Combinaison de thérapies avancées

Robert Battat M.D.
Directeur, CETRI
CENTRE D'EXCELLENCE CLINIQUE ET RECHERCHE TRANSLATIONNELLE MICI
Centre hospitalier de l'Université de Montréal
CHUM

Disclosures

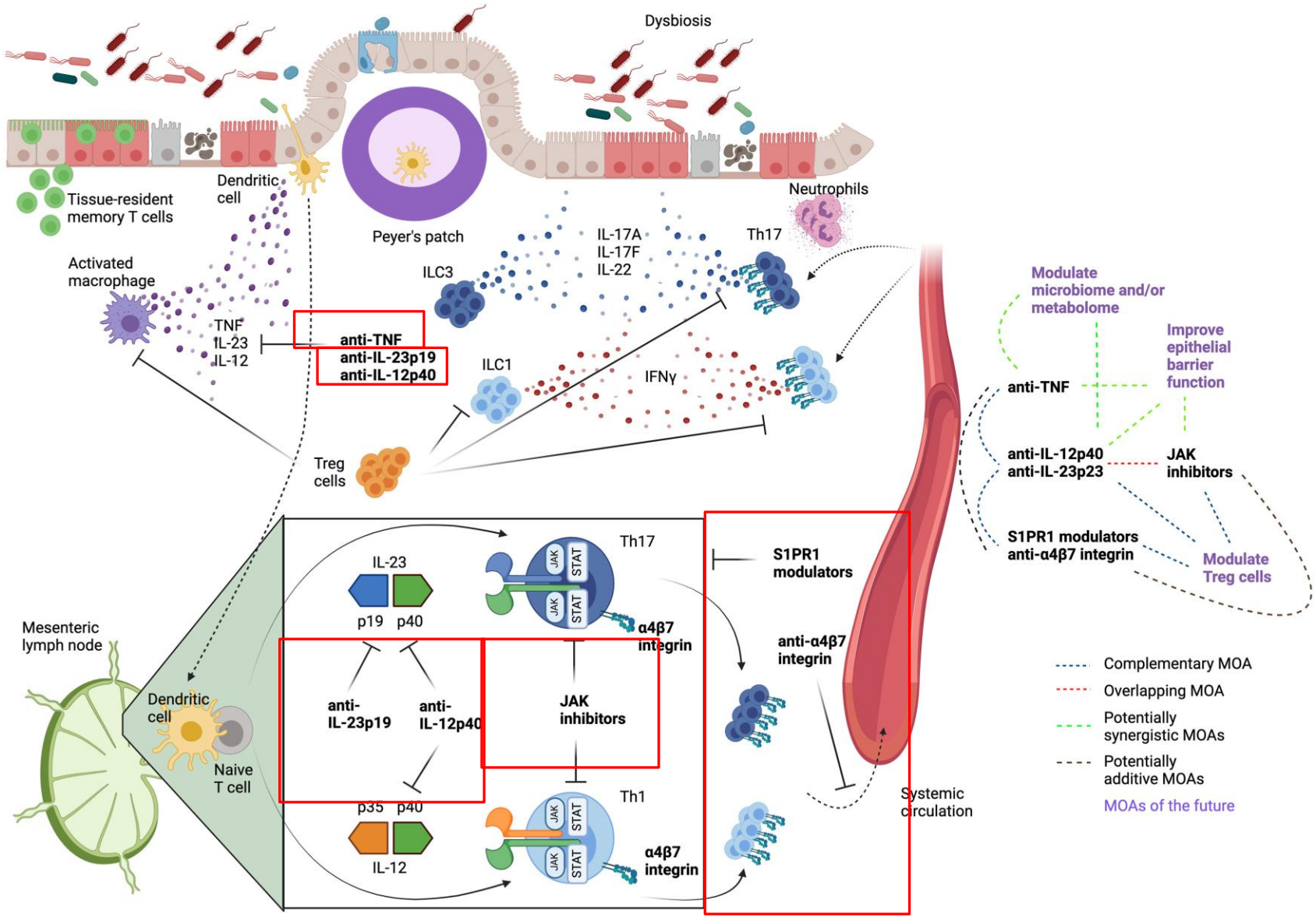
SPEAKER/CONSULTING/MODERATOR: BRISTOL MYERS SQUIBB, JANSSEN, ABBVIE, TAKEDA, FERRING, CELLTRION, PFIZER, MERCK, ELI LILLY

ADVISORY BOARDS: CELLTRION, ABBVIE, PFIZER, JANSSEN, BRISTOL MYERS SQUIBB, TAKEDA, MERCK, ELI LILLY

EDUCATIONAL GRANTS AND EDUCATIONAL SPONSORSHIPS: ABBVIE, JOHNSON AND JOHNSON INNOVATIVE MEDICINE, PFIZER, ELI LILLY, AMGEN, PENDOPHARM, MERCK, CELLTRION, ORGANON

Compétences CanMEDS

X	**Expert médical** (En tant qu'experts médicaux, les médecins assument tous les rôles CanMEDS et s'appuient sur leur savoir médical, leurs compétences cliniques et leurs attitudes professionnelles pour dispenser des soins de grande qualité et sécuritaires centrés sur les besoins du patient. Pivot du référentiel CanMEDS, le rôle d'expert médical définit le champ de pratique clinique des médecins .)
	Communicateur (En tant que communicateurs, les médecins développent des relations professionnelles avec le patient et ses proches ce qui permet l'échange d'informations essentielles à la prestation de soins de qualité.)
	Collaborateur (En tant que collaborateurs, les médecins travaillent efficacement avec d'autres professionnels de la santé pour prodiguer des soins sécuritaires et de grande qualité centrés sur les besoins du patient.)
	Leader (En tant que leaders, les médecins veillent à assurer l'excellence des soins, à titre de cliniciens, d'administrateurs, d'érudits ou d'enseignants et contribuent ainsi, avec d'autres intervenants, à l'évolution d'un système de santé de grande qualité.)
X	**Promoteur de santé** (En tant que promoteurs de la santé, les médecins mettent à profit leur expertise et leur influence en oeuvrant avec des collectivités ou des populations de patients en vue d'améliorer la santé. Ils collaborent avec ceux qu'ils servent afin d'établir et de comprendre leurs besoins, d'être si nécessaire leur porte-parole, et de soutenir l'allocation des ressources permettant de procéder à un changement.)
X	**Érudit** (En tant qu'érudits, les médecins font preuve d'un engagement constant envers l'excellence dans la pratique médicale par un processus de formation continue, en enseignant à des tiers, en évaluant les données probantes et en contribuant à l'avancement de la science.)
	Professionnel (En tant que professionnels, les médecins ont le devoir de promouvoir et de protéger la santé et le bien-être d'autrui, tant sur le plan individuel que collectif. Ils doivent exercer leur profession selon les normes médicales actuelles, en respectant les codes de conduite quant aux comportements qui sont exigés d'eux, tout en étant responsables envers la profession et la société. De plus, les médecins contribuent à l'autoréglementation de la profession et voient au maintien de leur santé.)



Battat et al. 2024

Therapy	MoA	Disease	Maintenance Dosing	Route
Infliximab	TNF	CD, UC	Q1-8W	IV/SC
Adalimumab	TNF	CD, UC	Q1-2W	IV/SC
Vedolizumab	$\alpha_4\beta_7$	CD, UC	Q2-8W	IV/SC
Ustekinumab	IL-12/23	CD, UC	Q8-12W	SC
Risankizumab	IL-23	CD, UC	Q8W	SC
Guselkumab			Q4W	
Mirikizumab			Q4W	
Upadacitinib	JAK-1	CD, UC	QD	PO
Ozanimod/Etrasimod	S1PRM	UC	QD	PO

Efficacy-CD

Therapy	MoA	NOC Date	Standard Maintenance Dosing
Infliximab	TNF	2004	Q8W
Upadacitinib	JAK-1	2023	QD
Guselkumab/ Risankizumab/ Mirikizumab	IL-23	2022	Q8W
Ustekinumab	IL-12/23	2016	Q8W
Adalimumab	TNF	2007	EOW
Vedolizumab	$\alpha_4\beta_7$	2016	Q8W

Efficacy-UC

Therapy	MoA	NOC Date	Standard Maintenance Dosing
Infliximab	TNF	2004	Q8W
Upadacitinib	JAK-1	2023	QD
Guselkumab	IL-12/23	2025	Q4W, Q8W
Vedolizumab	$\alpha_4\beta_7$	2016	Q8W
Ustekinumab, Risankizumab, Mirikizumab	IL-12/23	2016 2024	Q8W
Etrasimod	S1P	2023	QD
Adalimumab	TNF	2007	EOW

