Satellite symposium EAHP 2017

The evidence for switching stable patients to Inflectra

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Hospira
A Pfizer Company

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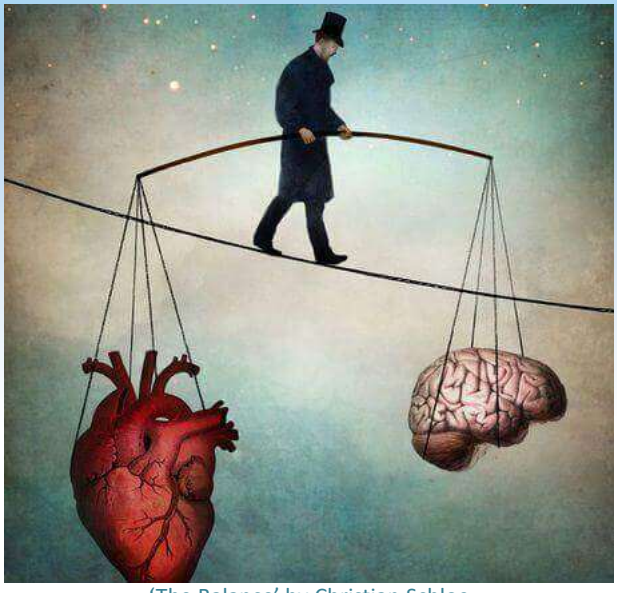
Disclosures

Silvio Danese has served as speaker, consultant and advisory board member for Abbvie, Astra Zeneca, Hospira, Johnson & Johnson, MSD, Mundipharma, Takeda, Vifor, and Pfizer

EAHP 2017–

"Hospital Pharmacists: Catalysts For Change"

Biosimilars in IBD



'The Balance' by Christian Schloe

Clinical studies that have examined switching to CT-P13* from Remicade

Study (Country)	Completion or Publication Date	Centres	Total Patients (No. Switched)	Indication/Use	Duration
PLANETRA extension[1] (International)	July 2013	69	302 (144)	Rheumatoid arthritis (RA)	48 weeks
PLANETAS extension[2] (International)	June 2013	40	174 (86)	Ankylosing spondylitis (AS)	48 weeks
Nikiphorou et al[3] (Finland)	November 2015	1	39 (39)	RA, AS, psoriatic arthritis (PsA), juvenile inflammatory arthritis (JIA), chronic reactive arthritis	56 weeks
Abdalla et al[4] (Ireland)	June 2016	1	34 (34)	RA, AS, PsA, IBD-related arthritis, JIA	91 weeks
Holroyd et al[5] (UK)	April 2016	1	56 (56)	RA, PsA, enteropathic arthritis (EA)	21 weeks
Malaiya et al[6] (UK)	April 2016	1	31 (30)	RA, AS, PsA	12 weeks[a]

1. Yoo DH et al. *Ann Rheum Dis.* 2017;76:355–63. 2. Park W et al. *Ann Rheum Dis.* 2017;76:346–54. 3. Nikiphorou E et al. *Expert Opin Biol Ther.* 2015;15(12):1677–83. 4. Abdalla A et al. *Open Access Rheumatol.* 2017;9:29–35. 5. Holroyd C et al. Presented at: BSR 2016. Abstract O52. 6. Malaiya R et al. Presented at: BSR 2016. Abstract 158.

[a]Converted from months.

