

Retirada de tratamiento en Artritis Idiopática Juvenil

Agustín Remesal
Reumatología Pediátrica
Hospital Infantil La Paz
27 de noviembre 2015



Hospital Universitario La Paz
SaludMadrid

Introducción

Últimos años

avances importantes en tratamiento de AIJ

Mayores expectativas para alcanzar

→ inactividad

→ remisión clínica



Introducción

Preliminary Criteria for Clinical Remission for Select Categories of Juvenile Idiopathic Arthritis



Retirada fármacos

6 meses

Tº Variable

12 meses

Debut



Enfermedad inactiva con medicación

Remisión clínica CON medicación

Remisión clínica SIN medicación

Introducción

AMERICAN COLLEGE OF RHEUMATOLOGY
EDUCATION • TREATMENT • RESEARCH

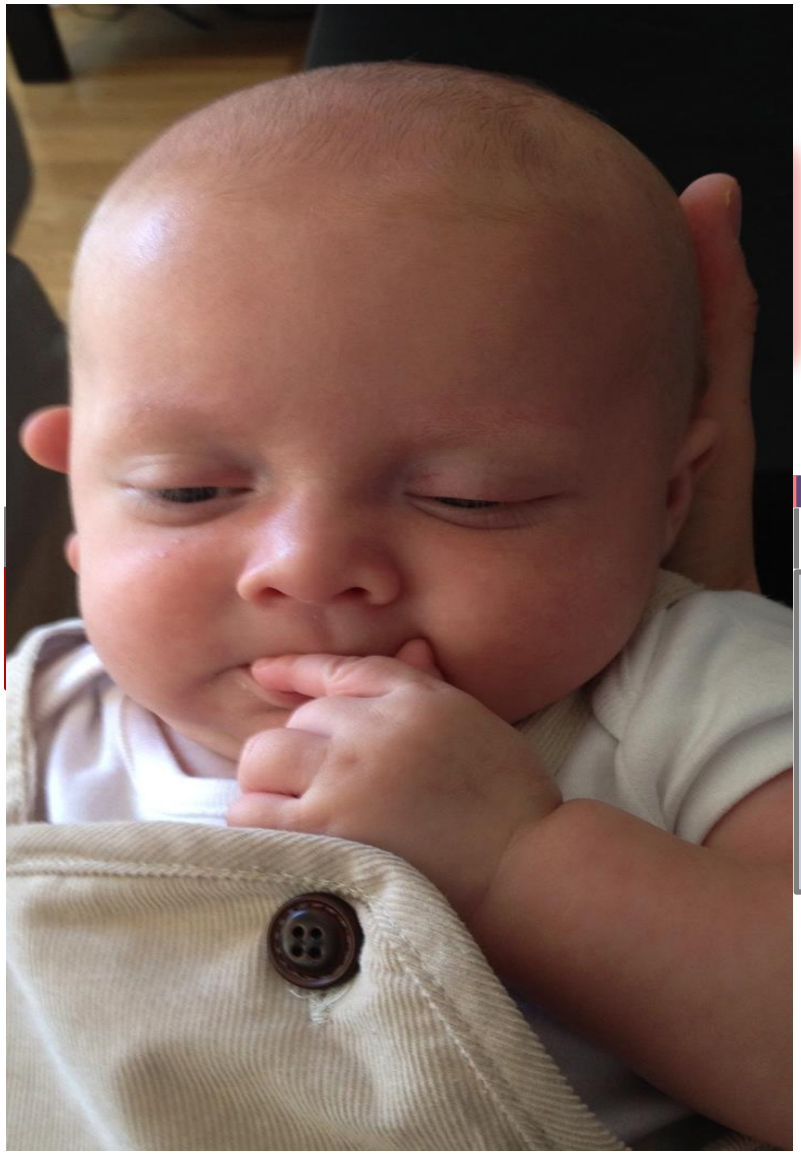
Debut



2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Initiation and Safety Monitoring of Therapeutic Agents for the Treatment of Arthritis and Systemic Features

TIMOTHY BEUKELMAN, MD, MSCE[1], NIVEDITA M. PATKAR, MD, MSPH[1], KENNETH G. SAAG, MD, MSc[1], SUE TOLLESON-RINEHART, PhD[2], RANDY Q. CRON, MD, PhD[1], ESI MORGAN DeWITT, MD, MSCE[3], NORMAN T. ILOWITE, MD[4], YUKIKO KIMURA, MD[5], RONALD M. LAXER, MDCM, FRCPC[6], DANIEL J. LOVELL, MD, MPH[3], ALBERTO MARTINI, MD[7], C. EGLA RABINOVICH, MD, MPH[8], and NICOLINO RUPERTO, MD, MPH[7]

Introducción



Retirada fármacos

Tº Variable

12 meses



Remisión clínica CON medicación

Remisión clínica SIN medicación

Introducción

Ausencia de
GUÍAS y RECOMENDACIONES
para retirada de tratamiento

Introducción

Debut → Enfermedad inactiva con medicación → Remisión clínica CON medicación → ✗



Práctica **clínica muy variable**:

empírica y dependiente del médico

Defining Juvenile Idiopathic Arthritis Remission and Optimum Time for Disease-Modifying Anti-Rheumatic Drug Withdrawal

Why We Need a Consensus

Broughton T and Armon K Pediatr Drugs 2012;14:7-12

Introducción

Debut

Enfermedad inactiva con medicación

Remisión clínica CON medicación



¿herramientas predictoras?

Esquema de la charla

ESTRATEGIAS DE RETIRADA

¿tiempo inactividad previo retirada?

¿reducción de dosis?

¿orden de retirada de fármacos?

¿categoría de AIJ?

Esquema de la charla

HERRAMIENTAS PREDICTORAS

¿Ecografía?

¿Biomarcadores *(Proteínas S100)*?

ESTRATEGIAS DE RETIRADA

casi todos los estudios realizados

Anti-TNF

ETN



ESTRATEGIAS DE RETIRADA

2009

Letters

When and how to stop etanercept after successful treatment of patients with juvenile idiopathic arthritis

F H M Prince,[1] M Twilt,[1,2] S C M Simon,[1] M A J van Rossum,[3] W Armbrust,[4] E P A H Hoppenreijs,[5] S Kamphuis,[1] M van Santen-Hoeufft,[6] Y Koopman-Keemink,[7] N M Wulffraat,[8] R ten Cate,[2] L W A van Suijlekom-Smit[1]

Ann Rheum Dis July 2009 Vol 68 No 7

ESTRATEGIAS DE RETIRADA

2010

The Journal of Rheumatology Volume 37, r

Discontinuation of Etanercept After Successful Treatment in Patients with Juvenile Idiopathic Arthritis

AGUSTIN REMESAL, JAIME DE INOCENCIO, ROSA MERINO and JULIA GARCIA-CONSUEGRA

A follow-up study of patients with juvenile idiopathic arthritis who discontinued etanercept due to disease remission

P. Pratsidou-Gertsi, M. Trachana, G. Pardalos, F. Kanakoudi-Tsakalidou

Clinical and Experimental Rheumatology

ESTRATEGIAS DE RETIRADA

2011

ARTHRITIS & RHEUMATISM
Vol. 63, No. 10, October 2011, pp 3163–3168
DOI 10.1002/art.30502
© 2011, American College of Rheumatology

BRIEF REPORT

Clinical Outcomes After Withdrawal of Anti–Tumor Necrosis Factor α Therapy in Patients With Juvenile Idiopathic Arthritis: A Twelve-Year Experience

Kevin Baszis, Jane Garbutt, Dana Toib, Jingnan Mao, Allison King, Andrew White, and Anthony French

ESTRATEGIAS DE RETIRADA

2013

Rheumatol Int (2013) 33:2657–2660
DOI 10.1007/s00296-012-2468-3

SHORT COMMUNICATION

Clinical remission in juvenile idiopathic arthritis after termination of *etanercept*

Jacek Postępski · Katarzyna Kobusińska · Edyta Olesińska · Violetta Osińska · Violetta Opoka-Winiarska

ESTRATEGIAS DE RETIRADA

2013

Rheumatol Int
DOI 10.1007/s00296-013-2884-z

SHORT COMMUNICATION

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

Estíbaliz Iglesias · Vicenç Torrente-Segarra · Rosa Bou · Silvia Ricart · María Isabel González · Judith Sánchez · Joan Calzada · Jordi Antón

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

Revisión de la literatura

Table 2

Main author (references)	Prince [2] ($N = 19$)	Remesal [4] ($N = 26$)	Pratsidou-Gertsi [3] ($N = 11$)	Baszis [5] ($N = 99$)[a]	Postepski [6] ($N = 39$)

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

¿mayor tiempo de inactividad con tto

=

menor tasa de recaída?

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

Revisión de la literatura

Table 2

Main author (references)	Prince [2] ($N = 19$)	Remesal [4] ($N = 26$)	Pratsidou-Gertsi [3] ($N = 11$)	Baszis [5] ($N = 99$)[a]	Postepski [6] ($N = 39$)
Duration of inactive disease prior to drug withdrawal modifies time to relapse	Yes[b]	No	Not assessed	No	Not assessed

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

¿influye en recaída?

- retirada **progresiva**
- retirada **directa**

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

Revisión de la literatura

Table 2

Main author (references)	Prince [2] ($N = 19$)	Remesal [4] ($N = 26$)	Pratsidou-Gertsi [3] ($N = 11$)	Baszis [5] ($N = 99$)[a]	Postepski [6] ($N = 39$)
Relapse differences between abrupt and progressive withdrawal	Yes[c]	No	No	Not applicable	Not assessed

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

FAMEs suspendidos antes que anti-TNF al alcanzar inactividad

Recaída tras suspender anti-TNF:

sugiere anti-TNF mantiene la inactividad

Non-systemic juvenile idiopathic arthritis outcome after reaching clinical remission with anti-TNF-α therapy: a clinical practice observational study of patients who discontinued treatment

¿orden óptimo de retirada de fármacos?



ESTRATEGIAS DE RETIRADA

Mayo 2015

Arthritis Care & Research
Vol. 67, No. 5, May 2015, pp 658–666
DOI 10.1002/acr.22477
© 2015, American College of Rheumatology

ORIGINAL ARTICLE

Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

CAROLINE Y. CHANG, RIKA M. L. MEYER, AND ANDREAS O. REIFF

Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

4 “ramas” de retirada de tratamiento

GRUPO 1

Anti-TNF + MTX: **1º MTX**

GRUPO 2

Anti-TNF + MTX: **1º anti-TNF**

GRUPO 3

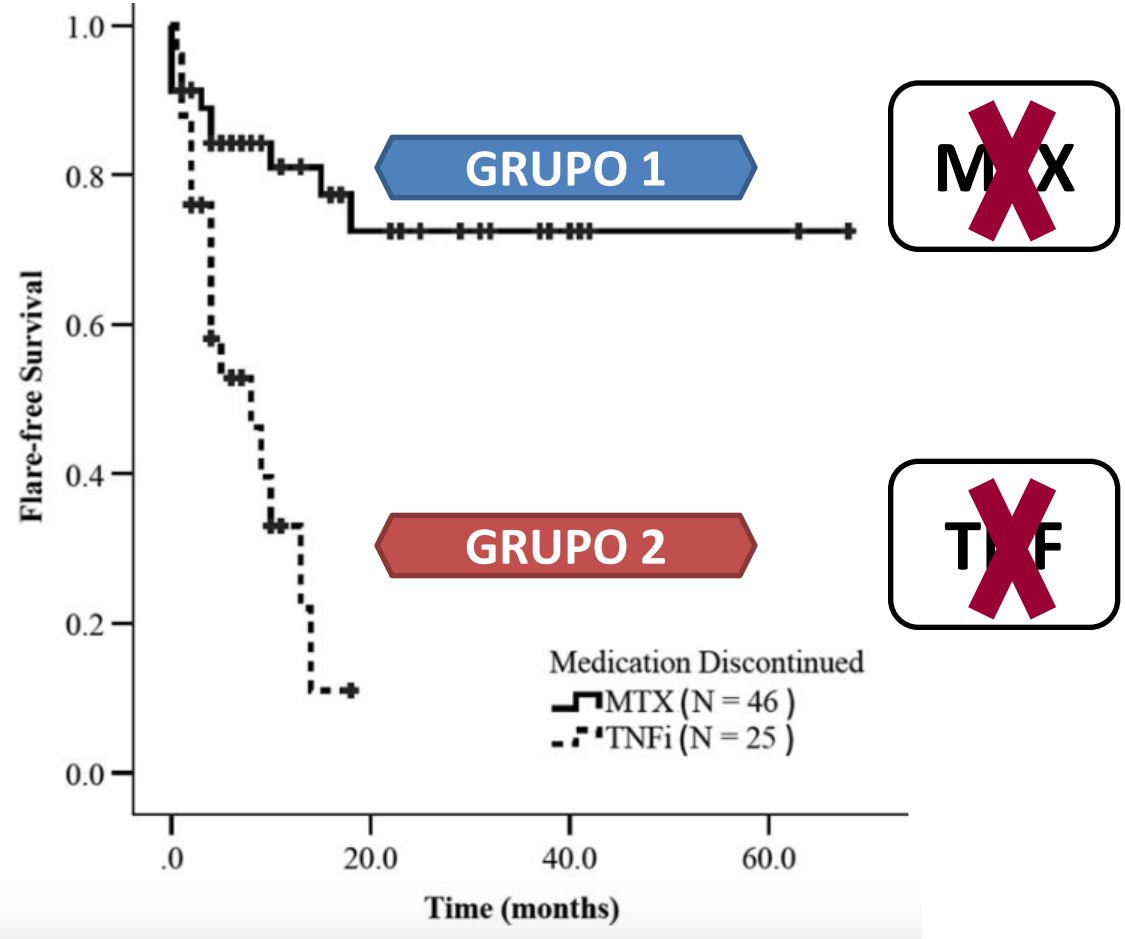
MTX en monoterapia

GRUPO 4

Anti-TNF en monoterapia

Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

Comparación: grupos de tto combinado



Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

Comparación: grupos de tto combinado

Permanecen INACTIVOS

		6 meses	12 meses
GRUPO 1	MTX	84%	81%
GRUPO 2	TNF	53%	22%

Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

Comparación: grupos en "monoterapia"

RECAÍDA 

		12 meses
GRUPO 3	MTX	50%
GRUPO 4	TNF	78%

Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

¿orden óptimo de retirada de fármacos?

