

ORIGINAL PAPERS

Initial experience with golimumab in clinical practice for ulcerative colitis

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ABSTRACT

Background: Golimumab is a TNF-blocking agent indicated as a second-line therapy in ulcerative colitis.

Purpose: To research the effectiveness and safety of golimumab in patients with ulcerative colitis in clinical practice.

Methods: Retrospective study of the effectiveness and safety of golimumab in patients with ulcerative colitis. All patients received golimumab 200 mg subcutaneously at week 0, and golimumab 100 mg subcutaneously at week 2. After the induction treatment, each patient received 50 mg sc. every 4 weeks in patients with body weight less than 80 kg, and 100 mg every 4 weeks in patients with body weight greater than or equal to 80 kg.

Results: Study of a group of 23 ulcerative colitis patients, 7 of whom were naive to any anti-TNF therapy, and 16 patients who had previously been treated with an anti-TNF agent other than golimumab (non-naive patients). The average treatment time with golimumab was 14.3 weeks. Globally, withdrawal of corticosteroids was observed in 74% of cases. Clinical response was observed in 85.5% of patients who had not received biological treatment previously, and in patients who had previously received biological treatment the response rate was 75%.

Conclusions: In this short study, golimumab seems to be an alternative treatment in naive and non-naive anti-TNF ulcerative colitis patients. It is also a safe therapy, given that there were no adverse effects in the patients studied.

Key words: Golimumab. Ulcerative colitis. TNF-blocking agent. Naive patient. Non-naive patient.

INTRODUCTION

Ulcerative colitis (UC) is a chronic disease characterized by diffuse mucosal inflammation within the colon, often with alternating periods of exacerbation and remission. Its treatment depends on the course or behavior of the disease, and although therapy with corticosteroids, 5-aminosalicylates, and immunomodulators is effective in most

cases, biological agents as anti-tumor necrosis factors (TNF) are necessary in cases where the disease is refractory or intolerant to therapeutic agents (1). The consequence of treatment failure in UC patients is a greater number of colectomies, and a possible alternative therapy in UC patients is a TNF-blocking agent, which has been shown to be effective, inducing clinical response and remission, and reducing the need for colectomy (2,3).

Golimumab is a recently introduced TNF-blocking agent. It is a completely human IgG₁ anti-TNF- α antagonist, subcutaneously administered, approved in 2013 by the European Medical Association (EMA) and Food and Drug Administration (FDA) for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to conventional therapy, including corticosteroids, 6-mercaptopurine and azathioprine, or who are intolerant to or have medical contraindications for such therapies (4). As golimumab was marketed only a short time ago, there are few data about its effectiveness and safety.

The objectives of this research were to analyze the response to golimumab in patients with ulcerative colitis in real clinical practice, and to assess any adverse effects during the treatment. The hypothesis *a priori* is that golimumab is a safe and effective therapy in these patients.

METHODS

A retrospective study was carried out in UC patients treated with golimumab in several hospitals in Andalusia (Spain). For this type of study formal consent is not required.

All patients received golimumab 200 mg subcutaneously at week 0 and golimumab 100 mg subcutaneously at week 2. After the induction treatment, each patient received, in accordance with the data

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sheet of the EMA (4), 50 mg sc. every 4 weeks in patients with body weight less than 80 kg, and 100 mg every 4 weeks in patients with body weight greater than or equal to 80 kg.

The Montreal classification (5) was used to characterize patients, considering the extent of the disease (E1: ulcerative proctitis; E2: left-sided UC, also known as distal UC; and E3: extensive UC) and its activity/severity (S0: UC in clinical remission; S1: mild UC; S2: moderate UC; and S3: severe UC). The Partial Mayo Score (6) was also considered for classifying patients.

The rate of response to the treatment was evaluated by the physician in terms of clinical (rectal bleeding and stool frequency reduction) according to the definitions of the European consensus on the diagnosis and management of UC (1). Clinical response was defined as a decrease from baseline in the partial Mayo score of at least 3 points, with an accompanying decrease in the subscore for rectal bleeding of at least 1 point or absolute subscore for rectal bleeding of 0 or 1. Also, reduction of the use of corticosteroids was considered.

Absolute figures were recorded, and mean values, ranges and percentages were calculated to show and analyze the results, using the SPSS software.

RESULTS

Twenty-three patients were included in this retrospective study, 18 (78.2%) men and 5 (21.7%) women, and the average age was 45 (range, 21-64). The mean age at diagnosis was 37.4 (range, 18-50). The mean time of the disease's progression was 7.5 years (range, 1-28).

Concerning the extent of the disease, 3 (15.8%) patients (2 men and 1 woman) had ulcerative proctitis (E1), 10 (43.4%) patients (8 men and 2 women) had left-sided UC (E2), and 10 (43.4%) patients (8 men and 2 women) had extensive UC (E3).

With regard to the disease's activity at the beginning of treatment with golimumab, 14 (60.9%) patients had moderate UC, and 9 (39.1%) patients had severe UC (S3). All of them were steroid dependent.

