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ORIGINAL ARTICLE

Real-Life Effectiveness and Safety of Golimumab and Its Predictors of Response in Patients with Ulcerative Colitis

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Abstract

Background Golimumab is a new anti-TNF-alpha monoclonal antibody for patients with ulcerative colitis.

Aims To assess the short- and long-term effectiveness and safety of golimumab in daily clinical practice and to identify predictors of response.

Methods Consecutive patients treated with golimumab in 22 Italian centers were enrolled. Clinical, laboratory, and endoscopic data were prospectively collected before and during treatment. A subgroup of patients completed a questionnaire to assess personal satisfaction with a golimumab autoinjector system.

Results A total of 196 patients were included. After 3 months, 130 patients were responders (66.3%) and showed significant reductions in mean partial, total, and endoscopic Mayo scores and in mean ESR, C-reactive protein, and fecal calprotectin levels ($p < 0.001$). Multivariate analysis revealed that a higher total Mayo score ($p < 0.001$, OR 1.5, 95% CI 1.2–1.8) and naïve status to anti-TNF-alpha ($p = 0.015$, OR 3.0, 95% CI 1.2–7.5) were predictive of a favorable response. Seventy-seven (39.3%) of the 130 responders maintained a response at month 12 of therapy. There were 17 adverse events, 28 patients needed hospitalization, and 15 patients underwent surgery. Self-administration of the drug was appreciated by most patients.

Conclusions The efficacy and safety of golimumab in daily clinical practice were confirmed for the short- and long-term treatment of patients with active ulcerative colitis. Patients naïve to the anti-TNF-alpha monoclonal antibody and those with a higher total Mayo score were more likely to respond to golimumab.

Keywords Inflammatory bowel disease · Ulcerative colitis · Biologics · Golimumab · Anti-TNF-alpha

Introduction

Anti-TNF-alpha monoclonal antibodies are commonly used to treat patients with moderate to severe ulcerative colitis (UC) [1, 2]. It is estimated that about 15% of patients with inflammatory bowel disease (IBD) require a course of a biologic drug during their disease [3].

Golimumab was the first anti-TNF-alpha monoclonal antibody to be synthesized using transgenic mice transfected with human genes [4]. Golimumab can be easily self-administered by patients using the ergonomic Smart-Ject® autoinjector system. The efficacy and safety of induction [5] and maintenance [6] therapy with golimumab were evaluated in UC patients in pivotal trials (the PURSUIT program). Following approval and marketing of drugs, real-life studies are needed to validate the benefits already demonstrated in randomized controlled trials (RCTs). The results of real-world studies complement data obtained in RCTs to provide

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a complete picture of the advantages and disadvantages of medicines used in clinical practice [7].

To date, few studies have been published on patients with UC treated with golimumab in daily clinical practice [8–11]. However, these studies had a relatively small sample size, thus limiting the generalizability of their results. Recently, a prospective open-label, single-arm, phase 4 study focused its attention on clinical response and quality of life of 205 UC patients treated with golimumab at week 54 [12]. Real-life studies have identified some factors possibly associated with a better response rate, such as a lack of previous exposure to anti-TNF-alpha monoclonal antibodies and short duration of disease [8–11]. However, more studies are needed to strengthen the results of these observations.

The primary end point of the present study was to assess the effectiveness and safety of golimumab in a real-life setting. The secondary aim was to evaluate the predictors of response. We also assessed patients' satisfaction with a system to self-administer golimumab.

Materials and Methods

Study Design

We conducted a multicenter, open-label, observational study in a cohort of UC patients cared for in 22 centers in southern Italy, who were treated with golimumab from June 2015 to February 2018. There were no exclusion criteria. The study was approved by the ethics committee of the coordinating center, and all patients provided written informed consent for their participation.

