

# Abordaje del paciente moderado: en busca de la ventana de oportunidad

-A propósito de un caso -



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Hospital Universitario Nacional de Colombia***



Canalde Youtube “william otero gastroenterologo”

# Historia clínica

Hombre de 30 años

Natural y procedente: Bogotá D.C

**MC:** *“Perdida de peso”*

**EA:** Inició un año antes (2012) con diarrea sanguinolenta (heces Bristol 6, 7), dolor abdominal, pérdida de peso (14 kg), palidez, astenia, no fiebre. Extra-institucional colitis ulcerativa y anemia secundaria. Manejado con hierro parenteral, transfusiones y mesalazina oral 3gr/día

# Antecedentes

**Acné**

**No cirugías**

**No alergias, no tóxicos**

**Familiares: Familiar de segundo grado colitis ulcerativa**

**Revisión de síntomas por sistemas: lo referido en enfermedad actual**

# Examen físico

**PA 100/70, T 36.3°C, FC 96 X` FR 14 X`**

**Peso 66 Kg Talla 178 cm IMC 20.8**

**CP: normal.**

**Abdomen normal.**

**Tacto rectal normal.**

**Neurològic normal.**

# Laboratorios

Hemograma: leucocitos , plaquetas normales

***Hb 7.8gr, Hcto 29% VCM 65fl, HCM 20pg***

**Ferritina 6.7 ng/mL, Hierro sérico 8 ng/mL**

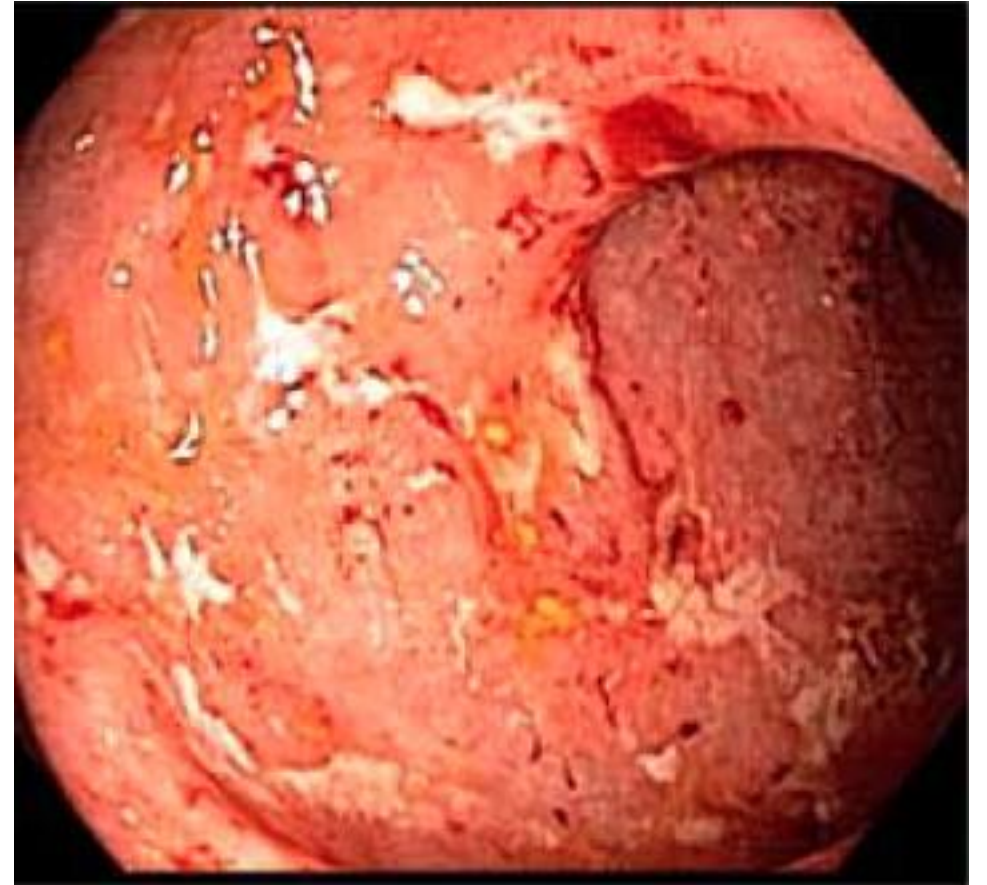
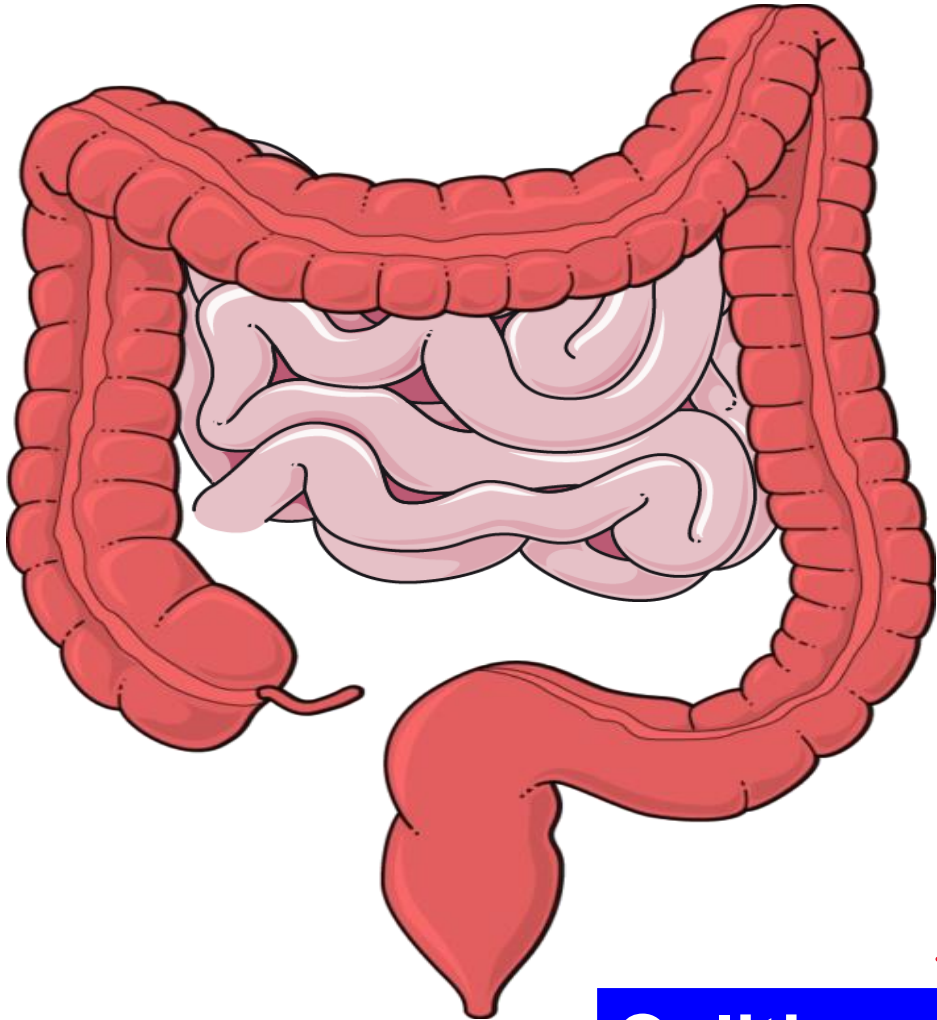
Perfil hepático normal.

Calprotectina 600 mcg/gr

Creatinina normal.

