RECOMENDACIONES PARA EL USO DE TERAPIA ANTI-TNF EN LA ENFERMEDAD DE BEHÇET

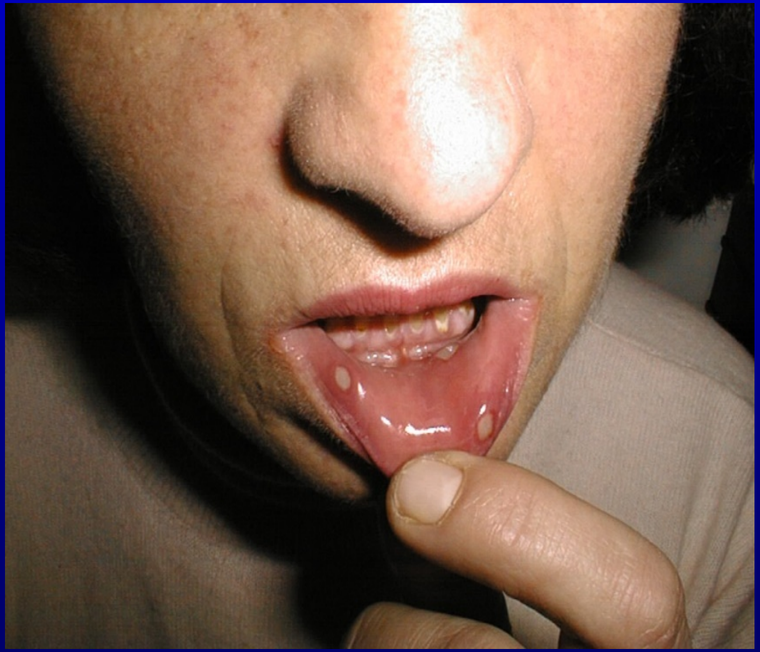
III Reunión Nacional en Enfermedades Autoinmunes Sistémicas

II Curso de Terapias Biológicas en Enfermedades Autoinmunes Sistémicas

30 Septiembre - 2 Octubre 2010
Hotel Meliá Lebreros
- Sevilla -

José Luis Callejas
Unidad Enfermedades Autoinmunes Sistémicas
H. Clínico San Cecilio de Granada

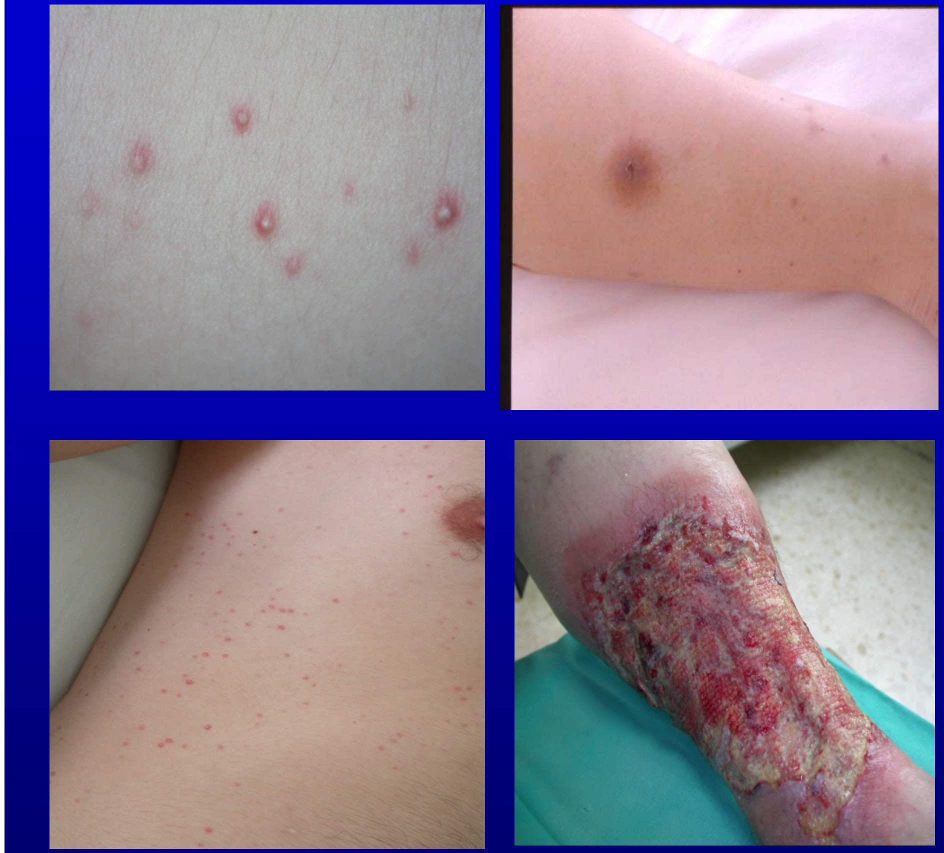
Erase una vez un turco que tenía una enfermedad de BEHÇET. Todos sus órganos se reunieron para determinar cuál de ellos era el más importante y, por tanto, candidato a ser tratado con antiTNF.



La mucosa oral dijo:

“ Yo casi siempre estoy afectada en la enfermedad y soy manifestación clínica obligatoria en los criterios diagnósticos; por tanto

Yo soy la MAS IMPORTANTE



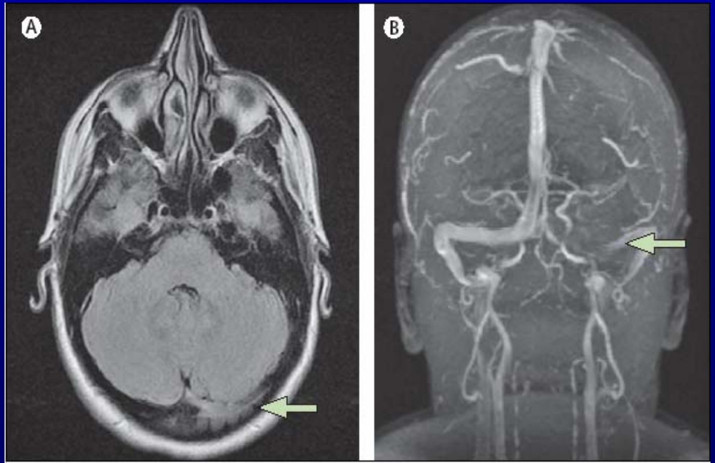
La PIEL dijo:

“ Yo puedo enfermar de muchas formas y además soy el escaparate para el resto de las personas

Yo soy la MAS IMPORTANTE

STUDY 1
10/03/2008
12:58:27
4 IMA 13 / 19
+LPH
RHP
MF 1.00
TR 3800.0
TE 98.0
TA 03:40
BW 100.0
M/ND
A2
HE
10cm
SP H40.9
SL 5.0
FoV 183*230
306*384s
Tra>Cor(-3.1)>Sag(-1.5)

El cerebro y la médula espinal, llenos de orgullo dijeron:



“ Nosotros pensamos, controlamos y transmitimos las órdenes.

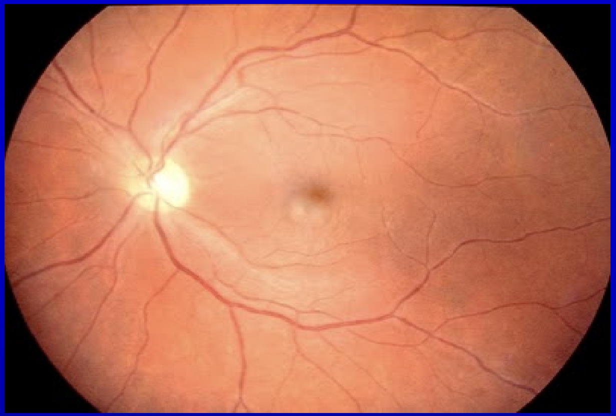
Somos por tanto los
ORGANOS MAS IMPORTANTES

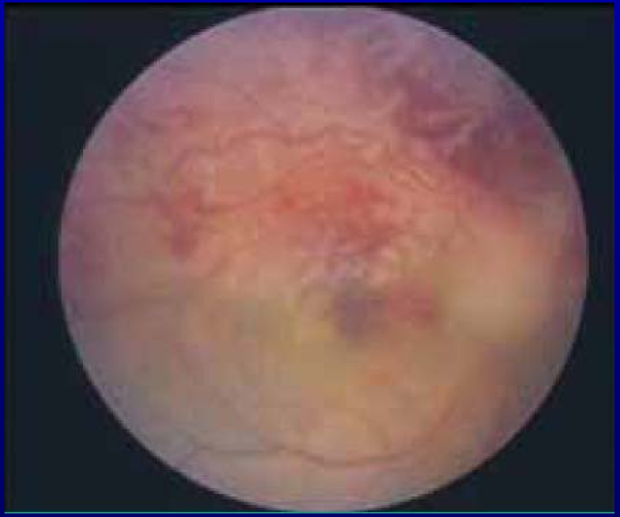
Las “partes nobles” llenas de orgullo dijeron:

“…..

……”

Somos por tanto los
ORGANOS MAS IMPORTANTES



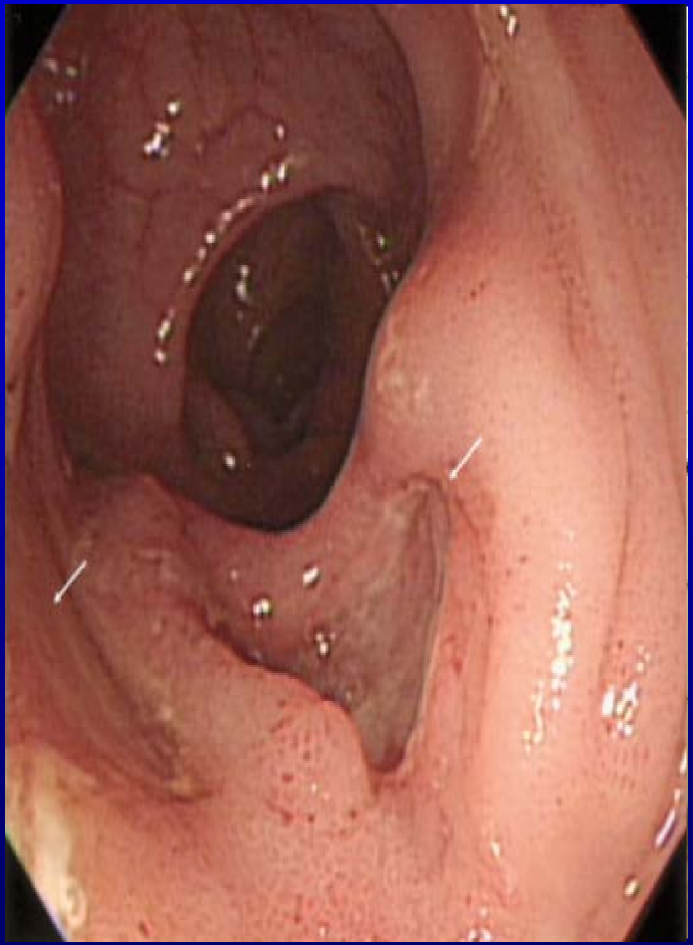


Los ojos llenos de orgullo dijeron:

“ Nosotros somos el órgano de los sentidos más importante, las puerta a la luz, los paisajes…”

Nosotros somos los más importantes

Y así, cada uno de los órganos del cuerpo fue exponiendo sus razones sin llegar a ningún entendimiento



Otro ojo, el del c… dijo, yo soy el más importante.

huelga
emebe@samarretak.com
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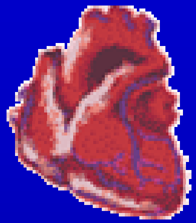

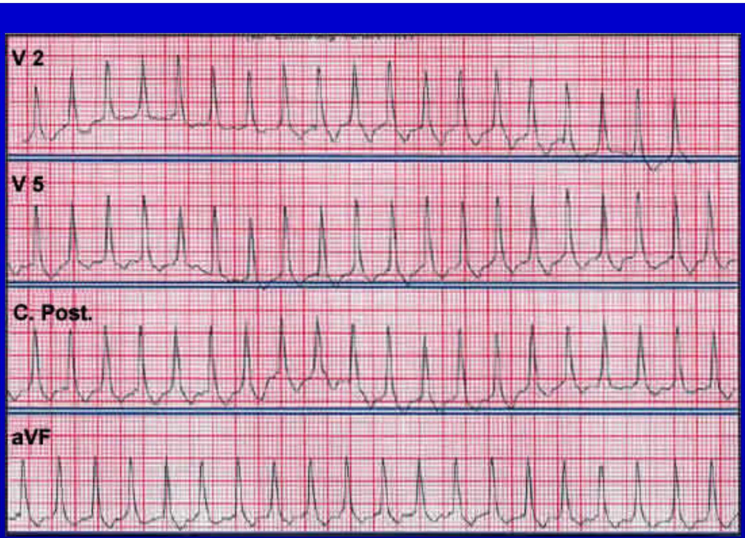
V 2
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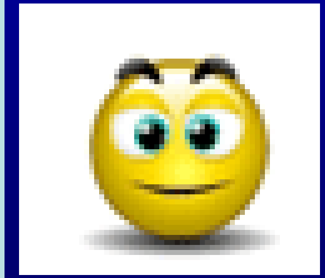
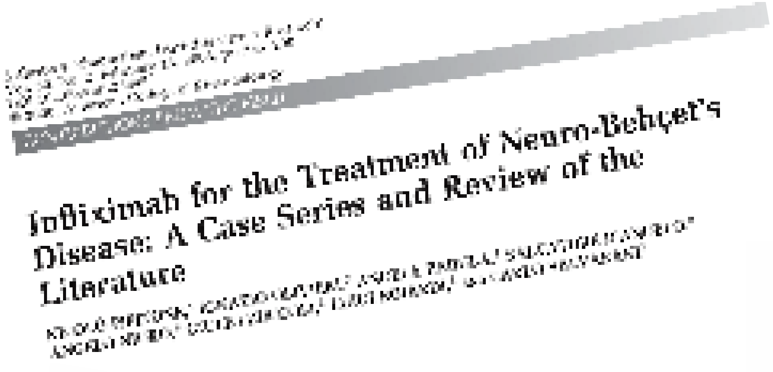
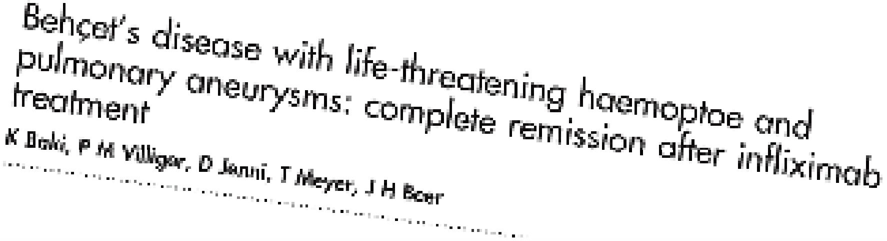


Ante el desastre, decidieron convocar una reunión de urgencia, en la cual se concluyó que

EN LA ENFERMEDAD DE BEHÇET TODOS LOS ORGANOS SOMOS IMPORTANTES Y, POR TANTO, CANDIDATOS AL TRATAMIENTO CON ANTI-TNF alfa

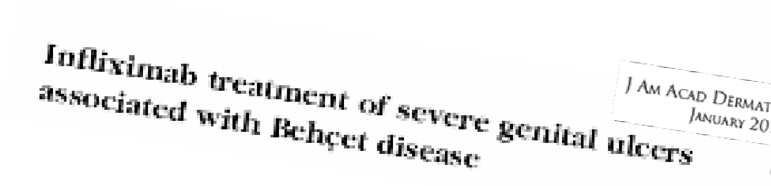


Infliximab for the Treatment of Neuro-Behçet's Disease: A Case Series and Review of the Literature



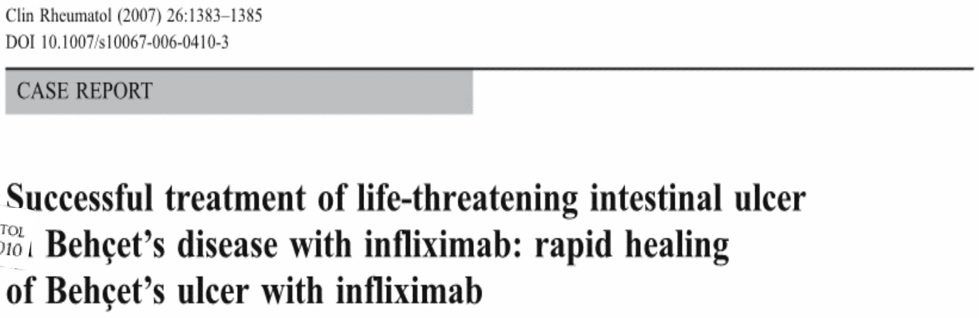
Behçet's disease with life-threatening haemoptoe and pulmonary aneurysms: complete remission after infliximab treatment

K Baki, P M Villiger, D Jenni, T Meyer, J H Beer



Infliximab treatment of severe genital ulcers associated with Behçet disease

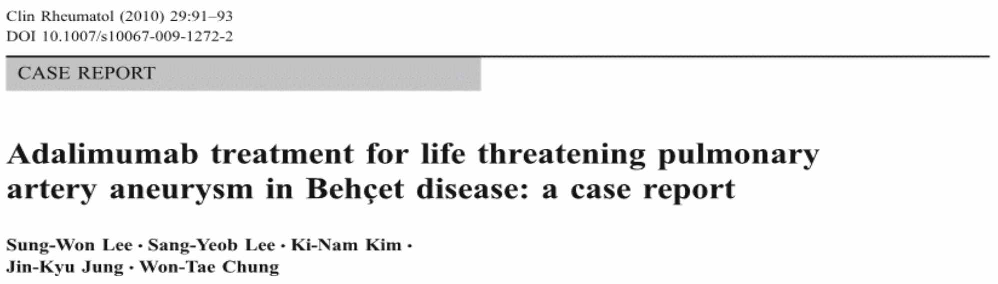
J Am Acad Dermatol
January 2010



Clin Rheumatol (2007) 26:1383–1385
DOI 10.1007/s10067-006-0410-3

CASE REPORT

Successful treatment of life-threatening intestinal ulcer in Behçet's disease with infliximab: rapid healing of Behçet's ulcer with infliximab

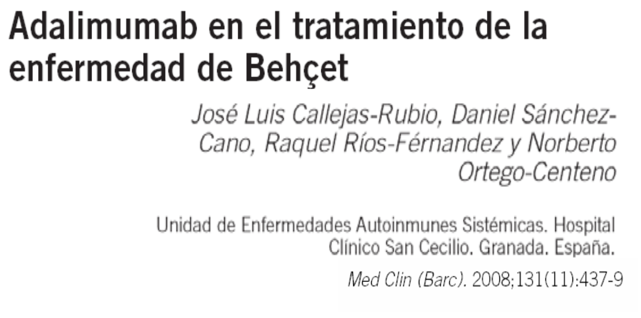


Clin Rheumatol (2010) 29:91–93
DOI 10.1007/s10067-009-1272-2

CASE REPORT

Adalimumab treatment for life threatening pulmonary artery aneurysm in Behçet disease: a case report

Sung-Won Lee · Sang-Yeob Lee · Ki-Nam Kim · Jin-Kyu Jung · Won-Tae Chung

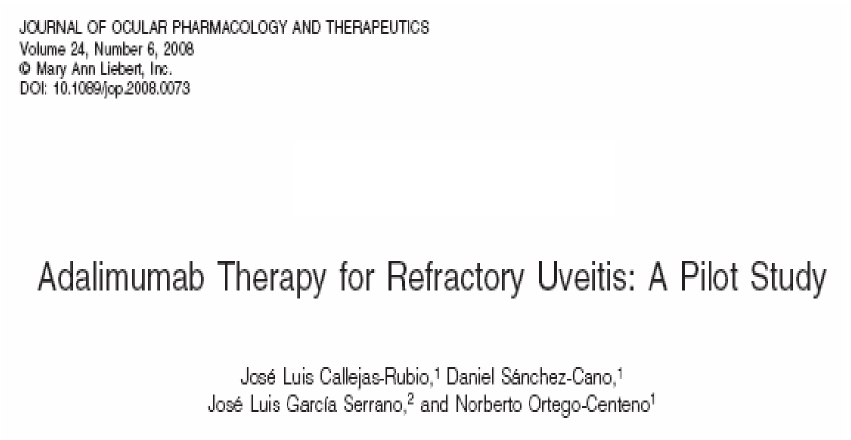


Adalimumab en el tratamiento de la enfermedad de Behçet

José Luis Callejas-Rubio, Daniel Sánchez-Cano, Raquel Ríos-Férnandez y Norberto Ortego-Centeno

Unidad de Enfermedades Autoinmunes Sistémicas. Hospital Clínico San Cecilio. Granada. España.

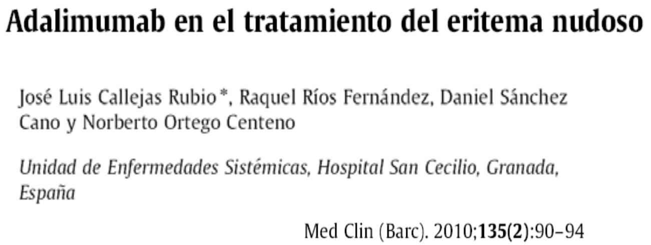
Med Clin (Barc). 2008;131(11):437-9



JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS
Volume 24, Number 6, 2008
© Mary Ann Liebert, Inc.
DOI: 10.1089/jop.2008.0073

Adalimumab Therapy for Refractory Uveitis: A Pilot Study

José Luis Callejas-Rubio,[1] Daniel Sánchez-Cano,[1]
José Luis García Serrano,[2] and Norberto Ortego-Centeno[1]

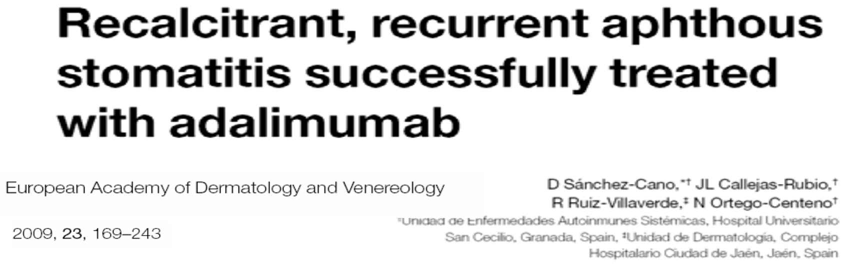


Adalimumab en el tratamiento del eritema nudoso

José Luis Callejas Rubio *, Raquel Ríos Fernández, Daniel Sánchez Cano y Norberto Ortego Centeno

Unidad de Enfermedades Sistémicas, Hospital San Cecilio, Granada, España

Med Clin (Barc). 2010;**135(2)**:90–94



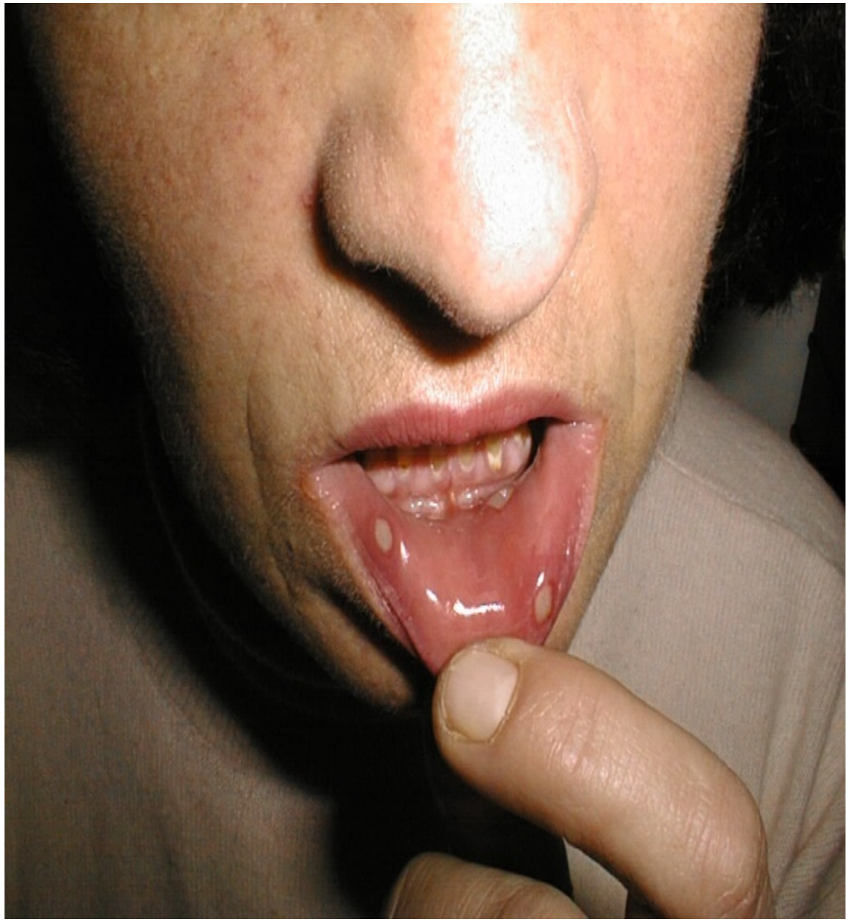
Recalcitrant, recurrent aphthous stomatitis successfully treated with adalimumab

