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Clinical Experience with Adalimumab in a Multicenter Swiss Cohort of Patients with Crohn's Disease

THESE

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par

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Clinical experience with adalimumab in a multicenter Swiss cohort of patients with Crohn's disease

Expérience clinique avec l'adalimumab dans une cohorte suisse multicentrique des patients atteints de maladie de Crohn

Background. Des études précédentes ont démontré l'efficacité et la tolérance de l'adalimumab chez les patients avec maladie de Crohn modérée ou sévère. Les patients qu'on rencontre dans la pratique quotidienne peuvent être différents des patients rigoureusement sélectionnés dans les études contrôlées.

But. Dans ce travail, nous résumons notre expérience avec l'adalimumab durant une période de 3 ans.

Méthodes. Nous avons analysé rétrospectivement les dossiers de 55 patients atteints d'une maladie de Crohn modérée ou sévère et traités par adalimumab dans les hôpitaux universitaires de Bâle, Zurich, Genève et Lausanne, ainsi que dans un cabinet médical à Olten. Les informations collectées étaient les suivantes : données démographiques, localisation, phénotype et durée de la maladie, traitements chirurgicaux précédents, traitements précédents par anti-TNF alpha ou immunosuppresseur, le traitement concomitant et l'activité de la maladie à la « baseline » et durant le traitement. La sévérité de la maladie à l'inclusion a été établie en utilisant le score Harvey-Bradshaw Index (HBI). Durant le traitement, la rémission a été définie avec un HBI≤4 et la réponse comme une réduction de l'HBI de plus de 3 points. L'analyse de régression logistique univariée a été utilisée pour déterminer si les variables étudiées étaient associées à la réponse ou à la rémission durant le traitement.

Résultats. L'âge moyen des patients a été de 37.5 ± 11.4 ans et la durée moyenne de maladie à été de 12.7 ans. 29 des 55 patients étaient des fumeurs. Le traitement d'induction a été effectué chez 31 patients avec l'adalimumab en sous-cutané 160 mg à la semaine 0 et 80 mg à la semaine 2 et chez 24 patients avec 80 mg à la semaine 0 et 40 mg à la semaine 2. Le traitement d'entretien a été de 40 mg en sous-cutané toutes les 2 semaines. 13 patients (23.6%) ont nécessité l'augmentation de la dose d'adalimumab pour maintenir la rémission ou la réponse.

Le taux de rémission et de réponse à la semaine 4-6 était de 52.7%, respectivement 83.6%. La rémission a été maintenue aux semaines 12, 24 et 52 chez 89.6%, 72.4%, respectivement 44.7% des patients. Le taux de rémission et de réponse n'a pas été influencé par le tabagisme, la location ou la durée de la maladie, la dose totale donnée durant le premier mois de traitement, la dose d'adalimumab par kilogramme-corps ou par le traitement précédent par infliximab. La rémission à la semaine 4-6 a été significativement plus élevée chez les patients intolérants à l'infliximab comparativement à ceux qui avaient perdu la réponse à l'infliximab (78.9% vs 42.1%, p=0.02). Le traitement par adalimumab a été bien toléré. Les effets secondaires les plus signalés ont été : la douleur au site d'injection (10.9%), l'asthénie (9%) et des infections (7.2%).

Conclusions. L'adalimumab a démontré une bonne efficacité et tolérance dans la pratique quotidienne chez les patients avec une maladie de Crohn modérée ou sévère.

