OPINION

Golimumab for ulcerative colitis: adding perspective to the pursuit

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Anti-TNF therapies have had a transformational effect on our treatment paradigms for ulcerative colitis (UC). Golimumab (GLM) received regulatory approval for the treatment of moderately to severely active UC, following demonstration of efficacy and safety in the induction (PURSUIT-SC) and maintenance (PURSUIT-M) trials.[1 2] The trial objective was to obtain regulatory approval, not to inform clinicians on optimising its use in clinical practice. In that sense, the inclusion of anti-TNF naive patients arguably represented 'low-hanging fruit'. Yet, trials leave a trail that subsequent studies must tread.

Adding to our understanding, Samaan and colleagues present a timely 'real-world' experience with GLM from two tertiary inflammatory bowel disease (IBD) centres.[3] The results are impressive: in a treatment refractory cohort (30% anti-TNF failures), 23/44 (52%), 15/44 (34%) and 13/44 (30%) achieved clinical response, remission and corticosteroid-free remission as defined by an Simple Clinical Colitis Activity Index (SCCAI) reduction >3 and<3, respectively.[3] Their observations corroborate with PURSUIT and real-world observational studies.[2 4–6] The imperfections, inherent to the retrospective design, challenge our perceptions through an incisive identification of myriad factors influencing successful outcomes. Through an elegant demonstration of the value of composite assessments (clinical, biomarkers and endoscopic scoring systems), the authors underscore the need for their wider adoption in clinical practice. We are only beginning to understand the manifold variables influencing anti-TNF pharmacokinetics, such as body weight, disease severity, drug levels and antibodies, concomitant immunomodulation, previous anti-TNF exposure, response and route of administration.[7]

Response rates in anti-TNF experienced patients were unsurprisingly lower (42% vs 65%) yet reassuring for a second anti-TNF. Our concepts with GLM therapeutic drug monitoring (TDM) are evolving and hold promise. Higher GLM levels correlated with higher response and remission rates at week 30 and 54 in PURSUIT.[2] Non-responders at week 6, dose-escalated to 100 mg, recaptured response at week 18, providing further proof of principle. Samaan and colleagues noted a statistically significant higher median dose (0.94 mg/kg) in responders than non-responders (0.79 mg/kg), affirming the potential for TDM in optimising GLM. We are learning that GLM levels of 2.5 µg/mL at week 6 and 1.4 µg/mL during steady state maintenance may be the aim for induction and maintenance of response.[3] Prospective validation of proposed GLM concentrations will provide clarity. Concomitant immunomodulation did not show benefit in PURSUIT.[2] Samaan and colleagues did not note a statistically significant difference either.

That less-severely ill patients did better is unsurprising.[2–6] High inflammatory burden, low albumin and faecal drug losses predict need for accelerated dosing with infliximab.[8] At its current fixed and non-weight-based dosing, GLM is unlikely to compete with infliximab in this realm, although plausibly equivalent for moderately active UC. Heavier patients may be underdosed with consequent decreased effect.[2 4–6]

It is presently unclear if any anti-TNF has particular advantage over others. Admixtures of disease activity, dosing and co-variables influence discrepancy and underpin the need for prospective and preferably randomised comparative studies[9 10]

Samaan and colleagues add credence to a small but growing body of evidence supporting the use of GLM in moderate

to severe UC. As good questions seek better answers, the prospect of such intellectual effort being rewarded through meaningful outcomes seems realistic. We must remain in pursuit…

Competing interests None declared.

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