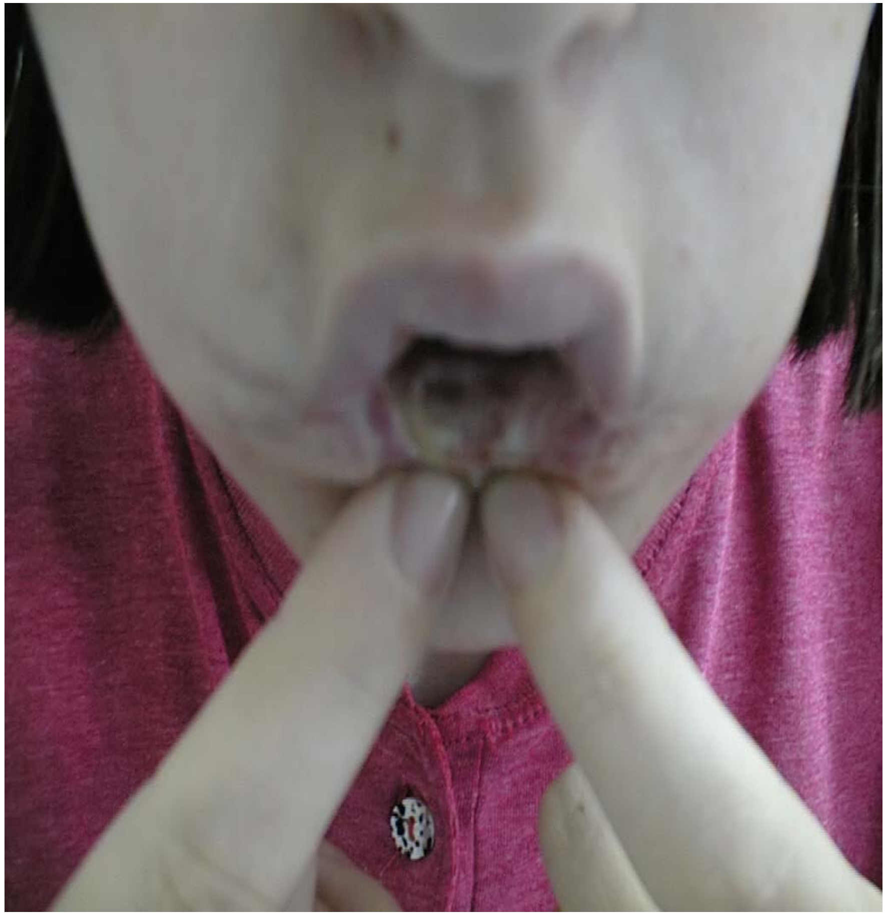
European Academy of Dermatology and Venereology

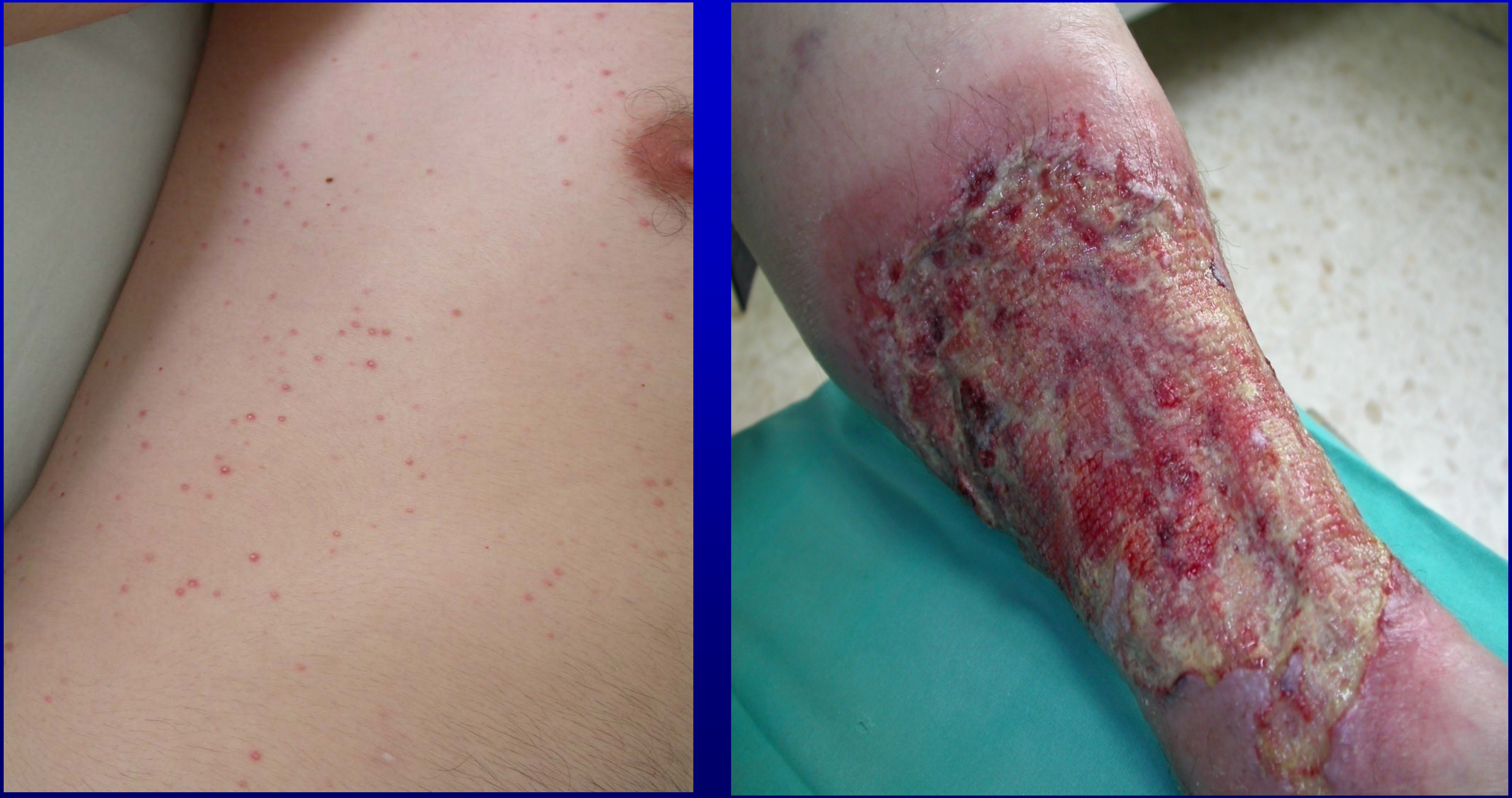
2009, **23**, 169–243

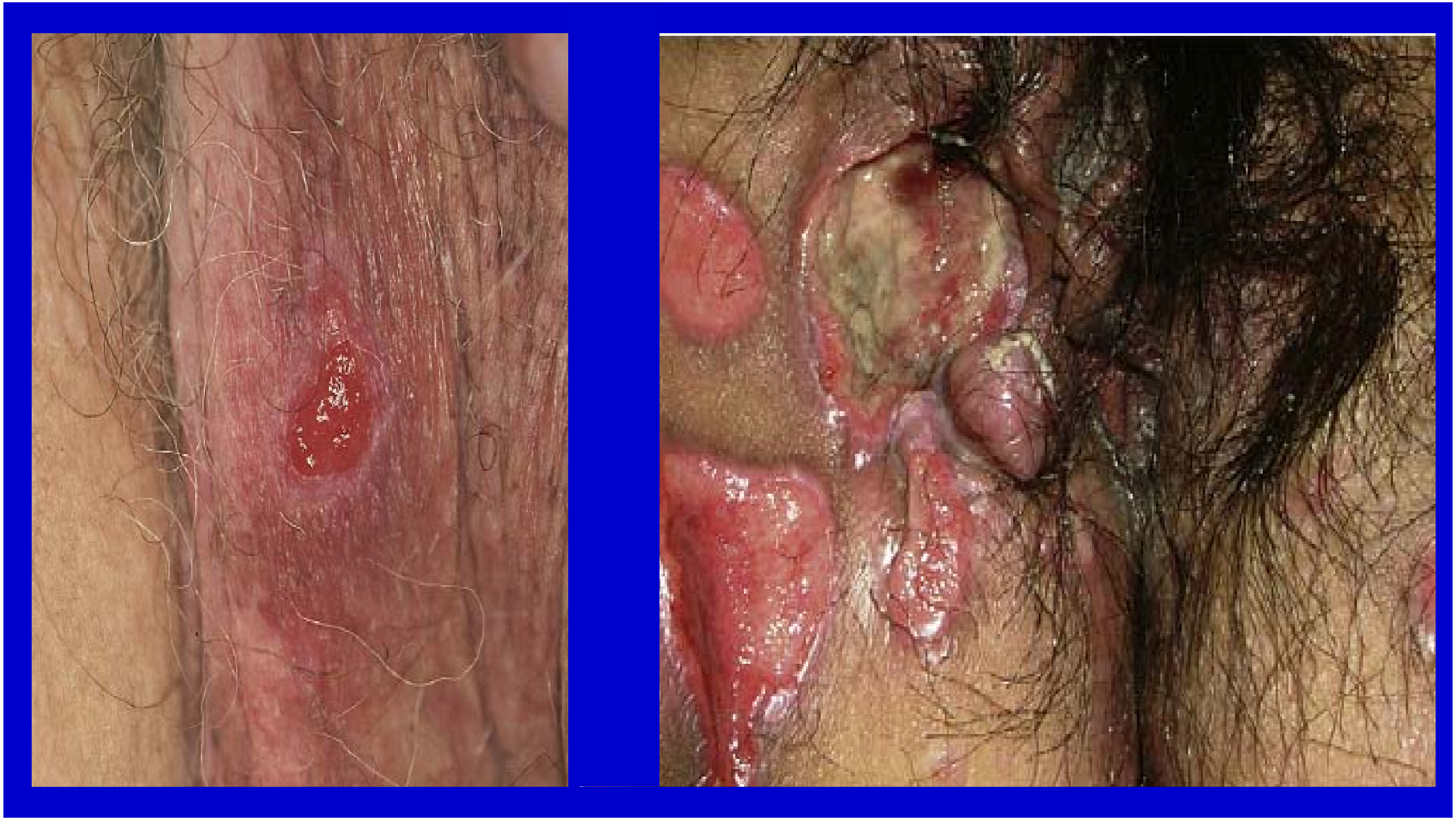
D Sánchez-Cano,[*,†] JL Callejas-Rubio,[†]
R Ruiz-Villaverde,[‡] N Ortego-Centeno[†]
[†]Unidad de Enfermedades Autoinmunes Sistémicas, Hospital Universitario San Cecilio, Granada, Spain, [‡]Unidad de Dermatología, Complejo Hospitalario Ciudad de Jaén, Jaén, Spain

unicef







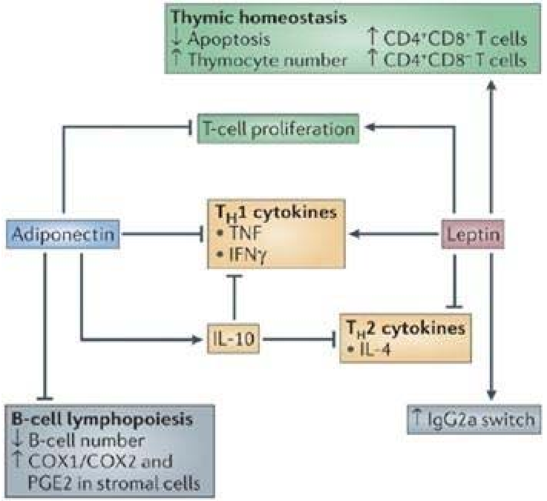


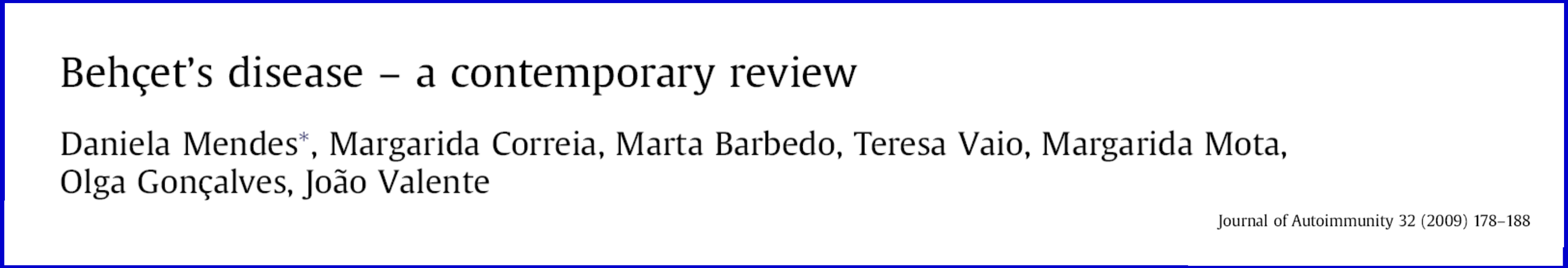
PREMIO
MOSCA COJONERA

Etiopathogenesis of Behcet's disease

Claudia Mendoza-Pinto [a], Mario García-Carrasco [a,b,*], Mario Jiménez-Hernández [a,g], Cesar Jiménez Hernández [a,g], Carlos Riebeling-Navarro [c], Arnulfo Nava Zavala [d], Mauricio Vera Recabarren [e], Gerard Espinosa [g], Javier Jara Quezada [f], Ricard Cervera [g]

Autoimmunity Reviews 9 (2010) 241–245

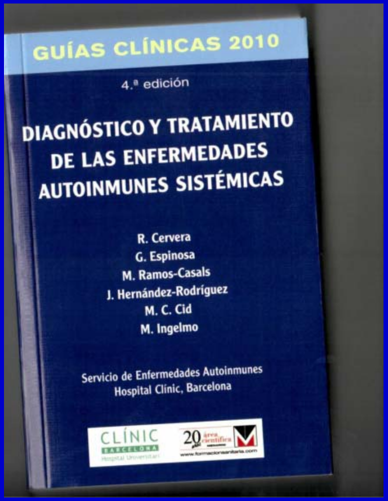

Thymic homeostasis
↓ Apoptosis
↑ Thymocyte number
↑ CD4+CD8+ T cells
↑ CD4+CD8− T cells
T-cell proliferation
Adiponectin
TH1 cytokines
• TNF
• IFNγ
Leptin
IL-10
TH2 cytokines
• IL-4
B-cell lymphopoiesis
↓ B-cell number
↑ COX1/COX2 and PGE2 in stromal cells
↑ IgG2a switch



Behçet's disease – a contemporary review

Daniela Mendes*, Margarida Correia, Marta Barbedo, Teresa Vaio, Margarida Mota,
Olga Gonçalves, João Valente

Journal of Autoimmunity 32 (2009) 178–188



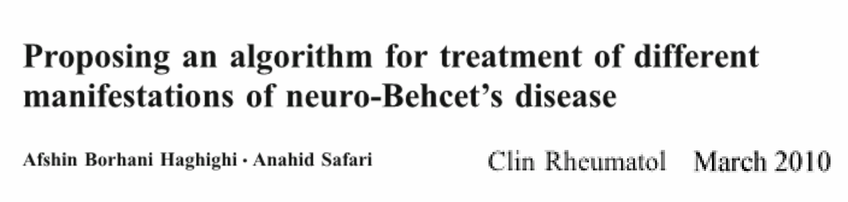
GUÍAS CLÍNICAS 2010

4.ª edición

DIAGNÓSTICO Y TRATAMIENTO DE LAS ENFERMEDADES AUTOINMUNES SISTÉMICAS

R. Cervera
G. Espinosa
M. Ramos-Casals
J. Hernández-Rodríguez
M. C. Cid
M. Ingelmo

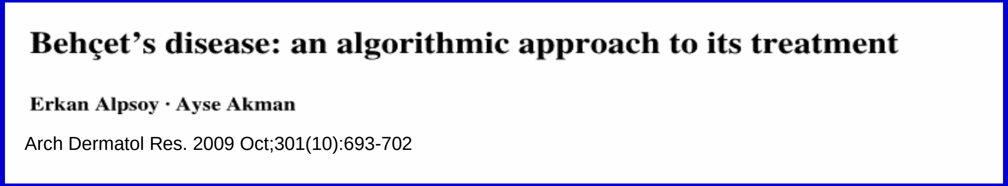
Servicio de Enfermedades Autoinmunes
Hospital Clínic, Barcelona



Proposing an algorithm for treatment of different manifestations of neuro-Behcet's disease

Afshin Borhani Haghighi · Anahid Safari

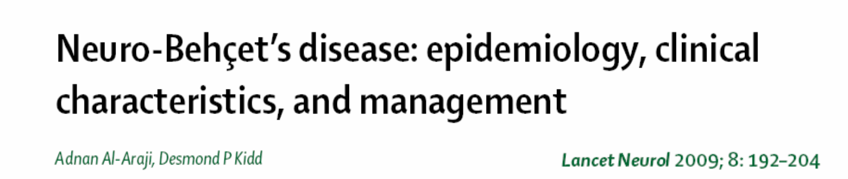
Clin Rheumatol March 2010



Behçet's disease: an algorithmic approach to its treatment

Erkan Alpsoy · Ayse Akman

Arch Dermatol Res. 2009 Oct;301(10):693-702



Neuro-Behçet's disease: epidemiology, clinical characteristics, and management

Adnan Al-Araji, Desmond P Kidd

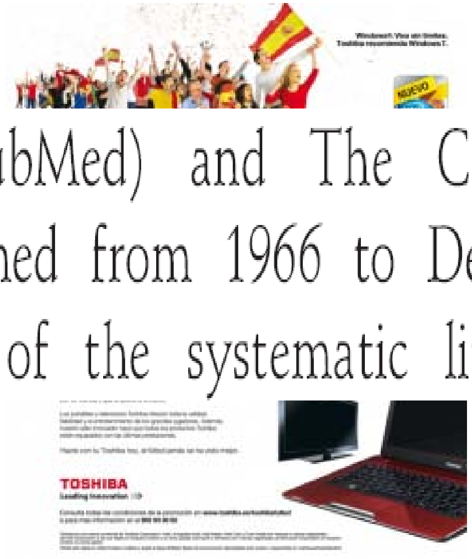
Lancet Neurol 2009; 8: 192–204

EULAR recommendations for the management of Behçet disease

G Hatemi,[1] A Silman,[2] D Bang,[3] B Bodaghi,[4] A M Chamberlain,[5] A Gul,[6] M H Houman,[7] I Kötter,[8] I Olivieri,[9] C Salvarani,[10] P P Sfikakis,[11] A Siva,[12] M R Stanford,[13] N Stübiger,[14] S Yurdakul,[1] H Yazici[1]

Ann Rheum Dis. 2009 Oct;68(10):1528-34.

Medline (via PubMed) and The Cochrane Library were searched from 1966 to December 2006. The results of the systematic literature



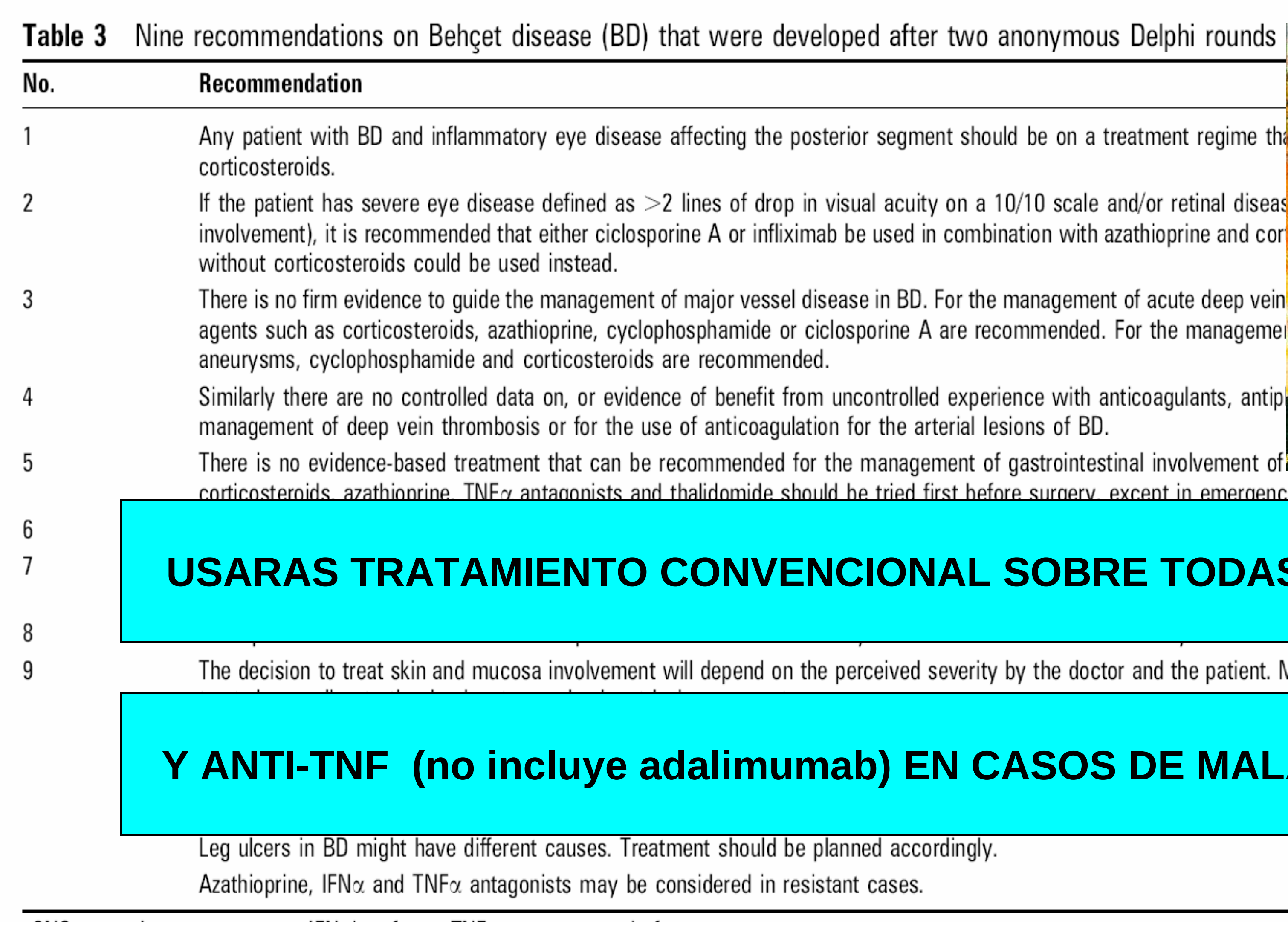
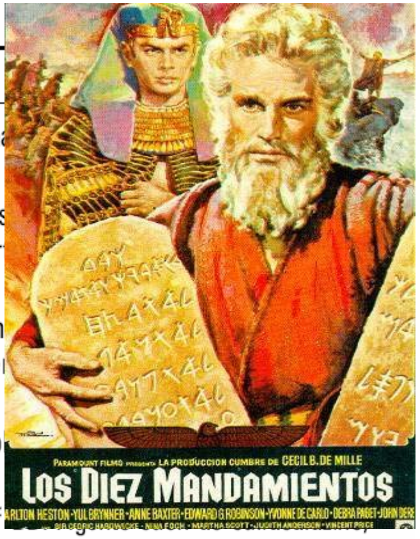


Table 3 Nine recommendations on Behçet disease (BD) that were developed after two anonymous Delphi rounds

No.	Recommendation
1	Any patient with BD and inflammatory eye disease affecting the posterior segment should be on a treatment regime th corticosteroids.
2	If the patient has severe eye disease defined as >2 lines of drop in visual acuity on a 10/10 scale and/or retinal diseas involvement), it is recommended that either ciclosporine A or infliximab be used in combination with azathioprine and cor without corticosteroids could be used instead.
3	There is no firm evidence to guide the management of major vessel disease in BD. For the management of acute deep vein agents such as corticosteroids, azathioprine, cyclophosphamide or ciclosporine A are recommended. For the manageme aneurysms, cyclophosphamide and corticosteroids are recommended.
4	Similarly there are no controlled data on, or evidence of benefit from uncontrolled experience with anticoagulants, antip management of deep vein thrombosis or for the use of anticoagulation for the arterial lesions of BD.
5	There is no evidence-based treatment that can be recommended for the management of gastrointestinal involvement of corticosteroids, azathioprine, TNFα antagonists and thalidomide should be tried first before surgery, except in emergencies.
6	
7	s,
8	
9	The decision to treat skin and mucosa involvement will depend on the perceived severity by the doctor and the patient. Mucocutaneous involvement should be
	Leg ulcers in BD might have different causes. Treatment should be planned accordingly.
	Azathioprine, IFNα and TNFα antagonists may be considered in resistant cases.


