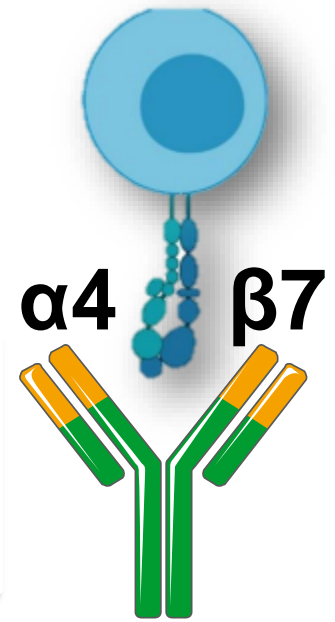
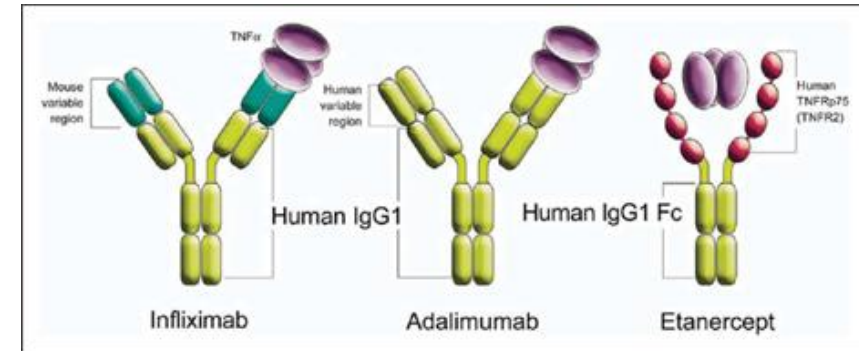


XI Congreso Venezolano de Enfermedad Inflamatoria Intestinal  
19, 20 Octubre 2022

# Anti TNF o Anti integrinas (Vedolizumab) como primera línea En colitis ulcerativa ?



**William Otero R MD, FAGA, FACP**  
**Profesor Titular de Medicina,**  
**Universidad Nacional de Colombia**  
**Hospital Universitario Nacional de Colombia**



**Presidente Dr Guillermo Veitía**  
**Caracas Venezuela**

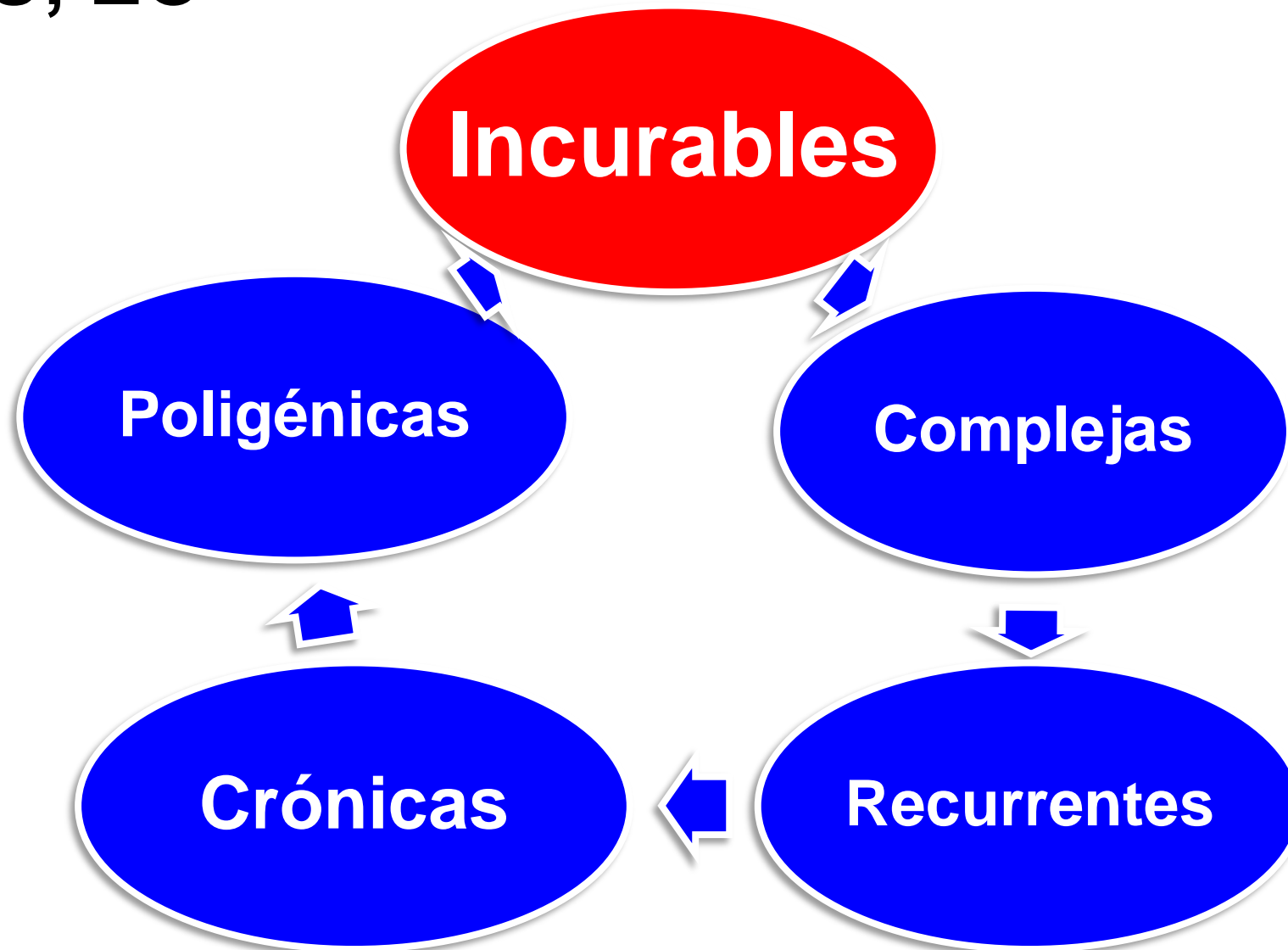


# Rapid Resolution of Chronic Colitis in the Cotton-top Tamarin With an Antibody to a Gut-Homing Integrin $\alpha 4\beta 7$

PAUL E. HESTERBERG, DAWN WINSOR-HINES, MICHAEL J. BRISKIN, DULCE SOLER-FERRAN, CHRISTOPHER MERRILL, CHARLES R. MACKAY, WALTER NEWMAN, and DOUGLAS J. RINGLER  
LeukoSite Inc., Cambridge, Massachusetts

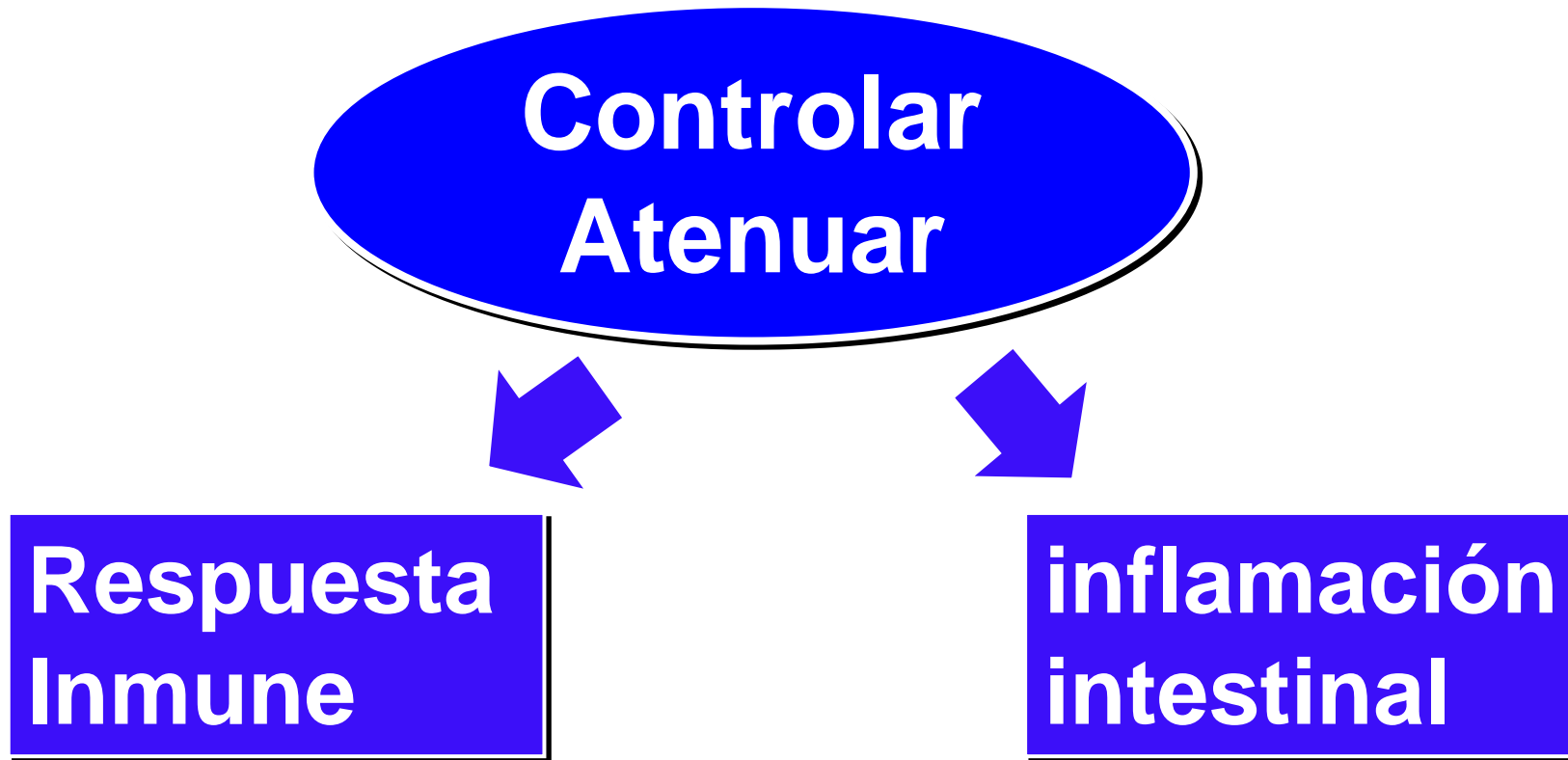
# Enfermedad inflamatoria intestinal, 2022

## CU, EC



# EII Tratamiento 2022

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# El Tratamiento 2022

Terapias de inducción

Rápido  
Comienzo  
De acción

Esteroides

Terapias biológicas

Terapias de  
Mantenimiento

Adecuado  
uso largo  
Plazo

Libre esteroides

AGA 2020  
ACG 2019

**Colitis Ulcerativa**



**15% curso agresivo**



**10 años**



**Anti TNF**

**70-80% recaen**

**Vedolizumab**

**10-40% No  
Responden**

**23-46% Pierden  
Respuesta 1 año**

**35% Pierden  
Respuesta 1 año**

Pudipeddi A, Med J Aust 2021;214:365-70  
Fumerey M, Clin Gastroenterol hepatol 2018;16:343-56  
Jeong DY, Autoimm Rev 2019;18:439-54  
Feuerstein JD, (AGA) Gastroenterology 2020;158:1450-61  
Schmidt E, Inflamm Bowel Dis 2018;24:2461-7

# CLINICAL PRACTICE GUIDELINES

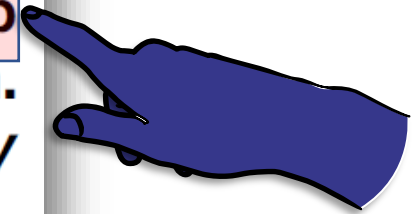
## AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis



Joseph D. Feuerstein,<sup>1</sup> Kim L. Isaacs,<sup>2</sup> Yecheskel Schneider,<sup>3</sup> Shazia Mehmood Siddique,<sup>3</sup> Yngve Falck-Ytter,<sup>4,5</sup> and Siddharth Singh,<sup>6</sup> on behalf of the AGA Institute Clinical Guidelines Committee

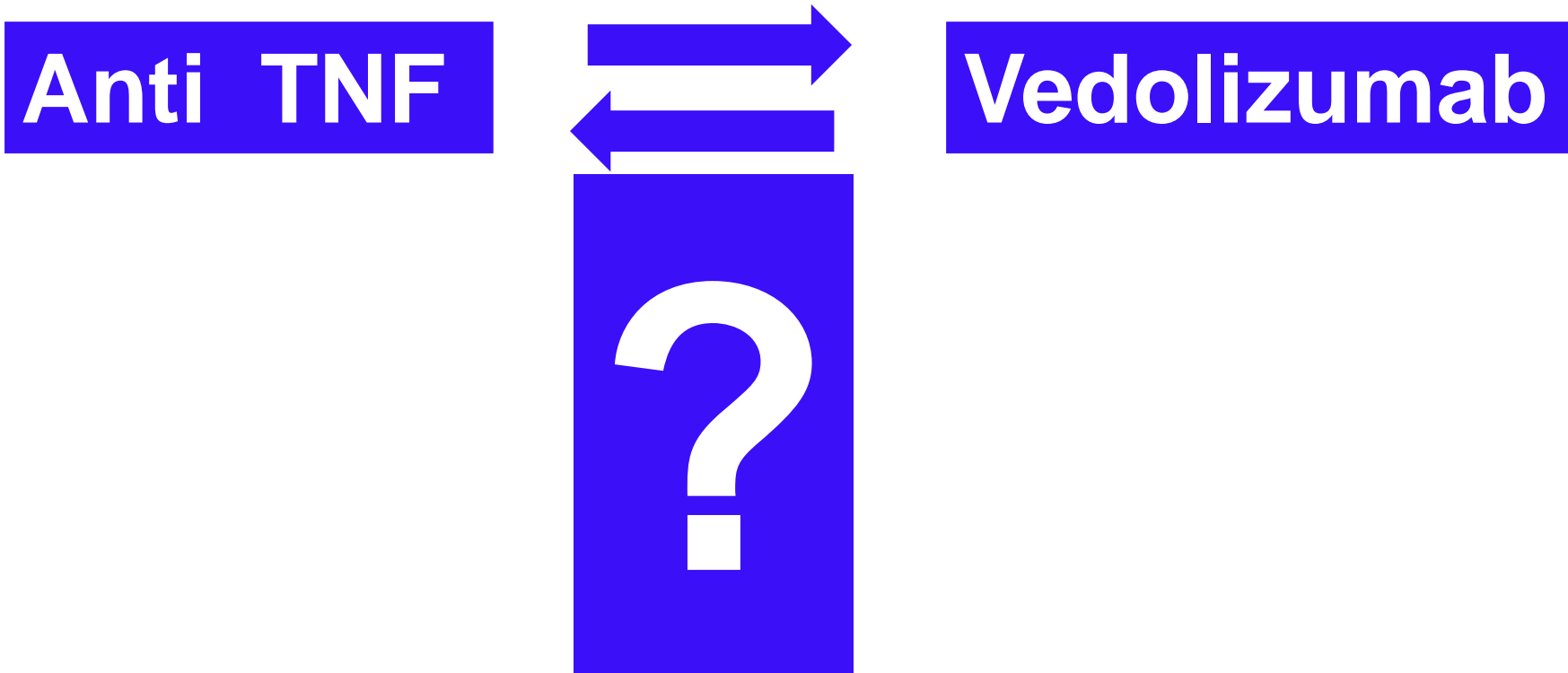
**2a. In adult outpatients with moderate to severe ulcerative colitis who are naïve to biologic agents, the AGA suggests using infliximab or vedolizumab rather than adalimumab, for induction of remission. (Conditional recommendation, moderate quality evidence)**

Comment: Patients, particularly those with less severe disease, who place higher value on the convenience of self-administered subcutaneous injection, and a lower value on the relative efficacy of medications, may reasonably chose adalimumab as an alternative.