*The molecule CT-P13 is marketed in different countries by different companies, under different brand names including Remsima and Inflectra

Clinical studies that have examined switching to CT-P13* from Remicade (cont'd)

Study (Country)	Completion or Publication Date	Centres	Total Patients (No. Switched)	Indication/Use	Duration
DANBIO[1] (Denmark)	June 2016	Not stated	693 (693)	RA, AS, PsA	12 weeks[a]
Batticciotto et al[2] (Italy)	June 2016	3	31 (31)	AS, PsA, EA, undifferentiated spondylarthritis (SpA)	26 weeks[a]
PROSIT-BIO[3]	January 2017	31	547 (97)	Crohn's disease (CD), ulcerative colitis (UC)	24 weeks
NOR-SWITCH[4] (Norway)	Planned completion January 2017	40	481 (240)	RA, CD, UC, SpA, PsA, psoriasis	52 weeks
Jung et al[5] (Korea)	April 2015	6	110 (36)	Inflammatory bowel disease	54 weeks

1. Glintborg B et al. Presented at: ACR 2016. Abstract 951.
2. Batticciotto A et al. Presented at: ACR 2016. Abstract 721.
3. Fiorino G et al. *Inflamm Bowel Dis.* 2017;23(2):233–43.
4. Jørgensen K et al. Presented at: UEGW 2016. Abstract #LB15.
5. Jung et al. *J Gastroenterol Hepatol* 2015;30:1705–12

[a]Converted from months.

*The molecule CT-P13 is marketed in different countries by different companies, under different brand names including Remsima and Inflectra

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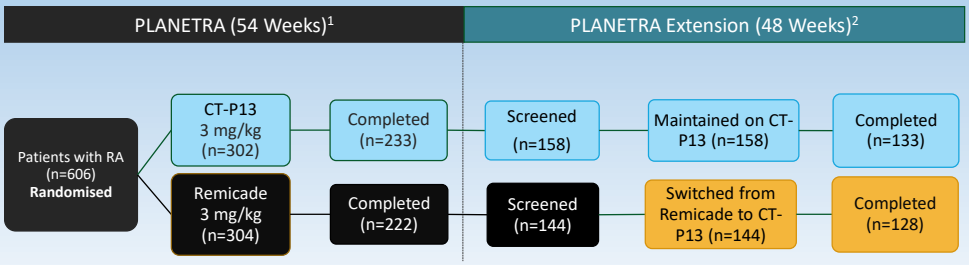
PLANETRA and PLANETAS

Hospira

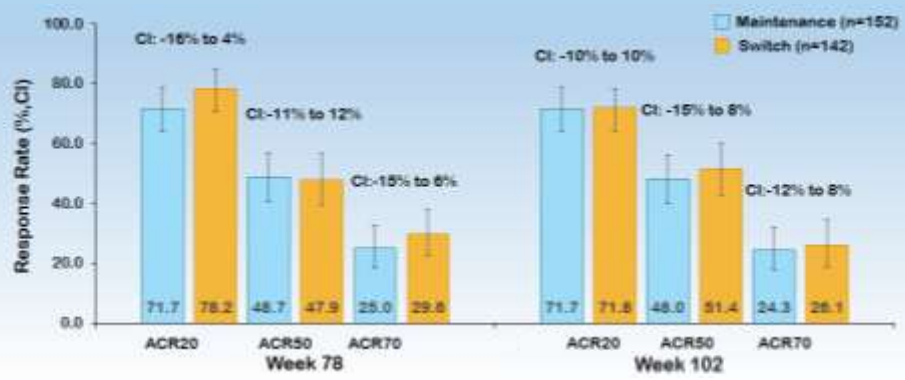
PLANETRA extension trial design



- Eligible patients with RA from PLANETRA were enrolled in a 48-week extension study to assess the efficacy and safety of switching from Remicade to CT-P13 (**switch** group) relative to maintenance on CT-P13 (**maintenance** group)[2]
- The objective of the study was to confirm long-term efficacy and safety of CT-P13 and to investigate switching from Remicade to CT-P13 in patients with RA[2]

1. Yoo DH et al. *Arthritis Res Ther.* 2016;18(1):82.
2. Yoo DH et al. *Ann Rheum Dis.* 2017;76:355–63.

Clinical response rates (ACR Criteria) at weeks 78 and 102 (efficacy population)