Patient Characteristics

All patients had confirmed UC based on the standard combination of clinical, laboratory, endoscopic, and histologic findings [13] and had been diagnosed at least 3 months before study inclusion. According to the Montreal classification of disease extent [14], patients were divided into three groups: extensive colitis (inflammation extending over the splenic flexure), distal colitis (inflammation involving the colon up to the splenic flexure), and proctitis (inflammation limited to the last 15 cm of the colon-rectum). Demographic information (age, gender, smoking status) and clinical data (extent and duration of UC, previous therapy, comorbidities) were collected. Patients were also divided into active smokers, non-smokers, and ex-smokers. The partial Mayo score (PMS) was used to determine clinical activity and the endoscopic Mayo score (EMS) for endoscopic activity [15]. Detailed information concerning the indication for treatment with golimumab, previous therapy (if any) with anti-TNF-alpha monoclonal antibodies and the reasons for their suspension, as well as prescribed concurrent medication was also collected. Regarding indications for golimumab administration, patients were subgrouped as follows: steroid resistance, steroid dependency, failure of a previous anti-TNF-alpha agent, and extra-intestinal manifestations. Steroid resistance was defined as persistence of symptoms despite an adequate dose of steroids (prednisone 1 mg/kg or equivalent) for at least 2 weeks [16]. Steroid dependence was defined as symptom relapse within 3 months of steroid withdrawal or during tapering [16]. Patients previously exposed to other anti-TNF-alpha monoclonal antibodies were subgrouped as follows: intolerant (patients with adverse events requiring drug discontinuation), primary non-responders, patients with loss of response, and patients in remission in whom the anti-TNF-alpha therapy was suspended.

Biomarkers of inflammation, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and fecal calprotectin before and during golimumab therapy, were also measured.

Treatment Schedule

Golimumab was administered according to the approved protocol: 200 mg of the drug at time 0 and 100 mg after 2 weeks; as maintenance therapy, patients received 50 or 100 mg every 28 days, according to body weight (100 mg for patients weighing > 80 kg).

Study Endpoints

Efficacy and safety during the induction period were assessed after the initial 3 months of therapy, while the long-term effectiveness and safety of treatment were assessed after 12 months of continuous treatment. The requirement for either laboratory or endoscopic examination during the follow-up period was left to the discretion of the participating investigators. The only obligation was to check the PMS at 3-month intervals (including by phone interview). Endoscopic evaluation (at the discretion of centers) to assess response to induction was performed between 8 and 12 weeks after initiation of golimumab and for maintenance between 48 and 54 weeks.

Patients were considered responders if they had a reduction of > 2 points in the PMS from basal values and in remission if the PMS was < 2 (with no one item > 1). Concerning endoscopic response, patients were considered responders if they had an EMS of 0 or 1. Patients treated for

extra-intestinal manifestations were considered responders if presenting signs and/or symptoms improved or resolved. In these patients, UC activity was also assessed by evaluating clinical, endoscopic, and laboratory parameters (ESR, CRP, and fecal calprotectin). During the maintenance period, patients in clinical remission (PMS ≤ 2) or with very mild clinical activity (PMS < 4) were considered responders. Finally, acceptance of subcutaneous administration of golimumab was assessed in a subgroup of patients who were asked to complete a five-item Likert questionnaire [17] after 12 weeks of therapy. Questions focused on the ease of administration, possible pain and local effects, confidence in self-administering the drug, and overall satisfaction with the injection device.

Statistical Analyses

Continuous and categorical variables of the study group were reported as medians/interquartile ranges (IQR) and absolute/percentage frequencies, respectively, and were compared (between responders and those in remission) using the Mann-Whitney, Pearson chi-square or Fisher's exact tests, where appropriate. To explore differences between responders and non-responders, several patient-related parameters were included in univariate and multivariate analyses. Variables significant ($p < 0.05$) in univariate analysis were further tested by multivariate analysis using a stepwise logistic regression model with backward stepwise selection of terms. The Wilcoxon signed-rank test was used to investigate any changes in investigated variables before the initiation of golimumab and after 3 months of therapy. The time interval (in months) from the beginning of treatment to the first loss of response was evaluated using the Kaplan-Meier method.

All analyses were performed using the SPSS software package v.13 (Chicago, IL, USA), and p values ≤ 0.05 were considered statistically significant.

Results

Baseline Characteristics of Patients

A total of 196 patients (116 males) were enrolled in the study and had a mean age at diagnosis of 38.1 ± 15 years and a mean duration of disease of 9.0 ± 8.0 years. The majority of patients had never smoked ($n = 140$; 71%), while a small number were ex-smokers ($n = 35$; 18%) or active smokers ($n = 21$; 11%). According to the Montreal classification for disease extent, 113 patients presented with pancolitis (58%), 76 with distal colitis (39%), and 7 with proctitis (3%). At enrollment, the median PMS, median total Mayo score (TMS), and median EMS were 6 (IQR 5–7), 9 (IQR 7–10), and 2 (IQR 2–3), respectively. The median ESR, C-reactive protein, and fecal calprotectin values were 25 mm/1st hour (IQR 15–38), 3 mg/dl (IQR 1–9), and 250 mg/kg (IQR 175–500), respectively.

