Approach to drug selection in the IBD multi-drug era

September 2021

Professor
Charlie W Lees

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THE UNIVERSITY of EDINBURGH
PREdiCCt
CHIEF SCIENTIST OFFICE
CENTRE FOR GENOMIC & EXPERIMENTAL MEDICINE

Disclosures

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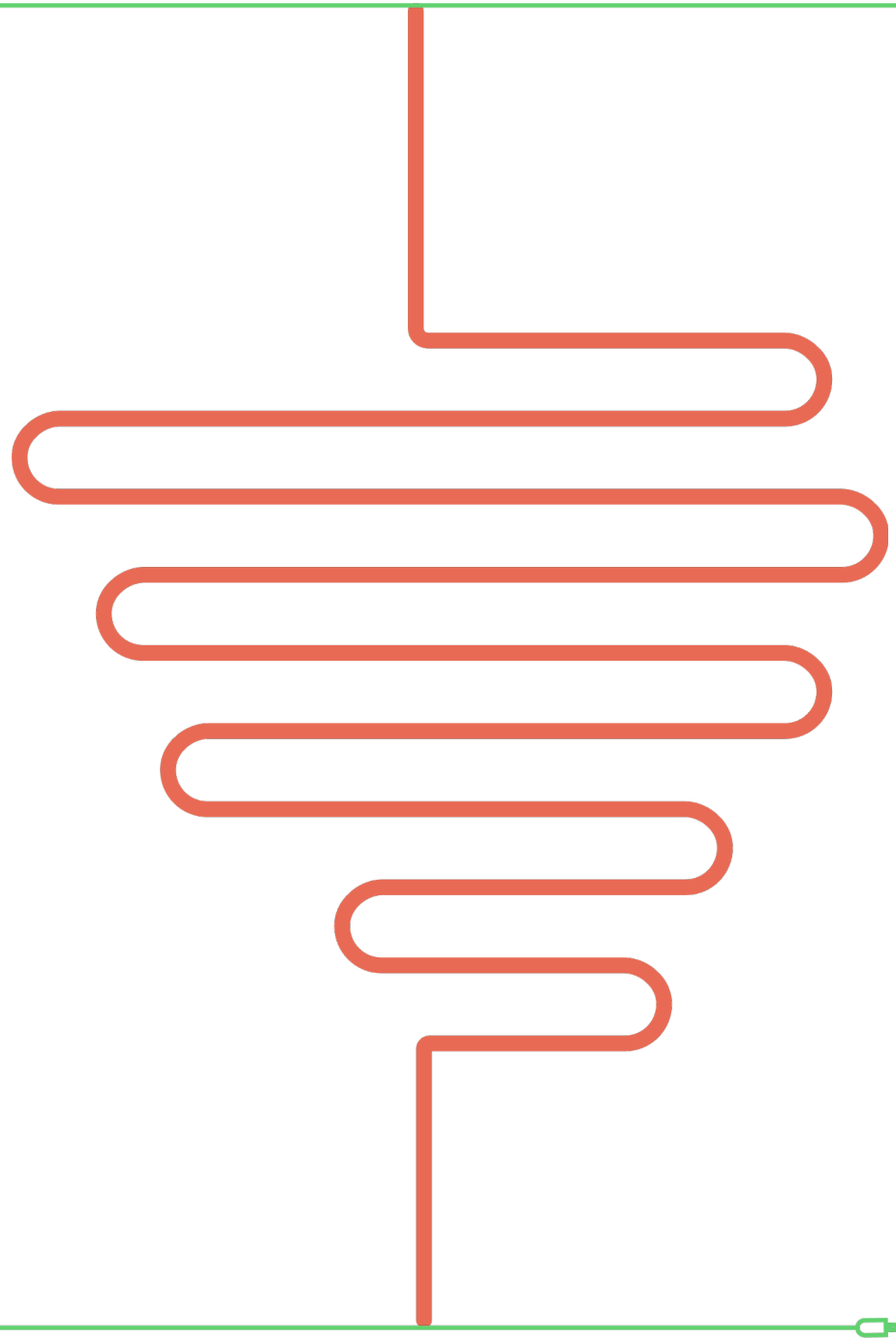
AbbVie, Pfizer, Janssen, Gilead, Dr Falk, Ferring, Hospira and Takeda



How does IBD impact on a person's life?

Physical aspects

- diarrhoea, urgency, blood in stool and pain
- joint pains, eye problems, skin rashes and mouth ulcers
- night sweats and fevers
- nausea and vomiting, loss of appetite and weight loss

Psychological aspects

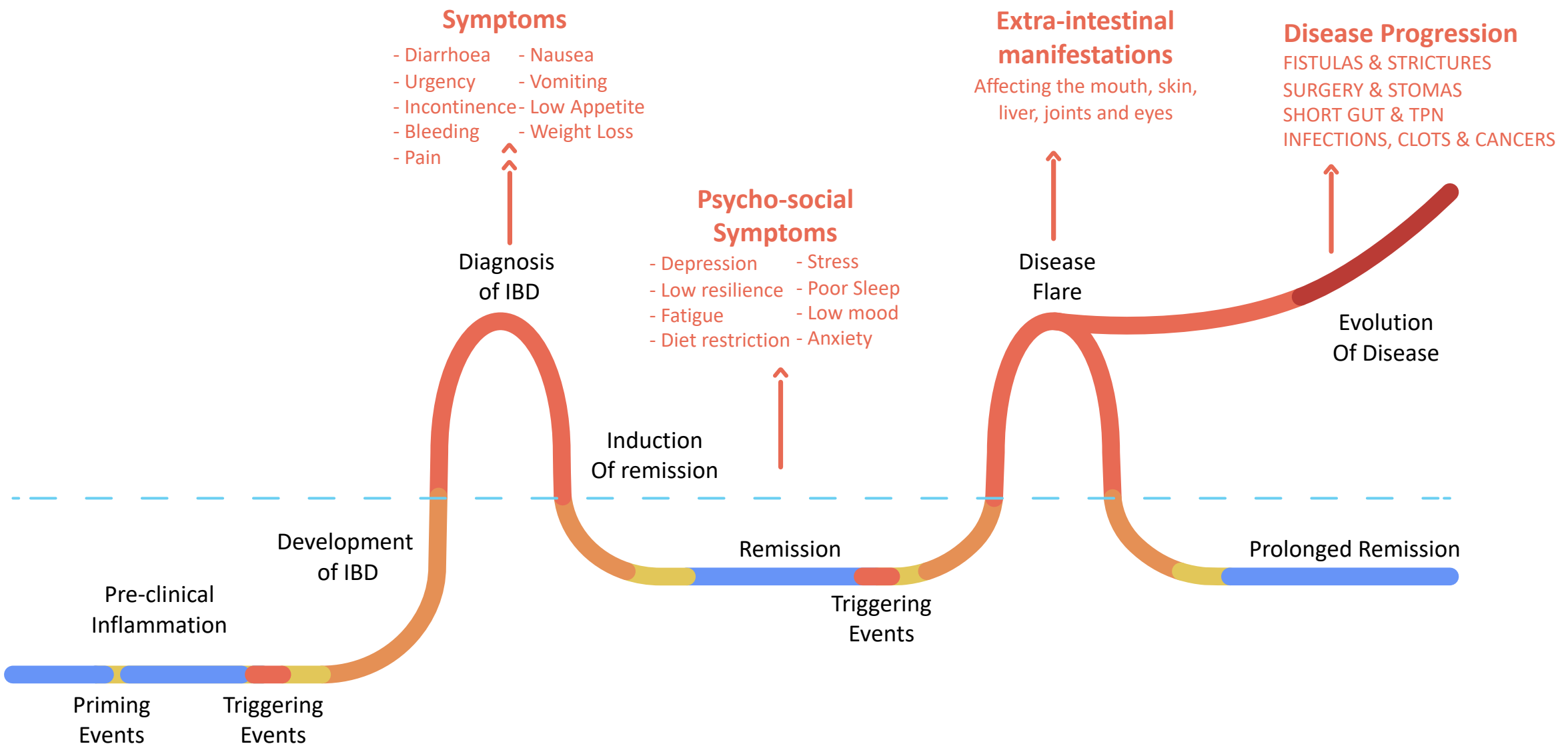
- fatigue and mental exhaustion
- anxiety and depression

Long-term complications of the disease

- hospitalisations for flares
- surgical interventions including stoma formation

Everyday life

- spending more time in the bathroom
- impact on studies and work - including absence and choice of job
- relationships and sex life, family planning and pregnancy
- regular medications required to maintain remission
- food choices may be restricted to manage / avoid flares


Symptoms
- Diarrhoea
- Urgency
- Incontinence
- Bleeding
- Pain
- Nausea
- Vomiting
- Low Appetite
- Weight Loss
Diagnosis of IBD
Psycho-social Symptoms
- Depression
- Low resilience
- Fatigue
- Diet restriction
- Stress
- Poor Sleep
- Low mood
- Anxiety
Induction Of remission
Extra-intestinal manifestations
Affecting the mouth, skin, liver, joints and eyes
Disease Flare
Disease Progression
FISTULAS & STRICTURES
SURGERY & STOMAS
SHORT GUT & TPN
INFECTIONS, CLOTS & CANCERS
Evolution Of Disease
Pre-clinical Inflammation
Development of IBD
Remission
Triggering Events
Prolonged Remission
Priming Events
Triggering Events

IBD inflammatory bowel disease

CD Crohn's disease

UC ulcerative colitis

- Mostly affect young people
- Lifelong with no known cure
- Global epidemiology trends striking
- Strong environmental influence
- Multiple genetic associations
- **Highly heterogenous phenotypes**

All artwork original (in collaboration with @ErikRVA)

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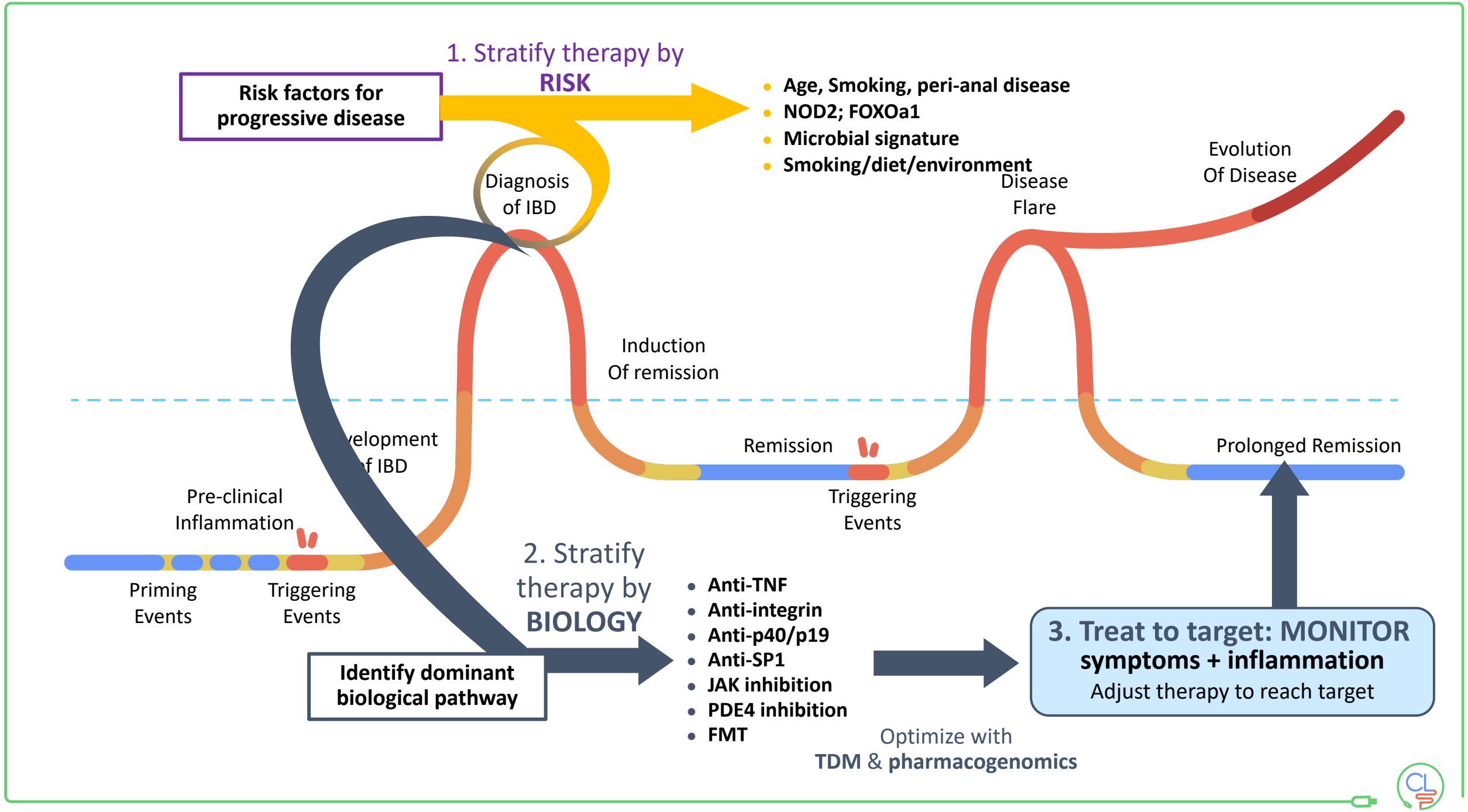
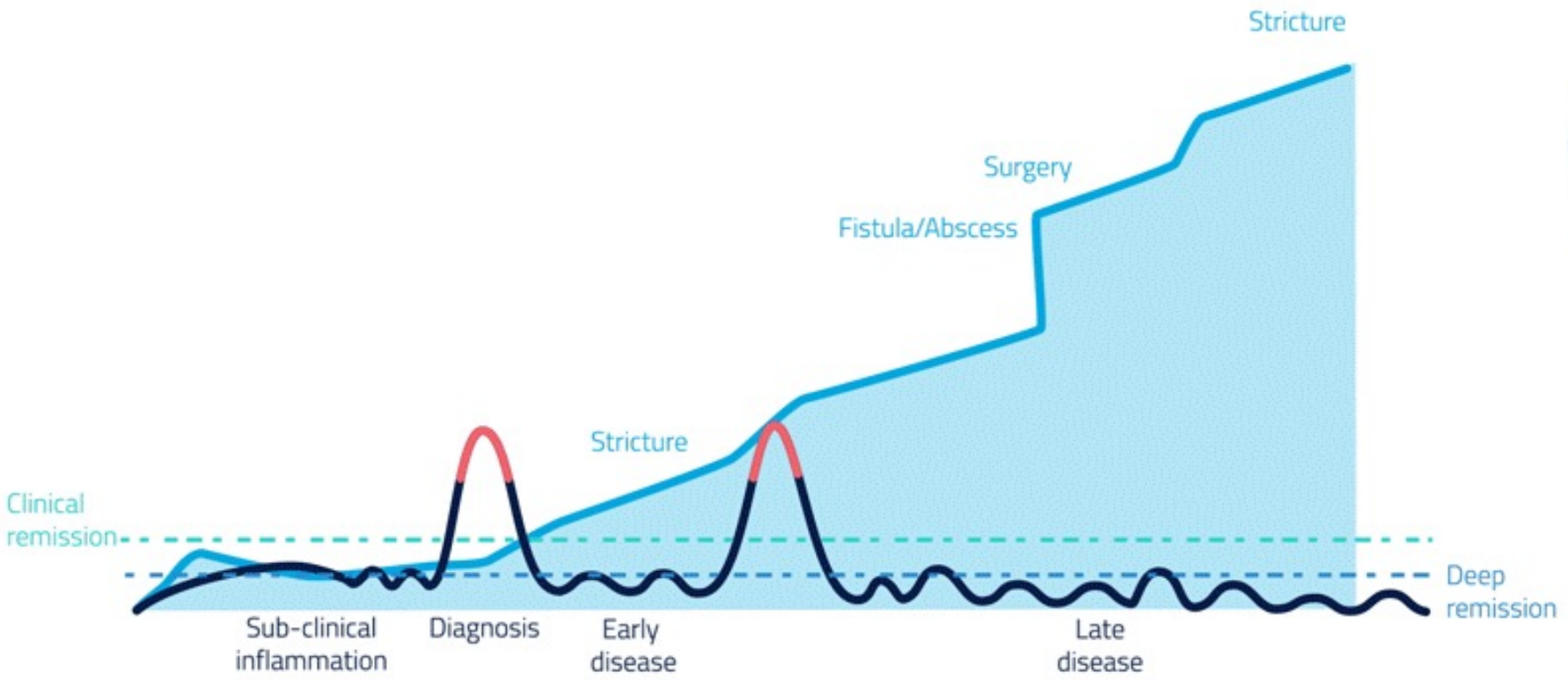
- Highly heterogenous phenotypes
- Treatment failure & disease progression is common
- **No good predictive models**


1. Stratify therapy by
RISK
Risk factors for progressive disease
Age, Smoking, peri-anal disease
NOD2; FOXOa1
Microbial signature
Smoking/diet/environment
Diagnosis of IBD
Disease Flare
Evolution Of Disease
Induction Of remission
Remission
Prolonged Remission
Triggering Events
Pre-clinical Inflammation
Priming Events
Triggering Events
2. Stratify therapy by
BIOLOGY
Identify dominant biological pathway
Anti-TNF
Anti-integrin
Anti-p40/p19
Anti-SP1
JAK inhibition
PDE4 inhibition
FMT
Optimize with
TDM & pharmacogenomics
3. Treat to target: MONITOR
symptoms + inflammation
Adjust therapy to reach target



Original artwork by Prof Charlie Lees
In collaboration with @ErikRVA

28-year-old male with Crohn's disease

- Diagnosed 9 years ago (2012) at the age of 19 years
- Terminal ileal distribution (L1) confirmed on colonoscopy and TI biopsy
- >50cm of TI inflammation on small bowel MRI scanning
- Non-smoker with no relevant family history
- Studying to be an electronics engineer

He is young and has extensive small bowel disease

- Started on combination therapy with IFX and AZA

- Excellent response
- He decides to discontinue IFX in 2013 …
  - We would strongly discourage this in 2021

- AZA continued to 2017 … stopped due to abnormal LFTs

AZA: azathioprine; IFX: infliximab;
LFTs: Liver Function Tests.

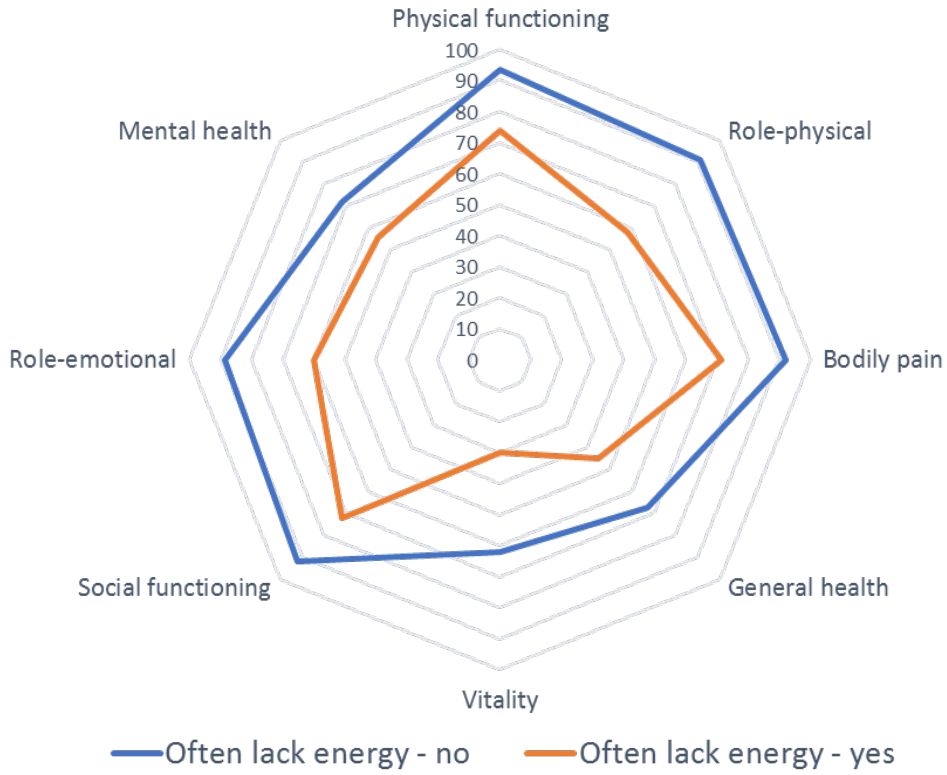
On no maintenance therapy, he develops fatigue

- “Brain fog” and profound fatigue
- Difficulties in concentrating
- He is off work

- No anaemia (Hb 150)
- Normal ferritin, vit B12, folate
- Slightly low Vitamin D

Fatigue is an important clinical problem in IBD

- 40% of IBD patients in clinical remission often lack energy
- Psychological well-being (anxiety, depression, sleep), clinical disease activity and female sex are independently related to fatigue
- Lack of energy significantly impact on health-related quality of life



Derikx et. al. OP22 ECCO 2021

On no maintenance therapy, his disease flares

- April 2018:
  - Urgent watery diarrhoea 7-8x /24h
  - CRP is normal but the FCAL is 761mcg/g
  - ADA monotherapy started
- October 2018:
  - Response to ADA has been excellent
  - BO x2 /24h; FCAL 26mcg/g

ADA: adalimumab; BO: bowel open; CRP: C-reactive protein; FCAL: faecal calprotectin.

He develops immunogenicity to ADA monotherapy

August 2019: ADA levels: undetectable; anti-drug antibodies: >200 ng/mL

- BO 5-6x /24h; abdo pain;
- Mental health issues: Depressive symptoms ++

- Joint pains – rheumatology
  - Painful swollen wrists and elbows; occasionally ankles and knees
  - Pauci-articular (Type I) enteropathic arthropathy
  - Joint hypermobility (Beighton's score 8/9)

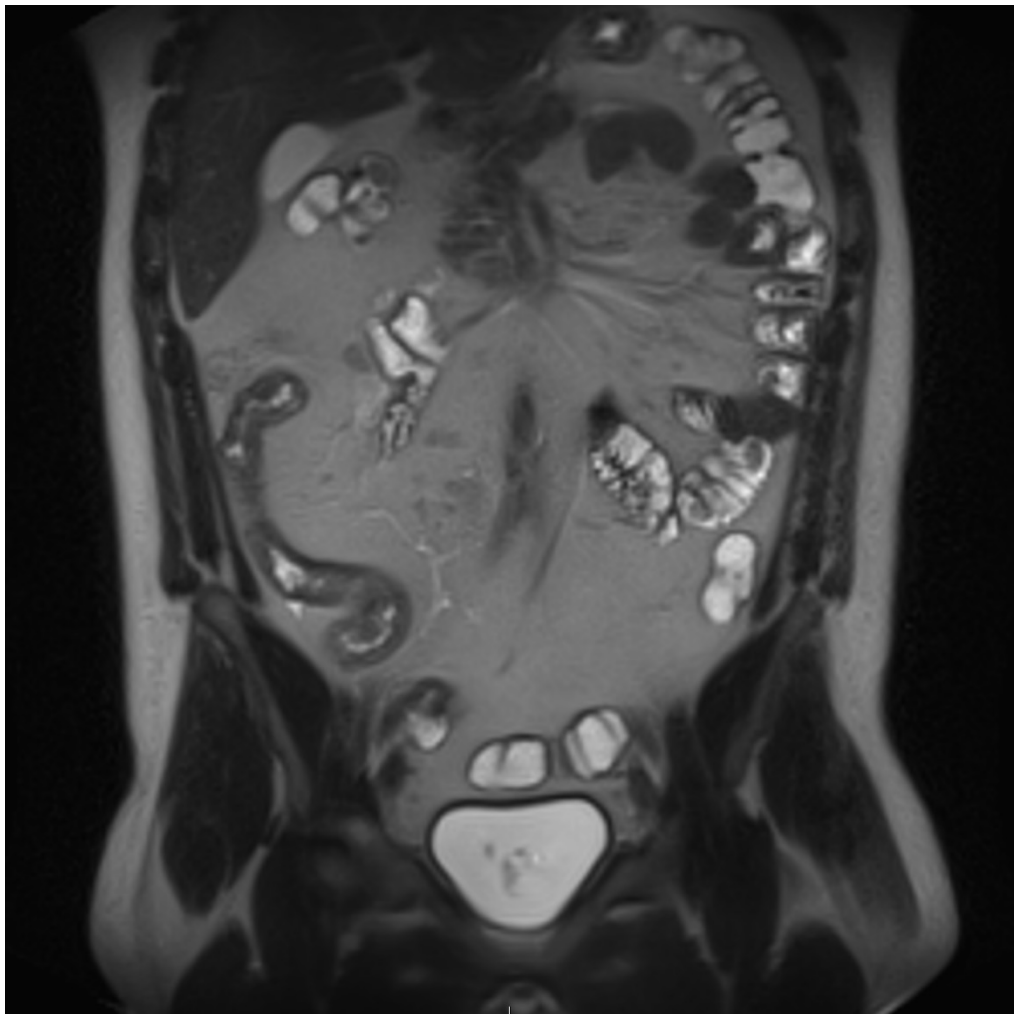
- Erythema nodosum on both shins

Disease is re-staged

- FCAL is 390mcg/g
- SBMRI 60cm of inflammation

- Options could be ustekinumab or vedolizumab

- Due to extra-intestinal manifestations of IBD … ustekinumab started



IBD: inflammatory bowel disease; FCAL: faecal calprotectin; SBMRI: small bowel MRI.

