Hospital Universitario 12 de Octubre
SaludMadrid

REUMATOLOGÍA PEDIÁTRICA
NOVEDADES EN EL ULTIMO AÑO

Jaime de Inocencio
Unidad de Reumatología Pediátrica



ULTIMOS 12 MESES EN REUMA PED

- Novedades desde la última reunión SERPE [Foro de Pamplona, Noviembre de 2012]
- Publicaciones que me han resultado interesantes
  - Sesgo personal
  - Igual no estamos todos de acuerdo
- Novedades en genética e inmunología
- Tendencias terapéuticas

ULTIMOS 12 MESES EN REUMA PED

- La reumatología pediátrica es una especialidad en la que no se producen múltiples novedades terapéuticas al año
- Multitud de consensos internacionales pero pocos estudios multicéntricos grandes
  - Con fármacos nuevos
  - Con fármacos conocidos pero administrados por distinta vía
    - Tocilizumab sc, Abatacept sc
  - Con fármacos ya conocidos pero para otra indicación
    - TCZ para AIJ poliarticular

ULTIMOS 12 MESES EN REUMA PED

NEWS & VIEWS

PAEDIATRIC RHEUMATOLOGY

Where are the innovations in paediatric rheumatology?

Thomas J. A. Lehman

NATURE REVIEWS | RHEUMATOLOGY

Rapid progress is being made in the field of rheumatology. Nevertheless, disappointingly, the limited resources of the paediatric rheumatology community are being expended on the publication of consensus guidelines that represent fossilization of old ideas rather than real innovation that leads to the improved care of children.

Lehman, T. J. A. *Nat. Rev. Rheumatol*. advance online publication XX Month 2013; doi:10.1038/nrrheum.2013.74

Lehman TJA. Nat Rev Rheumatol 2013; doi:10.1038/nrrheum.2013.74

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ARTRITIS IDIOPÁTICA JUVENIL

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GENÉTICA DE LA AIJ

NOVEDADES

AIJ. BASES GENÉTICAS

nature genetics

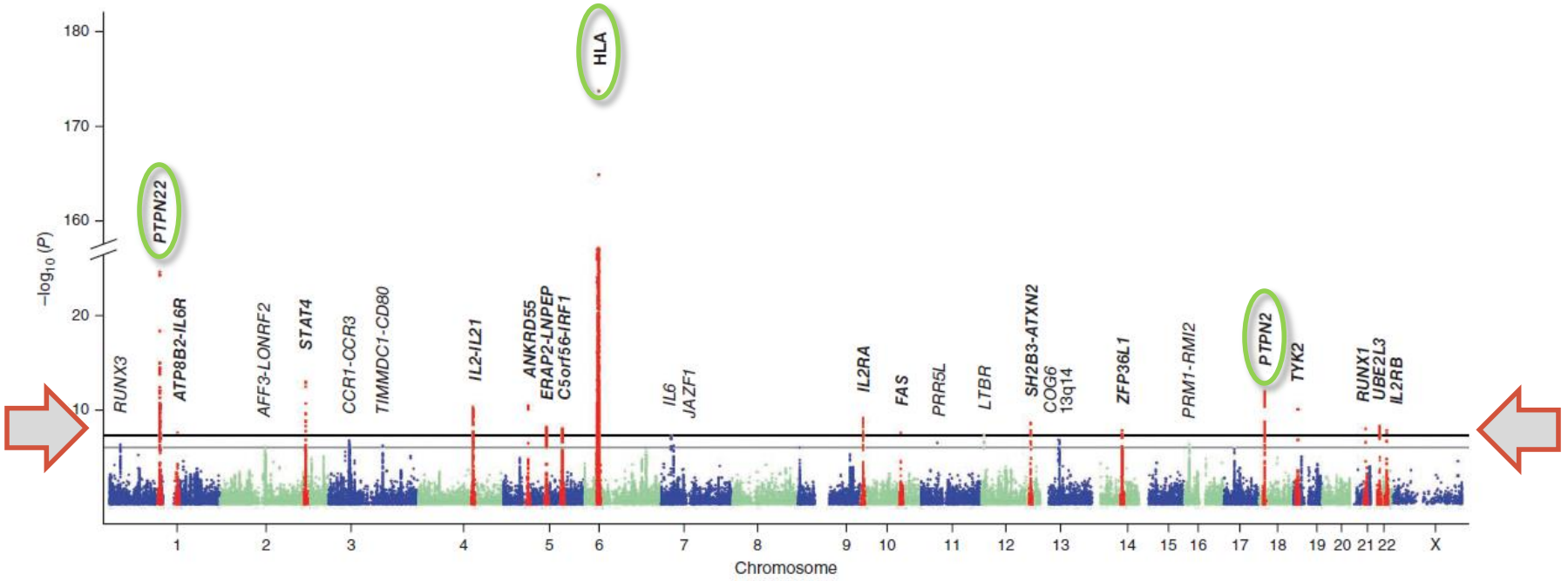
LETTERS

Dense genotyping of immune-related disease regions identifies 14 new susceptibility loci for juvenile idiopathic arthritis

Anne Hinks[1,2,22], Joanna Cobb[1,2,22], Miranda C Marion[3,4,22], Sampath Prahalad[5,6], Marc Sudman[7], John Bowes[1,2], Paul Martin[1,2], Mary E Comeau[3,4], Satria Sajuthi[3,4], Robert Andrews[8], Milton Brown[5], Wei-Min Chen[9], Patrick Concannon[9], Panos Deloukas[8], Sarah Edkins[8], Stephen Eyre[1,2], Patrick M Gaffney[10], Stephen L Guthery[11,12], Joel M Guthridge[10], Sarah E Hunt[8], Judith A James[10], Mehdi Keddache[13], Kathy L Moser[10], Peter A Nigrovic[14,15], Suna Onengut-Gumuscu[9], Mitchell L Onslow[7], Carlos D Rosé[14,15], Stephen S Rich[9], Kathryn J A Steel[1,2], Edward K Wakeland[16], Carol A Wallace[17], Lucy R Wedderburn[18], Patricia Woo[19], Boston Children's JIA Registry[20], British Society of Paediatric and Adolescent Rheumatology (BSPAR) Study Group[20], Childhood Arthritis Prospective Study (CAPS)[20], Childhood Arthritis Response to Medication Study (CHARMS)[20], German Society for Pediatric Rheumatology (GKJR)[20], JIA Gene Expression Study[20], NIAMS JIA Genetic Registry[20], TREAT Study[20], United Kingdom Juvenile Idiopathic Arthritis Genetics Consortium (UKJIAGC)[20], John F Bohnsack[11,12], Johannes Peter Haas[21], David N Glass[7], Carl D Langefeld[3,4], Wendy Thomson[1,2,23] & Susan D Thompson[7,23]

Hinks A *et al*. Nat Genet 2013; 45:664-9. doi: 10.1038/ng.2614.