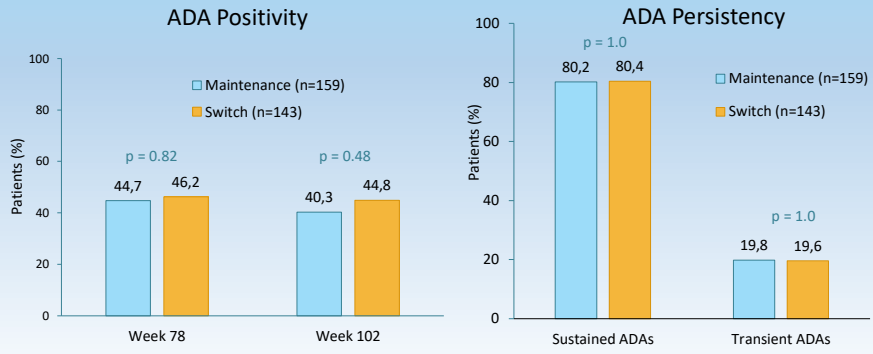


- ACR20, ACR50, and ACR70 responses did not differ significantly between maintenance and switch groups at weeks 78 and 102

ACR20/ACR50/ACR70, American College of Rheumatology definition of a 20%/50%/70% improvement; CI, 95% confidence interval.

Yoo DH et al. *Ann Rheum Dis.* 2017;76:355–63.

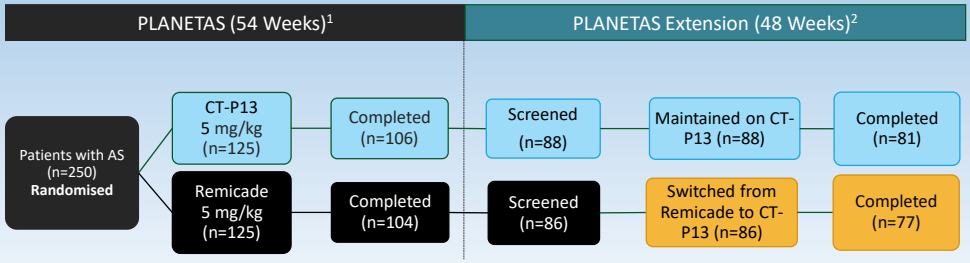
Antidrug Antibody (ADA) detection at weeks 78 and 102 (safety population)



- The percentage of patients positive for infliximab ADA and persistency of ADA was similar between treated groups at weeks 78 and 102

Yoo DH et al. *Ann Rheum Dis.* 2017;76:355–63.

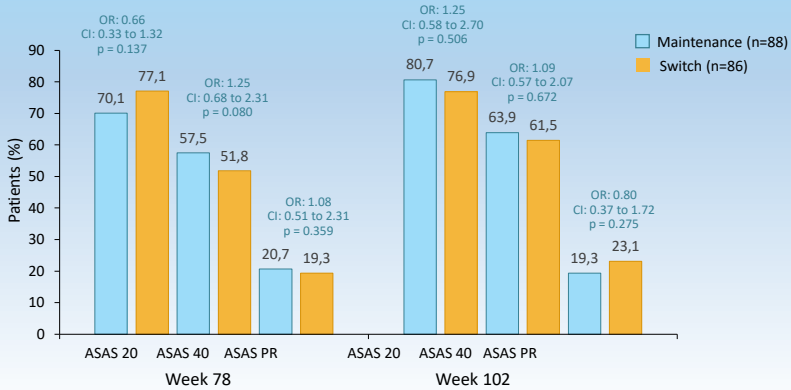
PLANETAS extension trial design



- Eligible patients with AS from PLANETAS were enrolled in a 48-week extension study to assess the efficacy and safety of switching from Remicade to CT-P13 (**switch** group) relative to maintenance on CT-P13 (**maintenance** group)[2]
- The objective of the study was to confirm long-term efficacy and safety of CT-P13 and to investigate switching from Remicade to CT-P13 in patients with AS[2]

