Health Monitor®

Clinician Update

Ulcerative Colitis

Scan here for a behind-the-scenes look at the case study on p. 21

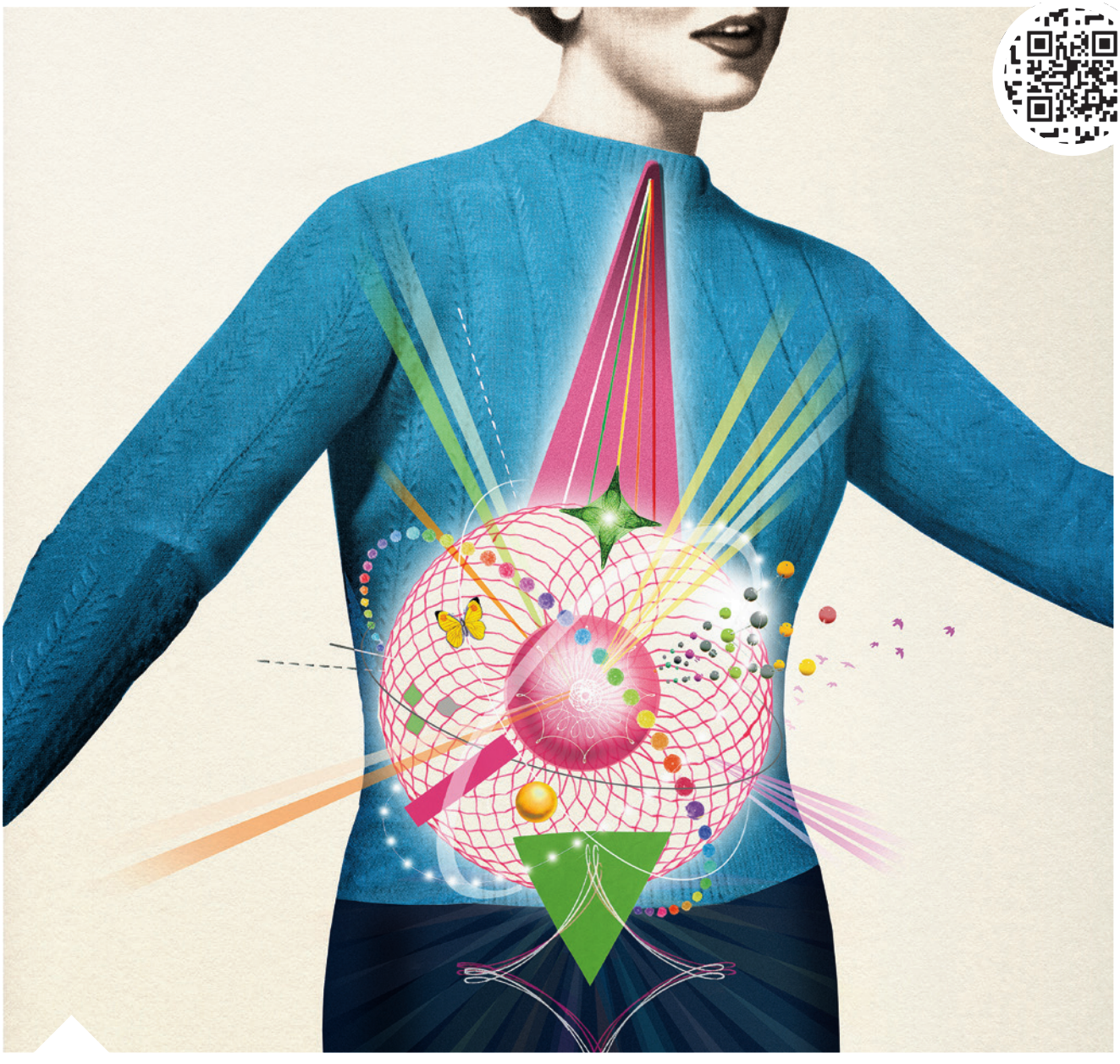

Illustration by Michela Buttignol

MODEL OF CARE

STRATEGIES *for* OPTIMIZING **BIOLOGIC THERAPY**

These targeted agents can not only control embarrassing symptoms, but also promote bowel healing to help achieve the ultimate goal: long-term remission.

Several biologic agents have been approved specifically for treating moderate-to-severe ulcerative colitis (UC), offering effective options beyond conventional therapy (e.g., mesalamines, corticosteroids and immunomodulators) and surgery. "We now have access to therapy that targets specific parts of the immune system," says Tauseef Ali, MD, FACG, AGAF, FACP, Chief of Gastroenterology and Medical Director of the Crohn's and Colitis Program at SSM Health St. Anthony Hospital, Oklahoma City. Compared with traditional first-line therapies, use of biologics has led to improved outcomes and quality of life (QoL), higher rates of long-term remission and possibly a reduced need for surgery in UC, he says.[1,2]

Additionally, biologics have a tolerable safety profile.[1,2] In fact, the American College of Gastroenterology (ACG) and American Gastroenterological Association (AGA) recognize the expanding role of biologics in UC treatment. Their guidelines for managing moderate-to-severe inflammatory bowel diseases support combining a biologic with an immunomodulator, such as methotrexate or thiopurines.[3,4]

"The rationale for combination therapy with biologics and immunomodulators is that the latter decrease the risk of immunogenicity against monoclonal antibodies by about 50%," says Siddharth Singh, MD, a gastroenterologist and Assistant Professor of Medicine at the University of California at San Diego and co-author of the AGA UC guideline.

Continued on next page ►

Immunomodulators also independently suppress the immune system and may have disease-modifying effects, explains Dr. Singh, adding that combination therapy may be particularly beneficial for patients with severe UC.

In all, 12 biologics with different mechanisms of action are indicated to treat UC, including anti-tumor necrosis factor (TNF) inhibitors, an integrin receptor antagonist and interleukin (IL) inhibitors. The latter class includes IL-23 inhibitors that gained FDA approval for UC over the past year and have expanded the field of biologic options. These agents target the p19 subunit of the IL-23 cytokine, which contributes to UC pathogenesis.[5] In clinical trials, patients with moderately to severely active UC who received these agents saw significantly higher rates of clinical remission after 12 weeks of induction therapy and 40 to 52 weeks of maintenance therapy, compared with placebo. Bowel urgency also was significantly reduced with IL-23p19 inhibitors.[6,7]

> "The more patients know about their disease and how biologics work, the more likely they are to stay adherent to treatment."
> —*Tauseef Ali, MD*

With so many options, choosing a biologic agent may seem overwhelming, particularly for patients. Yet experts note there are a few strategies that can help you and your patients zero in on the best option for them, including the following:

1. IDENTIFY APPROPRIATE CANDIDATES.

Once a patient's disease severity has been ascertained and reasonable treatment goals have been established, Dr. Ali suggests considering a biologic for patients with moderate-to-severe UC who are:

- Failing or cannot tolerate first-line therapies.
- At heightened risk of UC complications. This includes those with extensive disease or deep ulcers or who have extensive inflammation.
- Young or middle-aged and in the prime of their careers and family life.
- Steroid-dependent or -resistant. Short-term corticosteroid use can cause sleep disturbances, acne, weight gain and increased infection risk, while long-term use can lead to bone loss, hypertension, diabetes and cataracts.

However, biologics are contraindicated in patients with an active infection, as the medication can worsen it. Biologics are also not recommended for patients with active malignancies. In addition, certain agents must be used with caution in patients with serious comorbidities, such as heart failure, multiple sclerosis and other neurological disorders and severe liver disease.

In addition, Dr. Ali notes that if patients have recently received a live or live-attenuated vaccine, they may need to wait a couple weeks before starting a biologic, as the agent may interfere with vaccine response and increase risk of infection due to immunosuppression. Once patients start a biologic, they cannot receive live vaccines.

Also, ask if a patient is pregnant or breastfeeding or planning to do so. While most biologics are considered safe during pregnancy and breastfeeding, some agents could affect the fetus and breast milk.

2. MATCH THE BIOLOGIC TO PATIENT PREFERENCES AND NEEDS.

The choice of UC therapy should be based on shared decision-making, during which the patient's medical history and preferences are considered, says Kelly Colleen Cushing, MD, a gastroenterologist and Assistant Professor, University of Michigan Health System, Ann Arbor. Several key factors influence selection of a biologic[3,4,8,9] (see box on p. 5). When forming a treatment plan, Dr. Ali and Dr. Cushing suggest considering the following:

Past biologic use.

