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Comparative Study of Infliximab Versus Adalimumab in Refractory Uveitis due to Behçet's Disease: National Multicenter Study of 177 Cases

Belén Atienza-Mateo,[1] José Luis Martín-Varillas,[1] Vanesa Calvo-Río,[1] Rosalía Demetrio-Pablo,[1] Emma Beltrán,[2] Juan Sánchez-Bursón,[3] Marina Mesquida,[4] Alfredo Adan,[4] María Victoria Hernández,[4] Marisa Hernández-Garfella,[5] Elia Valls-Pascual,[6] Lucía Martínez-Costa,[6] Agustí Sellas-Fernández,[7] Miguel Cordero-Coma,[8] Manuel Díaz-Llopis,[9] Roberto Gallego,[9] José L. García-Serrano,[10] Norberto Ortego-Centeno,[10] José M. Herreras,[11] Alejandro Fonollosa,[12] Ángel M. Garcia-Aparicio,[13] Olga Maíz-Alonso,[14] Ana Blanco,[14] Ignacio Torre-Salaberri,[15] Cruz Fernandez-Espartero,[16] Vega Jovaní,[17] Diana Peiteado,[18] Esperanza Pato,[19] Juan Cruz,[20] Carlos Férnandez-Cid,[20] Elena Aurrecoechea,[21] Miriam García-Arias,[22] Santos Castañeda,[22] Miguel A. Caracuel-Ruiz,[23] Carlos A. Montilla-Morales,[24] Antonio Atanes-Sandoval,[25] Félix Francisco,[26] Santos Insua,[27] Senen González-Suárez,[28] Amalia Sanchez-Andrade,[29] Fernando Gamero,[30] Luis F. Linares Ferrando,[31] F. Romero-Bueno,[32] A. Javier García-González,[33] Raquel Almodóvar González,[34] Enrique Minguez Muro,[35] Carmen Carrasco-Cubero,[36] Alejandro Olive,[37] Águeda Prior,[37] Julio Vázquez,[38] Oscar Ruiz-Moreno,[39] Fernando Jiménez-Zorzo,[39] Javier Manero,[39] Santiago Muñoz Fernandez,[40] Cristina Fernández-Carballido,[41] Esteban Rubio-Romero,[42] Fred Antón Pages,[43] Francisco J. Toyos-Sáenz de Miera,[44] Myriam Gandia Martinez,[45] David Díaz-Valle,[19] Francisco J. López Longo,[16] Joan M. Nolla,[46] Enrique Raya Álvarez,[10] Marcelino Revenga Martínez,[47] Julio José González-López,[47] Paz Rodríguez-Cundin,[1] José L. Hernández,[1] Miguel A. González-Gay,[1] and Ricardo Blanco[1]

Objective. To compare the efficacy of infliximab (IFX) versus adalimumab (ADA) as a first-line biologic drug over 1 year of treatment in a large series of patients with refractory uveitis due to Behçet's disease (BD).

Methods. We conducted an open-label multicenter study of IFX versus ADA for BD-related uveitis refractory to conventional nonbiologic treatment. IFX or ADA was chosen as the first-line biologic agent based on physician and patient agreement. Patients received 3–5 mg/kg intravenous IFX at 0, 2, and 6 weeks and every 4–8 weeks thereafter, or 40 mg subcutaneous ADA every other week without a loading dose. Ocular parameters were compared between the 2 groups.

Results. The study included 177 patients (316 affected eyes), of whom 103 received IFX and 74 received ADA. There were no significant baseline differences between treatment groups in main demographic features, previous therapy, or ocular sign severity. After 1 year of therapy, we observed an improvement in all ocular parameters in both groups. However, patients receiving ADA had significantly better outcomes in some parameters, including improvement in anterior chamber inflammation (92.31% versus 78.18% for IFX; $P = 0.06$), improvement in vitritis (93.33% versus 78.95% for IFX; $P = 0.04$), and best-corrected visual acuity (mean ± SD 0.81 ± 0.26 versus 0.67 ± 0.34 for IFX; $P = 0.001$). A nonsignificant difference was seen for macular thickness (mean ± SD 250.62 ± 36.85 for ADA versus 264.89 ± 59.74 for IFX; $P = 0.15$), and improvement in retinal vasculitis was similar between the 2 groups (95% for ADA versus 97% for IFX; $P = 0.28$). The drug retention rate was higher in the ADA group (95.24% versus 84.95% for IFX; $P = 0.042$).

Conclusion. Although both IFX and ADA are efficacious in refractory BD-related uveitis, ADA appears to be associated with better outcomes than IFX after 1 year of follow-up.