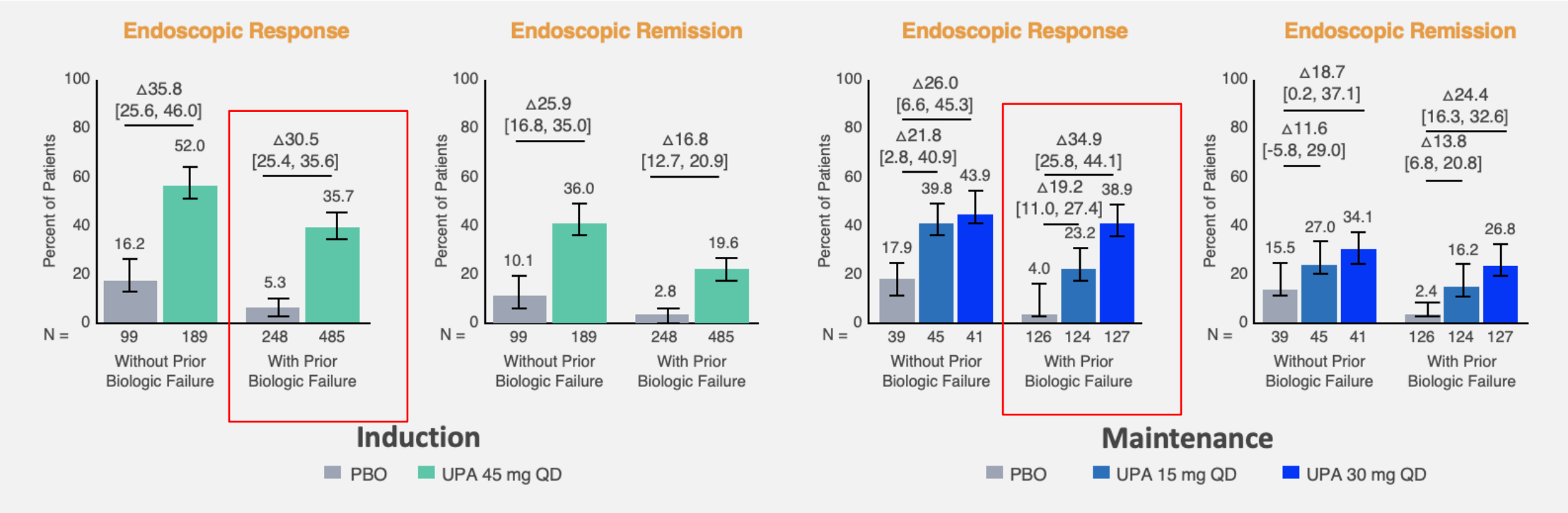
Factors for Efficacy

Effect size- delta between drug and placebo

Patient population

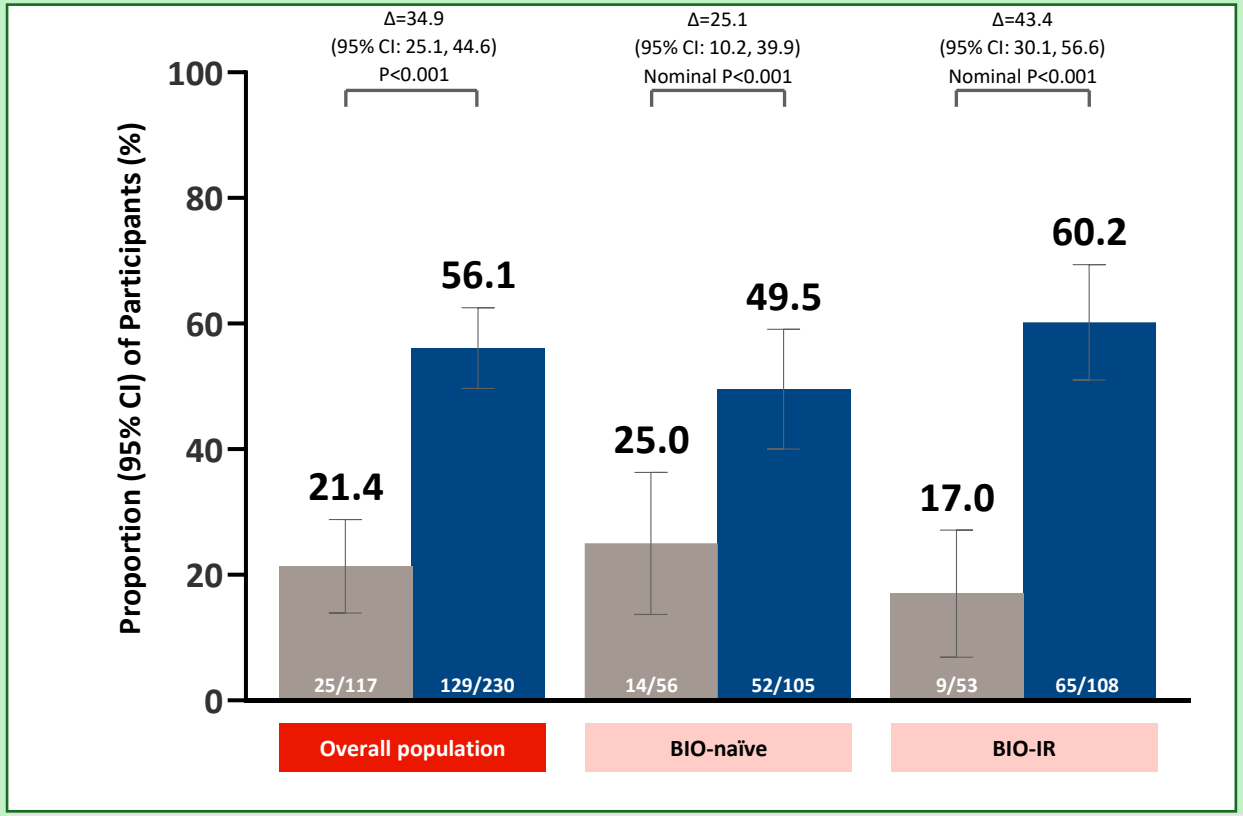
- bio-exposure status
- baseline severity
- Other characteristics (fistulae, strictures)
- Disease Duration

Upadacitinib CD



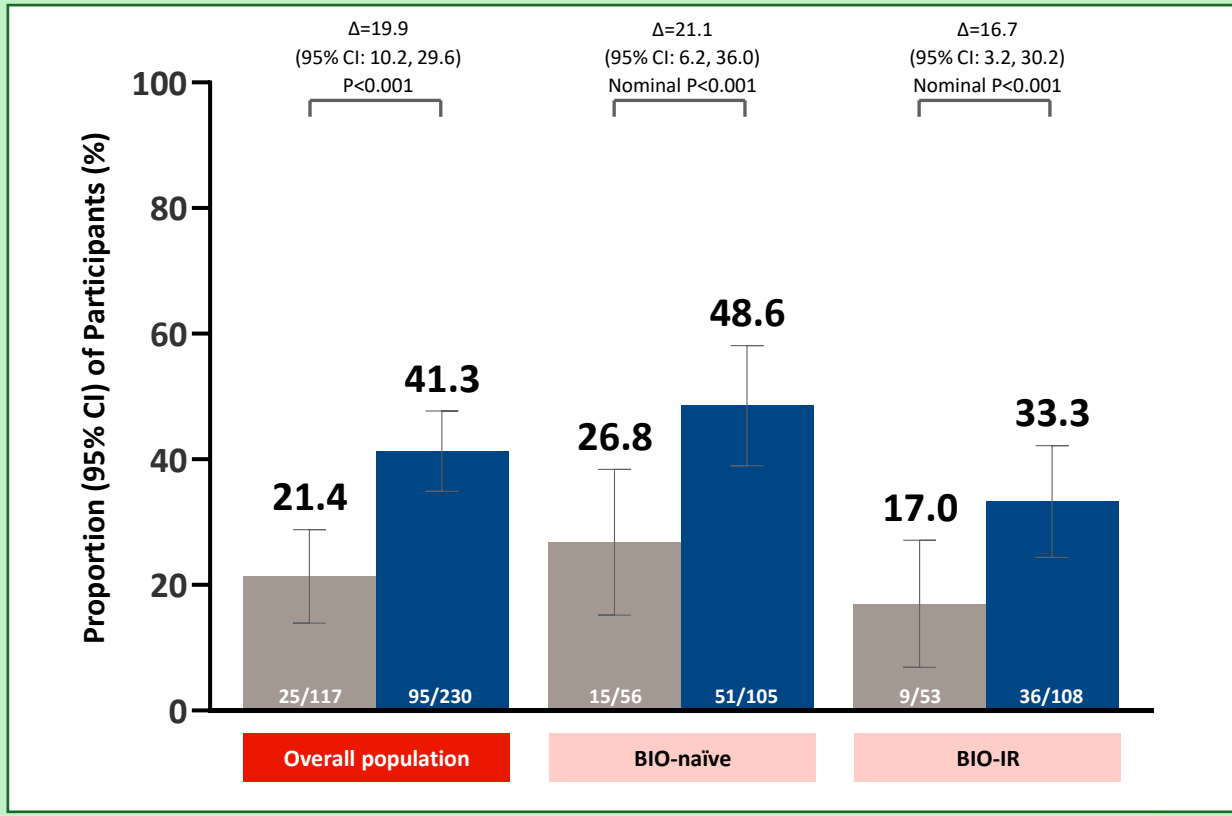
J Crohns Colitis 2023
Loftus et al., NEJM 2023

Clinical Remission at Week 12



Clinical remission: CDAI score <150

Endoscopic Response at Week 12



Endoscopic response: ≥50% improvement from baseline in SES-CD score

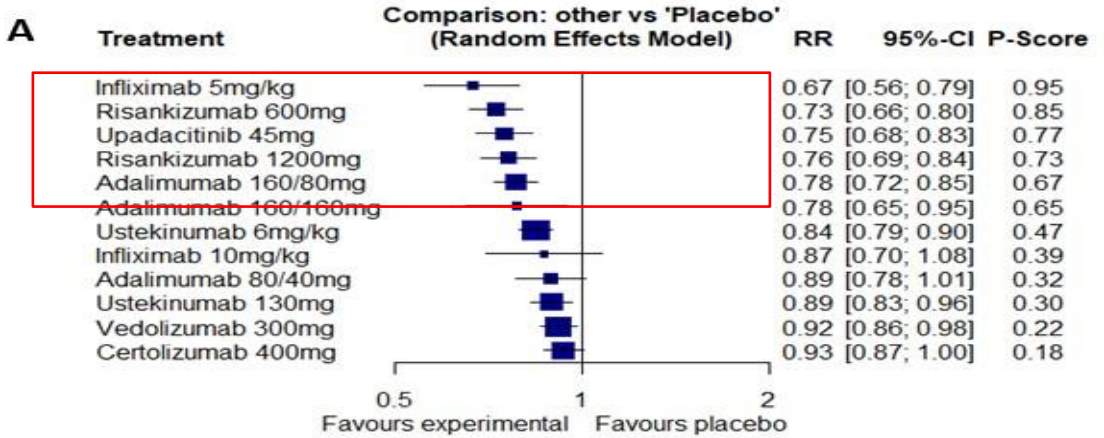
Placebo SC **GUS 400 mg SC q4w**

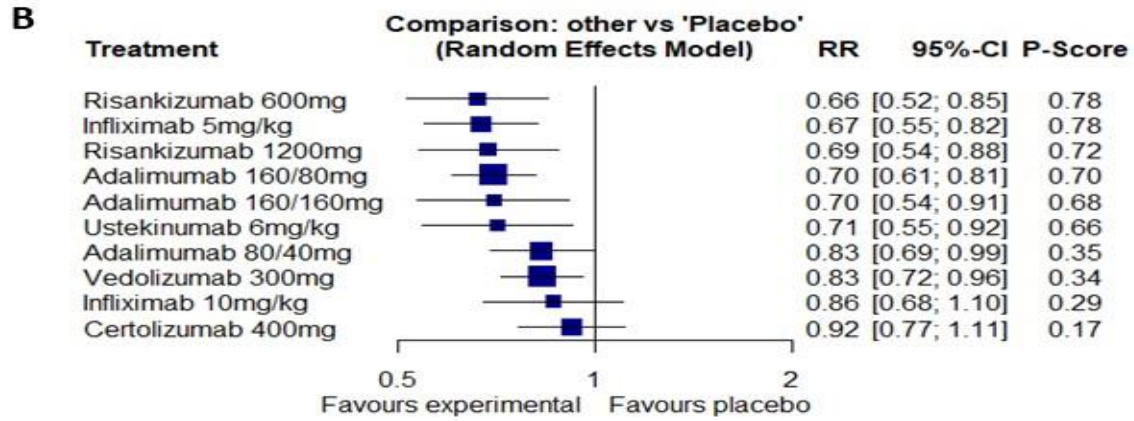
BIO-IR= history of inadequate response or intolerance to previous biologic therapy.

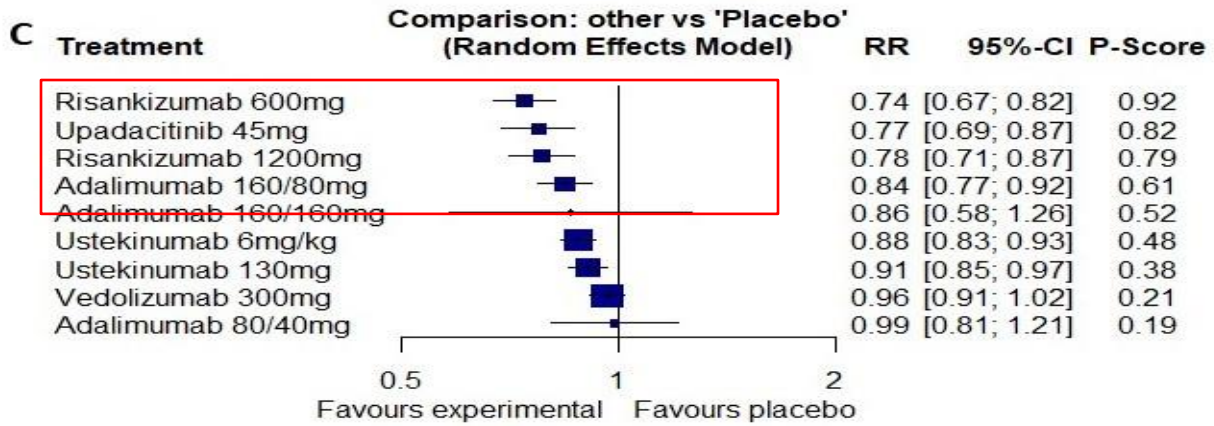
Note: Clinical remission at Week 12 was **multiplicity-controlled** for the overall population, not the BIO-naïve and BIO-IR subpopulations.

