1-1-2015

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Abstract

Ulcerative colitis (UC), a subdivision of inflammatory bowel disease, is a chronic disease of the large intestines. Ulcerative Colitis is normally a lifelong chronic illness with times of intense flairs and remission. During a flare, the lining of the colon becomes inflamed, and develops small ulcers causing patients to experience rectal bleeding, vomiting, anemia and diarrhea. The treatment options available to treat colitis are very small, causing many patients to need a total colectomy with in the first five years of their diagnosis. However, recent advancement in bio-technology has led to the development of a large array of new therapeutic agents intended to target the exact site in the multifaceted cascade of cytokine and chemokine effector molecules involved in UC pathogenesis. This article discusses the introduction of the chimeric monoclonal antibody to TNFa that has deeply affected the clinical treatment of moderate to severe ulcerative colitis, opening the door to a new era in the treatment of this disease. Studies discussed in this paper prove the effectiveness of both Remicade and Humira, two different biologics, given to patients with an active state of this disease.

Introduction

Acronyms: UC-ulcerative colitis IBD-inflamitory bowel disease
Ulcerative colitis (UC), a subdivision of inflammatory bowel disease (IBD), affects 1 to 2 million people in the United States each year. The reason for ulcerative colitis is not quite understood. However, the condition appears to be related to a combination of genetic and environmental factors. Minor symptoms include unformed stools, abdominal cramping, and diarrhea (Lichteger et al.,1994). As the severity of the disease increases, patients experience fatigue, loss of appetite, weight loss mucus present in the stool, intense rectal bleeding in addition to fever and anemia. UC can ensue at any time yet it is usually diagnosed in a person's teenage years. Roughly around 20% of people with UC have a close relative with IBD. (CCFA.org, 2015).

UC is normally a lifelong chronic illness with times of intense flairs and remission. A severe attack which can be a potentially fatal condition, is sometimes the first manifestation and is observed in about 15% of the patients with this disease. The introduction of corticosteroids sharply reduced the death rate. Corticosteroids remain as a pillar in the treatment of a severe attack of ulcerative colitis. The importance of achieving remission is undermined by the fact that the long-term colectomy rate in patients with a severe attack who achieve clinical and endoscopic remission after steroids is similar to those with a moderately severe or mild attack. The dependence on corticosteroid is a continuous problem. Steroid dependent patients may develop osteoporosis as they get older, in addition to dealing with weight gain, moon face, increase in appetite, as well as, acne and joint pain. Furthermore, the likelihood of a colectomy within the first five years from diagnosis ranges from 9% in patients with distal colitis to 35% in patients with complete colitis, normally because of unsuccessful medical therapy. The risk of recurring inflammatory bowel disease in the form of pouchitis ranges from 15.5% 1 year after the procedure to 45.5% 10 years after the procedure. Accordingly, new treatments for ulcerative colitis are needed (CCFA.org, 2015).

In recent years biological therapy has been the new method of treatment for those who are steroid dependent and or failing to respond to other treatments. Tumor necrosis factor α (TNF-α) is a key pro-inflammatory cytokine in patients with Crohn's disease, but is also found in amplified amounts in the intestinal tissue, stools, blood and urine of patients with ulcerative colitis. Infliximab, also known as Remicade, is an IgG1 monoclonal antibody that binds with intense strength to TNF-α, neutralizing its biologic activity (Simmons & Jewell, 2002). The question now becomes; will biological therapy be the answer to help induce clinical remission in those suffering from UC?

Material and methods

In order to answer the question proposed above, many research articles with relation to this topic have been read. Touro College's library database, the national website of Pubmed and Google Scholar were all used to obtain information for this paper. All of the articles and information that was accumulated through this research have been used in an attempt to conclusively determine if biological therapy will induce a remission in patients living with active state of ulcerative colitis.

