

**Switch from infliximab to infliximab biosimilar: efficacy and safety in a cohort of patients with different rheumatic diseases: Response to: Nikiphorou E, Kautiainen H, Hannonen P, 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 Opin Biol Ther. 2015;15:1677-1683**

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**Switch from Infliximab to Infliximab biosimilar: efficacy and safety in a cohort of patients with different rheumatic diseases.**

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**Running Title:** efficacy of the switch from originator to biosimilar

**Key words:** infliximab; biosimilar; switch; spondyloarthritis; rheumatoid arthritis

Dear Editor in Chief

We read with great interest the manuscript by Nikiphorou E et al. describing the effectiveness of infliximab-biosimilar CT-P13 (INB) used as a switch from Remicade (Infliximab) in patients with different established rheumatic diseases [1]. Thirty-nine patients on Infliximab (INX) were switched to biosimilar after a mean time (SD) of 4.1 (2.3) years. The authors reported that INB clinical effectiveness, during the first year of switching, was comparable to INX in both the patient-reported outcomes and disease-activity measures, with no immediate safety signals. Eleven patients (28.2%) discontinued INB due to INX antibodies detected prior to INB infusion (3/11); latent tuberculosis (1/11); new-onset neurofibromatosis (1/11); subjective reasons with no objective deterioration of disease (6/11). The authors suggested that subjective reasons, such as negative expectations, played a key role among INB discontinuations.

In this regard, we report herein our experience in a cohort of 23 patients followed in our Unit for different rheumatic diseases and switched, for local regulatory issues, to INB (Inflectra®) after a mean time (SD) of 71.65 (44.40) months on INX (Remicade®). More in detail, 11 out of 23 had psoriatic arthritis (7 with peripheral and 4 with axial involvement), 8/23 ankylosing spondylitis, 2/23 rheumatoid arthritis, 2/23 Crohn's disease and associated axial spondyloarthritis and 1/23 Behçet's disease and associated axial spondyloarthritis. At the time of the switch, all of the patients were in complete disease remission on INX at a dose of 5mg/kg every 8 weeks. After a mean time of 1.71 months (range, 1-2) from the start of INB a disease relapse occurred in 7 out of 23 patients (30.43%). Their mean (SD) duration of previous INX treatment was 62.28 (49.95) months. **Table 1** summarizes the clinical, demographic and therapeutic data of the 7 subjects unresponsive to INB. INB was then suspended and IFX was re-administered in all 7 patients at a dose of 5mg/kg every 8 weeks, in association with a tapering dose of oral corticosteroids. In 5/7, the readministration of INX promptly led to a remarkable clinical improvement (4/5), or at least a partial one (1/5), with a significant decrement of the disease activity indexes. No amelioration was observed in 2/7 subjects.

Among the 16 patients that were still on treatment with INB, 7 of them were under close observation and monitoring for uveitis relapse (1/7); recurrence of psoriatic lesions (1/7); arthralgia (4/7); referred worsening of global quality of life (1/7). No changes in the response to treatment were observed in 9 out of 23 subjects (39.13%). INB was well tolerated and no adverse events were noted.

In PLANETAS and PLANETRA studies INB demonstrated equivalent efficacy to INX at 30-week follow-up, with a comparable pharmacokinetic profile and immunogenicity both in patients affected by Ankylosing Spondylitis (AS) and Rheumatoid Arthritis (RA) [2, 3]. INB efficacy and safety have been confirmed also in the extension of the PLANETAS study in AS at 54-week follow-up [4]. Nevertheless, data on the effectiveness of the switch from INX to INB in patients in a stable disease remission while on IFX are scarce, and future studies are needed. For the above reason, real-life data should be welcome, even though from uncontrolled series, until further trials are performed. In our cohort of patients, 30% of subjects switched from IFX to INB while in disease remission showed a rapid worsening of disease activity indexes. Moreover, 30% of patients still on treatment with INB were under evaluation for the potential reduction of the interval between INB administrations either the potential increase of INB dosage or a further switch from INB to IFX, due to a suspected lack of efficacy. Overall, it is unlikely that in our cohort of patients, only subjective reasons have played a role in the poor outcome observed in most subjects. Indeed, we did not observe any change in the response to treatment in only 40% of cases. Limitations of our study were the small number of patients, the absence of a control group and the short-term follow-up. Until data from controlled ad-hoc studies are available, the interchangeability of IFX with INB, still remains a debated issue. For this reason, it is our opinion that a large-scale switch based on economic and regulatory affairs should be avoided, because of the loss of efficacy in a not negligible percentage of previously responsive patients.

## Declaration of Interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties

## References

1. Nikiphorou E, Kautiainen H, Hannonen P, Asikainen J, Kokko A, Rannio T, 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 Opin Biol Ther* 2015; 15:1677-83.
2. Yoo DH, Hrycaj P, Miranda P, Ramiterre E, Piotrowski M, Shevchuk S, et al. A randomised, double-blind, parallel-group study to demonstrate equivalence in efficacy and safety of CT-P13 compared with innovator infliximab when coadministered with methotrexate in patients with active rheumatoid arthritis: the PLANETRA study. *Ann Rheum Dis* 2013; 72:1613-20.
3. 4. Park W, Hrycaj P, Jeka S, Kovalenko V, Lysenko G, Miranda P, et al. A randomised, double-blind, multicentre, parallel-group, prospective study comparing the pharmacokinetics, safety, and efficacy of CT-P13 and innovator infliximab in patients with ankylosing spondylitis: the PLANETAS study. *Ann Rheum Dis* 2013; 72:1605-12.
4. Park W, Yoo DH, Jaworski J, Brzezicki J, Gnylorybov A, Kadinov V, et al. Comparable long-term efficacy, as assessed by patient-reported outcomes, safety and pharmacokinetics, of CT-P13 and reference infliximab in patients with ankylosing spondylitis: 54-week results from the randomized, parallel-group PLANETAS study. *Arthritis Res Ther* 2016; 18:25.

**Table 1.** Clinical, demographic and therapeutic characteristics of the refractory patient

Patient	Age	Gender	HLA B (B27/B51)	Diagnosis	Concomitant diseases and/or extra articular manifestations	Age at disease Onset	Age at diagnosis	Previous treatments	Duration of previous IFX treatment (months)	Concomitant treatments (during IFX and INB)
1	56	F	( - / + )	Axial SpA	Behçet's Disease	41	51	Etanercept 50mg/w Adalimumab 40mg/2w MTX, PDN NSAIDs	20	MTX, NSAIDs
2	23	M	( + / - )	Axial SpA	Crohn's Disease	23	23	NSAIDs SLZ, PDN	3	none
3	49	M	n.k	Axial SpA	none	30	36	NSAIDs, MTX, PDN	63	NSAIDs
4	64	M	( + / - )	Peripheral SpA	Psoriasis	44	46	NSAIDs, MTX, SLZ, PDN	136	MTX
5	60	F	n.k	Axial SpA	Crohn's Disease	46	50	NSAIDs, SLZ, PDN	63	NSAIDs
6	48	M	( - / + )	Axial SpA	Psoriasis	38	45	NSAIDs, Etanercept 50mg/w, PDN	19	MTX
7	41	M	( + / - )	Axial SpA	Psoriasis	14	28	NSAIDs, MTX	132	NSAIDs

**List of abbreviations:** M, male; F, female; W, week; MTX, methotrexate; PDN, prednisone; NSAIDs, non-steroidal anti-inflammatory drugs; SLZ, sulphasalazine; IFX, Infliximab