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Preferences and satisfaction of IBD patients after switching from adalimumab 40 mg weekly to 80 mg every other week given as a single injection: the ADASCAL study

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Abstract

Background: A recently registered device containing 80 mg of adalimumab (ADA) allows an alternative dose escalation regimen with ADA 80 mg every other week (EOW) given as a single subcutaneous injection instead of 40 mg every week. The ADASCAL study evaluated the preferences and satisfaction of inflammatory bowel disease (IBD) patients after switching their ADA regimen from 40 mg weekly to 80 mg EOW given with a single-dose pen.

Methods: In this multicentre cross-sectional study, patients in whom the ADA regimen was changed from 40 mg weekly to 80 mg EOW completed the Treatment Satisfaction Questionnaire for Medication (TSQM 1.4), a four-item questionnaire [a Likert-type 5-point scale for preferences, two closed questions for convenience and a 100-point visual analogue scale (VAS) to assess which escalated ADA regimen patients would prefer to continue] and two Health-Related Quality of Life (HRQoL) questionnaires: the generic European Quality of Life–5 Dimensions (EQ-5D) and disease-specific Spanish version of the Inflammatory Bowel Disease Questionnaire (SIBDQ-9).

Results: In total, 77 patients (64 Crohn's disease and 13 ulcerative colitis) were included. The TSQM score showed a notably high global satisfaction [83.4, standard deviation (SD) = 14.1] of patients with ADA 80 mg EOW given with a single-dose pen, with high TSQM scores for individual components: effectiveness (77.6, SD = 16.9), convenience (83.7, SD = 14.5) and side effects (86.1, SD = 23.4). Most of the patients (74%) preferred the ADA EOW regimen (59.7% had strong preference, 14.3% slight preference). ADA EOW interferes less with daily activity (59.7%) and with travel plans (81.8%). Most patients (77%) would prefer to continue with ADA EOW (mean VAS score of 84.7, SD = 24.1, where 100 indicates a preference for ADA EOW). Patients reported high HRQoL scores on both the EQ-5D (72.3, SD = 20.1) and SIBDQ-9 (75.1, SD = 14.7).

Conclusion: IBD patients in whom the ADA regimen was changed from 40 mg weekly to 80 mg EOW reported a higher preference for the EOW regimen and therefore most decided to continue with a single self-injection EOW.

Keywords: adalimumab, dose escalation, inflammatory bowel disease, patient-reported experience measures, single-dose pen

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Introduction

The inflammatory bowel diseases (IBDs), ulcerative colitis (UC) and Crohn's disease (CD), are chronic, relapsing inflammatory diseases of the gastrointestinal tract with heterogeneous behaviour and prognosis. Over the past two decades, the introduction and broad use of immunomodulatory agents including biologicals has revolutionized treatment of IBD. Adalimumab (ADA) is a fully humanized monoclonal antibody against tumour necrosis factor-alpha (TNFα) approved for induction and maintenance therapy in patients with CD[1] and UC.[2] However, a significant subset of CD or UC patients receiving subcutaneous (SC) ADA may have an inadequate response to induction or develop secondary loss of response during maintenance.[1,2] A post hoc analysis of the Crohn's trial of the fully Human antibody Adalimumab for Remission Maintenance (CHARM) trial reported that escalation of ADA dosing from 40 mg every other week (EOW) to 40 mg once a week regained clinical response in a large proportion of CD patients.[3] Subsequently, analysis of the ulcerative colitis long-term remission and maintenance with adalimumab 2 (ULTRA 2) trial demonstrated that escalation to 40 mg weekly doses of ADA was an effective strategy for UC patients with insufficient response or loss of response.[4] Recently, a device containing 80 mg of ADA (Humira® 80 mg/0.8 mL single-dose pen) has been developed and approved. According to the US Prescribing Information and European Summary of Product Characteristics, this 80 mg ADA injection can be used to deliver induction doses with fewer SC injections and will also allow for patients receiving escalated maintenance therapy with ADA an alternative regimen with 80 mg EOW (given as a single injection) instead of 40 mg once a week.[5,6]

Although optimization to weekly ADA demonstrated clinical benefits for CD and UC patients, the increased frequency of ADA injections could be considered inconvenient for patients and even have a negative effect on drug adherence. Therefore, treatment attributes such as the interval between ADA injections and number of injections necessary to deliver a dose are factors that may influence decisions in a maintenance regimen with ADA for IBD. In addition, in a 'patient-centred' provision of care, evaluating patient-reported experience measures regarding available dosing frequencies will allow a shared decision making that may increase acceptability, adherence and treatment success.[7] Several studies have evaluated patient preferences for SC *versus* intravenous administration of biologics for immune-mediated inflammatory diseases.[8] However, studies assessing patient satisfaction and preferences between ADA weekly compared with ADA EOW administered as a single SC injection are lacking.