Different types of ulcerative colitis

The symptoms present for a person with ulcerative colitis will vary based on the amount and severity of inflammation present and the site of the disease in the large intestines. Ulcerative proctitis, the mildest form of ulcerative colitis, is limited to the rectum (about 6 inches or less). Proctosigmoiditis is colitis that affects the rectum and sigmoid colon-which is located superior to the rectum. Proctosigmoiditis can be determined sometimes by the symptom of tenesmus (straining to have a bowel movement.) In addition, moderate pain on the lower left side of the abdomen may occur while the disease is present. The third version of colitis is known as left sided colitis. This presents as continuous inflammation that begins at the rectum and goes up as far as the splenic flexure (a bend in the colon near the spleen in the upper left abdomen). Symptoms for left side colitis

include severe pain on the left side of the abdomen, in addition to loss of appetite. Lastly, the most severe form of ulcerative colitis is pancolitis. Pancolitis affects the entire colon causing terrible abdominal pain, weight loss and complete loss of appetite (CCFA.org, 2015).

Climbing the medical ladder

Today, there are very effective treatments on the market to help control the disease with the goal of putting it into remission. The main aim of the different treatments is designed to decrease inflammation. This not only allows the colon to heal, but also relieves the symptoms of diarrhea, rectal bleeding and abdominal pain accompanied by the flare. Unfortunately, there is no "one size fits all" treatment plan for everyone suffering with this disease. One person may do just fine with the most minor suppository and live fine the rest of his life, while another may require more invasive treatment or need a complete colectomy. Therefore, the approach must be customized for each individual person because each person's disease is different. With the correct medical treatment, a patient can achieve remission with the hope of the state of remission lasting for months or even years. Nonetheless, ulcerative colitis may flare up at times from the reappearance of inflammation or from a specific trigger. Reoccurrence of a flare usually indicates the need to change the medication regimen for the patient. The choice of drugs to treat a patient is dependent upon the severity of the disease. The most commonly prescribed drugs fall into three basic categories:

Aminosalicylates: This class of drugs encompass 5-aminosalicylic acid commonly known as the 5-ASA . This class of drug is available in an oral form in addition to a suppository or an enema. The goal of the 5-ASA is to line the GI tract with the hope to decrease inflammation. In addition, Aminosalicylates are beneficial as a maintenance treatment in order to prevent a relapse of the disease (Colombel et al., 2010).

Corticosteroids: The job of steroids is to prevent the body from launching an inflammatory cascade. Additionally, corticosteroids work to keep the immune system properly balanced. Steroids are effective for short-term control of flare-ups. This class of drugs is known to help "put out the fire". Yet, corticosteroids are not recommended for long term use or as a maintenance drug for UC because of their tremendous amount of side effects. The goal of steroids is to buy the patient time, not fix the problem. A person who is unable to come off steroids without experiencing a relapse of the disease will then be prescribed a higher class of drugs to help manage the disease (Colombel et al., 2010).

Immunomodulators: Immunosuppressants work to control the body's immune system response in order to prevent ongoing inflammation. Immunomodulators are mostly used in people who have failed to respond to the 5-ASA and steroids have not been effective or have been minimally effective in controlling the disease. Furthermore, immunosuppressants are geared to allow people who are steroid dependent to eliminate the use of them (Sood et al., 2002).

Though these three possibilities of treatments have been shown to be effective, there are always patients who fail to respond to the three treatment options. These patients were left with no choice but to have surgery to rid them of the disease leaving them without a colon and remaining with a pouch for the rest of their lives. It had become evident that there was a need to help prevent patients from undergoing a complete colectomy.

TNF-a and inflammation

All humans have a large gastrointestinal mucosal surface that is continually being exposed to billions of potentially harmful antigens from our food, bacteria and the environment. However, the mucosal surface of the GI tract possesses an immune system that strongly controls the balance between immunogenic responsiveness and non-responsiveness-tolerance. Response to luminal antigens provokes "controlled" inflammation that is rapidly down regulated after eradication of the pathogen. However, this is not the case for someone with ulcerative colitis. In this disease this state of equilibrium is disturbed resulting in a state of chronic inflammation. During the start of the inflammation, antigen presenting cells, such as macrophages, cause the activation of T lymphocytes. T lymphocyte cells divide into two T helper T1 and T2 cells. T1 cells secrete interferon gamma (IFNy) which then enables macrophages to produces TNFa (Simmons & Jewell, 2002).

