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Primary care management of ulcerative colitis

***Abstract:** Ulcerative colitis (UC) is an inflammatory bowel disease marked by mucosal inflammation. UC has an impact on quality of life and places a financial burden on the healthcare system. This article focuses on the impact, presentation, diagnosis and classification, systemic manifestations, complications, management, and treatment associated with UC.*

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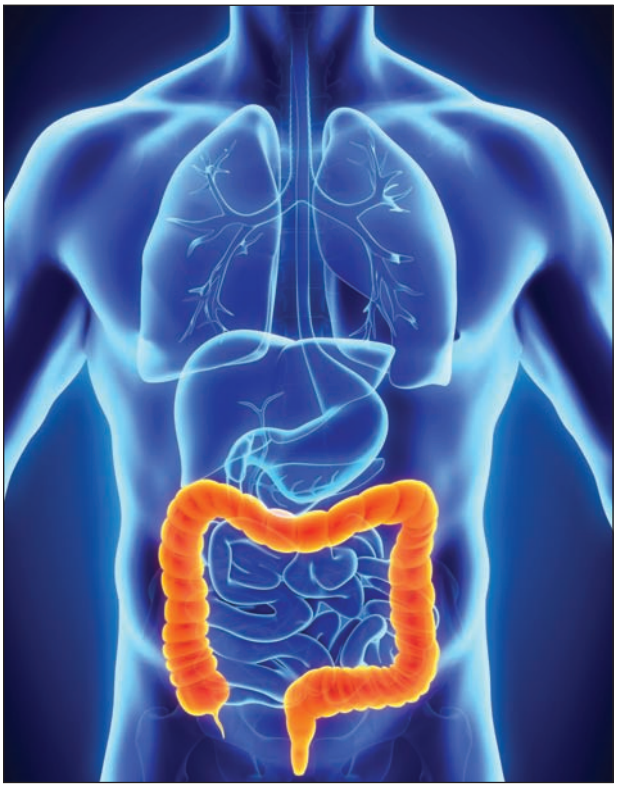
Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) marked by gastrointestinal (GI) mucosal inflammation due to altered microbiota, increased intestinal permeability, and immune system dysfunction.[1] UC is a chronic disease that causes inflammation and ulcerations in the lining of the large intestine, which includes the colon and rectum.[2] UC inflammation leads to small ulcers on the lining of the large intestines, which can lead to bleeding, pus, diarrhea, abdominal pain/cramping, nausea, and extreme fatigue.[3,4] (See *Erythema and ulceration of the colon in UC.*)

UC and Crohn disease have similar symptoms but are two distinct disease processes. UC affects the lining of the colon, whereas Crohn disease can affect the layers of the colon wall of the alimentary tract anywhere from the mouth to the anus and may even skip segments. At times, it is difficult to distinguish between UC or Crohn disease, and a diagnosis of intermediate colitis may be given.[3]

Twenty-five to 40% of patients' disease manifestations may include symptoms related to the eyes, joints, skin, bones, kidneys, and liver.[3] The most



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Keywords: American College of Gastroenterology Guidelines, gastrointestinal mucosal inflammation, IBD, inflammatory bowel disease, Mayo Score, Montreal classification of inflammatory bowel disease, Simple Clinical Colitis Activity Index, Truelove and Witts' severity index, ulcerative colitis

common symptoms are abdominal discomfort and blood or pus in diarrhea.[4] UC is characterized by periods of relapse with debilitating symptoms and remission. The disease etiology is essentially unknown but thought to be influenced by genetic determinants, environmental factors, and microbiome in the intestinal tract.[5,6]

UC has a profound impact on quality of life and places a financial burden on the healthcare system. The incidence of UC in the United States is 9 to 12 cases annually per 100,000 individuals, resulting in lost work days and steep hospital and medication costs.[7] Managing UC accounts for about 250,000 annual physician visits, 30,000 hospitalizations, and a loss of over one million work days per year.[8]

Background

The prevalence of UC in North America is 319 per 100,000 individuals.[9] It is estimated that up to 1.4 million individuals in the United States have been diagnosed with IBD.[10] UC appears to be more prevalent in the northern part of the world, especially among White individuals.[1]

