

# XI Curso SER Reumato 2 topics 022!

**Coordinadores:** Diego Benavent,  
Isabel Castrejón, Vanesa Calvo

**16 y 17 de septiembre de 2022**  
Hotel NH Collection Barcelona Constanza  
(Carrer de Dèu i Mata, 69-99)

#reumatopics22

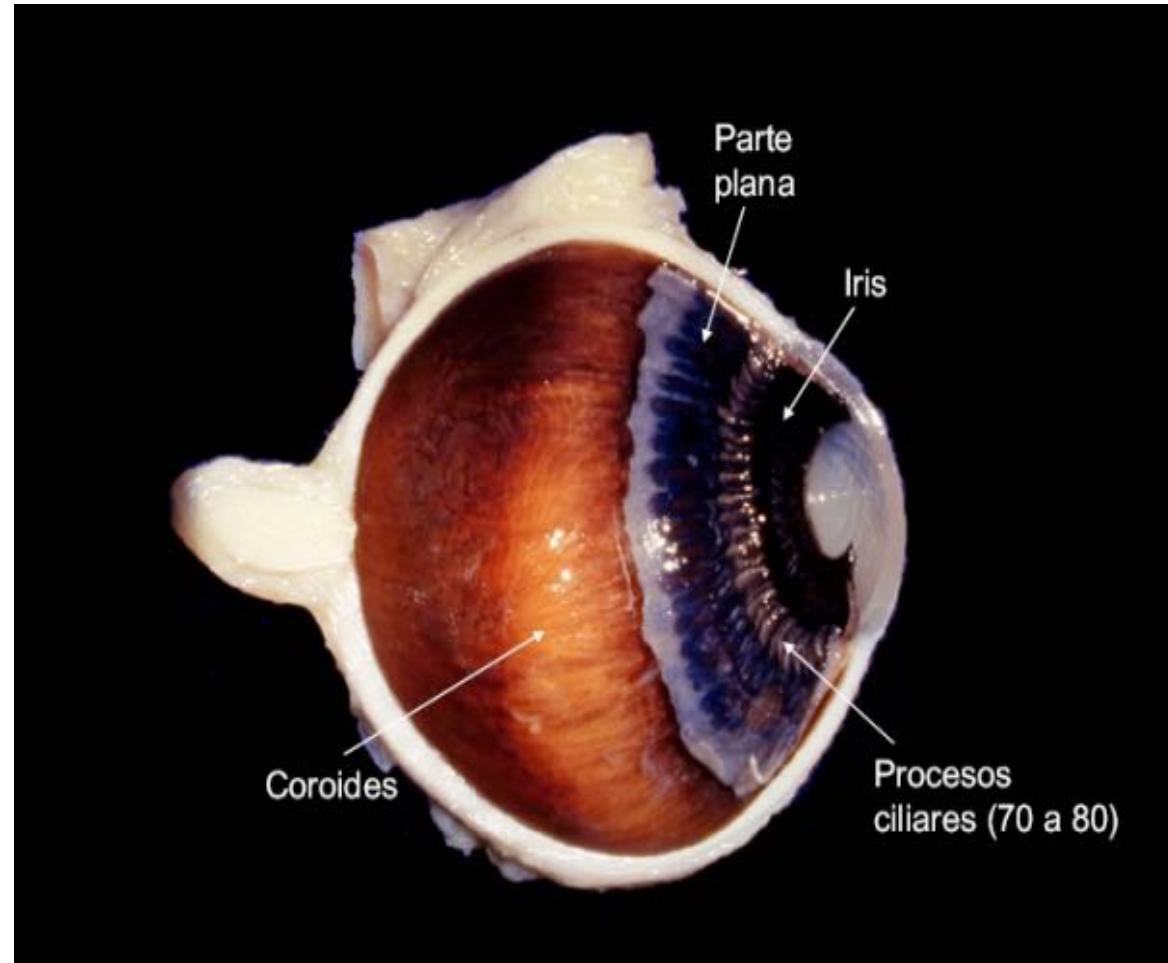
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# Actualización en uveítis

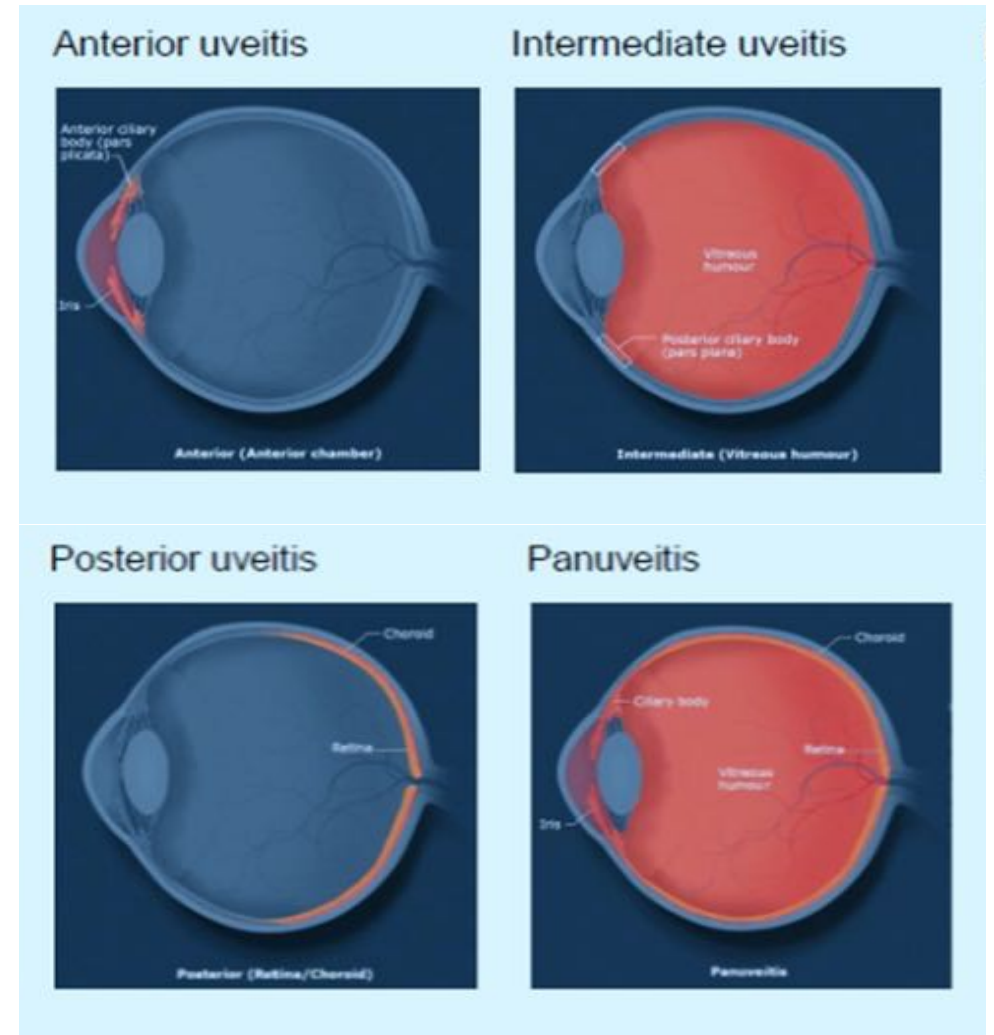
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Unidad de Uveítis.  
CAULE, León (Spain)  
IBIOMED*

# UVEÍTIS: Concepto



# Clasificación de las uveítis

- Clasificaciones:
  - 1) Anatómica: Ant/Int/Post/Pan
  - 2) Etiológica (Inmuno-mediada, infecciosa, neoplásica y traumática)
  - 3) Oftalmológica vs asociada a enfermedad sistémica
  - 4) Curso/Evolución: Debut, duración, curso
  - 5) Características en función de hallazgos.



# PERSPECTIVES

Standardization of Uveitis Nomenclature for Reporting Clinical Data. Results of the First International Workshop

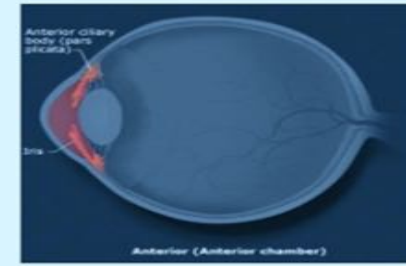
THE STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) WORKING GROUP

## Clasificación anatómica de las uveítis SUN 2005

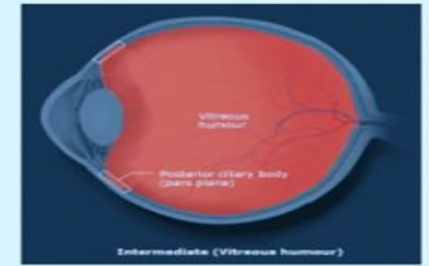
Tabla 2. Clasificación anatómica de la uveítis según el Grupo de Estandarización de la Nomenclatura

Tipo de uveítis	Localización primaria de la inflamación	Incluye (subtipos)
Uveítis anterior	Cámara anterior	Iritis Iridociclitis
Uveítis intermedia	Cavidad vítreo	Ciclitis anterior Pars planitis
Uveítis posterior	Retina o coroides	Ciclitis posterior Coroiditis focal, multifocal o difusa Coriorretinitis Retinocoroiditis Retinitis Neurorretinitis
Panuveítis	Cámara anterior, vítreo y retina o coroides	

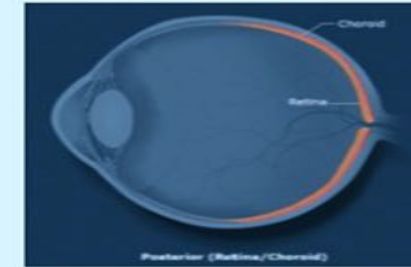
Anterior uveitis



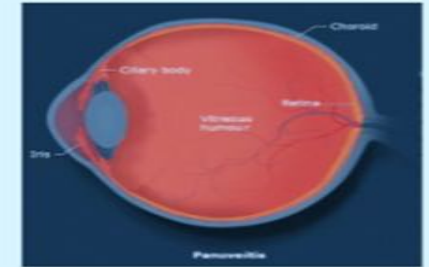
Intermediate uveitis



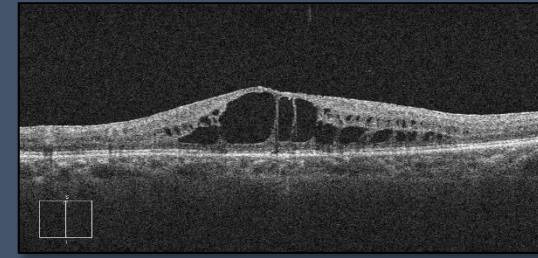
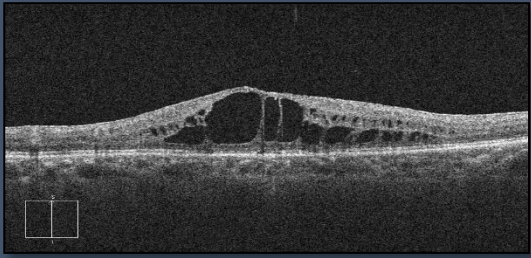
Posterior uveitis



Panuveítis



# EDEMA MACULAR



No cambia la localización de la uveítis

- Puede aparecer en cualquier uveítis: UA, UI, UP o PU
- Difusión de mediadores inflamatorios hacia polo posterior.
- Más frecuente en uveítis crónicas o muy intensas

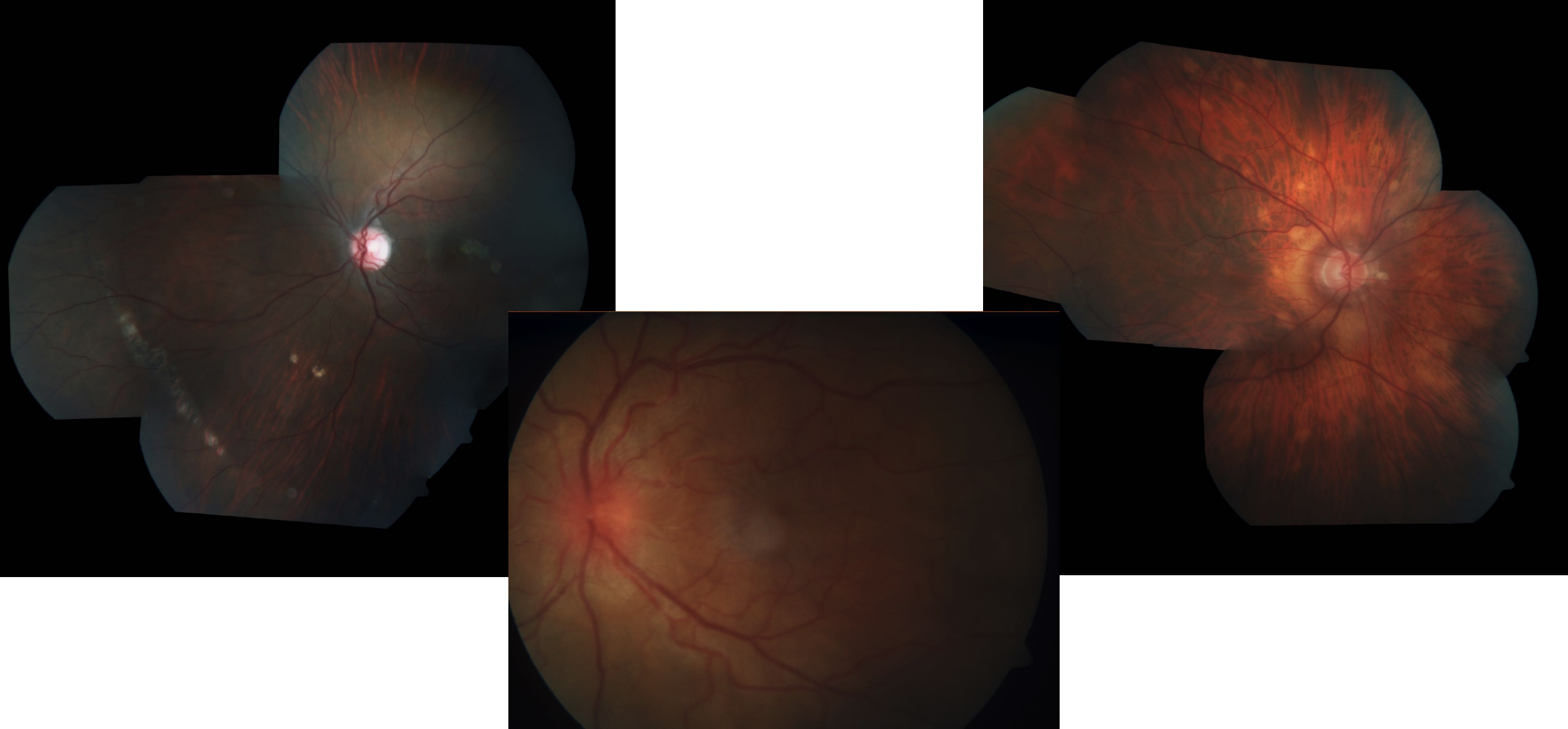
## *Problemas específicos del diagnóstico y clasificación de las uveítis NANI.*

**Enfermedad Heterogénea con Baja (Desconocida) prevalencia**

*Muchas dificultades para organizar, financiar, reclutar RCT's. Muy escasa y débil evidencia respecto a su epidemiología.*

**Dificultades para el diagnóstico de certeza. Ausencia de escalas de actividad**

*No hay una nomenclatura estandarizada; Ausencia de una escala de valoración completa y actualizada.*




¿PODEMOS JUNTAR  
CHURRAS CON MERINAS?





## An Update on the Epidemiology of Uveitis in an Urban Setting in Northern Madrid, Spain

Celia Sesmero-García, MD<sup>a</sup>, Mercedes Serrador, MD, PhD<sup>a,b</sup>, Marcelino Revenga, MD, PhD<sup>c,d</sup>, and Julio J Gonzalez-Lopez, MD, PhD, FEBO <sup>a,b</sup>

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### ABSTRACT

**Purpose:** To describe the incidence, prevalence and etiologies of uveitis in Madrid, Spain.

**Methods:** A retrospective cross-sectional study was performed in a single hospital. All consecutive cases of uveitis that attended the Hospital during year 2019 were included. Mean incidence and prevalence were calculated.

**Results:** Three hundred and one cases were included. Of these, 127 were incident. This represents an incidence of 21.24 new cases per 100,000 persons/year, and a prevalence was 50.43 cases per 100,000 persons. Mean age was  $56.89 \pm 18.78$  years, and 159 were women (52.8%). Sixty-two cases were infectious (20.6%). Age ( $p = .005$ ), initial visual acuity ( $p = .001$ ) and cystoid macular oedema (CMO;  $p = .010$ ) were found to be independent predictors of the final best corrected visual acuity (BCVA) in patients with uveitis.

**Conclusions:** Uveitis affects approximately 1 in 1800 persons in northern Madrid. Younger age, better initial visual acuities and the presence of CMO predicted better final BCVA.



## Epidemiology of Uveitis in Olmsted County, Minnesota: A Population-Based Follow-Up Study

Timothy T. Xu, MD<sup>a</sup>, Margaret M. Reynolds, MD<sup>a,b</sup>, David O. Hodge, MS<sup>c</sup>, and Wendy M. Smith, MD<sup>a</sup>

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### ABSTRACT

**Purpose:** To update the incidence of uveitis in a Midwestern U.S. county population.

**Methods:** Retrospective population-based cohort study. All Olmsted County, Minnesota residents diagnosed with uveitis from January 1, 2006 to December 31, 2015 were identified via the Rochester Epidemiology Project. Diagnoses were confirmed by a uveitis specialist.

**Results:** There were 371 incident uveitis cases, yielding an overall age- and sex-adjusted incidence rate of 26.9 per 100,000 per year (95% CI: 24.1–29.7). Females accounted for 202 (54.4%) cases, 306 (82.5%) were White, and 299 (80.6%) were anterior uveitis. Highest incidence was observed in patients  $\geq 65$  years old. No difference in incidence existed between sexes ( $p = .17$ ). Incidence rates increased with age for uveitis overall (all anatomic subtypes) ( $p < .001$ ), anterior uveitis ( $p < .001$ ), and posterior uveitis ( $p < .001$ ). Idiopathic uveitis accounted for 168 (45.3%) cases, more frequently diagnosed in females (50.0%) than males (39.6%) ( $p = .05$ ).

**Conclusion:** Uveitis incidence increased 1.6-fold over a 50-year span in this predominately White U.S. Midwestern county population.

# Epidemiology and Risk Factors in Non-infectious Uveitis: A Systematic Review

**TABLE 2** | Summary of large population-based epidemiologic studies worldwide published since Jan 2019\*.

Country	Year	Method	Sample size	Incidence (per 100,000 person-years)	Prevalence (per 100,000 persons)	% Non-infectious	Age	Sex	Location of Uveitis	Chronicity	Limitations
Australia (18)	2014–2015	Retrospective cohort	1,236 cases	21.5	36.3	86.6% non-infectious	Mean age of diagnosis 46.2	No significant difference between males and females	75% anterior	NA	<ul style="list-style-type: none"> <li>Authors acknowledge that unknown number of uveitis cases within Melbourne were not included due to external management (thus study likely underestimates true prevalence in urban Australia)</li> </ul>
Portugal (19)	2012–2017	Retrospective cohort	545 cases	3.9	12.4	45.5% non-infectious; 28.4% idiopathic	Mean age of diagnosis 47.8	No significant difference between males and females	47.5% anterior	NA	<ul style="list-style-type: none"> <li>Likely biased toward more severe diseases (referral center bias)</li> <li>Selection bias for northern Portuguese population</li> </ul>
Spain (20)	2016–2017	Retrospective cohort	529,855 sample size. 358 cases	NA	67.6	84% non-infectious	Mean age of diagnosis 47.0	No significant difference between males and females	83.2% anterior	NA	<ul style="list-style-type: none"> <li>Cross-sectional retrospective nature of the study limits evaluation of incidence of uveitis</li> </ul>
Sweden (21)	2013–2017	Retrospective cohort	2,483 cases	108 (2013–2017)	700 (2013–2017)	86% idiopathic; 9.2% non-infectious		No significant difference between males and females	93% anterior	NA	<ul style="list-style-type: none"> <li>Possible misclassification bias from using ICD-10 codes</li> <li>Selection bias</li> </ul>
Thailand (22)	2013–2018	Retrospective cohort	101,203 sample size. 586 cases with uveitis	NA	580	44% non-infectious; 36% idiopathic	Mean age of diagnosis was 46.3	No significant difference between males and females	50% anterior uveitis	57.7% acute	<ul style="list-style-type: none"> <li>Single center</li> <li>Tertiary military care center more biased toward more severe cases</li> <li>Selection bias for Thai population</li> </ul>
China (23)	2008–2018	Retrospective cohort	15,373 cases of uveitis	NA	NA	32.1% non-infectious, 53.4% idiopathic	Mean age of onset 35.4. Prevalence increased with age	Prevalence of systemic diseases in uveitis was 37.0% for males and 23.6% for females	62.8% panuveitis	NA	<ul style="list-style-type: none"> <li>Likely biased toward more severe diseases (referral center bias)</li> <li>Selection bias for Chinese uveitis patients</li> <li>No follow-up information</li> <li>Lack of information on</li> </ul>

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**Results:** Few epidemiologic studies from the United States, the estimated incidence and prevalence in the 20–50 years age group are the biggest risk factors for non-infectious uveitis. Protective factors include smoking, diabetes, celiac disease, and medications (bisphosphonates and etanercept).

