THE EVIDENCE

Recent studies demonstrating the possible impact of the nocebo effect

Reference biologic/ biosimilar biologic	Study design (Phase)	Indications	Follow-up post-switch	Evidence of a possible nocebo effect
1	Observ-ational, single-centre study (n=39)	RA, SpA, PsA, JIA, and chronic reactive arthritis	Variable	Of 39 Patients in Study, 11 patients (28.2%) discontinued CT-P13 treatment, with six patients discontinuing due to subjective reasons with no objective deterioration of disease. **Author conclusion:** **"Subjective reasons (negative expectations) may play a role among discontinuations of biosimilars".**
2	Observ-ational registry* (n=802)	RA, PsA, and SpA	3 months	Of 802 patients, 132 patients (16%) discontinued CT-P13 treatment, mainly due to perceived lack of effect (n=71/54%) or AEs (n=37/28%), although disease activity was largely unaffected in the majority of patients by the switch. **Author conclusion:** **"A nationwide non-medical switch from INX to CT-P13 had no apparent negative impact on disease activity".**
3	Observa-tional, multicentre, prospective cohort study (n=192)	RA, PsA, and SpA	6 months	Of 192 patients, 44 patients (23%) discontinued CT-P13 treatment, mainly due to perceived loss of efficacy (n=35) and AEs (n=23), although, in the majority of patients, no changes in efficacy, safety, or immunogenicity were observed. **Author conclusion:** **"Patients discontinued biosimilar infliximab mainly due to a subjective increase in BASDAI score and/or AEs, possibly explained by nocebo and/or attribution effects rather than pharmacological differencess".**
4	Observa-tional registry* (n=1548)	RA, PsA, and Sp	Variable	Of 1548 patients, ~9% stopped treatment during 5 months' follow up, with reasons for withdrawal reported as lack of effect (n=59), AEs (n=42), remission (n=2), cancer (n=4), death (n=1), and other/unknown (n=21). **Author conclusion:** **"Disease activity was largely unaffected in the majority of patients 3 months after switch to SB4 and comparable to the fluctuations observed in the 3 months prior to the switch. Longer follow-up will offer additional understanding of the potential efficacy and safety consequences of the non-medical switch".**

Biosimilars RIGHT

THE EVIDENCE

Reference biologic/ biosimilar biologic	Study design (Phase)	Indications	Follow-up post-switch	Evidence of a possible nocebo effect
5	Observa-tional register study (n=642)	RA, PsA, and Sp	Variable	635 of 642 (99%) patients agreed to transition of whom 625 patients (433 RA, 128 PsA, 64 AS) were included in the study. 600 patients were included in the historical cohort. Crude 6-months persistence rates of SB4 and ENB were: 90% (95%CI 88%-93%) versus 92% (95%CI 90%-94%). The transition cohort had a statistically significantly higher relative risk of discontinuation (adjusted HR 1.57, 95%CI 1.05-2.36) and smaller decreases in CRP (adjusted diff 1.8 (95%CI 0.3-3.2)) and DAS28-CRP (adjusted diff 0.15 (95%CI 0.05-0.25)) over six months compared with the historical cohort. **Author conclusion:** **"Non-mandatory transitioning from ENB to SB4 using a specifically-designed communication strategy showed a slightly lower persistence rate and smaller decreases in disease activity compared with a historical cohort, but these differences were considered as not being clinically relevant".**

*Data from observational data is limited by the lack of suitable control data.

AE, adverse event; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; JIA, juvenile idiopathic arthritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, axial spondyloarthritis.

1 Nikiphorou E, Kautiainen H, Hannonen P, Asikainen J, Kokko et al. Clinical effectiveness of CT-P13 (Infliximab biosimilar) used as a switch from Remicade (infliximab) in patients with established rheumatic disease. Report of clinical experience based on prospective observational data. Expert Opinion on Biological Therapy. 2015;15(12):1677–83.

2 Glintborg B. et al. A nationwide non-medical switch from originator infliximab to biosimilar CT-P13 in 802 patients with inflammatory arthritis: 1-year clinical outcomes from the DANBIO registry. Ann Rheum Dis. 2017 Aug;76(8):1426-1431. doi: 10.1136/annrheumdis-2016-210742. Epub 2017 May 4.

3 Tweehuysen L, van den Bemt BJF, van Ingen IL, de Jong AJL, van der Laan WH, van den Hoogen FHJ et al. Clinical and Immunogenicity Outcomes after Switching Treatment from Innovator Infliximab to Biosimilar Infliximab in Rheumatic Diseases in Daily Clinical Practice. (Abstract 627). Arthirtis & Theumatoloygy 2016;68 (suppl 10). Available from: http://acrabstracts.org/abstract/clinical-and-immunogenicity-outcomes-after-switching-treatment-from-innovator-infliximab-to-biosimilar-infliximab-in-rheumatic-diseases-in-daily-clinical-practice/ [Accessed 13 November 2016].

4 Glintborg B. et al. FRI0190 Clinical outcomes from a nationwide non-medical switch from originator to biosimilar etanercept in patients with inflammatory arthritis after 5 months follow-up. results from the danbio registry. Annals of the Rheumatic Diseases 2017;76:553–554.

5 Tweehuysen L, Huiskes V, van den Bemt B, Vriezekolk J et al. Open-label non-mandatory transitioning from originator Etanercept to Biosimilar SB4: 6-month results from a controlled cohort study. Arthritis Rheumatol. 2018 Apr 2. doi: 10.1002/art.40516. [Epub ahead of print]