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Current Research in Crohn's Disease and Ulcerative Colitis: Highlights from the 2010 ACG Meeting

A Review of Selected Presentations from
the 75th American College of Gastroenterology
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Course Description: This monograph summarizes key findings from the 2010 Annual Scientific Meeting of the American College of Gastroenterology.

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Statement of Need: The abstract review monograph *Current Research in Crohn's Disease and Ulcerative Colitis: Highlights from the 2010 ACG Meeting* presents the most current data updates emerging within this therapeutic area. New medical treatments, including biologic agents, have shown benefit for the treatment of Crohn's disease and ulcerative colitis. There is a clear educational need in the gastroenterology community for an updated understanding of these agents, including their effect on clinical indicators of disease, factors influencing their efficacy in various patient populations, safety considerations, and the development of new agents.

Target Audience: This program is designed for gastroenterologists involved in the management of patients with Crohn's disease or ulcerative colitis.

Learning Objectives: At the conclusion of this activity, participants should be able to:

1. Review the current role of biologic therapies in the treatment of Crohn's disease and ulcerative colitis.
2. Discuss factors associated with positive outcomes in these patients.
3. Outline novel therapies that may lead to new treatment options.

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Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are 2 types of chronic inflammatory bowel disease (IBD), both of which cause abdominal pain, changes in bowel habits, and rectal bleeding. In addition to these symptoms, up to 25% of individuals with IBD develop extraintestinal effects, including joint inflammation, skin lesions, eye complications, and osteopathy.[1]

CD involves a transmural process that can occur throughout the gastrointestinal tract; in contrast, UC involves inflammation that is restricted to the colon and affects the mucosa more evenly. CD is also marked by relapsing and remitting episodes that often develop into stricturing or perforating complications.[2] Onset of CD typically occurs in early adulthood, whereas onset of UC is characterized by 2 peaks—the first during adolescence/early adulthood and the second during later adulthood.[3]

In terms of prevalence, CD affects 26.0–198.5 individuals per 100,000 in the United States, whereas UC affects approximately 11 individuals per 100,000 in the United States.[4] Estimates from 2003 to 2005 show that IBD accounts for approximately 1.8 million visits to ambulatory healthcare settings and 76,374 visits to emergency departments each year.[5]

IBD is characterized by a dysregulated inflammatory response that leads to tissue damage and clinical symptoms; however, the etiologies of CD and UC are not well understood. Genetics appear to play a role, though incomplete concordance rates in twin studies support an environmental component for both conditions.[6] Infectious agents also appear to contribute to IBD susceptibility.

Conventional Treatment Approaches in Inflammatory Bowel Disease

The goal of medical treatment for IBD is to suppress inflammation in order to provide symptom relief and mucosal healing. Aminosalicylates (5-aminosalicylic acid [5-ASA]) remain the cornerstone of therapy for patients with active, mild to moderate UC.[7] The role of 5-ASA in patients with CD has been more controversial, however, as there are conflicting data as to whether these drugs are effective for treating active disease and maintaining remission in these patients.[8]

Corticosteroids also remain popular medications for inducing remission in both UC and CD. However, they cannot effectively maintain remission, and their association with significant adverse effects limit their long-term use.[9,10]

If IBD patients do not respond to first-line therapy, then immunosuppressive therapy with azathioprine and 6-mercaptopurine (6-MP) is often used. However, only 40% of patients receiving azathioprine remain in remission after 1 year.[11] Thus, additional safe and effective treatment options are needed for these patients.

Biologic Therapies

Over the past decade, the development of biologic therapies that target specific mediators of inflammation has revolutionized the treatment of IBD. The first biologic agent to demonstrate efficacy in patients with IBD was infliximab, a chimeric immunoglobulin (Ig)G1 monoclonal antibody targeted against the proinflammatory cytokine tumor necrosis factor (TNF)-α. Infliximab has proven effective as both induction and maintenance therapy for patients with CD.[12,13] TNF-targeted therapy has also demonstrated benefit in patients with UC; in a 2005 publication, infliximab demonstrated efficacy as induction and maintenance therapy in patients who had moderate to severe, active UC despite treatment with concurrent medications.[14]

Subsequently, other anti-TNF agents have shown positive results in patients with CD, including the recombinant human IgG1 monoclonal antibody adalimumab. Adalimumab has been shown to effectively induce and maintain remission in patients with CD, including patients who have not previously received a biologic agent[15-17] and those who do not respond to infliximab or who cannot tolerate the treatment.[18,19] In 2009, Afif and colleagues demonstrated the efficacy of adalimumab in patients with UC, including patients who can no longer tolerate infliximab or whose disease has lost response to infliximab.[20]

Another TNF-targeting agent that is useful in the treatment of CD is the pegylated Fab' fragment certolizumab pegol. Studies have shown that this drug can induce and maintain clinical response in patients with moderate to severe CD, including patients with secondary failure (loss of response and/or hypersensitivity) to infliximab.[21-23]

Most recently, the humanized monoclonal antibody natalizumab has been evaluated as a treatment for CD. Natalizumab is directed against α4-integrin, a cellular adhesion molecule present on leukocytes. The ENCORE trial demonstrated the efficacy of natalizumab in patients with moderate to severe, TNF inhibitor–refractory CD.[24] However, natalizumab is associated with signif-

icant adverse effects, including progressive multifocal leukoencephalopathy, a rare but severe neurologic complication, which has caused the US Food and Drug Administration to place stipulations on the use of this drug.

Recent Advances in Treatment: The 2010 ACG Meeting

Recent and ongoing studies have continued to explore the best ways of incorporating conventional and biologic agents into CD and UC treatment. Important questions include the optimal timing of therapy, use of concurrent medications, use of specific agents in different patient populations, and identification of predictive factors associated with response or lack of response to therapy. Moreover, additional novel agents and treatment strategies continue to be evaluated. Studies exploring these issues and others were presented at the 75th Annual Scientific Meeting of the American College of Gastroenterology (ACG), held in San Antonio, Texas, on October 15–20, 2010. Highlights from these clinical abstracts are provided on the following pages.