He makes an excellent response to ustekinumab

- After IV loading dose (Oct ‘19) at 6mg/kg:
  - Reduced BO’ing; no pain
  - Increased appetite and weight
  - Joint symptoms & E.N. resolve
  - Ongoing fatigue and bowel urgency

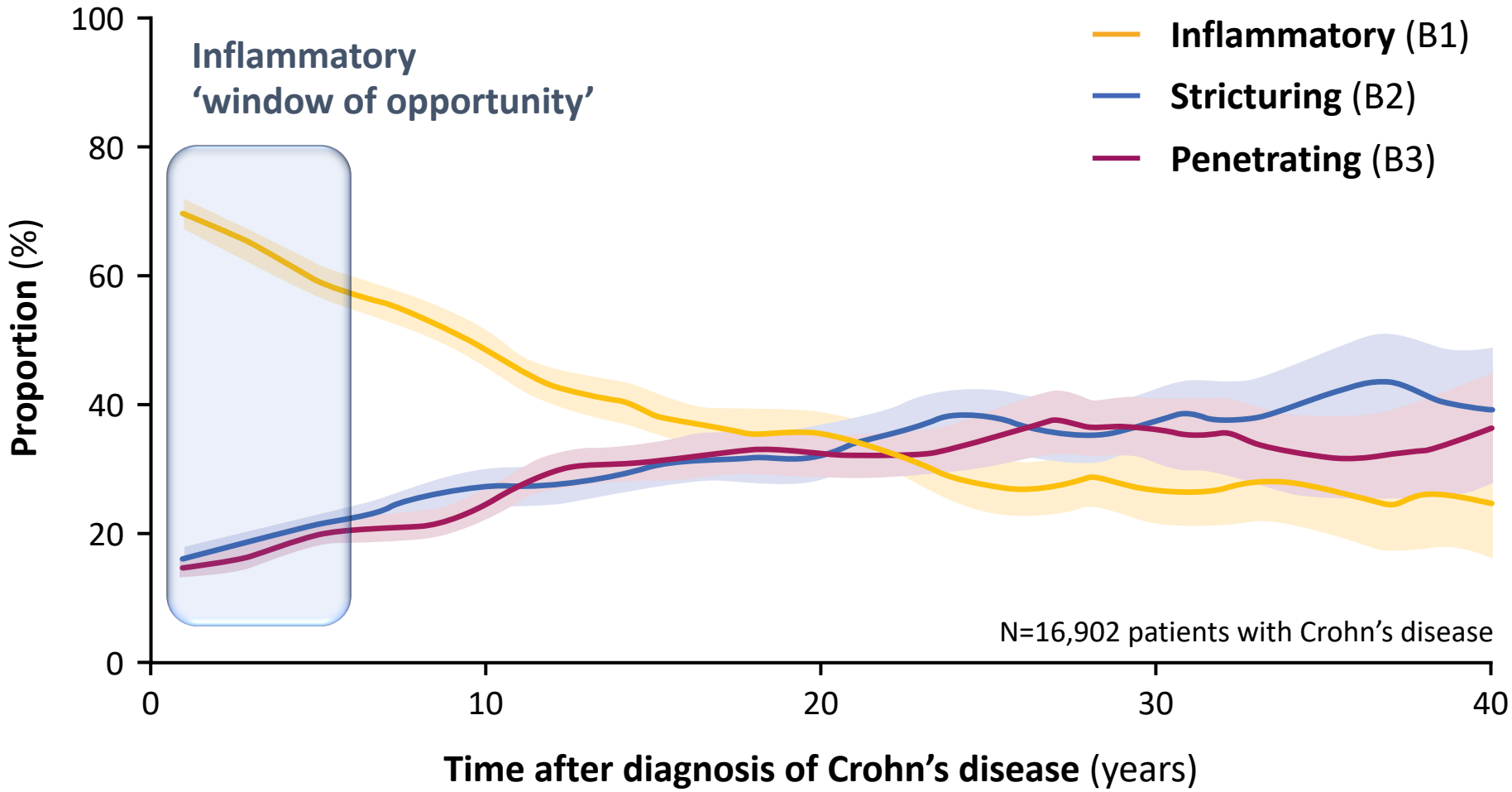
- May & Sept & Dec 2020 – phone & telemedicine clinics
  - Well!
  - BO 1-2/ 24h with normal stool; no urgency
  - Mood is good; Energy levels are normal
  - FCAL is 20mcg/g

BO: bowel open; E.N.: erythema nodosum; FCAL: faecal calprotectin; IV: intravenous.

March 2021

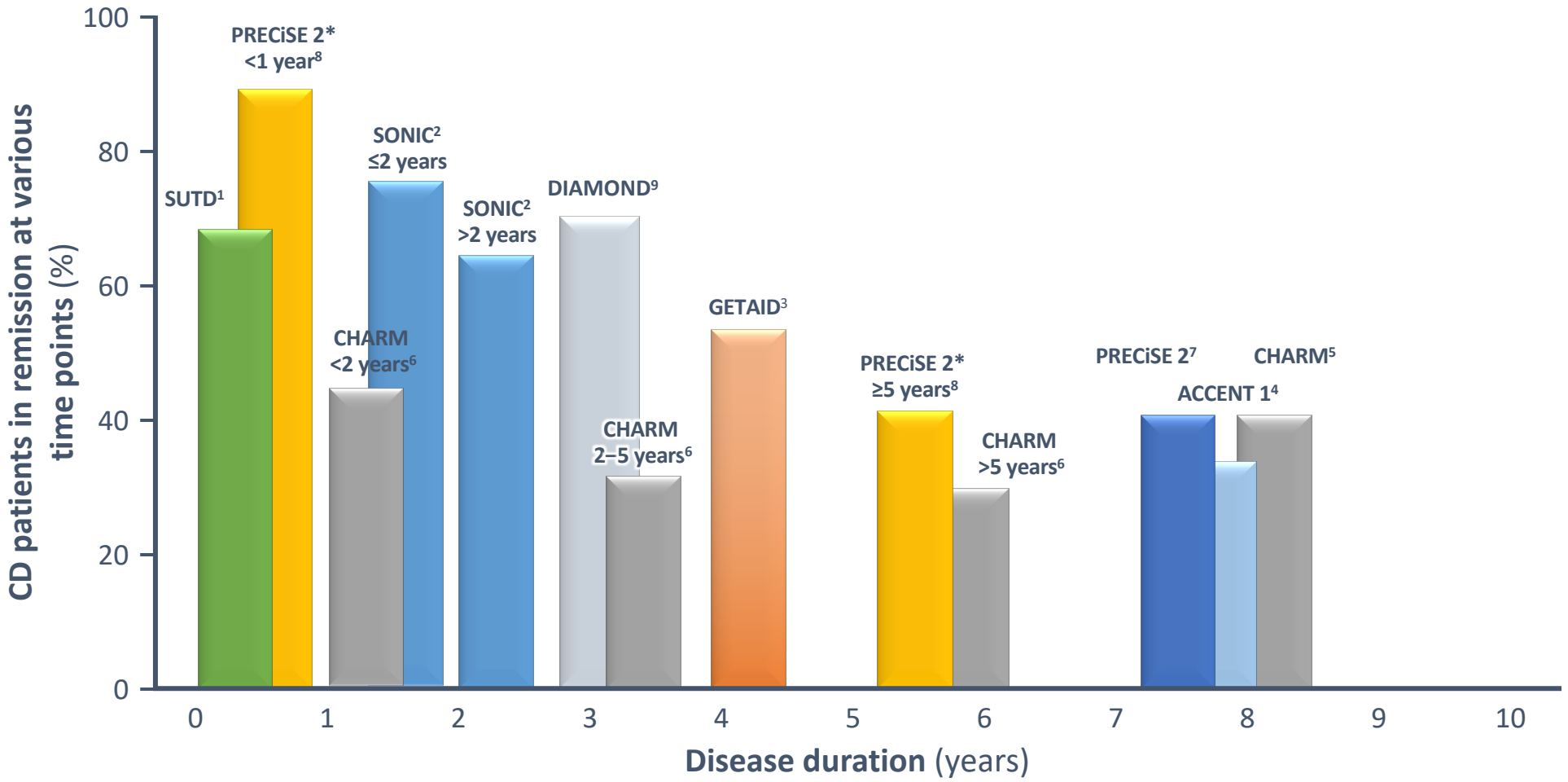
- Small bowel MRI – fibro-stenotic changes but no inflammation
- Occasional mild abdominal bloating – depends on diet
- Otherwise well
- FCAL <20mcg/g

Crohn's disease is progressive



Cleynen I, et al. *Lancet* 2016;387:156–167

Starting anti-TNF therapy: the importance of timing



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Original Article

Temporal Trends in Surgical Resection Rates and Biologic Prescribing in Crohn's Disease: A Population-based Cohort Study

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Abstract

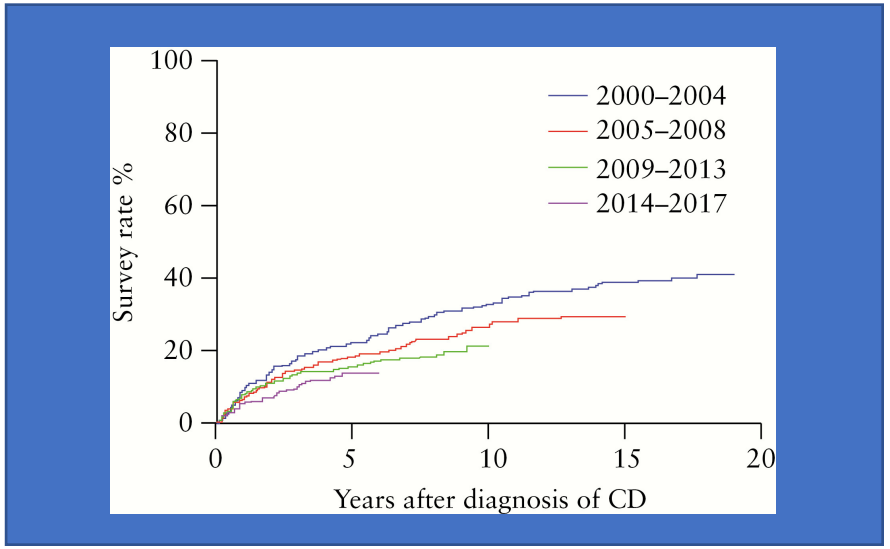
Background: The use of biologic therapy for Crohn's disease [CD] continues to evolve, however, the effect of this on the requirement for surgery remains unclear. We assessed changes in biologic prescription and surgery over time in a population-based cohort.

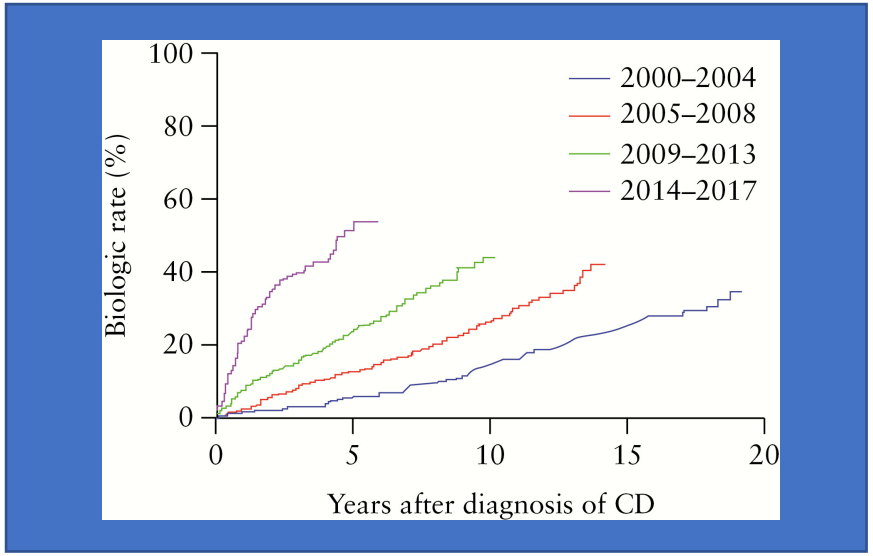
Methods: We performed a retrospective cohort study of all 1753 patients diagnosed with CD in Lothian, Scotland, between January 1, 2000 and December 31, 2017, reviewing the electronic health record of each patient to identify all CD-related surgery and biologic prescription. Cumulative probability and hazard ratios for surgery and biologic prescription from diagnosis were calculated and compared using the log-rank test and Cox regression analysis stratified by year of diagnosis into cohorts.

Results: The 5-year cumulative risk of surgery was 20.4% in cohort 1 [2000–2004],18.3% in cohort 2 [2005–2008], 14.7% in cohort 3 [2009–2013], and 13.0% in cohort 4 [2014–2017] p <0.001. The 5-year cumulative risk of biologic prescription was 5.7% in cohort 1, 12.2% in cohort 2, 22.0% in cohort 3, and 44.9% in cohort 4 p <0.001.

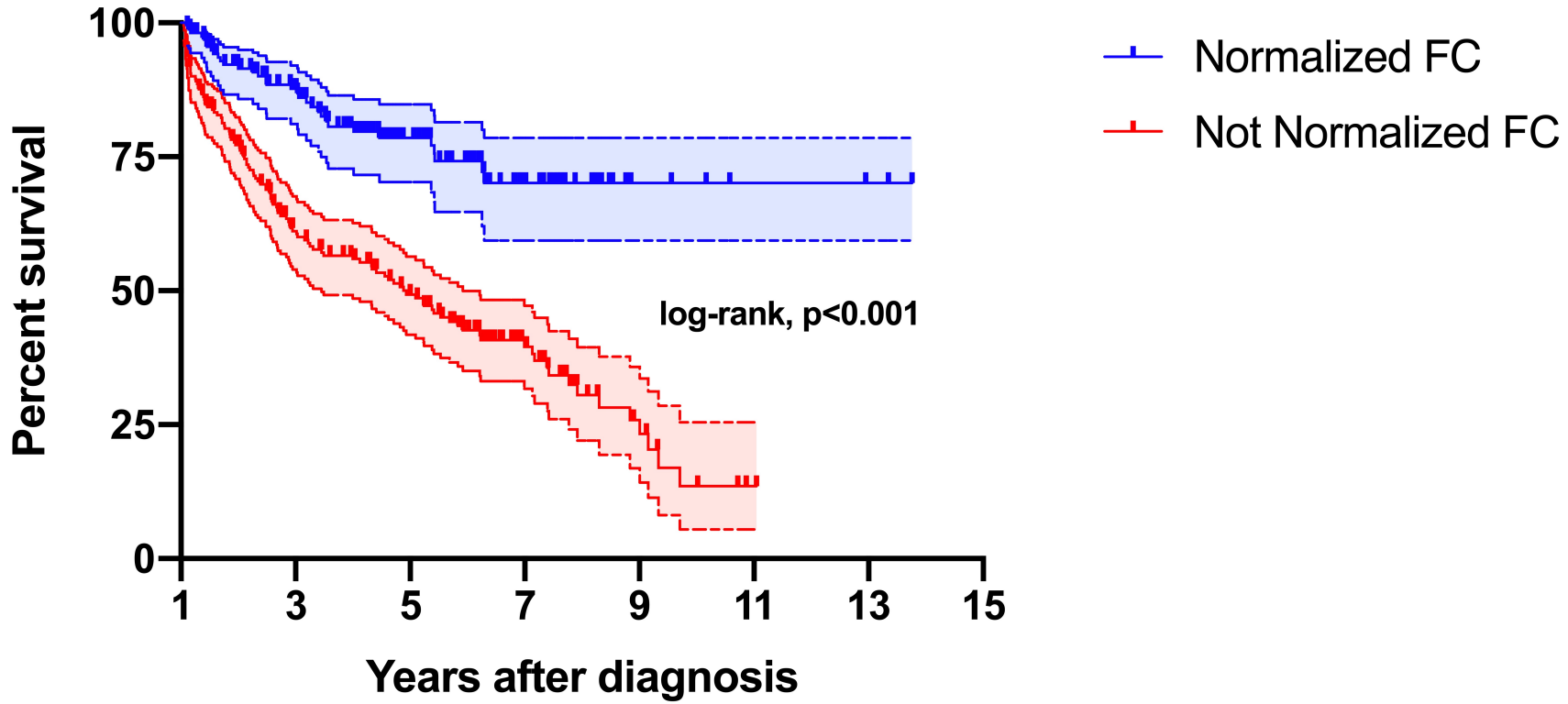
Conclusions: The increased and earlier use of biologic therapy in CD patients corresponded with a decreasing requirement for surgery over time within our cohort. This could mean that adopting a top-down or accelerated step-up treatment strategy may be effective at reducing the requirement for surgery in newly diagnosed CD.

Key Words: Crohn's disease; biologics; infliximab; adalimumab; vedolizumab; ustekinumab; surgery



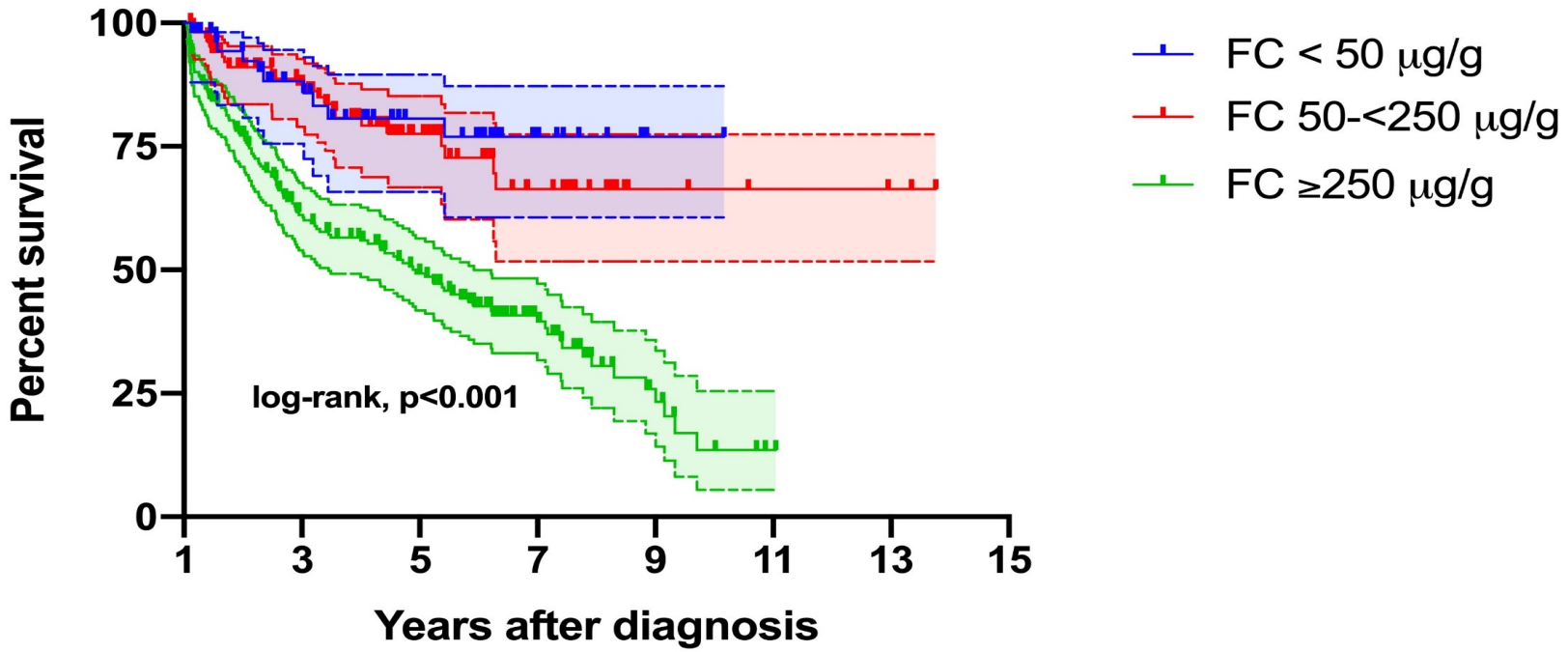


Normalisation of FC in first year of CD is associated with better outcomes over time



No. at risk						
Normalized FC	163	108	61	28	7	4
Not Normalized FC	212	108	72	33	11	2

Plevris N et al CGH 2020



No. at risk						
FC < 50 µg/g	56	38	23	10	2	1
FC 50-<250 µg/g	107	71	39	19	6	4
FC ≥ 250 µg/g	212	108	73	33	10	2

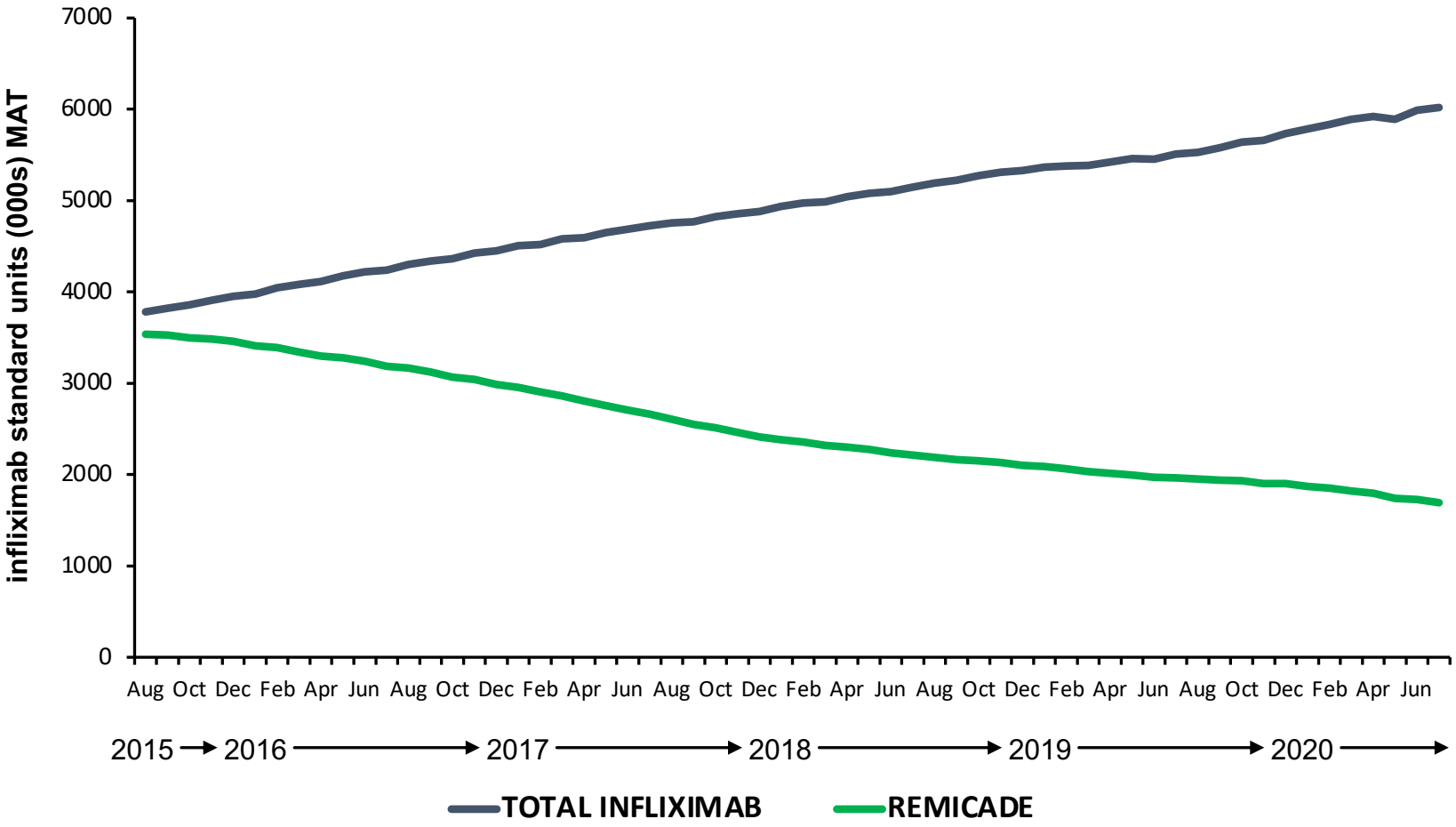
Plevris N et al CGH 2020

Early biologic use was the strongest predictor of FC normalisation

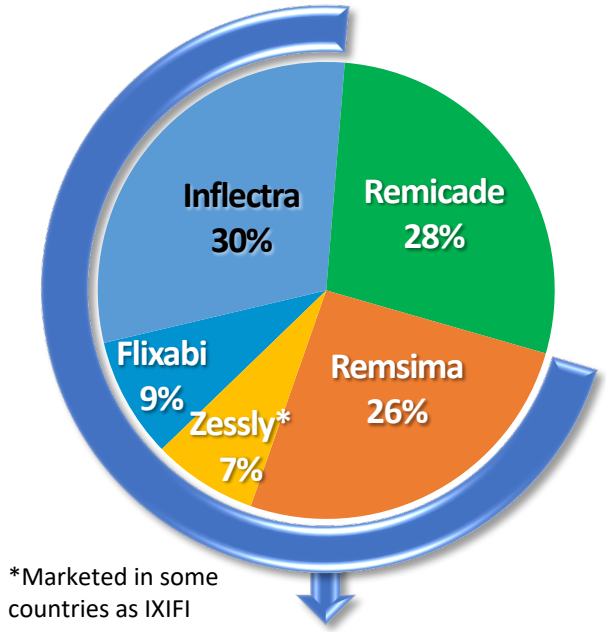
		Odds Ratio	95% Confidence Interval	p-value
Older Age		0.987	0.975-1.000	**0.045**
L4		0.290	0.155-0.542	**<0.001**
Treatment at diagnosis (<3 months)	Nil	Reference		
	Steroid mono-therapy	0.821	0.362-1.863	0.637
	IMM mono-therapy	0.945	0.418-2.138	0.893
	Biologic mono/combo-therapy	4.288	1.585-11.601	**0.004**
Higher Baseline FC*		0.127	0.048-0.336	**<0.001**

Plevris N et al CGH 2020

Total infliximab uptake in Europe has increased since biosimilars came to the market



July 2020 (MAT) market share of infliximab (EU)



*Marketed in some countries as IXIFI

72%

Biosimilar penetration

1. IMS MIDAS Unit Sales data by month (Feb 2020).

Infliximab and adalimumab biosimilars authorisations

	Biosimilar brand name	Molecule name	EMA authorisation[1]	Health Canada authorisation[2]	Japan authorisation[3]
Infliximab	**REMSIMA®/ INFLECTRA®**	CT-P13	10th Sept 2013	15th Jan 2014	4th July 2014
	FLIXABI® / RENFLEXIS®	SB-2	26th May 2016	1st Dec 2017	
	ZESSLY® / IXIFI®	PF-06438179 / GP1111	18th May 2018		2nd July 2018
	Infliximab biosimilar 2*	NI-071 / GS071			27th Sept 2017
Adalimumab	**AMGEVITA®**	ABP-501	21st Mar 2017		
	IMRALDI® / HADLIMA®	SB-5	24th Aug 2017	8th May 2018	
	HALIMATOZ® / HEFIYA® / HYRIMOZ®	GP-2017	26th July 2018		
	HULIO®	FKB327	16th Sept 2018		
	IDACIO®/ KROMEYA®	MSB-11022	2nd April 2019		

*Japanese Approved Name; EMA: European Medicines Agency

1. EMA. European Public Assessment Reports (EPARs). Available at: http://www.ema.europa.eu/ema (accessed Sept 2019); 2. Government of Canada. Drugs, health & consumer products – Review Decisions. Available at: https://hpr-rps.hres.ca/reg-content/summary-basis-decision.php (accessed Sept 2019); 3. GaBi Online – Generics and Biosimilars Initiative. Biosimilars approved in Japan. Available at: http://gabionline.net/Biosimilars/General/Biosimilars-approved-in-Japan (accessed Sept 2019).