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Clinical Experience with Adalimumab in a Multicenter Swiss Cohort of Patients with Crohn's Disease

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Key Words
Crohn's disease · Adalimumab · Response, adalimumab · Remission, Crohn's disease

Abstract
Background: Controlled clinical trials have demonstrated the efficacy and safety of adalimumab in patients with moderate-to-severe Crohn's disease (CD), but there is, however, only limited long-term experience with adalimumab in daily practice. ***Aim:*** To assess the long-term effectiveness and safety of adalimumab in a multicenter cohort of practice-based patients with moderate-to-severe CD. ***Methods:*** We retrospectively reviewed the charts of CD patients who received adalimumab over a 3-year period. Disease severity was scored using the Harvey-Bradshaw index (HBI). Remission was defined as an HBI of ≤ 4 and response as a reduction in the HBI of >3 points at evaluation compared to the baseline. Univariate logistic regression analysis was used to identify the predictive variables associated with response. ***Results:*** The charts of 55 patients were reviewed; remission and response rates observed at weeks 4–6 were 52.7 and 83.6%, respectively. Remission was maintained at weeks 12, 24 and 52 in 89.6, 72.4 and 44.7% of patients, respectively. Remission and response rates were not influenced by smoking status, disease location or duration, the first month total dose, or previous infliximab therapy. The remission rate at weeks 4–6 was significantly higher in patients intolerant of infliximab as compared to those who lost response to this drug. Adalimumab was well tolerated overall. ***Conclusion:*** Adalimumab can be considered a suitable option in patients with moderate-to-severe CD, demonstrating sustained long-term effectiveness.

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Introduction

Tumor necrosis factor α (TNF-α) has emerged as a central cytokine in the pathogenesis of Crohn's disease (CD), as is confirmed by the central role that TNF-α antagonists now play in the treatment of patients with moderate-to-severe or refractory CD. Infliximab (IFX), the first chimeric monoclonal TNF-α antibody, is an effective treatment for induction and maintenance of remission in patients with moderate-to-severe CD, including those with draining fistulas [1–4]. However, a proportion of patients develop antibodies to IFX, in particular with episodic therapy or in the absence of concomitant immunosuppressant medication. The presence of antibodies to IFX leads to infusion reactions, loss of response and delayed hypersensitivity reactions [5–7].

Adalimumab is a subcutaneously administered recombinant, fully human, immunoglobulin G1 monoclonal antibody that binds with high affinity and specificity to human TNF. Four pivotal, randomized, double-blind trials (CLASSIC-I, CLASSIC-II, CHARM and GAIN) in >1,400 patients demonstrated the clinical efficacy and safety of adalimumab in patients with moderate-to-severe CD [8–11]. Adalimumab was significantly more effective than placebo for induction of remission in patients naive to anti-TNF therapy (CLASSIC-I trial, 36 vs. 12% at week 4 with 160/80 mg regimen, $p = 0.004$) or in those who had either lost responsiveness or developed intolerance to IFX (GAIN trial, 21 vs. 7.2% at week 4, $p < 0.001$). The CHARM trial showed that, among patients who responded to open-label adalimumab induction, maintenance therapy with adalimumab 40 mg weekly or every other week for up to 1 year was associated with significantly greater remission rates than placebo at weeks 26 (47, 40 vs. 17%, $p < 0.001$) and 56 (41, 36 and 12%, $p < 0.001$). In another maintenance trial (CLASSIC-II), patients who were in remission after a short course of adalimumab and who were randomized to receive up to 1 year of treatment with adalimumab 40 mg weekly or every other week, were significantly more likely to remain in remission than those who received placebo (83, 79 vs. 44%, $p < 0.05$). Loss of efficacy can also be observed with adalimumab and an increased dose can be used to restore clinical response or remission. The role of antibodies to adalimumab in the loss of response is poorly characterized to date.

Adalimumab is generally well tolerated. In clinical trials, the rate of serious adverse events was low in patients treated with adalimumab and was similar to those treated with placebo [8–11].

Patients with CD seen in daily practice may differ from the selected patients included in randomized trials [12–15]. In a multicenter open-label single-arm study (CARE), adalimumab therapy showed substantial efficacy at week 4 (43% remission rate), which was sustained through week 20 (52% remission rate), including patients who had never responded to IFX [16]. Neither concomitant steroids nor immunosuppressants notably affected the results [17]. In this study, we analyzed our experience with adalimumab in current clinical practice over the past 3 years.

