

The economics of biological therapy for inflammatory bowel disease and the case for equality

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The introduction of infliximab in the late 1990s changed the perception of how Crohn disease (CD) could be treated. Following the emergence of further anti-tumor necrosis factor (anti-TNF) therapies, randomized controlled trials demonstrated the ability of TNF regimens to maintain remission, as compared with steroid therapies.^{1,2} Initially utilized as step-up therapies, over time, a top-down treatment approach in aggressive phenotypes has been advocated.³ Treatment paradigms are shifting towards a treat-to-target approach with the aim to induce mucosal healing and prevent long-term complications. By any measure, biologics have revolutionized the treatment of CD, and a fast expanding set of therapies with different classes and mechanisms of action further adds to the array of therapies at the clinician's disposal.

However, an almost global obstacle encountered by clinicians when attempting to utilize these agents is cost. Inevitably, biologics are significantly more expensive than conventional therapies for CD.⁴ Any successful treatment must be proved to be effective with benefits that outweigh the risks. However, finite resources mean that fiscal viability of a therapy is perhaps the most important element. With financial autonomy often lacking among clinicians, frustration can arise when attempting to institute biological treatments. This leads to diverse geographical distribution of biologic use even within Europe. It would appear that the lowest use per estimated number of patients with inflammatory bowel disease is in some Eastern European countries, including Poland.⁵

With this in mind, Eder et al⁶ aimed to analyze the utilization of tumor necrosis factor (TNF) inhibitors in Poland over a 5-year period. In Poland, anti-TNF therapy for CD is reimbursed in severe inflammatory or perianal disease, where conventional treatment has failed. Data from

the SATIMOS study, a prospective, multicenter safety study of TNF inhibitor use in Poland, was combined with data from the Polish National Health Fund (Narodowy Fundusz Zdrowia [NFZ]). The results were both illuminating and surprising.

A total of 256 people (women, 44%) from SATIMOS were included in the initial analysis. The basic phenotypic data were similar among men and women. However, disease duration prior to biological therapy was significantly longer in women than in men (9 years vs 5.5 years; $P = 0.02$). Furthermore, the proportion of women receiving biological treatment within 5 years of diagnosis was significantly lower than that of men (42.5% vs 57.7%; $P = 0.017$). A subsequent analysis of the NFZ data revealed that over the 5-year period significantly more men received anti-TNF treatment for CD compared with women (54% of men; 95% confidence interval [CI], 52–55 vs 46% of women; 95% CI, 45–48). Evidence suggests that the use of biologics is more beneficial early during disease course.⁷ It is not entirely clear from the data what is driving this worrying disparity, but it may lead to worse long-term outcomes in women. Indeed, similar results have been sporadically reported in the past. Dutch and German data previously highlighted a greater proportion of men receiving immunomodulators or biological therapy compared with women.^{8,9}

In reality, the reasons for undertreatment of women are likely multitudinous and intricate. Cultural and geographical causes are beyond the scope of this paper. However, pregnancy-related decisions are very likely to have a strong impact. Both anti-TNF and thiopurine therapies are generally considered low-risk during conception and pregnancy.¹⁰ Indeed, the risk of infertility, miscarriage, and other obstetrical complications increases with activity of inflammatory bowel disease. Despite this evidence, there is still a high risk of treatment discontinuation among

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pregnant women.¹⁰ From a physician's perspective, this paper is a stark reminder of the need to counsel women of childbearing age on the relative safety of biological therapies. From an institutional perspective, the decision of the NFZ to declare pregnancy a contraindication for biological therapy would appear unhelpful at best. Women who receive anti-TNF therapy much later in their disease course are likely to experience worse outcomes, and their care may generate greater health care costs. Both patients and clinicians require institutional reassurance that it is eminently sensible to use TNF inhibitors in women of childbearing age.

While the authors do concede that the study cohort is small, this does not negate the data. At the least, this study delves deeper into what, so far, has been an admittedly sporadic phenomenon. Biologics are still in their relative infancy. However, data seem to suggest that they offer a cost-effective treatment of active and severe inflammatory bowel disease.¹¹ It is important that these therapies are available as equally as possible across the society.

Note The opinions expressed by the author are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

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