Timeline: Edinburgh IBD unit biosimilar adoption

Biosimilar infliximab

Implementation of managed switch programme (Q1 – Q3 2016)
No Remicade by end of 2016

Bio-naive IFX patients started on CT-P13 (Q1 2015)

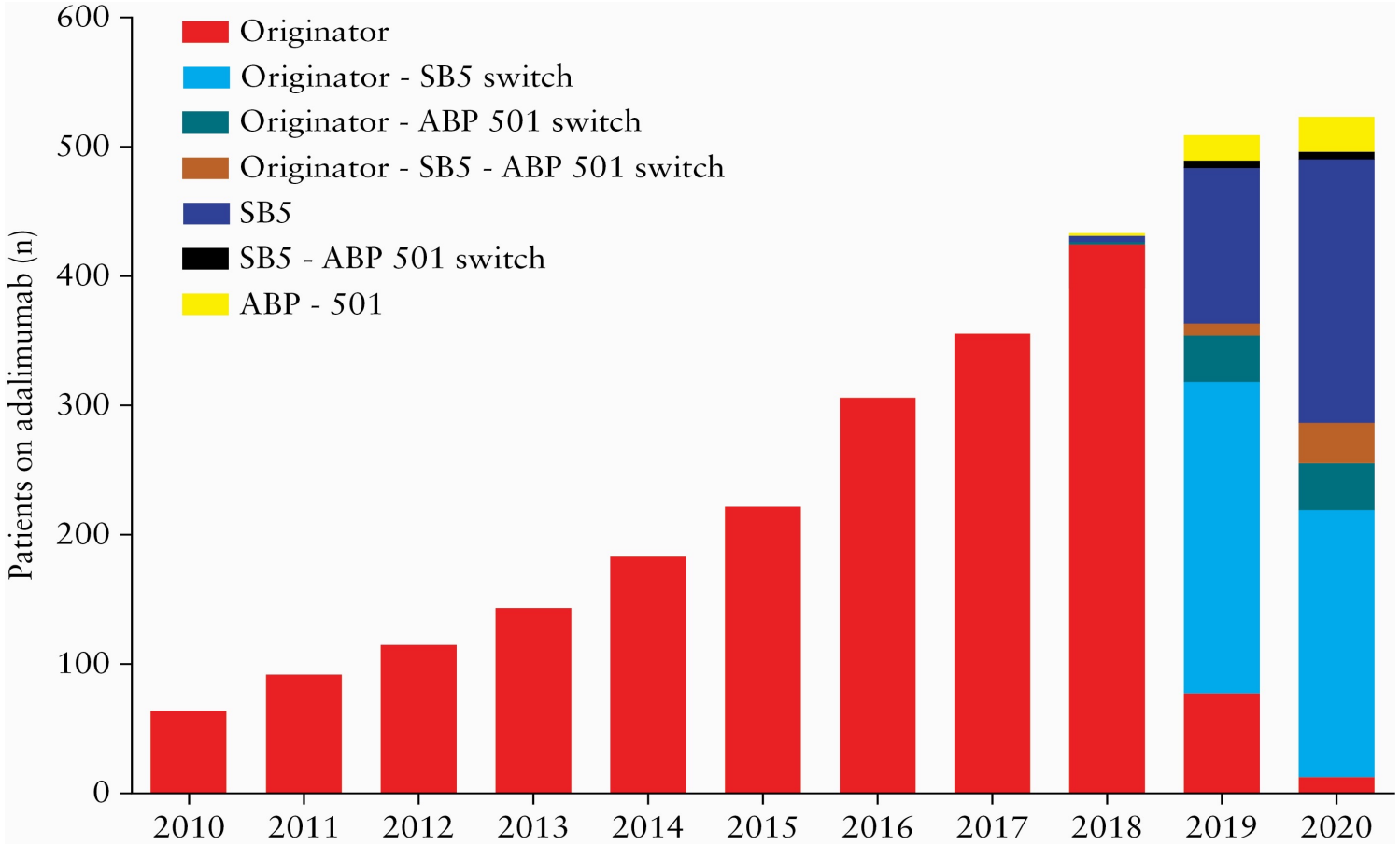
Development of managed switch programme (Q4 2015)

Managed switch programme: CT-P13 to IXIFI, started Q1 2020

Implementation of adalimumab managed switch programme

Biosimilar adalimumab

Adalimumab use over time

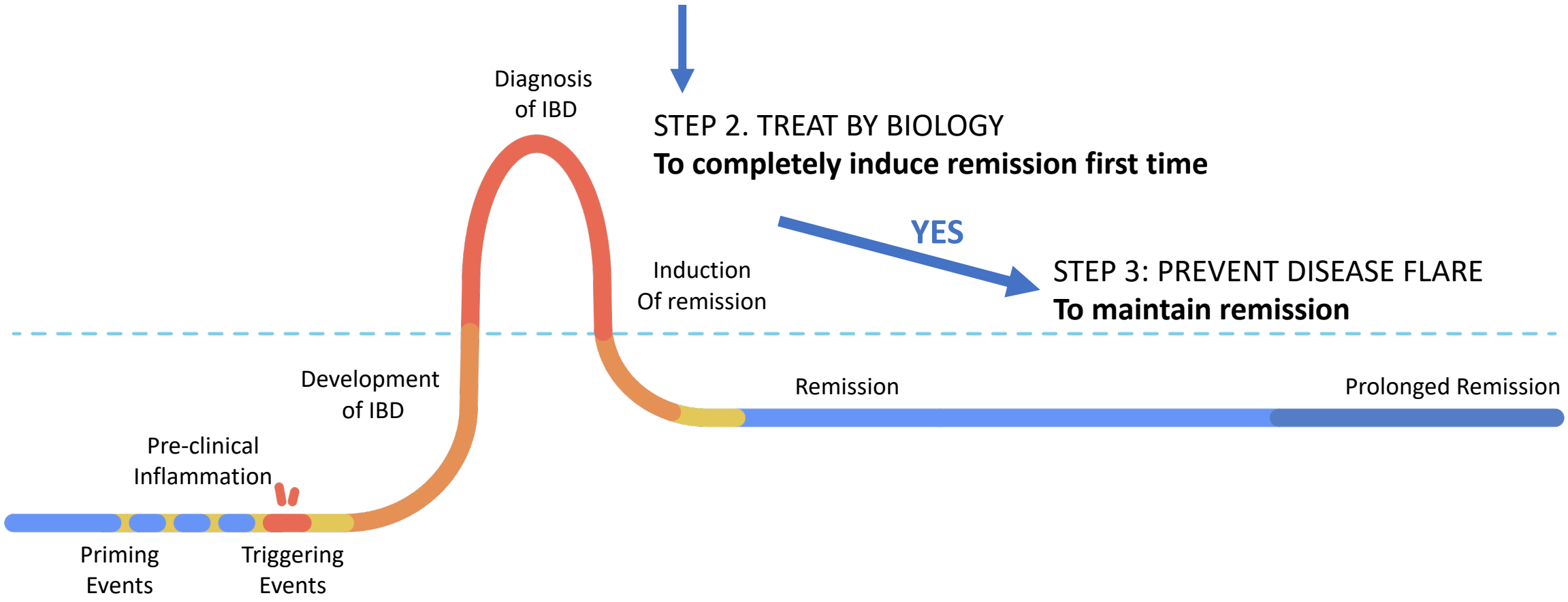


J Crohns Colitis, jjab100, https://doi.org/10.1093/ecco-jcc/jjab100

SCENARIO IBD_NO FLARES: induce remission, maintain remission, prevent flare, & therefore disease progression

STEP 1. STRATIFY by RISK

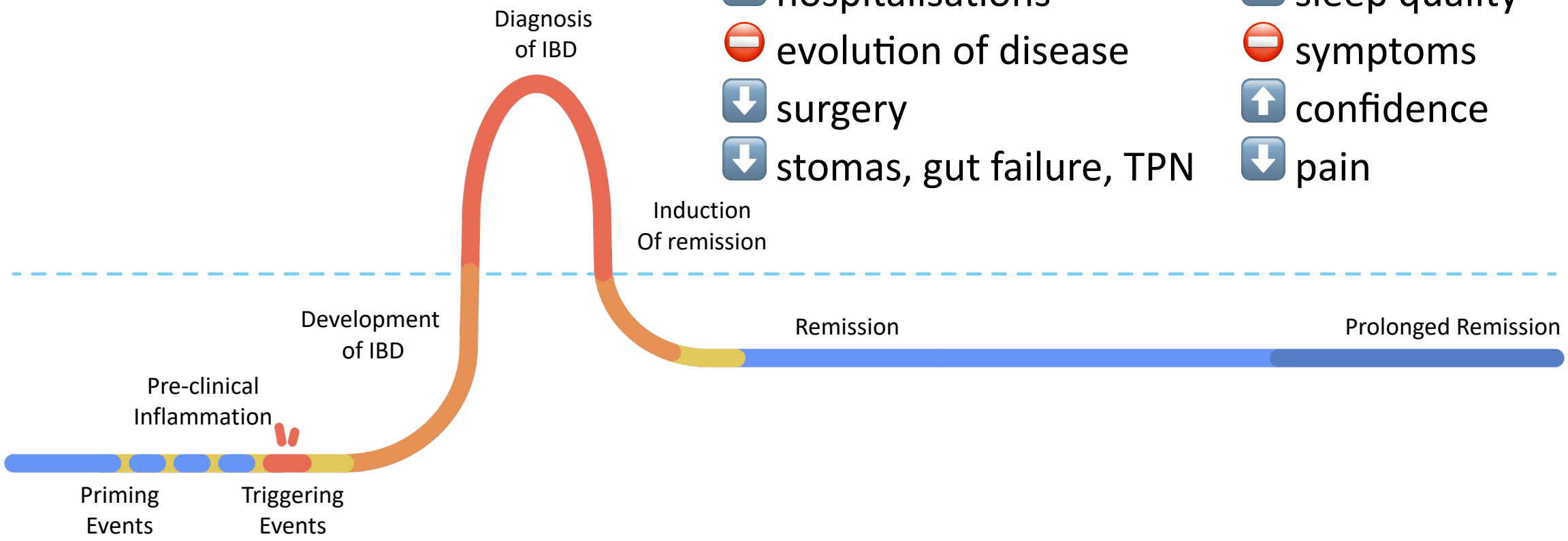
To overcome massive disease heterogeneity



What does success look like?

- ⬇️ cost
- ⬆️ quality of life
- ⬇️ hospitalisations
- ⛔ evolution of disease
- ⬇️ surgery
- ⬇️ stomas, gut failure, TPN

- ⬇️ fatigue
- ⬆️ mood
- ⬆️ sleep quality
- ⛔ symptoms
- ⬆️ confidence
- ⬇️ pain



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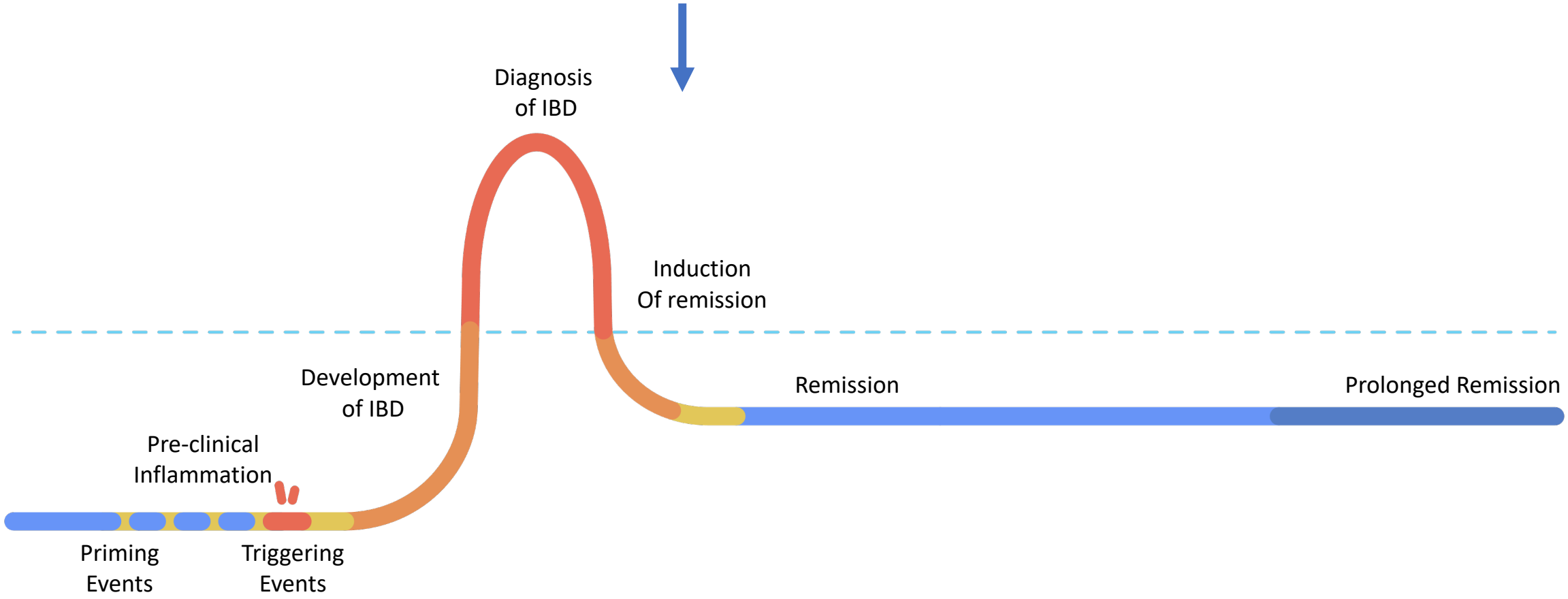
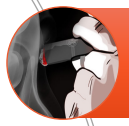


Layer in big data from multiple omics sources
- clinical and molecular phenotyping
- machine learning and AI
- hyper-personalized care

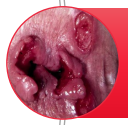
+ Risk factors

Young age
(Beaugerie L. et al, Gastroenterology. 2006;130:650-6. Loly C, et al. Scand J Gastroenterol. 2008;43:948-54)

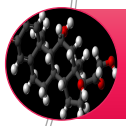


Smoking
(Franchimont D, et al. Eur J Gastroenterol Hepatol. 1998;10:821-5)

Extensive small bowel disease
(Munkholm P, et al. Gastroenterology. 1993;105:1716-33)

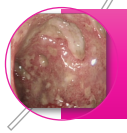


Peri-anal disease
(Beaugerie L. et al, Gastroenterol. 2006;130:650-6. Loly C, et al .Scand J Gastroenterol. 2008;43:948-54)



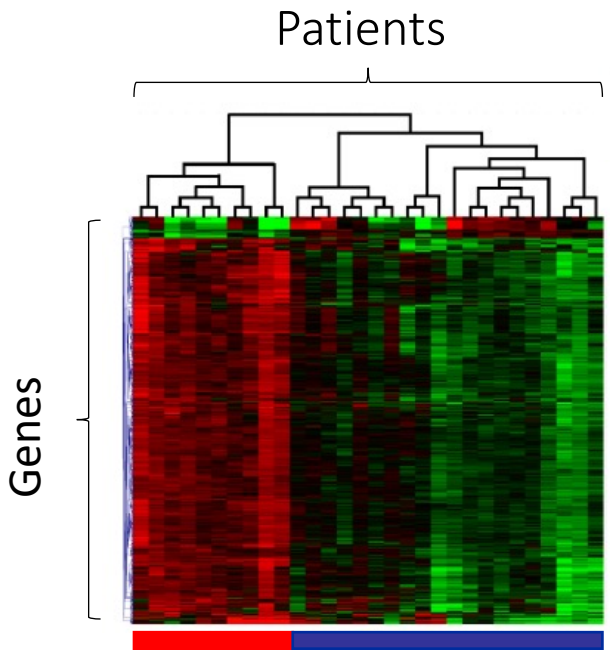
Steroids at diagnosis
(Beaugerie L, et al. Gastroenterology. 2006;130:650-6)

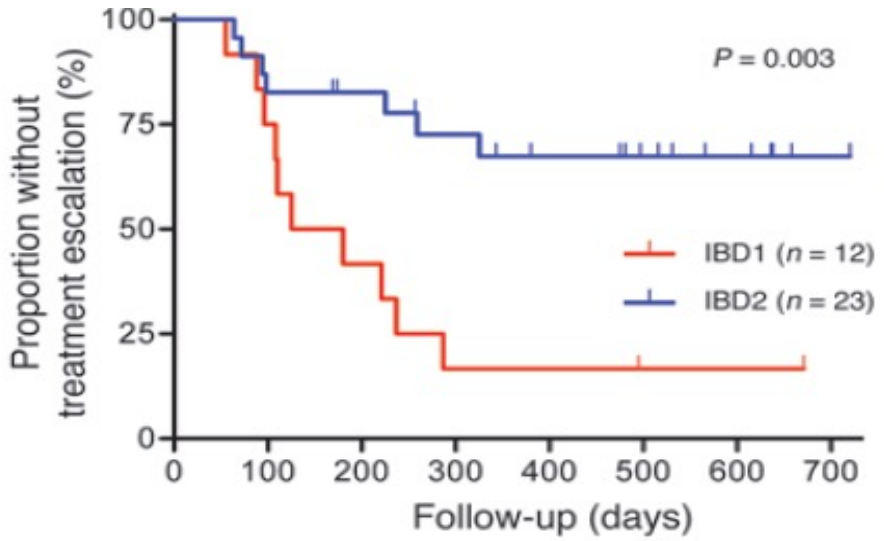
Weight loss
(Loly C, et al. Scand J Gastroenterol. 2008;43:948-54)



Deep ulcerations at endoscopy
(Allez M, et al. Am J Gastroenterol. 2002;89:454-9)

Predicting disease course in CD using CD8 transcriptomics





qPCR assay

Lee et al *JCI* 2011

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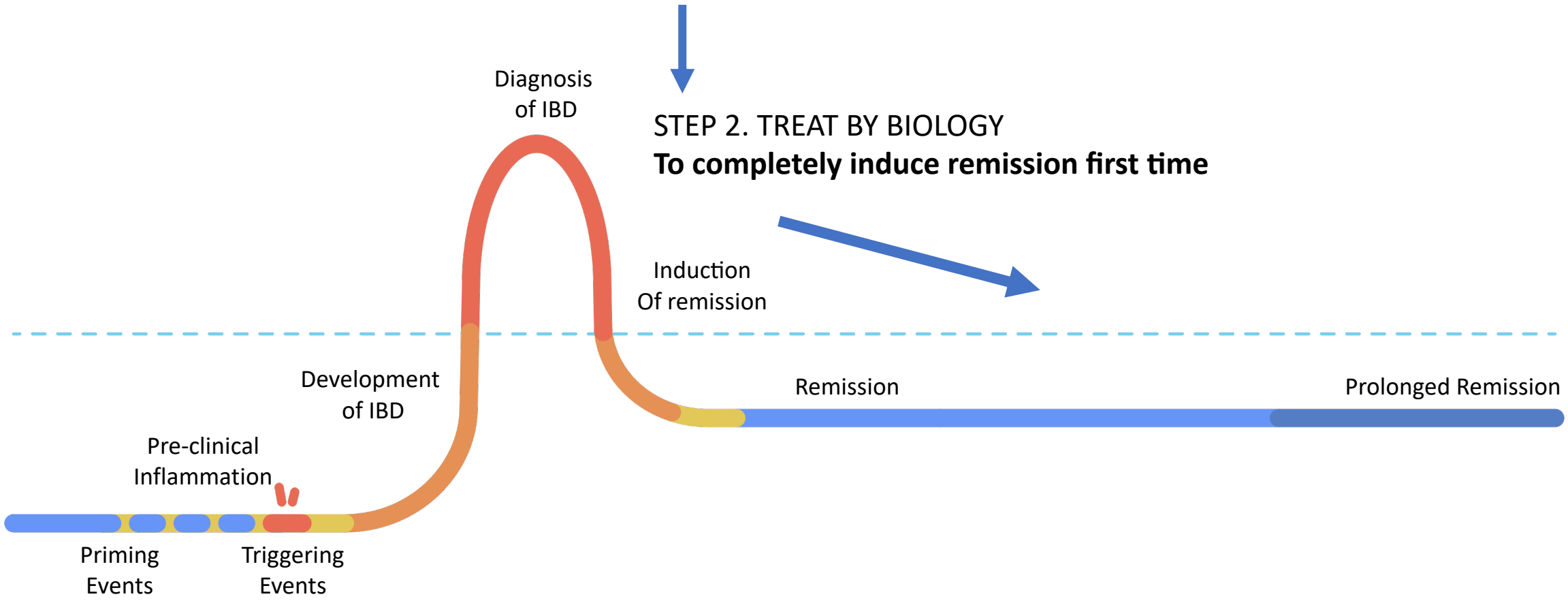
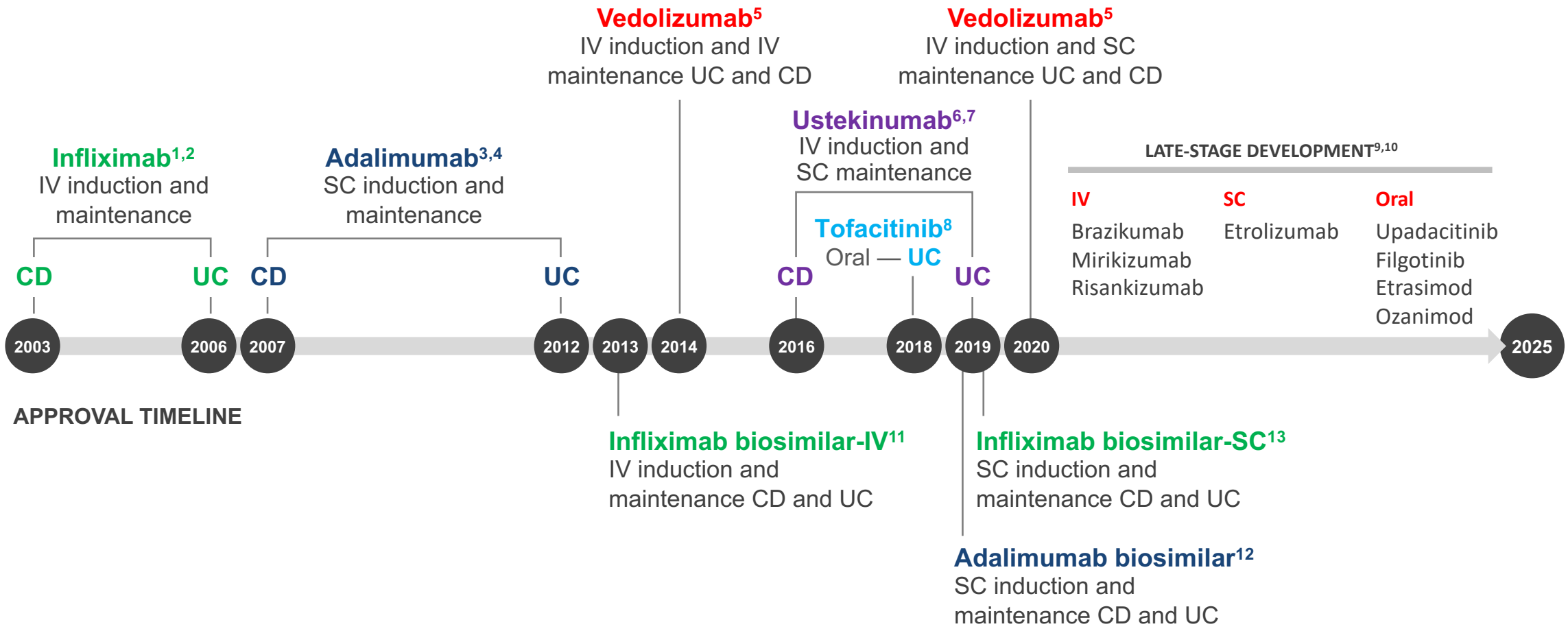


Advances in IBD therapy have provided patients and healthcare providers with a wealth of treatment options



CD, Crohn's disease; IBD, inflammatory bowel disease; IV, intravenous; SC, subcutaneous; UC, ulcerative colitis.

