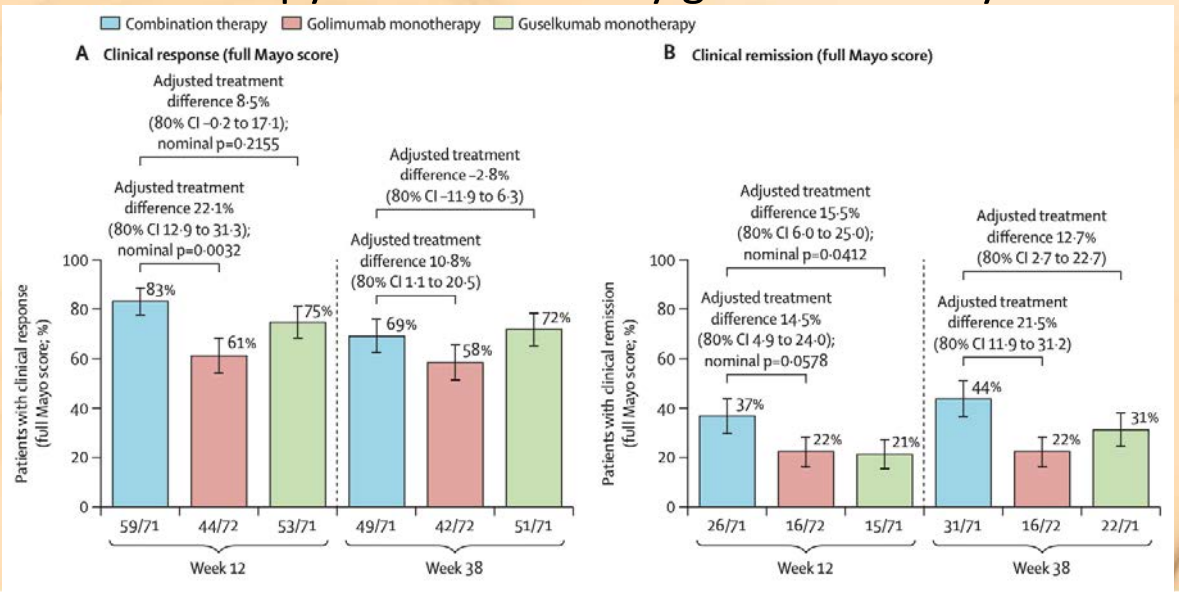
Summing it all up: Positioning oral small molecules relative to each other and to biologics

- In pediatric UC
  - Infliximab or vedolizumab as first therapy for steroid-dependent UC (consider where on the spectrum of steroid responsiveness)
  - Upadacitinib >Tofacitinib for refractory patients who have failed optimized anti-TNF
  - Likely after ustekinumab or anti-IL12/23 even in this setting
  - Earlier positioning of upadacitinib will depend on whether greater safety of the more selective JAK inhibition is demonstrated

Combining advanced therapies in UC

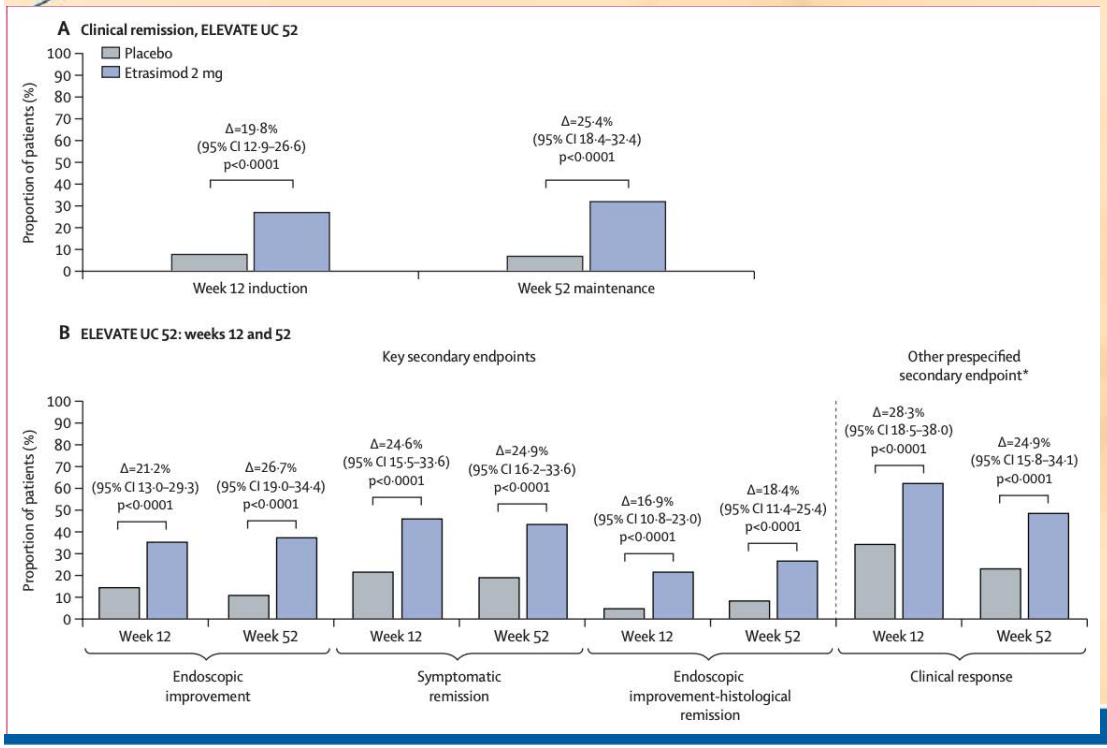
VEGA trial: (phase 2a, proof of concept, double-blind RCT) Golimumab plus Guselkumab combination therapy had numerically greater efficacy than either monotherapy