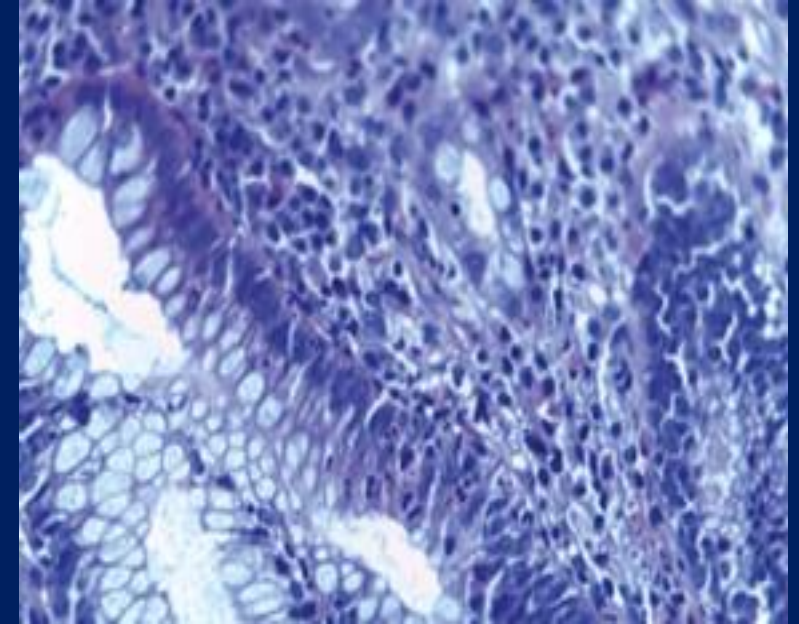
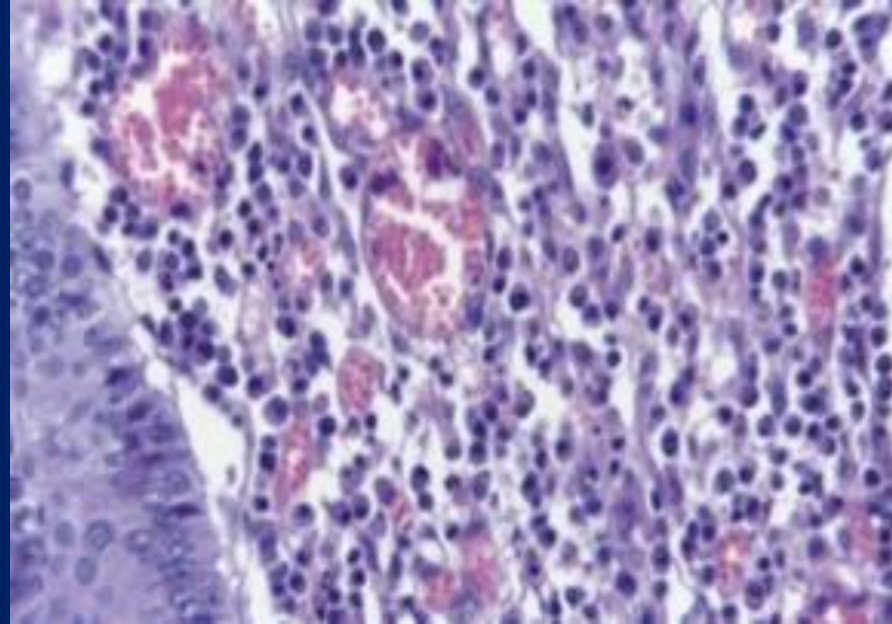
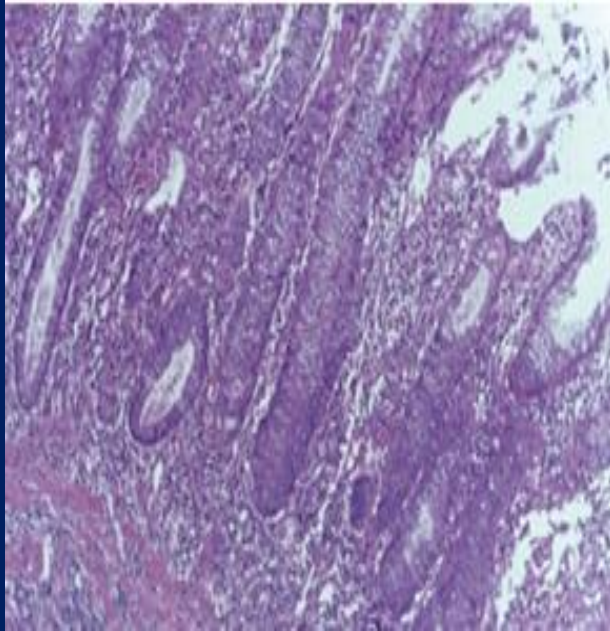
Colesterol triglicéridos, glicemia normales

# Colonoscopia Total



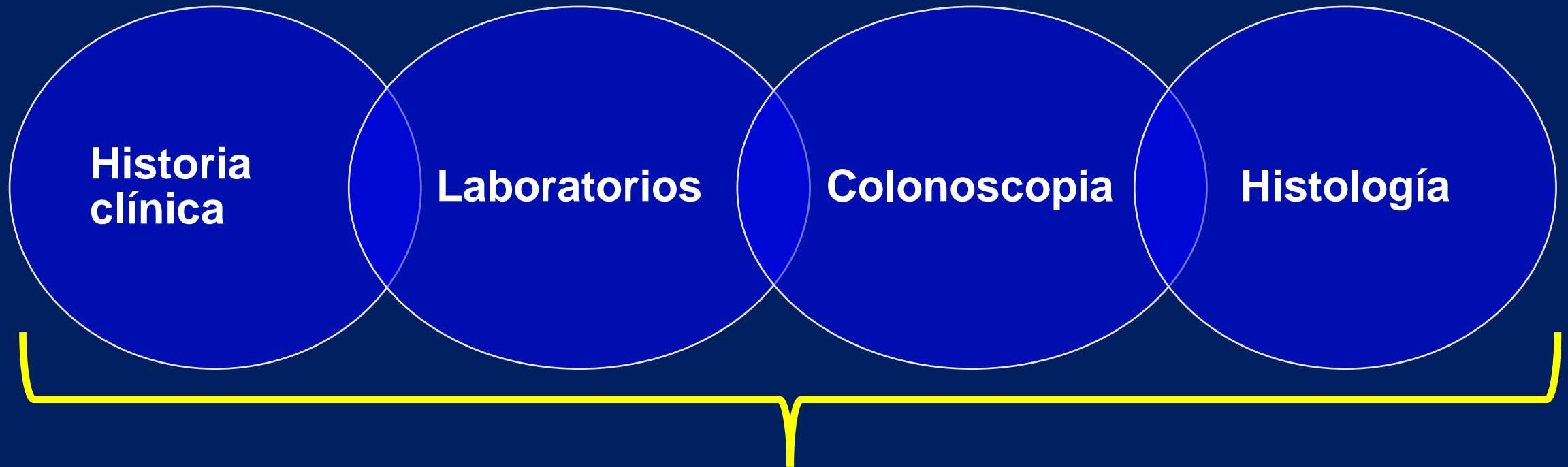
**Colitis extensa score endoscópico Mayo 3**

# Histología



**Criptas hiperplásicas, con gemación, infiltrado inflamatorio linfoplasmocitario escasos neutrófilos, microabscesos cripticos**

# Diagnóstico

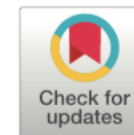


1. **Colitis ulcerativa con actividad moderada severa Montreal E3S3**
2. **Anemia ferropénica severa secundaria a colitis ulcerativa**



ARTÍCULO ORIGINAL

# Validación de un nuevo índice integral de enfermedad para evaluar el grado de actividad en pacientes mexicanos con colitis ulcerosa: un estudio de cohorte prospectivo



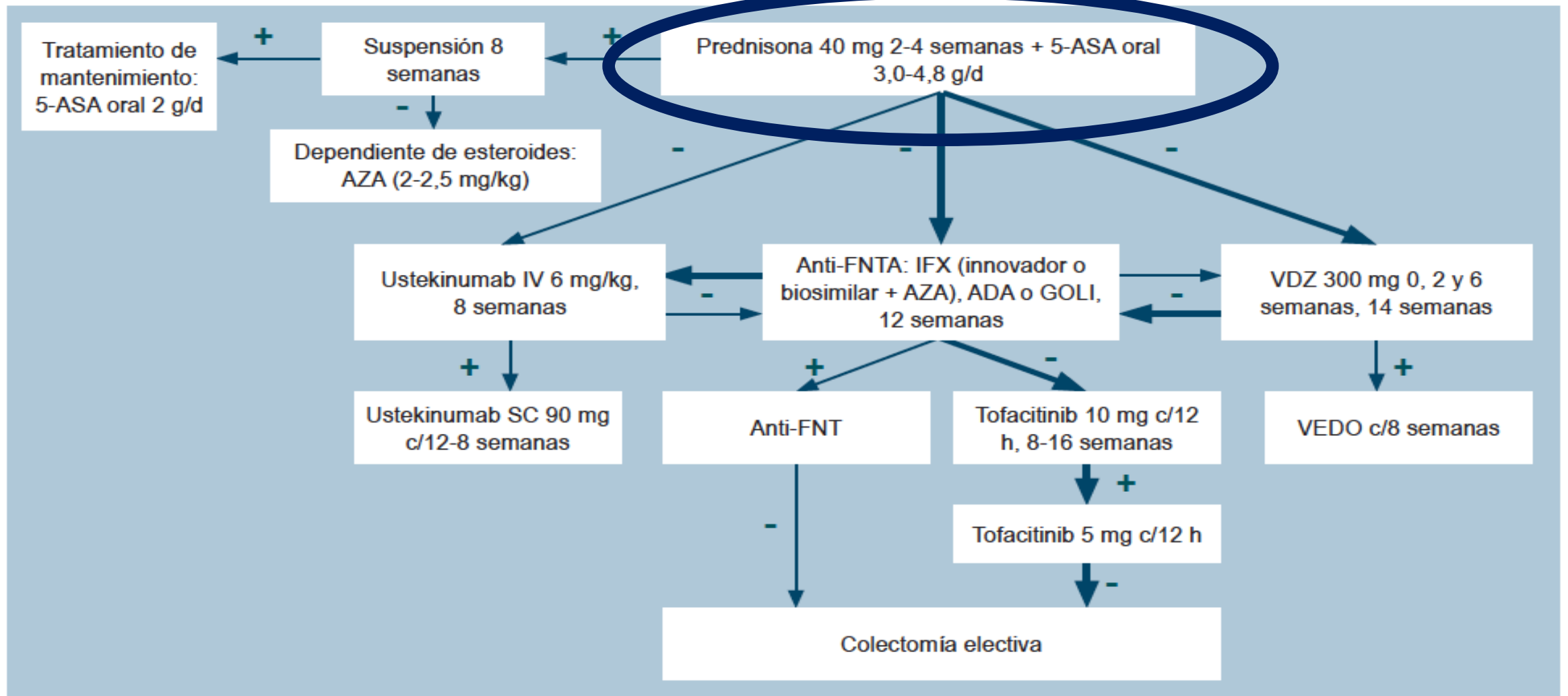
J.K. Yamamoto-Furusho<sup>a,\*</sup>, K.E. Bozada-Gutiérrez<sup>a</sup>, A. Sánchez-Rodríguez<sup>b</sup>,  
F. Bojalil-Romano<sup>a</sup>, R. Barreto-Zuñiga<sup>c</sup> y B. Martínez-Benitez<sup>d</sup>