POLIMORFISMOS en AIJ



- Analizan 123,000 SNPs [Polimorfismos de un único nucleótido]
- Mayor asociación con HLA [OR 6], PTPN22 [OR 1,6] y PTPN2 [OR 1,3]
  - HLA: SNP rs7775055 del haplotipo HLA-DRB1*0801–DQA1*0401–DQB1*0402
  - PTPN [Protein tyrosine phosphatase, non-receptor type 2 / 22. Proteína tirosina fosfatasa no-receptor] es una proteína que afecta a la respuesta del receptor de linfocitos T y B

Hinks A *et al*. Nat Genet 2013; 45:664-9. doi: 10.1038/ng.2614.

POLIMORFISMOS en AIJ

- Otros genes afectan a la IL2 [IL2RA, IL2-IL21 y IL2RB], así como otros genes relacionados con los linfocitos T, bien en su activación [SH2B3] o diferenciación [STAT4]
- Asociaciones ya conocidas por otros estudios y descritas en otras enfermedades autoinmunes
  - Enfermedad celiaca
  - Vitíligo
  - Artritis reumatoide
  - Diabetes tipo 1
  - Psoriasis
  - Cirrosis biliar primaria

Hinks A *et al*. Nat Genet 2013; 45:664-9. doi: 10.1038/ng.2614.

AIJ & ENF. AUTOINFLAMATORIAS

PEDIATRIC RHEUMATOLOGY

RESEARCH Open Access

Autoinflammatory gene polymorphisms and susceptibility to UK juvenile idiopathic arthritis

Anne Hinks[1], Paul Martin[1], Susan D Thompson[2], Marc Sudman[2], Carmel J Stock[3], Wendy Thomson[1], Thomas G Day[1], Jon Packham[4], Childhood arthritis prospective study (CAPS), BSPAR study group, Athimalaipet V Ramanan[5] and Rachelle P Donn[1*]

AIJ & ENF. AUTOINFLAMATORIAS

- Estudio genético de HIDS y TRAPS en 1.017 pacientes con AIJ de Reino Unido y 5.380 controles
- Analizan 37 SNPs [Polimorfismos de un único nucleótido] en las 7 categorías de AIJ
- Se asocian a AIJs
  - 3 de 4 polimorfismos de IL1
  - Polimorfismos de TNFRSF1A [TRAPS]
  - Polimorfismos en MVK [HIDS]
- Algunos se asocian a otras categorías de AIJ (RF+, ArE y APs) pero de manera menos significativa (asociación desaparece al eliminar AIJs del análisis)

Hinks A *et al*. Pediatr Rheumatol 2013; 11:14

AIJ POLI en REMISIÓN. GENETICA

arthritis research&therapy

RESEARCH Open Access

Genomic characterization of remission in juvenile idiopathic arthritis

Kaiyu Jiang[1,3†], Mark Barton Frank[2†], Yanmin Chen[1,3], Jeanette Osban[2] and James N Jarvis[1,3*]

- Jiang K *et al*. Arthritis Res Ther 2013 Aug; 15:R100 Epub

AIJ POLI en REMISIÓN. GENETICA

- El perfil genético de pacientes en remisión que han recibido tratamiento con MTX es distinto del de aquellos tratados con MTX+ETN
- Independientemente del tratamiento recibido los perfiles genéticos de los pacientes son diferentes del de los controles sanos → Remisión no es una vuelta a la normalidad
- Mayor cambio en granulocitos [innato] que linfocitos [adaptativo]
- Muchos de los genes con una expresión diferente se unen al factor de transcripción **HNF4α**, miembro de la superfamilia de receptores de hormonas esteroideas, y regulador de la respuesta inflamatoria mediada por citocinas → Parece estar implicado en el control de genes asociados a la remisión

Jiang K *et al*. Arthritis Res Ther 2013 Aug; 15:R100 Epub

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NOVIEMBRE 2012

AIJ POLIARTICULAR

ACR 2012. TCZ en AIJ Poliarticular

Table. Efficacy Endpoints

Randomized DB period (wks 16–40; ITT population: all pts who entered DB period)

	All PBO n = 81	All TCZ n = 82	p^a
Primary endpoint: JIA ACR30 flare (relative to wk 16), n (%)[b]	39 (48.1)	21 (25.6)	0.0024
Secondary endpoints (at wk 40 relative to day 0[c]; ITT population: all pts who entered DB period), n (%)			
JIA ACR30	44 (54.3)	61 (74.4)	0.0084
JIA ACR50	42 (51.9)	60 (73.2)	0.0050
JIA ACR70	34 (42.0)	53 (64.6)	0.0032

Initial lead-in period (at wk 16: ITT population)

	TCZ 10 mg/kg <30 kg BW n = 35	TCZ 8 mg/kg <30 kg BW n = 34	TCZ 8 mg/kg ≥30 kg BW n = 119	All TCZ N = 188
JIA ACR responses at wk 16,[d] n (%)				
JIA ACR30	31 (88.6)	26 (76.5)	111 (93.3)	168 (89.4)
JIA ACR50	28 (80.0)	24 (70.6)	104 (87.4)	156 (83.0)
JIA ACR70	22 (62.9)	14 (41.2)	81 (68.1)	117 (62.2)
JIA ACR90	11 (31.4)	8 (23.5)	30 (25.2)	49 (26.1)

ACR 2013. TCZ en AIJ Poliarticular

- CHERISH. Prolongación del periodo de observación a 104 semanas

Table. JIA ACR50/70 Responses and Percentage Change From Baseline in Components,[a] mean±SD

	All TCZ (N=82)	
	Week 40	**Week 104**
JIA ACR70 responders,[b] n (%)	65 (79.3)	71 (86.6)
JIA ACR90 responders,[b] n (%)	41 (50.0)	58 (70.7)
Active joints (0-71)	-82.4±24.9	-87.7±27.1
Joints with limitation in ROM (0-67)	-73.5±30.7	-81.3±31.7
Patient global[c] (VAS 0-100 mm)	-62.5±76.3	-75.4±43.8
Physician global (VAS 0-100 mm)	-85.3±16.8	-89.7±23.7
CHAQ-DI (0-3)	-66.0±44.7	-76.7±34.7
ESR (mm/h)	-76.5±22.0	-76.2±27.3



Brunner *et al*. Abstract #791. ACR 2013 San Diego

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DICIEMBRE 2012

AIJ SISTÉMICA

NEJM

New England Journal of Medicine

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Tocilizumab in Systemic Juvenile Idiopathic Arthritis

Fabrizio De Benedetti, M.D., Ph.D., Hermine I. Brunner, M.D., Nicolino Ruperto, M.D., M.P.H., Andrew Kenwright, B.Sc., Stephen Wright, M.D., Inmaculada Calvo, M.D., Ruben Cuttica, M.D., Angelo Ravelli, M.D., Rayfel Schneider, M.D., Patricia Woo, M.D., Ph.D., Carine Wouters, M.D., Ricardo Xavier, M.D., Lawrence Zemel, M.D., Eileen Baildam, M.D., Ruben Burgos-Vargas, M.D., Pavla Dolezalova, M.D., Stella M. Garay, M.D., Rosa Merino, M.D., Rik Joos, M.D., Alexei Grom, M.D., Ph.D., Nico Wulffraat, M.D., Zbigniew Zuber, M.D., Francesco Zulian, M.D., Daniel Lovell, M.D., M.P.H., and Alberto Martini, M.D., for the PRINTO and PRCSG*