The escalated ADA (ADASCAL) study aimed to evaluate the preferences and satisfaction of IBD patients after switching the ADA regimen from 40 mg once a week to 80 mg EOW given as a single SC injection. As a secondary objective, we assessed Health-Related Quality of Life (HRQoL) of patients receiving ADA 80 mg EOW.

Methods

Study design and patients

This was a multicentre cross-sectional study conducted between July 2019 and March 2020 at 10 IBD referral units all over Spain. Patients of at least 18 years of age with an established diagnosis of IBD treated with ADA for UC or CD were eligible. The study population consisted of consecutive patients receiving escalated maintenance therapy with ADA in whom the ADA regimen had been changed from 40 mg once a week to 80 mg EOW given as a single SC injection, and who had received at least four doses of the new regimen before inclusion. The modification in ADA regimen was decided by the attending gastroenterologists according to clinical practice. Patients on stable treatment with ADA 80 mg EOW were recruited and included consecutively during routine face-to-face visits after receiving information and giving written informed consent. Sociodemographic and clinical characteristics of patients were collected, and patients were asked to complete the questionnaires at the same scheduled routine visit. The ADA doses were delivered to patients as single-dose pre-filled pens of Humira® 40 mg/0.4 mL or Humira® 80 mg/0.8 mL at the hospital pharmacies of the participating centres. All patients self-administered ADA maintenance doses at home. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies were used in the design of the study and the preparation of the manuscript.[9]

Ethical considerations

The study was performed according to the Declaration of Helsinki's ethical guidelines and

was approved by the Clinical Research Ethics Committee of the leading centre (Hospital Universitario Clínico San Carlos, Madrid, Spain; C.I. 19/309-E_EPAOD, 17 July 2019).

Objectives and variables

The co-primary endpoints were patient preferences between escalated ADA dosing regimens and satisfaction with ongoing 80 mg EOW ADA given as a single self-injection. To evaluate satisfaction with ADA 80 mg single injection, EOW regimen patients completed the validated Treatment Satisfaction Questionnaire for Medication, version 1.4. (TSQM 1.4), which comprises 14 items across four domains exploring the effectiveness (3 items), side effects (5 items), convenience (3 items) and global satisfaction (3 items), with the treatment.[10,11] The total score was obtained by summing up each item score and the result was transformed into a 0–100 scale, where 0 indicated *extremely dissatisfied* and 100 *extremely satisfied*.

To assess patient preferences with ADA regimen modification from 40 mg every week to 80 mg EOW, we developed a four-item self-administered questionnaire. To minimize non-response rates, we kept the survey short and focused. A 5-point Likert-type scale ranked patient preference for the regimen, with options of expressing strong preference for weekly ADA 40 mg, slight preference for weekly ADA 40 mg, no preference, slight preference for ADA 80 mg EOW and strong preference for ADA 80 mg EOW. Two closed questions evaluated patient convenience and interference with work or daily activity and with travel or vacation plans. Lastly, a 100-point visual analogue scale (VAS) assessed which escalated ADA regimen (weekly or EOW) patients would prefer to continue (where 0 indicated a preference for ADA once a week, 100 for ADA EOW and 50 no preference). To validate the survey instrument, the initial content was first analysed by two IBD nurses and two IBD staff members and corrected, as necessary. The resulting questionnaire was tested in a random pilot sample of 10 IBD patients before full implementation. To assess test–retest reliability, we repeated the survey at least 10 days apart in a random sample of 15 patients from the leading centre.

