Meeting del 45° parallelo

IBD and liver hemisphere

30 Maggio 2024

Salone del Grano

Piazza Giuseppe Garibaldi, 2
Rovigo

Switching from intravenous to subcutaneous Vedolizumab and Infliximab

Luca Benazzato – Legnago (VR)

The evolution of Biologics Administration From Intravenous to Subcutaneous

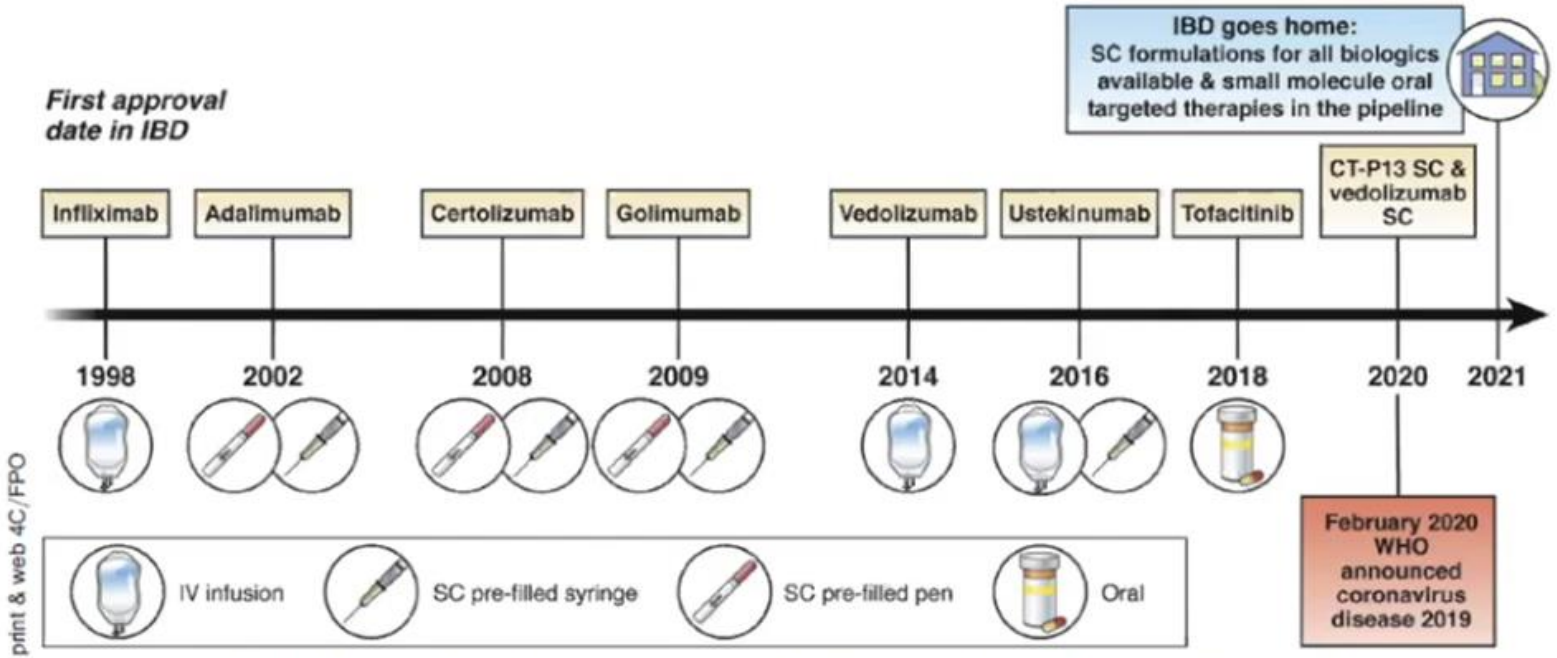
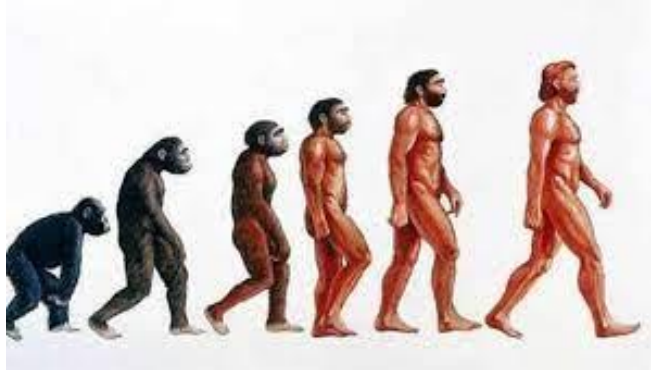


Figure 1. Evolution of advanced therapies administration in inflammatory bowel disease over time.

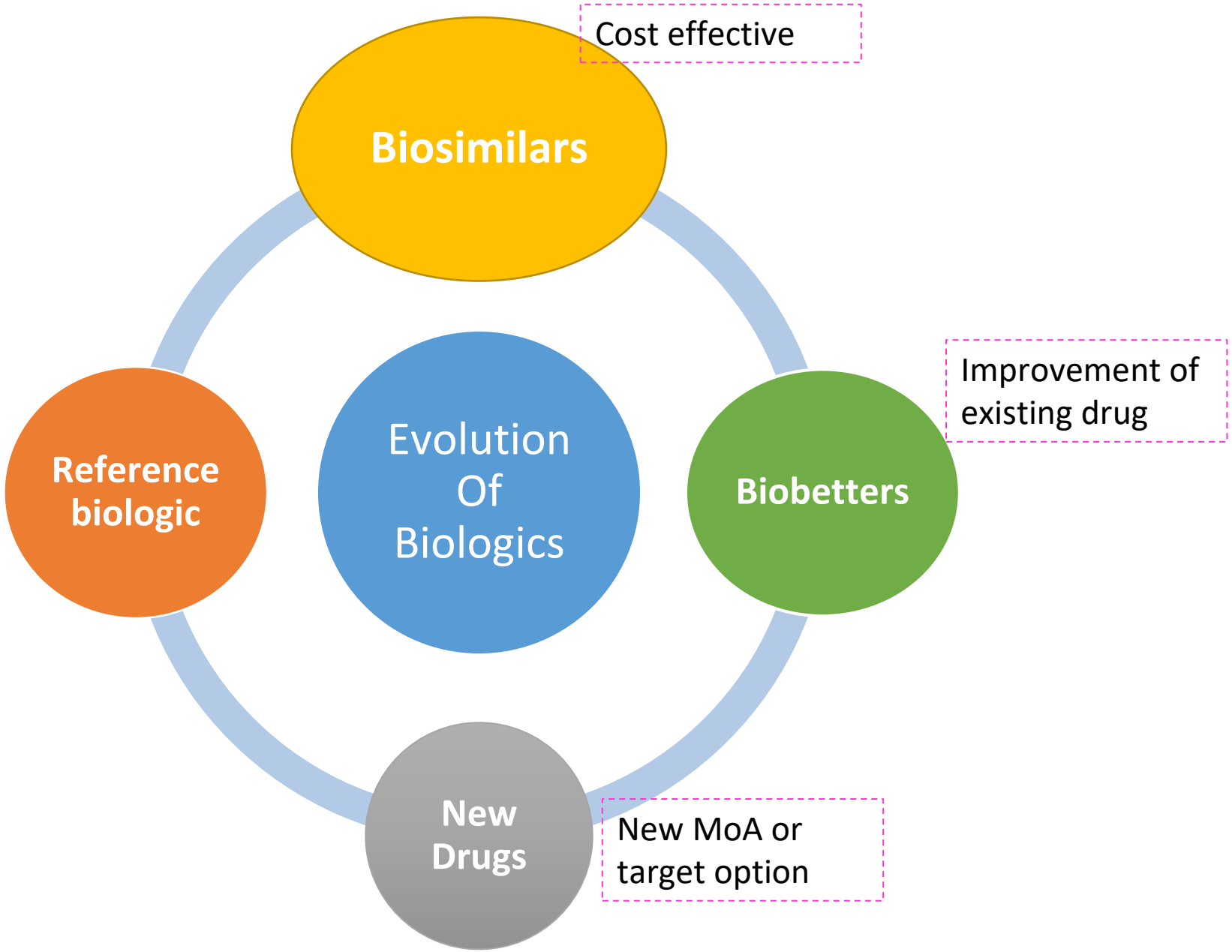
SC formulations could be defined as biobetters of IV ones?

Biobetter

Biobetter is a modified version of a specific biologic that enhances clinical outcome and/or drug pharmacology (pharmacokinetics and pharmacodynamics)



Improvement on reference biologics	Better medical outcomes
• Molecular stability • Increased half-life	• Increased serum trough level • Enhanced pharmacodynamics • Longer dosing frequency
• Changes in cytotoxicity • Combination of multiple targets • Reduced immunogenicity • Reduced pain (side effect)	• Improve efficacy • Increase patient compliance • Expansion of treatment patient group
• Formulation change	• Patient convenience and QoL


Cost effective
Biosimilars
Improvement of existing drug
Reference biologic
Evolution Of Biologics
Biobetters
New Drugs
New MoA or target option

Do we need biobetters?

- IBD highly impact on healthcare sistem budgets, due to long term treatment costs and reduction in work-related productivity of patients
- Decision to use the reference product or the biobetters should based on the balance between clinical outcomes and costs
- The introduction of biobetters could hypothetically:
  - lead to the achievement of better efficacy and/or drug pharmacology with a reductions in direct and indirect costs
  - Improve disease control

SUBCUTANEOUS INFLIXIMAB

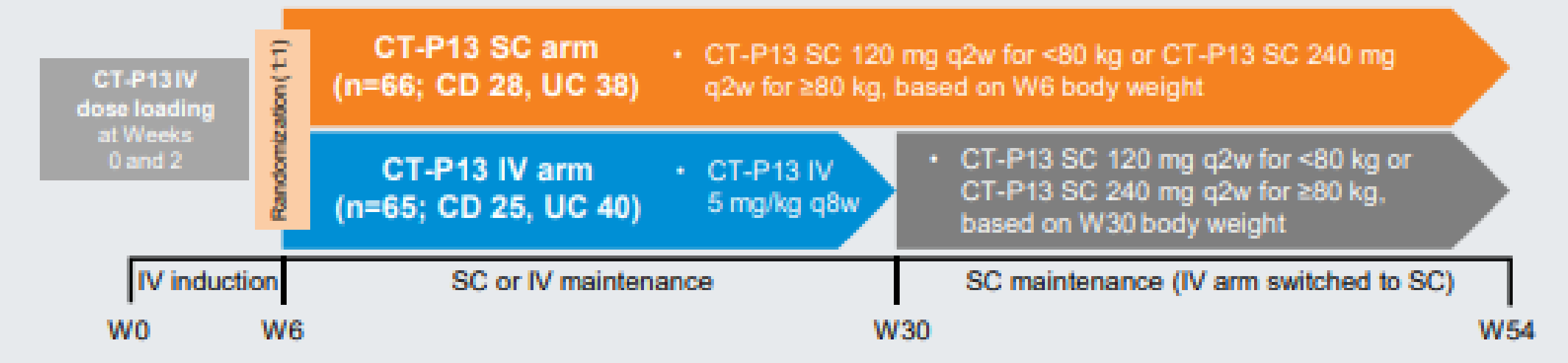
Infliximab: benchmark of TNF inhibitors for more than 20 yrs

- More than 20 yrs after approval, infliximab remains the efficacy benchmark of its category and one of the most prescribed medications in the field
- Extraintestinal complications
- The first infliximab biosimilar was approved for use in Europe for treating RA and IBD in 2013
- Until a new subcutaneous formulation of infliximab was recently approved for RA in 2019 and for IBD in 2020, infliximab was once available only as intravenous preparation

Randomized Controlled Trial: Subcutaneous vs Intravenous Infliximab CT-P13 Maintenance in Inflammatory Bowel Disease

Stefan Schreiber,[1,*] **Shomron Ben-Horin,**[2,*] Jaroslaw Leszczyszyn,[3] Robert Dudkowiak,[3,4]

131 adults with active CD/UC received CT-P13 IV at W0 and W2 and were randomized to CT-P13 SC or CT-P13 IV at W6; patients receiving CT-P13 IV switched to CT-P13 SC at W30