[1]Belén Atienza-Mateo, MD, José Luis Martín-Varillas, MD, Vanesa Calvo-Río, MD, PhD, Rosalía Demetrio-Pablo, MD, PhD, Paz Rodríguez-Cundin, MD, PhD, José L. Hernández, MD, PhD, Miguel A. González-Gay, MD, PhD, Ricardo Blanco, MD, PhD: Hospital Universitario Marqués de Valdecilla, Santander, Spain; [2]Emma Beltrán, MD: Hospital del Mar, Barcelona, Spain; [3]Juan Sánchez-Bursón, MD, PhD: Hospital de Valme, Sevilla, Spain; [4]Marina Mesquida, MD, PhD, Alfredo Adan, MD, PhD, María Victoria Hernández, MD: Hospital Clinic, Barcelona, Spain; [5]Marisa Hernández-Garfella, MD: Hospital General Universitario de Valencia, Valencia, Spain; [6]Elia Valls-Pascual, MD, Lucía Martínez-Costa, MD, PhD: Hospital Peset, Valencia, Spain; [7]Agustí Sellas-Fernández, MD: Hospital Vall d'Hebron, Barcelona, Spain; [8]Miguel Cordero-Coma, MD, PhD: Hospital de León, León, Spain; [9]Manuel Díaz-Llopis, MD, PhD,

INTRODUCTION

Behçet's disease (BD) is a systemic vasculitis characterized by recurrent oral and/or genital ulcers, skin lesions, and ocular involvement, although it can affect multiple organs (1,2). One of the major causes of disability in BD is uveitis. Several studies have indicated that the risk of severe visual loss ranges from 13–74% within 6–10 years after the onset of uveitis (3–6).

The prognosis of ocular involvement has improved over recent decades due to the use of conventional and biologic immunosuppressive therapies (7). According to the 2014 expert panel recommendations for the use of anti–tumor necrosis factor (anti-TNF) drugs in patients with ocular inflammatory disorders, infliximab (IFX; good-quality evidence) or adalimumab (ADA; moderate-quality evidence) may be considered as the first- or second-line glucocorticoid-sparing therapy for patients with ophthalmic manifestations of BD, and IFX may be considered as the first- or second-line treatment for acute exacerbations of preexisting BD (8).

In 2016, ADA was reported to be the only biologic drug that demonstrated efficacy in randomized double-blind, phase III studies of noninfectious intermediate posterior uveitis and panuveitis (the Efficacy and Safety of Adalimumab in Patients With Active Non-infectious Uveitis [VISUAL I] trial and the Efficacy and Safety of Adalimumab in Subjects With Inactive Non-infectious Uveitis [VISUAL II] trial) (9,10). Consequently, ADA was approved by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) for noninfectious non-anterior uveitis. However, underlying diseases included in the VISUAL trials were very heterogeneous. Furthermore, the VISUAL trials included very few cases of BD-related uveitis treated with ADA (12 patients [11%] in VISUAL I and 10 patients [9%] in VISUAL II). Therefore, conclusions regarding the efficacy of ADA in BD were limited. Moreover, little is known of differences in outcome for patients with BD-related uveitis treated with IFX versus those treated with ADA. Only one previous study has compared the efficacy of these 2 anti-TNF agents in adult patients with refractory noninfectious uveitis (11). However, that study included a very heterogeneous group of patients, including those with diseases unrelated to BD, such as juvenile idiopathic arthritis, spondyloarthritis, and sarcoidosis. Moreover, patients with refractory uveitis due to BD represented only 36% of the cases. Therefore, there was no specific comparison between IFX and ADA for refractory BD-related uveitis.

Taking into account all of these considerations, we aimed to compare the efficacy and safety of IFX versus ADA as the first-line biologic drug in a large series of patients with refractory uveitis exclusively due to BD who were followed up for 1 year.

PATIENTS AND METHODS

Study design, enrollment criteria, and definitions. We conducted an observational, open-label multicenter study including 177 patients with refractory uveitis due to BD who were treated with IFX or ADA as first-line biologic therapy. The dosing schedule was as follows: for IFX, 3–5 mg/kg intravenously (IV) at