To evaluate HRQoL, patients completed two validated questionnaires: the generic European Quality of Life–5 Dimensions (EQ-5D) and the disease-specific Spanish version of the 9-item Shortened Inflammatory Bowel Disease Questionnaire (SIBDQ-9). The EQ-5D is a generic HRQoL instrument that provides a standardized measure of health status, comprising five domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.[12] The EQ-5D index score ranges from −0.594 to 1, where higher scores indicate better HRQoL. The EQ-5D also includes a 100-point VAS, where 0 represents the worst imaginable health state and 100 the best imaginable one. SIBDQ-9 was developed and validated specifically for IBD patients and has shown excellent correlation with 36-item Inflammatory Bowel Disease Questionnaire (IBDQ-36).[13,14] SIBDQ-9 includes nine questions assessing the effect of IBD on social, emotional and physical well-being. The overall score was obtained by summing up each item score, and the result was transformed into a 0–100 scale, where 0 represents the worst health state.

Participating investigators completed sociodemographic and clinical characteristics of patients and evaluated IBD activity by means of the Partial Mayo Score (PMS) for UC patients and the Harvey–Bradshaw Index (HBI) for CD patients. Clinical remission was defined as a PMS of 0 or 1 for UC patients and as an HBI $\leqslant$4 for CD patients. To evaluate preferences for escalated ADA regimen, all investigators completed a 100-point VAS to evaluate the response to the question: 'Taking all aspects into account, which escalated adalimumab regimen do you prefer for your patients?' where 0 indicated a preference for ADA once a week, 100 for ADA EOW and 50 no preference.

Statistical analysis

Data were represented as mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and as frequencies and percentages for categorical variables. Continuous variables were compared using the Student's t test if normally distributed (Kolmogorov–Smirnov test) or the Mann–Whitney U test if not. Categorical variables were compared with the χ^2 test. We analysed the factors associated with a strong preference for the ADA 80 mg EOW regimen, including gender, age, employment status, type of disease, presence of perianal disease (for CD patients), extraintestinal manifestations and prior use of immunomodulator or biological treatment. Results

were presented as odds ratios (ORs) and their 95% confidence intervals (CIs). Variables with $p < 0.10$ in the univariate analysis were included in the multivariate model. The p values <0.05 were considered statistically significant. Test–retest reliability of the survey questionnaire was evaluated using Cohen's kappa for closed questions and intraclass correlation coefficient (ICC) for the numeric description scale. All statistical analyses were performed using the IBM/SPSS 22.0 software (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

A total of 77 consecutive patients, 13 with UC and 64 with CD, were included in the study. More than half were men ($n = 52$, 67.5%), with a mean age of 48.5 (SD = 14.1) years. No differences in sex, age or other sociodemographic characteristics were observed between patients with UC or CD (Table 1). More than half of the patients had received previous biologic treatment ($n = 44$, 57.2%), most frequently with infliximab ($n = 38$, 86.4%) (Table 2). The overall mean duration of exposure to ADA was 66 months (SD = 33.7), with a mean exposure to weekly ADA 40 mg of 40.5 months (SD = 24.8) and a mean exposure to ADA 80 mg EOW of 11.7 months (SD = 5.1) (Table 2). At inclusion, all UC patients were in clinical remission (mean PMS = 0.3, SD = 0.5). Mean HBI was 2 (SD = 2.5), with 87.1% of CD patients in clinical remission. With respect to the baseline characteristics and main outcomes, missing data accounted for less than 5% of the overall data.

Satisfaction with 80 mg ADA EOW

TSQM score reflected an extremely high satisfaction of patients with their current treatment with ADA 80 mg EOW given with a single-dose pen. The mean global satisfaction with treatment according to the TSQM was 83.4 (SD = 14.1), where 100 represents the maximum satisfaction. Patients reported notably high TSQM scores for individual components: effectiveness 77.6 (SD = 16.9), convenience 83.7 (SD = 14.5) and side effects 86.1 (SD = 23.4). There were no statistically significant differences in TSQM scores between UC and CD patients (Supplemental Table 1).