Hart, et al. Gastroenterology (2025)

Network Meta-Analyses
Induction of Remission in Crohn's disease





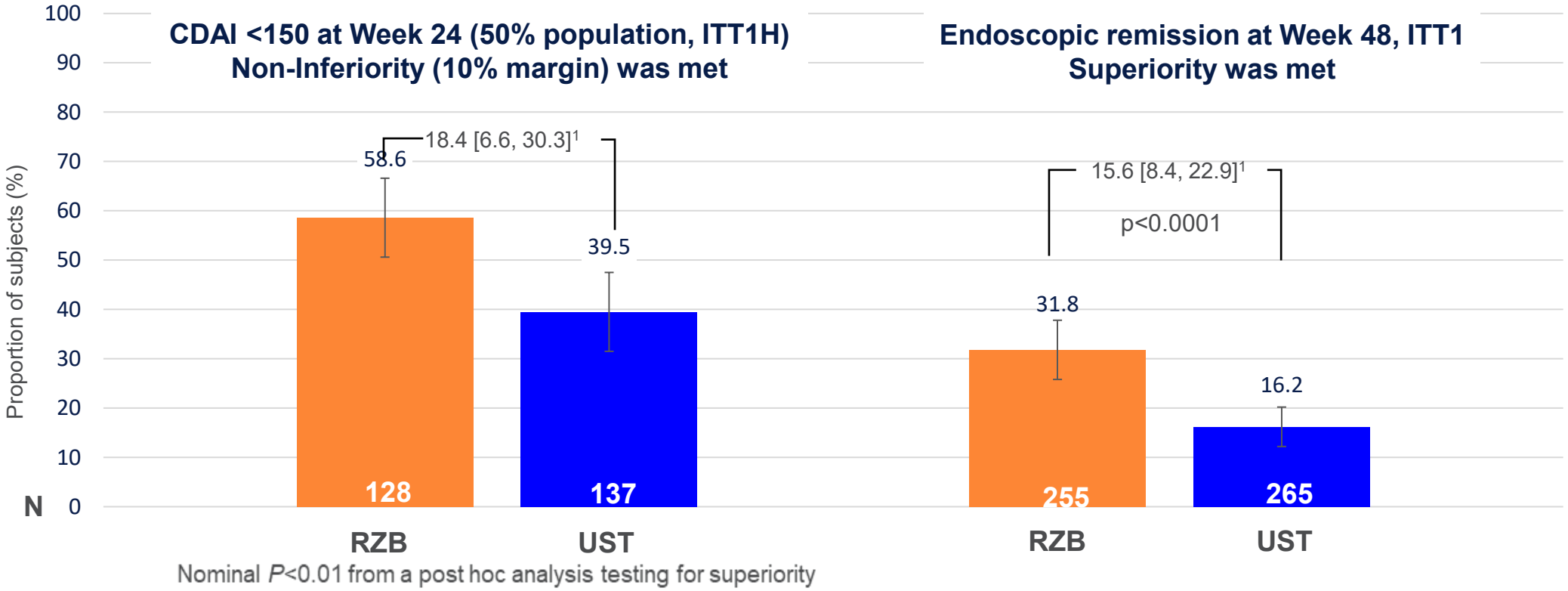


A=All patients
B=Bio-naive
C=Bio-exposed

Barberio et al. GUT 2023

Head to Head

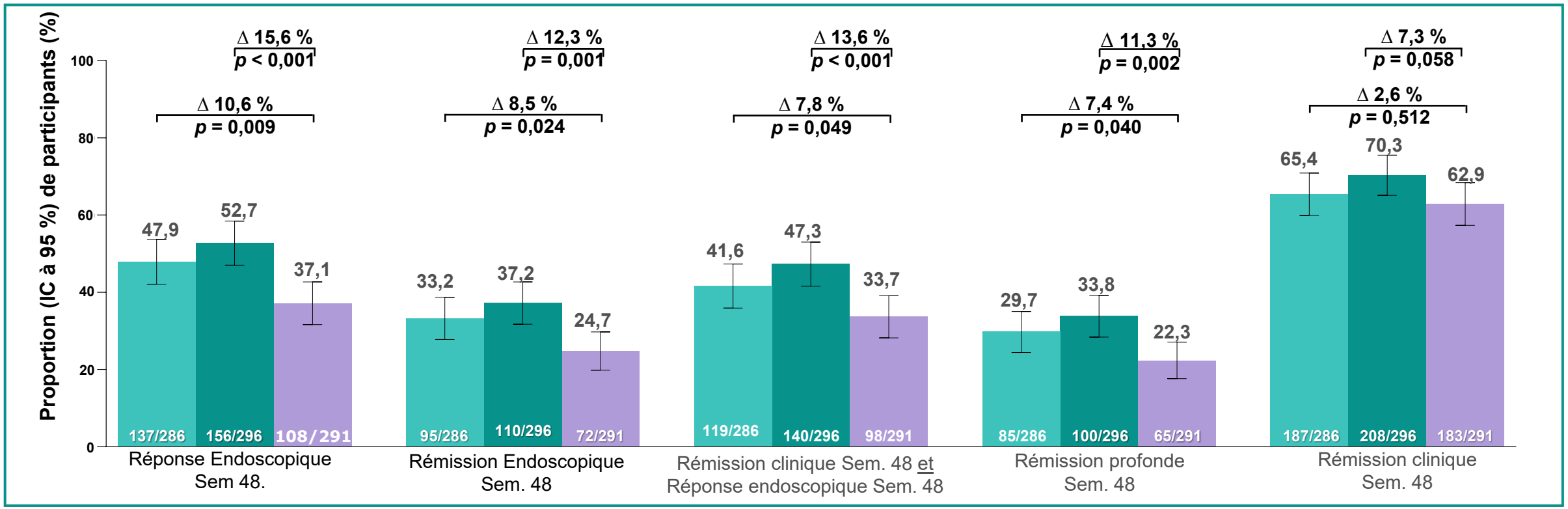
Crohn’s disease: Risankizumab vs. Ustekinumab



Error bars: 95% CI. Endoscopic remission: SES-CD ≤4 and at least a 2-point reduction versus baseline and no subscore >1 in any individual variable, as scored by a central reviewer. ITT1: includes subjects who were randomized to the UST or the selected RZB dose regimen group (RZB 600 mg IV followed by RZB 360 mg SC) and received at least one dose of study drugs during Part 1 of the study. ITT1H: The ITT1H population is a subset of the ITT1 population (approximately 50%) who reached Week 24 and is the population for the primary efficacy endpoint of clinical remission (CDAI <150) at Week 24. [1]Stratum-adjusted treatment difference (%) [95% CI] RZT–US .

Guselkumab *vs* Ustekinumab : Efficacité à la semaine 48

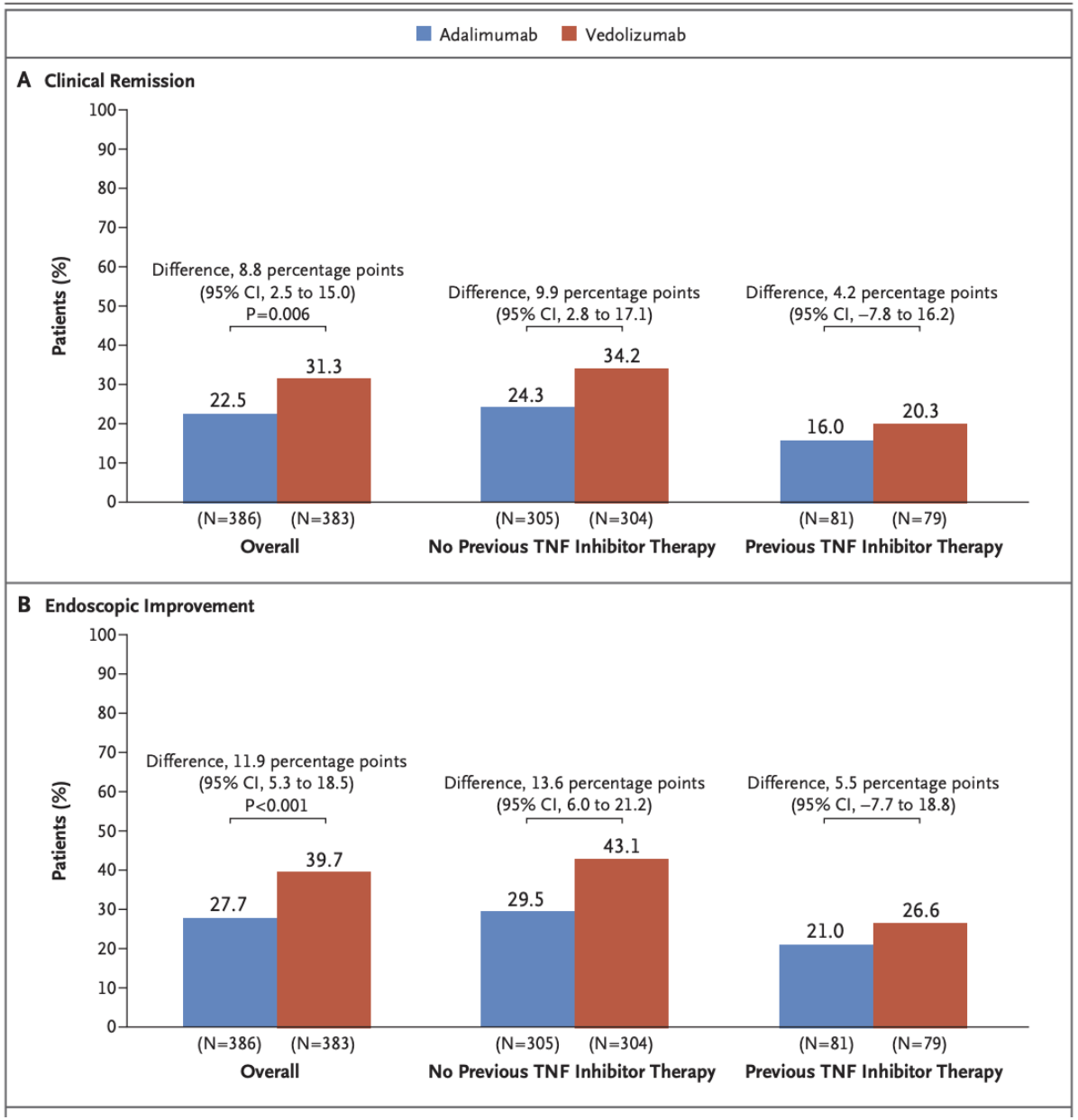
GALAXI 2 et 3 regroupées : Critères d'évaluation secondaires prédéfinis



Réponse endoscopique : amélioration ≥ 50 % par rapport au score SES-CD de départ ou score SES-CD ≤ 2
Rémission endoscopique : Score SES-CD ≤ 4 et réduction ≥ 2 points par rapport au début de l'étude; aucun sous-score > 1 associé à une quelconque variable individuelle.
Rémission clinique : indice CDAI < 150; rémission profonde : Rémission clinique et rémission endoscopique

Panaccione R, *et al.* Late breaking abstract (présentation). 18 au 21 mai, Digestive Disease Week® 2024, Washington(DC)

Head to Head- UC



Safety

Therapy
Vedolizumab
Ustekinumab
IL23i
Etrasimod
TNF-Antagonist
Upadacitinib

Green=Positive
Light Green= weak positive(i.e. observational or short term) data
Blue: Lack of Data
Orange = negative

Extra Intestinal Manifestations

Therapy
Infliximab
Adalimumab
Upadacitinib
Ustekinumab
IL23i
Vedolizumab

Green=Positive
Light Green= weak positive(i.e. observational or short term) data
Blue: Lack of Data
Orange = negative

Rheumatoid Arthritis, Ankylosing Spondylitis, Hidradenitis suppurativa

Therapy
Infliximab
Adalimumab
Upadacitinib
Ustekinumab
IL23i
Vedolizumab

Green=Positive
Light Green= weak positive(i.e. observational or short term) data
Blue: Lack of Data
Orange = negative

Psoriasis, Psoriatic Arthritis

Therapy
Infliximab
Adalimumab
Upadacitinib
Ustekinumab
IL23is
Vedolizumab

Green=Positive
Light Green= weak positive(i.e. observational or short term) data
Blue: Lack of Data
Orange = negative

Fistulae

Therapy
Infliximab
Upadacitinib
Adalimumab
Ustekinumab
Risankizumab
Vedolizumab

Green=Positive
Light Green= weak positive(i.e. observational or short term) data
Blue: Lack of Data
Orange = negative