Retirar el MTX antes que anti-TNF

ESTRATEGIAS DE RETIRADA

Retirada “directa” vs “progresiva”

2010

The Journal of Rheumatology Volume 37,

Discontinuation of Etanercept After Successful Treatment in Patients with Juvenile Idiopathic Arthritis

AGUSTIN REMESAL, JAIME DE INOCENCIO, ROSA MERINO and JULIA GARCIA-CONSUEGRA

A follow-up study of patients with juvenile idiopathic arthritis who discontinued etanercept due to disease remission

P. Pratsidou-Gertsi, M. Trachana, G. Pardalos, F. Kanakoudi-Tsakalidou

Mayo 2015

Arthritis Care & Research
Vol. 67, No. 5, May 2015, pp 658–666
DOI 10.1002/acr.22477
© 2015, American College of Rheumatology

ORIGINAL ARTICLE

Impact of Medication Withdrawal Method on Flare-Free Survival in Patients With Juvenile Idiopathic Arthritis on Combination Therapy

CAROLINE Y. CHANG, RIKA M. L. MEYER, AND ANDREAS O. REIFF

ESTRATEGIAS DE RETIRADA

Retirada “directa” vs “progresiva”

No hubo diferencias

PERO no recaída

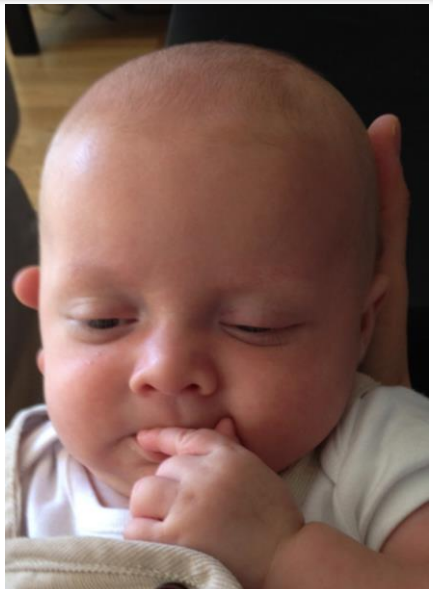
“hasta suspensión *COMPLETA* del anti-TNF”

NO durante rebaja progresiva

ESTRATEGIAS DE RETIRADA

Retirada “directa” vs “progresiva”

¿dosis *“bajas”* de anti-TNF *podrían* mantener la inactividad?



ESTRATEGIAS DE RETIRADA

2013

Rheumatol Int (2013) 33:2277–2282
DOI 10.1007/s00296-012-2642-7

ORIGINAL ARTICLE

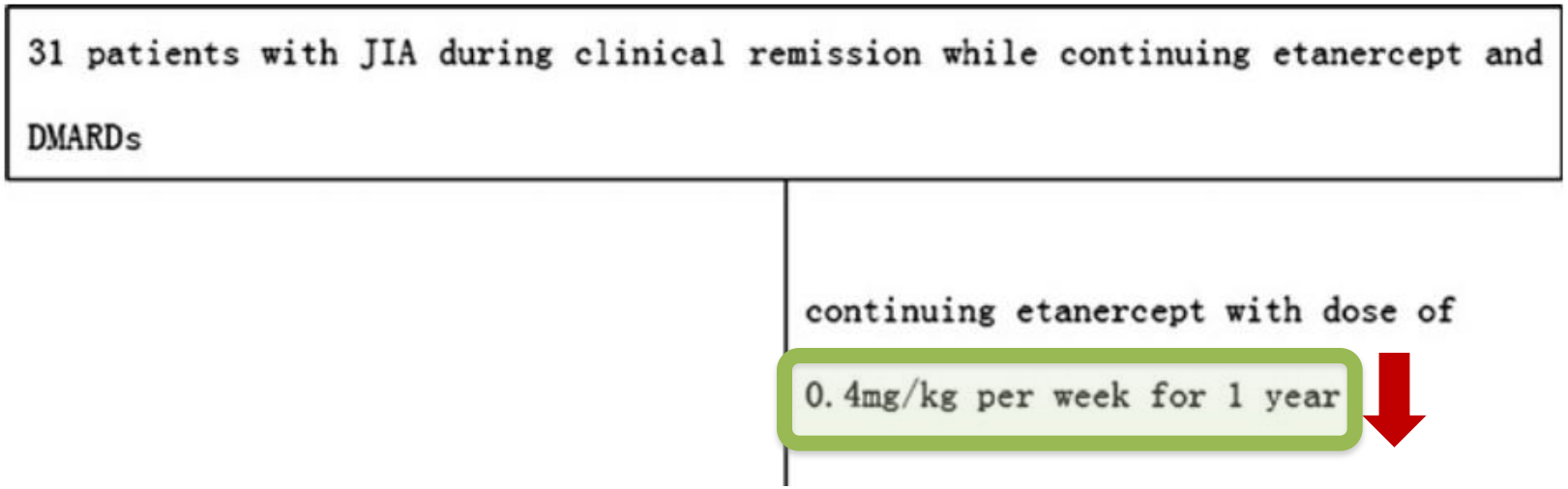
Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission

Yubo Cai · Xiaosheng Liu · Wenming Zhang · Jianrong Xu · Lanfang Cao

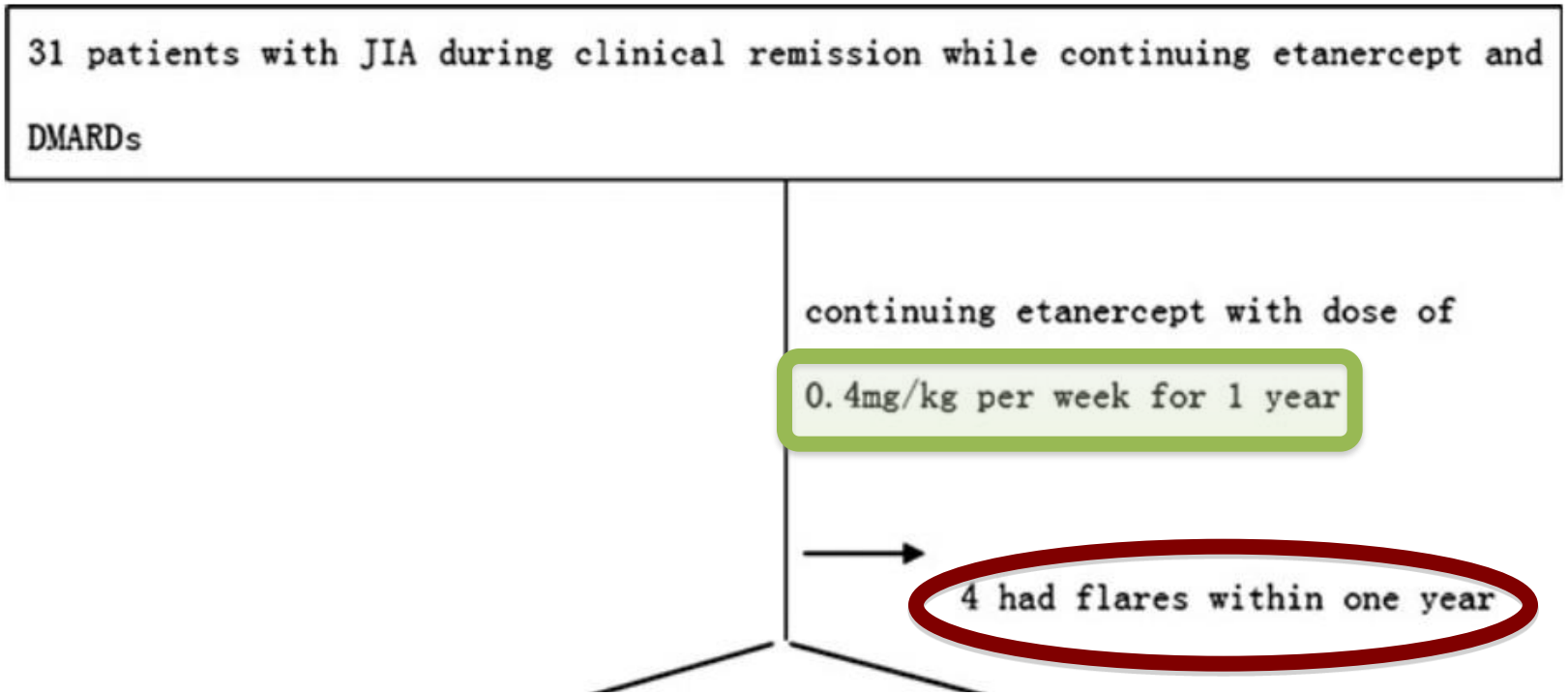
Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission

31 patients with JIA during clinical remission while continuing etanercept and DMARDs

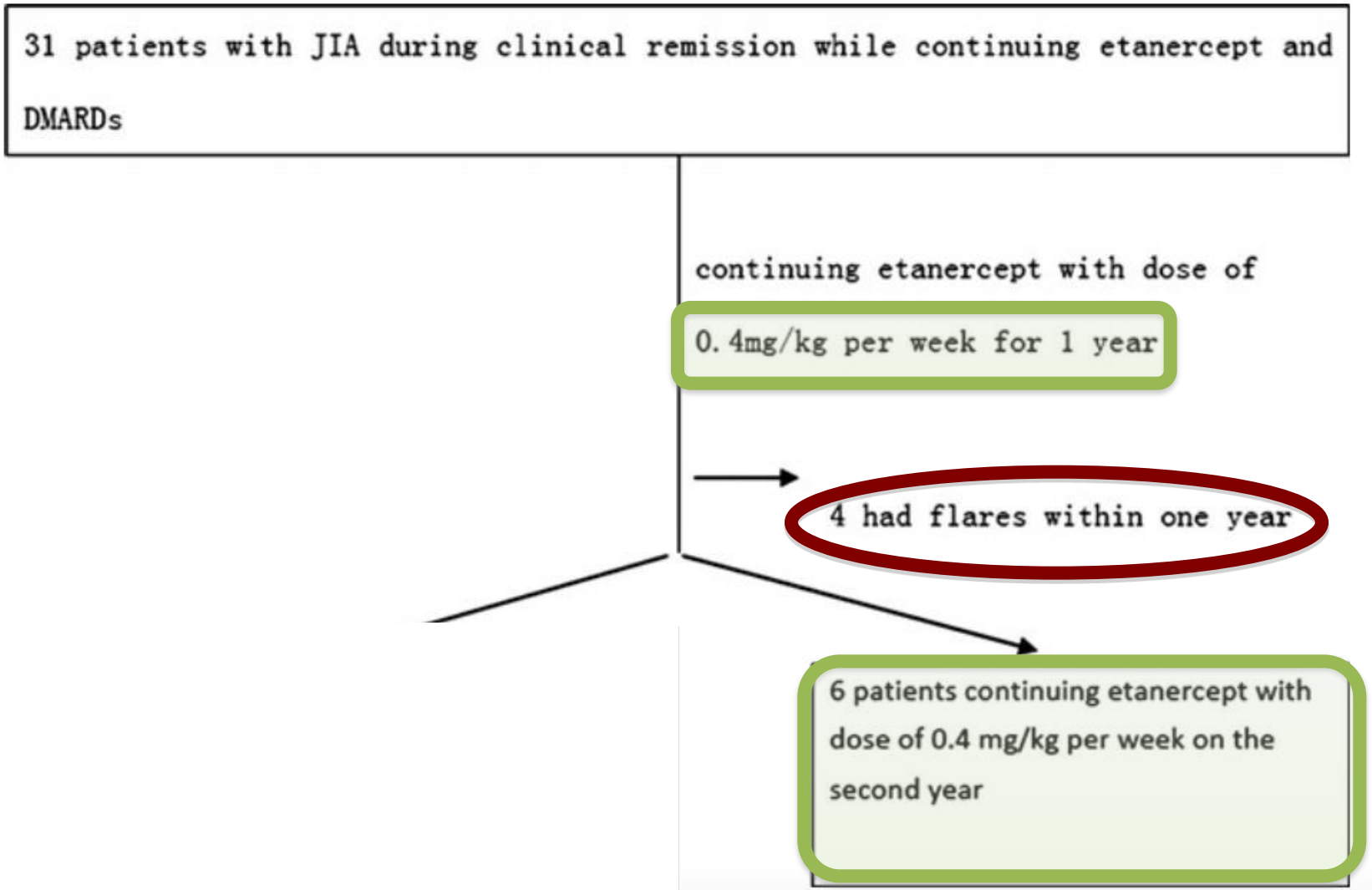
Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission