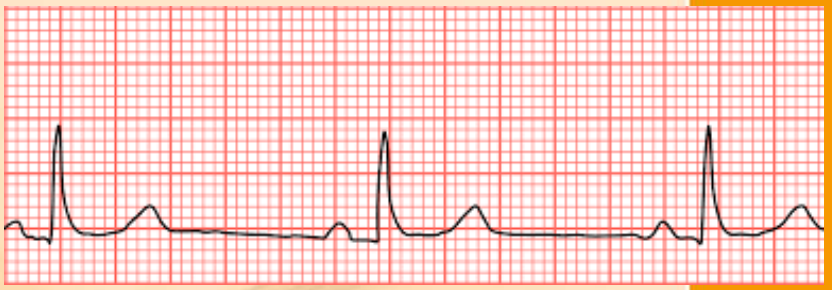
The rates of AE, serious AE and infections were not appreciably different between groups

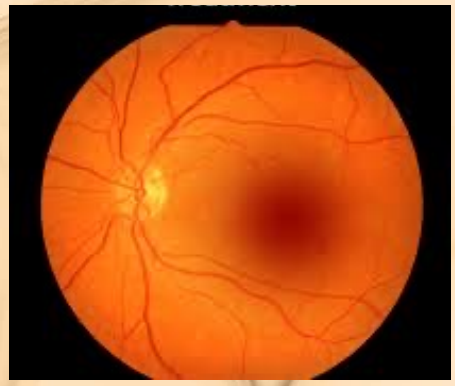


Feagan B et al Lancet Gastroenterol Hepatol 2023;8:307-20

Sphingosine 1 receptor modulators (S1Ps): Etrasimod ELEVATE UC trials