1. P&T Community. 21 May 2003. 2. P&T Community. 9 Mar 2006. 3. Abbott.11 Apr 2012. 4. Abbott. 30 Aug 2012. 5. Takeda. 28 May 2014. 6. Johnson & Johnson. 11 Nov 2016. 7. Johnson & Johnson. 21 Oct 2019. 8. Pfizer. 1 Aug 2018. 9. Pérez-Jeldres T, et al. Front Pharmacol. 2019;10:212. 10. Rawla P, et al. J Inflamm Res. 2018;11:215-26. 11. Cision PR Newswire. 10 Sep 2013. 12. Sandoz. 27 Jul 2018. 13. Nadpara N, et al. Dig Dis Sci. 2020;10.1007/s10620-020-06471-4.

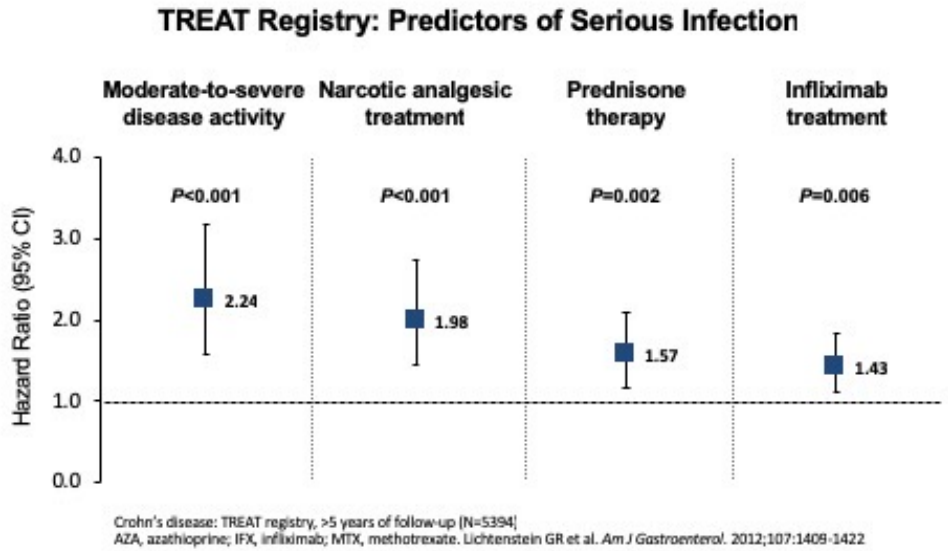
Chose the right drug for the right patient at the right time

STRIDE
Selecting targets of remission in inflammatory bowel disease

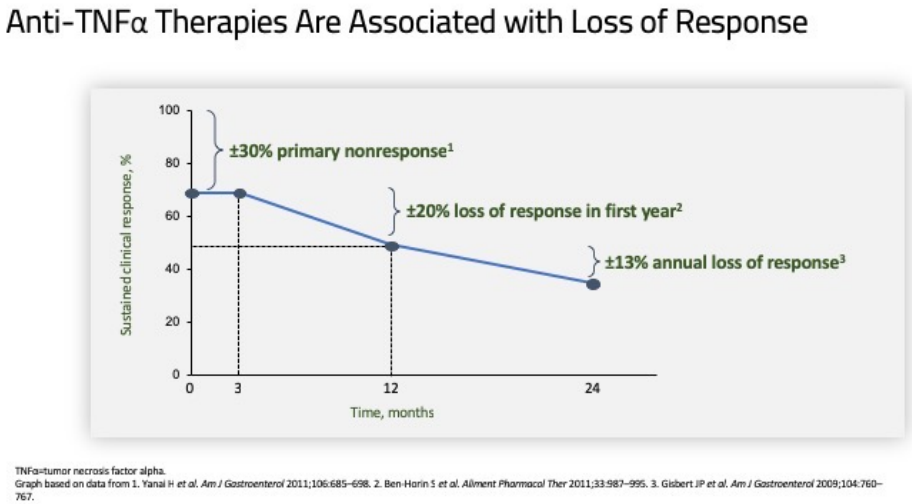
Treat to target[1]

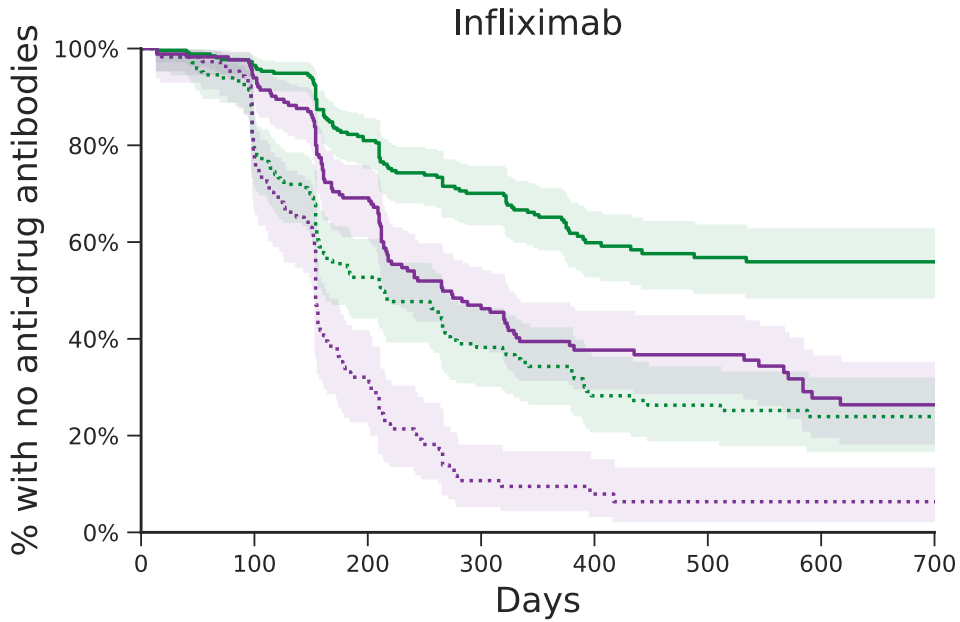
Lots of interesting questions here:

- precision medicine
- head to head studies
- drug sequencing
- role of biosimilars
- antibodies vs small molecules
- combination of therapies



Genes	Drugs	ADR
TPMT	Thiopurines	Myelosuppression
NUDT15	Thiopurines	Myelosuppression
HLA-DQA1*05	IFX, ADA	Immunogenicity
HLA-DRB1*07	Thiopurines	Pancreatitis





WHAT FACTORS DO YOU CONSIDER WHEN DETERMINING WHICH BIOLOGIC TO USE FIRST LINE?

Does your choice of a biologic for **first line use** affect the efficacy of subsequent therapy?

Does your choice of a biologic for first line use target the **underlying disease pathophysiology**?

How do the **safety profiles** of different biologics influence HCP prescribing and patient choice?

Can a therapy with a specific **mode of action** used first line, impact the efficacy of subsequent treatments?

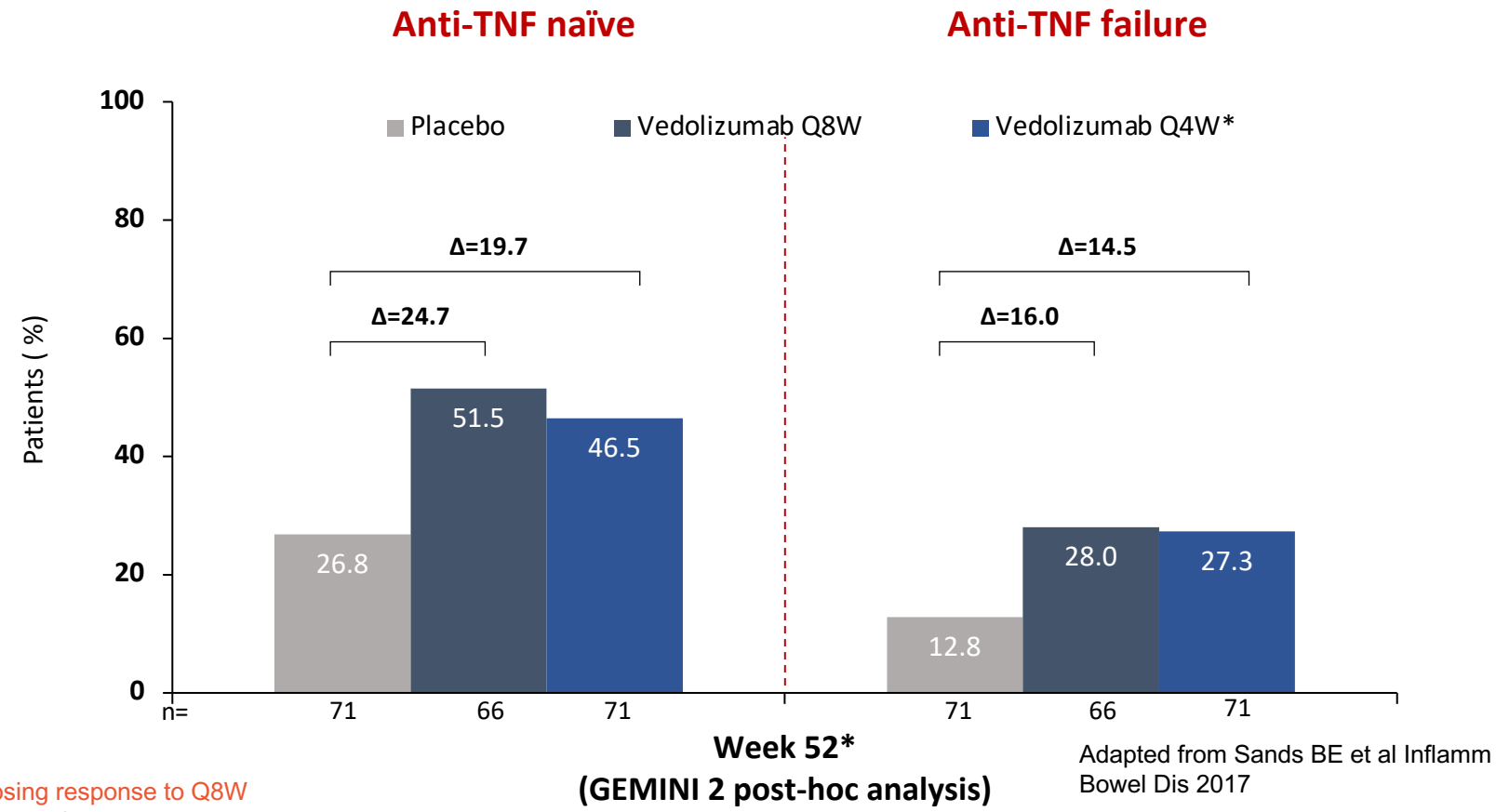
Therefore, does sequencing matter in the **context of a patient's long-term condition and lifelong treatment?**

What impact do **disease duration and disease severity** have on lifelong treatment?

EFFICACY OF VEDOLIZUMAB MAINTENANCE IS ATTENUATED FOLLOWING PRIOR USE OF ANTI-TNF

Crohn's disease

Clinical remission



Adapted from Sands BE et al Inflamm Bowel Dis 2017

*Q4W is approved for patients losing response to Q8W

*Week 52 in Week 6 CDAI 70 responders

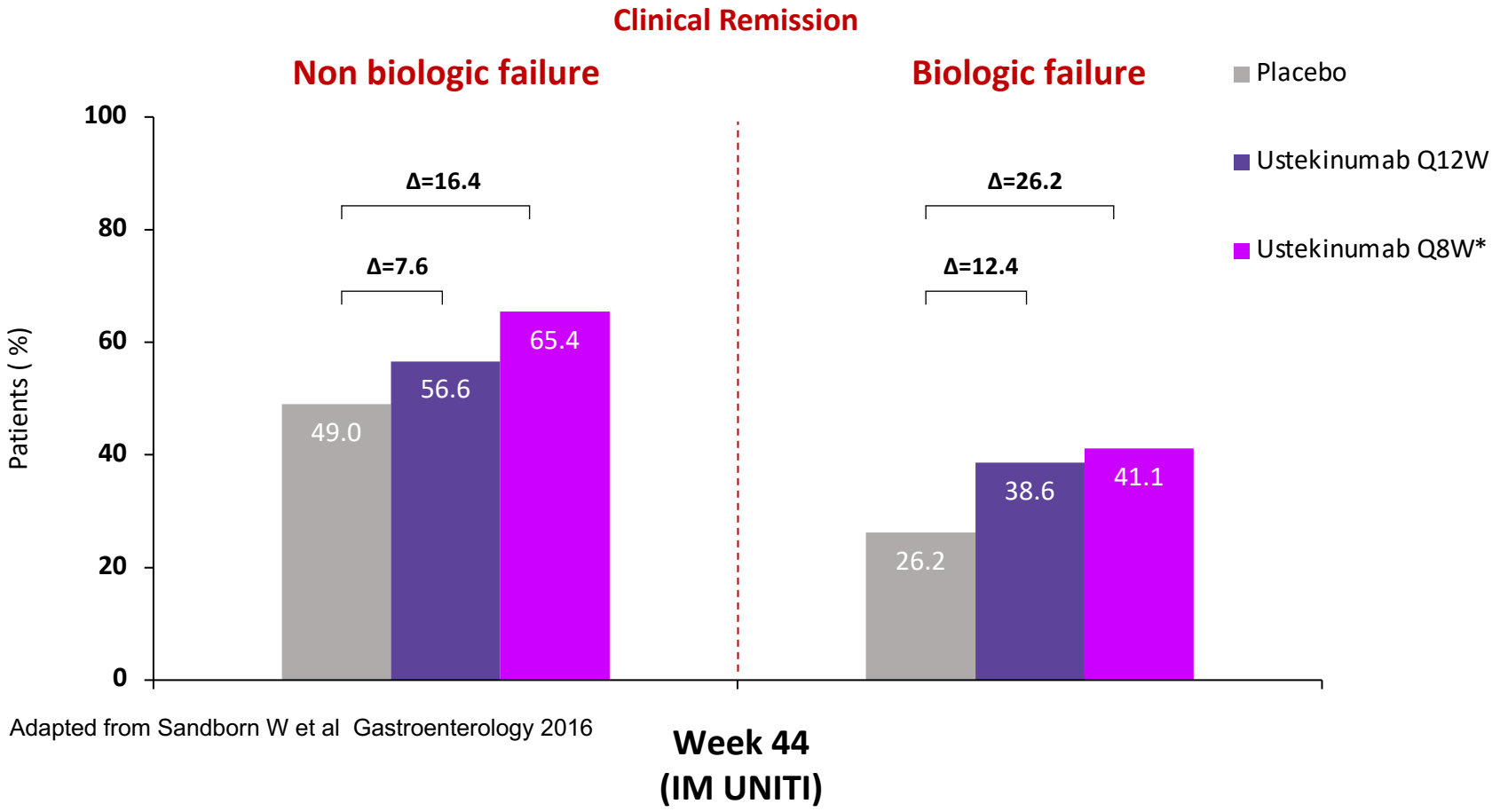
Clinical remission: Crohn's Disease Activity Index ≤150.

TNF: tumour necrosis factor therapy; Q4W, every 4 weeks; Q8W, every 8 weeks; CDAI: Crohn's Disease Activity Index

Sands BE, et al. Inflamm Bowel Dis. 2017;1:97-106 (supplementary appendix)

USTEKINUMAB EFFICACY AS MAINTENANCE THERAPY IN CROHN'S DISEASE

Crohn's disease



Adapted from Sandborn W et al Gastroenterology 2016

*Q8W is approved for patients losing response to Q12W

Clinical remission: Crohn's Disease Activity Index (CDAI) score <150 points;

CDAI-100 response: ≥100-point decrease in CDAI score TNF: tumour necrosis factor therapy; Q8W, every 8 weeks, Q12W, every 12 weeks

Sandborn W, et al. Gastroenterology. 2016;150 (4 Suppl):S157-158 (Abstract 768)

Received: 17 October 2019 | First decision: 15 November 2019 | Accepted: 10 March 2020
DOI: 10.1111/apt.15706
APT Alimentary Pharmacology & Therapeutics WILEY

The effectiveness of either ustekinumab or vedolizumab in 239 patients with Crohn's disease refractory to anti-tumour necrosis factor

Hadrien Alric[1] | Aurélien Amiot[2] | Julien Kirchgesner[3] | Xavier Tréton[4] | Matthieu Allez[5] | Yoram Bouhnik[4] | Laurent Beaugerie[3] | Franck Carbonnel[1] | Antoine Meyer[1]

Received: 10 February 2021 | First decision: 28 February 2021 | Accepted: 5 April 2021
DOI: 10.1111/apt.16377
APT Alimentary Pharmacology & Therapeutics WILEY

Comparison of short- and long-term effectiveness between ustekinumab and vedolizumab in patients with Crohn's disease refractory to anti-tumour necrosis factor therapy

Luc Manlay[1] | Gilles Boschetti[2] | Bruno Pereira[3] | Bernard Flourié[2] | Michel Dapoigny[1] | Maud Reymond[1] | Elisa Sollelis[1] | Claire Gay[2] | Mathilde Boube[1] | Anthony Buisson[1,4] | Stéphane Nancey[2]

Received: 8 April 2020 | First decision: 30 April 2020 | Accepted: 3 August 2020
DOI: 10.1111/apt.16057
APT Alimentary Pharmacology & Therapeutics WILEY

Comparative effectiveness of ustekinumab or vedolizumab after one year in 130 patients with anti-TNF-refractory Crohn's disease

Tristan Townsend[1] | Violeta Razanskaite[2] | Susanna Dodd[3] | Daniel Storey[1] | Stephanie Michail[1] | James Morgan[1] | Michael Davies[1] | Douglas Penman[4] | Christopher Watters[4] | Mira Swaminathan[5] | Joseph Sabine[4] | Adam Chapman[2] | Philip J Smith[1] | Paul K. Flanagan[4] | Ian Reilly[5] | Keith Bodger[3] | Sreedhar Subramanian[1]

Received: 9 January 2020 | First decision: 17 February 2020 | Accepted: 2 April 2020
DOI: 10.1111/apt.15745
APT Alimentary Pharmacology & Therapeutics WILEY

Ustekinumab is associated with superior effectiveness outcomes compared to vedolizumab in Crohn's disease patients with prior failure to anti-TNF treatment

Vince B. C. Biemans[1,2] | C. Janneke van der Woude[3] | Gerard Dijkstra[4] | Andrea E. van der Meulen-de Jong[5] | Mark Löwenberg[6] | Nanne K. de Boer[7] | Bas Oldenburg[8] | Nidhi Srivastava[9] | Jeroen M. Jansen[10] | Alexander G. L. Bodelier[11] | Rachel L. West[12] | Annemarie C. de Vries[3] | Jeoffrey J. L. Haans[2] | Dirk de Jong[1] | Frank Hoentjen[1] | Marieke J. Pierik[2] | on behalf of the Dutch Initiative on Crohn and Colitis (ICC)

Received: 17 October 2019 | First decision: 15 November 2019 | Accepted: 10 March 2020
DOI: 10.1111/apt.15706

APT Alimentary Pharmacology & Therapeutics WILEY

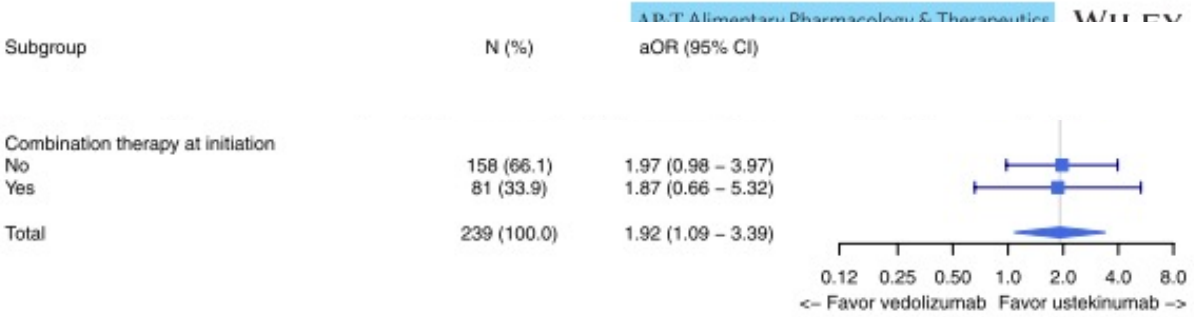
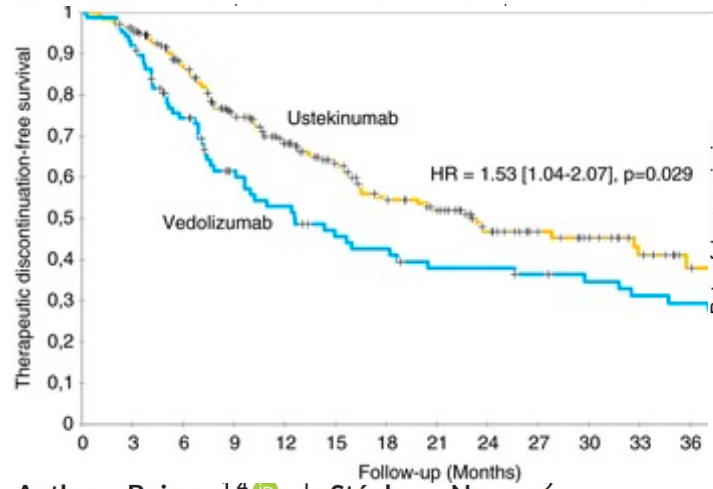
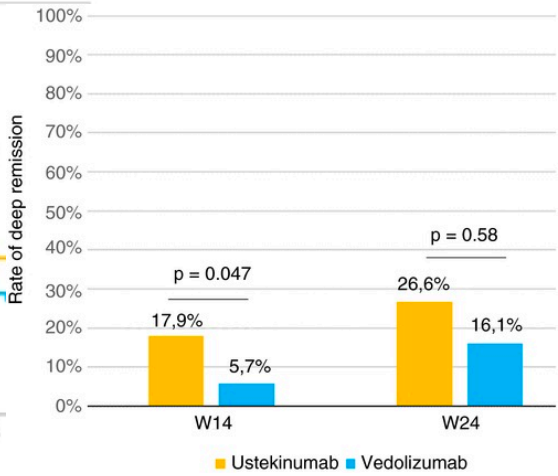


FIGURE 2 Remission rates at week 48 with vedolizumab or ustekinumab in patients Crohn's disease. Values are shown in Forest plot for subgroup analysis

Antoine Meyer[1]





Anthony Buisson[1,4] | Stéphane Nancey[2]

Received: 8 April 2020 | First decision: 30 April 2020 | Accepted: 3 August 2020
DOI: 10.1111/apt.16057