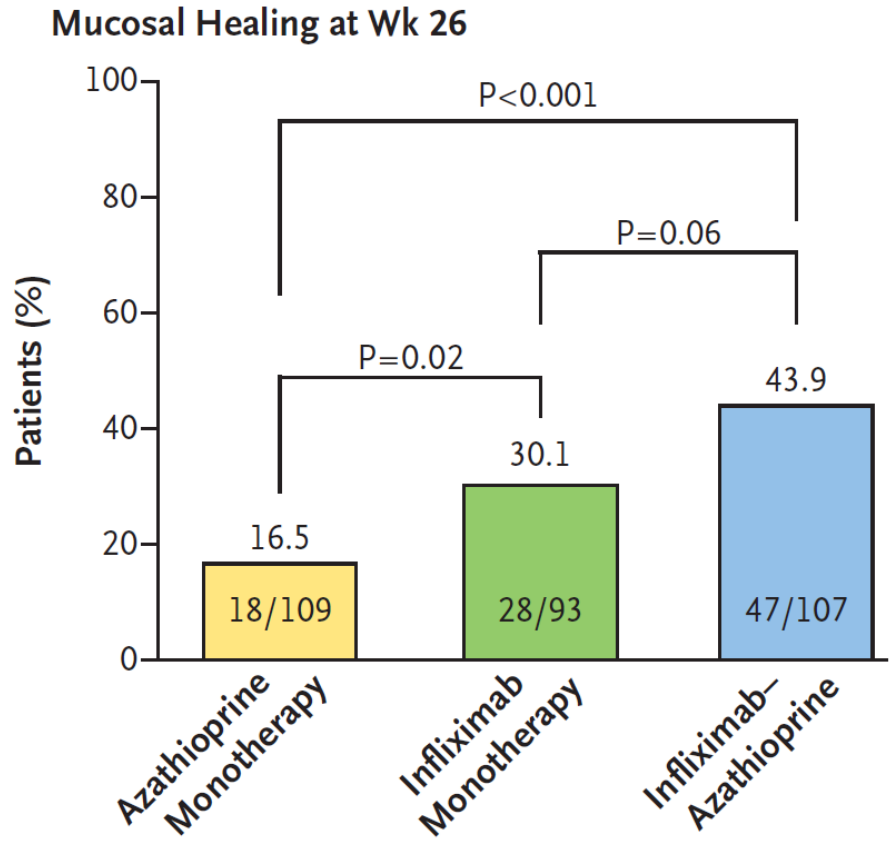
Pregnancy

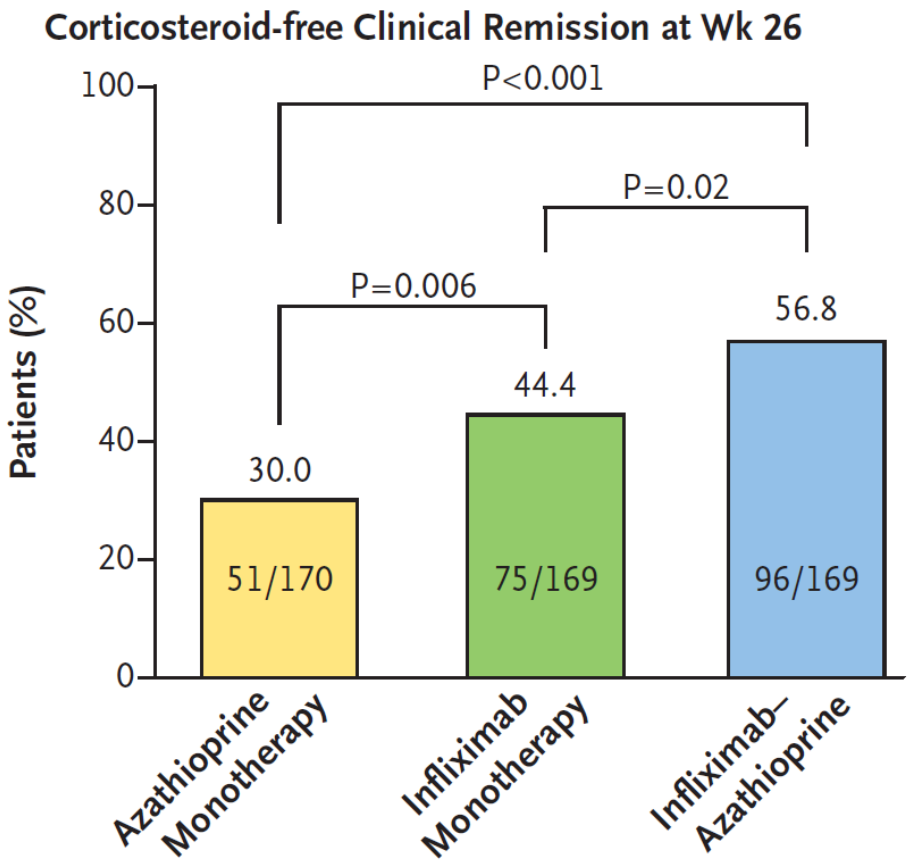
Therapy
Infliximab
Adalimumab
Vedolizumab
Ustekinumab
Risankizumab
Upadacitinib
Etrasimod

Green=Positive
Light Green= weak positive(i.e. observational or short term) data
Blue: Lack of Data
Orange = negative

Combined Advanced Targeted Therapy (CATT)

Combination Therapy in Crohn's - SONIC





Colombel J. et al. Infliximab, Azathioprine, or Combination Therapy for Crohn's Disease. NEJM. 2010

Problèmes d'innocuité avec les thiopurines ?

Lymphoma

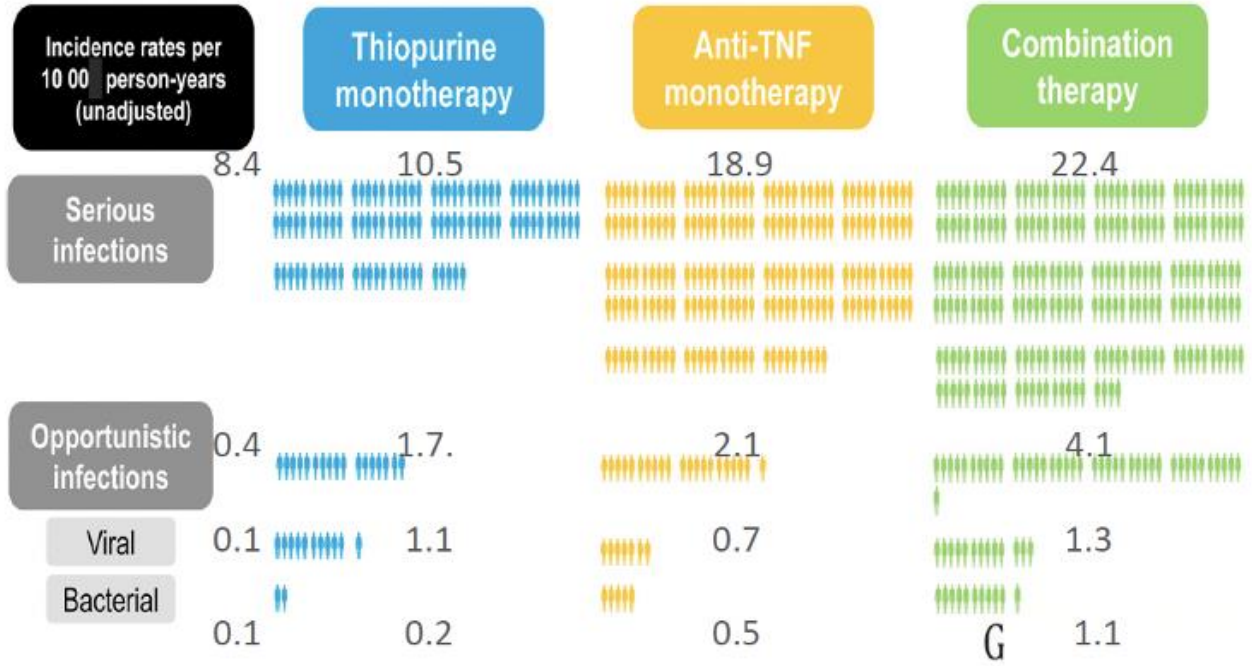
Incidence Rates per 1000 p/yrs

Unexposed 0.26

Thiopurine 0.54

Anti-TNF 0.41

Combined 0.95



De Boer. et al. JCC. 2018
Lemaitre M. et al. JAMA. 2017
Kirchgesner J. et al. Gastro. 2018

2 Agents Biologiques Ensemble

AP&T Alimentary Pharmacology & Therapeutics WILEY

Efficacy and safety of simultaneous treatment with two biologic medications in refractory Crohn's disease

Edward Yang[1] | Nicola Panaccione[2] | Natalie Whitmire[1] | Parambir S. Dulai[1] | Niels Vande Casteele[1] | Siddharth Singh[1] | Brigid S. Boland[1] | Angelina Collins[1] | William J. Sandborn[1] | Remo Panaccione[3] | Robert Battat[1,4]

ORIGINAL ARTICLE

Journal of Digestive Diseases WILEY

The use of combination biological or small molecule therapy in inflammatory bowel disease: A retrospective cohort study

Kerri Glassner[1] | Ayah Oglat[2] | Antonio Duran[3] | Pramoda Koduru[4] | Caroline Perry[1] | Amanda Wilhite[1] | Bincy P. Abraham[1]

Short Report

JCC JOURNAL of CROHN'S and COLITIS

Dual Targeted Therapy: A Possible Option for the Management of Refractory Inflammatory Bowel Disease

Giuseppe Privitera,[a,*] Sara Onali,[b] Daniela Pugliese,[b] Sara Renna,[c] Edoardo Savarino,[d] Anna Viola,[e] Davide Giuseppe Ribaldone,[f] Andrea Buda,[g] Cristina Bezzio,[h] Gionata Fiorino,[i,*] Massimo Claudio Fantini,[j] Franco Scaldaferri,[b] Luisa Guidi,[a,b] Silvio Danese,[i] Antonio Gasbarrini,[a,b] Ambrogio Orlando,[c] Alessandro Armuzzi[a,b]

ORIGINAL ARTICLE

ueg journal WILEY

Safety and efficacy of combining biologics or small molecules for inflammatory bowel disease or immune-mediated inflammatory diseases: A European retrospective observational study

Laurent Goessens[1] | Jean-Frédéric Colombel[2] | An Outtier[3] | Marc Ferrante[3] | Joao Sabino[3] | Ciaran Judge[4] | Reza Saeidi[5] | Louise Rabbitt[6] | Alessandro Armuzzi[7] | Eugeni Domenech[8] | George Michalopoulos[9] | Anneline Cremer[10] | Francisco Javier García-Alonso[11] | Tamas Molnar[12] | Konstantinos Karmiris[13] | Krisztina Gecse[14] | Joep Van Oostrom[14] | Mark Löwenberg[14] | Klaudia Farkas[12] | Raja Atreya[15] | Davide Giuseppe Ribaldone[16] | Christian Selinger[17] | Frank Hoentjen[18] | Benoit Bihin[19] | Shaji Sebastian[20] | European COMBIO study group | Jean-François Rahier[1]

)20;

Combination Biologic Therapy in Inflammatory Bowel Disease: Experience from a Tertiary Care Center

Lukasz Kwapisz, Laura E. Raffals, David H. Bruining, Darrell S. Pardi, William J. Tremaine, Sunanda V. Kane, Konstantinos A. Papadakis, Nayantara Coelho-Prabhu, John B. Kisiel, Valerie Heron, William A. Faubion, and Edward V. Loftus Jr.