1. Park W et al. *Arthritis Res Ther.* 2016;18(1):25.
2. Park W et al. *Ann Rheum Dis.* 2017;76:346–54.

Clinical response rates (ASAS Criteria) at weeks 78 and 102 (efficacy population)

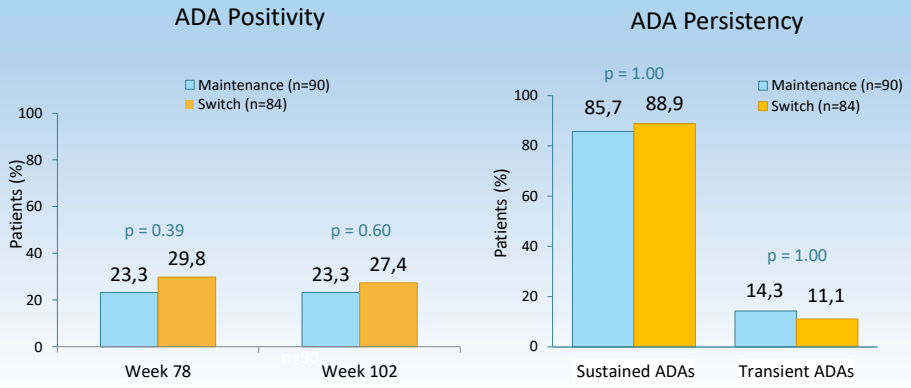


- ASAS 20, ASAS 40, and ASAS PR responses were similar between the maintenance and switch groups at weeks 78 and 102

ASAS 20/ASAS 40/ASAS PR, Assessment of SpondyloArthritis international Society 20%/40% improvement criteria/partial remission; CI, confidence intervals; OR, odds ratio.

Park W et al. *Ann Rheum Dis.* 2017;76:346–54.

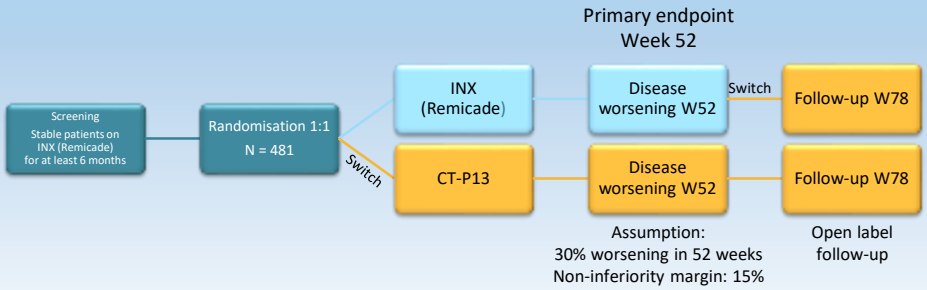
ADA positivity at weeks 78 and 102 (safety population)



- The percentage of patients positive for infliximab ADA and persistency of ADA was similar between treated groups at weeks 78 and 102

Park W et al. *Ann Rheum Dis.* 2017;76:346–54.

Study design and description[1-3]



- Primary endpoint: percentage of patients experiencing disease worsening

1. EudraCT Number: 2014-002056-40. https://www.clinicaltrialsregister.eu/ctr-search/trial/2014-002056-40/NO Accessed: March 2017.
2. ClinicalTrials.gov. The NOR-SWITCH Study. NCT02148640. https://clinicaltrials.gov/ct2/show/NCT02148640. Accessed: March 2017.
3. Jørgensen K et al. Presented at: UEGW 2016. Abstract LB15

Primary endpoint: disease worsening across indications

	INX (N=202)	CT-P13 (N=206)	Adjusted rate difference (95% CI)
Disease worsening (all indications)*	53 (26.2%)	61 (29.6%)	-4.4 (-12.7–3.9)

- The authors concluded that switch from INX (Remicade) to CT-P13 was not inferior to continued treatment with INX (Remicade)