PARAMOUNT FILMS presenta LA PRODUCCION CUMBRE DE CECIL B. DE MILLE
LOS DIEZ MANDAMIENTOS
ARLTON HESTON · YUL BRYNNER · ANNE BAXTER · EDWARD G. ROBINSON · YVONNE DE CARLO · DEBRA PAGET · JOHN DERE
SIR CEDRIC HARDWICKE · NINA FOCH · MARTHA SCOTT · JUDITH ANDERSON · VINCENT PRICE

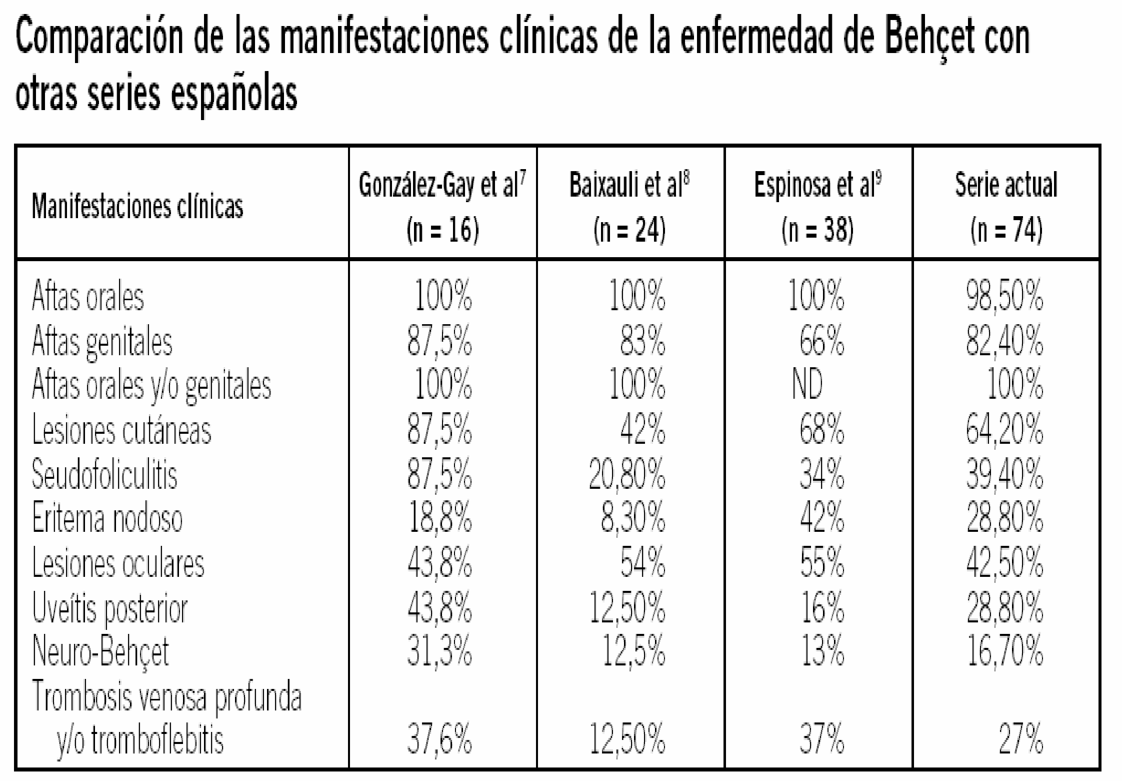
USARAS TRATAMIENTO CONVENCIONAL SOBRE TODAS LAS COSAS

Y ANTI-TNF (no incluye adalimumab) EN CASOS DE MALA EVOLUCION

Enfermedad de Behçet: estudio de 74 pacientes

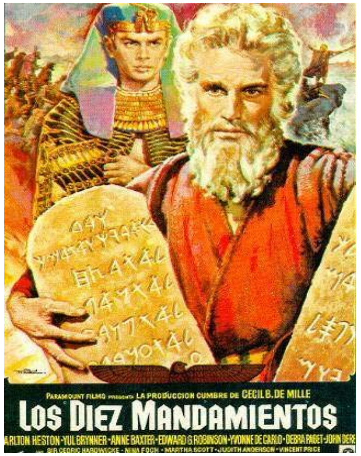
José María Ricart[a], José Todolí[b], Juan José Vilata[c], Javier Calvo[d],
José Román[e], Marisa Santaolaria[f] y Amparo Vayá[f]

Med Clin (Barc). 2006;127(13):496-9

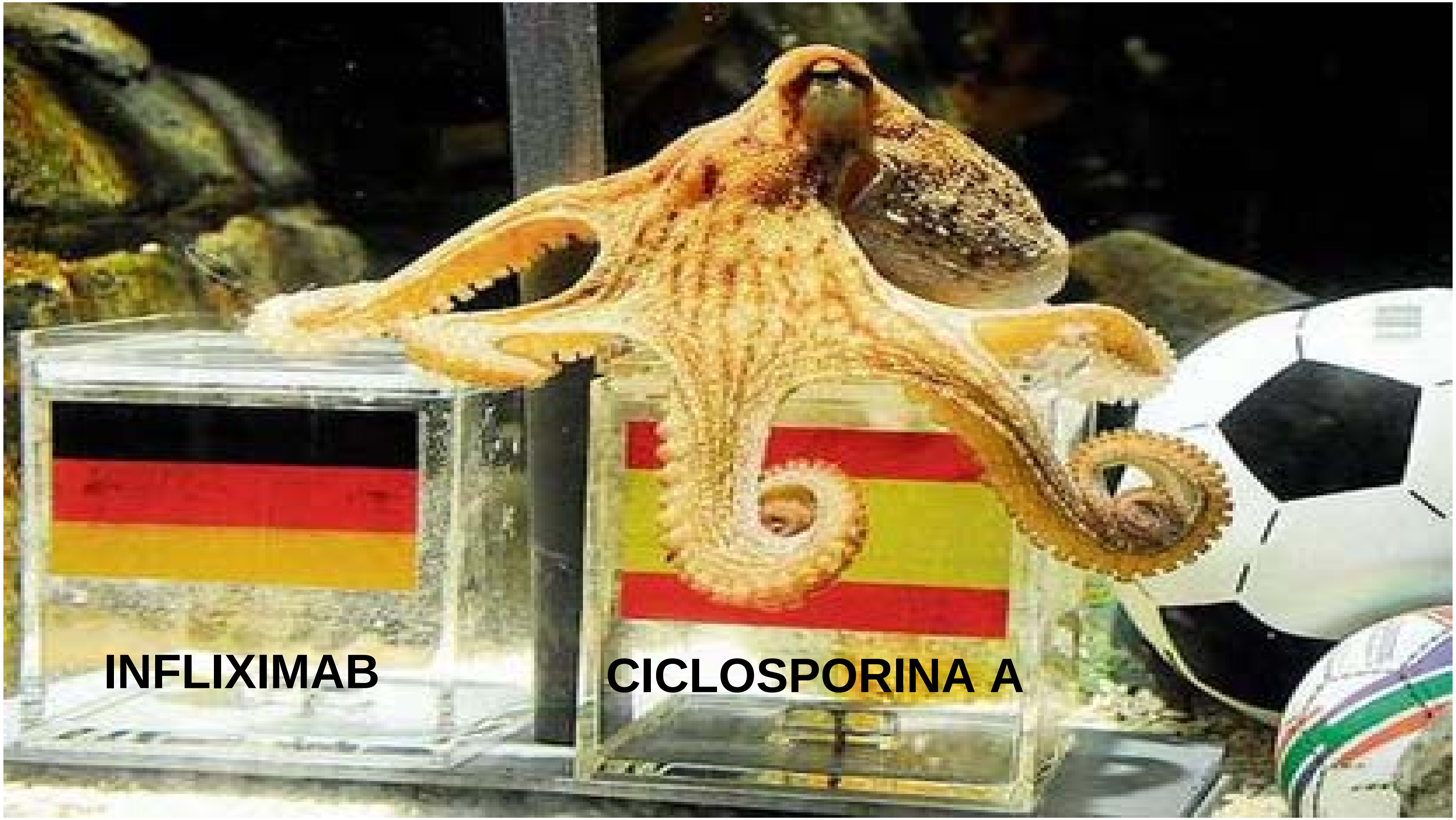


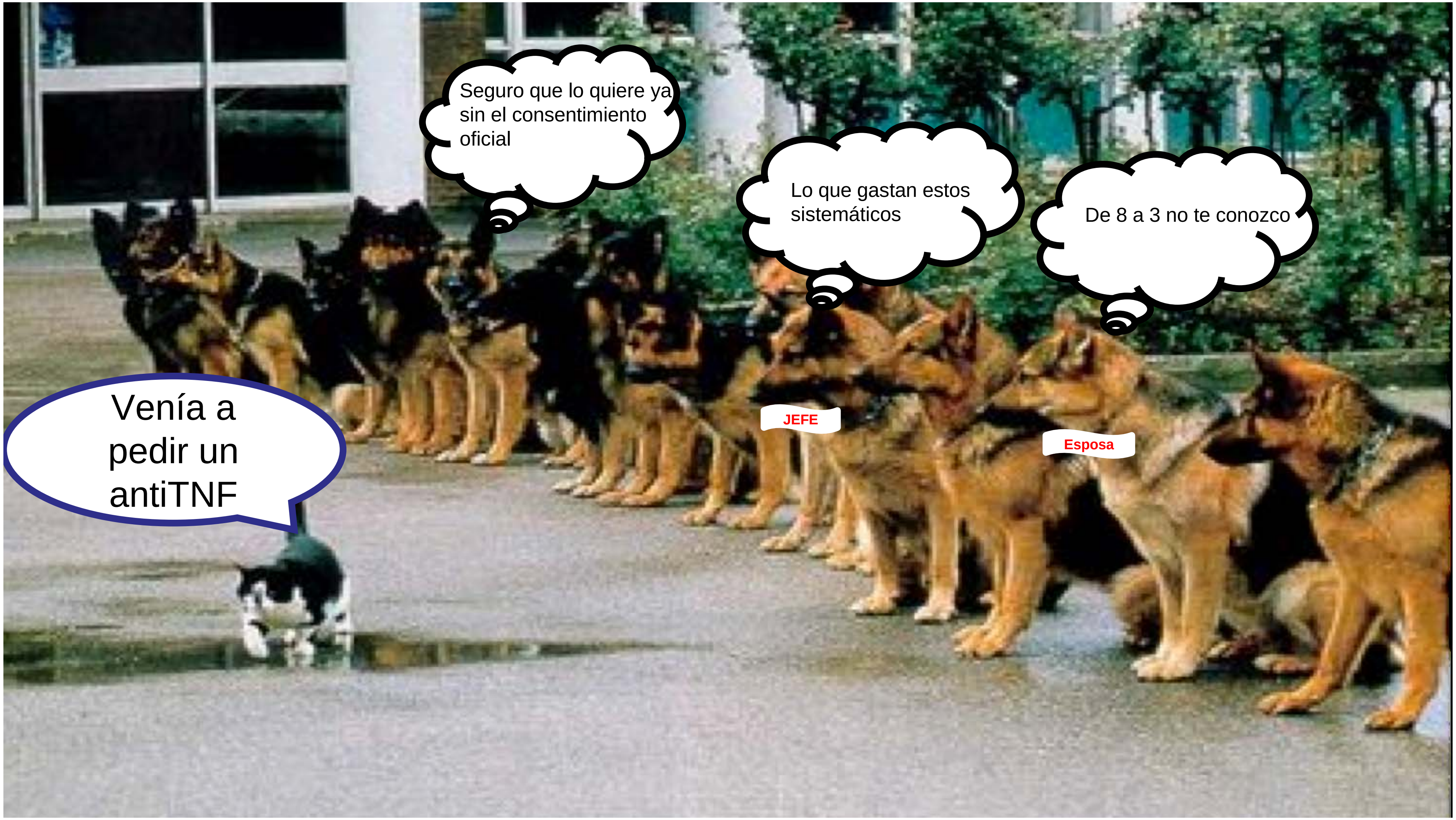
Comparación de las manifestaciones clínicas de la enfermedad de Behçet con otras series españolas

Manifestaciones clínicas	González-Gay et al[7] (n = 16)	Baixauli et al[8] (n = 24)	Espinosa et al[9] (n = 38)	Serie actual (n = 74)
Aftas orales	100%	100%	100%	98,50%
Aftas genitales	87,5%	83%	66%	82,40%
Aftas orales y/o genitales	100%	100%	ND	100%
Lesiones cutáneas	87,5%	42%	68%	64,20%
Seudofoliculitis	87,5%	20,80%	34%	39,40%
Eritema nodoso	18,8%	8,30%	42%	28,80%
Lesiones oculares	43,8%	54%	55%	42,50%
Uveítis posterior	43,8%	12,50%	16%	28,80%
Neuro-Behçet	31,3%	12,5%	13%	16,70%
Trombosis venosa profunda y/o tromboflebitis	37,6%	12,50%	37%	27%


PARAMOUNT FILMS presenta LA PRODUCCION CUMBRE DE CECIL B. DE MILLE
LOS DIEZ MANDAMIENTOS
ARLTON HESTON · YUL BRYNNER · ANNE BAXTER · EDWARD G. ROBINSON · YVONNE DE CARLO · DEBRA PAGET · JOHN DERE
SIR CEDRIC HARDWICKE · NINA FOCH · MARTHA SCOTT · JUDITH ANDERSON · VINCENT PRICE

If the patient has severe eye disease defined as >2 lines of drop in visual acuity on a 10/10 scale and/or retinal disease (retinal vasculitis or macular involvement), it is recommended that either ciclosporine A or infliximab be used in combination with azathioprine and corticosteroids; alternatively IFNα with or without corticosteroids could be used instead.


INFLIXIMAB
CICLOSPORINA A


Venía a pedir un antiTNF
Seguro que lo quiere ya sin el consentimiento oficial
Lo que gastan estos sistemáticos
De 8 a 3 no te conozco
JEFE
Esposa

Ocular Inflammation in Behçet Disease: Incidence of Ocular Complications and of Loss of Visual Acuity

R. OKTAY KAÇMAZ, JOHN H. KEMPEN, CRAIG NEWCOMB, SAPNA GANGAPUTRA, EBENEZER DANIEL, GRACE A. LEVY-CLARKE, ROBERT B. NUSSENBLATT, JAMES T. ROSENBAUM, ERIC B. SUHLER, JENNIFER E. THORNE, DOUGLAS A. JABS, AND C. STEPHEN FOSTER, ON BEHALF OF THE SYSTEMIC IMMUNOSUPPRESSIVE THERAPY FOR EYE DISEASES COHORT STUDY GROUP

The centers involved in the SITE Cohort Study are: the Uveitis Clinic, Casey Eye Institute, Oregon Health and Sciences University; the Laboratory of Immunology, National Eye Institute; the Ocular Immunology Service, Wilmer Eye Institute, Johns Hopkins University; the practice of C. Stephen Foster, formerly at the Massachusetts Eye and Ear Infirmary and now at the Massachusetts Eye Research and Surgery Institution; and the Ocular Inflammation Service, Scheie Eye Institute, University of Pennsylvania.

Am J Ophthalmol 2008;146:828–836.

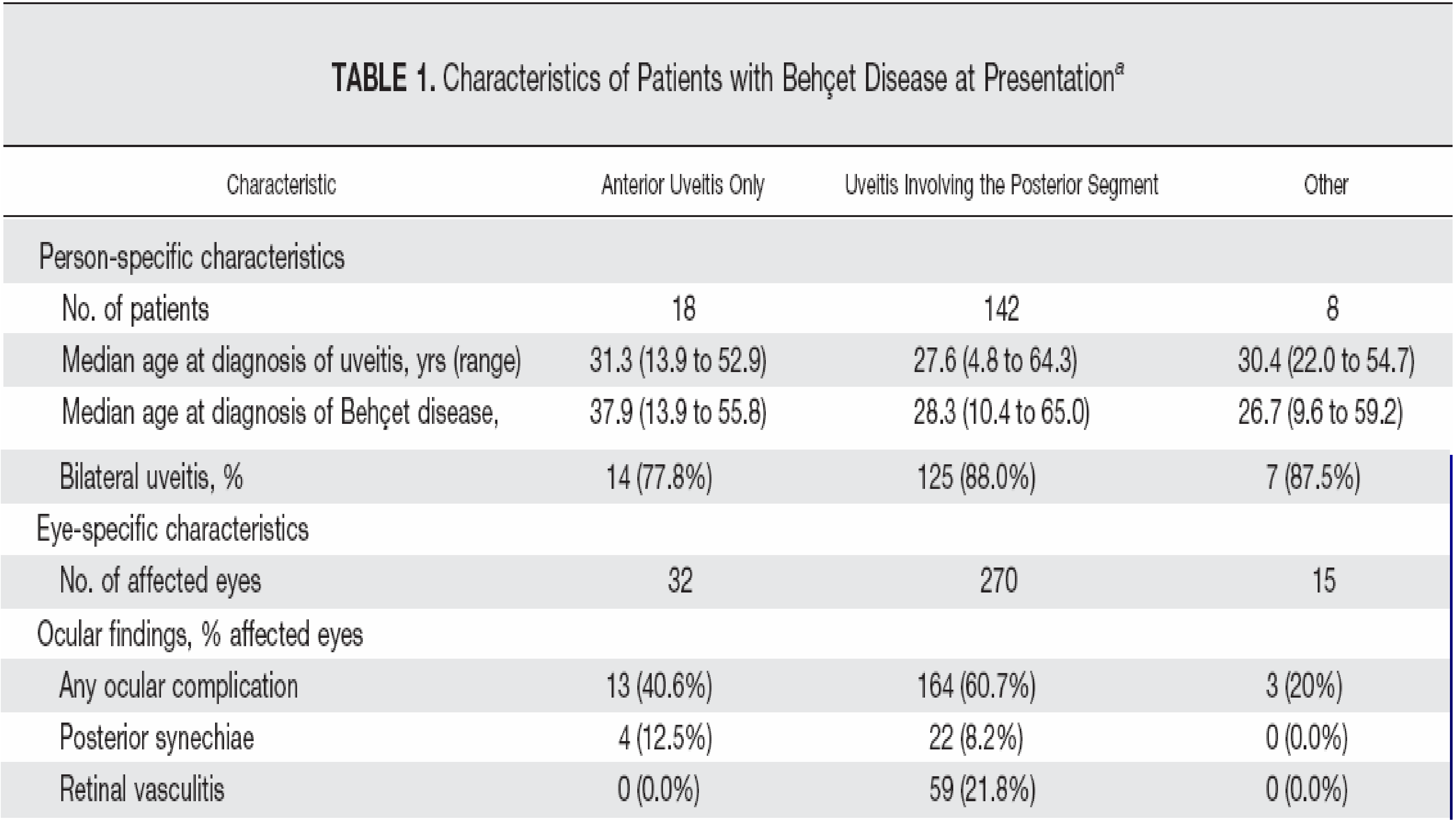


TABLE 1. Characteristics of Patients with Behçet Disease at Presentation[a]

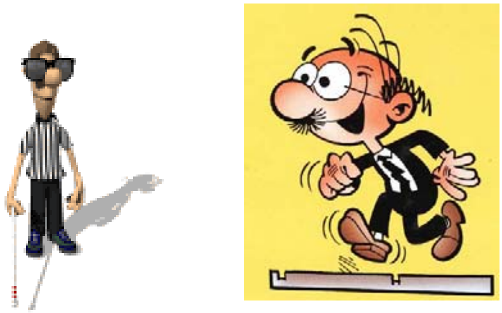
Characteristic	Anterior Uveitis Only	Uveitis Involving the Posterior Segment	Other
Person-specific characteristics			
No. of patients	18	142	8
Median age at diagnosis of uveitis, yrs (range)	31.3 (13.9 to 52.9)	27.6 (4.8 to 64.3)	30.4 (22.0 to 54.7)
Median age at diagnosis of Behçet disease,	37.9 (13.9 to 55.8)	28.3 (10.4 to 65.0)	26.7 (9.6 to 59.2)
Bilateral uveitis, %	14 (77.8%)	125 (88.0%)	7 (87.5%)
Eye-specific characteristics			
No. of affected eyes	32	270	15
Ocular findings, % affected eyes			
Any ocular complication	13 (40.6%)	164 (60.7%)	3 (20%)
Posterior synechiae	4 (12.5%)	22 (8.2%)	0 (0.0%)
Retinal vasculitis	0 (0.0%)	59 (21.8%)	0 (0.0%)

Ocular Inflammation in Behçet Disease: Incidence of Ocular Complications and of Loss of Visual Acuity

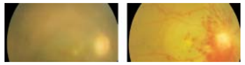
R. OKTAY KAÇMAZ, JOHN H. KEMPEN, CRAIG NEWCOMB, SAPNA GANGAPUTRA, EBENEZER DANIEL, GRACE A. LEVY-CLARKE, ROBERT B. NUSSENBLATT, JAMES T. ROSENBAUM, ERIC B. SUHLER, JENNIFER E. THORNE, DOUGLAS A. JABS, AND C. STEPHEN FOSTER, ON BEHALF OF THE SYSTEMIC IMMUNOSUPPRESSIVE THERAPY FOR EYE DISEASES COHORT STUDY GROUP

- CONCLUSIONS: Loss of VA and occurrence of ocular complications were common in patients with ocular inflammation associated with BD, even with aggressive therapy. Ongoing inflammation during follow-up, presence or occurrence of posterior synechiae, hypotony, and elevated IOP were associated with an increased risk of loss of VA.

Am J Ophthalmol 2008;146:828–836.



Infliximab Effects Compared to Conventional Therapy in the Management of Retinal Vasculitis in Behçet Disease



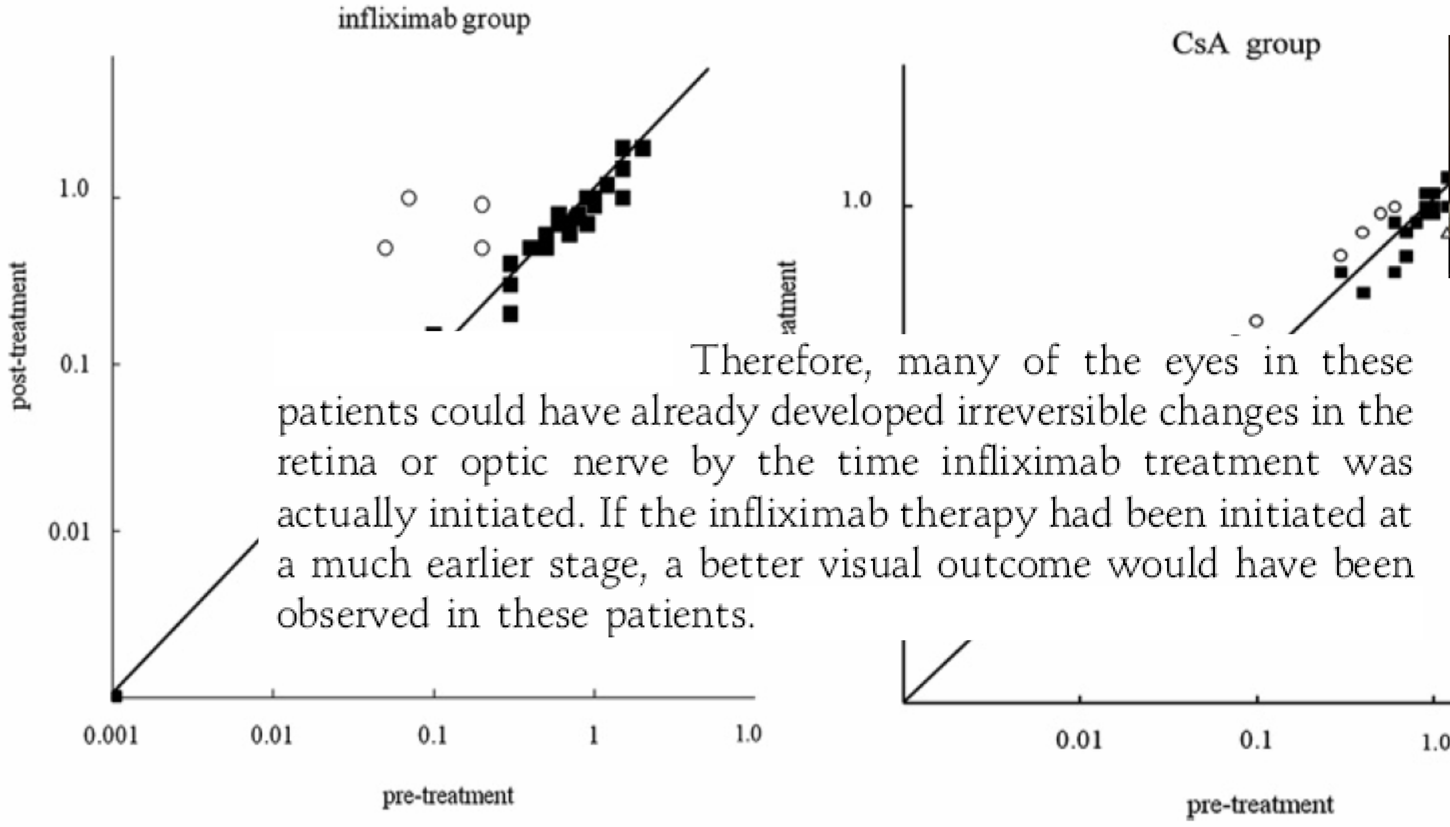
KHALID F. TABBARA AND AMAL I. AL-HEMIDAN

- CONCLUSIONS: Patients with Behçet disease had significant decrease in inflammation, improvement of visual acuity, and reduced ocular complications following infliximab when compared to conventional therapy. The number of relapses was less in the infliximab treatment group than the conventional therapy group.

Am J Ophthalmol 2008;146:845–850.

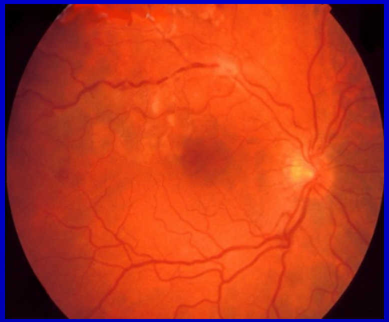
Table 1 Characteristics of patients with Behçet disease treated with infliximab (IFX)

Case	Age (years)	Sex	Interval between onset and infliximab (months)	Treatment before IFX administration	No of acute uveitis attacks		Concomitant treatment with IFX	Reason for conversion to IFX
					Before IFX	After IFX		
1	27	M	16	CsA	3	1	None	Resistance to CsA
2	32	M	60	CsA, PSL (0–30 mg)	6	0	None	Resistance to CsA
3	33	M	83	CsA, Col, PSL (5 mg)	5	0	Col	Resistance to CsA
4	39	M	70	CsA	5	0	None	Resistance to CsA
5	44	M	86	CsA	3	0	None	Resistance to CsA
6	63	M	72	PSL (15 mg)	0	0	PSL (12.5–15 mg)	Side effect of existent treatment
7	52	M	70	Col	1	0	None	Side effect of existent treatment
8	39	M	42	Az, Col, PSL (10 mg)	6	0	None	Side effect of existent treatment
9	42	M	110	CsA, PSL (10 mg)	0	0	PSL (9–10 mg)	Due to glaucoma operation
10	33	F	21	CsA, Col	3	0	None	Resistance to CsA
11	26	M	13	CsA, PSL (11 mg)	0	0	PSL (8–11 mg)	Resistance to CsA
12	34	M	21	CsA	3	0	None	Resistance to CsA
13	34	M	98	CsA	10	0	None	Resistance to CsA
14	40	M	16	Col, PSL (10 mg)	3	1	PSL (5–7.5 mg)	Resistance to existent treatment
15	26	F	31	CsA, PSL (10 mg)	0	0	PSL (5–10 mg)	Side effect of CsA
16	50	M	16	Col	2	0	Col	Resistance to Col
17	25	M	24	CsA	2	4	CsA	Resistance to CsA



Therefore, many of the eyes in these patients could have already developed irreversible changes in the retina or optic nerve by the time infliximab treatment was actually initiated. If the infliximab therapy had been initiated at a much earlier stage, a better visual outcome would have been observed in these patients.