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Highlights from the 2010 ACG Meeting

Incidence, Treatment Patterns, and Treatment Goals: Results from a Registry Study of Inflammatory Bowel Disease Patients in Rhode Island

60 Ocean State Crohn's and Colitis Area Registry (OSCCAR): Incidence of Crohn's Disease and Ulcerative Colitis in a Prospective, Population-based Inception Cohort in Rhode Island

S Shah, N Leleiko, S Lidofsky, R Bright, S Grabert, M Law, H Moniz, B Bancroft, K Suorsa, M Patel, J Vancura, A Harris, B Kalasapudi, E Cole, B Sands

P716 Presenting Symptoms at Diagnosis of Crohn's Disease and Ulcerative Colitis: Results from the Ocean State Crohn's and Colitis Area Registry (OSCCAR)

M Patel, S Shah, N Leleiko, S Lidofsky, R Bright, S Grabert, M Law, H Moniz, B Bancroft, K Suorsa, A Harris, J Vancura, B Kalasapudi, E Cole, B Sands

P283 Medical Therapy of IBD in the First Year After Diagnosis: Preliminary Results from the Ocean State Crohn's and Colitis Area Registry (OSCCAR)

A Harris, S Shah, N Leleiko, S Lidofsky, R Bright, S Grabert, M Law, H Moniz, B Bancroft, K Suorsa, M Patel, J Vancura, B Kalasapudi, E Cole, B Sands

Several abstracts presented at the 2010 ACG Annual Scientific Meeting were based on the prospective, population-based Ocean State Crohn's and Colitis Area Registry (OSCCAR), a novel inception cohort of patients with IBD living in Rhode Island. Researchers are using the registry to investigate trends in IBD incidence, natural history, and medical therapy.

Since January 1, 2008, OSCCAR has enrolled 180 Rhode Island residents newly diagnosed with CD, UC, or indeterminate colitis (IC). Diagnoses were confirmed using the National Institute of Diabetes and Digestive and Kidney Diseases IBD Genetics Consortium criteria. The registry excludes patients diagnosed prior to 2008, those unwilling to provide consent, and those imprisoned or pregnant at the time of diagnosis. Clinicians referring patients to the registry include 97 of the 98 gastroenterologists or colorectal surgeons in Rhode Island and 11 gastroenterologists or colorectal surgeons living in Massachusetts. Data collected from enrolled individuals included demographic data, medical history, information related to IBD, and questionnaires on quality of life and disease activity; blood, urine, and stool samples were also collected. Patients were followed quarterly during the first year and every 6 months thereafter. Researchers queried practice billing data and conducted chart reviews to capture missed referrals. The mean interval between diagnosis and enrollment was similar in 2008 and 2009 (66 and 64 days, respectively).

Shah and colleagues reported on the incidence of new cases of IBD in Rhode Island. Between January 1, 2008 and December 31, 2009, 237 new cases of CD and 274 new cases of UC/IC were identified. These numbers translated to unadjusted incidence rates of 21–27 cases per 100,000 for IBD, 10.4–11.6 cases per 100,000 for CD, 9.3–14.3 cases per 100,000 for UC, and 0.8–1.1 cases per 100,000 for IC.

The mean age of patients with CD was 38.8±20.0 years, with a bimodal distribution showing peaks in early adulthood and late middle age (Figure 1). The mean age among patients with UC/IC was 45.3±20.5 years.

Overall, 103 of 237 patients with CD and 77 of 274 patients with UC/IC enrolled in OSCCAR. The enrollees were primarily white (86.4% of CD patients and 93.5% of UC/IC patients) and had no history of smoking (68.9% and 63.6%, respectively) or nonsteroidal anti-inflammatory drug use (87.3% and 79.2%, respectively). Adults comprised 67.0% of patients with CD and 79.2% of those with UC/IC.

In a second analysis of the OSCCAR data, Patel and colleagues evaluated presenting symptoms in patients with CD (97 patients at baseline and 39 patients at Year 1) and patients with UC/IC (71 patients at baseline

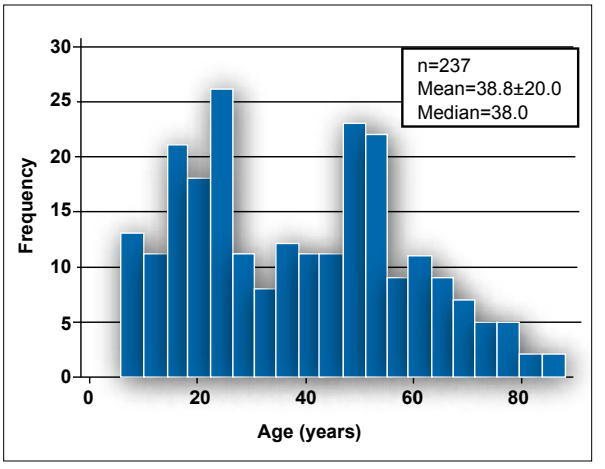

Figure 1. Age distribution of Crohn's disease in Rhode Island in 2008 and 2009.

Table 1. Top 10 Symptoms in Patients with Crohn's Disease

Symptom	Baseline % (n)	Year 1 % (n)
Abdominal pain	83.5 (81)	61.5 (24)
Tiredness or fatigue	81.4 (79)	61.5 (24)
Incontinence or leakage of stool	71.9 (18)	10.5 (4)
Abdominal tenderness	65.6 (63)	51.3 (20)
Cramping with a bowel movement	62.5 (60)	53.9 (21)
Loose stools or watery bowel movements	62.5 (60)	53.9 (21)
Abdominal bloating or distention	61.7 (58)	53.9 (21)
Sense of incomplete emptying after a bowel movement	59.3 (54)	51.3 (20)
Increased number or frequency of bowel movements	58.3 (56)	39.5 (15)
Weight loss	57.7 (56)	30.6 (11)

Table 2. Top 10 Symptoms in Patients with Ulcerative Colitis and Indeterminate Colitis

Symptom	Baseline % (n)	Year 1 % (n)
Loose stools or watery bowel movements	93.0 (66)	69.6 (16)
Urgent bowel movements	90.1 (64)	52.2 (12)
Increased number or frequency of bowel movements	88.6 (62)	39.1 (9)
Passage of blood with bowel movement	87.0 (60)	45.5 (10)
Cramping with a bowel movement	75.0 (51)	47.8 (11)
Foul smelling gas	72.5 (50)	47.8 (11)
Increased passage of gas	72.1 (49)	50.0 (11)
Tiredness or fatigue	70.0 (49)	69.9 (16)
Abdominal pain	68.6 (48)	69.9 (16)
Uncertainty whether gas/bowel movement is about to be passed	68.1 (47)	52.2 (12)

and 23 patients at Year 1). The most common symptoms reported by individuals with CD were abdominal pain and fatigue, present in 83.5% and 81.4%, respectively, at baseline; at Year 1, each symptom was present in 61.5% (Table 1). Other symptoms present in at least 60% of CD patients at baseline included incontinence/stool leakage (71.9%), abdominal tenderness (65.6%), cramping with a bowel movement (62.5%), loose stools or watery bowel movements (62.5%), and abdominal bloating or distention (61.7%). Symptoms present in at least 50% of CD patients at Year 1 included cramping with a bowel movement, loose stools or watery bowel movements, and abdominal bloating or distention (53.9% each), as well as abdominal tenderness and sense of incomplete emptying after a bowel movement (51.3% each).

