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Ulcerative Colitis and Its Advanced Therapies : A Comprehensive Review

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Abstract

Ulcerative colitis (UC) is a chronic idiopathic inflammatory bowel disease (IBD) characterised by continuous mucosal inflammation of the large bowel, typically starting in the rectum and extending to varying degrees to the proximal colon. Ulcerative colitis significantly impairs the quality of life of affected patients, and forms a substantial component of global health care burden. The causes of ulcerative colitis are unknown, but considered to be multifactorial, including genetic predisposition, immune system dysfunction, environmental risk factors, and alterations in the normal colonic microbiota. In this review, we provide an in-depth analysis of current understanding of ulcerative colitis, including epidemiology, disease causes and mechanisms, pathophysiology, clinical features, diagnosis, current and emerging treatments, complications, and future management approaches.

Keywords: Ulcerative colitis, inflammatory bowel disease, pathogenesis, diagnosis, treatment, biologics.

1. Introduction

Ulcerative colitis (UC) is a condition so much worse than its name suggests. It is a condition that comes and goes (relapsing and remitting) where areas of the bowel mucosa become inflamed.
The area of inflammation starts at the bottom of the bowel (rectum) and can spread up to affect the whole colon. In the UK the incidence is reported to be 12.6 cases per 100,000 person-years. From the Lothian region of Scotland we know the prevalence to be around 432 cases per 100,000 people. The disease tends to "first present" in two peaks of age, the first in the 2nd or 3rd decade of life and a second in people aged 50-80 years. The causes of the onset of ulcerative colitis are believed to be a combination of environmental factors, immune system dysfunction, factors affecting gut microbes and hereditary predisposition. Common symptoms include bloody diarrhoea, increased frequency of diarrhoea, abdominal pain, fatigue and in some cases incontinence of faeces.

Ulcerative colitis (UC) is classified according to the extent of disease into E1 (Proctitis – limited to the rectum), E2 (Left-sided Colitis – distal to the splenic flexure) and E3 (Extensive Colitis – proximal to the splenic flexure). Patients with left-sided and extensive colitis require more aggressive pharmacological therapy and have a greater need for colectomy and risk of developing colorectal cancer. Other factors that increase the risk of colorectal dysplasia or cancer in UC include duration of disease, ongoing disease activity (endoscopic and histological), colonic strictures, post-inflammatory polyps, a family history of colorectal cancer and the presence of primary sclerosing cholangitis (PSC), a chronic and often relapsing disease that results in inflammation and damage of the biliary ducts. PSC is seen in 3–7% of UC patients. Common extraintestinal manifestations include anaemia, musculoskeletal symptoms (arthropathy: axial or peripheral) and skin manifestations (erythema nodosum and pyoderma gangrenosum). In addition, patients with IBD can experience ocular symptoms (anterior uveitis or episcleritis). Most of the extraintestinal manifestations are linked to disease activity of the luminal symptoms, with the exception of ankylosing spondylitis and some forms of peripheral polyarthritis.

Table 1. Investigations for Ulcerative Colitis

Investigation	Type	Common Findings in UC	Notes
Blood Tests	Full blood count, U&E, CRP, Vitamin D, haematinics, liver biochemistry	Anaemia, thrombocytosis, raised inflammatory markers, low vitamin D	Consider pre-immunosuppressant screening (TPMT, viral serology). PSC may present with deranged LFTs.
Stool Cultures	C. difficile toxin, MC&S	Should be negative; infections can co-exist with UC	Thorough history including travel; recent antibiotics raise C. difficile risk.
Faecal Calprotectin	Neutrophil migration marker	50–100 µg/g gives 98–99% negative predictive value for IBD	Also used to monitor treatment response.
Endoscopy	Flexible sigmoidoscopy (acute); ileocolonoscopy (full assessment)	Erythema, oedema, loss of vascular pattern, ulcers	Mayo and UCEIS scores grade endoscopic severity.
Histology	Minimum two biopsies per bowel segment	Basal plasmacytosis, crypt atrophy, villous irregularity	Granulomas are more suggestive of Crohn's disease.
Imaging – AXR	Abdominal X-ray	Thumbprinting, lead-piping, toxic megacolon	

Imaging – CT/MRI	Cross-sectional imaging	Bowel wall oedema, inflammatory pseudopolyps	Small bowel imaging helps distinguish UC from Crohn's.