Dual Biologic and Small Molecule Therapy for the Treatment of Refractory Pediatric Inflammatory Bowel Disease

Michael T. Dolinger, MD, MBA, Elizabeth A. Spencer, MD, Joanne Lai, MD, David Dunkin, MD, and Marla C. Dubinsky, MD

Study	Year	UC or CD	# of patient	Combination (*n* exposed)	Results	Safety
Sands *et al.* [25]	2007	CD	79	Infliximab + natalizumab ($n=52$) vs. Infliximab + placebo ($n=27$)	Higher decrease in mean CDAI score in IFX + natalizumab group (38 points) compared to IFX+ placebo (3.5 points), but not significant ($P=0.085$).	Similar incidence of AEs among treatment and placebo
VEGA trial Feagan *et al.* [20▪]	2023	UC	214	Guselkumab + golimumab ($n=71$) vs. golimumab monotherapy ($n=72$) vs. guselkumab monotherapy ($n=71$)	At week 12, 83% of combination therapy group had achieved clinical response vs. 61% golimumab group vs. 75% guselkumab monotherapy group. At week 12, 18% had achieve endoscopic remissionin the combination therapy group vs. 10% in golimumab group vs. 8% in guselkumab group	Similar incidence of AEs among the 3 groups. Safety was analyzed up to week 50.
Explorer trial Colombel *et al.* [10▪]	2024	CD	55	Vedolizumab + adalimumab + methotrexate	Endoscopic remission at week 26 was 34.5% Clinical remsision at week 26 was 54.5% Post hoc Bayesian analysis showed higher rates of remission than monotherapy.	Similar incidence of AEs between triple therapy and monotherapy
Duet-CD	Ongoing phase 2b RCTs. Primary completion estimated: 2025-05-07	CD	715	Guselkumab + golimumab vs. golimumab vs. guselkumab At 3 differents doses	Not published yet	Not published yet
Duet-UC		UC	550		Not published yet	Not published yet
Ahmed *et al.* [15]	2022	UC and CD	279	Various combinations (e.g., TNF-α antagonists + antiintegrins, ustekinumab + antiintegrins)	Clinical remission at 6 months in 59%; endoscopic improvement in 34%. Observed in refractory patients.	Adverse events: 31%; Serious adverse events: 6.5%
Glassner *et al.* [26]	2020	CD, UC	50	Various combinations of biologics	Higher rates of clinical and endoscopic remission observed in combination therapy.	Increased risk of serious AEs compared to monotherapy.
Yang *et al.* [27]	2020	CD	22	Anti-TNF+ vedolizumab or ustekinumab (n=14) Ustekinumab + vedolizumab (n=8)	Clinical response in 50%, endoscopic response in 43%, remission in 26% after 1 year.	Similar rates of serious AEs between combination and monotherapy.
Privitera *et al.* [28]	2020	CD, UC	16	Vedolizumab + anti-TNF or ustekinumab	Improvement in intestinal and extraintestinal symptoms in the majority of patients.	No significant increase in serious AEs reported.

David A…Battat R Curr Opin Gastroenterol. 2025

Clinical Gastroenterology and Hepatology 2021;

Dual Biologic or Small Molecule Therapy for Treatment of Inflammatory Bowel Disease: A Systematic Review and Meta-analysis

Waseem Ahmed, MD,[*] Jonathan Galati, MD,[‡] Anand Kumar, MD,[*,§] Paul J. Christos, DrPH, MS,[||] Randy Longman, MD, PhD,[*] Dana J. Lukin, MD, PhD,[*] Ellen Scherl, MD,[*] and Robert Battat, MD[*]

Primary Outcomes

Outcome	Pooled rate	95% CI	Reported patients or combinations all studies
Primary outcomes[a]			
Number adverse events	115		
Adverse of events	31%	0.13–0.54	281
Clinical remission	59%	0.42–0.74	211
Endoscopic remission	34%	0.23–0.46	87

Ahmed W. et al. CGH. 2021

Secondary Outcomes

Outcome	Pooled rate	95% CI	Reported patients or combinations all studies
Secondary outcomes[a]			
Number of serious adverse events	21		
Serious adverse events	7%	0.02–0.13	281
Number of infections	62		
Infections	20%	0.13–0.27	281
Malignancy	2%	0.003–0.04	279
Clinical response	69%	0.52–0.84	138
Endoscopic response	43%	0.27–0.60	48
Steroid-free remission	46%	0.31–0.61	128
Need for surgery	12%	0.04–0.24	237
EIM response	50%	0.14–0.86	61

Ahmed W. et al. Dual Biologic or Small Molecule Therapy for Treatment of Inflammatory of Bowel Disease: A Systematic Review and Meta Analysis. CGH. 2021

Dual Therapy Characteristics

Characteristic	Data	Reported patients or combinations
Duration of treatment, wk	24 (13–32)	231
Previous biologics, wk	2 (2–4)	160
Corticosteroids at baseline	43%	88/204
Immunomodulator at baseline	44%	75/172
Previous exposure to therapy	61%	62/101
Indication for therapy		
Medically refractory intestinal disease	81%	225/279
EIM	12%	34/279
Both	5%	14/279
Other	2%	6/279

Dual therapy		
Anti-TNF and anti-integrin	48%	138/288
Anti-TNF and ustekinumab	7%	20/288
Anti-TNF and tofacitinib	3%	10/288
Vedolizumab and ustekinumab	19%	54/288
Vedolizumab and tofacitinib	11%	32/288
Ustekinumab and tofacitinib	6%	16/288
Anti-TNF and other	3%	8/288
Vedolizumab and other	3%	8/288
Ustekinumab and other	1%	2/288

Ahmed W. et al. Dual Biologic or Small Molecule Therapy for Treatment of Inflammatory of Bowel Disease: A Systematic Review and Meta Analysis. CGH. 2021

- “Adverse events occurred in three trials (13%)
- One trial ended due to drug-induced lupus attributed to adalimumab.
- One patient developed pneumonia
- another had reported basal cell skin cancer, recurrent Clostridium Difficile infection and Acinetobacter bacteremia in a patient with a recurrent history of all three diseases prior to initiation of DBT”

Yang et al. AP&T 2020

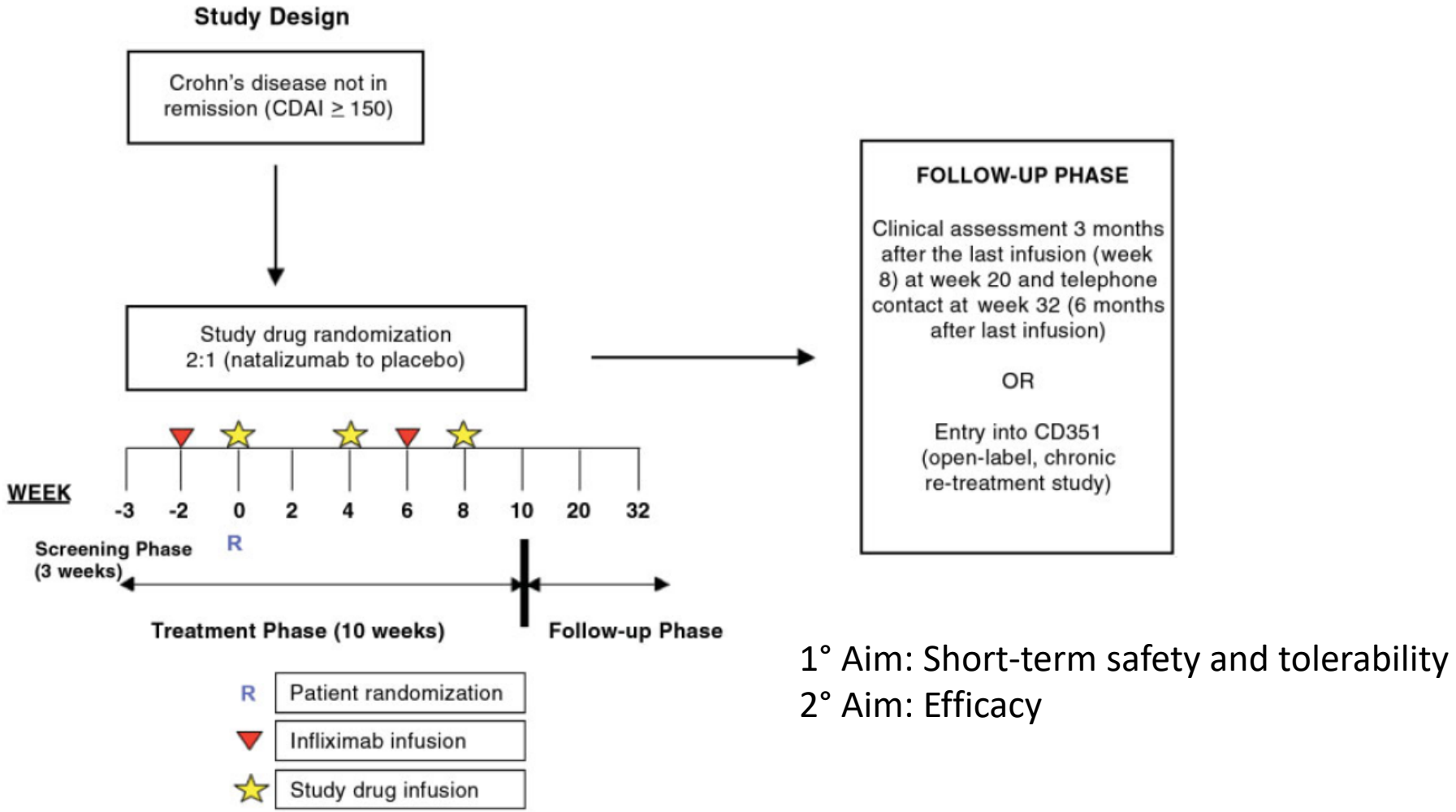
Serious Adverse Events

Dual therapy	Serious adverse event
Vedolizumab and ustekinumab	Bacterial enteric infection, abdominal wall abscess (n = 2), Pelvic abscess (n = 2), PICC line infection, PICC line infection and perianal abscess
Vedolizumab and golimumab	Peristomal cellulitis
Vedolizumab and tofacitinib	Deep vein thrombosis
Natalizumab and infliximab	Intestinal obstruction

Ahmed W. et al. Dual Biologic or Small Molecule Therapy for Treatment of Inflammatory of Bowel Disease:
A Systematic Review and Meta Analysis. CGH. 2021

Safety and Tolerability of Concurrent Natalizumab Treatment for Patients with Crohn's Disease Not in Remission While Receiving Infliximab

Bruce E. Sands, MD, MS[*] Richard Kozarek, MD[†] Jack Spainhour, MD[‡] Charles F. Barish, MD[§]
Scott Becker, MD[|] Lawrence Goldberg, MD[¶] Seymour Katz, MD[**] Ronald Goldblum, MD[††]
Rena Harrigan, MPH[††] Deborah Hilton, MS[††] and Stephen B. Hanauer, MD[‡‡]



1° Aim: Short-term safety and tolerability
2° Aim: Efficacy

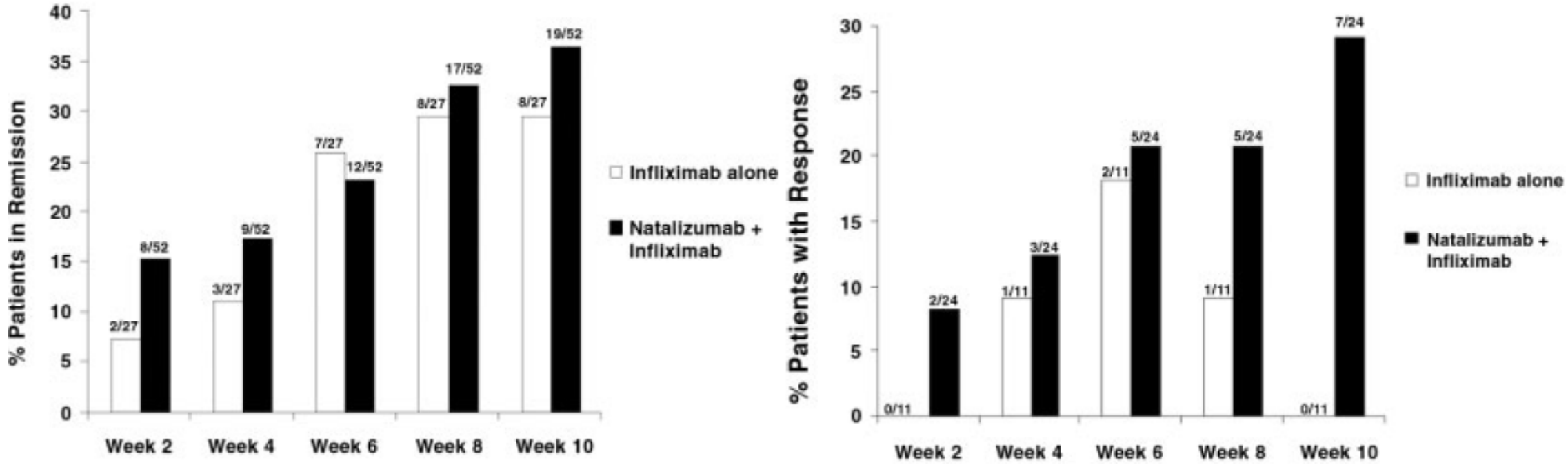
Sands B. et al. IBD. 2007

Safety

Adverse event	Placebo + infliximab (N = 27), n (%)	Natalizumab + infliximab (N = 52), n (%)
Headache	6 (22)	12 (23)
Fatigue	2 (7)	7 (13)
Exacerbation of Crohn's disease	4 (15)	5 (10)
Dizziness	1 (4)	5 (10)
Nasopharyngitis	3 (11)	5 (10)
Nausea	3 (11)	5 (10)
DNA antibody positive	3 (11)	4 (8)
Dyspepsia	1 (4)	4 (8)
Abdominal pain	0	3 (6)
Antinuclear antibody positive	1 (4)	3 (6)
Arthralgia	2 (7)	3 (6)
Back pain	2 (7)	3 (6)
Insomnia	1 (4)	3 (6)
Pyrexia	0	3 (6)
Upper respiratory tract infection	1 (4)	3 (6)