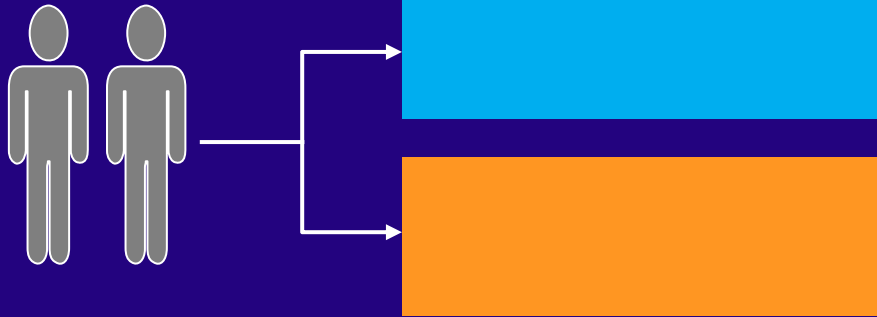
# Colitis ulcerativa

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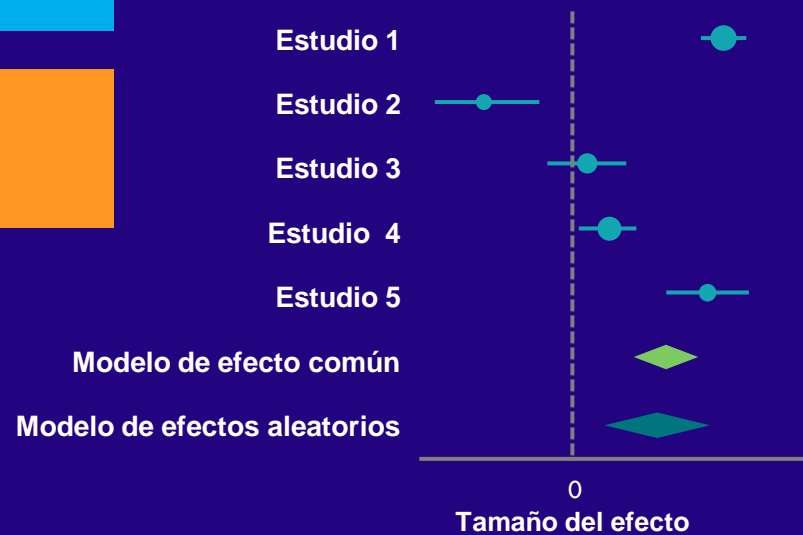


# Investigaciones científicas

ECC



Meta-análisis



Estudios del mundo real



Gurevitch J, et al. *Nature* 2018;555:175–182

Corrigan-Curay J, et al. *JAMA* 2018;320:867–868;

Peyrin-Biroulet L, et al. *J Crohns Colitis* 2017;S567–S775

Favalli E, et al. *BioMed Res Int* 2014;2014:831603

ORIGINAL ARTICLE

# Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis

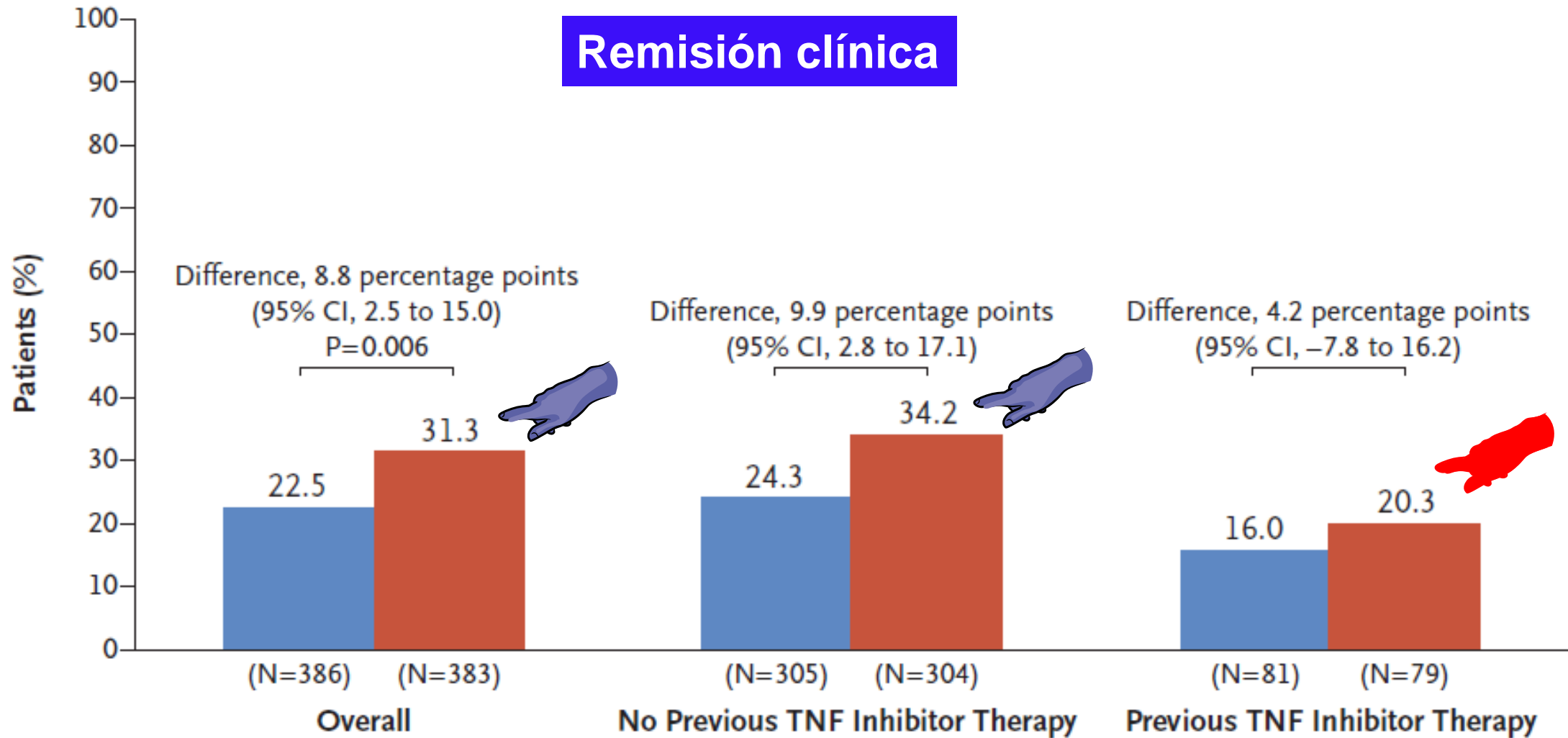
Bruce E. Sands, M.D., Laurent Peyrin-Biroulet, M.D., Ph.D., Edward V. Loftus, Jr., M.D.,  
Silvio Danese, M.D., Jean-Frédéric Colombel, M.D., Murat Törüner, M.D.,  
Laimas Jonaitis, M.D., Ph.D., Brihad Abhyankar, F.R.C.S., Jingjing Chen, Ph.D.,  
Raquel Rogers, M.D., Richard A. Lirio, M.D., Jeffrey D. Bornstein, M.D., and  
Stefan Schreiber, M.D., Ph.D., for the VARSITY Study Group\*

**Sands BE, N Engl J Med 2019;381:1215-26.**

# Varsity

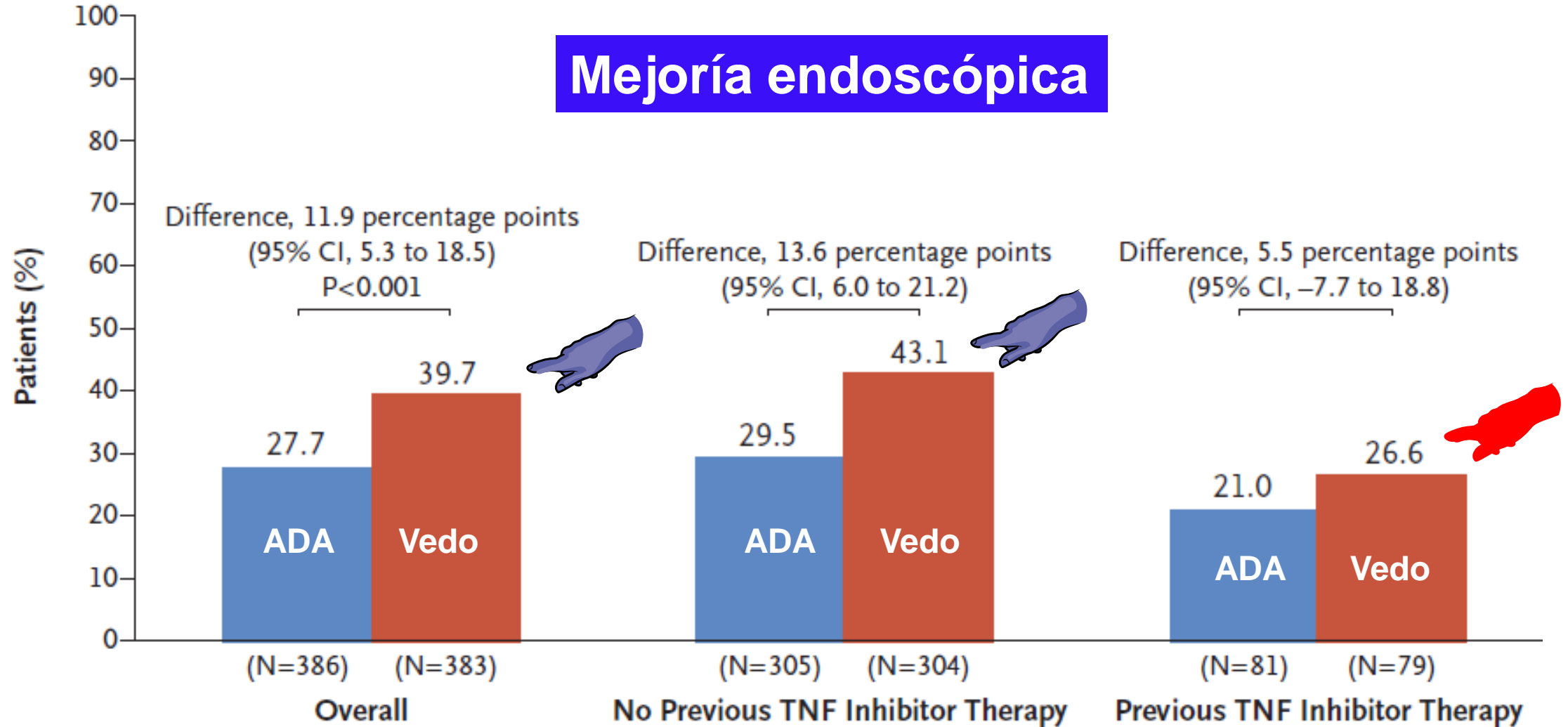
■ Adalimumab ■ Vedolizumab

## A Clinical Remission



# Varsity

## B Endoscopic Improvement



Sands BE, N Engl J Med 2019;381:1215-26.

# 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

Adalimumab SC  
40 mg Q2W  
n=386

Vedolizumab IV  
300 mg Q8W  
n=383

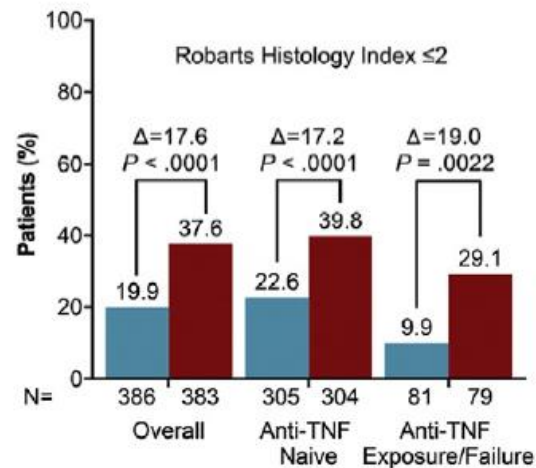
Baseline Histologic  
Disease Activity

Robarts Histology Index

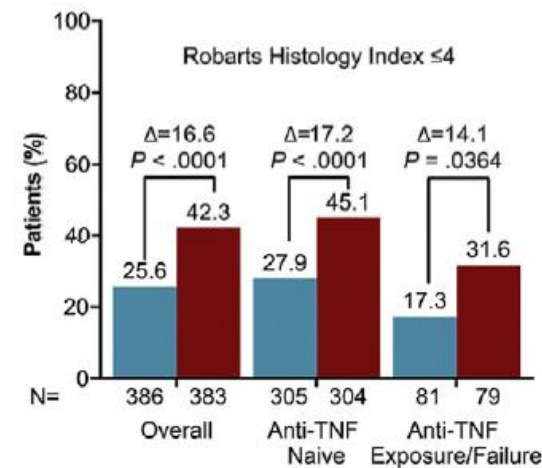
19.6  
Adalimumab SC  
40 mg Q2W

19.5  
Vedolizumab IV  
300 mg Q8W

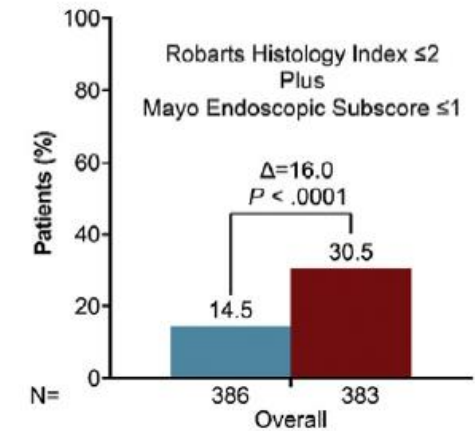
Vedolizumab-treated patients had higher rates of **histologic remission at Week 52**