Patient Preference Questionnaire

Figure 1 shows the results of the Patient Preference Questionnaire. Most patients (74%) preferred the ADA 80 mg EOW single self-injection (59.7% had a strong preference and 14.3% had a slight preference), followed by a lower proportion of patients (18.2%) who stated no preference for any regimen (Figure 1(a)). Regarding convenience, most patients considered that ADA 80 mg EOW interferes less with work or daily activity (59.7%) and with vacation or travel plans (81.8%) (Figure 1(b)). Finally, most patients would prefer to continue with ADA 80 mg EOW administered as a single injection, as reflected by a mean VAS score of 84.7 (SD = 24.1), where 100 indicated a preference for ADA EOW (Figure 1(c)). Overall, 77% of patients ($n = 57$) preferred to continue with ADA EOW (VAS score > 50), 7.8% ($n = 6$) with ADA once a week (VAS score < 50) and 18.2% ($n = 4$) had no preference (VAS score = 50).

There were no statistically significant differences in patient preferences, or their opinion on convenience, for ADA regimen by disease (UC or CD) or level of education (university studies or other) (Supplemental Table 2). In addition, there were no statistically significant differences according to the disease or the level of education in the VAS score evaluating which ADA regimen (once a week or EOW) patients would prefer to continue (Supplemental Table 2).

Test–retest reliability of the survey questionnaire was perfect for closed questions (Cohen's kappa 1), and excellent for the numeric description scale (ICC = 0.95, 95% CI = 0.92–0.98).

Predictors of strong preference of patients for ADA 80 mg EOW

None of the factors included in the univariate analysis showed an association with the strong preference of patients for the ADA 80 mg EOW regimen (Table 3).

Physician preference

All attending physicians reported a greater preference for the ADA 80 mg EOW regimen resulting in a mean VAS score of 93.0 (SD = 7.8), where 0 indicates a preference for ADA once a week and 100 for ADA EOW.

Table 1. Sociodemographic and clinical characteristics of patients.

	Total (*N* = 77)	**Ulcerative colitis (*n* = 13)**	**Crohn's disease (*n* = 64)**	***p***
Men, *n* (%)	52 (67.5)	11 (84.6)	41 (64.1)	0.202
Age, years, mean (SD)	48.5 (14.1)	53.9 (17.8)	47.4 (13.1)	0.229
Ethnicity, *n* (%)				
Caucasian	75 (97.4)	12 (92.3)	63 (98.4)	0.331
Other	2 (2.6)	1 (7.7)	1 (1.6)	
Level of education (*n* = 77), *n* (%)				
University	26 (41.9)	2 (18.2)	24 (47.1)	0.101
Other	36 (58.1)	9 (81.8)	27 (52.9)	
Employment situation (*n* = 70), *n* (%)				
Employed/self-employed	42 (60.0)	5 (45.5)	37 (62.7)	0.328
Other	28 (40.0)	6 (54.5)	22 (37.3)	
Diagnosis, *n* (%)				
Less than 10 years	20 (26.3)	7 (43.8)	13 (20.6)	0.234
More than 10 years	56 (73.7)	6 (46.2)	50 (79.4)	
Ulcerative colitis extension, *n* (%)				
Left		7 (53.8)		
Extensive		6 (46.2)		
Phenotype A – Crohn's disease, *n* (%)				
⩽16 years			4 (6.3)	
17–40 years			46 (71.9)	
>40 years			14 (21.9)	
Phenotype L–Crohn's disease (*n* = 63), *n* (%)				
L1 Terminal ileum			21 (33.3)	
L2 Colon			9 (14.3)	
L3 Ileocolon			27 (42.8)	
L4 Upper gastrointestinal tract			1 (1.6)	
L1 + L4			3 (4.8)	
L2 + L4			1 (1.6)	
L3 + L4			1 (1.6)	
Phenotype B – Crohn's disease, *n* (%)				
B1 Inflammatory			32 (50.0)	

(continued)

Table 1. (Continued)

	Total (*N* = 77)	Ulcerative colitis (*n* = 13)	Crohn's disease (*n* = 64)	*p*
B2 Stricturing			13 (20.3)	
B3 Penetrating			19 (29.7)	
Perianal disease, *n* (%)			25 (32.5)	
Extraintestinal manifestations, *n* (%)	22 (28.6)	1 (7.7)	21 (32.8)	
Peripheral arthropathy/spondylosis/ sacroiliitis, *n* (%)	17 (22.1)	0	17 (26.6)	
Erythema nodosum/pyoderma, *n* (%)	5 (6.5)	1 (7.7)	4 (6.3)	
Psoriasis, *n* (%)	1 (1.3)	0	1 (1.6)	
Uveitis, *n* (%)	3 (3.9)	0	3 (4.7)	

SD, standard deviation.