One hundred twenty-five patients (64%) were naïve to the anti-TNF-alpha monoclonal antibody therapy, while the remaining individuals had already been exposed to infliximab ($n = 47$), adalimumab ($n = 6$), or both ($n = 18$). Reasons for the discontinuation of previous anti-TNF-alpha treatment included intolerance in 22 (31%) patients, primary non-response in 7 (9.8%), and loss of response in 36 (50.7%); the remaining 6 patients (8.5%) had discontinued therapy because they had achieved complete remission. The indication for golimumab treatment was steroid-resistance in 38 (20%), steroid-dependence in 130 (66%), extra-intestinal manifestations in 6 (3%), and anti-TNF-alpha failure in 22 (11%). Regarding concurrent medications, 24 patients (12%) were treated with combination therapy (golimumab plus immunosuppressant), while 91 (46%) were on steroids at golimumab initiation. The median body mass index was 24 (IQR 22–27), and the median value of serum albumin was 4 g/dl (IQR 3–4). Seventy-five patients (38%) presented with significant clinical comorbidities for which concurrent therapies were deemed necessary. Twelve patients (6%) had latent tuberculosis and received isoniazid 300 mg/day, while 9 patients (4.5%) were HBV positive with a past or occult infection (all HBV-positive patients were followed up during the study with HBsAg and HBV-DNA evaluation every 3 months, and none received antiviral therapy during the study). Seventy-five (38%) had significant comorbidities (diabetes and/or ischemic or hypertensive heart disease), and 23 patients were > 65 years of age. The baseline characteristics of enrolled patients are shown in Table 1.

Induction of Response

One hundred thirty individuals (66.3%) were responders (a reduction of > 2 points on the PMS), and 47 (25%) showed complete clinical remission (PMS < 2) at 3 months of therapy (Fig. 1). Significant reductions in mean PMS ($p < 0.001$), TMS ($p < 0.001$), EMS ($p < 0.001$), ESR ($p < 0.001$), CRP ($p < 0.001$), and fecal calprotectin ($p < 0.001$) were observed after 3 months of treatment (Fig. 2). Thirty-three patients (44%) out of 75 who had a repeat endoscopy at 3 months showed mucosal healing. Of 91 patients receiving

Table 1 Baseline characteristics of enrolled patients

Number of patients (*n*)	196	–
Gender (*n*) (%)		
Female	80	41
Male	116	59
Age at diagnosis (mean ± SD) [median (IQR)]	38 ± 15	36 (25–48)
Disease duration at study inclusion (mean ± SD) [median (IQR)]	9 ± 8	7 (3–12)
≤ 2 years (*n*) (%)	37	19
> 2 years (*n*) (%)	159	81
BMI (mean ± SD) [median (IQR)]	25 ± 4	24 (22–27)
Smoking habit (*n*) (%)		
Active smoker	21	11
Non-smoker	140	71
Past smoker	35	18
Disease extent (*n*) (%)		
Pancolitis (E3)	113	58
Distal colitis (E2)	76	39
Proctitis (E1)	7	3
Naïve to anti-TNF-alpha (*n*) (%)	125	64
Previous anti-TNF-alpha (*n*) (%)	71	36
Infliximab	47	66
Adalimumab	6	8
Infliximab and adalimumab	18	26
Indication for golimumab (*n*) (%)		
Steroid resistance	38	20
Steroid dependence	130	66
Extra-intestinal manifestations	6	3
Failure of anti-TNF-alpha therapy	22	11
Latent tuberculosis (*n*) (%)		
No	184	94
Yes	12	6
Comorbidities (*n*) (%)[a]		
No	121	62
Yes	75	38
Reason for discontinuation of previous anti-TNF-alpha (*n*) (%)		
Intolerance	22	31
Primary non-response	7	10
Loss of response	36	50
Deep remission	6	9
HBV infection (*n*) (%)		
No	188	96
Yes	8	4
Concurrent immunosuppressants (*n*) (%)[b]		
No	172	88
Yes	24	12
UC activity at study inclusion (mean ± SD) [median (IQR)]		
Total Mayo score	8 ± 3	9 (7–10)
Partial Mayo score	6 ± 2	6 (5–7)
Endoscopic Mayo score	3 ± 1	2 (2–3)
ESR (normal values < 15 mm/1st hour)	29 ± 19	25 (15–38)
CRP (normal values < 0.5 mg/dl)	9 ± 16	3 (1–9)
Fecal calprotectin (normal values < 50 mg/kg)	418 ± 468	250 (175–500)
Patients on steroids at enrollment (*n*) (%)[c]		
No	105	54
Yes	91	46