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

# Estrategia de manejo en EII

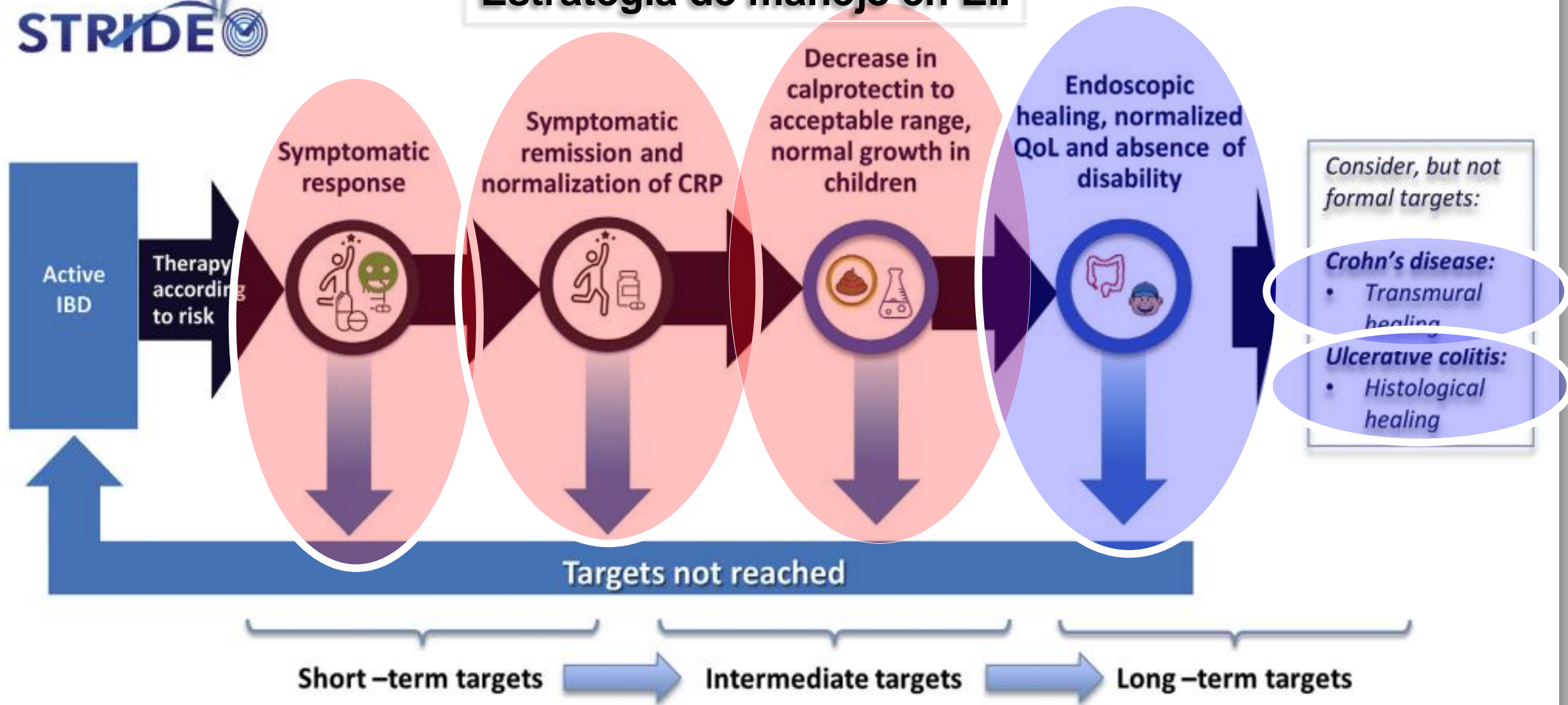
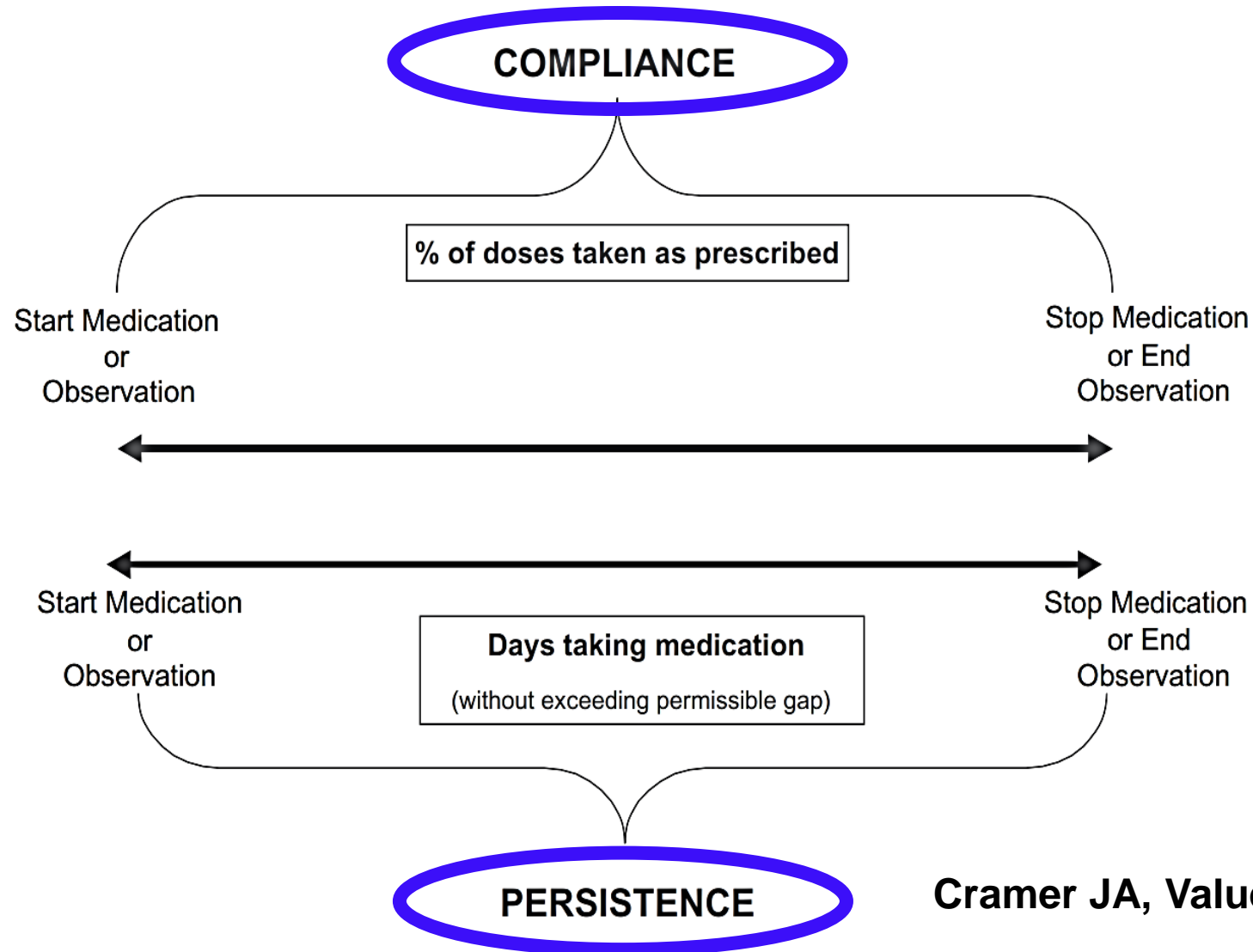


Figure 2. Treatment targets in CD and UC.

# Medication Compliance and Persistence: Terminology and Definitions

Joyce A. Cramer, BS,<sup>1</sup> Anuja Roy, MBA, MSc,<sup>2</sup> Anita Burrell, MBA,<sup>3</sup> Carol J. Fairchild, PhD,<sup>4</sup>  
Mahesh J. Fuldeore, PhD, RPh, MBA,<sup>5</sup> Daniel A. Ollendorf, MPH,<sup>6</sup> Peter K. Wong, PhD, RPh, MS, MBA<sup>7</sup>



**Persistencia**



**Proporción de Pacientes  
Continúan Con medicación**



**Marcador Subrogado**



**Efectividad Tolerabilidad  
Aceptación Mundo real**

Original Article

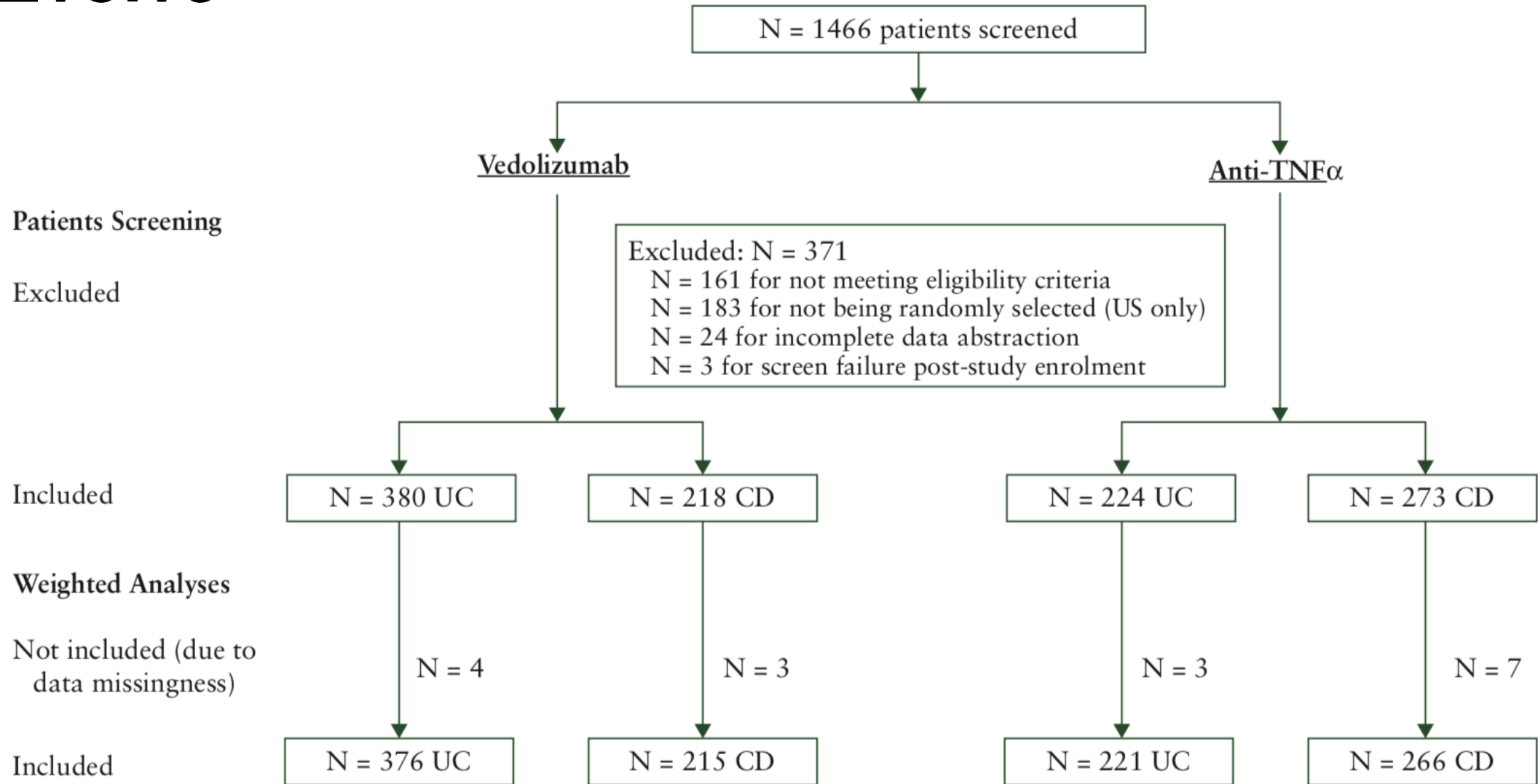
# Vedolizumab and Anti-Tumour Necrosis Factor $\alpha$ Real-World Outcomes in Biologic-Naïve Inflammatory Bowel Disease Patients: Results from the EVOLVE Study

Brian Bressler,<sup>a</sup> Andres Yarur,<sup>b</sup> Mark S. Silverberg,<sup>c</sup> Marielle Bassel,<sup>d</sup>  
Emanuelle Bellaguarda,<sup>e</sup> Chris Fourment,<sup>f</sup> Anthie Gatopoulou,<sup>g</sup>  
Pantelis Karatzas,<sup>h</sup> Uri Kopylov,<sup>i</sup> George Michalopoulos,<sup>j</sup>  
Spyridon Michopoulos,<sup>k</sup> Udayakumar Navaneethan,<sup>l</sup> David T. Rubin,<sup>m, </sup>  
Jesse Siffledeen,<sup>n</sup> Andrew Singh,<sup>o</sup> Konstantinos Soufleris,<sup>p</sup> Dara Stein,<sup>q</sup>  
Dirk Demuth,<sup>r</sup> Gerassimos J. Mantzaris<sup>s</sup>