Previous therapies received by the patients are shown in table I. Seven (30.4%) patients had never received treatment with biological agents, 4 (17.4%) patients had previously received a biological agent, and 12 (52.2%) patients had previously received two biological agents. Treatments associated with golimumab were mesalazine (100%), azathioprine (52.1%) and mercaptopurine (4.34%).

The average duration of UC to the beginning of golimumab treatment was 83 months (range, 6-336 months). The average treatment time with golimumab was 14.3 weeks (range, 4-36 weeks).

Globally, withdrawal of corticosteroids was observed in 74% of cases. Clinical response was observed in 85.5% of patients who had not previously received biological treatment, and in patients who had previously received biological treatment the response rate was 75% (no statistically significant difference was observed) (Fig. 1).

Clinical response in patients naive to biological agents was 100% in patients with extent E2, and 50% in patients with extent E3. Fifty per cent of patients E1 had no response. Response in non-naive patients was 44.4% in patients with extent E2, 50% in E3 patients, and 100% in patients with extent E1. Only in 9% of patients a colonoscopy was performed after the treatment so mucosa healing was not considered in this study.

Finally, no relevant adverse effects were reported in any of the treated patients. Any treatment was stopped as a result of any adverse event.

Table I. Therapies before beginning golimumab treatment

<i>Drug</i>	<i>Patients</i>	<i>Dose</i>	<i>Withdrawal</i>	<i>Cause of withdrawal</i>
Corticosteroids	100%	30 mg/day (70-20 mg/day)	-	-
Mesalazine	100%	3 g/day (2-4.8 g/day)	-	-
Azathioprine (AZA)	100%	2.5 mg/kg/day	31.5%	Adverse effects
6-mercaptopurine, because of failure of AZA	4.34%	1.5 mg/kg/day	-	-
Metotrexate, because of failure of AZA	8.69%	25 mg SC/week	100%	Adverse effects
Ciclosporine	4.34%	250 mg/day	100%	Partial response
Infliximab	69.56%	5 mg/kg week 0, 2 and 6; thereafter, every 8 weeks	100%	18.7%: lack of efficacy 25.0%: adverse effects 50.0%: no response 6.3%: requested by patient
Adalimumab	52.17%	160 mg/80mg/40 mg, every 15 days	100%	25%: lack of efficacy 50%: no response 25%: adverse effects
Apheresis	4.34%	10 columns, according to regime	100%	Partial response

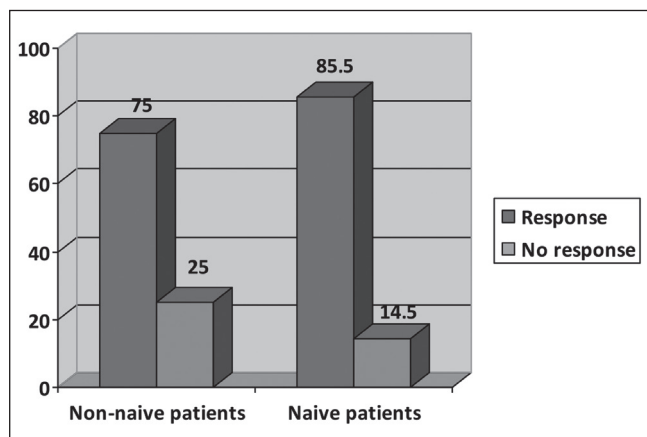


Fig. 1. Response to golimumab therapy in naive and non-naive patients.

DISCUSSION

The goals of UC therapy include resolution of gastrointestinal symptoms, healing of the colonic mucosa, prevention of long-term disease complications, and improvement of extra-intestinal symptoms; but no treatment achieves these objectives in each patient, and algorithms of therapy have been proposed (according to the course or behavior of the disease) including TNF-blocking agents (7,8).

This study shows the response to golimumab in a series of 23 UC patients. It is a first approximation to know results in patients with different UC activity, treated or not treated previously with biological agents. This research is not a prospective study, so it does not have the methodological characteristics of such studies. It is an analysis of the response to golimumab in clinical practice, without aiming to do anything more than showing our experience.

The PURSUIT-SC clinical trial recently demonstrated the efficacy of golimumab in patients with moderate to severe UC (9,10). It was effective in early remission as well as in long-term maintenance therapy. In our study, a good rate of response is obtained in UC patients and, perhaps, in patients naive to biological agents a better response is reached, although statistically significant differences were not observed between naive and non-naive biologic therapy patients. In PURSUIT-SC all patients were naive to anti-TNF therapy (previous treatment with TNF-blocking agents was an exclusion criterion), so we are showing the first experience (even though a very small one) of golimumab therapy in UC patients non-naive to anti-TNF therapy.

With regard to safety, anti-TNF agents have been related to uncommon but potentially serious adverse effects (11). In clinical trials of golimumab in patients with UC, the adverse events were rather similar in groups treated with placebo and golimumab, being mostly infectious problems or headache (9). In our study, we did not find any relevant adverse effect.

Nevertheless, the small number of patients included and the short length of treatment with golimumab (14 weeks) are important limitations of our study. So, though this study of real clinical practice reveals useful data, further studies about golimumab, and in larger series, are necessary to know the appropriate therapy in UC patients with different disease activity, different response to corticosteroids, and who have been previously treated with biological agents other than golimumab.

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