Reflecting the most recent comprehensive data, Nguyen and colleagues examined the rising hospitalization rates for IBD in the United States between 1998 and 2004. They found that an estimated 214,498 hospital admissions were related to UC, and the national cost for inpatient charges increased from $592 million to $945 million between 1998 and 2004.[11]

Kappelman and colleagues examined the direct healthcare costs of UC in the United States through a cross-sectional study designed to analyze the medical, surgical, and pharmaceutical claims in a patient database.[12] Results revealed that the mean total cost for patients with UC was $7,948 per year, and the mean and median annual UC-associated costs were $5,066 and $17,928, respectively. They also found the largest portion of pharmaceutical expenses was related to oral/rectal aminosalicylates. Kappelman and colleagues estimated the annual direct costs of IBD at $5.3 billion and the annual cost for UC alone at $2.7 billion.[12]

Erythema and ulceration of the colon in UC

Prominent erythema and ulceration in the colon are most severe in the rectosigmoid colon and extend into the ascending colon.

Source: Strayer D, Rubin E, eds. *Rubin's Pathology: Clinicopathologic Foundations of Medicine.* 7th ed. Philadelphia, PA: Wolters Kluwer; 2015:806.

Diagnosis and severity classification

Typically, the diagnosis of UC is made based on history, physical exam, symptomatology, diagnostic testing, and endoscopy. History should include a recall of the number of bowel movements, bleeding episodes, and incidences of waking up at night from pain or diarrhea, fever, and joint aches.[3] The physical exam should include an oral exam, abdominal exam, anal/rectal exam, skin exam, and various diagnostic tests. Differential diagnoses to consider include Crohn disease, ischemic colitis, and *Clostridium difficile* infection.[3]

According to the Crohn's and Colitis Foundation of America, diagnostic testing may include:

- blood and stool testing
- stool markers/cultures
- complete blood cell count
- erythrocyte sedimentation rate (ESR)
- C-reactive protein
- liver and kidney function panel
- electrolytes
- radiologic and diagnostic imaging
- barium enema
- computed tomography (CT) scan and CT enterography
- leukocyte scintigraphy
- magnetic resonance imaging and magnetic resonance enterography
- small bowel follow-through and small bowel enterocytes
- ultrasound
- X-rays.[3]

The gold standard for diagnosis is endoscopy with biopsies.[3] Family history may be helpful because the

number one risk factor for UC is a positive history in the immediate family. In addition to the above, fecal calprotectin has been found to be sensitive for detecting disease activity, although more so in UC than Crohn disease.[13] Genetic testing can help identify a patient's likelihood of developing symptoms and complications.[3]

Classifying the severity of UC can be as daunting as the disease itself. There is great variation depending on which instruments or criteria are utilized for the classification of disease severity. According to Peyrin-Biroulet and colleagues, although existing algorithms begin with classifying patients according to disease severity, there is no formal validated or consensus definition as to what constitutes mild, moderate, or severe IBD.[14] Examples of criteria used to diagnose the severity of UC include the Montreal classification of inflammatory bowel disease (MCIBD), Truelove and Witts' severity index, American College of Gastroenterology (ACG) Guidelines, Mayo Score, and Simple Clinical Colitis Activity Index (SCCAI).

MCIBD. This classification was developed by the Working Party of the 2005 Montreal World Congress of Gastroenterology. It is stratified into three categories: E1 (ulcerative proctitis-limited to rectum), E2 (left-sided/distal UC), and E3 (extensive UC or pancolitis, has involvement that extends to the splenic flexure).[15]

Truelove and Witts' severity index. This index was originally published in 1955 and was reproduced with permission by the National Institute for Health & Care Excellence in 2013.[16] It is stratified into three categories:

Mild: Fewer than four bowel movements/day, no more than small amounts of blood in the stool, afebrile, heart rate 90 beats/minute or less, no anemia, and ESR of 30 mm/h or below.

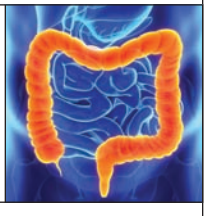
Moderate: Four to six bowel movements/day, mild-to-severe blood in stool, afebrile, heart rate 90 beats/minute or less, no anemia, and ESR of 30 mm/h or below.