The 5 most common symptoms at presentation in patients with UC and IC were loose stools/watery bowel movements (93%), urgent bowel movements (90.1%), increased number or frequency of bowel movements (88.6%), passage of blood with bowel movement (87.0%), and cramping with a bowel movement (75.0%; Table 2). At Year 1, the 5 most common symptoms were fatigue, abdominal pain, and loose stools/watery bowel movements (69.6% each), urgent bowel movements (52.2%), and uncertainty whether gas or a bowel movement is about to be passed (52.2%).

The researchers noted some differences in symptoms between pediatric and adult patients with CD. Although both adults and pediatric patients reported abdominal pain and fatigue as their most common symptoms, weight loss and decreased appetite were common in pediatric patients but not in adults.

Finally, Harris and colleagues used data from OSCCAR to investigate the frequency of medication use during the first year after IBD diagnosis. Baseline data were available for 103 patients with CD and 77 patients with UC or IC, and 12-month follow-up data were available for 49 and 30 patients, respectively.

The researchers found differences in treatment patterns based on IBD type (Tables 3 and 4). For patients with CD, 5-ASA was the cornerstone of treatment; this drug was used in 69.9% of patients at baseline, 66.7% at 6 months, and 63.3% at 12 months. Treatment with 5-ASA was also common in UC/IC, with use of this drug reported in 92.2% of patients at baseline, 79.6% at 6 months, and 76.7% at 12 months. At baseline, 42.7% of patients with CD and 50.6% of patients with UC/IC required steroids, a rate that dropped to 24.5% and 16.7%, respectively, by 12 months. Patients with CD were more likely than those with UC/IC to be receiving an immunomodulator (28.6% vs 10.0%) or anti-TNF agent (20.4% vs 10.0%) at 12 months. Differences in treatment patterns were also noted between adult and pediatric patients, with children more likely to receive an immunomodulator than adults. The investigators concluded that long-term follow-up of these patients should help researchers to better understand the effectiveness of different IBD therapies and their relative use in a clinical setting.

Table 3. Medication Use in Patients with Crohn's Disease

Class	Baseline (N=103) % (n)	3 Months (N=93) % (n)	6 Months (N=75) % (n)	9 Months (N=62) % (n)	Year 1 (N=49) % (n)
Antidiarrheals	2.9 (3)		0.0 (0)		0.0 (0)
5-aminosalicylic acid	69.9 (72)		66.7 (50)		63.3 (31)
Antibiotics	30.1 (31)		29.3 (22)		20.4 (10)
Budesonide	12.6 (13)	11.8 (11)	12.0 (9)	3.2 (2)	4.1 (2)
Any steroid	42.7 (44)	41.9 (39)	33.3 (25)	21.0 (13)	24.5 (12)
Immunomodulators	6.8 (7)		21.3 (16)		28.6 (14)
Biologics	4.9 (5)		16.0 (12)		20.4 (10)

Table 4. Medication Use in Patients with Ulcerative Colitis and Indeterminate Colitis

Class	Baseline (N=77) % (n)	3 Months (N=63) % (n)	6 Months (N=49) % (n)	9 Months (N=37) % (n)	Year 1 (N=30) % (n)
Antidiarrheals	10.4 (8)		2.0 (1)		0.0 (0)
5-aminosalicylic acid	92.2 (71)		79.6 (39)		76.7 (23)
Antibiotics	10.4 (8)		2.0 (1)		3.3 (1)
Any steroid	50.6 (39)	39.7 (25)	20.4 (10)	13.5 (5)	16.7 (5)
Immunomodulators	5.2 (4)		6.1 (3)		10.0 (3)
Biologics	0.0 (0)		6.1 (3)		10.0 (3)

Tumor Necrosis Factor Inhibitors

51 Mucosal Healing in Patients with Ulcerative Colitis Associates with a Reduced Colectomy Risk, High Incidence of Symptomatic Remission, and Corticosteroid-free State

W Sandborn, P Rutgeerts, W Reinisch, D Esser, Y Wang, Y Lang, C Marano, R Strauss, B Oddens, B Feagan, S Hanauer, G Lichtenstein, D Present, B Sands, J-F Colombel

The randomized, double-blind, placebo-controlled studies ACT 1 and ACT 2 demonstrated the efficacy of infliximab as induction and maintenance therapy in patients with UC. In the current analysis, Sandborn and colleagues analyzed data from patients enrolled in ACT 1 and ACT 2 and evaluated the association between mucosal healing at Week 8 and clinical outcomes. Mucosal healing was measured using the Mayo endoscopic subscore classification, in which 0=normal, 1=mild disease, 2=moderate disease, and 3=severe disease. The analysis was limited to patients in either study who were assigned to infliximab and who did not receive a colectomy or discontinue treatment prior to Week 8.

Among the 466 evaluable infliximab-treated patients, the endoscopy score at Week 8 was 0 in 26% of patients, 1 in 38%, 2 in 24%, and 3 in 12%. Week 8 endoscopy scores were significantly associated with a risk of colectomy, with the likelihood of remaining colectomy-free at Week 54 decreasing from 95% among patients with scores of 0 and 1, to 87% among patients with a score of 2, to 80% among patients with a score of 3 (P=.0004; Table 5). Week 8 endoscopy scores were also associated with symptomatic remission (defined as a stool frequency score of 0/1 and a rectal bleeding score of 1) and the need for corticosteroids. At Week 30, symptomatic remission rates ranged from 71% among patients with a score of 0 to 51%, 23%, and 10% among those with scores of 1, 2, and 3, respectively (P<.0001). The proportions of patients remaining corticosteroid-free were 62%, 46%, 20%, and 10% among patients with scores of 0, 1, 2, and 3, respectively (P<.0001).

An analysis of only patients from ACT 1 found a similar trend between Week 8 mucosal healing and Week 54 clinical outcomes. The extent of mucosal healing at Week 8 was also associated with outcomes in placebo-treated patients, though patients in this treatment arm were less likely than infliximab-treated patients to attain symptomatic remission or remain corticosteroid-free at Weeks 30 or 54.

Table 5. Kaplan-Meier Estimates of Time to Colectomy

Week 8 endoscopy score†	Number of colectomies	Colectomy-free probability at Week 54 (%)	*P*-value* (log rank)
0 (n=120)	6	95	.0004
1 (n=175)	8	95	
2 (n=114)	14	87	
3 (n=57)	10	80	

**P*-value indicates the difference in distributions of time to colectomy among the 4 endoscopy score subgroups.

†Patients randomized to infliximab (n=466). Patients who had a colectomy or discontinued before Week 8 were not included.