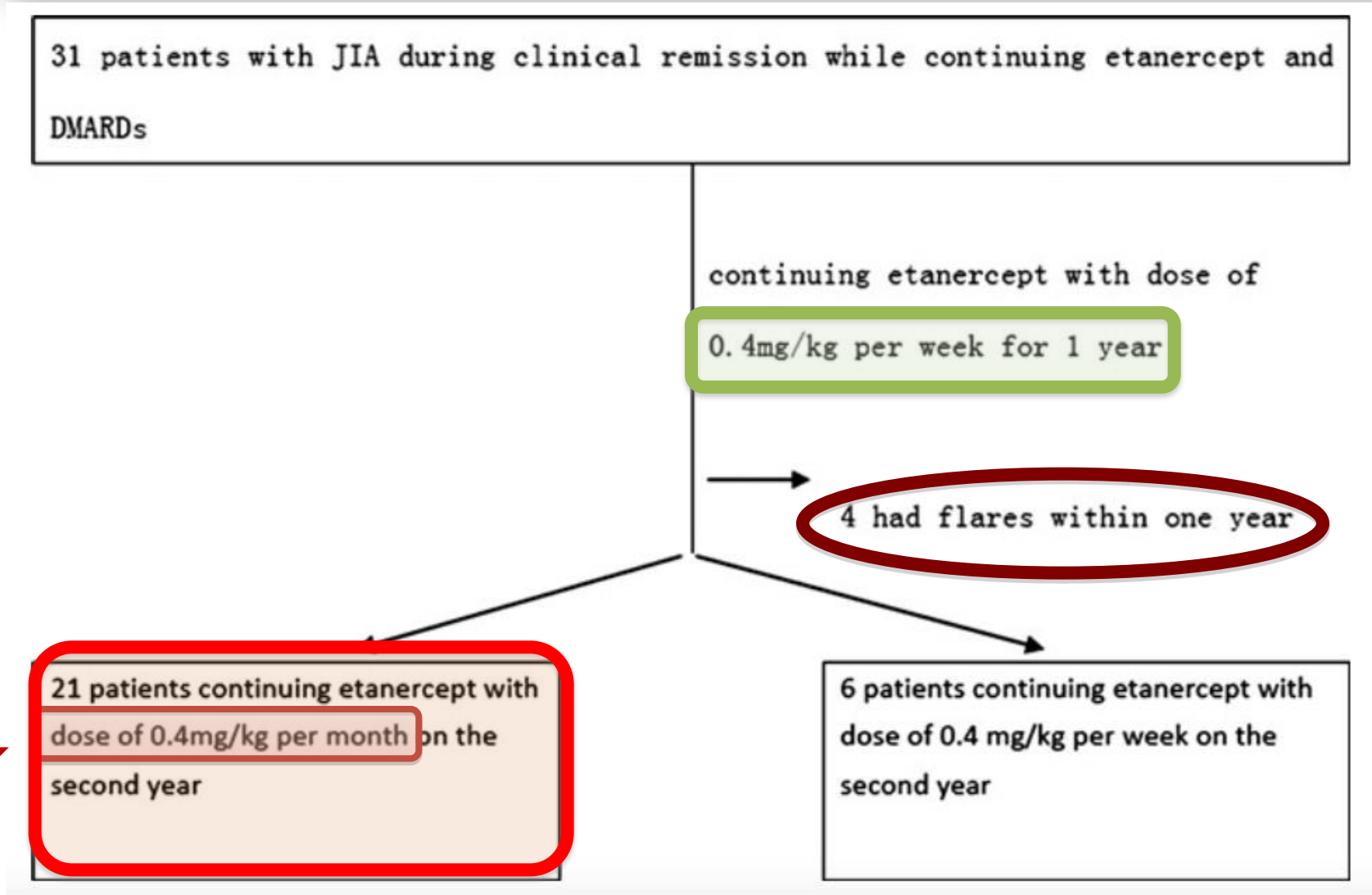
Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission



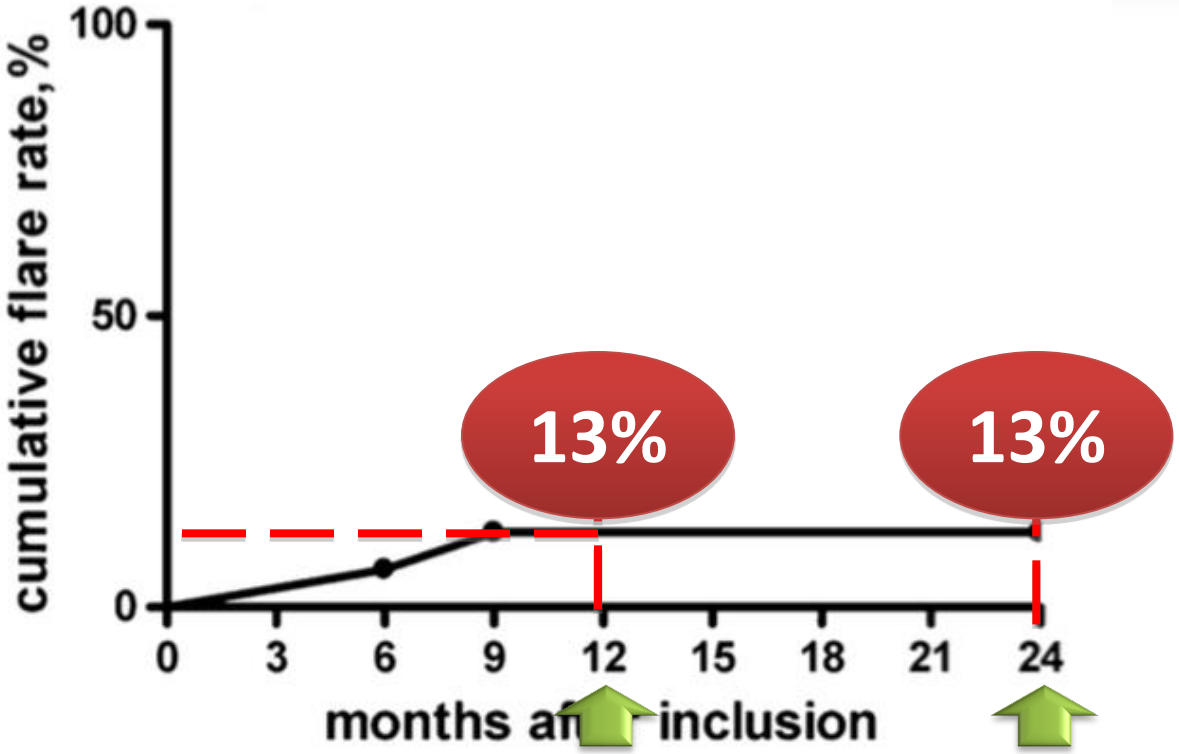
Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission



Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission



Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission



Months after inclusion	0	3	6	9	12	24
patients keeping remission	31	31	29	27	27	27

Clinical trial of etanercept tapering in juvenile idiopathic arthritis during remission

Método “step-down” puede ser útil en la retirada del ETN



LIMITACIONES

Análisis de AIJ agrupadas

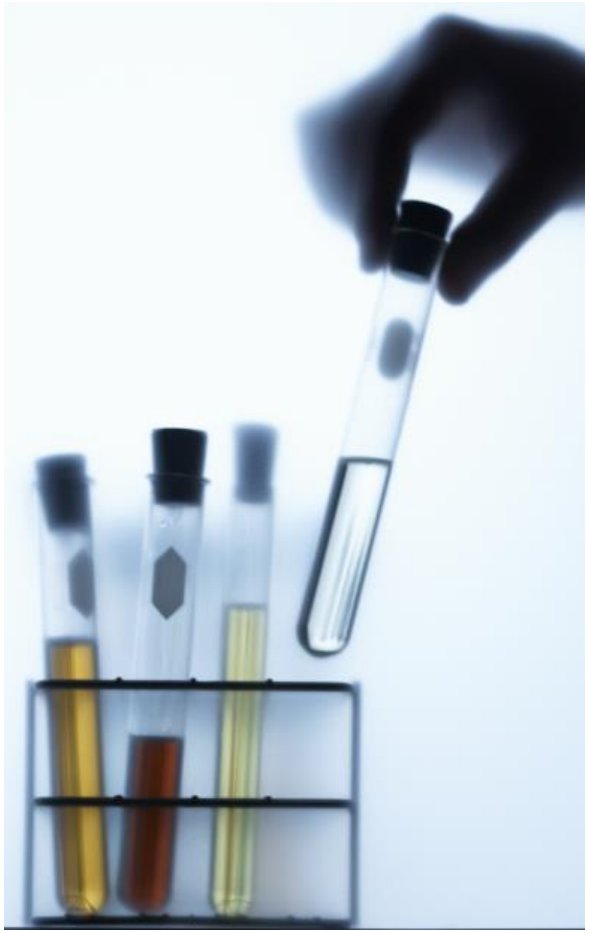
Mayoría clara de ARE

¿AIJ poli FR (+)?



LIMITACIONES

¿determinación de niveles de ETN?




PABLO
8


Coca-Cola
AZERBAIJAN
LAND OF FIRE

ECOGRAFÍA



Ventajas: barata, inocua, y "emparejada" a la EF

¿la actividad ecográfica predice recaídas al suspender tto?

ECOGRAFÍA

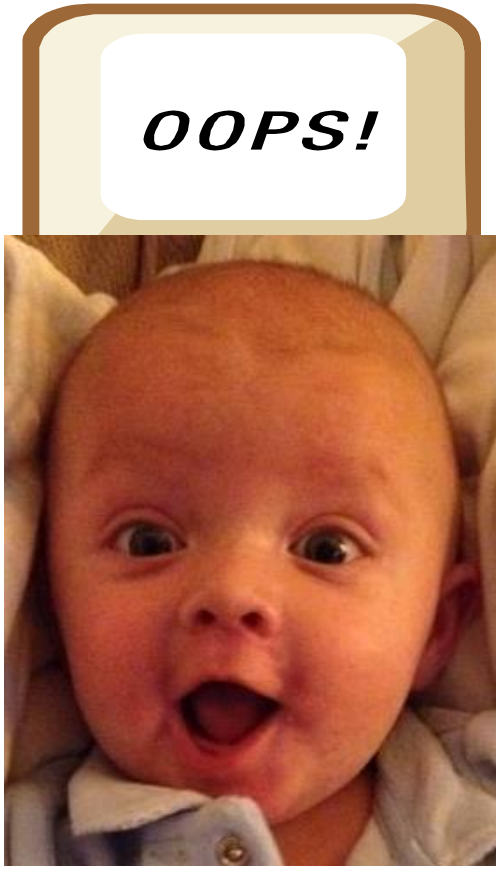
Clinical and Experimental Rheumatology 2014

Detection of synovitis by ultrasonography in clinically inactive juvenile idiopathic arthritis on and off medication

P. Collado[1], M.L. Gamir[2], J.C. López-Robledillo[3], R. Merino[4], C. Modesto[5], I. Monteagudo[6]

Objetivo: determinar alteraciones ECO AIJ en situación de CID con y sin tto

Detection of synovitis by ultrasonography in clinically inactive juvenile idiopathic arthritis on and off medication



Thirty-four patients with JIA were included in our study. They were clinically labelled by their clinicians as having ID after ≥6 months of follow-up prior to screening. Although the low values in the ssment reported by the inve port that those patients wer ate, 13 of them showed US-detected synovial pathology.