Severe: Six or more bowel movements/day, visible blood in stool, plus one of the systemic markers (fever over 100.04°F [37.8° C], heart rate over 90 beats/minute, anemia present, ESR over 30 mm/h).

ACG Guidelines. These guidelines generally follow the Truelove and Witts' criteria with the addition of the "fulminant" category, in which the patient has more than 10 bowel movements daily, has continuous bleeding (which requires blood transfusion), and colonic dilatation on abdominal X-ray.[8,17]

Mayo Score. This Likert-like scale looks at stool frequency, rectal bleeding, endoscopic findings, and physician's global assessment.[18] Stool frequency components include a normal number of stools for the patient; one or two stools/day more than normal; three to four stools more than normal; and over five stools more than normal. Rectal bleeding components include no blood, streaks of blood less than half the time, obvious blood with stool most of the time, or passing only blood. Endoscopic findings components are described as normal or inactive disease, mild, moderate, or severe disease.[18]

Individuals with UC are at higher risk for developing complications related to disease progression or complications of treatment.



SCCAI. This index scores bowel frequency during the day and night, urgency of defecation, blood in stool, general well-being, and extracolonic features.[19]

Identifying severity of disease can vary based on which criteria are used. It is critical for NPs to decide which instrument best fits their practice and to consistently use the same instrument.

Systemic manifestations and complications

Individuals with UC are at higher risk for developing complications related to disease progression or complications of treatment. Sequelae may affect many body organs/systems.

Manolakis and Cash summarized the existing literature and identified many of the possible systemic manifestations associated with a diagnosis of UC.[20] The following is a summary of their findings:

Ophthalmologic. Uveitis, episcleritis, keratopathy, keratoconjunctivitis sicca (dry eyes), and corticosteroid-induced cataracts or glaucoma (related to corticosteroid use for treatment).

Dermatologic. Some individual studies have demonstrated an increased risk for melanoma.

Bone health. Osteopenia and osteoporosis.

Gynecologic. Increased risk of abnormal Pap tests.

Psychological. Anxiety, depression.

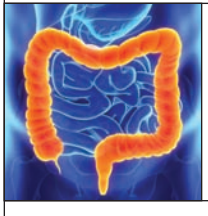
Opportunistic infections. Increased risk due to treatment with corticosteroids, antimetabolites, and anti-tumor necrosis factor medications.[20]

Additionally, patients with Crohn disease are at risk for complications, including stricturing, abscesses, and fistulae. Stricturing affects approximately 50% of patients with Crohn disease within 10 years of diagnosis. During this initial 10-year time frame, surgical resection is required in as many as 80% of patients with Crohn disease.[21]

Colorectal cancer

The longer a patient has a diagnosis of UC, the higher the risk of developing colorectal cancer (CRC). After 10 years of UC, the risk of bowel cancer is 1 in 50; it increases to 1 in 12 after 20 years and 1 in 6 after 30 years.[22] Diagnosis of CRC may be missed because the symptoms of UC and CRC are similar; therefore, routine screening for CRC is critical.[22]

Choi and colleagues completed a 40-year analysis of patients with UC through colonoscopic surveillance for neoplasia. They monitored 1,375 participants for a total of 15,234 patient-years. The authors found that 72 patients (5.2%) had positive detection of CRC. An additional 16 (1.2%) developed CRC after leaving surveillance. Fifty-four (61.4%) of the patients were male, and the median age at diagnosis was 55.5.[23]



ACG guidelines report anxiety in 19% of patients with UC and depression in 21% of patients.

The average duration of UC when the CRC was diagnosed was 23.5 years. The cumulative incidence of neoplasia by UC duration was 4.1% at 10 years, 14.1% at 20 years, 28% at 30 years, and 38.9% at 40 years; however, the overall risk of CRC by disease duration was low, with only 10% developing cancer at 40 years of disease duration.[23]

Psychological health

Patients with UC have periods of remission; however, they often have periods of relapse after enduring prolonged diarrhea, bloody stools, pain, fever, cramping, and other debilitating symptoms, which can cause profound psychological and emotional stress. The most recent ACG guidelines report anxiety in 19% of patients and depression in 21% of patients with no difference among inactive versus active disease. The benefits of treating depression were found to be significant, as there were noted to be less relapses and use of corticosteroids in the year following initiation of an antidepressant. Depression has also been an indicator for risk of nonadherence to the medication regimen.[24]