Table 6. Results by Infliximab (IFX) Adherence Level

	Adherent	Nonadherent
N (%)	466 (73)	172 (27)
Mean age (SD)	43 (15)	43 (15)
% Female	58	53
Mean IFX infusions (SD)	8 (0.7)	5 (0.8)
Hospitalization data		
% Hospitalized	8.2	12.2
Mean cost (SD)	$13,427	$37,783
Mean HLOS (SD)	5.92 (3.52)	12.76 (13.02)

HLOS=hospital length of stay; SD=standard deviation.

P1099 Adherence with Infliximab Therapy Decreases Hospitalization Rate and Inpatient Costs in Patients with Crohn's Disease

C Carter, H Waters, D Smith

Carter and colleagues evaluated CD patients to determine how adherence with the first year of infliximab therapy affected hospitalization-related outcomes and costs. In this retrospective analysis, the researchers assessed claims from a health plan claims database that were made between September 1, 2004 and June 30, 2009. The index date, defined as the first claim for an infliximab infusion, had to have occurred between September 1, 2005 and June 30, 2008. All patients must have been continuously enrolled for 12 months before this index date and 12 months after the index date. Other enrollment criteria included having at least 2 claims with an ICD-9 diagnosis code for CD before the index date, being at least 18 years of age at the index date, and having received at least 4 infliximab infusions with no more than 12 weeks between infusions. Adherence was measured for the 12 months following the index date, with those patients receiving 7–9 infusions during this period considered to be adherent and those receiving 4–6 infusions considered to be nonadherent.

The analysis included 638 patients with a mean age of 43 years (standard deviation [SD], 15 years); of these patients, 466 (73%) were adherent and 172 (27%) were nonadherent (Table 6). Females accounted for 58% of the adherent group and 53% of the nonadherent group. The mean number of infliximab infusions was 8 [SD, 0.7] in the adherent group and 5 [SD, 0.8] in the nonadherent group.

The researchers noted a trend toward a lower rate of CD-related hospitalizations among adherent versus nonadherent patients (8.2% vs 12.2%; *P*=.117). Moreover, among patients requiring hospitalization, adherent patients had significantly lower inpatient costs than nonadherent patients, whether costs were expressed as mean values ($13,427 vs $37,783; *P*=.001) or median values ($9,352 vs $28,864; *P*=.001). Adherent patients also had shorter mean and median hospital stays than nonadherent patients (5.9 vs 12.8 days and 5 vs 8 days, respectively; *P*=.015). The association between adherence and inpatient costs remained significant after controlling for baseline characteristics (*P*=.0002).

P1109 Predictors of Early and Sustained Response to Infliximab in Patients with Ulcerative Colitis

E Rostholder, A Ahmed, A Moss

To evaluate predictors associated with response to infliximab in patients with UC, Rostholder and colleagues conducted a retrospective study in which they examined demographic, clinical, and biochemical variables. Of 62 patients with complete data, 77% had a primary response to infliximab, 40% were in remission at 12 months, and 35% required colectomy within the 12-month study period. Factors associated with primary response to infliximab in a univariate analysis included age, disease duration, and prior use of azathioprine or 6-MP. Concomitant treatment with azathioprine or 6-MP was not associated with the likelihood of attaining remission or steroid-free remission at 12 months.

Disease duration was significantly associated with risk of progression to colectomy. Compared with patients diagnosed with UC within the past 2 years, those diagnosed at least 2 years previously were 80% less likely to progress to colectomy (95% confidence interval [CI], 0.1–0.6).

Half of the patients in the study (31 of 62) had steroid-refractory disease; among these cases, 65% of patients treated with infliximab had a primary response,

32% were in remission at 12 months, and 42% required colectomy. There was no association between concurrent azathioprine or 6-MP use and primary response to infliximab in these patients. However, age and disease duration remained significant factors.

P727 Clinical Utility of Infliximab in Treating Acute Exacerbation of Crohn's Disease in Treatment Naïve Patients

S Tyagi, M Cannon

The use of infliximab among patients who have been hospitalized for acute exacerbations of CD or UC has not been well studied. To characterize the use of infliximab in the inpatient setting, Tyagi and Cannon conducted a retrospective review of electronic medical records for all patients admitted to the William Beaumont Hospital in Royal Oak, Michigan with an acute flare-up of CD or UC who subsequently received infliximab on an inpatient basis between January 2007 and September 2009. These patients had received no prior anti-TNF therapy. Of the 2,000 patient records reviewed, 47 eligible patients were evaluated.

Among the 24 patients with CD, 22 (92%) showed a response to infliximab therapy, defined as relief from or resolution of symptoms resulting in early discharge and outpatient follow-up 6–8 weeks later for the next treatment dose. The remaining 8% of patients were nonresponders, defined as patients who required a prolonged hospital stay or surgery. Of the responding patients with CD, fistulizing disease was present in 32%, ileal involvement in 44%, and segmental disease in 24%.

Among the 23 patients with UC, 17 (74%) responded to infliximab. Factors associated with lack of response in these patients included smoking (odds ratio [OR], 7.14) and prior use of immunosuppressants (OR, 3.25).

52 Patient Response to Anti-TNF Dose Escalation in Crohn's Disease Using Health Claims Data

D Rubin, R Sederman

Rubin and Sederman used claims data to investigate the benefit of adalimumab and infliximab dose escalations in patients with CD. The response to dose escalation was assessed by determining whether the anti-TNF agent was continued.

Claims data were obtained from patients with a diagnosis of CD who were continuously enrolled for 6 months before and 3 months after their first anti-TNF agent claim and who had at least 1 claim with a postinduction anti-TNF agent. Infliximab dose escalation was defined as an interval of 4 weeks or less between maintenance doses or an increase of at least 75% in vials compared with induction therapy, using cost data. Adalimumab dose escalation was defined as a weekly dose of at least 40 mg, which is at least twice the recommended maintenance dose.

Data were available for 3,866 patients treated with infliximab; 60% of these patients were 30–60 years of age, and 56% were female. Infliximab dose escalation was reported in 28%; in 99% of these patients, infliximab was the first anti-TNF agent used. Data were also available for 935 patients treated with adalimumab; 69% of these patients were 30–60 years of age, and 61% were female. Adalimumab dose escalation was reported in 24%. In 65% of these patients, adalimumab was the first anti-TNF agent used; in the remaining 35%, infliximab was used as a first-line agent.

After controlling for age, gender, comorbidities, and the first anti-TNF agent, the mean time from induction to dose escalation was found to be 10.4 months for infliximab (95% CI, 8.7–12.0 months), 3.0 months for adalimumab (95% CI, 2.2–3.9 months), and 1.8 months for first-line infliximab/second-line adalimumab (95% CI, 1.2–2.4 months). In a similar adjusted analysis, the mean time to drug discontinuation after dose escalation was 12.6 months, 3.7 months, and 4.7 months, respectively.