## Contemporaneous Risk Factors for Visual Acuity in Non-Infectious Uveitis

Maxwell Pistilli, MEd, MS<sup>1</sup>, Sapna S. Gangaputra, MD, MPH<sup>2</sup>, Siddharth S. Pujari, MBBS, MPH<sup>3</sup>, Douglas A. Jabs, MD, MBA<sup>4,e</sup>, Grace A. Levy-Clarke, MD<sup>5,g</sup>, Robert B. Nussenblatt, MD, MPH<sup>6\*</sup>, James T. Rosenbaum, MD, FACR<sup>h,i</sup>, H. Nida Sen, MD, MS<sup>f</sup>, Eric B. Suhler, MD, MPH<sup>h,i,j</sup>, Jennifer E. Thorne, MD, PhD<sup>d,e</sup>, Nirali P. Bhatt, MD<sup>a</sup>, C. Stephen Foster, MD<sup>k,l</sup>, Hosne Begum, MBBS, MPH<sup>e</sup>, Tonetta D. Fitzgerald, BA<sup>a</sup>, Kurt A. Dreger, BS<sup>a,e</sup>, and John H. Kempen, MD, PhD<sup>l,m,n</sup> and the Systemic Immunosuppressive Therapy for Eye Diseases (SITE) Research Group\*\*

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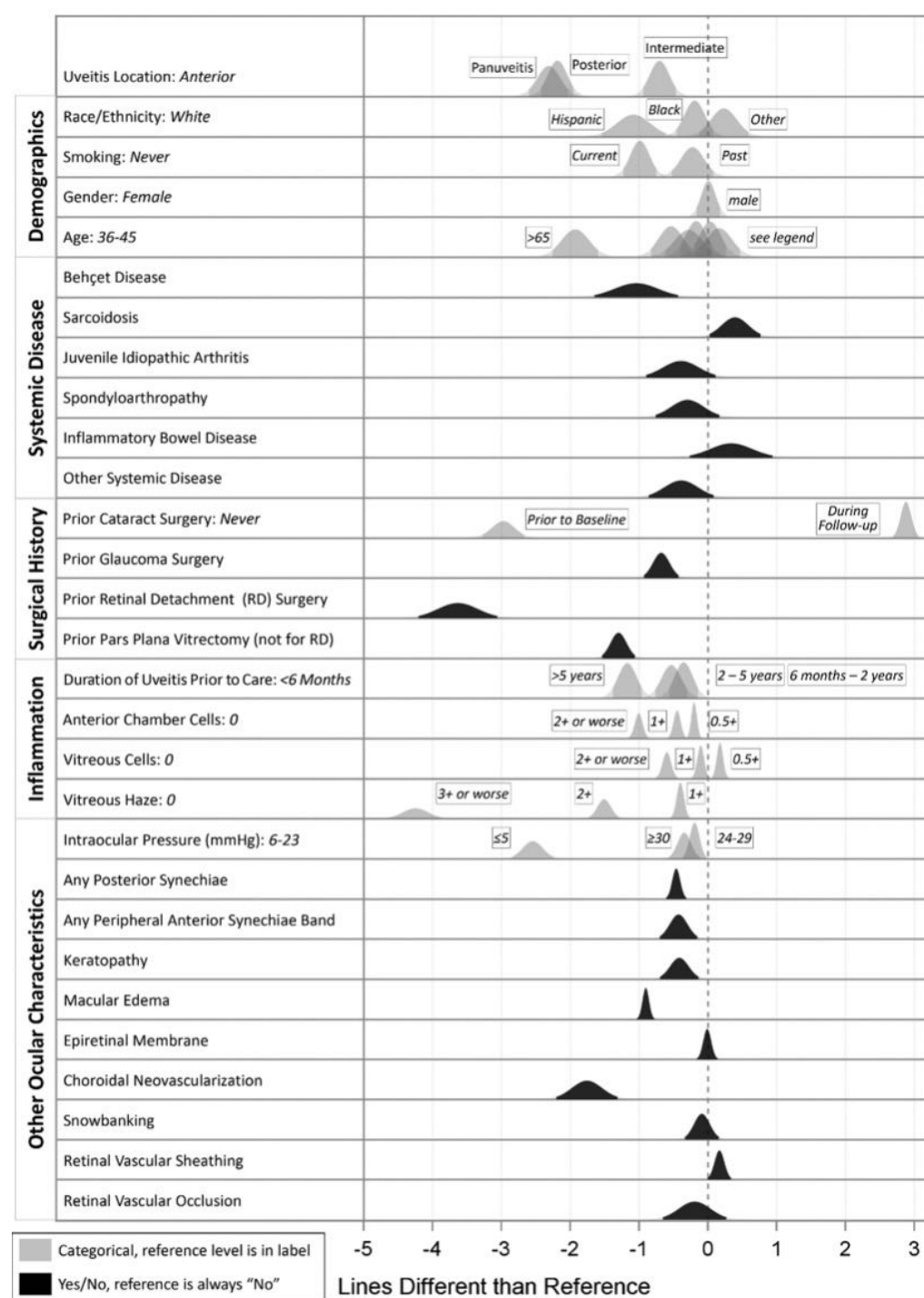
### ABSTRACT

**Introduction:** We evaluated the associations of clinical and demographic characteristics with visual acuity (VA) with over 5 years in a subspecialty noninfectious uveitis population.

**Methods:** Retrospective data from 5,530 noninfectious uveitis patients were abstracted by expert reviewers, and contemporaneous associations of VA with demographic and clinical factors were modeled.

**Results:** Patients were a median of 41 years old, 65% female, and 73% white. Eyes diagnosed  $\geq 5$  years prior to cohort entry had worse VA ( $-1.2$  lines) than those diagnosed  $< 6$  months prior, and eyes with cataract surgery performed prior to entry had worse VA ( $-5.9$  lines) than those performed during follow-up. Vitreous haze ( $-4.2$  lines for 3+ vs quiet), hypotony ( $-2.5$  lines for  $\leq 5$  mm Hg vs 6–23 mm Hg), and CNV ( $-1.8$  lines) all were strongly associated with reduced VA.

**Conclusion:** Factors associated with reduced VA included well-known structural complications, and lack of subspecialty care during cataract surgery.



## Development of classification criteria for the uveitides

The Standardization of Uveitis Nomenclature (SUN) Working Group<sup>\*,1,2,3</sup>

Uveitic Diseases Addressed by the SUN Developing Classification Criteria for the Uveitides Project

Anatomic class	Infectious*	Systemic Disease Associated	Eye-limited
Anterior	Cytomegalovirus anterior uveitis	Juvenile idiopathic arthritis-associated anterior uveitis	Fuchs uveitis syndrome
	Herpes simplex virus anterior uveitis	Spondyloarthritis/HLA-B27-associated anterior uveitis	
	Varicella zoster virus anterior uveitis	Tubulointerstitial nephritis with uveitis	
	Syphilitic anterior uveitis	Sarcoidosis-associated anterior uveitis	
Intermediate	Syphilitic intermediate uveitis	Multiple sclerosis-associated intermediate uveitis	Pars planitis
		Sarcoidosis-associated intermediate uveitis	Intermediate uveitis, non-pars planitis type
Posterior	Acute retinal necrosis	Sarcoidosis-associated panuveitis	Acute posterior multifocal placoid pigment epitheliopathy
	Cytomegalovirus retinitis		Birdshot chorioretinitis
	Syphilitic posterior uveitis		Multiple evanescent white dot syndrome
	Toxoplasmic retinitis		Multifocal choroiditis with panuveitis
	Tuberculous posterior uveitis		Punctate inner choroiditis Serpiginous choroiditis
Panuveitis	Syphilitic panuveitis	Behçet disease uveitis	Sympathetic ophthalmia
	Tuberculous panuveitis		
		Sarcoidosis-associated panuveitis	
		Vogt-Koyanagi-Harada disease (Early-stage and late-stage)	

\* Infectious uveitides refer to those with evidence of active infection. They do not include auto-inflammatory or auto-immune diseases triggered by a prior infection (e.g. reactive arthritis-associated uveitis).

# Classification Criteria for Serpiginous Choroiditis

THE STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) WORKING GROUP<sup>1,2,3,\*</sup>



## Abstract

**PURPOSE:** To determine classification criteria for serpiginous choroiditis.

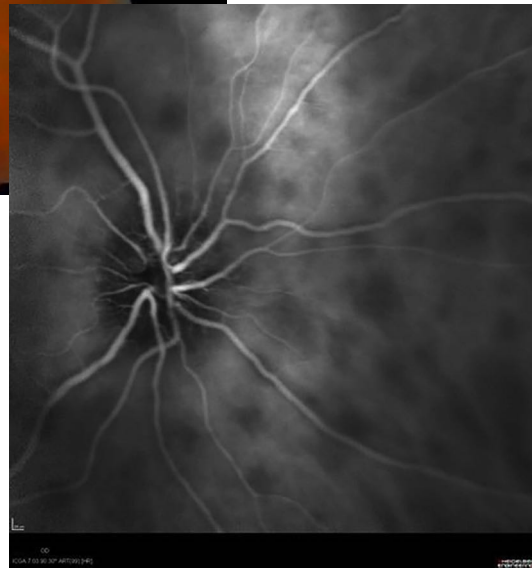
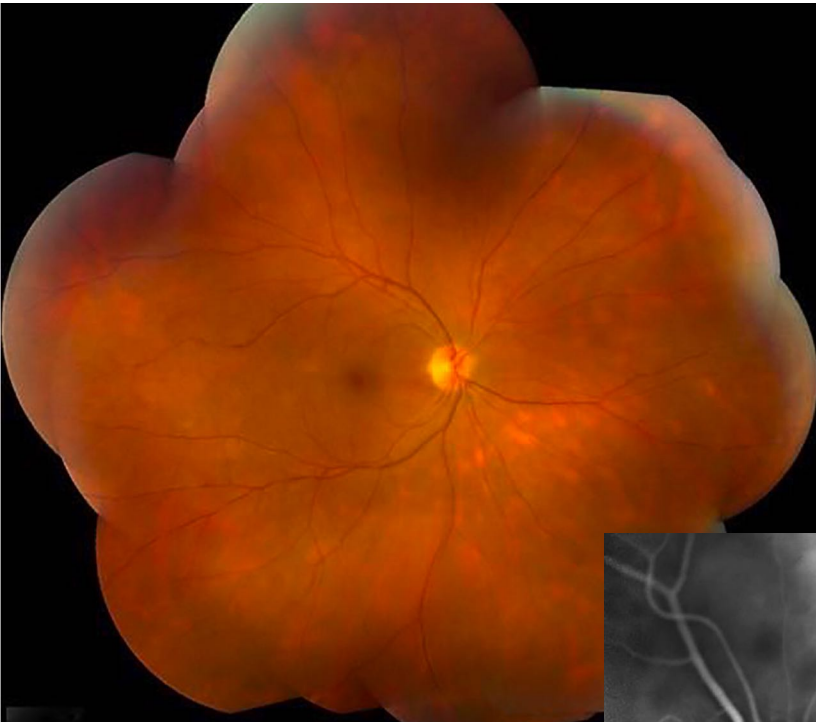
**DESIGN:** Machine learning of cases with serpiginous choroiditis and 8 other posterior uveitides.

**METHODS:** Cases of posterior uveitides were collected in an informatics-designed preliminary database, and a final database was constructed of cases achieving supermajority agreement on diagnosis, using formal consensus techniques. Cases were split into a training set and a validation set. Machine learning using multinomial logistic regression was used on the training set to determine a parsimonious set of criteria that minimized the misclassification rate among the infectious posterior uveitides / panuveitides. The resulting criteria were evaluated on the validation set.

**RESULTS:** One thousand sixty-eight cases of posterior uveitides, including 122 cases of serpiginous choroiditis, were evaluated by machine learning. Key criteria for serpiginous choroiditis included (1) choroiditis with an ameboid or serpentine shape; (2) characteristic imaging on fluorescein angiography or fundus autofluorescence; (3) absent to mild anterior chamber and vitreous inflammation; and (4) the exclusion of tuberculosis. Overall accuracy for posterior uveitides was 93.9% in the training set and 98.0% (95% confidence interval 94.3, 99.3) in the validation set. The misclassification rates for serpiginous choroiditis were 0% in both the training set and the validation set.

## Classification criteria for birdshot chorioretinitis

The Standardization of Uveitis Nomenclature (SUN) Working Group<sup>\*,1,2,3</sup>



### Abstract

**Purpose:** To determine classification criteria for birdshot chorioretinitis.

**Design:** Machine learning of cases with birdshot chorioretinitis and 8 other posterior uveitides.

**Methods:** Cases of posterior uveitides were collected in an informatics-designed preliminary database, and a final database was constructed of cases achieving supermajority agreement on diagnosis, using formal consensus techniques. Cases were split into a training set and a validation set. Machine learning using multinomial logistic regression was used on the training set to determine a parsimonious set of criteria that minimized the misclassification rate among the infectious posterior/panuveitides. The resulting criteria were evaluated on the validation set.

**Results:** One thousand sixty-eight cases of posterior uveitides, including 207 cases of birdshot chorioretinitis, were evaluated by machine learning. Key criteria for birdshot chorioretinitis included a multifocal choroiditis with: 1) the characteristic appearance a bilateral multifocal choroiditis with cream-colored or yellow-orange, oval or round choroidal spots (“birdshot” spots); 2) absent to mild anterior chamber inflammation; and 3) absent to moderate vitreous inflammation; or multifocal choroiditis with positive HLA-A29 testing and either: 1) classic “birdshot spots” or 2) characteristic imaging on indocyanine green angiography. Overall accuracy for posterior uveitides was 93.9% in the training set and 98.0% (95% confidence interval 94.3, 99.3) in the validation set. The misclassification rates for birdshot chorioretinitis were 10% in the training set and 0% in the validation set.

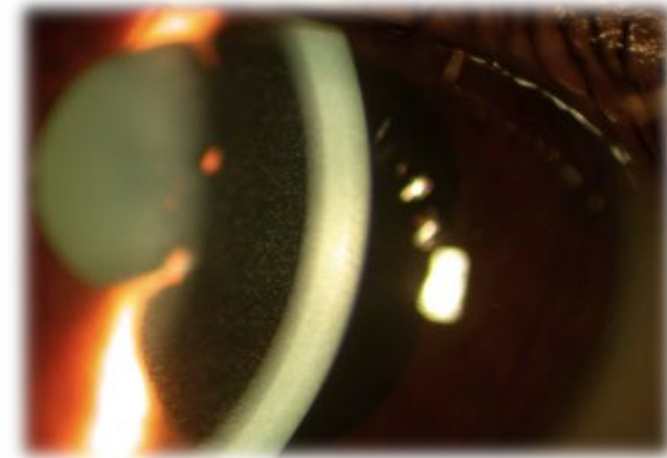
**Conclusions:** The criteria for birdshot chorioretinitis had a low misclassification rate and appeared to perform sufficiently well for use in clinical and translational research.

# VALORACIÓN DE LA ACTIVIDAD I

**Estratificación del grado de uveítis en función de las células en cámara anterior según el grupo de trabajo SUN (*Standardization of Uveitis Nomenclature*).**

Grado	Células por campo
0	<1
0.5+	1-5
1+	6-15
2+	16-25
3+	26-50
4+	>50

PERSPECTIVES  
Standardization of Uveitis Nomenclature for  
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International Workshop  
THE STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) WORKING GROUP



Tamaño del campo de 1mm a 1mm en lámpara de hendidura

## Clasificación de la actividad inflamatoria vítrea según el grado de opacidad vítreo.

Grado	Definición
0	Normal
Trazas o 0.5+	Margen de disco óptico ligeramente borroso
1+	Nervio óptico y vasos ligeramente borrosos
2+	Nervio óptico y vasos moderadamente borrosos
3+	Margen de la cabeza del nervio óptico borroso pero visible
4+	Cabeza del nervio óptico invisible



**PERSPECTIVES**  
Standardization of Uveitis Nomenclature for  
Reporting Clinical Data. Results of the First  
International Workshop

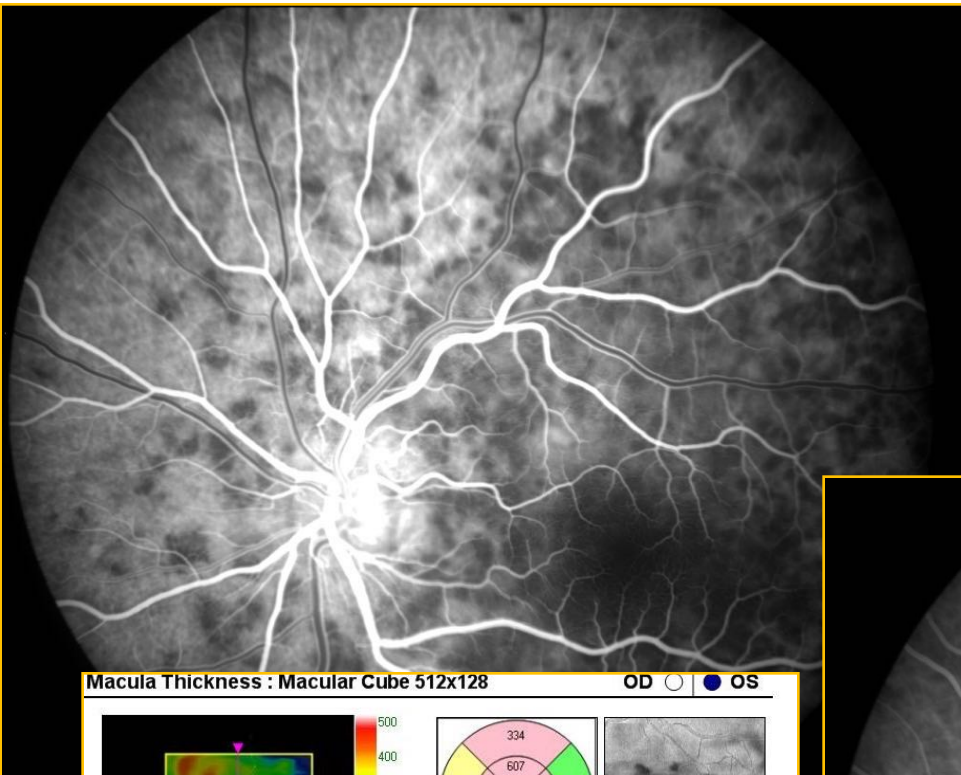


## Terminología de la actividad de la uveítis según el grupo de trabajo SUN.

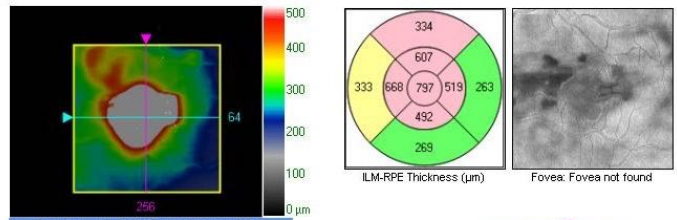
Término	Definición
Inactivo	Grado 0
Empeoramiento	Aumento en 2 grados el nivel de actividad o ascenso de grado 3+ a 4+
Mejoría	Descenso en 2 grados el nivel de actividad o descenso a grado 0
Remisión	Enfermedad inactiva $\geq$ 3 meses después de parar el tratamiento

Para la interpretación de la actividad, se utiliza el peor ojo: si uno mejora y el otro empeora, se considera empeoramiento

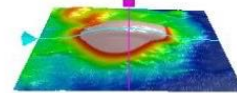
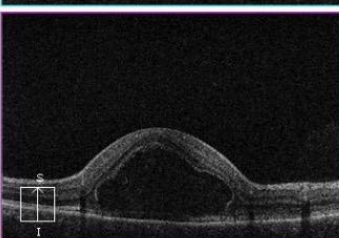
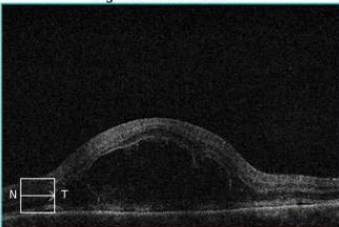
# VALORACIÓN DE LA ACTIVIDAD II



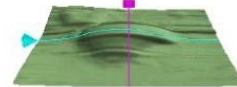
Macula Thickness : Macular Cube 512x128 OD  OS



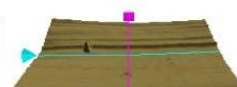
Overlay: ILM - RPE Transparency: 50 %  
High-definition mode



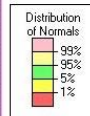
ILM - RPE



ILM



RPE



	Central Subfield Thickness (µm)	Cube Volume (mm <sup>3</sup> )	Cube Average Thickness (µm)
ILM - RPE	797	12.6	351

# Escala de actividad obsoleta

- Edema macular es el principal signo clínico en muchos pacientes y requiere pruebas complementarias (OCT, AFG) para su evaluación y seguimiento.
- Las vasculitis retinianas y uveítis posteriores también requieren pruebas complementarias para su evaluación y monitorización (AFG, ICG, Autofluorescencia...).
- Otras pruebas complementarias pueden ser cruciales para diagnosticar y monitorizar ciertos tipos de uveítis (CV, ERG...).

Escala incompleta, poco reproducible, poco plausible, cualitativa, no comparable, no universal....



# Development of a Core Outcome Set for Clinical Trials in Non-infectious Uveitis of the Posterior Segment

Mohammad O. Tallouzi, PhD,<sup>1,2,5</sup> Jonathan M. Mathers, PhD,<sup>1</sup> David J. Moore, PhD,<sup>1</sup> Nicholas Bucknall,<sup>3</sup> Melanie J. Calvert, PhD,<sup>1,5,6,†</sup> Philip I. Murray, PhD,<sup>2,4,†</sup> Alastair K. Denniston, PhD,<sup>4,5,7,‡</sup> for the COSUMO Working Group

Table 3. Final Core Outcome Set for Clinical Trials in Noninfectious Uveitis of the Posterior Segment

Outcome	Definition
<i>Issues Relating to Visual Function</i>	
Distance vision	A person's ability to see objects/people clearly from distance (beyond arm's length) (e.g., road signs, TV, cinema)
Near vision	A person's ability to see near objects (e.g., reading, seeing prices on a menu, seeing phone numbers and other close-up tasks)
Visual disturbance	A person reports blurred, hazy, foggy, grainy, or double vision; seeing flashing/shimmering lights or straight lines that appear bent, crooked, or wavy
<b>Issues Relating to Health-Related Quality of Life</b>	
Work/education-related impact	A person's performance and ability to maintain or continue work/employment or education
Driving/commuting-related impact	A person's ability to maintain or continue driving a vehicle or commuting by bicycle, train, bus, tram
Day-to-day usual activity-related impact	A person's ability to maintain and continue engagement in day-to-day activities (e.g., care for own self, shaving beard, washing face, gardening, shopping, cooking, and doing the washing), including social and leisure activities
Depression and mental well-being	Feelings of severe sadness or feeling depressed with loss of interest or lack of enjoyment
<b>Issues Relating to Treatment Side Effects</b>	
Treatment side effects	Describes undesired or unintended treatment effects that patients may experience
<b>Issues Relating to Disease Control</b>	
Anterior segment inflammation	Inflammation in the front of the eye between the cornea and the iris
Vitreous inflammation/haze	Inflammation/haze/cloudiness of vitreous jelly located between the lens and the retina
Retinal vasculitis	Inflammation of the blood vessels of the retina (the light sensitive layer at the back of the eye)
Retinitis/choroiditis/chorioretinitis	Inflammation of the retina or choroid layers (the light sensitive layer and the supporting blood vessel layer at the back of the eye)
Flare/relapse/recurrence	Recurrence or increase of inflammation in the front or back of the eye that may be associated with effects on vision
Intraocular pressure	Change in the pressure inside the eye above or below the normal range and if left untreated may permanently damage the sight
UME	Fluid that builds up in the central part of the retina causing swelling of the macula; the macula is responsible for detailed central vision
Structural changes	Changes to the structure of the eye including retinal scarring, optic nerve damage (including glaucoma), formation or progression of band keratopathy—white, chalky deposits on the surface of the cornea (the “window” of the eye) that may cause pain and a reduction in vision, formation or progression of epiretinal membrane—a thin layer of scar tissue that forms on the surface of the retina usually at the macula (the sensitive central part of the retina) that may reduce vision

# Quantitative Assessment of Experimental Ocular Inflammatory Disease

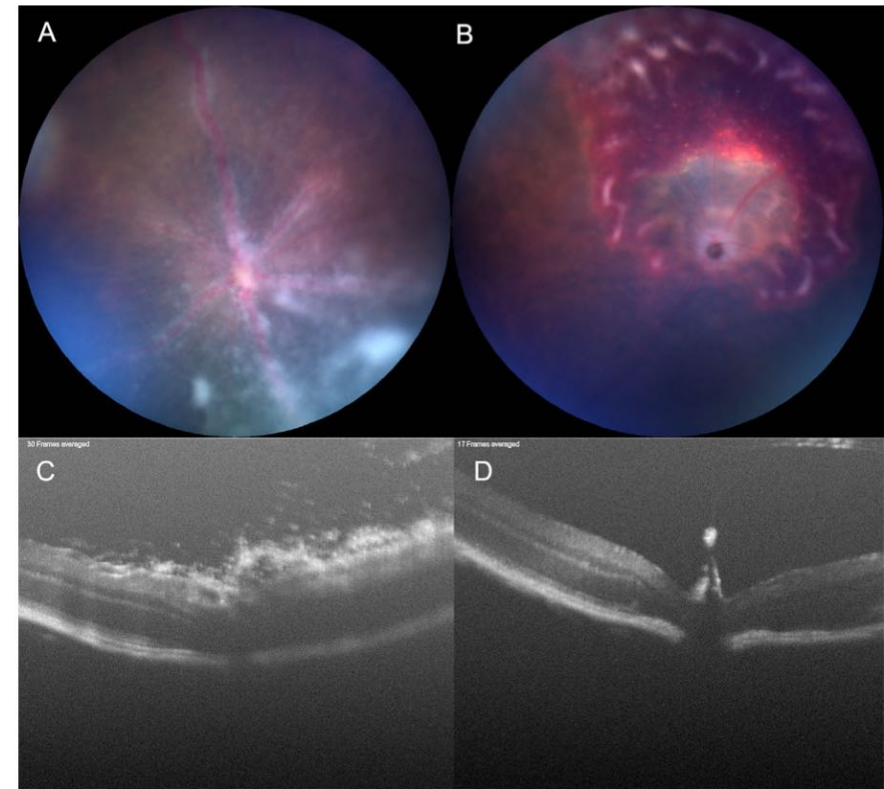
Lydia J. Bradley<sup>1</sup>, Amy Ward<sup>1</sup>, Madeleine C. Y. Hsue<sup>1</sup>, Jian Liu<sup>2</sup>, David A. Copland<sup>2</sup>, Andrew D. Dick<sup>1,2,3</sup> and Lindsay B. Nicholson<sup>1\*</sup>

<sup>1</sup> School of Cellular and Molecular Medicine, University of Bristol, Bristol, United Kingdom, <sup>2</sup> Academic Unit of Ophthalmology, Translational Health Sciences, University of Bristol, Bristol, United Kingdom, <sup>3</sup> University College London, Institute of Ophthalmology, London, United Kingdom

**TABLE 1** | Scheme for scoring clinical ocular inflammation.

Score	Optic disc	Retinal vessels	Retinal tissue infiltration	Structural damage
1	Minimal inflammation	Cuffing: 1–4 mild	1–4 small lesions or 1 linear lesion	Retinal lesions or retinal atrophy involving 1/4 to 3/4 of retinal area
2	Mild inflammation	Cuffing: >4 mild or 1–3 moderate	5–10 small lesions or 2–3 linear lesions	Panretinal atrophy with multiple small lesions (scars) or ≤3 linear lesions (scars)
3	Moderate inflammation	Cuffing: >3 moderate	>10 small lesions or >3 linear lesions	Pan-retinal atrophy with >3 linear lesions or confluent lesions (scars)
4	Severe inflammation	Cuffing: >1 severe	Linear lesion confluent	Retinal detachment with folding
5	Not visible (white-out or extreme detachment)	Not visible (white-out or extreme detachment)	Not visible (white-out or extreme detachment)	Not visible (white-out or extreme detachment)

A blinded observer assigns scores to retinal photographs for changes that relate to inflammation of the optic disc, retinal vessels and retinal tissue and a score for structural damage. These scores can then be summed independently (score of 0-20) or given as a summary score of the average of all features (score of 0-5) (10, 21, 54).