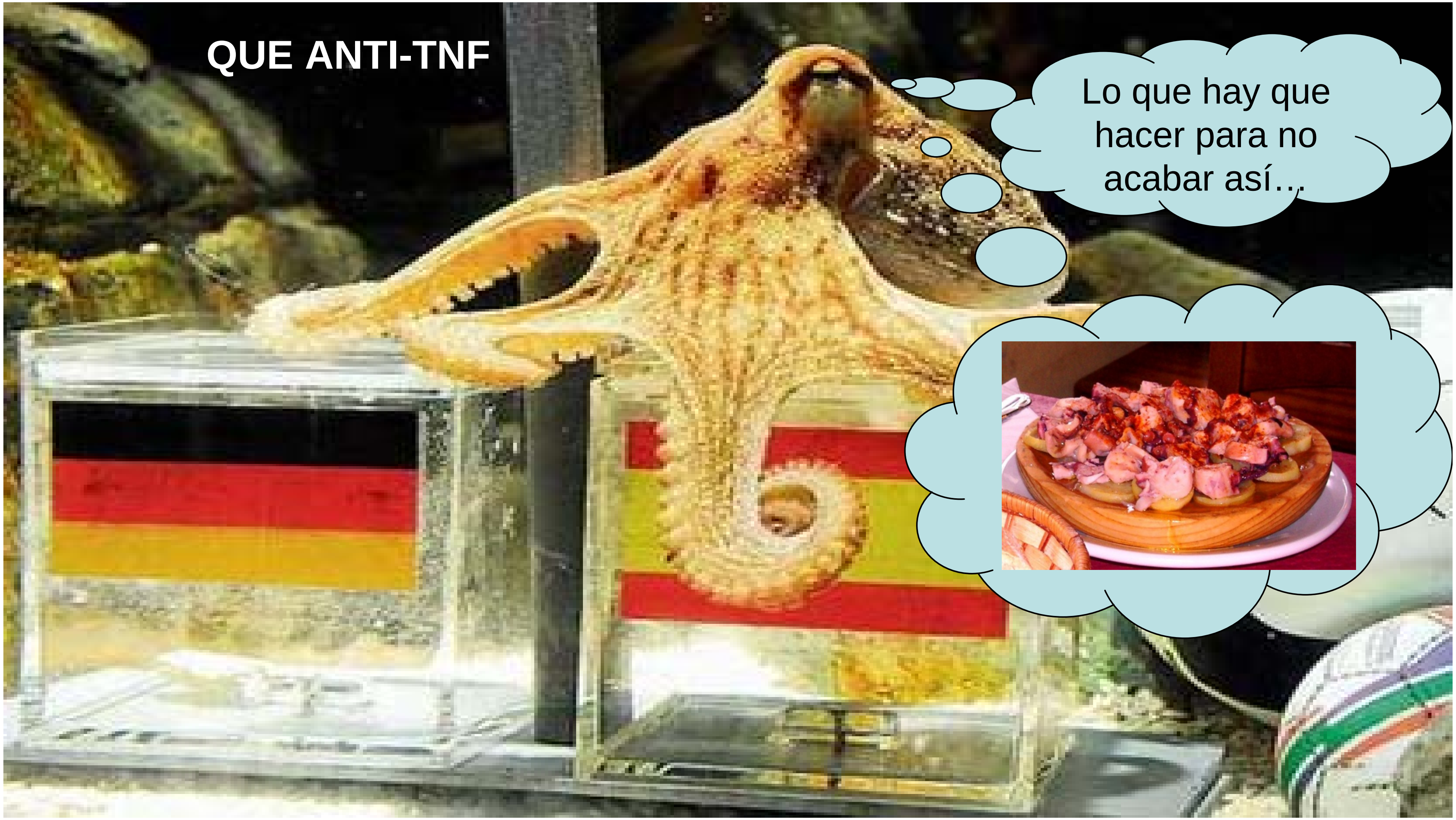
e 2 Visual acuity changes seen for each therapy. Best-corrected visual acuity (BCVA) was measured at the initiation point and 6 months after the
istration. With infliximab, the vision improved or was unchanged in 97% of the eyes, compared with 93% in the CsA group. Open circle, more than
nes of improvement; black square, unchanged; open triangle, a decrease of less than two lines. Statistical analysis was performed using the
–Whitney U test.

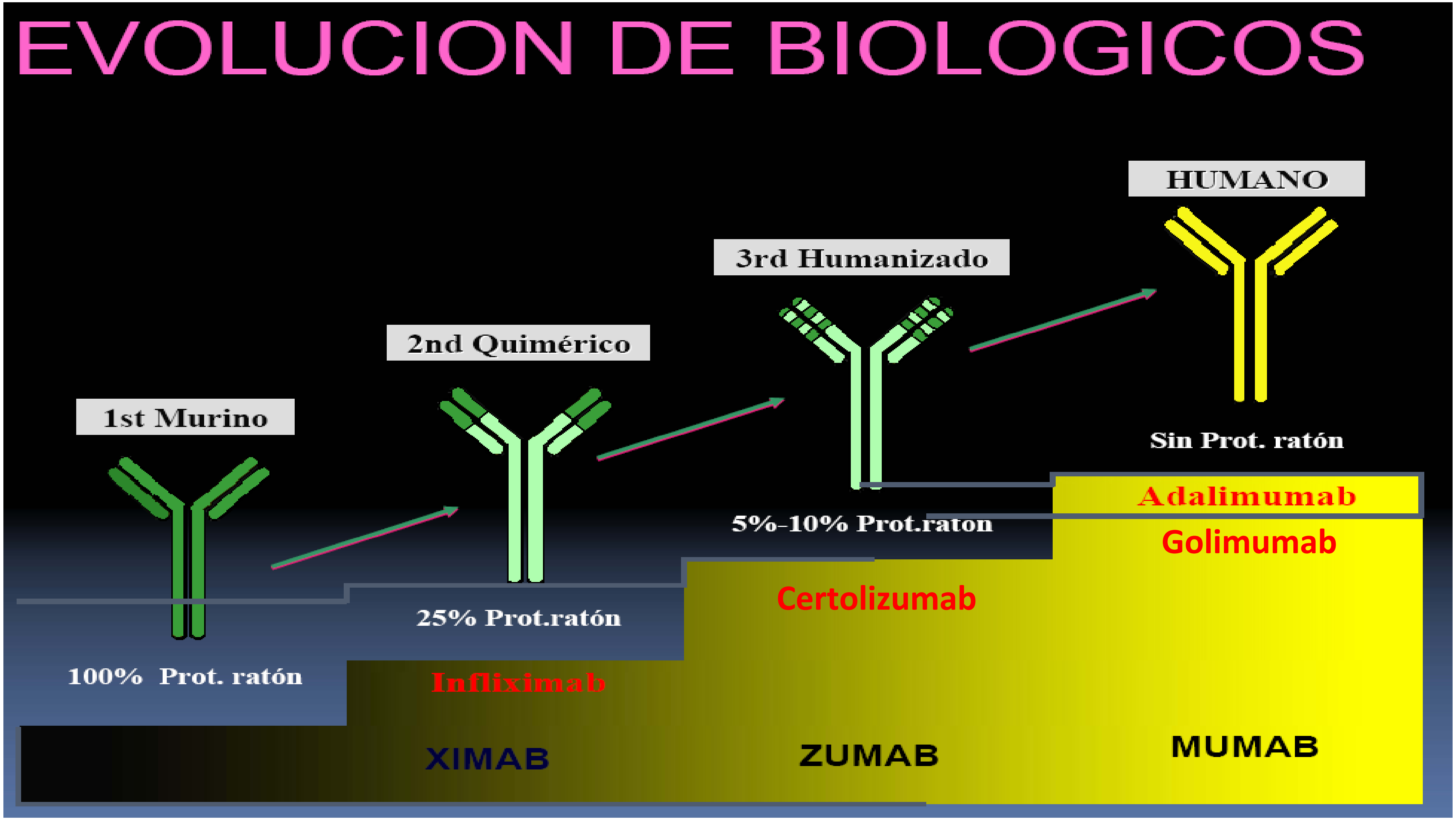


CON LA INFLAMACION EN EL OJO.......

TOLERANCIA
CERO

QUE ANTI-TNF


Lo que hay que hacer para no acabar así…



EVOLUCION DE BIOLOGICOS

1st Murino

100% Prot. ratón

2nd Quimérico

25% Prot.ratón

3rd Humanizado

5%-10% Prot.raton

HUMANO

Sin Prot. ratón

Infliximab

Certolizumab

Adalimumab

Golimumab

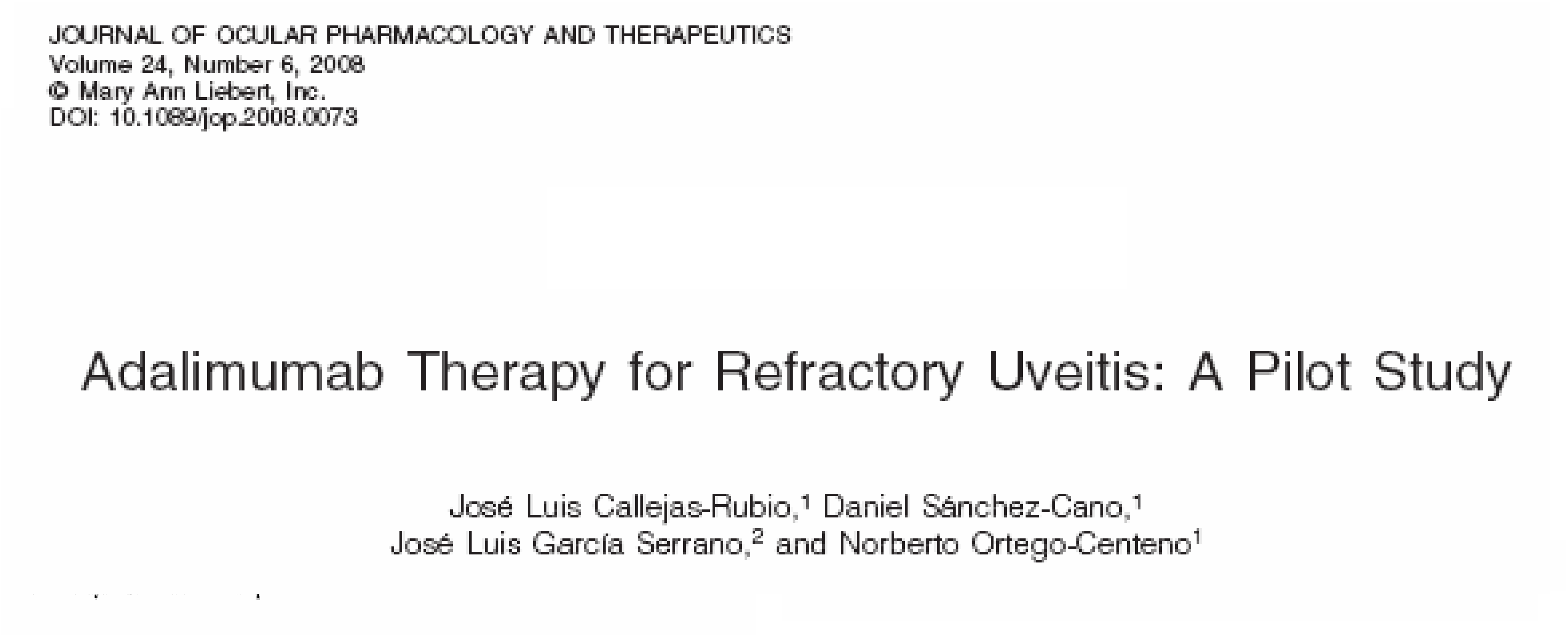
XIMAB

ZUMAB

MUMAB

INDICACIONES DE LA EMEA

	AR	EA	CROHN	PSORIASIS
ETANERCEPT	MENOR EFICACIA EN UVEITIS			
INFLIXIMAB	**SI**	**SI**	**SI**	**SI**
ADALIMUMAB	**SI**	**SI**	**SI**	**SI**
CERTOLIZUMAB	NINGUN CASO NI EN BEHÇET NI EN UVEITIS			
GOLIMUMAB				



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Adalimumab Therapy for Refractory Uveitis: A Pilot Study

José Luis Callejas-Rubio,[1] Daniel Sánchez-Cano,[1]
José Luis García Serrano,[2] and Norberto Ortego-Centeno[1]

Clinical Experience with Adalimumab in the Treatment of Ocular Behçet Disease

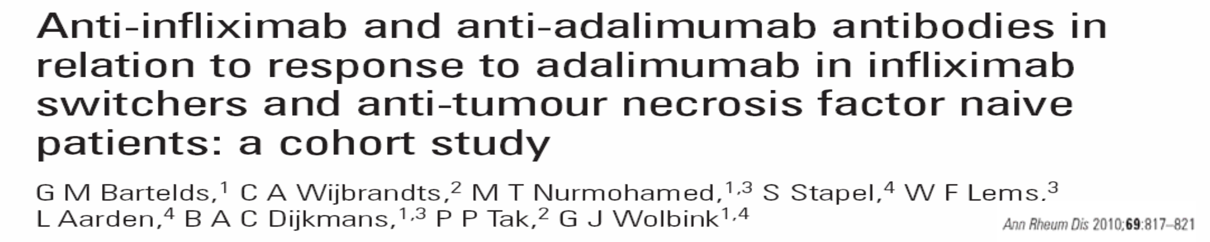
Ocul Immunol Inflamm. 2010 Jun;18(3):226-32.

9-1178-y

[redacted]

witching to adalimumab in an infliximab-allergic
severe Behçet disease-related uveitis

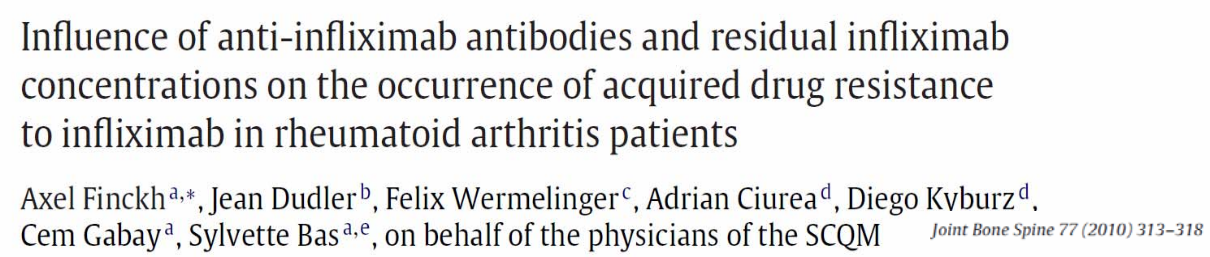
geru Ohno · Haruko Ideguchi ·
hiro Takeno · Yoshiaki Ishigatsubo



Anti-infliximab and anti-adalimumab antibodies in relation to response to adalimumab in infliximab switchers and anti-tumour necrosis factor naive patients: a cohort study

G M Bartelds,[1] C A Wijbrandts,[2] M T Nurmohamed,[1,3] S Stapel,[4] W F Lems,[3]
L Aarden,[4] B A C Dijkmans,[1,3] P P Tak,[2] G J Wolbink[1,4]

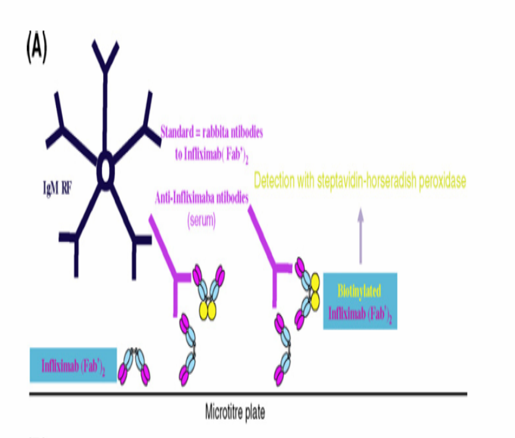
Ann Rheum Dis 2010;**69**:817–821

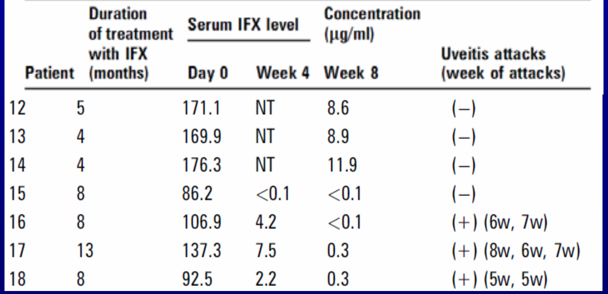


Influence of anti-infliximab antibodies and residual infliximab concentrations on the occurrence of acquired drug resistance to infliximab in rheumatoid arthritis patients

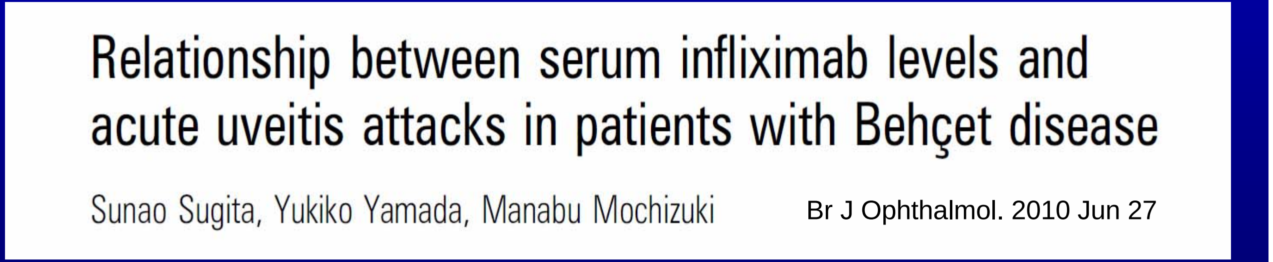
Axel Finckh[a,*], Jean Dudler[b], Felix Wermelinger[c], Adrian Ciurea[d], Diego Kyburz[d],
Cem Gabay[a], Sylvette Bas[a,e], on behalf of the physicians of the SCQM

Joint Bone Spine 77 (2010) 313–318


(A)
IgM RF
Standard = rabbita ntibodies to Infliximab(Fab')2
Detection with steptavidin-horseradish peroxidase
Anti-Infliximaba ntibodies (serum)
Biotinylated Infliximab (Fab')2
Infliximab (Fab')2
Microtitre plate



Patient	Duration of treatment with IFX (months)	Serum IFX level Day 0	Week 4	Concentration (µg/ml) Week 8	Uveitis attacks (week of attacks)
12	5	171.1	NT	8.6	(−)
13	4	169.9	NT	8.9	(−)
14	4	176.3	NT	11.9	(−)
15	8	86.2	<0.1	<0.1	(−)
16	8	106.9	4.2	<0.1	(+) (6w, 7w)
17	13	137.3	7.5	0.3	(+) (8w, 6w, 7w)
18	8	92.5	2.2	0.3	(+) (5w, 5w)



Relationship between serum infliximab levels and acute uveitis attacks in patients with Behçet disease

Sunao Sugita, Yukiko Yamada, Manabu Mochizuki

Br J Ophthalmol. 2010 Jun 27

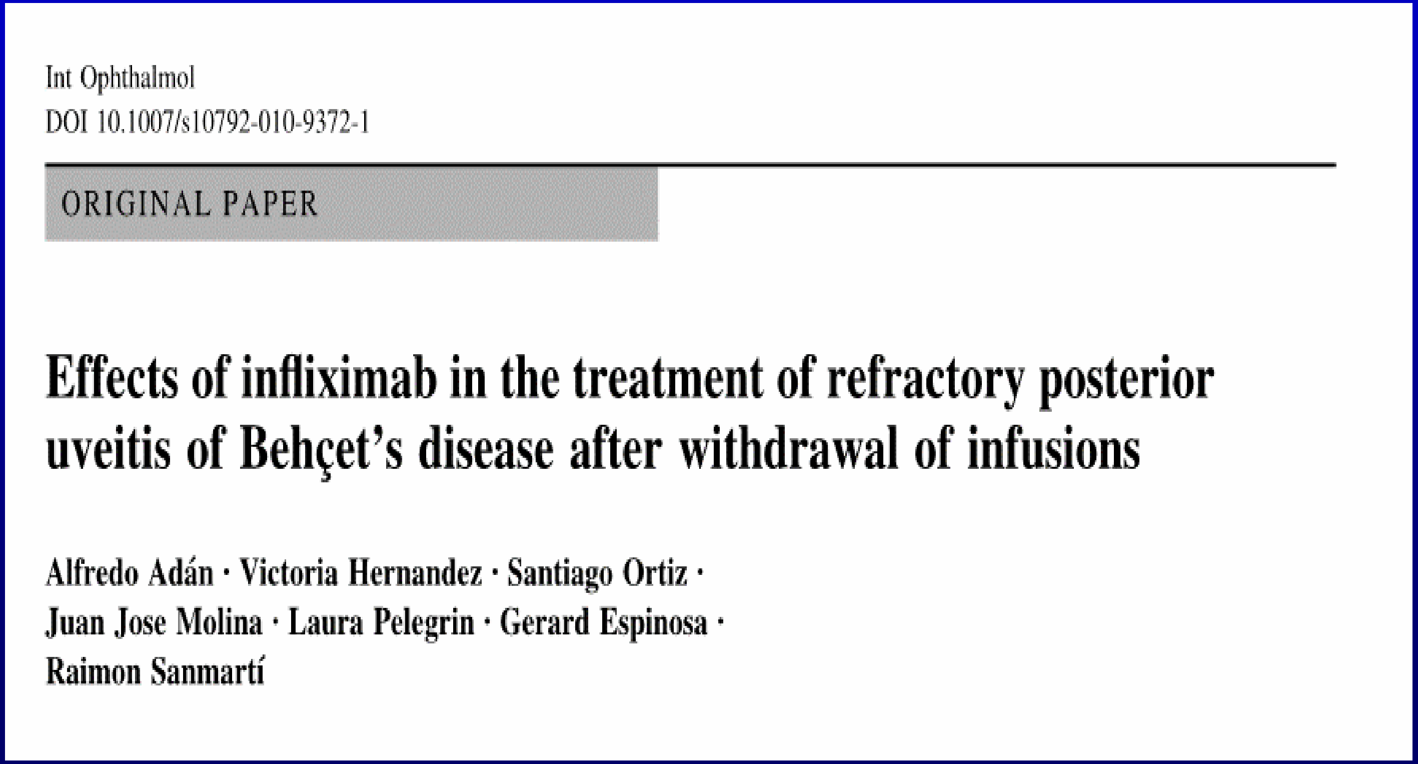
Timing of recurrent uveitis in patients with Behcet's disease receiving infliximab treatment

Yamada Y, Sugita S, Tanaka H, Kamoi K, Takase H, Mochizuki M. Br J Ophthalmol. 2010 Jun 11

¿ DURANTE CUANTO TIEMPO?

