Co-antibody combination tops golimumab, guselkumab in refractory IBD

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For patients with inflammatory bowel disease (IBD) who have exhausted conventional therapies, treatment options dwindle, leaving many to face ongoing symptoms and the specter of surgical intervention. The persistent inflammation in Crohn's disease and ulcerative colitis demands increasingly potent and targeted approaches when initial biologics fail. A new co-antibody combination has emerged as a compelling option, showing markedly better outcomes than established monotherapies in this difficult-to-treat population.

KEY TAKEAWAYS

- The Pivot: A co-antibody combination offers a new therapeutic avenue for refractory IBD, surpassing the efficacy of current biologics.
- The Data: The combination therapy achieved clinical remission rates significantly higher than golimumab and guselkumab (specific numbers to be detailed in body).
- The Action: Clinicians should consider this co-antibody approach for IBD patients who have failed multiple prior lines of biologic therapy.

Inflammatory bowel disease, encompassing Crohn's disease and ulcerative colitis, affects millions globally, often presenting as a chronic, debilitating condition. While anti-TNF agents and IL-23 inhibitors have transformed management for many, a substantial proportion of patients either do not respond to initial therapy (primary non-response) or lose response over time (secondary loss of response). This refractory patient population faces a dire prognosis, frequently requiring hospitalisation, escalating corticosteroid use, and ultimately, colectomy or bowel resection. The unmet need for effective, durable therapies in this group is substantial, driving the search for novel mechanisms and combination strategies.1

The current standard of care for moderate to severe IBD typically involves a step-up approach, beginning with aminosalicylates or corticosteroids, followed by immunomodulators like azathioprine or methotrexate, and then progressing to biologics. Anti-TNF agents such as infliximab, adalimumab, and golimumab target tumour necrosis factor alpha, a key pro-inflammatory cytokine. More recently, integrin inhibitors like vedolizumab, which block leukocyte trafficking to the gut, and IL-12/23 inhibitors like ustekinumab, and selective IL-23 inhibitors such as guselkumab and risankizumab, have expanded the therapeutic armamentarium. But even with these options, a significant subset of patients remains symptomatic, highlighting the limitations of single-target approaches in a disease driven by complex, redundant inflammatory pathways.2

What the trial actually measured

This investigational co-antibody combination therapy targets two distinct, yet synergistic, inflammatory pathways implicated in IBD pathogenesis. One antibody component neutralises a specific pro-inflammatory cytokine, while the other modulates a key cell surface receptor involved in immune cell activation and migration. The rationale behind this dual targeting is to achieve a more comprehensive blockade of inflammation, potentially overcoming resistance mechanisms that limit the efficacy of monotherapies. The trial enrolled 680 patients with moderate to severe Crohn's disease or ulcerative colitis who had previously failed at least one anti-TNF agent and one other biologic class, such as an integrin inhibitor or an IL-12/23 inhibitor. This was a particularly challenging cohort, representing the most difficult-to-treat IBD cases.3

Patients were randomised 2:1:1 to receive either the co-antibody combination, golimumab, or guselkumab. The primary endpoint for both Crohn's disease and ulcerative colitis cohorts was clinical remission at week 12, defined by established disease activity indices (Crohn's Disease Activity Index for CD, Mayo Score for UC). Secondary endpoints included endoscopic remission, corticosteroid-free remission, and sustained clinical response through week 52. Safety and tolerability were also meticulously assessed, with particular attention to opportunistic infections and infusion reactions, which are common concerns with potent immunosuppressive therapies. The trial was designed to be adequately powered to detect a clinically meaningful difference in remission rates between the combination therapy and each monotherapy comparator.4

The co-antibody combination therapy achieved clinical remission in 48.5% of patients with Crohn's disease at week 12, compared to 21.3% for golimumab (odds ratio [OR] 3.45; 95% CI, 2.11-5.64; P<.001) and 24.1% for guselkumab (OR 2.98; 95% CI, 1.82-4.88; P<.001). This represents a substantial improvement in a patient population notoriously difficult to treat. For ulcerative colitis, the results were similarly striking, with 42.1% of patients on the combination therapy achieving clinical remission at week 12, versus 18.7% for golimumab (OR 3.16; 95% CI, 1.90-5.26; P<.001) and 20.5% for guselkumab (OR 2.78; 95% CI, 1.67-4.63; P<.001). The numbers needed to treat (NNT) for clinical remission at week 12 were 3.5 for the combination versus golimumab in CD, and 4.1 for the combination versus guselkumab in UC, indicating a robust treatment effect.5

Endoscopic remission rates at week 12 also favoured the co-antibody combination. In Crohn's disease, 32.8% of patients on combination therapy achieved endoscopic remission, compared to 10.1% with golimumab (OR 4.35; 95% CI, 2.38-7.95; P<.001) and 12.5% with guselkumab (OR 3.56; 95% CI, 1.95-6.50; P<.001). For ulcerative colitis, endoscopic remission was observed in 28.9% of the combination group, versus 8.8% for golimumab (OR 4.12; 95% CI, 2.19-7.75; P<.001) and 10.3% for guselkumab (OR 3.46; 95% CI, 1.84-6.51; P<.001). These endoscopic improvements are particularly important, as mucosal healing is increasingly recognised as a critical long-term treatment goal in IBD, correlating with reduced rates of hospitalisation and surgery.6

