GASTRO ENTEROLOGIA BELLUNO

Con il patrocinio di

PROGRESSI E NUOVE FRONTIERE IN
GASTROENTEROLOGIA ED ENDOSCOPIA DIGESTIVA
BELLUNO
15-16 GIUGNO 2023

Cosa c'è all'orizzonte MICI

Giammarco Mocci

MD, PhD

Department of Internal Medicine, Gastroenterology Unit

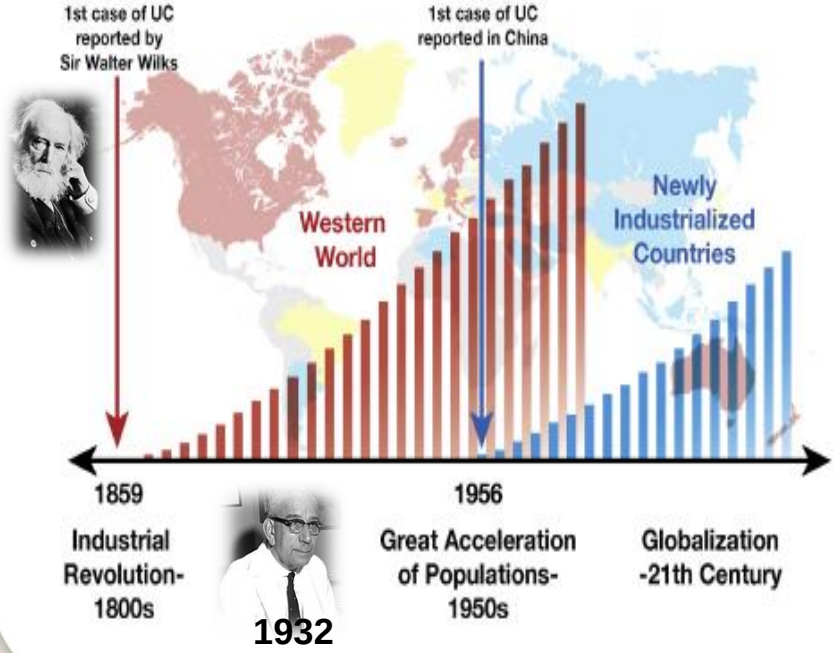
ARNAS "G. Brotzu" Cagliari

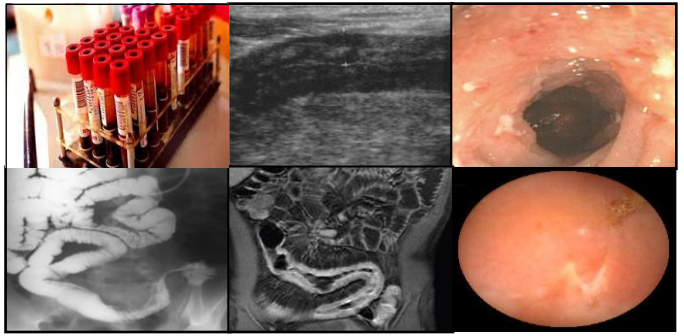
Disclosures

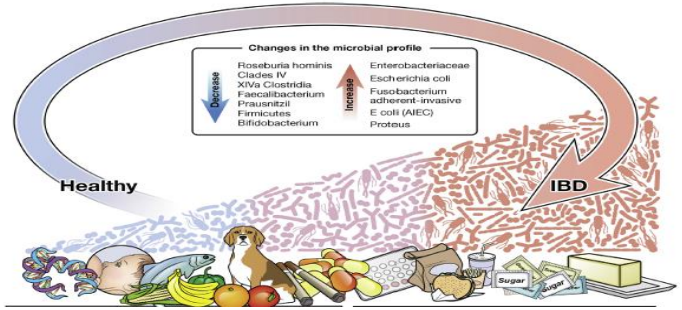
- Consultant: AbbVie, Amgen, Biogen, Celltrion, Chiesi, Ferring, Galapagos, Janssen, MSD, Pfizer, Sandoz, Takeda, Vifor Pharma, Zambon

- Lecture fees: AbbVie, Amgen, Aurora Biopharma, Biogen, Ferring, Janssen, MSD, Omega Pharma, Pfizer, Sandoz, Takeda

The Global Burden of Inflammatory Bowel Disease

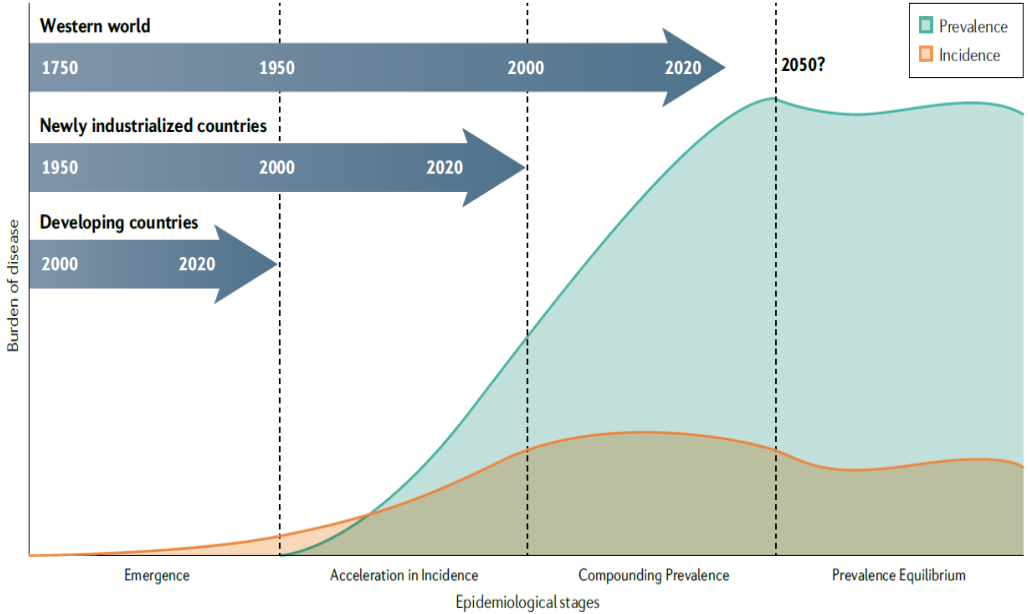




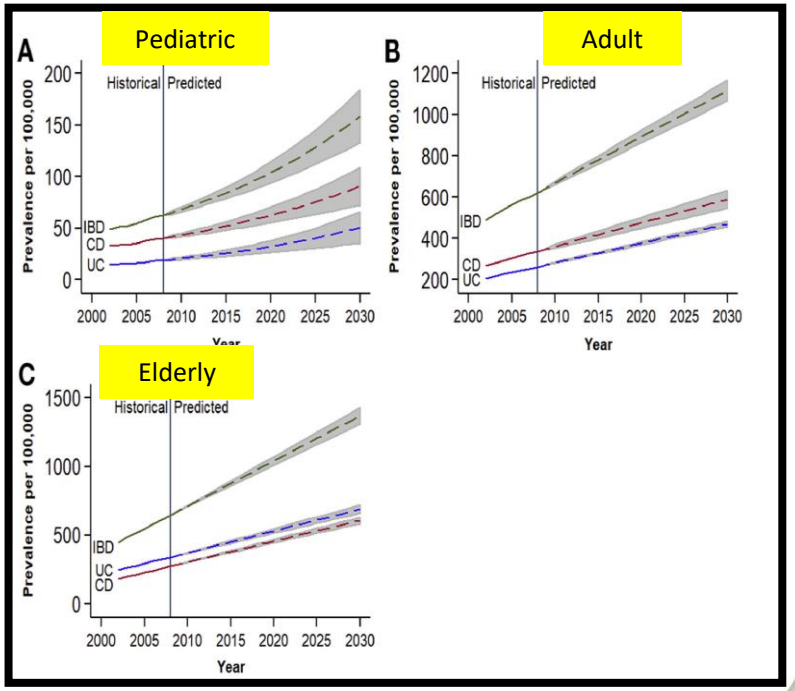


Kaplan GG *et al, Gastroenterology* 2017

The Global Burden of Inflammatory Bowel Disease

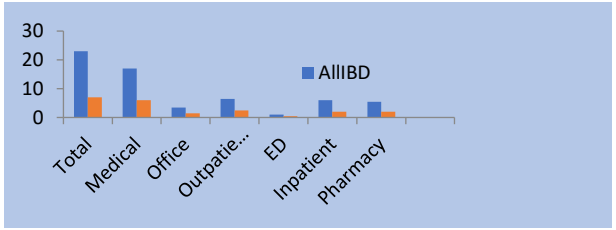


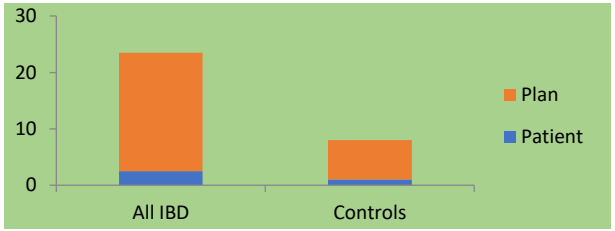
Kaplan GG and Windsor JW, *Nature Reviews, Gastroenterology & Hepatology* 2021