Patients and Methods

We performed a retrospective chart review of patients with CD who had been treated with adalimumab at the University Hospitals of Lausanne, Geneva, Zurich and Olten between April 2005 and April 2008, and 55 patients who had received adalimumab were identified. The diagnosis of CD was confirmed in all cases by a review of patients' medical records including clinical notes, endoscopic, radiographic or histological documents.

The information collected included patient demographics, disease location, disease phenotype, disease duration, prior surgical procedures, smoking status, previous anti-TNF and immunosuppressant use, concomitant medication, disease activity at baseline and during treatment (table 1). Disease severity for luminal CD was scored using the Harvey-Bradshaw index (HBI) [18]. For patients with previous surgical resections, other causes of diarrhea, such as bile salt malabsorption, small bowel bacterial overgrowth, or deficient water absorption secondary to proctocolectomy, were eliminated before considering them for adalimumab therapy.

The first clinical evaluation was performed at weeks 4–6. Subsequent assessments of the efficacy of treatment were performed at weeks 12, 24 and 52. The clinical evolution of luminal CD was classified into 3 categories: remission, response, and non-response. Remission was defined as an HBI of ≤4 and response as a reduction in the HBI of ≥3 points at the evaluation week compared to the baseline index [19]. The non-response category included all the remaining patients.

Data on clinical safety were collected at every medical visit and the patients were also instructed to contact the physician's office if any illness or adverse reaction occurred. Patients were considered intolerant to IFX if they were unable to continue the treatment due to reactions judged by the clinician to be linked to the perfusion. Loss of responsiveness to IFX was accepted if patients did not achieve remission with an increased IFX regimen after loss of efficacy at a standard dose.

We used univariate logistic regression analysis to see if the predictive variables tested (table 2, 3) were implicated in the response rate. The variables which had a p value of <0.3 were tested, then together in a multivariate analysis in order to control for the confounding effect of each. A p value of <0.05 was considered to be statistically significant. Data are expressed according to a per-protocol analysis. All quantitative variables are expressed as the mean ± standard error.

Table 1. Demographic and baseline clinical characteristics (55 patients)

Patient characteristics	n
Gender	
Male	21 (38.2%)
Female	34 (61.8%)
Mean age, years	37.5
Disease duration, years	
Mean ± SD	12.67 ± 11.4
Range	1–41
Smokers	
Yes	29 (52.7%)
No	26 (47.3%)
Disease location (Vienna classification)	
L1: Ileal	9 (16.3%)
L2: Colonic	11 (20%)
L3: Ileocolonic	35 (63.6%)
L4: Upper (esophageal)	1 (1.8%)
Disease behavior	
(Vienna classification; patients may appear more than once)	
B1: non-stricturing non-penetrating	35 (63.6%)
B2: stricturing	7 (12.7%)
B3: penetrating	23 (41.8%)
Surgery for Crohn's disease	
Ileal resection	5 (9%)
Ileocolonic resection	12 (21.8%)
Colonic resection	7 (12.7%)
Proctocolectomy	4 (7.3%)
None	23 (41.8%)
Previous IFX therapy (n = 43)	
Side effects	23/43 (53.4%)
Loss of response	19/43 (44.2%)
No/insufficient response	1/43 (2.3%)
Never given	12/55 (21.9%)
Type of IFX therapy	
Regular	18/43 (41.9%)
Episodic	25/43 (58.1%)
Concomitant treatment	
Budesonide	4 (7.3%)
Prednisone	25 (45.4%)
Azathioprine	5 (9%)
Methotrexate	3 (5.4%)
Indication of adalimumab	
Intolerance to IFX	19 (34.5%)
Loss of response to IFX	19 (34.5%)
Corticodependence	10 (18.1%)
Other reason[a]	7 (12.7%)
Adalimumab induction regimen	
160/80 mg	31 (56.4%)
80/40 mg	24 (43.6%)

The values are the number of patients with percentages in parentheses. IFX = Infliximab.

