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Biosimilar CT-P13 in treating ulcerative colitis in the real world

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Conflicts of interest: none to declare.

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Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) arising from an interaction between genetic and environmental factors.^{1, 2}

In UC, the anti-tumor necrosis factor (TNF) infliximab, a chimeric IgG1 antibody, is approved to treat patients with steroid-refractory or steroid-dependent disease. The undoubted benefits of a better disease control are partly limited by the high cost of the infliximab originator (Remicade).

The biosimilar infliximab CT-P13 was approved for UC in Europe based on two randomised controlled trials in patients *naïve* to TNF inhibitors, comparing infliximab originator with CT-P13 in ankylosing spondylitis (PLANETAS, a phase 1 study) and rheumatoid arthritis (PLANETRA, a phase 3 study).³ This extrapolation of indication has been debated in gastroenterology because the mechanisms of action for infliximab might differ between indications.⁴

To date a fair number of studies about switching from infliximab originator to infliximab biosimilar in UC have been available from open cohort studies in secondary or tertiary centres.⁵⁻¹³

A randomised, double-blind, parallel-group, multicentre, non-inferiority (non-inferiority margin of 15%) trial (NOR-SWITCH) was the first study to show that switching from an originator to a biosimilar TNF inhibitor was not inferior to continued treatment with the originator drug.¹⁴ The authors calculated that 394 patients were required to exclude a difference in favour of infliximab originator. For the originator the risk difference of disease worsening was not statistically significant. The presumption of the study should be that, being involved patients with different immune-mediated disorders, the conclusions should be extended to all six relevant indications. Nevertheless, the authors highlighted that the study was not powered to show non-inferiority in individual diseases. So, also the data obtained by this study do not definitively resolve the issue of the equivalence between originator and CT-P13 in the individual diseases.

Tursi *et al.* recently published a prospective, observational, multicentre study performed in primary

IBD centres in Italy in which 29 adult outpatients with UC were treated with biosimilar infliximab CT-13 between 1st of May 2015 and 1st of October 2016 and a 12-month follow-up was performed (where available).¹⁵ A group of patients was *naïve* to infliximab, another group switched Remicade to biosimilar infliximab CT-P13. The need of treatment discontinuation was left to the investigators' judgement, as well as concomitant medications including oral and topical aminosalicylates, steroids and immunosuppressants.

No adverse events were observed during follow-up, confirming the good safety profile of the drug.

The authors concluded that biosimilar IFX CT-P13 was effective in real life even when managed in primary IBD centres. They argued that their results were better, regarding clinical response, mucosal healing and clinical remission, than those reported in literature. However, it should be noted that the reported efficacy derives from a *per protocol* analysis: the data of 100% of clinical remission and of mucosal healing come from the only 6 (of 29 enrolled) patients that concluded the 12 months follow up. The data from an *intention to treat* analysis, when all the patients will have concluded the follow up, or at least more details on why other patients have stopped taking infliximab, will be of great clinical interest.

In conclusion, data from randomised clinical trials and from primary IBD centres are in the right direction to provide us more data on the equivalence between infliximab originator and the biosimilar infliximab CT-P13, but larger cohort and *intention to treat* analysis are needed to obtain the definitive answer.

References

1. Ardesia M, Villanacci V, Fries W. The aged gut in inflammatory bowel diseases. Minerva

Gastroenterol Dietol 2015;61:235-47.

2. Actis GC, Pellicano R. Comorbid immunopathological affections in outpatients with inflammatory bowel disease: a prospective study. *Minerva Gastroenterol Dietol* 2016;6:270-1.
3. Yoo DH, Hrycaj P, Miranda P, Ramitterre 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.
4. Danese S, Gomollon F, Governing Board and Operational Board of ECCO. ECCO position statement: the use of biosimilar medicines in the treatment of inflammatory bowel disease (IBD). *J Crohns Colitis* 2013;7:586–89.
5. Buer LC, Moum BA, Cvancarova M, Warren DJ, Medhus AW, Hoivik ML. Switching from Remicade(R) to Remsima(R) is safe and feasible: a prospective, open-label study. *J Crohns Colitis* 2017;11:297-304.
6. Smits LJ, Derikx LA, de Jong DJ, Boshuizen RS, van Esch AA, Drenth JP, *et al.* Clinical outcomes following a switch from Remicade(R) to the biosimilar CT-P13 in inflammatory bowel disease patients: a prospective observational cohort study. *J Crohns Colitis* 2016;10:1287–93.
7. Fiorino G, Manetti N, Armuzzi A, Orlando A, Variola A, Bonovas S, *et al.* The PROSIT-BIO Cohort: A prospective observational study of patients with inflammatory bowel disease treated with infliximab biosimilar. *Inflamm Bowel Dis* 2017;23:233-43.
8. Farkas K, Rutka M, Balint A, Nagy F, Bor R, Milassin Á, *et al.* Efficacy of the new infliximab biosimilar CT-P13 induction therapy in Crohn's disease and ulcerative colitis: experiences from a single center. *Expert Opin Biol Ther* 2015;15:1257–62.
9. Gecse KB, Lovász BD, Farkas K, Banai J, Bene L, Gasztanyi B, *et al.* Efficacy and safety of the

biosimilar infliximab CT-P13 treatment in inflammatory bowel diseases: a prospective, multicentre, nationwide cohort. *J Crohns Colitis* 2015;10:133–40.

10. Jahnsen J, Detlie TE, Vatn S, Ricanek P. Biosimilar infliximab (CT-P13) in the treatment of inflammatory bowel disease: a Norwegian observational study. *Expert Rev Gastroenterol Hepatol* 2015;9(Suppl 1):45–52.
11. Jung YS, Park DI, Kim YH, Lee JH, Seo PJ, Cheon JH, *et al.* Efficacy and safety of CT-P13, a biosimilar of infliximab, in patients with inflammatory bowel disease: a retrospective multicenter study. *J Gastroenterol Hepatol* 2015;30:1705–12.
12. Kang YS, Moon HH, Lee SE, Lim YJ, Kang HW. Clinical experience of the use of CT-P13, a biosimilar to infliximab in patients with inflammatory bowel disease: a case series. *Dig Dis Sci* 2015;60:951–6.
13. Keil R, Wasserbaeur M, Zádorvá Z, Hajer J, Drastich P, Wohl P, *et al.* Clinical monitoring: infliximab biosimilar CT-P13 in the treatment of Crohn’s disease and ulcerative colitis. *Scand J Gastroenterol* 2016;51:1062–8.
14. Jørgensen KK, Olsen IC, Goll GL, Lorentzen M, Bolstad N, Haavardsholm EA, *et al.* Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial. *Lancet* 2017; published online May 11. DOI: 10.1016/S0140-6736(17)30068-5.
15. Tursi A, Allegretta L, Chiri S, Della Valle N, Elisei W, Forti G, *et al.* Effectiveness and safety of infliximab biosimilar CT-P13 in treating ulcerative colitis: a real-life experience in IBD primary centers. *Minerva Gastroenterol Dietol*. 2017 Mar 14. doi: 10.23736/S1121-421X.17.02402-3.
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