Twelve months after infliximab dose escalation, 36% of patients remained on infliximab. Six months after adalimumab dose escalation, 38% of patients who had received first-line adalimumab and 33% of those who had received first-line infliximab remained on treatment. The researchers noted a longer mean time on maintenance therapy among patients who had undergone dose escalation than those who had not for infliximab (23.0 vs 13.5 months), adalimumab (6.7 vs 4.9 months), and first-line infliximab/second-line adalimumab (6.5 vs 3.0 months). Finally, the proportion of patients receiving prescription therapy for CD or undergoing surgery within 6 months of anti-TNF discontinuation was 47–62% among patients who had undergone dose escalation and 53–60% among those who had not.

34 52-Week Efficacy with Adalimumab in Patients with Moderately to Severely Active Ulcerative Colitis Who Failed Corticosteroids and/or Immunosuppressants

W Reinisch, W Sandborn, A Kumar, P Pollack, A Lazar, R Thakkar

To assess the safety and efficacy of adalimumab in patients with moderately to severely active UC, Reinisch and colleagues reported Week 52 results from an open-label extension study that enrolled 390 UC patients with a Mayo score of 6–12 and an endoscopy subscore of 2–3 despite concurrent use of oral corticosteroids and/or immunosuppressants. (Use of concurrent medications was not required if patients had been treated with corticosteroids or immunosuppressants during the past

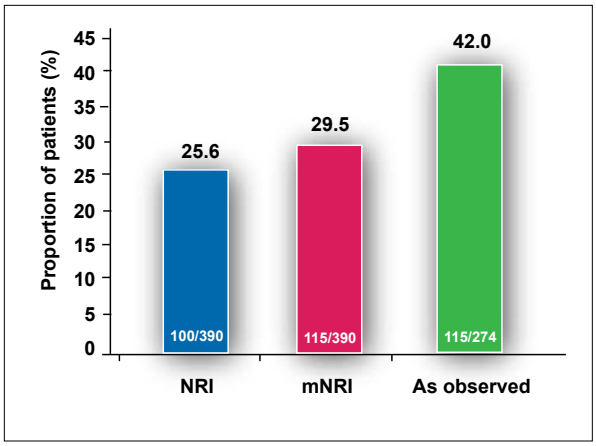

Figure 2. Clinical remission at Week 52. All randomized patients pooled.

mNRI=modified nonresponder imputation; NRI=nonresponder imputation.

Table 7. Secondary Endpoints at Week 52

	NRI N=390 N (%)	mNRI N=390 N (%)	As observed N=274 N (%)
Clinical response	166 (42.6)	209 (53.6)	209 (76.3)
Endoscopy subscore ≤1	148 (37.9)	182 (46.7)	182 (66.4)
Rectal bleeding subscore ≤1	185 (47.4)	246 (63.1)	246 (89.1)*
Stool frequency subscore ≤1	145 (37.2)	175 (44.9)	175 (63.4)*

All randomized adalimumab groups pooled. *N=276.

mNRI=modified nonresponder imputation; NRI=nonresponder imputation.

5 years and were found to be nonresponsive or intolerant to such treatment.) No prior biologic agents were permitted. During the double-blind induction period, patients received 1 of 3 treatments: adalimumab 80/40 (80-mg dose followed 2 weeks later by 40-mg dose), adalimumab 160/80 (160-mg dose followed 2 weeks later by 80-mg dose), or placebo. At Week 8, patients moved into the open-label extension period, during which patients received adalimumab 40 mg every other week, with dose escalation to 40 mg every week permissible beginning at Week 12.

The primary endpoint for this study was the proportion of patients attaining clinical remission (Mayo score ≤2 with no individual subscore >1) at Week 8; this endpoint was achieved in a significantly higher proportion of patients in the adalimumab 160/80 group than the placebo group (18.5% vs 9.2%; *P*=.031). The investigators also assessed the response to open-label adalimumab at Week 52 in a pooled analysis of all randomized patients (Figure 2). In a nonresponder imputation (NRI) analysis, in which a missing Week 52 Mayo score or escalation to weekly dosing was counted as lack of remission or response, 25.6% of patients attained clinical remission with open-label adalimumab. In a modified NRI analysis that did not count dose escalations as failures, the Week 52 clinical remission rate was 29.5%. Finally, in the as-observed analysis, 42.0% of patients attained clinical remission at Week 52.

Clinical response was defined as a decrease in Mayo score of at least 3 points and at least 30% from baseline plus a decrease in the rectal bleeding subscore (RBS) of at least 1 or an absolute RBS of no more than 1. Using this definition, Week 52 clinical response rates were 42.6% in the NRI analysis, 53.6% in the modified NRI analysis, and 76.3% in the as-observed analysis. In the NRI analysis, the proportion of patients attaining Week 52 subscores of no more than 1 was 37.9% for endoscopy, 47.4% for rectal bleeding, and 37.2% for stool frequency (Table 7).

No new safety concerns were noted in the open-label treatment period. No deaths or lymphomas were reported, and rates of infectious adverse events and serious infectious adverse events were 89.5 and 4.0 per 100 person-years, respectively.

P721 Concomitant Use of Adalimumab and Immunomodulators or Corticosteroids Compared with Adalimumab Alone: Pooled Safety Analysis

W Sandborn, J-F Colombel, J Lewis, M Osterman, A Robinson, B Huang, P Pollack, R Thakkar

To further characterize the safety profile of adalimumab administered in conjunction with other therapies, Sandborn and colleagues conducted a pooled analysis of serious infection rates in patients with CD using data from several lead-in and long-term studies of adalimumab: CLASSIC I, CLASSIC II, CHARM, GAIN, and ADHERE. The analysis included 638 patients who received adalimumab with immunomodulators—such as 6-MP, azathioprine, or methotrexate—at lead-in study baseline and 821 patients receiving adalimumab without immunomodulators at baseline.

Overall, serious infection rates were numerically higher among patients using adalimumab with immunomodulators than among patients receiving adalimumab alone (10.0% vs 7.2%; *P*=.058). The highest serious

Table 8. Treatment-emergent Serious Infections by Baseline Concomitant Therapy

Therapy	N	SI n (%)	SI E/ 100-PY	*P*-value*
ADA alone	528	30 (5.7)	3.2	
ADA+IMM (no CS)	370	33 (8.9)	5.3	.064
ADA+CS (no IMM)	293	29 (9.9)	7.0	.034
ADA+IMM+CS	268	31 (11.6)	8.6	.005

*Comparing proportion, versus adalimumab (ADA) alone.