N Engl J Med 2012;367:2385-95.
DOI: 10.1056/NEJMoa1112802
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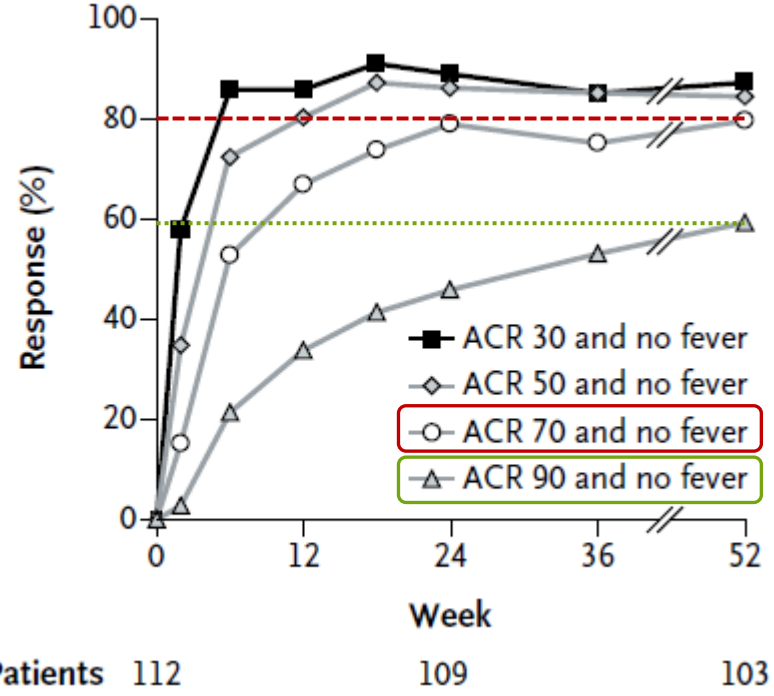
TOCILIZUMAB en AIJs

- Estudio multicéntrico realizado en 43 centros
- Dos fases
  - **Fase 1**. Estudio aleatorizado [en proporción 2:1], doble ciego, controlado con placebo, de 12 semanas de duración
  - TCZ 12 mg/kg/2 sem <30 kg y 8 mg/kg en ≥30 kg
  - **Fase 2**. Estudio abierto de extensión de hasta 5 años de seguimiento.

De Benedetti F *et al*. N Engl J Med 2012; 367:2385-95

TOCILIZUMAB en AIJs

- **112 pacientes** de 2-17a con enf ≥6 meses de evolución y respuesta inadecuada a PDN
- En **fase 1** [**12 sem**]
- En **fase 2** [**52 sem**]



De Benedetti F *et al*. N Engl J Med 2012; 367:2385-95

TOCILIZUMAB en AIJs

- Seguridad [n=112]
  - **Neutropenia ~20%.** Grado III [500-1,000/mm^3] en 17 [15%], grado IV [<500/mm^3] en 2 [2%]
  - **Elevación de ALT/GPT** ≥ 2,5 VR **~20%** [21/112]
  - **Elevación** de al menos 1 valor de **Colesterol** total o LDL: **31%** [vs 14% del grupo Placebo]
  - **Tasa de infecciones** de 3,4 por paciente-año con TCZ y 2,9 con PBO.
  - **Reacciones**: Rash 12%, Urticaria 7%, Eccema 6%
  - No TBC o infecciones oportunistas

De Benedetti F *et al*. N Engl J Med 2012; 367:2385-95

New England Journal of Medicine

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two Randomized Trials of Canakinumab in Systemic Juvenile Idiopathic Arthritis

Nicolino Ruperto, M.D., M.P.H., Hermine I. Brunner, M.D., Pierre Quartier, M.D., Tamás Constantin, M.D., Nico Wulffraat, M.D., Gerd Horneff, M.D., Riva Brik, M.D., Liza McCann, M.D., Ozgur Kasapcopur, M.D., Lidia Rutkowska-Sak, M.D., Rayfel Schneider, M.D., Yackov Berkun, M.D., Inmaculada Calvo, M.D., Muferet Erguven, M.D., Laurence Goffin, M.D., Michael Hofer, M.D., Tilmann Kallinich, M.D., Sheila K. Oliveira, M.D., Yosef Uziel, M.D., Stefania Viola, M.D., Kiran Nistala, M.D., Carine Wouters, M.D., Rolando Cimaz, M.D., Manuel A. Ferrandiz, M.D., Berit Flato, M.D., Maria Luz Gamir, M.D., Isabelle Kone-Paut, M.D., Alexei Grom, M.D., Bo Magnusson, M.D., Seza Ozen, M.D., Flavio Sztajnbok, M.D., Karine Lheritier, Ph.D., Ken Abrams, M.D., Dennis Kim, M.D., M.P.H., Alberto Martini, M.D., and Daniel J. Lovell, M.D., M.P.H., for the PRINTO and PRCSG*

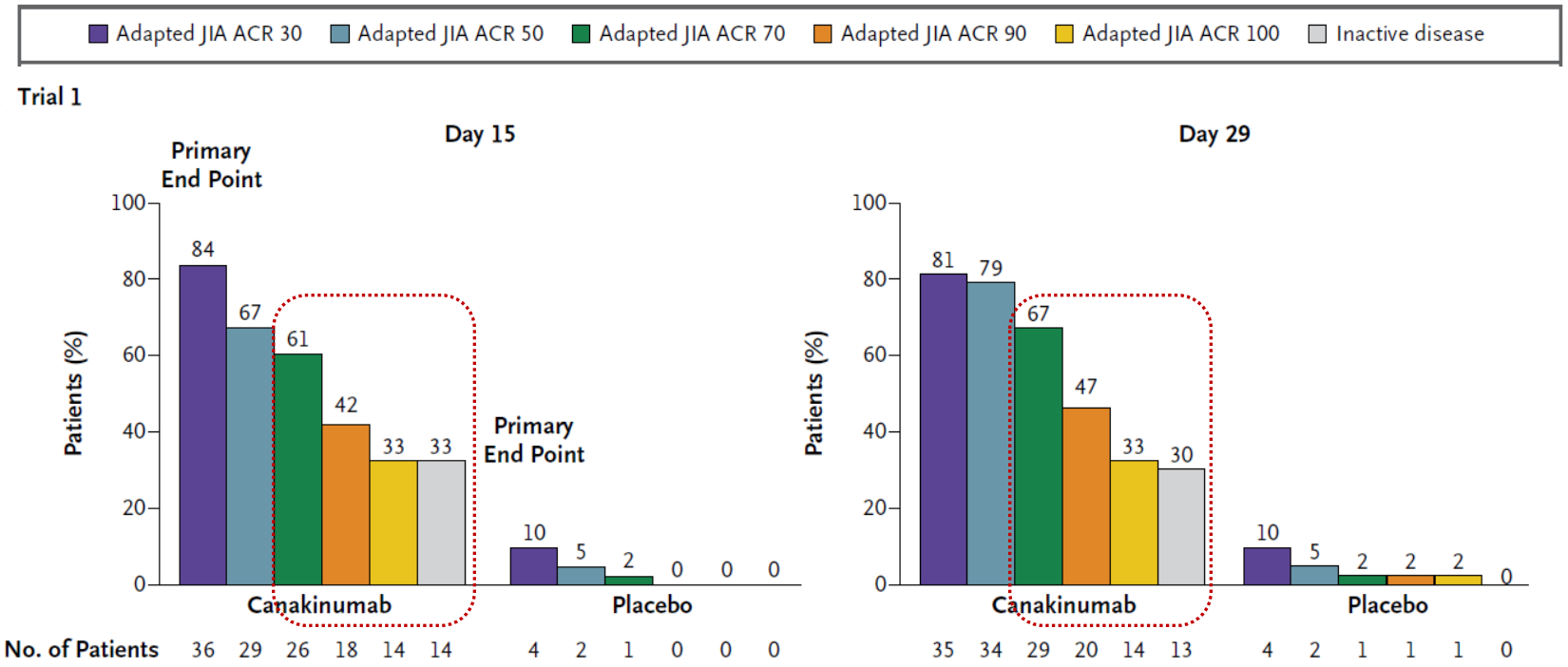
N Engl J Med 2012;367:2396-406.
DOI: 10.1056/NEJMoa1205099
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CANAKINUMAB en AIJs