Schreiber, Gastroenterology 2021

Mean pre-dose through levels

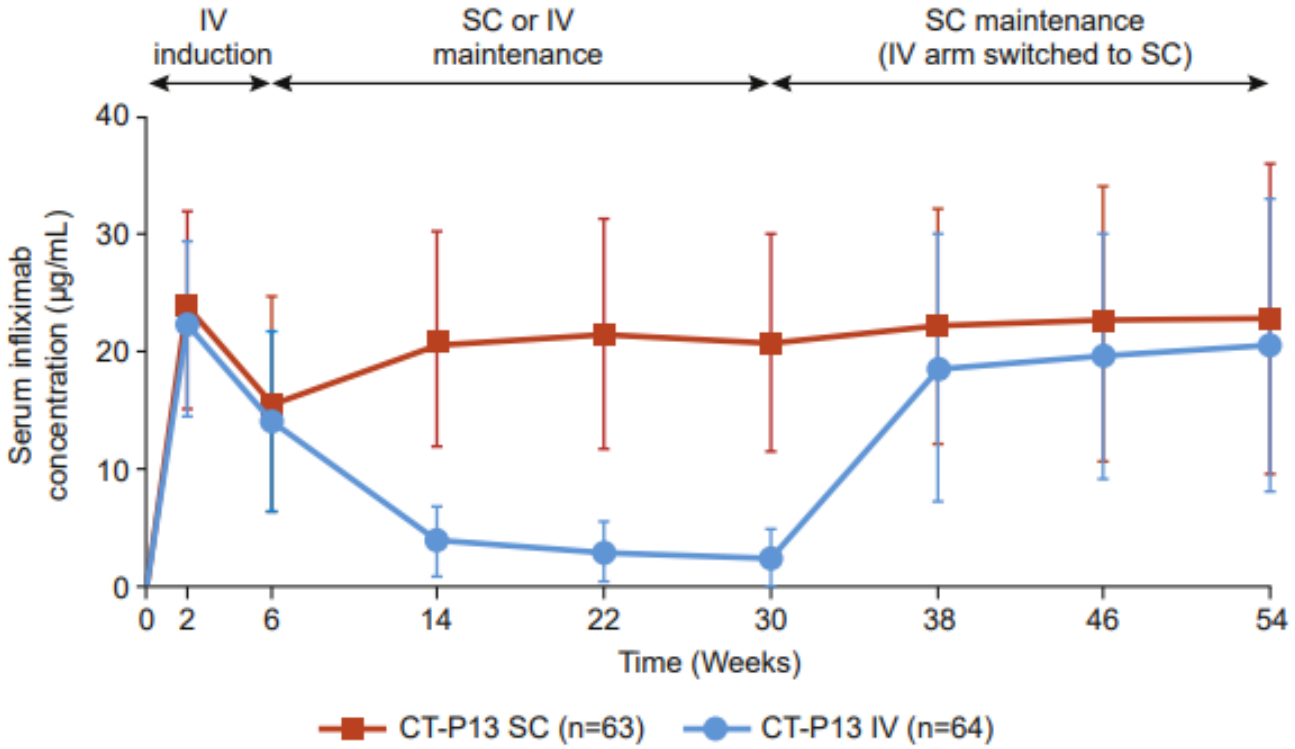
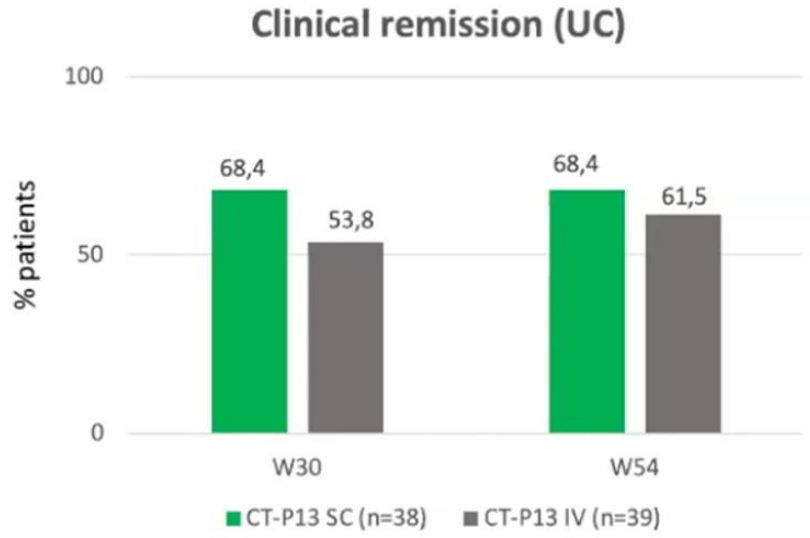
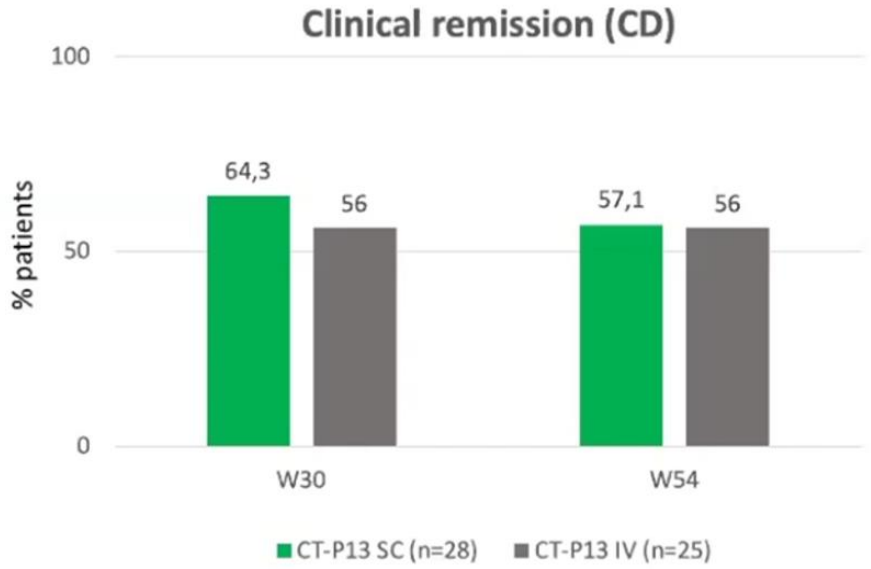


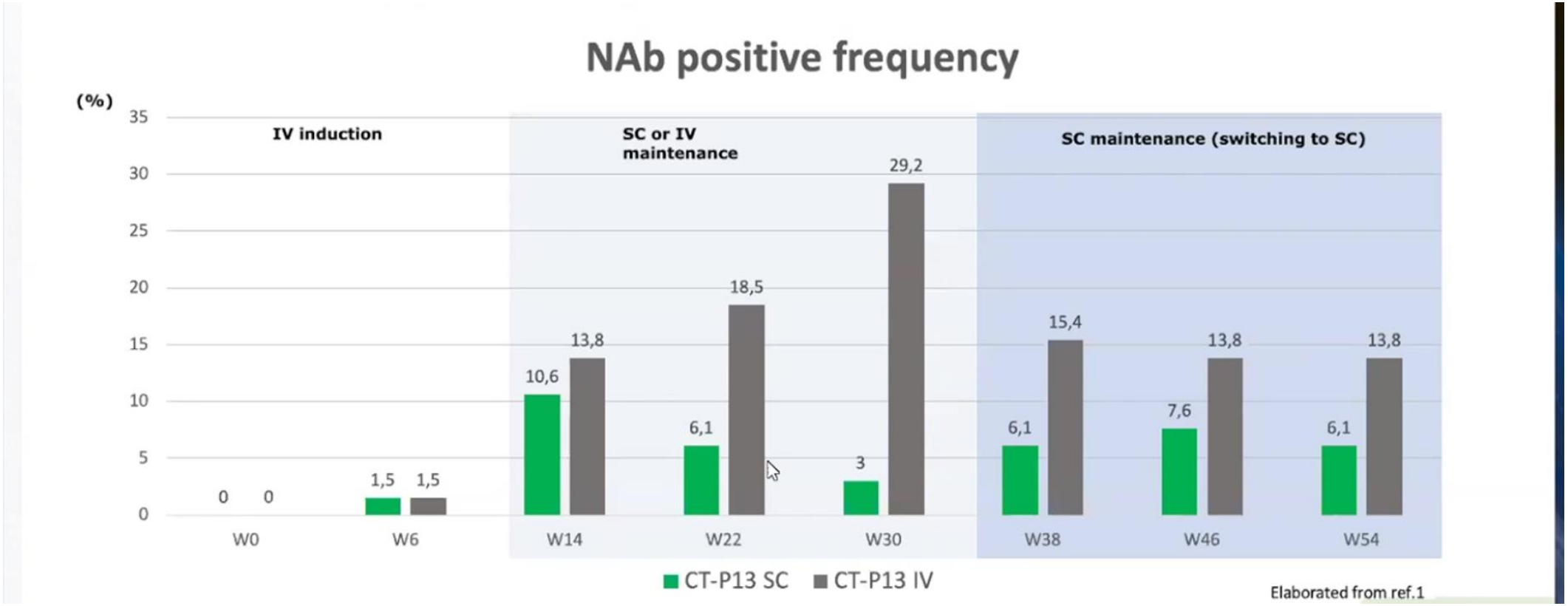
Figure 2. Mean (±SD) predose serum infliximab concentration[a] for CT-P13 SC and CT-P13 IV arms (PK population). PK, pharmacokinetic; SD, standard deviation. [a]Concentrations below the lower limit of quantification (BLQ) before W0 were set to zero; other concentrations BLQ were set to the lower limit of quantification.

Efficacy


Clinical remission (UC)
100
50
0
% patients
68,4
53,8
68,4
61,5
W30
W54
CT-P13 SC (n=38)
CT-P13 IV (n=39)


Clinical remission (CD)
100
50
0
% patients
64,3
56
57,1
56
W30
W54
CT-P13 SC (n=28)
CT-P13 IV (n=25)

Immunogenicity



Efficacy and Safety of Elective Switching from Intravenous to Subcutaneous Infliximab [CT-P13]: A Multicentre Cohort Study

Philip J. Smith,[a] Lisa Critchley,[a] Daniel Storey,[a] Belle Gregg,[a] June Stenson,[a]

- 181 IBD (60 UC, 115 CD)

	All [*n* = 181]	Ulcerative colitis [*n* = 60]	Crohn's disease [*n* = 115]	IBD-U [*n* = 6]
Concomitant immunomodulator, *n* [%]	107 [59.1%]	33 [55.0%]	70 [60.9%]	4 [66.7%]
Immunomodulator use, *n* [%]:				
6-MP	14 [7.7%]	8 [13.4%]	5 [4.4%]	1 [16.7%]
AZA	82 [45.3%]	23 [38.3%]	56 [48.7%]	3 [50.0%]
MTX	11 [6.1%]	2 [3.3%]	9 [7.8%]	0 [0.0%]
6-TGN levels, mean [SD]	267.5 [118.5]	249.4 [128.4], *n* = 19	271.6 [116.4], *n* = 47	306.0 [108.6], *n* = 4
Infliximab frequency prior to switch:				
8-weekly	131 [72.4%]	48 [80.0%]	78 [67.8%]	5 [83.3%]
6-weekly	34 [18.8%]	5 [8.3%]	28 [24.3%]	1 [16.7%]
4-weekly	16 [8.8%]	7 [11.7%]	9 [7.8%]	0 [0%]