38%

ECOGRAFÍA



¿**actividad ecográfica** en pacientes clínicamente inactivos aumenta **riesgo de recaída tras suspensión**?



ECOGRAFÍA

2013

Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

Silvia Magni-Manzoni,[1] Carlo Alberto Scirè,[1] Angelo Ravelli,[2,3] Catherine Klersy,[1] Silvia Rossi,[1] Valentina Muratore,[1] Chiara Visconti,[1] Stefano Lanni,[1] Pietro Merli,[1] Carlomaurizio Montecucco,[1,4]

Ann Rheum Dis 2013;**72**:223–228. doi:10.1136/annrheumdis-2011-201264

Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

- 39 pacientes CID 3 meses
- 22 (57%) sin tratamiento

- Ecografía “ciega” 52 articulaciones de cada paciente
- Seguimiento 2 años o hasta recaída

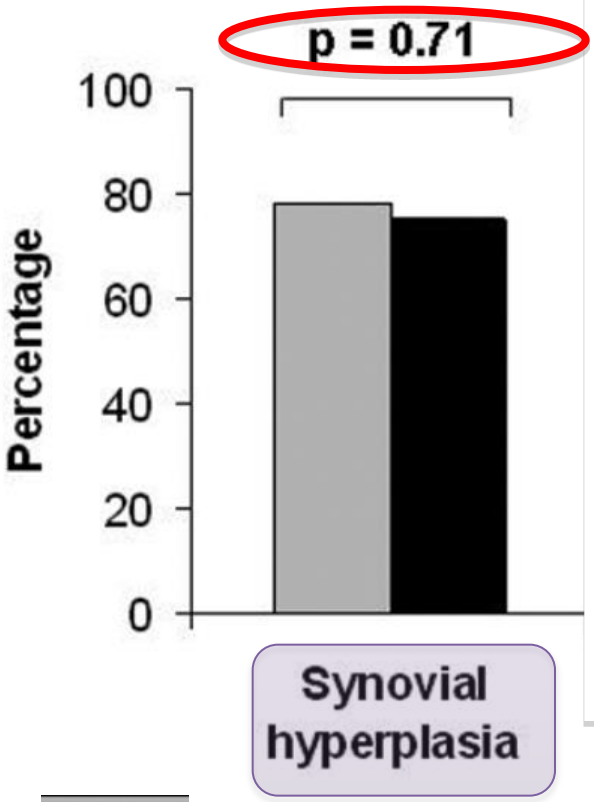
Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

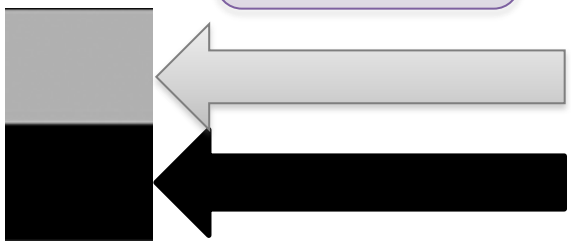
alteraciones ecográficas
al entrar en estudio