**Table 1** Novel integral disease index of UC activity (NIDI) or Yamamoto-Furusho Index.

Disease Activity	Number of bloody stools per day	Hemoglobin	hs-CRP	Albumin	Endoscopic findings	Histopathologic findings
0 Remission	Usual (no blood)	> 12	≤0.20	≥3.5	Normal mucosa	Normal
1 Mild	2-3	12 to 10	0.21- 0.35	3.4-3.0	Erythema, decreased vascular pattern, mild friability	Mild activity
2 Moderate	4-6	9.9 to 8	0.36-1.0	2.9-2.5	Marked erythema, absent vascular pattern, friability and erosions	Moderate activity
3 Severe	> 6	< 8	> 1.0	< 2.5	Spontaneous bleeding and ulcerations	Intense Activity

# Tratamiento

## Colitis ulcerativa izquierda o extensa activa moderada-grave



# Tratamiento

Se ordenó hospitalización , el paciente y su familia prefirieron “esperar la evolución”

Prednisona 40mg/día

5-ASA oral gránulos 3gramos/día

Enemas 4 gramos

Empíricamente metronidazol 500 mg C/8 h  
por la sospecha de *C.difficile*

# Pruebas complementarias

Prueba de tuberculina

Rx Tòrax

Anticitomegalovirus

Anti hepatitis C

VIH

EBV

HBsAg, Anti-Core Total

Ac Anti-superficie

Toxinas A y B Cd

# Evolución

6 semanas  
1 Deposición Bristol 3-4  
No sangrado  
No urgencia

5- ASA oral y tópica  
Retiro gradual prednisolona

Hb 13gr, VSG 16  
PCR 0,3mg/dL  
Albumina 4g/L  
Calprotectina 100

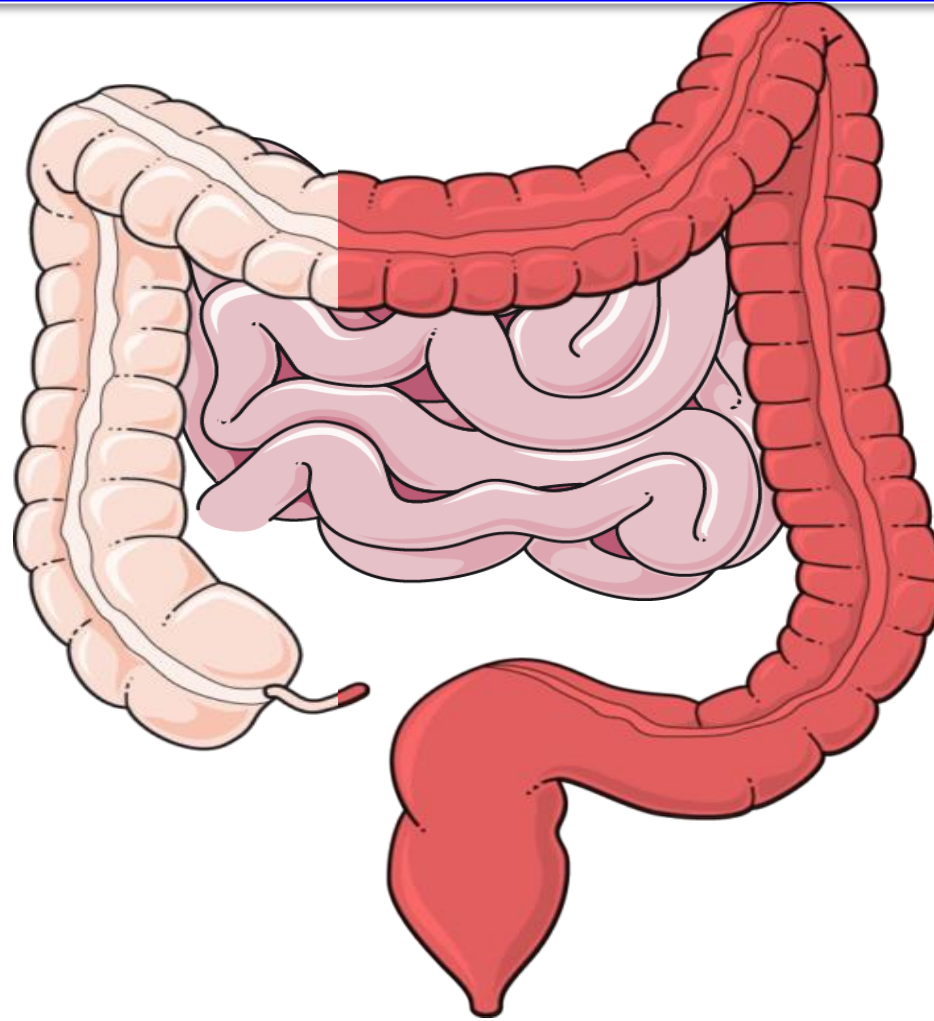
3 meses recurrencia  
de síntomas

Peso 72kg

Sangrado intermitente  
Hb 12gr  
Calprotectina fecal 250mcg/gr



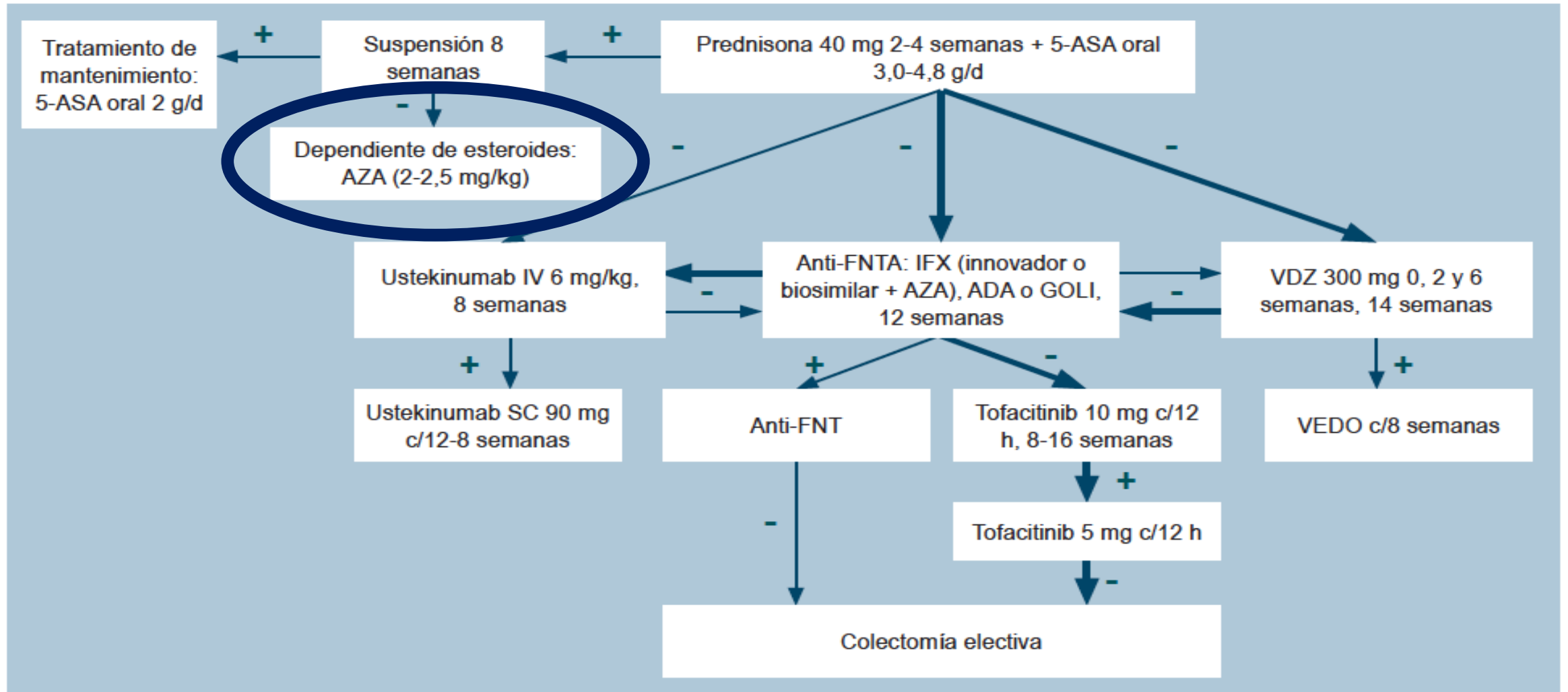
# Colonoscopy



**Colitis ulcerativa E3 S2**

# Tratamiento

## Colitis ulcerativa izquierda o extensa activa moderada-grave



# Evolución



**Remisión clínica durante 8 semanas**

# Evolución

Cuadro 10 días  
5-6 deposiciones  
Bristol 6-7

Dolor abdominal

Sangrado  
incontinencia de urgencia



Peso 71,5kg  
FC 86 FR 16 T 37°C  
Hb 11gr

**Recaída de colitis ulcerativa actividad moderada (Truelove)**

# Evolución

Prednisolona 40mg/día  
Azatioprina 150mg/día  
5-ASA oral 3gramos  
Descarta infección