- 2 ensayos clínicos realizados en 63 centros PRINTO o PRCSG
- **Ensayo 1**
  - Aleatorización a **dosis única** de CNK *sc* [4 mg/kg, máx 300 mg] o placebo → 84 pacientes de 2-19a

Ruperto N *et al*. N Engl J Med 2012; 367:2396-406

CANAKINUMAB en AIJs



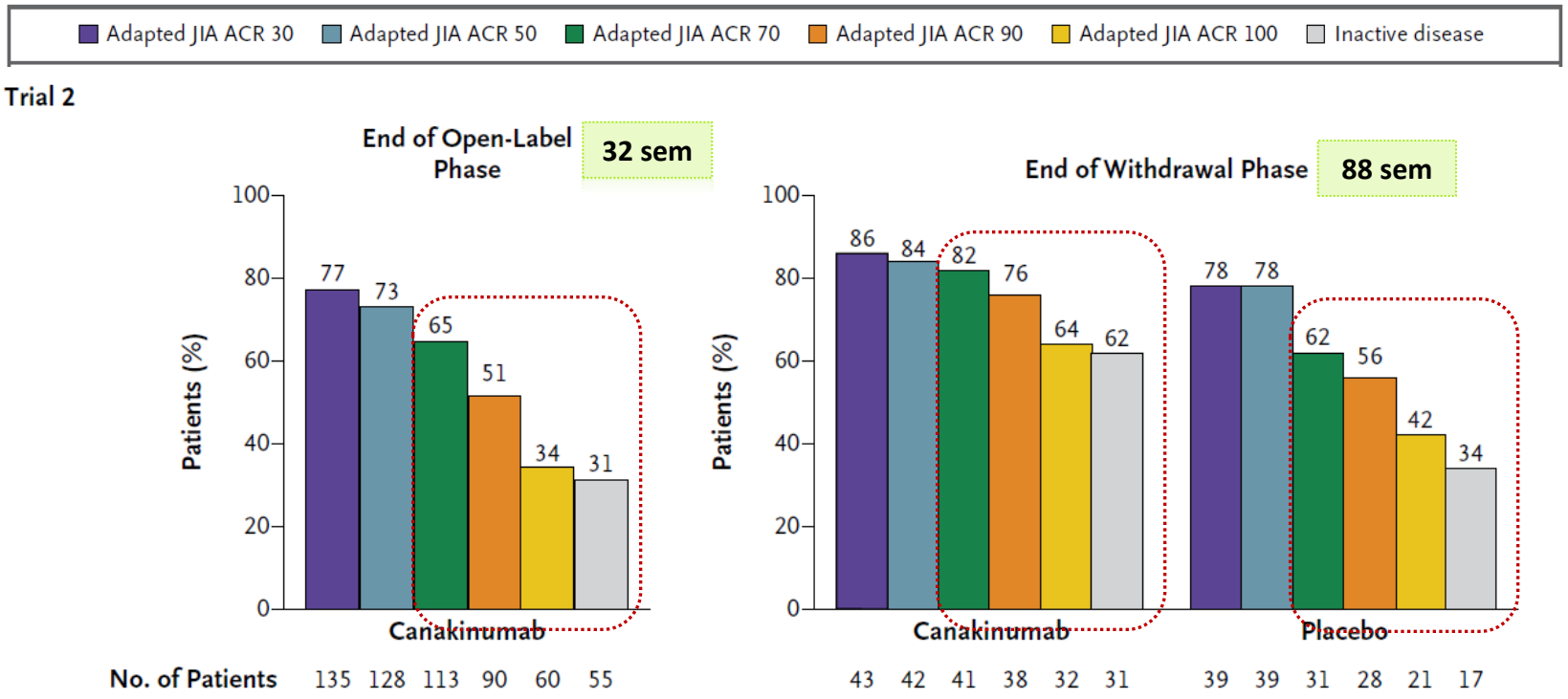
Ruperto N *et al*. N Engl J Med 2012; 367:2396-406

CANAKINUMAB en AIJs

- **Ensayo 2**
  - Dos partes
  - **1. Fase abierta** a la que también accedían los pacientes que en el Ensayo 1 alcanzaron el ACRPed30 modificado a los 15 días
  - CNK cada 4 semanas desde la 12 a la semana 32
  - **2. Fase de retirada** se aleatorizaba 1:1 a aquellos con respuesta ACRPed30 adaptado y con dosis estables o que no recibían PDN, a continuar recibiendo CNK o placebo

Ruperto N *et al*. N Engl J Med 2012; 367:2396-406

CANAKINUMAB en AIJs



Ruperto N *et al*. N Engl J Med 2012; 367:2396-406

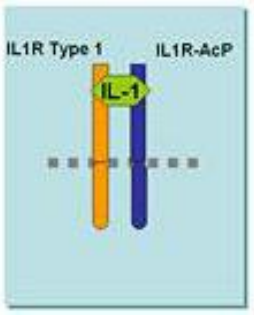
CANAKINUMAB en AIJs

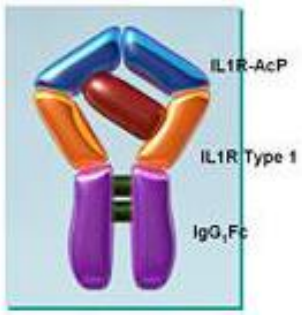
- Eficacia
  - Dosis media de esteroides reducida de 0,34 a 0,05 mg/kg/día. El 33% los suspendieron
- Seguridad
  - Neutropenia [6-12%] y Trombopenia [6%]
  - Infecciones graves en 4-5% del grupo CNK y 2-4% del grupo Placebo
  - 7 SAM [5 en CNK y 2 en PBO], 2 fallecimientos:
    - Urosepsis + SAM [8 dosis de CNK + 6 PBO]
    - SAM con hemorragia pulmonar [3 dosis CNK]