Quality of life

At the time of survey, patients reported a notably high HRQoL for all five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) of the EQ-5D (Supplemental Table 3). The mean total EQ-5D index score was 0.867 (SD = 0.167), where 1 represents the best imaginable health. There were no differences in the total EQ-5D score between patients with UC (0.892, SD = 0.138) and CD (0.862, SD = 0.17) ($p = 0.567$). The mean EQ-5D VAS score was 72.3 (SD = 20.1), where 100 represents the best imaginable health, with no differences between patients with UC (76.9, SD = 15.8) and CD (71.3, SD = 20.8) ($p = 0.361$).

Similarly, patients reported high HRQoL in the disease-specific SIBDQ-9, with a mean score of 75.1 (SD = 14.7), where 100 represents the best imaginable health. There were no differences in SIBDQ-9 mean score between patients with UC (80.3, SD = 17.6) and CD (73.9, SD = 13.9) ($p = 0.155$).

Discussion

In the current health care environment in which a wide variety of anti-TNF options are available with proven effectiveness but differing routes of administration and dosing regimens, patient-reported experience measures may play a greater role in the selection of treatments and regimens. The ADASCAL study evaluated for the first-time preferences and satisfaction of IBD patients after switching from ADA from 40 mg weekly to 80 mg EOW given with the new 80 mg single-dose pen. Patients expressed their satisfaction with the EOW regimen that requires fewer injections to deliver escalated doses of ADA and preferred it to the weekly regimen.

Escalation to 40 mg weekly doses of ADA is safe and beneficial for IBD patients with insufficient response or loss of response to ADA 40 mg EOW.[3,4] However, the more frequent SC injections could be considered inconvenient for the patients in their everyday lives. In Japan, an alternative dose escalation regimen with ADA 80 mg EOW (given as two SC 40 mg injections) improved CD activity in patients who had lost response to maintenance ADA with no new safety signals.[15] Furthermore, a recent study evaluating ADA trough levels and occurrence of anti-ADA antibodies in patients with inactive IBD under stable maintenance therapy with dose-escalated ADA reported the pharmacokinetic equivalence between ADA 40 mg weekly and 80 mg EOW dose regimens.[16]

In situations where different treatment regimens are expected to have generally similar efficacy and safety profiles, patient preferences are an important factor in deciding which regimen to use. Our study demonstrated a clear preference of IBD patients for the ADA EOW regimen using the 80 mg single-dose pen. This regimen not only has

Table 2. Prior use of biologics or immunosuppressants, and time of exposure to ADA: total and with each escalated regimen (ADA 40 mg once a week and 80 mg EOW).

	Total (*N* = 77)	Ulcerative colitis (*n* = 13)	Crohn's disease (*n* = 64)	*p*
Prior exposure to biologics, *n* (%)				
Yes	44 (57.2)	10 (76.9)	34 (53.1)	0.114
No	33 (42.8)	3 (23.1)	30 (46.9)	
Treatment, *n* (%)				
Infliximab	38 (86.4)	13 (100)	25 (80.6)	0.16
ADA	6 (13.6)	0	6 (19.4)	
Vedolizumab	0	0	0	–
Golimumab	0	0	0	–
Ustekinumab	0	0	0	–
Last biologic, *n* (%)				
Infliximab	32 (93.9)	3 (9.4)	29 (90.6)	–
Total exposure to ADA, months				
Mean (SD)	66.0 (33.7)	45.0 (25.2)	70.3 (32.5)	0.005
Median (IQR)	58 (40–100)	43.7 (28.7–56.5)	66.4 (42.0–102.2)	0.02
ADA 40 mg every week, months				
Mean (SD)	40.5 (24.8)	37.5 (25.7)	41.1 (24.7)	0.628
Median (IQR)	22 (11–38)	23. (10.2–34.8)	22.1 (11.6–40.8)	0.812
ADA 80 mg EOW, months				
Mean (SD)	11.7 (5.1)	9.9 (6.6)	12.0 (4.7)	0.285
Median (IQR)	13 (8–15)	9.2 (3.9–15.3)	12.6 (9.0–16.0)	0.146
IMM with ADA 80 mg EOW				
Yes	33 (42.9)	4 (30.8)	29 (45.3)	0.258
No	44 (57.1)	9 (69.2)	35 (54.7)	

