

New biologics in the management of Crohn's disease: focus on certolizumab pegol

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Abstract: Crohn's disease (CD) is a chronic inflammatory condition involving the gastrointestinal tract characterized by recurrent exacerbations and remission. The disease frequently occurs in the lower part of the small bowel, but can affect any part of the digestive tract, from the mouth to the anus. The traditional goals of treatment of Crohn's disease were to induce and maintain clinical remission. More recently targets such as mucosal healing, reduced hospitalization and surgery, and improved quality of life are becoming increasingly achievable. The general principles for treatment should consider clinical activity, site and behavior of disease; however, the appropriate choice of medication depends on many factors that are the best tailored to the individual patient. This review focuses on certolizumab pegol, the first Fc-free PEGylated Fab' fragment of humanized monoclonal antibody that binds and neutralizes human tumor necrosis factor alpha. Data on indication, pharmacokinetics, efficacy, safety, and influence on quality of life are reviewed.

Keywords: Crohn's disease, certolizumab (CDP870), antiTNF- α agents

Introduction

Crohn's disease is a chronic inflammatory condition involving the gastrointestinal tract characterized by recurrent exacerbations and remission. The disease frequently occurs in the lower part of the small bowel, but can affect any part of the digestive tract, from the mouth to the anus. The most common symptoms are abdominal pain, often in the lower right region of the abdomen, diarrhea, often with blood and/or mucus in the stool, weight loss, anorexia, fever, and extra-intestinal manifestations (ie, localized to the eyes, skin, and joints).¹ In addition, approximately 10% of Crohn's disease patients have perianal fistulas at the diagnosis.²

The goal of treatment should be to induce clinical remission, while bearing in mind the most appropriate means of maintaining remission. This actually may require a "step up" regimen, where less potent/toxic approaches are used as first-line therapy, although in selected patients, a "top down" approach using as first-line biological therapy could be appropriate.

Epidemiology, genetic background and pathogenesis

A consistent geographical variation in incidence rates has been reported varying from 3.6 to 15.6 cases per 100,000 person-years in North America, 0.7 to 9.8 cases per 100,000 in Europe, and 0.5 to 4.2 cases per 100,000 in Asia.³

The wide regional and racial variation suggests an important genetic component in the pathophysiology of the disease or a distinct environmental contribution.

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The disease tends to occur slightly more frequently in women (50% to 60%) than in men,⁴ and while most patients are diagnosed in their twenties and thirties, about 10% to 15% are diagnosed in childhood.⁵

Crohn's disease is widely believed to originate from a dysregulated immune response to luminal bacteria, in a genetically susceptible host.⁶ The inheritance model is non-Mendelian but complex–polygenic, with several genes involved together and interacting with environmental factors.

Concordance data in monozygotic twins (36% to 58%) and the high relative risk for first-degree relative (up to 20 to 35) have provided strong epidemiological evidence for a genetic contribution.⁷ These observations led to development of genetic investigations with two broad strategies: one has investigated candidate genes whereas the other used hypothesis-free methods like genome-wide scanning.

The NOD2 gene (nucleotide-binding oligomerization domain 2) on chromosome 16q12 was the first susceptibility gene for Crohn's disease to be successfully identified in 2001 among Caucasians.⁸ NOD2 gene encodes an intracellular receptor predominantly expressed in monocytes and Paneth cells.⁹ The coded protein is activated by muramyl dipeptide (MDP), a component of peptidoglycan in bacterial cell walls and subsequently will activate the nuclear factor- κ B signaling pathway, and stimulate secretion of antimicrobial peptides including defensins.¹⁰ NOD2 variants are more prevalent in patients with ileal Crohn's disease and seems to predispose for a stricturing phenotype and need for surgery.^{11–16}

More recently, a number of genome-wide association studies¹⁷ and a meta-analysis¹⁸ have identified more than 30 Crohn's disease susceptibility loci.

The contribution of environmental factors is more puzzling. Given that the incidence of disease appears to increase as countries become more developed, it is likely that some components of disease are triggered by an industrial environmental (diet or changes in exposure to pathogens); moreover, higher incidence of disease is associated with higher socioeconomic status.⁹ Of the environmental factors thought to affect disease susceptibility, only smoking and appendectomy have a substantive evidence base.^{3,20}

In conclusion, the current hypothesis on pathogenesis suggests that Crohn's disease is the result of an exaggerated immune response against intestinal microflora by activation of T cells and overexpression of inflammatory cytokines in a genetically predisposed host.¹⁸ The classic immunological paradigm focuses especially on type 1 helper T-cell (Th1) cytokines, especially tumor necrosis factor alpha (TNF- α),

although more recently the Th17 pathway is receiving increasing attention.^{21,22}

Principles of medical therapy

The main goal of the treatment of Crohn's disease is to induce clinical remission. The appropriate choice of medication depends on many factors that are the best tailored to individual patient. The choice is often influenced by the balance between drug potency and site effects, previous response to treatment, or presence of extra-intestinal manifestation.