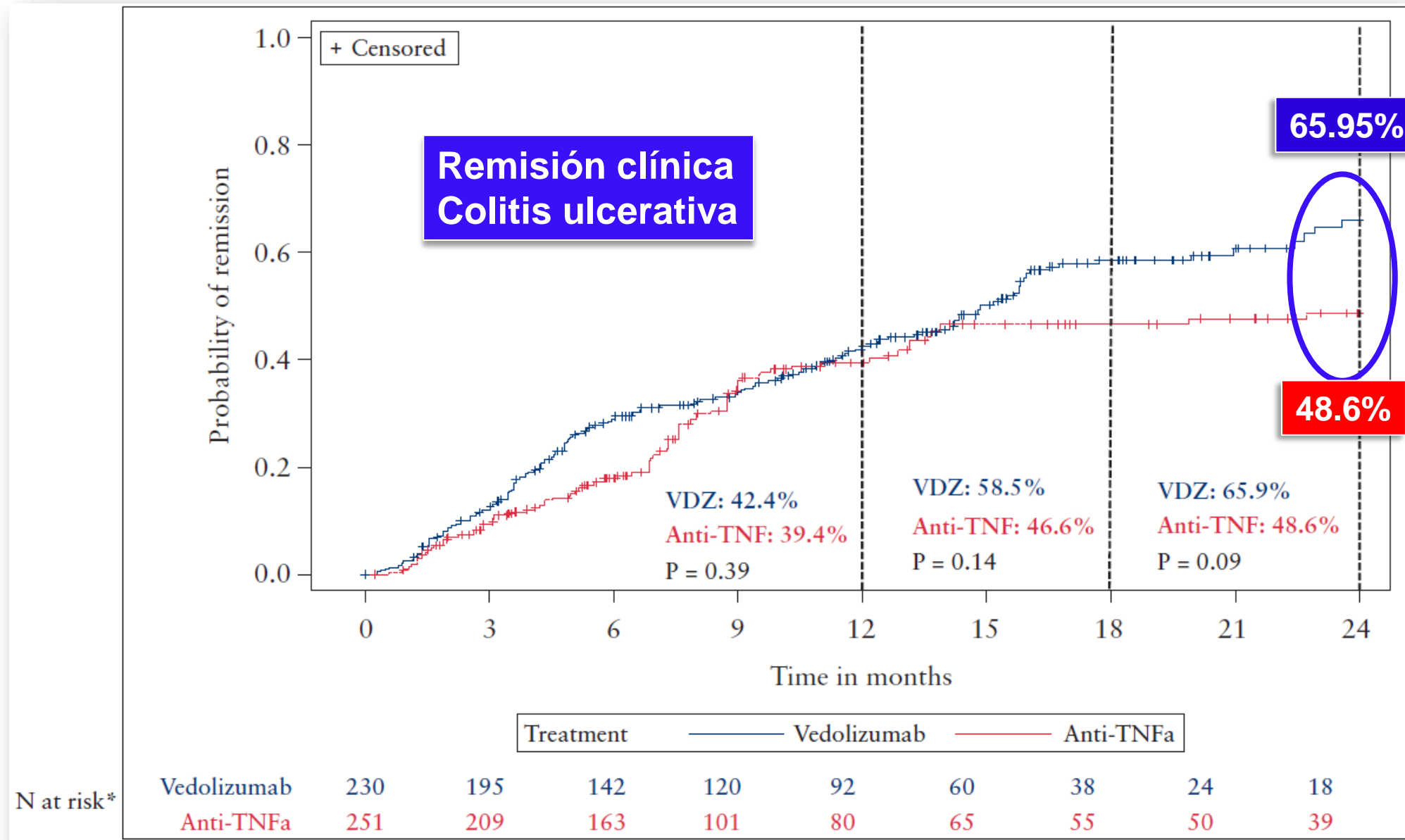


USA  
Canadá  
Grecia

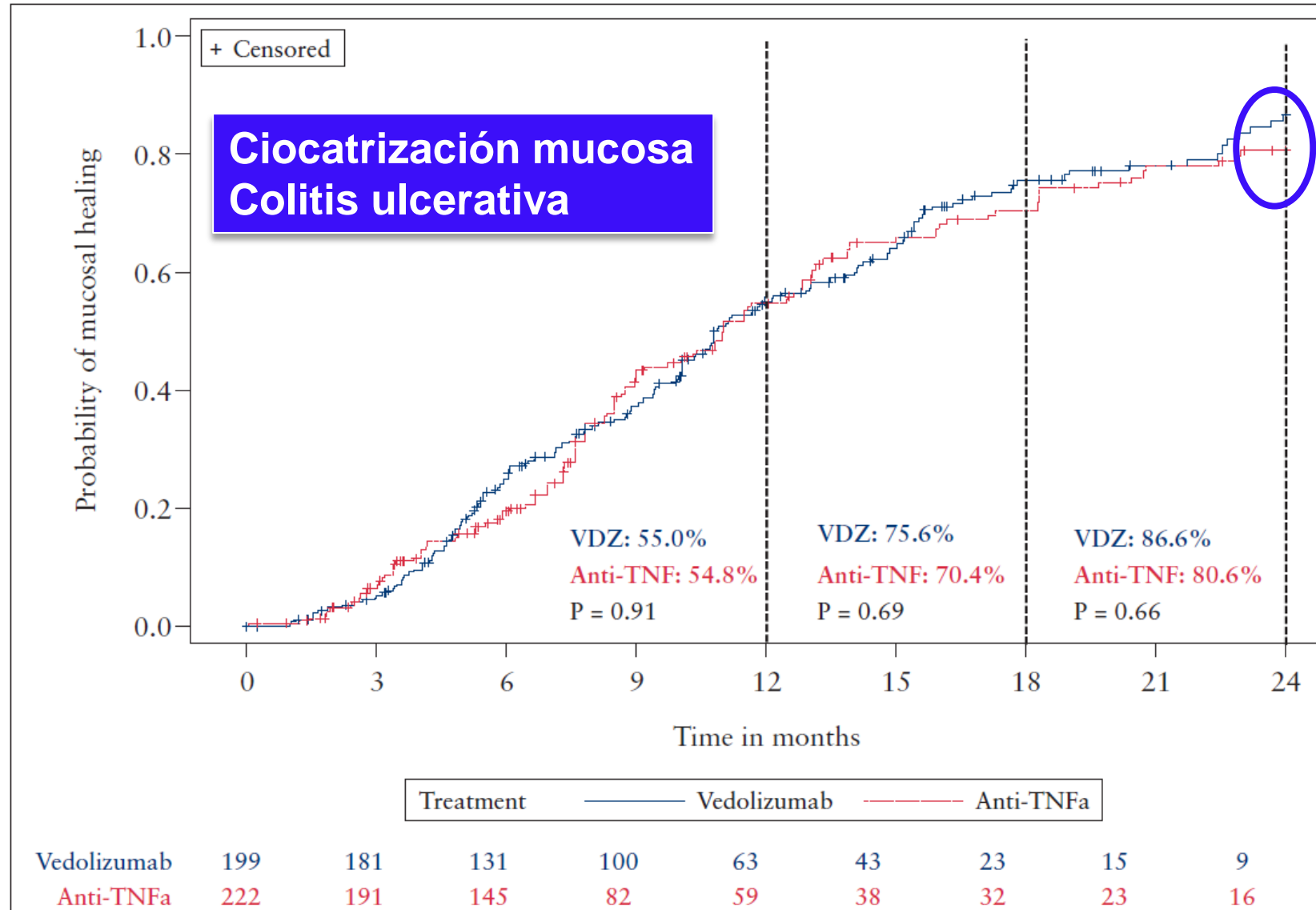
# Evolve



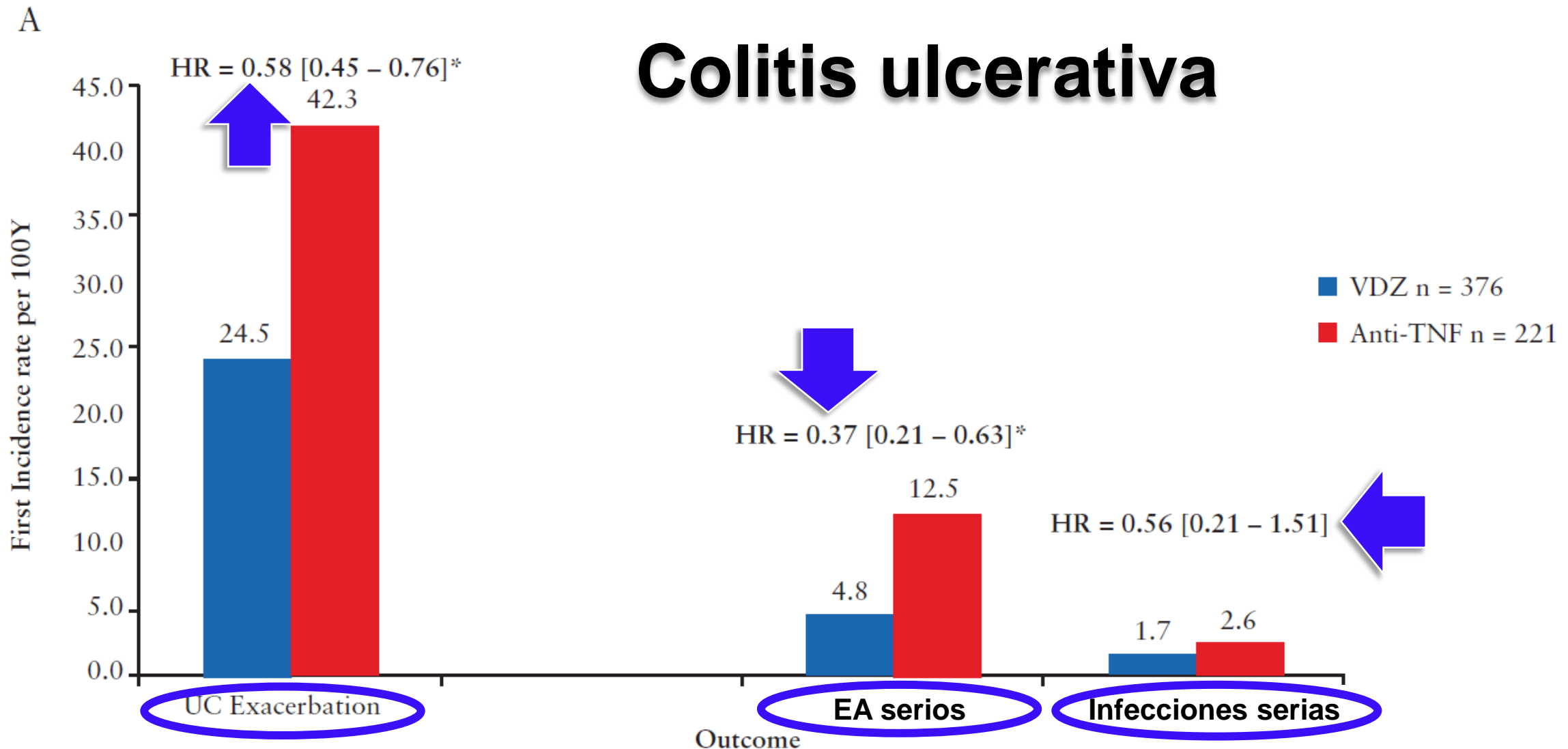
# Estudio EVOLVE






# Estudio EVOLVE



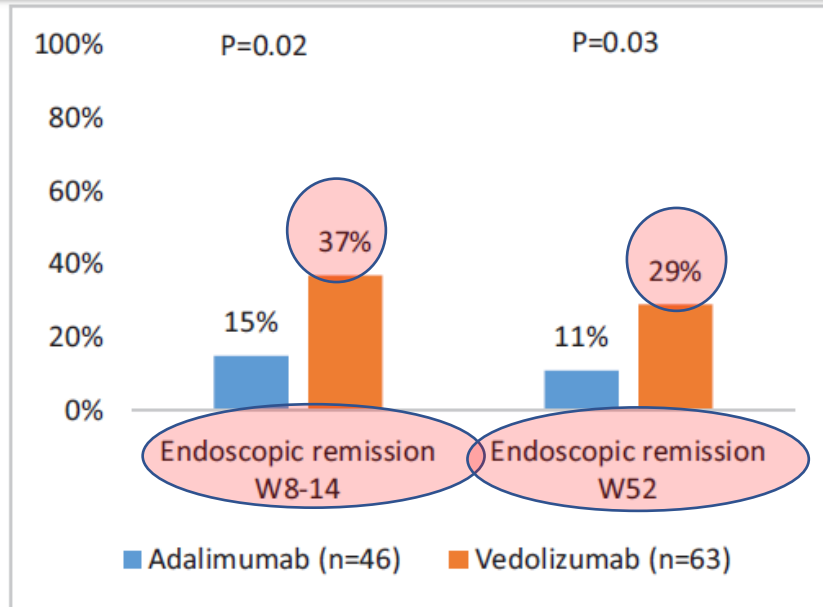
## Colitis ulcerativa



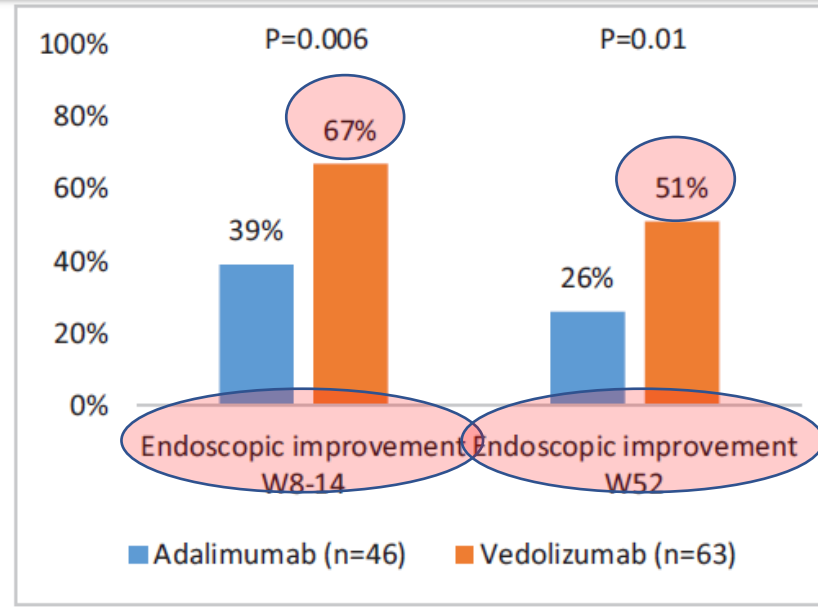
# Translating Results from VARSITY to Real World: Adalimumab vs Vedolizumab as First-line Biological in Moderate to Severe IBD

Annick Moens, PhD,<sup>\*,†</sup>  Bram Verstockt, PhD,<sup>\*,†</sup> Dahham Alsoud, PhD,<sup>†</sup> João Sabino, PhD,<sup>\*,†</sup>  
Marc Ferrante, PhD,<sup>\*,†</sup>  and Séverine Vermeire, PhD,<sup>\*,†</sup> 