Roberto Gallego, MD, PhD: Hospital Universitario La Fe, Valencia, Spain; [10]José L. García-Serrano, MD, PhD, Norberto Ortego-Centeno, MD, PhD, Enrique Raya Álvarez, MD, PhD: Hospital Universitario San Cecilio, Granada, Spain; [11]José M. Herreras, MD, PhD: Hospital Universitario IOBA, Valladolid, Spain; [12]Alejandro Fonollosa, MD, PhD: Hospital de Cruces, Bilbao, Spain; [13]Ángel M. Garcia-Aparicio, MD: Hospital de Toledo, Toledo, Spain; [14]Olga Maíz-Alonso, MD, Ana Blanco, MD: Hospital Universitario de Donostia, San Sebastián, Spain; [15]Ignacio Torre-Salaberri, MD: Hospital Universitario de Basurto, Bilbao, Spain; [16]Cruz Fernandez-Espartero, MD, Francisco J. López Longo, MD, PhD: Hospital Universitario de Móstoles, Madrid, Spain; [17]Vega Jovaní, MD, PhD: Hospital General de Alicante, Alicante, Spain; [18]Diana Peiteado, MD, PhD: Hospital La Paz, Madrid, Spain; [19]Esperanza Pato, MD, David Díaz-Valle, MD, PhD: Hospital Clínico San Carlos, Madrid, Spain; [20]Juan Cruz, MD, Carlos Férnandez-Cid, MD: Hospital de Pontevedra, Pontevedra, Spain; [21]Elena Aurrecoechea, MD, PhD: Hospital Sierrallana, Torrelavega, Spain; [22]Miriam García-Arias, MD, Santos Castañeda, MD, PhD: Hospital Universitario de la Princesa, IIS-Princesa, Madrid, Spain; [23]Miguel A. Caracuel-Ruiz, MD, PhD: Hospital Universitario Reina Sofía, Córdoba, Spain; [24]Carlos A. Montilla-Morales, MD, PhD: Hospital Clínico Universitario de Salamanca, Salamanca, Spain; [25]Antonio Atanes-Sandoval, MD, PhD: Complejo Hospitalario Universitario A Coruña, A Coruña, Spain; [26]Félix Francisco, MD: Hospital Doctor Negrín, Las Palmas de Gran Canaria, Spain; [27]Santos Insua, MD: Hospital Universitario Santiago de Compostela, A Coruña, Spain; [28]Senen González-Suárez, MD: Hospital de Cabueñes, Gijón, Spain; [29]Amalia Sanchez-Andrade, MD, PhD: Hospital Lucus Augusti, Lugo, Spain; [30]Fernando Gamero, MD: Hospital San Pedro Alcántara, Cáceres, Spain; [31]Luis F. Linares Ferrando, MD, PhD: Hospital Virgen de la Arrixaca, Murcia, Spain; [32]F. Romero-Bueno, MD, PhD: Jiménez Díaz Foundation University Hospital, Madrid, Spain; [33]A. Javier García-González, MD: Instituto de Investigación Hospital 12 de Octubre, Madrid, Spain; [34]Raquel Almodóvar González, MD: Hospital Universitario Fundación de Alcorcón, Madrid, Spain; [35]Enrique Minguez Muro, MD, PhD: Hospital Clínico de Zaragoza, Zaragoza, Spain; [36]Carmen Carrasco-Cubero, MD: Hospital de Mérida, Mérida, Spain; [37]Alejandro Olive, MD, PhD, Águeda Prior, MD: Germans Trias i Pujol Hospital, Barcelona, Spain; [38]Julio Vázquez, MD: Hospital de Ferrol, A Coruña, Spain; [39]Oscar Ruiz-Moreno, MD, PhD, Fernando Jiménez-Zorzo, MD, Javier Manero, MD: Hospital Universitario Miguel Servet, Zaragoza, Spain; [40]Santiago Muñoz Fernandez, MD, PhD: Hospital Universitario Infanta Sofía, Madrid, Spain; [41]Cristina Fernández-Carballido, MD, PhD: Hospital General Universitario de Elda, Alicante, Spain; [42]Esteban Rubio-Romero, MD: Hospital Universitario Virgen del Rocío, Sevilla, Spain; [43]Fred Antón Pages, MD: Complejo Asistencial de Palencia, Palencia, Spain; [44]Francisco J. Toyos-Sáenz de Miera, MD, PhD: Hospital Virgen de la Macarena, Sevilla, Spain; [45]Myriam Gandia Martinez, MD, PhD: Hospital Puerta del Mar, Cádiz, Spain; [46]Joan M. Nolla, MD, PhD: Hospital Universitari de Bellvitge, Barcelona, Spain; [47]Marcelino Revenga Martínez, MD, PhD, Julio José González-López, MD, PhD: Hospital Universitario Ramón y Cajal, Madrid, Spain.

Drs. Atienza-Mateo, Martín-Varillas, and Calvo-Río contributed equally to this work.

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0, 2, and 6 weeks and every 4–8 weeks thereafter; and for ADA, 40 mg subcutaneously every other week without loading dose.

All of the BD patients had uveitis refractory to glucocorticoids and had previously received at least 1 conventional synthetic immunosuppressive drug. Of the 177 patients, 103 received IFX and 74 received ADA. Partial information on 124 patients in this series was previously reported (12). Patients were followed up at 52 uveitis referral units in Spanish hospitals. Patients were diagnosed as having BD according to the proposed International Criteria for BD (13), and all patients fulfilled the recently proposed criteria for BD (14).

Since uveitis is an off-label indication for IFX, written informed consent was requested and obtained from all patients in the IFX group. Written informed consent was also obtained from patients in the ADA group, since ADA was prescribed before approval by the EMA and the FDA for the treatment of noninfectious and non-anterior uveitis.