RAPHAEL
QUE SABE NADIE
DISCO EXCLUSIVAMENTE PROMOCIONAL

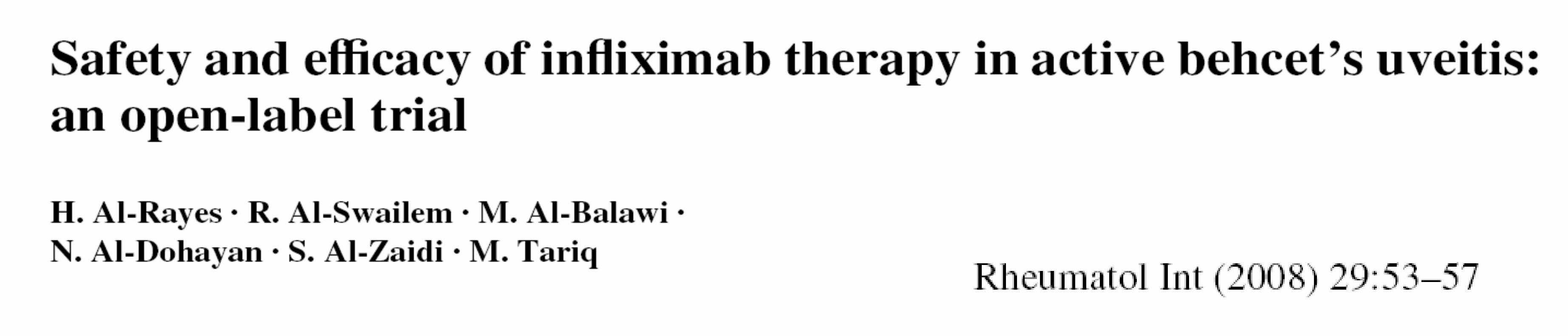
FOTOSEARCH


Int Ophthalmol
DOI 10.1007/s10792-010-9372-1

ORIGINAL PAPER

Effects of infliximab in the treatment of refractory posterior uveitis of Behçet's disease after withdrawal of infusions

Alfredo Adán · Victoria Hernandez · Santiago Ortiz ·
Juan Jose Molina · Laura Pelegrin · Gerard Espinosa ·
Raimon Sanmartí



Safety and efficacy of infliximab therapy in active behcet's uveitis: an open-label trial

H. Al-Rayes · R. Al-Swailem · M. Al-Balawi ·
N. Al-Dohayan · S. Al-Zaidi · M. Tariq

Rheumatol Int (2008) 29:53–57

n = 10 pacientes

Pauta inicial: 2 dosis de 5mg/kg/d de infliximab los días 0-14

7/10…70% de recidivas

ciclos cada 8 semanas

Sin brotes en 36 meses

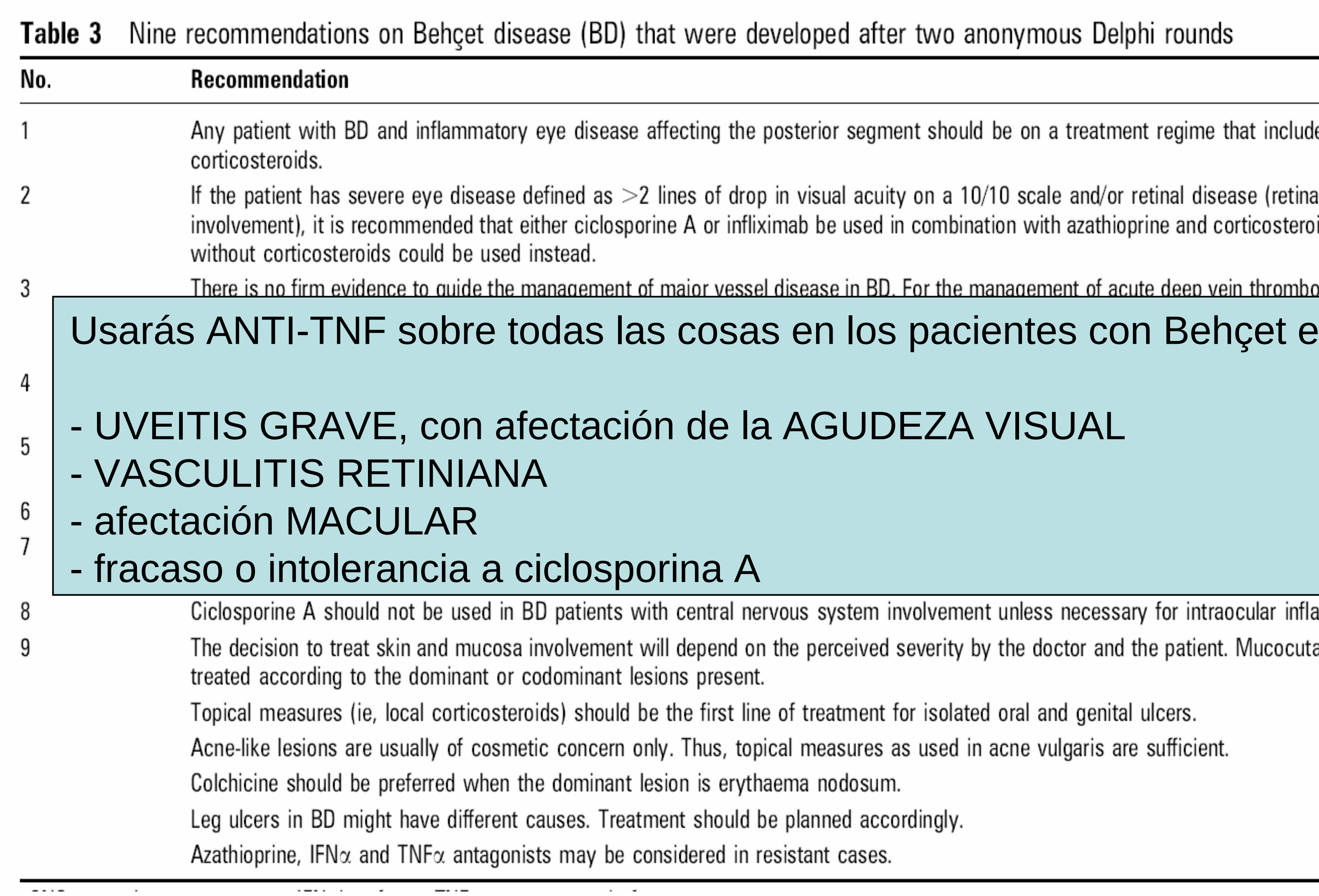
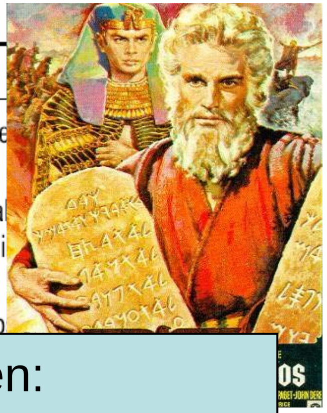


Table 3 Nine recommendations on Behçet disease (BD) that were developed after two anonymous Delphi rounds

No.	Recommendation
1	Any patient with BD and inflammatory eye disease affecting the posterior segment should be on a treatment regime that include corticosteroids.
2	If the patient has severe eye disease defined as >2 lines of drop in visual acuity on a 10/10 scale and/or retinal disease (retina involvement), it is recommended that either ciclosporine A or infliximab be used in combination with azathioprine and corticosteroi without corticosteroids could be used instead.
3	There is no firm evidence to guide the management of major vessel disease in BD. For the management of acute deep vein thrombo
4	the
5	
6	
7	ids,
8	Ciclosporine A should not be used in BD patients with central nervous system involvement unless necessary for intraocular inflammation.
9	The decision to treat skin and mucosa involvement will depend on the perceived severity by the doctor and the patient. Mucocutaneous involvement should be treated according to the dominant or codominant lesions present. Topical measures (ie, local corticosteroids) should be the first line of treatment for isolated oral and genital ulcers. Acne-like lesions are usually of cosmetic concern only. Thus, topical measures as used in acne vulgaris are sufficient. Colchicine should be preferred when the dominant lesion is erythaema nodosum. Leg ulcers in BD might have different causes. Treatment should be planned accordingly. Azathioprine, IFNα and TNFα antagonists may be considered in resistant cases.



Usarás ANTI-TNF sobre todas las cosas en los pacientes con Behçet en:

- UVEITIS GRAVE, con afectación de la AGUDEZA VISUAL
- VASCULITIS RETINIANA
- afectación MACULAR
- fracaso o intolerancia a ciclosporina A

RECOMENDACIONES PARA EL USO DE TERAPIA ANTI-TNF EN LA ENFERMEDAD DE BEHÇET

III Reunión Nacional en Enfermedades Autoinmunes Sistémicas
II Curso de Terapias Biológicas en Enfermedades Autoinmunes Sistémicas
30 Septiembre - 2 Octubre 2010
Hotel Meliá Lebreros
- Sevilla -

José Luis Callejas
Unidad Enfermedades Autoinmunes Sistémicas
H. Clínico San Cecilio de Granada

UEAS
Unidad de Enfermedades Autoinmunes Sistémicas

Long-term efficacy of infliximab in refractory posterior uveitis of Behçet's disease: a 24-month follow-up study

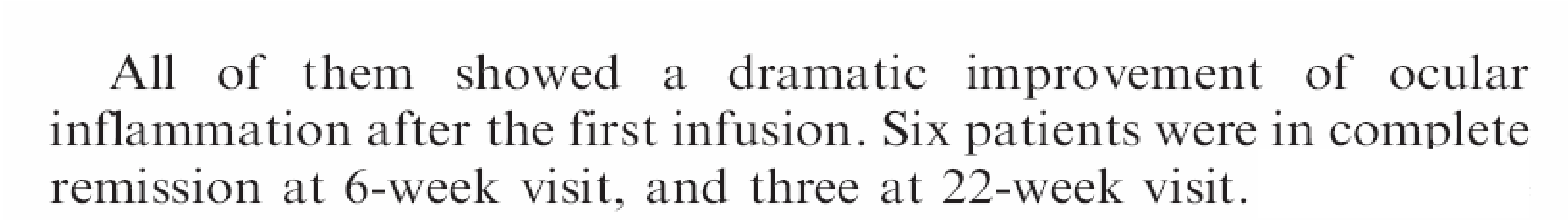
L. Niccoli, C. Nannini, M. Benucci[2], D. Chindamo, E. Cassarà, C. Salvarani[3], L. Cimino[4], G. Gini[1], I. Lenzetti[1] and F. Cantini

Rheumatology 2007;46;1161–1164

TABLE 1. Baseline demographic, and concurrent clinical manifestations in 12 patients with BD and RPU.

all subjects received infliximab 2-h intravenous infusions at the dose of 5 mg/kg at weeks 0, 2, 6, 14, 22, 30, 38, 46 and 54.

Previous therapy	
CS,AZA,CsA	5/12 (42%)
CS,AZA,MTX	5/12 (42%)
CS,AZA,CyC	2/12 (16%)



All of them showed a dramatic improvement of ocular inflammation after the first infusion. Six patients were in complete remission at 6-week visit, and three at 22-week visit.

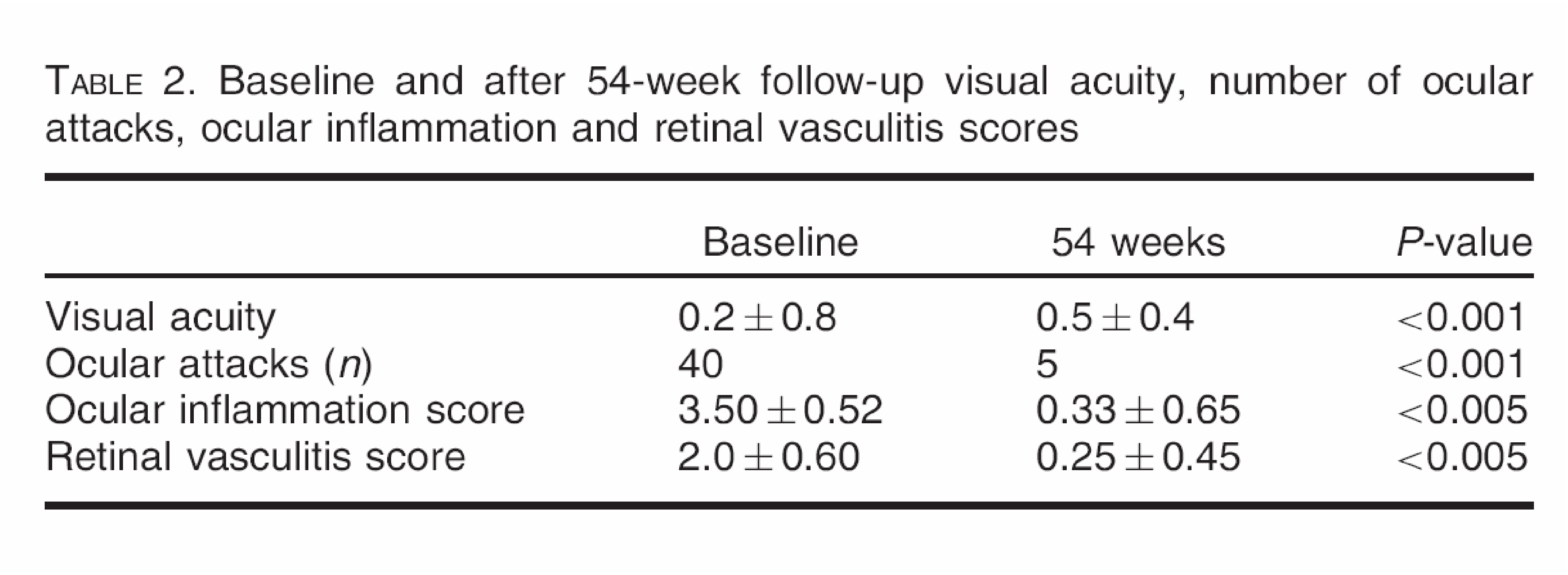


TABLE 2. Baseline and after 54-week follow-up visual acuity, number of ocular attacks, ocular inflammation and retinal vasculitis scores

	Baseline	54 weeks	*P*-value
Visual acuity	0.2 ± 0.8	0.5 ± 0.4	<0.001
Ocular attacks (*n*)	40	5	<0.001
Ocular inflammation score	3.50 ± 0.52	0.33 ± 0.65	<0.005
Retinal vasculitis score	2.0 ± 0.60	0.25 ± 0.45	<0.005

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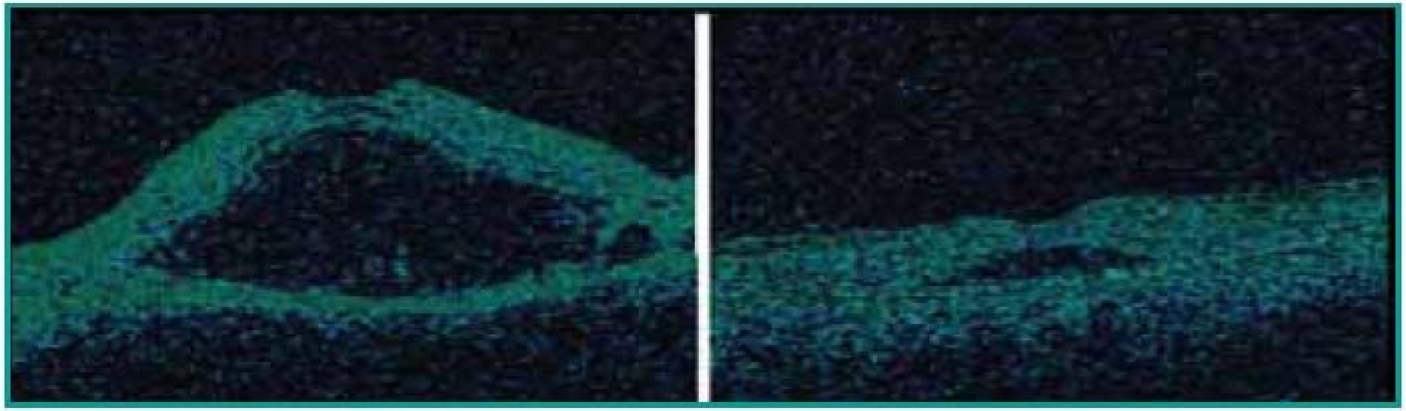
DOI: 10.1089/jop.2007.0104

Adalimumab Therapy for Refractory Uveitis: A Pilot Study

MANUEL DIAZ-LLOPIS,[1–3] SALVADOR GARCÍA-DELPECH,[1] DAVID SALOM,[1]
PATRICIA UDAONDO,[1] MARISA HERNÁNDEZ-GARFELLA,[1] ARTURO QUIJADA,[1]
and F. JAVIER ROMERO[2,4]



Patient no./ sex/age, year	*Diagnosis*	*Anatomic location*
1/F/24	Idiopathic	Posterior
2/M/34	Behçet disease	Panuveítis
3/M/41	Sarcoidosis	Panuveítis
4/F/54	BSCR	Posterior
5/M/35	Behçet disease	Panuveítis
6/M/28	Behçet disease	Panuveítis
7/F/42	Idiopathic	Panuveítis
8/F/26	Idiopathic	Intermediate
9/M/42	Idiopathic	Intermediate
10/M/35	VKH	Panuveítis
11/F/46	BSCR	Posterior
12/M/28	VKH	Panuveítis
13/M/25	Idiopathic	Intermediate
14/M/36	Idiopathic	Posterior
15/F/39	Idiopathic	Posterior
16/F/27	Idiopathic	Anterior
17/F/32	Crohn disease	Panuveítis
18/F/37	Idiopathic	Panuveítis
19/M/29	Idiopathic	Panuveítis

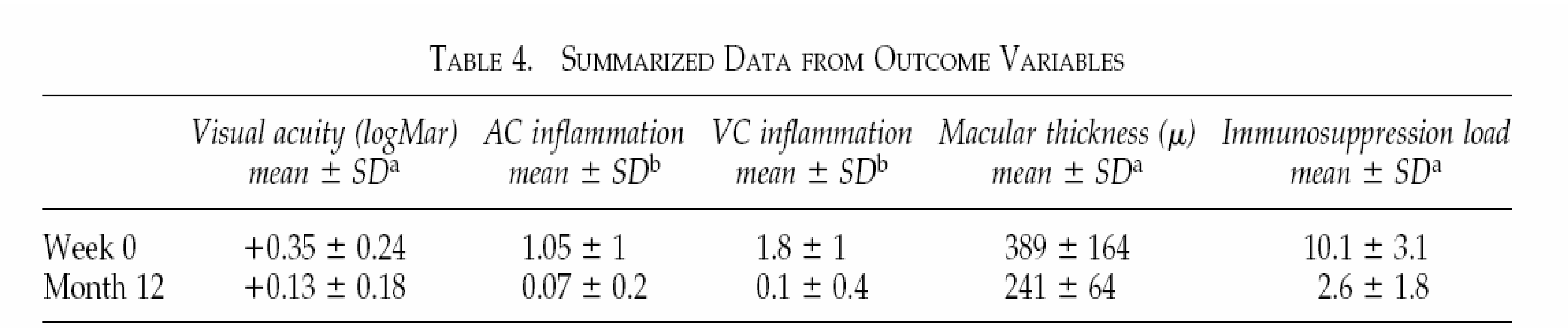
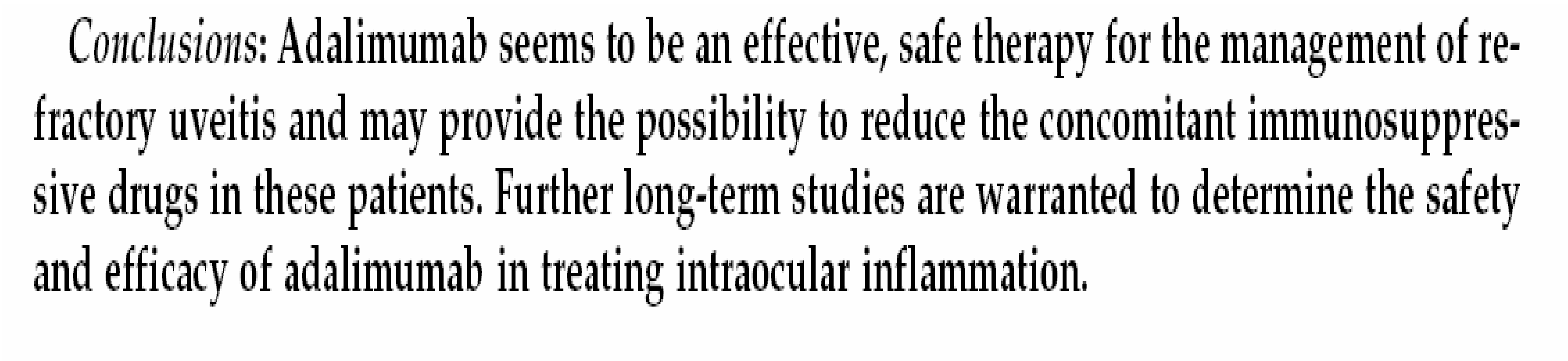
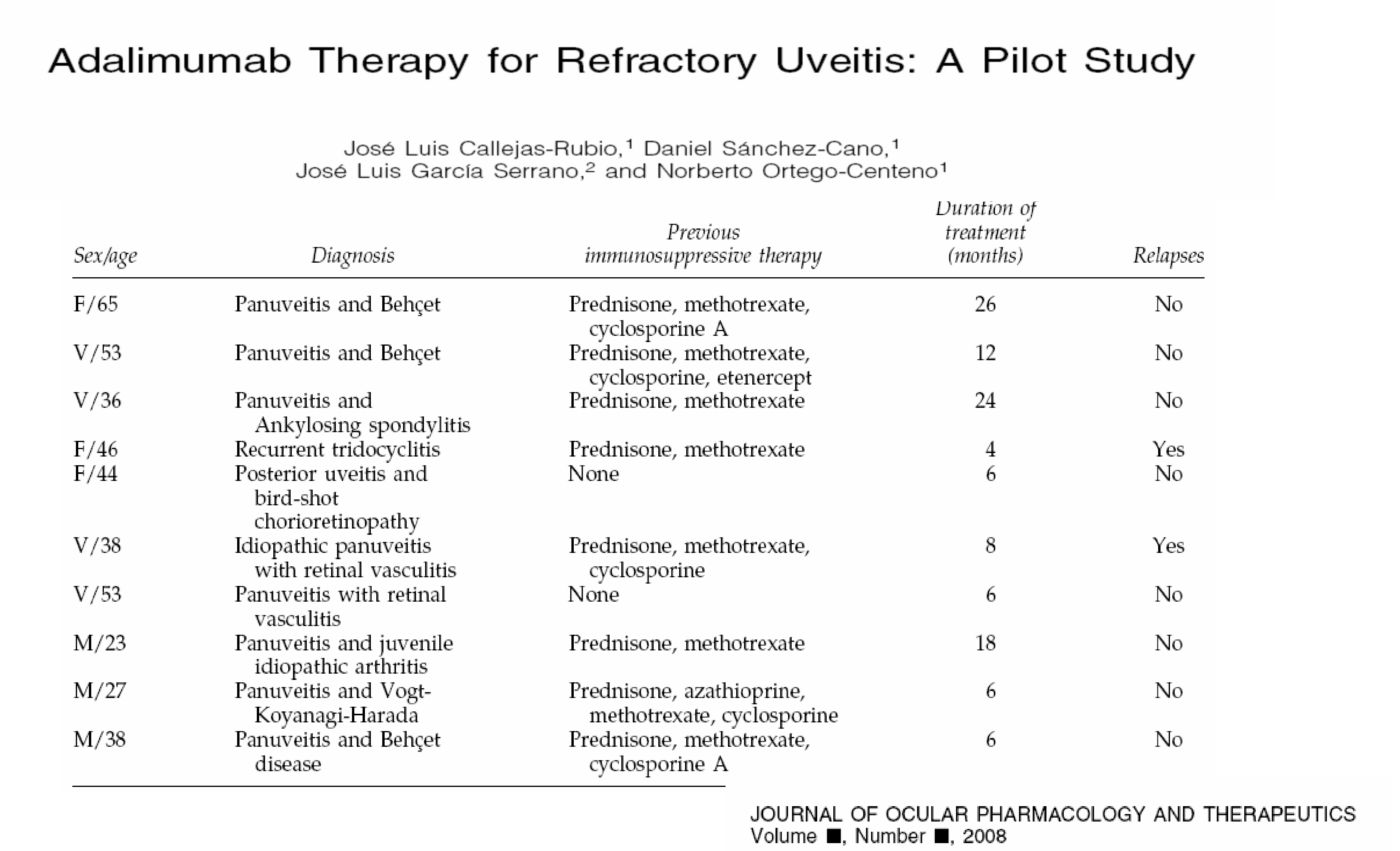


TABLE 4. SUMMARIZED DATA FROM OUTCOME VARIABLES

	Visual acuity (logMar) mean ± SD[a]	AC inflammation mean ± SD[b]	VC inflammation mean ± SD[b]	Macular thickness (μ) mean ± SD[a]	Immunosuppression load mean ± SD[a]
Week 0	+0.35 ± 0.24	1.05 ± 1	1.8 ± 1	389 ± 164	10.1 ± 3.1
Month 12	+0.13 ± 0.18	0.07 ± 0.2	0.1 ± 0.4	241 ± 64	2.6 ± 1.8



Conclusions: Adalimumab seems to be an effective, safe therapy for the management of refractory uveitis and may provide the possibility to reduce the concomitant immunosuppressive drugs in these patients. Further long-term studies are warranted to determine the safety and efficacy of adalimumab in treating intraocular inflammation.