If therapeutic levels of a biologic achieved no or inadequate response, it's unlikely that another biologic within the same class would be more effective. "In that case, we would likely try a different class of medications," says Dr. Cushing. However, she notes that some patients may have a delayed response to the initial biologic. For example, subtherapeutic levels may have occurred due to pharmacokinetics or the presence of antidrug antibodies. In such cases, the patient may respond to drug optimization (e.g., a higher dose or shorter interval between doses); other options include adding an immunomodulator or trying another drug within the same class.

Delivery method.

Patient preference for the biologic's route of administration also should be considered. Some biologics are administered via IV infusion, which may appeal to patients who prefer fewer injections or are averse to self-injecting. By contrast, other patients may prefer the convenience of subcutaneous (SC) self-injection at home.

Frailty.

Frail patients are vulnerable to serious infections. TNF inhibitors induce systemic immune suppression and are associated with an increased risk for infection, which may make non-TNF inhibitors preferable. However, this rule may not apply to seniors who are in good health. "Patient frailty, rather than age, should determine whether to avoid systemic immune suppression with a TNF inhibitor," notes Dr. Cushing.

Targeted symptoms.

If a patient struggles with fecal urgency—an especially distressing symptom—an IL-23p19 inhibitor (indicated for UC) may be a good option, as this class has been shown to improve bowel urgency, says Dr. Ali.[1,2] If a gut-specific mechanism of action is preferred, an integrin receptor antagonist can target the gut while minimizing adverse effects to other organs, he adds.

Comorbidities.

If a patient with UC has a comorbid inflammatory disease, such as psoriasis or psoriatic arthritis, Dr. Ali recommends choosing a biologic that is indicated for both conditions, such as an anti-TNF blocker or dual IL-12/23 inhibitor. And "if the patient is undergoing cancer treatment, a gut-selective biologic should be chosen over a systemic immune suppressive because the latter increases infection risk," says Dr. Cushing.

3. DISPEL MISCONCEPTIONS.

"The more patients know about their disease and how biologics work, the more likely they are to stay adherent to treatment," says Dr. Ali. Many patients harbor misconceptions about biologics that need to be clarified before treatment starts. Dr. Ali notes common examples and how to dispel them:

"Biologic equals 'seriously ill.' "

When biologics are given as second-line therapy, the goal is remission, not palliation. "Some patients feel that biologics are a last-resort treatment, but they are not," he says.

"Biologics start working immediately."

Many patients think they'll feel better as soon as they start a biologic, but patients typically won't notice an effect for weeks or even months, notes Dr. Ali. "Once they do see an effect, it's usually worth the wait."

"Biologics are dangerous."

Biologics, in general, have a more benign safety profile

Key factors to consider when choosing biologic therapy[2-5]

Patient characteristics

- Age
- Comorbidities (e.g., heart failure, renal disease) that may contraindicate use or warrant caution with certain biologics
- Vulnerability to infection
- History of malignancy
- Pregnancy
- Individual goals and preferences

Disease characteristics

- Disease severity
- Perianal disease
- Presence of extraintestinal manifestations (e.g., joint pain, skin disorders)
- Co-existing inflammatory disease (e.g., rheumatoid arthritis, psoriasis)

Treatment-related considerations

- Overall efficacy (short- and long-term) and the need for a rapid response
- Tolerability and safety (including patient concerns about side effects)
- Previous biologic therapy
- Immunogenicity
- Administration modality
- Need for flexible treatment (e.g., easy interruption or restart)
- Insurance coverage

than accepted first-line therapies. "Though fatal infections have been reported with some biologics, these have been extremely rare."

"If this biologic works, I'll never need another."

Impress upon patients that they may need to change biologics at some point. Immunogenicity, low serum drug levels and intermittent or episodic therapy can cause patients to lose response to a biologic over time.[10]

"I can stop the biologic as soon as I feel better."

Many patients do not realize biologics are continuous long-term regimens, says Dr. Ali. "Tell the patient, 'A biologic can help you stay in remission, but it cannot cure your disease. If you stop taking it, the inflammation will come back.' "

To further dispel misconceptions and fill potential knowledge gaps, refer patients to evidence-based resources such as the Crohn's & Colitis Foundation (*crohnscolitisfoundation.org)*, which offers educational resources, access to an online support community and more. It's also important to inform patients about mental health services to help with depression or anxiety, which can thwart medication adherence, notes Dr. Ali.

4. HELP PATIENTS OVERCOME ACCESS ISSUES.

The choice of biologic frequently hinges on the patient's insurance. Many payers will require step therapy with an aminosalicylate before they consider biologic coverage. "We prescribe based on what's best for the patient," explains Dr. Cushing, "but we have to work within the confines of what insurance will cover." She notes that often an insurer will mandate a specific TNF inhibitor as the first-choice biologic therapy. Still, she says, "More insurers are becoming open to alternative first-line therapies besides anti-TNFs, and some insurers may be receptive to appeals for prior authorization."

The Crohn's & Colitis Foundation website offers customizable letters to help with appeals, as well as links to programs for patients who need help affording their medication. Also, many pharmaceutical companies offer financial assistance and copay assistance to help patients access medications, notes Dr. Ali.

–by Pete Kelly

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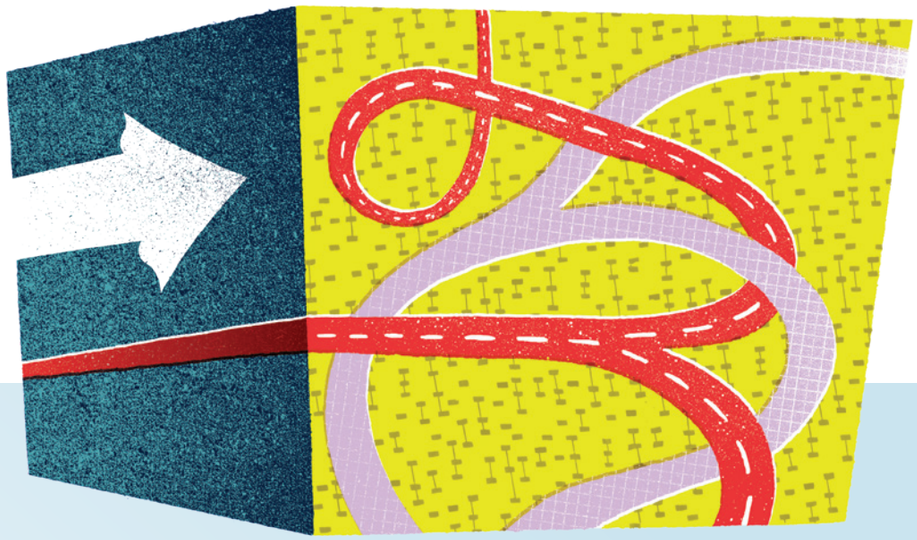

Illustration by Lizzie Roberts / Ikon Images

PRACTICE PEARLS

MANAGING COMMON COMORBIDITIES

Early recognition and treatment of coexisting conditions are crucial for improving patient outcomes and quality of life.

While gut symptoms are the hallmark of inflammatory bowel disease (IBD), up to 47% of patients with ulcerative colitis or Crohn's disease develop extraintestinal manifestations (EIMs), which are related complications that affect other parts of the body. (In some surveys, patients say that EIMs are more bothersome than IBD itself.) Meanwhile, the medications used to treat common comorbidities in patients with IBD may also cause problems.[1,2]

In addition, research shows that common immunologic comorbidities, such as inflammatory arthritis and uveitis, can affect the course of ulcerative colitis (UC), impacting treatment choices to manage both UC and comorbid manifestations.[1] To help ensure comprehensive management of patients with UC, here are expert strategies for diagnosing and treating common comorbidities and related complications.

Joint problems

"Joint pain is the most common extraintestinal manifestation of IBD," says David T. Rubin, MD, co-director of the Digestive Diseases Center at the University of Chicago.