Malignancy or systemic infectious diseases, including hepatitis B or C infection, were excluded before starting anti-TNF treatment, as previously described (12,15–21). To exclude latent tuberculosis (TB), patients underwent a tuberculin skin test (purified protein derivative) and/or an interferon-γ assay (QuantiFeron) and a chest radiograph, as indicated by the Spanish National Guidelines for all patients receiving biologic drugs. If latent TB was present, prophylaxis with isoniazid was initiated at least 4 weeks before beginning biologic treatment and maintained for 9 months.

Uveitis was anatomically classified according to the Standardization of Uveitis Nomenclature (SUN) Working Group (22). Remission was defined as the absence of signs of any intraocular inflammation for at least 3 months. Intraocular inflammation was considered to be present if there was anterior or posterior chamber inflammation, retinal vasculitis, papillitis, or cystoid macular edema (CME). A relapse was defined as a new flare of uveitis in a patient whose disease was in remission (23).

The conventional immunosuppressive drugs and dosages given most frequently before ADA or IFX treatment were cyclosporin A (CsA; 3–6 mg/kg/day orally), methotrexate (MTX; 7.5–25 mg/week subcutaneously), and azathioprine (AZA; 100–150 mg/day orally). Consistent with the VISUAL I and VISUAL II trials, the maintenance dose of ADA was 40 mg subcutaneously every other week. However, the VISUAL I and II trials were published after the present study had begun, and therefore, patients from our series did not receive a loading dose of ADA. Patients in the IFX group received a standard loading dose of 3–5 mg/kg IV at weeks 0, 2, and 6 and a maintenance dose every 4–8 weeks thereafter. The anti-TNF agents were administered in combination with conventional immunosuppressive drugs in 78 of 102 patients receiving IFX (76.5%) and in 52 patients receiving ADA (70.3%) and as monotherapy in the remaining cases. The conventional drugs used in combination with ADA and IFX are shown in Table 1.

Outcome variables. The outcome variables were efficacy, safety, and drug retention rate. To determine efficacy, intraocular inflammation, macular thickness, visual acuity, degree of immunosuppression load, number of relapses, and glucocorticoid-sparing effect were assessed. These outcome variables were recorded at baseline, 1 week, 2 weeks, 1 month,

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Address correspondence to Miguel A. González-Gay, MD, PhD, or Ricardo Blanco, MD, PhD, Hospital Universitario Marqués de Valdecilla, Rheumatology Division, Avenida Valdecilla s/n, 39008 Santander, Spain. E-mail: miguelaggay@hotmail.com or rblanco@humv.es.

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Table 1. Baseline features of and follow-up data for a series of 177 patients receiving IFX or ADA for refractory uveitis due to Behçet's disease*

	IFX (n = 103)	ADA (n = 74)	*P*
No. of patients/no. of affected eyes	103/185	74/131	–
Age, mean ± SD years	40.4 ± 10.1	38.7 ± 1.3	0.29
Sex, no. of men/no. of women	55/48	39/35	0.93
HLA–B51 positive, %	69.4	68.9	0.74
Duration of uveitis before anti-TNF therapy, median (IQR) months	36 (12–72)	24 (12–60)	0.69
Ocular features at start of anti-TNF therapy			
Anterior chamber inflammation grade, median (IQR)	1 (0–2)	1 (0–2)	0.25
Vitritis grade, median (IQR)	1 (0–2)	1 (0–2)	0.12
BCVA, mean ± SD	0.50 ± 0.35	0.56 ± 0.34	0.08
Macular thickness, mean ± SD μm	331.11 ± 131.97	346.37 ± 136.14	0.49
No. of patients with retinal vasculitis	114	78	0.51
No. of patients with choroiditis	41	10	<0.01
Uveitis pattern, no. (%)			
Bilateral	82 (79.61)	57 (77.03)	0.68
Unilateral	21 (20.39)	17 (22.97)	0.68
Anterior	11 (10.68)	14 (18.92)	0.19
Posterior	28 (27.18)	14 (18.92)	0.19
Panuveitis	64 (62.14)	45 (60.81)	0.19
Intermediate	0 (0)	1 (1.35)	0.19
Treatment before start of anti-TNF therapy, %			
Oral glucocorticoids	95	88	0.08
Intravenous pulse MP	31	31	0.98
CsA	75	78	0.65
AZA	57	42	0.049
MTX	44	42	0.77
Other treatments	4	2	0.41
Prednisone dosage at start of anti-TNF therapy, mean ± SD, mg/day	54.35 ± 15.84	53.37 ± 17.52	0.37
Combined treatment, %†	76.5	70.3	0.35
AZA	21.8	19.2	–
CsA	41.1	55.7	–
MTX	33.3	21.1	–
CYC	1.3	0.0	–
MMF	1.3	3.8	–
FK-506	1.3	0.0	–
Follow-up data			
Duration of follow-up, mean ± SD months	31.52 ± 23.51	26.48 ± 18.57	0.13
Remission, no. (%)	78 (76.47)‡	61 (82.43)	0.34
No. of relapses, mean ± SD	1.13 ± 2.62	1.66 ± 8.62	0.61
Drug discontinuation, no. (%)	57 (55.33)	21 (28.37)	<0.01
Reason for discontinuation, no. (%)			
Remission	20 (19.41)	6 (8.1)	0.58
Inefficacy	18 (17.47)	11 (14.86)	0.09
Severe side effects/toxicity	8 (7.76)	4 (5.4)	0.58
Other	11 (10.68)	0 (0)	0.03
Serious side effects per 100 patient-years, mean ± SD	4 ± 1.48	4 ± 2.46	0.40