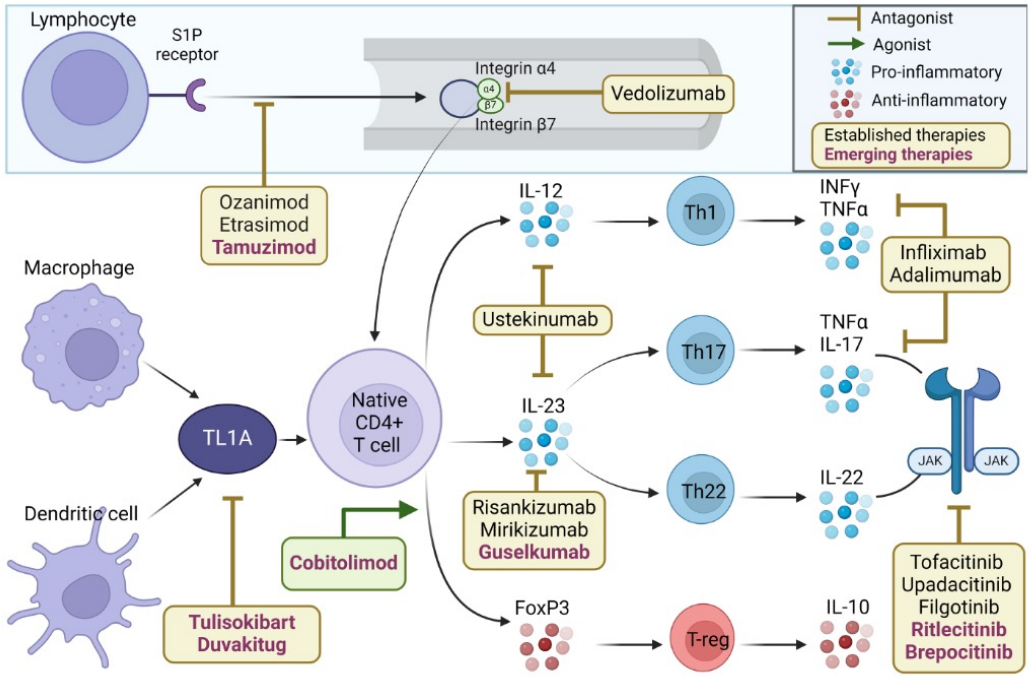






Sandborn W et al Lancet 2023;401:1159-71

The future



- Anti-TL1A: (Anti-inflammatory & Anti-fibrotic potential) Tulisokibart, Duvakitug
- MicroRNA therapy (miR-124): Obefazimod
- Anti-IL 1a/b DVD IG: Lutikizumab
- RIPK1 inhibitors: intestinal barrier integrity