APT Alimentary Pharmacology & Therapeutics WILEY

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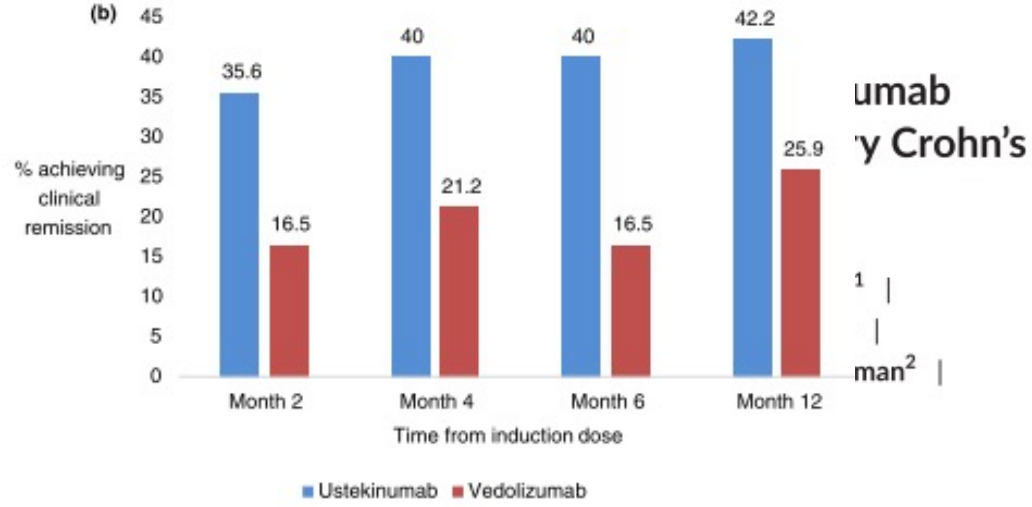

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Tristan To
Stephanie
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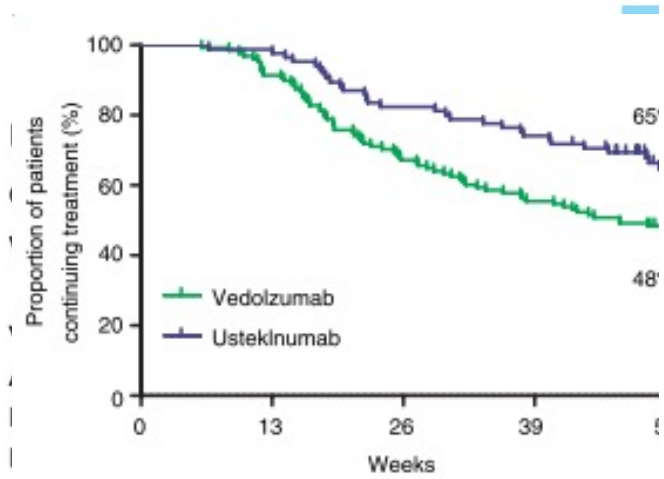
man[2]

Received: 9 January 2020 | First decision: 17 February 2020 | Accepted: 2 April 2020
DOI: 10.1111/apt.15745



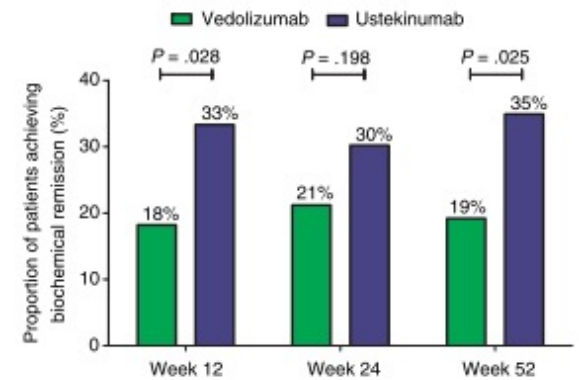
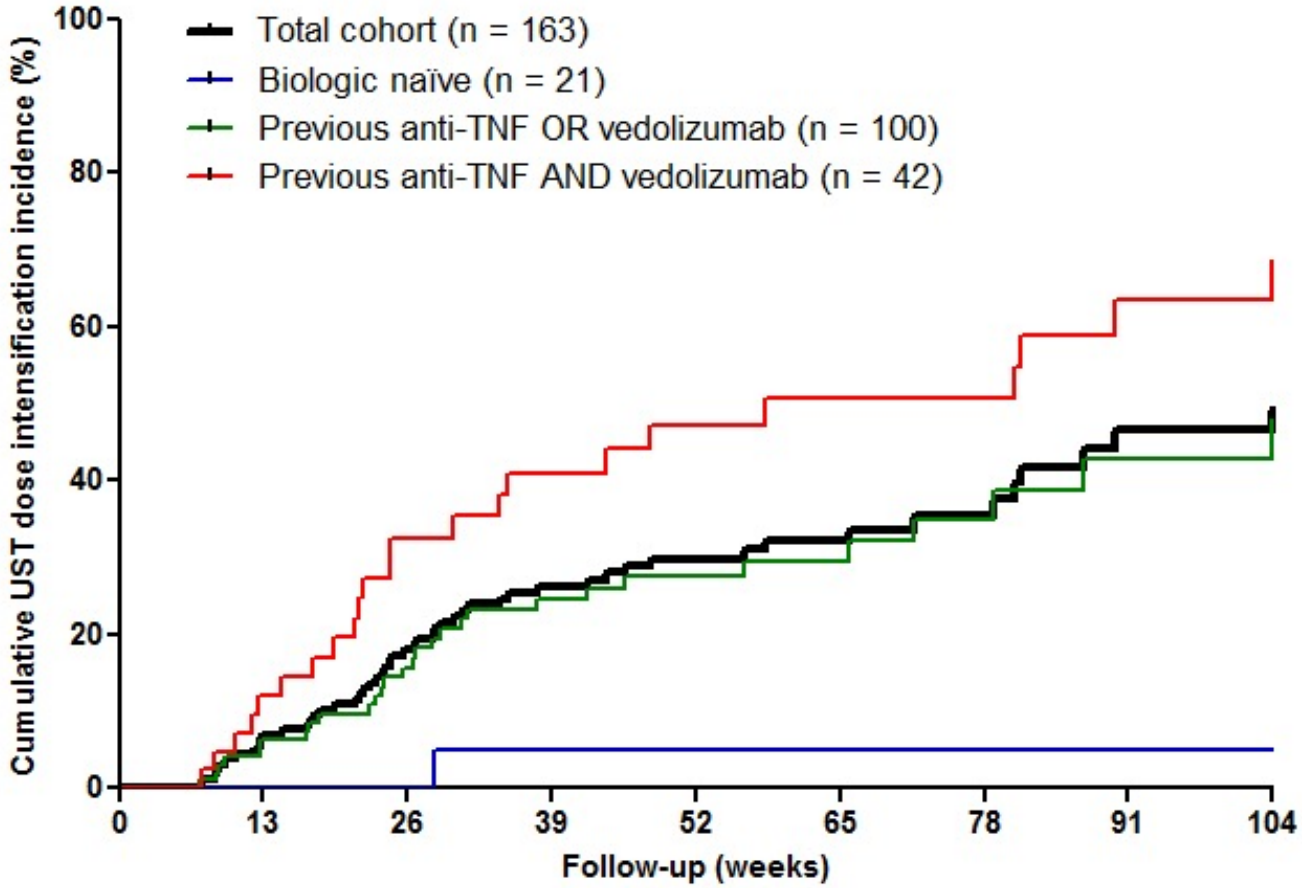


FIGURE 3 Unadjusted proportion of Crohn's disease patients achieving biochemical remission (CRP ≤5 mg/L and faecal calprotectin ≤250 μg/g). CRP, C-reactive protein

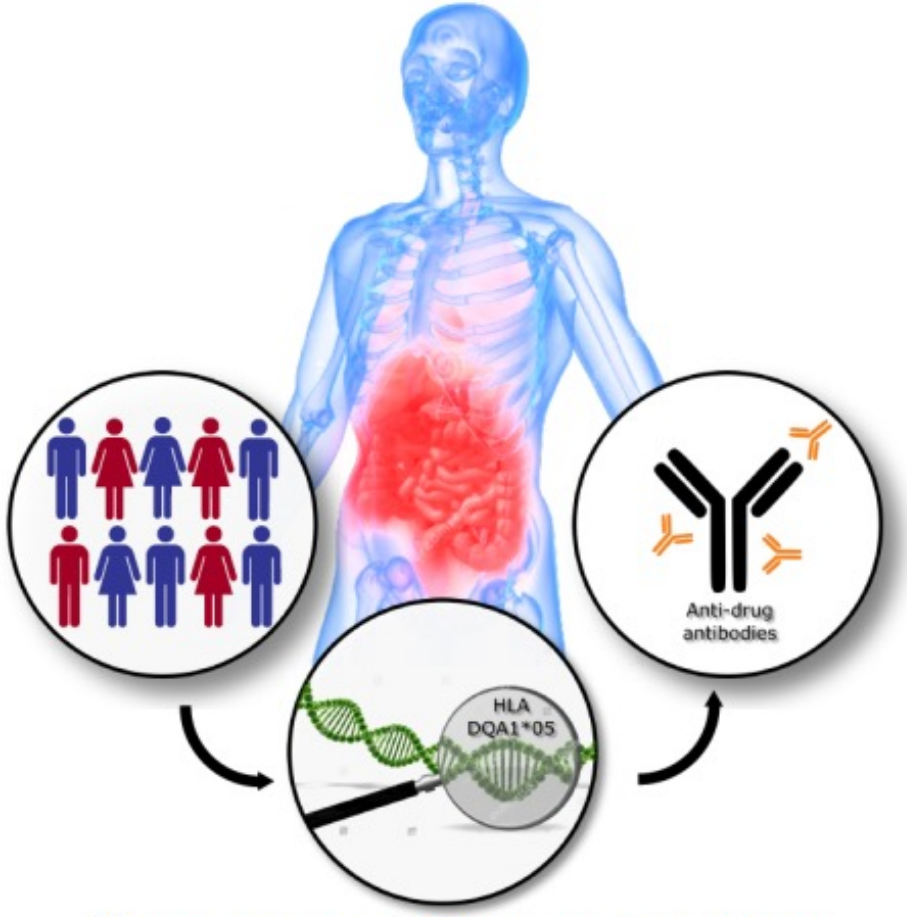
Frank Hoentjen[1] | Marieke J. Pierik[2] | on behalf of the Dutch Initiative on Crohn and Colitis (ICC)

Edinburgh IBD Unit ustekinumab audit in Crohn's disease
USTE dose intensification over time *(*unpublished data)*



HLA-DQA1*05 testing might help select anti-TNF and combination immunomodulator therapies.

		Immunomodulator status	
		Appropriate and tolerated	Contraindicated *or* not tolerated
DQA1*05	Pos	**IFX combo ADAL combo**	**Avoid anti-TNF**
	Neg	**IFX combo ADAL combo /** ?mono	**ADAL mono**



Sasonovs et al Gastroenterology. 2019 Oct 7. pii: S0016-5085(19)41414-5. doi: 10.1053/j.gastro.2019.09.041. [Epub ahead of print]

Therapeutic targets in IBD

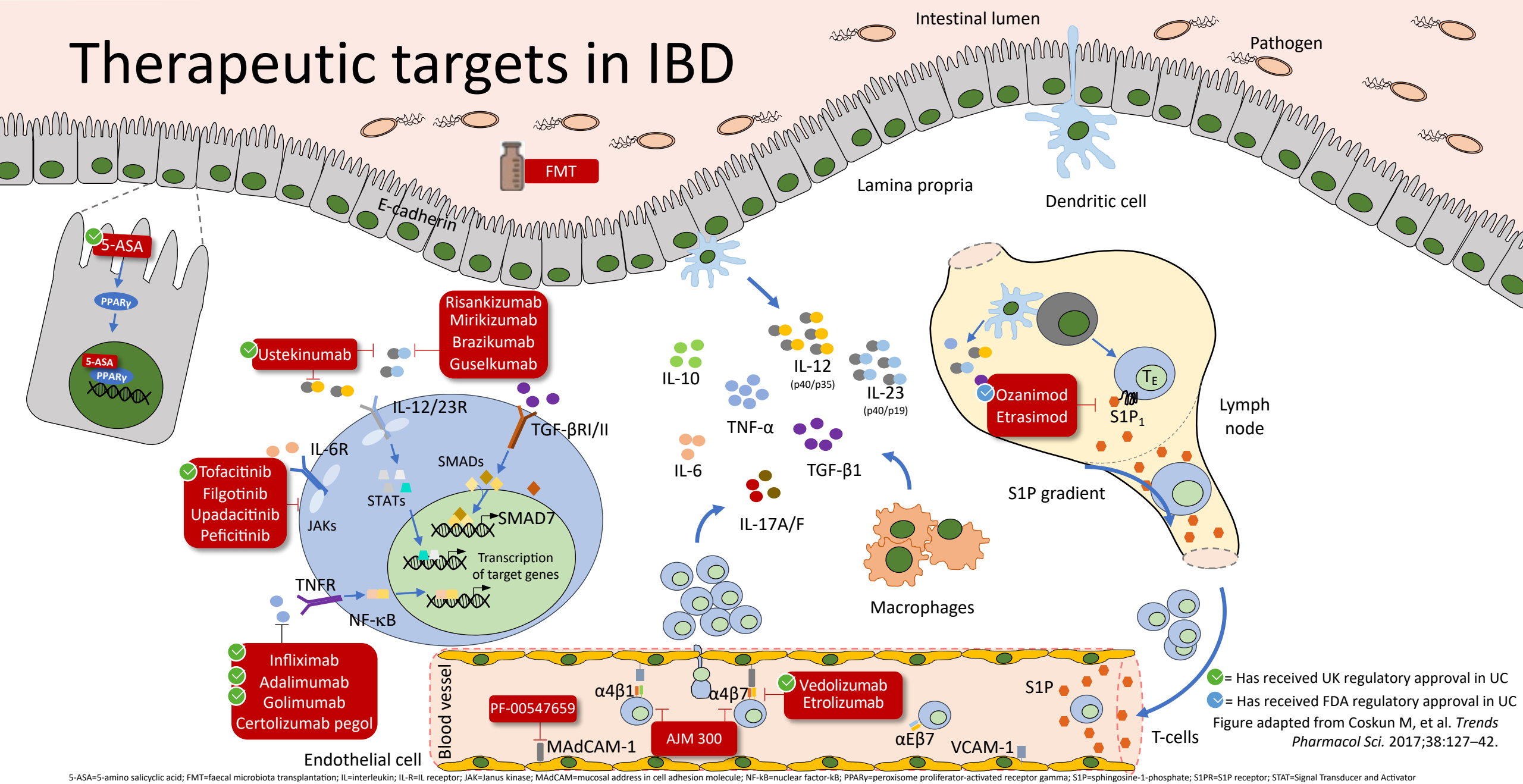


Figure adapted from Coskun M, et al. *Trends Pharmacol Sci.* 2017;38:127–42.

5-ASA=5-amino salicyclic acid; FMT=faecal microbiota transplantation; IL=interleukin; IL-R=IL receptor; JAK=Janus kinase; MAdCAM=mucosal address in cell adhesion molecule; NF-kB=nuclear factor-kB; PPARγ=peroxisome proliferator-activated receptor gamma; S1P=sphingosine-1-phosphate; S1PR=S1P receptor; STAT=Signal Transducer and Activator of Transcription; Tε=effector T-cell; TGF-b=Transforming Growth Factor-b; TGF-bR=TGF-b receptor; TNF-α=Tumour Necrosis Factor alpha; TNFR=TNF receptor; VCAM=Vascular Cell Adhesion Molecule

1. Coskun M, et al. Trends Pharmacol Sci. 2017;38:127–42; **2.** NICE, Ulcerative colitis: management [NG130]. 2019. https://www.nice.org.uk/guidance/ng130/chapter/Recommendations#maintaining-remission-in-people-with-ulcerative-colitis. Accessed 26 July 2021. **3.** NICE, Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy [TA329]. 2015. http://www.nice.org.uk/guidance/TA329. Accessed 26 July 2021. **4.** NICE, Vedolizumab for treating moderately to severely active ulcerative colitis [TA342]. 2015. http://www.nice.org.uk/guidance/TA342. Accessed 26 July 2021. **5.** NICE, Tofacitinib for moderately to severely active ulcerative colitis. [TA547]. 2018. http://www.nice.org.uk/guidance/TA547. Accessed 26 July 2021. **6.** NICE, Ustekinumab for treating moderately to severely active ulcerative colitis. [TA633]. 2020. http://www.nice.org.uk/guidance/TA633. Accessed 26 July 2021. **7.** Ozanimod pharmaceutical information. Available at https://www.sps.nhs.uk/medicines/ozanimod/ Accessed 21 July 2021

Inflammatory bowel disease head-to-head trials

Conventional vs conventional therapy	Mesalazine vs Asacol in UC[1]
	Budesonide-multi-matrix System (MMX™) vs Asacol in UC[2]
	MMX® Mesalamine vs Delayed-release Mesalamine in UC[3]
Biologic vs conventional therapy	SONIC: Infliximab + Azathioprine vs Infliximab vs Azathioprine in CD[4]
	UC-SUCCESS: Infliximab + Azathioprine vs Infliximab vs Azathioprine in UC[5]
Comparison of therapeutic strategies	Top-Down vs Step-Up Strategies in CD: Infliximab + Azathioprine vs Methylprednisolone or Budesonide[6]
	REACT: Treatment Algorithm vs Usual Care for Management of CD[7]
	CALM: Tight Control vs Clinical Management Algorithm in CD[8]
Biologic vs biosimilar	NOR-SWITCH and 3.4: Originator Infliximab vs Biosimilar CT-P13 in CD[9-10]
Biologic vs biologic	*VARSITY[11] (vedo > ada in UC); SEAVUE[12] (ada = uste in CD)*

1. Kamm MA et al. Gastroenterology. 2007;132:66-75. 2. Sandborn WJ et al. Gastroenterology. 2012;143:1218-26. 3. D'Haens G et al. Am J Gastroenterol. 2012;107:1064-77. 4. Colombel JF et al. N Engl J Med. 2010;362:1383-95. 5. Panaccione R et al. Gastroenterology. 2014;146:392-400.e3. 6. D'Haens G et al. Lancet. 2008;371:660-7. 7. Khanna R et al. Lancet. 2015;386:1825-34. 8. Colombel JF et al. Lancet. 2017;390:2779-89. 9. Jørgensen KK et al. Lancet. 2017;389:2304-16. 10. Ye BD et al. Lancet 2019;393:1699-1707. 11. Sands B et al. NEJM 2019;381:1215-26. 12. Sand BE. DDW 2021

Infliximab, Azathioprine, or Combination Therapy for Crohn's Disease

2010. SONIC

RDBT/ IFX vs AZA vs IFX+AZA/ Mod-Sev CD/ Remission

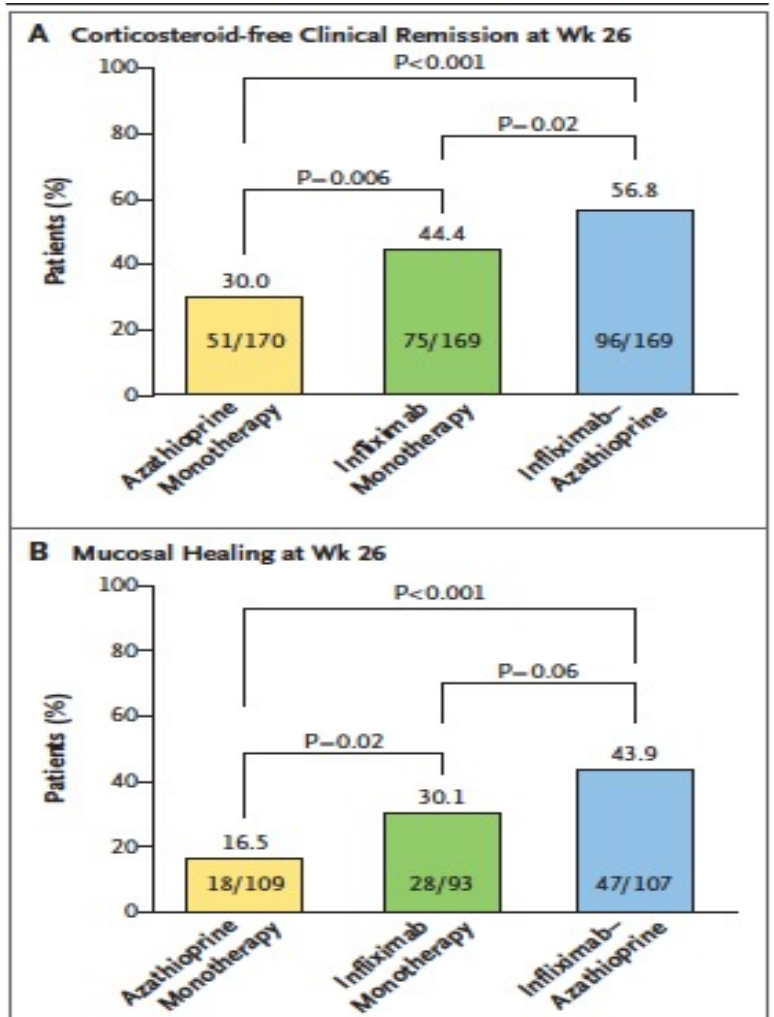


Figure 2. Patients with Corticosteroid-free Clinical Remission (Panel A) and Mucosal Healing (Panel B) at Week 26.

Primary end point: corticosteroid-free clinical remission at w26;
Secondary end points: mucosal healing w26, rate of any remission,response-70, response-100, IBDQ score, steroid dose, CRP level from baseline to w26.

Steroid free remission w26: 56.8% combo vs 44.4% IFX alone vs 30% AZA; p=0.006/ p<0.001
Mucosal healing w26: combo 43.9% vs 30.1% IFX alone vs 16.5% AZA; p=0.02/p<0.001
Antibodies w30: 0.9% combo vs 14.6% IFX; p<0.001
No differences in serious infections.

Conclusion: Patients with moderate to severe active CD treated with IFX+ AZA or IFX monotherapy were more likely to have steroid free remission than AZA alone. Combotherapy superior to both monotherapies.

6. Colombel JF et al. N Eng J Med 2010; 362:1383-1395

2008. SUTD

Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn's disease: an open randomised trial

OL/ conventional vs IFX+AZA/ New CD/ Remission

Primary outcome: free steroid remission (CDAI<150) without surgery need w26 and 52.
Secondary: time to relapse, mean CDAI and IBDQ scores; mean CRP and endoscopic severity scores.

Remission without surgery w26: 60% E-combo vs 35.9% conventional; p=0.006.
Remission without surgery w54: 61.5% E-combo vs 42.2% conventional ; p=0.028.
No differences in serious adverse events related to treatment.

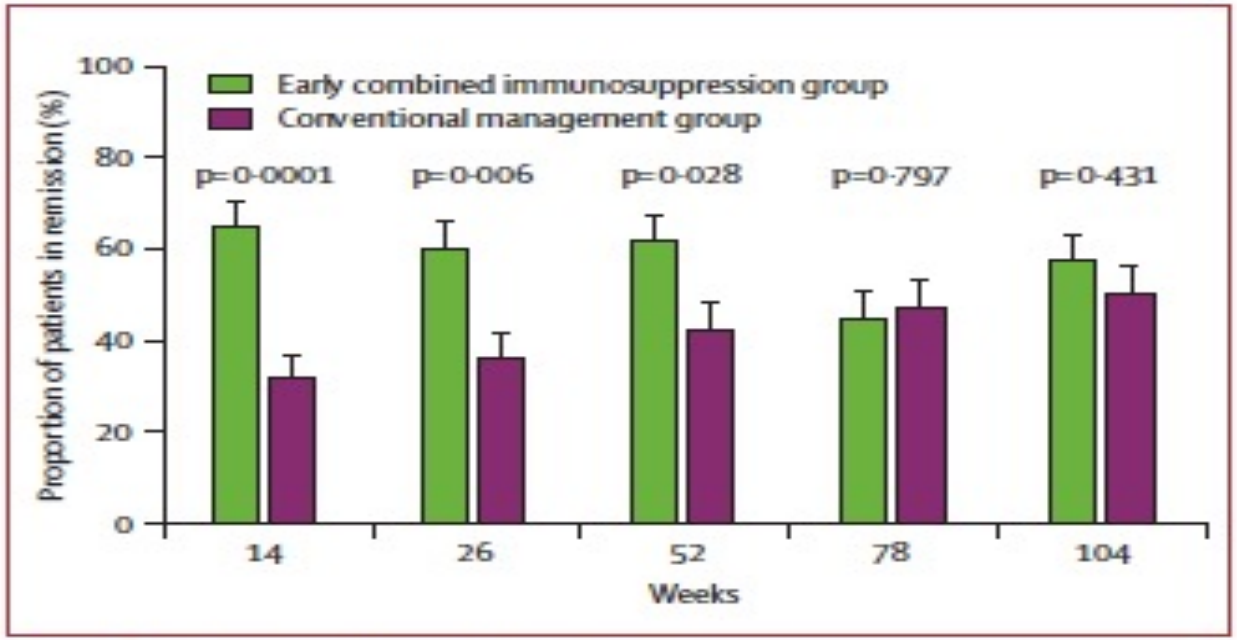


Figure 2: **Proportions of patients in remission**

Conclusions: Combined therapy more effective than conventional for induction and reduction of steroid use in recently diagnosed CD.