* IFX = infliximab; ADA = adalimumab; IQR = interquartile range; BCVA = best-corrected visual acuity; MP = methylprednisolone; CsA = cyclosporin A; AZA = azathioprine; MTX = methotrexate; CYC = cyclophosphamide; MMF = mycophenolate mofetil.
† Patients receiving conventional immunosuppressive drugs in combination with the anti–tumor necrosis factor (anti-TNF) agent.
‡ Data were available for 102 patients.

3 months, 6 months, and 1 year after the start of IFX or ADA treatment. They were assessed in each center according to a follow-up protocol agreed upon beforehand.

The degree of intraocular inflammation was evaluated according to the SUN Working Group criteria (22). Vitritis was assessed using the Nussenblatt scale (24). The best-corrected visual acuity (BCVA) was estimated using a Snellen chart. Following SUN recommendations (22), improvement in anterior uveitis activity was defined as either a 2-step decrease in the level of inflammation or a decrease to grade 0 for the level of inflammation

(on a scale comprised of the grades 4, 3, 2, 1, 0.5, and 0). Inactive anterior uveitis (grade 0) was defined as <1 cell per field in the anterior chamber on slit lamp examination. Worsening activity was defined as either a 2-step increase in the level of inflammation or an increase to grade 4. Similar definitions were used for improvement in and worsening of vitritis.

Fluorescein angiography (FA) was performed to assess the presence of vasculitis. FA results were reviewed for the presence of vasculitis, papillitis, and CME. Retinal vasculitis was defined as a retinal angiographic leakage, staining, and/or occlusion on FA (4). Choroiditis and retinitis were considered active or inactive depending on the presence or absence, respectively, of activity data on ophthalmoscopic examination and/or FA.

Macular thickness was measured by high-definition optical coherence tomography (OCT), a noninvasive imaging technique that uses light waves to obtain high-resolution cross-sectional images of the retina. Scans were obtained using a 512 × 128 scan pattern. Macular thickening was defined as a macular thickness >250 μm, whereas CME was considered to be present if macular thickness was >300 μm.

The degree of immunosuppression was calculated according to the semiquantitative scale proposed by Nussenblatt et al (25,26). This grading scheme provides a combined, single numeric score for the total immunosuppression load per unit of body weight per day. Each agent (prednisone, CsA, AZA, MTX, and other immunosuppressants) was graded on a scale of 0–9, except for mycophenolate mofetil, which was graded on a scale of 0–7. For patients receiving multiple medications, the sum of the grading scores for each drug was used to calculate the total immunosuppression score on a scale of 0–15 at the baseline visit and at each subsequent visit. Topical or periocular glucocorticoid therapy was excluded from the calculation of the immunosuppression load. The biologic agent dose was not used to calculate the final immunosuppression load.

Statistical analysis. Results are expressed as the mean ± SD for normally distributed variables and as the median (interquartile range [IQR]) for non-normally distributed variables. Continuous variables were compared by Student's 2-tailed *t*-test (for normally distributed variables) or Mann-Whitney U test (for non-normally distributed variables). The chi-square test or Fisher's exact test was used for dichotomous variables. Wilcoxon's signed rank test was used to compare continuous variables between the 2 treatment groups. BCVA, anterior chamber inflammation, vitritis, retinal vasculitis, and OCT findings were assessed at baseline (first visit before the initiation of anti-TNF treatment), 1 week, 2 weeks, 1 month, 3 months, 6 months, and 1 year and compared between time points within each group. In addition, mixed linear models were used with repeated-measures data to accommodate the effects of treatment and time and the covariation between observations for the same subject at different times. This mixed model allows greater flexibility in modeling covariance structures for repeated-measures data, and adequately accounts for the within-subject time-dependent correlations. Further, Bonferroni correction for multiple comparisons was performed in order to control for the family-wise error rate. *P* values less than 0.05 were considered significant. Statistical analysis was performed using Statistica software (StatSoft).

RESULTS

Baseline demographic and clinical features of the patients in the IFX and ADA groups. A total of 177 patients (316 affected eyes) with uveitis refractory to conventional immunosuppressive therapy were studied (Table 1). Of these patients, 103 (58%) were treated with IFX and 74 (42%) were treated with ADA as a first-line biologic agent. In both groups, men slightly outnumbered women (55 men and 48 women in the IFX group versus 39 men and 35 women in the ADA group; $P = 0.93$). The mean age was similar in both groups (mean ± SD 40.4 ± 10.1 years in the IFX group and 38.7 ± 11.3 years in the ADA group; $P = 0.29$). HLA–B51 was present in a similar proportion of patients in both groups (69.4% in the IFX group versus 68.9% in the ADA group; $P = 0.74$). In most cases uveitis was bilateral (79.61% in the IFX group versus 77.03% in the ADA group; $P = 0.68$).