Quality of life

Managing UC can be time-consuming, expensive, and life-altering. Dealing with the symptoms, lost days of work, adverse reactions of medications, and increased risks of complications can have effects on patients' physical well-being; their social and professional lives and overall quality of life may also suffer.[25]

Two studies examined health-related quality of life (HRQOL) and both identified factors associated with lower HRQOL scores. The first study by Tabibian and colleagues examined HRQOL and adherence in 135 participants and found that lower HRQOL scores were associated with higher levels of perceived stress and numbers of relapses over the previous 2-year period.[25]

In a study by Luo and colleagues, 214 patients were recruited to examine HRQOL through perceived stress and coping strategies. The authors found that better HRQOL was associated with regular follow-up, no use of corticosteroids, lower relapse and hospitalization rates, disease remission, an MCIBD score of E1, lower Mayo Score, and lower levels of perceived stress.[26]

Many patients may experience disease symptoms for years before seeking medical care due to symptom embarrassment, fear of cancer, and associated costs. Primary care providers might diagnose the symptoms as another GI disease and not consider IBD. It is essential for primary care providers to include IBD in the differential diagnosis.

Treatment and goals

The ultimate goal for UC treatment is complete remission. Management of UC includes medical management, exercise, and dietary control.

Toronto Consensus Guidelines. The Toronto Consensus Guidelines committee was formed to review existing literature and develop recommendations for treatment of patients with mild-to-severe active UC. In brief, types of medications to treat UC include 5-aminosalicylates,

Summary of the *Toronto Consensus Guidelines*[27]

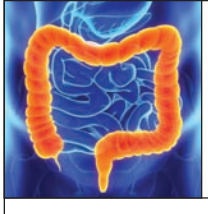
Recommendation statement #	Diagnosis and severity	Recommendation
Statements regarding 5-aminosalicylates (5-ASA)		
1	Mild-to-moderate active ulcerative proctitis	First line: Rectal 5-aminosalicylate (5-ASA)
2	Mild-to-moderate active left-sided UC	Alternative first line: 5-ASA enemas
3	Mild-to-moderate active UC of any disease beyond proctitis	Alternative first line: Oral 5-ASA
4	Mild-to-moderate active UC of any disease beyond proctitis	Alternative first line: Combination of rectal and oral 5-ASA
5	Patients with UC	Evaluate at 4-8 weeks for response
6	Complete remission with oral or rectal 5-ASA for ulcerative proctitis or left-sided UC	Maintain therapy
7	Complete remission with 5-ASA for mild-to-moderate UC of any disease extent	Continue oral therapy
8	Selected 5-ASA-naive patients with UC with symptomatic remission on oral corticosteroids	Oral 5-ASA and assess for corticosteroid-free complete remission
9	Failure to respond to oral 5-ASA	Recommendation against switching to another 5-ASA oral formulation
10	Using 5-ASA to induce or maintain complete remission	Recommend once-daily dosing
Statements regarding corticosteroids		
11	Moderate-to-severe UC	First line: Oral corticosteroids
12	Mild-to-moderate active UC-failure to respond to 5-ASA	Second line: Oral corticosteroids
13	Mild-to-moderate active left-sided UC or proctitis-failure to respond to rectal 5-ASA	Second line: Rectal corticosteroids
14	Patients with UC	Recommend against oral corticosteroids to maintain complete remission
15	Mild-to-moderate UC of any disease extent	Alternative first line: Oral budesonide MMX
16	Patients with UC	Within 2 weeks of induction of corticosteroids, evaluate for lack of symptomatic response, need for therapy modification
17	Patients with UC	Recommend against the use of thiopurine monotherapy
18	Patients with UC–symptomatic remissions on oral corticosteroids	Recommend thiopurine monotherapy as option for maintenance with corticosteroid-free remission
19	Patients with UC	Recommend against methotrexate monotherapy
Statements regarding anti-TNF therapy and other agents		
20	Patients with UC-failure to thiopurine or corticosteroids	Recommend anti-TNF therapy
21	Starting anti-TNF therapy	Recommendation: Do not use anti-TNF as monotherapy–Combine with thiopurine or methotrexate