2. Epidemiology

Ulcerative colitis, or UC, shows up more often than Crohn's disease around the world. You'll see both in wealthier, industrialized places like North America and Western Europe, but rates in Asia are going up fast. Each year, anywhere between 1.2 and 20.3 people per 100,000 get diagnosed, and overall prevalence runs from about 7.6 all the way up to 245 per 100,000. While we still don't fully understand what causes UC, research points toward a mess of genetic and environmental factors.

Risk Factors

UC seems to start when the gut microbiome gets thrown off or the lining of the intestine breaks down. That damage can come from a bunch of outside influences—gut infections, NSAIDs, or antibiotics. The connection between stomach bugs and developing IBD is strongest in the year after a Salmonella or Campylobacter infection. One big study found women who take NSAIDs for a couple weeks or more have higher chances of getting IBD.

Family History and Genetics

If someone in your family has IBD, your risk goes up—but not as much as you'd think. Only about 10–25% of people with IBD have a close relative with the same issue. UC turns up more often in people of Jewish descent and shows up less in African American and Hispanic groups. Genetic work is ongoing; HLA-DQA1 variants stick out as big risk factors, and other genes linked to how the gut lining holds up—like CDH1 and LAMB1—keep showing up.

Other Contributing Factors

Surprisingly, smoking actually lowers your risk for UC, but quitting puts you back at risk. Still, doctors want everyone to stop smoking since it's terrible for health overall. What you eat might play a part, but there's no single diet guaranteed to trigger UC.

Signs and Symptoms

UC usually shows up as bloody diarrhea, stomach pain, feeling like you need to rush to the toilet, and tenesmus (the sensation of incomplete evacuation). Sometimes, patients lose weight or get mild fevers, but those are less common. Symptoms tend to creep up over a few weeks rather than coming on all at once.

Extraintestinal Manifestations

UC isn't just about the gut—it can mess with your skin, joints, eyes, and liver. Skin issues like erythema nodosum and pyoderma gangrenosum are pretty common. Erythema nodosum often matches up with the main gut symptoms, while pyoderma gangrenosum can do its own thing. Arthritis is the most common issue outside the intestines and can affect joints in either the arms and legs or the spine.

Severity Classification

Doctors sort UC by how severe it is—mild, moderate, severe, or fulminant. Mild cases mean fewer than four bowel movements a day, sometimes with blood, but no major inflammation signs. Moderate cases hit four or more bloody stools a day, but with just a hint of other symptoms. Severe UC is rough: more than six bloody stools daily, plus fever, rapid heartbeat, or anemia.

Diagnosis

Diagnosing UC takes a mix of gut symptoms, seeing continuous inflammation in the colon via endoscopy (usually starting at the rectum), and confirming things under the microscope.
Sometimes, a patch of inflammation near the appendix shows up (called a cecal patch), and that's not Crohn's disease. Biopsies help confirm the diagnosis, but aren't always clear cut.

Laboratory Investigations

Checking stool samples is important—it rules out infections. Blood tests often show raised inflammation markers like ESR and CRP, but not always. Fecal calprotectin and fecal lactoferrin are more reliable indicators of gut inflammation, yet none of these tests is a slam dunk.

Diagnostic Tests

- Blood tests: Look for white cell counts, anemia, and inflammation.

- Stool tests: Help find blood, white cells, or bugs that cause diarrhea.

- Flexible sigmoidoscopy and colonoscopy: Best tools for confirming UC, seeing how far it goes, and ruling out other stuff like Crohn's, diverticular disease, or cancer.
- Fecal calprotectin: Non-invasive marker—also good for checking treatment progress.

- CT scan and barium enema: CT gives detailed images to spot complications like toxic megacolon.

Pathogenesis and Aetiology

We don't know all the details, but UC appears to come from a tangled mix of genes, environment, and a misfiring immune system. Some findings hint that babies born small to moms with UC are more likely to get the disease later.

HLA-B27 shows up in a lot of UC patients, but that doesn't mean it causes the disease or signals a big risk. Dietary ingredients and bacterial antigens might worsen things when the gut barrier is already leaky.

On the outside, the colon looks red, swollen, and loses its normal blood vessel pattern. The surface is rough and flaky. With UC, shallow ulcers lead to little "islands" of healthy tissue called pseudopolyps. Sometimes the bowel swells and the muscles get thick, but rarely the outside wall gets involved—when it does, that usually signals severe disease.