Regarding previous therapy, there were no significant differences between the 2 groups with regard to the administration of oral glucocorticoids (95% in the IFX group versus 88% in the ADA group [$P = 0.08$]; mean ± SD maximum daily prednisone dosage 54.35 ± 15.84 mg/day in the IFX group versus 53.37 ± 17.52 mg/day in the ADA group; $P = 0.37$) or IV pulse methylprednisolone (31% in both groups; $P = 0.98$). The percentages of patients treated with CsA, MTX, and cyclophosphamide were also similar between groups (Table 1). However, a significantly higher percentage of patients in the IFX group (57%) than in the ADA group (42%) received AZA before the start of anti-TNF treatment ($P = 0.049$). No significant differences in the dosages of the conventional immunosuppressive drugs were observed between the IFX and ADA groups (for CsA, mean ± SD 4.9 ± 0.8 mg/kg/day versus 4.8 ± 0.8 mg/kg/day [$P = 0.88$]; for MTX, 15.6 ± 4.6 mg/week versus 16.7 ± 3.6 mg/week [$P = 0.17$]; and for AZA, 137.2 ± 32.3 mg/day versus 127.4 ± 25.3 mg/day [$P = 0.14$]). Moreover, the immunosuppression load score was similar in both groups (mean ± SD 9.07 ± 4.14 in the IFX group versus 8.01 ± 5.24 in the ADA group; $P = 0.2$).

The median period between the onset of uveitis and the beginning of anti-TNF therapy was also similar in both groups (36 months [IQR 12–72 months] in the IFX group versus 24 months [IQR 12–60 months] in the ADA group; $P = 0.69$).

Visual outcome, glucocorticoid-sparing effect, and immunosuppression load score after 1 year of ADA or IFX therapy. The standard loading dose of IFX (3–5 mg/kg IV) was given at 0, 2, and 6 weeks, and patients then received a maintenance dose every 4–8 weeks. The numbers of patients

receiving each specific IFX dosing regimen were as follows: 3 mg/kg IV and maintenance dose every 4 weeks (n = 1), every 6 weeks (n = 2), and every 8 weeks (n = 5); 4 mg/kg IV and maintenance dose every 4 weeks (n = 1); and 5 mg/kg IV and maintenance dose every 4 weeks (n = 15), every 6 weeks (n = 18), every 7 weeks (n = 1), and every 8 weeks (n = 60).

During the first year of treatment, we observed an improvement in all ocular parameters in both the IFX and ADA groups. Nevertheless, outcomes for the following parameters were significantly better in the ADA group: anterior chamber inflammation (improvement in 92.31% in the ADA group versus 78.18% in the IFX group; $P = 0.06$), vitritis (improvement in 93.33% in the ADA group versus 78.95% in the IFX group; $P = 0.04$), and BCVA (mean ± SD 0.81 ± 0.26 in the ADA group versus 0.67 ± 0.34 in the IFX group; $P = 0.001$). Patients in the ADA group had a greater improvement in macular thickness but the difference between treatment groups was not significant (mean ± SD 250.62 ± 36.85 μm in the ADA group versus 264.89 ± 59.74 μm in the IFX group; $P = 0.15$). A similar proportion in both groups experienced improvement in retinal vasculitis (97% in the IFX group versus 95% in the ADA group; $P = 0.28$). The drug retention rate at 1 year was better in the ADA group (95.24% versus 84.95% in the IFX group; $P = 0.042$).

More rapid improvement of anterior chamber inflammation and vitritis was seen in the IFX group (data not shown). This finding may be explained by the fact that the patients in our series did not receive an ADA loading dose. However, better results were achieved in the patients in the ADA group after 1 year of therapy, with a significantly greater proportion of patients experiencing improvement in anterior chamber inflammation and vitritis, and a significantly higher BCVA and drug retention rate compared to the IFX group.

In order to capture within-patient correlation of repeated observations, we performed a mixed linear model using as covariates the factors shown in Table 1 that had a P value of less than or equal to 0.1, as well as other plausible confounders. After adjustment for the presence of basal choroiditis and use of oral glucocorticoids or AZA before anti-TNF onset, improvement in BCVA at 12 months remained significantly better in the ADA group compared to the IFX group ($P = 0.007$). The improvement in BCVA values at different time points in the study is shown in Figure 1. When the model included the presence of vitritis, age, sex, or duration of uveitis before starting anti-TNF therapy, the results did not change. However, once the model was adjusted for these variables, there were no significant differences between the 2 treatment groups with regard to vitritis, retinitis, or OCT measurements.