Adalimumab Therapy for Refractory Uveitis: A Pilot Study

José Luis Callejas-Rubio,[1] Daniel Sánchez-Cano,[1]
José Luis García Serrano,[2] and Norberto Ortego-Centeno[1]

Sex/age	*Diagnosis*	*Previous immunosuppressive therapy*	*Duration of treatment (months)*	*Relapses*
F/65	Panuveitis and Behçet	Prednisone, methotrexate, cyclosporine A	26	No
V/53	Panuveitis and Behçet	Prednisone, methotrexate, cyclosporine, etenercept	12	No
V/36	Panuveitis and Ankylosing spondylitis	Prednisone, methotrexate	24	No
F/46	Recurrent tridocyclitis	Prednisone, methotrexate	4	Yes
F/44	Posterior uveitis and bird-shot chorioretinopathy	None	6	No
V/38	Idiopathic panuveitis with retinal vasculitis	Prednisone, methotrexate, cyclosporine	8	Yes
V/53	Panuveitis with retinal vasculitis	None	6	No
M/23	Panuveitis and juvenile idiopathic arthritis	Prednisone, methotrexate	18	No
M/27	Panuveitis and Vogt-Koyanagi-Harada	Prednisone, azathioprine, methotrexate, cyclosporine	6	No
M/38	Panuveitis and Behçet disease	Prednisone, methotrexate, cyclosporine A	6	No

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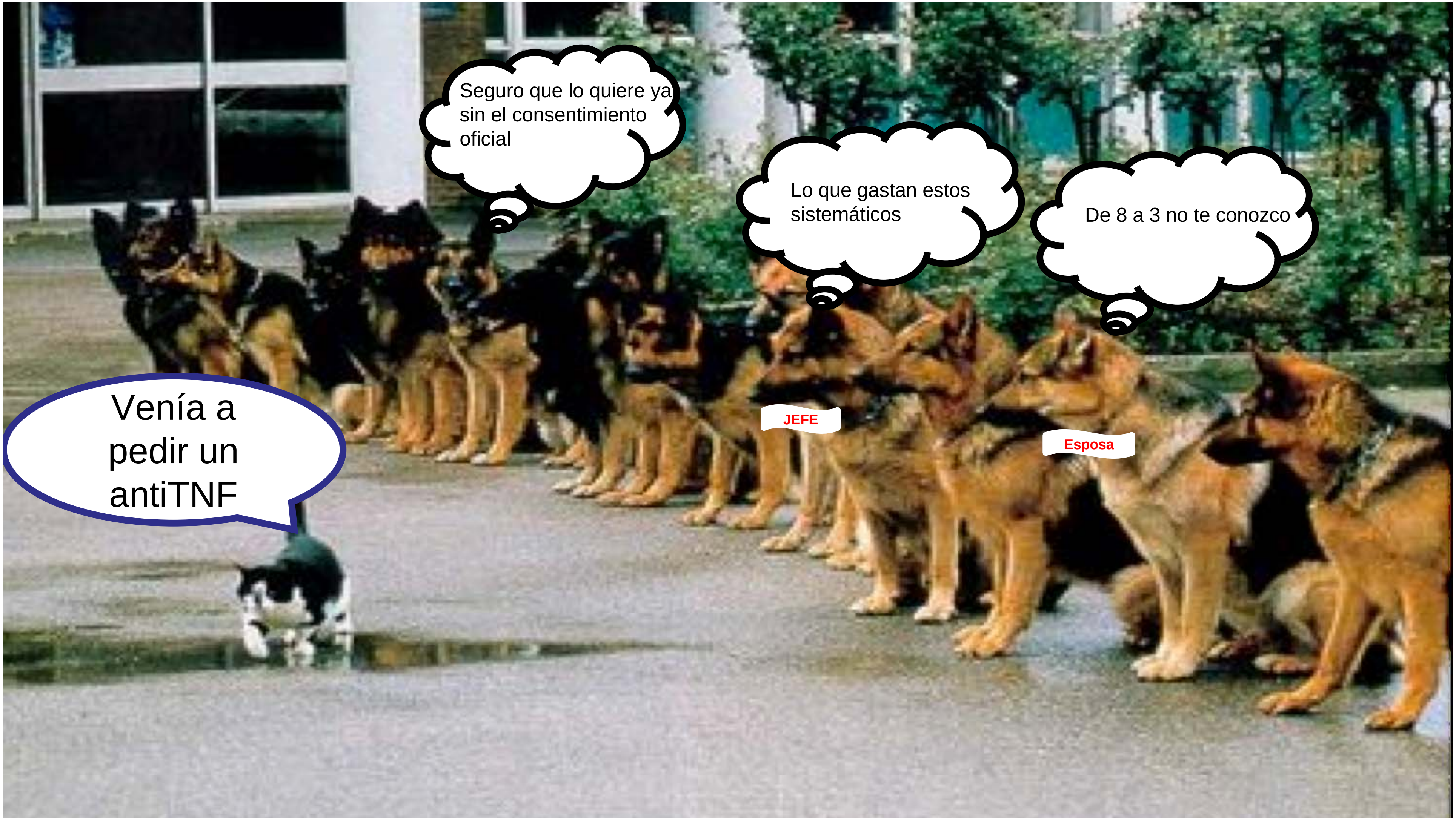
Volume ■, Number ■, 2008


Venía a pedir un antiTNF
Seguro que lo quiere ya sin el consentimiento oficial
Lo que gastan estos sistemáticos
De 8 a 3 no te conozco
JEFE
Esposa

Junio 2009
AÑO 2 · Nº 2

Cuadernos de Autoinmunidad

PUBLICACIÓN OFICIAL DE LA SOCIEDAD ANDALUZA DE ENFERMEDADES AUTOINMUNES

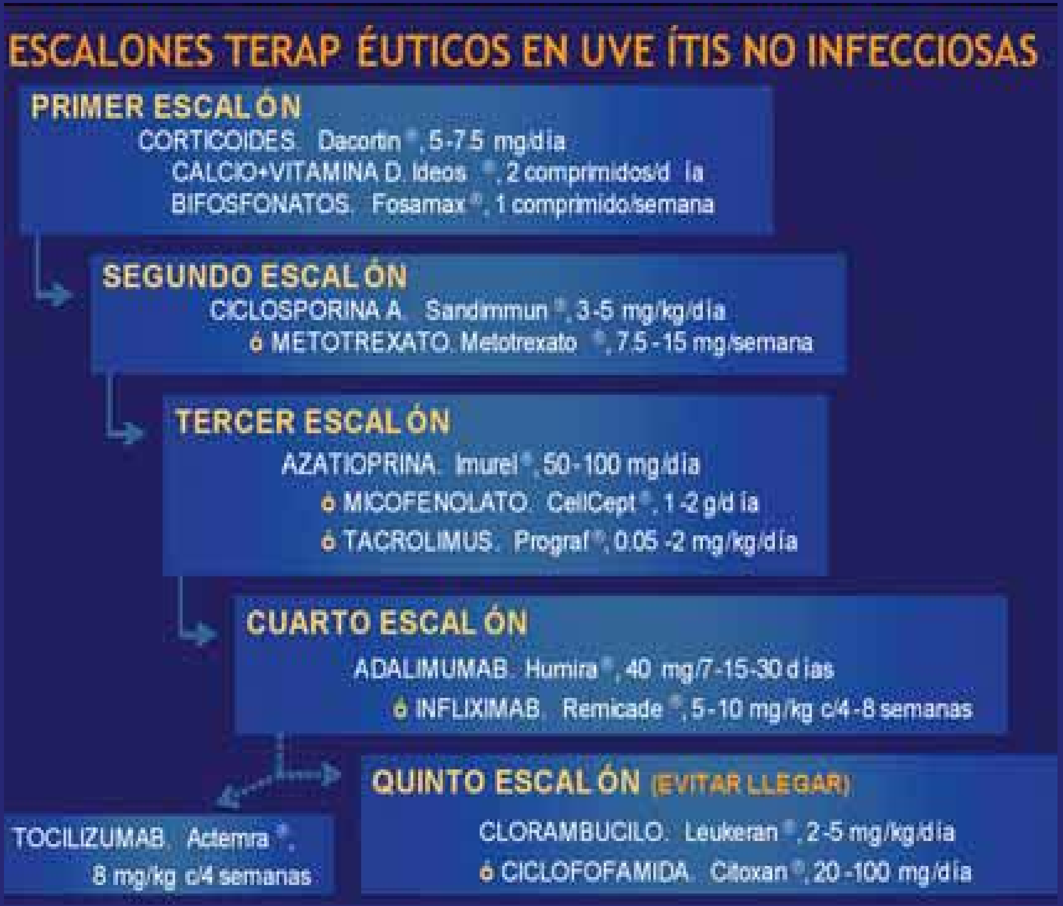
MONOGRÁFICO

UVEÍTIS E INFLAMACIÓN OCULAR

PRINCIPIOS GENERALES DEL TRATAMIENTO DE LAS UVEÍTIS NO INFECCIOSAS

Dr. Roberto Gallego Pinazo [1], Dr. David Salom Alonso [1], Dr. Salvador García Delpech [1], Dr. Manuel Díaz Llopis [1,2]

1 Hospital Universitario La Fe de Valencia. Servicio de Oftalmología
2 Facultad de Medicina. Universidad de Valencia



ESCALONES TERAPÉUTICOS EN UVEÍTIS NO INFECCIOSAS

PRIMER ESCALÓN
CORTICOIDES. Dacortin®, 5-7.5 mg/día
CALCIO+VITAMINA D. Ideos®, 2 comprimidos/día
BIFOSFONATOS. Fosamax®, 1 comprimido/semana

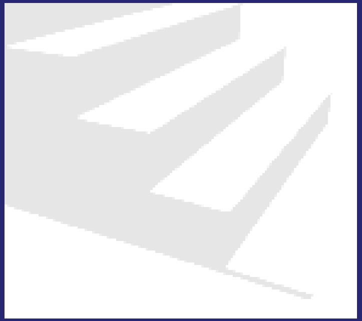
SEGUNDO ESCALÓN
CICLOSPORINA A. Sandimmun®, 3-5 mg/kg/día
ó METOTREXATO. Metotrexato®, 7.5 - 15 mg/semana

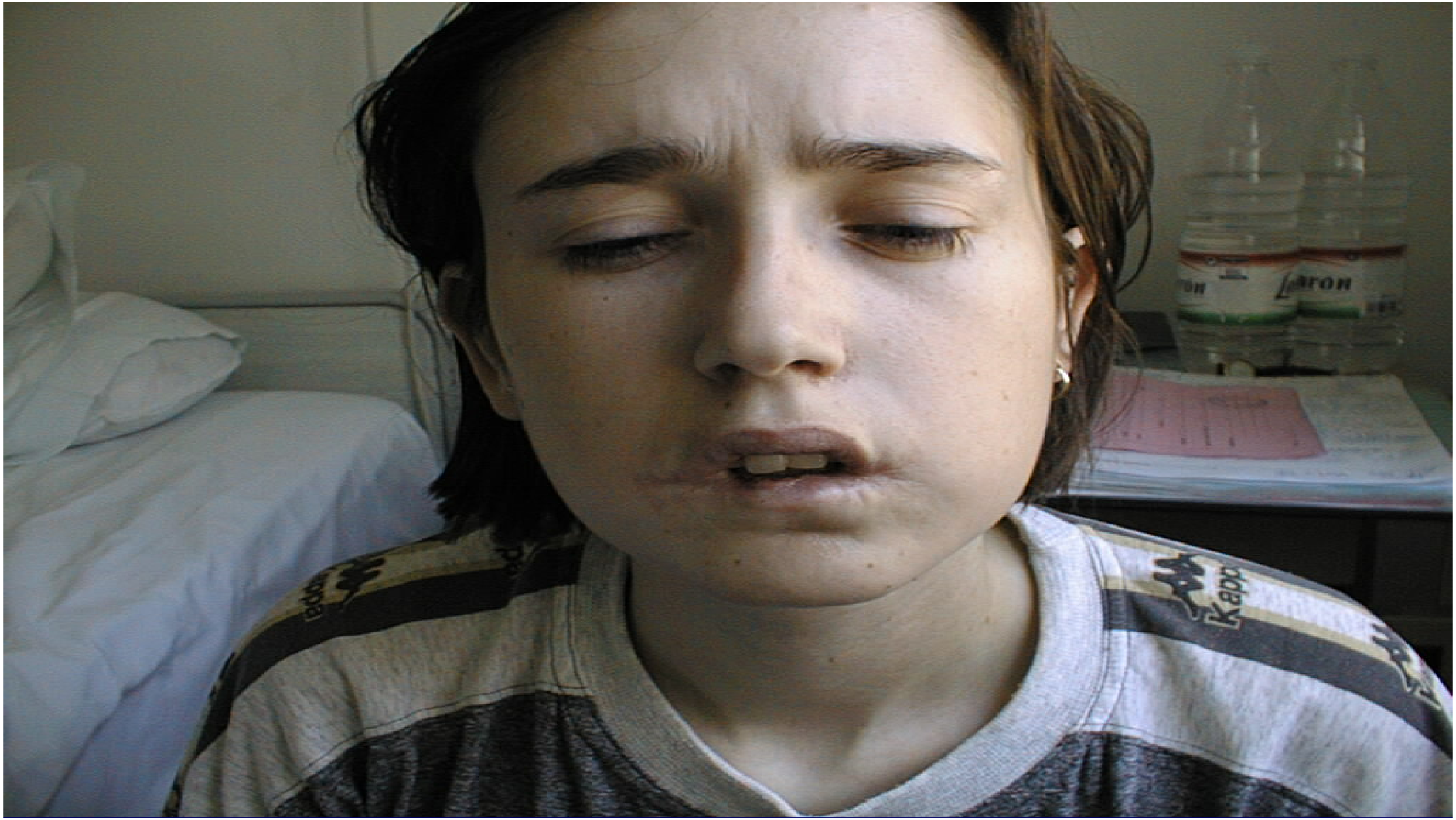
TERCER ESCALÓN
AZATIOPRINA. Imurel®, 50 - 100 mg/día
ó MICOFENOLATO. CellCept®, 1-2 g/día
ó TACROLIMUS. Prograf®, 0.05 -2 mg/kg/día

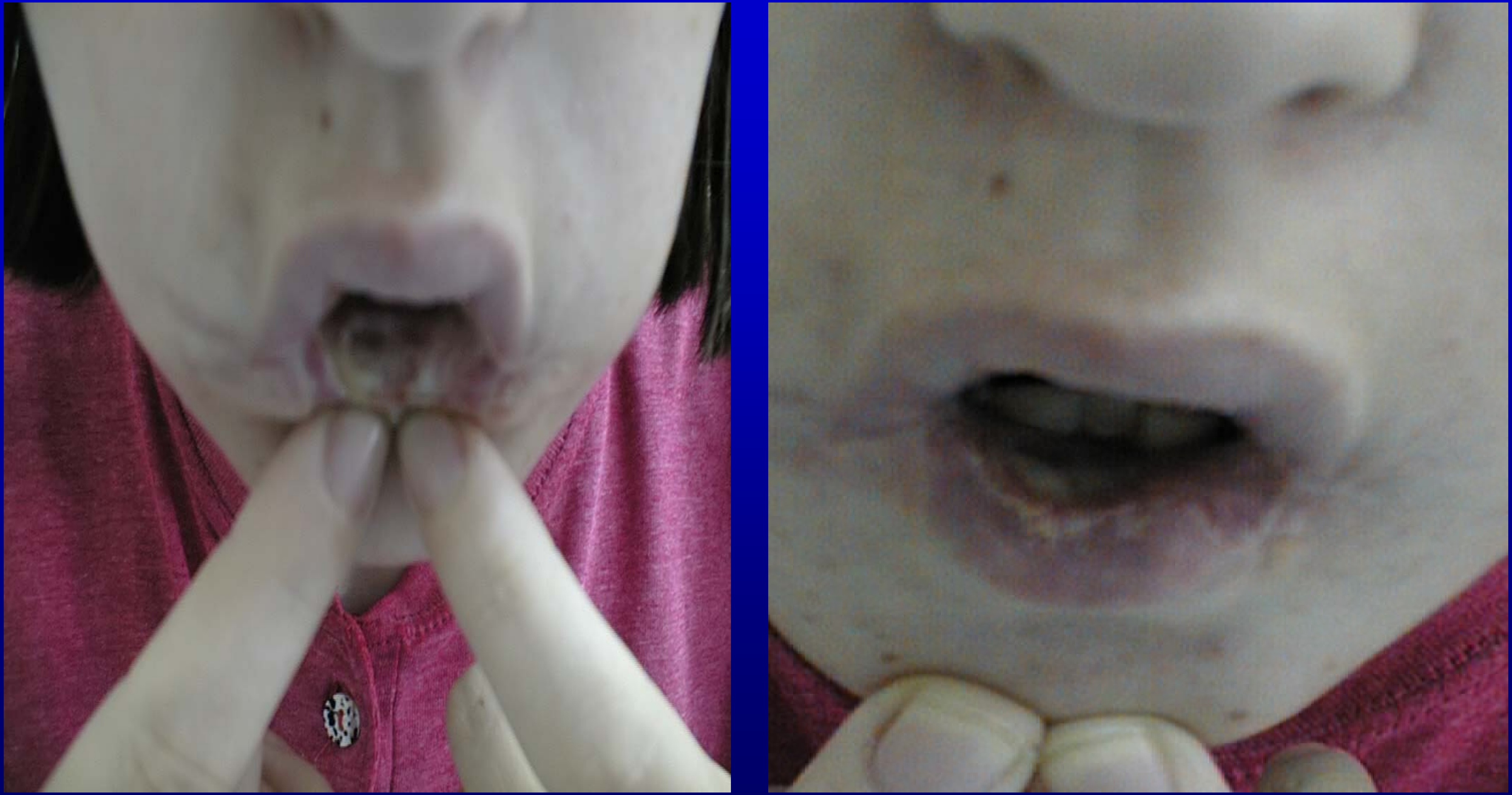
CUARTO ESCALÓN
ADALIMUMAB. Humira®, 40 mg/7-15-30 días
ó INFLIXIMAB. Remicade®, 5 - 10 mg/kg c/4 -8 semanas

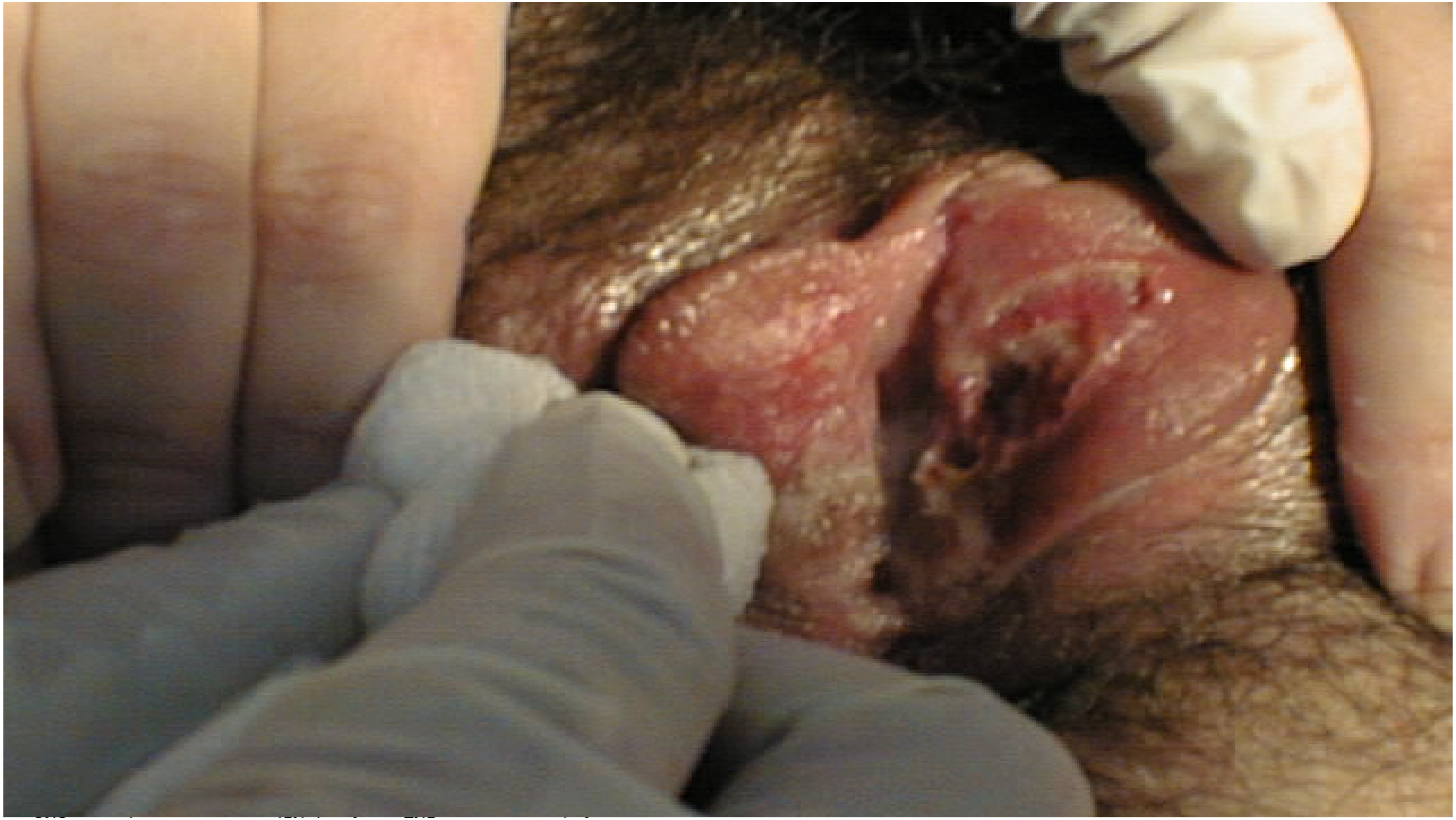
QUINTO ESCALÓN (EVITAR LLEGAR)
CLORAMBUCILO. Leukeran®, 2-5 mg/kg/día
ó CICLOFOFAMIDA. Citoxan®, 20 -100 mg/día

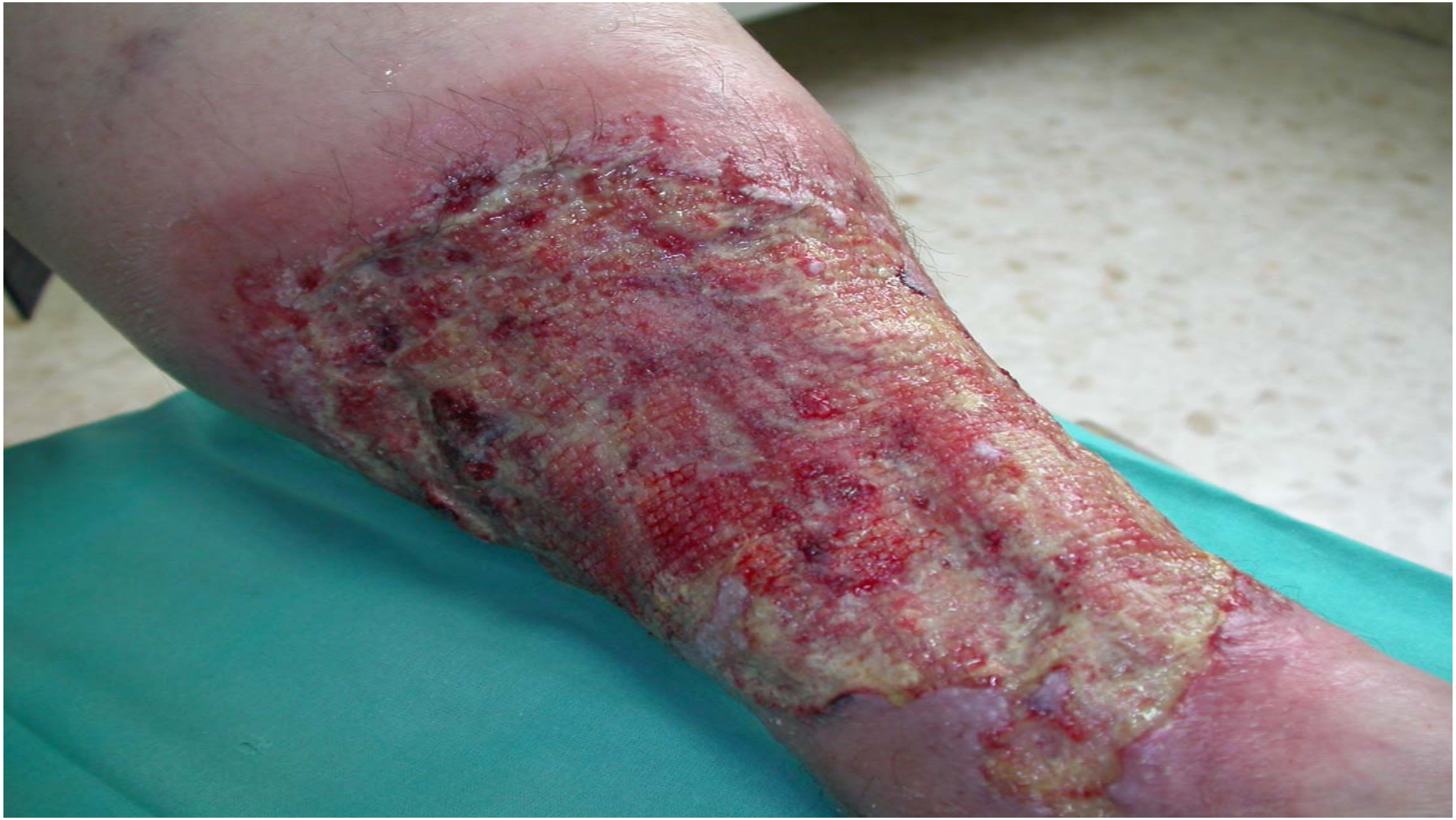
TOCILIZUMAB. Actemra®,
8 mg/kg c/4 semanas