Under the microscope, early UC shows bleeding, loss of the mucous layer, and formation of crypt abscesses—pretty much the classic feature for this disease.

Genetic Factors

People with the right genetic setup show weird immune responses, attacking their own gut flora and ending up with inflamed colon tissue. Having a family member with UC boosts your risk, and identical twins show strong genetic ties. Several gene regions are involved—some overlap with Crohn's—and one, CDH1, also links with colorectal cancer. Chromosomal instability (measured by telomeric associations in blood cells) can push cancer risk higher.

Immune Mechanisms

Autoantibodies hitting intestinal cells, along with ANCA and ASCA antibodies, are hallmarks of IBD. Fewer UC cases in people who had their appendix out before age 20 suggests the appendix actually influences immune system responses**.**

Environmental Factors

Sulfate-reducing bacteria crank out harmful sulfide, and you find more of them in UC patients, especially during flare-ups. The gut microbiome shifts in active UC, including lower Klebsiella levels (which return to normal after surgery). NSAIDs are used more by UC patients, and about a third of those who flare say they recently took these drugs. Low antioxidant intake (vitamins A and E), stress, and milk consumption might make the disease act up.

Treatment

Treating UC depends on how bad it is and what the patient wants. Most people start with milder therapy and step up if things get worse.

Aminosalicylates (5-ASA)

5-ASA drugs (like sulfasalazine, mesalamine, olsalazine, and balsalazide) anchor treatment for mild to moderate UC. You can take them by mouth, rectally, or by enema. If it's just the left colon, topical meds work for up to 90% of patients. Combining oral and rectal therapy is most effective, but many people choose the pills—they're just easier.

Corticosteroids

Steroids kick the disease into remission fast, but you don't want to stay on them long-term. For milder flares, budesonide MMX targets the colon with fewer side effects. More serious flares call for systemic steroids like prednisone, either orally or intravenously. If UC is only in the distal colon, steroid enemas might do the trick.

Thiopurines

Drugs like azathioprine and mercaptopurine help keep UC in remission—meta-analyses say you need to treat about five patients to keep one in remission compared to placebo. They take 6–12 weeks to work fully, so steroids are often used short-term when starting these meds.

Anti-TNF Agents

Three drugs— infliximab (IV), adalimumab, and golimumab (both subcutaneous)—are approved for moderate to severe UC. They work solo or combined with thiopurines to induce and maintain remission.

Calcineurin Inhibitors

Cyclosporine is mostly for hospitalized patients with severe UC who don't respond to IV steroids. It's not a routine drug anymore, since infliximab works just as well and is usually preferred. Tacrolimus isn't used much; the evidence behind it just isn't strong.

Selective Adhesion Molecule Inhibitors

Vedolizumab came out in 2014. It's a monoclonal antibody that blocks leukocytes from getting into the gut, dialing back inflammation. It works well for moderate to severe UC after traditional therapy fails.

Probiotics

VSL-3 shows some promise in mild to moderate UC flares, but there's not enough evidence to recommend it for long-term maintenance. Other probiotics don't have strong backing for routine use.

First-Line Drug Summary

First-line treatment focuses on aminosalicylates; steroids are for tougher cases or when 5-ASA doesn't cut it. Immunomodulators like azathioprine, mercaptopurine, and cyclosporine come in when initial therapy fails—they take a few months to work and tamp down the immune system.

Surgery

You need surgery when UC leads to toxic megacolon, perforation, heavy bleeding, failed medical treatment, steroid dependence, or cancer. Around 10–15% of people with UC end up needing surgery. With acute severe UC, surgeons usually do a total colectomy with a Hartmann pouch. Down the line, you might get a permanent ileostomy or an ileal pouch-anal anastomosis if suitable.

Complications

UC ramps up the risk for colorectal cancer—especially if the disease covers the left side or is extensive. If it's just proctitis or proctosigmoiditis, cancer risk isn't much higher than normal, so extra screening isn't needed. After 20 years with UC, cancer risk hits about 5–10%, and keeps climbing the longer you have it. That's why regular colonoscopies are crucial.