2 grupos de pacientes



Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

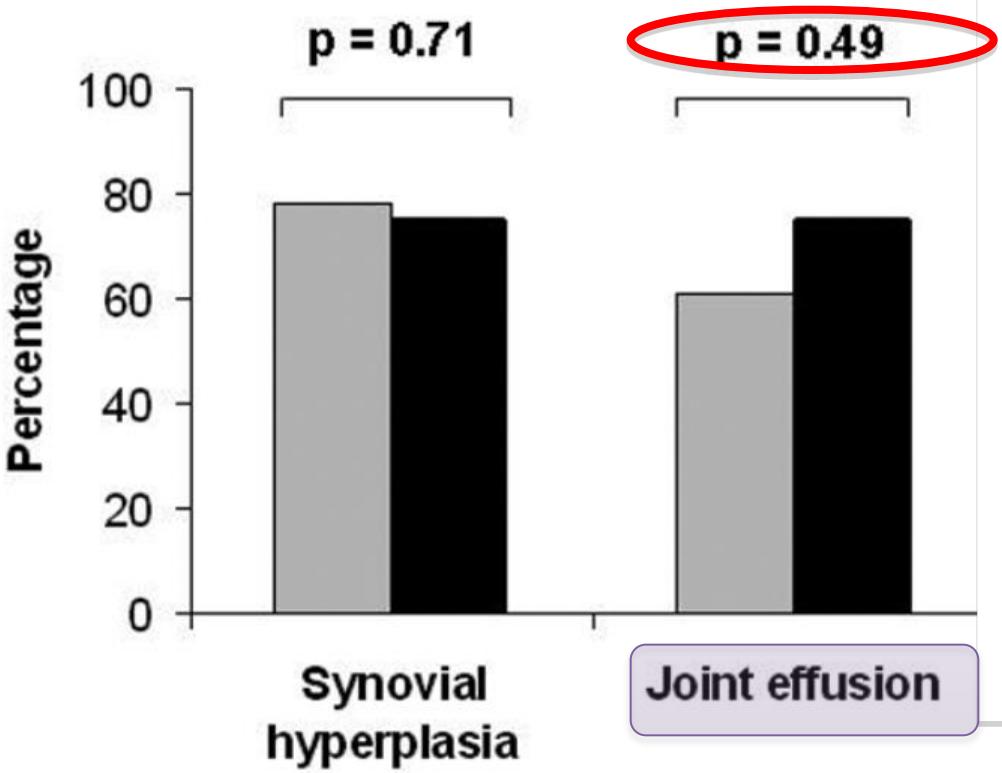


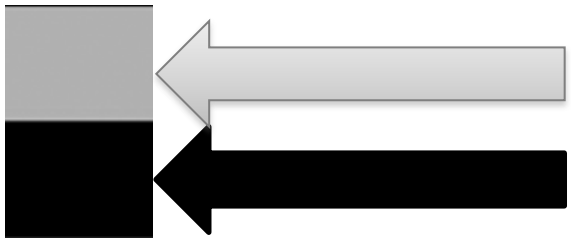


Remisión persistente

Recaída

Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

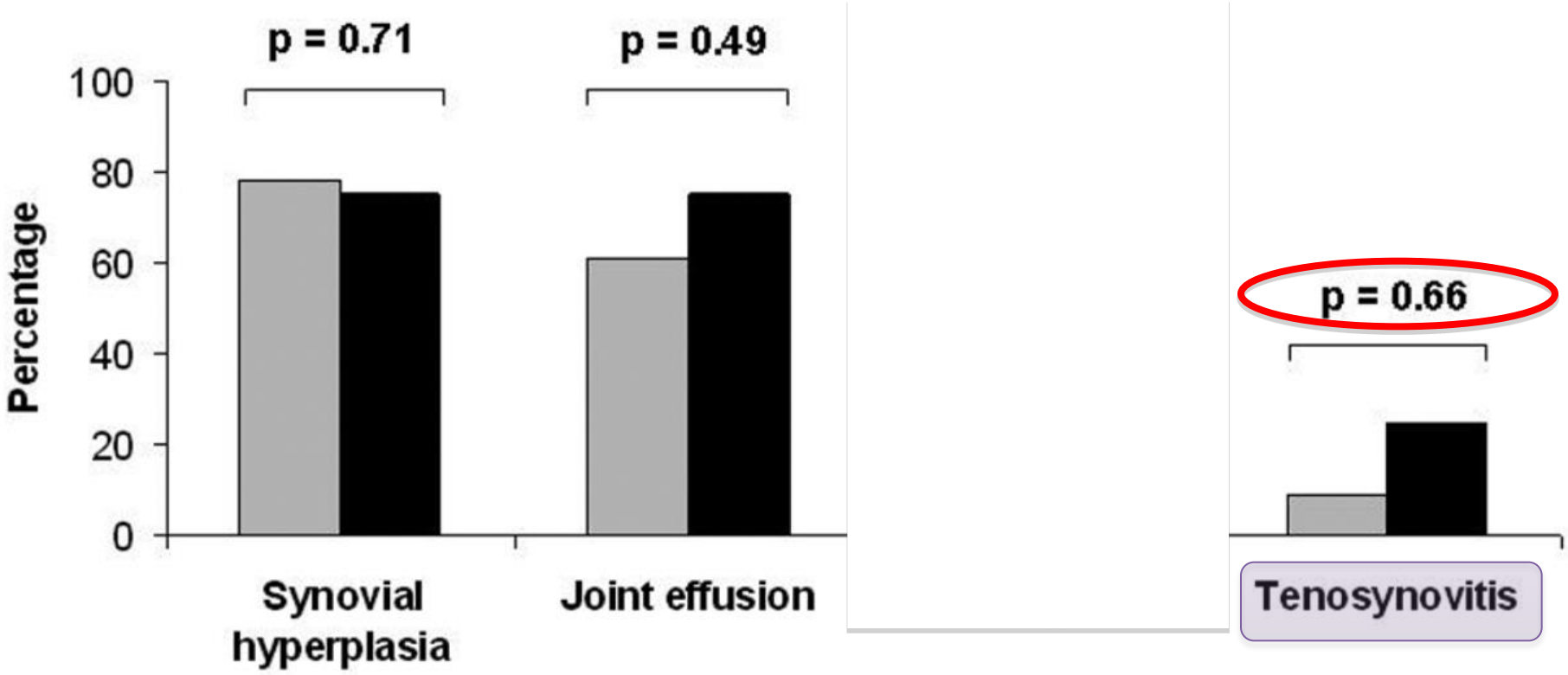


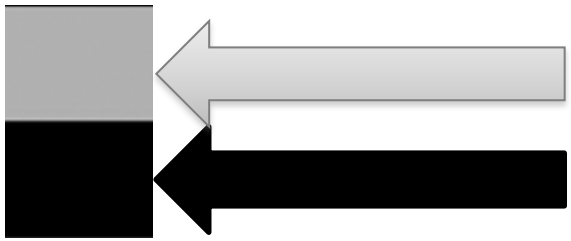


Remisión persistente

Recaída

Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

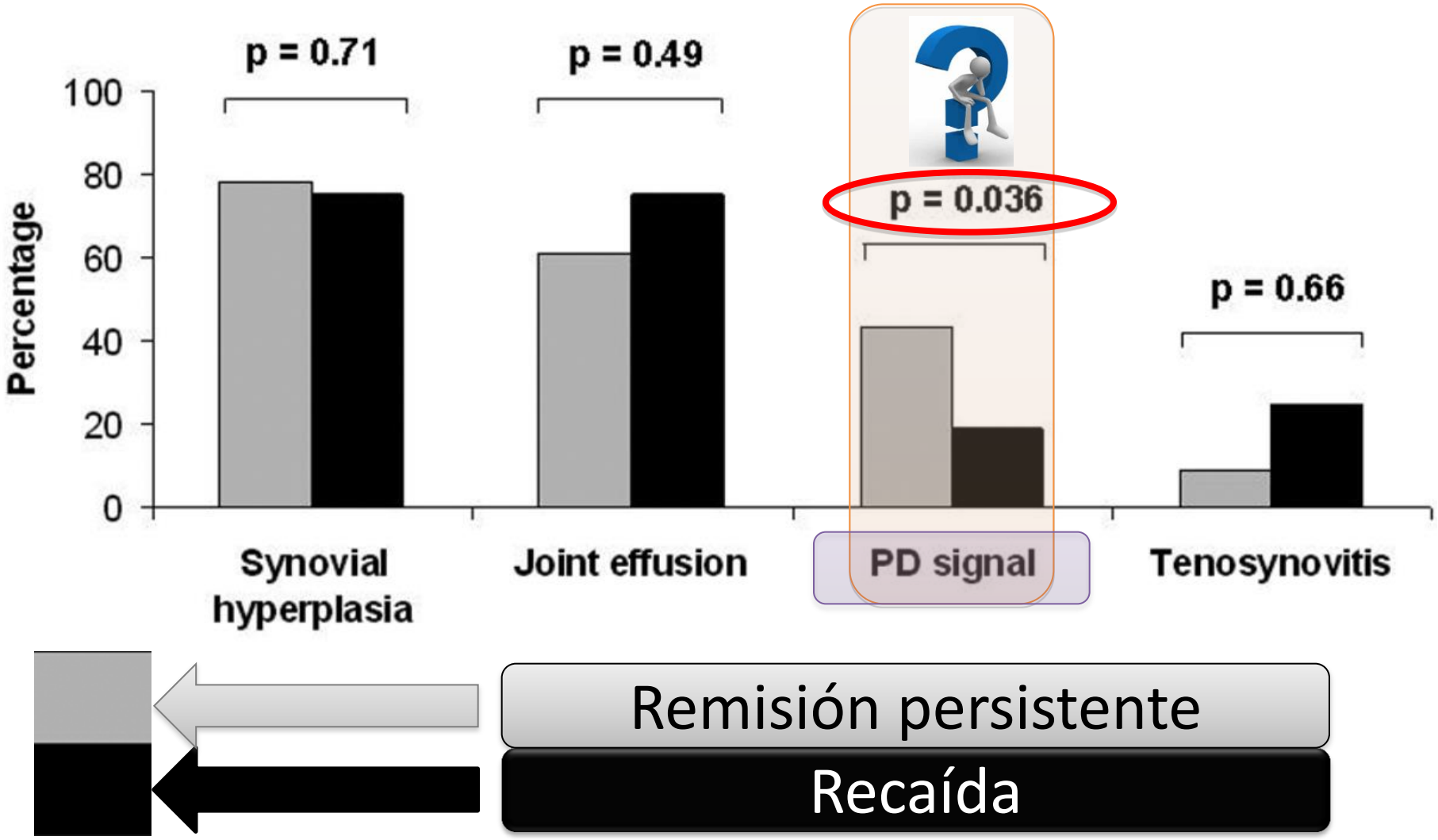




Remisión persistente

Recaída

Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis



Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

45 articulaciones recayeron



sólo 17

alteraciones ecográficas al entrar en estudio

Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis

sion. These findings suggest that the ultrasound demonstration of ongoing synovial pathology in JIA patients with clinically defined inactive disease does not predict an early flare of synovitis. The lack of predictive value of ultrasound was reinforced by





Proteínas S100

Proteínas S100

2010

Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission

A Randomized Clinical Trial

Dirk Foell, MD
Nico Wulffraat, MD
Lucy R. Wedderburn, MD, PhD
Helmut Wittkowski, MD
Michael Frosch, MD
Joachim Gerß, PhD
Valda Stanevicha, MD
Dimitrina Mihaylova, MD
Virginia Ferriani, MD
Florence Kanakoudi Tsakalidou, MD
Ivan Foeldvari, MD
Ruben Cuttica, MD
Benito Gonzalez, MD
Angelo Ravelli, MD
Raju Khubchandani, MD
Sheila Oliveira, MD
Wineke Armbrust, MD
Stella Garay, MD
Jelena Vojinovic, MD
Ximena Norambuena, MD
María Luz Gamir, MD
Julia García-Consuegra, MD
Loredana Lepore, MD
Gordana Susic, MD
Fabrizia Corona, MD
Pavla Dolezalova, MD
Angela Pistorio, MD, PhD
Alberto Martini, MD
Nicolino Ruperto, MD, MPH
Johannes Roth, MD
for the Paediatric Rheumatology International Trials Organization (PRINTO)



Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission

DISEÑO



364 AIJ en remisión con MTX

Aleatorización en 2 grupos

GRUPO 1

6meses

GRUPO 2

12meses

Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission

DISEÑO

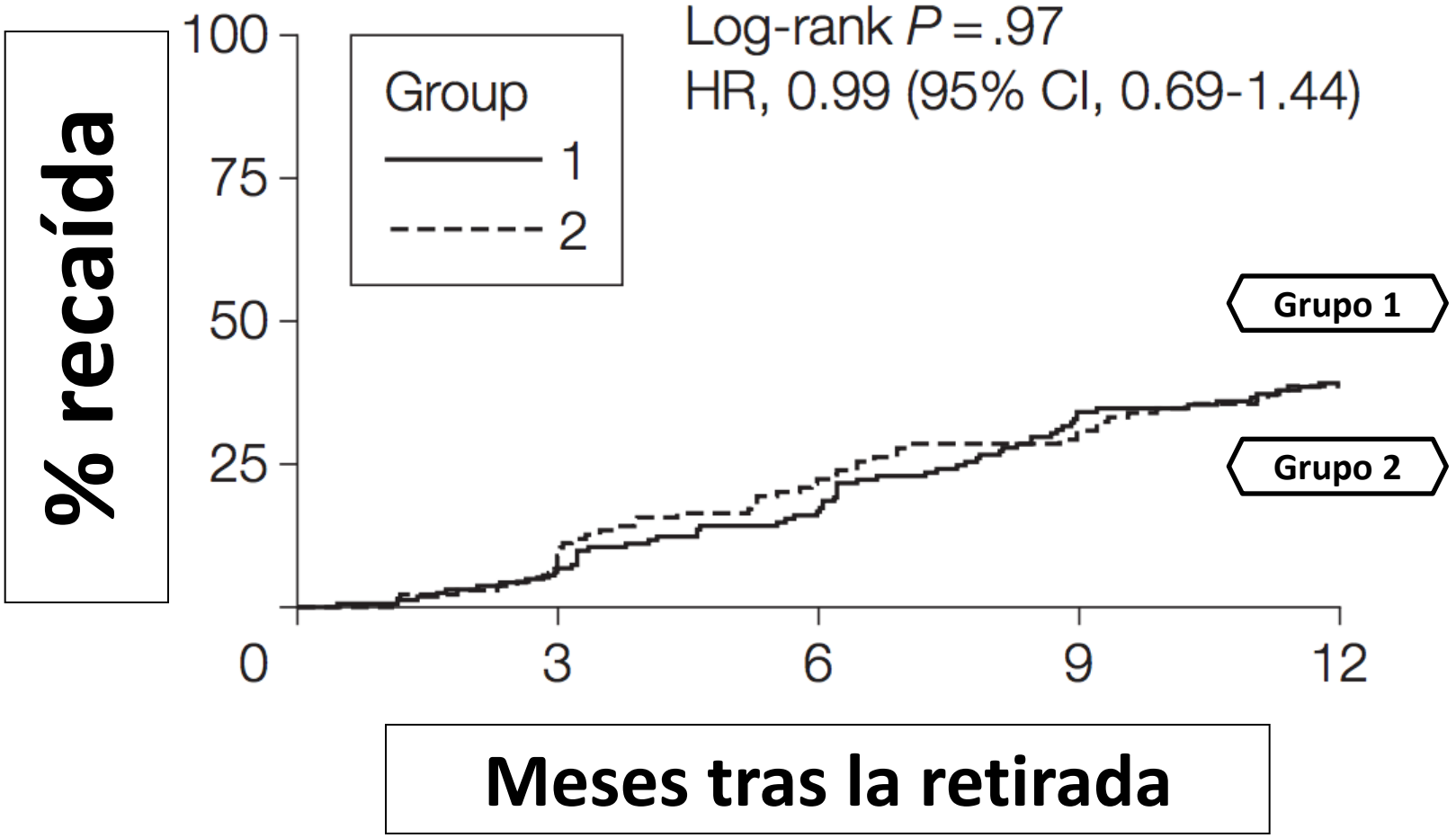


Niveles séricos de **MRP8/14** al suspender MTX



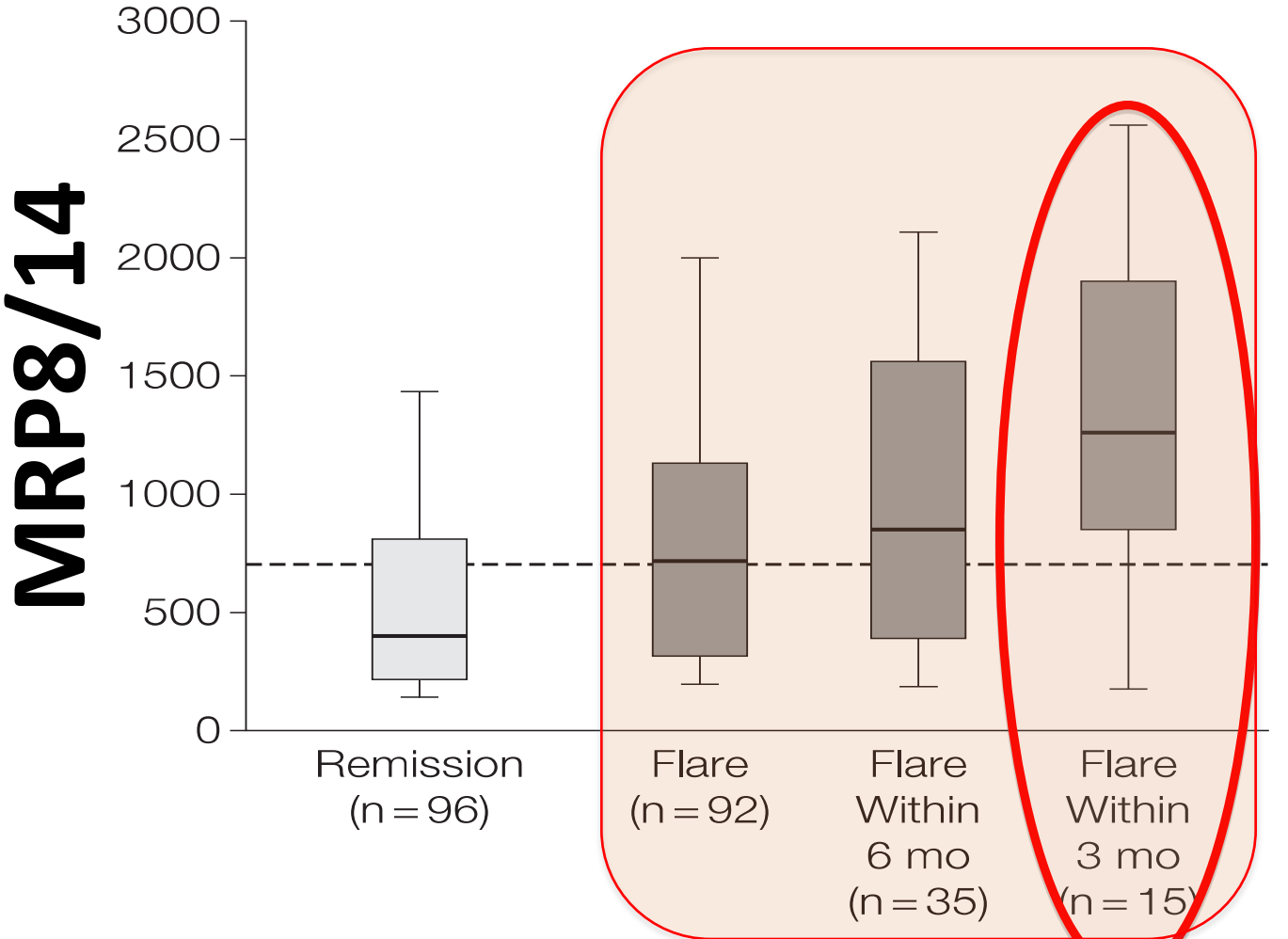
Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission

Tiempo de tto previo a retirada



Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission

MRP8/14 mayor en los que recayeron



Proteínas S100

2012

Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Joachim Gerss,[1,2] Johannes Roth,[3] Dirk Holzinger,[2,3,4] Nicolino Ruperto,[5] Helmut Wittkowski,[4] Michael Frosch,[4] Nico Wulffraat,[6] Lucy Wedderburn,[7] Valda Stanevicha,[8] Dimitrina Mihaylova,[9] Miroslav Harjacek,[10] Claudio Len,[11] Claudia Toppino,[12] Massimo Masi,[13] Kirsten Minden,[14] Traudel Saurenmann,[15] Yosef Uziel,[16] Richard Vesely,[17] Maria Teresa Apaz,[18] Rolf-Michael Kuester,[19] Maria Jesus Rua Elorduy,[20] Ruben Burgos-Vargas,[21] Maka Ioseliani,[22] Silvia Magni-Manzoni,[23] Erbil Unsal,[24] Jordi Anton,[25] Zsolt Balogh,[26] Stefan Hagelberg,[27] Henryka Mazur-Zielinska,[28] Tsivia Tauber,[29] Alberto Martini,[5,30] Dirk Foell[2,3] for the Paediatric Rheumatology International Trials Organization (PRINTO)

Ann Rheum Dis 2012;**71**:1991–1997

Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

¿Retirada Fármacos?