New therapeutic approaches over the last decade have focused on the immunological mechanisms associated with the pathogenesis of Crohn's disease, especially the blocking of TNF- α .

TNF is a proinflammatory cytokine which is a key mediator of inflammation. It can be detected at high concentrations in diseased areas of the bowel wall and in blood and feces of patients.^{26–28} AntiTNF- α acts by binding to both soluble and trans-membrane forms of TNF- α , inhibiting its immediate pro-inflammatory actions, and the production of other pro-inflammatory mediators. In vitro studies have demonstrated that antiTNF- α agents reduce the production of chemokines and upregulation of endothelial adhesion molecules; this in turn decreases the migration of inflammatory cells, reduces granulocyte-macrophage colony-stimulating factor (GM-CSF) production in intestinal mucosal T cells, and may in turn induce T cells apoptosis.

Infliximab was the first antiTNF- α antibody approved by FDA for treatment of Crohn's disease. However, its chimeric composition has been associated with problems of immunogenicity, which may lead to infusion reactions and loss of efficacy.²⁹ More recently several other biologics have been investigated for treatment of Crohn's disease: adalimumab, natalizumab, CDP871, and certolizumab. The last named has been approved by FDA for adults with moderate to severe Crohn's disease not responding to conventional therapy.³⁰

Our aim is to provide a comprehensive, up-to-date review of indication, pharmacokinetics, efficacy, safety, and influence on quality of life of certolizumab.

Mechanism of action of certolizumab pegol (CDP870)

Certolizumab pegol is the first Fc-free PEGylated Fab' fragment of humanized monoclonal antibody that binds and neutralizes human TNF- α . The pharmacokinetic properties of the Fab' fragment in vivo are usually poor. However, attachment of the 40 kDa polyethylene glycol (PEG) moiety markedly increases the half-life of certolizumab to a value

comparable with that of the whole-antibody product. The Fab' fragment was engineered with a single free-cysteine residue in the hinge region, which enables site-specific attachment of PEG without affecting the ability of the Fab' fragment to bind and neutralize TNF- α . The structure of certolizumab pegol differs from that of other antiTNF- α agents that have been tested for treatment of Crohn's disease. Infliximab, adalimumab, and etanercept are all based on the human IgG1 Fc, are capable of fixing complement and binding to Fc receptors, and therefore have the potential for Fc-mediated effect.

The mechanisms of action believed to be essential for the efficacy of antiTNF- α agents in Crohn's disease are:

Induction of apoptosis of both monocytes and T cells;^{31–34}

Neutralization of soluble and membrane-bound TNF- α ;³³

Antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC);³⁵

Reverse signaling via mTNF- α .³⁶

In vitro studies have demonstrated that infliximab, certolizumab, adalimumab, and etanercept are all able to neutralize soluble TNF- α and membrane-bound TNF- α . Infliximab and adalimumab are comparable in their ability to mediate complement-dependent cytotoxicity, and antibody-dependent cell-mediated cytotoxicity. Moreover, they equally increase the proportion of cells undergoing apoptosis and the level of granulocyte degranulation. Etanercept mediated these effects to a lesser degree, while certolizumab pegol did not exhibit increased levels of apoptosis, suggesting that these mechanisms are not essential for the efficacy of antiTNF- α agents in Crohn's disease.³² This probably happens because certolizumab pegol does not contain Fc region, which is normally present in a complete antibody, and therefore does not fix complement or cause antibody-dependent cell-mediated cytotoxicity.³⁸

Despite the fact that certolizumab pegol is a monovalent antibody fragment, its in vitro potency is greater than that of bivalent antibody adalimumab and infliximab.³⁹

The site-specific addition of two molecules of PEG to the antibody fragment increases the plasma half-life to approximately 2 weeks, thus reducing the frequency of dosing.