[a] Refractory to certolizumab (n = 3), to azathioprine (n = 1), extraintestinal manifestations (n = 2), no response to IFX (n = 1).

Results

This cohort comprised 55 patients (21 men and 34 women, mean age 37.5 ± 11.4 years) treated with adalimumab between April 2005 and April 2008. The demographic data and baseline clinical characteristics are summarized in table 1. The mean duration of CD was 12.7 (range 1–41) years. Description of disease location of luminal CD followed the usual distribution. One patient had ileal, colonic and esophageal disease. The mean HBI before treatment was 10.9 ± 5 points. Twenty-nine patients were smokers. Adalimumab was administered to patients intolerant to IFX, to those who had lost response to IFX, or to those who were corticodependent. Seven patients were treated thus for other reasons, 2 of whom had severe spondylarthropathy. The indication for adalimumab therapy in the 4 patients who had an HBI of <4 points at inclusion was intolerance to IFX (1 patient), lupus-like syndrome with IFX (1 patient) and corticodependence (2 patients). These patients were considered to be in remission if their HBI remained <4, or were deemed non-responders if their HBI value rose during the follow-up period. Of those who had already received IFX, 25 patients had episodic infusions and 18 patients had regular treatment. All patients received subcutaneous injections of adalimumab at weeks 0 and 2 at a dose of 160/80 mg (31 patients) or 80/40 mg (24 patients) and then 40 mg every other week. The results of detailed subgroup analysis are summarized in tables 2 and 3.

Adalimumab Induces and Maintains Clinical Remission and Response in CD Patients

At weeks 4–6, in per-protocol analysis, remission had been induced in 29 patients (52.7%) and response was noted in 46 patients (83.6%). An adalimumab-induced remission was maintained in 26 patients (89.6%) at week 12, and in 21 patients (72.4%) at week 24. The evolution over time of remission and response rates in per-protocol analysis is shown in figure 1. However in a intention-to-treat analysis remission was noticed in 47.3% patients at week 24 and in 31% patients at week 52. Response rates at the same time points were 54.5 and 34.5%, respectively. Thirteen patients (23.6%) required an increase in the adalimumab dose: 9 patients to 40 mg every week, 2 patients to every 10 days, 1 patient to 80 mg every week, and another to 80 mg every 2 weeks, because of incomplete response or loss of response. Of these 13 patients, 6 (46.1%) achieved remission and another 2 patients responded. In 1 patient, the dose was reduced to 40 mg ev-

Table 2. Response by subgroups at 4–6 weeks

Variable	Category	Response n (%)	Nonresponse n (%)	Univariate regression		Multivariate regression	
				OR (95% CI)	p	OR (95% CI)	p
Age, years		38.3	33.4	1.04 (0.97–1.12)	0.249	1.04 (0.97–1.12)	0.268
Gender	Female	29 (85.3%)	5 (14.7%)	1			
	Male	17 (80.9%)	4 (20.1%)	0.73 (0.17–3.10)	0.673		
Smoking status	Non-smoker	23 (88.5%)	3 (11.4%)	1			
	Smoker	23 (79.3%)	6 (20.7%)	0.50 (0.11–2.24)	0.366		
Disease duration, years	<7	15 (83%)	3 (17%)	1			
	<7–15	16 (84%)	3 (17%)	1.00 (0.17–5.72)	1		
	>15	15 (83%)	3 (17%)	0.94 (0.16–5.39)	0.942		
Disease location	Ileitis (L1)	8 (80%)	2 (20%)	1			
	Colitis (L2)	10 (91%)	1 (9%)	2.22 (0.17–8.86)	0.542		
	Ileocolitis (L3)	28 (82.3%)	6 (17.3%)	1.04 (0.19–6.07)	0.968		
Previous resection (any segment)	No	18 (78.3%)	5 (21.7%)	1			
	Yes	28 (87.5%)	4 (12.5%)	1.94 (0.46–8.22)	0.366		
Previous IFX therapy	Never	9 (75%)	3 (25%)	1			
	Episodic	21 (84%)	4 (16%)	1.57 (0.29–8.41)	0.595		
	Regular	16 (88.9%)	2 (10.1%)	2.40 (0.34–6.97)	0.380		
Indication for adalimumab	Loss of response to IFX	17 (89.4%)	2 (10.6%)	1		1	
	Intolerance to IFX	17 (89.4%)	2 (10.6%)	0.94 (0.12–7.48)	0.957	1	
	Other[a]	12 (70.5%)	5 (20.5%)	0.27 (0.04–1.61)	0.149	0.33 (0.07–1.68)	0.182
First-month total dose, mg	120 (80+40)	19 (79.2%)	5 (21%)	1			
	240 (160+80)	27 (87.1%)	4 (13%)	1.00 (0.99–1.02)	0.434		
First-month total dose/weight, mg/kg	<2.5	17 (80.9%)	4 (19.1%)	1		1	
	2.5–3.5	13 (76.4%)	4 (23.6%)	0.72 (0.15–3.43)	0.682	1	
	>3.5	16 (94.1%)	1 (5.9%)	3.56 (0.36–5.20)	0.278	3.87 (0.38–39.03)	0.251