*UC: Increase in partial-Mayo (p-Mayo) score of ≥ 3 points from randomisation and a minimum p-Mayo score of ≥ 5 points
CD: Increase in HBI of ≥ 4 points from randomisation and a HBI score of ≥7 points
RA/PsA: Increase in DAS28 of ≥ 1.2 from randomisation and a minimum DAS score of 3.2
AS/SpA: Increase in ASDAS of ≥1.1 from randomisation and a minimum ASDAS of 2.1
Psoriasis: Increase in PASI of ≥ 3 points from randomisation and a minimum PASI score of 5

If a patient did not fulfill the formal definition, but experienced a clinically significant worsening according to both the investigator and patient and which led to a major change in treatment this was considered as a disease worsening but recorded separately in the Case Report Form.

ASDAS, Ankylosing Spondylitis Disease Activity Score; AS, ankylosing spondylitis; CD, Crohn's Disease; CRF, DAS28, Disease Activity Score in 28 joints; HBI, Harvey-Bradshaw Index; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, spondylarthritis; UC, ulcerative colitis.

Jørgensen K et al. Presented at: UEGW 2016. Abstract #LB15

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PROSIT-BIO

Study design and description

Key inclusion criteria
- Previously diagnosed either as UC or CD based on clinical, radiological, endoscopic, and histological criteria

Naive to anti–TNF-α (n=311)

Previous exposure to anti–TNF-α (n=139)

Switched from originator infliximab (n=97)

→ CT-P13

Week 8	Week 32	Week 54
Primary failure/ loss of response[a]	Estimated efficacy endpoint[b]	Primary endpoint[c]

Mean follow-up of 4.3 ±2.8 months

Primary endpoint:
- Evaluation of safety in terms of the rate of SAEs along the first year since introduction of CT-P13

Secondary endpoints:
- Efficacy evaluated in terms of clinical remission/response and treatment persistency
- Immunogenicity evaluated as the occurrence of infusion reactions and loss of response
- Predictive factors of safety and efficacy

[a]Primary failure to CT-P13 was defined as no or minor clinical response at 8 weeks after the induction regimen or deterioration of clinical condition leading to surgery, early therapy change, or withdrawal. Loss of response was studied among responders at Week 8 using time-to-event methods for censored observations (ie, patients withdrawn from the study because of AEs, and patients who had not lost response on the final data collection date, were considered "censored").

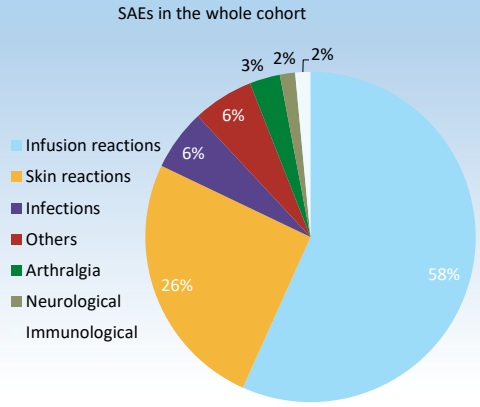
[b]Estimated efficacy was calculated using time-to-event methods for censored observations up to 32 weeks from the beginning of therapy.

[c]Evaluation of safety in terms of rate of SAEs along the first year since the introduction of the CT-P13 biosimilar in Italy.

CD=Crohn's disease; IBD=inflammatory bowel disease; SAE=serious adverse event; TNF=tumuor necrosis factor; UC=ulcerative colitis.

Fiorino G et al. *Inflamm Bowel Dis*. 2017;23(2):233–43.