Efficacy study of certolizumab pegol (CDP870)

At the moment three clinical trials have evaluated the short-term efficacy of certolizumab for induction of clinical response and remission in patients with active Crohn's disease.⁴⁰

In these studies the clinical response was defined as a decrease of ≥ 100 points from baseline Crohn's Disease

Activity Index (CDAI) and remission was defined as a CDAI score of ≤ 150 points.

The phase II trial by Winter⁴¹ was a randomized, multicenter, placebo-controlled study, which aimed to evaluate the efficacy and safety of a single intravenous (iv) administration of different doses of certolizumab in adult patients with moderate to severe Crohn's disease. At the screening, patients were randomized into four treatment groups: certolizumab 1.25 mg/kg, 5 mg/kg, 20 mg/kg, or placebo. The 5 mg/kg dose of certolizumab was equivalent to a 400 mg subcutaneous dose of certolizumab. Ninety-two adult patients were enrolled into the study and were permitted to receive concomitant medication (azathioprine, methotrexate, antibiotics, mesalazine, corticosteroids) provided that dose had been stable prior to the start of the study. No significant differences in baseline demographics between treatment groups were found.

At week 4 (primary endpoint) there were no statistically significant differences in clinical response for any of the certolizumab groups compared with placebo (Table 1). A post-hoc analysis at week 2 indicated that the certolizumab 10 mg/kg dose had induced remission in a statistically significant number of patients compared with placebo: 47.0% (95% CI 0.4–73.7) vs 16% (95% CI 0.0–32.4) ($p = 0.041$). Moreover, at week 4 47.1% of patients treated with certolizumab 10 mg/kg were in remission compared with 20% of placebo group. However, these rates of response were not sustained at week 12 when only 23.5% of patients in certolizumab 10 mg/kg were in remission compared with 32% of patients in the placebo group.

The lack of difference of clinical response between the certolizumab-treated groups and placebo was probably due to the high response rate observed in the placebo group (52% to 60%). This finding was in contrast to the relatively low placebo response rate observed in a similar study with infliximab (12% to 17%). Patient response rate may be influenced by a variety of factors, such as use of corticosteroids, surgery and concomitant therapy. In addition, high placebo response rates may also be an artifact of the calculation of CDAI score, because of the high degree of subjectivity of this index as an indicator of disease activity.

Table 1 Clinical response to certolizumab pegol (CDP870) vs placebo at week 4⁴¹

CDAI	CDP870 dose			Placebo
	5 mg/kg	10 mg/kg	20 mg/kg	
Response (%)	60.0	58.8	47.8	56.0%
(95% CI)	(38.8–81.2)	(32.5–85.2)	(25.2–70.4)	(34.5–77.5)

The phase II, multicenter, randomized, double-blind placebo-controlled, dose-response trial by Schreiber et al was designed to assess the efficacy and safety of subcutaneous certolizumab 100 mg, 200 mg, 400 mg, or placebo administered at week 0, 4, and 8.⁴² Efficacy assessments were performed every 2 weeks up to week 12, with a further 8-week follow-up evaluation for safety. A total of 291 patients were included in the study. Concomitant therapy with steroids, mesalamine or immunosuppressants was permitted if the patient was on a stable dose that could be continued throughout the 12-week duration of the double-blind phase. Patient characteristics were generally well balanced among treatment groups, although the mean age of patients receiving certolizumab was higher than in the placebo group. The greatest difference among the groups was a small preponderance of women in the placebo group. The use of concomitant medications were broadly similar among groups; the greater difference was observed for overall glucocorticoid use: 39.7% in the placebo group and 30.6% in the certolizumab 400 mg group.

For the primary endpoint, all doses of certolizumab produced at week 2 a statistical benefit compared with placebo (Table 2). Certolizumab also showed significantly higher efficacy compared with placebo at week 4, 8, and 10 (only for 400 mg dose). Patients receiving the 400 mg dose showed the highest response rate at all time points, with the highest response observed at week 10 (52.8% vs 30.1% in placebo group). However, at week 12 the difference between the certolizumab- and placebo-treated groups did not reach statistical significance. There was no effect of gender or concomitant therapy on the clinical response rate. The same was observed for the remission rate at weeks 4 and 12. A post-hoc analysis according to baseline C-reactive protein (CRP) concentration was performed since CRP serum concentration usually provides an objective criterion of inflammatory activity.⁴³ Increased serum concentrations of CRP have been reported as a regular feature of patients with active disease. In asymptomatic patients, increased levels of this protein may indicate subsequent clinical relapse. Indeed, in patients with baseline CRP levels of 10 mg/L or greater, treatment with certolizumab 400 mg resulted in a statistically significant benefit at all time

points throughout the 12-week study in terms of both rates of clinical response and remission. In patients with baseline CRP less than 10 mg/L, none of active treatments achieved a statistical difference from placebo, both of clinical response and remission rates. In patients with baseline CRP concentration ≥ 7 to 10 mg/L who received certolizumab 400 mg, the clinical response rates at week 12 showed statistically significant difference from placebo. Accordingly, placebo response rates decreased with increasing baseline CRP level.