TNFa is an inflammatory mechanism that has been shown to play a vital role in the pathogenesis of IBD. The transcribing of the TNFa gene in stimulated macrophages, platelets, monocytes, adipocytes and T cells results in the secretion of TNFa. Circulating TNFa binds to 2 TNFa receptors facilitating numerous biological effects including activation of other macrophages, further expansion of the T cell response, and initiation of granuloma formation. TNFa also lengthens inflammation by triggering NF-kB dependent pathways, which contribute to ulceration and degradation of the mucosa through the release of MMP (matrix metalloproteins). TNFa triggers other inflammatory mediators, such as, IL6 therefore strengthening the early sequence of the inflammatory cascade. Increased TNFa production and NFKb have been shown to be abundant in lamina propria mononuclear cells derived from UC patients with ulcerative colitis through stool, urine and blood tests (Hassan et al., 2007).

Recent advancement in bio-technology have thankfully led to

the development of a large array of new therapeutic agents intended to target the exact site in the multifaceted cascade of cytokine and chemokine effector molecules involved in UC pathogenesis. In particular, the introduction of the chimeric monoclonal antibody to TNFa has deeply affected the clinical treatment of moderate to severe ulcerative colitis, opening the door to a new era in the treatment of this disease.

Infliximab

Infliximab is the first and most widely studied biological agent for ulcerative colitis. As of 2006, Infliximab has been approved by the FDA for the treatment of ulcerative colitis. "This biologic is a chimeric monoclonal antibody to TNFa composed of a "human" IgGI constant region (75%) and murine-derived antigen binding variable region (25%)" (Sands & Kaplan, 2007). Infliximab is able to bind powerfully to both soluble and membrane-bound TNFa receptors. The actual mechanism of Infliximab is not completely understood, direct neutralization of TNFa does not entirely explain its effect. Infliximab has been found to apply a proapoptotic effect on monocytes and T cells in the lamina propria of the gut. The proapoptotic effect in infliximab may be exerted, preventing the production of granulocyte macrophage colony-stimulating factor, which is a growth factor that stimulates granulocyte growth and differentiation and activates neutrophils with greater adhesion (Sands & Kaplan, 2007).

Patients were eager to try this treatment option hoping to get their disease under control. A study was conducted in March 2002 testing the safety and efficacy of Infliximab. This study consisted of two large double-blind, placebo controlled trials known as the Active Ulcerative Colitis Trials 1 and 2 (ACT 1 and ACT 2). Both trails were done on 364 patients with moderate to severe ulcerative colitis. All participants in ACT 1 who were considered eligible were screened for a confirmed diagnosis of ulcerative colitis via biopsy and endoscopies. Eligible patients had active colitis with a Mayo score of 6 to 12 points (scores range from 0-12 with higher scores indicating more severe disease activity). Additionally, eligible patients also had active disease on the sigmoidoscopy exam results (despite simultaneous treatment with steroids alone or in combination with immunosuppressant's, aza or 6mp). ACT 2 allowed study participants who had only failed 5 ASA's to participate. Patients formerly exposed to infliximab or any other anti-TNF agents were omitted. Patients who were eligible were randomly assigned to be administered intravenous infusions or infliximab at a dose of 5mg or 10mg per kilogram of weight or a placebo at weeks 0, 2, and 6 and then every 8 weeks. Patients were monitored through week 54 in ACT 1 and week 30 in ACT 2 (Rutgeerts et al., 2005).