No asiste a control

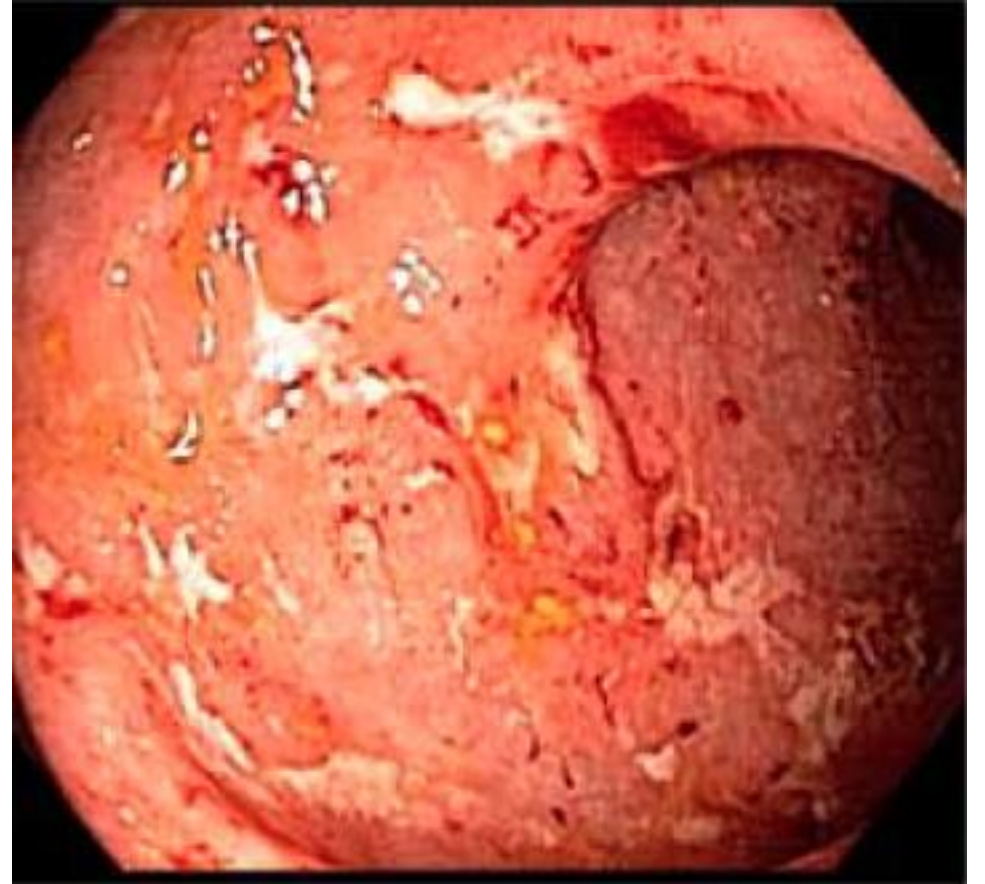
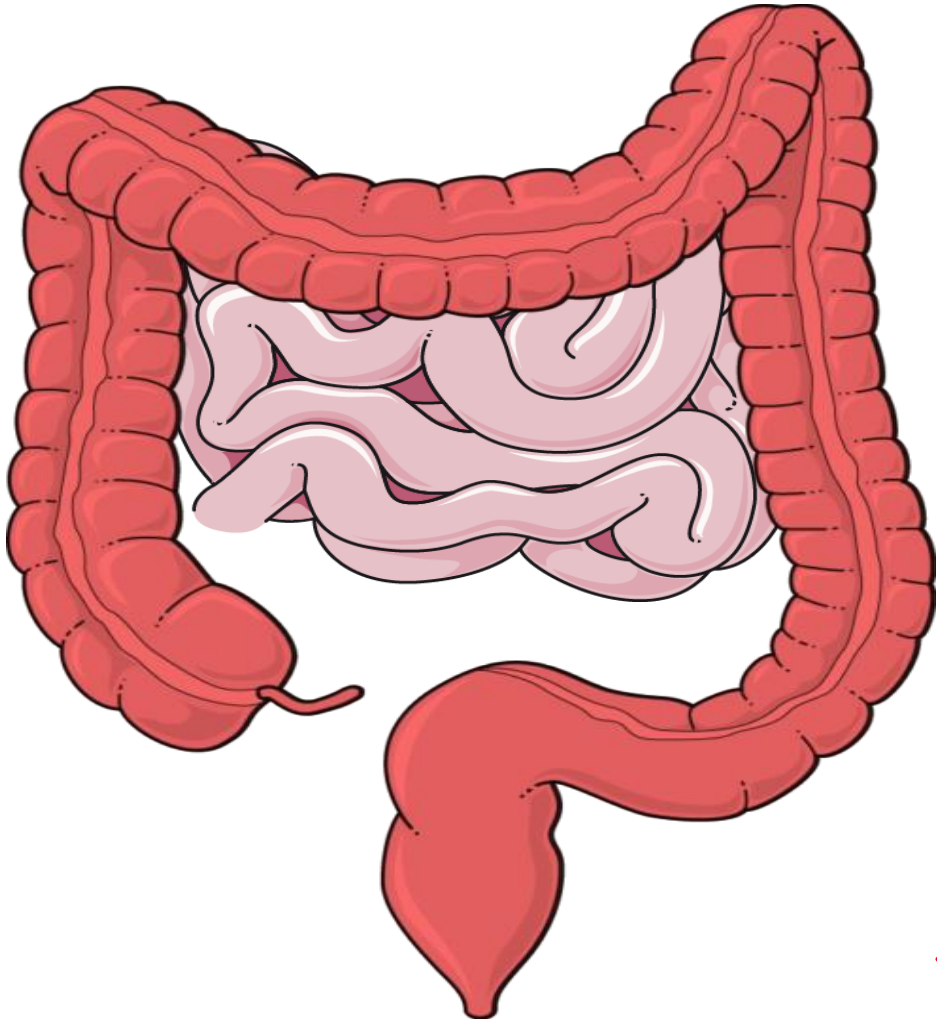
Hb 11.6gr  
Gestión de riesgo  
Control endoscópico



Disminución síntomas  
Disminución prednisolona

Asiste a los 5 meses  
Prednisolona 20mg/día  
Azatioprina 150mg/día  
5-ASA oral 3gramos

# Colonoscopy



Colitis ulcerativa E3 S2 score endoscópico Mayo 3

# Seguimiento

HBsAg

no reactivo

**Colitis ulcerativa dependiente de esteroides**

**Vedolizumab (No fue aprobado)**

**Se Inició de infliximab 5mg/kg semana 0,2 y 6, cada 8**

**Azatioprina 150mg/día**

VIH

Negativo

PPD

Negativa

Rx de tórax

Normal

# Evolución

Remisión clínica  
15 meses CON  
Infliximab

Colonoscopia  
Actividad en recto-  
sigmoides

Actividad de la enfermedad  
< 2kg, Hb 9gr CF 400mcg/gr

Descartar infecciones  
Mesalazina espuma



*Perdida de respuesta a  
Anti TNF*



*Cambio de antiTNF ?*





***Medición de niveles Infliximab  
Y anticuerpos neutralizantes***



***Cambio de blanco terapéutico  
Farmacodinamia***

# Infliximab Activity and Neutralizing Antibody

ARUP test code 2008320

## Infliximab Activity

16.25 ug/mL

### INTERPRETIVE INFORMATION: Infliximab Activity and Neutralizing Ab

This test measures the capacity of infliximab to neutralize TNF-alpha activity. Additionally, infliximab neutralizing antibodies (NAB) are titered (reporting the highest dilution of patient sera in which NAB activity is detected).

This test is used to evaluate secondary response failures to infliximab therapy. Secondary response failure is defined as loss of clinical response after initial improvement of clinical signs and symptoms. Therapeutic decision should rest on both the clinical response and the knowledge of the fate of the drug including the emergence of immunogenicity in individual patients.

Circulating infliximab levels have been shown to vary considerably between patients. These differences relate to route and frequency of administration and patient-related features such as age, gender, weight, drug metabolism, and concomitant medications such as methotrexate and other immunosuppressants.

Infliximab Activity	Infliximab Neutralizing Ab. Titer	Interpretation
Not Detected	Not Detected	A higher dosage of infliximab or shortening the dosing interval may be appropriate.
Not Detected	1:20 or greater	A change to another anti-TNF-alpha drug may be appropriate.
0.65 ug/mL or greater	Not Detected	A change to another type of therapy (not targeting TNF-alpha) may be appropriate.
0.65 ug/mL or greater	1:20 or greater	Repeat testing is suggested to rule out decreasing infliximab activity and/or increasing infliximab neutralizing antibodies.

Not Detected

(Ref Interval: Not Detected)

See Note

Access ARUP Enhanced Report using either link below:

H - high

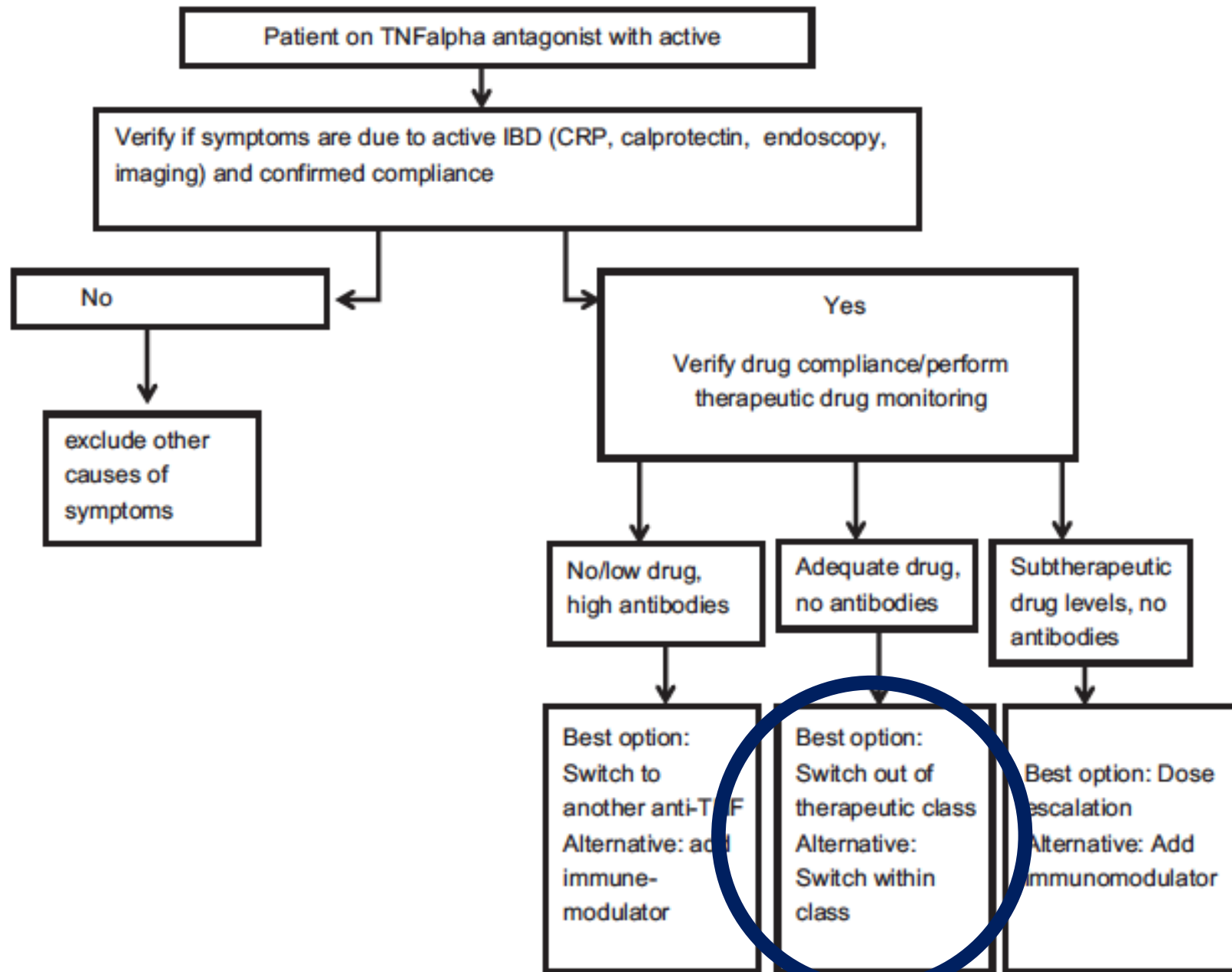
L - low

\* - abnormal

C - critical

Niveles 6-10 mcg  
Remisión endoscópica 80%  
12-15mcg > remisión  
endoscópica-histológica