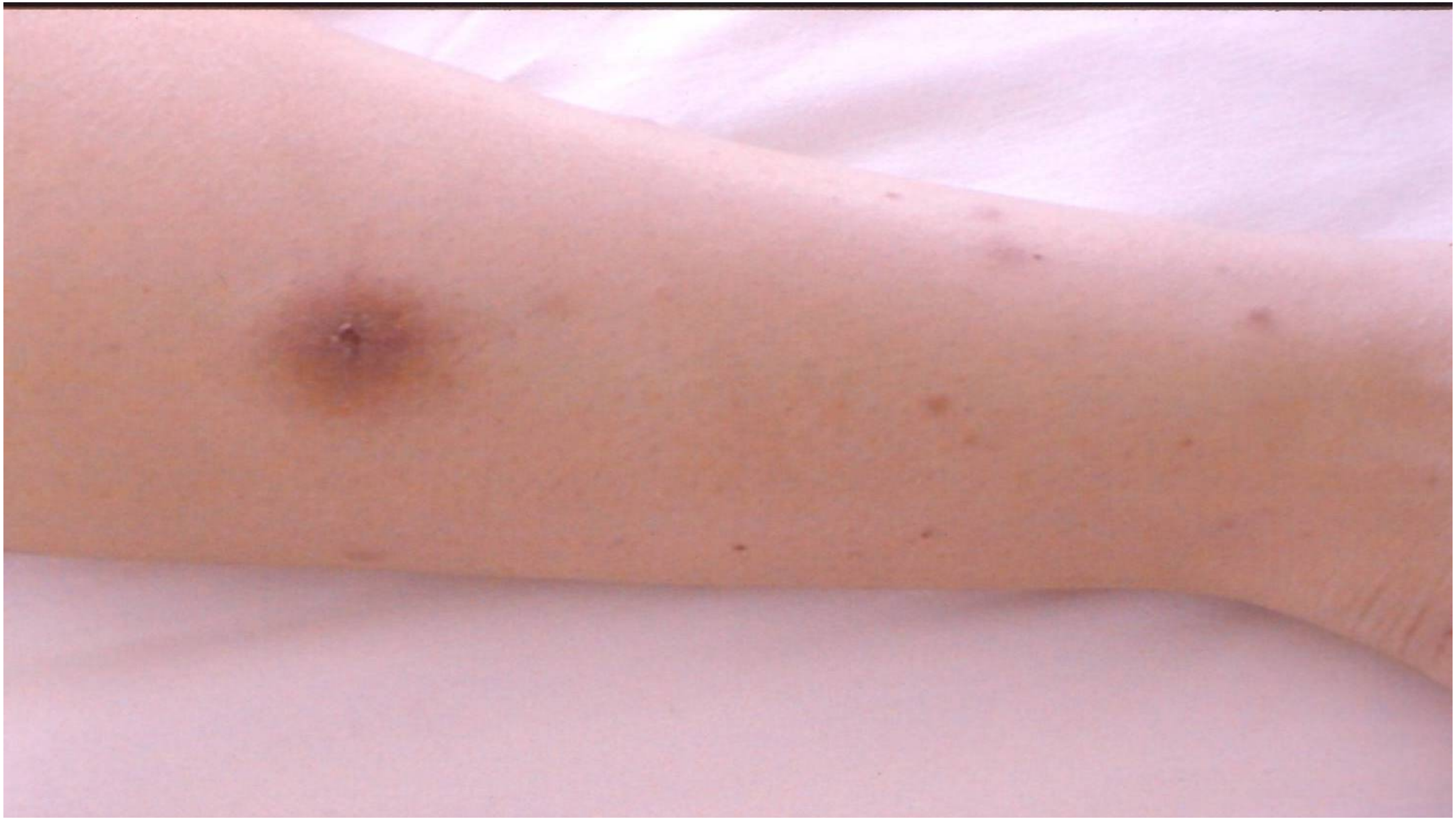


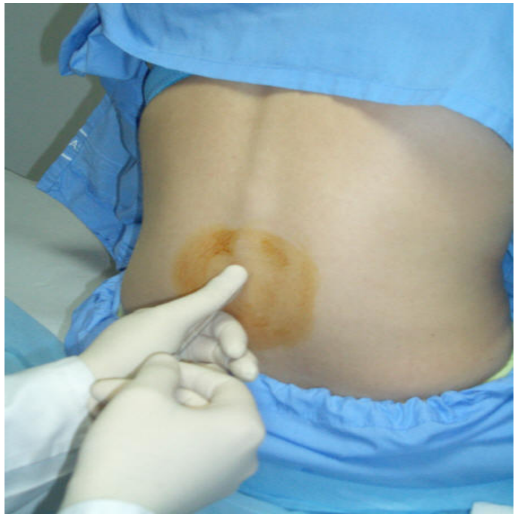


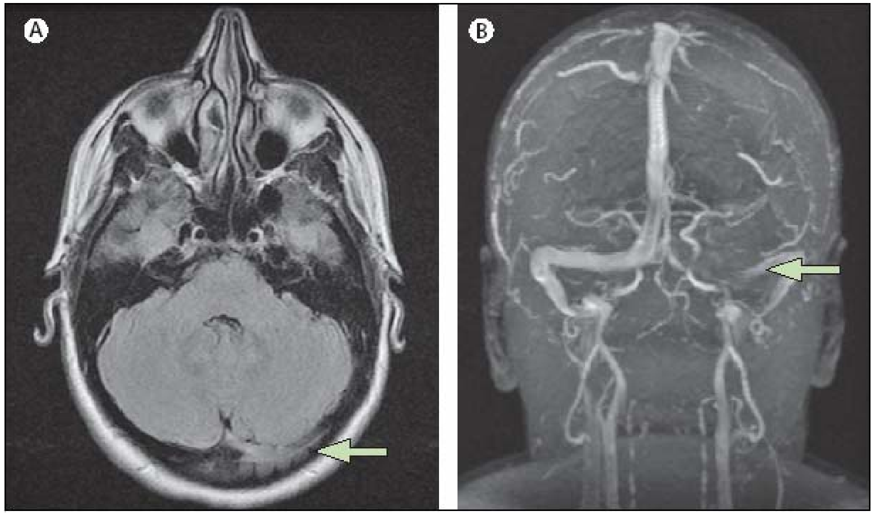








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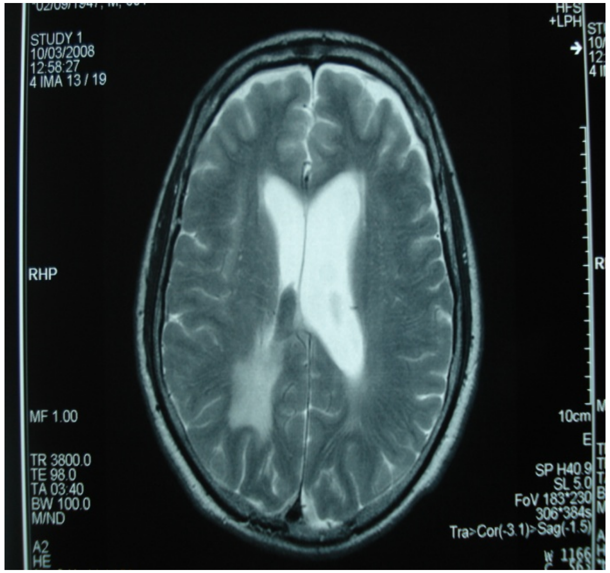
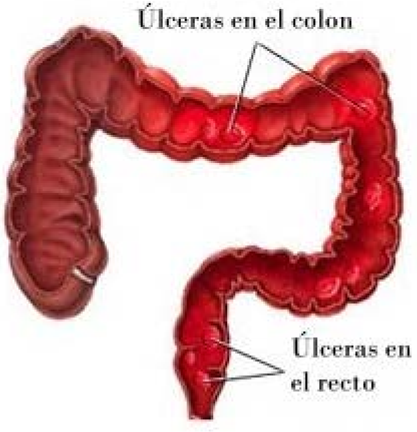
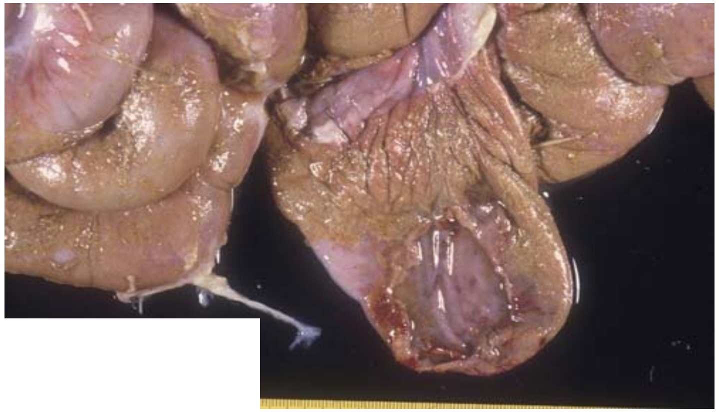
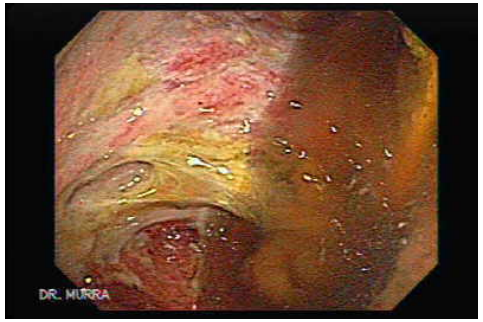

HFS
+LPH
STUDY 1
10/03/2008
12:58:27
4 IMA 13 / 19
RHP
MF 1.00
10cm
E
TR 3800.0
TE 98.0
TA 03:40
BW 100.0
M/ND
SP H40.9
SL 5.0
FoV 183*230
306*384s
Tra>Cor(-3.1)>Sag(-1.5)
A2
HE
W 1166

MANIFESTACIONES GASTROINTESTINALES


Úlceras en el colon
Úlceras en el recto





Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 59, No. 2, February 15, 2008, pp 285–290
DOI 10.1002/art.23345
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CONTRIBUTIONS FROM THE FIELD

Infliximab for the Treatment of Neuro-Behçet's Disease: A Case Series and Review of the Literature

NICOLÒ PIPITONE,[1] IGNAZIO OLIVIERI,[2] ANGELA PADULA,[2] SALVATORE D'ANGELO,[2] ANGELO NIGRO,[2] GIULIO ZUCCOLI,[1] LUIGI BOIARDI,[1] AND CARLO SALVARANI[1]

Table 3 Nine recommendations on Behçet disease (BD) that were developed after two anonymous Delphi rounds

No.	Recommendation
1	Any patient with BD and inflammatory eye disease affecting the posterior segment should be on a treatment regime that includes azathioprine and systemic corticosteroids.
2	or
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7	ls,
8	
9	be treated according to the dominant or codominant Topical measures (ie, local corticosteroids) should Acne-like lesions are usually of cosmetic concern Colchicine should be preferred when the dominant Leg ulcers in BD might have different causes. Tre Azathioprine, IFNα and TNFα antagonists may be considered in resistant cases.

Visto en videosydiver

PROHIBIDO BAÑARSE

TABLE 1. Recommendations for the prescription of anti-TNF agents in BD

Subset	New manifestation	Recurrent/refractory cases
Parenchymal CNS involvement	Not recommended	In patients refractory to treatment with pulse cyclophosphamide and prednisolone (1 mg/kg/day), or in those who relapse while on maintenance with AZA[b] and prednisolone (<7.5 mg/day) infliximab[c] may be tried
Intestinal inflammation	Not recommended	In patients that have failed two immunosuppressive agents[b] and require prednisolone at a dosage >7.5 mg/day, Infliximab[c] may be used
Major vessel involvement	Not enough data	Not enough data
Mucocutaneous manifestations	Not recommended	In patients with poor quality of life despite, or intolerant to, adequate doses[b] of AZA, colchicine or thalidomide and require prednisolone at a dosage >7.5 mg/day, etanercept[d] or Infliximab[c] may be used

Adalimumab en el tratamiento de la enfermedad de Behçet

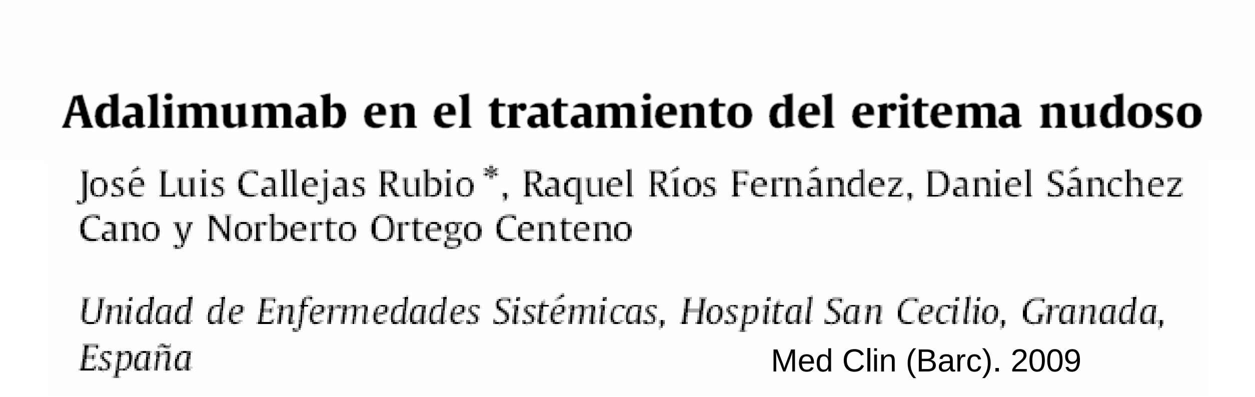
José Luis Callejas-Rubio, Daniel Sánchez-Cano, Raquel Ríos-Férnandez y Norberto Ortego-Centeno

Unidad de Enfermedades Autoinmunes Sistémicas. Hospital Clínico San Cecilio. Granada. España.

Med Clin (Barc). 2008;131(11):437-9

Características clínicas de los pacientes

Edad (años)	**Sexo**	**Motivo**	**Tratamientos previos**	**Respuesta**	**Seguimiento (meses)**
34	Mujer	Vasculitis cutánea	PD, CQ, MTX	RC	18
36	Mujer	Aftas recalcitrantes y artritis	PD, CQ, MTX	EA grave	1
38	Varón	Panuveítis con vasculitis retiniana	PD, MTX, CYC-A	RC	6
53	Varón	Panuveítis con vasculitis retiniana	PD, MTX, CYC-A	RC	10
55	Mujer	Panuveítis con vasculitis retiniana	PD, MTX, CYC-A	RC	26

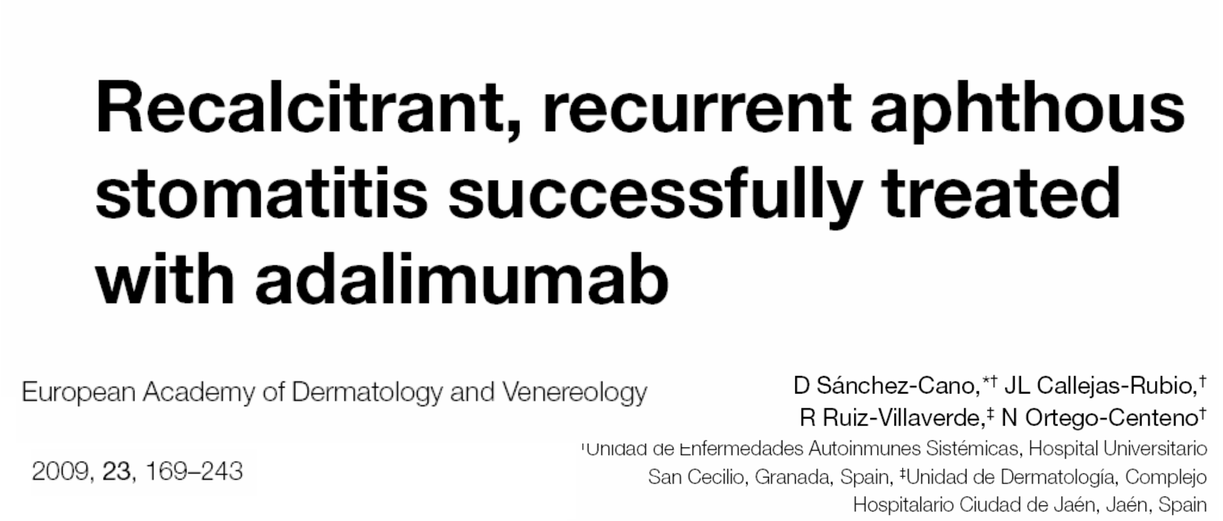


Adalimumab en el tratamiento del eritema nudoso

José Luis Callejas Rubio [*], Raquel Ríos Fernández, Daniel Sánchez Cano y Norberto Ortego Centeno

Unidad de Enfermedades Sistémicas, Hospital San Cecilio, Granada, España

Med Clin (Barc). 2009



Recalcitrant, recurrent aphthous stomatitis successfully treated with adalimumab

European Academy of Dermatology and Venereology

2009, **23**, 169–243

D Sánchez-Cano,[*†] JL Callejas-Rubio,[†]
R Ruiz-Villaverde,[‡] N Ortego-Centeno[†]
[†]Unidad de Enfermedades Autoinmunes Sistémicas, Hospital Universitario
San Cecilio, Granada, Spain, [‡]Unidad de Dermatología, Complejo
Hospitalario Ciudad de Jaén, Jaén, Spain

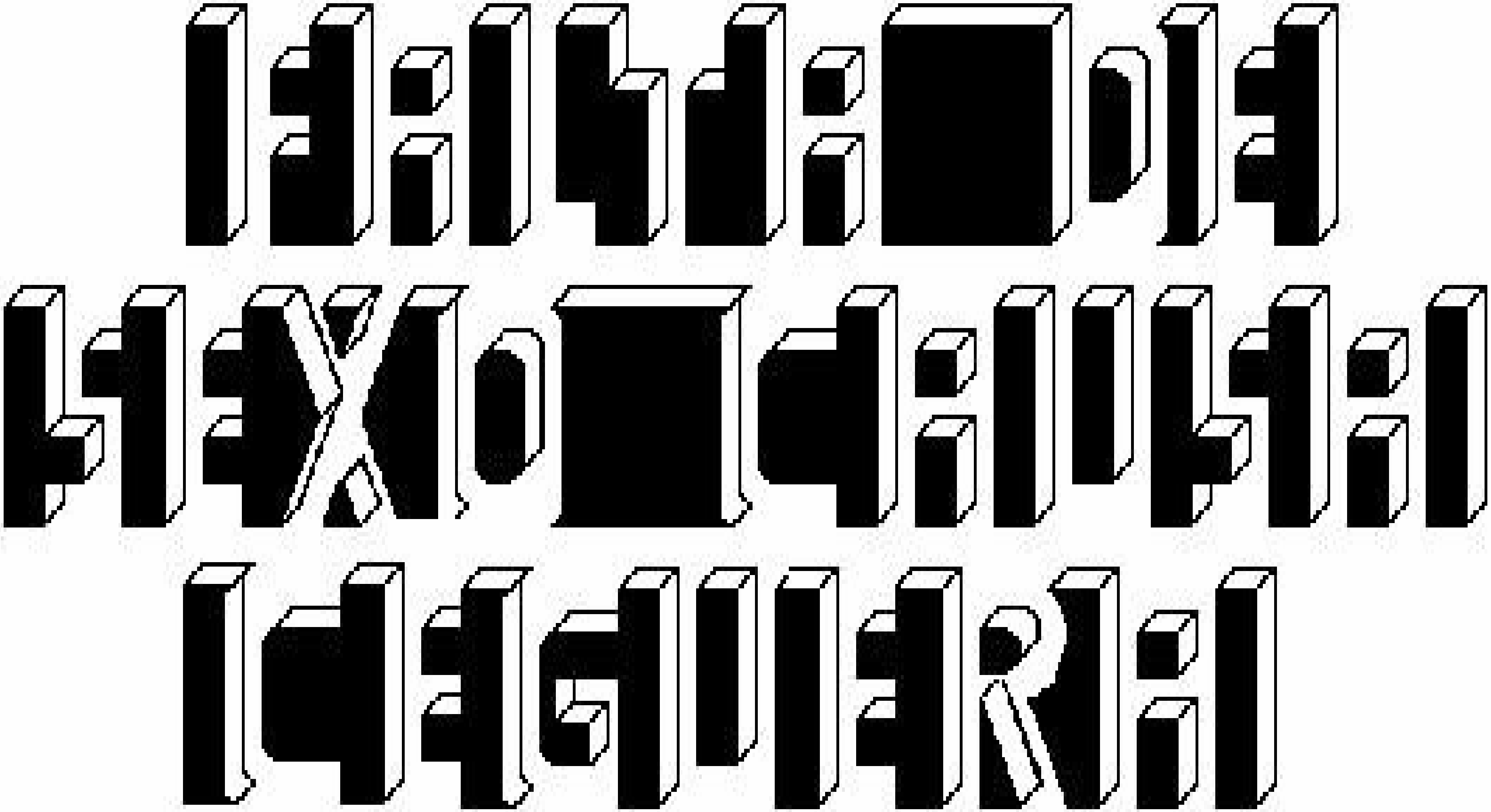
REVIEW

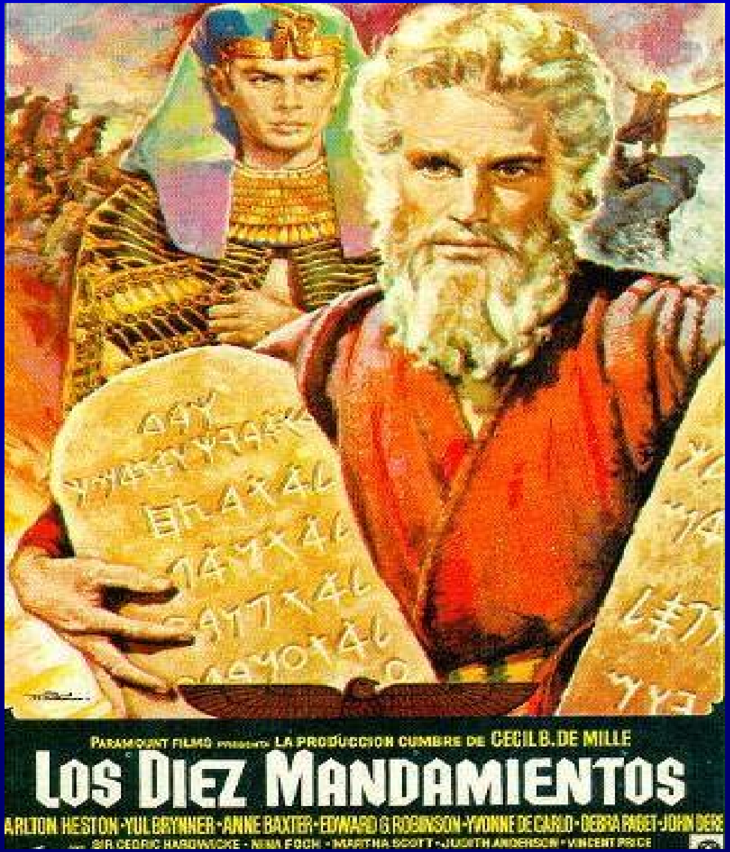
Tumor necrosis factor-alpha inhibitor treatment for sarcoidosis

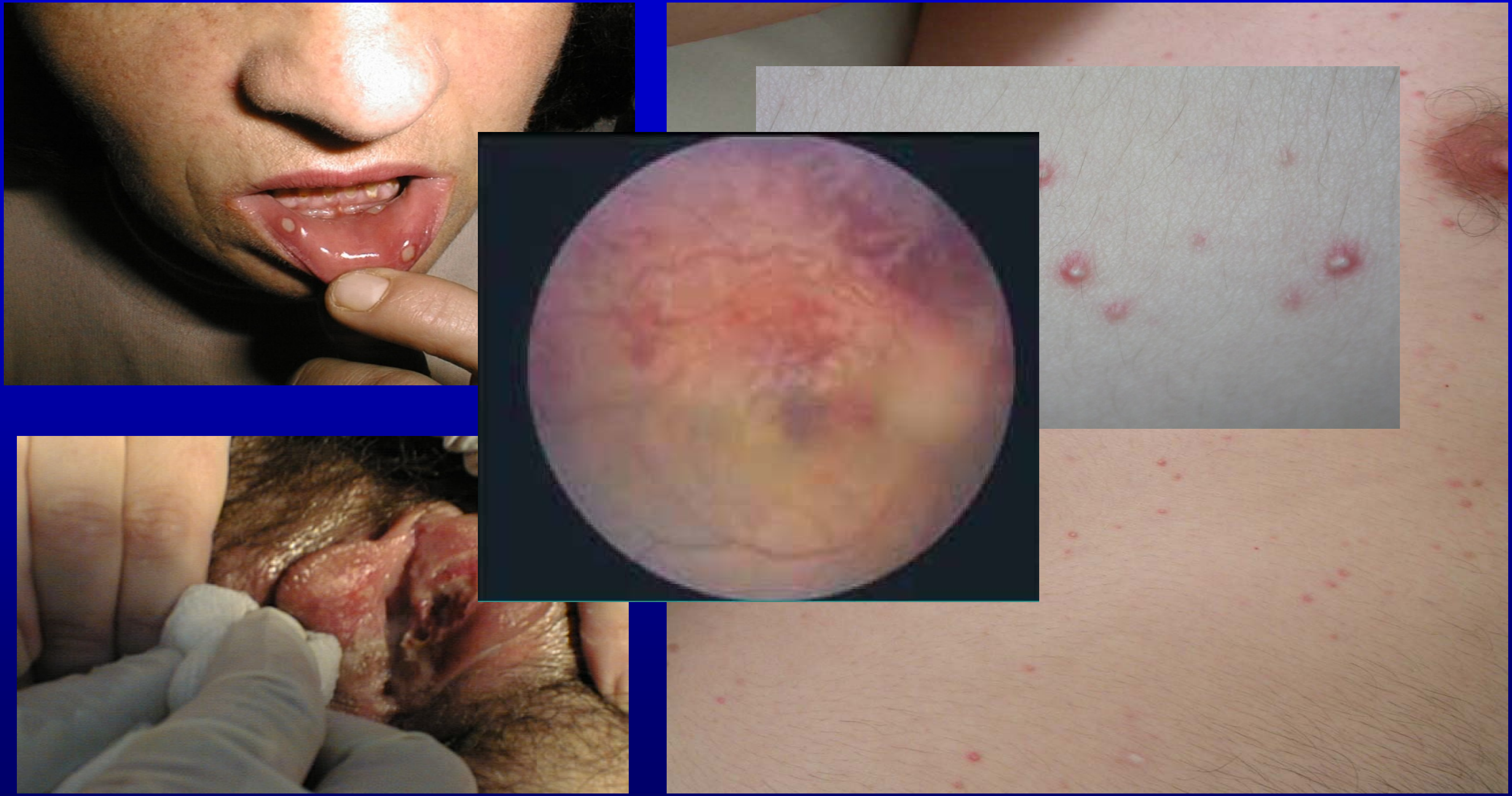
José Luis Callejas-Rubio
Lourdes López-Pérez
Norberto Ortego-Centeno

Unit of Autoimmune Systemic
Diseases, Hospital Clinico San Cecilio,
Granada, Spain