ADA, adalimumab; EOW, every other week, IMM, immunosuppressant; IQR, interquartile range; SD, standard deviation.

a longer interval between ADA doses but also the need for fewer SC injections to deliver a dose. Everyday life of patients seems less affected with the ADA EOW regimen since it interferes less with work or daily activity and with travel or vacation plans. The reported benefit was higher for travel plans, perhaps because depending on the duration of the trip, it may not be necessary to carry a drug that requires special transport conditions. A study evaluating preferences for the type and frequency of administration of biologics in rheumatoid arthritis patients demonstrated that the longest possible interval between injections was the most appealing treatment attribute for the ideal SC biologic.[17] The need for regular injections impacts the acceptance of treatment and hence adherence, especially in patients with IBD in long-lasting remission, like the population

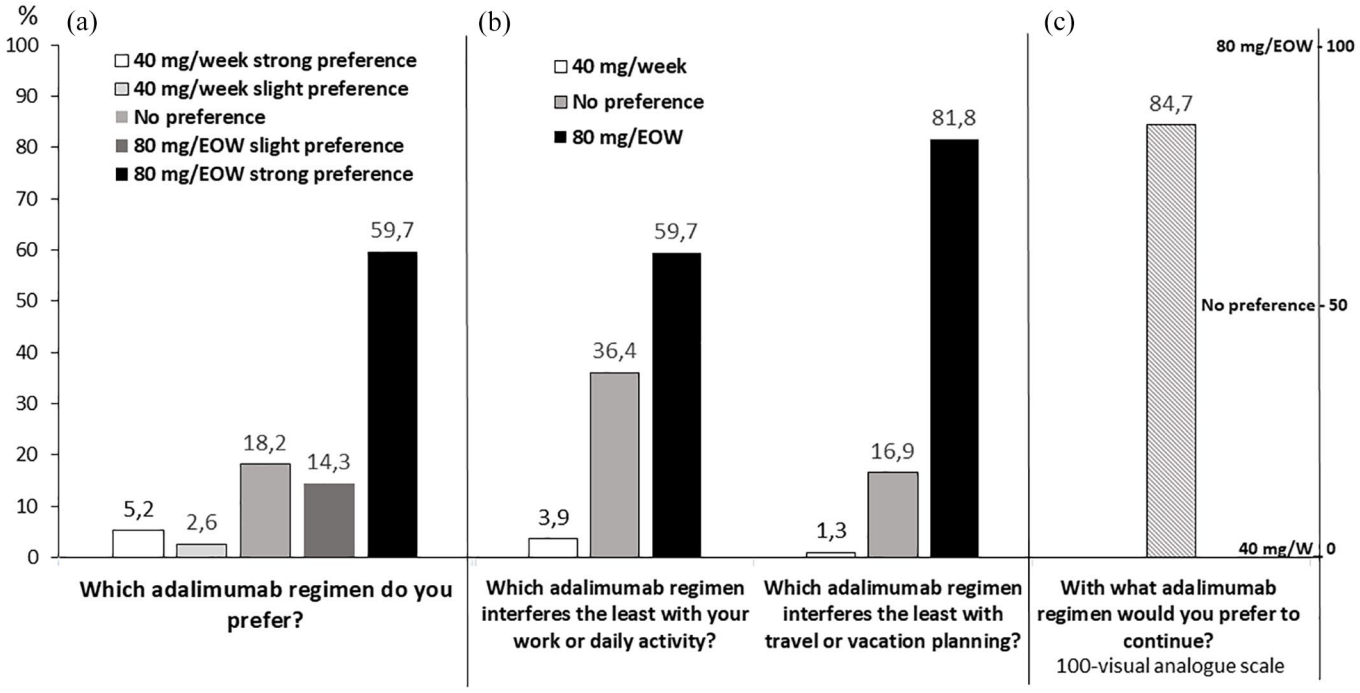

Figure 1. Self-administered questionnaire to evaluate preferences for adalimumab 40 mg weekly or 80 mg every other week: (a) a 5-point Likert-type scale for preferences, (b) two closed questions for convenience and (c) a 100-point visual analogue scale to evaluate the patient preference to continue with one or another adalimumab regimen.

included in our study. Therefore, assessing preferences for treatment in IBD patients in stable remission is a necessary step towards improving outcomes by ensuring satisfaction and adherence.