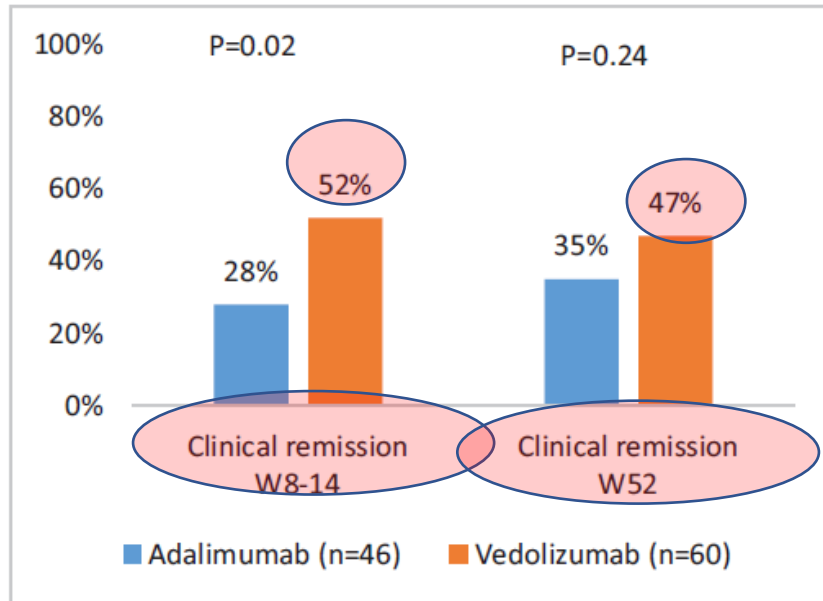
# Desenlaces en CU



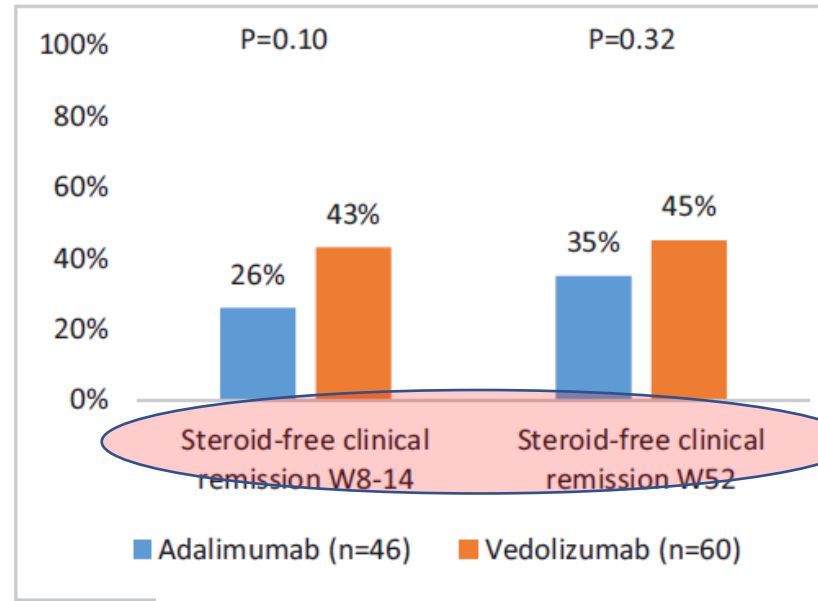
A



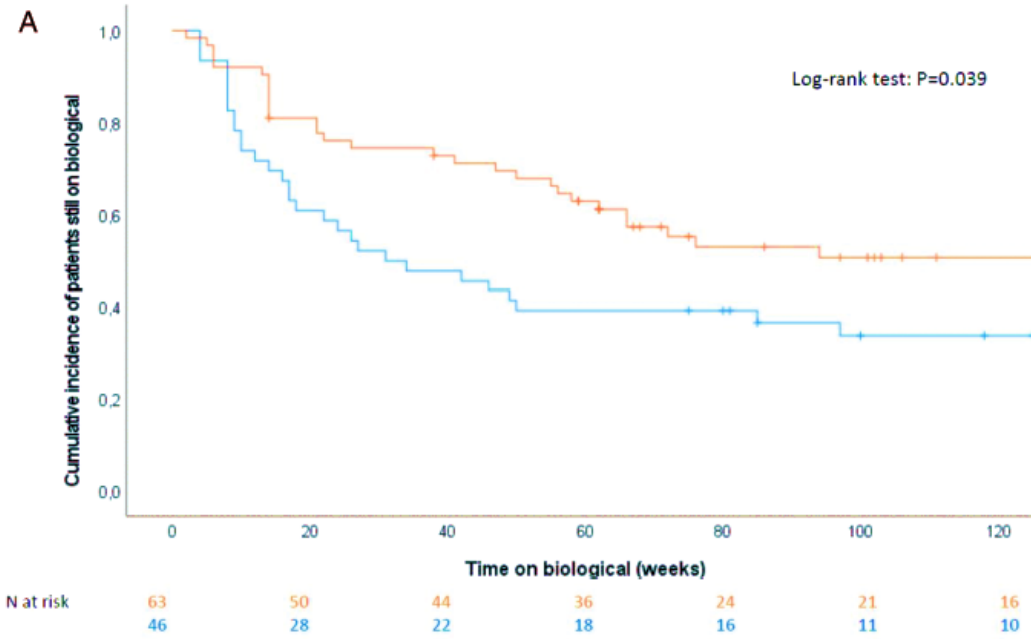
B



C

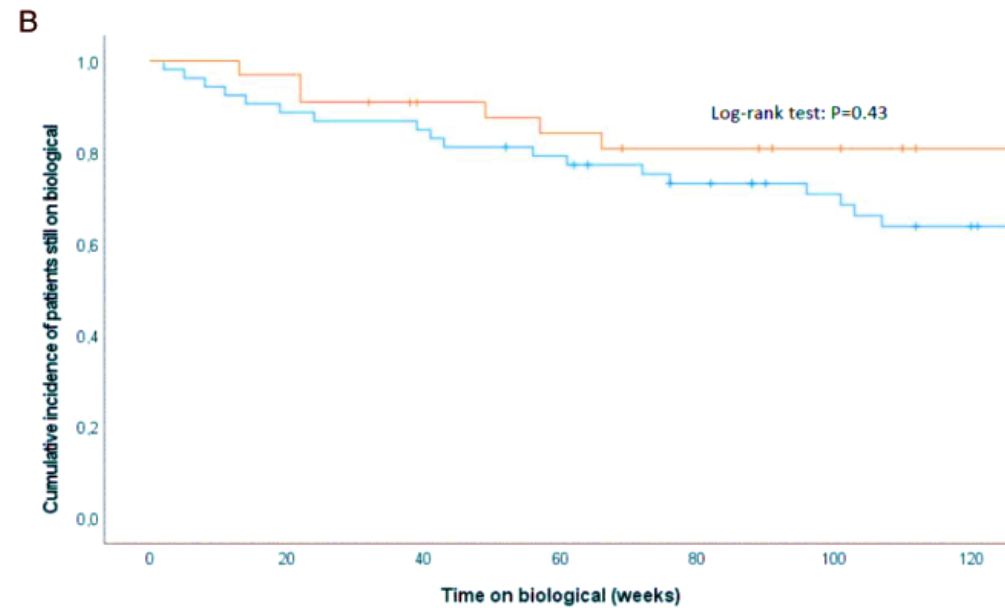


D



**Persistencia CU**

- Vedolizumab
- Adalimumab



**Persistencia EC**

- Vedolizumab
- Adalimumab

**Superior treatment persistence with ustekinumab in Crohn's disease and vedolizumab in ulcerative colitis compared with anti-TNF biological agents: real-world registry data from the Persistence Australian National IBD Cohort (PANIC) study**

Yanna Ko<sup>1,2</sup>  | Sudarshan Paramsothy<sup>1,2,3</sup>  | Yunki Yau<sup>1</sup> | Rupert W. Leong<sup>1,2,3</sup> 

# Persistencia de Biológicos CU Moderada-Severa

Persistencia



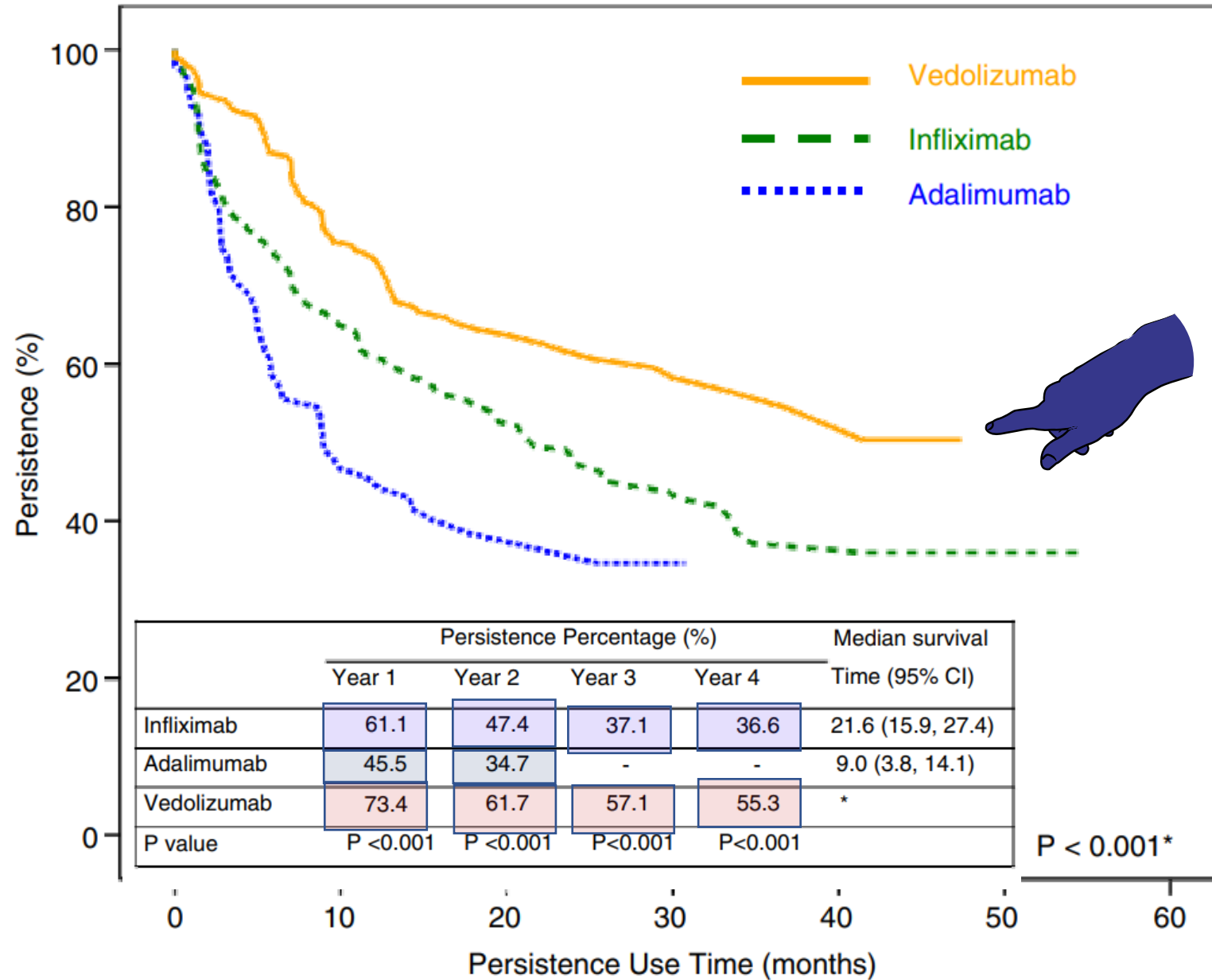
Proporción de Pacientes continúan Con medicación



Marcador Subrogado



Efectividad  
Tolerabilidad  
Aeptación  
Mundo real

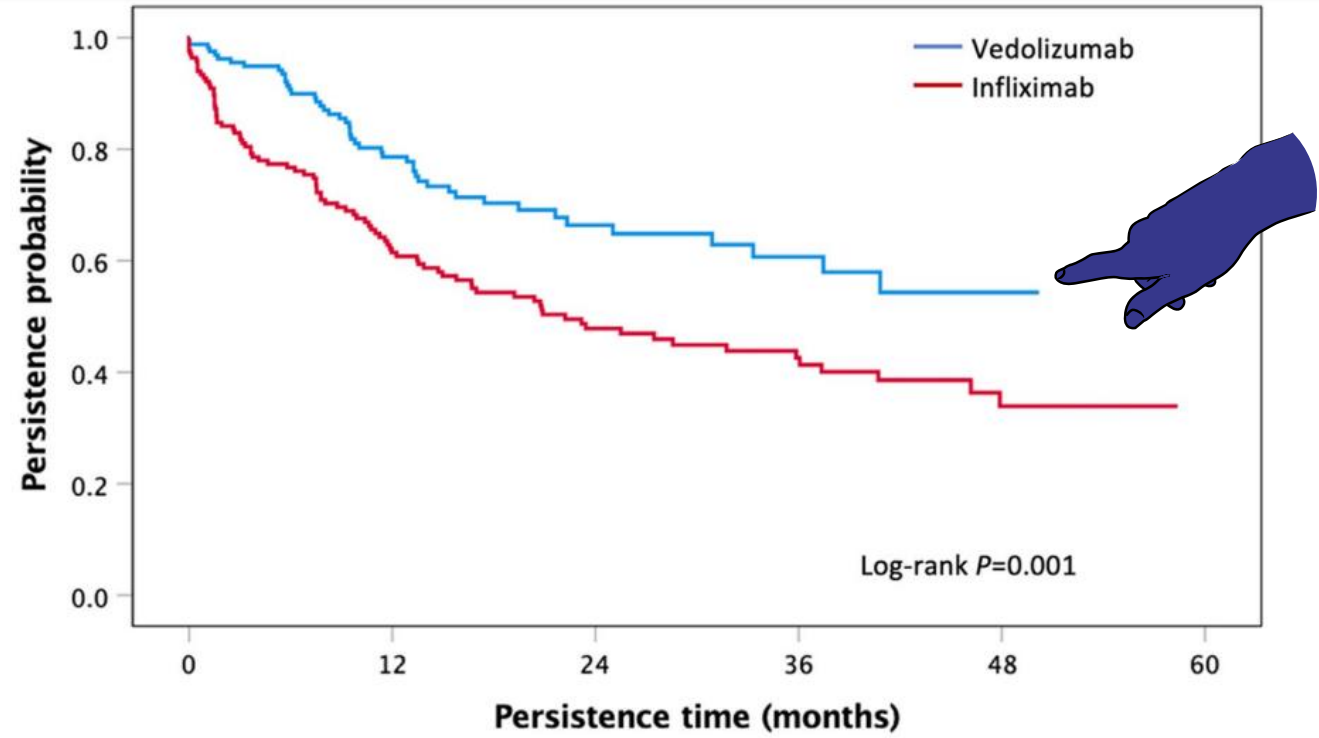


**Vedolizumab has longer persistence than  
infliximab as a first-line biological agent  
but not as a second-line biological agent  
in moderate-to-severe ulcerative colitis:  
real-world registry data from the  
Persistence Australian National IBD  
Cohort (PANIC) study**

Aviv Pudipeddi, Yanna Ko, Sudarshan Paramsothy and Rupert W. Leong , for the PANIC  
Study Group – Persistence in Australian National IBD Cohort

# PANIC : Persistence Australian National IBD Cohort study

**Primera línea**



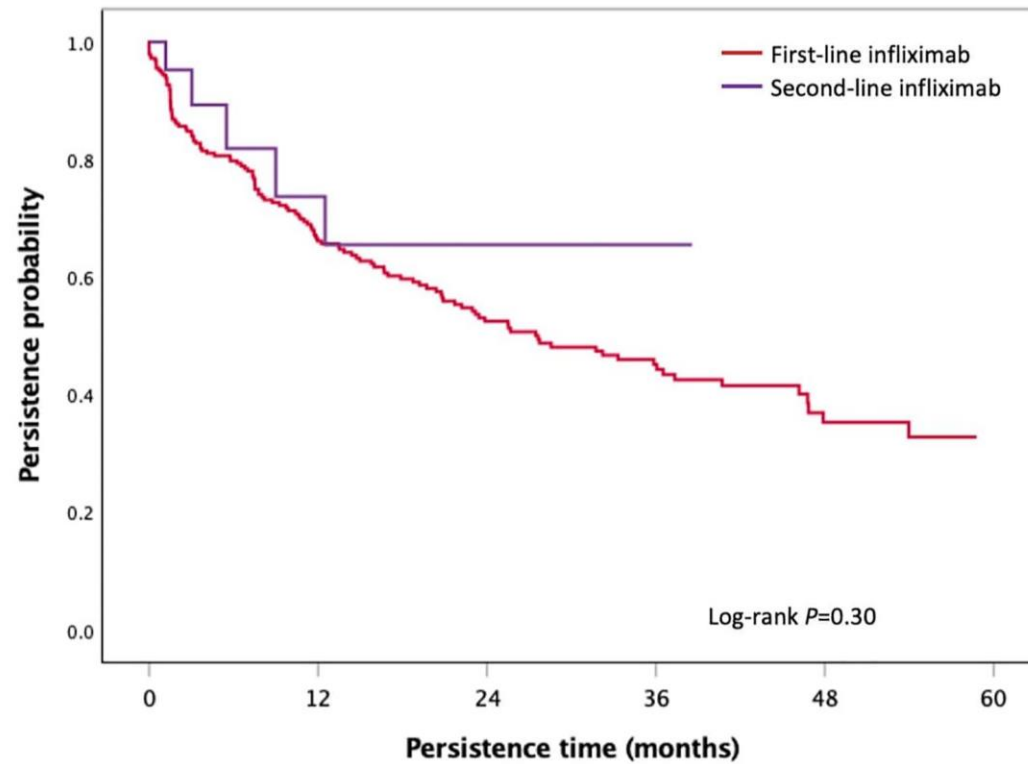
|                              | Persistence Percentage (95%CI) (%) |                     |                     |                     | Median survival time in months (95% CI) |
|------------------------------|------------------------------------|---------------------|---------------------|---------------------|---|
|                              | 12 months                          | 24 months           | 36 months           | 48 months           |   |
| Infliximab                   | 61.5<br>(52.0-71.0)                | 47.9<br>(38.1-57.7) | 43.8<br>(34.1-53.5) | 33.9<br>(24.6-43.2) | 22.2 (12.7–31.7)                        |
| Vedolizumab                  | 78.6<br>(72.3-84.8)                | 66.4<br>(59.3-73.5) | 60.7<br>(53.3-68.1) | 54.3<br>(46.8-61.8) | > 50.2*                                 |
| <i>P</i> -value <sup>†</sup> | <0.001 <sup>‡</sup>                | <0.001 <sup>‡</sup> | <0.001 <sup>‡</sup> | <0.001 <sup>‡</sup> |   |