# Adalimumab for Treatment of Noninfectious Uveitis

## *Immunogenicity and Clinical Relevance of Measuring Serum Drug Levels and Antidrug Antibodies*

Miguel Cordero-Coma, MD, PhD,<sup>1,2</sup> Sara Calleja-Antolín, MD,<sup>3</sup> Irene Garzo-García, MD,<sup>1</sup>  
Ana M. Nuñez-Garnés, MD,<sup>3</sup> Carolina Álvarez-Castro, MD,<sup>4</sup> Manuel Franco-Benito, MD,<sup>1</sup>  
Jose G. Ruiz de Morales, MD, PhD<sup>2,3</sup>

- Ophthalmologic examination
  - Snellen best-corrected visual acuity
  - Slit-lamp examination of AC (AC cells graded using SUN classification)
  - Vitreous haze (evaluation of vitreal inflammatory activity)
  - OCT (to measure cystoid macular edema)
  - Fluorescein angiography (vasculitis and retinal angiographic leakage)

### Ophthalmologic response to treatment

Complete response	Partial response or improvement	No response
<ul style="list-style-type: none"> <li>• Grade 0 cells in both anterior and posterior segment in addition to absence of any other sign of intraocular inflammation on ophthalmologic, OCT, and FA examination</li> </ul>	<ul style="list-style-type: none"> <li>• New onset from either baseline visit or when compared with previous clinical examination of any of the following:                             <ol style="list-style-type: none"> <li>1. a 2-step decrease in the SUN grading scheme (eg, anterior chamber cells, vitreous haze) or decrease to grade 0</li> <li>2. resolution of cystoid macular edema (1-mm central retinal thickness &lt;300 mm and absence of intraretinal or subretinal fluid in OCT examination)</li> <li>3. absence of any retinal angiographic leakage in FA examination</li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>• Persistent intraocular inflammation without any finding consistent with the criteria of partial response or improvement</li> </ul>

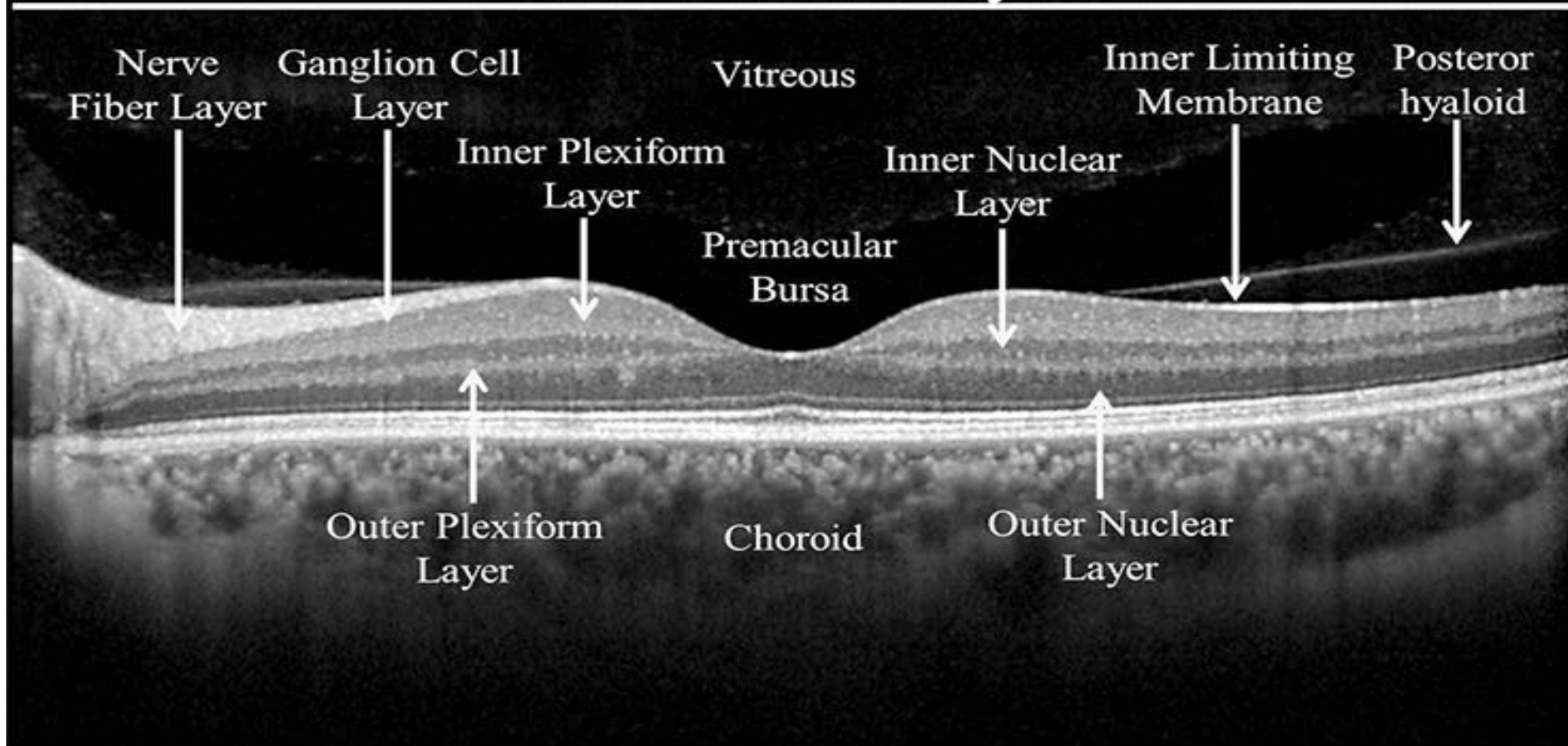
• AC, anterior chamber; OCT, Optical coherence tomography; SUN, Standardization of Uveitis Nomenclature

• Cordero-Coma M, et al. Ophthalmology 2016; Sept 27 [Epub ahead of print]

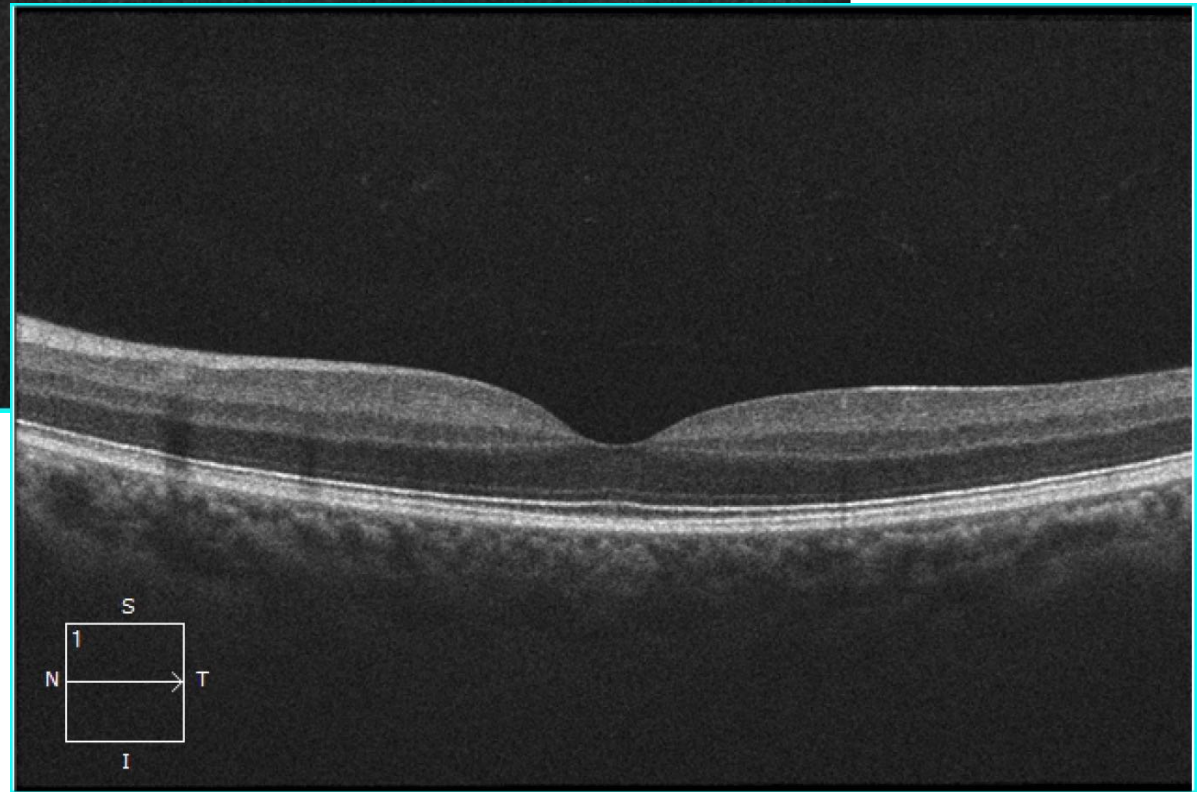
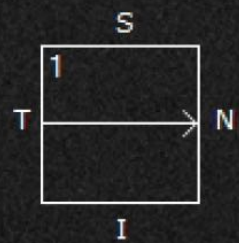
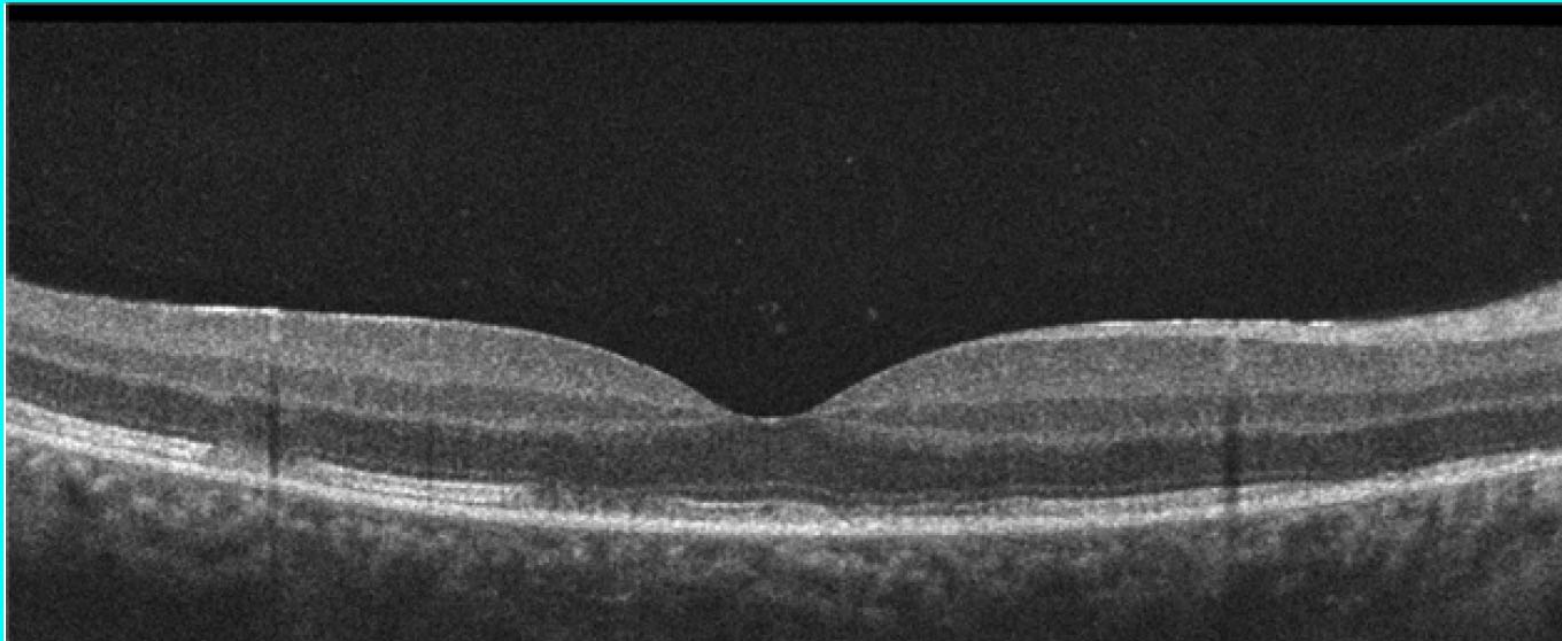
# Development of an activity disease score in patients with uveitis (UVEDAI)

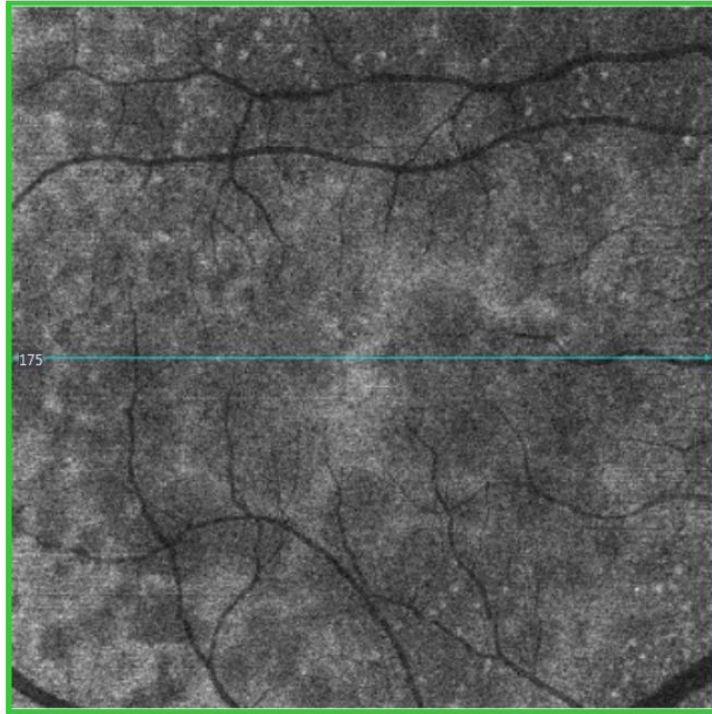
Esperanza Pato<sup>1</sup> · M<sup>a</sup> Auxiliadora Martin-Martinez<sup>2</sup> · Adela Castelló<sup>3</sup> · Rosalía Méndez-Fernandez<sup>4,5</sup> ·  
Santiago Muñoz-Fernández<sup>6</sup> · Miguel Cordero-Coma<sup>7</sup> · Lucia Martinez-Costa<sup>8</sup> · Elia Valls<sup>9</sup> · Miguel Reyes<sup>10</sup> ·  
Félix Francisco<sup>11</sup> · Mar Esteban<sup>12</sup> · Alex Fonollosa<sup>13</sup> · Fernando Sanchez-Alonso<sup>2</sup> · Cruz Fernández-Espartero<sup>14</sup> ·  
Teresa Diaz-Valle<sup>15</sup> · José Miguel Carrasco<sup>16</sup> · Emma Beltran-Catalán<sup>17</sup> · Marisa Hernández-Garfella<sup>18</sup> ·  
María Victoria Hernández<sup>19</sup> · Laura Pelegrin<sup>20</sup> · Ricardo Blanco<sup>21</sup> · David Diaz-Valle<sup>4,5</sup>

# OCT Imaging of the Vitreoretinal Interface and Inner Retinal Layers

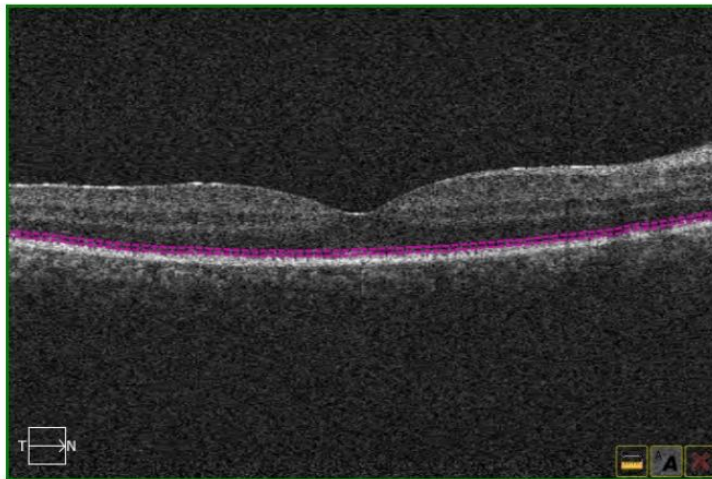






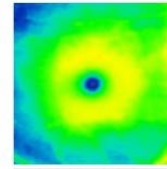


Elipsoide IS/OS: Desplazamiento = -45 µm Grosor = 21 µm

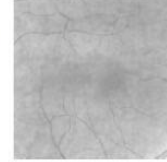


Corte: 175

Mapa de grosor



Fondo de ojo OCT



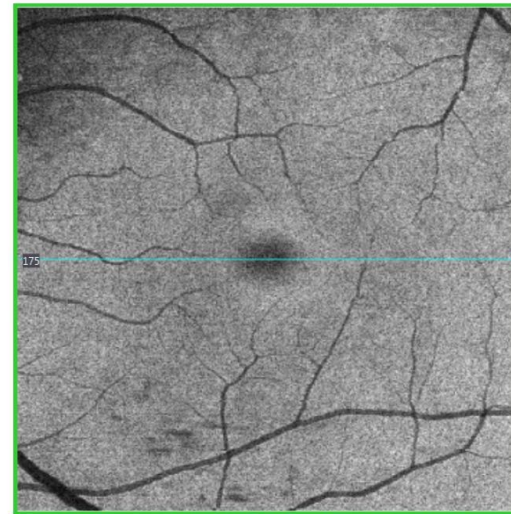
Retin medi:

Elipsoi IS/OS:

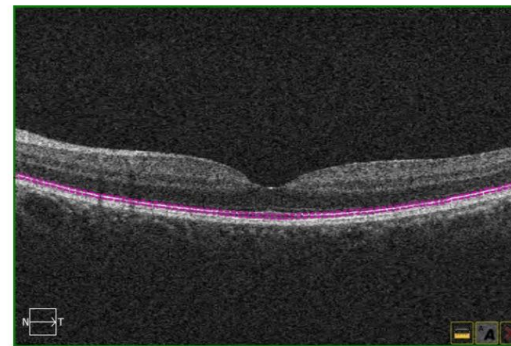
Coroid

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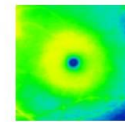


Elipsoide IS/OS: Desplazamiento = -45 µm Grosor = 21 µm

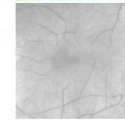


Corte: 175

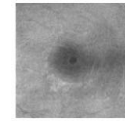
Mapa de grosor



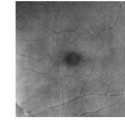
Fondo de ojo OCT



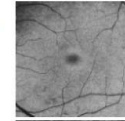
VRI



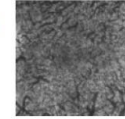
Retina media



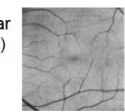
Elipsoide IS/OS



Coroides



Personalizar - (Coroidal)



Personalizar - (Mediorretinal)