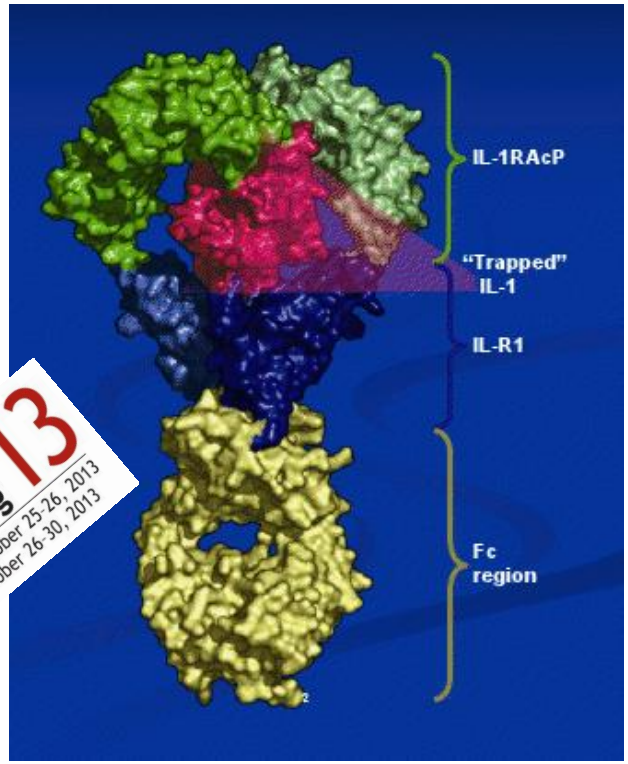
Ruperto N *et al*. N Engl J Med 2012; 367:2396-406

RILONACEPT en AIJ SISTÉMICA

- Ensayo RAPPORT [RAndomized Placebo Phase Study Of Rilonacept in the Treatment of SoJIA]
- Rilonacept. Proteína de fusión que contiene los dominios extracelulares de los 2 componentes requeridos para la transmisión de señal de activación de IL1unidos al fragmento Fc de la IgG1 humana:
  - El receptor tipo I
  - La proteína accesoria al receptor







ACR/ARHP 13 Annual Meeting
San Diego
Pre-Meeting Courses: October 25-26, 2013
Scientific Sessions: October 26-30, 2013

Ilowite N *et al*. Abstract #1780. ACR 2013 San Diego

RILONACEPT en AIJ SISTÉMICA

- n=71 AIJs con artritis en al menos 2 articulaciones
- Valoran resultado utilizando un índice ACR 30 adaptado [ACR 30 + no fiebre durante 2 semanas + rebaja PDN según protocolo durante las primeras 12 semanas]
- Resultados a la semana 4:

	Rilonacept	Placebo
ACR 30 adaptado	26/35 (79%)	13/33 (39%)
ACR 50 adaptado	21/35 (60%)	10/33 (30%)
ACR 70 adaptado	14/35 (40%)	4/33 (12%)

ACR/ARHP 13 Annual Meeting
San Diego
Pre-Meeting Courses: October 25-26, 2013
Scientific Sessions: October 26-30, 2013

Ilowite N *et al*. Abstract #1780. ACR 2013 San Diego

RITUXIMAB en AIJ SISTÉMICA

- Seguimiento a 5 años de 60 niños con AIJs
- Edad 1-18 años
- Refractarios a MTX, CsA, GGIV y/o anti TNF
- 5/60 [8%] refractarios a TCZ, 36 [60%] tomaban PDN
- Protocolo de tratamiento: 375 mg/m^2/semana x 4 dosis

Ciclos RTX	Nª de pacientes	%
1	60	100
2	36	60
3	19	32
4	5	8



Alexeeva E *et al*. Abstract #2170. ACR 2013 San Diego

RITUXIMAB en AIJ SISTÉMICA

- Control 6 meses después de recibir RTX [n=60]
  - Manifestaciones sistémicas resueltas en 45/60 [75%]
- Evolución con RTX
  - No mejoría en 25% [15 pacientes]
  - No control de la artritis en 13% [8 pacientes]
  - 7% recaída articular [n=4], 12% recaída enf sistémica [7]

Tiempo	n	Remisión		ACR 50	ACR 70	ACR 90
6 meses	60	25%		40%	35%	-
12 meses	45	30%		55%	45%	-
2 años	39	43%		80%	75%	70%
3 años	32	33%		85%	80&	75%
4 años	27	33%		95%	95%	93%

Alexeeva E *et al*. Abstract #2170. ACR 2013 San Diego

HT PULMONAR en AIJ SISTÉMICA

Arthritis Care & Research

Pulmonary Hypertension and Other Potentially Fatal Pulmonary Complications in Systemic Juvenile Idiopathic Arthritis

Yukiko Kimura MD[1], Jennifer E. Weiss MD[1], Kathryn L. Haroldson BS[1], Tzielan Lee MD[2], Marilynn Punaro MD[3], Sheila Oliveira MD[4], Egla Rabinovich MD[5], Meredith Riebschleger MD[6], Jordi Antón MD, PhD[7], Peter R. Blier MD, PhD[8], Valeria Gerloni MD[9], Melissa M Hazen MD[10], Elizabeth Kessler MD[11], Karen Onel MD[12], Murray H Passo MD[13], Robert M Rennebohm MD[14], Carol A Wallace MD[15], Patricia Woo MD[16], Nico Wulffraat MD[17], and the CARRAnet Investigators

- Kimura Y et al. Arthr Care Res 2013; 65:745-52

HT PULMONAR en AIJ SISTÉMICA

- Publican 25 casos de HT Pulmonar [16], Enf. Intersticial Pulmonar [7] y Proteinosis Alveolar [5] en pacientes con AIJs
- Comparan con el resto de la serie CARRA [n=389]:
  - Mayor porcentaje de mujeres
  - Más persistencia de síntomas sistémicos
  - Exposición a IL1ra, TCZ, Esteroides, GGIV, CsA y Ciclofosfamida

  - 80% diagnosticados después de 2004
  - 20/25 presentaron SAM
  - 68% fallecieron una media de 10 meses después del diagnóstico de la enfermedad pulmonar

Kimura Y et al. Arthr Care Res 2013; 65:745-52

MÁS SOBRE AIJ

UN POCO DE TODO

CORTICOIDES INTRAARTICULARES en el TRATAMIENTO de la AIJ

Arthritis Care & Research

ORIGINAL ARTICLE

Delineating the Role of Multiple Intraarticular Corticosteroid Injections in the Management of Juvenile Idiopathic Arthritis in the Biologic Era

CHARALAMPIA PAPADOPOULOU,[1] MIKHAIL KOSTIK,[1] MARIA ISABEL GONZALEZ-FERNANDEZ,[1] MAREK BOHM,[1] JUAN CARLOS NIETO-GONZALEZ,[1] ANGELA PISTORIO,[1] STEFANO LANNI,[1] ALESSANDRO CONSOLARO,[2] ALBERTO MARTINI,[2] AND ANGELO RAVELLI[2]

Papadopoulou C *et al*. Arthritis Care Res 2013; 65:1112-20

CIA y TRATAMIENTO de AIJ

- Hexacetónido de Triamcinolona
  - Anestesia general o local
  - Reposo relativo durante 24 horas [cadera 72 horas]
- **220** pacientes y **1,096** artic infiltradas [mediana 4, RIQ 3-6]
  - **71,3% AIJ de curso poliarticular** [Poliartritis FR negativo u Oligoartritis extendida]
  - Mediana de evolución de la enfermedad 0,6 años
  - Mediana de edad 3,7 años
  - 61,8% recibieron tratamiento sistémico →
  - **38,2% no recibieron tratamiento sistémico**