CI, confidence interval

**Infliximab de Segunda línea**



**No se modifica la Persistencia**



|                              | Persistence Percentage (95%CI) (%) |                     |                     |                     | Median survival time in months (95% CI) |
|------------------------------|------------------------------------|---------------------|---------------------|---------------------|---|
|                              | 12 months                          | 24 months           | 36 months           | 48 months           |   |
| First-line IFX               | 66.1<br>(60.2-71.9)                | 52.5<br>(46.3-58.7) | 45.1<br>(38.9-51.3) | 35.3<br>(29.4-41.2) | 27.6 (18.7–36.6)                        |
| <u>Second-line IFX</u>       | 73.7<br>(55.3-92.1)                | 65.5<br>(45.6-85.4) | 65.5<br>(45.6-85.4) | -                   | > 38.6*                                 |
| <i>P</i> -value <sup>†</sup> | 0.53                               | 0.32                | 0.09                | n/a                 |   |

CI, confidence interval; IFX, infliximab; n/a, not applicable

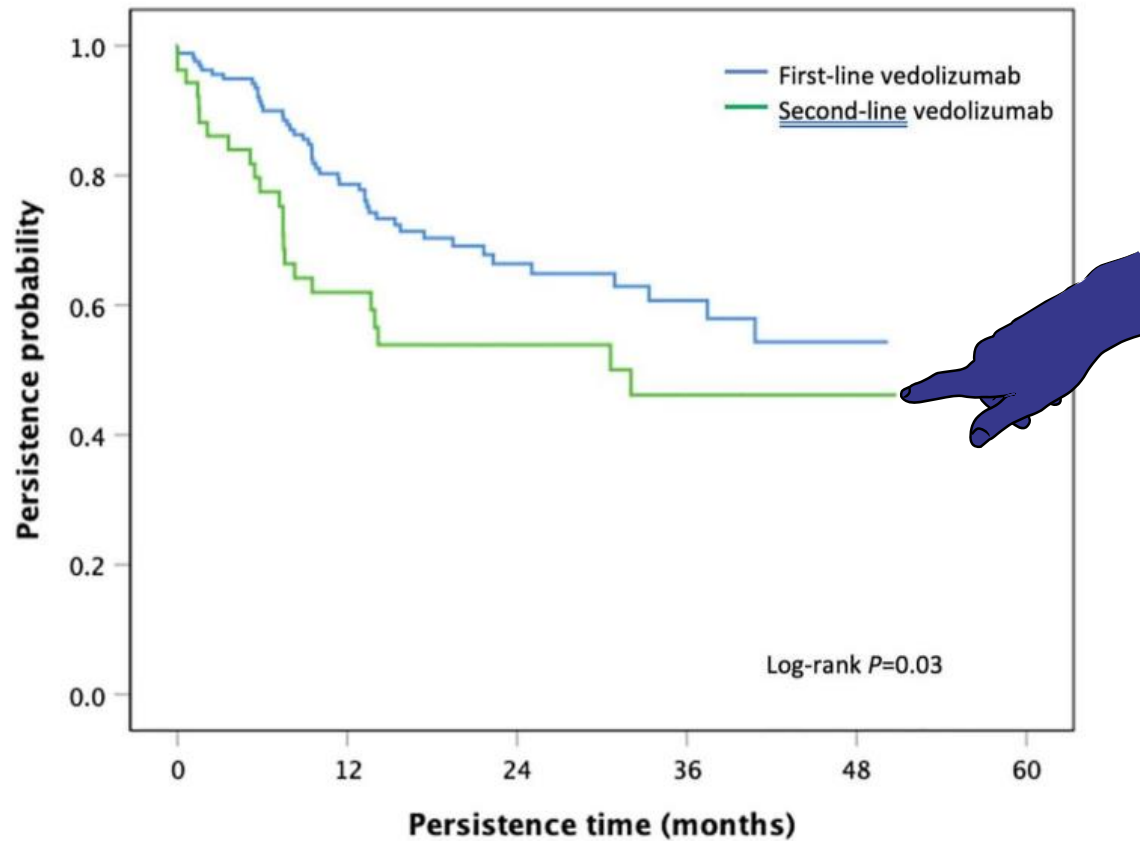
\*The median survival or its confidence interval cannot be exactly calculated when event rate is higher than 50%.

<sup>†</sup>Based on Bonferroni correction, statistical significance defined as  $P<0.017$

**Vedolizumab de Segunda línea**



**Disminuye la Persistencia**



|                              | Persistence Percentage (95%CI) (%) |                     |                     |                     | Median survival         |
|------------------------------|------------------------------------|---------------------|---------------------|---------------------|-------------------------|
|                              | 12 months                          | 24 months           | 36 months           | 48 months           | Time in months (95% CI) |
| First-line VED               | 78.6<br>(72.4-84.8)                | 66.4<br>(59.3-73.5) | 60.7<br>(53.3-68.1) | 54.3<br>(46.8-61.8) | > 50.2*                 |
| <u>Second-line VED</u>       | 62.0<br>(48.9-75.1)                | 53.9<br>(40.5-67.3) | 46.2<br>(32.8-59.6) | -                   | 32.0^a                  |
| <i>P</i> -value <sup>†</sup> | 0.02                               | 0.13                | 0.04                | n/a                 |                         |

CI, confidence interval; VED, vedolizumab; n/a, not applicable

# Effectiveness and Safety of Vedolizumab in Anti-TNF-Naïve Patients With Inflammatory Bowel Disease—A Multicenter Retrospective European Study

Uri Kopylov, MD,<sup>\*,a</sup> Bram Verstockt, MD,<sup>†,a</sup> Luc Biedermann, MD,<sup>‡</sup> Shaji Sebastian, MD,<sup>§</sup> Daniela Pugliese, MD,<sup>¶</sup> Elena Sonnenberg, MD,<sup>||</sup> Peter Steinhagen, MD,<sup>\*\*</sup> Naila Arebi, MD,<sup>††</sup> Yulia Ron, MD,<sup>‡‡</sup> Torsten Kucharzik, MD,<sup>§§</sup> Xavier Roblin, MD,<sup>¶¶</sup> Bella Ungar, MD,<sup>\*†</sup> Ariella Bar-Gil Shitrit, MD,<sup>|||</sup> Sandro Ardizzone, MD,<sup>\*\*\*</sup> Pauliina Molander, MD,<sup>†††</sup> Marina Coletta, MD,<sup>‡‡‡</sup> Laurent Peyrin-Biroulet, MD,<sup>§§§</sup> Peter Bossuyt, MD,<sup>¶¶¶</sup> Irit Avni-Biron, MD,<sup>||||</sup> Emmanouela Tsoukali, MD,<sup>\*\*\*\*</sup> Mariangela Allocca, MD,<sup>††††</sup> Konstantinos Katsanos, MD,<sup>‡‡‡‡</sup> Tim Raine, MD,<sup>§§§§</sup> Taina Sipponen, MD,<sup>††††</sup> Gionata Fiorino, MD,<sup>¶¶¶¶</sup> Shomron Ben-Horin, MD,<sup>\*</sup> Rami Eliakim, MD,<sup>\*</sup> Alessandro Armuzzi, MD,<sup>¶</sup> Britta Siegmund, MD,<sup>||</sup> Daniel C. Baumgart, MD,<sup>\*\*</sup> Nikolaos Kamperidis, MD,<sup>††</sup> Nitsan Maharshak, MD,<sup>‡‡</sup> Christian Maaser, MD,<sup>§§</sup> Gerassimos Mantzaris, MD,<sup>\*\*\*\*</sup> Henit Yanai, MD,<sup>||||</sup> Dimitriou K. Christodoulou, MD,<sup>‡‡‡‡</sup> Iris Dotan, MD,<sup>||||,a</sup> and Marc Ferrante, MD<sup>†,a</sup>

**Pérdida de respuesta es menor en “Naive” versus Exposición previa Anti TNF**

> Ann Clin Lab Sci. 2021 Sep;51(5):678-685.

# **Alterations in MAdCAM1-Positive Mucosal Capillaries and Integrin $\alpha_4\beta_7$ -Positive Lymphocytes in Crohn's Disease Treated with Anti-TNF $\alpha$ Biologics**

Mamoun Younes <sup>1</sup>, Andrew W DuPont <sup>2</sup>, Brooks D Cash <sup>2</sup>, Atilla Ertan <sup>2</sup>

**Menos eficacia Vedolizumab  
pos ANTI TNF**





**Menor expresión  
MAdCAM1**

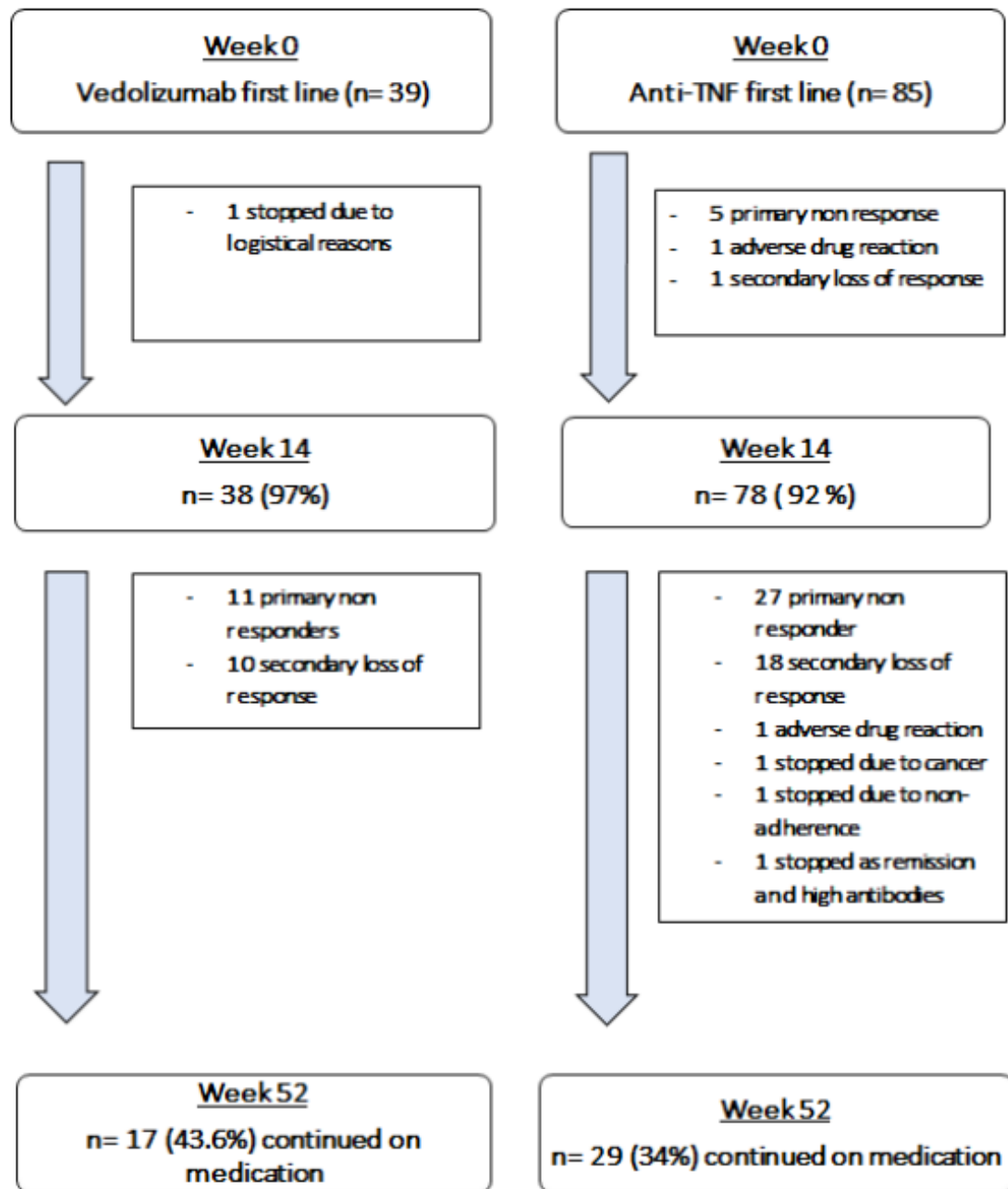
**Farmacocinética  
Vedolizumab**

**Niveles 22.5 vs  
36.0 µgr/ml**

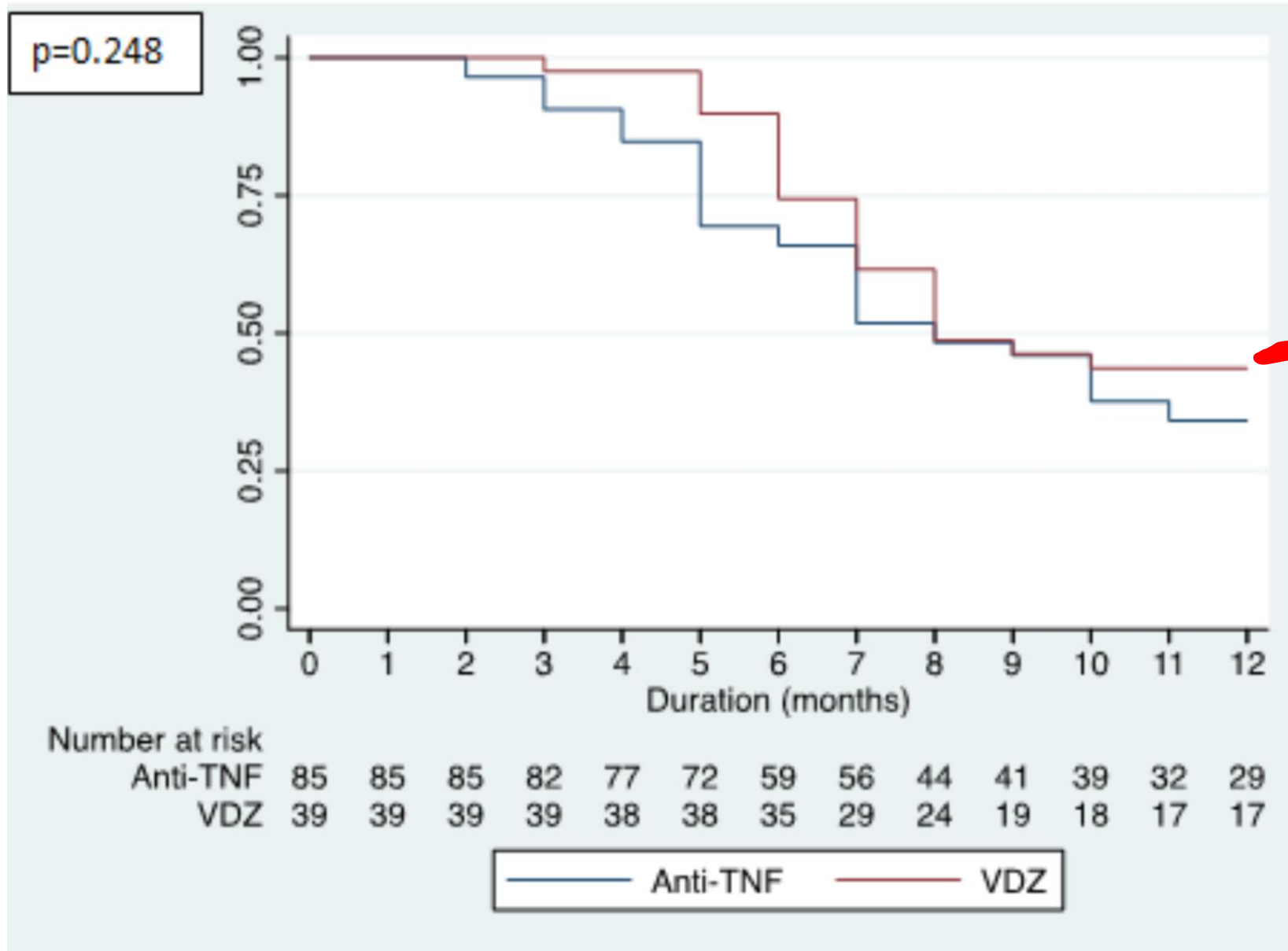
Liefferinckx C, Eur J Gastroenterol Hepatol 2019;31:478-85  
Biancheri P, Inflamm Bowel Dis 2013;19:259-64