Smith, JCC 2022, 16, 1436

Treatment persistence

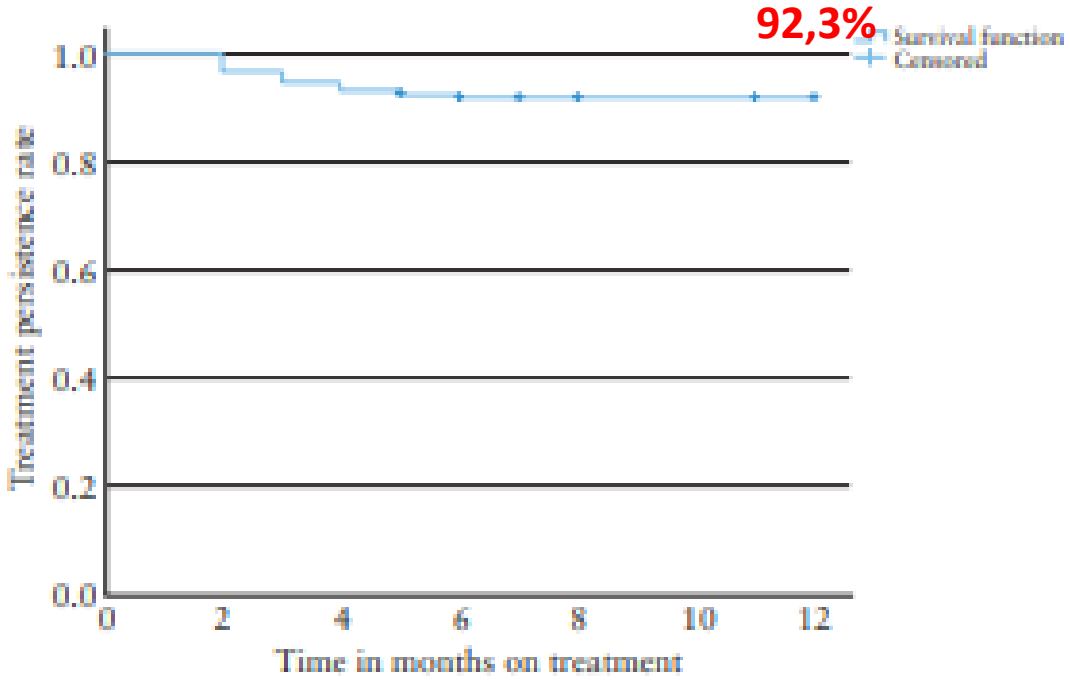
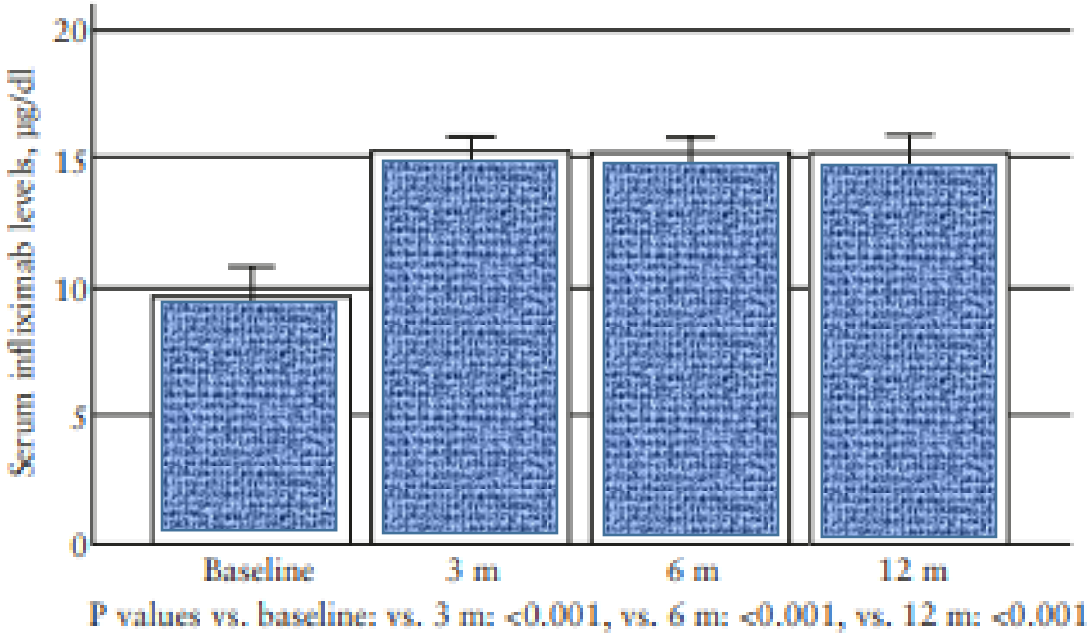


Figure 1. Kaplan–Meier curve of treatment persistence with subcutaneous [SC] infliximab [CT-P13] in patients switching from intravenous infliximab.

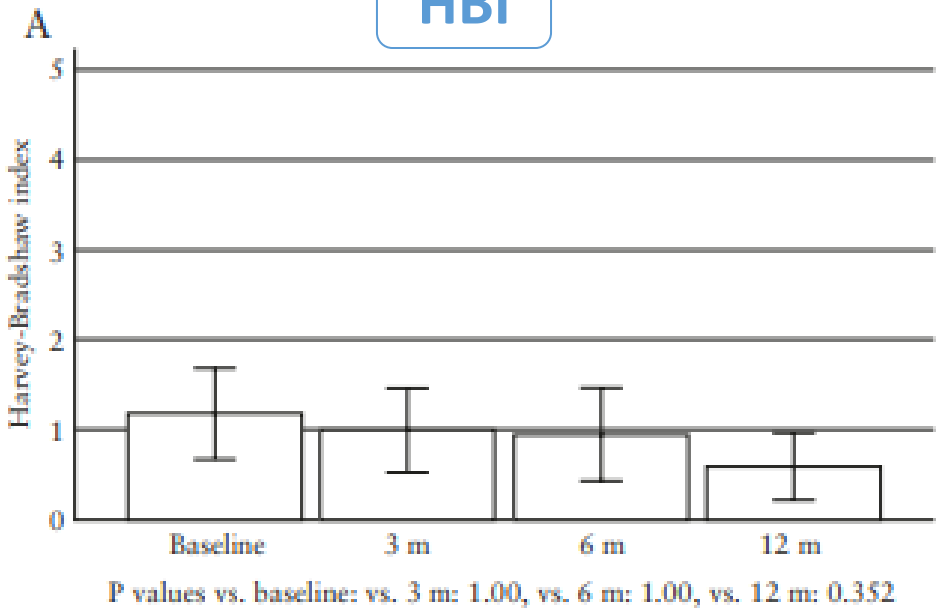
25% dei pazienti proveniva da un regime ottimizzato al momento dello switch

Serum IFX levels



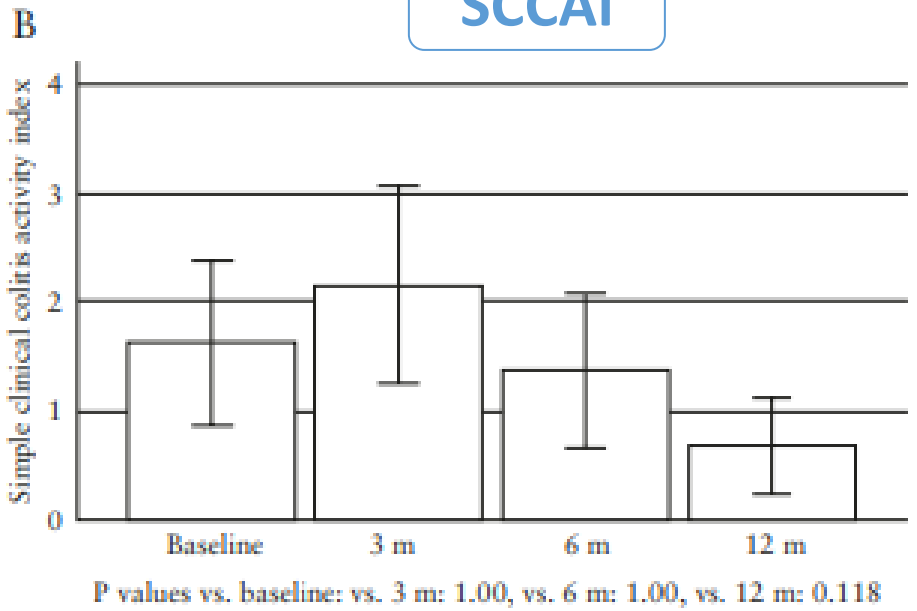
Smith, JCC 2022, 16, 1436

HBI



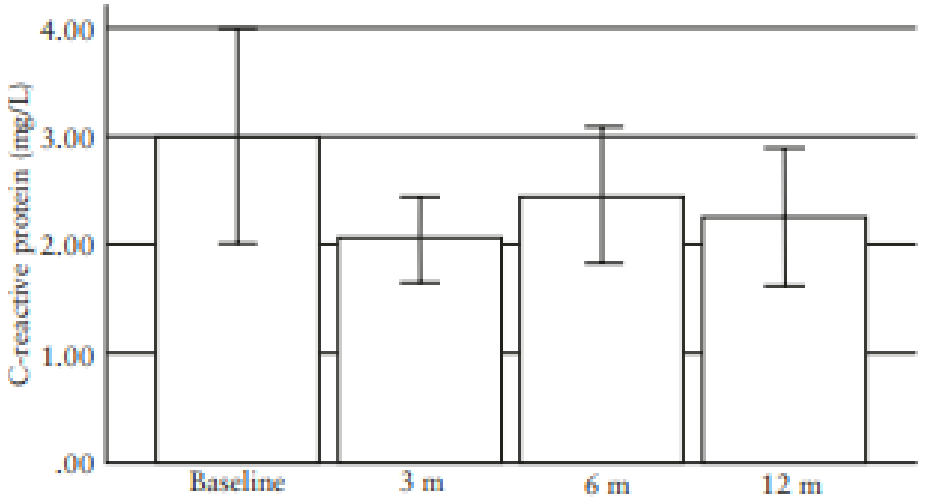
P values vs. baseline: vs. 3 m: 1.00, vs. 6 m: 1.00, vs. 12 m: 0.352

SCCAI



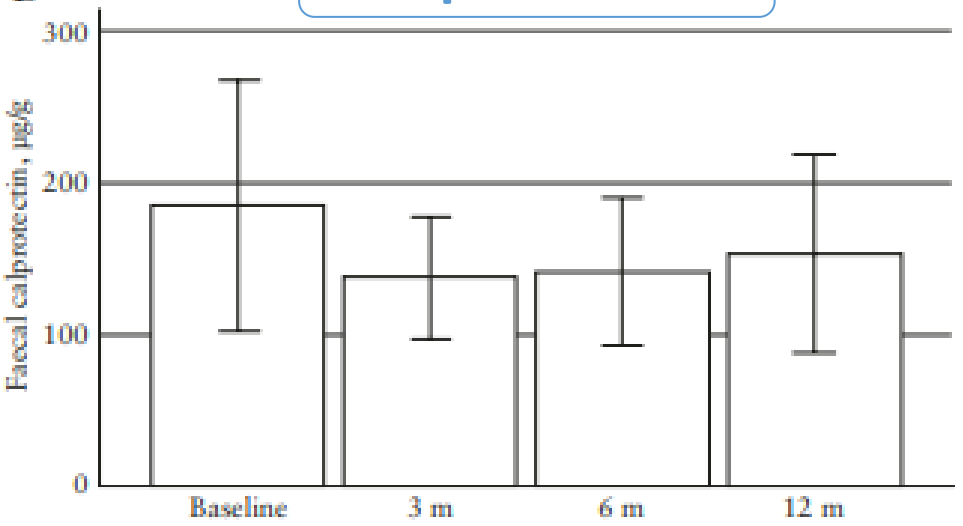
P values vs. baseline: vs. 3 m: 1.00, vs. 6 m: 1.00, vs. 12 m: 0.118