# PRACTICAL OCT-ANGIOGR

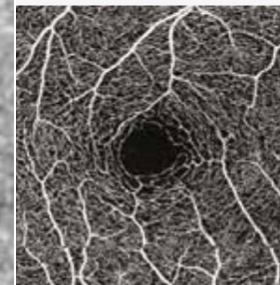
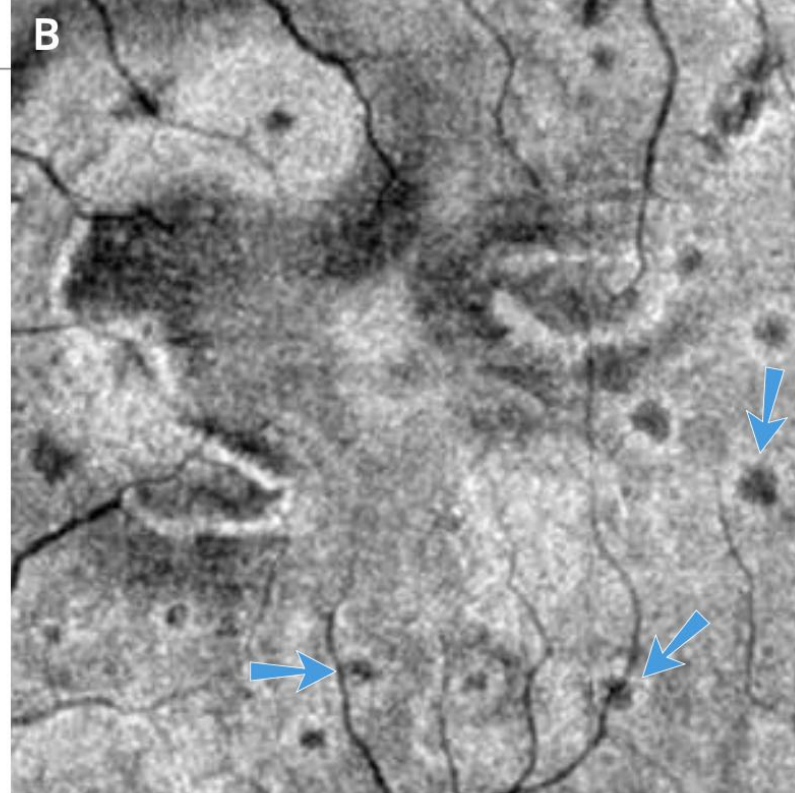
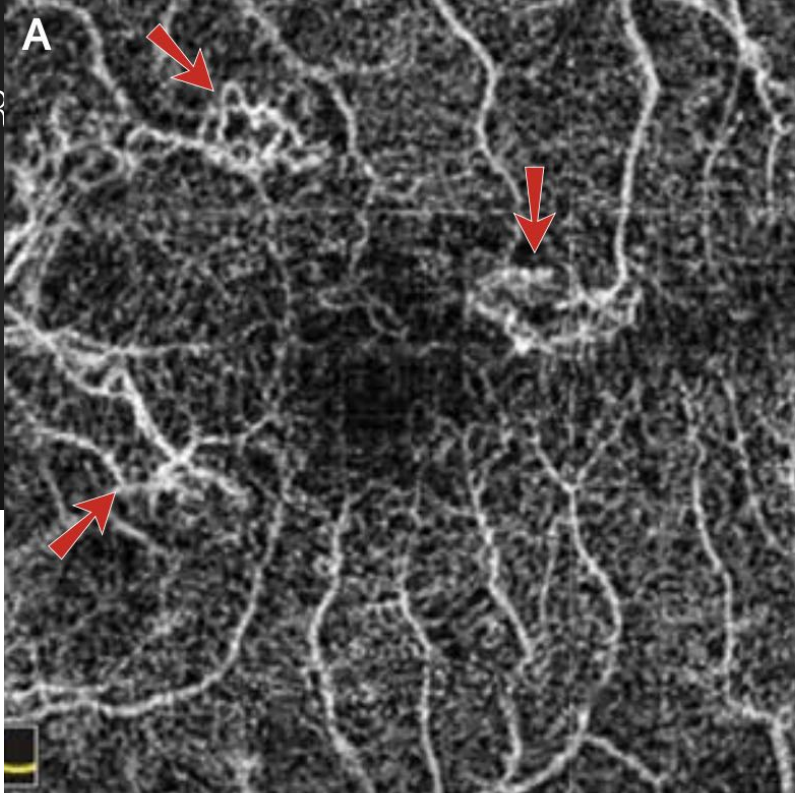
Neovascularization, edema, ischemia and degeneration

Dr Sylvia Nigham-Buttet  
Sandrine Ayrault  
Dr Corinne Delahaye-Mazza

and

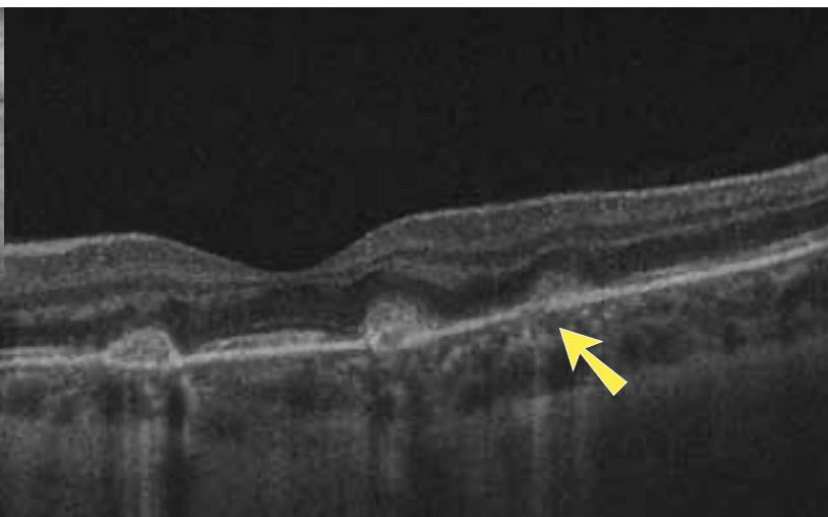
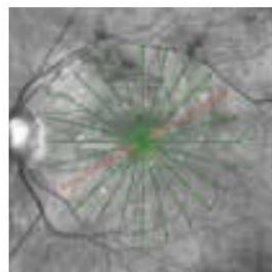
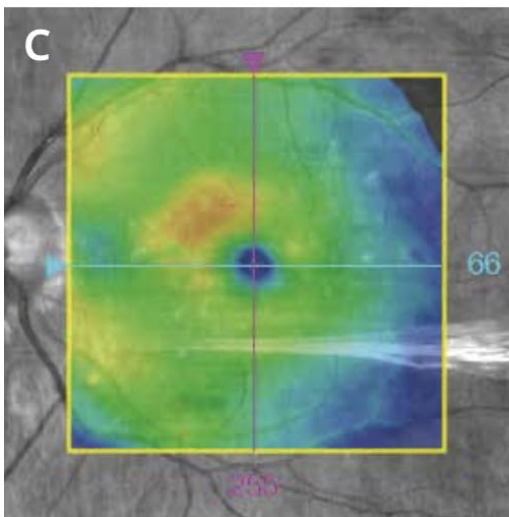
Dr Typhaine Grenier  
Dr Gabriel Quintini  
Dr Franck Fajnkuchen  
Pr Salomon Yves Cohen

Preface by Pr Eric Souied



## OCT-Angiography map

These maps are a reconstruction of the microvasculature of the retina and choroid.



the ILM<sup>(1)</sup> and the IPL<sup>(2)</sup>.

the IPL<sup>(2)</sup> and the OPL<sup>(3)</sup>.

the OPL<sup>(3)</sup> and the RPE<sup>(4)</sup>.

3) OPL: Outer plexiform layer

4) RPE: Retinal pigment epithelium

... maps are a 2D representation of the microvasculature over a particular area of

... surface provides 2D maps of the microvasculature, according to clinically interesting segmentation

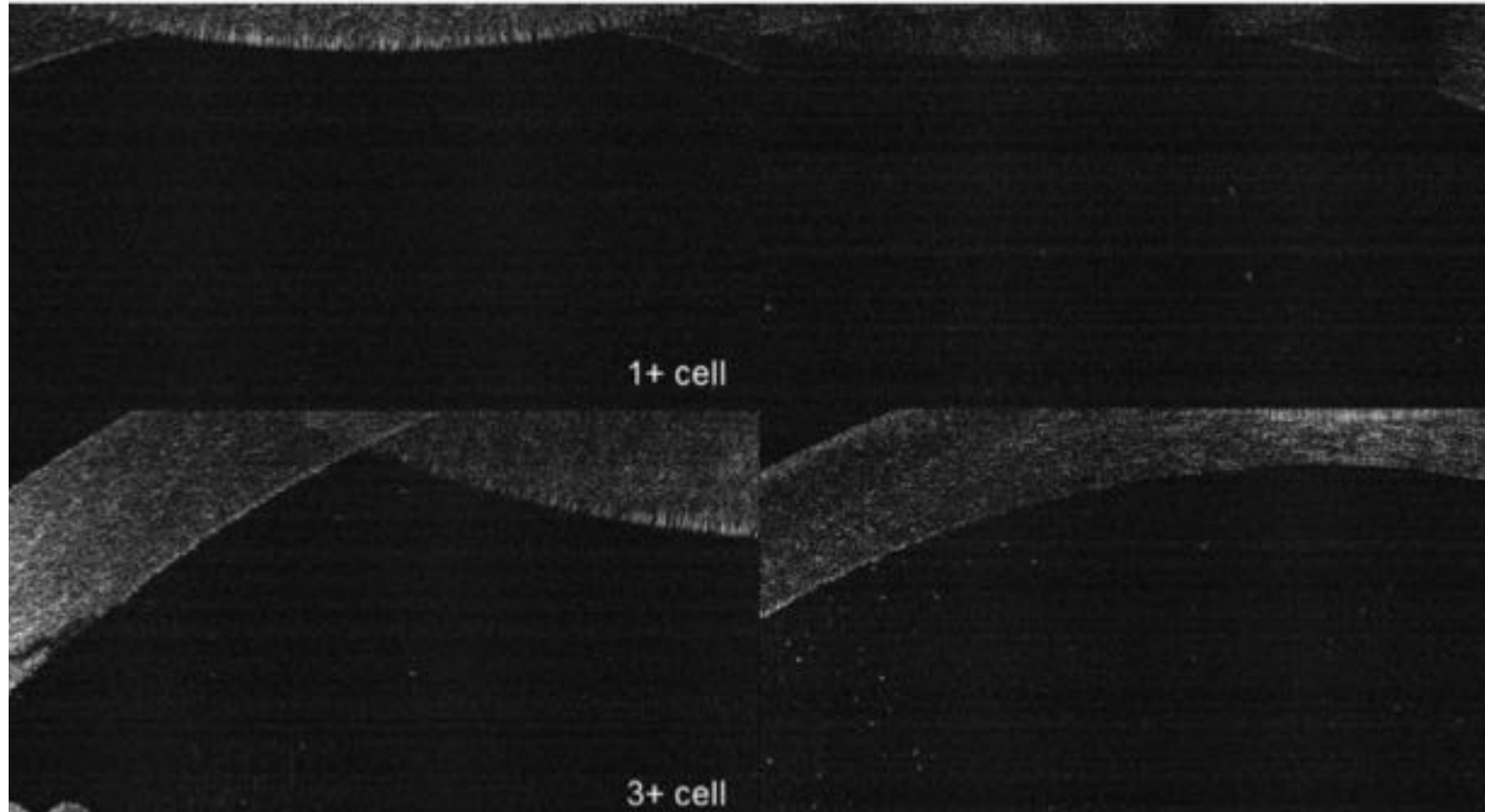
... membrane layer

# Automated Analysis of Anterior Chamber Inflammation by Spectral-Domain Optical Coherence Tomography

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Sumit Sharma, MD,<sup>1</sup> Careen Y. Lowder, MD, PhD,<sup>1</sup> Amit VasANJI, PhD,<sup>2</sup> Kimberly Baynes, COA,<sup>1</sup>  
Peter K. Kaiser, MD,<sup>1</sup> Sunil K. Srivastava, MD<sup>1</sup>

- 114 ojos de 70 pacientes con uveítis anterior activa.



Number of Cells Seen on Individual Line Scan as Determined by Manual Grading

Clinical Examination Grade	No. of Eyes	Average No. of Cells on OCT Line Scan	Range of Cells on OCT Line Scan
0	24	0.13	0-1
1/2+	5	1.2	0-3
1+	16	2.6	1-4
2+	15	5.7	3-8
3+	11	15.5	7-28
4+	12	41.2	23-75

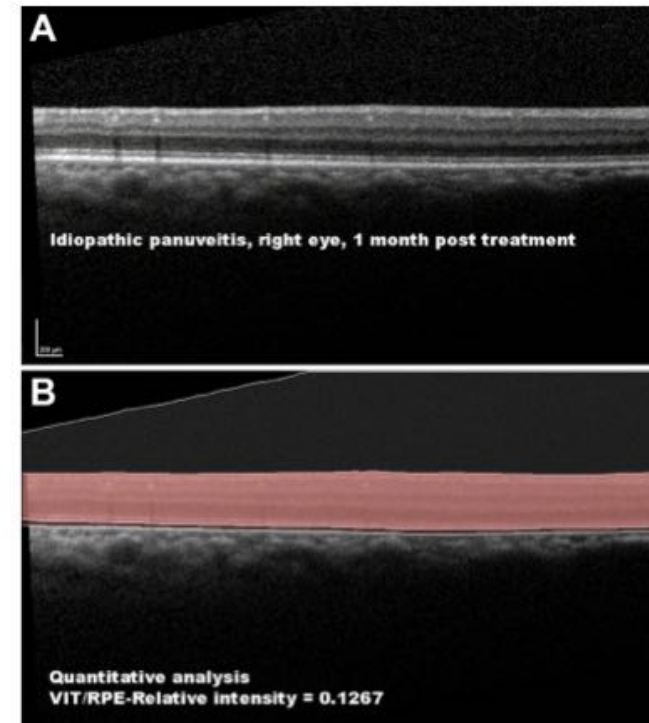
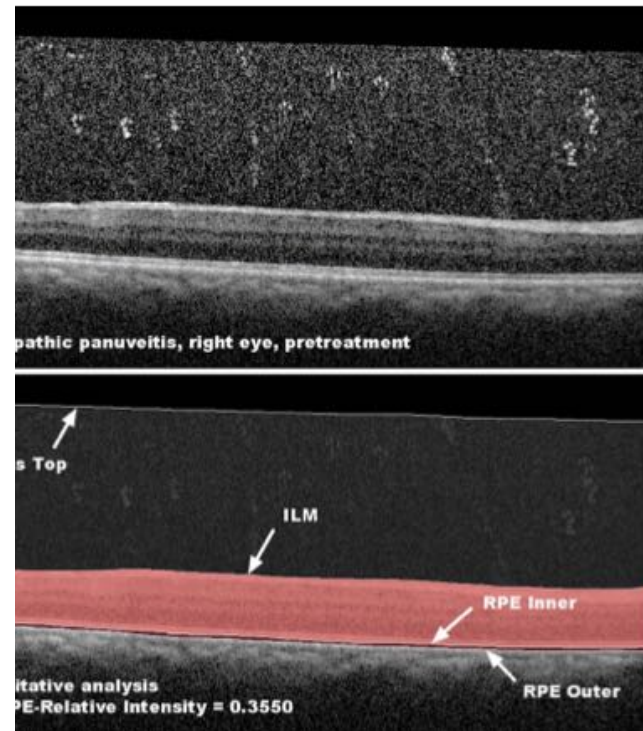
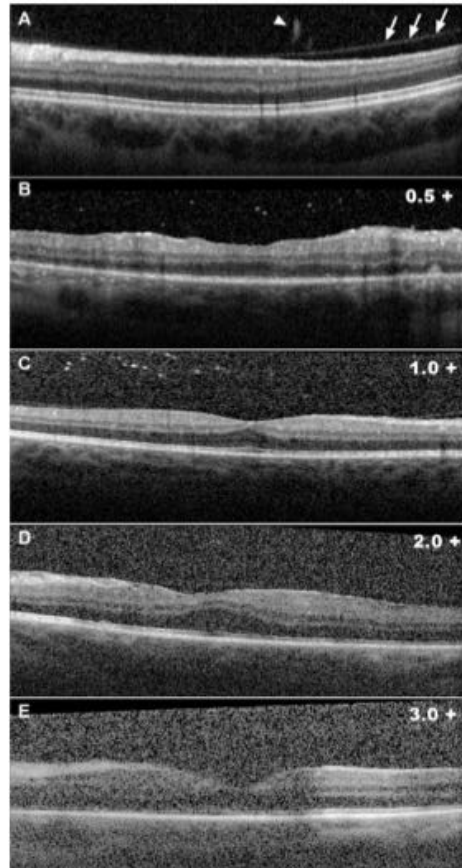
OCT = optical coherence tomography.

Table 3. Clinical Grade with Corresponding Automated and Manual Cell Counts from 3-Dimensional Volume Scans

Clinical Examination	Average No. of Cells Automated	Average No. of Cells Manual	Average Cell Density/mm <sup>3</sup>
0	13.6	9.2	0.268
1/2+	17.5	10.0	0.366
1+	23.5	16.33	0.463
2+	40.3	31.5	0.783
3+	121.6	138.6	2.372
4+	527.2	936.8	11.05

# Objective Measurement of Vitreous Inflammation Using Optical Coherence Tomography

Pearse A. Keane, MD, FRCOphth,<sup>1</sup> Michael Karampelas, MD, FEBO,<sup>1,2</sup> Dawn A. Sim, FRCOphth,<sup>1</sup> Srinivas R. Sadda, MD,<sup>3</sup> Adnan Tufail, MD, FRCOphth,<sup>1</sup> H. Nida Sen, MD, MHSc,<sup>4</sup> Robert B. Nussenblatt, MD, MPH,<sup>4</sup> Andrew D. Dick, MD, FMedSci,<sup>5</sup> Richard W. Lee, MRCOphth, PhD,<sup>5</sup> Philip I. Murray, PhD, FRCOphth,<sup>6,7</sup> Carlos E. Pavesio, MD, FRCOphth,<sup>1</sup> Alastair K. Denniston, PhD, FRCOphth<sup>7,8</sup>



FULL TEXT LINKS



*Acta Ophthalmol.* 2021 Nov;99(7):756–764. doi: 10.1111/aos.14739. Epub 2021 Jan 9.

## Swept-source optical coherence tomography objective composite activity score for uveitis

Victor Llorenç<sup>1,2</sup>, Alba R Serrano<sup>1</sup>, Marina Mesquida<sup>2</sup>, Phoebe Lin<sup>3</sup>, Cristina Esquinas<sup>4</sup>, Maite Sainz-de-la-Maza<sup>1,2</sup>, Christina Metea<sup>3</sup>, Anna Bosch<sup>5</sup>, Maria Calvo<sup>5</sup>, Ariel Balter<sup>3</sup>, Yukiko Nakamura<sup>3</sup>, Blanca Molins<sup>2</sup>, Carmen Alba<sup>1</sup>, Eric Suhler<sup>3</sup>, Alfredo Adán<sup>1,2</sup>

Affiliations

PMID: 33421360 DOI: [10.1111/aos.14739](https://doi.org/10.1111/aos.14739)

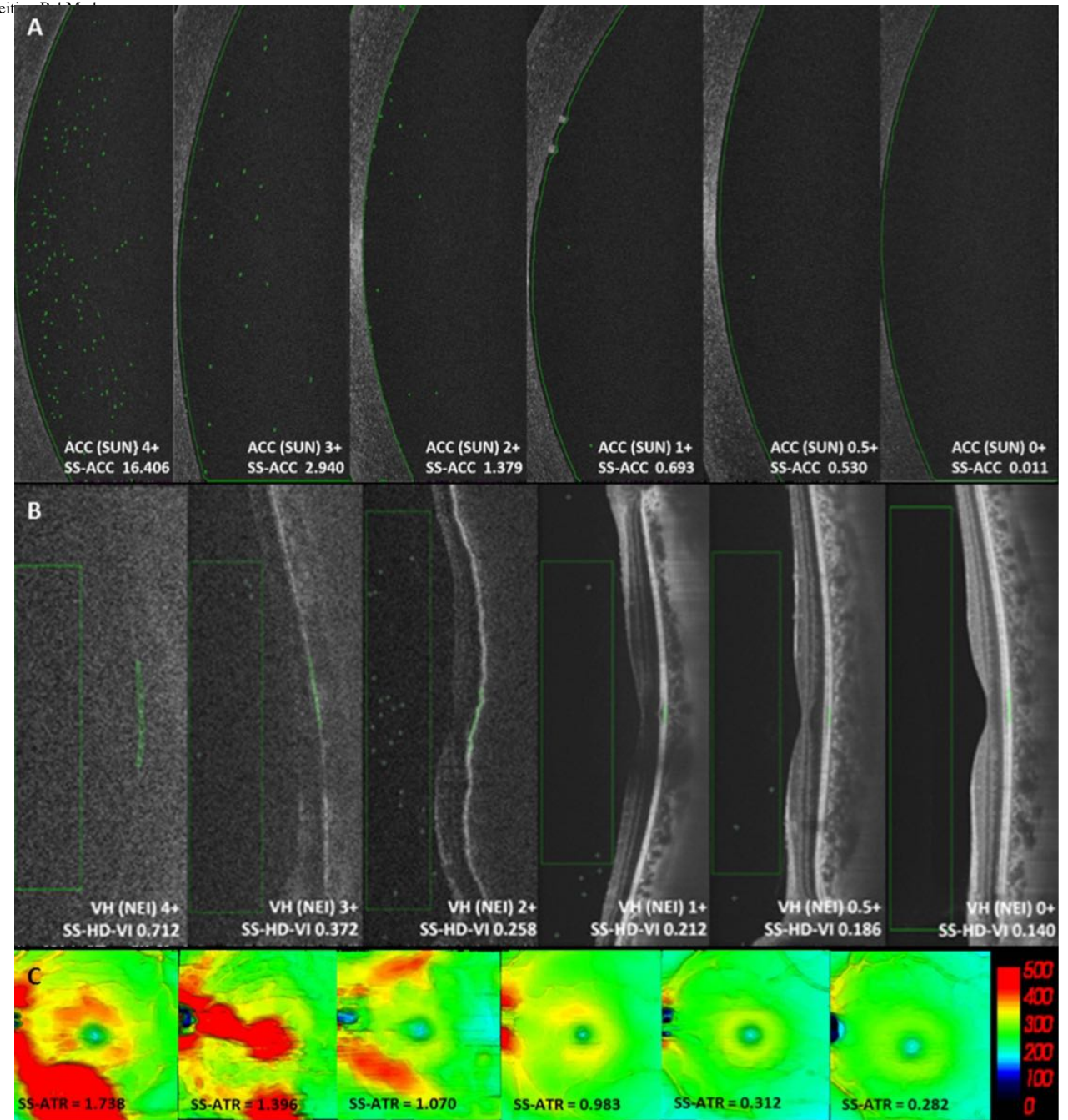
### Abstract

**Purpose:** To develop an objective intraocular inflammation composite score.

**Methods:** Cross-sectional study. Non-invasive image acquisition and processing were conducted from April 2017 to April 2019. Inflammation-grade stratified eyes from patients with active, inactive uveitis and healthy controls were recruited. After clinical assessment, four anterior and posterior segment image acquisition protocols per eye, using swept-source optical coherence tomography (SS-OCT), were performed at inclusion. Eight imaging biomarkers in three domains: anterior, intermediate and posterior were studied. They were ranked and selected by discriminatory power and correlation with clinical scores. A final SS-OCT-derived composite uveitis activity score (SS-UAS) was developed through multiple linear regression.

**Results:** We studied 224 eyes with uveitis (165 active and 59 inactive) from 165 patients (mean age 46.6 SD 15.5 years; 55.3% women) and 38 eyes from 19 healthy controls (mean age 43.6 SD 17.1; 47% women). The selected SS-OCT-derived biomarkers to build the final score were anterior chamber hyper-reflective dots (anterior), high-definition relative vitreous intensity (intermediate) and the averaged thickened retinal index (posterior). Swept-source (SS)-UAS was highly discriminant between active and inactive, and between active and healthy eyes (means 2.06 SD 1.86, 0.93 SD 0.44, and 0.96 SD 0.38, respectively, both  $p < .001$ , Mann-Whitney U). Construct validity (Cronbach's alpha = 0.7), internal consistency, criterion validity and reliability (concordance correlation coefficient intra-rater = 0.99, 95% CI: 0.98–0.99; inter-rater = 0.98, 95% CI: 0.96–0.99) were favourable.

