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INVITED EDITORIAL

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Editorial: Infliximab induction therapy in paediatric Crohn's disease — A cost-effective strategy? Authors' reply

We thank Chanchlani et al. for their editorial.[1] They raised the important question of how to maximise cost-effectiveness of anti-tumour necrosis factor (TNF) treatment in children with inflammatory bowel disease (IBD). The incidence and prevalence of IBD are increasing, resulting in increased healthcare costs. To optimise cost-effectiveness of anti-TNF therapy, effectiveness should be maximised and cost minimised.

To optimise effectiveness, selecting the right patients to start directly with infliximab is paramount. The ECCO/ESPGHAN guideline recommends considering first-line infliximab for patients with predictors of poor outcome (POPO), such as extensive disease, stricturing disease behaviour and growth delay.[2] A prospective observational study showed that, regardless of the presence of any POPO, 217 children with moderate-to-severe Crohn's disease who received early anti-TNF (<90 days of diagnosis), had a higher risk ratio of achieving sustained steroid-free mild or inactive disease without treatment intensification at 1 year than patients not receiving early anti-TNF (RR 5.50 [95% CI 2.51–12.05], $p < 0.001$).[3] Clinical and standard laboratory values still insufficiently capture the full extent of disease heterogeneity; emerging data on –omics should help identify eligible patients for first-line infliximab.

Another way to maximise effectiveness is by optimising infliximab. Guidelines recommend to proactively measure a trough level at the fourth infusion and to start a concomitant immunomodulator.[2] Colman et al showed that, 22 weeks after receiving infliximab, there was no difference in trough levels in patients who received optimised infliximab monotherapy (in 54% of patients, infliximab was intensified when trough level was <5 μg/mL at 4th infusion) or in those receiving infliximab with azathioprine.[4] Additionally, antibodies to infliximab may be reversed by adding an immunomodulator or increasing the dose, thereby improving durability of infliximab.[5,6]

Use of biosimilars has led to great reduction of costs. Furthermore, the use of subcutaneous infliximab may be a feasible alternative in children with IBD in the near future and reduce indirect costs.[7]

Theoretically, another way to minimise costs is to stop infliximab. Within paediatric care, infliximab is generally not discontinued once started. In adults, a prediction model assessed the risk of relapse in patients who stopped anti-TNF treatment, but this needs to be further updated and validated before implementation in clinical practice.[8] To our knowledge, no such model is available for children. Within the TISKids study, two clusters of patients were identified based on immune serum profiling involving 30 infliximab-modulated proteins. Low concentrations of these proteins were associated with better disease outcomes at 1 year and could support the decision to stop infliximab after five infusions.[9] However, more information and validation are crucial before we will be able to identify patients who may de-escalate infliximab.

In conclusion, increasing cost-effectiveness of first-line infliximab further necessitates optimising effectiveness while minimising costs. Future studies should focus on selecting the appropriate patients to start first-line infliximab, and explore predictive factors of those who could discontinue infliximab.

AUTHOR CONTRIBUTIONS

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LINKED CONTENT

This article is linked to Vuijk et al papers. To view these articles, visit https://doi.org/10.1111/apt.18000 and https://doi.org/10.1111/apt.18033

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