PCR



P values vs. baseline: vs. 3 m: 0.056, vs. 6 m: 0.794, vs. 12 m: 0.229

Calprotectine



P values vs. baseline: vs. 3 m: 1.00, vs. 6 m: 1.00, vs. 12 m: 1.00

Smith, JCC 2022, 16, 1436

INFLAMMATORY BOWEL DISEASE

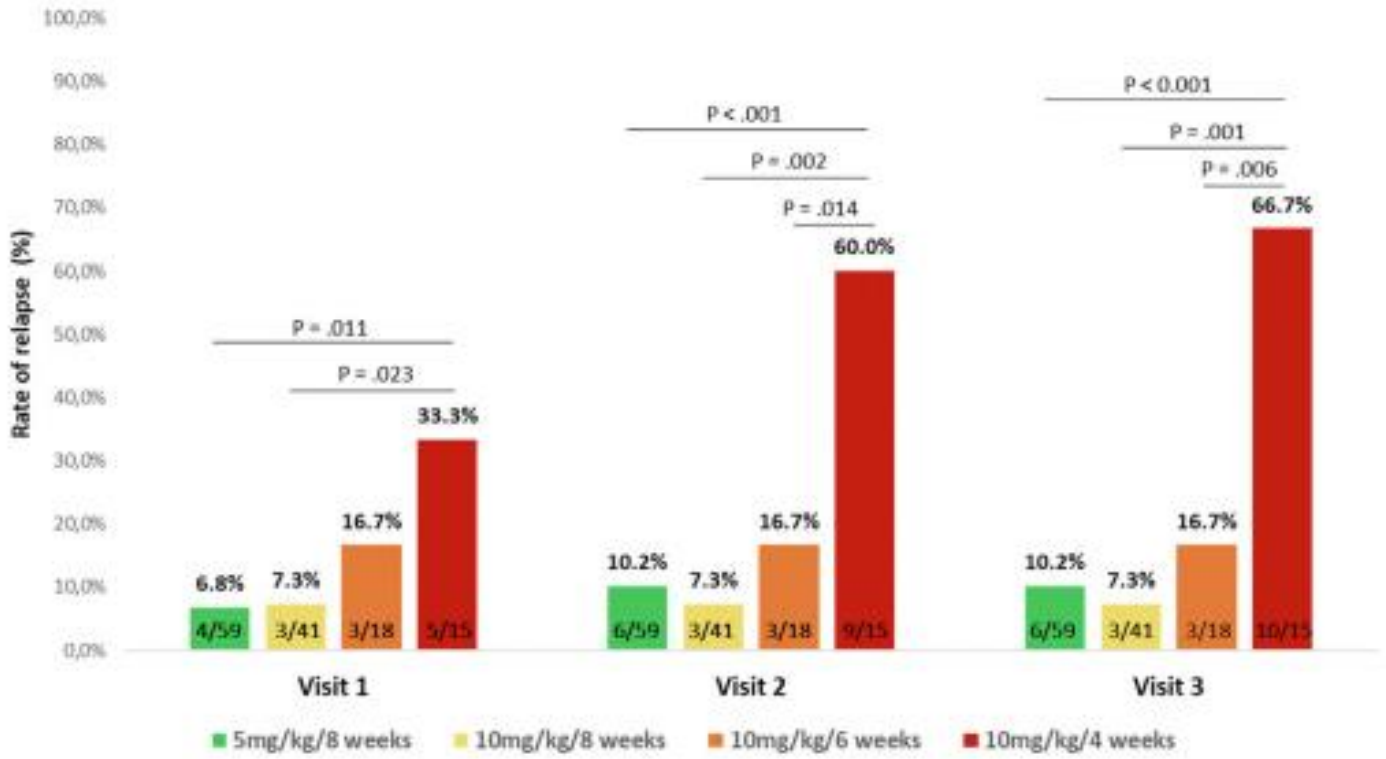
Effectiveness of Switching From Intravenous to Subcutaneous Infliximab in Patients With Inflammatory Bowel Diseases: the REMSWITCH Study

Anthony Buisson,[1,2] Maria Nachury,[3] Maud Reymond,[1] Clara Yzet,[6] Pauline Wils,[3]

Rate of relapse

Disease activity at baseline	
Harvey-Bradshaw index	0 (0–1)
Partial Mayo score	0 (0–1)
C-reactive protein level, mg/L	1 (0–3.4)
Fecal calprotectin level, μg/g	39 (16–112)
Medications at baseline	
Infliximab maintenance therapy duration, y	5.4 ± 3.8
Intravenous infliximab maintenance regimen	
5 mg/kg every 8 wk	59 (44.4)
10 mg/kg every 8 wk	41 (30.8)
10 mg/kg every 6 wk	18 (13.5)
10 mg/kg every 4 wk	15 (11.3)

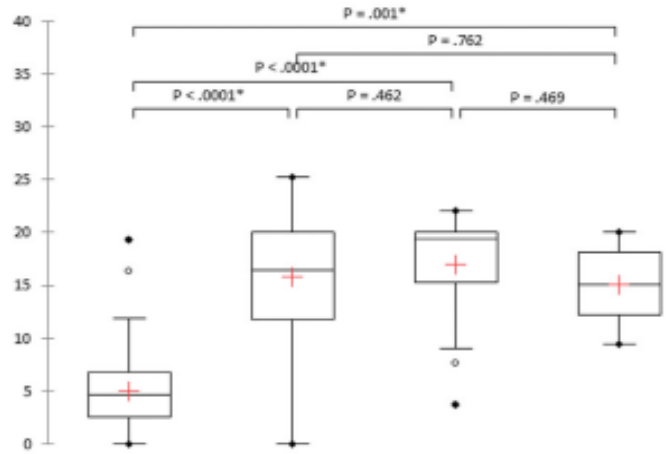
Among 184 eligible patients, 72.3% (133 of 184) agreed to switch



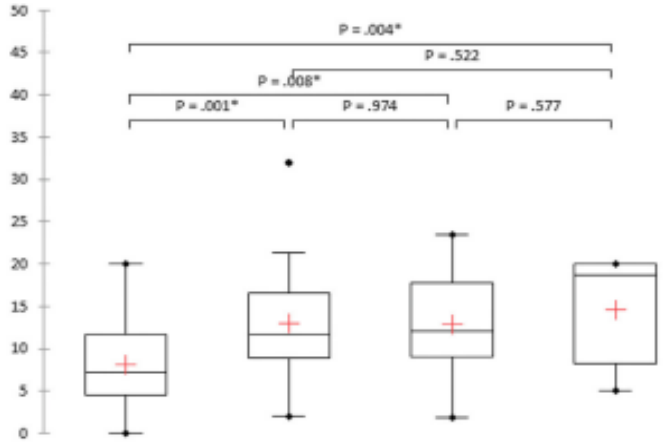
Clinical Gastroenterology and Hepatology 2023;21:2338–2346