5. D'Haens et al. Lancet 2008; 371: 660-67

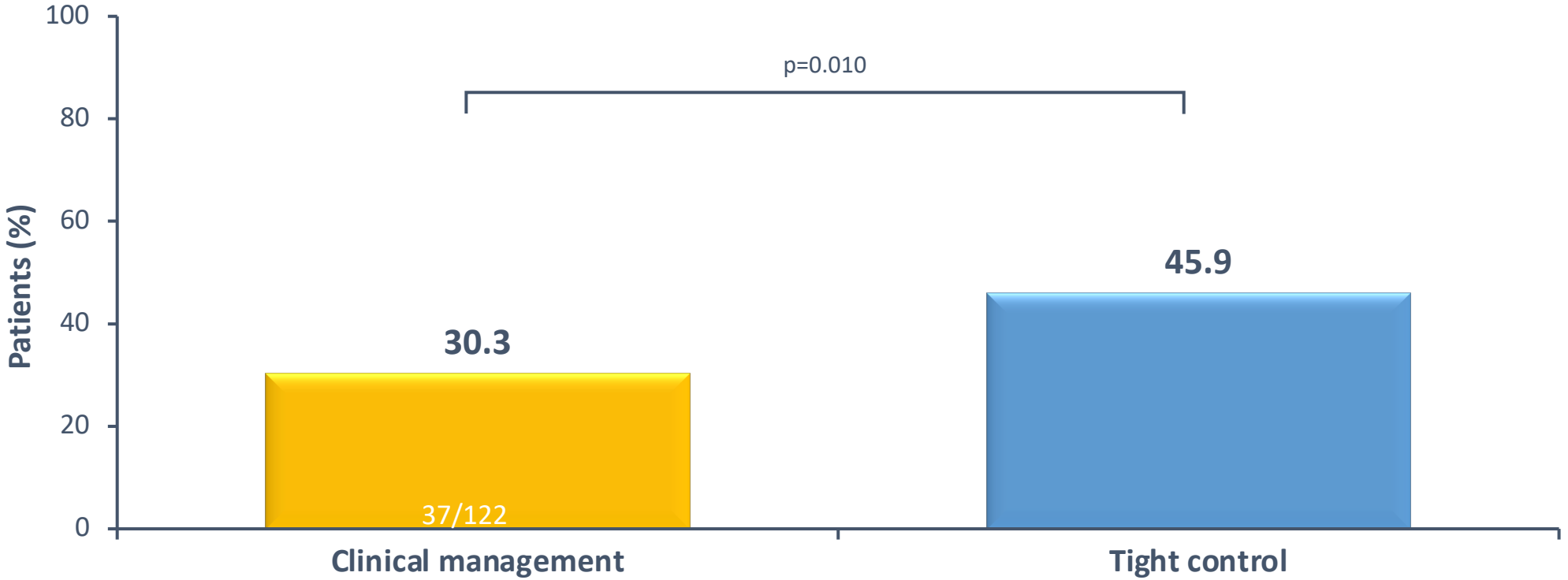
CALM: Evidence for the success of treating to target in IBD

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

Colombel JF, et al. *Lancet 2018*

CALM: Primary endpoint at Week 48

Tight control resulted in significantly more patients achieving **mucosal healing (CDEIS <4) with no deep ulcerations** than clinical management



FCP (≥250 µg/g) **was the most frequent failure criterion driving treatment optimization in the tight-control group**

Colombel JF, et al. *Lancet* 2018

SEAVUE: A phase 3b, multicentre, randomised, blinded, head-to-head trial[1]

SEAVUE

AIM: To compare the efficacy and safety of ***Stelara® to that of adalimumab*** in the treatment of ***biologic-naïve patients with moderately-to-severely active CD***

1. Primary outcome measure:

- Percentage of Participants with **Clinical Remission (CDAI score <150)** at Week 52

2. Major secondary outcome measures:

- Percentage of Participants with **Corticosteroid-free Remission** at Week 52
- Percentage of Participants with **Clinical Response** at Week 52
- **PRO-2 Symptom Remission** at Week 52
- Percentage of Participants with **Clinical Remission** at Week 16
- Percentage of Participants with **Endoscopic Remission** at Week 52

1. Sands BE, et al. Oral presentation 775d. Digestive Disease Week (DDW) 2021; **2.** Clinicaltrials.gov. NCT03464136. Available at: https://clinicaltrials.gov/ct2/show/NCT03464136 [accessed August 2021].

SEAVUE enrolled biologic-naïve patients with active CD[1,2]

SEAVUE

Key inclusion criteria:

- **Not previously received an approved biologic (including biosimilars) for CD**
- **CD or fistulising CD of ≥3 months duration**, with colitis, ileitis or ileocolitis
- **Moderately-to-severely active CD** (baseline CDAI of ≥220 and ≤450)
- **≥1 ulcerations** (SES-CD of ≥3)
- **Failed or was intolerant to conventional therapy** or is corticosteroid dependent
- **Participants must discontinue** AZA, MP or MTX ≥3 weeks prior to baseline

1. Sands BE, et al. Oral presentation 775d. Digestive Disease Week (DDW) 2021; **2.** Clinicaltrials.gov. NCT03464136. Available at: https://clinicaltrials.gov/ct2/show/NCT03464136 [accessed August 2021].

MP: mercaptopurine; AZA: azathioprine; CD: Crohn's disease; CDAI: Crohn's disease activity index; MTX: methotrexate; SES-CD: simple endoscopic score for Crohn's disease.

SEAVUE: Study design[1]

SEAVUE

The citrate-free 40 mg/0.4 mL ADA formulation was used[1]

Treat-through study design

Dosing as per US prescribing information (in line with SmPCs)[2,3]
Monotherapy (no IMMs)

Randomisation (n=386)

Week 0	Week 2	Week 4	Week 8	Week 52	Week 56	Week 76
Stelara® ~6 mg/kg* IV + 4 PBO SC injections	2 PBO SC injections	1 PBO SC injection	Stelara® 90 mg SC q8w† + 1 PBO SC injection q2w			
ADA 160 mg SC + PBO IV	ADA 80 mg SC	ADA 40 mg SC q2w				

Corticosteroid tapering, if applicable, to begin at Weeks 8 or 16

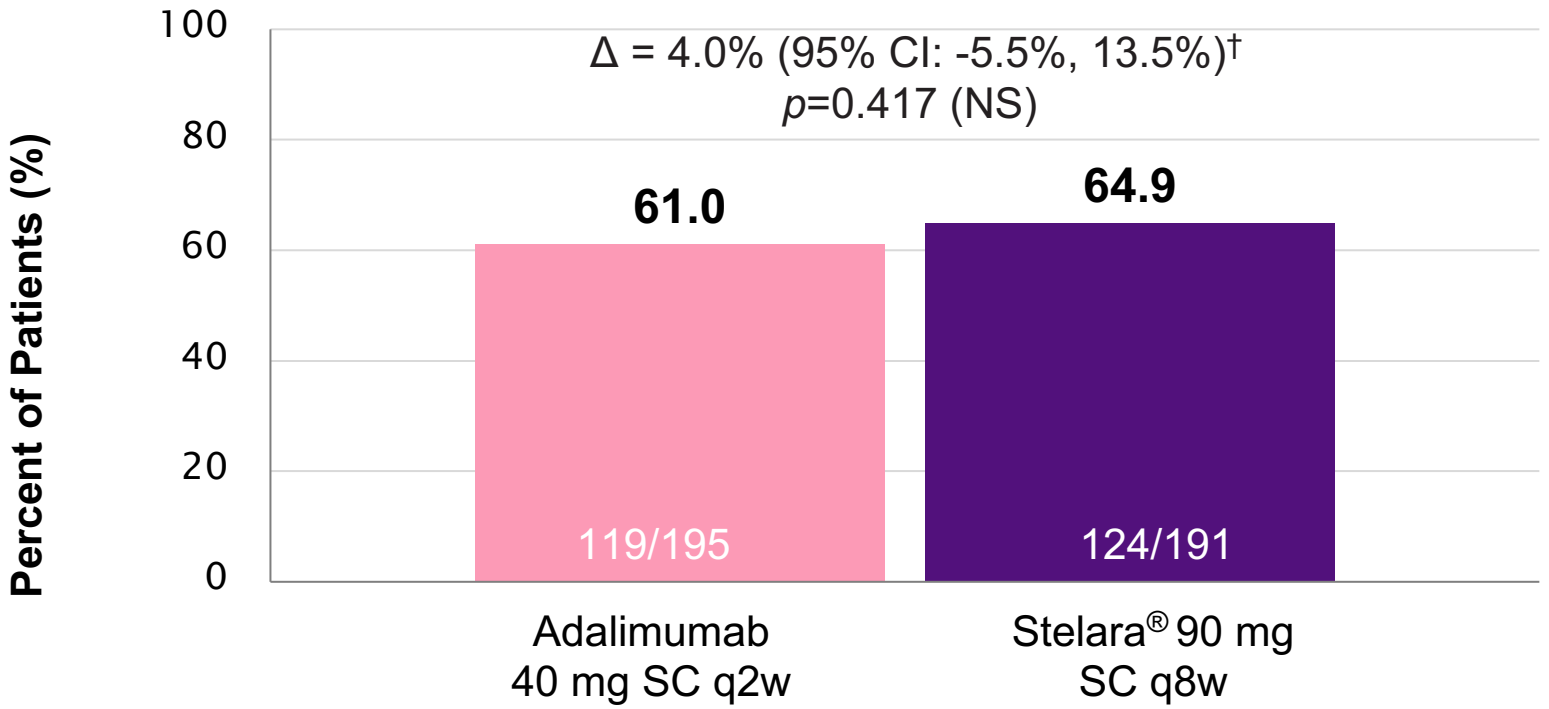
Study visits q8w

PRIMARY ENDPOINT

1. Sands BE, et al. Oral presentation 775d. Digestive Disease Week (DDW) 2021; **2.** Stelara® SmPC. Available at: https://www.medicines.org.uk/emc [accessed August 2021];
3. Humira® SmPC. Available at: https://www.medicines.org.uk/emc [accessed August 2021].

PRIMARY ENDPOINT
Clinical remission* at Week 52 (CDAI <150)

SEAVUE



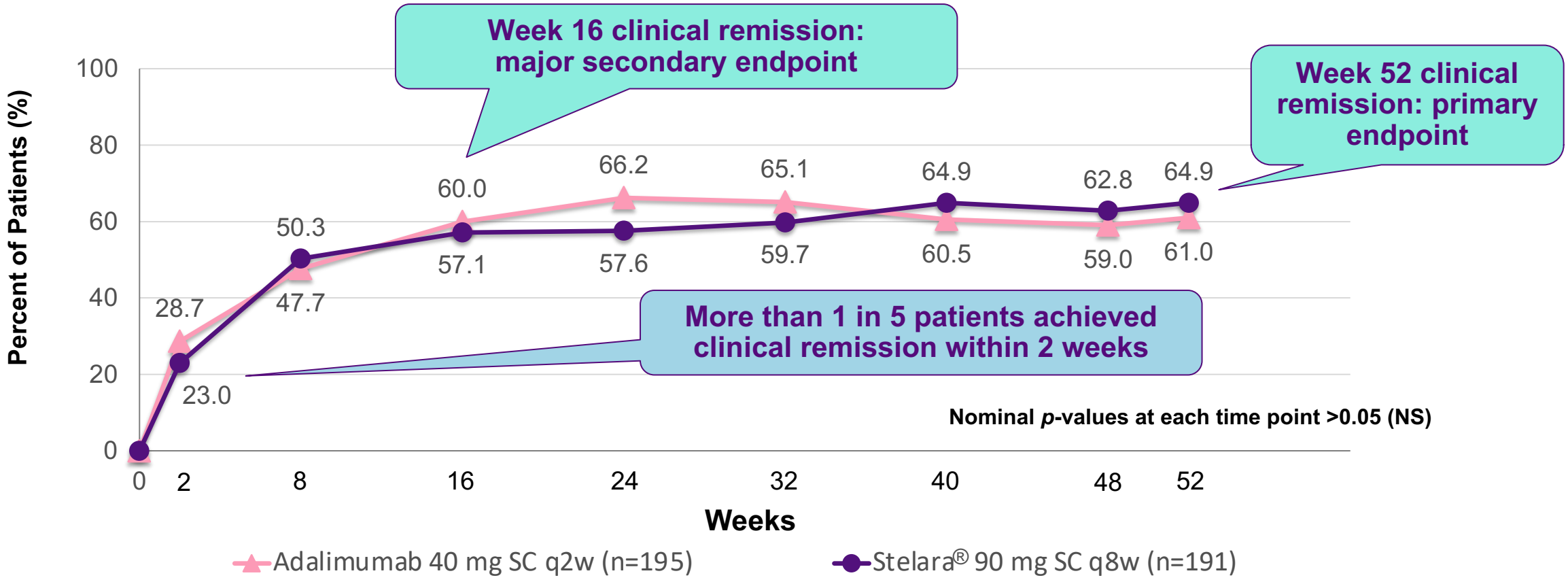
*Patients who had a prohibited CD-related surgery, had prohibited concomitant medication changes, or discontinued study agent due to lack of efficacy or due to an AE indicated to be of worsening CD prior to the designated analysis timepoint are considered not to be in clinical remission, regardless of their CDAI score. Patients who had insufficient data to calculate the CDAI score at the designated analysis timepoint are considered not to be in clinical remission. †The confidence intervals were based on the Wald statistic with Mantel-Haenszel weight.

Sands BE, et al. Oral presentation 775d. Digestive Disease Week (DDW) 2021.

AE: adverse event; CD: Crohn's disease; CDAI: Crohn's disease activity index; CI: confidence interval; NS: not statistically significant; q2w: every 2 weeks; q8w: every 8 weeks; SC: subcutaneous.

Clinical remission* through Week 52 (CDAI <

SEAVUE



*Patients who had a prohibited CD-related surgery, had prohibited concomitant medication changes, or discontinued study agent due to lack of efficacy or due to an AE indicated to be of worsening CD prior to the designated analysis timepoint are considered not to be in clinical remission, regardless of their CDAI score. Patients who had insufficient data to calculate the CDAI score at the designated analysis timepoint are considered not to be in clinical remission.

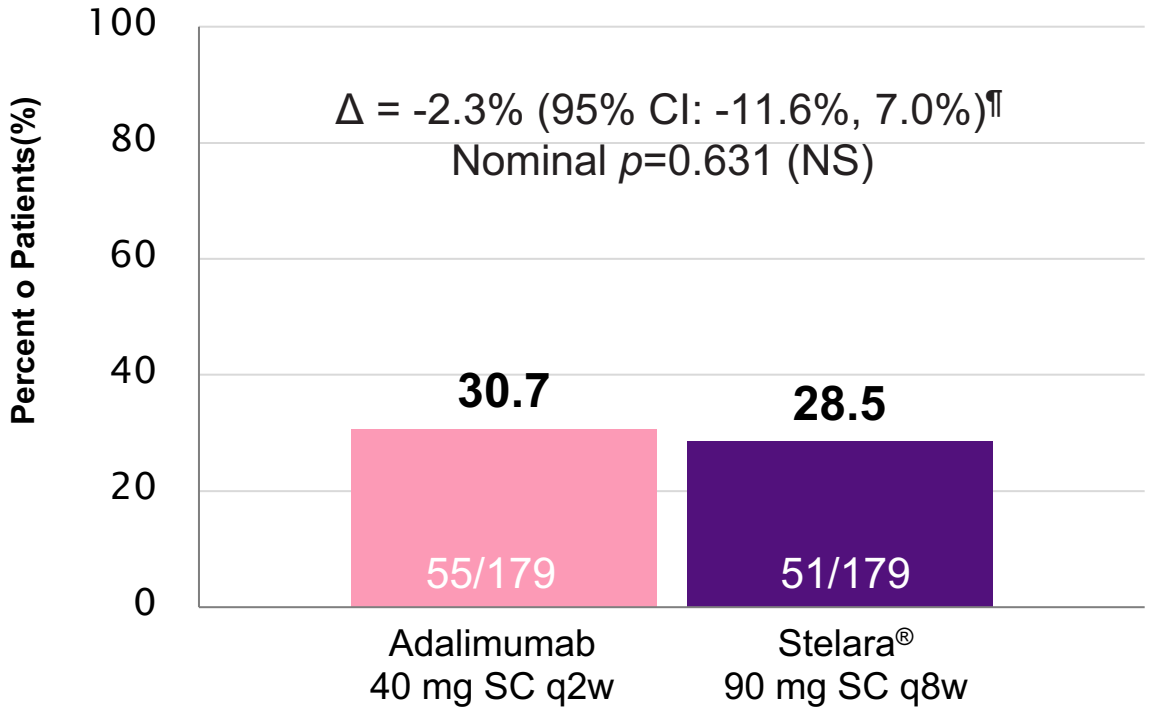
Sands BE, et al. Oral presentation 775d. Digestive Disease Week (DDW) 2021.

AE: adverse event; CD: Crohn's disease; CDAI: Crohn's disease activity index; NS: not statistically significant; q2w: every 2 weeks; q8w: every 8 weeks; SC: subcutaneous.

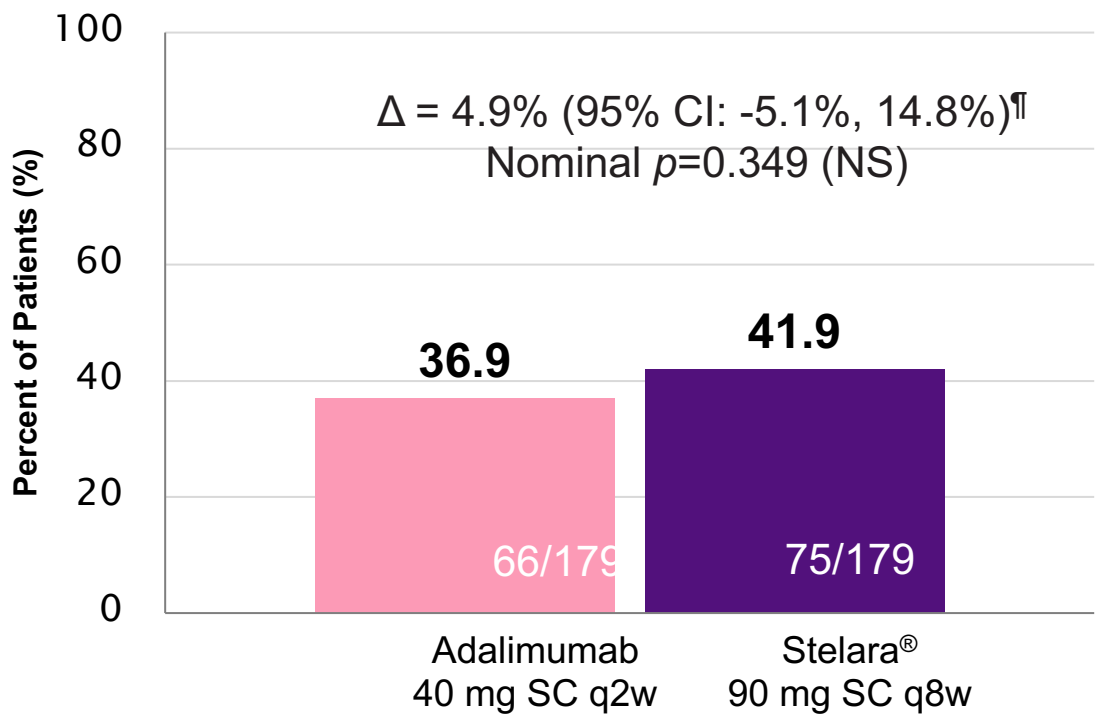
Endoscopic remission* and response† at Week 52

SEAVUE

Major Secondary Endpoint: Endoscopic remission‡,§



Major Secondary Endpoint: Endoscopic response‡,§



Adapted from Sands BE, et al. 2021

*Endoscopic remission defined as SES-CD ≤3 or SES-CD=0 for patients who entered the study with an SES-CD=3. Evaluated in patients with SES-CD ≥3 at baseline. †Endoscopic response defined as reduction in SES-CD by 50% from baseline or SES-CD ≤3 or SES-CD =0 for patients who enter the study with an SES-CD =3. ‡Patients who had a prohibited CD-related surgery, had prohibited concomitant medication changes, or discontinued study agent due to lack of efficacy or due to an AE indicated to be of worsening CD prior to the designated analysis timepoint are considered not to be in endoscopic remission/response, regardless of their SES-CD score. §Patients who had insufficient data to calculate the SES-CD score at the designated analysis timepoint are considered not to be in endoscopic remission/response. ¶The confidence intervals were based on the Wald statistic with Mantel-Haenszel weight. Sands BE, et al. Oral presentation 775d. Digestive Disease Week (DDW) 2021.

AE: adverse event; BL: baseline; CD: Crohn's disease; CI: confidence interval; NS: not statistically significant; q2w: every 2 weeks; q8w: every 8 weeks; SES-CD: simple endoscopic score for Crohn's disease.

ULCERATIVE COLITIS

The number of biologic prescriptions for patients with UC has increased

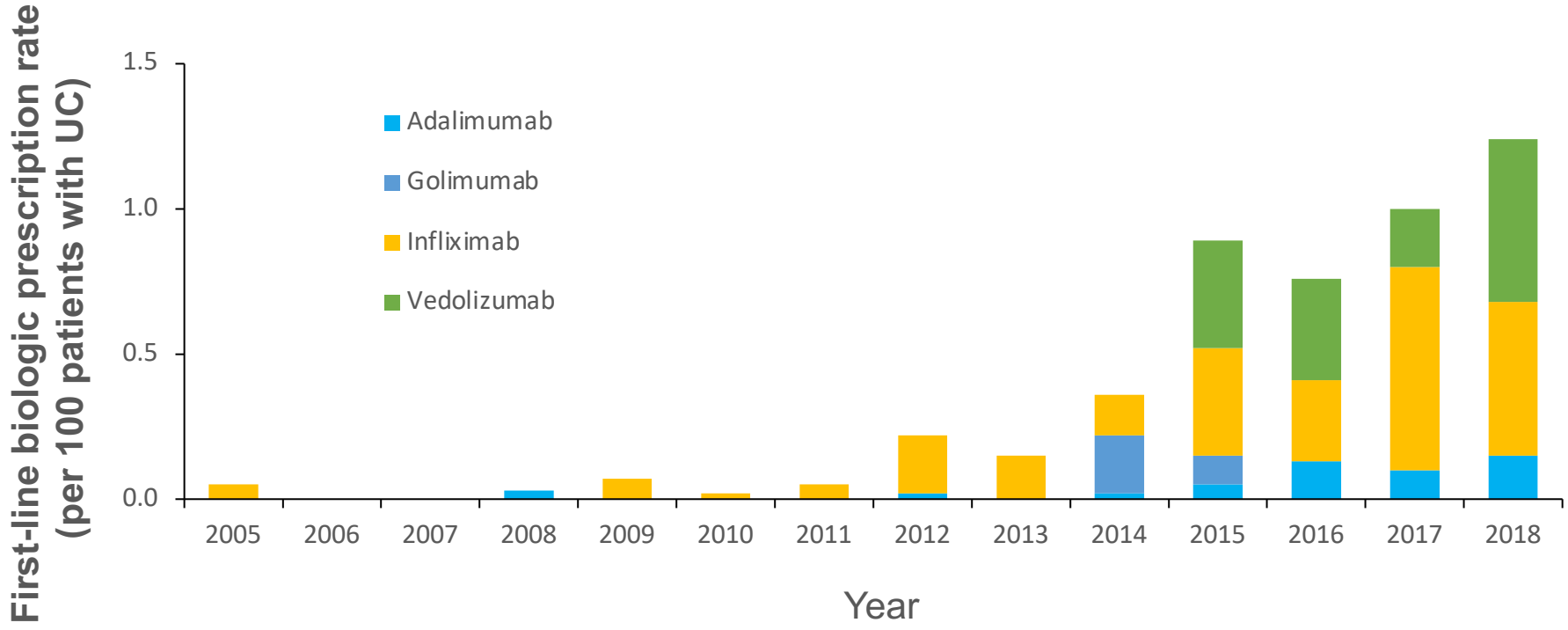


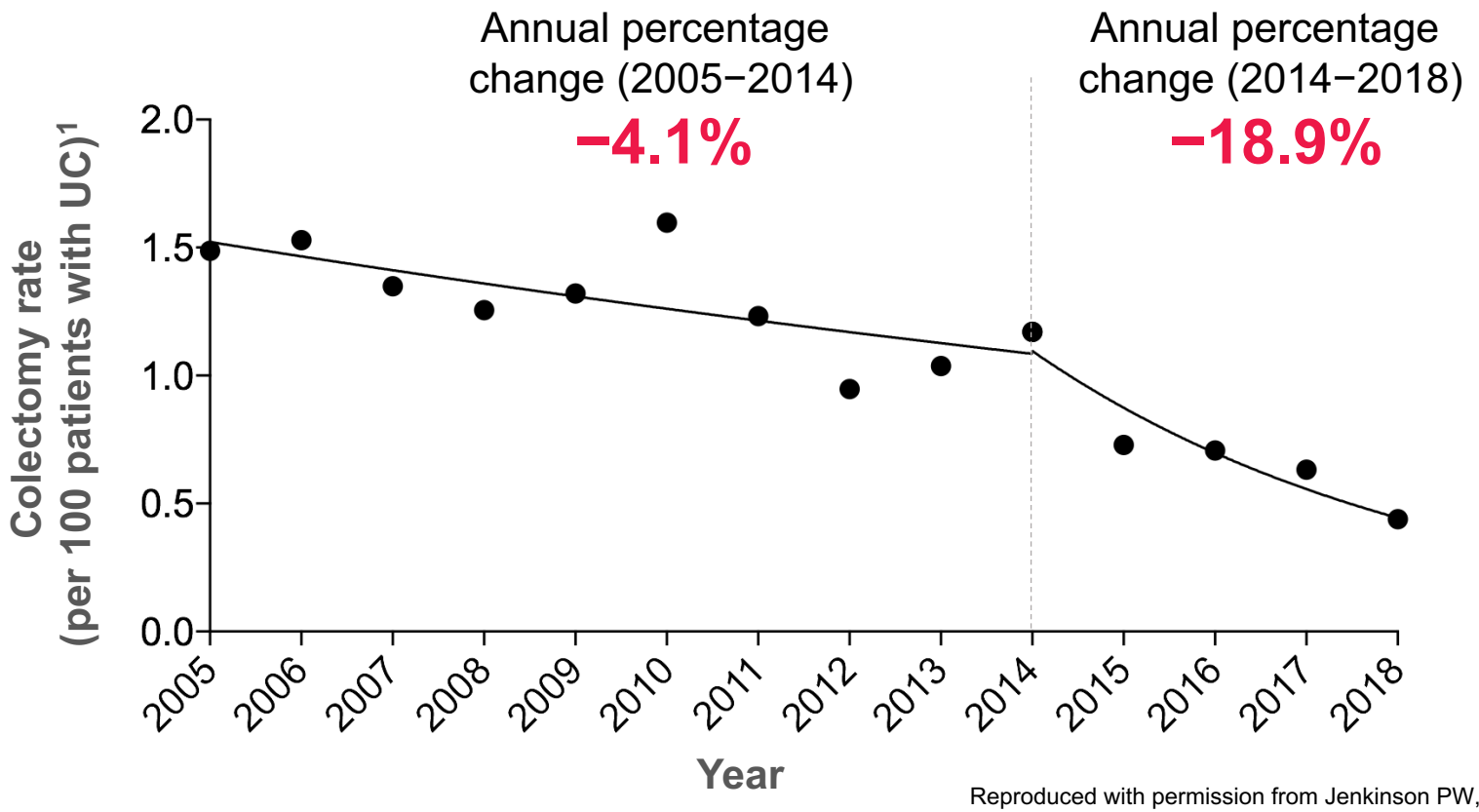
Figure adapted with permission from Jenkinson PW, et al. 2020.