[a]Clinically relevant comorbidities considered were diabetes and/or ischemic and hypertensive heart disease

[b]Concomitant immunosuppressants (23 patients were treated with thioprines and 1 with methotrexate)

[c]Patients on steroids at enrollment: patients receiving oral steroids at any dosages at initiation of golimumab

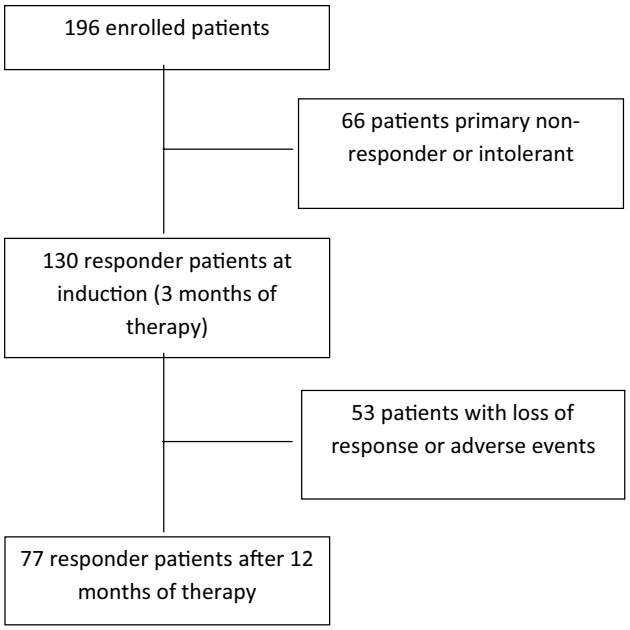

Fig. 1 Study flow chart of enrolled patients during the year of therapy with golimumab

corticosteroids at baseline, 34 (37.4%) were able to discontinue steroids after 3 months.

Response rates at month 3 in patients treated with golimumab as the first, second, or third anti-TNF-alpha treatment are shown in Fig. 3. A significantly higher proportion of patients were responders to golimumab when it was used as the first anti-TNF-alpha agent compared with patients who had previously failed two anti-TNF-alpha agents (72.8% vs. 44.4%, $p=0.015$).

Clinical response did not appear to differ among patients with intolerance, primary non-response, secondary failure, or complete response to a previous anti-TNF-alpha regimen. All six patients treated for extra-intestinal manifestations (three peripheral arthritis, two spondylitis, and one pyoderma gangrenosum) showed significant clinical improvement or resolution.

Factors Predictive of Response at 3 Months

When the baseline features of enrolled patients were considered, univariate analysis showed that naïve status to anti-TNF-alpha monoclonal antibody treatment ($p=0.01$), higher CRP values ($p=0.0001$), higher TMS ($p=0.0001$), higher PMS ($p=0.0001$), and higher EMS ($p=0.006$) were predictive of response to golimumab (Table 2). In multivariate analysis, only TMS ($p<0.001$, OR 1.5, 95% CI 1.2–1.8) and naïve status to anti-TNF-alpha monoclonal antibody ($p=0.015$, OR 3.0, 95% CI 1.2–7.5) were positive predictors of response.

Maintenance of Response

Ninety-nine patients (73%) received a maintenance dose of 50 mg/28 days of golimumab, while the remaining 39 (27%) received 100 mg/28 days. Dose was not escalated in any patient following loss of response because this was not allowed by the Italian Medicine Agency (AIFA). During the maintenance period, out of 130 responder patients at 3 months, 77 (59.2%) completed 12 months of therapy with golimumab, while 53 (40.8%) discontinued therapy because of loss of response or adverse events (Fig. 1).

The 77 long-term responders showed a stable PMS of ≤ 4 throughout the study period, with 66 of these (85.7%) achieving complete clinical remission with a PMS < 2 (Fig. 4). Of the 52 patients with a repeat endoscopy at 12 months, 36 (69%) also experienced endoscopic remission (EMS ≤ 1).