Quality of Care and the Role of the Primary Care Physician

With UC hitting multiple body systems and some treatments causing their own problems, primary care doctors are vital for keeping patients safe and healthy. The American Gastroenterological Association set out ten quality measures in 2011 to guide care. PCPs have to monitor medication, watch for complications from drugs, handle preventive care, and make sure patients see a specialist quickly if things flare up.

Recent Advancements

Drugs that have completed phase III Clinical Trials

Agent	Target	Mode of Delivery	Dose	Primary Endpoint	Outcome (Drug vs Placebo)
CT-P13	TNF	SC	120 mg every 2 weeks	LIBERTY-UC: clinical remission at week 52	43.2% vs 20.8% (p<0.001)
Etrolizumab	α4β7 and αEβ7 integrins	SC	105 mg every 4 weeks	HICKORY: remission wk14 HICKORY: remission wk66 HIBISCUS I: remission wk10 HIBISCUS II: remission wk10	18.5% vs 6.3% (p=0.003) 24.1% vs 20.2% (p=0.50) 19.4% vs 6.9% (p=0.017) 18.2% vs 11.1% (p=0.17)
Carotegrast methyl (AJM300)	α4 integrin	Oral	960 mg three times daily	Clinical response at week 8	45% vs 21% (p<0.001)
Mirikizumab	IL-23/p19 subunit	IV (induction) / SC (maintenance)	Induction: 300 mg Q4W Maintenance: 200 mg Q4W	LUCENT 1: remission wk12 LUCENT 2: remission wk40	24.2% vs 13.3% (p<0.001) 49.9% vs 25.1% (p<0.001)

Upadacitinib	JAK1	Oral	Induction: 45 mg daily	U-ACHIEVE: remission wk8	26% vs 5% (p<0.001)
			Maintenance : 15–30 mg daily	U- ACCOMPLISH: remission wk8 U-ACHIEVE (maintenance): remission wk52	33% vs 4% (p<0.001) 52% (30mg) vs 12% (p<0.001) 42% (15mg) vs 12% (p<0.001)
Etrasimod	S1PR1, S1PR4, S1PR5	Oral	2 mg once daily	ELEVATE UC 12: remission wk12 ELEVATE UC 52: remission wk12 ELEVATE UC 52: remission wk52	25% vs 15% (p=0.026) 27% vs 7% (p<0.001) 32% vs 7% (p<0.001)

Subcutaneous CT-P13

CT-P13 is a biosimilar of infliximab whose intravenous formulation has an established record of safety and efficacy in inflammatory bowel disease. A subcutaneous (SC) formulation delivering 120 mg/mL was subsequently developed, offering patients the convenience of home self- administration and eliminating the need for regular infusion centre attendance. The SC formulation has received approval from the European Medicines Agency (EMA) for the same indications as intravenous infliximab.

The maintenance efficacy of SC CT-P13 in UC was examined in the LIBERTY-UC Phase 3 trial. Eligible patients had moderate-to-severe UC (modified Mayo score 5–9 with endoscopic sub-score ≥2) and received open-label induction with intravenous CT-P13 (5 mg/kg) at weeks 0, 2, and 6. Of 548 enrolled patients, 79.9% achieved a clinical response and were randomised at week 10 in a 2:1 ratio to SC CT-P13 120 mg or placebo every two weeks for 54 weeks. The primary endpoint of clinical remission at week 54 was attained by 43.2% of SC CT-P13 recipients versus 20.8% in the placebo group ($p < 0.0001$). Statistically significant improvements were also recorded for clinical response, endoscopic-histological mucosal improvement, and corticosteroid-free remission. The safety profile was comparable between the two groups.

Etrolizumab

Etrolizumab is a humanised subcutaneous monoclonal antibody directed against the β7 subunit shared by both the α4β7 and αEβ7 integrins. By obstructing β7-mediated interactions with

MAdCAM-1 and E-cadherin, it simultaneously curtails leukocyte homing to the gut and inhibits retention of intramucosal lymphocytes. Animal data suggest tissue selectivity confined to mucosal surfaces, without effect on migration to non-mucosal sites.

The etrolizumab clinical development programme in UC encompassed five trials involving over 2,000 patients globally — three placebo-controlled and two head-to-head against an active TNFi comparator.