The main end point was a clinical response at week 8. Secondary end points included a clinical response or remission with stoppage of corticosteroids at week 30 in both studies and at week 54 in ACT 1.

Of the 364 patients in ACT 1, 121 were given a placebo, 121 received 5 mg of infliximab, and 122 to received 10 mg of infliximab. Treatment was stopped early by 74 patients in the placebo group, 45 patients in the group receiving 5 mg of infliximab, and 49 patients in the group getting 10 mg. Of the 364 patients in ACT 2, 123 were given a placebo, 121 received 5 mg of infliximab, and 120 were administered 10 mg. At week 8, in ACT 1, clinical remission was achieved in 69.4% of patients receiving 5 mg of infliximab and 61.5 % of patients in the group receiving 10 mg of infliximab. However, in the placebo group only 37.2 percent of patients achieved clinical response. In ACT 2, at week 8, 64.5 % of the patients in the group receiving 5 mg of infliximab and 69.2 % of patients receiving 10 mg of infliximab exhibited a clinical response, in comparison to the 29.3 % of patients in the placebo group. Additionally, at the end of weeks 54 and 30 significantly higher percentage of patients receiving Infliximab as opposed to the placebo went into complete remission and were able to discontinue the use of steroids (Rutgeers et al., 2005).

Antibodies against Infliximab

A common concern when starting biologics is the possibility of a buildup of antibodies towards the drug. One study tested serum samples from participants to check for a buildup of antibodies to the drug. At week 54, 229 patients in ACT 1 had serum samples available for testing of antibody build up to Infliximab. Only 14 patients had a positive test after the first infusion, 36 presented negative tests and 179 patients had inconclusive tests. In ACT 2 from the 188 patients who had serum samples available for testing, 12 presented a positive test for antibodies, 34 negative, and 142 inconclusive. Furthermore, in ACT 2 a clinical response still occurred in 11 patients who tested positive for antibodies.

The study further tested the safety of this drug. In both studies, the proportions of patients with adverse events were similar in the placebo group and the two Infliximab groups. In ACT 1, serious adverse events occurred in 25.6% of patients in the placebo group, 21.5% of patients receiving 5 mg of Infliximab, and 23.8% percent of patients receiving 10 mg of infliximab. In ACT 2, the percentages of serious adverse events were 19.5% in the placebo group, 10.7% in the 5mg group, and 9.2% in the 10mg group. Based on these numbers, it was concluded that adverse events were more common in the placebo group showing that the medication was effective. Serious adverse events were most commonly related to the gastrointestinal system.

Among adverse events in ACT 1, basal-cell carcinoma developed in one patient treated with 10 mg of infliximab. In ACT 2, basal-cell carcinoma developed in one patient who received placebo, and rectal adenocarcinoma developed in one patient treated with 5 mg of infliximab. Three neurologic events occurred only in patients treated with infliximab. One patient in ACT 2 (receiving 5mg of infliximab) presented a lupus-like reaction (Rutgeers et al.,2005).

The incidence of infections was similar among the groups in both studies. In ACT 1, infections occurred in five patients in the placebo group, three patients in the group receiving 5 mg of infliximab, and eight patients in the group receiving 10 mg of infliximab. In ACT 2, severe infections occurred in one patient in the placebo group, two patients in the group receiving 5 mg of infliximab, and three patients in the group receiving 10 mg of Infliximab. In ACT 1, tuberculosis developed in one patient treated with 10 mg of infliximab (Rutgeers et al., 2005).

This study proves that Infliximab is twice as likely two induce clinical remission in patients with moderate to severe ulcerative colitis in comparison to a placebo. Because the results of the study proved to be positive for adult patients put on Infliximab doctors wanted to use this drug to treat young children failing to respond to other medical therapy as well. Consequently, a study was done to test the safety and efficacy of the use of Remicade in pediatric patients with a moderate to severe form of the disease. A total of 60 pediatric patients ranging from ages 6-17 years old who had active ulcerative colitis and had not responded to or tolerated other treatment options like immuno-suppressants, steroids or 5ASA, were given 5 mg/ of infliximab at weeks 0, 2, and 6. The primary end point was response at week 8. At week 8, those whose responded well to the drug were randomly assigned to groups given Infliximab every 8 or 12 weeks and were monitored through week 54 (Hyams et al., 2012).