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About one third of patients experience joint pain and stiffness, with some research suggesting the figure is even higher, notes Dr. Rubin. Arthritis and arthralgia may affect both younger and older patients. The Crohn's & Colitis Foundation (CCF) identifies three types of arthritis as commonly afflicting people with IBD:[2]

Peripheral arthritis, which typically affects joints in the limbs such as the knees, hips, elbows and shoulders, though the fingers may become symptomatic, too. Diagnosis is based on medical history, physical examination and exclusion of other potential causes of joint pain with lab tests and imaging. Severity of joint symptoms generally parallel those of the gastrointestinal tract. Fortunately, no joint destruction occurs and peripheral arthritis usually resolves when underlying IBD is effectively treated. "If you treat the bowel, the joints get better," says Dr. Rubin.

Axial arthritis, or spondylitis, which causes pain and stiffness in the lower spine and sacroiliac joints. Symptoms may arise months or years before a patient reports IBD symptoms. "These large joints in your lower back and pelvis can be inflamed independently of IBD disease activity," says Dr. Rubin. "So you can fix the IBD, but the problems with the large joints will still progress." Left untreated, inflammation can produce permanent joint damage and vertebral fusion that limits range of motion. Therefore, it's crucial to coordinate care with a rheumatologist.

Ankylosing spondylitis (AS) is a less common but more severe form of spinal arthritis that's diagnosed in a small portion (2% to 3%) of IBD patients. AS typically afflicts younger patients, especially males, and those with Crohn's disease are more at risk than those with ulcerative colitis. As with axial arthritis, successful treatment of IBD will not alter the course of AS. Damage to joints in the lower spine and sacroiliac joints can dramatically limit range of motion. Again, the key to minimizing damage is coordinated care with a rheumatologist.

Other forms of arthritis should also be considered. For example, some studies have suggested that IBD patients have an increased risk for rheumatoid arthritis, yet overall findings have been inconsistent.[3]

Skin disorders

Skin issues are the second most common EIM of IBD. They include:

Erythema nodosum, which occurs more commonly in Crohn's disease, affects about 6% of patients, producing nodules that are painful and tender.[4] Skin symptoms parallel bowel symptoms, but erythema nodosum "responds well when the bowel is treated," says Dr. Rubin.

Pyoderma gangrenosum is less common, but produces severe, painful ulcers, often on the legs. Patients with ulcerative colitis have a greater risk for these skin manifestations, which occur independently of disease activity in the bowel. Topical corticosteroids and tacrolimus ointments may be useful, but many patients require oral corticosteroids.[5]

Psoriasis. People with Crohn's disease and ulcerative colitis are 59% to 65% more likely to develop psoriasis.[6] The skin changes of psoriasis are unrelated to disease activity in the gut. Psoriasis is associated with comorbidities such as obesity and habits such as smoking, but the increased prevalence is also linked to therapy.

While TNF inhibitors are commonly prescribed for management of psoriasis, in some cases the drugs can have the paradoxical effect of triggering the skin condition. One meta-analysis found that 5.6% of IBD patients treated with a TNF inhibitor developed psoriasis or psoriasiform rashes.[7] In the event a TNF inhibitor is suspected of triggering psoriasis, consider consulting with a dermatologist to determine if topical therapy is sufficient to control psoriasis activity, says Kelly Colleen Cushing, MD, a gastroenterologist at the Brighton Center for Specialty Care in Michigan. "In cases where topical therapy is not sufficient, the anti-TNF therapy is often discontinued and a new class of therapy is started," notes Dr. Cushing.

Bone disease

Between 30% and 60% of IBD patients have lower-than-average bone density, according to the CCF, leaving them vulnerable to osteoporosis and related skeletal disorders and their sequelae. For example, people with IBD are 40% more likely than age- and sex-matched control subjects to suffer bone fractures.[6]

Baseline bone density testing is recommended for patients who have suffered a previous fragility-related fracture, postmenopausal women, males over 50 years, hypogonadal males and any IBD patient with more than 3 months of corticosteroid therapy.[8]

In addition, several steps can reduce patients' risk for bone disorders. First, it's important to optimize IBD therapy, as chronic inflammation disturbs healthy bone metabolism. How-

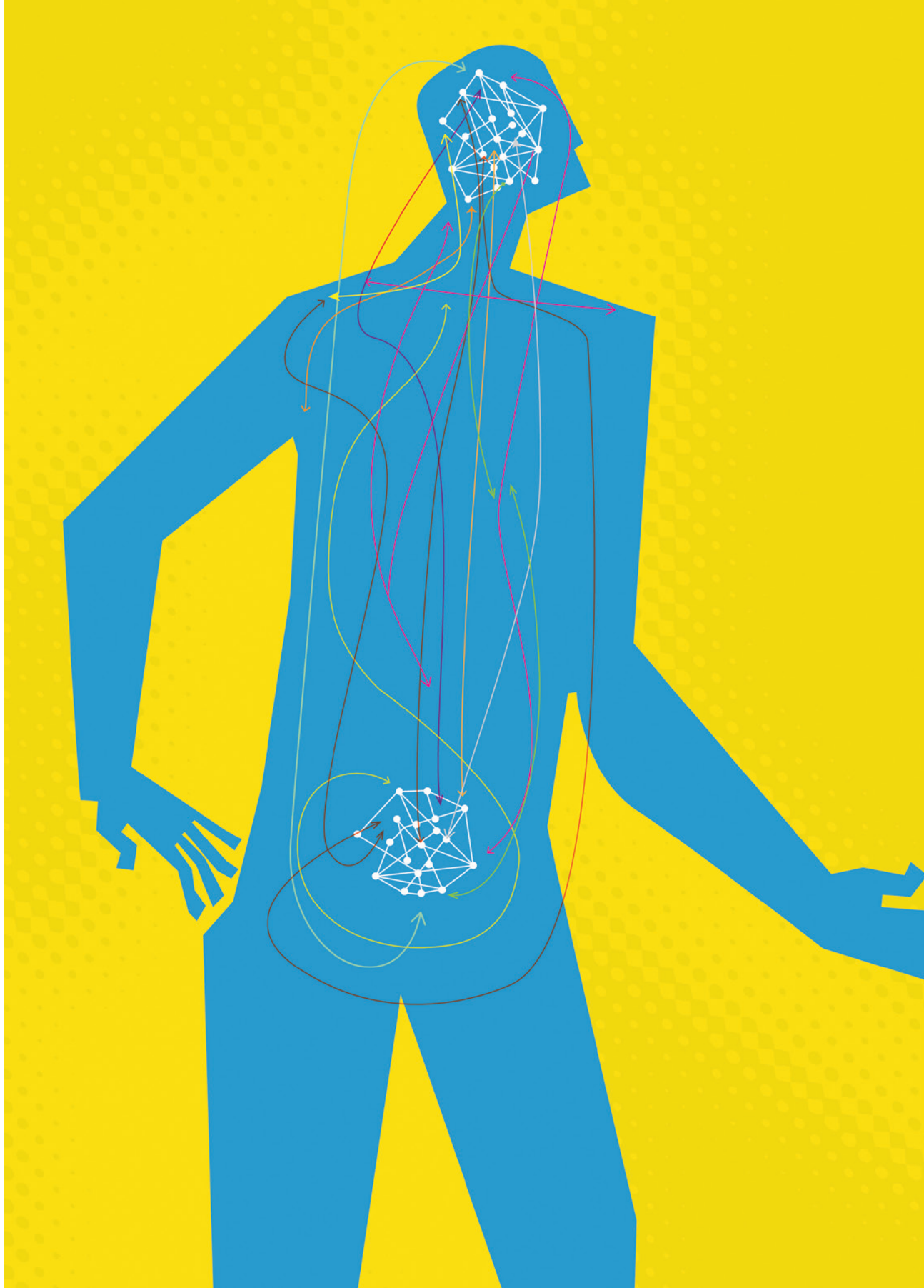

Illustration by Mark Mcginnis

ever, limit corticosteroids, as the increased threat of osteoporosis and bone fractures is largely linked to long-term use of the drugs. "It's one of many reasons why we want to limit excessive steroid exposure," says Dr. Cushing. Also, consider nutritional supplements such as calcium and vitamin D, particularly for patients who have undergone surgery to remove portions of the small bowel and may not adequately absorb bone-building nutrients. Patients with inadequate dietary intake may benefit from supplementation.