Tº Variable

Remisión clínica CON medicación

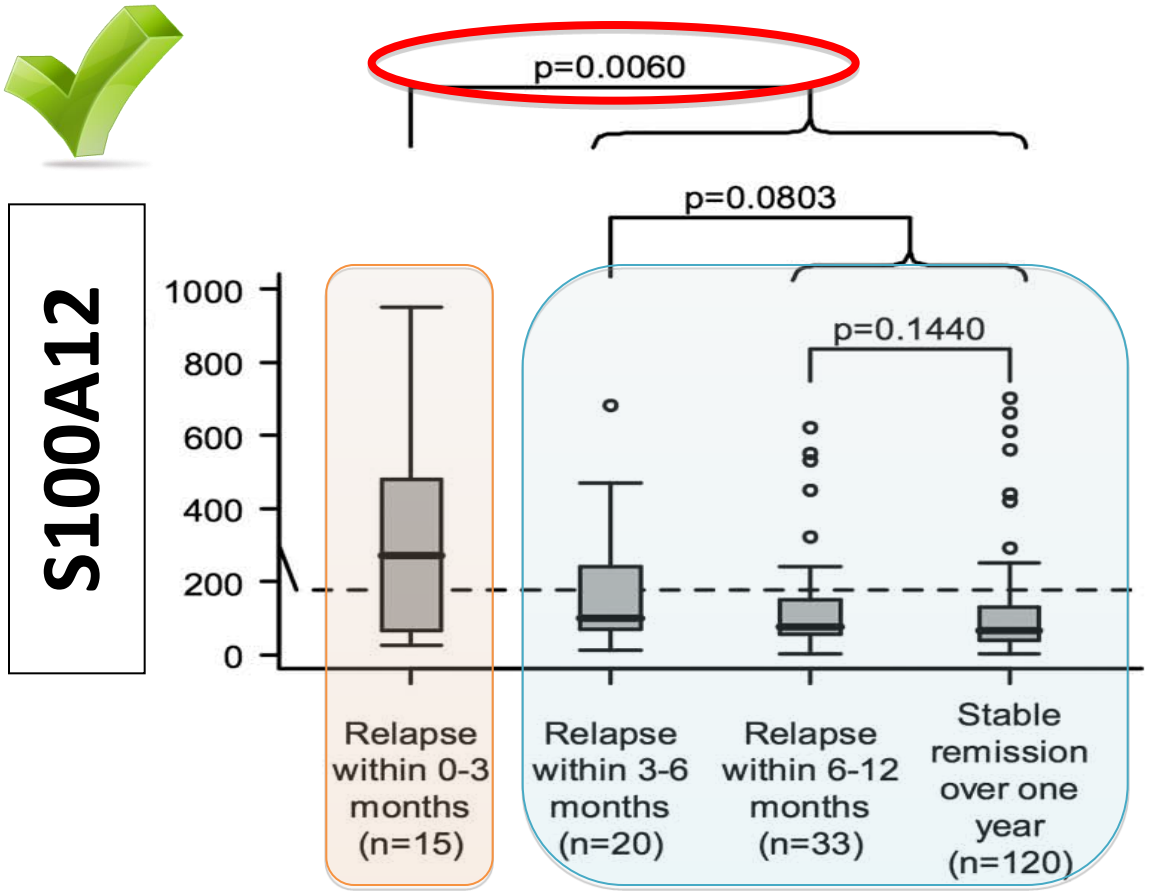
S100A12

MRP8/14

hsCRP

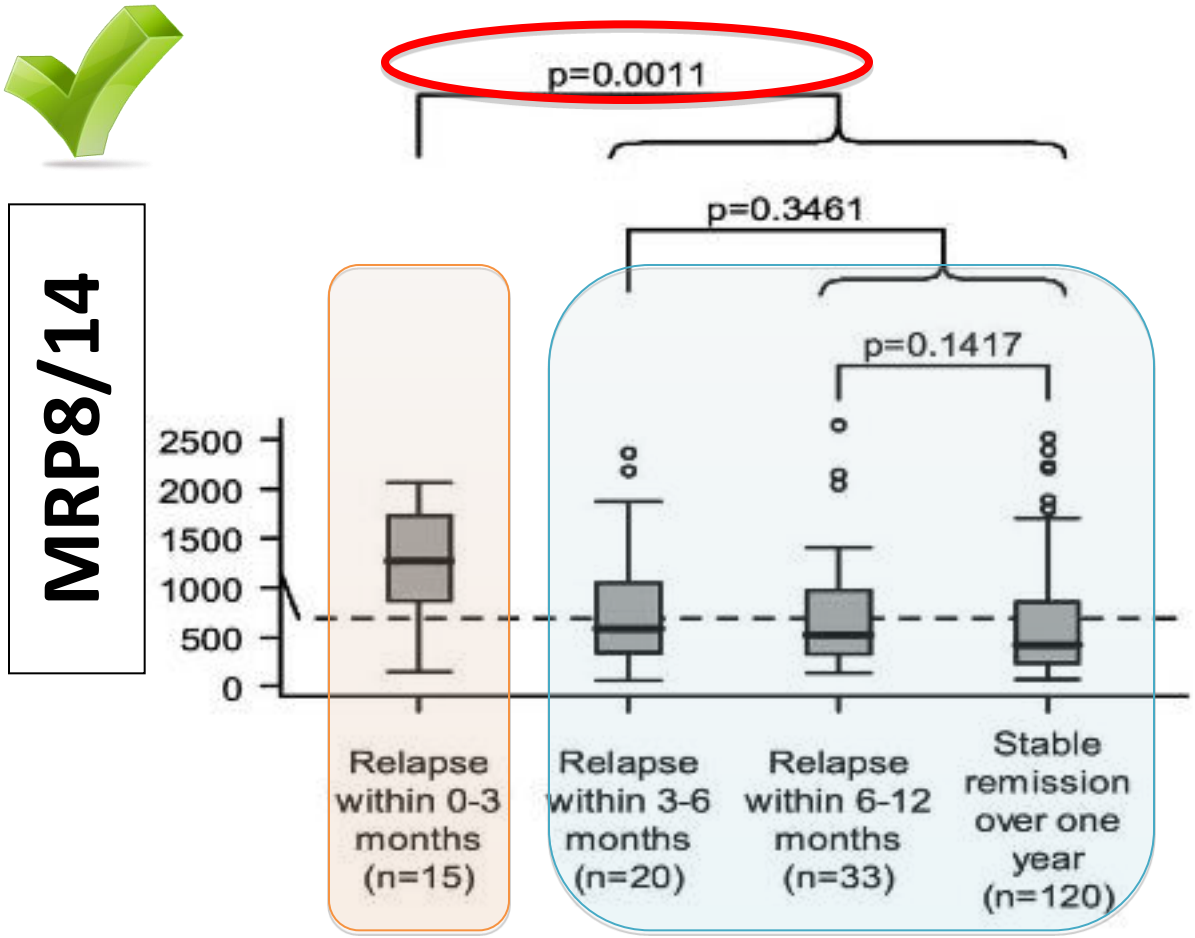
Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de **recaída PRECOZ** = 3 meses



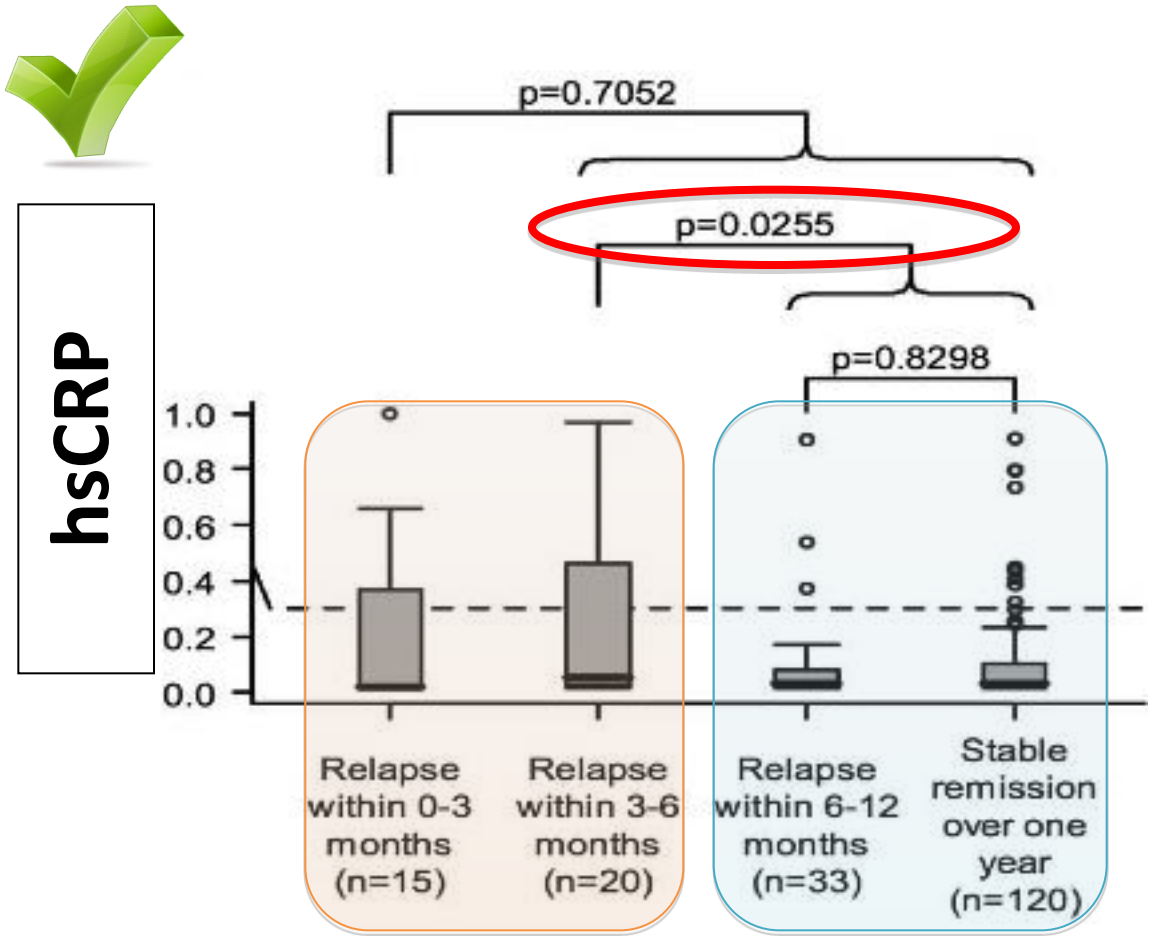
Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de **recaída PRECOZ** = 3 meses



Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de **recaída TARDÍA** = 6 meses



Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de recaída

S100A12

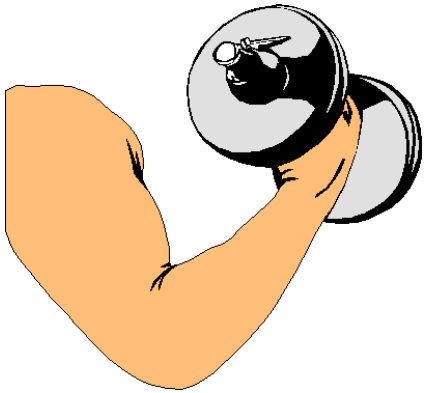


MRP8/14

Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de recaída

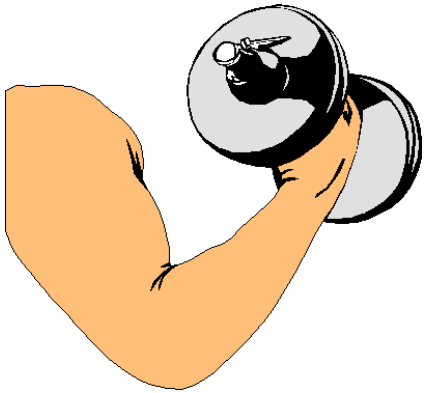
S100A12 + hsCRP



Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de recaída

MRP8/14 + hsCRP



Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Riesgo de recaída

Mejor combinación biomarcadores

S100A12 / hsCRP



Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

¿Retirada Fármacos?



Tº Variable

Remisión clínica CON medicación

S100A12
hsCRP

Remisión inestable = continuar tratamiento

Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

¿Retirada Fármacos?