Evolution of serum IFX levels after the switch

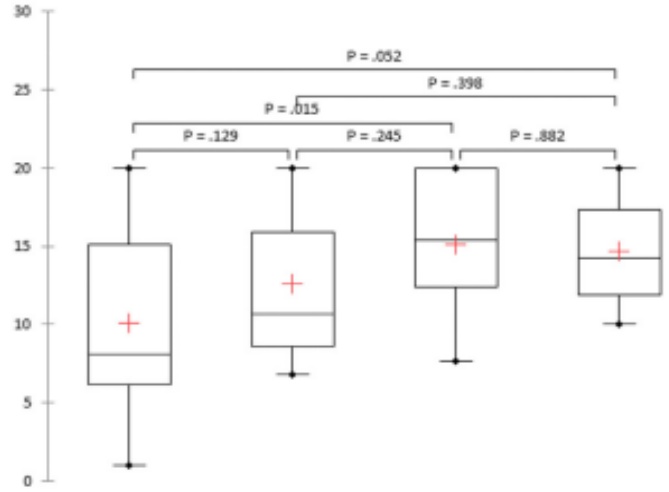
IFX 5 mg/kg/8 wks



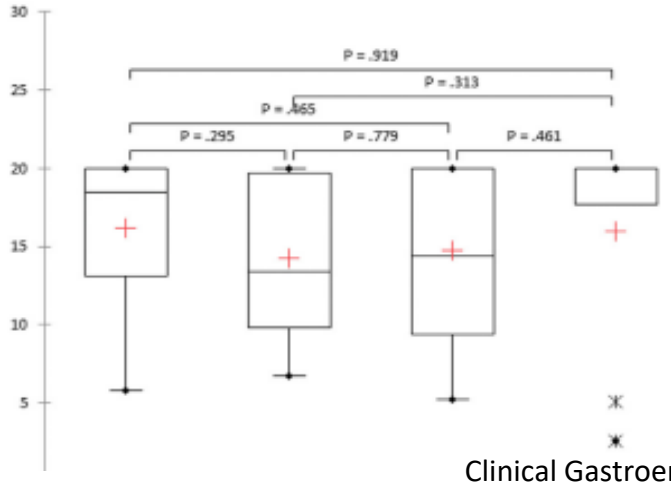
IFX 10 mg/kg/8 wks



IFX 10 mg/kg/6 wks



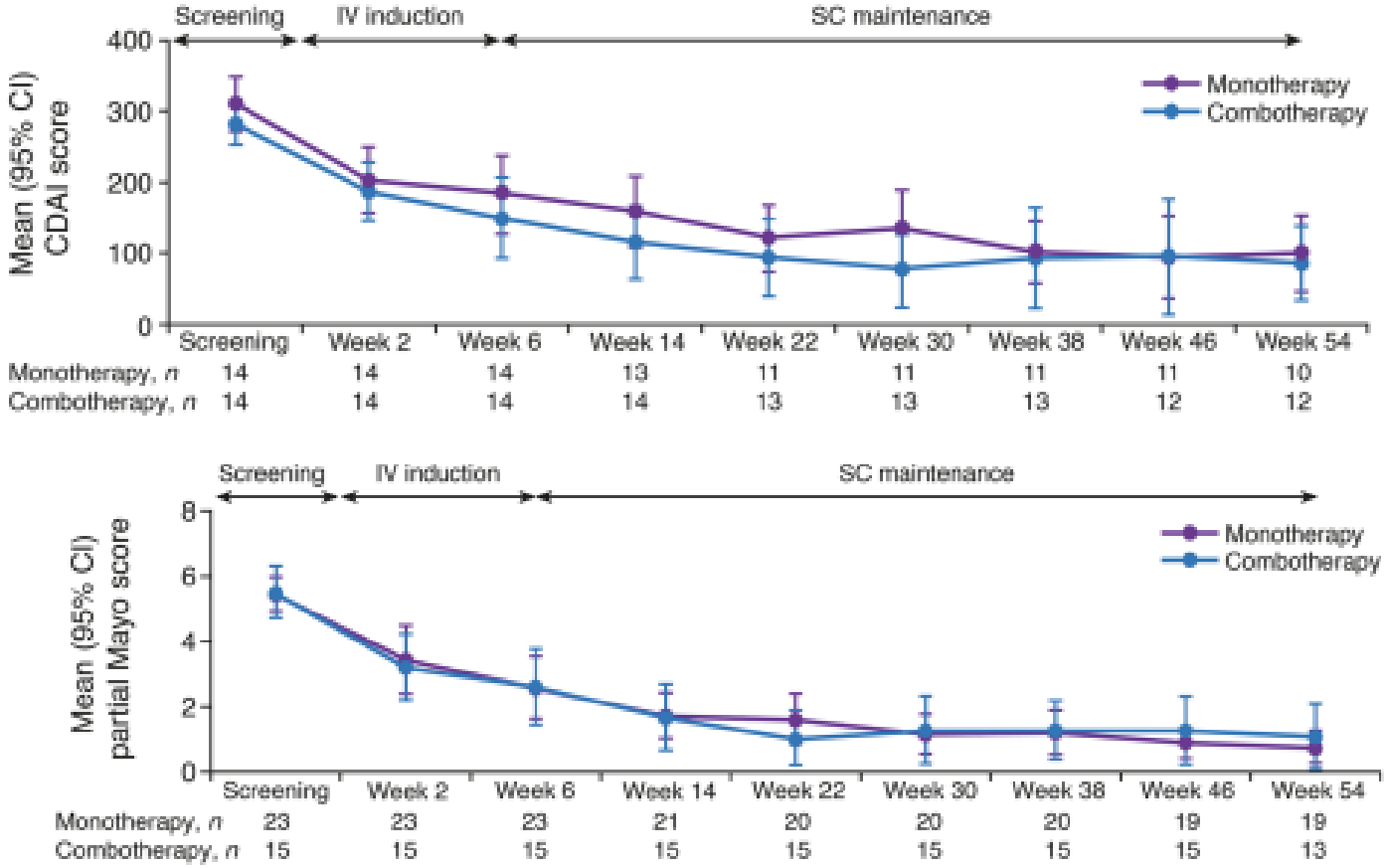
IFX 10 mg/kg/4 wks



Clinical Gastroenterology and Hepatology 2023;21:2338–2346

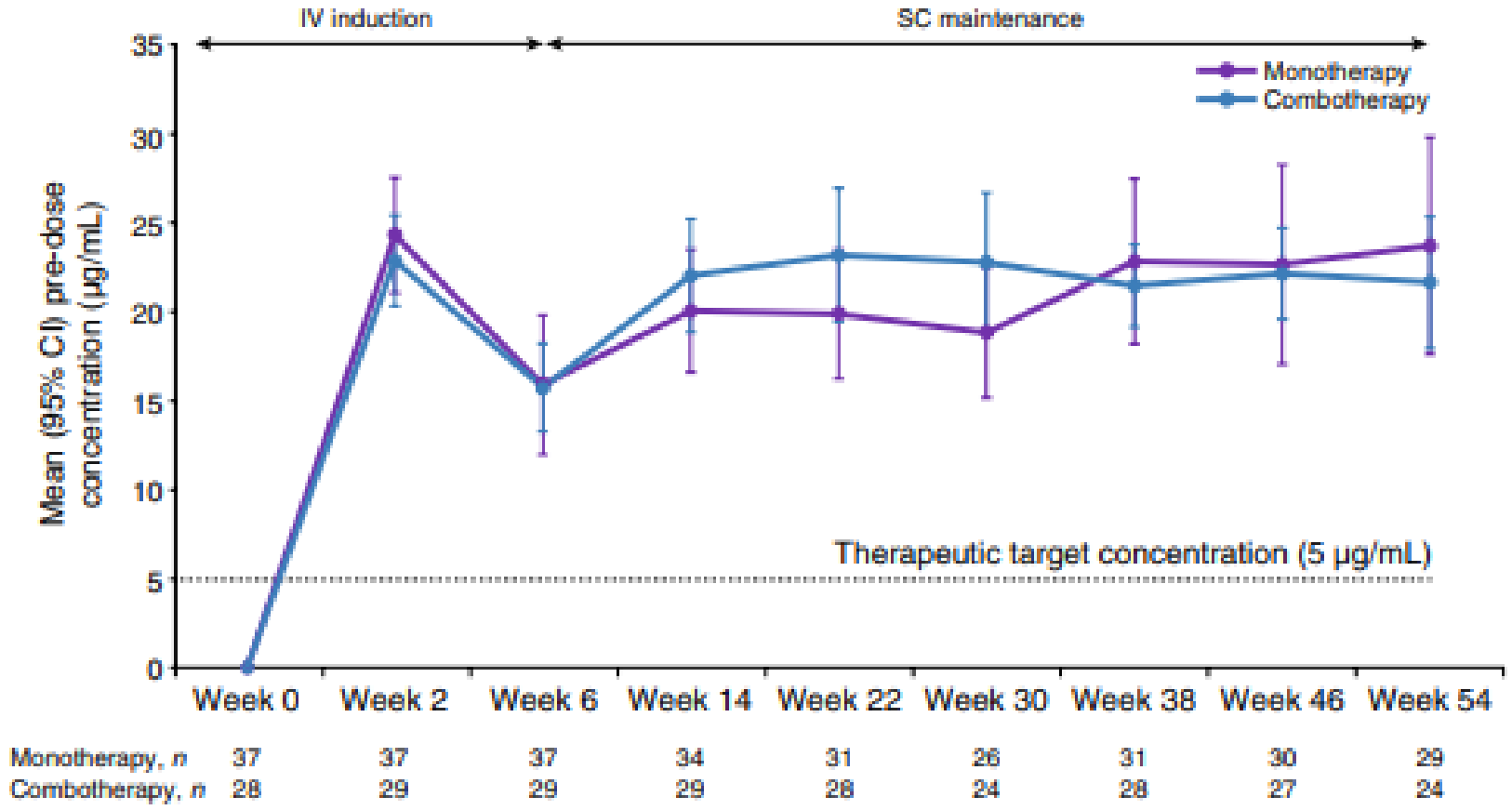
Subcutaneous Infliximab Monotherapy Versus Combination Therapy with Immunosuppressants in Inflammatory Bowel Disease: A Post Hoc Analysis of a Randomised Clinical Trial

Geert D'Haens[1] · Walter Reinisch[2] · Stefan Schreiber[3] · Fraser Cummings[4] · Peter M. Irving[5,6] · Byong Duk Ye[7] · Dong-Hyeon Kim[8] · SangWook Yoon[8] · Shomron Ben-Horin[9]



D'Haens 2024

	Ada+
Mono	65.5%
Combo	48%



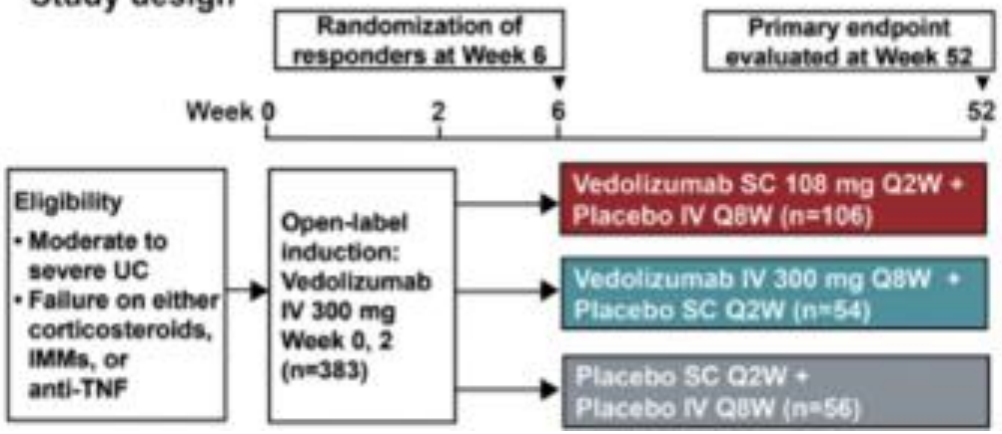
D'Haens 2024

SUBCUTANEOUS VEDOLIZUMAB

Efficacy and Safety of Vedolizumab Subcutaneous Formulation in a Randomized Trial of Patients With Ulcerative Colitis

William J. Sandborn,[1] Filip Baert,[2] Silvio Danese,[3] Željko Krznarić,[4] Taku Kobayashi,[5] Xiaopan Yao,[6] Jingjing Chen,[6] Maria Rosario,[6] Siddharth Bhatia,[7] Krisztina Kisfalvi,[6] Geert D'Haens,[8] and Séverine Vermeire[9]

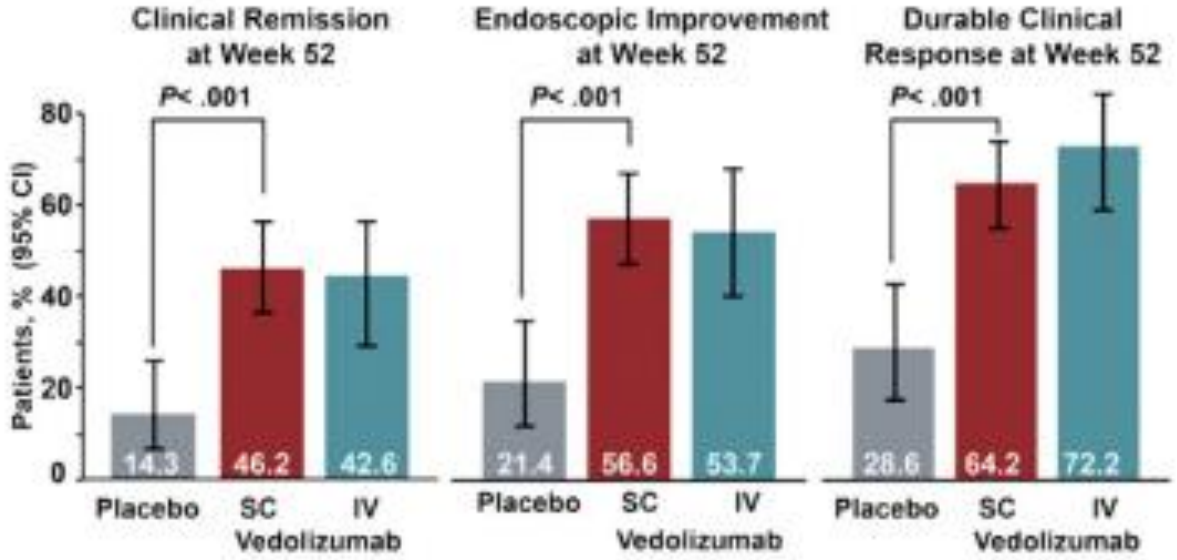
Study design



Safety / tolerability

n (%)	Placebo (N=56)	Vedolizumab SC (N=106)	Vedolizumab IV (N=54)
Adverse events	43 (76.8)	69 (65.1)	41 (75.9)
Serious adverse events	3 (5.4)	6 (5.7)	1 (1.9)
Abdominal and GI infections	5 (4.7)	2 (3.7)	1 (1.8)
Injection site adverse events	0	11 (10.4)	1 (1.9)

Efficacy



Vedolizumab SC effective as maintenance therapy in patients with moderate to severe UC after clinical response to IV induction

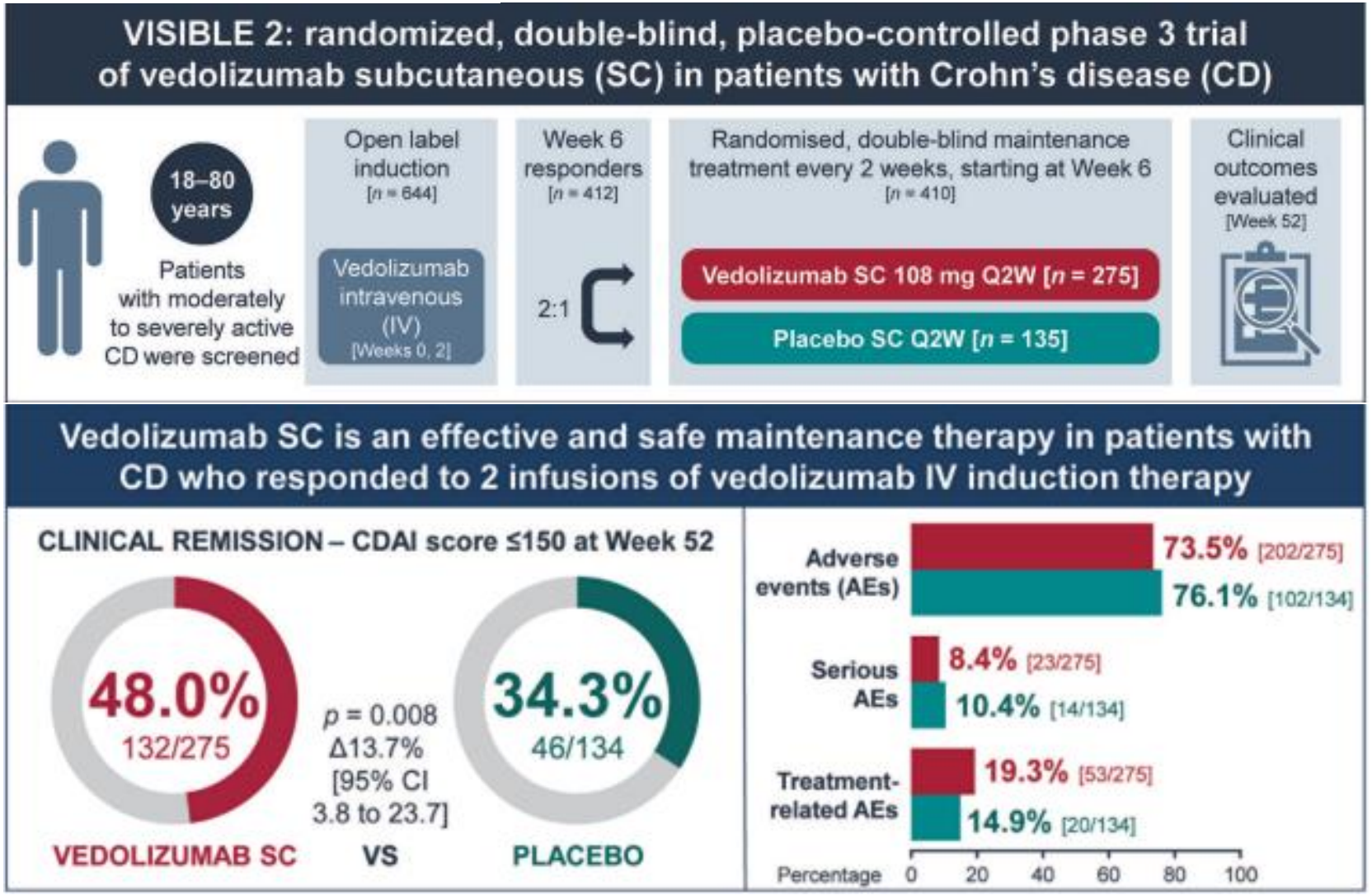
Vedolizumab SC safety / tolerability profile consistent with the well-established profile of vedolizumab IV

Sandborn, Gastroenterology 2020

Original Article

Efficacy and Safety of Subcutaneous Vedolizumab in Patients With Moderately to Severely Active Crohn's Disease: Results From the VISIBLE 2 Randomised Trial

Séverine Vermeire,[a] Geert D'Haens,[b] Filip Baert,[c] Silvio Danese,[d]



Vermeire, JCC 2022

Transitioning from Intravenous to Subcutaneous Vedolizumab in Patients with Inflammatory Bowel Disease [TRAVELESS]

Esther Ventress,[a] David Young,[a,b] Sohail Rahmany,[c] Clare Harris,[b] Marion Bettey,[c] Trevor Smith,[c] Helen Moyses,[d] Magdalena Lech,[b] Markus Gwiggner,[c] Richard Felwick,[c] J. R. Fraser Cummings[b,c,d]