Liver disease

Having IBD increases the risk for several diseases of the liver, with the most prevalent and worrisome being primary sclerosing cholangitis (PSC), or inflammation of the bile ducts.[2] In a Canadian population-based study of IBD patients, PSC occurred most often in males with ulcerative colitis (3%).[6] "Inflammation of the bile ducts in PSC occurs independently of IBD disease activity in the gut," explains Dr. Cushing, and disturbs the normal flow of bile. Early symptoms are itching and jaundice, which can progress to fatigue. Complications include infection, cirrhosis, colon cancer and cancer of the bile duct (cholangiocarcinoma). "PSC requires continuous monitoring and collaboration with our colleagues in hepatology," says Dr. Cushing.

Eye disorders

Uveitis, or inflammation of the uvea (the middle layer of the eye) and associated tissues, affects about 10% of IBD patients, according to the CCF. Symptoms include redness, pain and sensitivity to light. The patient may also complain of blurred vision and headaches. Untreated uveitis can result in glaucoma and vision loss, so refer a patient with this eye condition to an ophthalmologist.[9]

Unchecked inflammation may also cause episcleritis, which affects the outer coating of the white of the eye, causing redness and pain. However, episcleritis is usually self-limiting and often clears up when gut symptoms are adequately treated.[2]

Cancer

IBD and its treatment are linked to an increased risk for certain cancers, including:

Colorectal cancer, which is a significant cause of death in IBD patients, accounting for 10% to 15% of mortality,[10] though rates appear to be declining, notes Dr. Rubin. "We know that colon cancer risk is reduced because our prevention strategies and our therapies are working," he says. Unchecked inflammation in the intestinal tract is the likely explanation for the heightened risk for colorectal cancer in IBD. The American Cancer Society recommends that an IBD patient undergo a colonoscopy within 8 years of diagnosis and suggests follow-up colonoscopies every 1 to 3 years, depending on the initial findings and the patient's other risk factors.[11,12]

Lymphoma. IBD patients as a group have a modestly increased risk for lymphoma. "That has been predominantly driven by one of our older therapies, the thiopurines," says Dr. Rubin. (TNF inhibitors carry a warning about reports of lymphoma and other malignancies in patients treated with the agents, which primarily occurred in adolescents and young males on combination therapy with azathioprine or 6-mercaptopurine.) If a patient is a candidate for combination therapy, discuss the risks and benefits of thiopurines.

Skin cancer. Patients with IBD have a four- to seven-fold increased risk for skin cancer, primarily basal cell carcinoma.[13] The American College of Gastroenterology (ACG) calls for IBD patients receiving immunosuppression to wear sunscreen and sun-protective clothing when outdoors and to undergo evaluation by a dermatologist, with subsequent surveillance determined on a case-by-case basis.[14]

Cervical cancer. While data regarding an increased risk for cervical cancer in women with IBD are conflicting, there is consistent evidence linking chronic immunosuppression to the malignancy. Therefore, the ACG recommends annual cervical cancer screening for women on immunosuppressive therapy.[14]

> "Joint pain is the most common extraintestinal manifestation…if you treat the bowel, the joints get better."
>
> —David T. Rubin, MD

Cardiovascular disease

People with IBD have an increased risk for cardiovascular disease (CVD).[15] What's more, the prevalence of venous thromboembolism (VTE) is at least three times higher among IBD patients than in the general population, with the risk significantly increased during hospitalization, surgery and periods of high disease activity.[16] In addition, one JAK inhibitor has a warning about an increased risk of pulmonary thromboembolism and death at certain dosages.[17] Therefore, presence of some forms of CVD may influence choice of therapy. "For example, we avoid prescribing anti-TNF medication in patients with significant heart failure out of concern that it could make their condition worse," says Dr. Cushing.

Fatigue

One study found that two thirds of patients with IBD reported fatigue.[18] Sleep disturbances, disease activity, depression and anxiety were the strongest predictors of persistent fatigue among 2,429 patients with Crohn's disease or ulcerative colitis followed over a 6-month period. Referral to a sleep specialist, mental health provider and regular exercise may provide some relief, though sufficient data are lacking. And while findings are inconsistent, some evidence suggests that curbing inflammation may help improve fatigue: One study found that patients who were started on a biologic and achieved clinical remission were less likely to have persistent fatigue after 1 year of treatment.[19]

–by Timothy Gower

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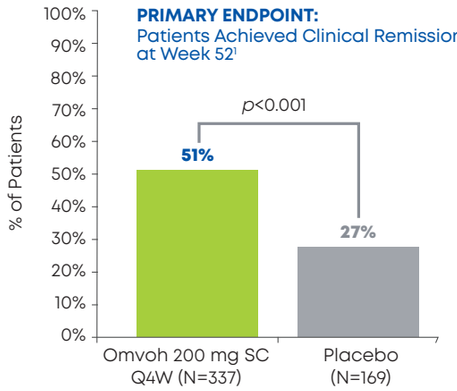
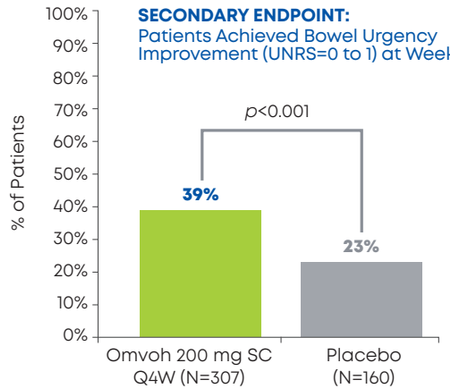
For your adult patients with moderately to severely active ulcerative colitis (UC) who had inadequate response to their current treatment[1]

MAKE THE URGENT CHANGE WITH OMVOH

AMONG PATIENTS WHO ACHIEVED CLINICAL RESPONSE WITH OMVOH AT WEEK 12[1]

Omvoh demonstrated sustained clinical remission and reduced bowel urgency at Week 52[1]





Nearly 2 in 3 patients taking Omvoh achieved clinical response at Week 12[1]

65% of patients (n=517/795) taking Omvoh achieved clinical response* after 12 weeks of induction dosing vs 43% (n=115/267) with placebo (secondary endpoint), and nearly 1 in 4 (24%, n=191/795) achieved clinical remission[a] vs 15% (n=40/267) with placebo (primary endpoint).[1]

[a]Clinical remission based on mMS is defined as: SF=0 or 1, RB=0, and centrally read ES=0 or 1 (excluding friability).[1]

*Clinical response is defined as a decrease in the mMS of ≥2 points with ≥30% decrease from baseline, and either a decrease of ≥1 point in RB from baseline or RB=0 or 1.[1]

INDICATION

Omvoh™ is an interleukin-23 antagonist indicated for the treatment of moderately to severely active ulcerative colitis in adults.[1]

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS: Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients.

Please see Important Safety Information below.

Lilly

omvoh™ (mirikizumab-mrkz)

300 mg/15 mL infusion | 100 mg/mL injection

UC-1 AND UC-2 TRIAL DESIGN

Omvoh was studied in two Phase 3, randomized, double-blind, placebo-controlled clinical trials of adult patients with moderately to severely active UC. Patients (N=1279) were randomized 3:1 to receive Omvoh 300 mg IV infusion or placebo every 4 weeks (Q4W) for 12 weeks (Week 0, 4, and 8) in the induction study (UC-1). Patients who achieved clinical response with Omvoh at Week 12 in UC-1 (N=581) were re-randomized 2:1 to receive Omvoh 200 mg SC injection or placebo Q4W for 40 weeks in the maintenance study (UC-2) (52 weeks of continuous therapy). The primary endpoint was the proportion of patients in clinical remission at Week 12 in UC-1 and Week 40 in UC-2.[1]

At baseline of UC-1, all patients had inadequate response, loss of response, or intolerance to at least one corticosteroid, immunomodulator, biologic treatment (TNF blocker, vedolizumab), or tofacitinib. In UC-2, patients who were on concomitant UC therapies during UC-1 were required to continue on stable doses of oral aminosalicylates and immunomodulator agents. Corticosteroid tapering was required for patients who were receiving oral corticosteroids at baseline and achieved clinical response in UC-1.[1]

Patients with an mMS of 5 to 9 at baseline of UC-1 were included for efficacy analyses. Patients had a median mMS of 7, and 58% had severely active disease (mMS 7 to 9). Patients' baseline therapies included 41% of patients receiving oral corticosteroids, 24% receiving immunomodulators, and 75% receiving aminosalicylates. Patients' prior treatment experiences include: 57% were biologic- and JAKi-naive, 41% had failed at least one biologic, 3% had failed a JAKi, and 2% had previously received but had not failed a biologic or JAKi.[1]

Bowel urgency was assessed using an Urgency Numeric Rating Scale (UNRS) ranging from 0 (no urgency) to 10 (worst possible urgency) during UC-1 and as a secondary endpoint in UC-2. Bowel urgency improvement was evaluated as the proportion of patients with a baseline UNRS weekly average score of ≥3 achieving a weekly average score of 0 to 1 at Week 12 in UC-1 and Week 40 in UC-2.[1,2,4]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS - Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis during intravenous infusion, have been reported with Omvoh administration. Infusion-related hypersensitivity reactions, including mucocutaneous erythema and pruritus, were reported during induction. If a severe hypersensitivity reaction occurs, discontinue Omvoh immediately and initiate appropriate treatment.