CS=corticosteroid; E=events; IMM=immunomodulator; PY=person-years; SI=serious infections.

infection event rate was observed with adalimumab plus immunomodulators and corticosteroids, at 8.6 per 100 person-years, followed by 7.0 per 100 person-years for adalimumab plus corticosteroids (no immunomodulators), 5.3 per 100 person-years for adalimumab plus immunomodulators (no corticosteroids), and 3.2 per 100 person-years for adalimumab alone (Table 8). Each of the combinations had a significantly higher serious infection event rate than adalimumab alone. These findings suggest that among patients with CD who are receiving adalimumab, those receiving concomitant immunosuppressants and corticosteroids at baseline have the highest risk of developing a treatment-related serious infection.

Novel Approaches

50 Interferon-β-1A in Active Moderate to Severe Ulcerative Colitis: Efficacy and Safety from a Phase IIA Multicenter Study

P Mannon, R Panaccione, P Miner, A McAllister, J O'Gorman, F Cataldi

The cytokine interleukin (IL)-13 has been identified as a potential therapeutic target for UC, as it is active in a mouse model of UC and has been shown to cause direct damage to the gut epithelium.[1,2] Type I interferons (IFNs) are known to block IL-13 production and receptor signaling in human CD4-positive T cells. In an open-label pilot study of 16 patients with moderately active UC, the type I IFNβ-1a was associated with an 81% clinical response rate and a 44% remission rate after 12 weeks.[3] Moreover, IFNβ was associated with decreases in IL-13 production in responding patients.

In the current study, Mannon and colleagues reported results of a multicenter, randomized, double-blind, placebo-controlled phase IIa study evaluating IFNβ in patients with moderate to severe UC. Patients were 18–65 years of age, had an established diagnosis of UC for at least 6 months, and had a modified Mayo score of 6–13. Active disease in at least 20 cm at screening endoscopy was required. Patients were required to be receiving stable doses of concomitant corticosteroids, azathioprine/6-MP, or 5-ASA, in any combination.

A total of 123 patients were randomly assigned to intramuscular IFNβ 30 µg (62 patients) or placebo (61 patients) twice weekly for 12 weeks, with a safety evaluation at Week 16. The investigators reported no difference between arms for the primary endpoint, Week 8 clinical response, which was defined as a decrease from baseline in total Mayo score of at least 3 points and at least 30% plus a decrease in the RBS of at least 1 point or an absolute RBS of 0 or 1. In an intent-to-treat analysis, 53% of IFN-treated patients and 44% of placebo-treated patients achieved clinical response (*P*=.35).

Of the 122 patients evaluable for the secondary endpoint, which was defined as a decrease in Short Clinical Colitis Activity Index score of at least 3 points at Week 8, there was a trend toward a higher rate of patients attaining clinical response with IFN versus placebo (64% vs 46%; *P*=.05).

The researchers reported that IFN was well tolerated, with a safety profile consistent with that of previous reports. There were no serious infections. Serious adverse events occurred in 4 patients, 3 of whom were in the placebo arm; these events included worsening of UC (2 patients receiving placebo and 1 patient receiving IFN) and 1 tibia fracture in a placebo-treated patient.

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P723 Randomized, Double-blind, Placebo-controlled Trial of *Andrographis paniculata* Extract (HMPL-004) in Patients With Moderately Active Crohn's Disease

W Sandborn, S Targan, V Byers, T Tang

Sandborn and colleagues evaluated the safety and efficacy of treatment with the herbal extract HMPL-004 in patients with moderately active CD. HMPL-004 is an extract of *Andrographis paniculata* that has been shown

to inhibit multiple proinflammatory cytokines, including TNF-α, IL-1β, and nuclear factor-κB.[1]

This randomized, double-blind, placebo-controlled trial enrolled patients in the United States and Ukraine with moderate CD, defined as a Crohn's Disease Activity Index (CDAI) between 220 and 400 points with C-reactive protein (CRP) levels above the upper limit of normal despite stable doses of concomitant medications. A total of 101 patients were randomly assigned to oral HMPL-004 1,200 mg/day (51 patients) or placebo (50 patients). The investigators reported a nonsignificant trend toward benefit with HMPL-004 versus placebo for the primary endpoint, defined as a CDAI reduction of 100 points at Week 8, with clinical response rates of 37.3% for HMPL-004 and 22% for placebo (*P*=.087). The proportion of patients who achieved a CDAI reduction of 70 points was 49% in the HMPL-004 group and 32% in the placebo group (*P*=.061). Remission rates, defined as a CDAI less than 150 points, were 29.4% and 14%, respectively (*P*=.069).

Mean CRP levels declined significantly from baseline to Week 8 in both groups, from 23.5 mg/L to 11.8 mg/L in the HMPL-004 group (*P*=.004) and from 14.2 mg/L to 10.0 mg/L in the placebo arm (*P*=.008). There was a trend toward a greater CRP reduction between baseline and Week 8 with HMPL-004 versus placebo (11.7 mg/L vs 4.2 mg/L; *P*=.068).

Adverse event rates were similar with HMPL-004 and placebo (64% and 56%, respectively), and no adverse events were considered to be "probably" or "definitely" related to the study medication. Infection-related events among patients receiving HMPL-004 included an increase in skin rash and slight increases in bronchitis and urinary tract infections. Serious adverse events included CD exacerbation (2 patients in the HMPL-004 arm and 3 patients in the placebo arm) and 1 case of lung cancer in the placebo arm.

The investigators noted that a dose-ranging study of HMPL-004 for active UC showed significant efficacy with the agent dosed at 1,800 mg/day but not at the 1,200-mg/day dose used in the current study. A planned study will investigate higher doses of HMPL-004 in patients with CD.

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58 Briakinumab (Anti-Interleukin 12/23P40, ABT874) for Treatment of Crohn's Disease (CD)

R Panaccione, W Sandborn, G Gordon, S Lee, A Safdi, S Sedghi, B Feagan, S Hanauer, A Kumar, R Carcereri

Briakinumab is a human monoclonal antibody directed against IL 12/23p40. In this randomized, placebo-controlled study, Panaccione and colleagues evaluated briakinumab for induction and maintenance therapy in patients with CD. A total of 230 patients with moderately to severely active CD (CDAI of 220–400) were randomly assigned to briakinumab 700 mg (n=139), briakinumab 400 mg (n=45), or placebo (n=46) administered by infusion at Weeks 0, 4, and 8. Patients who responded to treatment, defined as having a CDAI decrease of at least 70 points from baseline to Week 12, were eligible for maintenance therapy. The maintenance regimen varied depending on the induction regimen each patient received; patients who received induction therapy with briakinumab 400 mg (n=21) or placebo (n=14) received the same therapy for maintenance, whereas patients who received briakinumab 700 mg for induction therapy were randomly assigned to maintenance with briakinumab 700 mg (n=21), briakinumab 200 mg (n=21), or placebo (n=22). In all cases, maintenance therapy was administered at Weeks 12, 16, and 20, with an assessment at Week 24.