The phase III randomized, double-blind, placebo-controlled trial by Sandborn et al PRECISE 1 (Pegylated antibody fRagment Evaluation in Crohn's dIsease: safety and Efficacy 1)⁴⁴ was designed to evaluate the efficacy and safety of certolizumab 400 mg or placebo subcutaneously at week 0, 2, 4 and then every 4 weeks. Patients were followed through week 26. Randomization was performed centrally and was stratified according to the serum level of CRP (≥ 10 mg/L <10 mg/L) and concomitant therapy. Patients could receive concomitant therapy with stable doses of mesalamine, steroids, and immunosuppressive drugs. The baseline characteristics were similar in the two groups of patients. The study was conducted on 662 adults with moderate-to-severe Crohn's disease. Among patients with a baseline CRP level of at least 10 mg/L, 37% of patients in the certolizumab groups had a response at week 6 as compared with 26% in placebo group ($p = 0.04$). In the overall population, response rates at week 6 were 35% in the certolizumab group and 27% in the placebo group ($p = 0.02$). At weeks 6 and 26, 23% of patients in the certolizumab groups had a response compared with 16% of patients in the placebo group ($p = 0.02$). Use of immunosuppressive agents, concomitant steroids, previous treatment with infliximab and smoking status were not associated with the magnitude of response. At week 26, 30% of patients in the certolizumab group had fistula closure as compared with 31% in the placebo group.

Another important endpoint is to achieve and maintain long-term remission in Crohn's disease. Two studies have assessed the long-term efficacy of certolizumab for maintenance of response and remission, PRECISE 2⁴⁵ and PRECISE 3.⁴⁶ In PRECISE 2, there was an induction phase in which 668 patients received three subcutaneous injections doses of certolizumab 400 mg at week 0, 2, and 4. At week 6, 64.1% patients (428/668) had clinical response and were then randomized to the maintenance phase, receiving certolizumab 400 mg/kg or placebo every 4 weeks up to week 26. At week 26, in the certolizumab group response rate was 63% compared with 36% in the placebo group ($p < 0.001$); in addition, 48% of patients in the certolizumab group had

Table 2 Global benefit at week 2 post-injection of certolizumab pegol (CDP870) vs placebo⁴²

Placebo	15.1% (95% CI, 6.2–24.0)
CDP870 100 mg	29.7% (95% CI, 18.6–40.8) ($p = 0.033$)
CDP870 200 mg	30.6% (95% CI, 19.2–41.9) ($p = 0.026$)
CDP870 400 mg	33.3% (95% CI, 21.8–44.9) ($p = 0.010$)

remission at week 26 compared with 29% in the placebo group ($p < 0.001$).

The study was centrally randomized and group assignment was stratified according to serum CRP level (≥ 10 mg/L or < 10 mg/L), concurrent use of steroids, and immunosuppressive agents. In the intention to treat analysis, response rates at week 26 were greater among patients receiving maintenance therapy with certolizumab than among those receiving placebo, both for patients receiving concomitant immunosuppressive agents (61% vs 33%) ($p < 0.001$) and those without (64% vs 39%) ($p < 0.001$). No significant interactions between group assignment and smoking status or body mass index were found.

Among patients with a baseline CRP serum level of less than 10 mg/L, response rates at week 26 were significantly greater in the certolizumab group (64%) compared with placebo groups (39%) ($p < 0.001$); similarly remission rate was 54% in the certolizumab group compared with 31% in the placebo group ($p < 0.001$).

The PRECISE 3 was an open label extension study that recruited patients from PRECISE 1 and 2. Patients enrolled received certolizumab 400 mg subcutaneously every 4 weeks. Two populations were analyzed: patients induced and treated for 24 weeks with certolizumab (PRECISE 1 and 2); patients who responded to induction therapy with certolizumab, but were than randomized to placebo in PRECISE 2.

At week 80, more than 80% of patients achieved a clinically meaningful response and remission rate. Therefore, certolizumab 400 mg administered every 4 weeks was an effective long-term maintenance therapy for patients who had responded to certolizumab induction therapy.