Infections

Omvoh may increase the risk of infection. Do not initiate treatment with Omvoh in patients with a clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Omvoh. Instruct patients to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops or an infection is not responding to standard therapy, monitor the patient closely and do not administer Omvoh until the infection resolves.

Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Omvoh. Do not administer Omvoh to patients with active TB infection. Initiate treatment of latent TB prior to administering Omvoh. Consider anti-TB therapy prior to initiation of Omvoh in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after Omvoh treatment. In clinical trials, subjects were excluded if they had evidence of active TB, a history of active TB, or were diagnosed with latent TB at screening.

Hepatotoxicity

Drug-induced liver injury in conjunction with pruritus was reported in a clinical trial patient following a longer than recommended induction regimen. Omvoh was discontinued. Liver test abnormalities eventually returned to baseline. Evaluate liver enzymes and bilirubin at baseline and for at least 24 weeks of treatment. Monitor thereafter according to routine patient management. Consider other treatment options in patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Immunizations

Avoid use of live vaccines in patients treated with Omvoh. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Prior to initiating therapy, complete all age-appropriate vaccinations according to current immunization guidelines. No data are available on the response to live or non-live vaccines in patients treated with Omvoh.

ADVERSE REACTIONS

Most common adverse reactions (≥2%) associated with Omvoh treatment are upper respiratory tract infections and arthralgia during induction, and upper respiratory tract infections, injection site reactions, arthralgia, rash, headache, and herpes viral infection during maintenance.

MR HCP ISI UC APP

See Brief Summary of Prescribing Information on subsequent pages. See Instructions for Use included with the device.

ES=endoscopic subscore; IV=intravenous; mMS=modified Mayo score; Q4W=every 4 weeks; RB=rectal bleeding subscore; SC=subcutaneous; SF=stool frequency subscore; TNF=tumor necrosis factor; UC=ulcerative colitis; UNRS=Urgency Numeric Rating Scale.

References: 1. Omvoh (mirikizumab-mrkz). Prescribing Information. Lilly USA, LLC. **2.** D'Haens G, Dubinsky M, Kobayashi T, et al. Mirikizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2023;388(26):2444-2455. doi:10.1056/NEJMoa2207940 **3.** Data on File. DOF-MR-US-0018. Lilly USA, LLC. **4.** Dubinsky MC, Irving PM, Panaccione R, et al. Incorporating patient experience into drug development for ulcerative colitis: development of the Urgency Numeric Rating Scale, a patient-reported outcome measure to assess bowel urgency in adults. *J Patient Rep Outcomes*. 2022;6(1):31. doi:10.1186/s41687-022-00439-w

Omvoh™ (mirikizumab-mrkz) injection, for intravenous or subcutaneous use

Brief Summary: Consult the package insert for complete prescribing information.

INDICATIONS AND USAGE
Omvoh is an interleukin-23 antagonist indicated for the treatment of moderately to severely active ulcerative colitis in adults.

CONTRAINDICATIONS
Omvoh is contraindicated in patients with a history of serious hypersensitivity reaction to mirikizumab-mrkz or any of the excipients *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS
Hypersensitivity Reactions
Serious hypersensitivity reactions, including anaphylaxis during intravenous infusion, have been reported with Omvoh administration. Infusion-related hypersensitivity reactions, including mucocutaneous erythema and pruritis, were reported during induction [see *Adverse Reactions*]. If a severe hypersensitivity reaction occurs, discontinue Omvoh immediately and initiate appropriate treatment.

Infections
Omvoh may increase the risk of infection *[see Adverse Reactions]*.

Do not initiate treatment with Omvoh in patients with a clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing Omvoh. Instruct patients to seek medical advice if signs or symptoms of clinically important acute or chronic infection occur. If a serious infection develops or an infection is not responding to standard therapy, monitor the patient closely and do not administer Omvoh until the infection resolves.

Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Omvoh.

Do not administer Omvoh to patients with active TB infection. Initiate treatment of latent TB prior to administering Omvoh. Consider anti-TB therapy prior to initiation of Omvoh in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after Omvoh treatment.

In clinical trials, subjects were excluded if they had evidence of active TB, a past history of active TB, or were diagnosed with latent TB at screening.

Hepatotoxicity
A case of drug-induced liver injury (alanine aminotransferase [ALT] 18x the upper limit of normal (ULN), aspartate aminotransferase [AST] 10x ULN, and total bilirubin 2.4x ULN) in conjunction with pruritus was reported in a clinical trial subject following a longer than recommended induction regimen. Omvoh was discontinued. Liver test abnormalities eventually returned to baseline.

Evaluate liver enzymes and bilirubin at baseline and for at least 24 weeks of treatment. Monitor thereafter according to routine patient management.

Consider other treatment options in patients with evidence of liver cirrhosis. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. Interrupt treatment if drug-induced liver injury is suspected, until this diagnosis is excluded. Instruct patients to seek immediate medical attention if they experience symptoms suggestive of hepatic dysfunction.

Immunizations
Avoid use of live vaccines in patients treated with Omvoh. Prior to initiating therapy with Omvoh, complete all age-appropriate vaccinations according to current immunization guidelines. No data are available on the response to live or non-live vaccines in patients treated with Omvoh.

ADVERSE REACTIONS
The following topics are also discussed in detail in the Warnings and Precautions section:
Hypersensitivity Reactions
Infections
Tuberculosis
Hepatotoxicity

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Omvoh was studied up to 12 weeks in subjects with moderately to severely active ulcerative colitis in a randomized, double-blind, placebo-controlled induction study (UC-1). In subjects who responded to induction therapy in UC-1, long-term safety up to 52 weeks was evaluated in a randomized, double-blind, placebo-controlled maintenance study (UC-2) and a long-term extension study *[see Clinical Studies]*.

In the induction study (UC-1), 1279 subjects were enrolled of whom 958 received Omvoh 300 mg administered as an intravenous infusion at Weeks 0, 4, and 8. In the maintenance study (UC-2), 581 subjects were enrolled of whom 389 received Omvoh 200 mg administered as a subcutaneous injection every 4 weeks.

Table 1 summarizes the adverse reactions reported in at least 2% of subjects and at a higher frequency than placebo during UC-1.

Table 1: Adverse Reactions[a] in Subjects with Ulcerative Colitis through Week 12 in a Placebo-Controlled Induction Study (UC-1)

Adverse Reactions	OMVOH 300-mg Intravenous Infusion[b] N=958 n (%)	Placebo N=321 n (%)
Upper respiratory tract infections[c]	72 (8%)	20 (6%)
Arthralgia	20 (2%)	4 (1%)

[a] Reported in at least 2% of subjects and at a higher frequency than placebo.
[b] Omvoh 300 mg as an intravenous infusion at Weeks 0, 4, and 8.
[c] Upper respiratory tract infections includes related terms (e.g., COVID-19, nasopharyngitis, pharyngitis, rhinitis, sinusitis, and upper respiratory tract infection).

In the induction study (UC-1), infusion-related hypersensitivity reactions were reported by 4 (0.4%) subjects treated with Omvoh and 1 (0.3%) subject treated with placebo.

Table 2 summarizes the adverse reactions reported in at least 2% of subjects and at a higher frequency than placebo during the 40-week controlled period of UC-2.