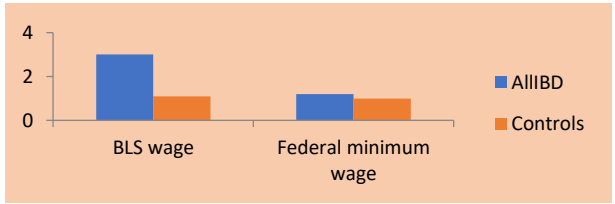


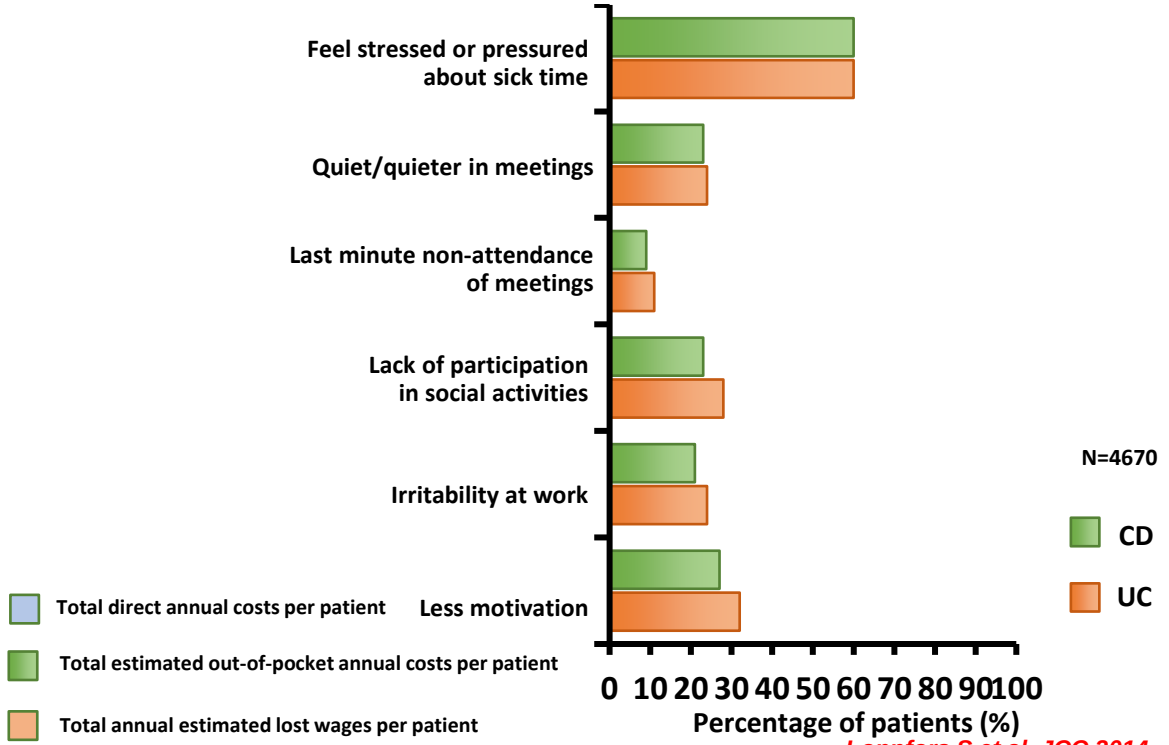
Coward S *et al*, *Gastroenterology* 2019

SOCIAL BURDEN IN IBD









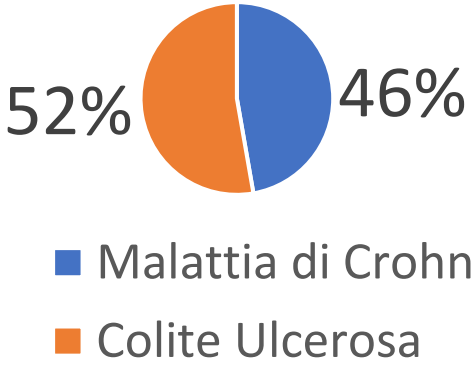
Park KT et al. IBD 2020

Lonnfors S et al. JCC 2014

Indagine BETTER - BisogniAssistEnziali, Lavorativi, Legali e Sociali per la cura dei pazienti affeTti da malaTtiE infiammatoRie Croniche dell'Intestino

AMICI ITALIA

1350 PAZIENTI



Il 72% ha avuto difficoltà a frequentare regolarmente la scuola/università a causa della malattia infiammatoria cronica intestinale

Il 79,73% ha avuto bisogno di prendere dei giorni di assenza dalla scuola a causa della malattia infiammatoria cronica intestinale

Per **il 71,75%** La sua malattia ha influenzato la sua capacità di lavorare

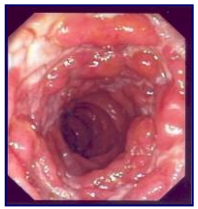
Il **59,24%** ha dovuto prendere un congedo dal lavoro a causa della sua malattia

Past, present, future

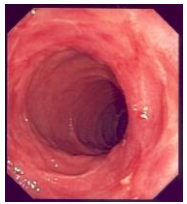
Raising the bar in treatments objectives for IBD patients….

Symptom improvement → Clinical remission → Steroid-free remission → Mucosal healing → Deep remission → PROs & mucosal healing → Disease cure

Treatment of Crohn's Disease With Anti-TNF Chimeric Monoclonal Antibody (cA2)



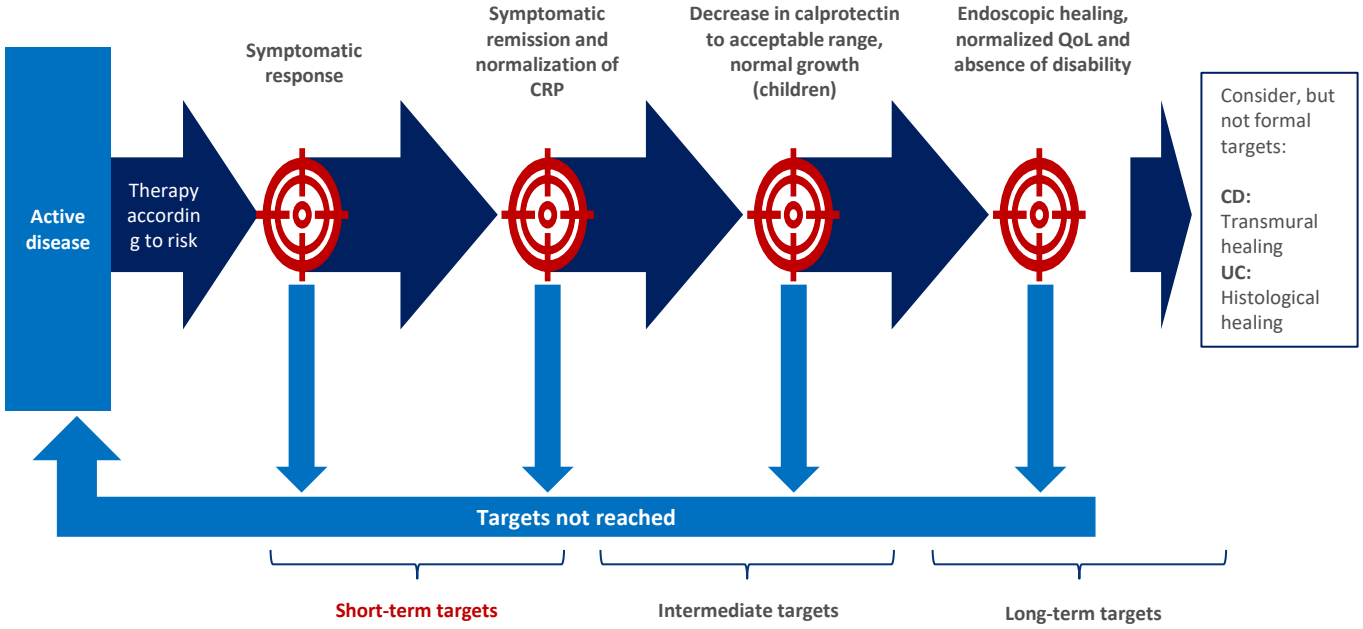
Before



After

Van Dullemen HM, et al. Gastroenterology 1995

Treatment Targets in Crohn's Disease and in Ulcerative Colitis: STRIDE –II CONSENSUS



Adapted Turner D, et al. Gastroenterology 2020.

CALM: Evidence for a T2T approach in IBD

CALM

Tight control VS **Clinical management**

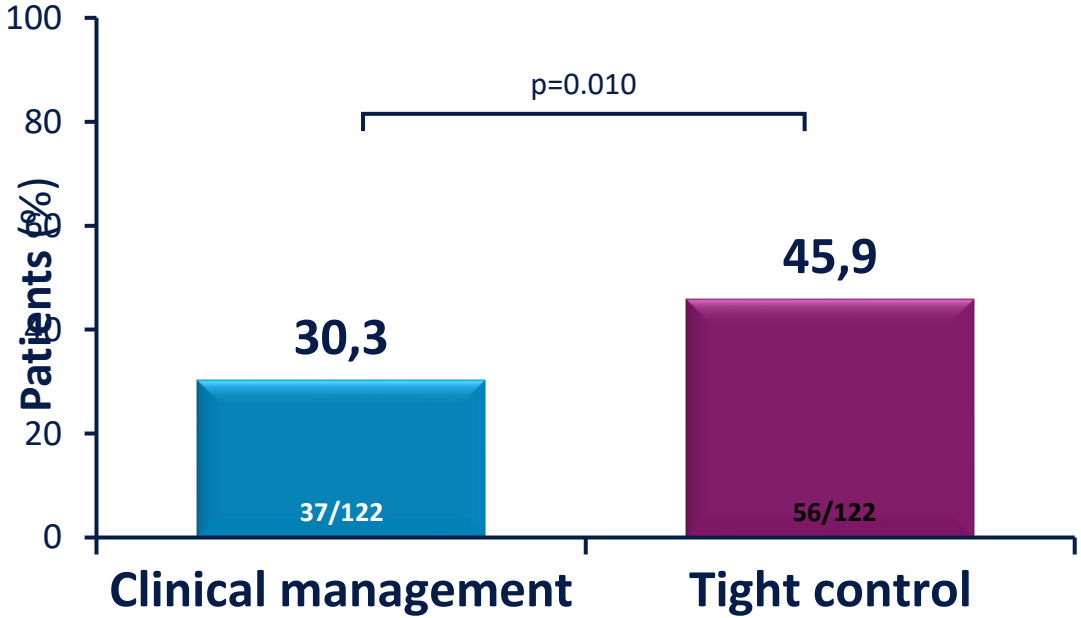
- Open-label, multicentre study in patients with **early*** moderate-to-severe CD
- Patients (n=244) randomised to:
  - **Tight control (treat-to-target approach)** – Treatment optimisation based on **biomarkers (CRP, FCP), steroid use and clinical symptoms (CDAI)**
  - **Clinical management** – Treatment optimisation based on **steroid use and clinical symptoms (CDAI)**
- Monitored **every 12 weeks**
- Primary endpoint was **mucosal healing (CDEIS <4)** with absence of deep ulcers at week 48

CALM is the **first study** to show that timely **optimisation of therapy based on clinical symptoms combined with biomarkers** in **early CD** results in **improved clinical and endoscopic outcomes** than optimisation based on symptoms alone

Colombel JF, et al. *Lancet* 2017

CALM: primary endpoint at 48 weeks after randomisation

CDEIS <4 and no deep ulcerations



Endoscopic scoring is based on site read. Cochran-Mantel-Haenszel test stratified by smoking status (yes/no) and weight (<70/≥70 Kg) at screening. NRI analysis.
NRI: non-responder imputation.