- Joinpoints identified at 2012 and 2015
- 30% annual percentage change over the entire study period

UC=ulcerative colitis.

Jenkinson PW, et al. *Colorectal Dis*. 2020. doi: 10.1111/codi.15491.

Proportion of patients with uc undergoing colectomy has fallen since 2005



Reproduced with permission from Jenkinson PW, et al. 2020.[1]

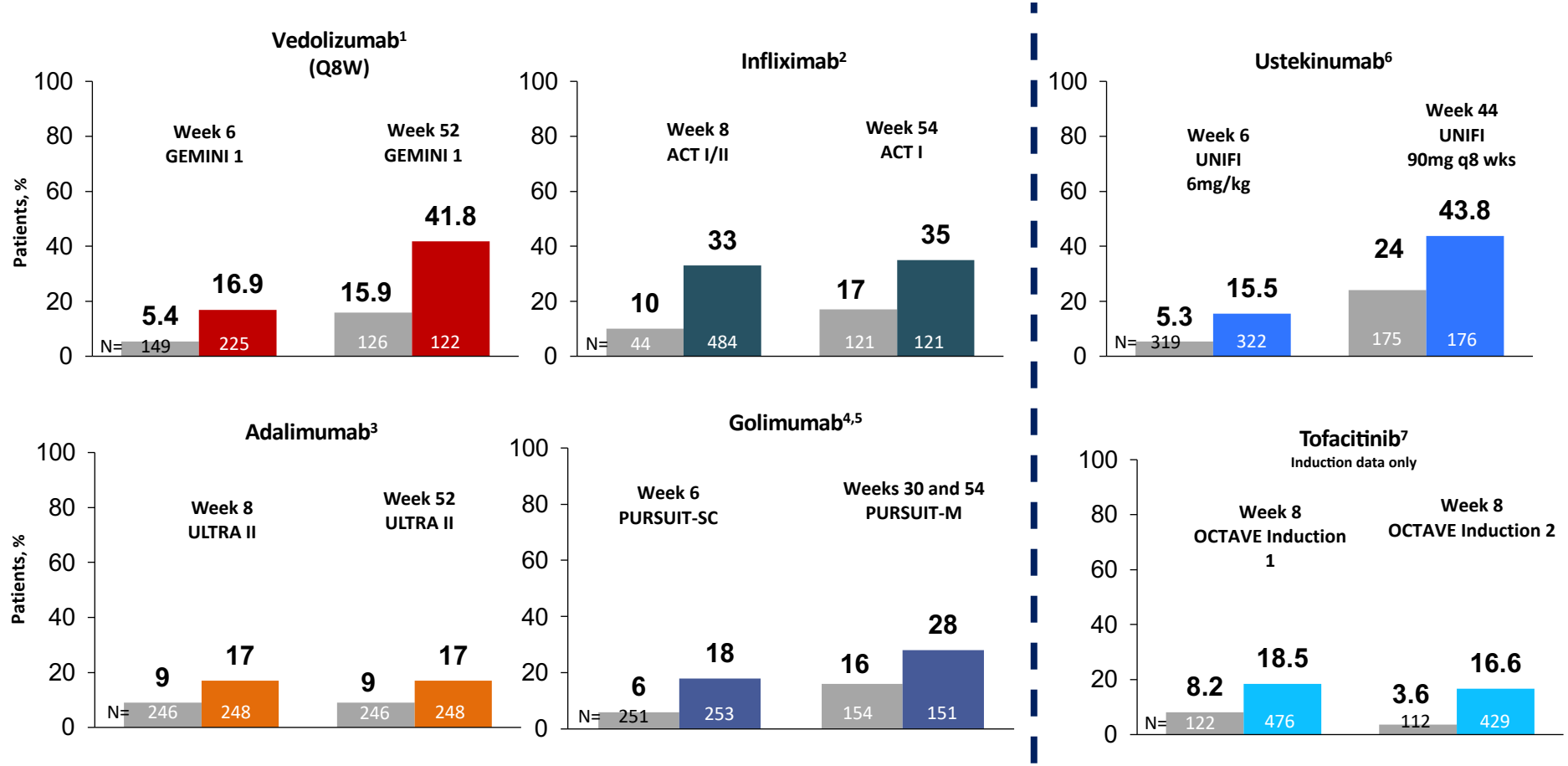
Many factors have contributed to this reduction in colectomy incidence, including an increasing number of treatment options[2]

- Joinpoint identified at 2014; *P*=0.019
- Significant increase in the rate of change of colectomy after 2014

UC=ulcerative colitis.

1. Jenkinson PW, et al. *Colorectal Dis*. 2020. doi: 10.1111/codi.15491. **2**. Worley G, et al. *Aliment Pharmacol Ther*. 2020. doi: 10.1111/apt.16202.

TARGETED THERAPIES: CLINICAL REMISSION* IN UC



Grey bar, placebo; other colors, active treatments. *Clinical remission was defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point, except for tofacitinib studies, in which clinical remission was defined as total Mayo score ≤2; no subscore >1; rectal bleeding subscore of 0. 1. Feagan BG et al. N Engl J Med 2013; 369: 699-710. 2. Rutgeerts P, et al. *N Engl J Med.* 2005;353:2462-76. 3. Sandborn WJ, et al. *Gastroenterology.* 2012;142:257-65. 4. Sandborn WJ, et al. Gastroenterology. 2014;146:85-95. 5. Sandborn WJ. *Gastroenterology*. 2014;146:96-109. 6. Sands B, et al. *N Engl J Med.* 2019;381:1201-14.. 7. Sandborn et al. N Engl J Med 2017; 376:1723-1736

UC treatment pathway example

Active UC

1. **Assess severity and extent**
   - Mild: BO 1−3 per day. No systemic symptoms
   - Moderate: BO 4−6 per day without systemic symptoms
   - Severe: BO >6 per day with systemic symptoms

   → If acute UC, admit to hospital and follow ASUC protocol

2. **Optimise 5-ASA therapy**, depending on severity and extent
   Treat active symptoms as per guidance

3. **Assess response** with calprotectin (fCAL) and Mayo score

4. **If patient does not respond**, is steroid-dependent or has received >1 course of steroids in the past 12 months consider the recommended treatment options but also consider surgery

5. Ensure complete screening, counselling and vaccination per local recommendations

Options available

- Thiopurine[1]
- Infliximab plus thiopurine[2]
- Adalimumab[2]
- Golimumab[2]
- Vedolizumab[3]
- Tofacitinib[4]
- Ustekinumab[5]

Diagram adapted from NHS Lothian UC Pathway, courtesy of Prof Charlie Lees.

ASUC=acute severe ulcerative colitis; BO=bowels opened; fCAL=faecal calprotectin; NICE=National Institute for Health and Care Excellence; UC=ulcerative colitis.

1. NICE, Ulcerative colitis: management [NG130]. 2019. https://www.nice.org.uk/guidance/ng130/chapter/Recommendations#maintaining-remission-in-people-with-ulcerative-colitis. Accessed 26 July 2021. **2.** NICE, Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy [TA329]. 2015. http://www.nice.org.uk/guidance/TA329. Accessed 26 July 2021. **3.** NICE, Vedolizumab for treating moderately to severely active ulcerative colitis [TA342]. 2015. http://www.nice.org.uk/guidance/TA342. Accessed 26 July 2021. **4.** NICE, Tofacitinib for moderately to severely active ulcerative colitis. [TA547]. 2018. http://www.nice.org.uk/guidance/TA547. Accessed 26 July 2021. **5.** NICE, Ustekinumab for treating moderately to severely active ulcerative colitis. [TA633]. 2020. http://www.nice.org.uk/guidance/TA633. Accessed 26 July 2021.

Case 2 (1/5): 26yrs female teacher; uC 2013

- Traumatic birth – prolonged neonatal icu admission as a baby
- Grandmother with UC; aunt with Crohn's disease

2013: Initial induction therapy with prednisolone 40mg /day reducing over 8 weeks plus adcal

- Oral and topical 5-ASA with excellent response FCAL <20mcg/g
- BO x1 /day no blood and no pain; good energy levels;
- weight reduction from 94 to 84kg by good diet and exercise

May 2017 enrolled into PREdiCCt Study

Case 2 (2/5)

July 2018: Routine FCAL in clinic is 977mcg/g

- Symptoms flare (reduction in 5-ASA dose) and needs prednisolone
- FCAL is 232mcg/g after steroids; continues on Mezavant 4.8g as monotherapy
- October 2019: FCAL 15mcg/g

July 2020: virtual clinic; well; BO 2x/day no blood, no urgency, no pain

- Diet is good and weight down; enjoying cycling; mood is good despite the pandemic

October 2020: FLARE CLINIC

- BO 20x/24h; blood; fatigue; CRP 187mg/L; albumin 34g/L; FCAL 1133mcg/g; admitted for iv steroids
- Flexible sigmoidoscopy: severe confluent colitis with deep ulcers
- IFX 10mg/kg x2

Case 2 (3/5)

7 December 2020: Telemedicine clinic

- Flare precipitated “from the stress around my recent and very protracted house moved that got delayed by cladding issues and then COVID issues”
- Very happy with infliximab; prednisolone at 15mg od;
- Stop 5-ASA and start azathioprine 75mg once daily
  - AZA poorly tolerated; plans to switch to subcut IFX
- She is desperate to get back to school. She works as a secondary teacher. I am happy for her to back now and she is relieved to hear this.

29 December 2020: flaring 10d after steroids finish; an extra iv dose of IFX (dose 4) arranged

- BO 6x/24 and still blood; some urgency; CRP 2mg/L albumin 41g/L – continue with subcut IFX
- Restart 5-ASA and check FCAL … 1091mcg/g

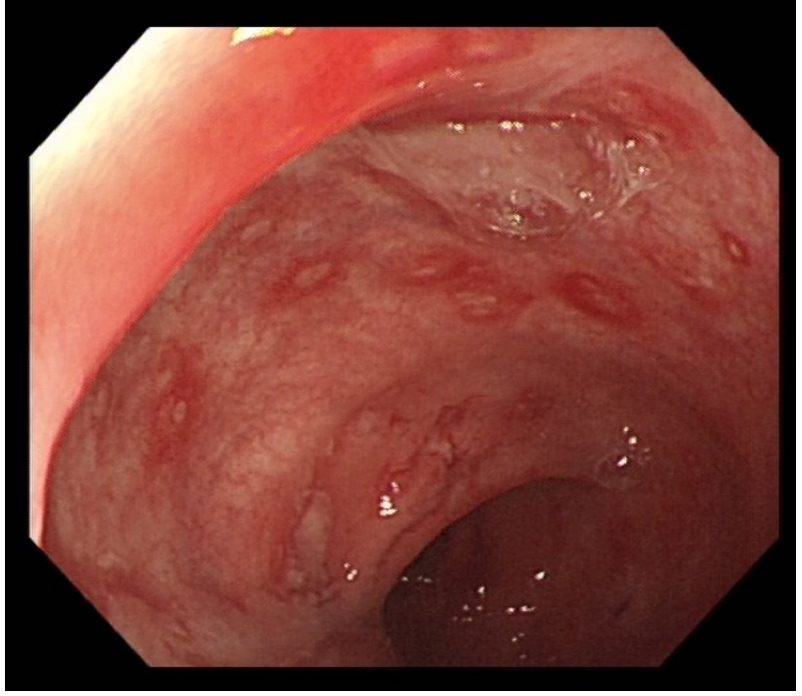
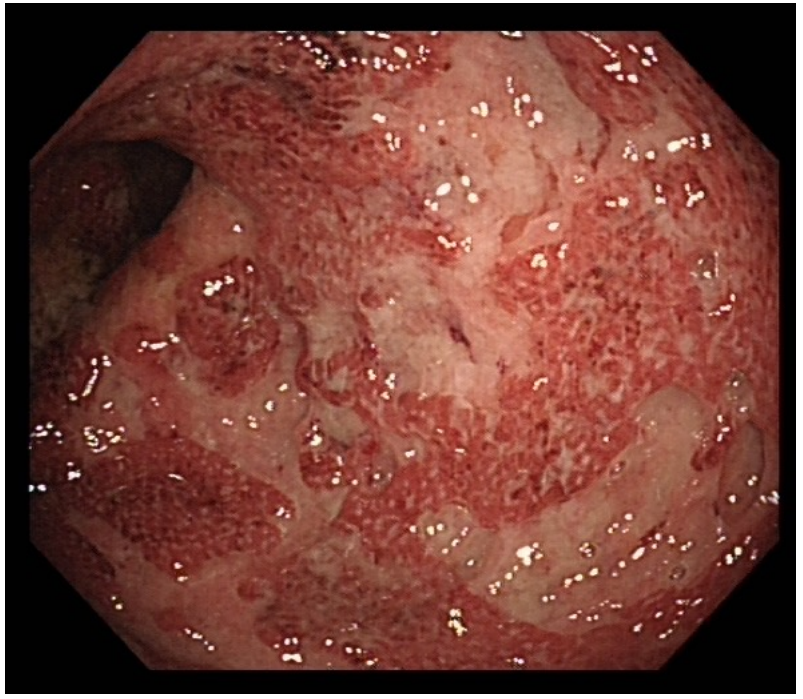
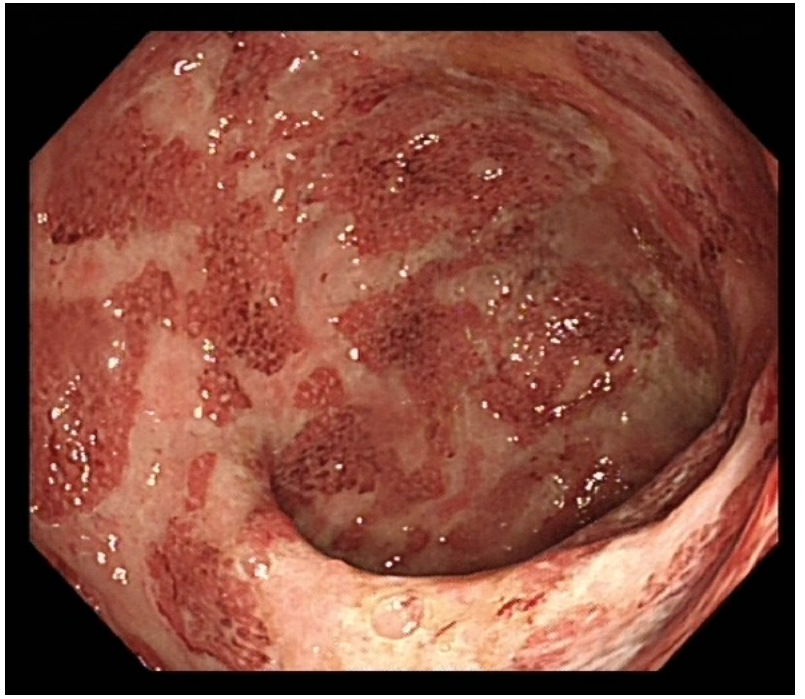
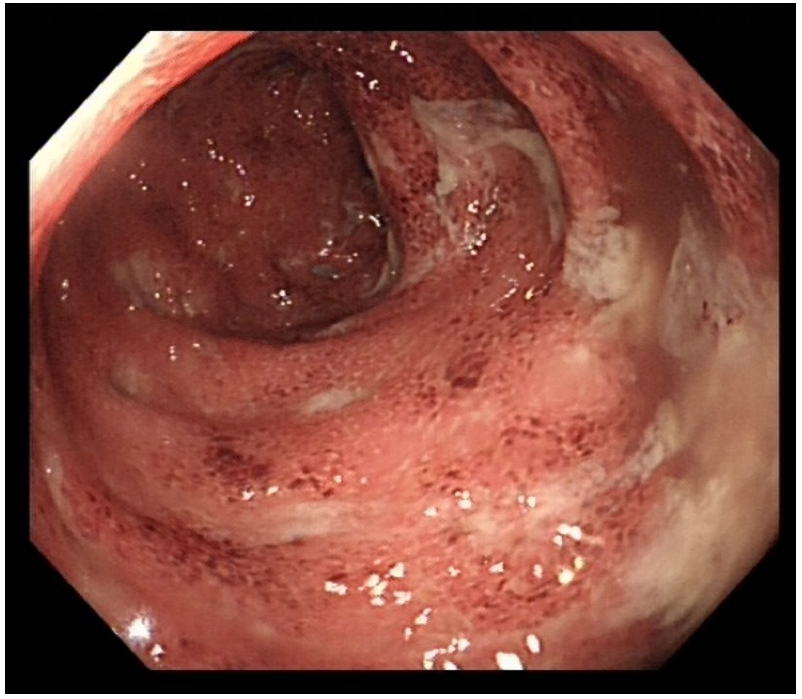
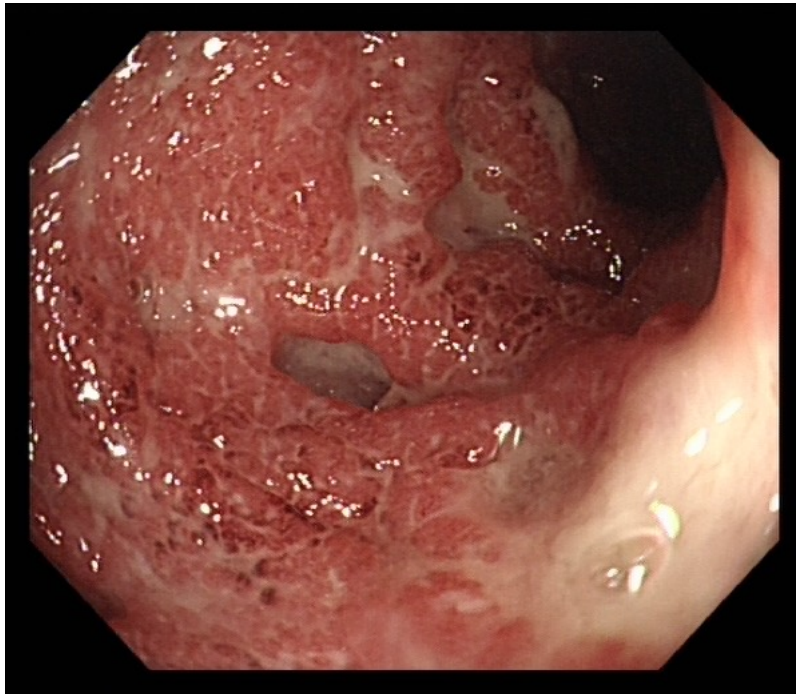
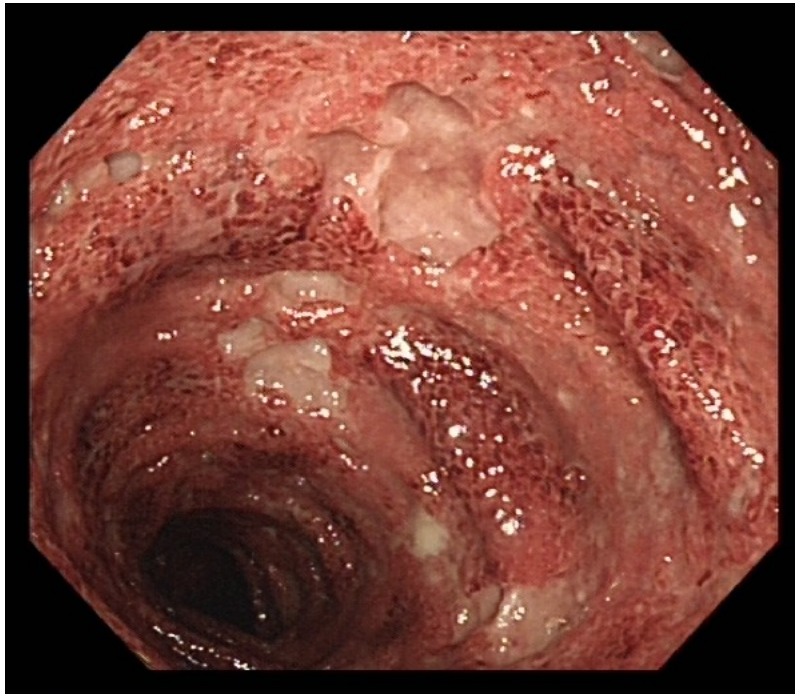
Case 2 (4/5)

19 February: face-to-face clinic

- Astra Zeneca Covid vaccine 9th February
- Decreased BO; less blood

18th March 2021: Acute admission from clinic

- iv steroids plus vedo

Case 2 (4/5)

19 February: face-to-face clinic

- Astra Zeneca Covid vaccine 9th February
- Decreased BO; less blood

18th March 2021: Acute admission from clinic

- iv steroids plus vedo

April 2021: further acute admission: CyA started ("it is a wonder drug")
    - Mild resting tremor
    - Accelerated steroid withdrawal
- Vedo loading continues – 3rd iv dose (week 6) om 5th May; will start subcut on 2nd July

Well; bloods normal; FCAL 156mcg/g; **stop CyA after 10 weeks**

Case 2 (5/5)

10 days after CyA stops … BO'ing inreases from x2/day to x5/day with increased blood

- CRP 17mg/L and FCAL 961mcg/g
- **Vedo stopped; tofacitinib started at 10mg bd**

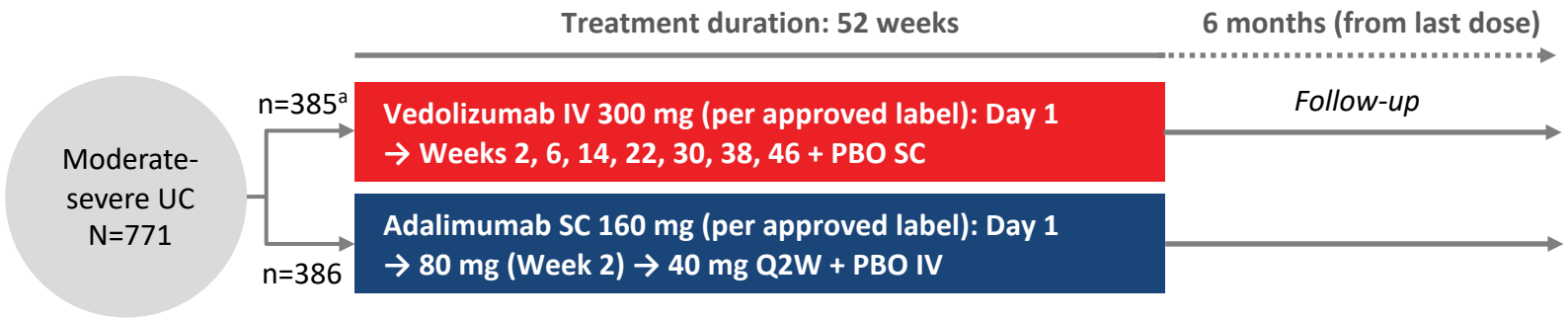
1 to 2 days after starting TOFA bleeding stopped

- Within 5 days bowels opening twice per day; nil nocturnal, no pain,
- Fever and sweats stopped;
- Within 14 days: energy levels near normal
- CRP dropped from 17mg/L to 1mg/L

FCAL dropped from 961mcg/g (18th June) to 26mcg/g (25th August)