In terms of remission rates at Week 6, there was no significant difference among briakinumab 700 mg, briakinumab 400 mg, and placebo (17.3%, 13.3%, and 8.7%, respectively). Week 12 remission rates were 22.3%, 28.9%, and 10.9%, respectively, with only the briakinumab 400-mg arm achieving a statistically significant difference from placebo (*P*=.030). Among patients who received maintenance therapy, Week 24 remission rates were 57.1%, 52.4%, and 28.6%, respectively. Among the subset of patients who received briakinumab 700 mg for induction therapy and were re-randomized to maintenance therapy, Week 24 remission rates were 57.1% with briakinumab 700 mg, 42.9% with briakinumab 200 mg, and 47.6% with placebo.

Briakinumab was associated with a serious adverse event rate of 4.5% and a serious infection rate of 0.5%. In the placebo group, serious adverse events occurred in 8.7% of patients; 2.2% of placebo-treated patients developed nonmelanoma skin cancer. During maintenance therapy, serious adverse event rates with briakinumab and placebo were 2.2% and 7.1%, respectively. Serious infections developed in 1.1% of patients receiving briakinumab as maintenance therapy. One patient receiving briakinumab died from respiratory distress failure due to pancreatitis 2 months after the last dose.

Commentary

Gary R. Lichtenstein, MD

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Obtaining population-based cohort information allows clinicians to more knowledgeably discuss with patients the natural history of their disease and what they can expect from treatment. For example, if individuals present with severe disease at onset, we want to be able to tell them their risk of progressing to colectomy, staying in remission, and/or having disease flares. Knowing these risks also helps the physician decide which patients might need more aggressive medical care. At the 2010 ACG Meeting, a new patient registry was presented—the Ocean State Crohn's and Colitis Area Registry—that could help to provide clinicians with a better understanding of the natural history of IBD in the United States. There are already several population-based cohorts worldwide, but patients in other countries may not be representative of patients in the United States, and those registries previously established in the United States may not be representative of the entire country. For example, Olmstead County, Minnesota, has a large patient registry, but this region may not be representative of areas in the Northeast such as New York City and Philadelphia. With OSCCAR, however, researchers have data from the entire state of Rhode Island, which could be more representative of other areas in the country.

Another topic of significant interest at the 2010 ACG Meeting was how best to use anti-TNF agents to treat IBD, and in particular, how to predict which patients will respond to these drugs. In one recent landmark study, researchers reported that UC patients who achieved mucosal healing shortly after administration of infliximab subsequently had a reduced colectomy rate. Mucosal healing is also associated with achieving a corticosteroid-free state, suggesting that this clinical finding could be a predictor of long-term efficacy.

A second study looking at predictors of success with anti-TNF therapy found that adherence was a significant factor. In this retrospective study, analysis of information from a health plan database demonstrated that CD patients who adhere to therapy are less likely to be hospitalized, have shorter mean and median hospital stays, and have lower inpatient costs than patients who do not adhere with therapy. Thus, clinicians must not only administer medication but also educate patients and help them understand why taking their medication is important.

Another study, by Rostholder and colleagues, identified factors that can predict which individuals with UC will benefit from infliximab. In a retrospective analysis, age and duration of disease were found to be significant factors, but there was no association between success with infliximab and concurrent antimetabolite use. This finding is in contrast to those of the SONIC study, in which CD patients who were naïve to immunomodulators and anti-TNF therapy did benefit from combination treatment with azathioprine plus infliximab. One possible explanation for this observed difference is that patients in Rostholder's study might have failed antimetabolite medications prior to starting anti-TNF therapy.

Examining the use of anti-TNF therapy in an inpatient setting, researchers demonstrated that infliximab is an effective treatment for acute exacerbations of CD or UC among hospitalized patients. In a retrospective review of electronic medical records, patients who presented at a single hospital over a period of approximately 2.5 years were evaluated. These patients had not previously received anti-TNF therapy. While anti-TNF therapy was usually effective, smoking and prior use of immunosuppressants were found to be associated with lack of response in UC patients.

A similar study used health claims data to determine the effect of anti-TNF dose escalations and found that infliximab, adalimumab, and first-line infliximab/second-line adalimumab showed differences in terms of mean time from induction to dose escalation and mean time from dose escalation to drug discontinuation. While these differences are interesting, the retrospective nature of this particular study limits our ability to conclude that one agent is better than another. If a larger, prospective study confirms these differences, however, then physicians might begin using one agent more frequently, and insurers might embrace use of one particular agent over another.

In another study evaluating anti-TNF agents, the efficacy of adalimumab was evaluated in patients with moderately to severely active UC who had failed corticosteroids and/or immunosuppressants and who had not previously been exposed to biologics. Among individuals who received 160 mg adalimumab as a loading dose followed by 80 mg adalimumab 2 weeks later, 42% of patients in the as-observed analysis obtained clinical remission (Mayo score ≤2 with no individual subscore >1) at Week 52. Improvements were also seen in the study's secondary endpoints: clinical response, endoscopy subscore, rectal bleeding subscore, and stool frequency subscore.

In addition to evaluating existing therapies, data on several novel treatments were presented at the 2010 ACG Meeting. For example, interferon β was evaluated in a phase II, multicenter, double-blind, placebo-controlled study as a treatment for moderate-to-severe UC. Patients in this study had moderately active disease with the presence of endoscopic inflammation and were on stable doses of steroids, 5-ASA, and/or immune modulators (including azathioprine or 6-MP). The overall finding of the study was that 64% of patients treated with interferon β showed a decrease of at least 3 points in their Short Clinical Colitis Activity Index score at Week 8, compared to 46% of placebo-treated patients. While promising, this agent will need to be further evaluated in a large, phase III trial, and a dose ranging study should be performed to better define appropriate doses for different individuals.

A new herbal agent currently being studied is HMPL-004, which has been shown in vitro to inhibit TNF-α, nuclear factor κB, and IL-1β. In a large, multicenter, double-blind, placebo-controlled trial, there was a nonsignificant trend towards benefit with HMPL-004 versus placebo for the study's primary endpoint, which was defined as a 100-point decrease in Crohn's Disease Activity Index score. While this was a negative study, the drug's lack of response may be a dosing-related issue. A dose ranging study for UC found that HMPL-004 was effective at 1,800 mg/day but not at the 1,200-mg/day dose used in the current study. Perhaps a higher dose will also prove effective in CD, but this has yet to be determined.