Papadopoulou C *et al*. Arthritis Care Res 2013; 65:1112-20

CIA y TRATAMIENTO de AIJ

	Patients who had the joint injected (n = 220)	No. of injected joints	Joints with remission†	Joints with synovitis flare†	*P*
Knee	186 (84.5)	298	236 (79.2)	62 (20.8)	< 0.0001
Ankle	168 (76.4)	245	132/241 (54.8)	109/241 (45.2)	0.14
Subtalar	67 (30.5)	88	57/87 (65.5)	30/87 (34.5)	0.004
Elbow	64 (29.1)	84	71 (84.5)	13 (15.5)	< 0.0001
Proximal interphalangeal	58 (26.4)	128	100/127 (78.7)	27/127 (21.3)	< 0.0001
Wrist	57 (25.9)	83	49/82 (59.8)	33/82 (40.2)	0.08
Metacarpophalangeal	51 (23.2)	109	79/107 (73.8)	28/107 (26.2)	< 0.0001
Metatarsophalangeal	14 (6.4)	16	12/14 (85.7)	2/14 (14.3)	0.008
Foot interphalangeal	14 (6.4)	21	18/20 (90.0)	2/20 (10.0)	0.0003
Shoulder	8 (3.6)	11	5/7 (71.4)	2/7 (28.6)	–
Intertarsal	8 (3.6)	10	9 (90.0)	1 (10.0)	–
Hip	2 (0.9)	2	1/1 (100.0)	0/1 (0.0)	–
Temporomandibular	1 (0.5)	1	1 (100.0)	0 (0.0)	–
Total number of injected joints	–	1,096	770/1,079 (71.4)	309/1,079 (28.6)	< 0.0001

* Values are the number (percentage) unless otherwise indicated.
† Of the total number of joints for which the outcome could be assessed.

Papadopoulou C *et al*. Arthritis Care Res 2013; 65:1112-20

CIA y TRATAMIENTO de AIJ

- Factores de riesgo:
  - ANA negativo
  - Elevación de PCR > 0,46 mg/dl
  - No asociar MTX al tiempo de la infiltración
  - Curso articular: Poli peor que Oligo

Cox regression model*		
Risk factor	**HR (95% CI)**	***P*†**
ANA status: negative (reference category: positive)	2.97 (1.71–5.18)	0.0004
CRP level >0.46 mg/dl (reference category: ≤0.46 mg/dl)	2.40 (1.48–3.88)	0.0001
Ongoing or newly started methotrexate: no (reference category: yes)	1.91 (1.30–2.81)	0.0011
Disease course		0.017
Polyarthritis (reference category: oligoarthritis)	2.04 (1.12–3.71)	
Systemic arthritis (reference category: oligoarthritis)	1.13 (0.41–3.06)	

* The event of interest was flare of synovitis. Complete data were available for 189 patients. HR = hazard ratio; 95% CI = 95% confidence interval; ANA = antinuclear antibody; CRP = C-reactive protein.
† *P* values refer to the likelihood ratio test.

Papadopoulou C *et al*. Arthritis Care Res 2013; 65:1112-20

COMO SUSPENDER ANTI-TNF

- Estudio retrospectivo monocéntrico de pacientes con AIJ Poliarticular controlados entre Enero 2000-Diciembre 2011
- Utilizan criterios de enfermedad inactiva de Wallace *et al*
- **n=194**, 4 brazos de tratamiento:
  - Anti TNF + MTX, suspenden MTX primero (n=45)
  - Anti TNF + MTX, suspenden anti TNF primero (n=19)
  - MTX en monoterapia (n=32)
  - Anti TNF en monoterapia (n=6)
- Después de 23 m de seguimiento enf. inactiva 129/194 (66%)

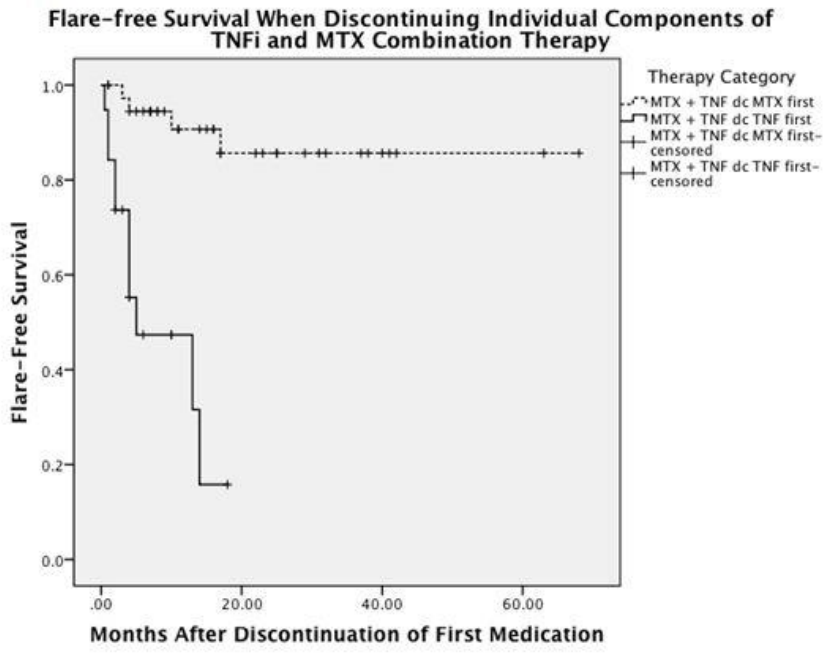


Chang CY *et al*. Abstract #282. ACR 2013 San Diego

COMO SUSPENDER ANTI-TNF

- Entre los pacientes que recibieron **terapia combinada** mantuvieron más tiempo la remisión aquellos pacientes a quienes se suspendió primero el MTX (90%) que aquellos a quienes se suspendió antes el anti TNF (47%)