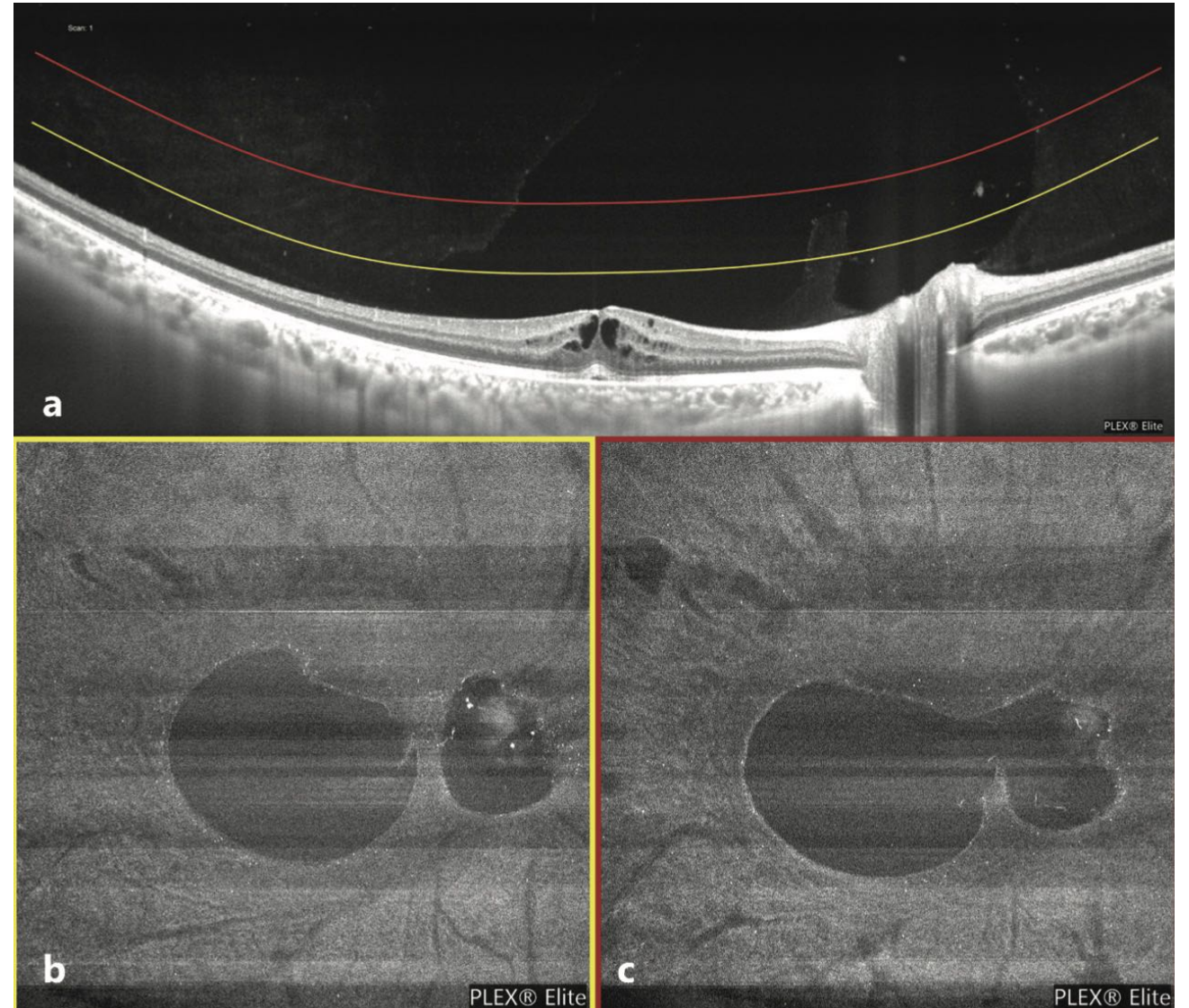
**Conclusions:** Global intraocular inflammation can potentially be staged and scored objectively, continuously, consistently and in a valid manner through the combined processing of SS-OCT scans.



# The Vitreous in Uveitis: Characterizing the Invisible with Optical Coherence Tomography




Francesco Pichi, MD<sup>a,b</sup> and Ester Carreño, MD, PhD <sup>c,d</sup>

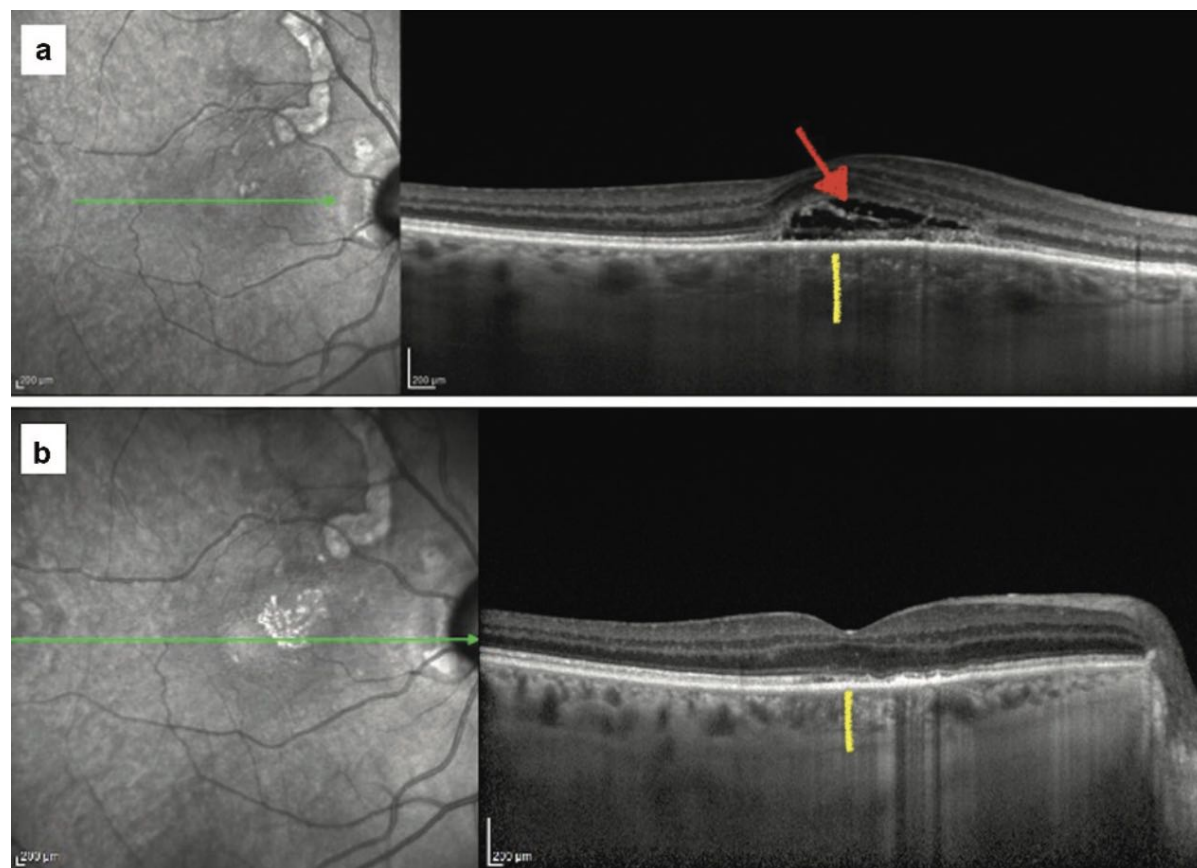
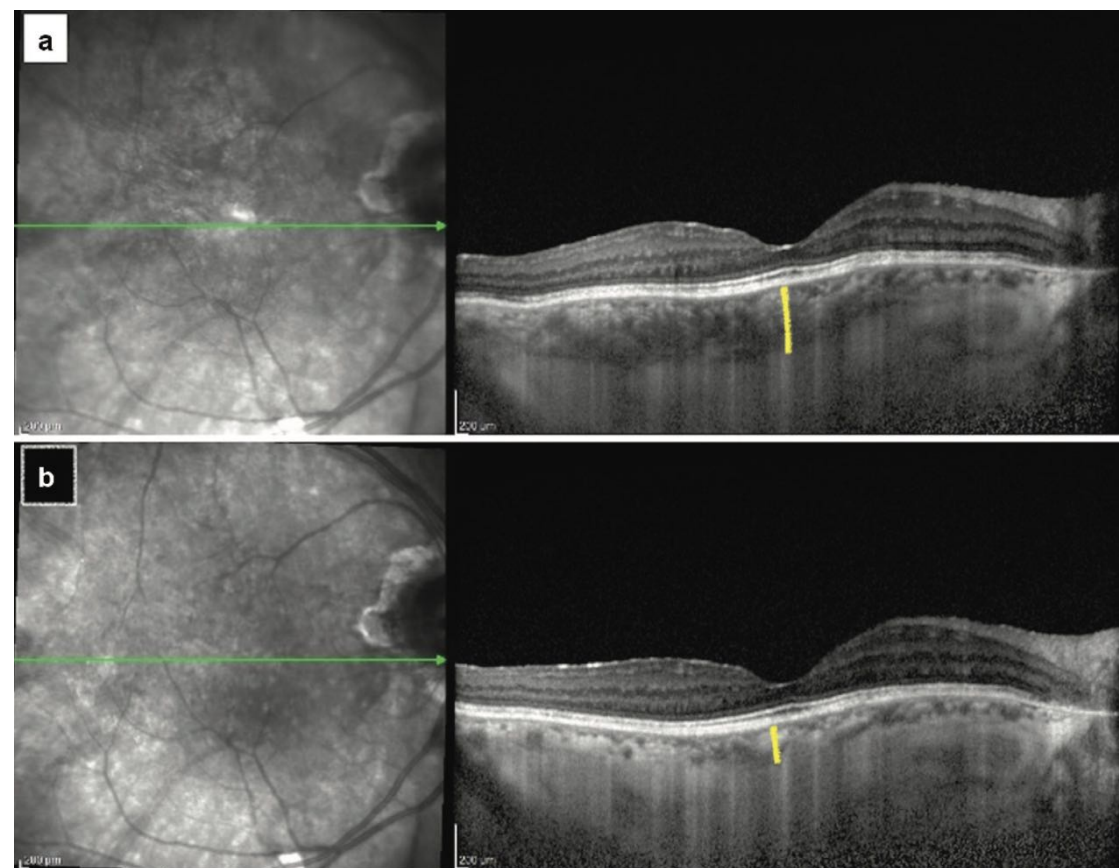
<sup>a</sup>Eye Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates; <sup>b</sup>Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, Ohio, USA; <sup>c</sup>Department of Ophthalmology, University Hospital Fundación Jiménez Díaz, Madrid, Spain; <sup>d</sup>Department of Ophthalmology, University Hospital Rey Juan Carlos, Madrid, Spain

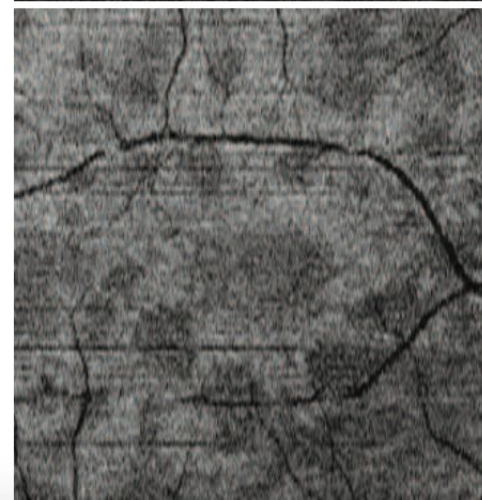
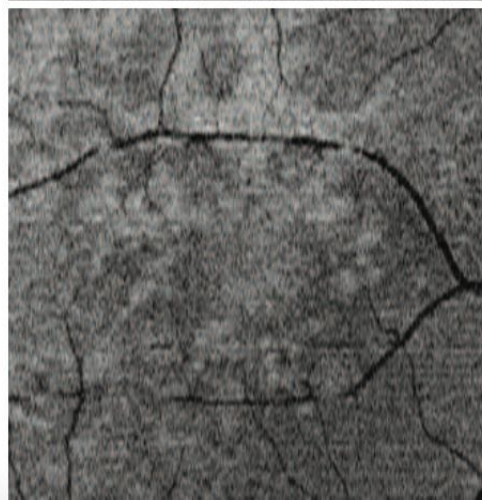
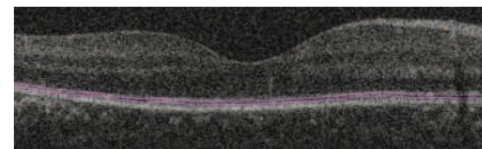
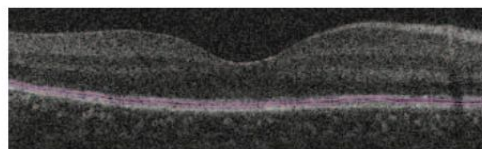
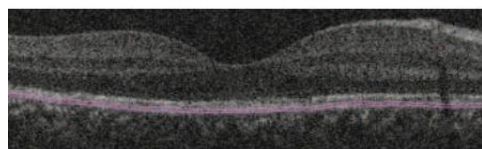
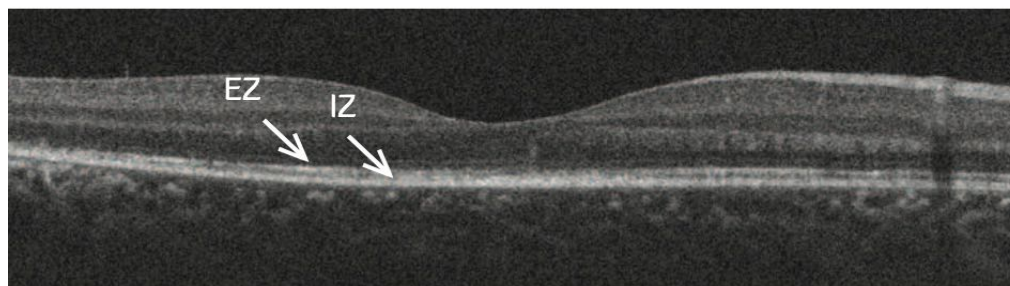
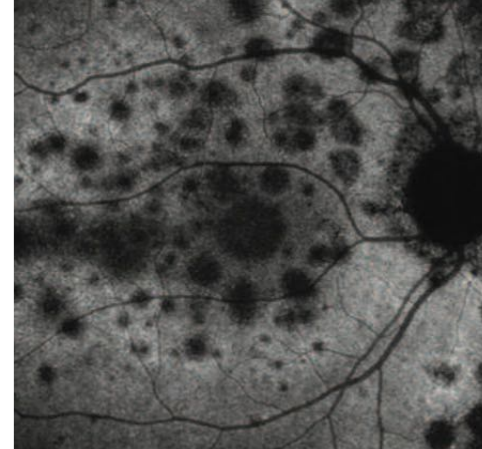
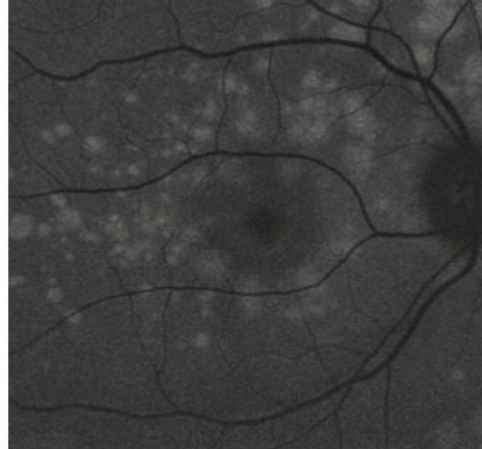




# Outcome Measures for Disease Monitoring in Intraocular Inflammatory and Infectious Diseases (OCTOMERIA): Understanding the Choroid in Uveitis with Optical Coherence Tomography (OCT)

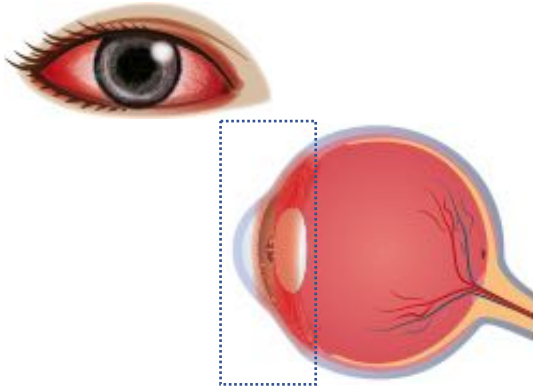
Rupesh Agrawal, MD <sup>a,b,c,d,e\*</sup>, Rei Chern Weng<sup>a\*</sup>, Alex Fonollosa, PhD<sup>f,g</sup>, Lena Giralt, MD<sup>f</sup>, Joseba Artaraz, MD<sup>f</sup>, Peizeng Yang, PhD<sup>h</sup>, Fanfan Huang, MD <sup>h</sup>, Bingyao Tan, PhD<sup>d,i,j</sup>, Leopold Schmetterer, PhD<sup>d,i,j,k,l,m,n</sup>, Alok Sen, MS<sup>o,p</sup>, Vishali Gupta, MD <sup>q</sup>, and Wei Xin, MMed<sup>b</sup>





# Uveítis anterior vs no-anterior no-infecciosa

## UVEÍTIS ANTERIOR



## CURSO CLÍNICO



- ▼ Curso clínico limitado (ridges and valleys)<sup>1</sup>
- ▼ Menor incidencia de complicaciones oculares<sup>2</sup>
- ▼ Mejor pronóstico global<sup>2</sup>
- ▼ Tratamiento tópico efectivo<sup>3-5</sup>

## MANEJO TERAPÉUTICO<sup>3-5</sup>

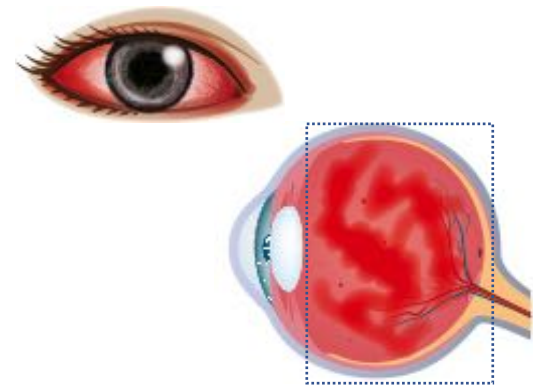


Inicialmente  
tópico



Tratamiento sistémico  
necesario sólo en casos  
seleccionados

## UVEÍTIS NO-ANTERIOR



## CURSO CLÍNICO

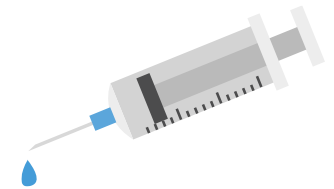


- ▼ Curso clínico prolongado<sup>1</sup>
- ▼ Mayor incidencia de complicaciones oculares<sup>2</sup>
- ▼ Peor pronóstico global<sup>2</sup>
- ▼ Tratamiento tópico ineficaz<sup>3-5</sup>

## MANEJO TERAPÉUTICO<sup>3-5</sup>



Inicialmente  
sistémico



Tratamiento local  
fundamentalmente co-  
adyuvante, solo en casos  
seleccionados.

# Tratamiento local frente a tratamiento sistémico en uveítis NANI



# Injectable Fluocinolone Acetonide Long-Acting Implant for Noninfectious Intermediate Uveitis, Posterior Uveitis, and Panuveitis

## Two-Year Results

Glenn J. Jaffe, MD,<sup>1</sup> Phoebe Lin, MD, PhD,<sup>1</sup> Robert T. Keenan, MD, MPH,<sup>2</sup> Paul Ashton, PhD,<sup>3</sup> Cindy Skalak, RN, COT,<sup>4</sup> Sandra S. Stinnett, DrPH<sup>1</sup>

ocular pressure (IOP) rise. At baseline, 1 study eye (9%) required pressure-lowering drops; 2 additional study eyes (18%) required them during the follow-up period. Filtering procedures were performed in 2 of these eyes (18.1%). No FAi explantations were required, nor were any participants lost to follow-up during the investigation.

**Conclusions:** It is feasible to place a long-acting FAi in an outpatient setting, without prolonged adverse events attributed to the implant injection procedure. The FAi effectively controlled intraocular inflammation in all eyes in the study, and at the last follow-up, all implanted eyes demonstrated an improvement in visual acuity. Elevated IOP that occurred in 18% of FAi-implanted eyes was managed by standard means. The FAi implant is a promising approach for patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis who do not respond to, or are intolerant to, conventional therapy. *Ophthalmology* 2016;123:1940-1948 © 2016 by the American Academy of Ophthalmology.

# Benefits of Systemic Anti-inflammatory Therapy versus Fluocinolone Acetonide Intraocular Implant for Intermediate Uveitis, Posterior Uveitis, and Panuveitis

## Fifty-four—Month Results of the Multicenter Uveitis Steroid Treatment (MUST) Trial and Follow-up Study

**Conclusions:** Visual outcomes of fluocinolone acetonide implant and systemic treatment for intermediate uveitis, posterior uveitis, and panuveitis were similarly favorable through 54 months. The implant maintained a clear advantage in controlling inflammation through 54 months. Nevertheless, with systemic therapy, most patients also experienced greatly improved inflammatory status. Macular edema improved equally with longer follow-up. Based on cost effectiveness and side-effect considerations, systemic therapy may be indicated as the initial treatment for many bilateral uveitis cases. However, implant therapy is a reasonable alternative, especially for unilateral cases and when systemic therapy is not feasible or is not successful. *Ophthalmology* 2015;122:1967-1975 © 2015 by the American Academy of Ophthalmology.

JAMA | Original Investigation

# Association Between Long-Lasting Intravitreal Fluocinolone Acetonide Implant vs Systemic Anti-inflammatory Therapy and Visual Acuity at 7 Years in Intermediate, Posterior

**CONCLUSIONS AND RELEVANCE** In 7-year extended follow-up of a randomized trial of patients with severe intermediate, posterior, or panuveitis, those randomized to receive systemic therapy had better visual acuity than those randomized to receive intravitreal fluocinolone acetonide implants. Study interpretation is limited by loss to follow-up.

Writing Committee for the Multicenter Uveitis Steroid Treatment

# Long-Term Intravitreal Dexamethasone Implant Outcomes in Uveitis

Carmen Alba-Linero, Anna Sala-Puigdollers, Barbara Romero, Victor Llorenç, Alfredo Adan & Javier Zarranz-Ventura

## Dexamethasone Inserts in Noninfectious Uveitis

### A Single-Center Experience

Dominika Pohlmann, MD,<sup>1,\*</sup> Gerrit A. vom Brocke, MD,<sup>1,\*</sup> Sibylle Winterhalter, MD,<sup>1</sup> Theresa Steurer, MD,<sup>2</sup> Sabrina Thees,<sup>1</sup> Uwe Pleyer, MD<sup>1</sup>

TABLE 1. Baseline characteristics of study patients and eyes treated with the intravitreal dexamethasone implant for uveitis.