Table 2: Adverse Reactions[a] in Subjects with Ulcerative Colitis through Week 40 In a Placebo-Controlled Maintenance Study (UC-2)

Adverse Reactions	OMVOH 200-mg Subcutaneous Injection[b] N=389 n (%)	Placebo N=192 n (%)
Upper respiratory tract infections[c]	53 (14%)	23 (12%)
Injection site reactions[d]	34 (9%)	8 (4%)
Arthralgia	26 (7%)	8 (4%)
Rash[e]	16 (4%)	2 (1%)
Headache	16 (4%)	2 (1%)
Herpes viral infection[f]	9 (2%)	1 (1%)

[a] Reported in at least 2% of subjects and at a higher frequency than placebo
[b] Omvoh 200 mg as a subcutaneous injection at Week 12 and every 4 weeks thereafter for up to an additional 40 weeks.
[c] Upper respiratory tract infections includes related terms (e.g., COVID-19, nasopharyngitis, pharyngitis, rhinitis, sinusitis, and upper respiratory tract infection).
[d] Injection site reactions includes related terms (e.g., erythema, hypersensitivity, pain, reaction, and urticaria at the injection site).
[e] Rash is composed of several similar terms.
[f] Herpes viral infection includes related terms (e.g., herpes zoster, herpes simplex, and oral herpes.)

Infections
In UC-1 through Week 12, infections were reported by 145 (15%) subjects treated with Omvoh 300 mg and 45 (14%) subjects treated with placebo. Serious infections were reported by less than 1% in both groups. Serious infections in the Omvoh group included intestinal sepsis, listeria sepsis, and pneumonia.

In the maintenance study (UC-2) through Week 40 (a total of 52 weeks of treatment), infections were reported by 93 (24%) subjects treated with Omvoh 200 mg and 44 (23%) subjects treated with placebo. A case of COVID-19 pneumonia was reported as a serious infection in the Omvoh group.

Hepatic Enzyme Elevations
In UC-1 through Week 12, alanine aminotransferase (ALT) ≥5X ULN was reported by 1 (0.1%) subject treated with Omvoh 300 mg and 1 (0.3%) subject treated with placebo. Aspartate aminotransferase (AST) ≥5X ULN was reported by 2 (0.2%) subjects treated with Omvoh 300 mg and no subject treated with placebo. These elevations have been noted with and without concomitant elevations in total bilirubin.

In the maintenance study (UC-2) through Week 40 (a total of 52 weeks of treatment), 3 (0.8%) subjects treated with Omvoh 200 mg reported ALT ≥5X ULN and 3 (0.8%) subjects reported AST ≥5X ULN; with or without concomitant elevations in total bilirubin. No subjects treated with placebo experienced similar elevations *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS
Pregnancy
Pregnancy Exposure Registry
There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Omvoh during pregnancy. Pregnant women exposed to Omvoh and healthcare providers are encouraged to call Eli Lilly and Company at 1-800-Lilly-Rx (1-800-545-5979).

Risk Summary
Available data from case reports of mirikizumab-mrkz use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Although there are no data on mirikizumab-mrkz, monoclonal antibodies can be actively transported across the placenta, and mirikizumab-mrkz may cause immunosuppression in the in utero-exposed infant. An enhanced pre- and post-natal development study conducted in pregnant monkeys at a dose 69 times the maximum recommended human dose (MRHD) revealed no adverse developmental effects to the developing fetus, or harm to infant monkeys from birth through 6 months of age. There are risks of adverse pregnancy outcomes associated with increased disease activity in women with inflammatory bowel disease *(see Clinical Considerations)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations
Disease-Associated Maternal and Embryo/Fetal Risk
Published data suggest that the risk of adverse pregnancy outcomes in women with inflammatory bowel disease (IBD) is associated with increased disease activity. Adverse pregnancy outcomes include preterm delivery (before 37 weeks gestation), low birth weight (less than 2500 g) infants, and small for gestational age at birth.

Fetal/Neonatal Adverse Reactions
Transport of endogenous IgG antibodies across the placenta increases as pregnancy progresses, and peaks during the third trimester. Because mirikizumab-mrkz may interfere with immune response to infections, risks and benefits should be considered prior to administering live vaccines to infants exposed to Omvoh in utero. There are no data regarding infant serum levels of mirikizumab-mrkz at birth and the duration of persistence of mirikizumab-mrkz in infant serum after birth. Although a specific timeframe to delay live virus immunizations in infants exposed in utero is unknown, a minimum of 2 months after birth should be considered because of the half-life of the product.

Data
Animal Data
An enhanced pre- and postnatal development study was conducted in cynomolgus monkeys administered mirikizumab-mrkz by intravenous injection during organogenesis to parturition at a dose of 300 mg/kg twice weekly (69 times the MRHD based on exposure comparisons). Mirikizumab-mrkz crossed the placenta in monkeys. No maternal toxicity was noted in this study. No mirikizumab-mrkz-related effects on morphological, functional, or immunological development were observed in infant monkeys from birth through 6 months of age. However, incidences of embryo/fetal loss were higher in the treated groups compared to control (6.7% [1 of 15] in controls vs 26.7% [4 of 15] at 300 mg/kg (69 times the MRHD, based on exposure comparisons) but were within the range of historical control data. Following delivery, most adult female cynomolgus monkeys and all infants from the mirikizumab-mrkz-treated group had measurable serum concentrations up to 28 days postpartum. In the infant monkeys, mean serum concentrations were approximately 4.8 times the respective mean maternal concentrations.

Lactation
Risk Summary
There are no data on the presence of mirikizumab-mrkz in human milk, the effects on the breastfed infant, or the effects on milk production. Endogenous maternal IgG and monoclonal antibodies are transferred in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to mirikizumab-mrkz are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Omvoh and any potential adverse effects on the breastfed infant from Omvoh or from the underlying maternal condition.

Pediatric Use
The safety and effectiveness of Omvoh have not been established in pediatric patients.

Geriatric Use
Of the 795 Omvoh-treated subjects in the two clinical trials, 64 subjects (8%) were 65 years of age and older, while 10 subjects (1%) were 75 years of age and older. These clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger adult subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects. No clinically meaningful differences in the pharmacokinetics of mirikizumab-mrkz were observed in subjects 65 years of age and older compared to younger adult subjects *[see Clinical Pharmacology]*.

DOSING
Recommended Dosage
Induction Dosage
The recommended induction dosage of Omvoh is 300 mg administered by intravenous infusion over at least 30 minutes at Week 0, Week 4, and Week 8 *[see Dosage and Administration]*.

Maintenance Dosage
The recommended maintenance dosage of Omvoh is 200 mg administered by subcutaneous injection (given as two consecutive injections of 100 mg each) at Week 12, and every 4 weeks thereafter *[see Dosage and Administration]*.

PATIENT COUNSELING INFORMATION
Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Hypersensitivity Reactions
Advise patients to discontinue Omvoh and seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions *[see Warnings and Precautions]*.

Infections
Advise patients that Omvoh may lower the ability of their immune system to fight infections and to contact their healthcare provider immediately if they develop any symptoms of infection *[see Warnings and Precautions]*.

Tuberculosis
Advise patients to contact their healthcare provider if they experience symptoms suggestive of TB (e.g., unexplained fever, cough, or difficulty breathing) *[see Warnings and Precautions]*.

Hepatotoxicity
Inform patients that Omvoh may cause liver injury. Advise patients to seek immediate medical attention if they experience symptoms suggestive of liver dysfunction (e.g., unexplained rash, nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine) *[see Warnings and Precautions]*.

Immunizations
Advise patients that vaccination with live vaccines is not recommended during Omvoh treatment and immediately prior to or after Omvoh treatment. Medications that interact with the immune system may increase the risk of infection following administration of live vaccines. Instruct patients to inform their healthcare provider that they are taking Omvoh prior to receiving a vaccination *[see Warnings and Precautions]*.

Pregnancy
Advise patients who are exposed to Omvoh during pregnancy to contact Eli Lilly and Company *[see Use in Specific Populations]*.

Administration
Instruct patients in preparation and administration of Omvoh, including choosing anatomical sites for subcutaneous administration, and proper subcutaneous injection technique. Instruct patients in the technique of pen disposal *[see Instructions for Use]*.