In the Phase 3 HICKORY trial, induction over 14 weeks included both an open-label cohort and a randomised placebo-controlled cohort. Remission was achieved by 18.5% of etrolizumab- treated patients versus 6.3% on placebo ($p = 0.0033$). However, during the 52-week maintenance phase, remission rates did not differ between those continuing etrolizumab and those switched to placebo (24.1% vs 20.2%; $p = 0.50$). The maintenance Phase 3 LAUREL trial, which followed an open-label induction period, also failed to meet its primary endpoint of clinical remission at week 62.

The two HIBISCUS trials (I and II) were identical Phase 3, double-blind, placebo- and adalimumab-controlled studies enrolling TNFi-naive patients with moderate-to-severe UC refractory to conventional therapy. Patients were randomised to etrolizumab 105 mg SC every 4 weeks, standard-dose adalimumab induction, or placebo. In HIBISCUS I, clinical remission at week 10 was achieved in 19.4% (etrolizumab) versus 6.9% (placebo; $p = 0.017$). HIBISCUS II did not demonstrate a statistically significant difference (18.2% vs 11.1%; $p = 0.17$). Etrolizumab did not show superiority over adalimumab across key secondary endpoints in either trial.
Investigators attributed this, in part, to an over-optimistic assumption of a 25% absolute remission rate difference in the sample size calculation.

The GARDENIA trial, comparing etrolizumab with infliximab in TNFi-naive patients using a treat-through design, found no difference in clinical response at week 10 or clinical remission at week 54 (18.6% vs 19.75%; $p = 0.81$). The 105 mg dose selected for Phase 3 was informed by the Phase 2

EUCALYPTUS trial which, despite comparing two doses against placebo, was limited by a small sample size (n = 81 etrolizumab-treated patients) with two-thirds being prior TNFi users, raising concerns about dose selection generalisability.

Carotegrast Methyl (AJM300)

Carotegrast methyl is an orally administered small molecule that antagonises α4 integrin. Its active metabolite, HCA2969, selectively blocks α4β7 and α4β1 integrin interactions with cell adhesion molecules, sharing the mechanism of natalizumab. Given natalizumab's association with progressive multifocal leukoencephalopathy (PML), early investigations of carotegrast methyl were deliberately limited to induction phases. Phase IIa data in moderate-to-severe UC already refractory to conventional therapies demonstrated significant improvements over placebo across clinical response, clinical remission, and endoscopic and histological endpoints.

A Phase 3 multicentre, randomised, double-blind, placebo-controlled trial conducted in Japan enrolled patients who had not responded to conventional therapy. Unlike many comparable trials, patients with disease limited to the rectum were eligible. Following a two-week single-blind placebo run-in period designed to minimise placebo response bias, patients with active disease (Mayo score 6–10, endoscopic sub-score ≥2, rectal bleeding sub-score ≥1) were randomised to oral carotegrast methyl or placebo three times daily after meals for 8 weeks. The primary endpoint of clinical response at week 8 was achieved in 45% of the active group versus 21% in placebo recipients (p = 0.00028). Patients without endoscopic remission or cessation of rectal bleeding at week 8 continued treatment to 24 weeks, at which point significantly greater proportions on carotegrast methyl achieved clinical and symptomatic remission and endoscopic response. JCV seroconversion occurred in 16% of carotegrast methyl patients versus 7% on placebo at week 8, though no PML cases emerged. Nasopharyngitis was the most common adverse event in both groups (~10–11%). Carotegrast methyl was approved in Japan in 2022 for moderate UC with inadequate response to aminosalicylates.

Mirikizumab

Mirikizumab is an IgG4-variant monoclonal antibody that selectively binds the p19 subunit of IL-23. Phase 2 data across three dose regimens showed the strongest signal with 200 mg exposure-based dosing (22.6% remission at week 12 vs 4.8% placebo; p = 0.004), supporting advancement to Phase 3.

In the Phase 3 LUCENT 1 induction trial, moderate-to-severe UC patients were randomised 3:1 to intravenous mirikizumab 300 mg or placebo every 4 weeks for 12 weeks. Clinical remission was significantly higher with mirikizumab (24.2% vs 13.3%; p = 0.00006). Induction responders were then re-randomised in the LUCENT 2 maintenance trial to subcutaneous mirikizumab 200 mg or placebo every 4 weeks. At week 40, the primary endpoint of clinical remission was met by 49.9% on mirikizumab versus 25.1% on placebo (p < 0.001), with statistically significant endoscopic remission rates in both conventional therapy-failure and advanced therapy-failure subgroups. Further studies underway include an open-label extension (LUCENT 3), a paediatric/adolescent Phase 2 trial (SHINE 1), and a Phase 3b head-to-head trial against vedolizumab (LUCENT ACT).