- NLRX-1 agonists: reduces reactive oxygen species
- GLP-2 agonists: intestinal repair
- Anti-TREM1: Macrophages

Noor N et al Aliment Pharmacol Ther. 2024;60:1244-60

Association of disease duration and clinical remission rates

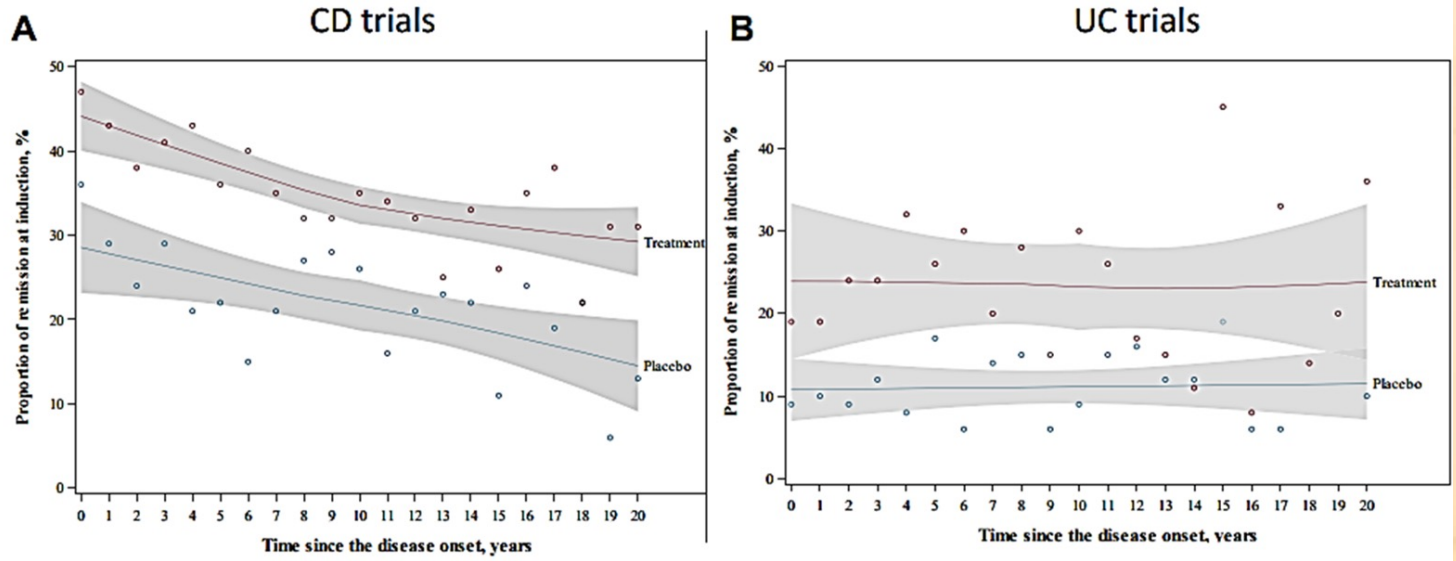
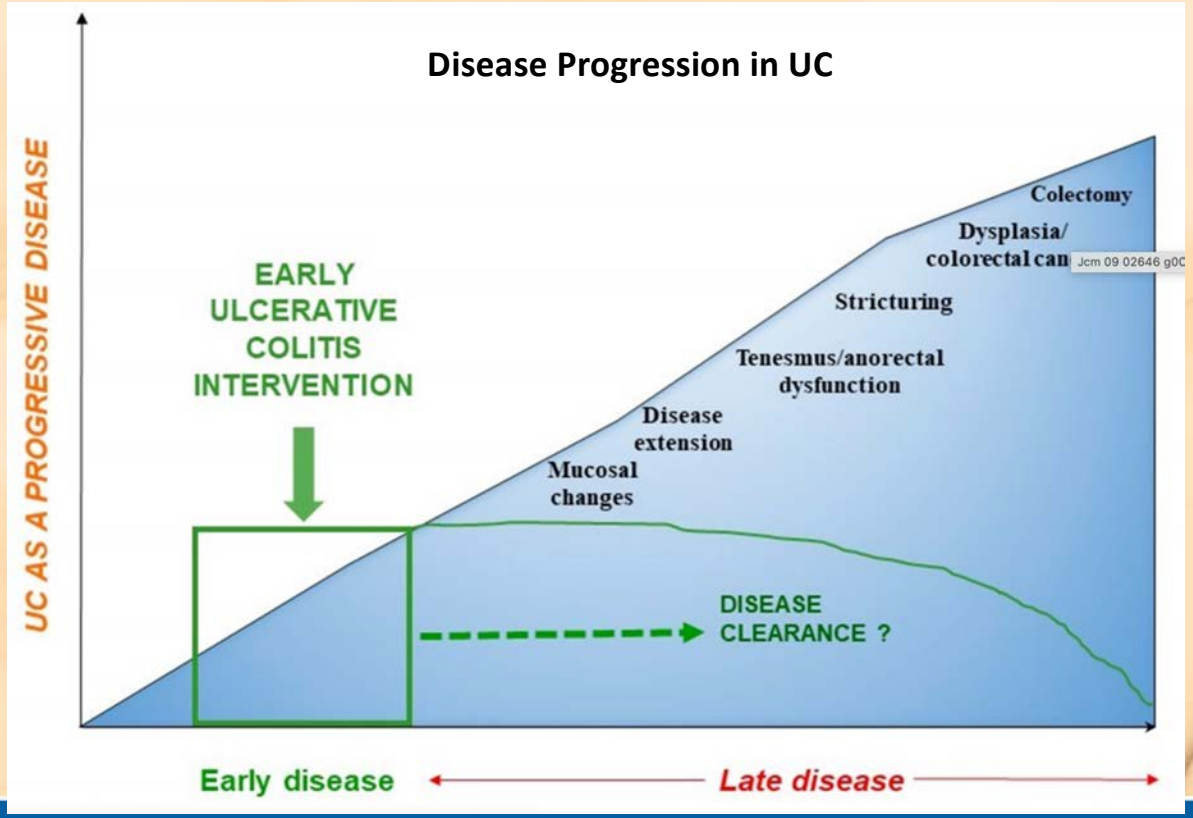