Instruct patients or caregivers to administer two 100-mg prefilled pens to achieve the full 200-mg dose of Omvoh.

Additional information can be found at www.Omvoh.com

See Instructions for Use accompanying the product device.

MR HCP BS UC APP

PP-MR-US-0147

Omvoh™ (mirikizumab-mrkz) injection,
for intravenous or subcutaneous use

MR HCP BS UC APP

Illustration by Jeannie Phan

PATIENT ENGAGEMENT

EDUCATING PATIENTS ON **NONDRUG THERAPIES FOR UC**

Certain interventions are clearly beneficial, but others lack evidence and could even cause harm. Here's what to know.

CONTINUED ON NEXT PAGE

Although living with ulcerative colitis (UC) is stressful, combining pharmacotherapy with other interventions can help patients have more control over their health and quality of life. While lifestyle changes focusing on diet and exercise can greatly benefit patients, certain nondrug therapies are not as well studied—and may be not only a waste of money, but also dangerous.

Consider this: About half of all patients with UC may use some type of complementary and alternative medicine (CAM), including herbs and supplements. People often choose CAM because they believe it may cure or improve their condition; others turn to CAM because they are concerned about potential medication side effects or feel their treatment isn't working. What's more, it's not uncommon for patients who use CAM to be less adherent to traditional treatment.[1]

Given the varying levels of evidence, it's important to talk openly with patients about which interventions they're using or interested in trying, stresses Rebecca Matro, MD, Clinical Associate Professor of Medicine and Director of the IBD Intestinal Ultrasound Program at Scripps Clinic, San Diego. Below are some common nondrug therapies and how to guide patients on options that may help—and those that should be used with caution.

Dietary changes

Knowing what to eat can be particularly difficult for those with UC: According to the American Gastroenterological Association (AGA), dietary guidance on UC is often controversial and a source of uncertainty for physicians and patients alike.[2] In 2024, the AGA published a clinical practice update on diet and nutritional therapies for inflammatory bowel disease (IBD), recommending the following:

- Encourage patients to follow the Mediterranean diet (emphasizing plant-based foods and healthy fats) unless contraindicated. By eating less red meat and processed foods, patients may have fewer disease flares.
- Patients with intestinal strictures may have trouble with fibrous plant-based foods. These foods should be cooked and processed until soft and less fibrous, and patients are advised to chew carefully to aid digestion.
- All patients should be screened for malnutrition, as well as vitamin D and iron deficiencies.

Dr. Matro agrees with advising patients to follow the Mediterranean diet, noting that certain elimination diets—such as those that exclude gluten, lactose and FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols)—may also help alleviate symptoms. She also notes that the Crohn's Disease Exclusion Diet, a type of partial enteral nutrition, has been effective for inducing and maintaining remission in adults and children with mild-to-moderate Crohn's disease for a short period of time,[3,4] and it may be helpful for those with UC as well.

"During times of disease flare, we will often recommend a low-fiber and low-residue diet, because fiber may increase symptoms of abdominal pain, bloating and diarrhea," explains Dr. Matro. "Most patients who are in remission do not need to restrict fiber, but because some have symptoms with certain types of fiber or specific vegetables, they will limit foods that bother them." In addition, some studies recommend that patients choose a diet based on foods they enjoy eating and evaluate whether symptoms and markers of inflammation improve.[3] In general, the goal is to eat low-glycemic index, anti-inflammatory and nonprocessed foods free of artificial dyes and sugars.[4]

> "Stress increases the risk of flares, and it's important that, as physicians, we ask about stress levels and issues in patients' lives that may be impacting their disease."
>
> —*Rebecca Matro, MD*

Illustration by Jeannie Phan

Exercise

Regular physical activity is particularly important and has been shown to be beneficial and safe for patients with UC. In fact, exercise can help relieve stress, improve overall health and may prevent worsening of UC.[5] According to research, low-to-moderate intensity exercise is effective, though not as much is known about high-intensity exercise. While exercise is anti-inflammatory, it also changes blood flow to the gut, so patients should be counseled based on individual needs and tolerance.[6]

Clinicians can start by asking how active patients are and addressing difficulties they may have in staying active. Dr. Matro's recommendations: "Maintaining hydration and building up exercise volume gradually—just like you would recommend for anyone else starting an exercise program. Specific recommendations vary depending on the patient and where they are starting. In general, I encourage low- to moderate-intensity exercise like walking, swimming, biking, yoga, and light strength training."

Stress reduction and social support

Chronic stress can create a vicious cycle: Living with UC can be stressful—and stress can make UC worse. Though how this happens is unknown, research suggests it may be the effect of inflammation on the gut-brain axis.[7] According to Dr. Matro, "Stress increases the risk of flares, and it's important that, as physicians, we ask about stress levels and issues in patients' lives that may be impacting their disease." Patients with UC should also be asked if they're struggling with anxiety and depression so that those who need help can be referred to their primary care provider or a mental health professional for appropriate treatment.

One effective way to manage stress is with cognitive behavioral therapy (CBT).[5,7] In CBT, patients learn to recognize and change unhelpful patterns of thinking and behavior. Other methods for improving quality of life include meditation, relaxation (e.g., breathing exercises and progressively contracting and releasing muscles) and yoga.[5]

In addition, support groups can provide a forum where people can share their stories, find answers and be part of a community. Online support can be found at the Crohn's & Colitis Foundation (*crohnscolitisfoundation.org/find-a-support-group*); *InflammatoryBowelDisease.net*; *MyCrohnsAndColitisTeam.com*; and *facebook.com/groups/UlcerativeColitisSupport*.

Herbal and nutritional supplements

Though supplements are not well regulated, it's common for patients to use them, says Dr. Matro. She emphasizes that precautions must be taken when using any supplement, particularly herbs. "Some herbal sup-

plements may have drug-drug interactions with other medications patients are taking. They may also cause side effects like nausea and bloating, and possibly liver test abnormalities." That said, there are a few supplements that may be helpful as adjuncts to medication, says Dr. Matro. These include:

Curcumin. "One supplement that we recommend is curcumin. There's evidence that it has anti-inflammatory properties and has been shown to improve symptoms and QoL scores, especially when used in combination with other medications. But as with all supplements that are not regulated, I counsel about use and suggest selecting a reputable brand that has been tested by an independent organization, such as Evinature." She adds that studied doses range from 1.5-3 g/day.

Probiotics. According to one analysis of 25 studies, 21 of them found that patients with UC had improved symptoms while using probiotics.[8] Still, Dr. Matro says, "There are limited high-quality studies showing effectiveness of probiotics in IBD." However, she does recommend brands such as VSL#3 or Visbiome for UC maintenance therapy for patients who have had a total colectomy with J pouch surgery and have recurrent pouchitis. For other patients, she emphasizes the importance of eating a healthy diet with a variety of fruits and vegetables.

Cannabis. In one study, 92.7% of patients with UC endorsed cannabis as effective in managing their symptoms, reporting better quality of life than nonusers on some measures.[9] Dr. Matro notes that in her practice, patients who use cannabis have reported improvement in abdominal pain, diarrhea, nausea, vomiting, joint pain and appetite. However, she cautions that with overuse, there is a risk for cannabinoid hyperemesis syndrome, marked by side effects such as episodic nausea, vomiting and abdominal pain. "I do not proactively recommend cannabis for patients, but if patients are interested or they do report use, I think it is important to have a conversation about it," Dr. Matro stresses.

The bottom line

The most important steps patients need to take, Dr. Matro explains: minimize stress, adhere to their medications for UC and comorbid conditions and remain in communication with their providers. "Being in touch with their care team, and if there is a change in their symptoms, letting their doctor know—is very important," she emphasizes. "That way, HCPs can intervene before things may get more severe." ●

—by Heather Anderson

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PATIENT: JESSICA, 34, HAD ULCERATIVE COLITIS (UC) THAT HAD BECOME RESISTANT TO THERAPY.