The median values of ESR, CRP, fecal calprotectin, PMS, TMS, and EMS during the year of treatment are shown in online supplementary Fig. 1. Univariate analysis did not identify any predictors of long-term response.

Safety

Seventeen patients experienced an adverse event during therapy (8.9%) and four (2.0%) a serious adverse event: a perianal abscess ($n=2$), active tuberculosis despite a negative TB Gold test before golimumab treatment ($n=1$), and *Clostridium difficile* infection ($n=1$). The other adverse events included skin reactions to golimumab (dermatitis localized at the site of drug injection), rhinosinusitis, and headache.

Seventy-five patients (38%) had significant comorbidities (diabetes and/or ischemic or hypertensive heart disease). Only three patients in this group developed adverse events, one of which was serious, which was not significantly different compared with patients without comorbidities. Four (17.4%) of the 23 patients over 65 years of age and treated with golimumab experienced adverse events, of which 2 were serious (8.7%). These results were not significantly different compared with those in younger patients (17.4% vs. 8%, $p=0.2$).

Hospitalization and Surgery

Twenty-eight patients (14.3%) were hospitalized for worsening UC ($n=24$, 85.7%) or severe adverse events ($n=4$, 14.3%), and 15 patients (6.5%) underwent colectomy. As expected, the rate of hospital admissions and surgery was significantly higher in the non-responder group than in the responder group (5.2% vs. 20.2%, $p=0.003$; 0% vs. 12.6%, $p=0.0005$, respectively).