VARSITY IS THE FIRST HEAD-TO-HEAD SUPERIORITY STUDY COMPARING TWO BIOLOGICS IN UC

Phase IIIb randomised, double-blind, double-dummy, multicentre, active-controlled study

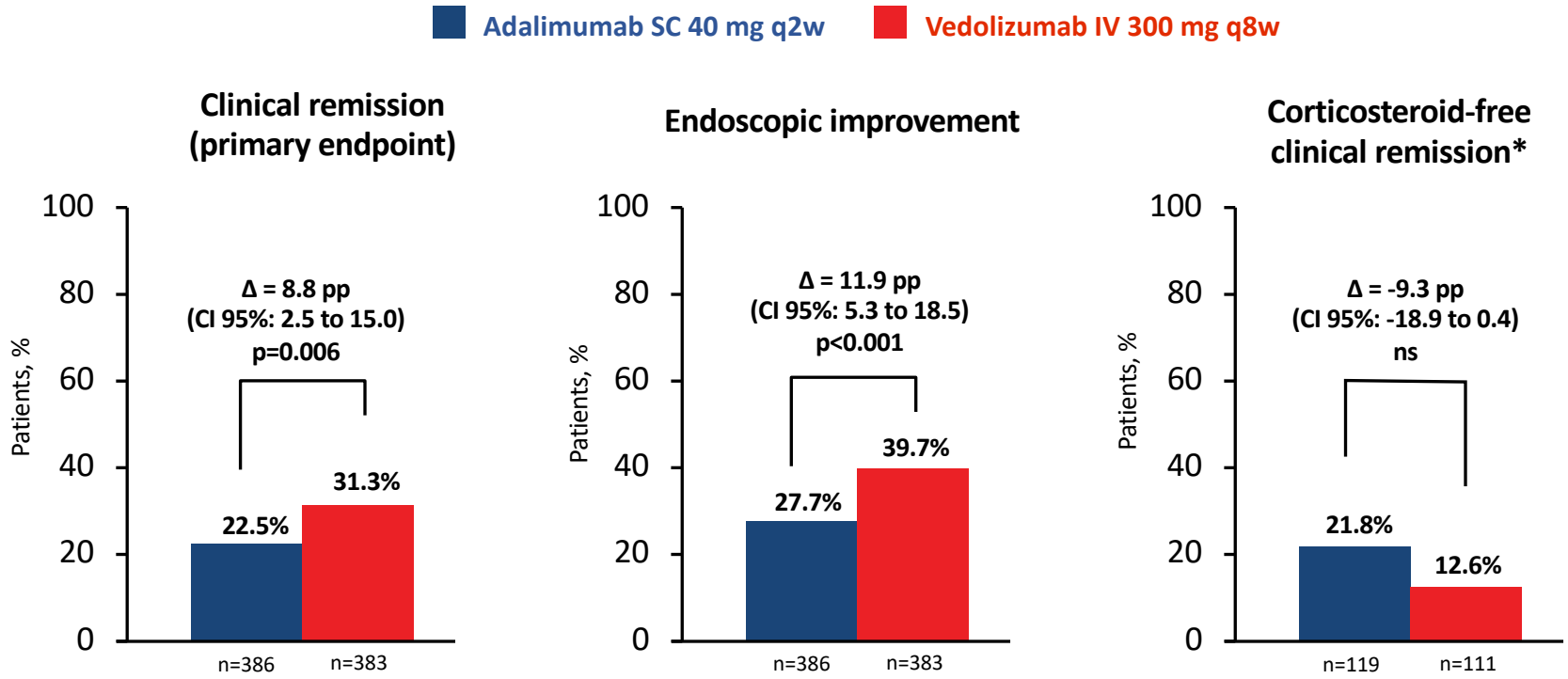


Adapted from Sands BE et al New Engl J Med 2019

- Objective: Evaluate efficacy and safety of vedolizumab IV compared with adalimumab SC over 52 weeks
- Primary endpoint: Clinical remission at Week 52 (complete Mayo score ≤2 and no individual subscore >1)
- Secondary endpoints:
  - Mucosal healing at Week 52 (Mayo endoscopic subscore ≤1)
  - Corticosteroid-free clinical remission at Week 52 (among those with baseline corticosteroid use)

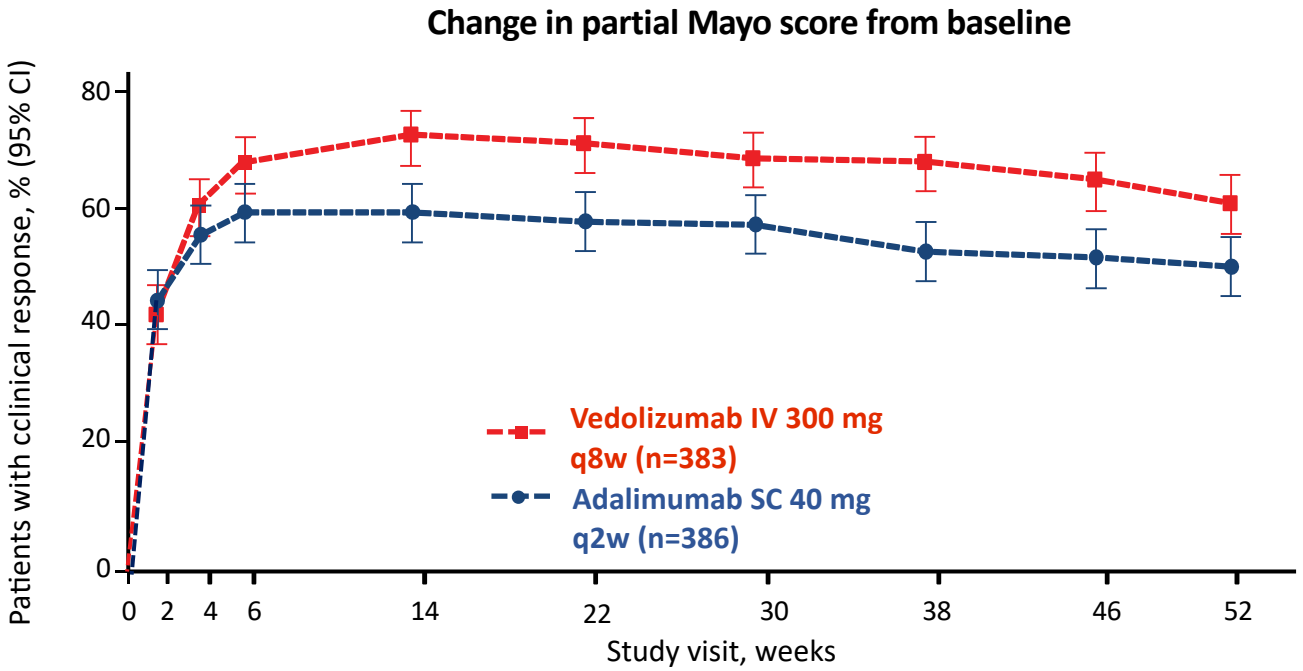
[a] Includes two patients randomized but not dosed.
IV: intravenous; PBO: placebo; Q2W: every 2 weeks; SC: subcutaneous; UC: ulcerative colitis.
Sands BE, et al. *New Engl J Med.* 2019;381:1215–26.

VEDOLIZUMAB SUPERIOR TO ADALIMUMAB IN ACHIEVING CLINICAL REMISSION AND ENDOSCOPIC IMPROVEMENT AT WEEK 52



*In the subgroup of patients receiving corticosteroids at baseline.
Clinical remission defined as complete Mayo score ≤2 and no individual subscore >1; Endoscopic improvement defined as Mayo endoscopic subscore ≤1.
IV: intravenous; ns: non-significant; pp: percentage points; qXw: every X weeks; SC: subcutaneous.
Sands BE, et al. *New Engl J Med*. 2019;381:1215–26.

DIFFERENCES IN CLINICAL RESPONSE BETWEEN VEDOLIZUMAB AND ADALIMUMAB WERE SUSTAINED TO WEEK 52



Adapted from Sands BE et al *N Engl J Med* 2019

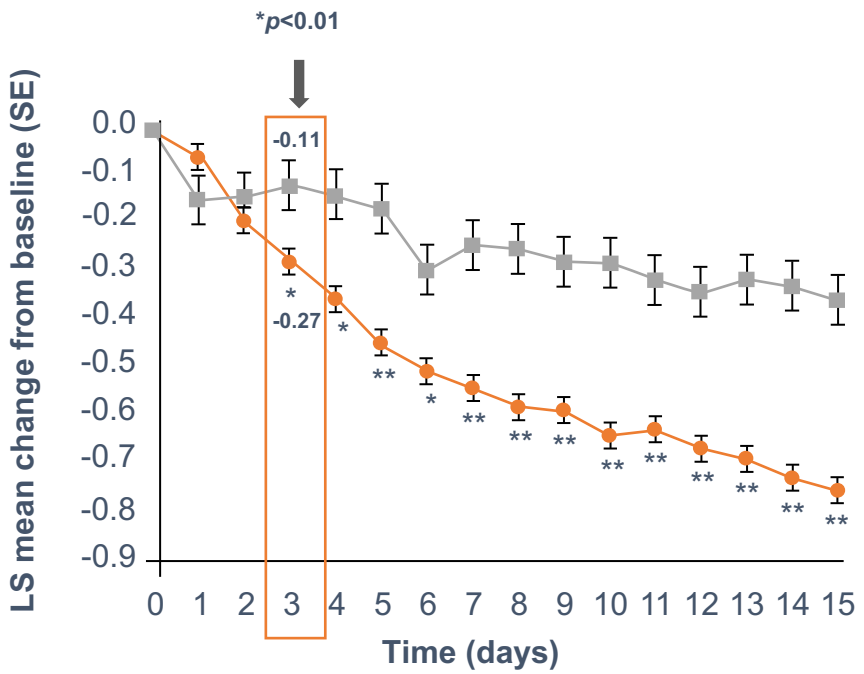
Clinical response based on partial Mayo score: Reduction in partial Mayo score of ≥2 points and ≥25% from baseline, with an accompanying decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore of ≤1 point. Patients with missing clinical response status were considered nonresponders.
CI: confidence interval; IV: intravenous; qXw: every X weeks; SC: subcutaneous; UC: ulcerative colitis.
Sands BE, et al. *N Engl J Med.* 2019;381:1215–26.

Tofacitinib in UC

Post-hoc analysis† of pooled data from OCTAVE Induction 1 and OCTAVE Induction 2 (FAS, observed case)

Daily Mayo stool frequency and rectal bleeding subscores were calculated using patient diary data collected daily during the first 15 days of induction therapy. Partial Mayo Score subscore data were first collected at Day 15

Stool frequency

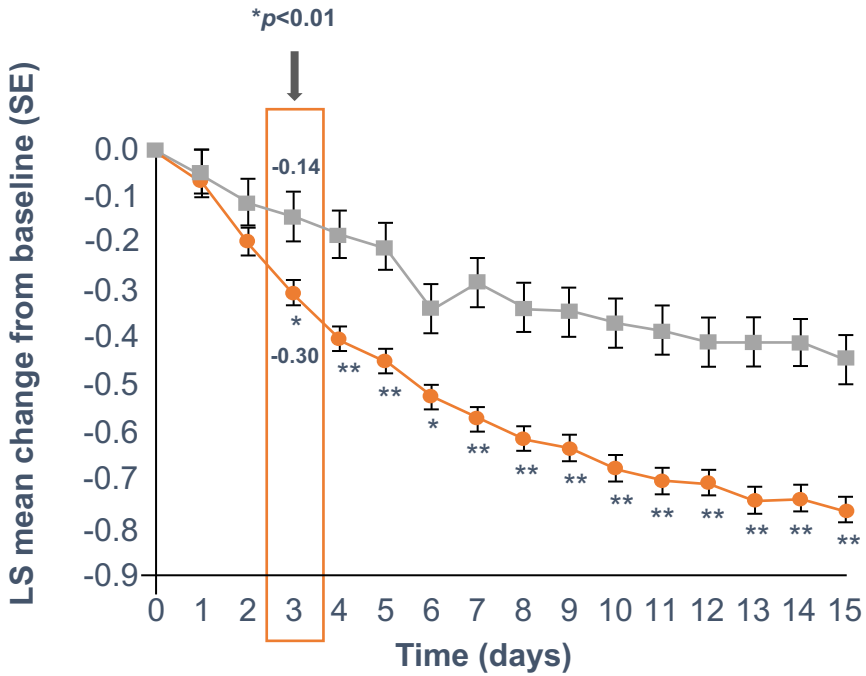


Placebo (n=234)

Tofacitinib 10 mg BID (n=905)

*p<0.01; **p<0.0001 for tofacitinib versus placebo

Rectal bleeding



Figures adapted with permission from Hanauer S *et al. Clin Gastroenterol Hepatol* 2019;17(Suppl):139–147.

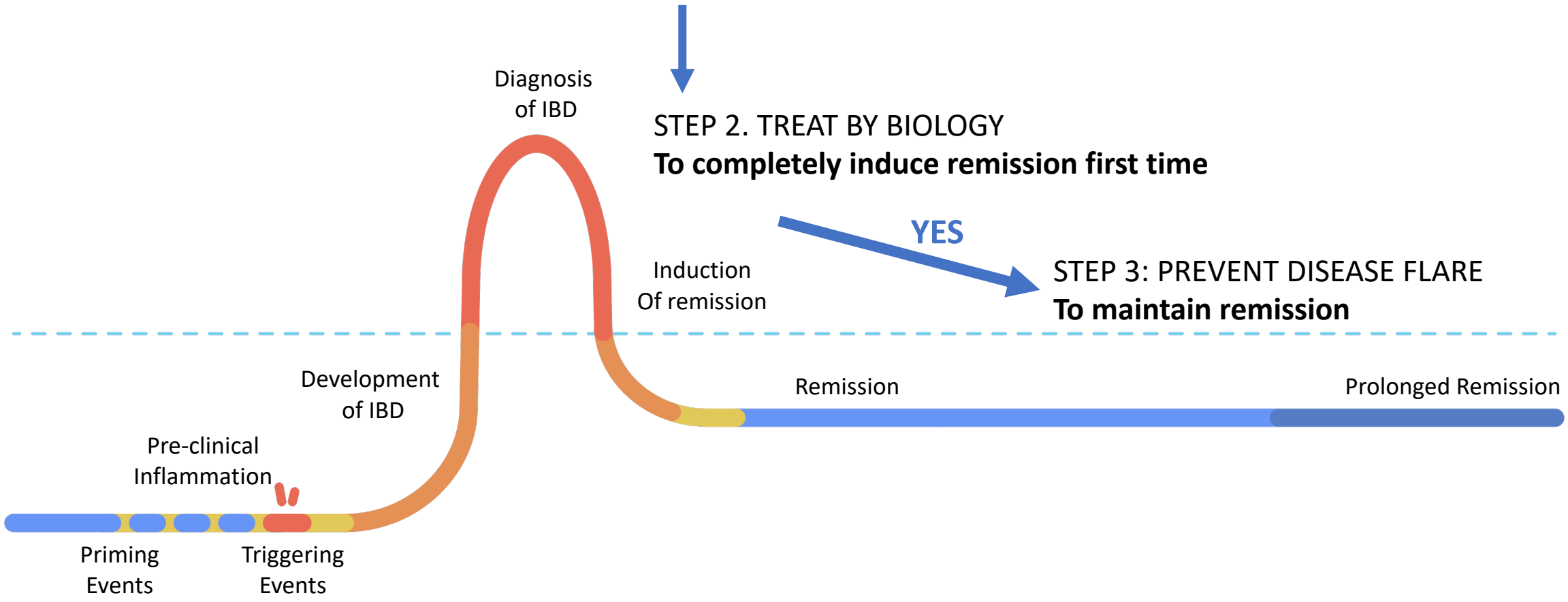
†Consideration should be made for multiple testing and inclusion of unadjusted *p*-values when interpreting data.
BID=twice daily; FAS=full analysis set; LS=least-squares; SE=standard error.

1. Hanauer S et al. *Clin Gastroenterol Hepatol* 2019;17:139–147. 2. Hanauer S et al. *Clin Gastroenterol Hepatol* 2019;17(suppl):139–147.

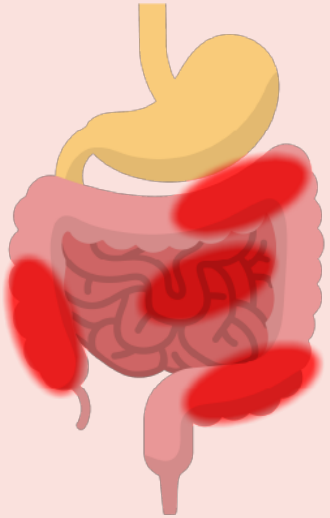
SCENARIO IBD_NO FLARES: induce remission, maintain remission, prevent flare, & therefore disease progression

STEP 1. STRATIFY by RISK

To overcome massive disease heterogeneity



Crohn´s Disease



Strong relation seen with:
- Lack of fiber
- Lack of Omega-3
- Ultra-processed foods
- Lack of Vitamin D*

Not-enough-evidence diets in IBD
- Low FODMAP
- Gluten free
- Dairy free
- Prebiotic rich diets
- Paleo/Keto diet
- Vegan/vegetarian diet

IBD

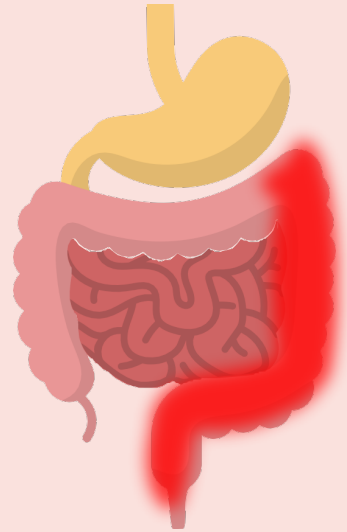
Risk
- Omega 3 fats
- Fiber
- Nuts
- Vitamin D

Risk
- Saturated fats
- Red Meat
- Sugars
- Emulsifiers

Improve
- Exclusive enteral nutrition (small bowel CD)

Common Deficiencies
- Iron
- Folate
- Vitamin D, B12
- Calcium, Magnesium, Zinc

Ulcerative Colitis



Strong relation seen with:
- Red meat
- Sweet beverages

Nutrients 2021, 13, 1387.
Alim Pharmacol Ther.2014; 39:834-842
Inflamm Bowel Dis 2016:22:345-354
Inflamm Bowel Dis. 2016; 22: 1403-11
Eur J Clin Nutr. 2017; 71:566
Gastroenterology. 2020; 159: 873-883
Nutrients 2020, 12, 2296

IOIBD Dietary Recommendations for Patients With IBDs

Diet	UC	CD	Clarifications
Fruits			If stricture reduce insoluble fiber
Vegetables			If stricture reduce insoluble fiber
Refined sugars/ Carbohydrates			
Wheat/gluten			Associated with ileitis in mouse model
Red/processed meat			
Poultry			
Pasteurized Dairy			Lactase deficiency & intolerance frequent in IBD
Unpasteurized Dariy			
Dietary fats (trans fat, palm oil, dairy fats)			
Alcohol			
Maltodextrins/artificial sweeteners			
Emulsifiers and thickeners			E433, polysorbate-80, E466, and carboxymethylcellylose
Carrageenans			In dairy-based deserts, frozen meals & processed meat
Titanium dioxide & other nanoparticules			

RED: prudent to avoid. GREEN: Prudent to increase. PINK: May be prudent to avoid

PREdiCCt

PREdiCCt aims:

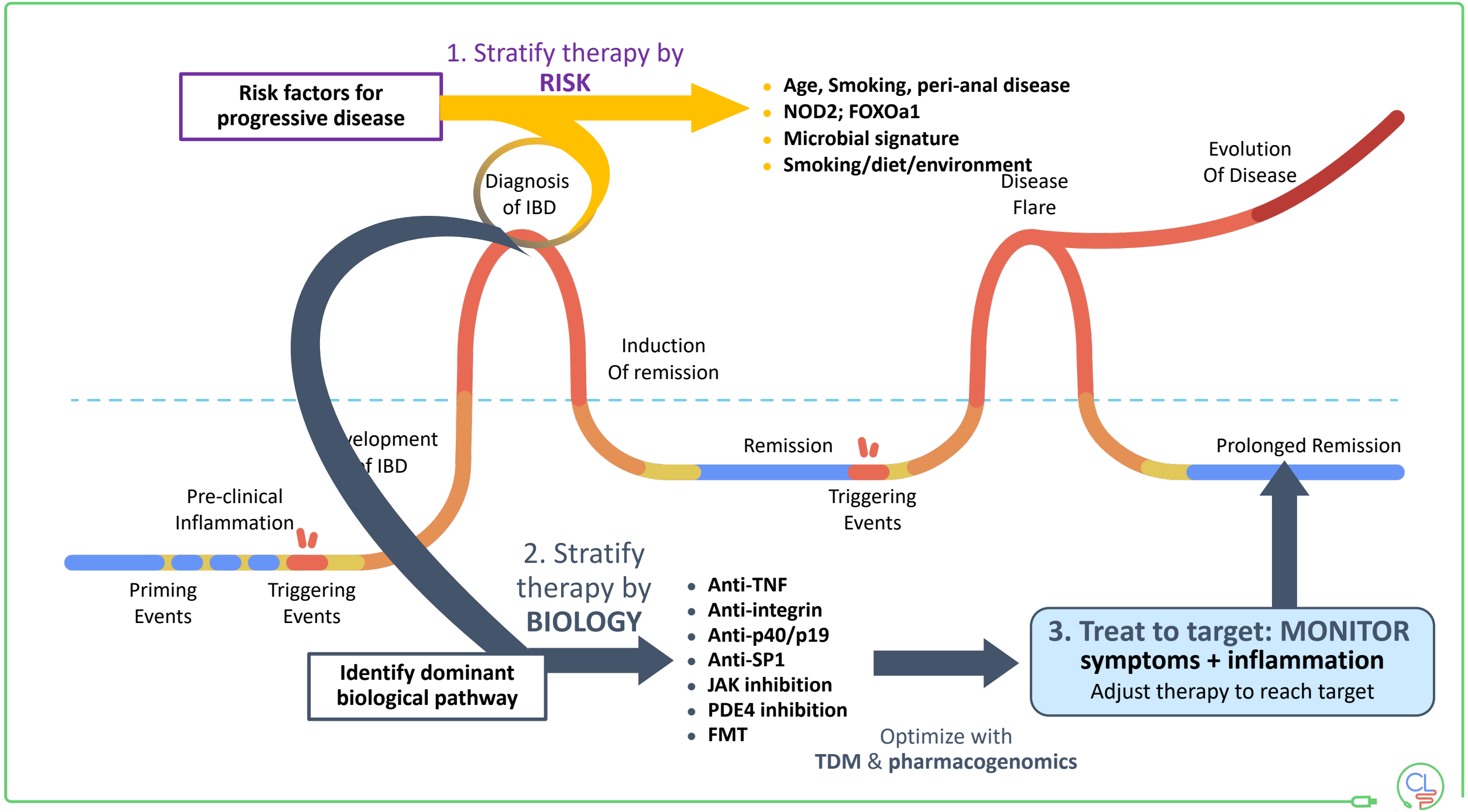
To determine which aspects of
a) baseline habitual diet,
b) the environment,
c) genetic variation and
d) the gut microbiota
are **associated with & predict disease flare in Crohn's disease and UC**.

The primary objectives are to test associations with:

1. Total animal protein intake
2. Dietary fibre
3. N-6 polyunsaturated fatty acids
4. Dietary emulsifiers
5. Total bacterial gene count in stool

Dr Charlie Lees PhD FRCP(Ed)
@charlie_lees charlielees.com

PREdiCCt


1. Stratify therapy by
RISK
Risk factors for progressive disease
Age, Smoking, peri-anal disease
NOD2; FOXOa1
Microbial signature
Smoking/diet/environment
Diagnosis of IBD
Disease Flare
Evolution Of Disease
Induction Of remission
Remission
Prolonged Remission
Triggering Events
Pre-clinical Inflammation
Priming Events
Triggering Events
2. Stratify therapy by
BIOLOGY
Identify dominant biological pathway
Anti-TNF
Anti-integrin
Anti-p40/p19
Anti-SP1
JAK inhibition
PDE4 inhibition
FMT
Optimize with
TDM & pharmacogenomics
3. Treat to target: MONITOR
symptoms + inflammation
Adjust therapy to reach target

Prof Charlie W Lees
Chair of Gastroenterology
Consultant Gastroenterologist
UKRI Future Leaders Fellow (*#UKRIFLF*)

Centre for Genomics and Experimental Medicine
IGMM & Edinburgh IBD UNIT

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Mathew Lyons
Laura Lucaciu
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Lee Murphy
Chris Weir
Linda Williams
Kate Covil
Jon Rhodes
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Key UK scientific partners
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Luke Jostins (Oxford)
Miles Parkes (UK IBD Bioresource)
Tariq Ahmad (PANTS studies)
Nick Kennedy (Exeter)
Catalina Vallejos (IGMM)
Chris Lamb (Newcastle)

Digital media: @erikRVA

National IBD Doctors Annual Meeting 2021

CLINICAL CHALLENGES & PEARLS

IN CONTEMPORARY IBD CARE

FERRING
PHARMACEUTICALS