Age, mean ±SD (median,IQR)	56 ± 16.62 (57–24)
Sex, % female	41 / 63 64.9%
N eyes (patients)	
Indications (% , n)	
Uveitis anatomic class	
Phenotypic diagnosis	
Systemic therapies (% , n)	
Immunomodulatory therapy	
Previous local therapies (% , n)	

at least one immunosuppressant drug. This may suggest that local therapy with the intravitreal dexamethasone implant may help controlling the disease and allow the reduction of systemic treatment and collateral dise effects in certain cases. In our opinion, the main drivers for treatment selection between systemic therapy or dexamethasone implant are the presence of systemic symptomatology and the laterality (unilateral or bilateral) of uveitis. In our opinion, the intravitreal dexamethasone implant would be the treatment of choice in exclusively ocular and unilateral disease.

5. Infliximab (10.9%, 5/40)  
6. Tocilizumab (8.4%, 4/40)  
7. Others (16.85%, 7/40)

(16.1%, 13/79)  
(8.8%, 7/79)  
(6.3%, 5/79)  
(1.2%, 1/79)

CME = cystoid macular edema; IQR =interquartile; MTX = methotexate; double therapy: steroids+second-line agent; Triple therapy: steroids+second line agents x2JIA = juvenile idiopathic arthritis. IRVAN = idiopathic retinitis vasculitis aneurysm and neuroretinitis. TINU = tubulointerstitial nephritis and uveitis. VKH = Vogt-Koyanagi-Harada.

Pohlmann et al · Dexamethasone Inserts in Uveitis

Table 3. Central Retinal Thickness by Number of Dexamethasone Inserts

Time Point	No. of Dexamethasone Inserts					
	1	2	3	4	5	6
Baseline						
Mean (µm)	465	460	476	478	480	439
No.	109	76	47	31	17	12
SD	±142	±129	±140	±119	±151	±125
1 mo						
Mean (µm)	318	314	309	295	275	259
SD	±80	±88	±66	±57	±39	±50
P value	<0.001	<0.001	<0.001	<0.001	<0.001	0.002
3 mos						
Mean (µm)	342	352	337	364	345	331
SD	±93	±101	±98	±131	±124	±123
P value	<0.001	<0.001	<0.001	<0.001	0.011	0.019
6 mos						
Mean (µm)	388	408	398	467	431	438
SD	±106	±145	±134	±170	±126	±230
P value	<0.001	0.004	0.001	0.861	0.308	0.959

SD = standard deviation.  
Boldface indicates statistical significance.

Table 5. Percentages of Patients with Best-Corrected Visual Acuity Gain to 0.3 Logarithm of the Minimum Angle of Resolution (Snellen Equivalent, 20/40)

Dexamethasone Insert	1 Month	3 Months	6 Months
First	28% (31/109)	31% (34/109)	26% (28/109)
Second	26% (20/78)	24% (19/78)	27% (21/78)
Third	29% (14/48)	27% (13/48)	19% (9/48)
Fourth	26% (8/31)	26% (8/31)	16% (5/31)
Fifth	12% (2/17)	18% (3/17)	6% (1/17)

## *Problemas específicos del tratamiento sistémico de las uveítis NANI.*

**Ausencia de guías terapéuticas**

*Escasísimos ensayos clínicos randomizados. Estudios sobre tratamiento de muy bajo nivel de evidencia.*

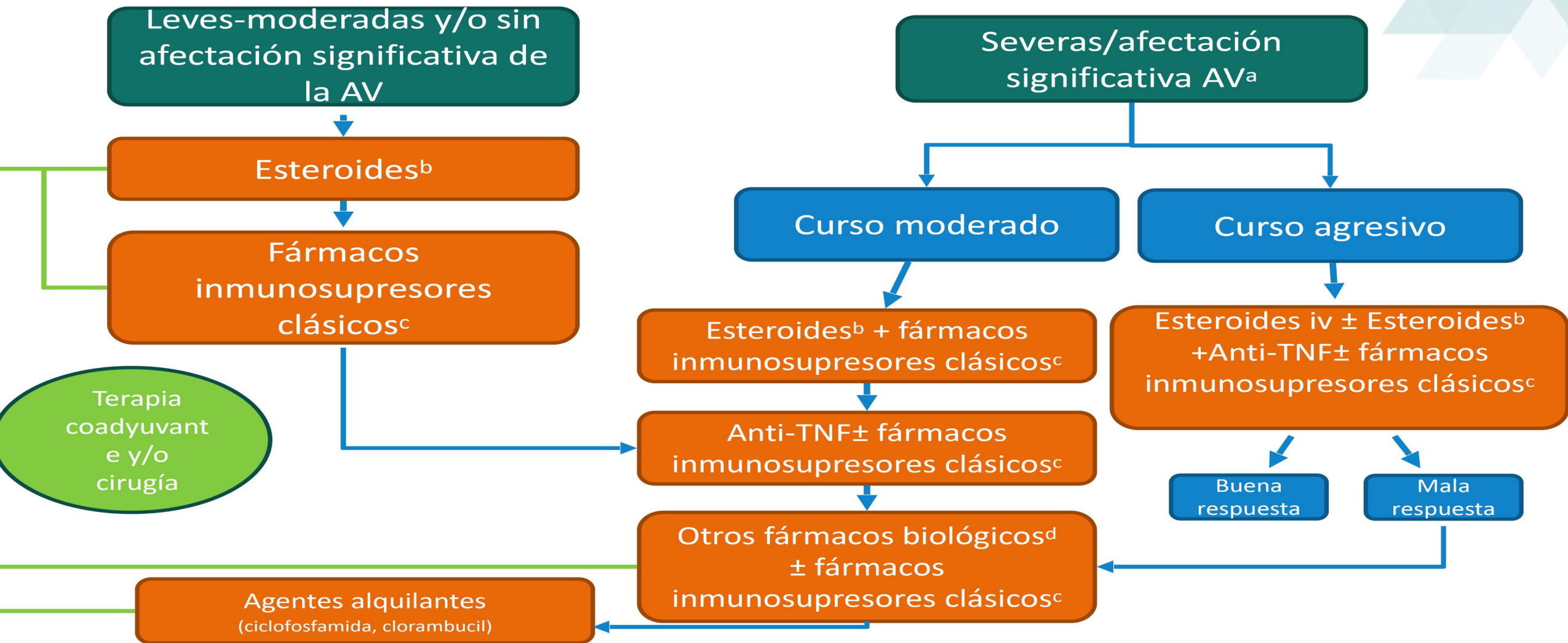
**Ausencia de escalas para valorar respuesta a tratamiento/monitorización**

*No hay una nomenclatura estandarizada; Ausencia de una escala de valoración completa y actualizada.*

**Escasas opciones de tratamiento**

*La mayor parte de los tratamientos off-label.*

# Algoritmo de tratamiento en uveítis no-anteroiores no-infecciosas



<sup>a</sup>Behçet, AII, VKH, Oftalmía Simpática, PUK, escleritis, coroidopatías inflamatorias agresivas (serpiginosa etc)

<sup>b</sup>Tópica, loco-regional y/o sistémica; <sup>c</sup>Metotrexate, azatioprina, micofenolato mofetil, ciclosporina A

<sup>d</sup>Anti-TNF de primera elección son infliximab y adalimumab; <sup>e</sup>Otros anti-TNF (golimumab, certolizumab), interferon, tocilizumab, rituximab



# Factores que influyen en la elección de los fármacos inmunosupresores/Inmunomoduladores en la uveítis no infecciosa



# Guidance on Noncorticosteroid Systemic Immunomodulatory Therapy in Noninfectious Uveitis

## Fundamentals Of Care for Uveitis (FOCUS) Initiative

Table 4. Evidence Supporting Use of Biologics and Recommendation

Originator Biologic	No. of Studies	Anatomic Location*	Disease Entities or Cause	Outcomes			Evidence Level (No. of Publications)	Recommendation Level
				Inflammation Control	Visual Acuity Stability or Improvement	Steroid Sparing		
<b>Anti-tumor necrosis factor</b>								
Infliximab	24	Anterior, posterior, retinal vasculitis	BD	Yes	Yes	Yes	2B (3), 3B (2), 4 (8)	B
		Anterior uveitis, intermediate uveitis, posterior uveitis, panuveitis	Pediatric NIU (uveitis entities include JIA, BD, sarcoidosis, VKH disease)	Yes	Yes	Yes	2B (1), 4 (2), 5 (1)	C
		Anterior uveitis, intermediate uveitis, posterior uveitis, panuveitis	Other uveitis entities (including BD, BCR, sarcoidosis, idiopathic vasculitis, VKH disease)	Yes	Yes	Yes	2B (2), 3B (1), 4 (4)	B
Adalimumab	15	Anterior uveitis, intermediate uveitis, posterior uveitis, panuveitis	NIU (including different uveitis entities: BD, idiopathic uveitis, sarcoidosis, BSR, TINU, VKH disease, pars planitis; other: HLA-B27, JIA)	Yes	Yes	Yes	1B (4), 2B (4), 4 (5), 5 (2)	A
Golimumab	2	Anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis	NIU	Yes	Yes	Yes	4	C
Etanercept	2	Anterior, intermediate, posterior uveitis	NIU, sarcoidosis	X	X	X	2B	B
Certolizumab	No studies fulfilling inclusion criteria		—	—	—	—	—	D
<b>Anti-interleukin 1</b>								
Anakinra/canakinumab	1	Anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis	BD	Yes	—	—	4	C
Gevokizumab	1	Posterior uveitis, panuveitis, and/or retinal vasculitis	BD	Yes	—	—	2B	C
<b>Anti-interleukin 2</b>								
Daclizumab	7	Anterior uveitis, intermediate uveitis, posterior uveitis, or panuveitis; retinal vasculitis	NIU (including different uveitis entities such as: idiopathic anterior uveitis and panuveitis; MCP; scleritis, idiopathic panuveitis; sarcoid panuveitis; HSV-associated anterior scleritis; idiopathic keratouveitis)	Yes	Yes	Yes	2B (5) and 4 (2)	B
<b>Anti-interleukin 6</b>								
Tocilizumab	2	Anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis; also note retinal vasculitis with and without uveitis	NIU (including different uveitis entities)	Yes	Yes	X	4	C

Table 4. (Continued.)

Originator Biologic	No. of Studies	Anatomic Location*	Disease Entities or Cause	Outcomes			Evidence Level (No. of Publications)	Recommendation Level
				Inflammation Control	Visual Acuity Stability or Improvement	Steroid Sparing		
Sarilimumab	Ongoing CT, no results		NIU (including different uveitis entities)	—	—	—	—	D
<b>Anti-interleukin 17</b>								
Secukinumab	4 (2 publications)	Intermediate uveitis, posterior uveitis, panuveitis	NIU (including different uveitis entities: Behçet's uveitis noninfectious; non-Behçet's uveitis; quiescent, non-infectious, non-Behçet's uveitis)	Yes	X <sup>†</sup>	Yes	1B (1) and 2B (3)	B
<b>Anti-CD-20</b>								
Rituximab	1	Anterior uveitis, posterior uveitis, and retinal vasculitis	BD	Yes <sup>‡</sup>	—	—	2B	C
<b>Anti-CD-52</b>								
Alemtuzumab	1	Not specified	BD	Yes	—	Yes	2B	C
<b>Interferons</b>								
Interferon alfa-2a and -2b	15	Anterior uveitis, intermediate uveitis, posterior uveitis or panuveitis or retinal vasculitis	BD and other uveitis entities including pars planitis, VKH disease, idiopathic panuveitis, uveopapillitis	Yes	Yes	Yes	2B (6), 3B (1), 4 (6), 5 (2)	B
Pegylated interferon alfa-2b	1	Nonanterior uveitis	BD	—	—	Yes <sup>§</sup>	2B	C
Interferon β	1	Intermediate uveitis or uveitis associated with multiple sclerosis	Patients with primary intermediate uveitis or uveitis associated with multiple sclerosis	Yes <sup>  </sup>	Yes	—	2B	C
<b>Others</b>								
Intravenous immunoglobulins	1	Posterior uveitis	BCR	—	Yes	—	2B	C



Conferencia de consenso

Documento de recomendaciones sobre el tratamiento con inmunodepresores de la uveítis no anterior, no infecciosa, no neoplásica

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Methods

This is a project promoted and endorsed by the Spanish Society of Ocular Inflammation (SEIO). The Autoimmune Diseases Group of the Spanish Society of Internal Medicine, Spanish Society of Immunology and Spanish Society of Rheumatology also endorse this project.



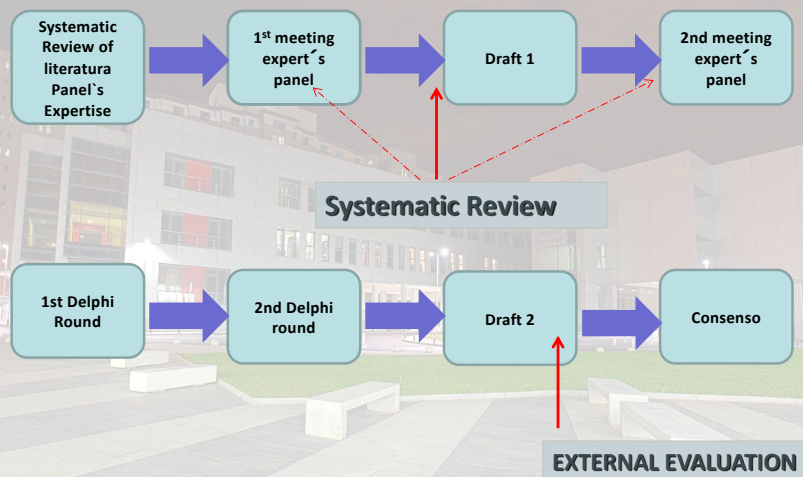
Efficacy and safety of immunomodulatory drugs in patients with non-infectious intermediate and posterior uveitis, panuveitis and macular edema: A systematic literature review

Alejandro Gómez-Gómez<sup>a,b</sup>, Estíbaliz Loza<sup>c</sup>, M<sup>a</sup> Piedad Rosario<sup>c</sup>, Gerard Espinosa<sup>d</sup>, José M García Ruiz de Morales<sup>e</sup>, José M Herrera<sup>f</sup>, Santiago Muñoz-Fernández<sup>g,h</sup>, Luis Rodríguez-Rodríguez<sup>g,h</sup>, Miguel Cordero-Coma<sup>i,\*</sup>, on behalf of the Spanish Society of Ocular Inflammation (SEIO)

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CONSENSUS DOCUMENT



A. Gómez-Gómez et al. / Seminars in Arthritis and Rheumatism 50 (2020) 1299–1306

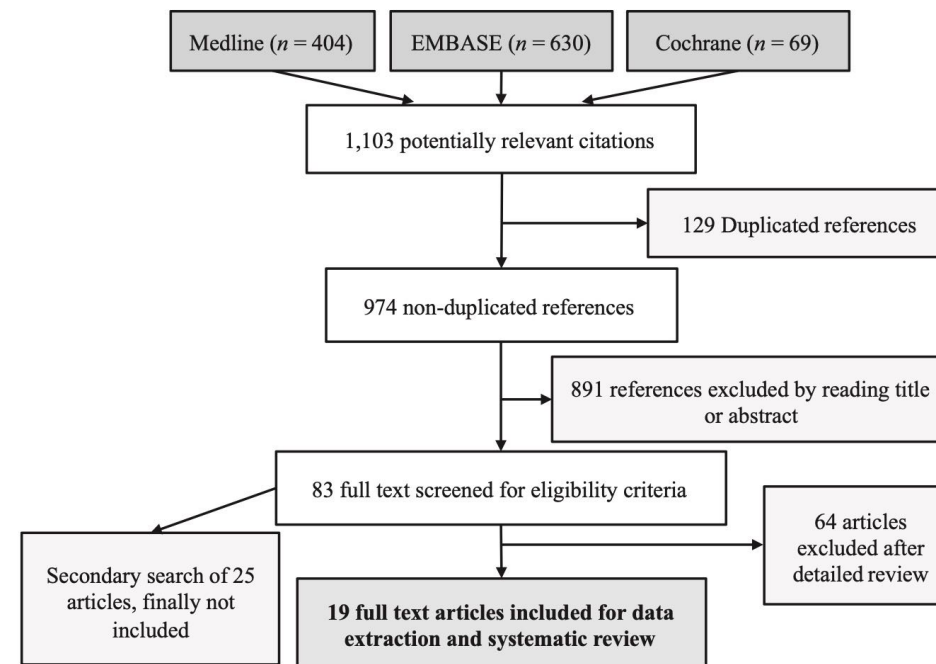


Fig. 1. Studies flow chart

# Definiciones

**Table 1**

Definitions of the consensus document on non-neoplastic, non-infectious uveitis.

Activity	Presence of cell grade in the anterior chamber and/or vitreous cavity > 0 according to the SUN scale <sup>55</sup> and/or the presence of inflammatory lesions of the posterior segment and/or inflammatory macular oedema and/or the presence of active vasculitis in the FAG and/or the presence of findings suggestive of inflammation in other complementary tests of special interest in the said condition
Remission	Absence of activity after three months without treatment
Control of the disease	Absence of activity after three months with treatment
Therapeutic objective	Control of inflammation, or in its absence, the lowest possible degree of activity after a balance of the risks and benefits of the therapeutic options available
Significant improvement	Decrease in cell grade (in anterior chamber and vitreous cavity) of at least 2 degrees on the SUN scale or reaching grade 0 on that same scale or, in the case of active uveitis without presence of inflammatory cell reaction, significant improvement in those tests (OCT, FAG etc.) that detected the inflammation, before receiving the treatment, in the said patient
Worsening	Any cell grade increase (anterior chamber and vitreous cavity) according to the SUN scale and/or the appearance of signs of inflammation in the available complementary tests (OCT, FAG, etc.) and/or a negative progression in the result of these tests if these were already suggestive of inflammation at the beginning
Response to treatment	Significant improvement of the patient after an acceptable period using appropriate pharmacological doses for that specific drug and that particular patient. All clinical responses that do not meet the requirements for significant improvement will be considered partial responses.
Therapeutic failure	Absence of disease control with a given drug despite using the drug/s doses that were appropriate for that particular patient and that specific drug during a reasonable period of time
Uveitic macular oedema	Central macular thickness (central 1-mm of SD-OCT, <i>Macular cube strategy</i> ) higher than 315 microns with signs suggestive of intraocular inflammation not attributable to another concomitant condition <sup>a</sup>
Vasculitis	Staining of the vascular wall and progressive extravascular diffusion of contrast in FAG during angiographic intervals with signs suggesting inflammation not attributable to another concomitant condition

FAG: indocyanine green angiography; mm: millimetre; OCT: optical coherence tomography; SD: spectral domain; SUN: Standardization of Uveitis Nomenclature.

<sup>a</sup> Source: Grover S, Murthy RK, Brar VS, Chalam KV. Normative data for macular thickness by high-definition spectral-domain optical coherence tomography (spectralis).

**Tabla 4**

Resultados del Delphi y grado de acuerdo para cada recomendación

Recomendación	Media	DS	Mediana	P25	P75	Mín.	Máx.	% ≥7
<i>Recomendación 1.</i> No todos los pacientes con pars planitis requieren tratamiento inmunomodulador sistémico. En casos graves, especialmente si son bilaterales, se recomienda iniciar tratamiento con corticoides sistémicos junto con un inmunomodulador como AZA, MMF o MTX	6,3	3,2	6	4,5	10	1	10	89%
<i>Recomendación 2.</i> En pacientes con pars planitis se recomienda valorar el uso de corticoides tópicos, locorreregionales y/o intravítreos, así como de ciclopléjicos/midriáticos en casos determinados de afectación muy asimétrica y/o unilateral, afectación de la cámara anterior, y si existiese edema macular asociado	9,3	1,5	10	9	10	5	10	92,8%
<i>Recomendación 3.</i> En pacientes con pars planitis, en ausencia de control de la inflamación pasado un periodo de 4-6 meses y/o intolerancia al tratamiento pautado, el panel recomienda cambiar a otro inmunosupresor clásico o iniciar terapia biológica (añadida al inmunomodulador)								

**Uveítis intermedias***Pars planitis (uveítis intermedia idiopática)*

La pars planitis puede asociarse en algunos casos a EM<sup>15</sup>, y su inflamación no se resuelve muchas veces tan rápido como en otras zonas del ojo. Su tratamiento se basa en el uso de corticoides sistémicos así como de inmunomoduladores y terapias coadyuvantes locales.

*Recomendación 1.* No todos los pacientes con pars planitis requieren tratamiento inmunomodulador sistémico. En casos graves, especialmente si son bilaterales, se recomienda iniciar tratamiento con corticoides sistémicos junto con un inmunomodulador como AZA, MMF o MTX (NE 2 a; GR B; GA 89%).

Los glucocorticoides sistémicos pueden pautarse de 2 formas. Como bolos intravenosos de metilprednisolona (125 a 500 mg/día durante 3 días), seguidos de prednisona 0,5 mg/kg/día (o equivalente) en pauta descendente. O como corticoides orales a dosis de prednisona 0,5-1 mg/kg/día (o equivalente) en pauta descendente. El objetivo en ambos casos es la suspensión de los mismos o su mantenimiento con dosis mínimas ( $\leq 5$  mg/día)<sup>13</sup>.

No existe evidencia para seleccionar un fármaco inmunomodulador “de elección”<sup>16-19</sup>. En base a estudios observacionales y experiencia de los expertos, se recomendarían AZA, MMF y MTX<sup>20-22</sup>.

*Recomendación 2.* En pacientes con pars planitis se recomienda valorar el uso de corticoides tópicos, locorreregionales y/o intravítreos, así como de ciclopléjicos/midriáticos en casos determinados de afectación muy asimétrica y/o unilateral, afectación de la cámara anterior, y si existiese edema macular asociado (NE 4; GR C; GA 92,8%).