Upadacitinib

Upadacitinib is a selective oral JAK1 inhibitor approved in 2022 for moderate-to-severe UC. It demonstrates greater selectivity for JAK1 inhibition over other JAK family members and TYK2. The Phase 3 programme comprised two parallel induction trials (U-ACHIEVE [UC1] and U- ACCOMPLISH [UC2]) and a maintenance study (U-ACHIEVE [UC3]).

Clinical remission at week 8 (adapted Mayo score ≤2, rectal bleeding score 0, stool frequency score ≤1,

endoscopic sub-score ≤1 without friability) was significantly higher with upadacitinib 45 mg daily compared to placebo: 26% vs 5% (UC1; $p < 0.001$) and 33% vs 4% (UC2; $p < 0.001$). Benefits in biologic-experienced subgroups were similarly robust.

In the maintenance trial (UC3), the primary endpoint of clinical remission at week 52 was met by 52% on upadacitinib 30 mg and 42% on 15 mg, versus 12% on placebo ($p < 0.001$ for each dose). Biologic-experienced patients maintained clinically meaningful remission advantages at both doses. Mucosal healing (Mayo endoscopic sub-score 0 and Geboes score <2) was achieved in 19% (30 mg) and 18% (15 mg) versus 5% on placebo, with all secondary endpoints statistically significant ($p < 0.0001$).

The most common adverse events during induction were nasopharyngitis (4–5%), creatine phosphokinase elevations (5%), and acne (5–7%). Herpes zoster was reported in 3 patients across both induction studies. In the maintenance phase, herpes zoster occurred in 4% on both upadacitinib doses versus none on placebo; two patients in the 30 mg arm developed venous thromboembolism. No major adverse cardiovascular events occurred in any upadacitinib maintenance arm. A key practical advantage is rapid onset: post-hoc analysis of induction trials showed improvements in stool frequency and rectal bleeding within the first day of treatment.

Conclusion

Advanced therapies- biologics and small molecules are front and center when it comes to treating moderate-to-severe or steroid-dependent ulcerative colitis. Even with a growing list of medications, remission rates from major studies still just sit around 20–40%. That gap shows we need more breakthroughs. The drugs coming down the pipeline bring something new—some target fresh pathways, like TLR9 agonism; some are more selective, like focusing just on IL-23; and others are easier for patients to take. It's exciting, but it makes things a little messier in the clinic. Now, doctors have to juggle more choices and figure out which meds make sense for which patients, weighing things like inflammation level, comorbidities, extra-intestinal symptoms, the patient's preferred route, how quickly relief is needed, and cost.bDirect comparison studies are rare. The VARSITY trial showed vedolizumab works better than adalimumab, but the HIBISCUS and GARDENIA trials found etrolizumab wasn't much different compared to adalimumab or infliximab. Meta-analyses put upadacitinib at the top for starting remission, even for folks who've tried biologics before, but the differences between trial eras and endpoints mean you can't take those rankings at face value. Small molecules really shine for those who want pills instead of injections, quicker relief (especially with JAK inhibitors—sometimes within a week), no risk of immune reactions, and the possibility of using them as solo therapy. But, they're not without their worries—selective JAK inhibitors still raise the risk of shingles, and we don't have the full picture yet on long-term heart or cancer risks, especially for upadacitinib and filgotinib. The new selective IL-23 inhibitors are shaking things up, especially when comparing them to ustekinumab, which targets both IL-12 and IL-23. Real- world and study data suggest selective IL-23 inhibitors might still work even after ustekinumab, and they seem to outperform ustekinumab in psoriasis, giving doctors a reason to use them one after another. What about using two advanced therapies at once? The idea is to mix agents with different mechanisms to boost results, and early reports—from a review covering 266 patients— show pretty solid remission rates (40–70%) and serious side effects in about 1 out of 10. The VEGA study hints at benefits from combining guselkumab and golimumab. But before combo therapy becomes routine, we need bigger studies, longer follow-up, and better cost-effectiveness data. As choices keep multiplying, the real challenge is predicting which drug works best for which person. We'll need reliable biomarkers and a smarter, more personalized approach if we want to get the most out of these new treatments for UC.

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