# Comparative effectiveness of a second-line biologic in patients with ulcerative colitis: vedolizumab followed by an anti-TNF versus anti-TNF followed by vedolizumab

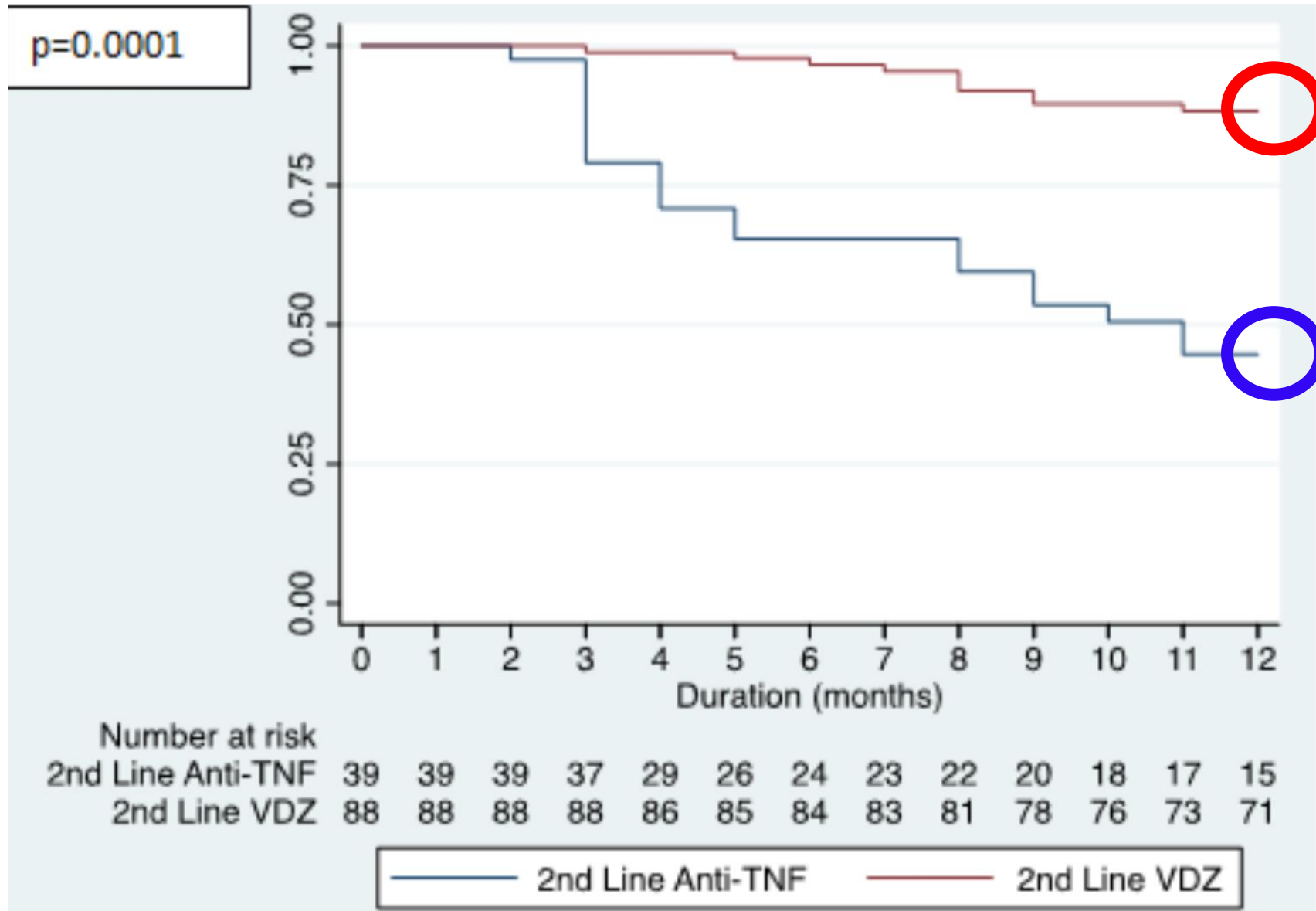
Charles Miller <sup>1</sup>, Hanson Kwok,<sup>1</sup> Paul Harrow,<sup>1</sup> Roser Vega,<sup>1</sup> Edward Seward <sup>1</sup>, Shameer Mehta,<sup>1</sup> Farooq Rahman,<sup>1</sup> Sara McCartney <sup>1</sup>, Ioanna Parisi,<sup>1</sup> Samuel Hsiang Lim,<sup>2</sup> Esha Sharma,<sup>2</sup> Mark A Samaan,<sup>2</sup> Aaron Bancil,<sup>3</sup> Klaartje Bel Kok,<sup>3</sup> Ahmed Shalabi,<sup>4</sup> Emma L Johnston,<sup>4</sup> Dev Katarey,<sup>5</sup> Nina Taherzadeh,<sup>5</sup> Charles Murray,<sup>5</sup> Mohammed Tauseef Sharip,<sup>6</sup> Martyn J Carter,<sup>6</sup> Shiva T Radhakrishnan <sup>7</sup>, Simon Peake,<sup>7</sup> Imran Khakoo,<sup>8</sup> Mahmood Wahed,<sup>8</sup> Sebastian Povlsen,<sup>9</sup> Mehul Patel,<sup>9</sup> Patrick DuBois,<sup>9</sup> Jemima Finkel,<sup>10</sup> Clive Onnie,<sup>10</sup> Stuart Bloom<sup>1</sup>



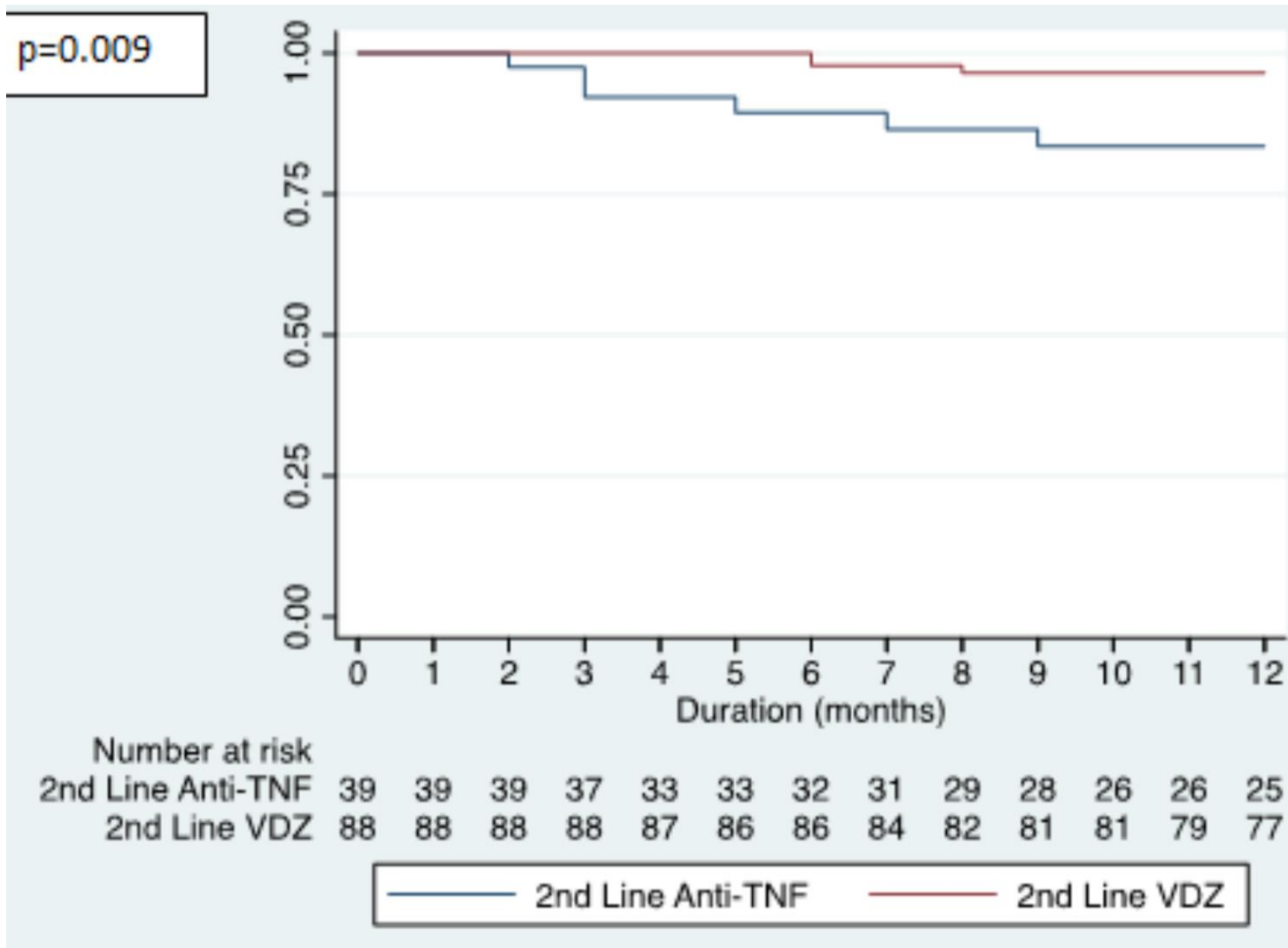
# Persistencia en primera línea Anti TNF vs Vedolizumab