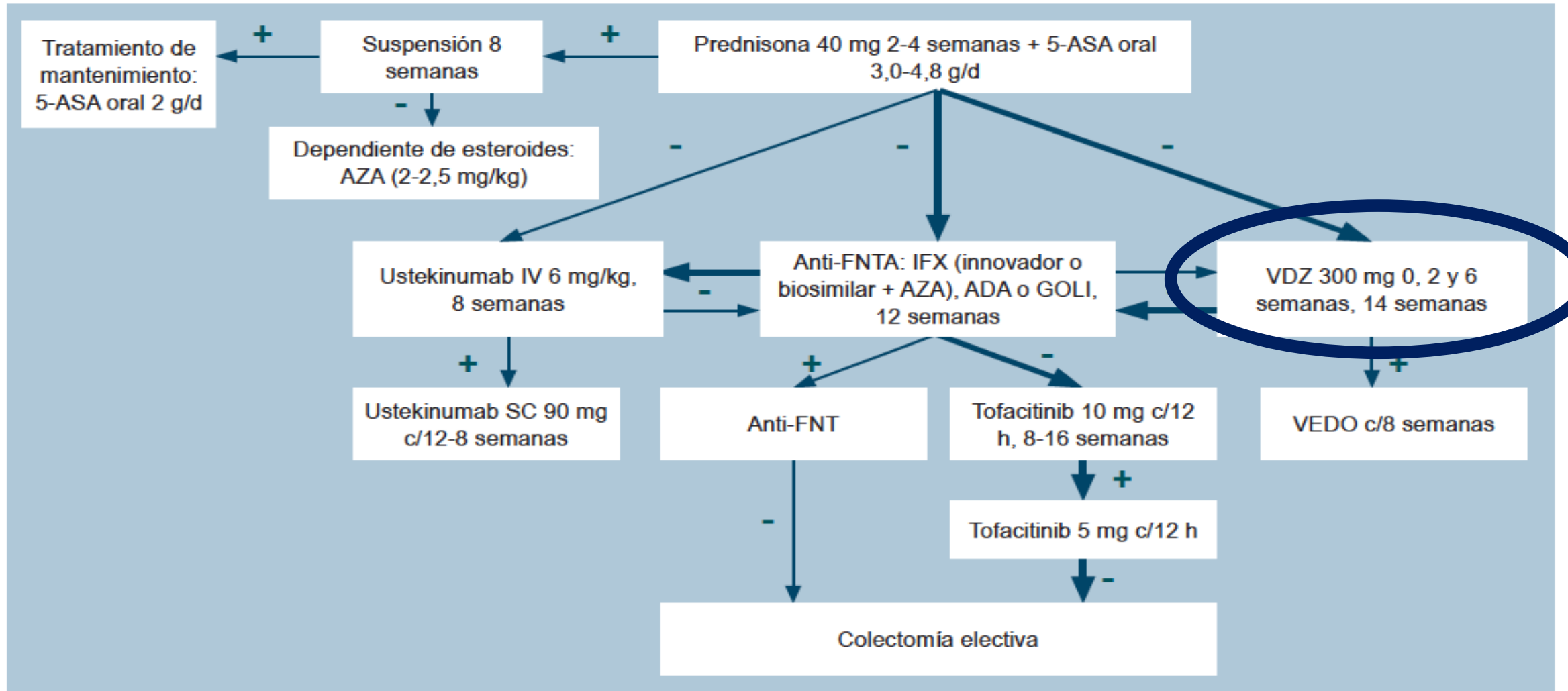
Año 2016



**Figure 1** Management of patients with LOR. CRP, C reactive protein; LOR, loss of response.

# Tratamiento

## Colitis ulcerativa izquierda o extensa activa moderada-grave



**Vedolizumab Cu-EC Moderada – Severa  
300 mg IV 0-2-6 semanas- C/ 8 semanas**

**Respuesta  
Inadecuada  
Terapia  
convencional**

**Pérdida Respuesta  
Inmunosupresores  
Anti TNF**

**Problemas  
Seguridad**

**Entyvio, EMA 2019**

# Evolución

Vedolizumab  
300mg cada  
8 semanas

Azatioprina  
100mg/día  
Fue  
Suspendida

5-ASA Oral  
3gramos

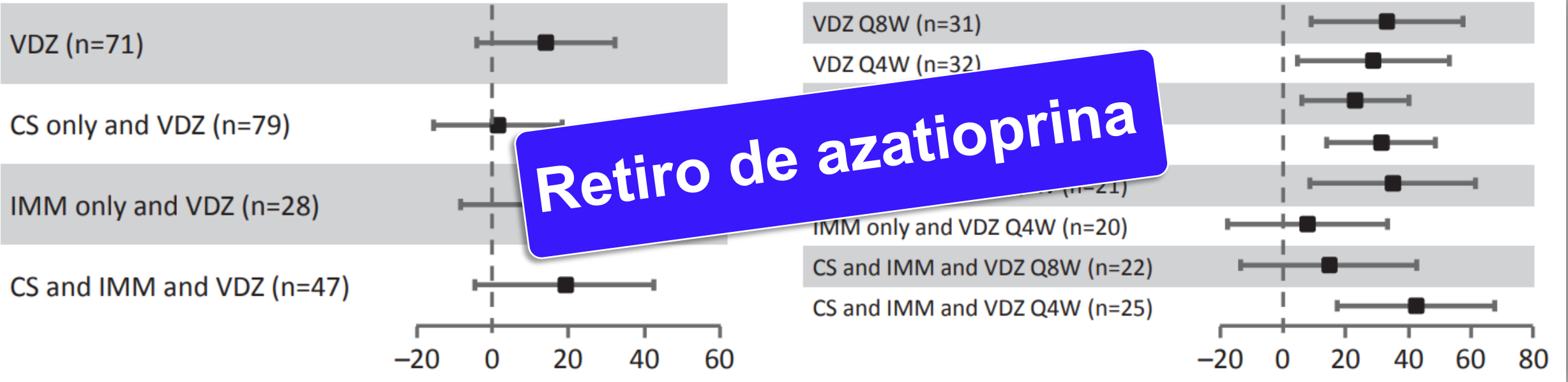
Desde hace 5 años  
78Kg- asintomático



ELSEVIER

### Should we use vedolizumab as mono or combo therapy in ulcerative colitis?

Charlotte Hedin <sup>a</sup>, Jonas Halfvarson <sup>b,\*</sup>

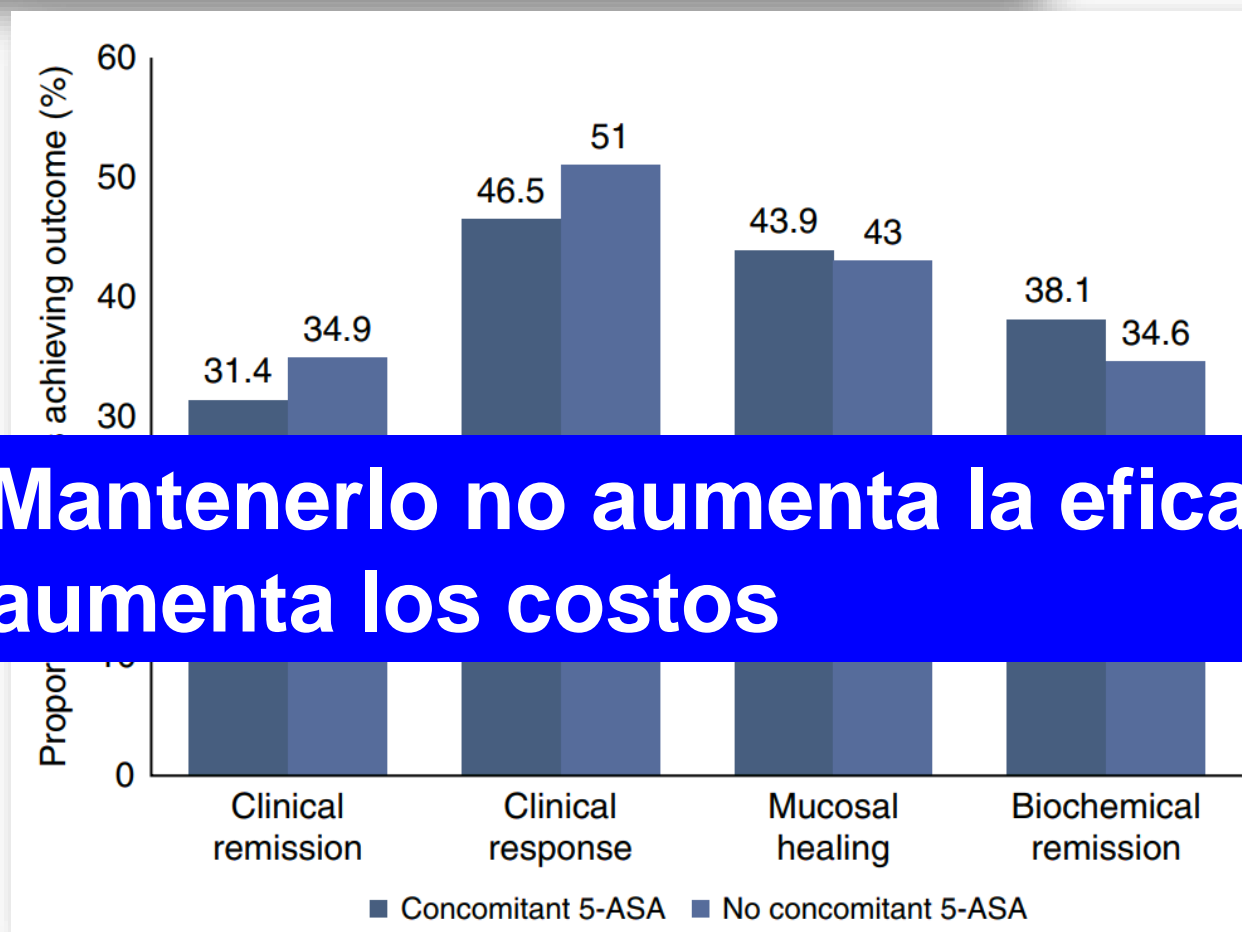


**Retiro de azatioprina**

# No Benefit of Concomitant 5-Aminosalicylates in Patients With Ulcerative Colitis Escalated to Biologic Therapy: Pooled Analysis of Individual Participant Data From Clinical Trials

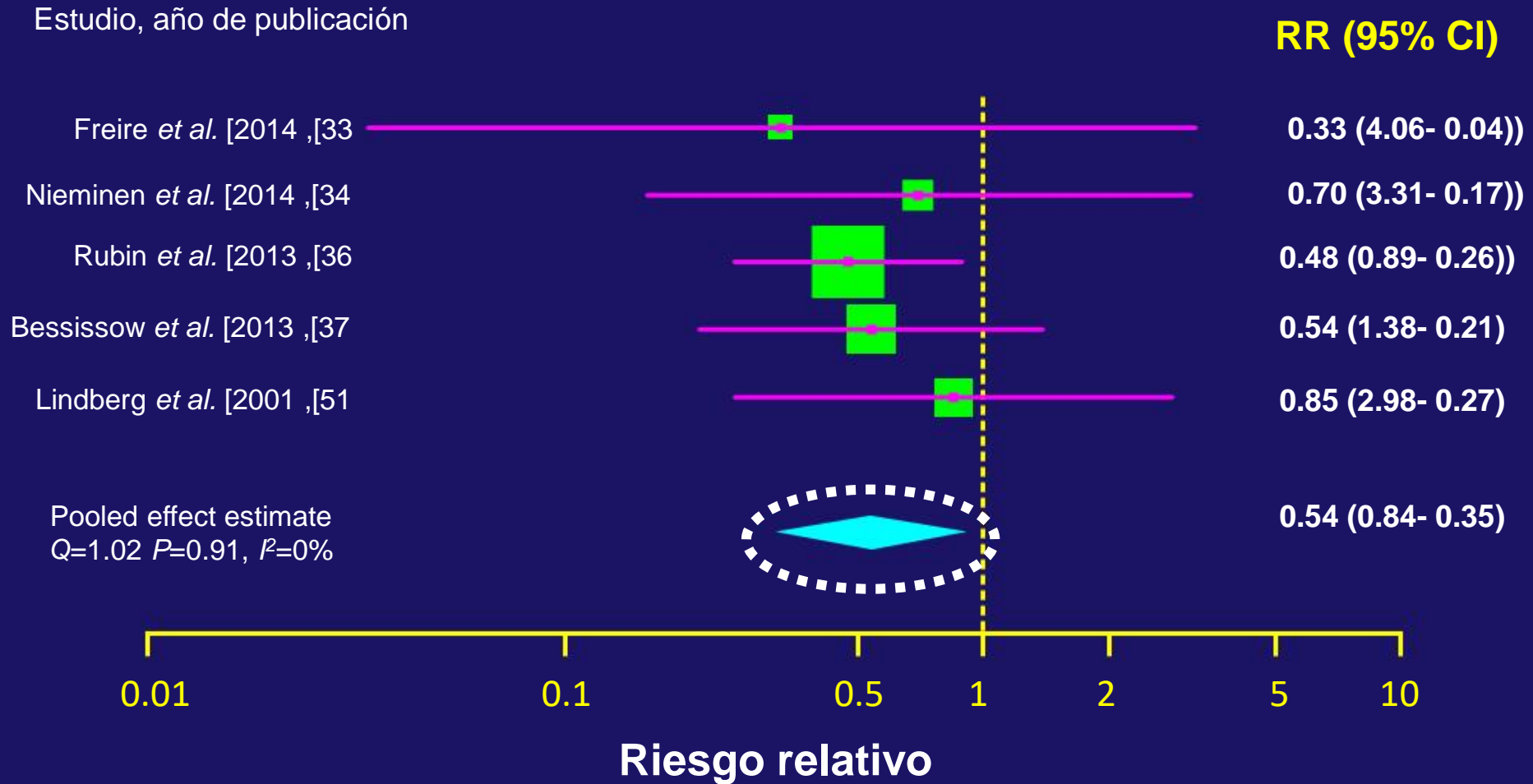
Siddharth Singh, MD, MS<sup>1,2</sup>, James A. Proudfoot, MS<sup>3</sup>, Parambir S. Dulai, MD<sup>1</sup>, Vipul Jairath, MD, PhD<sup>4,5</sup>, Mathurin Fumery, MD<sup>6</sup>, Ronghui Xu, PhD<sup>3,7</sup>, Brian G. Feagan, MD<sup>4</sup> and William J. Sandborn, MD<sup>1</sup>

Am J Gastroenterol. 2018;113:1197-1205.