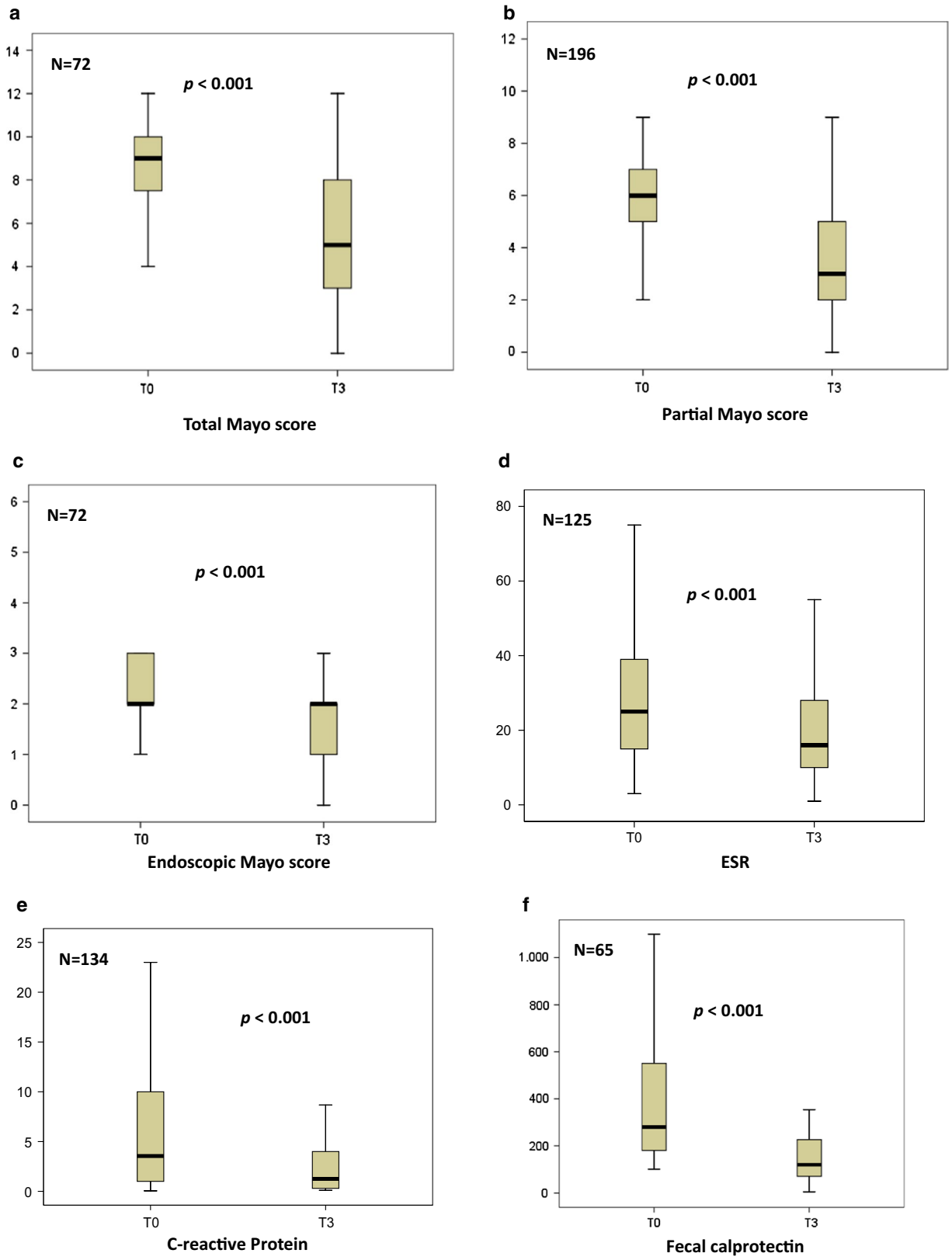

Fig. 2 Median values of total Mayo score (**a**), partial Mayo score (**b**), endoscopic Mayo score (**c**), erythrocyte sedimentation rate (ESR) (**d**), C-reactive protein (**e**), and fecal calprotectin (**f**) at baseline and after 3 months of therapy

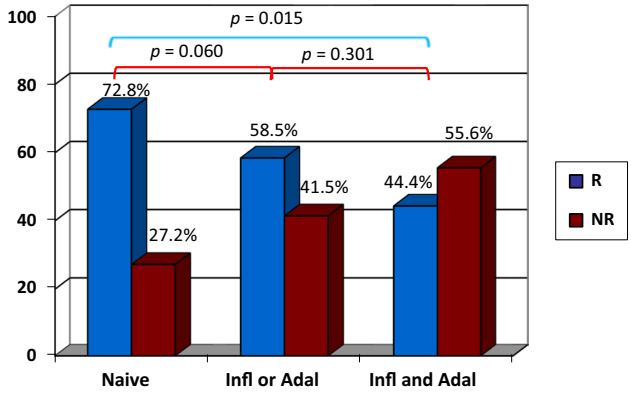

Fig. 3 Responder and non-responder rates in patients naïve to anti-TNF-alpha and in patients previously treated with one or two anti-TNF-alpha monoclonal antibodies. *Adal* adalimumab, *Infl* infliximab, *NR* non-responder, *R* responder

Acceptance of the Golimumab Smart-Ject® Autoinjector System

Patient acceptance of the golimumab Smart-Ject® autoinjector system was also determined in a subset of 43 patients. Thirty-seven (86%) patients reported the Smart-Ject® device was easy to use and painless, and almost all of the subset ($n=42$, 98%) agreed that there were no local effects at the site of injection. Thirty patients (70%) were self-confident using the system, and 34 (79%) were satisfied. No significant differences were found between the patients regarding age, gender, previous treatment with anti-TNF-alpha monoclonal antibodies, or disease status at week 12.

Discussion

We conducted a real-life prospective study on a heterogeneous group of UC patients treated with golimumab. Patients differed regarding disease extent and severity, and number of previous therapies, and 75 (38%) had relevant comorbidities. The design of the study did not include an obligation to carry out laboratory and endoscopic examinations, and each center followed their usual daily clinical practice. We were able to obtain initial information for all enrolled patients, but several clinical, laboratory, and endoscopic data were not available for evaluation at the different time points (see online supplementary Fig. 1).

RCTs are characterized by low external validity [7]. Thus, it is important to collect data on the efficacy and safety of a treatment in daily clinical practice where a heterogeneous population of patients is receiving the compound. Such studies may be biased by the lack of a control group, but they are very useful for evaluating effectiveness, which is a measure of the success of a therapy when provided in an average clinical setting. Consequently, a real-life study has high external validity (i.e., no bias in terms of selection or allocation of patients is possible), and the results are widely generalizable.