# Effect of Corticosteroid-Sparing Treatment With Mycophenolate Mofetil vs Methotrexate on Inflammation in Patients With Uveitis

## A Randomized Clinical Trial

S. R. Rathinam, MD, PhD; John A. Gonzales, MD; Radhika Thundikandy, MD; Anuradha Kanakath, MD; S. Bala Murugan, MD; R. Vedhanayaki, MD; Lyndell L. Lim, MBBS, DMedSci; Eric B. Suhler, MD, MPH; Hassan A. Al-Dhibi, MD; Thuy Doan, MD, PhD; Jeremy D. Keenan, MD, MPH; Maya M. Rao, MPH; Caleb D. Ebert, MPH; Hieu H. Nguyen, MS; Eric Kim, MA; Travis C. Porco, PhD, MPH; Nisha R. Acharya, MD, MS; for the FAST Research Group

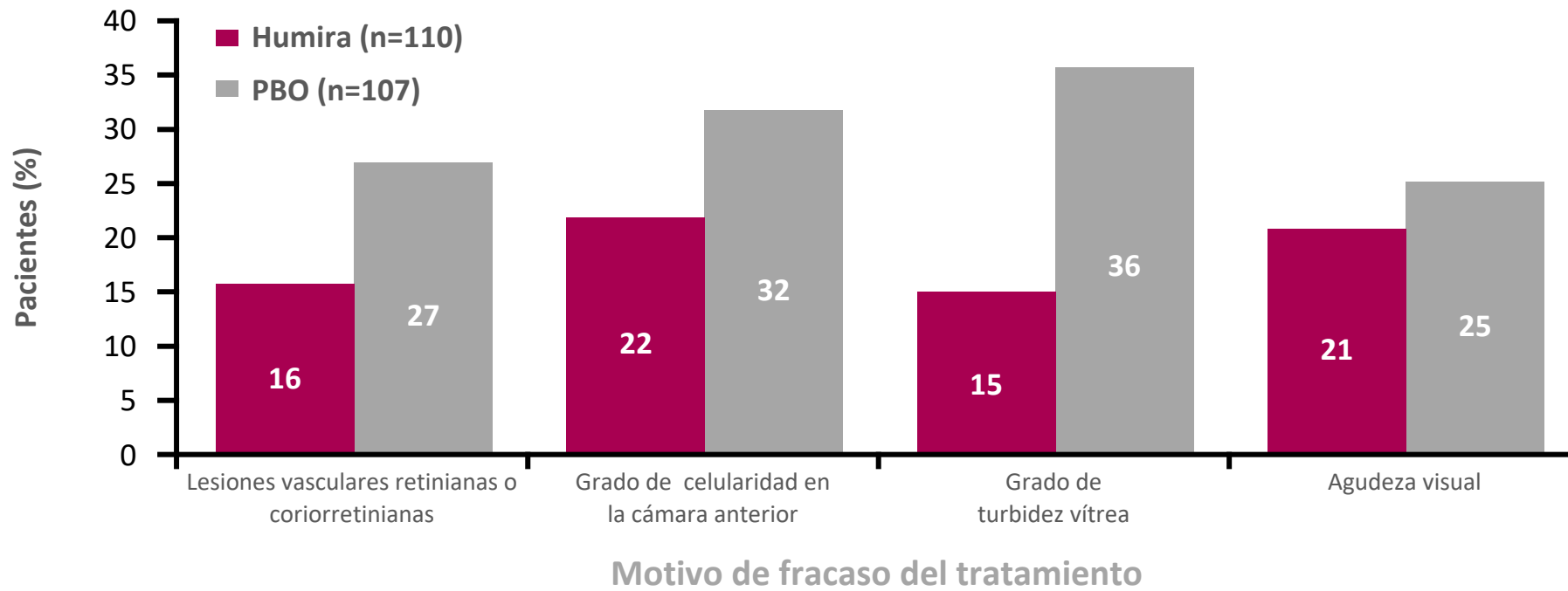
**Table 2. Six-Month Results From a Randomized Clinical Trial Comparing Methotrexate and Mycophenolate Mofetil for Noninfectious Uveitis**

Patient-Level Characteristics	Methotrexate (n = 96)	Mycophenolate Mofetil (n = 98) <sup>a</sup>	Absolute Risk Difference for Treatment Success, % (95% CI)	OR Estimate for Treatment Success (95% CI) <sup>b</sup>	P Value
<b>Primary Analysis</b>					
Treatment success, No. (%) <sup>c</sup>	64 (66.7)	56 (57.1)	9.5 (−5.3 to 21.8)	1.50 (0.81 to 2.81)	.20
Treatment failure, No. (%)	32 (33)	42 (43)			
<b>Secondary Analyses</b>					
Reason for treatment failure, no./No. (%)					
Efficacy <sup>c</sup>	26/32 (81)	38/42 (90)			.55
Intolerability <sup>d</sup>	3/32 (9)	2/42 (5)			
Safety <sup>e</sup>	3/32 (9)	2/42 (5)			
Treatment success by anatomical location, no./No. (%)					
Anterior uveitis and intermediate uveitis/ intermediate uveitis only	6/18 (33.3)	14/22 (63.6)	−30.3 (−51.6 to 1.1)	0.29 (0.08 to 1.05)	.07 <sup>f</sup>
Posterior uveitis/panuveitis	58/78 (74.4)	42/76 (55.3)	19.1 (3.6 to 30.6)	2.35 (1.16 to 4.90)	.02 <sup>f</sup>
Treatment success at 12 mo, no./No. (%)					
Continued on randomized antimetabolite <sup>g</sup>	48/60 (80)	40/54 (74)	5.9 (−12.2 to 17.0)	1.40 (0.57 to 3.56)	.47
Switched to other antimetabolite <sup>h</sup>	20/29 (69)	7/20 (35)	34.2 (6.6 to 52.6)	4.17 (1.32 to 13.16)	.02
Missed doses, mean (SD), % <sup>i</sup>	4.6 (1.0)	4.3 (0.5)			.87
<b>Eye-Level Characteristics</b>					
	<b>Methotrexate (n = 185 eyes)</b>	<b>Mycophenolate Mofetil (n = 181 eyes)</b>			<b>P Value<sup>k</sup></b>
Change in logMAR visual acuity, median (IQR) <sup>l</sup>	−0.10 (−0.32 to 0.00)	−0.12 (−0.31 to 0.00)			.83
Reduction in central macular thickness, median (IQR) [No., μm <sup>m</sup> ]	−26.00 (−89.00 to 5.00) [42]	−14.00 (−80.00 to 3.25) [55]			.95

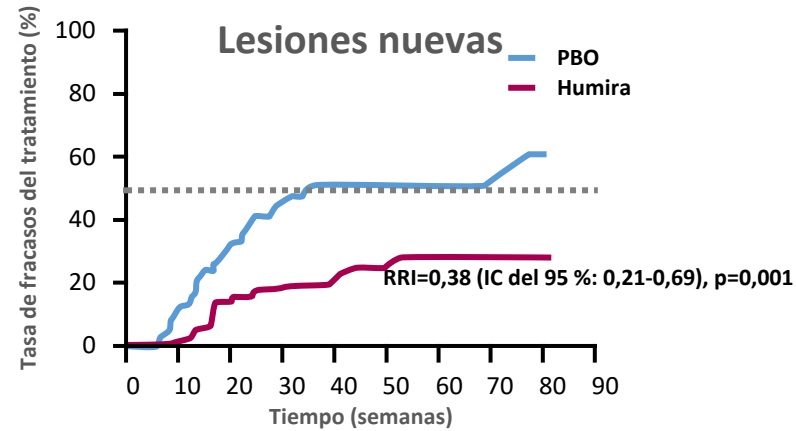
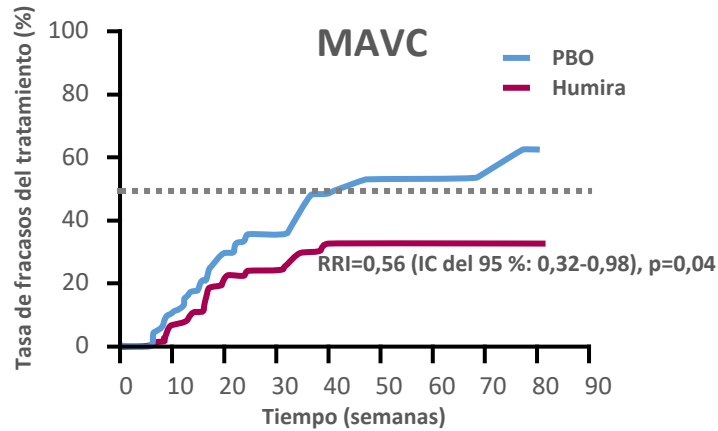
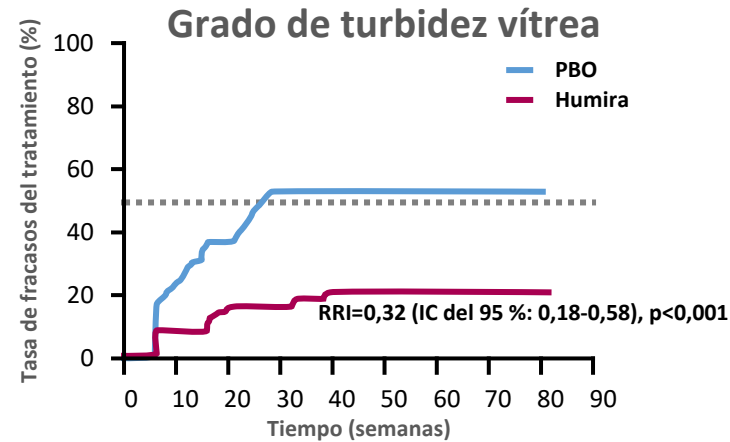
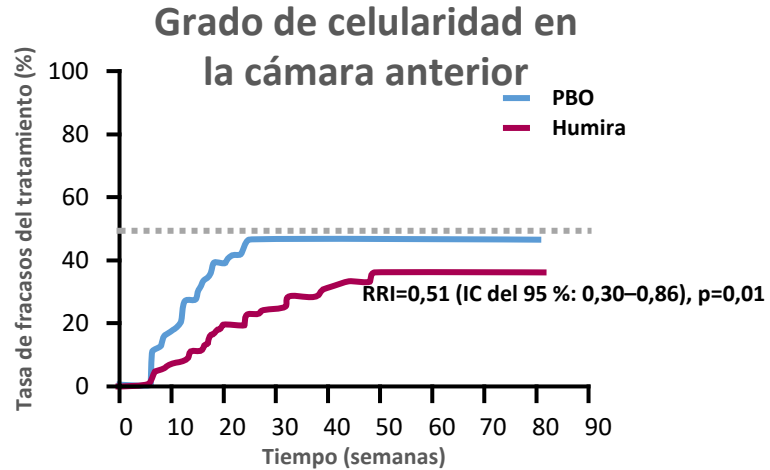
ORIGINAL ARTICLE

## Adalimumab in Patients with Active Noninfectious Uveitis

Adalimumab for prevention of uveitic flare in patients with inactive non-infectious uveitis controlled by corticosteroids (VISUAL II): a multicentre, double-masked, randomised, placebo-controlled phase 3 trial



# Componente del fracaso del tratamiento: criterio de valoración principal



Humira redujo significativamente el empeoramiento del grado de celularidad de la cámara anterior, el grado de turbidez vítrea, la MAVC y la aparición de lesiones nuevas.

\*Población ITT

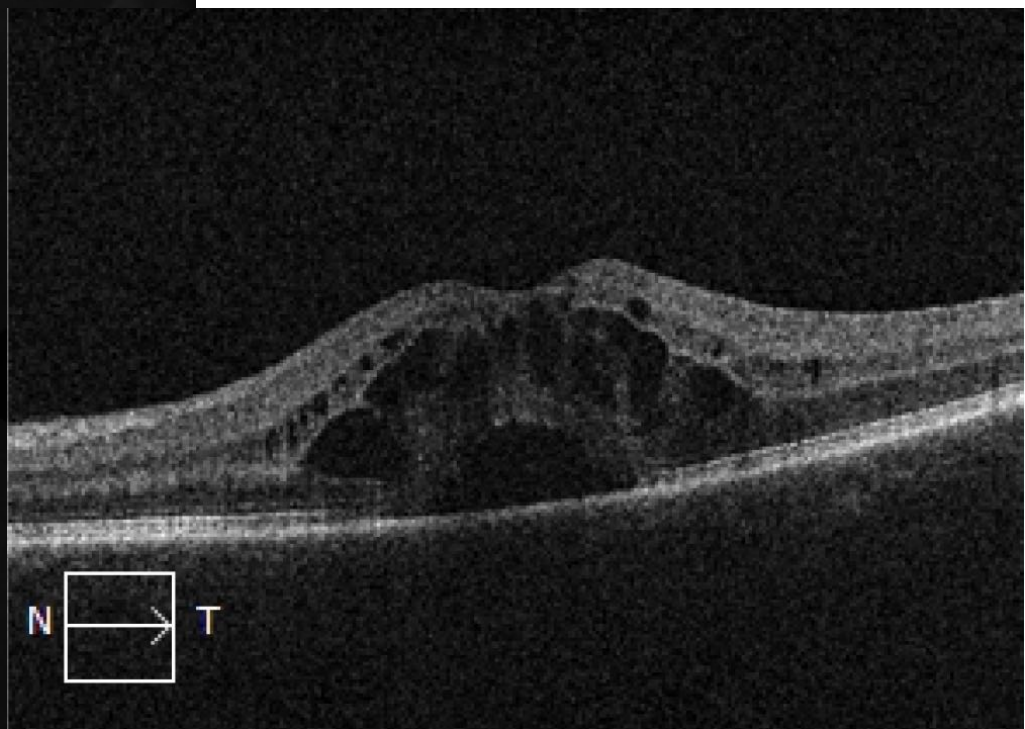
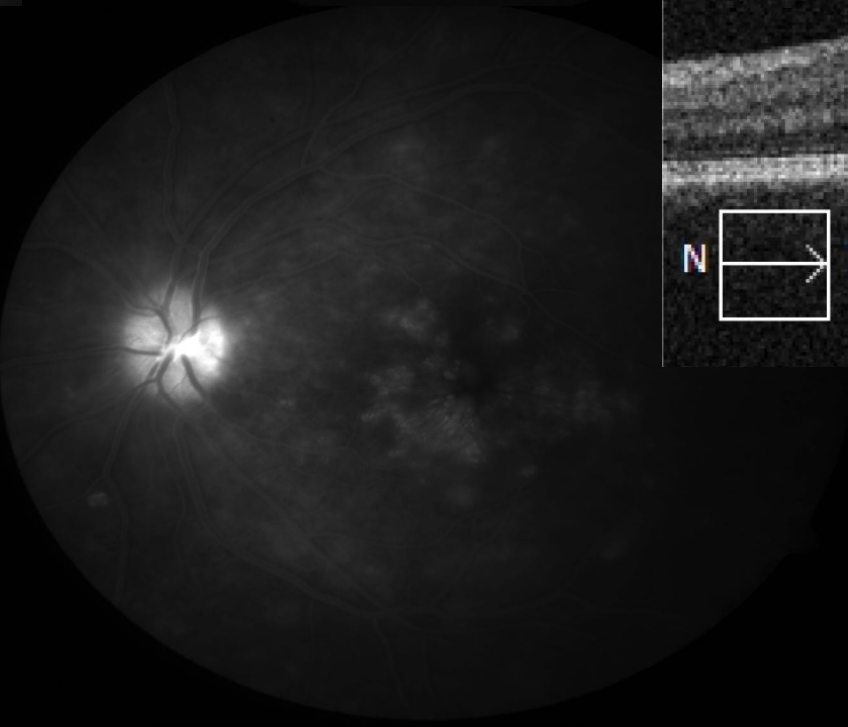
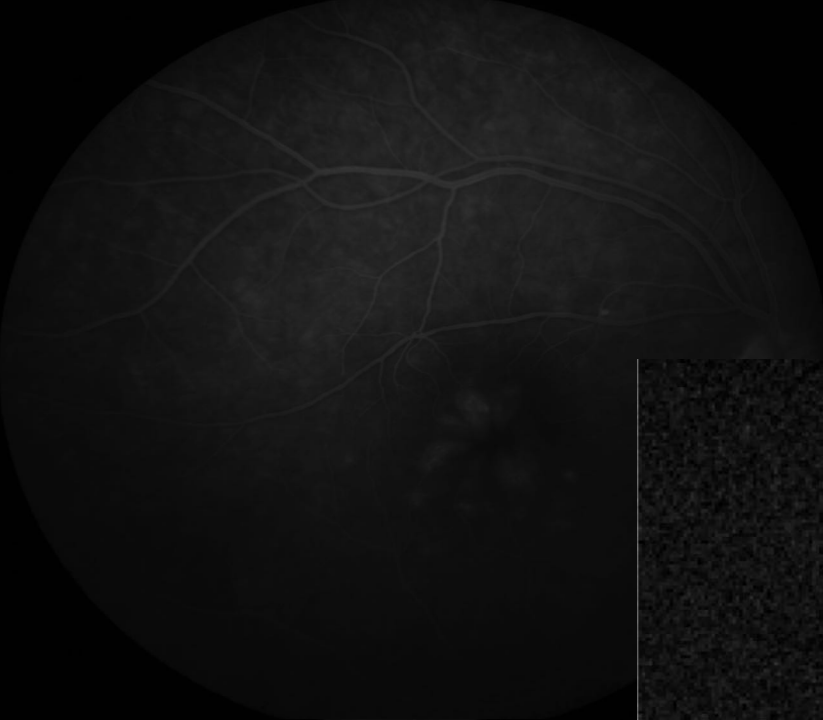
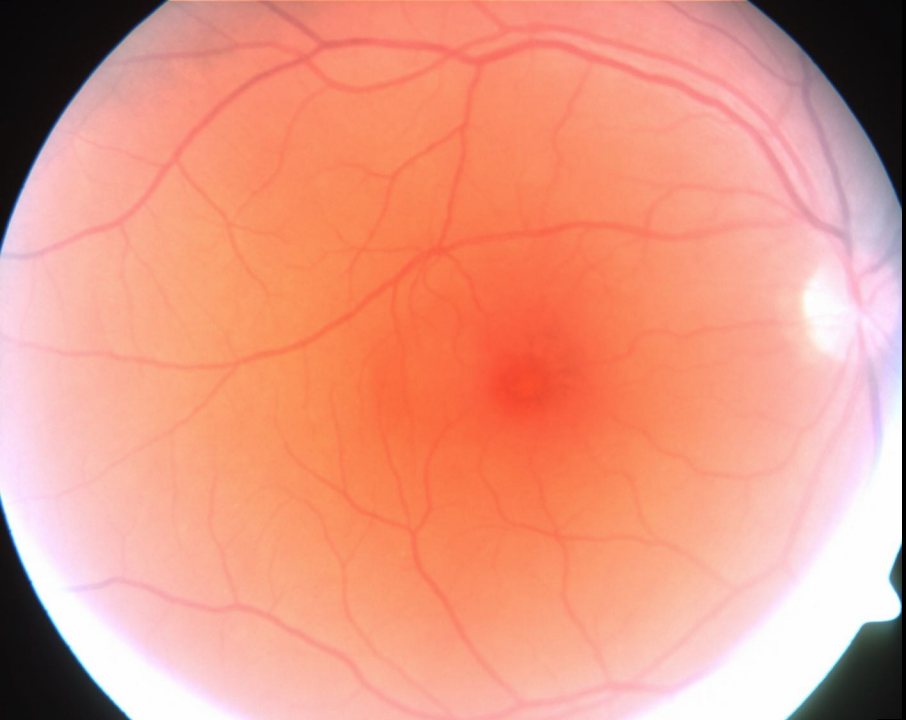


# Criterios de valoración secundarios ordenados especificados previamente (población ITT)

Variables secundarias ordenadas*	PBO (n=107)		Humira (n=110)		Valor de p
	n	Media	n	Media	
<b>1. Variación del grado de celularidad en la cámara anterior</b>					
Ojo izquierdo	102	0,59	101	0,35	
Ojo derecho	102	0,69	101	0,36	
Diferencia, media (IC del 95 %)		-0,29 (-0,51 a -0,07)			0,011 <sup>†</sup>
<b>2. Variación del grado de turbidez vítrea</b>					
Ojo izquierdo	103	0,33	101	0,11	
Ojo derecho	103	0,45	101	0,13	
Diferencia, media (IC del 95 %)		-0,27 (-0,43 a -0,11)			<0,001 <sup>†</sup>
<b>3. Variación de la MAVC, logMAR</b>					
Ojo izquierdo	103	0,12	101	0,07	
Ojo derecho	103	0,13	101	0,04	
Diferencia, media (IC del 95 %)		-0,07 (-0,11 a -0,02)			0,003 <sup>‡</sup>
<b>4. Tiempo hasta la aparición de signos de EMQ en la semana 6 o después (pacientes sin EMQ en el momento basal) [análisis especificado previamente]</b>					
Mediana	45	6,2	55	11,1	
RRI (IC del 95 %)		0,70 (0,39 a 1,26)			0,231 <sup>‡</sup>
<b>5. Variación porcentual del GRC [análisis especificado previamente]</b>					
Ojo izquierdo	100	20,2	100	9,6	
Ojo derecho	102	22,0	101	8,2	
Diferencia, media (IC del 95 %)		-11,4 (-20,9 a -1,8)			0,020 <sup>‡</sup>

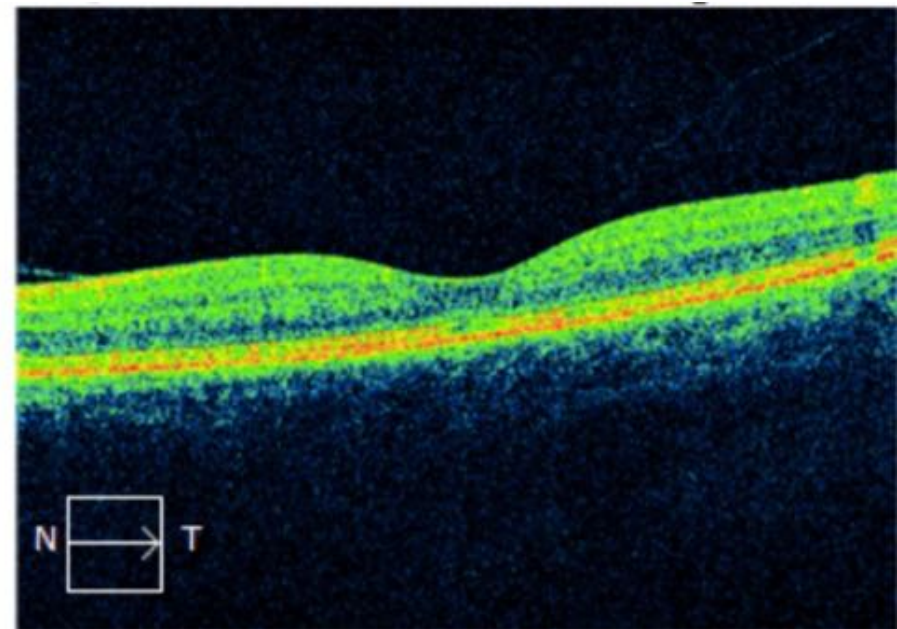
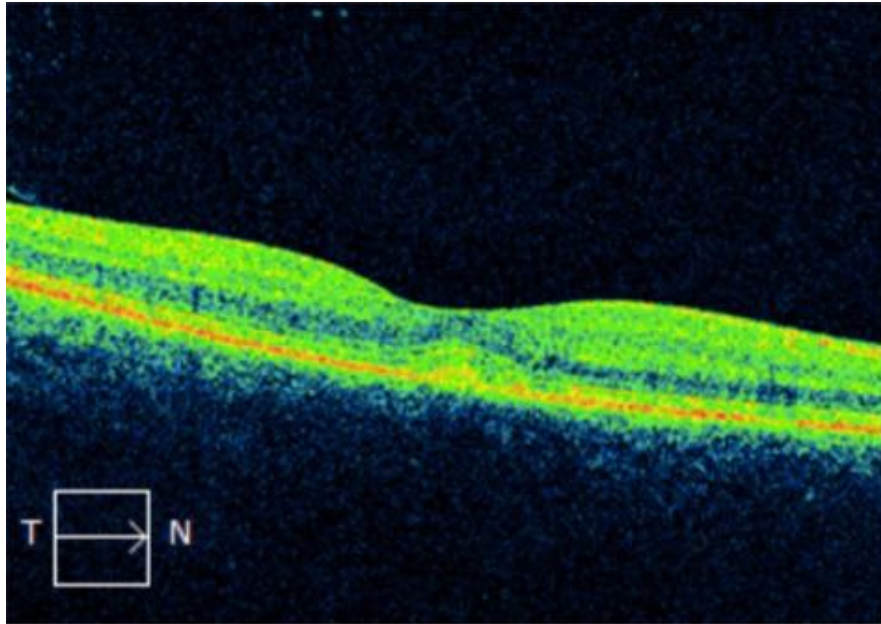
\*Salvo que se indique lo contrario, los datos reflejan la variación desde el mejor estado alcanzado antes de la semana 6 y la visita final o de suspensión preliminar; <sup>†</sup>Valor de p del análisis de la varianza con el tratamiento como factor y ajustado para las observaciones agrupadas; <sup>‡</sup>valor de p bilateral de la prueba del rango logarítmico

EMQ, edema macular quístico; GRC, grosor de la retina central  
Brezin A, et al. SOE 2015, Presentación oral FP-UVE0065.