Colombel JF, et al. *Lancet* 2017

REACT2: Randomized Evaluation of an Algorithm for Crohn's Treatment

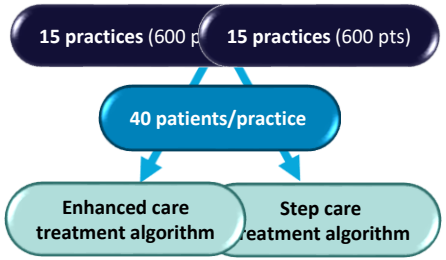
Primary endpoint:

- Risk of CD-related complications at 1 year, measured at practice level

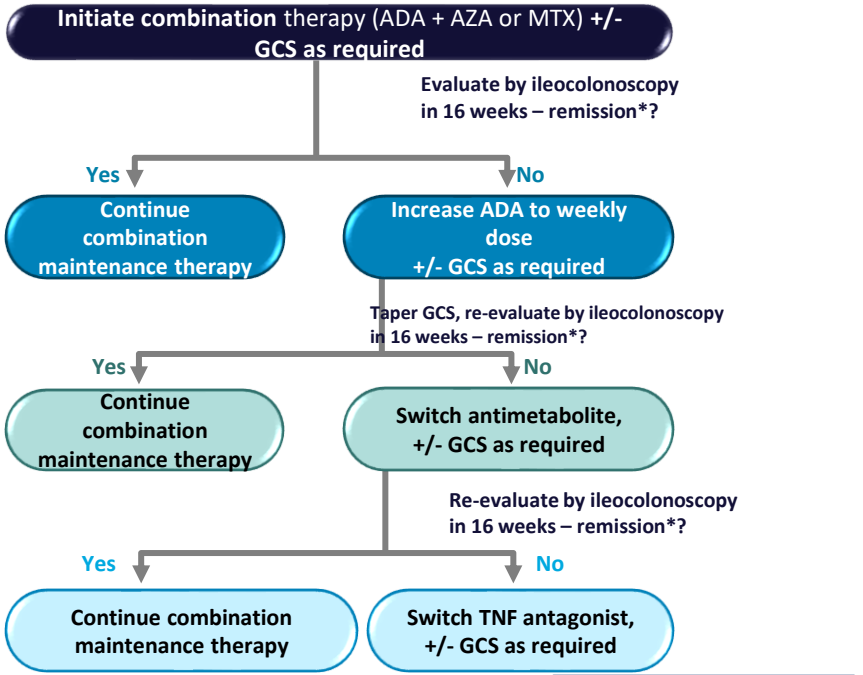
CD-related complications include:

1) **CD-related hospitalisations for CD-related surgeries and non-surgical CD events**
   (eg disease flare, bowel obstruction; excluding hospitalisation for side effects of study medication)
2) **Bowel damage events not requiring hospitalisation**
   (eg symptomatic bowel obstruction, cutaneous fistula, abscess)

Usual care versus enhanced care

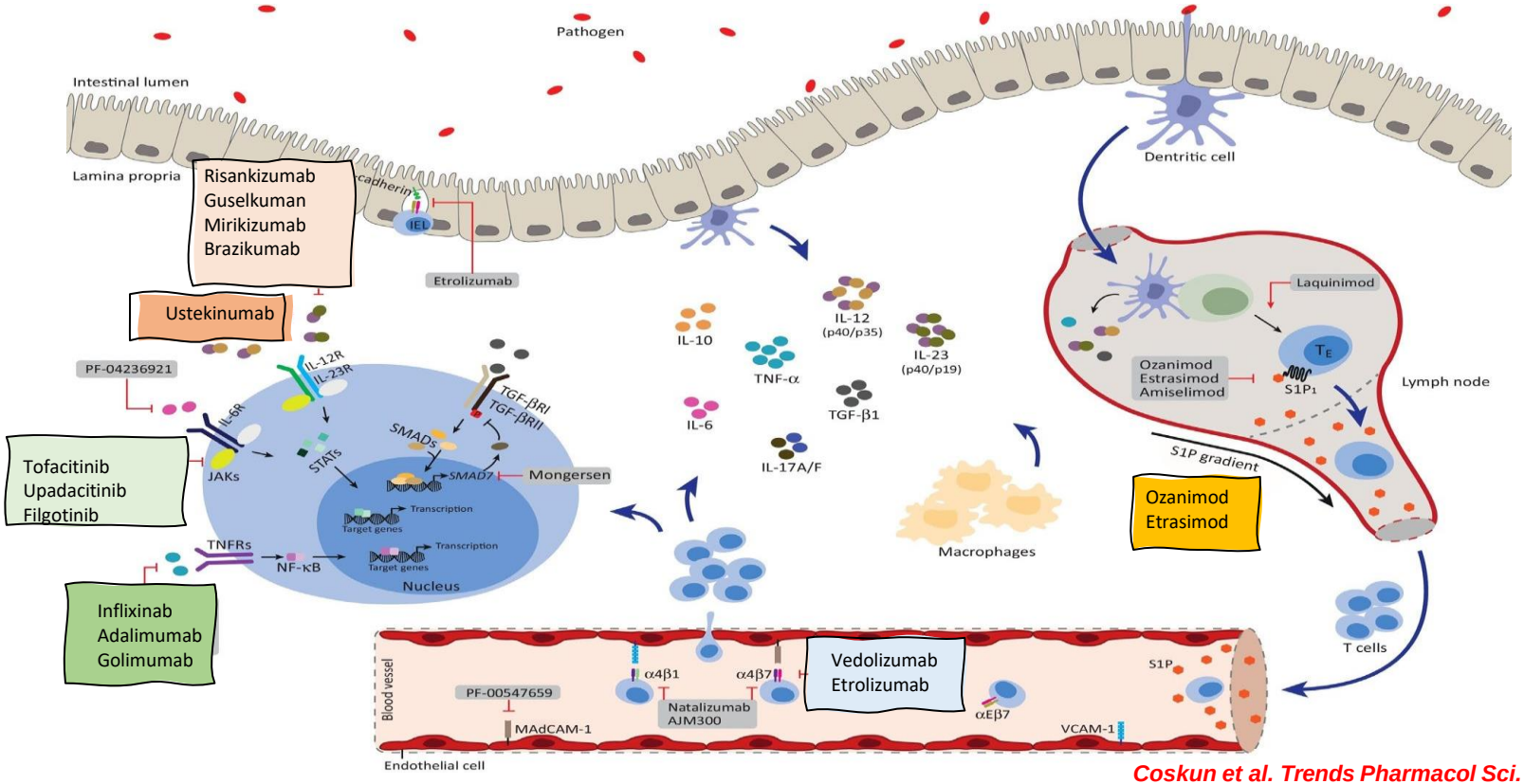


Active luminal CD (HBI >4, 1 large ulcer)



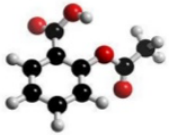
cluster randomisation

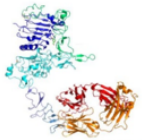
*Remission defined as HBI ≤4, no large ulcers, no GCS. GCS: glucocorticoids. www.clinicaltrials.gov:NCT01698307.



Coskun et al. Trends Pharmacol Sci. 2017

Future panorama of IBD drugs

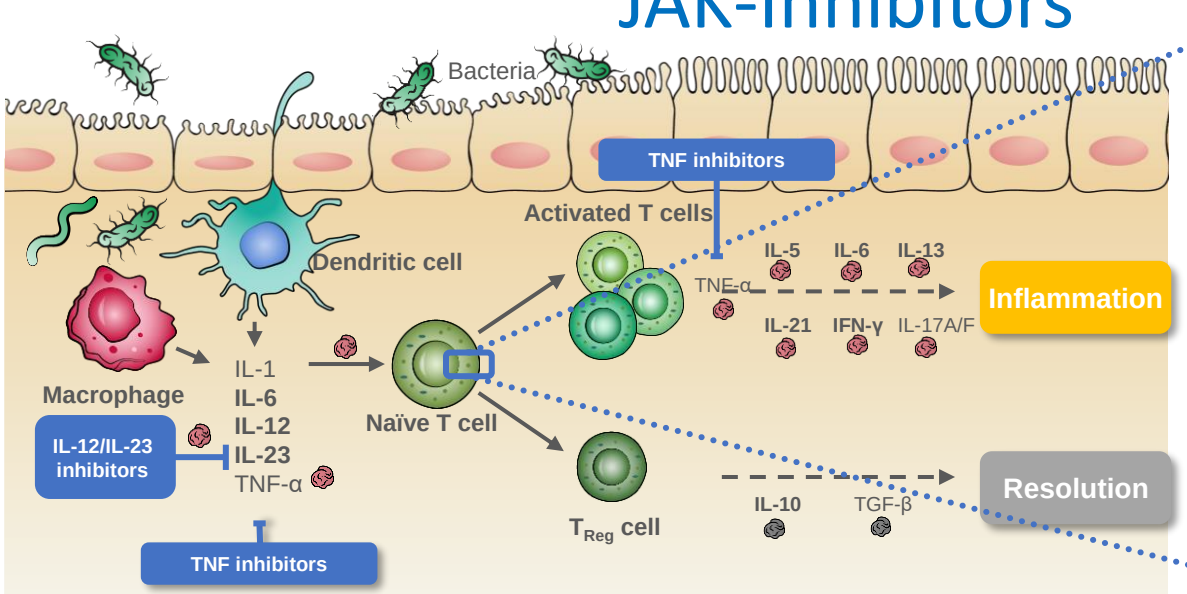




	Small molecules	Monoclonal antibodies
	Small organic compounds	Proteins
Molecular weight	Small (<1000 daltons)	Large (e.g. mAb = 150 kDa)
Route of administration	Oral	Parenteral
Preparation	Chemical synthesis	Biologically produced
MoA	Receptor or enzyme inhibition	Depletion
Location of target	Intracellular	Extracellular
Metabolism	Liver and gut CYPs into no active and active metabolites	Proteolytic degradation to peptides and amino acids
Target specificity	Less (compared to biologics) • Toxicities generally non-specific/not related to target ("off-target toxicity")	High target specificity • Toxicity generally related to target/pharmacology or "on-target toxicity"
Half-life	Short (compared to antibodies) • Minutes – hours - days	Long – especially molecules with Fc or IgG FcRn receptor, protects IgG from catabolism
Distribution	Potential for extensive distribution within the body	More limited distribution within body • Initially, largely confined to vascular space
Immunogenicity	Generally not a concern	Common challenge in animals and humans

Adapted from Mócsai A *et al. BMC Medicine* 2014; Zhao L *et al. Acta Pharmacologica Sinica* 2012