Figure 1



Chang CY *et al*. Abstract #282. ACR 2013 San Diego

ARTROCENTESIS y SEDACIÓN

European Journal of Pediatrics

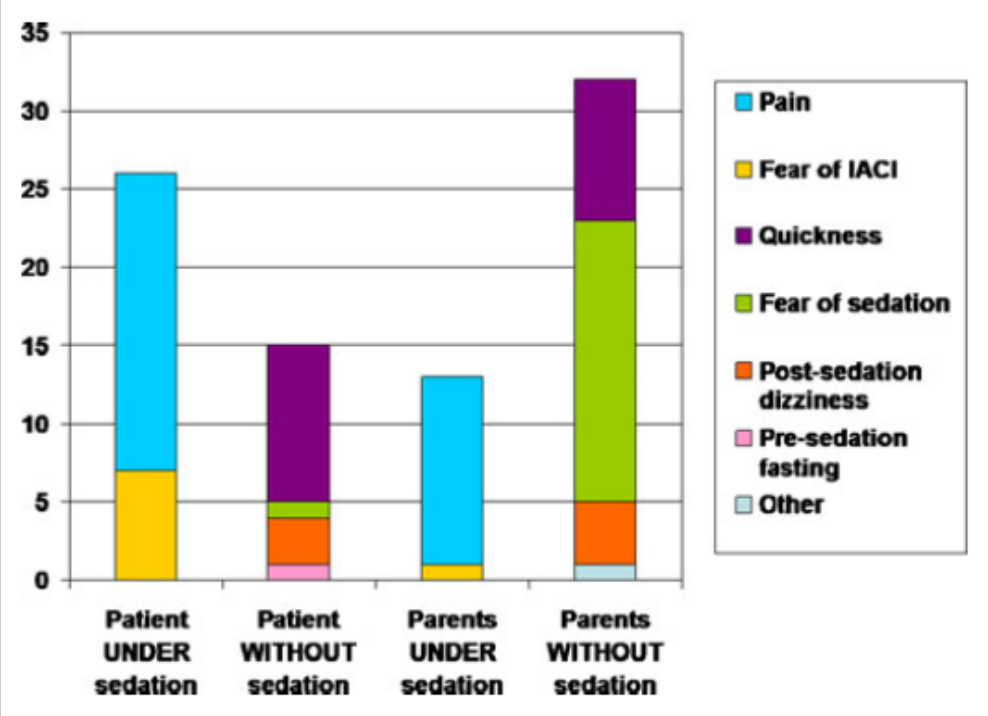
Sedation for intra-articular corticosteroid injections in juvenile idiopathic arthritis: the views of patients and their parents

Rocío Casado · Javier Lumbreras · Jaime de Inocencio · Agustín Remesal · Rosa Merino · Julia García-Consuegra

- 45 niños con AIJ que habían recibido CIAs con y sin sedación
- Analiza la percepción del riesgo y preferencias de los niños y de los padres sobre la utilización de sedación [sevofluorano] *vs*. ningún tipo de analgesia para realizar artrocentesis

Casado R *et al*. Eur J Pediatr 2013; 172:144-13

ARTROCENTESIS y SEDACIÓN



- Pacientes prefieren
  - Sedación para evitar dolor, en menores [26/45]
  - No analgesia por su rapidez y evitar la sensación de mareo post-sedación, en mayores [15/45]
- Padres prefieren
  - Sedación para evitar dolor
  - No analgesia por miedo a los efectos 2^{rios} de la sedación [18/32]

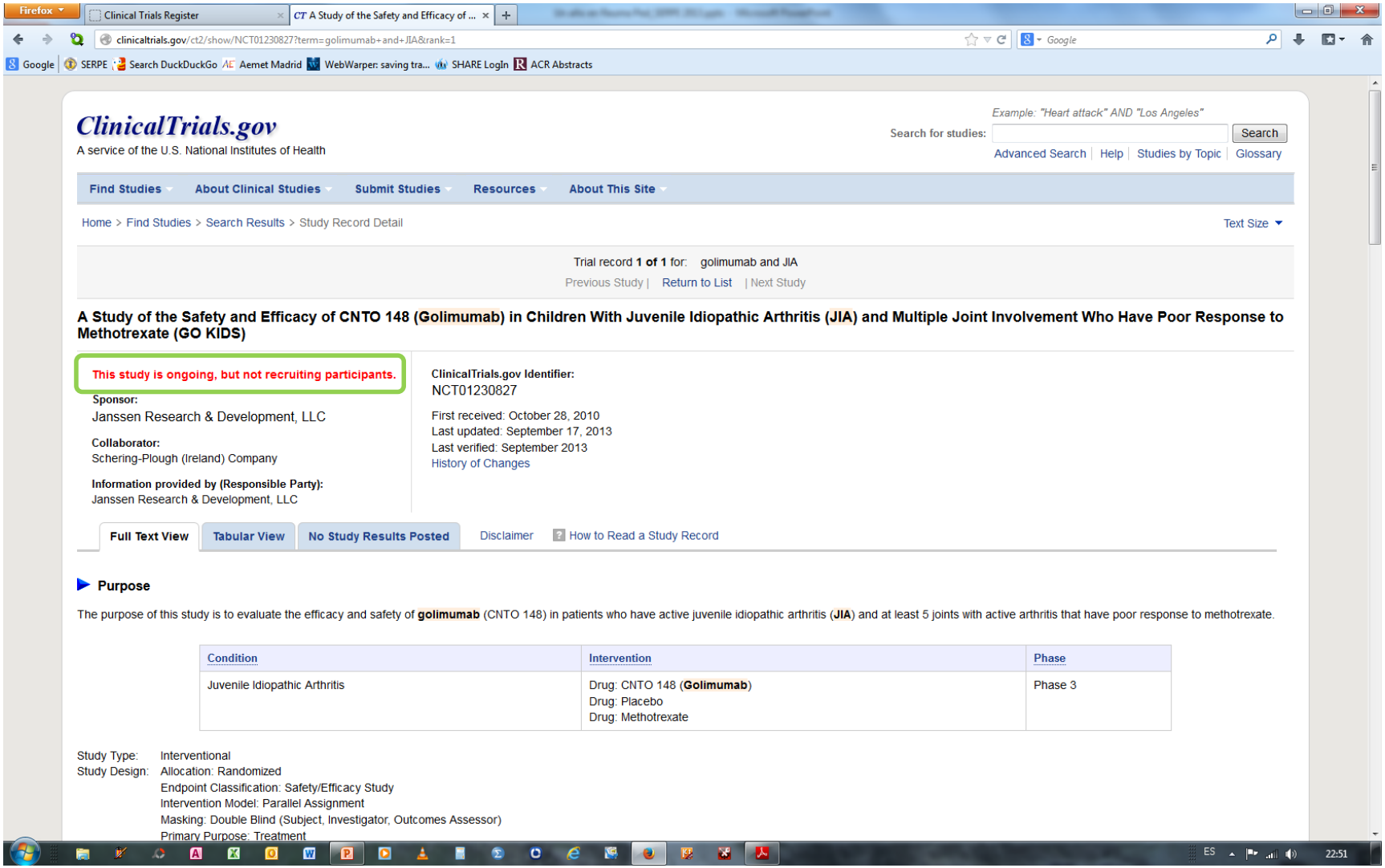
Casado R *et al*. Eur J Pediatr 2013; 172:144-13

Hospital Universitario 12 de Octubre
SaludMadrid

ENSAYOS EN MARCHA

ANTI-TNFα, ABATACEPT y NUEVAS MOLÉCULAS en PEDIATRÍA

GOLIMUMAB en AIJ Poliarticular



Clinical Trials Register | A Study of the Safety and Efficacy of ...

clinicaltrials.gov/ct2/show/NCT01230827?term=golimumab+and+JIA&rank=1

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ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Example: "Heart attack" AND "Los Angeles"
Search for studies: Search
Advanced Search | Help | Studies by Topic | Glossary

Find Studies | About Clinical Studies | Submit Studies | Resources | About This Site

Home > Find Studies > Search Results > Study Record Detail

Text Size

Trial record 1 of 1 for: golimumab and JIA
Previous Study | Return to List | Next Study

A Study of the Safety and Efficacy of CNTO 148 (Golimumab) in Children With Juvenile Idiopathic Arthritis (JIA) and Multiple Joint Involvement Who Have Poor Response to Methotrexate (GO KIDS)

This study is ongoing, but not recruiting participants.