Sands B. et al. IBD. 2007

Dual Biologic RCT: Efficacy

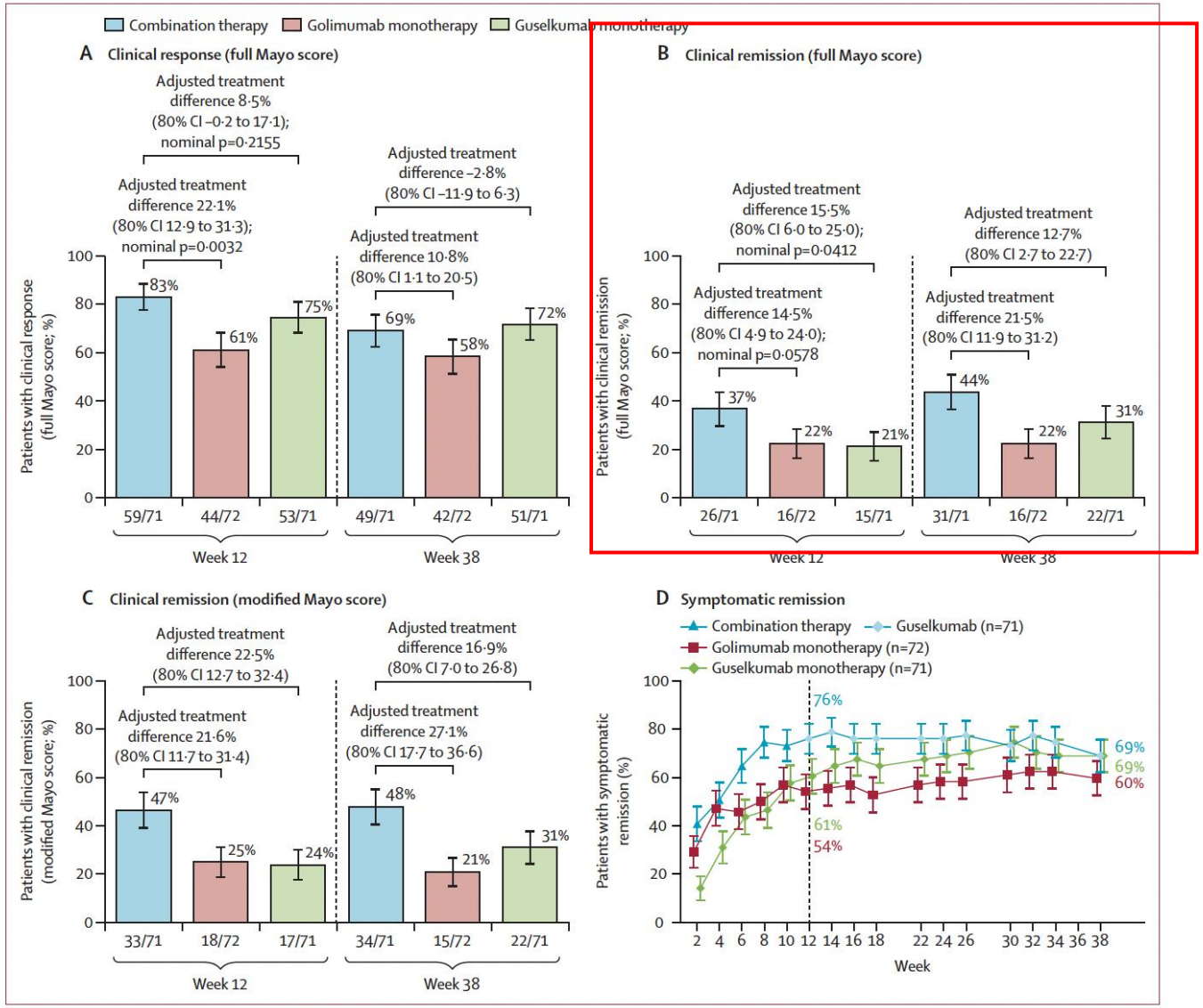


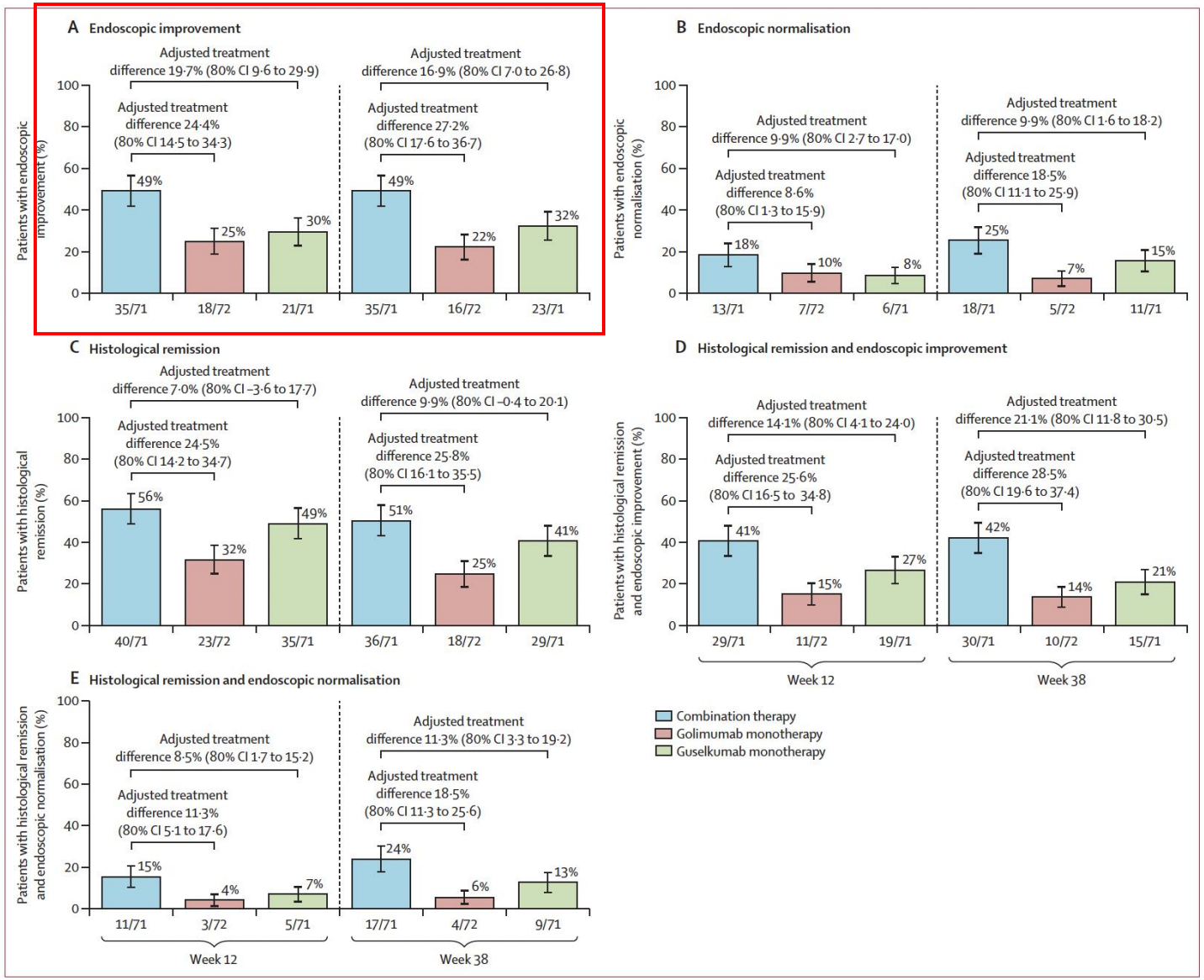
Elevated Baseline CRP

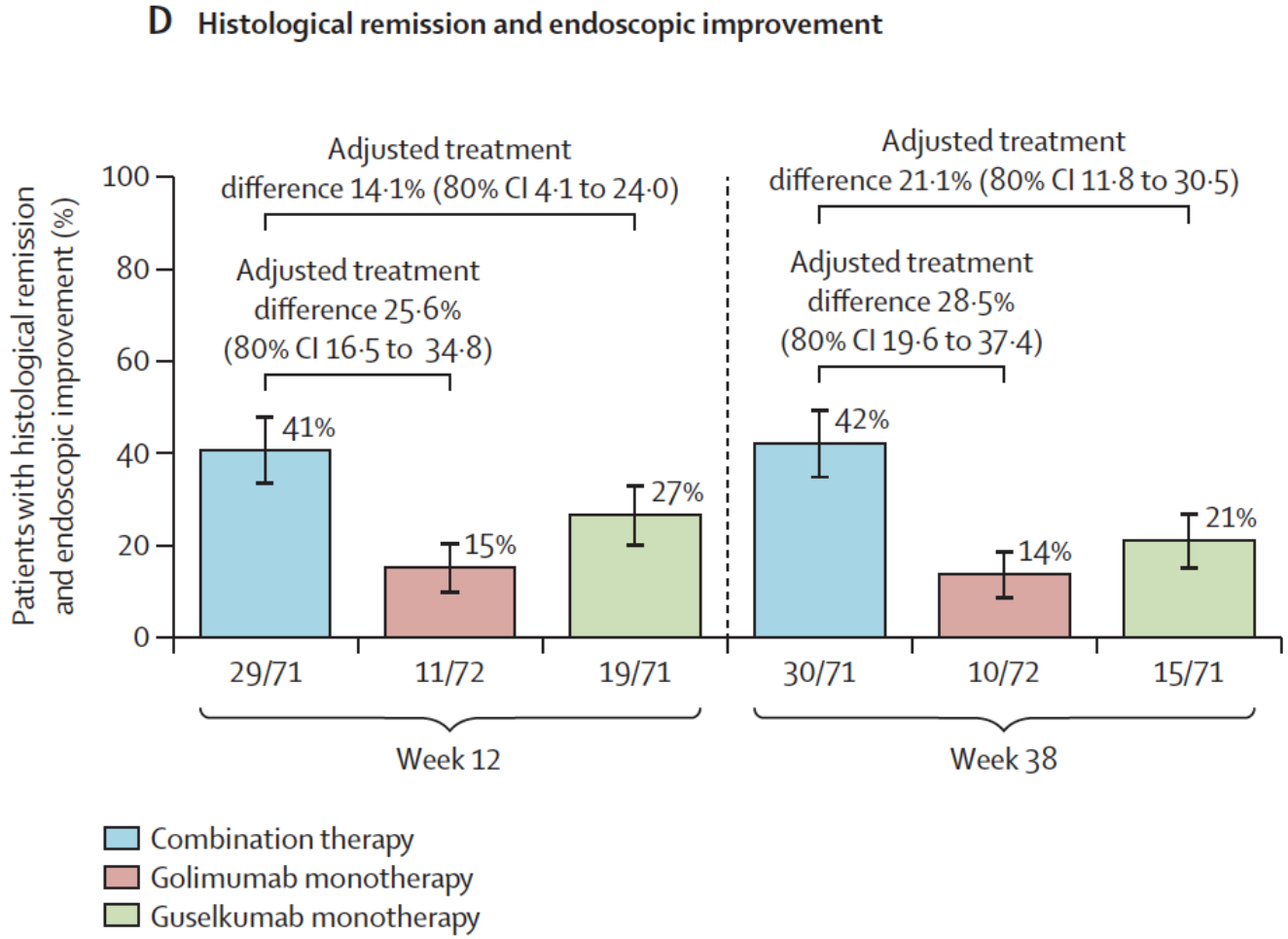
Sands B. et al. IBD. 2007

Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial

*Brian G Feagan, Bruce E Sands, William J Sandborn, Matthew Germinaro, Marion Vetter, Jie Shao, Shihong Sheng, Jewel Johanns, Julián Panés, for the VEGA Study Group**