JAK-Inhibitors



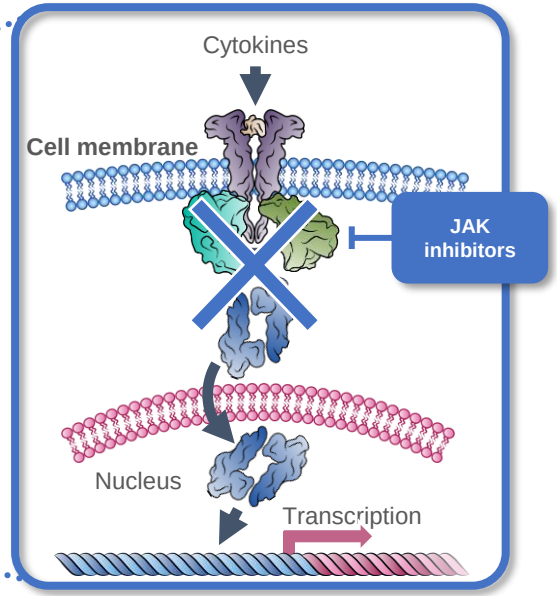


Figure adapted from: Neurath 2014,[3] Neurath MF 2017[4] and Yeshi *et al.* 2020[5]

JAK inhibitors partially and reversibly inhibit the activity of intracellular JAK proteins[2]

1. Salas A, et al. Nat Rev Gastroenterol Hepatol 2020; 17:323–337; 2. Danese S, et al. Gut 2019; 10:1893–1899;
3. Neurath MF. Nat Rev Immunol 2014; 14:329–342; 4. Neurath MF. Nat Rev Gastroenterol Hepatol 2017; 14:269–278; 5. Yeshi K, et al. J Clin Med 2020; 9:1273

New JAK-Inhibitors

Drug	Target	Gut selectivity	IBD type	Status
Tofacitinib	JAK1/JAK3	No	CD UC	Phase 2 completed (NCT00615199, NCT01393626) FDA/EMA approved
Peficitinib	JAK1/JAK3	No	CD UC	No studies Phase 2 completed (NCT01959282)
Upadacitinib	JAK1	No	CD UC	Phase 3 completed (NCT03345836), active not recruiting (NCT03345823) FDA/EMA approved
Filgotinib	JAK1	No	CD UC	Phase 3 active, not recruiting (NCT02914561), enrolling by invitation (NCT02914600) EMA approved, FDA rejected
Izencitinib (TD-1473)	pan-JAK	Yes	CD UC	Phase 2 terminated (NCT03635112) Phase 2b/3 terminated (NCT03758443)
Ivarmacitinib (SHR0302)	JAK1	No	CD UC	Phase 2 completed (NCT03677648) Phase 2 completed (NCT03675477)
OST-122 (Oncostellae)	JAK3/TYK2/ARK5	Yes	CD UC	No studies Phase 1b/2a recruiting (NCT04353791)
Deucravacitinib (BMS-986165)	TYK2	No	CD UC	Phase 2 recruiting (NCT03599622) Phase 2 active, not recruiting (NCT03934216)
Brepocitinib (PF-06700841)	JAK1/TYK2	No	CD UC	Phase 2 active, not recruiting (NCT03395184) Phase 2 completed (NCT02958865)
Ritlecitinib (PF-06651600)	JAK3	No	CD UC	Phase 2 active, not recruiting (NCT03395184) Phase 2 completed (NCT02958865)

Herrera DeGuise C et al. Front Med 2023

The NEW ENGLAND JOURNAL of MEDICINE

OR

Upadacitinib In
Therapy f

E.V. Loftus, Jr., J. Panés, A
R. Panaccione, W. Reinis
B.S. Boland, C. Phillips,
E. Dub

May 18, 2023

U.S. FDA Approves RINVOQ® (upadacitinib) as a Once-Daily Pill for Moderately to Severely Active Crohn's Disease in Adults

- *The co-primary endpoints of endoscopic response (visible reduction of intestinal lining damage) and clinical remission were achieved by significantly more patients treated with RINVOQ (upadacitinib) at week 12 and week 52 versus placebo*[1]
- *Clinical response was achieved by significantly more patients treated with RINVOQ (upadacitinib) versus placebo as early as week 2 in induction studies*[1]
- *This indication marks the seventh FDA approval for RINVOQ across gastroenterology, rheumatology and dermatology*[1]

NORTH CHICAGO, Ill., May 18, 2023 /PRNewswire/ -- AbbVie (NYSE: ABBV) today announced that the U.S. Food and Drug Administration (FDA) has approved RINVOQ® (upadacitinib) for the treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response or intolerance to one or more TNF blockers.[1] This is the seventh FDA approval for RINVOQ across rheumatology, dermatology, and gastroenterology, where it is now indicated in both ulcerative colitis and Crohn's disease.[1]

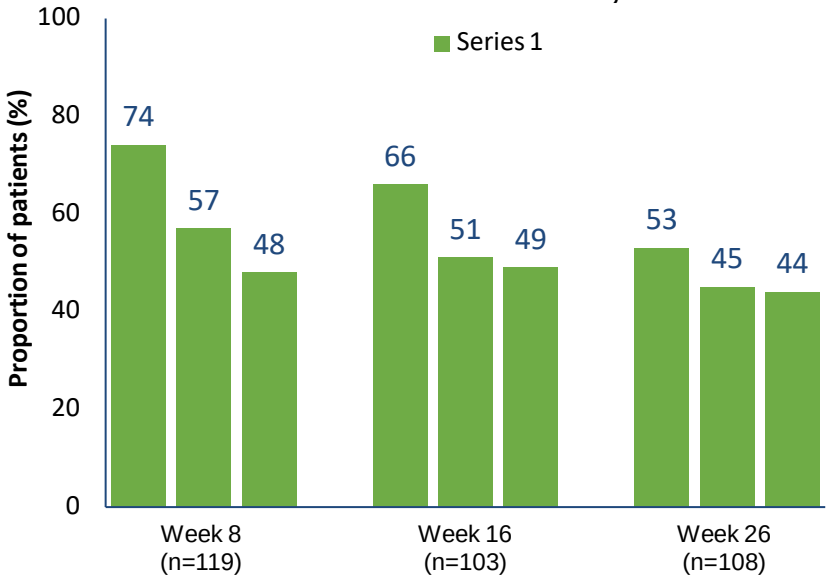
Access the multimedia news release here: https://www.multivu.com/players/English/9145751-abbvie-fda-crohns-disease/

Loftus EV et al. N Engl J Med 2023

Multicentre UK TOFA Experience: Study Design and Clinical Outcomes

- Retrospective, multicentre, observational cohort study†
- 134 patients with UC commenced on tofacitinib between October 2018 and October 2019
  - 83% had previously been treated with ≥1 biologic
- Patients received tofacitinib 10 mg BID for at least 8 weeks followed by a dose reduction to 5 mg BID
  - Subsequent dose escalation in maintenance was at clinician discretion
- Disease activity was assessed using SCCAI or PMS, dependent on study site
  - Clinical response was defined as a reduction in SCCAI or PMS ≥3
  - Clinical remission was defined as SCCAI ≤2 or a PMS ≤1
- Other clinical outcomes included biochemical markers of disease activity, endoscopic healing and steroid use

Clinical response, clinical remission and CS-free remission at Weeks 8, 16 and 26



†Data were collected from 4 tertiary referral IBD centres in the UK: Guy's and St. Thomas' Hospitals NHS Foundation Trust; Royal Devon and Exeter Hospital NHS Foundation Trust; Oxford University Hospitals NHS Foundation Trust; King's College Hospital NHS Foundation Trust.
BID=twice daily; CS=corticosteroid; IBD=inflammatory bowel disease; PMS=partial Mayo score; SCCAI=Simple Clinical Colitis Activity Index.

Honap S, et al. *J Crohns Colitis*. 2020

Multicentre UK Tofacitinib Experience: Safety Data

52 (**39%**) patients reported an adverse event, of which 15 (**11%**) were deemed serious adverse events†

The most frequently reported adverse event was lipid abnormality, occurring in 27 patients (**20%**)

Discontinuation due to adverse events was uncommon, occurring in 2 patients (**1.5%**)

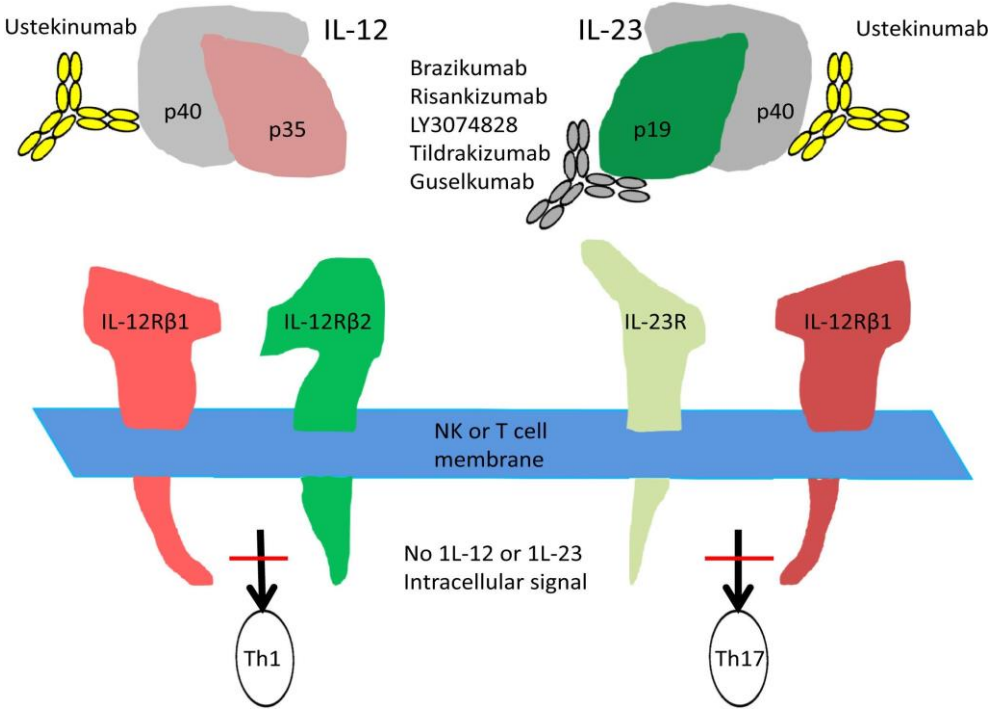
There were **3 cases** of herpes zoster infection: tofacitinib was discontinued in 1 patient and the other 2 patients were able to continue a reduced dose after antiviral treatment

No cases of venous thromboembolism or MACE were reported

†Adverse events were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) version 20.1. Serious adverse events included those that were life-threatening, resulted in persistent/permanent or significant disability/incapacity or that led to hospitalisation.
MACE=major adverse cardiovascular event.