(Continues)

Recommendation statement #	Diagnosis and severity	Recommendation
22	Patients with UC-dependent on corticosteroids	Anti-TNF therapy for corticosteroid-free induction/remission
23	Patients with UC	Evaluate symptomatic response at 8-12 weeks
24	Patients with UC who respond to anti-TNF therapy	Continue anti-TNF therapy
25	Patients with UC-suboptimal response to anti-TNF therapy	Dose intensification
26	Patients with UC who lose response to anti-TNF maintenance therapy	Recommend optimizing dose to recapture remission
27	Patients with UC	Recommend dose optimization by therapeutic drug monitoring
28	Primary failure to anti-TNF therapy	Switch to vedolizumab over other anti-TNFs
29	Patients with secondary failure to an anti-TNF therapy	Switch to another anti-TNF agent or to vedolizumab based on therapeutic drug monitoring
30	Moderate-to-severe active UC-failure to corticosteroids, thiopurines, or anti-TNF therapies	Recommend vedolizumab
31	Patients with UC	Evaluate for lack of symptomatic response to vedolizumab at 8-14 weeks
32	Patients with UC-responding to vedolizumab	Continue vedolizumab therapy
33	Patients with UC	Recommend against fecal microbial transplant
34	Patients with UC	Recommend against probiotics outside the setting of a clinical trial

Source: Bressler B, Marshall JK, Bernstein CN, et al. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: The Toronto Consensus. *Gastroenterology*. 2015;148(5):1035-1058.e3. Used with permission.

corticosteroids, thiopurines, anti-tumor necrosis factor (anti-TNF) agents, and humanized monoclonal antibodies (see *Summary of the Toronto Consensus Guidelines*).[27] The Toronto Consensus Guidelines committee reported that, at the time of the development of the guidelines, there were insufficient data to support the use of fecal microbial transplant, and the quality of studies examining probiotic use was insufficient to warrant supporting recommendations.[27]



The ultimate goal for UC treatment is complete remission, and management includes medical management, exercise, and dietary control.

Exercise. Many experts have posited that exercise is beneficial in treating UC and obtaining complete remission. Liu and colleagues completed a study in mice designed to examine if prior (before disease) voluntary exercise would attenuate colonic inflammation and meliorate clinical symptoms. The authors hypothesized that exercise increases glucocorticoid production and upregulates peroxisome proliferator-activated receptor gamma (PPAR-γ) (involved in regulation of the inflammatory response) activity in the colon.[28] Results revealed that exercise significantly increased the expression of PPAR-γ and elevated corticosteroid levels in the colon and supported the hypothesis that exercise prior to active UC could be beneficial in suppressing inflammation.[28]

Another study from 2015 found that among patients with Crohn disease in remission, exercise correlated with reduced risk of disease activity at 6 months. The same was true of patients with UC; however, the findings were not statistically significant among the population in this study. In addition to remission, exercise improves bone density.[29]

Dietary control. Many experts believe that the increased consumption of fats and refined carbohydrates

may increase risk of disease relapse.[6] The Western diet is typically abundant with carbohydrates, and digestion of these carbohydrates can vary naturally (even more so for patients with IBD).[30] The Western diet is also often high in carbohydrates, red meats, fats, starches, sugars, and low in fiber.

According to Uranga and colleagues, mucosal inflammation, increased permeability, and immune system dysfunction may be caused by several factors, including dietary habits.[1] The use of probiotics and prebiotics may be helpful in controlling symptoms and preventing relapse and is the focus of intense ongoing research; however, there is not currently enough evidence to support this.[1]

Walton and colleagues completed a study on the adherence of patients with UC to healthy eating guidelines. Eighty-one participants completed a 24-hour diet recall designed to assess nutrient intake compared with national recommended intake values. The authors found that nutritional knowledge was limited, numerous food groups were largely avoided, and almost half of the participants avoided dairy products.[31]

The authors also noted that fat intake was above and energy intake was significantly below the national recommendations. Not surprisingly, results also revealed that 12% of the participants had osteopenia, 6% osteoporosis, and 31% anemia, which may be indicative of nutrient deficiencies.[31]

Vaccinations. It is essential to review the vaccination record of all patients diagnosed with UC. According to the 2017 ACG guidelines, all children, adolescents, and adults with IBD should receive vaccinations according to the current guidelines published by the CDC, the Advisory Committee on Immunization Practices, and the Infectious Disease Society of America.[24] Patients with IBD should receive nonlive vaccines regardless of immunosuppression status.[24] Before a live vaccine is considered, the immunosuppression status of the patient needs to evaluated and the prescribing label for the specific vaccine reviewed. The prescribing labels list specific contraindications for the live vaccine based on the immunosuppression status of the patient.