PRECISE 4 was an open label extension study that assessed the effectiveness of re-induction followed by maintenance therapy with certolizumab in patients who had experienced a significant clinical worsening of Crohn's disease.⁴⁷ Patients who withdrew after week 2 in PRECISE 1 or week 6 in PRECISE 2 with clinical worsening entered in PRECISE 4 and received re-induction with certolizumab 400 mg subcutaneously at week 0, 2, 4 and then every 4 weeks. The rates of response at week 4 (45.7%), 24 (57.1%) and 52 (69.3%) indicated that re-induction with a single dose of certolizumab followed by a standard 4-weekly stable dose could restore clinical response and remission.

Another important issue to evaluate is the efficacy of certolizumab in patients previously treated with infliximab.

About one third of patients with active Crohn's disease who had been treated with infliximab had no response to this drug after three induction doses.⁴⁸ In addition, about one third

of patients who might initially respond to infliximab therapy may subsequently lose the response or become intolerant over the first year of therapy. In PRECISE 2 a significant difference in the response rate at week 26 between the certolizumab group and the placebo group was found for patients who had previously received infliximab (44% vs 25%) ($p < 0.001$).

In WELCOME, a 26-week open label induction, double-blind maintenance trial,^{40,49} 539 patients who had loss of response or intolerance to infliximab received certolizumab 400 mg subcutaneously at weeks 0, 2, and 4. At week 6, 62.2% patients had clinical response and 39.3% had remission.

These data were confirmed a study that reported the efficacy of certolizumab for induction of response and remission in a case series of 21 Crohn's disease patients who were refractory or had lost response to infliximab.⁵⁰ At week 4, 52% patients achieved clinical response and 42% were in remission.^{40,50} These findings are in contrast with CHARM,⁵¹ which reported efficacy of adalimumab as maintenance therapy for moderate to severe Crohn's disease. In this trial, patients who were naïve to antiTNF therapy had slightly better results at weeks 26 and 56 than patients who had previously received antiTNF therapy; however the difference did not reach statistical significance.

The concomitant use of immunomodulator with an antiTNF agent has been a topic of great interest and debate. Initially, it was assumed that the use of concomitant immunomodulators could improve the efficacy of antiTNF- α therapy (specifically infliximab), probably by decreasing immunogenicity. Subsequently, data emerged suggesting that the efficacy of TNF antagonists used as monotherapy was equivalent to combination therapy with TNF antagonists and immunomodulators.⁵² Preliminary data from the pivotal SONIC (Study of Biologic and Immunomodulator Naïve Patients in Crohn's Disease) trial have been reported.⁵³ This study compared the efficacy outcomes in patients with Crohn's disease naïve to immunomodulators treated with azathioprine, infliximab, or a combination of azathioprine and infliximab. Patients eligible for the study had received previous treatment only with corticosteroids and/or 5-aminosalicylates. Due to the characteristics of the inclusion criteria, patients had a short duration of Crohn's disease, approximately 2 years before study entry. Week 26 steroid-free remission (CDAI < 150) was the primary endpoint, with week 54 endoscopic remission as a second important endpoint. At week 26, patients receiving azathioprine in combination with infliximab had the highest rate of remission (57%) compared with infliximab alone

(44%) or azathioprine alone (30%). Endoscopic remission rates paralleled clinical remission rates, and patients on combination therapy fared the best, while those receiving infliximab alone fared second best, and those on azathioprine alone fared the worst. Mucosal healing at week 26 was shown in 43.9% of the patients treated with infliximab + azathioprine, 30.1% of those treated with infliximab alone, and 16.5% of those treated with azathioprine alone.

Certolizumab safety

A recently study⁵¹ analyzed the safety data collected from patients who were enrolled in the different clinical trials using certolizumab. 1313 patients who had received continuous treatment with certolizumab 400 mg were entered in the study. All patients received ≥ 4 week of certolizumab and were stratified into 4 groups based on the duration of treatment (> 3 months; > 6 months; > 9 months; > 12 months). Rates of common adverse event were stable across exposure categories with the exception of infections, which increased with duration of exposure to certolizumab (47.5% if > 4 weeks vs 60% if > 6 months).

In PRECISE 1 there were 4 cases of cancer (2 in the certolizumab group and 2 in the placebo group) and 7 cases of serious infections (2%) in the certolizumab group and 3 cases in the placebo group (1%).

In PRECISE 2 serious adverse events occurred in 6% of patients in the certolizumab group and 7% in the placebo group.