Honap S, et al. *J Crohns Colitis*. 2020

Drugs targeting T-cell differentiation in IBD: anti-IL-23 agents



Deepak et al. Gastroenterol Clin N Am 2017

Induction

ADVANCE[1]

Patients with (~60%) & without (~40%) prior biologic failure

Randomization 2:2:1 N = 931

- RZB 1200 mg IV — N = 372
- RZB 600 mg IV — N = 373
- PBO IV — N = 186

MOTIVATE[1]

Patients with prior biologic failure (100%)

Randomization 1:1:1 N = 618

- RZB 1200 mg IV — N = 205
- RZB 600 mg IV — N = 206
- PBO IV — N = 207

IV dosing:

Wk: 0 (BL), 4, 8, 12

Co-primary Endpoints‡:

- Clinical Remission (SF/AP)
- Endoscopic Response

Clinical responders to 12 weeks of RZB IV induction[2,*]

Maintenance

FORTIFY[2]

Randomization 1:1:1 N = 542

- Corticosteroid taper
- RZB 360 mg SC Q8W — N = 179
- RZB 180 mg SC Q8W — N = 179
- Withdrawal (PBO SC) Q8W — N = 184

SC dosing:

W: 0, 8, 16, 24, 32, 40, 48, **52**

Co-primary Endpoints‡:

- Clinical Remission (SF/AP)
- Endoscopic Response

OLE rescue starting at W16†

RZB 1200 mg IV x 1 → RZB 360 mg SC Q8W

W: 0, 16, 52

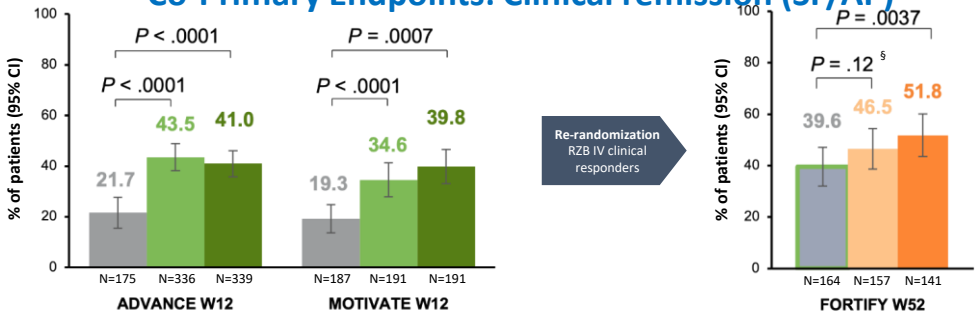
[1]D'Haens G et al. *Lancet.* 2022.; [2]Ferrante M et al. *Lancet.* 2022

Baseline Demographics and Disease Characteristics

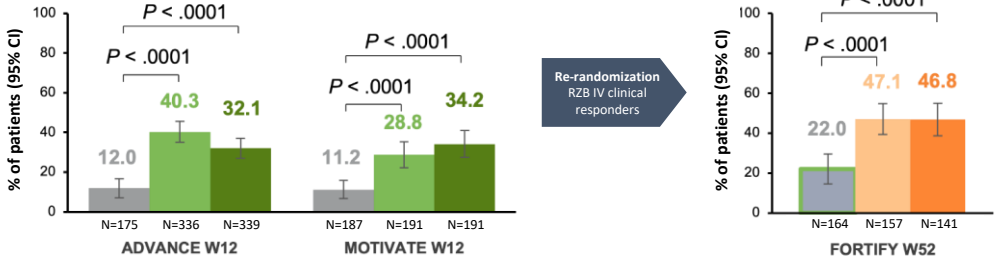
	ADVANCE			MOTIVATE		
	Placebo IV N=175	RZB 600 mg IV N=336	RZB 1200 mg IV N=339	Placebo IV N=187	RZB 600 mg IV N=191	RZB 1200 mg IV N=191
Male, n (%)	88 (50.3%)	189 (56.3%)	183 (54.0%)	99 (52.9)	92 (48.2)	102 (53.4)
Age, mean years (SD)	37.1 (13.4)	38.3 (13.3)	37.0 (13.2)	39.3 (13.5)	40.2 (13.6)	39.3 (12.9)
Disease duration, mean years (SD)	8.2 (7.1)	9.0 (8.8)	8.9 (8.4)	12.5 (9.7)	10.9 (7.7)	11.8 (9.1)
Fecal calprotectin (mg/kg), median (range)	1200 (30-26786)	960 (30-14690)	1045 (30-28800)	987.5 (30-28800)	1367.0 (30-28800)	1220.0 (30-16877)
hs-CRP (mg/L), mean (SD)	16.3 (21.3)	18.1 (26.9)	16.2 (21.9)	20.4 (25.7)	19.3 (26.3)	20.7 (25.3)
CDAI, mean (SD)	319.2 (59.4)	311.2 (62.4)	311.5 (68.4)	319.6 (69.8)	310.7 (63.6)	312.4 (61.2)
SES-CD*, mean (SD)	13.8 (6.8)	14.7 (7.7)	13.4 (6.5)	15.0 (8.1)	14.4 (7.6)	15.1 (7.6)
Average daily stool frequency, mean (SD)	6.1 (2.8)	5.8 (2.7)	5.6 (2.8)	6.4 (2.9)	6.2 (3.1)	5.9 (2.8)
Average daily abdominal pain score, mean (SD)	1.9 (0.6)	1.8 (0.6)	1.9 (0.5)	1.8 (0.5)	1.9 (0.5)	1.9 (0.56)
Corticosteroid use*, n (%)	49 (28.0%)	102 (30.4%)	103 (30.4%)	68 (36.4)	65 (34.0)	62 (32.5)
Immunomodulator use, n (%)	42 (24.0%)	88 (26.2%)	73 (21.5%)	40 (21.4)	36 (18.8)	53 (27.7)
Biologics failure history*, n (%)						
0	78 (44.6%)	141 (42.0%)	141 (41.6%)	0	0	0
1	41 (23.4%)	100 (29.8%)	98 (28.9%)	88 (47.1)	92 (48.2)	88 (46.1)
>1	56 (32.0%)	95 (28.3%)	100 (29.5%)	99 (52.9)	99 (51.8)	103 (53.9)
Ustekinumab failure history, n (%)	19 (19.6%)	43 (22.1%)	48 (24.2%)	40 (21.4)	36 (18.8)	33 (17.3)

[1]D'Haens G et al. *Lancet*. 2022

Co-Primary Endpoints: Clinical remission (SF/AP)†



Co-primary Endpoints: Endoscopic response‡



PBO IV | RZB 600 mg IV | RZB 1200 mg IV | Withdrawal (PBO SC) | RZB 180 mg SC | RZB 360 mg SC

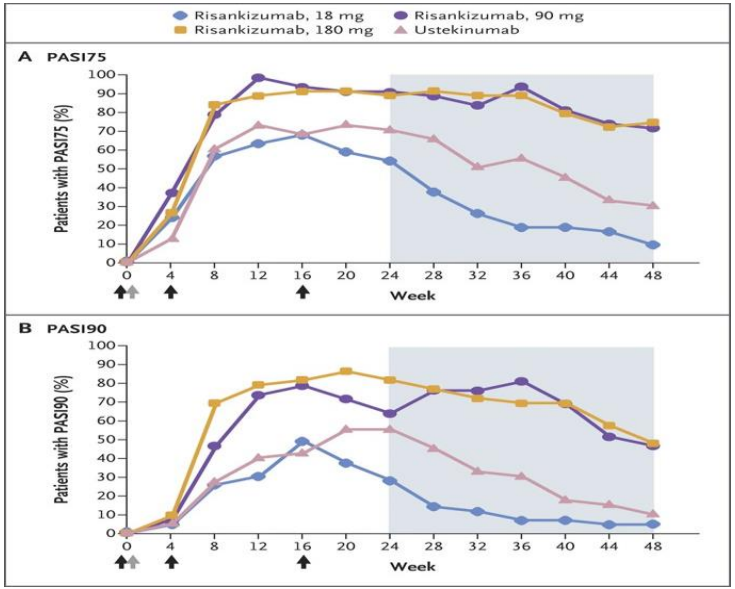
KEY TAKEAWAYS

- Significantly higher rates of clinical remission (SF/AP) and endoscopic response were achieved with 600 mg & 1200mg IV RZB vs PBO at W12 of both induction studies and with 360 mg SC RZB vs withdrawal (PBO SC) at W52 of the maintenance study
- At FORTIFY W52, the 180 mg SC RZB treatment arm did not achieve statistical significance compared to the withdrawal (PBO SC) arm for clinical remission (SF/AP)§
- Numerically higher rates of efficacy were generally observed with RZB in the patients without previous bio-failure

[1]D'Haens G et al. *Lancet.* 2022.; [2]Ferrante M et al. *Lancet.* 2022

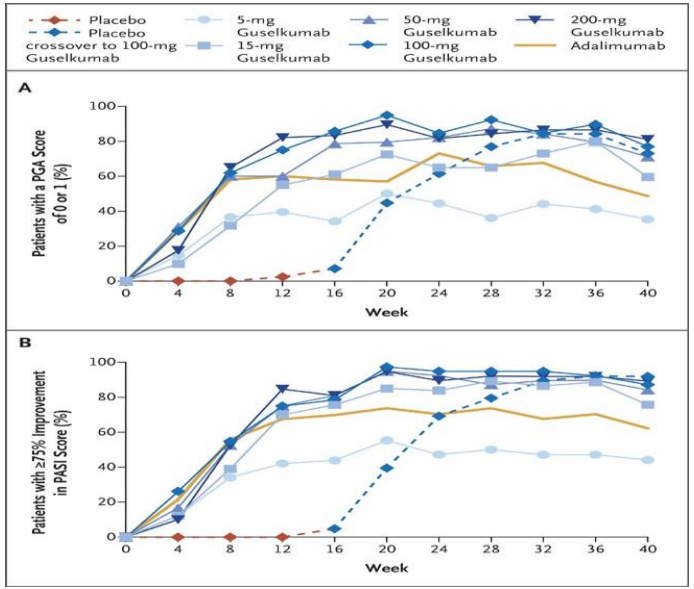
Will Anti-IL 23 (p19 inhibitors) be better than what we have?