Results

The study done proved Remicade to be highly effective in treating children with moderate to severe form of the disease. At week 8, Infliximab induced a response in 73.3% of patients. Additionally, 68.3% of patients achieved mucosal healing at week 8. Those who achieved remission at week 8, were randomly assigned to receive Infliximab, 5mg every 8 weeks through week 46 or every 12 weeks through week 42. At week 54, twice as many patients in the group that received Remicade every 8 weeks achieved remission compared with the group that received Remicade every 12 weeks. Serious unfortunate events and infusion reactions occurred in comparable quantities in the 8 and 12 week groups. No deaths, cancers, serious infections, or tuberculosis were reported in either group given Remicade. Infliximab was safe and effective, inducing a response at week

8 in 73.3% of pediatric patients with moderate to severely active ulcerative colitis who did not respond to other medical intervention. Those given the every 8 week infusion ended up with a higher clinical remission rate than those who were given infusion every 12 weeks (Hyams., 2012) .

Today, Remicade is approved for children and adults. It is known to be one of the most effective methods of treatment for those suffering with an active state of the disease. Remicade is known to save people form undergoing a complete colectomy in addition to giving them a new lease on life. The studies above help strengthen this point showing how effective this biologic can be.

Adalimumab

Another biologic on the rise is known as Humira has been approved by the FDA in 2012. Humira is a treatment method for moderate to severe active ulcerative colitis in adult patients who have failed to respond to conventional therapy. Humira is a fully humanized monoclonal antibody against TNFa. Unlike Remicade, Humira is administered subcutaneously. Because Adalimumab is fairly new on the market it is still being tested today. The main studies that assessed the effectiveness of Adalimumab in UC are the induction and maintenance trials, known as ULTRA 1 and ULTRA 2 (Ammuzi et al., 2013).

ULTRA 1 was an 8 week randomized, double-blind, placebo controlled trial studying the use of Humira as an induction therapy in patients with moderate- severe UC despite the use of conventional therapy. In the ULTRA 1 trial 576 patients were randomly selected to receive either placebo or one of two different regimens of Adalimumab. The first regimen was 160/80mg. patients were given 160mg at week 0 followed by 80mg at week 2 and 40mg at weeks 4 and 6. The second regimen was 80/40mg. 80mg were given at week 0, 40mg were given at week 2, 4, 6. At the same time patients were still receiving stable treatment with oral corticoid steroids or immunosuppressants (Sandborn et al., 2013).

The primary endpoint of the trail was clinical remission at week 8. The patients who participated had moderately to severely active UC, with a Mayo score of 6–12 and simultaneous treatment with at least oral corticosteroids, mercaptopurine/AZA or did not respond or could not endure prior corticosteroids or immunomodulators.

The primary endpoint of clinical remission was achieved with the higher dose of Adalimumab 160/80mg showing results of 18.5% percent response and 9.2% placebo. The amount of patients who achieved clinical remission at week 8 in the placebo group compared to the group receiving Humira at a regimen of 80/40mgand 80/40mg was a difference of point .6%. These

results show that Humira is much more effective when given to patients at a higher regimen. Additionally, Adalimumab treatment was tolerated well at both doses. The safety profile was comparable to that of placebo. Ulcerative colitis was the most common adverse event which led to discontinuation of 4% of the placebo group, 3.8% of the 80/40mg group and 3.6% of the 160/80mg group (Sandborn et al., 2013).