A final study presented at the 2010 ACG Meeting looked at an IL-12/23p40 antagonist known as briakinumab. This study found no significant difference between briakinumab 700 mg, briakinumab 400 mg, and placebo in terms of remission rates at Week 6, but the 400-mg arm showed a statistically significant difference compared to placebo at Week 12. There were no unexpected safety issues, but this study was powered for efficacy rather than safety. Further evaluation will be needed via future clinical trials. Overall, the IL-12/23 antibodies are a very promising group of agents, and I suspect they will get more attention in the future. Another IL-12/23 antagonist, ustekinumab, is currently FDA-approved for psoriasis and is also undergoing trials for treatment of CD.

Conclusions

Despite the advancements we have made in treating patients with anti-TNF therapy and other drugs, a large number of CD patients still need surgery. Since we aim to avoid surgery in most cases, there remains an unmet need for better medical therapy. Discovering new agents, testing them, and defining the patient population in which they might work is therefore a critical project. New agents add to our medical capabilities, help to lessen the need for surgery and hospitalizations, and improve patients' quality of life.

While evaluating new treatments is important, we also need to optimize existing therapies. Many of the studies discussed above evaluated FDA-approved drugs such as the anti-TNF agents. These medications have made a major impact in helping us to better treat patients, but we cannot always predict which patients will benefit from these drugs. By examining the predictive value of demographic and clinical factors, such as mucosal healing, clinical trials help us determine which populations will benefit from certain therapies.

Finally, early aggressive treatment is an area that has been extensively discussed. If we can use clinical parameters such as serologic markers or genetics to predict that an individual is likely to need surgery, then clinicians can start with more aggressive treatment. While early aggressive treatment has been studied for CD, there has not yet been any corresponding research for UC, so further research in this area is needed. Natural history studies could also come into play here, as they could help us to better understand what will occur if these patients are not treated with aggressive therapy.

USF Health CB2011 104 Post-Event Questionnaire
Current Research in Crohn's Disease & Ulcerative Colitis:
Highlights from the 2010 ACG Meeting

This Post-Event Questionnaire may be:
1.) Completed and submitted online 2.) Printed, completed, and faxed to: 813-974-3217
3.) Mailed to USF Health, 12901 Bruce B. Downs Blvd, MDC 46, Tampa, FL 33612 (Attn: Pam LeClair)

According to the OSCCAR data presented by Patel & colleagues, which were the most common Sx reported by individuals w/ CD?

- ○ Abdominal pain and fatigue
- ○ Weight loss and decreased appetite
- ○ Loose stools, watery/urgent bowel movements
- ○ Foul smelling gas and increased passage of gas

According to the study by Sandborn & colleagues in which mucosal healing at Week 8 was evaluated as a predictor of clinical outcomes, what was a patient's likelihood of remaining colectomy-free at Week 54 if they had an endoscopy score of 2 at Week 8?

○ 20% ○ 80% ○ 87% ○ 95%

According to the data presented by Carter & colleagues, how does adherence with infliximab therapy affect hospitalization rates and inpatient costs in patients with CD?

- ○ Adherent patients had a lower rate of CD-related hospitalizations
- ○ Among patients requiring hospitalization, adherent patients had lower inpatient costs
- ○ Adherent patients had shorter hospital stays
- ○ All of the above are true

In the study by Rostholder & colleagues, which of the following factors was ***NOT*** associated with primary response to infliximab?

- ○ Age
- ○ Disease duration
- ○ Prior use of azathioprine or 6-MP
- ○ Concomitant treatment with azathioprine or 6-MP

In the study conducted by Tyagi & Cannon, what % of CD patients who were hospitalized with acute flare-ups responded to infliximab therapy?

○ 18% ○ 55% ○ 65% ○ 92%

In the study by Rubin & Sederman, patients treated w/ infliximab, adalimumab, and first-line infliximab/second-line adalimumab who had undergone dose escalation were found to have a mean time on maintenance therapy that was ***???*** that of patients who had not undergone dose escalation.

○ Longer than ○ Shorter than ○ Equal to ○ Not compared to

In the adalimumab study by Reinisch & colleagues, what % of patients in the NRI analysis achieved a clinical response at Week 52?

○ 34.7% ○ 42.6% ○ 56.8% ○ 92.7%

According to the pooled safety analysis performed by Sandborn & colleagues, which treatment combination showed the highest serious infection event rate?

- ○ Adalimumab alone
- ○ Adalimumab plus corticosteroids
- ○ Adalimumab plus immunomodulators
- ○ Adalimumab plus immunomodulators and corticosteroids

In the study of *Andrographis paniculata* extract presented by Sandborn and colleagues, what dose of HMPL-004 was used?

○ 200 mg/day ○ 1,200 mg/day ○ 1,800 mg/day ○ 2,400 mg/day

In the study of briakinumab presented by Panaccione & colleagues, which Tx arm showed the highest remission rate at Week 12?

○ Briakinumab 200 mg ○ Briakinumab 400 mg ○ Briakinumab 700 mg ○ Placebo

USF Health CB2011 104 Post-Event Questionnaire
Current Research in Crohn's Disease & Ulcerative Colitis:
Highlights from the 2010 ACG Meeting

	Y	N
Were ***YOUR*** objectives met in reviewing this material?	○	○

If no, please explain.

	Y	N
Were the ***PROGRAM'S*** objectives met when reviewing this material?		
Review the current role of biologic therapies in the treatment of Crohn's disease and ulcerative colitis	○	○
Discuss factors associated with positive outcomes in these patients	○	○
Outline novel therapies that may lead to new treatment options	○	○

Response Definition: 1=Not useful 2=Somewhat useful 3=Quite useful 4=Very useful

Rate the usefulness of the following topics:

	1	2	3	4
IBD incidence, treatment patterns, and treatment goals	○	○	○	○
Tumor necrosis factor inhibitors	○	○	○	○
Novel approaches / new treatments	○	○	○	○
Overall, to what extent did you find the abstract summaries useful?	○	○	○	○
To what extent did you find the commentary useful?	○	○	○	○

Of the information presented, what percentage is useful to you?

○ 0 - 20% ○ 21 - 40% ○ 41 - 60% ○ 61 - 80% ○ 81 - 100%

Response Definition: 1=Strongly Disagree 2=Disagree 3=Neutral 4=Agree 5=Strongly Agree 6=No Opinion 7=N/A

As a result of reading this monograph from the 2010 ACG Meeting...

	1	2	3	4	5	6	7
I increased my knowledge of current research in CD and UC	○	○	○	○	○	○	○
I am more aware of new biologic therapies for CD and UC	○	○	○	○	○	○	○
The monograph provided information relevant to my practice	○	○	○	○	○	○	○
The monograph addressed my most pressing questions	○	○	○	○	○	○	○
The monograph was based on current information	○	○	○	○	○	○	○

The material was free of commercial bias or influence

○ Yes ○ No

The following information is required for your certificate:

Please enter the required information in the space below: ***Full name & credentials - Address - City, State, Zip - Phone - Email***