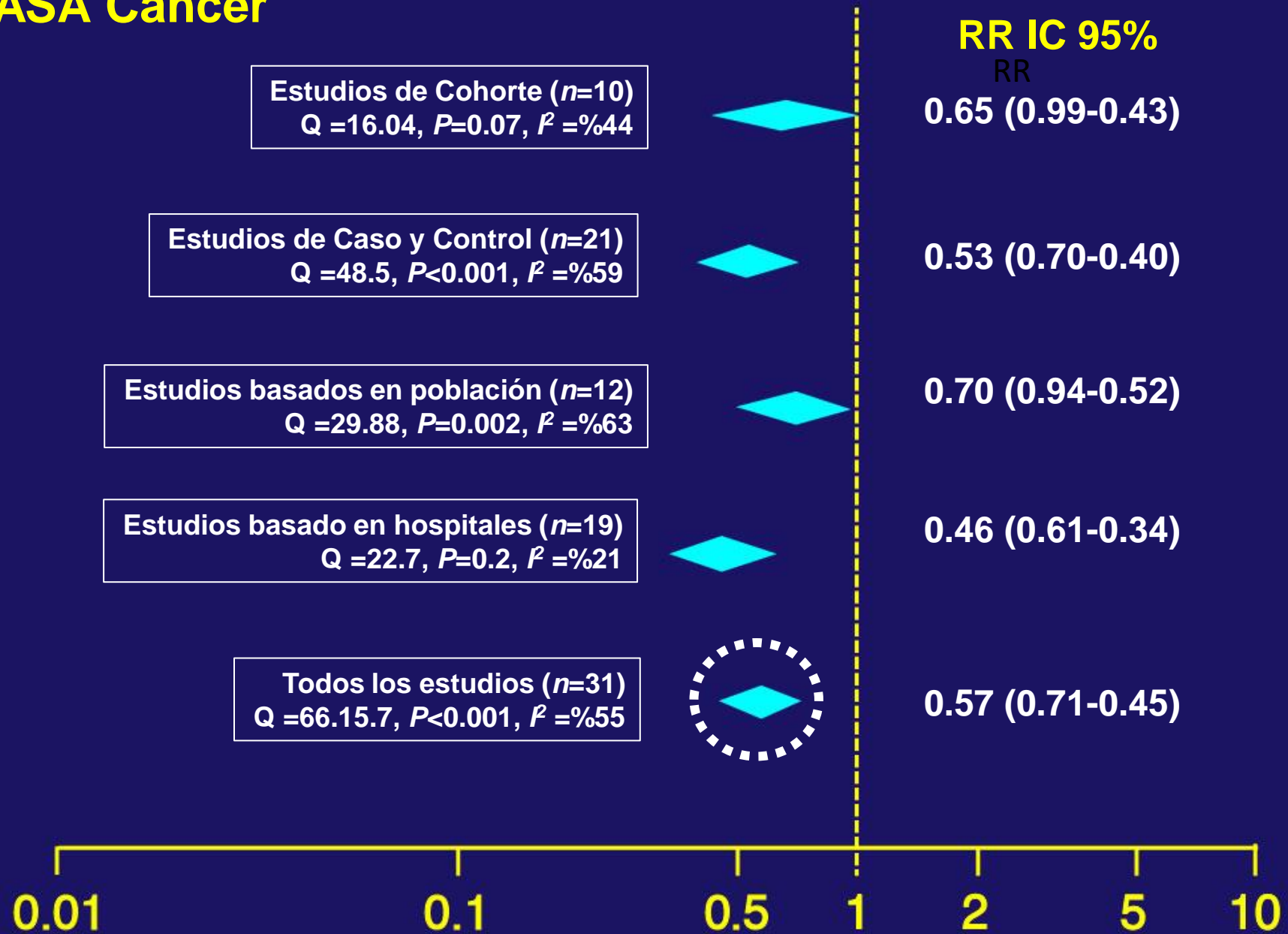


**Mantenerlo no aumenta la eficacia  
aumenta los costos**

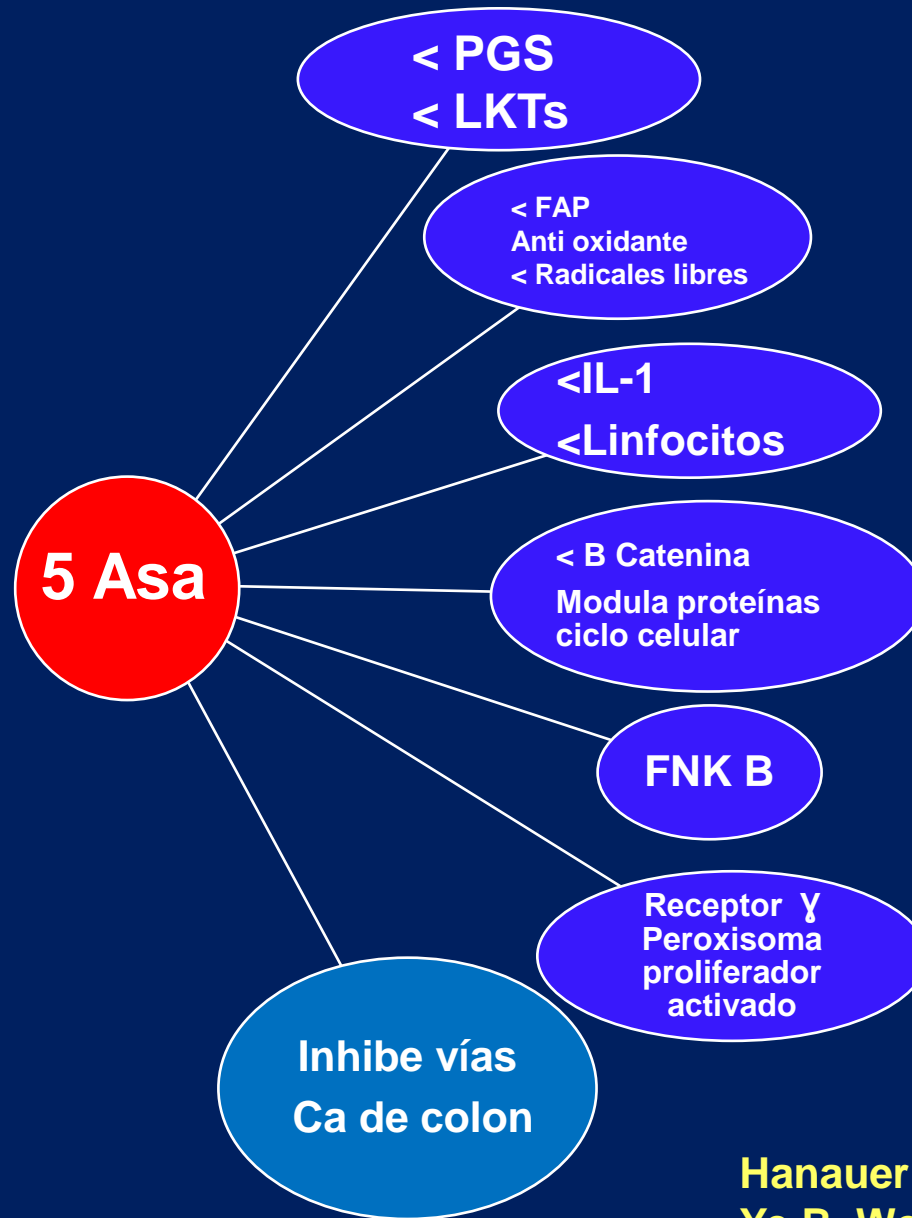
# 5 ASA Displasia



# 5 ASA Cáncer



# 5 Asa Mecanismos De acción



Actúa localmente  
Inhibiendo la Inflamación  
de la mucosa colónica

Hanauer SB. Dig Dis 2016;34:122-4  
Ye B, World J Gastroenterol Pharmacol Ther 2015;6:137-44  
Aliment Pharmacol Ther. 2017;45:1179-1192.

## ARTICLE

Translational Therapeutics

# 5-Aminosalicylic acid inhibits stem cell function in human adenoma-derived cells: implications for chemoprophylaxis in colorectal tumorigenesis

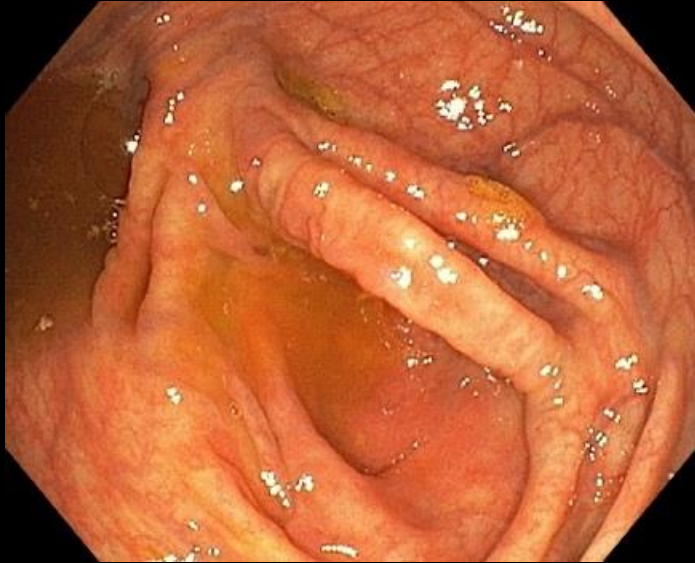
Steven William Dixon <sup>1,2</sup>, Tracey Jane Collard<sup>1</sup>, Eleanor May Harrisdotter Mortensson<sup>1</sup>, Danny Nigel Legge <sup>1</sup>, Adam Christian Chambers<sup>1</sup>, Alexander Greenhough <sup>1,3</sup>, Tom Julian Creed<sup>2</sup> and Ann Caroline Williams <sup>1</sup>

**Propiedades anti neoplásicas intrínsecas**

**Dixon SW, et al . Br J Cancer 2021; 124:1959-69;**

**Table 4.** Guideline recommendation for chemoprevention in IBD

Guideline/publication date	Recommendation
Magro et al. [42] ECCO 2017	“Chemoprevention with mesalamine compounds may reduce the incidence of colorectal cancer in ulcerative colitis. There is insufficient evidence to recommend for or against chemoprevention with thiopurines”
Rubin et al. [44] American College of Gastroenterology 2019	“No medical therapy has demonstrated sufficient prevention of dysplasia or CRC to avoid colonoscopic surveillance in UC.” (Key concept statement)
Lamb et al. [43] British Society of Gastroenterology Consensus 2019	“We recommend that patients with ulcerative colitis or IBD-U with left-sided or more extensive disease should be advised to take mesalazine in doses of at least 2 g daily to reduce risk of colorectal cancer.” We suggest that thiopurines may reduce the risk of colorectal cancer in patients with ulcerative colitis and IBD-U, but evidence for a chemopreventive role from methotrexate, calcineurin inhibitors, anti-TNF, and anti-integrin agents is lacking at present and they cannot be currently recommended solely for chemoprevention against colorectal cancer (GRADE: weak recommendation, low-quality evidence. Agreement: 93%)
Singh et al. [45] American Gastroenterology Association 2020	“In adult outpatients with moderate to severe UC, who have failed 5-ASAs, and have escalated to therapy with biologic agents, tofacitinib, and/or immunomodulators, there may be no benefit to continuing 5-ASAs over stopping 5-ASAs”



**Protocolo biopsias  
4 cada 10 cm  
Patología  
Colitis ulcerativa  
inactiva**

## CALPROTECTINA EN MATERIA FECAL

>1000.0

ug/g

Método: TECNOLOGIA SMC : ELISA AUTOMATIZADO.

DATO CONFIRMADO

SE DEBE CORRELACIONAR EL RESULTADO CON LOS HALLAZGOS CLÍNICOS, LA HISTORIA CLÍNICA Y PRUEBAS DE LABORATORIO RELACIONADAS.