Tº Variable

Remisión clínica CON medicación

S100A12
hsCRP

Remisión estable = suspender tratamiento

Proteínas S100

Agosto 2015

Anink *et al. Arthritis Research & Therapy* (2015) 17:200
DOI 10.1186/s13075-015-0723-1

arthritis research&therapy

RESEARCH ARTICLE Open Access

CrossMark

MRP8/14 serum levels as a predictor of response to starting and stopping anti-TNF treatment in juvenile idiopathic arthritis

Janneke Anink[1*], Lisette W. A. Van Suijlekom-Smit[1], Marieke H. Otten[1], Femke H. M. Prince[1], Marion A. J. van Rossum[2], Koert M. Dolman[3], Esther P. A. H. Hoppenreijs[4], Rebecca ten Cate[5], Simona Ursu[6], Lucy R. Wedderburn[6], Gerd Horneff[7], Michael Frosch[8], Thomas Vogl[9], Faekah Gohar[10], Dirk Foell[10], Johannes Roth[9] and Dirk Holzinger[10]

MRP8/14 serum levels as a predictor of response to starting and stopping anti-TNF treatment in juvenile idiopathic arthritis

OBJETIVO

Niveles séricos de **MRP8/14**

Predictores de **respuesta a anti-TNF** en **AIJ no sistémica**

Predictores de **recaída tras suspensión** en **AIJ no sistémica**

MRP8/14 serum levels as a predictor of response to starting and stopping anti-TNF treatment in juvenile idiopathic arthritis

DISEÑO

- MRP8/14 al **iniciar** anti-TNF

88 AIJ no sistémica

- MRP8/14 al **suspender** anti-TNF

26 AIJ no sistémica

MRP8/14 serum levels as a predictor of response to starting and stopping anti-TNF treatment in juvenile idiopathic arthritis

MRP8/14 predice respuesta

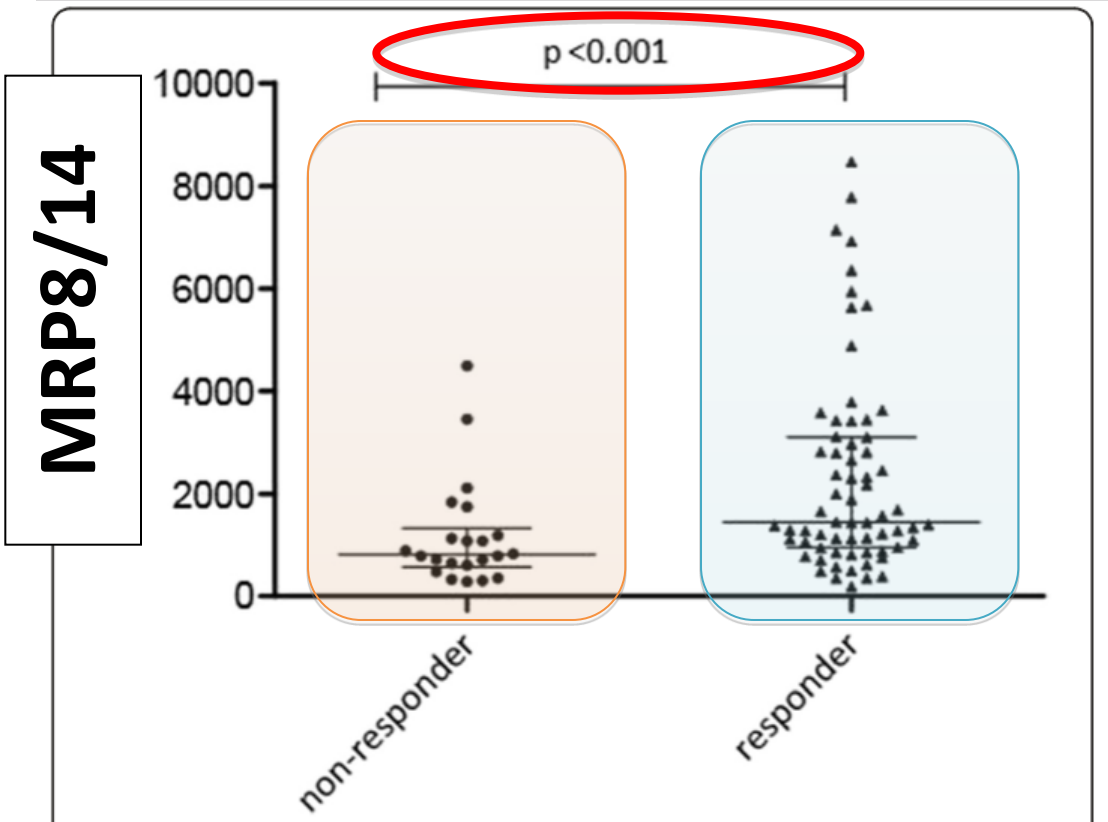
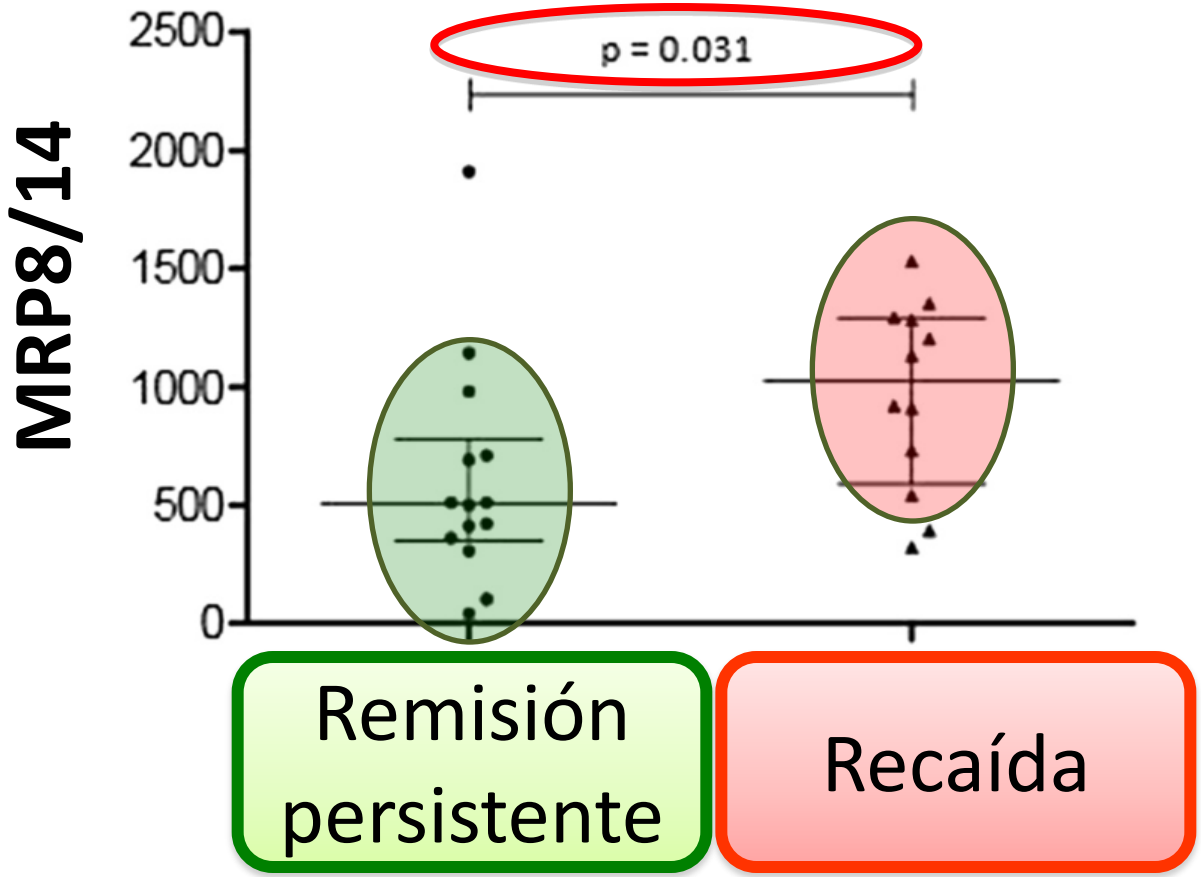


Fig. 1 Differences in myeloid related protein (*MRP*)8/14 serum levels between non-responders and responders before starting treatment

MRP8/14 serum levels as a predictor of response to starting and stopping anti-TNF treatment in juvenile idiopathic arthritis

MRP8/14 y **riesgo de recaída**



MRP8/14 serum levels as a predictor of response to starting and stopping anti-TNF treatment in juvenile idiopathic arthritis

MRP8/14

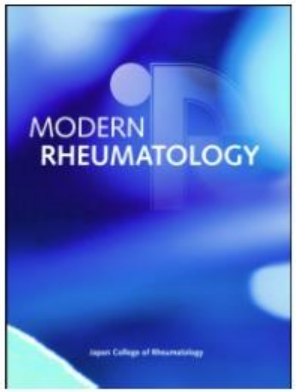
Puede ser herramienta útil

RETIRADA DE TRATAMIENTO ANTI-TNF EN **AIJ no sistémica**



Proteínas S100

Octubre 2015



Modern Rheumatology

ISSN: 1439-7595 (Print) 1439-7609 (Online) Journal homepage: http://www.tandfonline.com/loi/imor20

Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

Yuichi Yamasaki, Syuji Takei, Hiroyuki Imanaka, Yasuhito Nerome, Tomohiro Kubota, Yukiko Nonaka, Harumi Akaike, Tomoko Takezaki & Yoshifumi Kawano

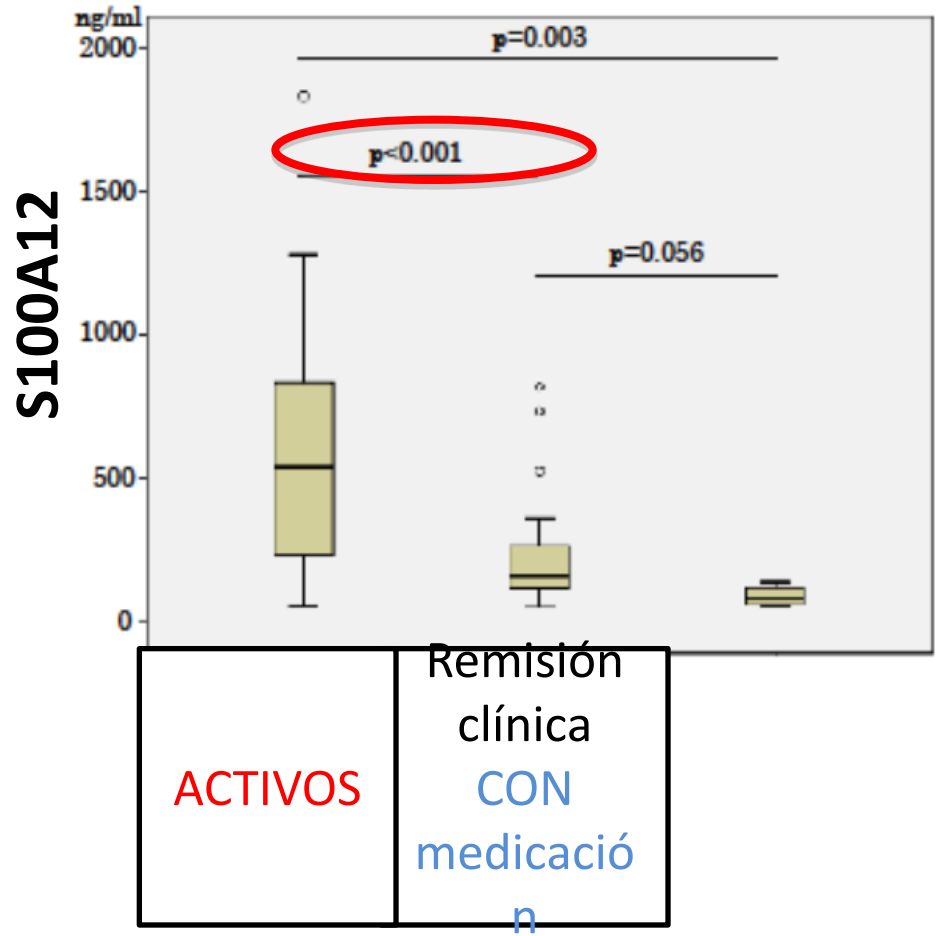
Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

DISEÑO

- **44** AIJ oligo/poliarticulares (**no AIJs**) en tto con MTX +/- biológico
- **S100A12** y **VEGF** en:
  - Activos
  - Remisión