The most relevant outcome of this study was that most patients preferred to continue with the ADA 80 mg EOW regimen administered as a single injection because of the reduction in the frequency and number of SC injections. Only six patients preferred to return to the previous 40 mg weekly regimen, which suggests there has been no nocebo effect motivated by the distrust of patients with a new regimen with fewer ADA injections at longer intervals. Of note, there were no differences in patient preferences, opinion on convenience and the decision of which regimen patients chose to continue according to the disease (UC or CD) or level of education, highlighting the consistency of our results. Furthermore, there were no predictors associated with strong preference for the ADA EOW regimen. The rate of patients choosing to continue with the ADA EOW regimen was broadly in keeping with results of a previous study of the 80 mg EOW regimen, although it is not clear whether the dose was administered with the 80 mg single-dose pen or given as two 40 mg injections.[16]

As a secondary objective, the study assessed the preference of the investigators regarding the most suitable ADA escalated regimen for their patients. All attending physicians reported a preference for the ADA 80 mg EOW regimen. Since the 80 mg single-dose pen was offered at a discounted price (per milligram of ADA) in many centres, some investigators considered that the ADA 80 mg EOW regimen could be a cost-efficient strategy for IBD patients under escalated maintenance therapy with ADA 40 mg every week.[18]

In the present study, patients reported notably high degrees of satisfaction for all individual components of the validated TSQM with their current treatment with ADA 80 mg EOW given with a single-dose pen. Moreover, patients reported high HRQoL in the generic EQ-5D score and in the disease-specific SIBDQ-9. A major study weakness is that patients were required to be on stable treatment with ADA 80 mg EOW, which makes the high remission and satisfaction rates with ongoing regimen observed in the study

Table 3. Univariate analysis of factors associated with strong preference for adalimumab 80 mg every other week.

	Strong preference (*n*)	Strong preference (%)	Total (*n*)	OR	95% CI	*p*
Sex						
Male	32	61.5	52	1		0.643
Female	14	56	25	0.795	0.302–2.093	
Age, years						
⩽40	15	60	25	1		0.998
41–54	16	59.3	27	0.97	0.32–2.939	
⩾55	15	60	25	1	0.999–1	
Level of education						
University	15	57.7	26	1		0.15
Other	27	75	36	2.2	0.744–6.502	
Employment situation						
Employed or self-employed	24	57.1	42	1		0.367
Other	19	67.9	28	1.583	0.581–4.309	
Inflammatory bowel disease						
Crohn's disease	37	57.8	64	1		0.444
Ulcerative colitis	9	69.2	13	1.642	0.457–5.882	
Perianal disease (Crohn's disease patients)						
No	23	61.5	39	1		0.814
Yes	14	59	25	0.885	0.321–2.444	
Extraintestinal manifestations						
No	32	58.2	55	1		0.659
Yes	14	63.6	22	1.257	0.453–3.484	

CI, confidence interval; OR, odds ratio.

predictable. It would be expected that patients who discontinue their treatment with any of the ADA escalated regimens may be more likely to be unsatisfied with their treatment. Another main limitation of our study is the cross-sectional design in which information on satisfaction and HRQoL with the prior ADA weekly regimen cannot be collected, and so comparisons between the two escalated ADA regimens are not possible. Furthermore, the study did not evaluate clinical, endoscopic or histological outcomes with both escalated ADA dosing regimens, which would enable a more detailed comparison of clinical effectiveness of both regimens.

In conclusion, IBD patients in whom the ADA regimen was changed from 40 mg once a week to 80 mg EOW given with a single-dose pen reported a higher preference for the EOW regimen. This regimen interferes less with daily activity and with travel plans. According to the TSQM results, patients had a notably high level of satisfaction with the current EOW regimen. Therefore, most patients would prefer to continue with ADA

80 mg EOW given as a single SC injection. Assessing patient preferences for treatment in IBD is a necessary step towards improving outcomes by ensuring satisfaction and adherence.