Transitioning from intRavenous to subcutAneous VEdolizumab in patients with infLammatory bowEl diSeaSe (TRAVELESS)

54 remained on IV

178 adults with IBD treated with IV vedolizumab offered the option to transition to home administered SC vedolizumab

124

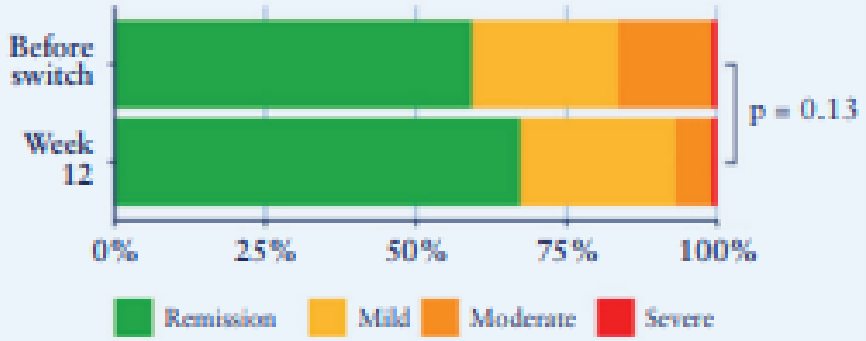
Efficacy, safety and satisfaction review 12 weeks after transition

Maintenance of baseline status:

✔ 84%

✘

No change in disease activity following transition for patients established (median 24 months) on vedolizumab



Well tolerated

All ADRs reported by > 5%

Adverse drug reaction (ADR)	Patients, n (%)
Injection site reaction	18 (15%)
Joint pain	10 (8%)
Rash	10 (8%)
Headache	7 (6%)

High patient satisfaction following transition

Median patient time saved per infusion

Estimated annual savings for this Trust

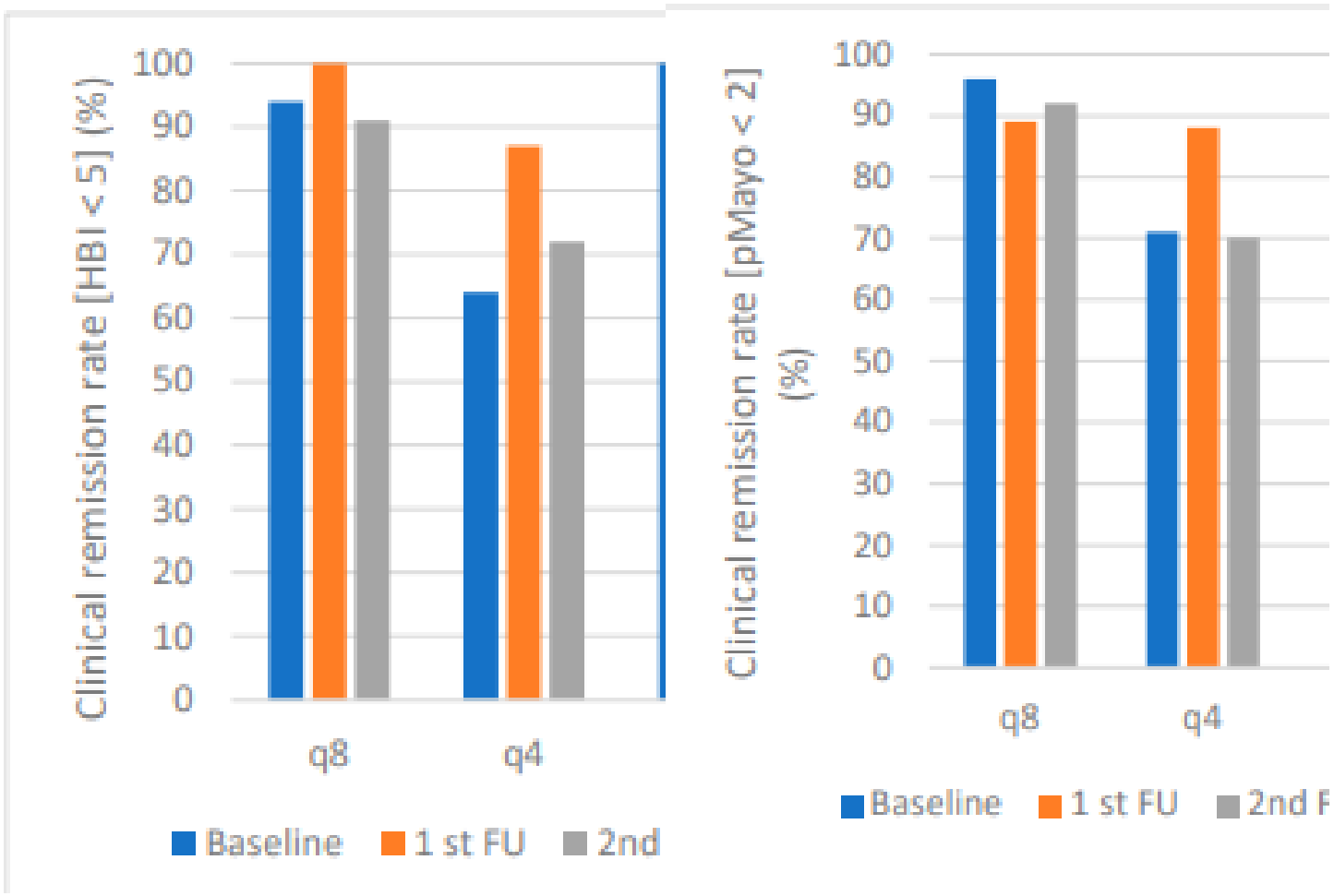
£572k

Article

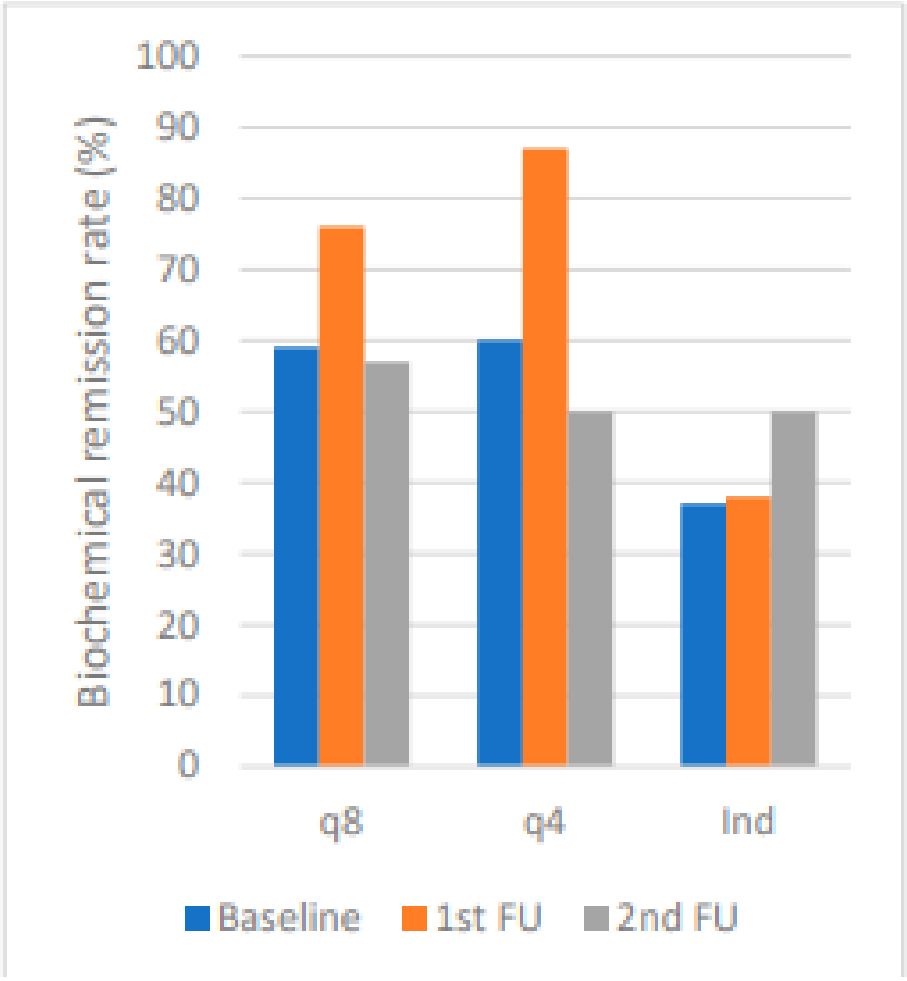
Remission Is Maintained after Switch from Dose-Optimised Intravenous Treatment to Subcutaneous Treatment with Vedolizumab in Inflammatory Bowel Disease

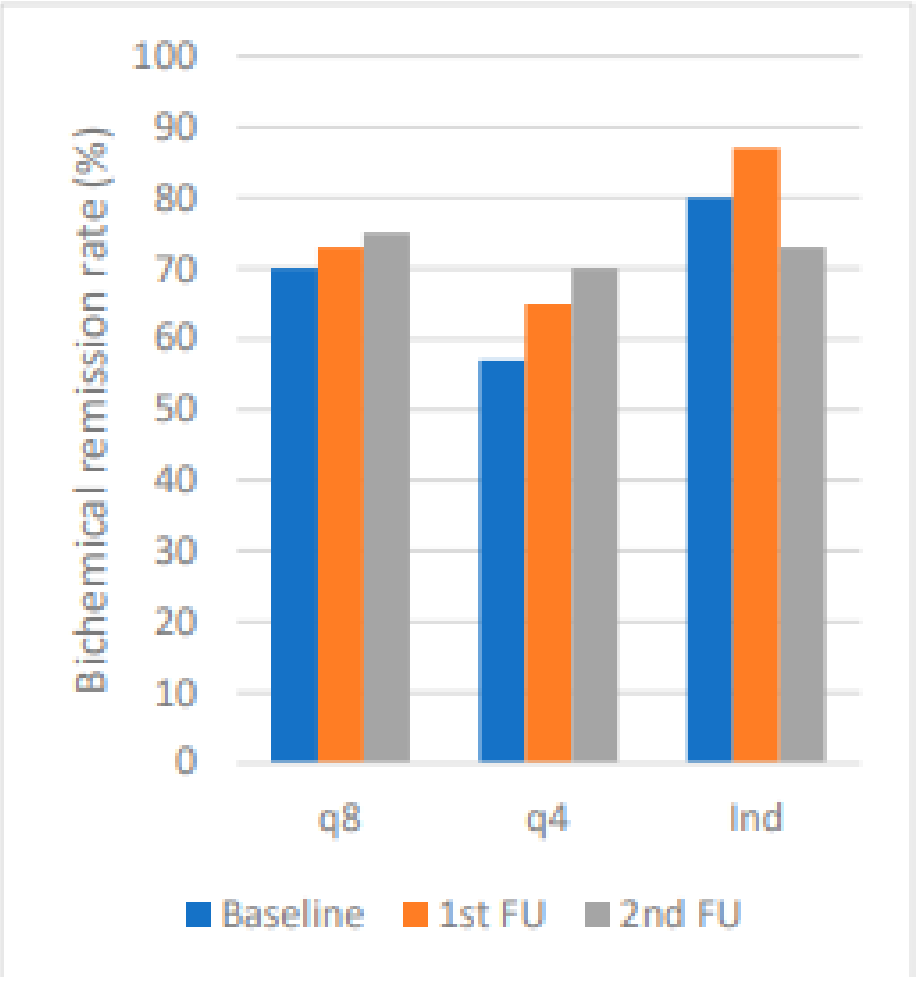
Špela Pintar [1,†], Jurij Hanžel [1,2,†], David Drobne [1,2], Matic Koželj [1], Tina Kurent [1], Nataša Smrekar [1] and Gregor Novak [1,2,*]

- Real world efficacy of switching to sc treatment
- 135 pts (38% CD, 62% UC)
- Median time 1st follow-up 14.5 weeks
- Median time 2nd follow up 40 weeks