In our study, 130 UC patients (66%) showed a clinical response after 3 months of therapy with golimumab. These results are in line with other real-life studies, which report clinical response rates at induction ranging from 65 to 80% [10–13]. In these studies, assessment of response at induction was determined after about 3 months in all [8–11] but one, where evaluation was conducted after 8 weeks of therapy [11]. The rate of anti-TNF-alpha-naïve patients in these studies ranged from 27% [10] to 89% [11]. In our study we found that naïve patients responded better to golimumab treatment compared with patients who had failed two anti-TNF-alpha monoclonal antibody treatments, although no significant difference emerged when naïve patients were compared with patients who had failed only one anti-TNF-alpha treatment. Naïve to anti-TNF-alpha status was also found to be associated with a better response in multivariate analysis. These results are similar to those reported by Taxonera et al. [11]. However, in this study, multivariate analysis did not show a significant improvement in the clinical response of naïve patients, probably because the population of enrolled patients was smaller. None of the other real-life studies reported a better response to golimumab in naïve patients [8–10]. However, the rates of anti-TNF-alpha naïve patients in these studies were 30%, 27%, and 88%, respectively, so the results could be related to the unequal number of naïve patients compared with treatment-experienced patients. Multivariate analysis revealed a significant association between higher TMS and better response to golimumab in our population, but this association was not found in any of the previously published studies. In the studies by Bosca Watts et al. [9] and Tursi et al. [10], short disease duration (<2 years) was significantly associated with better response, while steroid-dependence was associated with a lower rate of response ($p=0.01$) only in the study by Tursi et al. [10], but our data did not confirm these associations. However, real-life studies (both prospective and retrospective) cannot provide conclusions concerning factors predictive of response but only hypotheses, which must be confirmed in specifically designed studies.

Regarding long-term response, about 39% of our patients maintained sustained response after 12 months of therapy. Similar findings were only found in the study of Taxonera et al. [11] who reported that 46.5% of their patients were long-term responders. In our study, endoscopic healing (EMS ≤ 1) was achieved by 33 out of 75 patients (44%) after 3 months and maintained in 36 out of 52 patients (69%) after 12 months of therapy.

The rate of mucosal healing was 19.3% at 6 months of therapy in the study of Tursi et al. [10], while no endoscopic

Table 2 Univariate analysis of predictors of response in responder and non-responder patients after 3 months of therapy with golimumab

Gender (*n*) (%)	Response to golimumab				*p* value
	No (*n* = 66)		Yes (*n* = 130)		
Female	23	29	57	71	0.226
Male	43	37	73	63	
Age at diagnosis (mean ± SD) [median (IQR)]	38 ± 16	36 (25–51)	37 ± 14	37 (27–48)	0.678
BMI (mean ± SD) [median (IQR)]	25 ± 4	25 (22–28)	25 ± 4	25 (22–27)	0.719
Disease duration at study inclusion (mean ± SD) [median (IQR)]	8 ± 6	6 (3–12)	10 ± 8	8 (4–14)	
≤ 2 years (*n*) (%)	15	41	22	59	0.533
> 2 years (*n*) (%)	49	35	91	65	
Smoking habit (*n*) (%)					
Active smoker	7	33	14	67	0.679
Non-smoker	45	32	95	68	
Past smoker	14	40	21	60	
Disease extent (*n*) (%)					
Pancolitis (E3)	40	35	73	65	0.600
Distal colitis (E2)	25	33	51	67	
Proctitis (E1)	1	14	6	86	
Naive to anti-TNF-alpha (*n*) (%)	34	27	91	73	0.011
Previous anti-TNF-alpha (*n*) (%)	32	45	39	55	
Infliximab	19	40	28	60	0.562
Adalimumab	3	50	3	50	
Infliximab and adalimumab	10	56	8	44	
Indication for golimumab (*n*) (%)					
Steroid resistance	13	35	24	65	0.315
Steroid dependence	41	32	87	68	
Extra-intestinal manifestations	1	17	5	83	
Failure of anti-TNF-alpha therapy	11	50	11	50	
Concurrent immunosuppressants (*n*) (%)					
No	58	34	114	66	0.969
Yes	8	33	16	67	
UC activity at study inclusion (mean ± SD) [median (IQR)]					
Total Mayo score (T0)	7 ± 3	8 (5–9)	9 ± 2	9 (8–10)	0.0001
Partial Mayo score (T0)	5 ± 2	5 (3–6)	6 ± 2	7 (5–7)	0.0001
Endoscopic Mayo score (T0)	2 ± 1	2 (2–3)	3 ± 1	3 (2–3)	0.009
ESR (T0)	27 ± 19	23 (15–35)	29 ± 19	25 (15–39)	0.406
CRP (T0)	6 ± 11	1 (1–7)	8 ± 12	4 (1–9)	0.034
Fecal calprotectin (T0)	355 ± 287	250 (160–500)	418 ± 532	243 (175–500)	0.981
Serum albumin (T0)	4 ± 1	4 (3–4)	4 ± 0	4 (3–4)	0.664
BMI (T0) (mean ± SD) [median (IQR)]	25 ± 4	25 (22–28)	25 ± 4	25 (22–27)	0.719
Steroids at study inclusion (*n*) (%)					
Yes	30	37	50	63	0.345
No	36	31	80	69	