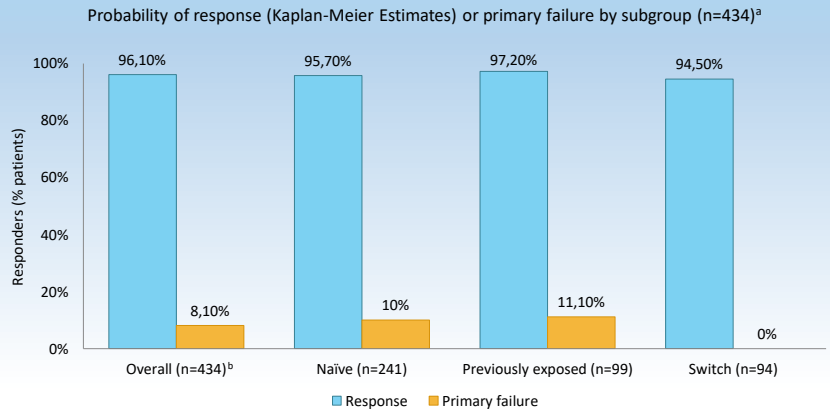
Primary endpoint: adverse events for overall study population



- 12.1% of patients (66/547) reported SAEs, leading to discontinuation of CT-P13 in 16 patients (2.9%)
  - No significant difference in the incidence of SAEs leading to discontinuation was found among the three cohorts
- 6.9% of patients (38/547) suffered infusion reactions, which led to discontinuation in 5.3% of patients
  - Infusion reactions were observed more frequently in pre-exposed patients in the whole cohort (no difference between patients with UC and CD)

CD, Crohn's disease; SAE, serious adverse event; TNF, tumour necrosis factor; UC, ulcerative colitis.
Fiorino G et al. *Inflamm Bowel Dis*. 2017;23(2):233–43.

Secondary endpoint: probability of response and primary failure

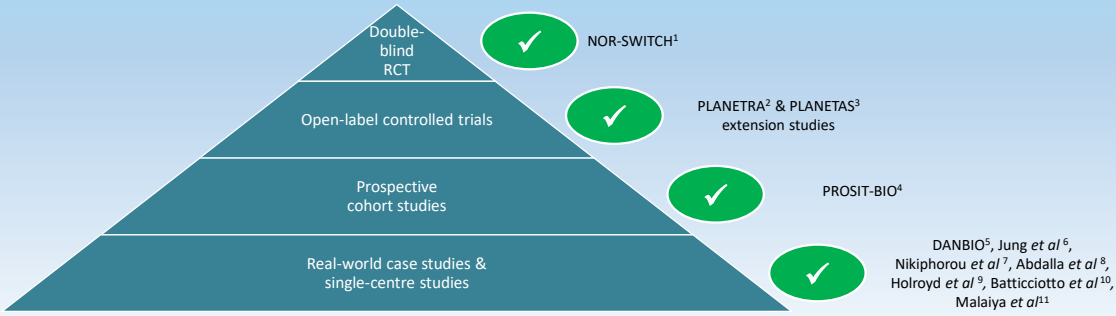


[a]Data presented are at the 8-week time point, which was calculated after the first 8 weeks, therefore 8 weeks actually represents 16 weeks from the start of treatment.

[b]18.6% (74/399) of the overall cohort's responders at Week 8 lost response during follow-up, which includes from week 8 onward.

Fiorino G et al. *Inflamm Bowel Dis*. 2017;23(2):233–43.

Conclusions



Available data indicates that switching to biosimilar infliximab CT-P13 shows similar safety and efficacy to remaining on innovator infliximab

1. Jørgensen K et al. Presented at: UEGW 2016. Abstract #LB15. 2. 1. Yoo DH et al. *Ann Rheum Dis.* 2017;76:355–63. 3. Park W et al. *Ann Rheum Dis*. 2017;76:346–54. 4. Fiorino G et al. *Inflamm Bowel Dis.* 2017;23(2):233–43. 5. Glintborg B et al. Presented at: ACR 2016. Abstract 951. 6. Jung et al. *J Gastroenterol Hepatol* 2015;30:1705–12 7. Nikiphorou E et al. *Expert Opin Biol Ther*. 2015;15(12):1677–83. 8. Abdalla A et al.*Open Access Rheumatol*. 2017;9:29–35. 9. Holroyd C et al. Presented at: BSR 2016. Abstract O52. 10. Batticciotto A et al. Presented at: ACR 2016. Abstract 721. 11. Malaiya R et al. Presented at: BSR 2016. Abstract 158.