ULTRA 2 was a 52 week study evaluating the efficacy of Humira as a maintenance therapy in UC patients. The ULTRA 2 trial included 494 patients displaying moderate-severe ulcerative colitis and failed to respond to conventional treatment. ULTRA 2 evaluated patients through week 52 but did not have an open-label phase after induction like in ULTRA 1. ULTRA 2 included two treatment possibilities: 248 patients received Adalimumab 160/80mg (160 mg at week 0, 80 mg at week 2, and 40 mg every other week starting at week 4) and a placebo group consisting of 246 patients. Participants were randomly assigned to treatment groups. The two primary endpoints were remission at week 8 and 52 (Sandborn et al., 2013).

Overall, clinical remission at week 8 was achieved in 16.5% of patients on Humira compared to 9.3% on placebo. The results for week 52 for the Adalimumab and placebo groups were 17.3% and 8.5%. Secondary endpoints encompassed clinical response and mucosal healing. The differences between adalimumab and placebo were substantial at weeks 8 and 52 in favor of adalimumab (Ammuzi et al., 2013).

A subclass analysis of ULTRA 2 evaluated the one-year maintenance outcomes in patients who responded to therapy with Adalimumab. Patients who attained clinical response at week 8 were evaluated at week 52 to determine if they achieved several outcomes such as clinical remission, clinical response and mucosal healing. At week 8, approximately half of the Humira treated patients achieved clinical response. Of those, 30.9% from the placebo, 49.6% for the 160/80mg and 43.1% for the 80/40mg achieved clinical remission, clinical response and mucosal healing at week 52. Furthermore, of the week 8 responders who were dependent on corticosteroids, 21.1% achieved steroid-free remission and 37.8% were able to discontinue steroids at week 52 (Sandborn et al., 2013).

Aside from the ULTRA trials, there is further clinical experience on the use of Adalimumab for UC. Data from a study on a small group of 30 patients from Spain validated that Adalimumab induction and maintenance therapy was effective in patients who previously failed other therapies including infliximab. At weeks 4 and 12, clinical response was achieved in 16 (53%) and 18 (60%) of patients, and clinical remission was achieved in 3(10%) and 8 (27%) of the patients. Adalimumab was continued in 50%

of the patients after the 48week follow-up. Total colectomy was necessary in six (20%) of patients. Nevertheless, patients who reached clinical response at week 12 evaded colectomy over the long term (Denese et al., 2013).

Adalimumab vs. Infliximab

Real-life data on the use of anti-TNF agents in UC was obtained from a Canadian group. This was a forthcoming study with a long-term follow-up of 53 patients treated with either Remicade or Humira. Effectiveness was evaluated using physician's worldwide assessment focusing on stabilization of bowel frequency, nonappearance of blood with defecation and tapering of corticosteroids until it can be discontinued. Responses to induction therapy were 96.4% for infliximab and 80% for Adalimumab. Responses to maintenance therapy were similar: infliximab 77.8% and Adalimumab 70.0% (Denses et al.,2013).

Based on research present above, Remicade tends to produce better results when given to patients with active disease. There haven't been any studies found showing that Remicade does not induce remission to those experiencing moderate to severe ulcerative colitis.

Administering biologics

However, due to the way the two biologics are administered may be enough of a reason for a patient to prefer one over the other. Remicade is administered as a 2-hour IV infusion so that it goes right into the bloodstream and starts to work. Doctors will normally give a patient 5mg per infusion. Some adult patients who at first respond to treatment or completely fail to respond to 5mg/kg may do well if their dose is increased to 10mg/kg. Remicade is first given at weeks 0, 2, and 6. Patients will then stay on maintenance therapy, which is every 8 weeks, which could be as few as 6times per year (REMICADE.com, 2014).

Humira, on the other hand, is given via self-injection under the skin, typically every other week (after the initial starting doses). Humira needs to be kept in a refrigerator in its original bottle and protected from light until it's ready to be used. The recommended dose regimen for adult patients taking Humira is 160 mg initially on Day 1 (given as four 40 mg injections in one day or as two 40 mg injections per day for two sequential days), followed by 80 mg two weeks later. When this is completed patients continue two weeks later with a dose of 40 mg every other week (HUMIRA.com, 2013).