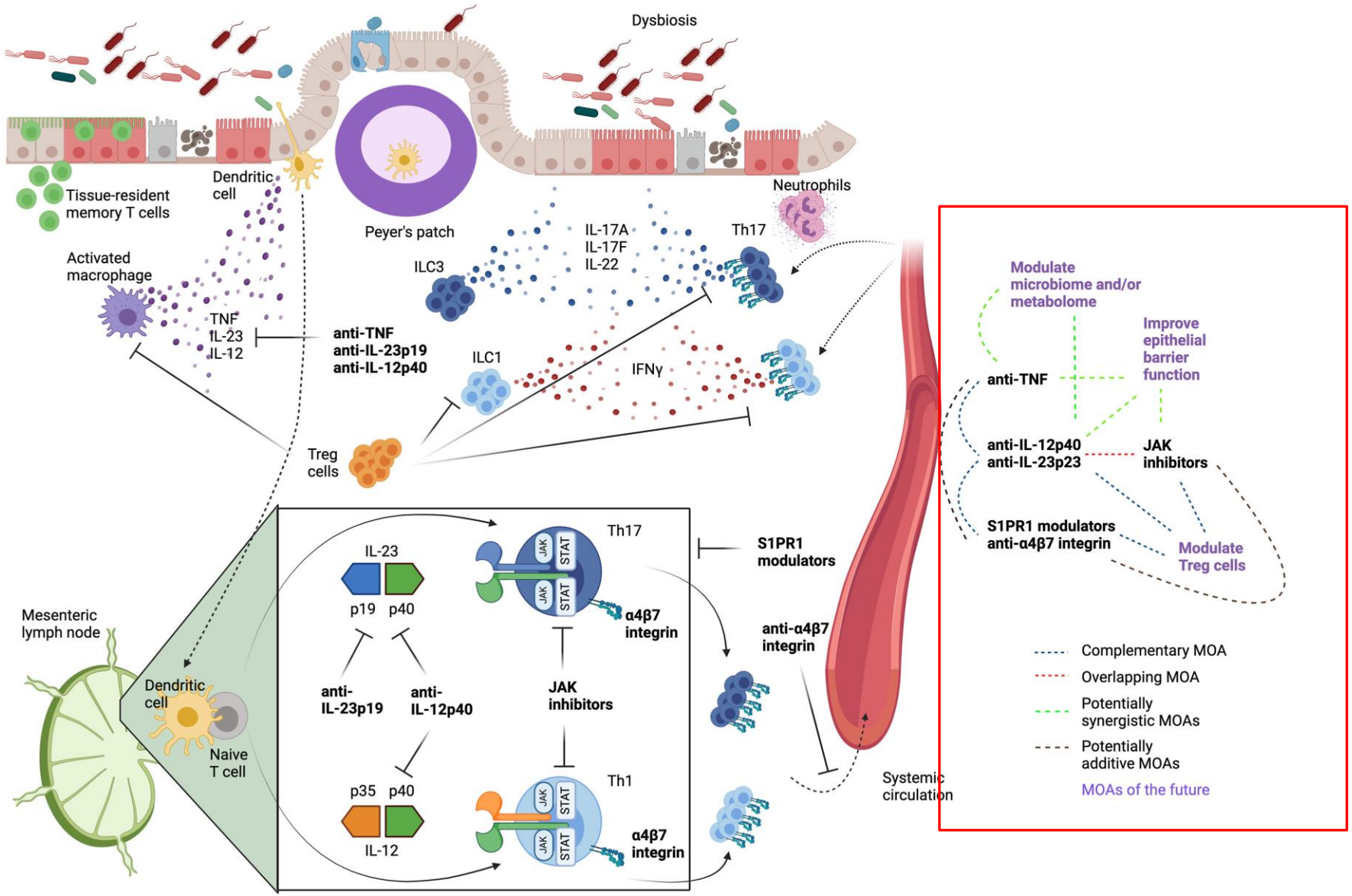

Combination therapy
Golimumab monotherapy
Guselkumab monotherapy
A Clinical response (full Mayo score)
Adjusted treatment difference 8·5% (80% CI −0·2 to 17·1); nominal p=0·2155
Adjusted treatment difference 22·1% (80% CI 12·9 to 31·3); nominal p=0·0032
Adjusted treatment difference −2·8% (80% CI −11·9 to 6·3)
Adjusted treatment difference 10·8% (80% CI 1·1 to 20·5)
Patients with clinical response (full Mayo score; %)
83%
61%
75%
69%
58%
72%
59/71
44/72
53/71
49/71
42/72
51/71
Week 12
Week 38
B Clinical remission (full Mayo score)
Adjusted treatment difference 15·5% (80% CI 6·0 to 25·0); nominal p=0·0412
Adjusted treatment difference 14·5% (80% CI 4·9 to 24·0); nominal p=0·0578
Adjusted treatment difference 12·7% (80% CI 2·7 to 22·7)
Adjusted treatment difference 21·5% (80% CI 11·9 to 31·2)
Patients with clinical remission (full Mayo score; %)
37%
22%
21%
44%
22%
31%
26/71
16/72
15/71
31/71
16/72
22/71
Week 12
Week 38
C Clinical remission (modified Mayo score)
Adjusted treatment difference 22·5% (80% CI 12·7 to 32·4)
Adjusted treatment difference 21·6% (80% CI 11·7 to 31·4)
Adjusted treatment difference 16·9% (80% CI 7·0 to 26·8)
Adjusted treatment difference 27·1% (80% CI 17·7 to 36·6)
Patients with clinical remission (modified Mayo score; %)
47%
25%
24%
48%
21%
31%
33/71
18/72
17/71
34/71
15/72
22/71
Week 12
Week 38
D Symptomatic remission
Combination therapy
Guselkumab (n=71)
Golimumab monotherapy (n=72)
Guselkumab monotherapy (n=71)
Patients with symptomatic remission (%)
76%
61%
54%
69%
69%
60%
Week


A Endoscopic improvement
Adjusted treatment difference 19·7% (80% CI 9·6 to 29·9)
Adjusted treatment difference 24·4% (80% CI 14·5 to 34·3)
Adjusted treatment difference 16·9% (80% CI 7·0 to 26·8)
Adjusted treatment difference 27·2% (80% CI 17·6 to 36·7)
Patients with endoscopic improvement (%)
49%
25%
30%
49%
22%
32%
35/71
18/72
21/71
35/71
16/72
23/71
B Endoscopic normalisation
Adjusted treatment difference 9·9% (80% CI 2·7 to 17·0)
Adjusted treatment difference 8·6% (80% CI 1·3 to 15·9)
Adjusted treatment difference 9·9% (80% CI 1·6 to 18·2)
Adjusted treatment difference 18·5% (80% CI 11·1 to 25·9)
Patients with endoscopic normalisation (%)
18%
10%
8%
25%
7%
15%
13/71
7/72
6/71
18/71
5/72
11/71
C Histological remission
Adjusted treatment difference 7·0% (80% CI −3·6 to 17·7)
Adjusted treatment difference 24·5% (80% CI 14·2 to 34·7)
Adjusted treatment difference 9·9% (80% CI −0·4 to 20·1)
Adjusted treatment difference 25·8% (80% CI 16·1 to 35·5)
Patients with histological remission (%)
56%
32%
49%
51%
25%
41%
40/71
23/72
35/71
36/71
18/72
29/71
D Histological remission and endoscopic improvement
Adjusted treatment difference 14·1% (80% CI 4·1 to 24·0)
Adjusted treatment difference 25·6% (80% CI 16·5 to 34·8)
Adjusted treatment difference 21·1% (80% CI 11·8 to 30·5)
Adjusted treatment difference 28·5% (80% CI 19·6 to 37·4)
Patients with histological remission and endoscopic improvement (%)
41%
15%
27%
42%
14%
21%
29/71
11/72
19/71
30/71
10/72
15/71
Week 12
Week 38
E Histological remission and endoscopic normalisation
Adjusted treatment difference 8·5% (80% CI 1·7 to 15·2)
Adjusted treatment difference 11·3% (80% CI 5·1 to 17·6)
Adjusted treatment difference 11·3% (80% CI 3·3 to 19·2)
Adjusted treatment difference 18·5% (80% CI 11·3 to 25·6)
Patients with histological remission and endoscopic normalisation (%)
15%
4%
7%
24%
6%
13%
11/71
3/72
5/71
17/71
4/72
9/71
Week 12
Week 38
Combination therapy
Golimumab monotherapy
Guselkumab monotherapy