Figure 3. Rate of remission induction by duration of disease at initiation of treatment for *(A)* CD and *(B)* UC trials. The *dots* denote proportion of an outcome averaged per the respective year.

Ben-Horin S, Gastroenterology 2022;162:482-494

Early intervention in UC?



Solitano V et al J Clin Med 2020;8: 2646

Monitoring of therapy in UC: Current treat to target guidelines

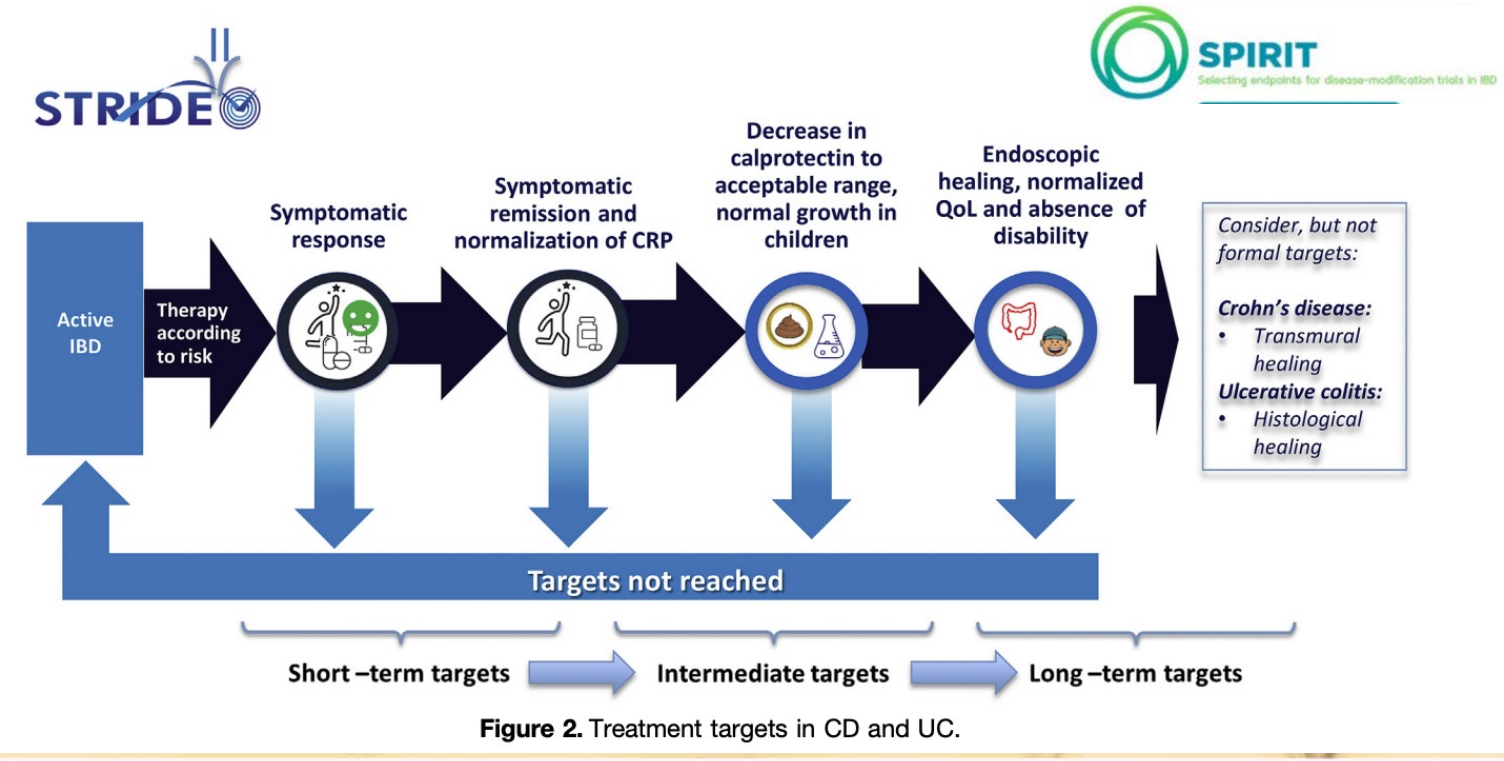


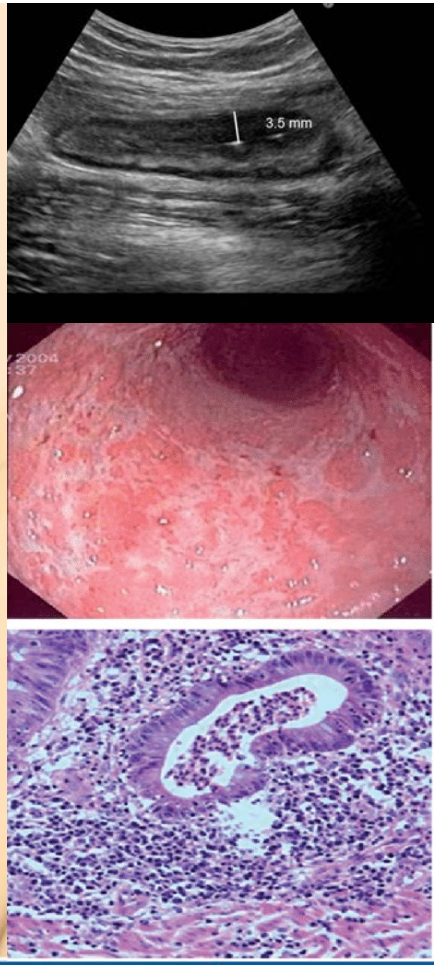
Figure 2. Treatment targets in CD and UC.

Turner D et al Gastroenterol 2021;160:1570-83

Extending Treat to target in UC?

- **Super Sonic-UC**: Intestinal ultrasound at w8 accurately predicted endoscopic remission at 6-12 months

- **VERDICT**: Optimal treatment target in UC: symptoms, endoscopic and histologic outcomes



Dolinger M et al J Crohns Colitis 2025;19:jjaf075
Jairath V et al BMJ Open Gastroenterol 2024;11:e001218