

represented in the infliximab group), and steroid refractoriness (more frequent in patients receiving adalimumab).²

In addition, the way biologics were used in this series contradict the assumption that this experience represents their 'real use' in Crohn's disease.^{2–7} Firstly, cotreatment with immunosuppressors was given in just 16% of cases in the infliximab group.^{2, 6} Secondly, and surprisingly, only 77% of the infliximab-treated patients were able to complete the induction treatment, mainly due to severe adverse events in eight (18%) patients; this is not generally seen in clinical series.^{2, 3} Thirdly, the definition of loss of response considered the same interval of time (2 weeks) for both drugs, ignoring their different biological behaviour.⁴ Finally, in the adalimumab group, 16 patients dropped out before the scheduled 54 weeks for clinical worsening or loss of response ($n = 8$), in spite of which therapy was never intensified.^{5, 6}

All these considerations prevent us to accept the conclusion that 'the efficacy of infliximab and adalimumab is comparable.' As the authors correctly state, 'future prospective double-blind studies in patients matched for clinical variables are required to further assess the efficacy and safety of different anti-TNFs in CD.' Until such data are made available, it is probably premature to judge these drugs according to the data presented by Zorzi *et al.*

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Letter: persistence of anti-infliximab antibodies after discontinuation of infliximab in patients with IBD

C. Steenholdt*, J. Brynskov* & K. Bendtzen†

*Department of Gastroenterology, Herlev Hospital, Herlev, Denmark.

†Institute for Inflammation Research, Rigshospitalet, University Hospital of Copenhagen, Copenhagen, Denmark.
E-mail: steenholdt@brygge.dk

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SIRS, In an interesting article, Ben-Horin *et al.* report that anti-infliximab (IFX) antibodies (Ab) are detectable in only a small minority of IBD patients at 1 year after discontinuation of IFX (3 of 16 patients, 19%).¹ We have recently monitored the decline of anti-IFX Ab in 56 IBD patients and found that 77%, 62%, 36%, 25% and 0%, respectively, had detectable anti-IFX Ab when tested 0–1, 1–2, 2–3, 3–4 and >4 years after discontinuation of IFX.²

There may be several explanations for these discrepancies, including the larger sample size of our study, a different composition of patients with Crohn's disease and ulcerative colitis (Ben-Horin included nine and seven, we included 46 and 10), and the extent of repeated anti-IFX Ab measurements in individual patients.

The use of different assays may also add to the conflicting findings. While our radioimmunoassay (RIA) uses anti-human λ Ab for detection, as in the capture ELISA used by Ben-Horin *et al.*, binding in RIA takes place in fluid-phase and without addition of TNF- α .³ This RIA has been extensively clinically validated in IBD and other diseases.^{3–6} It has a higher sensitivity for anti-IFX Ab detection than bridging and capture ELISAs, and is capable of detecting all subtypes of anti-IFX Ab including monovalent IgG4 Ab, which predominate during long-term immunisations.⁷

This subclass of Ab, although detectable in capture ELISA, are not detected in bridging ELISAs.⁷ Solid-phase assays may also give false negative results due to epitope masking.⁷ Finally, anti-idiotypic Ab may go unnoticed in

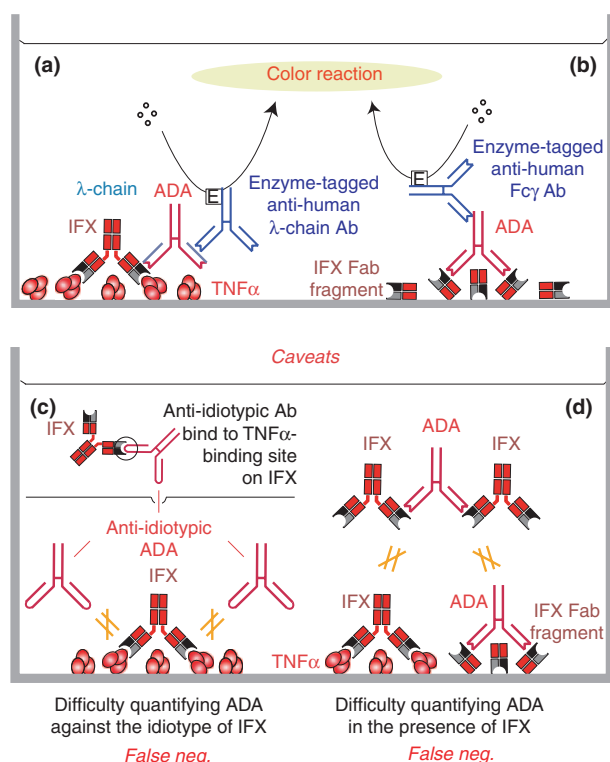


Figure 1 | (a) Capture ELISAs for detection of anti-drug Ab (ADA) against IFX. λ- light chain ADA, captured to IFX pre-bound to TNF-α-plated wells, are detected by enzyme-labeled anti-human λ-chain Ab. (b) λ- and κ- light chain ADA, captured on F(ab')₂ fragments of IFX or F(ab')₂ fragments (not shown), are detected by enzyme-labeled anti-human Fc-γ Ab. False-negative ADA testings may arise from matrix effects, e.g. epitope masking due to protein aggregation (not shown), failure to detect anti-idiotypic ADA (c), or high drug sensitivity (d). Note that functionally monovalent IgG4 ADA are not detected in bridging ELISA (not shown).⁷

ELISAs where the capture phase consists of IFX bound to high-level TNF-α-coated plastic (Figure 1), a problem also noted by Ben-Horin *et al.*⁸

Our conclusion is that anti-IFX Ab can persist for years after discontinuing the drug. The impact on efficacy and safety of pre-existing anti-IFX Ab prior to IFX retreatment remains to be definitively established.

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