One year after the initiation of anti-TNF therapy, a reduction in the immunosuppression load score was observed in both groups (from a mean ± SD of 9.07 ± 4.14 in the IFX group and 8.01 ± 5.24 in the ADA group at baseline [$P = 0.2$] to 5.47 ± 3.19 in the IFX group and 4.79 ± 3.52 in the ADA group at 1 year [$P = 0.38$]). The median daily dose of prednisone was reduced in both groups, from 30 mg (IQR 20–45) at baseline to 5 mg (IQR 0–10) at 1 year in the IFX group and from 20 mg (IQR 10–45) at baseline to 5 mg (IQR 2.5–10) at 1 year in the ADA group ($P = 0.9$).

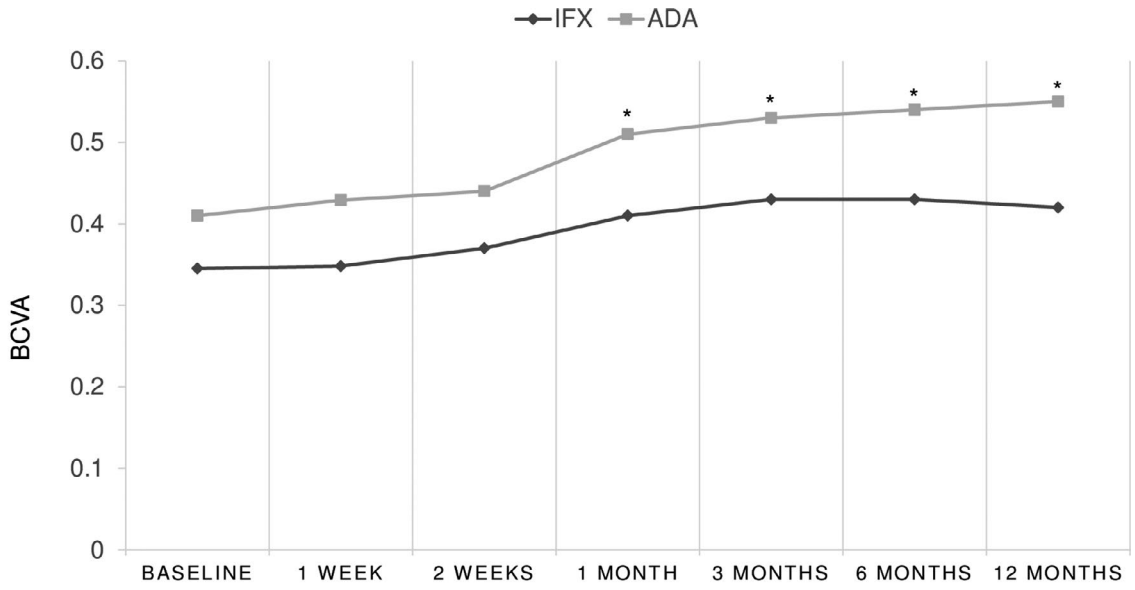

Figure 1. Adjusted best-corrected visual acuity (BCVA) at the indicated time points in the patients with Behçet's disease–related uveitis treated with infliximab (IFX) and those treated with adalimumab (ADA). Values are the mean.

Follow-up data and side effects of ADA and IFX. After a mean ± SD follow-up of 31.52 ± 23.51 months in the IFX group and 26.48 ± 18.57 months in the ADA group, ocular remission was achieved in 78 (76.47%) of 102 patients receiving IFX and in 61 (82.43%) of the patients receiving ADA ($P = 0.34$). However, the drug retention rate was significantly higher in the ADA group than in the IFX group (71.62% versus 44.12%; $P < 0.001$). IFX was discontinued in 57 (55.33%) of the patients and ADA in 21 (28.37%) of the patients ($P < 0.01$). IFX was discontinued because of remission in 20 patients. In the remaining 37 patients the reasons for IFX discontinuation were inefficacy (n = 18), preference for a different route of administration (n = 9), toxicity/side effects (n = 8), colon carcinoma (n = 1), and desire for pregnancy (n = 1). ADA was discontinued due to remission in 6 patients and was discontinued in the remaining 15 patients due to inefficacy (n = 11) or toxicity/side effects (n = 4).

Eight patients in the IFX group and 4 patients in the ADA group discontinued treatment due to severe side effects or toxicity. The 8 withdrawals from the IFX group were due to infusion reactions in 4 cases, and TB, *Mycobacterium avium* pneumonia, severe oral ulcers, and palmoplantar skin reaction in 1 case each. The 4 patients who discontinued ADA therapy withdrew because of lymphoma, bacterial pneumonia, severe local reaction at the injection site, and *Escherichia coli* bacteremia. Data on remission, relapses, treatment discontinuation, and serious sides effects are shown for both groups in Table 1.