IFX = Infliximab. [a] Corticodependence (n = 10) and other (n = 7) merged because of small numbers.

Table 3. Remission by subgroups at 4–6 weeks

Variable	Category	Remission n	Non-remission n	p value
Smoker status	Smoker	12 (41.4%)	17 (58.6%)	0.075
	Non-smoker	17 (65.4%)	9 (34.6%)	
Previous IFX therapy	Regular	10 (55.5%)	8 (44.5%)	0.719
	Episodic	12 (48%)	13 (52%)	
	Never	7 (58.3%)	5 (41.7%)	
Indication for adalimumab	Loss of response to IFX	8 (42.1%)	11 (57.9%)	0.012
	Intolerance to IFX	15 (78.9%)	4 (21.1%)	

IFX = Infliximab.

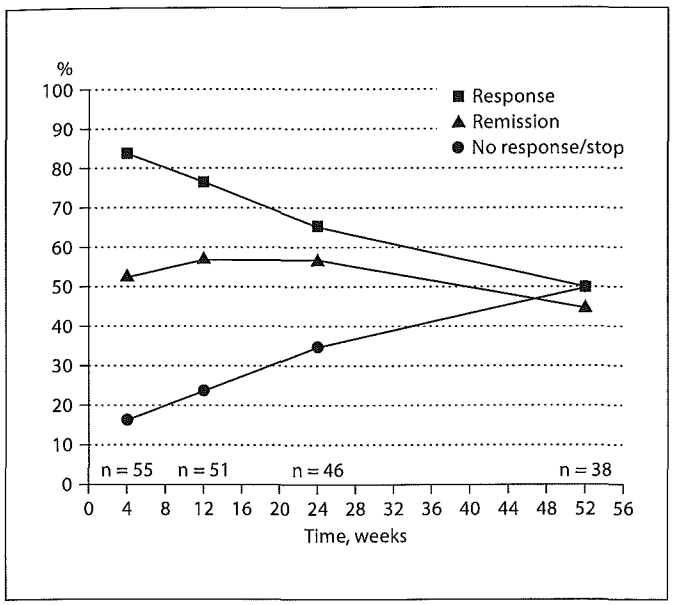

Fig. 1. Response and remission rate over time in per-protocol analysis.

Table 4. Adverse events observed over the 3-year period

Type of adverse event	n
None	30
Perianal abscesses	2
Asthenia	5
Pain at injection site	6
Pruritis at injection site	2
Rash	1
Headache	3
Nausea	2
Diarrhea	1
Dizziness	2
Phlebitis	1
Gynecological side effect	1
Labial herpes	1
Lupus-like syndrome	1

ery 4 weeks because of fatigue. The response rate was not significantly higher in the group of patients with previous abdominal surgery (table 2).