SI EL RESULTADO NO COINCIDE CON EL ESTADO CLÍNICO O PRUEBAS RELACIONADAS, SE SUGIERE REALIZAR NUEVAMENTE LA MEDICIÓN DE LA PRUEBA EN 4 A 6 SEMANAS, PARA DETERMINAR EL ESTADO INFLAMATORIO.

\*\* Valores de Referencia\*\*:

Intervalo normal: Menor de 50 ug/g

Valores un poco elevados: 50 – 200 ug/g

Valores considerablemente elevados: Mayor de 200 ug/g

Fecha Validación: 10-Mar-2022 11:19 am



# Estrategia de manejo en EII

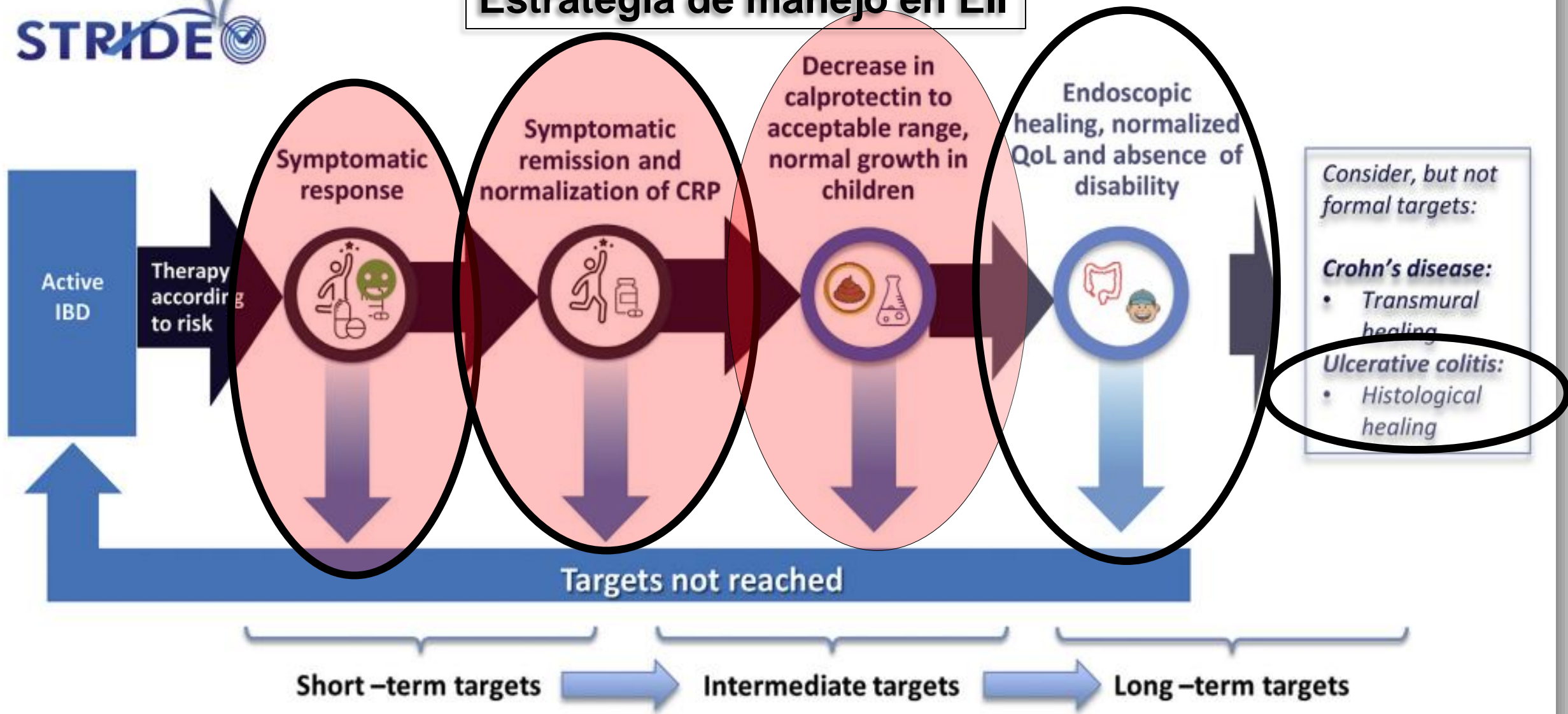


Figure 2. Treatment targets in CD and UC.

# Histologic Outcomes With Vedolizumab Versus Adalimumab in Ulcerative Colitis: Results From An Efficacy and Safety Study of Vedolizumab Intravenous Compared to Adalimumab Subcutaneous in Participants With Ulcerative Colitis (VARSITY)



Laurent Peyrin-Biroulet,<sup>1</sup> Edward V. Loftus Jr,<sup>2</sup> Jean-Frédéric Colombel,<sup>3</sup> Silvio Danese,<sup>4</sup> Raquel Rogers,<sup>5</sup> Jeffrey D. Bornstein,<sup>5</sup> Jingjing Chen,<sup>5</sup> Stefan Schreiber,<sup>6</sup> Bruce E. Sands,<sup>3</sup> and Richard A. Lirio<sup>5</sup>

## Histologic Outcomes in Ulcerative Colitis from the VARSITY Study

### Study Design

Study Duration 52 weeks

Randomized  
N=769

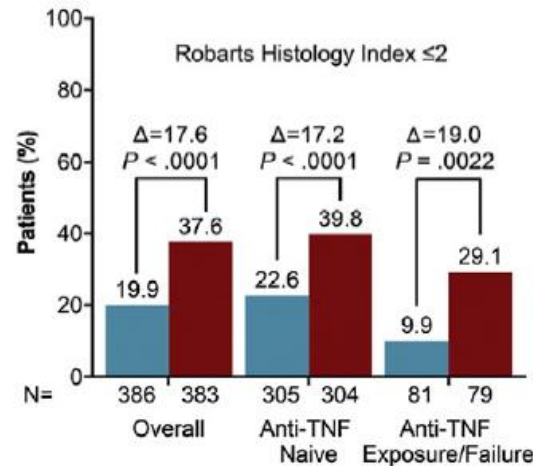


Baseline Histologic Disease Activity

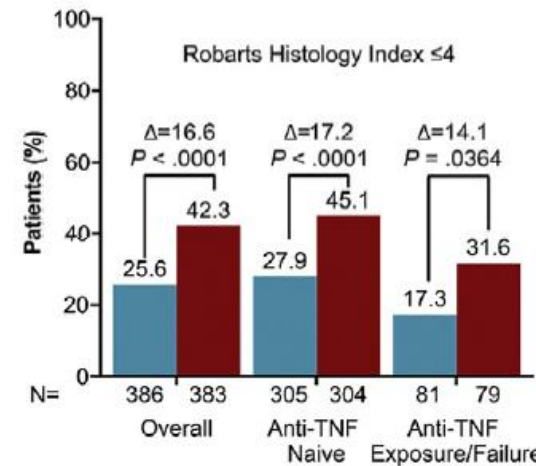
Robarts Histology Index

19.6	19.5
Adalimumab SC 40 mg Q2W	Vedolizumab IV 300 mg Q8W

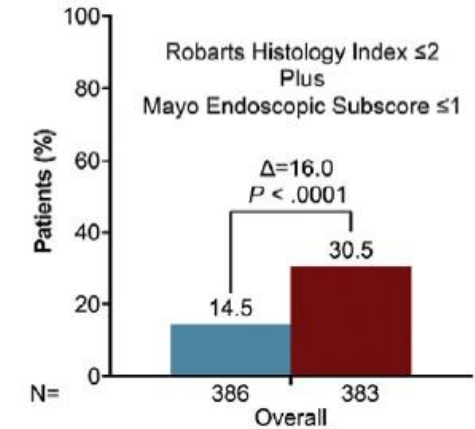
Vedolizumab-treated patients had higher rates of **histologic remission at Week 52**



Vedolizumab-treated patients had higher rates of **minimal histologic disease activity at Week 52**



Vedolizumab-treated patients had higher rates of **histologic remission plus endoscopic improvement at Week 52**



Gastroenterology

**Table 1** Novel integral disease index of UC activity (NIDI) or Yamamoto-Furusho Index.

Disease Activity	Number of bloody stools per day	Hemoglobin	hs-CRP	Albumin	Endoscopic findings	Histopathologic findings
0 Remission	Usual (no blood)	> 12	≤0.20	≥3.5	Normal mucosa	Normal
1 Mild	2-3	12 to 10	0.21- 0.35	3.4-3.0	Erythema, decreased vascular pattern, mild friability	Mild activity
2 Moderate	4-6	9.9 to 8	0.36-1.0	2.9-2.5	Marked erythema, absent vascular pattern, friability and erosions	Moderate activity
3 Severe	> 6	< 8	> 1.0	< 2.5	Spontaneous bleeding and ulcerations	Intense Activity

# Evolución

**Peso 78 kg, Asintomático 1 deposición Bristol 3-4**  
**Excelente calidad de vida, Ingeniero exitoso**  
**Albumina normal**  
**Cuadro hemático normal**  
**Vitamina D normal**  
**Perfil Hepático normal.**  
**Colonoscopia normal.**  
**Histología normal**  
**“Vedolizumab man” (Video)**

**Conclusión: Colitis ulcerativa  
Falla secundaria a anti TNF**

**Se consideró Empíricamente  
2do Anti TNF *Farmacocinética* ?**

**Se optó por niveles de Infliximab 2016  
y acs anti Infliximab, *farmacodinamia***

**Vedolizumab: 5 años en remisión profunda  
Clínica, endoscópica e histológica**

***Vedo en Jóvenes y  
Adultos mayores***

***Muchas gracias!!***