Possible side effects

As always, all drugs come along with side effects. The usual side effects of biologics are nausea, headaches and fatigue. However, with time these side effects usually subside. More serious side effects have been experienced by patients especially those 65 years and older. Patients have had serious infections caused by viruses,

fungi or bacteria that have spread all through the body, including tuberculosis (TB) and histoplasmosis. Some of these infections have been deadly. Rare cancers have been reported in children and teenage patients taking TNF-blocker medicines. T-cell lymphoma, an uncommon form of deadly lymphoma, has transpired typically in teenage or young adult males with ulcerative colitis who were taking Remicade or Humira. (REMICADE.com, 2014; HUMIRA.com, 2013). To help prevent serious side effects, patients are required to go for blood work initially every other week and then monthly in order to monitor their blood count. Though the side effects listed above are scary, a patient needs to weigh the benefits and the risks together. Prolonged, untreated inflammation is the number one cause of colon cancer a number one leading death in the United States today.

Immunosuppressants + Biologics

Seeing the results biologics produce on their own, doctors questioned if combining immunosuppressants with biologics to treat patients would have an even greater outcome than just using biologics alone. Their thought process was as follows; the job of immunosuppressants is to stop the production of white blood cells by interfering with transcribing DNA and preventing the division and multiplying of many more white blood cells. Biologics on the other hand, are geared to stop an inflammatory response by binding with TNFa. Therefore, it was thought by combining these two drugs the likelihood of the patient achieving a remission is two times more likely than just treating them with one drug.

Initial data is available from a UC study that had a similar design to SONIC (which was a study designed to test the same combination in Crohn's patients) (Colombel et al., 2012). The study included 239 patients with moderate-severe UC who were unexperienced to biologics, were failing corticosteroids and were either unexperienced to AZA or had stopped AZA three months before entering the study. Patients were randomly assigned to receive AZA 2.5 mg/kg, infliximab 5 mg/kg or infliximab 5 mg/kg plus AZA 2.5 mg/kg for 16 weeks. The primary endpoint was steroid-free remission at week 16 and secondary endpoints included response and mucosal healing both at week 16. Preliminary results showed that the primary endpoint was achieved in the infliximab plus AZA group compared with the AZA alone. Additionally, infliximab plus AZA was greater to AZA or infliximab monotherapy in inducing steroid-free remission in patients. Patients treated with an infliximab plan of action were more likely to achieve response and mucosal healing than those treated with AZA monotherapy. What does this study mean for anti-TNF therapy moving forward? It is tough to make any precise conclusions and more data is needed. Nonetheless, the limited data (only from infliximab experience) point that anti-TNF therapy in combination with immunosuppressants may be more effective in early UC compared with monotherapy at

16 weeks. Though remission is achieved in a greater percentage when the two classes of drugs are combined, it is not recommended to combine the two because of increased risk of side effects (Denese et al., 2013).

Conclusion

Recent advancement in bio-technology have thankfully led to the development of a large array of new therapeutic agents intended to target the exact site in the multifaceted cascade of cytokine and chemokine effector molecules involved in UC pathogenesis. In particular, the introduction of the chimeric monoclonal antibody to TNFa has deeply affected the clinical treatment of moderate to severe ulcerative colitis, opening the door to a new era in the treatment of this disease. Studies discussed in this paper show the effectiveness of both Remicade and Humira given to patients with an active state of this disease. Additionally, doctors tested the possibility of combining a biologic with an immunosupressent. Though remission nearly doubled, side effects were likely to double as well. Therefore, doctors are not pushing the combination of the two drugs unless there is no other option.

With the recent introduction to biologics, patients suffering with ulcerative colitis in an unmanageable state are able to try a new treatment option with the hope of avoiding surgery. Remicade and Humira have both been proven to put patients with an active state of the disease into full remission.

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