RISANKIZUMAB > USTEKINUMAB IN PSORIASIS



Papp KA et al. N Engl J Med 2017

GUSELKUMAB > ADALIMUMAB IN PSORIASIS



Gordon et al. N Engl J Med 2015

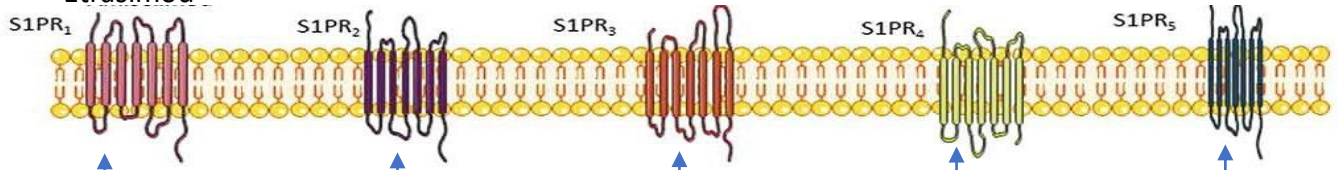
S1P modulators

Fingolimod
Ozanimod
Etrasimod

Fingolimod

Fingolimod
Etrasimod

Fingolimod
Ozanimod
Etrasimod

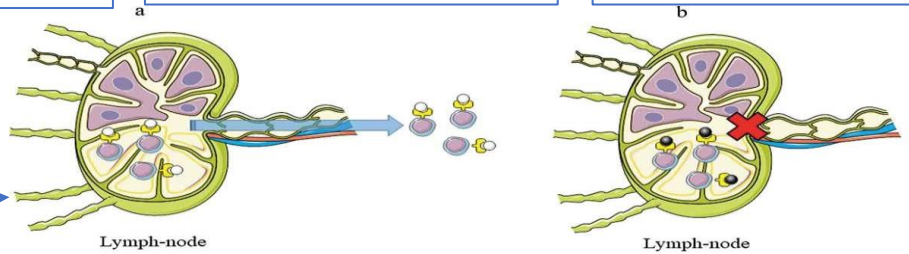


Associated with immunomodulation & bradicardia

Associated with cardiac, pulmonary and cancer related events

Associated with immunosuppressive effects

Associated with CNS effects



Argollo et al. Expert Opin Biol Ther 2020

S1P modulators

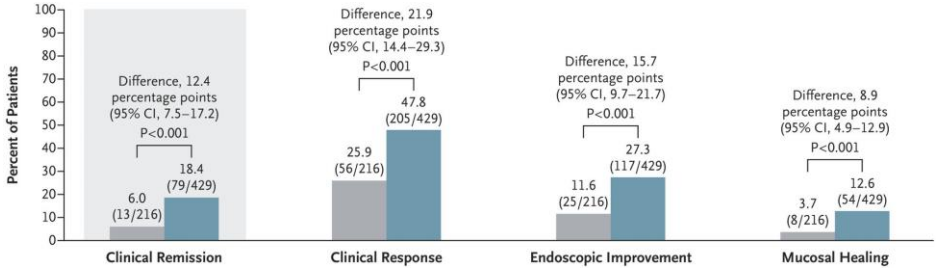
Drug	Target	Route	IBD type	Drug stage	EMA approved (indication)
Ozanimod	S1P1 and S1P5	Oral	CD UC	Phase II/III recruiting Phase III completed	UC, MS
Etrasimod	S1P1, S1P4 and S1P5	Oral	CD UC	Phase II/III recruiting Phase III recruiting	

Modified from Grossberg et al. Aliment Pharmacol Ther. 2022

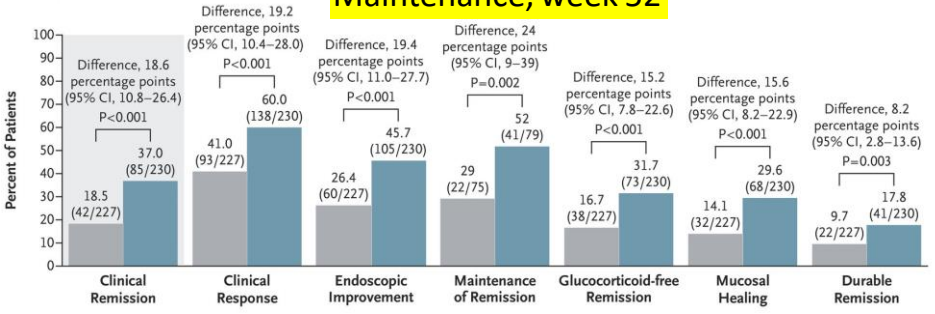
Ozanimod as Induction and Maintenance Therapy for UC

(Phase III True North Study)