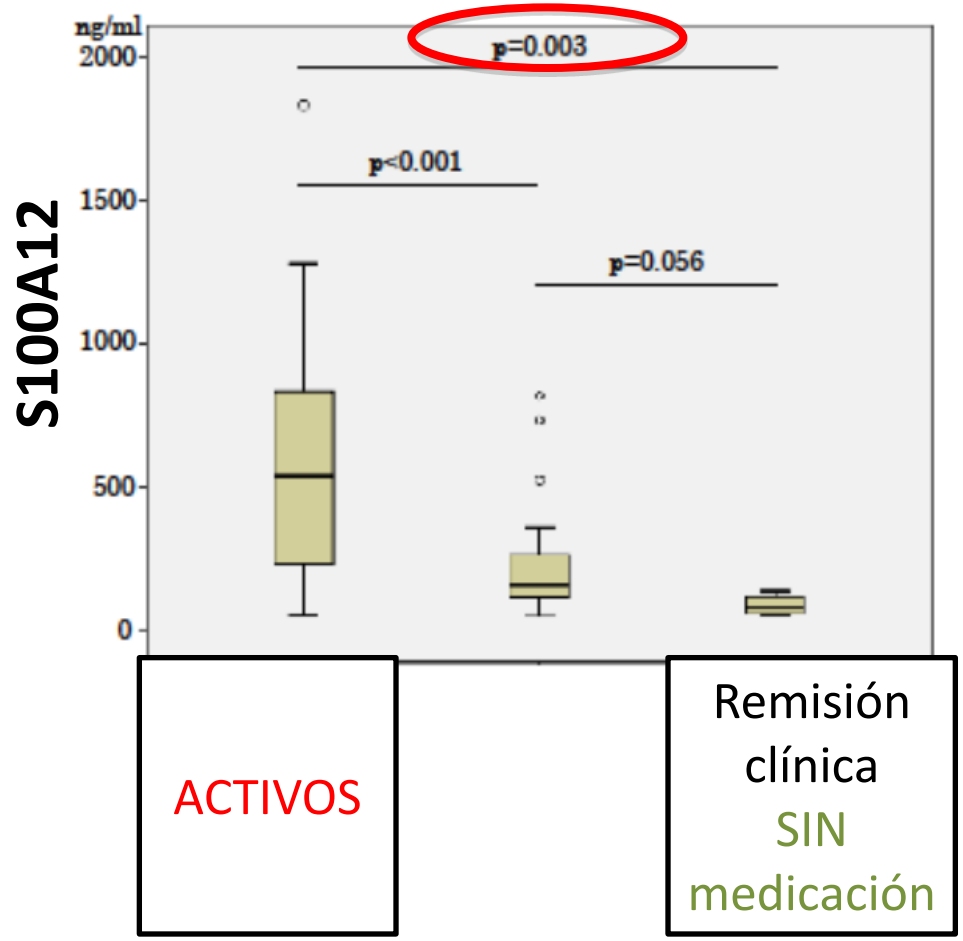
Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

S100A12 > en pacientes activos



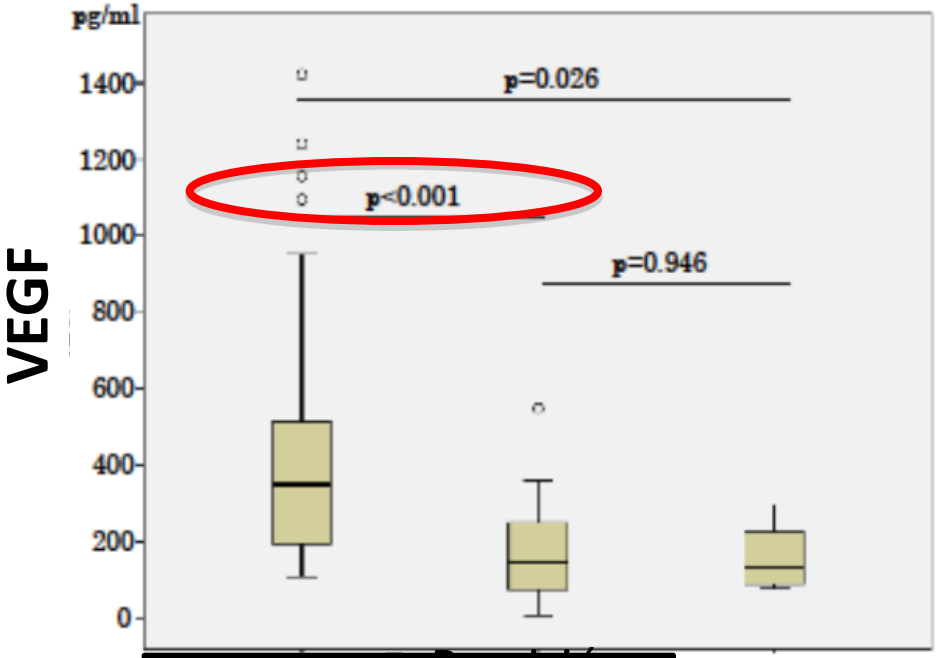
Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

S100A12 > en pacientes activos



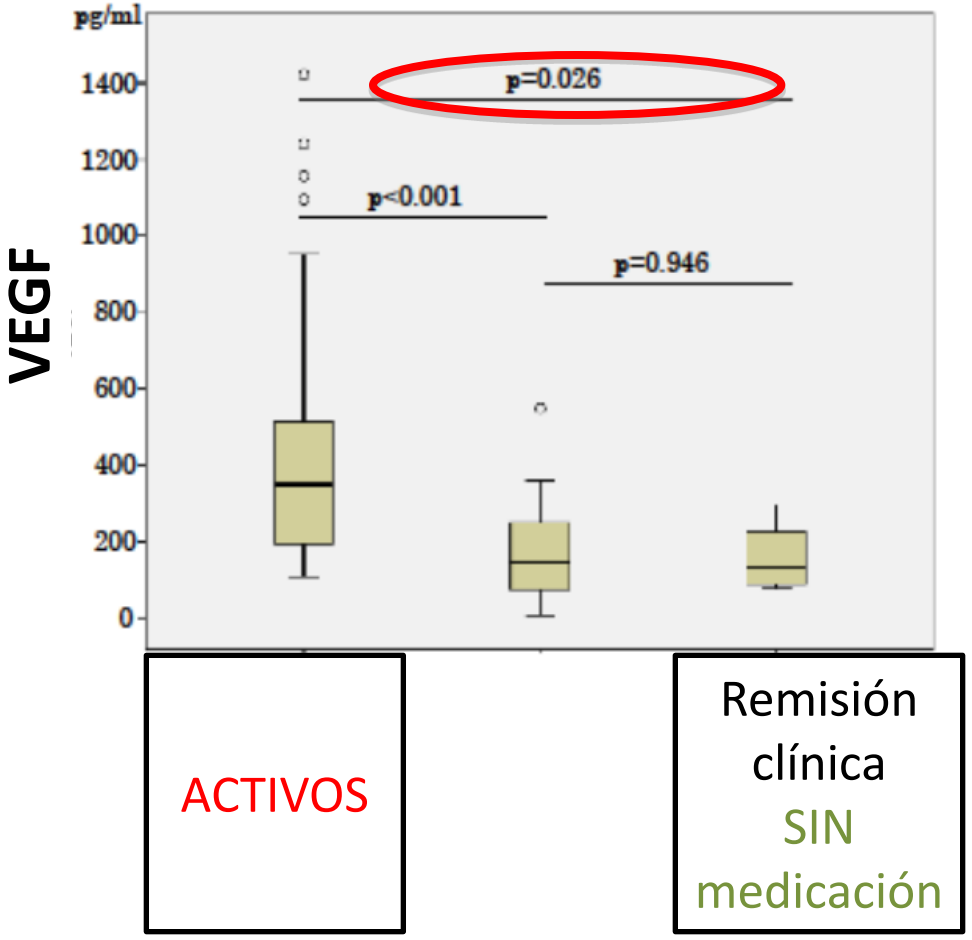
Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

VEGF > en pacientes activos



Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

VEGF > en pacientes activos



Prediction of long-term remission of oligo/ polyarticular juvenile idiopathic arthritis with S100A12 and Vascular Endothelial Growth Factor

S100A12

¿utilidad también
en retirada de tratamiento
en AIJ poli/oligo ?



Proteínas S100

LIMITACIONES

1.VP de MPR8/14 no es 100%

2.¿pueden ser de utilidad real en la práctica diaria?

Proteínas S100

2014

Arthritis Care & Research
Vol. 66, No. 6, June 2014, pp 949–955
DOI 10.1002/acr.22248
© 2014, American College of Rheumatology

BRIEF REPORT

Validation of Relapse Risk Biomarkers for Routine Use in Patients With Juvenile Idiopathic Arthritis

FRIEDERIKE ROTHMUND,[1] JOACHIM GERSS,[2] NICOLINO RUPERTO,[3] JAN DÄBRITZ,[1] HELMUT WITTKOWSKI,[1] MICHAEL FROSCH,[4] NICO M. WULFFRAAT,[5] LUCY R. WEDDERBURN,[6] DIRK HOLZINGER,[7] FAEKAH GOHAR,[1] SEBASTIAAN J. VASTERT,[5] RIVA BRIK,[8] CHANTAL JOB DESLANDRE,[9] JOSE ANTONIO MELO-GOMES,[10] CLAUDIA SAAD MAGALHÃES,[11] ROBERTO BARCELLONA,[12] RICARDO RUSSO,[13] MARCO GATTORNO,[3] ALBERTO MARTINI,[14] JOHANNES ROTH,[2] AND DIRK FOELL,[7] FOR THE PAEDIATRIC RHEUMATOLOGY INTERNATIONAL TRIALS ORGANISATION (PRINTO)

Validation of Relapse Risk Biomarkers for Routine Use in Patients With Juvenile Idiopathic Arthritis

- ***Bühlmann*** MRP8/14 Calprotectin Elisa
- ***PhiCal*** Calprotectin Elisa
- ***CircuLex*** S100A12/EN-RAGE Elisa

Validation of Relapse Risk Biomarkers for Routine Use in Patients With Juvenile Idiopathic Arthritis

Comparación con ELISA usado en los trabajos

Methotrexate Withdrawal at 6 vs 12 Months in Juvenile Idiopathic Arthritis in Remission
A Randomized Clinical Trial

Phagocyte-specific S100 proteins and high-sensitivity C reactive protein as biomarkers for a risk-adapted treatment to maintain remission in juvenile idiopathic arthritis: a comparative study

Joachim Gerss,[1,2] Johannes Roth,[3] Dirk Holzinger,[2,3,4] Nicolino Ruperto,[5] Helmut Wittkowski,[4] Michael Frosch,[4] Nico Wulffraat,[6] Lucy Wedderburn,[7] Valda Stanevicha,[8] Dimitrina Mihaylova,[9] Miroslav Harjacek,[10] Claudio Len,[11] Claudia Toppino,[12] Massimo Masi,[13] Kirsten Minden,[14] Traudel Saurenmann,[15] Yosef Uziel,[16] Richard Vesely,[17] Maria Teresa Apaz,[18] Rolf-Michael Kuester,[19] Maria Jesus Rua Elorduy,[20] Ruben Burgos-Vargas,[21] Maka Ioseliani,[22] Silvia Magni-Manzoni,[23] Erbil Unsal,[24] Jordi Anton,[25] Zsolt Balogh,[26] Stefan Hagelberg,[27] Henryka Mazur-Zielinska,[28] Tsivia Tauber,[29] Alberto Martini,[5,30] Dirk Foell[2,3] for the Paediatric Rheumatology International Trials Organization (PRINTO)

Ann Rheum Dis 2012;**71**:1991–1997



Validation of Relapse Risk Biomarkers for Routine Use in Patients With Juvenile Idiopathic Arthritis

CONCLUSIONES



Compared to experimental assays, the tested commercial ELISAs produced a similar correlation between high serum levels of MRP-8/MRP-14 and S100A12 with the individual relapse risk.

Validation of Relapse Risk Biomarkers for Routine Use in Patients With Juvenile Idiopathic Arthritis

CONCLUSIONES



We therefore conclude that the risk-adapted stratification of decisions to stop or continue with therapy after achieving JIA remission using MRP-8/MRP-14 and S100A12 biomarker assays is feasible in clinical practice.



Comentarios

Casi todos los estudios anti-TNF (ETN) y MTX

Faltan estudios sobre otros biológicos ANK, abatacept, tocilizumab etc.

Comentarios

Ecografía

por el momento

NO parece herramienta útil

para decidir retirada tratamiento

a diferencia de AR de adultos

Scire CA et al. Ultrasonographic evaluation of joint involvement in early rheumatoid arthritis in clinical remission: power Doppler signal predicts short-term relapse. Rheumatology 2009

Peluso G et al. Clinical and ultrasonographic remission determines different chances of relapse in early and long standing rheumatoid arthritis. Ann Rheum Dis 2011

Comentarios

Biomarcadores inmunológicos

parecen actualmente

las herramientas

más prometedoras



Comentarios

FUTURO



¿determinación de niveles de fármaco?

Muchas gracias