DISCUSSION

In this multicenter study, we report on 177 cases of refractory BD-related uveitis treated with IFX (n = 103) or ADA (n = 74) as first-line biologic therapy. After 1 year of follow up, a significantly greater improvement in BCVA, as well as a significantly higher drug retention rate, was achieved in patients treated with ADA than in those treated with IFX. However, more rapid improvement in anterior chamber inflammation and vitritis was observed in the IFX group compared to the ADA group, which could be explained in part by the fact that patients in the ADA group did not receive a loading dose of 80 mg along with a subsequent dose of 40 mg at 1 week as performed in the VISUAL trials, since our study was carried out before the VISUAL trials were published.

Several studies have demonstrated the presence of high levels of TNF—a potent and central ubiquitous proinflammatory cytokine—in serum and aqueous humor from patients with uveitis, including cases with BD-related uveitis (27–29). The anti-TNF agents IFX (a human–mouse chimeric IgG1 monoclonal antibody specific for TNF, administered IV) and ADA (a fully human IgG1 monoclonal antibody also specific for TNF, administered subcutaneously) have demonstrated efficacy in the treatment of BD-related uveitis refractory to conventional immunosuppressive therapy (12,26,30–38).

In fact, ADA has recently been approved by the FDA and EMA for use in noninfectious intermediate, posterior uveitis and panuveitis, including cases due to BD. However, there are few studies comparing the efficacy of IFX and ADA for the induction and maintenance of remission in these patients with refractory uveitis (11,39,40). Moreover, those studies generally include patients with heterogeneous diseases, with patients with BD making up a minority of the total reported cases.

The present study compared the efficacy of IFX versus ADA as a first-line biologic drug in a large series of patients with BD-related uveitis refractory to conventional immunosuppressive drugs. Before the initiation of biologic therapy, all patients had received systemic high-dose glucocorticoids and one or more conventional synthetic immunosuppressive drugs. However, despite this treatment uveitis remained active.

Although our study showed a rapid and sustained improvement in all ocular parameters for patients in both anti-TNF drug groups, a significant difference was observed between the 2 groups with regard to BCVA improvement, which was greater in the ADA group. It is possible that the differences between the ADA group and the IFX group would have been even more evident if we had performed an intent-to-treat study instead of a per-protocol analysis because a higher percentage of patients discontinued IFX due to inefficacy.

The drug retention rate was also higher in the ADA group. This finding could be explained in part by the route of administration since ADA is given subcutaneously in a rapid and comfortable manner. Moreover, infusion reactions occur more frequently with IFX due to its chimeric nature, and the occurrence of anti-drug antibodies may also be higher with IFX.

Minor adverse effects, such as mild infusion reaction to IFX and local reactions at the site of the injection of ADA, were the most commonly observed side effects. Severe complications leading to discontinuation of the biologic therapy were observed in 8 cases in the IFX group and 4 in the ADA group. The treatment was discontinued due to inefficacy in 18 cases in the IFX group and 11 in the ADA group, comprising a low percentage of cases (17.5% and 14.9%, respectively).

We realize that this study has several limitations due to its observational nature. Therefore, further randomized, controlled trials comparing IFX and ADA head-to-head are needed.

In conclusion, we observed favorable results of both ADA and IFX therapy for BD-related refractory uveitis after 1 year of treatment, with significantly greater improvement in BCVA and higher drug retention rate in the ADA group than the IFX group.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version

to be published. Dr. González-Gay had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Atienza-Mateo, Martín-Varillas, Calvo-Río, González-Gay, R. Blanco.

Acquisition of data. Atienza-Mateo, Martín-Varillas, Calvo-Río, Demetrio-Pablo, Beltrán, Sánchez-Bursón, Mesquida, Adan, Hernández, Hernández-Garfella, Valls-Pascual, Martínez-Costa, Sellas-Fernández, Cordero-Coma, Díaz-Llopis, Gallego, García-Serrano, Ortego-Centeno, Herreras, Fonollosa, Garcia-Aparicio, Maíz-Alonso, A. Blanco, Torre-Salaberri, Fernandez-Espartero, Jovaní, Peiteado, Pato, Cruz, Férnandez-Cid, Aurrecoechea, García-Arias, Castañeda, Caracuel-Ruiz, Montilla-Morales, Atanes-Sandoval, Francisco, Insua, González-Suárez, Sanchez-Andrade, Gamero, Linares Ferrando, Romero-Bueno, García-González, Almodóvar González, Muro, Carrasco-Cubero, Olive, Prior, Vázquez, Ruiz-Moreno, Jiménez-Zorzo, Manero, Muñoz Fernandez, Fernández-Carballido, Rubio-Romero, Pages, Toyos-Sáenz de Miera, Martinez, Díaz-Valle, López Longo, Nolla, Álvarez, Martínez, González-López, Rodríguez-Cundin, González-Gay, R. Blanco.

Analysis and interpretation of data. Atienza-Mateo, Martín-Varillas, Calvo-Río, Demetrio-Pablo, Hernández, González-Gay, R. Blanco.

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