ECCO position on biosimilars


ECCO Position Statement

ECCO Position Statement on the Use of Biosimilars for Inflammatory Bowel Disease—An Update

Silvio Danese,[a,b] Gionata Fiorino,[c] Tim Raine,[d] Marc Ferrante,[e] Karen Kemp,[f] Jaroslaw Kierkus,[g] Peter L. Lakatos,[h] Gerassimos Mantzaris,[i] Jenneke van der Woude,[j] Julian Panes,[k] Laurent Peyrin-Biroulet[l]

JCC

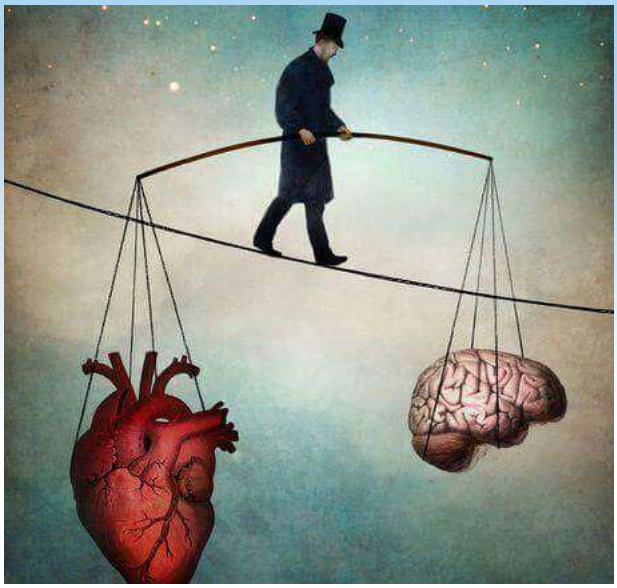
Switching from the originator to a biosimilar in patients with IBD is acceptable.

- Studies of switching can provide valuable evidence for safety and efficacy.
- Scientific and clinical evidence is lacking regarding reverse switching, multiple switching, and cross-switching among biosimilars in IBD patients

Switching from originator to a biosimilar should be performed following appropriate discussion between physicians, nurses, pharmacists, and patients, and according to national recommendation.

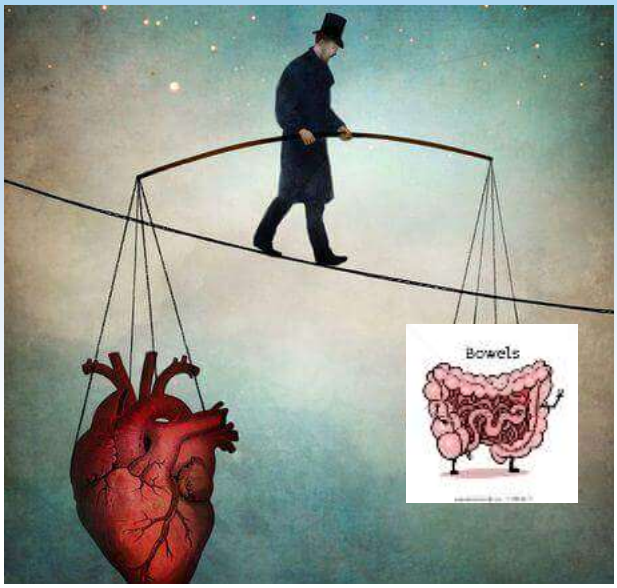
Danese S et al. *J Crohn's Colitis*. 2017:26–34 doi:10.1093/ecco-jcc/jjw198

Biosimilars in IBD



'The Balance' by Christian Schloe

Biosimilars in IBD



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