BMI body mass index, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *UC* ulcerative colitis

information was reported in the other real-life studies [8, 9, 11].

We found a significant reduction in laboratory biomarkers of inflammations (ESR, C-reactive protein, and fecal calprotectin) after 3 months of therapy (Fig. 1), in agreement with Tursi et al. [10] and Bosca Watts et al. [9]. In the latter study, 9 of the 33 enrolled patients required treatment intensification within the first 14 weeks of therapy (in 5 patients the dose was increased from 50 to 100 mg, and in 4 patients the dose interval was shortened to 2 weeks), and 7

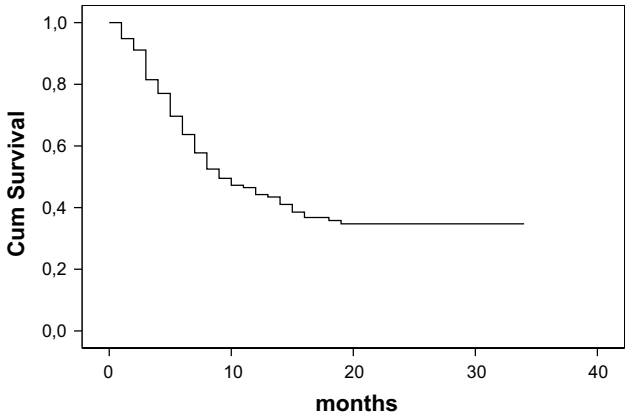

Fig. 4 Kaplan-Meier persistence curve for treatment with golimumab during the year of therapy

(77.8%) achieved clinical remission [9]. Taxonera et al. also reported that dose escalation of golimumab was necessary in 31 patients during maintenance therapy and that 71% of them regained response [11]. However, none of our patients underwent treatment intensification as it was not allowed by the Italian Medicine Agency (AIFA).

Our study is not large enough to assess the safety of golimumab in the real-life setting. However, 17 patients (8.6%) experienced an adverse event during therapy and 4 (2%) a serious adverse event. There were no significant differences between responders and non-responders regarding the rate of adverse events or serious adverse events. There was no difference in the rate of adverse events in the subgroup of 75 patients (38%) with significant clinical comorbidities. The rate of adverse events in the 23 patients > 65 years of age treated with golimumab in our study was higher than in younger patients, but the difference was not statistically significant ($p = 0.2$).

To the best of our knowledge, this is the first study to investigate the opinions of IBD patients using the golimumab Smart-Ject® autoinjector system. However, two studies have confirmed that patients with rheumatoid arthritis preferred the golimumab autoinjection system to prefilled syringes [18, 19]. Our results showed that patients liked the Smart-Ject® autoinjector since they found it easy to use and it did not cause any local effects at the injection site.

In conclusion, our study suggests that golimumab is an effective and safe drug for the treatment of patients with UC. It can be used in daily clinical practice, even in older patients and those with comorbidities, and patients persistently show a favorable response even after a year of therapy. Golimumab seems to be associated with a better response in patients with a higher TMS and in those who are naïve to anti-TNF-alpha. Golimumab was also a valid therapeutic option in patients who had failed one anti-TNF-alpha agent but not in those who had failed two such agents, suggesting that, for these patients, switching to a drug with a different mechanism of action could be a better choice.

Author's contribution FB: planning the study, drafting the article, analysis and interpretation of data. AA, GB, FWG, AR, MBP, MC, AT, WF, ACP, GC, LG, and SM: planning the study, critical revision of the article and interpretation of data. MRV: analysis of data. AL, RC, CF, ES, MM, GP, LS, AM, MP, RS, CR, CS, PP, GI, AAz, ON, NB, MR, GR, LF, and RM: critical revision of the article for important intellectual content.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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