Therapeutics and Clinical Risk Management 2008:4(6) 1305–1313




PARAMOUNT FILMS presenta LA PRODUCCION CUMBRE DE CECIL B. DE MILLE
LOS DIEZ MANDAMIENTOS
ARLTON HESTON · YUL BRYNNER · ANNE BAXTER · EDWARD G. ROBINSON · YVONNE DE CARLO · DEBRA PAGET · JOHN DERE
SIR CEDRIC HARDWICKE · NINA FOCH · MARTHA SCOTT · JUDITH ANDERSON · VINCENT PRICE



Junio 2009
AÑO 2 · Nº 2

Cuadernos de Autoinmunidad

PUBLICACIÓN OFICIAL DE LA SOCIEDAD ANDALUZA DE ENFERMEDADES AUTOINMUNES

MONOGRÁFICO

■ UVEÍTIS E INFLAMACIÓN OCULAR

PRINCIPIOS GENERALES DEL TRATAMIENTO DE LAS UVEÍTIS NO INFECCIOSAS

Dr. Roberto Gallego Pinazo [1], Dr. David Salom Alonso [1], Dr. Salvador García Delpech [1], Dr. Manuel Díaz Llopis [1,2]

1 Hospital Universitario La Fe de Valencia. Servicio de Oftalmología

2 Facultad de Medicina. Universidad de Valencia

Immunosuppressive therapy for ocular diseases

Aliza Jap[a,b] and Soon-Phaik Chee[b,c,d]

Current Opinion in Ophthalmology 2008, 19:535–540

JOURNAL OF OCULAR PHARMACOLOGY AND THERAPEUTICS
Volume 24, Number 3, 2008
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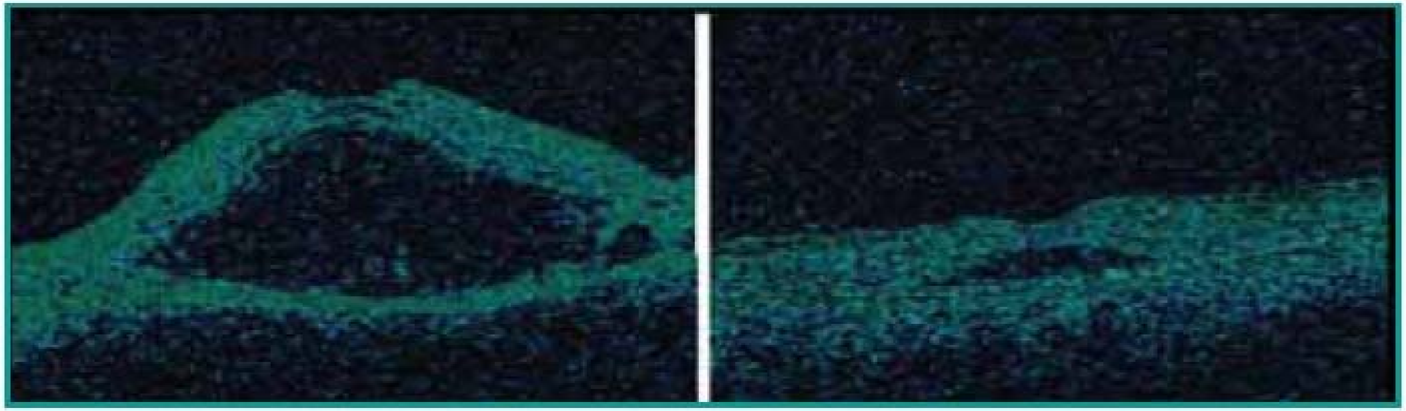
DOI: 10.1089/jop.2007.0104

Adalimumab Therapy for Refractory Uveitis: A Pilot Study

MANUEL DIAZ-LLOPIS,[1–3] SALVADOR GARCÍA-DELPECH,[1] DAVID SALOM,[1]
PATRICIA UDAONDO,[1] MARISA HERNÁNDEZ-GARFELLA,[1] ARTURO QUIJADA,[1]
and F. JAVIER ROMERO[2,4]



Patient no./ sex/age, year	*Diagnosis*	*Anatomic location*
1/F/24	Idiopathic	Posterior
2/M/34	Behçet disease	Panuveítis
3/M/41	Sarcoidosis	Panuveítis
4/F/54	BSCR	Posterior
5/M/35	Behçet disease	Panuveítis
6/M/28	Behçet disease	Panuveítis
7/F/42	Idiopathic	Panuveítis
8/F/26	Idiopathic	Intermediate
9/M/42	Idiopathic	Intermediate
10/M/35	VKH	Panuveítis
11/F/46	BSCR	Posterior
12/M/28	VKH	Panuveítis
13/M/25	Idiopathic	Intermediate
14/M/36	Idiopathic	Posterior
15/F/39	Idiopathic	Posterior
16/F/27	Idiopathic	Anterior
17/F/32	Crohn disease	Panuveítis
18/F/37	Idiopathic	Panuveítis
19/M/29	Idiopathic	Panuveítis

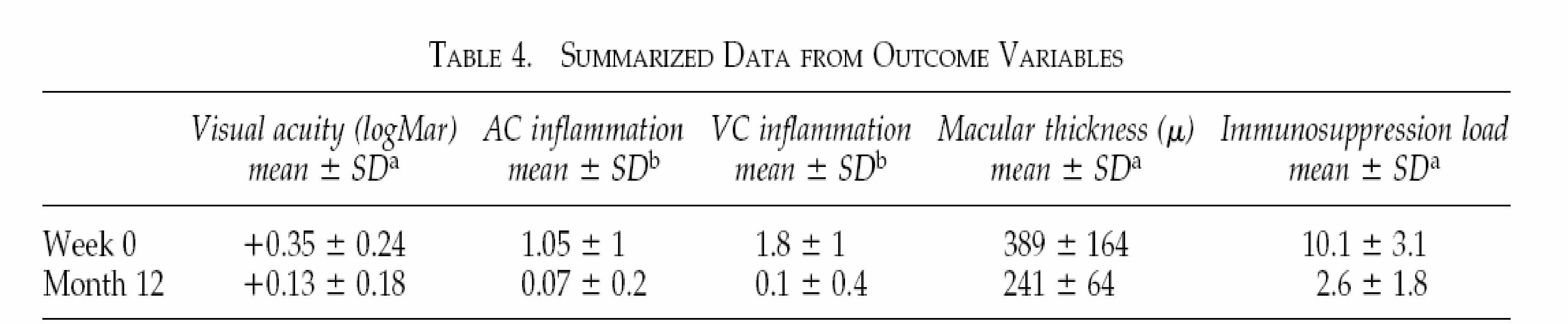
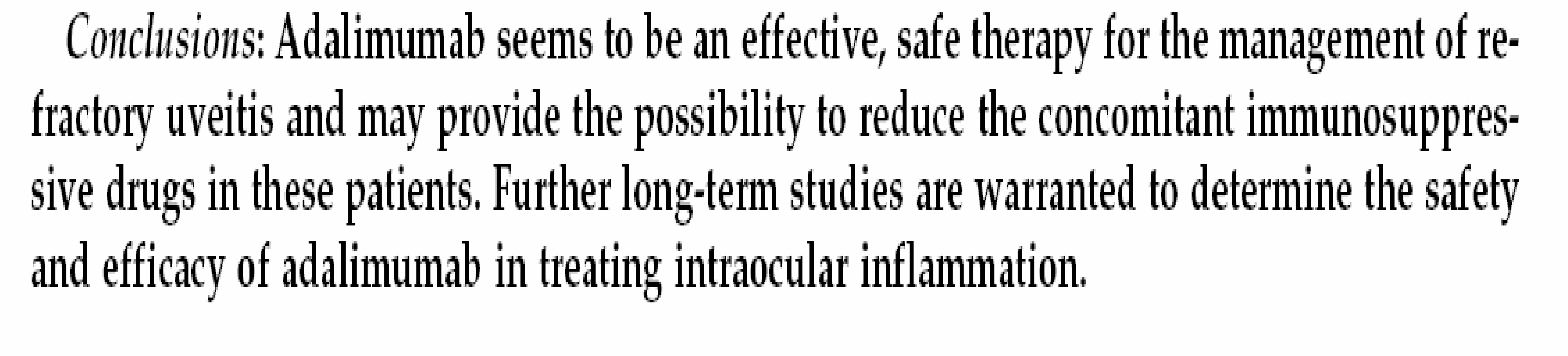
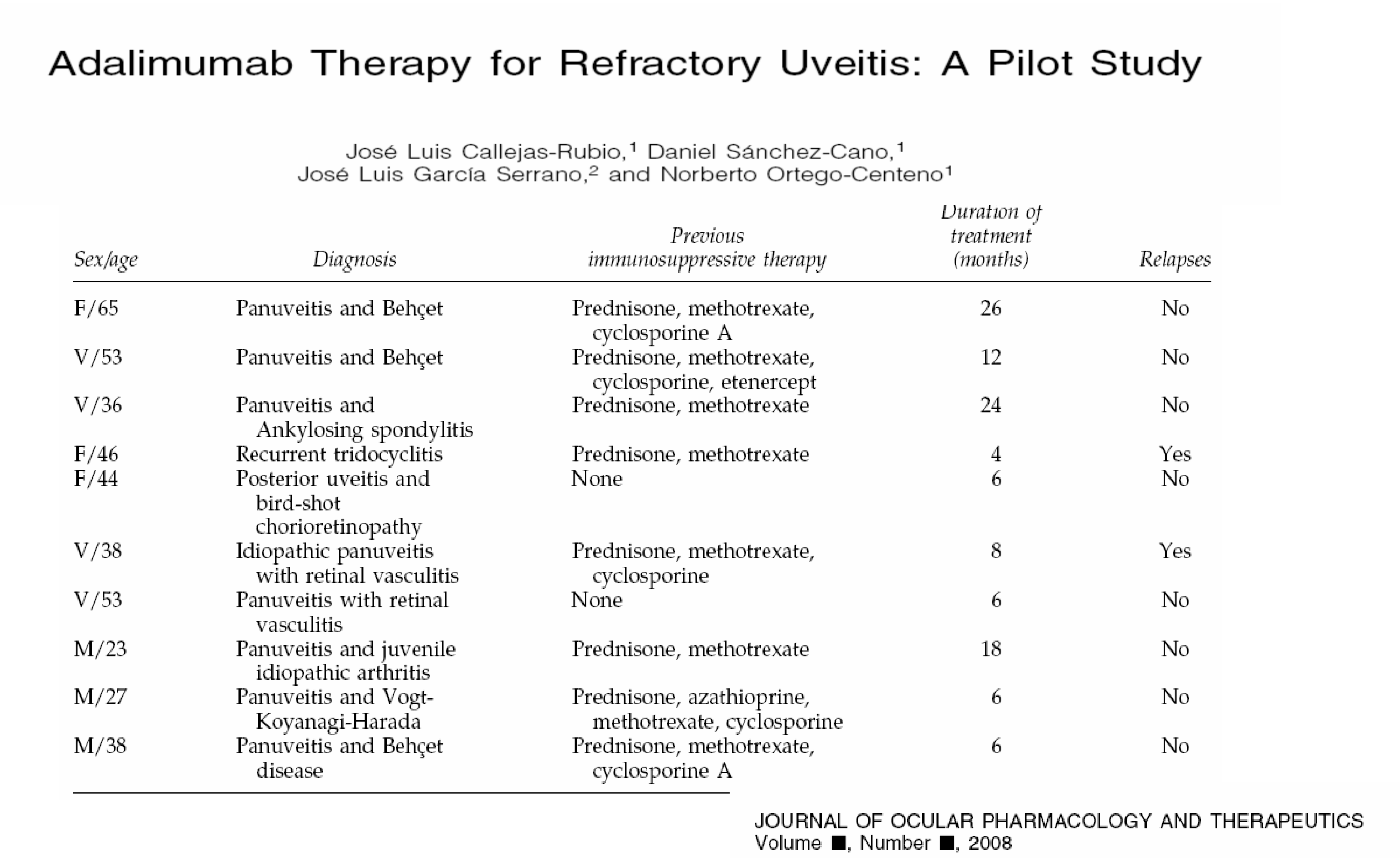


TABLE 4. SUMMARIZED DATA FROM OUTCOME VARIABLES

	Visual acuity (logMar) mean ± SD[a]	*AC inflammation mean ± SD*[b]	*VC inflammation mean ± SD*[b]	*Macular thickness (μ) mean ± SD*[a]	*Immunosuppression load mean ± SD*[a]
Week 0	+0.35 ± 0.24	1.05 ± 1	1.8 ± 1	389 ± 164	10.1 ± 3.1
Month 12	+0.13 ± 0.18	0.07 ± 0.2	0.1 ± 0.4	241 ± 64	2.6 ± 1.8



Conclusions: Adalimumab seems to be an effective, safe therapy for the management of refractory uveitis and may provide the possibility to reduce the concomitant immunosuppressive drugs in these patients. Further long-term studies are warranted to determine the safety and efficacy of adalimumab in treating intraocular inflammation.



Adalimumab Therapy for Refractory Uveitis: A Pilot Study

José Luis Callejas-Rubio,[1] Daniel Sánchez-Cano,[1]
José Luis García Serrano,[2] and Norberto Ortego-Centeno[1]

Sex/age	*Diagnosis*	*Previous immunosuppressive therapy*	*Duration of treatment (months)*	*Relapses*
F/65	Panuveitis and Behçet	Prednisone, methotrexate, cyclosporine A	26	No
V/53	Panuveitis and Behçet	Prednisone, methotrexate, cyclosporine, etenercept	12	No
V/36	Panuveitis and Ankylosing spondylitis	Prednisone, methotrexate	24	No
F/46	Recurrent tridocyclitis	Prednisone, methotrexate	4	Yes
F/44	Posterior uveitis and bird-shot chorioretinopathy	None	6	No
V/38	Idiopathic panuveitis with retinal vasculitis	Prednisone, methotrexate, cyclosporine	8	Yes
V/53	Panuveitis with retinal vasculitis	None	6	No
M/23	Panuveitis and juvenile idiopathic arthritis	Prednisone, methotrexate	18	No
M/27	Panuveitis and Vogt-Koyanagi-Harada	Prednisone, azathioprine, methotrexate, cyclosporine	6	No
M/38	Panuveitis and Behçet disease	Prednisone, methotrexate, cyclosporine A	6	No

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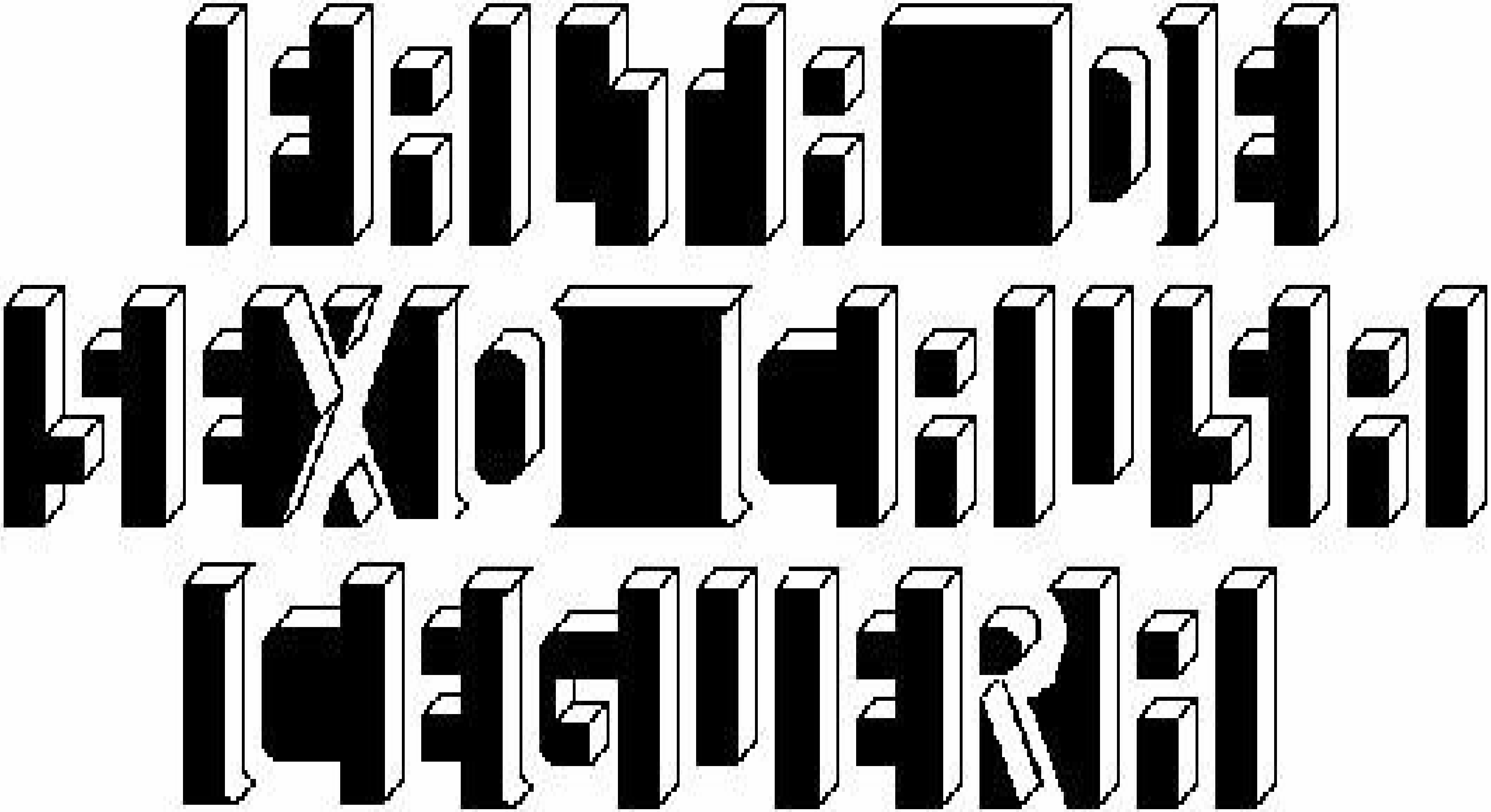
Volume ■, Number ■, 2008



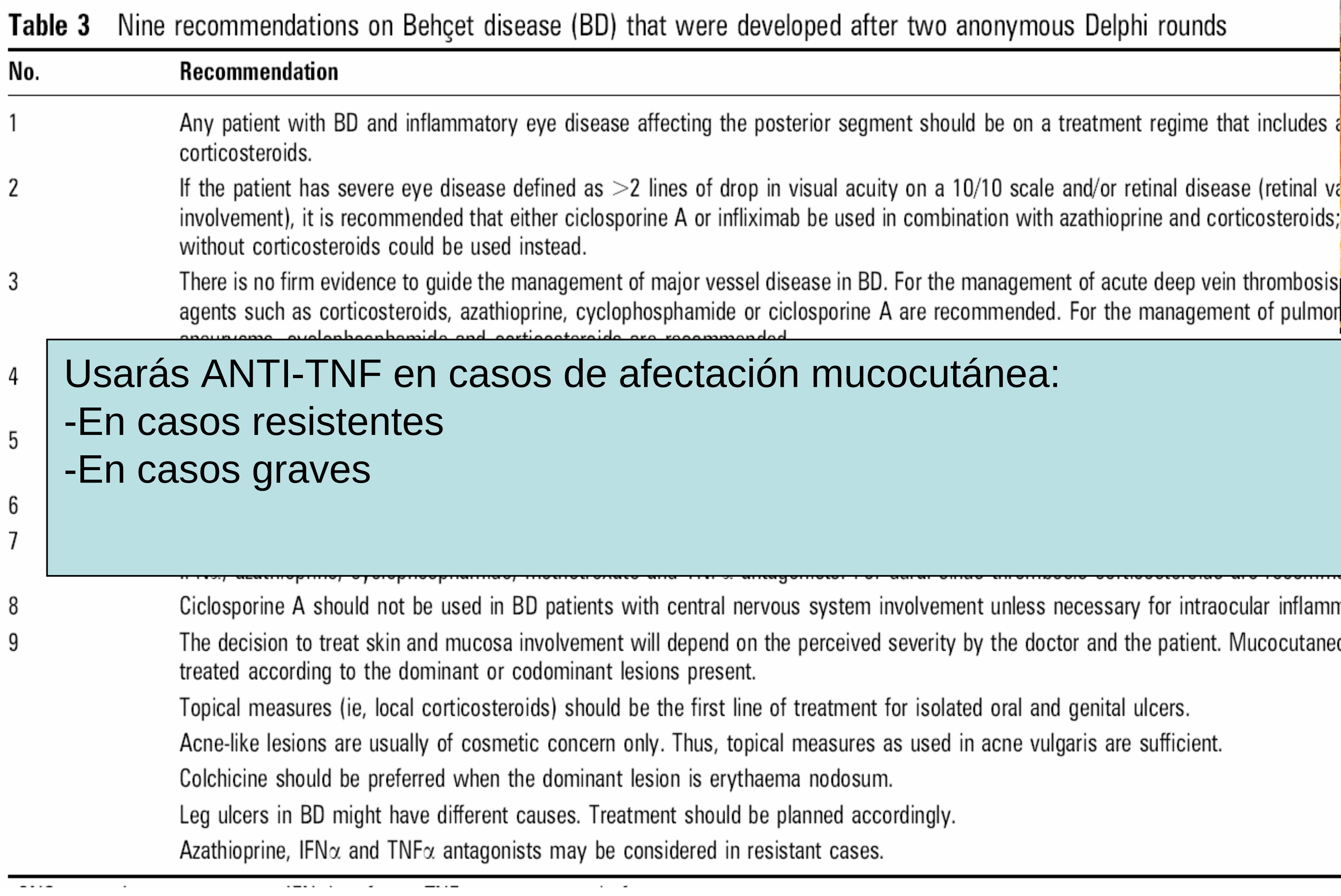


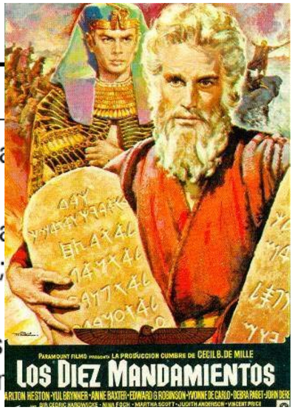
Table 3 Nine recommendations on Behçet disease (BD) that were developed after two anonymous Delphi rounds

No.	Recommendation
1	Any patient with BD and inflammatory eye disease affecting the posterior segment should be on a treatment regime that includes corticosteroids.
2	If the patient has severe eye disease defined as >2 lines of drop in visual acuity on a 10/10 scale and/or retinal disease (retinal involvement), it is recommended that either ciclosporine A or infliximab be used in combination with azathioprine and corticosteroids; without corticosteroids could be used instead.
3	There is no firm evidence to guide the management of major vessel disease in BD. For the management of acute deep vein thrombosis agents such as corticosteroids, azathioprine, cyclophosphamide or ciclosporine A are recommended. For the management of pulmon
4	the
5	e,
6	
7	oids,
8	Ciclosporine A should not be used in BD patients with central nervous system involvement unless necessary for intraocular inflammation.
9	The decision to treat skin and mucosa involvement will depend on the perceived severity by the doctor and the patient. Mucocutaneous involvement should be treated according to the dominant or codominant lesions present. Topical measures (ie, local corticosteroids) should be the first line of treatment for isolated oral and genital ulcers. Acne-like lesions are usually of cosmetic concern only. Thus, topical measures as used in acne vulgaris are sufficient. Colchicine should be preferred when the dominant lesion is erythaema nodosum. Leg ulcers in BD might have different causes. Treatment should be planned accordingly. Azathioprine, IFNα and TNFα antagonists may be considered in resistant cases.

Usarás ANTI-TNF en casos de afectación mucocutánea:

-En casos resistentes

-En casos graves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LOS DIEZ MANDAMIENTOS

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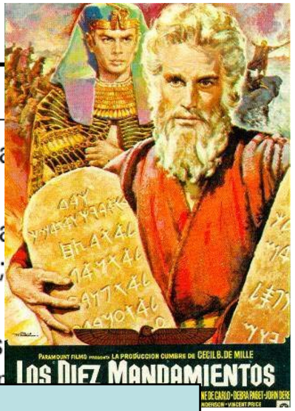
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LOS DIEZ MANDAMIENTOS

- Afectación Gastrointestinal:
    - no hay tratamientos basados en la evidencia
    - sulfasazalina, azatioprina, talidomida o anti-TNF alfa deberían ser usados antes de la cirugía

-Afectación SNC:
    - no hay estudios controlados
    - pueden usarse IFN, azatioprina, ciclofosfamida, metotrexate o anti TNF alfa

CRITERIOS CLASIFICATORIOS PARA LA ENFERMEDAD DE BEHÇET
(Grupo Internacional de Estudio para la Enfermedad de Behçet. 1990)

ULCERAS ORALES RECURRENTES:

- un mínimo de 3 episodios al año

Más 2 de las siguientes

ULCERAS GENITALES RECURRENTES

LESIONES OCULARES: uveitis anterior
“ posterior
vasculitis retiniana

LESIONES CUTANEAS: eritema nudoso
pseudofoliculitis
pápulo-pústulas
acneiformes en post-adolescentes sin cortis

TEST PATERGIA POSITIVO

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HLA-B51 (+)

TEST PATERGIA POSITIVO

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Med Clin (Barc): 2009: en prensa

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D Sánchez-Cano,[*†] JL Callejas-Rubio,[†]
R Ruiz-Villaverde,[‡] N Ortego-Centeno[†]
[†]Unidad de Enfermedades Autoinmunes Sistémicas, Hospital Universitario San Cecilio, Granada, Spain, [‡]Unidad de Dermatología, Complejo Hospitalario Ciudad de Jaén, Jaén, Spain