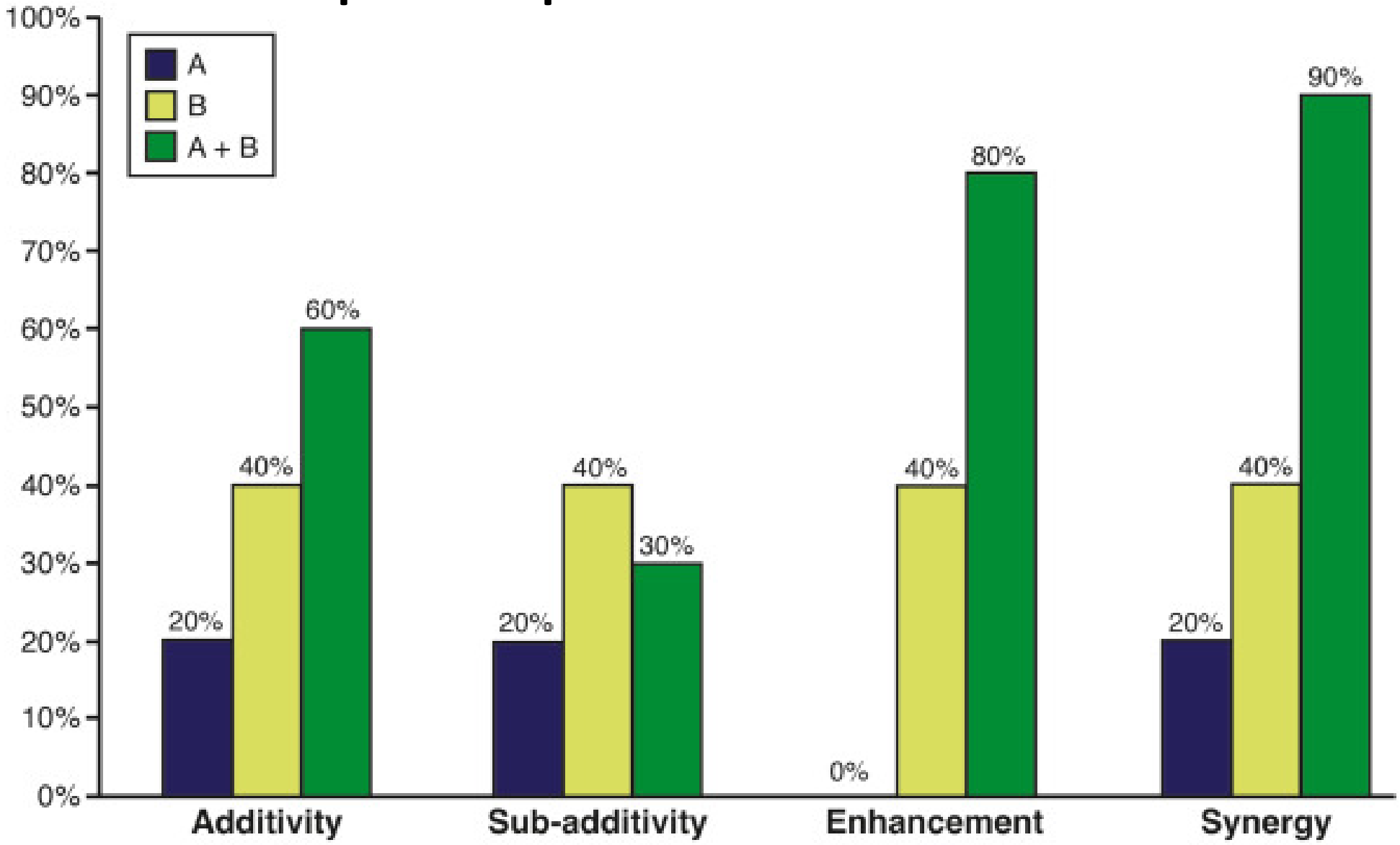
- *Feagan et al., Lancet 2023*

Sélection du traitement



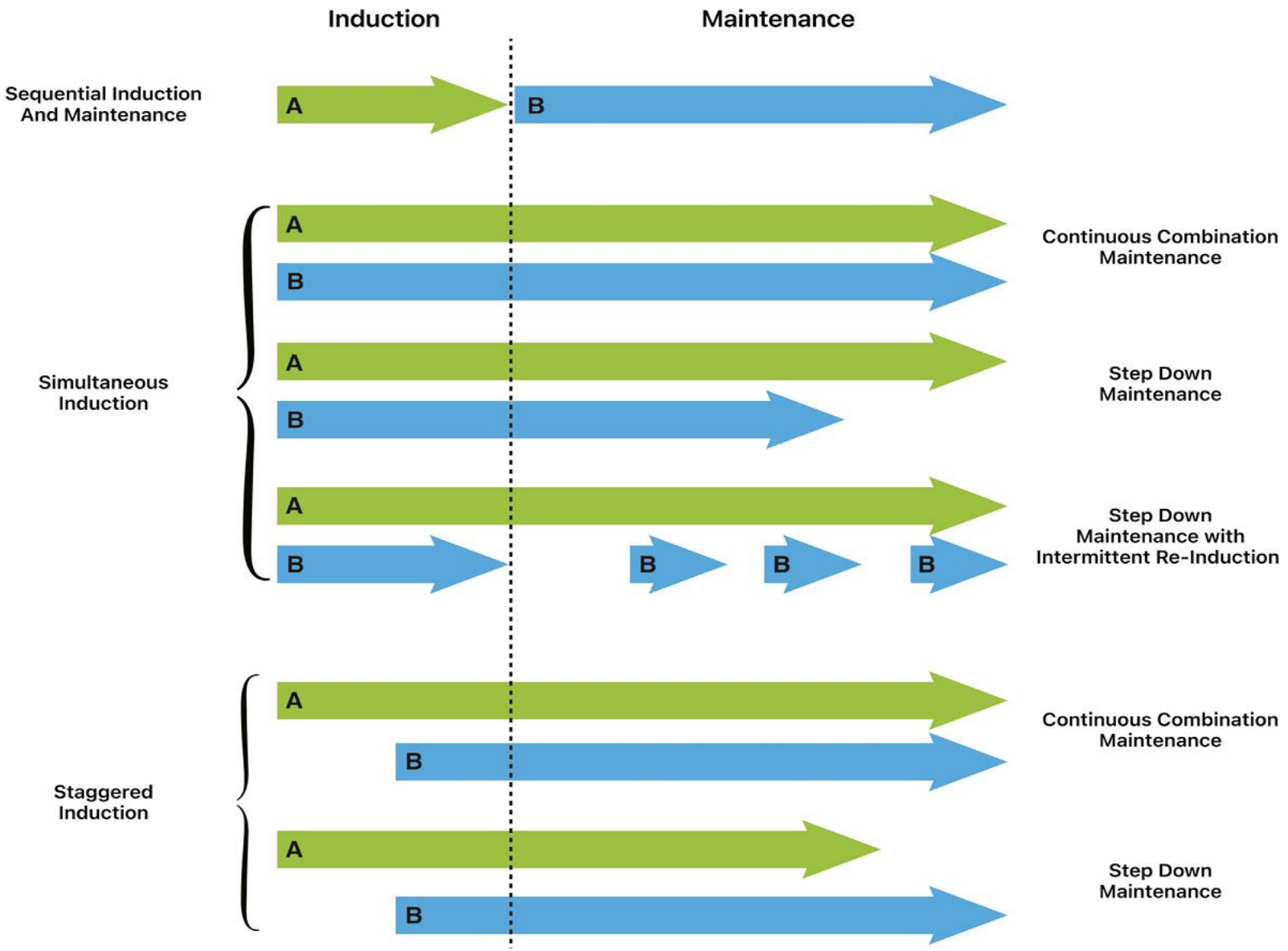
Battat et al. CGH, 2024

Buts thérapeutique

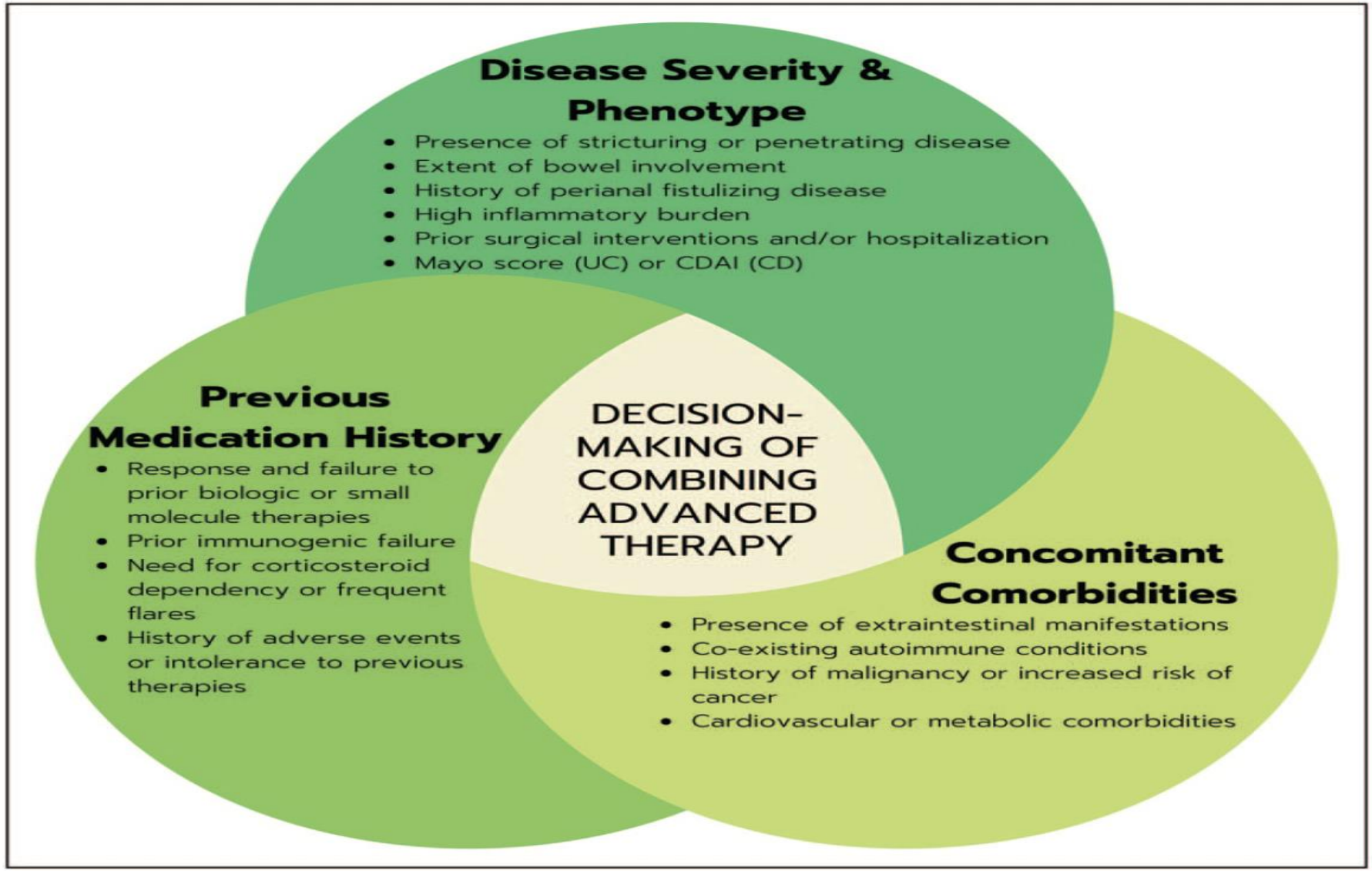


Battat et al., CGH 2024

Approche thérapeutique



Battat et al., CGH 2024



David A…Battat R Curr Opin Gastroenterol. 2025

Table 1. Special Considerations in CATT

Disease	Agent to consider for inclusion in combination				
	TNF antagonist	JAK inhibitor	Anti-integrin	IL23 or IL12/23 antagonist	S1P inhibitor
Fistulizing Crohn's disease	Yes	Possible	Possible	Possible	–
Atopic dermatitis	–	Yes	–	–	–
Hidradenitis suppurativa	Yes	–	–	–	–
Pyoderma gangrenosum	Yes	–	–	–	–
Rheumatoid arthritis	Yes	Yes	–	–	–
Psoriatic diseases	Yes	Yes	–	Yes	–
Ankylosing spondylitis	Yes	Yes	–	–	–
Uveitis	Yes	–	–	–	–
Multiple sclerosis	–	–	–	–	Yes

CATT, Combined advanced targeted therapies; IL, interleukin; JAK, Janus kinase; TNF, tumor necrosis factor.

Battat et al. 2024 CGH

Sélection du medicament

- Inclure le mécanisme d'action naïf si possible
- Si le traitement précédent est réessayé
- Raison de l'échec :
    - pK: TDM? Dose-Optimized
    - Immunogenicity
    - Mechanistic failure: PNR or 2LOR
    - Need for surgery
  - Preuve d'échec :
    - biomarkers, CTE/MRE, endoscopy

Sélection des patients

- risque élevé de développer des complications liées à la maladie
- échec d'un traitement conventionnel
- échec d'au moins 1 à 2 monothérapies biologiques ou à petites molécules.
- Qui NE PAS considérer (2025) :
  - Naïf face à une option thérapeutique raisonnable
  - Essai clinique
  - Bénéfice de la chirurgie
  - Sécurité
    - Maladies comorbides
    - Immunosuppression pour les troubles immunitaires alternatifs*Non-compliance
  - CU?

Combinations?

- TNF antagonist +
  - Vedolizumab- OUI
  - IL12/23-OUI
  - Jaki- NO
- Vedolizumab +
  - TNF antagonist-OUI
  - IL12/23-OUI
  - Jaki- OUI
- IL23, 12/23 +
  - Vedolizumab- OUI
  - TNF antagonist-OUI
  - Jaki- ?
- S1P +
  - No data
  - Vedolizumab –probable oui

Suivi

- Monitoring sur Tx
  - Suivi proche
  - qmois labo + CRP/FCAL x 3, en suite q3mo
  - 6mo endoscopie+/- CTE/MRE
  - TDM?
  - PPx:
    - Immunizations
    - Dermatologie
    - Age-appropriate & IBD specific cancer screening

De-Escalation?

- Maladie extra-intestinale?
- Corticosteroid or immunomodulateur?
- Patient preference?
- TDM pre- de-escalation?
- Avoir une stratégie de sortie et un plan pour redémarrer la bithérapie
- Si la cicatrisation de la muqueuse est obtenue à 6 mois et que le patient est d'accord :
  - Maintenir le traitement si le patient n'en a jamais reçu.
  - Effectuer un TDM en monothérapie.
  - Évaluation non invasive de l'activité de la maladie à 3 mois.
  - Évaluation endoscopique +/- enteroIRM/scan à 6 mois.

Merci

Diplôme d'études spécialisées en MICI à l'Université de Montréal

Directrice D.E.S MICI UdM: Dr Katarzyna Orlicka
katarzyna.orlicka.med@ssss.gouv.qc.ca

CHUM

Merci!