Special consideration should be given for international travel, military, or those who work in risk areas, as they may also require vaccines such as rabies, anthrax, or typhoid.[32] The CDC website provides immunization schedules for all age groups as well as vaccine-specific recommendations for travel and emergency situations.[32] Patients with IBD should be referred to a travel medicine or infectious disease specialist prior to travel.[24]

Summary of Concert's Referral Points[33]

Referral source	Indication for referral
Gastroenterologist	Severe disease, endoscopic intervention or surveillance, and initiation of immunosuppressive medication
Surgeon	Intra-abdominal abscess, massive bleeding, stricture, intestinal obstruction, or perforation of the bowel
Rheumatologist	Extraintestinal manifestations–arthritis (may precede overt bowel disease)
Dermatologist	Skin manifestations (erythema nodosum, pyoderma gangrenosum, and others)
Ophthalmologist	Uveitis, iritis, episcleritis, and others
Hospitalization	Dehydration, inability to tolerate oral intake, failure of oral/topical therapy, and need for I.V. therapy/surgical intervention. Severe abdominal pain assessment for toxic megacolon may require immediate surgery.

The primary care provider is an integral part of the healthcare team for patients with UC (see *Summary of Concert's Referral Points*).[33] Additional referrals should be considered for psychological, financial, and family/social support. Concert and colleagues state that patients with disease of more than 7-year duration should have annual colonoscopic surveillance.[33] Once the patient with UC is evaluated and stabilized by specialists, the primary care provider can resume the primary role for management. Collaboration between the provider and appropriate specialists should be ongoing as needed.

Implications for nursing research, practice, and education

A major implication for future research is the fact that there currently are no commonly agreed-upon criteria for defining the severity of UC. In addition, limited information exists as to etiology of IBD and more specifically, UC. Determining the genetic component of IBD is essential. While current research is focused on discovering medications to induce

Patient and provider resources

American Gastroenterological Association
www.gastro.org

ACG
www.acg.gi.org

ACG Patient Education and Resource Center
http://patients.gi.org/topics/inflammatory-bowel-disease

Crohn's and Colitis Foundation
www.ccfa.org

National Institute of Diabetes and Digestive and Kidney Diseases
niddk.nih.gov

Society of Gastroenterology Nurses and Associates
www.sgna.org

remission and prevent relapses of UC, treating a disease process is difficult when the pathology is essentially unknown.[3]

Additional areas for research include discovering ways to minimize complications and better ways to predict/prevent UC in high-risk individuals.[3] Primary care providers must be educated on the identification of UC symptoms as well as best practice guidelines for acute and maintenance therapy. Remission is the treatment goal and can only be achieved if the proper maintenance treatment is initiated once the patient is in remission.

NPs must be aware that UC is a life-altering disease process that affects more than just the abdomen and GI tract. Patients should be assessed for anxiety and/or depression related to the daily process of managing UC, the adverse reactions of medications, and possible complications.

Healthcare providers play an essential role in educating patients regarding the natural progression of UC and the importance of adherence to long-term treatment. In addition to following evidence-based guidelines for medical management, partnering with patients through open communication and psychosocial support can improve patient treatment adherence.[34] Patient educational resources are available, including support groups, printed materials, computer and smartphone apps to track and manage disease symptoms, webcasts, and enrollment in clinical trials (see *Patient and provider resources*).

Reaching remission

UC is a life-altering, possibly debilitating disease process, and much is still unknown about the etiology of the disease process. Existing literature supports efforts to decrease severity of disease and reduce the incidence of relapses through diet, exercise, and medical management. Screening, vaccinating, monitoring for complications/sequelae, and referral to specialists are critical to effective care of the patient with UC in order to achieve complete remission. NP

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