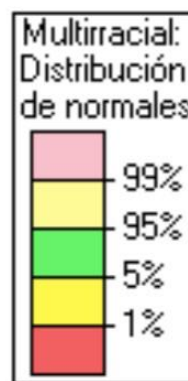
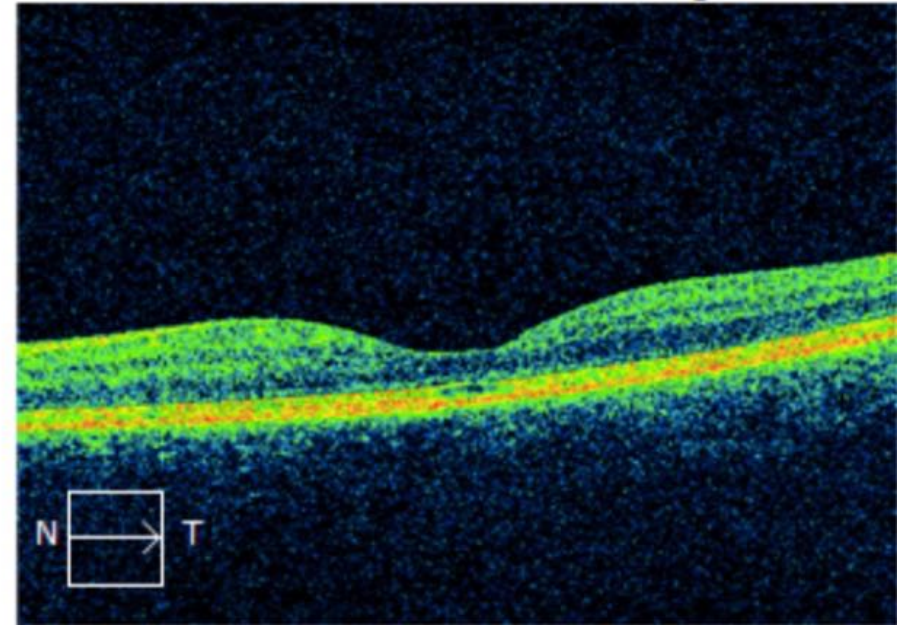
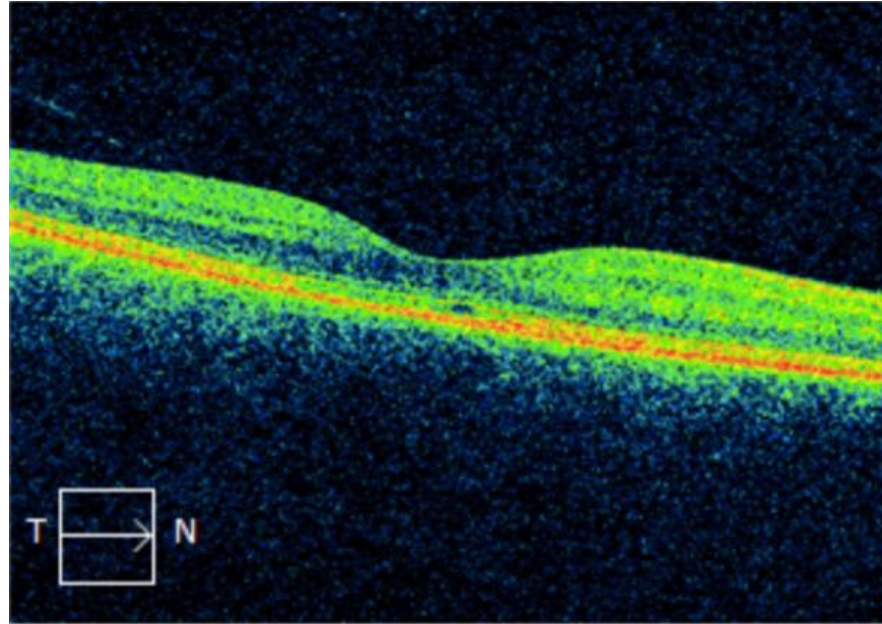


Edema refractario a:  
ADA  
ADA + Ozurdex  
ADA + CsA  
IFX + Tacrolimus

4 meses tras inicio de TCZ 8mg/4sem i.v.



# 10 meses tras TCZ



# Long-Term Effects of Tocilizumab Therapy for Refractory Uveitis-Related Macular Edema

ORIGINAL ARTICLE

## Tocilizumab in Uveitic Macular Edema Refractory to Previous Immunomodulatory Treatment

Christoph M.E. Deuter, MD<sup>1</sup>, Manfred Zierhut, MD<sup>1</sup>, Annette Igney-Oertel, MD<sup>2</sup>, Theodoros Xenitidis, MD<sup>2</sup>, Alexandra Feidt, MD<sup>1</sup>, Bianka Sobolewska, MD<sup>1</sup>, Nicole Stuebiger, MD<sup>3</sup>, and Deshka Doycheva, MD<sup>1</sup>

Marina Mesquida, MD,<sup>1</sup> Blanca Molins, PhD,<sup>2</sup> Victor Llorenç, MD, PhD,<sup>1</sup> Maite Sainz de la Maza, MD, PhD,<sup>1</sup> Alfredo Adán, MD, PhD<sup>1</sup>

Table 1. Patient Characteristics, Previous Treatments, and Response to Tocilizumab Therapy

### Anti-IL6-Receptor Tocilizumab in Refractory and Noninfectious Uveitic Cystoid Macular Edema: Multicenter Study of 25 Patients

NURIA VEGAS-REVENGA, VANESA CALVO-RÍO, MARINA MESQUIDA, ALFREDO ADÁN, MARÍA VICTORIA HERNÁNDEZ, EMMA BELTRÁN, ELIA VALLS PASCUAL, DAVID DÍAZ-VALE, GISELA DÍAZ-COROVÉS, MARISA HERNANDEZ-GARFELLA, LUCÍA MARTÍNEZ-COSTA, INMACULADA CALVO, ANTONIO ATANES, LUIS F. LINARES, CONSUELO CARRASCO-CUBERO, CARMEN GONZÁLEZ-VELA, ROSALÍA DEMETRIO-PABLO, ELENA AURRECOECHEA, LUCÍA C. DOMÍNGUEZ-CASAS, BELÉN ATIENZA-MATEO, JOSÉ LUIS MARTÍN-VARILLAS, NATALIA PALMOU-FONTANA, JOSÉ L. HERNÁNDEZ, MIGUEL A. GONZÁLEZ-GAY, RICARDO BLANCO



Patient	Follow-up with Tocilizumab (mos)	Central Foveal Thickness (µm)					Best-Corrected Visual Acuity*			
		Baseline	1 Mo	3 Mos	6 Mos	12 Mos	Baseline	3 Mos	6 Mos	12 Mos
14	14	424	234	277	197	221	0.8	0.7	0.5	0.5
18	18	896	524	182	176	163	2	2	2	2
16	16	500	313	408	345	254	0.4	0.4	0.2	0.2
16	16	260	243	247	246	230	0.3	0.3	0.2	0.2
15	15	590	469	324	320	351	0.3	0.3	0.4	0.3

RHEUMATOLOGY

Original article

doi:10.1093/rheumatology/kex480

### Anti-interleukin 6 receptor tocilizumab in refractory uveitis associated with Behçet's disease: multicentre retrospective study

Belén Atienza-Mateo<sup>1,\*</sup>, Vanesa Calvo-Río<sup>1,\*</sup>, Emma Beltrán<sup>2</sup>, Lucía Martínez-Costa<sup>3</sup>, Elia Valls-Pascual<sup>3</sup>, Marisa Hernández-Garfella<sup>2</sup>, Antonio Atanes<sup>4</sup>, Miguel Cordero-Coma<sup>5</sup>, Joan Miquel Nolla<sup>6</sup>, Carmen Carrasco-Cubero<sup>7</sup>, Javier Loricera<sup>1</sup>, María C. González-Vela<sup>1</sup>, Nuria Vegas-Revenga<sup>1</sup>, Carlos Fernández-Díaz<sup>1</sup>, Rosalía Demetrio-Pablo<sup>1</sup>, Lucía C. Domínguez-Casas<sup>1</sup>, José Luis Martín-Varillas<sup>1</sup>, Natalia Palmou-Fontana<sup>1</sup>, José L. Hernández<sup>8,†</sup>, Miguel Á. González-Gay<sup>1,†</sup> and Ricardo Blanco<sup>1,†</sup>

10	7	F/24	JIA	14	PDN, CyA, MTX, ADA, RTX	No
11	7	F/24	JIA	14	PDN, CyA, MTX, ADA, RTX	No

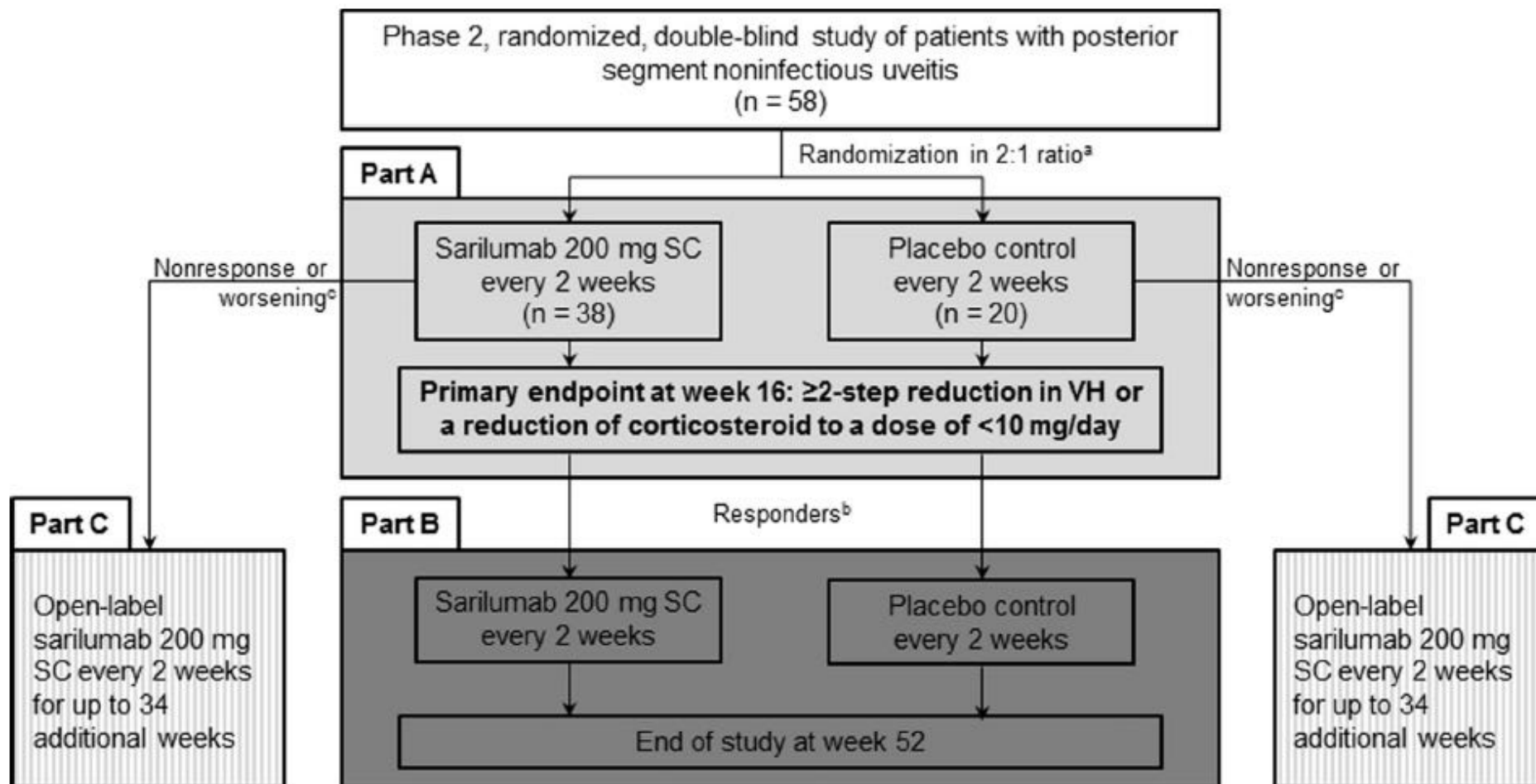
ABT = abatacept; ADA = adalimumab; CyA = cyclosporine A; F = female; prednisone; RTX = rituximab.

\*Logarithm of the minimum angle of resolution units.

# Efficacy and Safety of Sarilumab for the Treatment of Posterior Segment Noninfectious Uveitis (SARIL-NIU):

## The Phase 2 SATURN Study

Jarmila Heissigerová, MD, PhD,<sup>1</sup> David Callanan, MD,<sup>2</sup> Marc D. de Smet, MD, PhD,<sup>3</sup> Sunil K. Srivastava, MD,<sup>4</sup> Michala Karkanová, MD,<sup>5</sup> Olga Garcia-Garcia, MD, PhD,<sup>6</sup> Sibel Kadayifçilar, MD,<sup>7</sup> Yilmaz Orzyazgan, MD,<sup>8</sup> Robert Vitti, MD,<sup>9</sup> Kristine Erickson, OD, PhD,<sup>9</sup> Aditya Athanikar, MD,<sup>9</sup> Karen Chu, MS,<sup>9</sup> Namrata Saroj, OD,<sup>9</sup> Preethi A. Sundaram, PhD,<sup>10</sup> Rafael Varona, MD,<sup>10</sup> Valerie Corp-dit-Genti, MS,<sup>10</sup> Ronald Buggage, MD,<sup>10</sup> Yenchieh Cheng, PhD,<sup>9</sup> Yuhwen Soo, PhD,<sup>9</sup> Quan Dong Nguyen, MD, MSc<sup>11</sup>



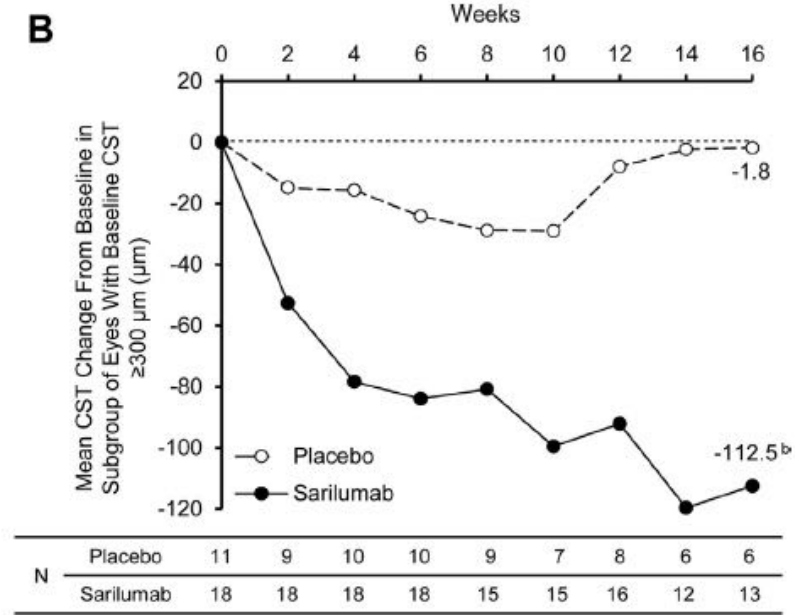
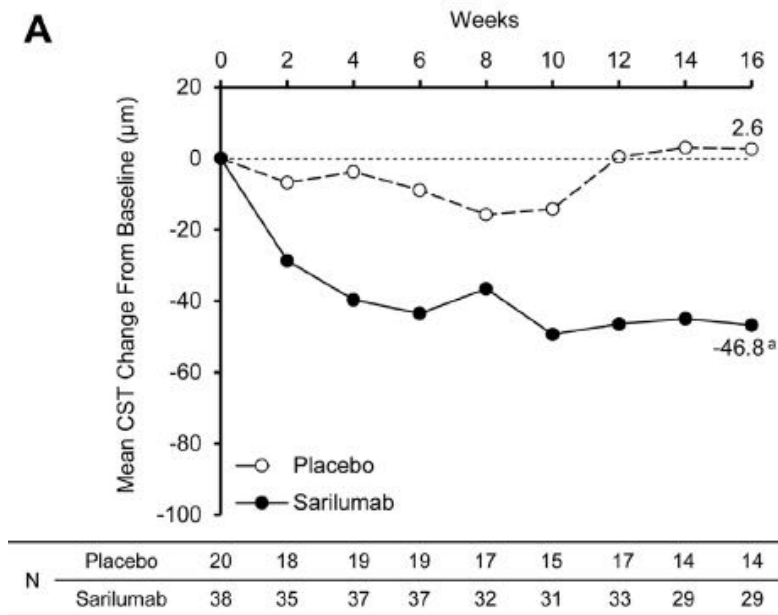
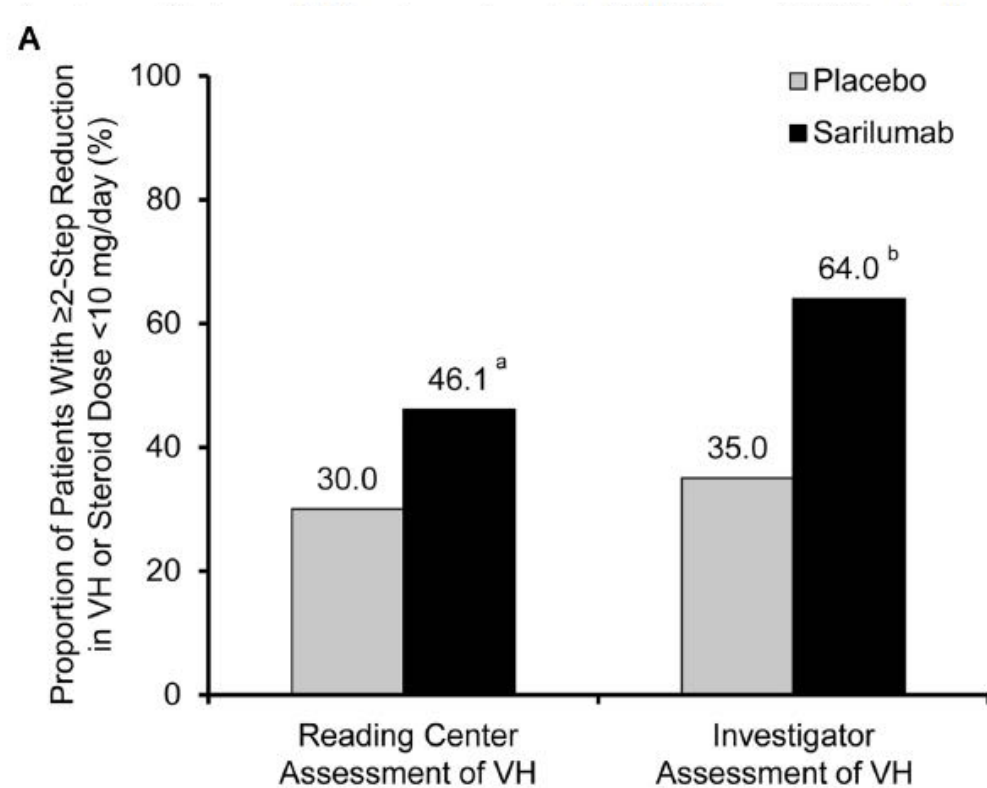
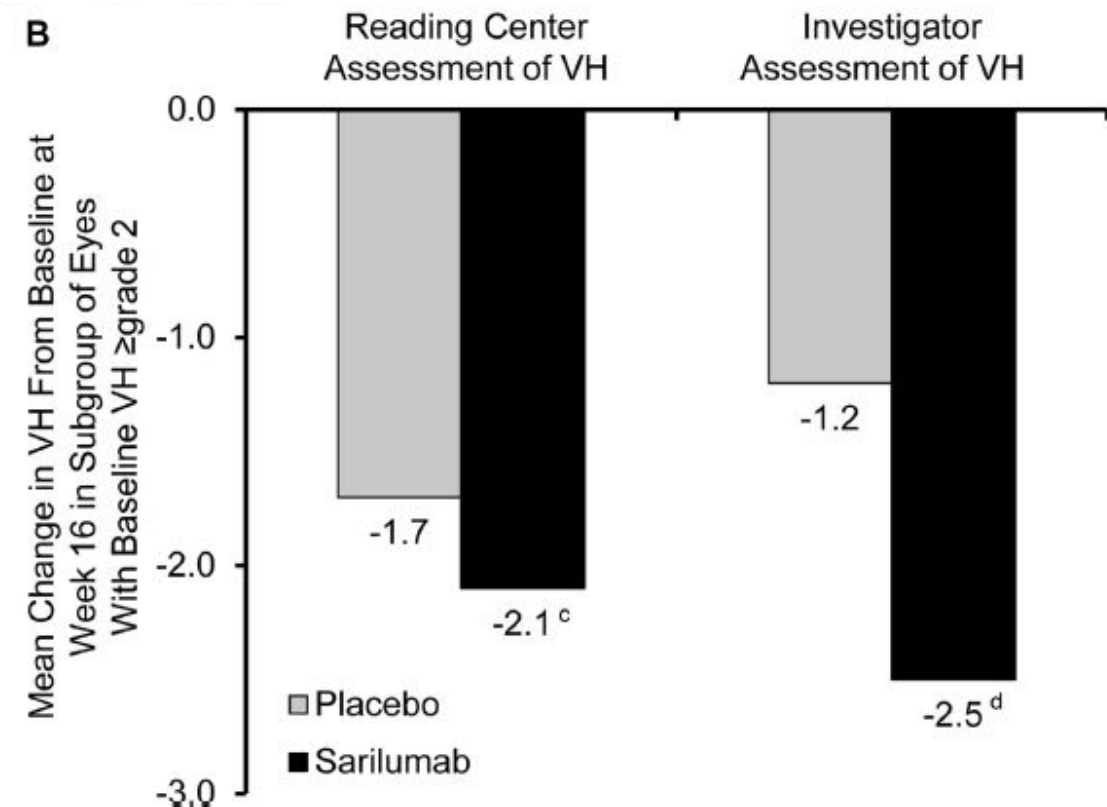


Figure 4. Anatomical Mean changes in visual hypermetropia (VH) in placebo. Modified from [1].



rough week .0683 and <sup>b</sup>



# PERFIL CLÍNICO

- Diversas cuestiones (burocráticas, legales, enfermedades asociadas del paciente, edad...) a tener en cuenta previamente.
- Predominio celularidad (vítrea/CA): ADA
- Predominio Edema Macular: TCZ
- ¿Predominio Vasculitis retiniana: IFX?



# Conclusiones

- Las NINA suponen uno de los grupos más heterogéneos de enfermedades inmunomediadas. Exigen individualización.
- No obstante, hay datos que nos permiten diagnosticar y tomar decisiones cada vez más fundamentadas y ajustadas al paciente
- Las decisiones basadas en cada vez más datos, y algoritmos que los tengan en cuenta, serán más probablemente acertadas.
- La evidencia en el tratamiento de las uveítis NINA es escasa.