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Author contributions

C.T. designed the study, designed the study-specific questionnaire, collected data and wrote the paper. D.O. extracted data from database and performed statistical analysis. C.A. collected data and contributed with critical revision of the manuscript. The remaining authors selected and included the patients, and collected data. All authors read and approved the final version of the manuscript.

Conflict of interest statement

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Supplemental material

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References

1. Colombel JF, Sandborn WJ, Rutgeerts P, *et al.* Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial. *Gastroenterology* 2007; 132: 52–65.
2. Sandborn WJ, van Assche G, Reinisch W, *et al.* Adalimumab induces and maintains clinical remission in patients with moderate-to-severe ulcerative colitis. *Gastroenterology* 2012; 142: 257–265.
3. Sandborn WJ, Colombel JF, Schreiber S, *et al.* Dosage adjustment during long-term adalimumab treatment for Crohn's disease: clinical efficacy and pharmacoeconomics. *Inflamm Bowel Dis* 2011; 17: 141–151.
4. Wolf D, D'Haens G, Sandborn WJ, *et al.* Escalation to weekly dosing recaptures response in adalimumab-treated patients with moderately to severely active ulcerative colitis. *Aliment Pharmacol Ther* 2014; 40: 486–497.
5. US Prescribing Information, https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125057s415lbl.pdf (accessed 12 June 2021).
6. EU SmPC, https://www.ema.europa.eu/en/documents/product-information/humira-epar-product-information_en.pdf (accessed 12 June 2021).

7. Sylwestrzak G, Liu J, Stephenson JJ, *et al.* Considering patient preferences when selecting anti-tumor necrosis factor therapeutic options. *Am Health Drug Benefits* 2014; 7: 71–81.
8. Overton PM, Shalet N, Somers F, *et al.* Patient preferences for subcutaneous versus intravenous administration of treatment for chronic immune system disorders: a systematic review. *Patient Prefer Adherence* 2021; 15: 811–834.
9. von Elm E, Altman DG, Egger M, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370: 1453–1457.
10. Atkinson MJ, Sinha A, Hass SL, *et al.* Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. *Health Qual Life Outcomes* 2004; 2: 12.
11. Jubert-Esteve E, Del Pozo-Hernando LJ, Izquierdo-Herce N, *et al.* Quality of life and side effects in patients with actinic keratosis treated with ingenol mebutate: a pilot study. *Actas Dermosifiliogr* 2015; 106: 644–650.
12. EuroQol Group. EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* 1990; 16: 199–208.
13. Alcalá MJ, Casellas F, Fontanet G, *et al.* Shortened questionnaire on quality of life for inflammatory bowel disease. *Inflamm Bowel Dis* 2004; 10: 383–391.
14. Casellas F, Alcalá MJ, Prieto L, *et al.* Assessment of the influence of disease activity on the quality of life of patients with inflammatory bowel disease using a short questionnaire. *Am J Gastroenterol* 2004; 99: 457–461.
15. Motoya S, Watanabe M, Wallace K, *et al.* Efficacy and safety of dose escalation to adalimumab 80 mg every other week in Japanese patients with Crohn's disease who lost response to maintenance therapy. *Inflamm Intest Dis* 2018; 2: 228–235.
16. Paul S, Williet N, Nancey S, *et al.* No difference of adalimumab pharmacokinetics when dosed at 40 mg every week or 80 mg every other week in IBD patients in clinical remission after adalimumab dose intensification. *Dig Dis Sci* 2021; 66: 2744–2749.
17. Huynh TK, Ostergaard A, Egsmose C, *et al.* Preferences of patients and health professionals for route and frequency of administration of biologic agents in the treatment of rheumatoid arthritis. *Patient Prefer Adherence* 2014; 8: 93–99.
18. Ferreiro-Iglesias R, Jardi A, Quiroga A, *et al.* P553 Efficacy, safety and cost-efficiency of adalimumab 80 mg every other week in previously intensified IBD patients under treatment with adalimumab 40 mg every week. *J Crohns Colitis* 2019; 13: S390–S391.