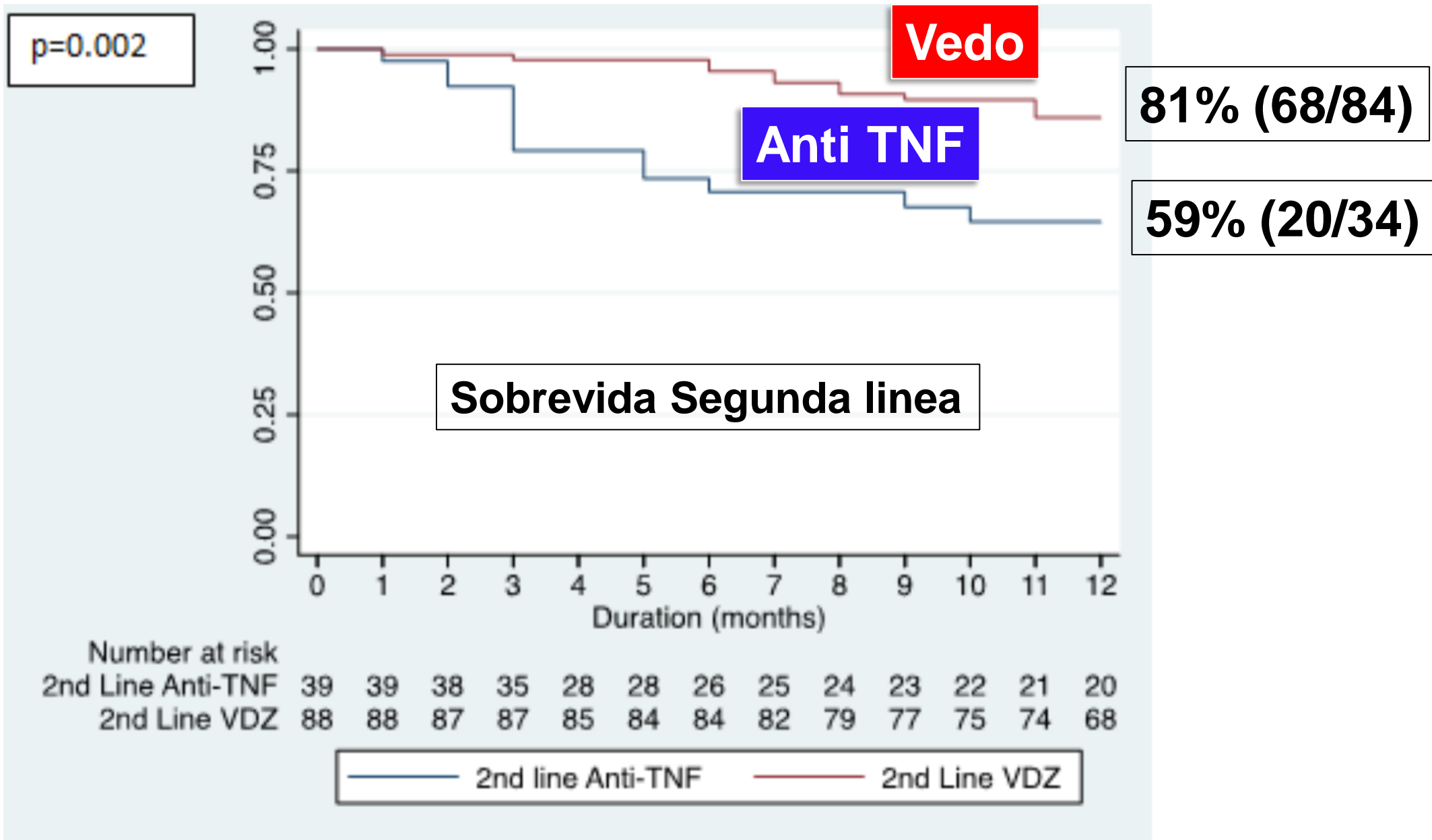


# Persistencia en segunda línea Anti TNF vs Vedolizumab



# Tasa de sobrevida libre de colectomía

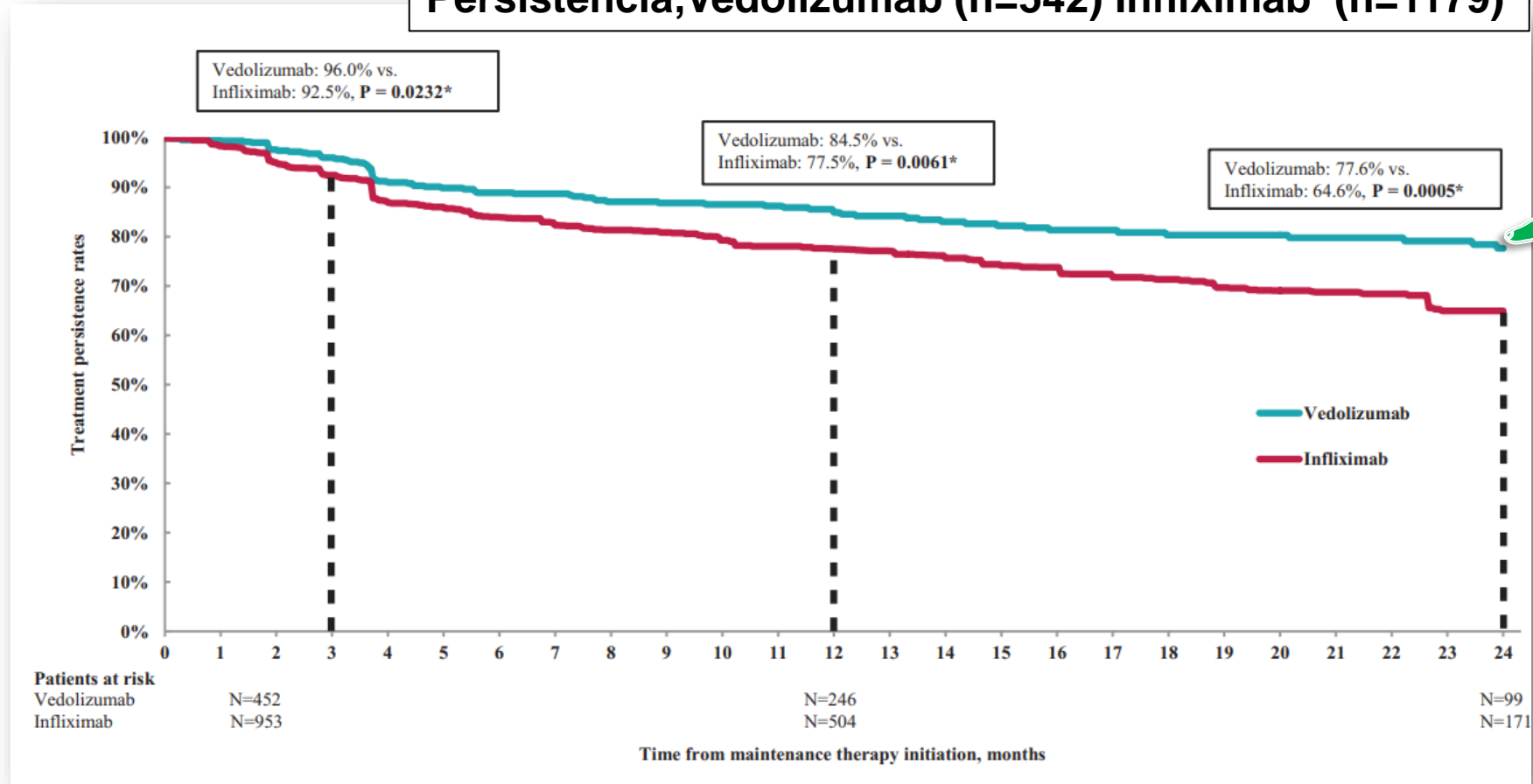




# Comparison of Real-World Treatment Outcomes With Vedolizumab Versus Infliximab in Biologic-Naive Patients With Inflammatory Bowel Disease

Haridarshan Patel, PharmD,<sup>\*</sup> Dominick Latremouille-Viau, MA,<sup>†</sup> Rebecca Burne, PhD,<sup>†</sup> Sherry Shi, MSc,<sup>†</sup> and Shashi Adsul, MD, MBA<sup>‡</sup>

## Persistencia, Vedolizumab (n=542) Infliximab (n=1179)



# Intensificaciòn de la dosis

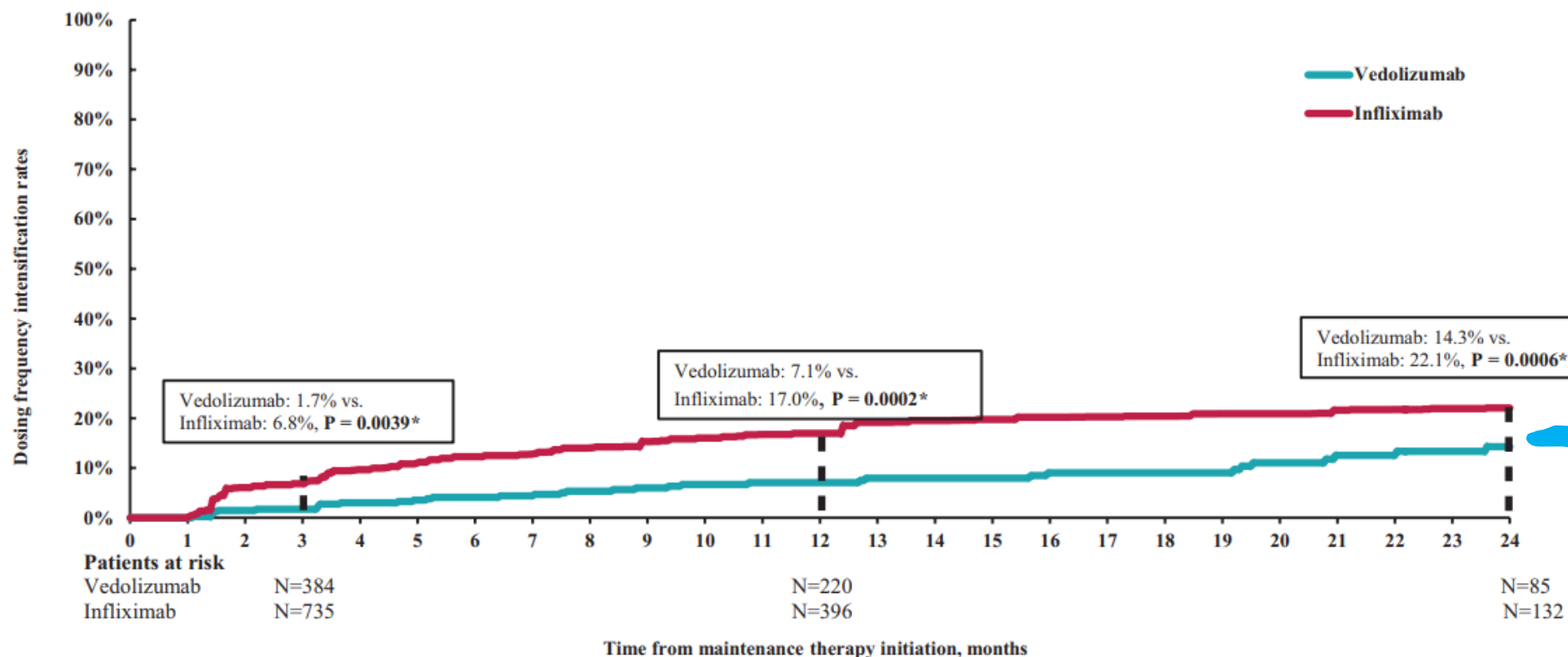
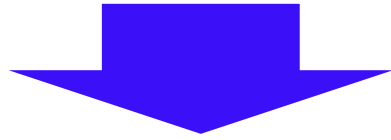
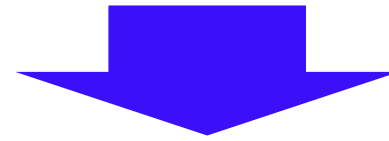


FIGURE 2. Weighted Kaplan–Meier curves of dosing frequency intensification in IBD patients (vedolizumab, N = 407; infliximab, N = 911). \*Statistically significant at the 5% level. Dose escalation via increased dose is not included in this end point. Only dose escalation via intensification of dosing frequency is included.

**Vedolizumab superior**



**Adalimumab e infliximab  
en múltiples Objetivos terapéuticos**



**Remisión clínica  
Remisión endoscópica  
Remisión histológica**

# **Paciente Candidato para Vedolizumab**

# Colitis ulcerativa o EC moderada a severa

## Vedolizumab

Corta evolución  
Infecciones previas  
Cáncer extraintestinal  
Vitamina D normal  
PCR Baja  
Adulto mayor  $\geq 65$  años  
***No exposición Anti TNF***  
***??***

## Anti TNF

Colitis aguda severa  
*Embarazo*  
*Extraintestinales*

# ElI manifestaciones extraintestinales







Paralelas  
Actividad  
Intraluminal

Independientes  
Actividad  
Intraluminal

Artritis periférica tipo 1  
Eritema nodoso  
Estomatitis aftosa  
Epiescleritis

Artritis periférica tipo 2  
Artritis axial  
Pioderma gangrenoso  
Escleritis  
Uveitis  
Colangitis esclerosante primaria

# Vedolizumab and Extraintestinal Manifestations in Inflammatory Bowel Disease

Jurij Hanzel<sup>1,2,7</sup>  · Christopher Ma<sup>2,3</sup>  · Niels Vande Castele<sup>2,4</sup>  · Reena Khanna<sup>5</sup>  · Vipul Jairath<sup>2,5,6</sup>  · Brian G. Feagan<sup>2,5,6,8</sup> 

**Manifestaciones  
Enfermedad inmune  
Sistémica Primaria**









**Fisiopatología**

**Secundarias  
Inflamación intestinal**

**Atracción anormal de linfocitos por expresión ectópica  
de citoquinas y moléculas adhesión intestinales  
Reacción cruzada con autoanticuerpos contra intestino**

# Vedolizumab and Extraintestinal Manifestations in Inflammatory Bowel Disease

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## Vedolizumab

**Eficaz Extraintestinales  
Asociadas con actividad**

**Exacerbación  
Antecedentes anti TNF**

**No hay ECC  
Análisis pos hoc  
Se necesitan estudios  
Bien diseñados**

Hanzel J, *Drugs* 2021; 81:333–347

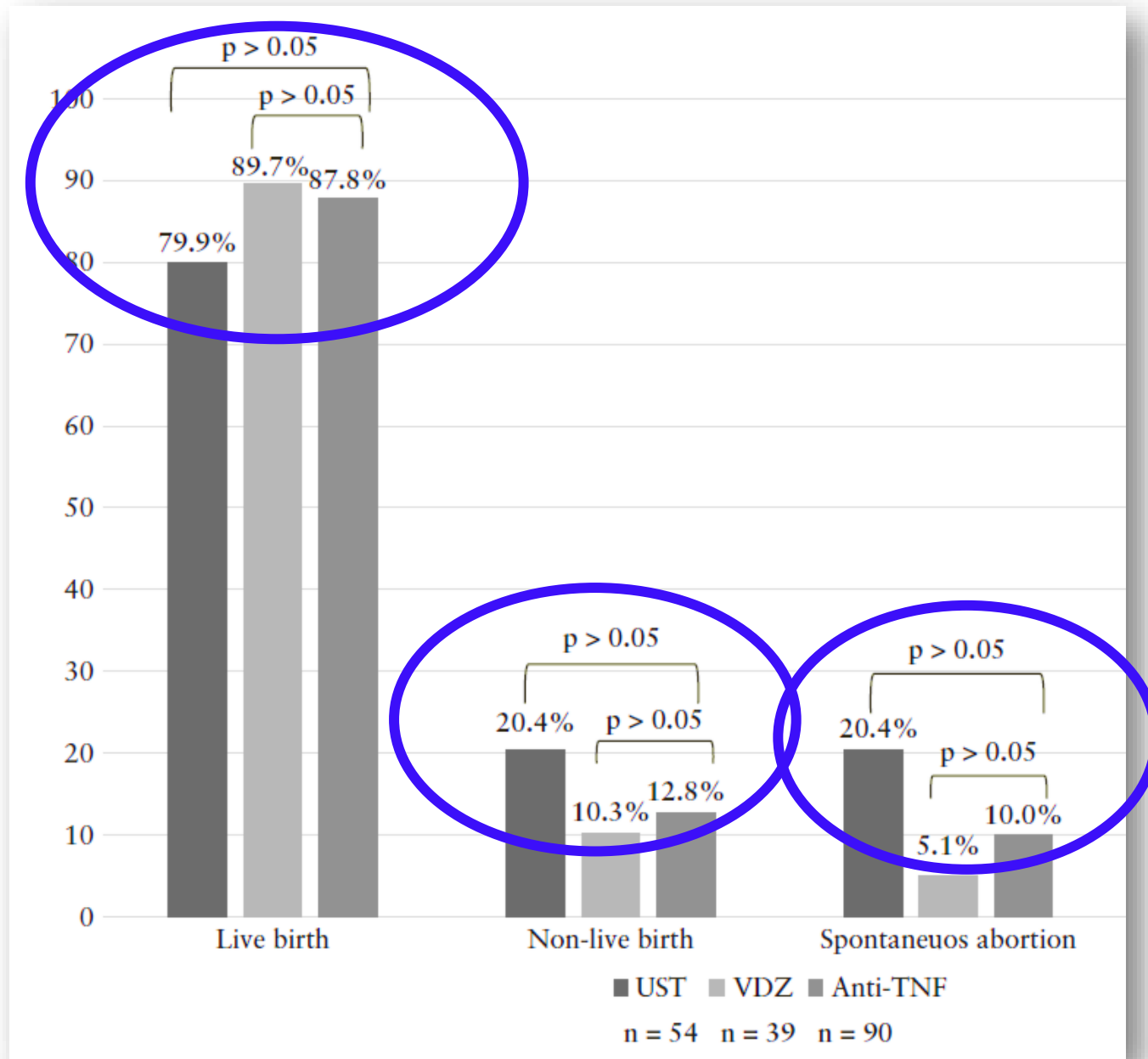
## **Safety of Ustekinumab and Vedolizumab During Pregnancy – Pregnancy, Neonatal, and Infant Outcome: A Prospective Multicentre Study**

Katarina Mitrova,<sup>a,b</sup> Barbora Pipek,<sup>c,d,e</sup> Martin Bortlik,<sup>f,g,h</sup> Ludek Bouchner,<sup>i</sup> Jan Brezina,<sup>j</sup> Tomas Douda,<sup>k</sup> Tomas Drasar,<sup>l</sup> Pavel Klvana,<sup>m</sup> Pavel Kohout,<sup>n</sup> Vaclav Leksa,<sup>o</sup> Petra Minarikova,<sup>h</sup> Ales Novotny,<sup>p</sup> Pavel Svoboda,<sup>e</sup> Jan Skorpik,<sup>q</sup> Jan Ulbrych,<sup>r,s</sup> Marek Veinfurt,<sup>t</sup> Blanka Zborilova,<sup>t</sup> Milan Lukas,<sup>a</sup> Dana Duricova<sup>a,g</sup>; the Czech IBD Working Group



**Mitrova K, J Crohn's Colitis 2022 Online Sept 2,**

# Embarazo



# Vedolizumab USA



**> 261.000 patients**  
**> 36.000 mèdicos**

**Takeda 2022**

# ***Mensajes para la casa***

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**Vedolizumab en “bionative” superior anti TNF**

**Vedo inicial no disminuye eficacia anti TNF**

**Persistencia de Vedo supera anti TNF**

**Mejor estrategia CU Vedo --- Anti TNF**

**Vedo 2da línea menor eficacia ?**

**Vedo en extraintestinales paralelas con EI**

***Muchas gracias!***