Although these results indicate that certolizumab does not increase the risk of serious adverse events, they should be interpreted with caution because the sample size was not large and the follow up might not have been long enough to pick up serious adverse events. Moreover, differences in the molecular structure compared with the other antiTNF agents may explain the different side-effects but data are lacking thus far.

Another issue is the potential development of anti-certolizumab antibodies and their clinical implications. In Schreiber's study,⁴⁵ anticertolizumab antibodies were found in the 12.3% of patients receiving certolizumab 400 mg while in PRECISE I anticertolizumab antibodies were found in

the 8% of patients and 4% of those receiving concomitant immunosuppressive therapy.⁴⁴ The plasma concentration of certolizumab appeared to be lower in the presence of antibodies, but no decrease in efficacy was reported.

Comparative efficacy of infliximab, adalimumab and certolizumab

Three antiTNF agents have been approved by the FDA for treatment of Crohn's disease (Table 3). However it is difficult to directly compare the efficacy of certolizumab with infliximab and adalimumab in the absence of head-to-head studies. Nevertheless, the results of maintenance trials of these three drugs are similar; basically patients who had a clinical response at an early time point were randomized to receive either placebo or antiTNF agents and the rates of remission were taken at weeks 26 and 30.

In ACCENT1,⁵² the maintenance trial with infliximab, 58% of patients responded to open label therapy at week 2 and 30; 39% of patients were in remission on infliximab 5 mg/kg compared with 21% patients receiving placebo.

In CHARM,⁵³ the maintenance trial with adalimumab, 58% patients responded to open label therapy at week 4 and 26 compared with 40% patients receiving placebo.

In PRECISE 2 study,⁴⁵ 64% patients responded to certolizumab 400 mg; 48% were in remission compared 29% patients in the placebo group.

Therefore the efficacy of these three agents for induction and remission was roughly similar. At the moment selection of antiTNF agents for induction or salvage therapy is based on local availability and regulatory restriction. However, while adalimumab and certolizumab have proven effective in patients with loss of response to infliximab, no controlled data on infliximab as salvage therapy are available.

Effect of certolizumab on quality of life

Patients with Crohn's disease have poor health-related quality of life (HRQL). This is usually estimated with the inflammatory bowel disease questionnaire (IBDQ) which assesses 4 aspects of a patient's life:⁵⁴

Table 3 Principal characteristics of infliximab, abalimumab and certolizumab

	Infliximab	Adalimumab	Certolizumab
Biological characteristics	Recombinant chimeric mouse-human nonoclonal antiTNF- α antibody	Recombinant fully human monoclonal antiTNF- α antibody	Fc-free pegylated antiTNF- α
Apoptotic effects	Yes	Yes	No
Administration route	Intravenous	Subcutaneous	Subcutaneous

- 1) symptoms directly related to primary bowel symptoms;
- 2) systemic symptoms;
- 3) emotional function;
- 4) social function.

The IBDQ scores range from 32 to 224, higher scores indicating better quality of life. An increase of at least 16 points in the total score is regarded as clinically meaningful.⁵⁵

In Schreiber's phase II study, for all treatment groups, there was an increase in IBDQ total scores within 2 weeks of treatment that paralleled the change in CDAI scores. The large change from baseline at week 2 was observed in the certolizumab 400 mg group (22.8 points compared with 10.6 points in the placebo group) ($p = 0.002$). At week 12, the IBDQ total scores were 156.5 ± 37.36 in the certolizumab group compared with 140.5 ± 35.88 in the placebo group.⁴²

In PRECISE 2, 60% patients in the certolizumab group had a IBDQ response at week 26 compared with 43% in the placebo group ($p < 0,001$).

These data suggest that certolizumab 400 mg might significantly improve the quality of life in patients with moderate to severe Crohn' disease.

Conclusion

AntiTNF agents have an important role in the treatment of Crohn's disease refractory to conventional therapy. Compared with adalimumab and infliximab, certolizumab pegol is similarly effective for a rapid induction of response (about 50% of patients) and long-term maintenance of clinical response or remission.

Moreover, certolizumab significantly improves quality of life in patients with active Crohn's disease.

Certolizumab appears to be safe since no clinical trials have reported an increased risk of serious adverse events; however, more data from longer duration studies and larger numbers of patients are still needed.

Of note, certolizumab might be an additional treatment option in patients who have lost response to or were intolerant to other antiTNF agents.

Disclosures

The authors have conflicts of interest to disclose.

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