Pintar, Medicina 2024



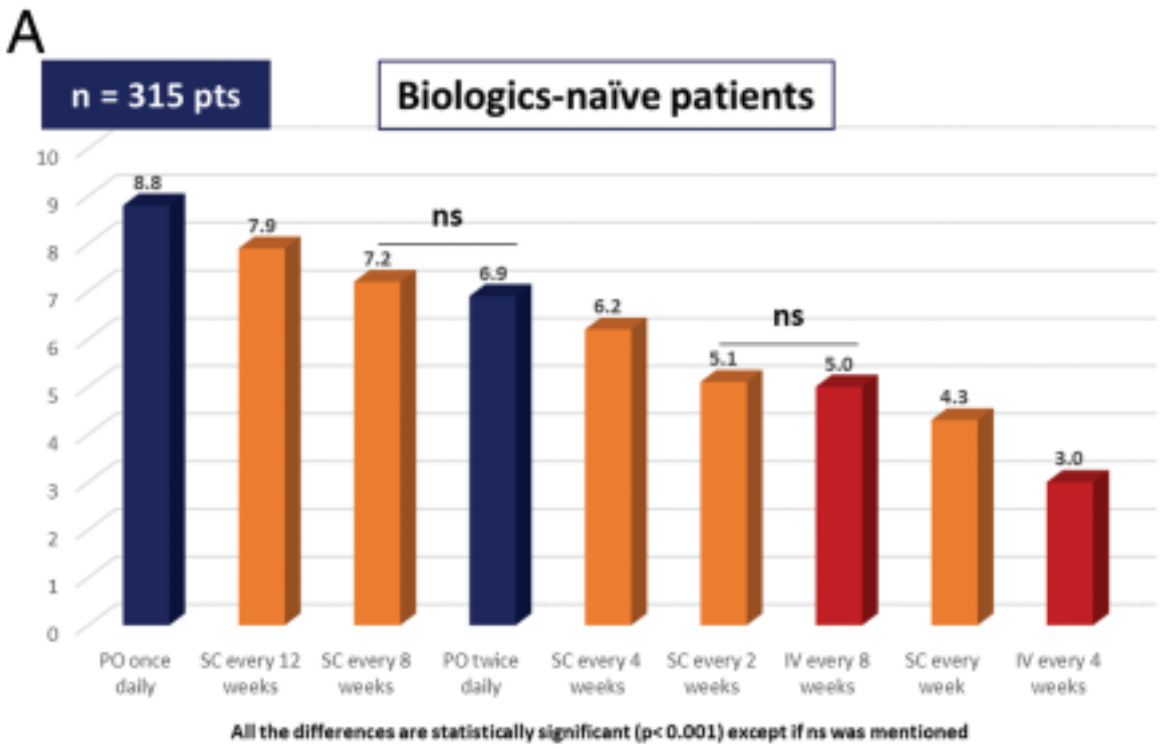


Pintar, Medicina 2024

Comparative Acceptability of Therapeutic Maintenance Regimens in Patients With Inflammatory Bowel Disease: Results From the Nationwide ACCEPT2 Study

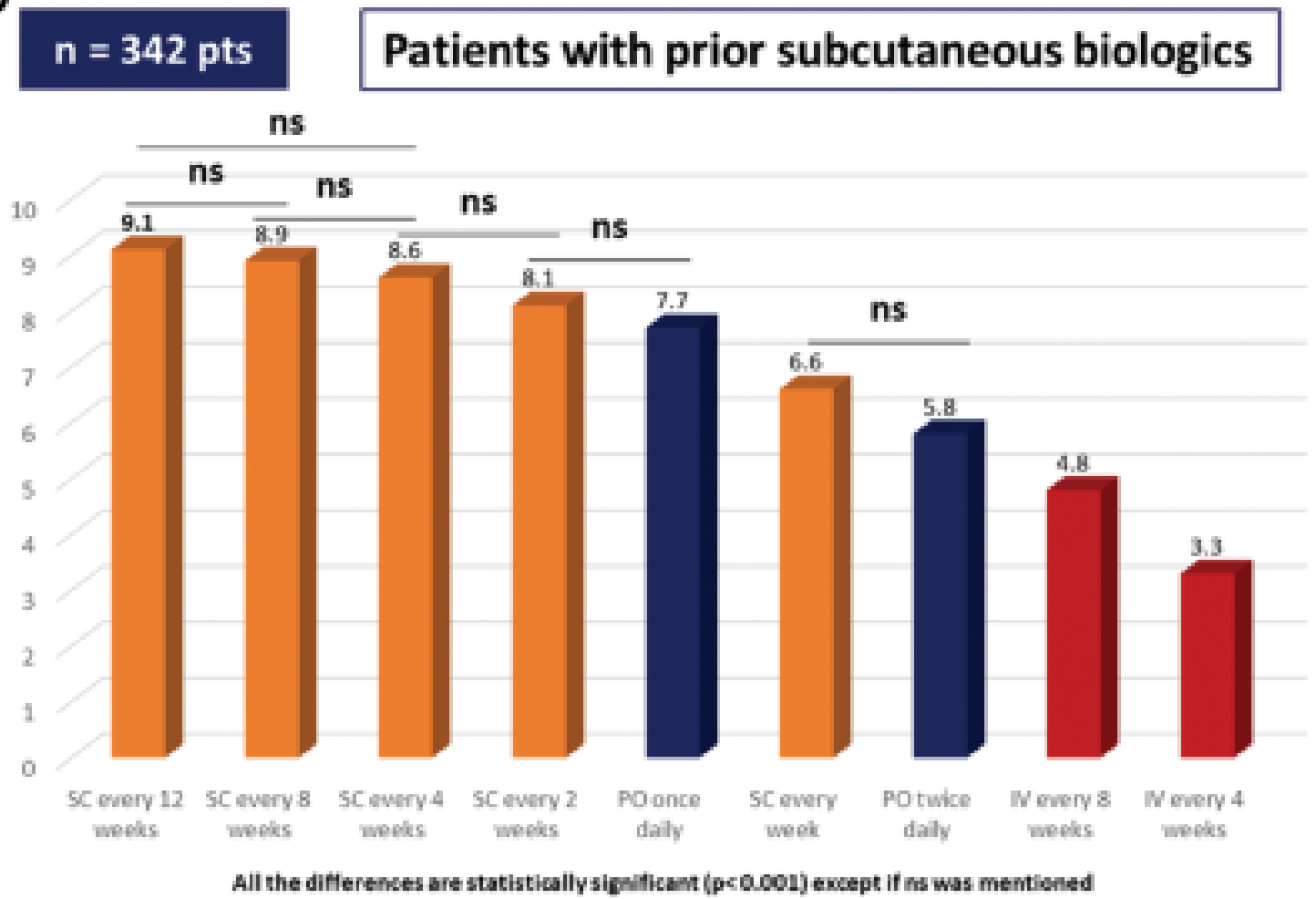
Anthony Buisson, MD, PhD,[*,†,] Mélanie Serrero, MD,[‡] Laurie Orsat, MSc,[*]

- 1850 pts included
- Dedicated questionnaire including acceptability numerical scales (ANS)



Buisson, IBD 2023, 29, 579-588

B



Buisson, IBD 2023, 29, 579-588

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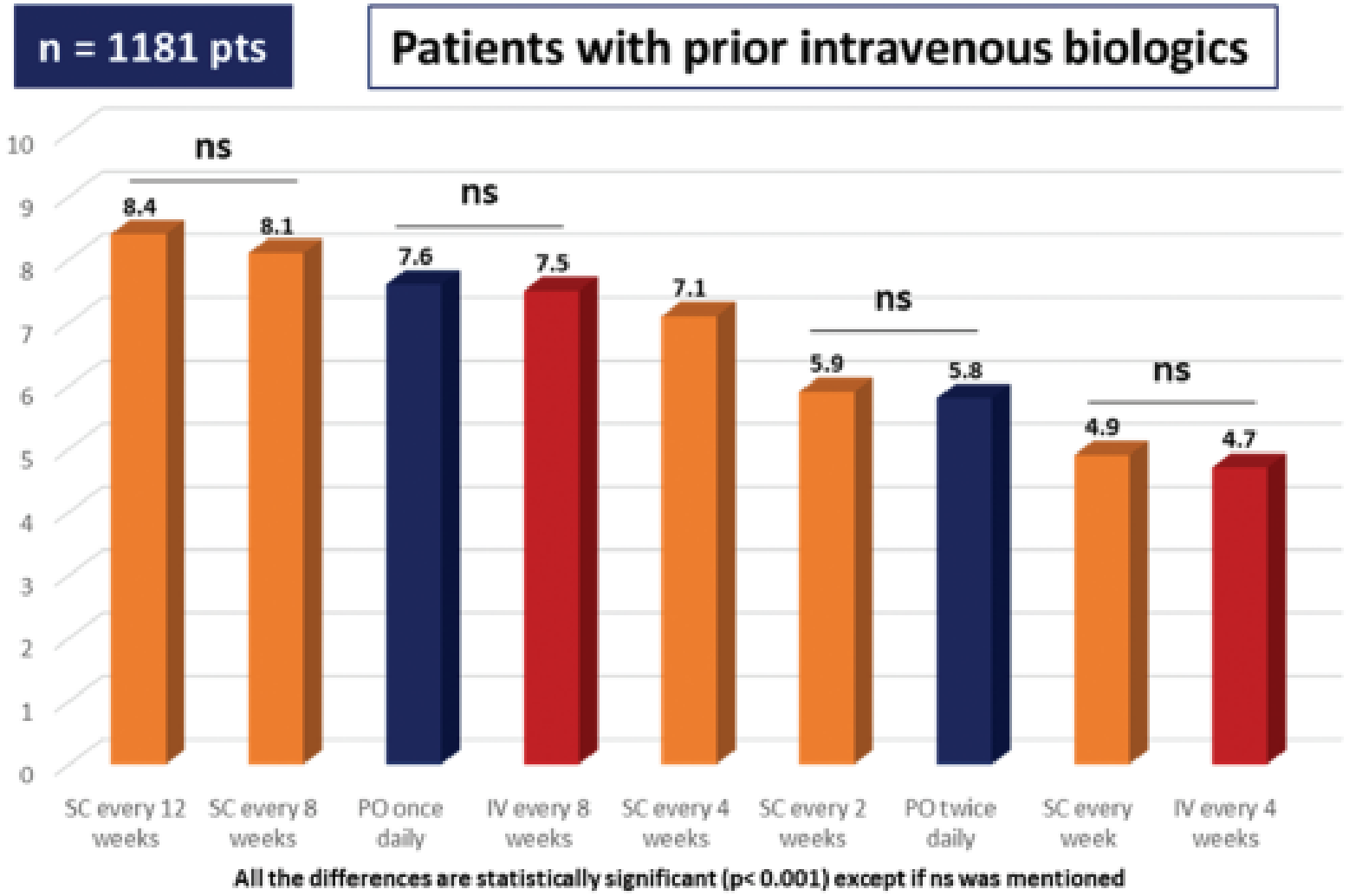


Buisson, IBD 2023, 29, 579-588

Article

Inflammatory Bowel Disease Patients' Acceptance for Switching from Intravenous Infliximab or Vedolizumab to Subcutaneous Formulation: The Nancy Experience

Clotilde Remy [1,†], Bénédicte Caron [1,2,†], Celia Gouynou [1], Vincent Haghnejad [1,2], Elodie Jeanbert [3], Patrick Netter [4], Silvio Danese [5] and Laurent Peyrin-Biroulet [1,2,*]

- 130 pts included
  - 27.7% vedolizumab
  - 72.3% infliximab
- 77% pts accepted the switch

Multivariate analysis: short duration of treatment associated with higher switch acceptance rate

Reasons for Patient's Refusal for Switching from IV to SC Formulation	Total	IFX	VDZ
Fear of loss of efficacy, n (%)	10 (34.5)	7 (30.4)	3 (50.0)
Impact on medical follow-up	10 (34.5)	9 (39.1)	1 (16.7)
Increased frequency of administration	3 (10.3)	2 (8.7)	1 (16.7)
Self-administered injection	4 (13.8)	3 (13.0)	1 (16.7)
Other	2 (6.9)	2 (8.7)	0 (0.0)