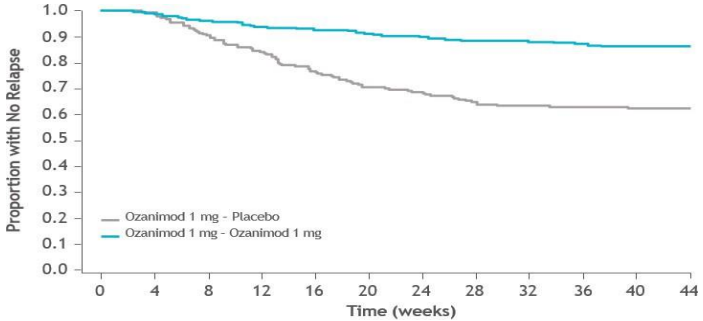
Induction, week 10



Maintenance, week 52



Time to Disease Relapse in the Maintenance Period



Sandborn et al. N Engl J Med 2021

OZANIMOD

ETROLIZUMAB

TOFACITINIB

CT-P13 SC

ETRASIMOD

INFLIXIMAB

GOLIMUMAB

USTEKINUMAB

ADALIMUMAB

VEDOLIZUMAB

UPADACITINIB

CERTOLIZUMAB

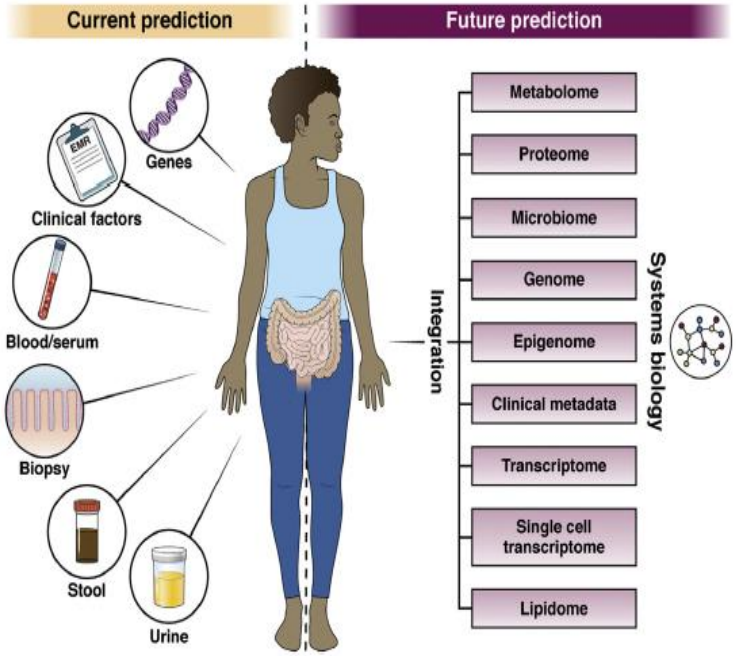
MIRIKIZUMAB

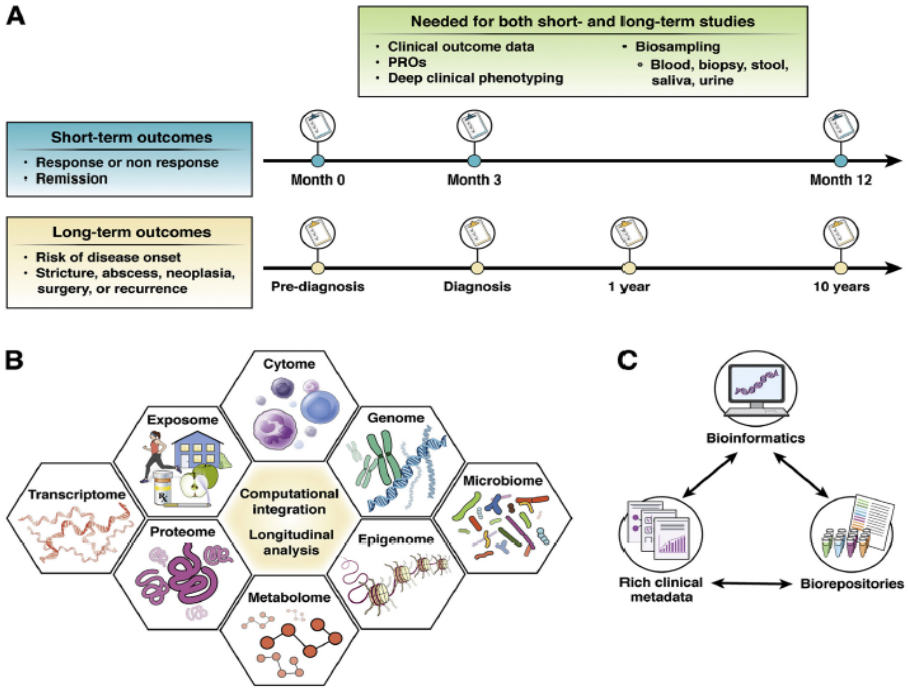
RISANKIZUMAB

GUSELKUMAB

FILGOTINIB

PRECISION MEDICINE IN IBD: THE FUTURE

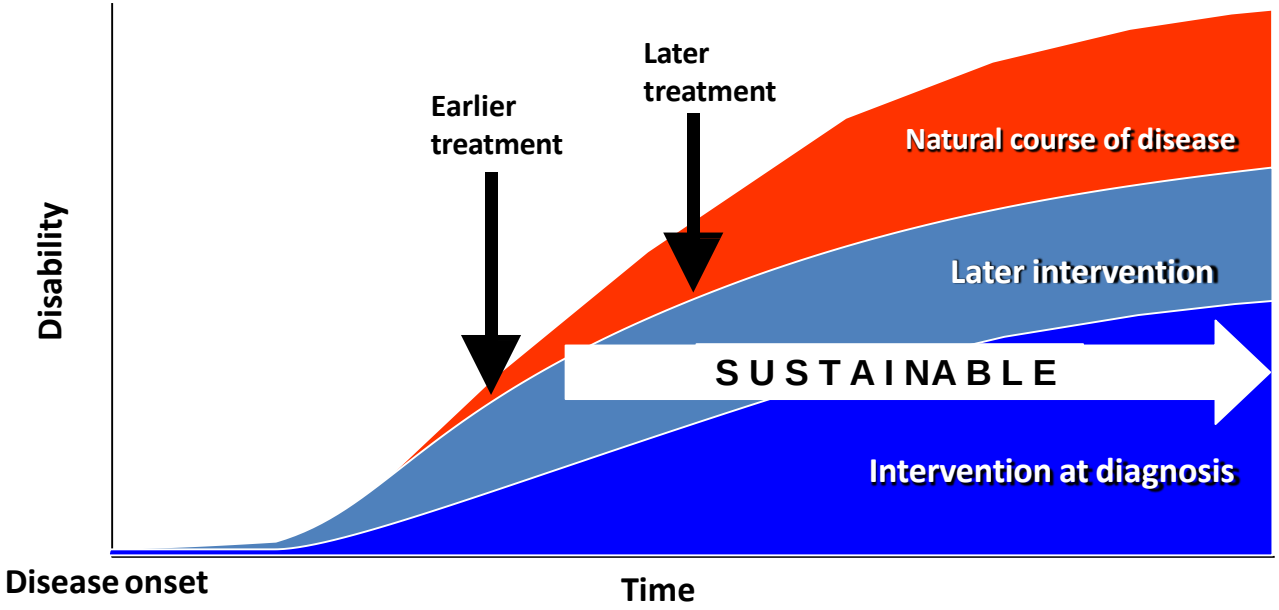




Lamb CA et al. *Gastroenterology 2022*

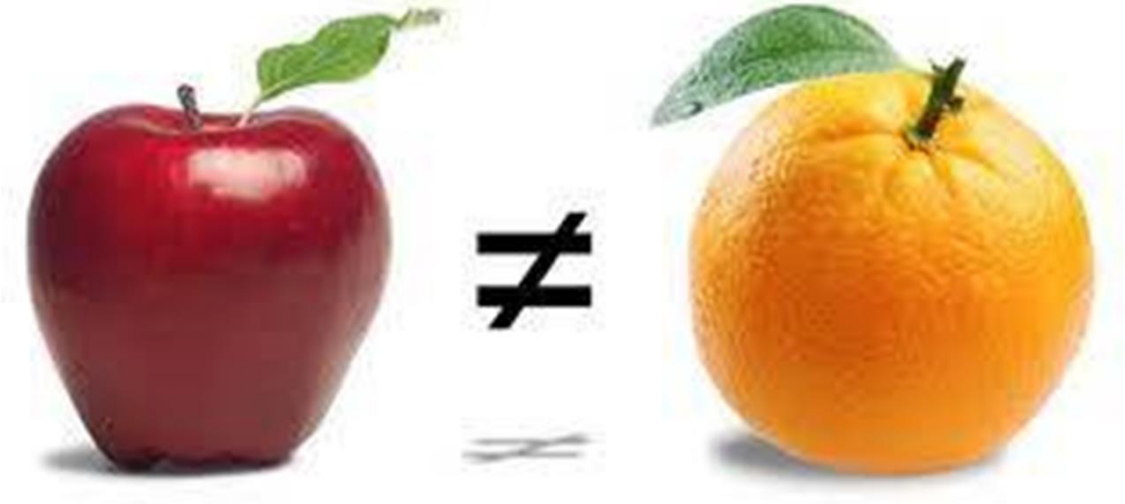
BIOSIMILARS: HIGHER ACCESSIBILITY TO BIOLOGICS ?

Earlier and more intensive use of Anti TNF-α as the first line therapy

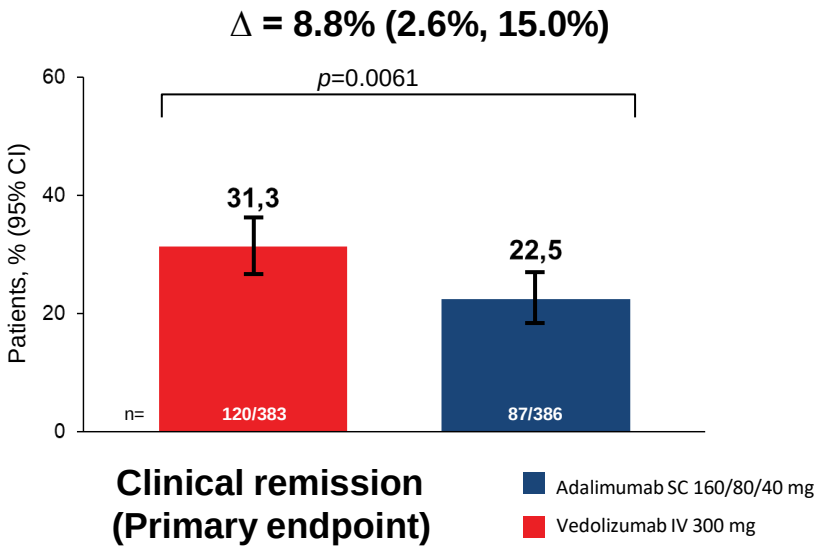


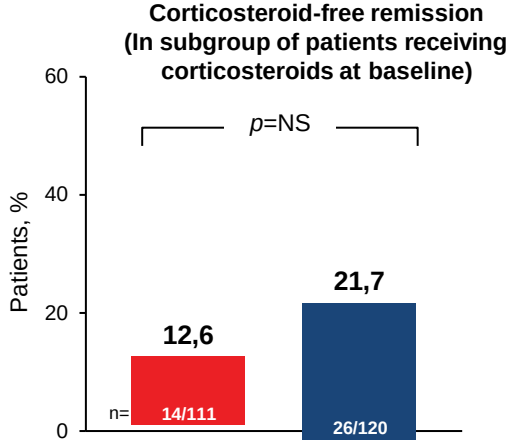
Adapted from Jones J, Panaccione R. *Curr Opinion Gastroenterol* 2008

Comparing efficacy of molecules in the absence of head-to-head trials is biased



VARSITY: VDZ superior to ADA in achieving clinical remission at Week 52 in UC: Head to Head trial





Sands BE, et al. New Engl J Med

Problems with RCT: Poor external validity

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*

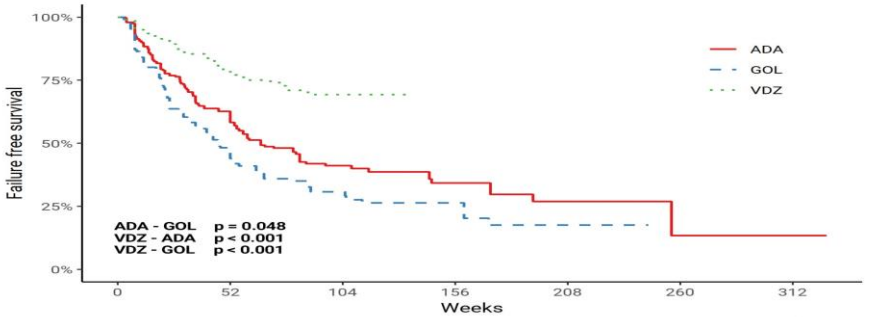
Table 1. Demographic and Disease Characteristics of the Patients at Baseline.*

Characteristic	Adalimumab (N=386)	Vedolizumab (N=385)
Age — yr	40.5±13.4	40.8±13.7
Male sex — no. (%)	216 (56.0)	234 (60.8)
White race — no. (%)†	341 (88.3)	345 (89.6)
Body weight — kg	73.4±18.4	72.7±17.0
Current smoker — no. (%)‡	23 (6.0)	19 (4.9)
Duration of ulcerative colitis — yr§	6.4±6.0	7.3±7.2
Total score on the Mayo scale¶	8.7±1.5	8.7±1.6
Fecal calprotectin level — μg/g‖	2771±4064	2929±5920
Previous treatment with a TNF inhibitor with documented reason for discontinuation — no. (%)	81 (21.0)	80 (20.8)
Previous therapy with a TNF inhibitor with documented failure — no. (%)	79 (20.5)	72 (18.7)

Sands BE et al. NEJM 2019

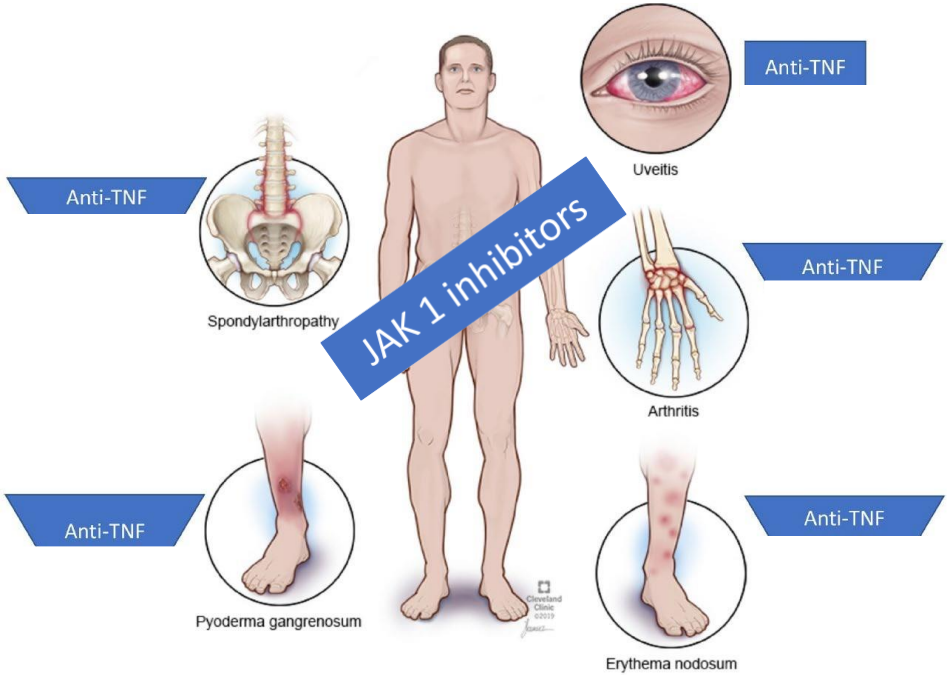
A Propensity Score Weighted Comparison of Vedolizumab, Adalimumab, and Golimumab in Patients with Ulcerative Colitis: Real-Life Data from the Sicilian Network for Inflammatory Bowel Disease (SN-IBD)

Variable	VDZ (n=187)	ADA (n=168)	GOL (n=108)	p
Previous lines of biologics, n (%)				
0 (naïve)	66 (35.3%)	104 (61.9%)	58 (53.7%)	<0.001
1	62 (33.2%)	53 (31.5%)	35 (32.4%)	
2	53 (28.3%)	9 (5.4%)	14 (13.0%)	
3	6 (3.2%)	2 (1.2%)	1 (0.9%)	