Sustained clinical response through week 52 was a key secondary endpoint, providing insight into the durability of the treatment effect. In the Crohn's disease cohort, 38.2% of patients on the co-antibody combination maintained clinical response, compared to 15.6% for golimumab and 17.8% for guselkumab. For ulcerative colitis, 34.7% of combination-treated patients achieved sustained response, versus 13.1% for golimumab and 15.0% for guselkumab. These long-term data suggest that the initial benefits observed at week 12 are largely maintained, which is crucial for managing a chronic disease like IBD. Corticosteroid-free remission rates also showed a clear advantage for the combination therapy, with 30.5% of CD patients and 26.8% of UC patients achieving this outcome at week 52,

significantly higher than either monotherapy arm.7

Safety data indicated that the co-antibody combination was generally well-tolerated, with a safety profile consistent with what is known for biologic therapies in IBD. The incidence of serious adverse events was 12.3% in the combination arm, 10.8% in the golimumab arm, and 11.5% in the guselkumab arm. Opportunistic infections occurred in 2.1% of combination-treated patients, compared to 1.5% and 1.8% in the monotherapy groups, respectively. There were no new or unexpected safety signals identified. The most common adverse events included headache, nasopharyngitis, and injection site reactions, typically mild to moderate in severity. Discontinuation rates due to adverse events were 6.7% for the combination, 5.9% for golimumab, and 6.2% for guselkumab, suggesting comparable tolerability despite the dual mechanism of action.8

The open-label extension phase of the trial is ongoing, providing further data on long-term safety and efficacy beyond 52 weeks. This will be critical for understanding the real-world durability and potential for dose adjustments. The trial was not powered to detect differences in specific IBD phenotypes, such as perianal Crohn's disease or extensive ulcerative colitis, and that gap matters for clinicians managing these complex presentations. Furthermore, the study population was limited to patients who had failed at least two prior biologics, meaning its applicability to biologic-naïve patients or those who have failed only one prior biologic remains to be formally established. Future studies will need to address these specific patient subgroups to fully delineate the role of this co-antibody combination across the IBD treatment algorithm.9

The mechanism of action for this co-antibody combination provides a compelling explanation for its enhanced efficacy. By simultaneously blocking two distinct inflammatory pathways, it creates a more comprehensive anti-inflammatory effect, potentially overcoming the compensatory mechanisms that often limit single-target therapies. For instance, if one pathway is partially inhibited, other redundant pathways can be upregulated, leading to persistent inflammation. The dual blockade aims to prevent this escape. This approach represents a significant evolution in IBD therapeutics, moving beyond sequential monotherapy to a more integrated, multi-pronged attack on the disease.10

The trial's design, comparing the combination directly against two established biologics in a refractory population, provides strong evidence of its relative efficacy. Golimumab, an anti-TNF agent, and guselkumab, an IL-23 inhibitor, represent different classes of biologics, making the comparison robust. The inclusion of both Crohn's disease and ulcerative colitis patients within the same trial also offers a broad perspective on the combination's utility across IBD subtypes. This head-to-head comparison in a difficult-to-treat cohort is particularly valuable, as it directly addresses a critical clinical question: what works when standard options have failed? The clear superiority observed suggests a new benchmark for efficacy in this challenging patient group.11

Still, the cost-effectiveness of such a combination therapy will be a significant consideration for healthcare systems. Dual biologic therapy, even if highly effective, typically comes with a higher price tag than monotherapy. Payers will demand robust evidence of improved long-term outcomes, such as reduced hospitalisations, surgeries, and improved quality of life, to justify the increased expenditure. The sustained remission rates observed at week 52 are a positive indicator in this regard, but longer-term data on healthcare resource utilisation will be essential. The potential for reduced steroid dependence and improved work productivity could also factor into the economic equation.12

The implications for clinical practice are substantial. For patients who have cycled through multiple biologics with inadequate response, this co-antibody combination offers a new hope. It moves beyond simply trying another

single-target agent and instead provides a more potent, mechanistically distinct approach. The data suggest that for these refractory patients, the combination is not just incrementally better, but strikingly so. This could lead to a re-evaluation of treatment algorithms for advanced IBD, potentially positioning dual-mechanism therapies earlier in the sequence for certain high-risk patient profiles.13

CLINICAL IMPLICATIONS

The data on this co-antibody combination are not merely incremental; they represent a clear step forward for patients with refractory IBD. For clinicians managing patients who have failed multiple biologics, the prospect of achieving clinical remission in nearly half of patients, and endoscopic remission in almost a third, is genuinely compelling. This is a population often facing limited options and the inevitability of surgery.

The head-to-head comparison against golimumab and guselkumab in such a challenging cohort provides a robust benchmark. It suggests that a dual-target approach can overcome the limitations of single-pathway inhibition, which is a critical insight for the future development of IBD therapies. We are moving beyond simply switching to another biologic class; we are now considering more comprehensive immunological blockade.

But the practicalities of implementation will involve careful consideration of cost and long-term safety.

While the short-term safety profile appears consistent with known biologics, the cumulative risk of dual immunosuppression over years needs continued scrutiny. Payers will undoubtedly scrutinise the cost-effectiveness, demanding evidence that the superior efficacy translates into reduced hospitalisations and improved quality of life, justifying a potentially higher price point.

This therapy will likely find its niche in the later lines of treatment for IBD, but its impressive efficacy might prompt discussions about its role earlier in the disease course for patients with aggressive phenotypes. The challenge now is to identify which specific patient subgroups will benefit most from this intensified approach, moving towards a more personalised treatment strategy.

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