Effect of Smoking on Adalimumab Efficacy at Weeks 4–6

The remission and response rates were higher among the non-smokers, but without any statistically significant difference.

Effect of Disease Duration or Location on Adalimumab Efficacy at Weeks 4–6

Because of the long mean disease duration of our cohort, we chose to separate the patients into 3 almost equal groups: CD known for <7 years, for 7–15 years and for >15 years. The remission and response rates were almost similar within these 3 groups. The location of the intestinal segment(s) involved was not found to play a significant role in patients' clinical response to the adalimumab therapy.

Effect of the First-Month Total Dose on Adalimumab Efficacy at Weeks 4–6

Remission and response rates were not different between the groups who received adalimumab 240 or 120 mg during the first month of treatment. The total first-month adalimumab dose was divided by the patient's weight and patients were then grouped into 3 dose-adjusted groups according to the total dose per kilogram over the first month: <2.5, 2.5–3.5 and >3.5 mg/kg. We did not find any statistically significant difference between these 3 groups with regard to the response rate.

Impact of Prior IFX Treatment on Adalimumab Efficacy at Weeks 4–6

The response rate was not influenced by the absence of previous IFX treatment or by its regular as opposed to episodic use. In contrast, the remission rate at weeks 4–6 was significantly higher among patients intolerant to IFX, compared to those who had lost response to this medication (78.9 vs. 42.1%, p = 0.02).

Safety of Adalimumab Treatment

Overall, subcutaneous injections of adalimumab were well tolerated (table 4). Thirty of the 55 patients reported no adverse event. The most common side effect was pain at the injection site (10.9%), followed by asthenia (9%) and infections (7.2%). One patient stopped the treatment because of intolerable fatigue and another because of gynecological side effects. One case of lupus-like syndrome was noted. In our cohort, no fatal complication, malignancy, neurologic or cardiovascular complication was noted during the whole observation period.

Discussion

The purpose of our retrospective cohort study was to evaluate the effectiveness of adalimumab in our Crohn's patients over a period of 3 years in daily clinical practice. Adalimumab treatment was effective in the induction and maintenance of remission in patients with moderate-to-severe CD. The results in our cohort appear better than the remission and response rates noticed in the CLASSIC I trial (36 and 59%, respectively, at week 4) [8] and the GAIN trial (21 and 52%, respectively, at week 4) [11]. The fact that in our cohort the first evaluation occurred later than in those trials, i.e. that our patients had a supplementary third injection, may have contributed to the improved results. In the per-protocol analysis, 44.7% patients were in remission and 50% still in response at week 52. These long-term results for remission are similar to those at week 56 in the CLASSIC II trial [9]. The limited size of our cohort, the lack of placebo controls and the absence of restricted inclusion criteria may have contributed to the differences noticed in our patients. In addition, we used the HBI rather than the Crohn's Disease Activity Index to evaluate patients, which could also in part explain the difference from the randomized trial. The remission and response rates in our cohort are also comparable to those of the CARE study [16, 17], although in this multicenter cohort all patients received a 160/80-mg induction regimen.

The proportion of our patients who needed a dose increase and the benefit obtained from this strategy were similar to those reported in the CHARM trial [20]. In our cohort, the mean time to dose increase was relatively long: 7 (range 1–24) months. Our results thus confirm that in clinical practice this strategy should be explored before considering another treatment in patients who lose response or fail to achieve complete remission with a standard adalimumab regimen. In a small study, a higher percentage of patients were previously reported to require an adalimumab dose increase (nearly 60% at 6 months) after using a suboptimal induction regimen of 80/40 mg [12]. In another 2 cohorts, only 13.2 and 29% of patients required a dose increase [14, 15].