Macaluso FS et al. Dig Liver Dis. 2020

Treatment options for extraintestinal manifestations in IBD



Greuter T, et al. Gut 2021

PRIORITIZING EFFICACY

- UC
  - JAK1-preferential inhibitors
  - Infliximab
- CD
  - P19 inhibitors ??
  - Anti-TNFs

PRIORITIZING SAFETY

- P19 or P40 inhibitors
- Vedolizumab

PRIORITIZING COST

- Biosimilars (for now Anti-TNFs)

Emerging role of dual biologic therapy for the treatment of IBD

Table 1 Summary of trials, case reports and retrospective studies on dual biological therapy for inflammatory bowel disease

Ref.	Study type	No. of patients	Disease	Treatment used
Sands *et al*[14], 2007	RCT	79	CD	IFX + natalizumab
Anita and Michael [16], 2016	CR	1	CD	VDZ + ADA
Bethge *et al*[17], 2017	CR	1	UC	VDZ + ETN
Liu and Loomes[9], 2017	CR	1	CD	UST + VDZ
Huff-Hardy *et al* [10], 2017	CR	1	CD	UST + VDZ
Roblin *et al*[19], 2018	CR	1	UC	GOL + VDZ
Buer *et al*[20], 2018	CS	10	4 × CD, 6 × UC	Anti-TNF + VDZ
Mao *et al*[21], 2018	CS	4	CD	VDZ + UST/GOL
Olbjørn *et al*[11], 2020	CS	13	9 × CD, 4 × UC	IFX + UST/VDZ
Glassner *et al*[22], 2020	Retrospective	50	CD + UC	UST + ANTI-TNF/VDZ, tofacitinib + VDZ/UST/anti-TNF, Cyclosporin, rituximab, SEC, leflunomide, tacrolimus
Yang *et al*[23], 2020	Retrospective	22	CD	VDZ + UST/anti-TNF, UST + anti-TNF
Privitera *et al*[24], 2020	Retrospective	16	11 × CD, 5 × UC	UST + CZP/IFX/ADA/VDZ, VDZ + ADA/SEC/IFX/CZP/aprelimast
Kwapisz *et al*[26], 2021	Retrospective	15	14 × CD, 1 × UC	VDZ + anti-TNF/UST, UST + anti-TNF/VDZ
Goessens *et al*[27], 2021	Retrospective	98	58 × CD, 40 × UC	ADA + VDZ/UST, VDZ + INF + azathioprine, VDZ + UST + azathioprine, UST + ETN, IFX + VDZ + methotrexate, CZP + VDZ + methotrexate
No author listed [15], 2022	RCT	214	UC	GOL + guselkumab

Table 2 Summary of infections reported in randomised controlled trial and case studies of patients on dual biologic therapy for inflammatory bowel disease

Ref.	Infections documented
Sands *et al*[14], 2007	Nasopharyngitis
Buer *et al*[20], 2018	Tonsillitis × 2
	Sinusitis × 1
Olbjørn *et al*[11], 2020	Skin infection
Mao *et al*[21], 2018	Clostridium difficile × 2
	Hand, foot and mouth disease
	Influenza
Yang *et al*[23], 2020	Pneumonia
	Clostridium difficile
	Actinetobacter bacteraemia
Privitera *et al*[24], 2020	Perianal abscess
Kwapisz *et al*[26], 2021	Salmonella
	Clostridium difficile
	4 × patients needing antibiotics
Goessens *et al*[27], 2021	Osteomyelitis
	Enterocutaneous fistula infection
	Perianal abscess
	Viral URTI
	Campylobacter
	Pneumonia
	Herpetic meningoencephalitis
	Oesophageal candidiasis
	Influenza

McCormack MD *et al. WJG* 2023

DUET-CD and DUET-UC Study

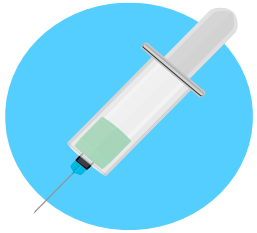
JNJ78934804
guselkumab/golimumab co-formulation
Three dose regimens

DUET Studies
48-week Phase 2b Study
with a 192-week extension

Efficacy

Safety

Guselkumab
monotherapy



Golimumab
monotherapy

Placebo

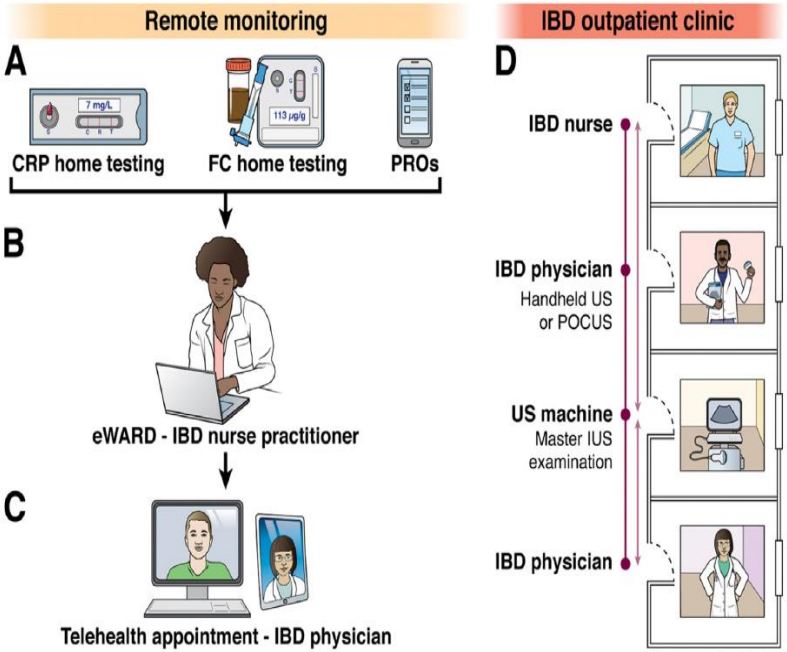
DUET-CD

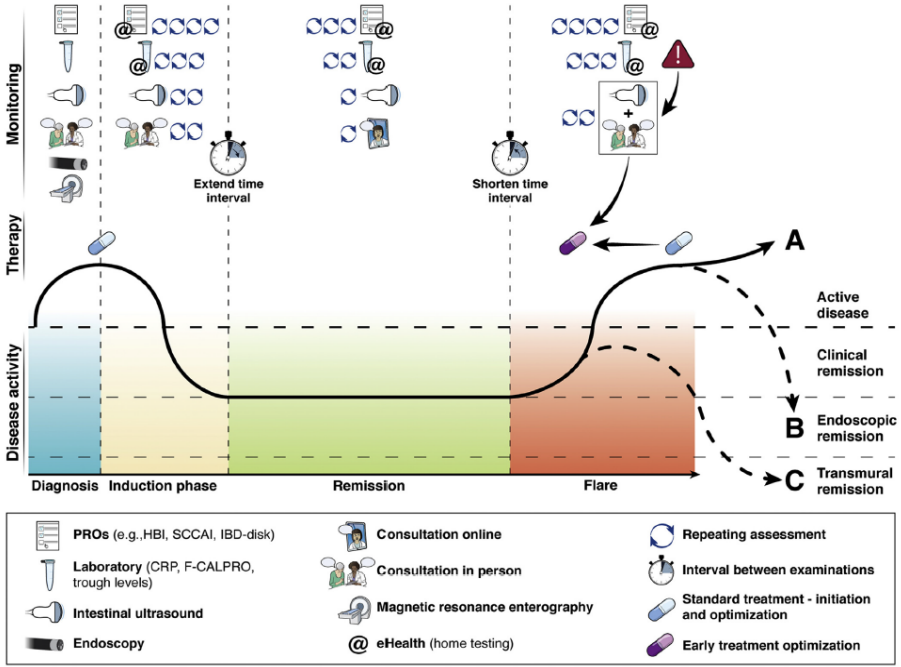
- Moderately to severely active CD (CDAI 220-450 AND SF ≥ 4 or AP ≥2 AND SES-CD score ≥ 6 OR ≥ 4 for isolated ileal disease)
- Prior inadequate response to at least one approved advanced therapy

DUET-UC

- Moderately to severely active UC (modified Mayo score of 5 to 9, inclusive, and screening endoscopy subscore ≥ 2)
- Prior inadequate response to at least one approved advanced therapy

DISEASE MONITORING: THE FUTURE





Wilkens R et al. *Gastroenterology 2022*

DECALOGO DELLA QUALITA' DI CURA: CONFRONTO TRA PAZIENTI E GASTROENTEROLOGI

Dal confronto delle risposte di pazienti e medici in merito ai criteri prioritari per la definizione della qualità delle cure (decalogo), appare evidente come vi sia un allineamento solo su alcuni aspetti. Colpiscono infatti le differenze nella valorizzazione di aspetti legati alla personalizzazione delle terapie e alla partecipazione attiva del paziente nelle scelte terapeutiche

Cfr. dati report pazienti

PAZIENTI

1. Sentire di essere accolto e supportato in un percorso di cura e assistenza condiviso e adattato alle mie esigenze
2. Poter dare voce alle mie priorità ed esigenze rispetto alla gestione della malattia e alle cure disponibili e sentirmi parte attiva delle scelte che riguardano il mio stato di salute
3. Sapere che posso contare su cure adeguate a me e al mio stato di salute anche in situazioni di emergenza
4. Essere reso partecipe di tutte le informazioni rilevanti relative al mio stato di salute
5. Poter accedere facilmente a un servizio di cura prevedibile, condiviso e trasparente
6. Essere rispettato e tutelato nei miei bisogni e desideri di cura
7. Poter esprimere al medico tutte le mie preoccupazioni e i miei dubbi e sentirmi ascoltato e compreso
8. Potermi affidare a degli specialisti competenti ed esperti della mia malattia e della sua cura
9. Sentire che i miei bisogni e le mie aspettative di cura - specifici del mio essere donna o uomo - sono compresi e presi in considerazione dal sistema sanitario
10. Sentire che i miei bisogni e le mie aspettative di cura – specifici del momento di vita e di salute che sto attraversando - sono compresi e presi in considerazione dal sistema sanitario

V/s

GASTROENTEROLOGI

1. Potermi affidare a degli specialisti competenti ed esperti della mia malattia e della sua cura
2. Poter accedere facilmente a un servizio di cura prevedibile, condiviso e trasparente
3. Sapere che posso contare su cure adeguate a me e al mio stato di salute anche in situazioni di emergenza
4. Sentire che i miei bisogni e le mie aspettative di cura - specifici del mio essere donna o uomo - sono compresi e presi in considerazione dal sistema sanitario
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Barello S. et al. Journal of Crohn's and Colitis 2020

Grazie per l'attenzione