"Her worsening UC made it difficult to have a healthy work-life balance"

PHYSICIAN:

Tauseef Ali, MD, FACP, FACG, AGAF

Medical Executive Director, SSM Health Digestive Institute and SSM Health Crohn's and Colitis Center, Oklahoma City

Illustration by Juhee Kim

History:

Jessica, a marketing manager with a mid-sized company, was diagnosed with ulcerative colitis (UC) approximately 4 years ago. Her initial symptoms included abdominal pain, diarrhea, bowel urgency, blood in stool and weight loss, all of which caused her to take more time off from work and triggered a drop in her quality of life. What used to be routine for her—including frequent in-person meetings and travel—was becoming increasingly difficult.

To treat her worsening symptoms, Jessica's primary care physician started her on oral mesalamine, followed by corticosteroids and a short course of thiopurine. When these failed to produce much relief, she was sent to a specialist, who prescribed a TNF-alpha inhibitor. While it initially improved Jessica's symptoms, she had to discontinue it after it was discovered that she had developed antibodies to it. The ensuing pain and discomfort only served to exacerbate the anxiety and mild depression that she had been treated for since her college days, all of which put a strain on her marriage as well.

Initiating treatment:

When she came to see me about 6 months ago, Jessica was still traveling and working long hours, while trying to meet her obligations as a mother of two school-aged children. Her treatment goals for her moderate-to-severe UC were to reduce her symptoms, achieve remission and improve her quality of life, which would allow her to reduce her absenteeism and achieve a better work-life balance.

With these goals in mind, and given her past treatment failures, I suggested to Jessica that we initiate therapy with a relatively new biologic that targets the p19 subunit of IL-23 (IL-23p19) to fight inflammation related to UC. This agent has had very promising results in patients like Jessica, whose disease is progressing in spite of treatment. She was hesitant at first because the drug requires a time commitment up front that she felt she couldn't afford. (It's initiated as three IV infusions, each 4 weeks apart, followed by two self-injections every 4 weeks.) But when we discussed its potential efficacy versus the other drugs she had tried, and the potential benefits to her in terms of work and family, she agreed to start it.

Jessica began seeing an improvement in her UC symptoms after the second infusion and has been faithful to taking her medication ever since. Not only did her UC symptoms improve, but her anxiety and depression—for which I advised her to seek counseling—began to lessen as well.

Considerations:

This case is a good example of a newer, more-targeted therapy that we can offer to patients like Jessica whose moderate-to-severe UC is interfering with their quality of life despite trying other medications, including TNF inhibitors. In addition, the agent has been shown to be effective for improving three key symptoms—stool frequency, rectal bleeding and bowel urgency—regardless of past biologic use. Although there may come a time when Jessica loses response to her medication, for now it represents a significant advance in her UC care and aligns perfectly with her goals for treatment, including bowel healing. ●

NEW!

KOL ON DEMAND VIDEO

Scan here for more insight on Jessica's case.

Q&A

Expert insight on managing ulcerative colitis

Illustration by John S. Dykes Collection

Avoiding triggers

Q: What lifestyle changes do you recommend to help patients avoid flare-ups?

A: Many of my patients attribute stressful events as a trigger for their symptoms. I advise them to avoid such situations, if possible, and learn to manage their stress with mindfulness techniques, meditation and yoga. Certain foods can also be problematic, so I advise avoiding ones they feel trigger bowel symptoms, such as lactose/dairy, caffeine, high-fiber foods, alcohol and foods containing high amounts of sugar/artificial sweetener. And, since processed foods and red meat have been linked with inflammation, I recommend limiting these foods as well.

I also encourage incorporating exercise into their daily routine, which helps both physically and emotionally. Even just taking a walk after meals can be of benefit. Finally, because sleep disturbances are often seen in patients with ulcerative colitis (UC), establishing a good nighttime routine (e.g., keeping a consistent sleep schedule, avoiding digital screens before bed, sleeping in a dark, cool bedroom) is helpful for improving sleep.

*–**Asma Khapra, MD, AGAF,** Assistant Professor of Medical Education, University of Virginia School of Medicine*

Treatment options

Q: Recently, biologics that target IL-23p19 have become available. What's been your experience with these agents?

A: In patients with moderate-to-severe UC, newer IL-23p19 biologics are some of the safest options, and based on clinical trial data, they have been shown to be effective in both bio-naïve and bio-failure patients. IL-23s have demonstrated good clinical response and remission of UC. For my patients, some of the biggest benefits are improvement in rectal bleeding and stool frequency, as well as improvement in urgency, which can be a game-changer for some UC patients.

Finally, IL-23p19 biologics require only three initial IV infusions followed by maintenance with subcutaneous (SC) self-injection every four or eight weeks. This ease of administration allows patients to travel or go away to college without disruption of their daily lives. I also think it improves adherence. Having biologics like this, with good efficacy, safety and ease of administration, is very beneficial for patients.

*–**Asma Khapra, MD, AGAF***

Taking a targeted approach

Q: What is the "treat to target" strategy, and why is it helpful?

A: The treat to target approach means that we define a target to achieve and then continue to watch, adjust and change our therapy accordingly. The reason to define and then go after a target is to achieve better clinical outcomes. In patients with inflammatory bowel diseases like UC, these targets are defined to improve symptoms and prevent complications ranging from surgery to hospitalization or cancer. Experts define the three types of treatment targets as follows:

- Short-term targets: resolution of diarrhea, abdominal pain and rectal bleeding. These are essential to improve QoL and enable patients to conduct daily activities.
- Intermediate targets: improving markers of inflammation like blood marker CRP or the stool marker calprotectin.
- Long-term goals: improving endoscopic findings of inflammation, such as resolution of ulcers, and–more recently–controlling the microscopic level of inflammation, also known as deep remission.

Long-term goals are essential to prevent complications such as cancer development or the need for surgery.

*–**Tauseef Ali, MD, FACG, AGAF,** Chief of Gastroenterology; Medical Director, Crohn's and Colitis Program, SSM Health St. Anthony Hospital, Oklahoma City*

Addressing psychosocial issues

Q: What are some underappreciated challenges of living with an inflammatory bowel disease?

A: Some common challenges are related to sexual health, mental health, and pain management. Patients with UC also have concerns about how their diagnosis, medications and surgeries will affect their sexual relationships. Bringing their partner to visits and being open about concerns early on can help make it easier to address these issues. In addition, depression and anxiety are more common in these patients than the general population, so it is important to screen for these symptoms. Treatment may include referral to a mental health provider, medication and stress management. Finally, pain and fatigue are also common. Fatigue can be due to several factors, including inflammation, side effects of medication, vitamin or nutrient deficiencies and poor sleep from gastrointestinal symptoms. Pain can be related or unrelated to their disease and can be gastrointestinal or extraintestinal. Treatment for pain and fatigue will vary based on the cause, but it is important for physicians to ask patients about such symptoms so they can identify the cause and address it appropriately.

*–**Rebecca Matro, MD,** Clinical Associate Professor of Medicine; Director of the IBD Intestinal Ultrasound Program, Scripps Clinic, San Diego*

"Newer IL-23p19 biologics are some of the safest options."
—Asma Khapra, MD, AGAF

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Clinician Update

DECISION TOOL

ASSESSING SEVERITY OF UC SYMPTOMS

Ulcerative colitis (UC) not only affects quality of life, it can also damage the bowel if left uncontrolled. This underscores the importance of engaging patients about how they're feeling day to day. When assessing worsening symptoms—which may require a change in therapy—consider the criteria below.

ASK PATIENTS THE FOLLOWING:

1. **On how many days over the last two weeks have you felt tired?**
   _____DAYS

2. **In the last two weeks did your bowel condition prevent you from going out socially?**
   - No, not at all.
   - Yes, some of the time.
   - Yes, most of the time.
   - Yes, all of the time.

3. **On how many days over the last two weeks have you felt generally unwell?**
   _____DAYS

4. **On how many days over the last two weeks have you felt pain in your abdomen?**
   _____DAYS

5. **On how many nights in the last two weeks have you had to get up to use the toilet because of your bowel condition after you have gone to bed?**
   _____NIGHTS

6. **On how many days over the last two weeks has your abdomen felt bloated?**
   _____DAYS

7. **In the last two weeks have you felt upset?**
   - No, not at all.
   - Yes, some of the time.
   - Yes, most of the time.
   - Yes, all of the time.

8. **On how many days over the last two weeks have you had to rush to the toilet?**
   _____DAYS

Source: Alrubaiy L, et al. *J Crohns Colitis*. 2015;9(1)66-76.