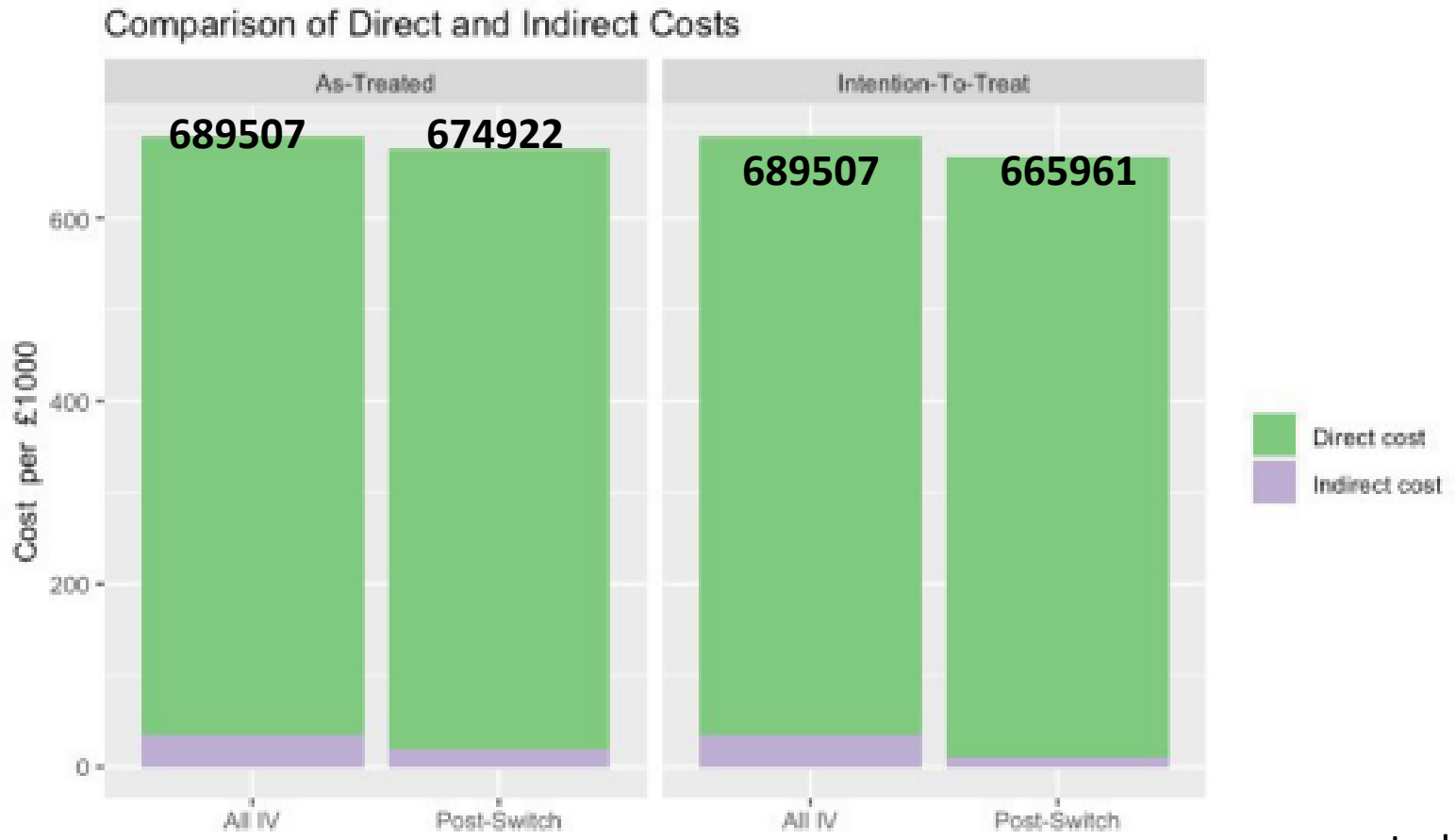
n, number; %, percentage; IV, intravenous; SC, subcutaneous; IFX, infliximab; VDZ, vedolizumab.

Remy, J Clin Med 2022

Impact on direct and indirect costs of switching pts with IBD from i.v. to s.c. IFX

- All adult pts with IBD on standrad dose CT-P13 (5 mg/kg) were eligible to switch
- 98/169 pts (58%) switched within 3 months
- Real life direct and indirect costs in a tertiary centre

Isabel Carbery, BMJ 2023

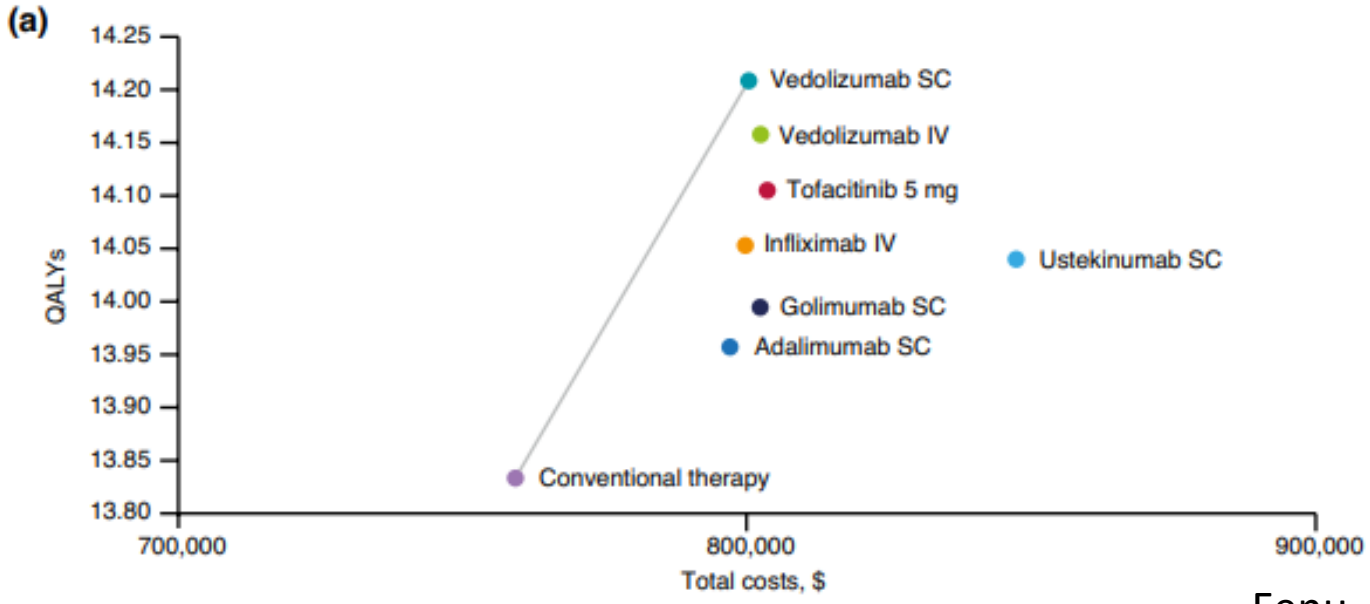


Isabel Carbery, BMJ 2023

Cost Effectiveness of Subcutaneous Vedolizumab for Maintenance Treatment of Ulcerative Colitis in Canada

Markov model to evaluate *vedo costs*, *QUALYs*, *cost effectiveness* vs conventional therapy, ada sc, ifx i.v., gol sc, tofa, uste s.c., vedo i.v.

This model predicts the number of patients achieving clinical response and remission after treatment induction



Fenu, Pharmacoeconomics 2022

Costi

VDZ vs	$/anno
Ustekinumab sc	↓ 47,024
Tofacitinib 5 mg	↓ 3251
Vedolizumab i.v.	↓ 2120
Golimumab	↓ 2004
IFX i.v.	↑ 582
Ada	↑ 3293
conventional	↑ 41,024

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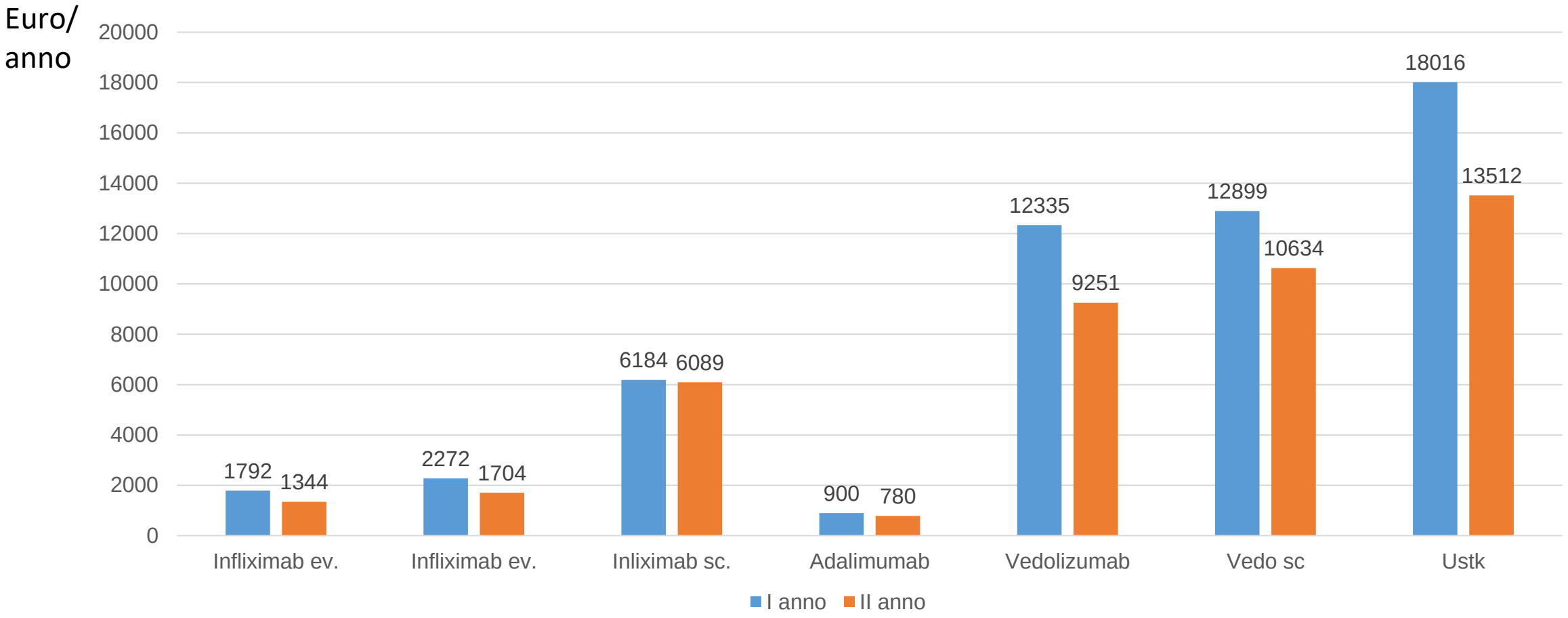
Spesa annuale/trattamento (ULSS9)

Paziente di 70 kg, senza ottimizzazione

	I anno terapia	II anno
Infliximab ev. biosimilare	1792	1344
Infliximab e.v.	2272	1704
Infliximab s.c.	6184 (568 + 5616)	6089
Adalimumab	900 (180 + 720)	780
Vedolizumab	12335	9251
Vedolizumab s.c.	12899 (3083+9816)	10634
Ustekinumab	18016 (6756+11260)	13512


Euro/ anno
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
1792
1344
2272
1704
6184
6089
900
780
12335
9251
12899
10634
18016
13512
Infliximab ev.
Infliximab ev.
Inliximab sc.
Adalimumab
Vedolizumab
Vedo sc
Ustk
I anno
II anno

Switching from i.v. to s.c. infliximab and vedolizumab

- Multicenter, retrospective study
- CD and UC moderate-severe activity
- 231 pts (168 IFX, 68%; 73 VDZ, 32%)
- Time to switch:
  - Week 6 in 83 pts (36%)
  - Median time to switch: 13 months
- At 6 months:
  - 12 pts (5,2%) underwent reverse switch
  - 9 (3.9%) discontinued therapy
  - 6 (2.6%) required optimization
  - 5 (2.2%) required systemic steroids

D'Amico, IGIBD 2023

Clinical activity at baseline:
low probability of corticosteroid free remission at 3 and 6 months (multivariate analyses)

Switch a sottocute: pro e contro

- Comodità del paziente
- Minor accesso ad amb. infusionale
- Ottimizzazione risorse
- Minore immunogenicità
- Costi?

- Saturazione dell'ambulatorio
- Il paziente deve comunque ritirare il farmaco ogni 2 mesi
- Aderenza alla terapia?
- Costi?

Conclusioni

IBD goes home

Vedolizumab e Infliximab sottocute hanno dimostrato pari efficacia rispetto alla formulazione ev. nel mantenimento della remissione

Valida alternativa alla formulazione ev. nei pazienti motivati

L'impatto dei costi della terapia s.c. non è facile da calcolare, e bisogna tenere in considerazione l'elevato costo (diretto) del sottocute

Resta da definire il timing più adeguato per il passaggio alla terapia sottocutanea, ma è fondamentale che il paziente sia stabilizzato


ngiyabonga
danke
謝謝
teşekkur ederim
спасибо
dank je
thank you
gracias
tapadh leat
mochchakkeram
bedankt
hvala
mauruuru
dziękuje
go raibh maith agat
sukriya
kop khun krap
obrigado
arigató
dakujem
grazie
merci
감사합니다