In a per-protocol analysis, we observed that over 52 weeks adalimumab treatment was stopped in half of the patients. This dropout rate was progressive during the observation period. The reasons for discontinuation were either no response, loss of response despite dose increase (14/19 patients) or adverse reaction (5/19 patients).

Smoking status had no effect on either the rate of clinical remission or the response rate in patients treated with adalimumab. This observation is consistent with the results of the sub-analysis in the CLASSIC I trial, where the efficacy of adalimumab treatment at week 4 was not affected by smoking status [21]. Hinojosa et al. [13] also reported no difference in the 4-week response rate of active smokers with luminal CD as compared to former smokers.

The efficacy of adalimumab therapy in our cohort was not influenced by disease duration. In the CHARM trial, Colombel et al. [10] showed a significantly better remission rate at weeks 26 and 56 with adalimumab in patients with a CD duration of <2 or >5 years. We were unable to separate our patients into the same 3 groups (disease duration <2, 2–5 and >5 years) because our patients had a longstanding diagnosis of CD. Our results suggest that a disease duration of >7 years has no greater impact on response.

We failed to show a correlation between the total first month dose adapted to body weight or the response or remission rate to adalimumab therapy. These results suggest that the dose during the first month as currently administered should suffice in the majority of patients. However, the small size of the cohort and the retrospective nature of the analysis do not exclude the possibility that a dose-weight relationship might exist in a larger group of patients. Indeed, as the affinities and molecular weight of IFX and adalimumab are comparable, one could have expected that such a relationship might exist. Other characteristics of adalimumab may explain this difference as compared to IFX, such as the human nature of the antibody or differences in the binding sites of the antibodies.

The majority of our patients had been treated with IFX before receiving adalimumab. The remission and response rates at weeks 4–6 were not statistically different in patients naive to IFX compared to those who had already been treated with IFX. Similarly, no difference was found in the response to adalimumab between patients whose previous IFX therapy was interrupted because of loss of response or because of intolerance. This last observation was also reported by Hinojosa et al. [13]. In contrast, however, the remission rate at weeks 4–6 was significantly higher in the subgroup of patients intolerant to IFX. This suggests that patients who did not lose their response to IFX may benefit more from another anti-TNF agent. Patients who have lost response may represent a group of patients who may better benefit from a change in the treatment target, different from TNF.

Overall, adalimumab was well tolerated in our cohort. The rate of side effects was similar to that already reported in randomized trials, in which patients underwent

more stringent selection and monitoring [8–10]. Pain at the injection site, asthenia and infections were the most common adverse events. Despite these reassuring results, the safety issues surrounding anti-TNF therapies continue to be of great significance and clinicians need to remain vigilant. Colombel et al. [22] recently assessed global adalimumab safety in a collective of 2,228 patients exposed to adalimumab in pivotal randomized trials, open-label extensions and phase IIIb studies, CHOICE and CARE. The rates of opportunistic infections and malignant neoplasms were found to be <2% of patients. Such rates justify careful monitoring of all patients, even when stable in remission.

Our study has several limitations. Firstly, the data presented are based on a retrospective review and not on a uniform analysis with precise time points. Secondly, even if this is the largest cohort of open-label clinical experience in patients with CD to date, the number of patients analyzed at 24 and 52 weeks is still low. Thirdly, our patients had a long-standing CD history prior to adalimumab therapy. It remains to be studied if adalimumab used in a top-down scheme might improve the results reported here. Although nonsignificant, the odds ratio values cannot be taken as proof that none of the variables mentioned in table 2 may have an effect. The large confidence intervals indicate that the calculated odds ratio remains imprecise.

In conclusion, our data suggest that adalimumab is as effective in inducing and maintaining remission in patients with moderate-to-severe or refractory CD seen in daily practice as reported during randomized trials. Our results further suggest that patients with intolerance to IFX represent a group particularly well suited to further adalimumab therapy. The safety of adalimumab is also confirmed in daily practice. However, results from larger cohorts should be awaited before reaching firm conclusions.

Disclosures

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