Ulcerative Colitis (proctitis)

An example of the value of biosimilar medicines

The management and prescribing guidelines for UC again show a dominance of biosimilar medicines [33]

Medical treatment for UC has two main goals:

- achieving remission (control or resolution of inflammation, leading to symptom resolution)
- maintaining remission.

Over the last several years, biosimilars have become available for the treatment of inflammatory bowel disease (IBD) such as UC and other inflammatory diseases. Biologic therapies offer a distinct advantage in IBD treatment because their mechanisms of action are more precisely targeted to the factors responsible for IBD. For example, biologic agents act more selectively than corticosteroids, which affect the whole body and may produce major side effects. These therapies target proteins that have already been proven to be involved in IBD. Biologics have an increasingly important role in early intervention to maintain remission and avoid complications and to reduce the risk of surgical intervention.

Biologics known as anti-tumour necrosis factor (anti-TNF) agents bind and block a small protein called tumour necrosis factor alpha (TNF-alpha) that promotes inflammation in the intestine as well as other organs and tissues. All anti-TNF medications have been shown to not only reduce the symptoms of IBD, but also help heal the inflamed intestine.

While anti-TNF medications are not effective for every individual, many patients benefit from this class of medication. It may take up to eight weeks after starting an anti-TNF to notice an improvement in symptoms, though many experience more immediate improvement.

Examples of classes of anti-TNF medications used in UC and Crohn's disease include:

- Anti-TNF agents
- Integrin receptor antagonists
- JAK inhibitors

Clinical efficacy

A value exemplar

In clinical trials, all the biosimilar drugs approved to treat moderate to severe UC[34] have been shown to be more effective than a placebo at decreasing symptoms (inducing remission) and preventing their return (maintaining remission).

Biosimilar medicines, as well as the original reference biologic versions in brackets, approved for UC include:

- Adalimumab (Humira)
- Infliximab (Remicade)
- Vedolizumab (Entyvio)
- Ustekinumab (Stelara)
- Golimumab (Simponi)

These treatments are an option when other, more standard therapies have failed to help, which occurs for about 20-40% of patients.

Adalimumab and infliximab are already available as biosimilars. The exclusivities on the other three treatments are all due to expire over the next VPAS period, between 2024 and 2028[35]. Therefore, more UC patients will be able to be treated and sooner, unless a high VPAS rate prevents biosimilar competition.

Data from clinical studies suggest that 30-65% of
UC patients will achieve remission (the absence of
symptoms and inflammation) after taking these
medications for one year, with the rate of responders (patients who benefit from biologic drugs) versus non-responders varying depending on the treatment.

These medicines can prevent some patients with moderate to severe UC from requiring surgery or hospitalisation.

Biosimilar medicines have already made a remarkable contribution to widening patient access to better, more consistent treatments that reduce health inequalities while also providing significant NHS savings.

The utilisation of biosimilars in UC has therefore meant:

- Admissions avoidance – Patients needing medicine through devices such as inhalers require consistency in delivery to support adherence and reduce exacerbations.
- Outpatient and elective admissions reduction – Biosimilars for the management of UC have reduced the need for surgery and improved patient outcomes.
- Supporting patients waiting for elective treatment – Patients waiting for treatment are being managed with the use of medicines to alleviate symptoms.
- Inequality reduction – Closing diagnosis gaps in circulatory, endocrine and respiratory conditions will help improve health outcomes for all and reduce inequalities.

Clinical studies

In a study of 134 adults with UC carried out by the charity Crohn's & Colitis UK, researchers found that:

- 56.9% of those who took adalimumab were responders.
- 62.5% of those who took infliximab were responders.
- 47.5% of those who took vedolizumab were responders.

The percentage of people with UC receiving biologic drugs has increased substantially since 1998, when infliximab became the first approved biologic. Now, about 16% of the patient population is estimated to use biologics – either the original reference product or the biosimilar treatments that have followed. According to a 2020 study of more than 500 patients with UC, the introduction and utilisation of biologics may be responsible for a marked decline in the number of patients who need to undergo surgery. In the pre-biologics era, about 20% of patients with UC needed a colectomy (surgery to remove the colon) during their first hospitalisation, and 30% required a colectomy within a year of their first hospitalisation.

Since the introduction of biologics, those rates have declined to 5.3 and 11.9% respectively, suggesting that biologics have spared many patients from losing their colons. And as more biologic treatments have lost their exclusivity, the NHS has been able to expand the treatment owing to the availability of biosimilars. This has led to the prevalence of biologics in UC, as can be seen by the orange bars in the chart below. Not all patients with UC experience improvements while taking biologics. The drugs do not always bring about remission or prevent the need for surgery, or sometimes they have reduced effectiveness over time or even no benefits at all. However, there is no indication that the number of non-responders is different between originator biological medicines and the biosimilar alternatives. The UK medicines regulator MHRA36 says:

"Once authorised, a biosimilar product is considered to be interchangeable with their Reference Product (RP), which means a prescriber can choose the biosimilar medicine over the RP (or vice versa) and expect to achieve the same therapeutic effect. Likewise, a biosimilar product is considered to be interchangeable with another biosimilar to the same RP."

As a result of interchangeability, switching patients from one product to another (RP or biosimilar) has become clinical practice. The decision rests with the prescriber in consultation with the patient, in line with the principles of shared decision making; both need to be aware of the brand name of the product received.

Biologic-treated inflammatory bowel disease (CD & UC) patients are significantly less likely to undergo colectomy (7.3%) than UC patients not receiving biologic therapy (11.0%) (p <.001). The same is true for CD patients receiving biologic therapy, who are less likely to undergo colectomy (9.3%) than CD patients not receiving biologic therapy (12.1%) (p <.001).
Khoudari et al., Clin Gastroenterol Hepatol 2022