Sponsor:
Janssen Research & Development, LLC

Collaborator:
Schering-Plough (Ireland) Company

Information provided by (Responsible Party):
Janssen Research & Development, LLC

ClinicalTrials.gov Identifier:
NCT01230827

First received: October 28, 2010
Last updated: September 17, 2013
Last verified: September 2013
History of Changes

Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

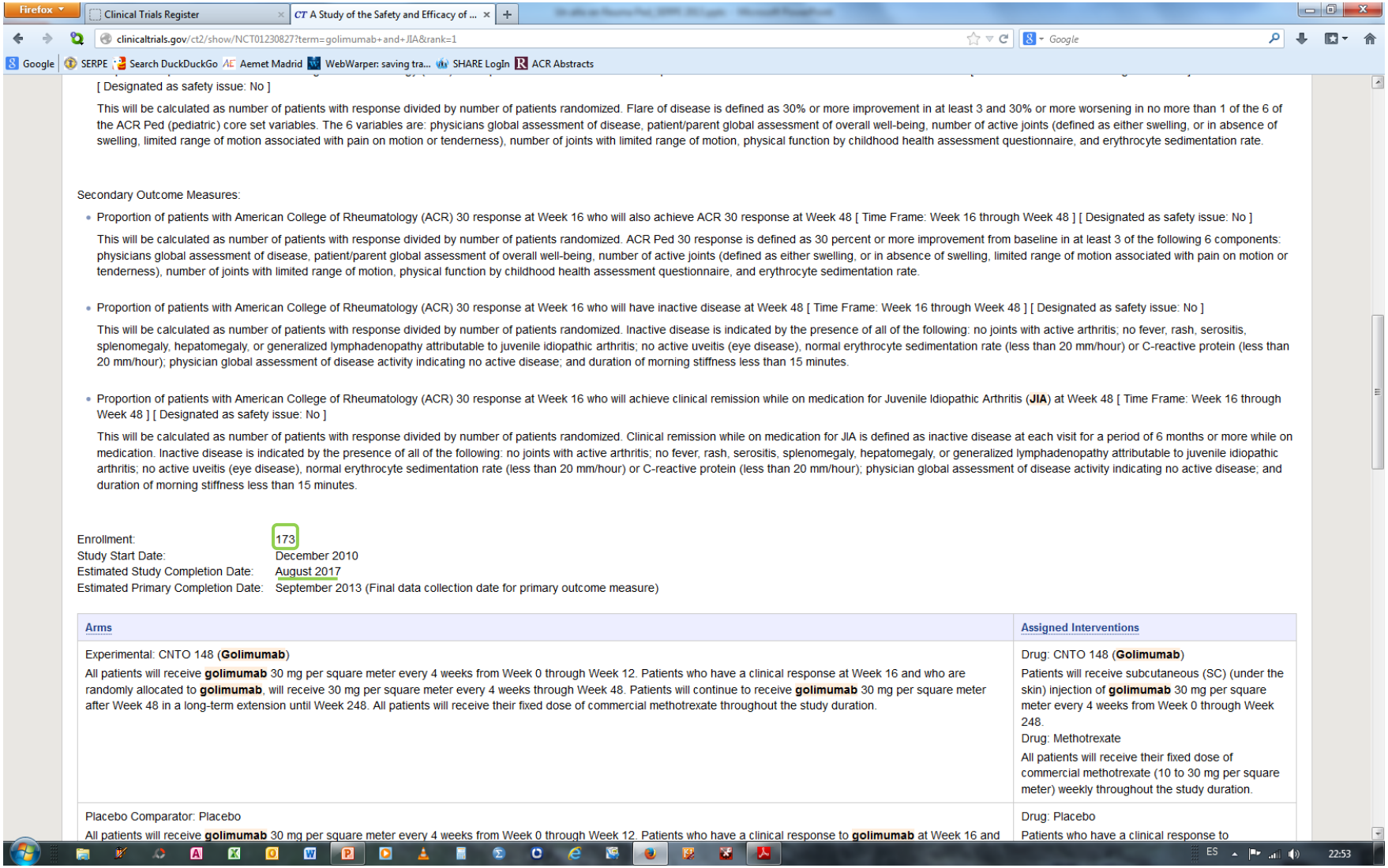
Purpose

The purpose of this study is to evaluate the efficacy and safety of **golimumab** (CNTO 148) in patients who have active juvenile idiopathic arthritis (**JIA**) and at least 5 joints with active arthritis that have poor response to methotrexate.

Condition	Intervention	Phase
Juvenile Idiopathic Arthritis	Drug: CNTO 148 (**Golimumab**) Drug: Placebo Drug: Methotrexate	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

GOLIMUMAB en AIJ Poliarticular



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clinicaltrials.gov/ct2/show/NCT01230827?term=golimumab+and+JIA&rank=1

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[Designated as safety issue: No]

This will be calculated as number of patients with response divided by number of patients randomized. Flare of disease is defined as 30% or more improvement in at least 3 and 30% or more worsening in no more than 1 of the 6 of the ACR Ped (pediatric) core set variables. The 6 variables are: physicians global assessment of disease, patient/parent global assessment of overall well-being, number of active joints (defined as either swelling, or in absence of swelling, limited range of motion associated with pain on motion or tenderness), number of joints with limited range of motion, physical function by childhood health assessment questionnaire, and erythrocyte sedimentation rate.

Secondary Outcome Measures:

- Proportion of patients with American College of Rheumatology (ACR) 30 response at Week 16 who will also achieve ACR 30 response at Week 48 [Time Frame: Week 16 through Week 48] [Designated as safety issue: No]

  This will be calculated as number of patients with response divided by number of patients randomized. ACR Ped 30 response is defined as 30 percent or more improvement from baseline in at least 3 of the following 6 components: physicians global assessment of disease, patient/parent global assessment of overall well-being, number of active joints (defined as either swelling, or in absence of swelling, limited range of motion associated with pain on motion or tenderness), number of joints with limited range of motion, physical function by childhood health assessment questionnaire, and erythrocyte sedimentation rate.

- Proportion of patients with American College of Rheumatology (ACR) 30 response at Week 16 who will have inactive disease at Week 48 [Time Frame: Week 16 through Week 48] [Designated as safety issue: No]

  This will be calculated as number of patients with response divided by number of patients randomized. Inactive disease is indicated by the presence of all of the following: no joints with active arthritis; no fever, rash, serositis, splenomegaly, hepatomegaly, or generalized lymphadenopathy attributable to juvenile idiopathic arthritis; no active uveitis (eye disease), normal erythrocyte sedimentation rate (less than 20 mm/hour) or C-reactive protein (less than 20 mm/hour); physician global assessment of disease activity indicating no active disease; and duration of morning stiffness less than 15 minutes.

- Proportion of patients with American College of Rheumatology (ACR) 30 response at Week 16 who will achieve clinical remission while on medication for Juvenile Idiopathic Arthritis (**JIA**) at Week 48 [Time Frame: Week 16 through Week 48] [Designated as safety issue: No]

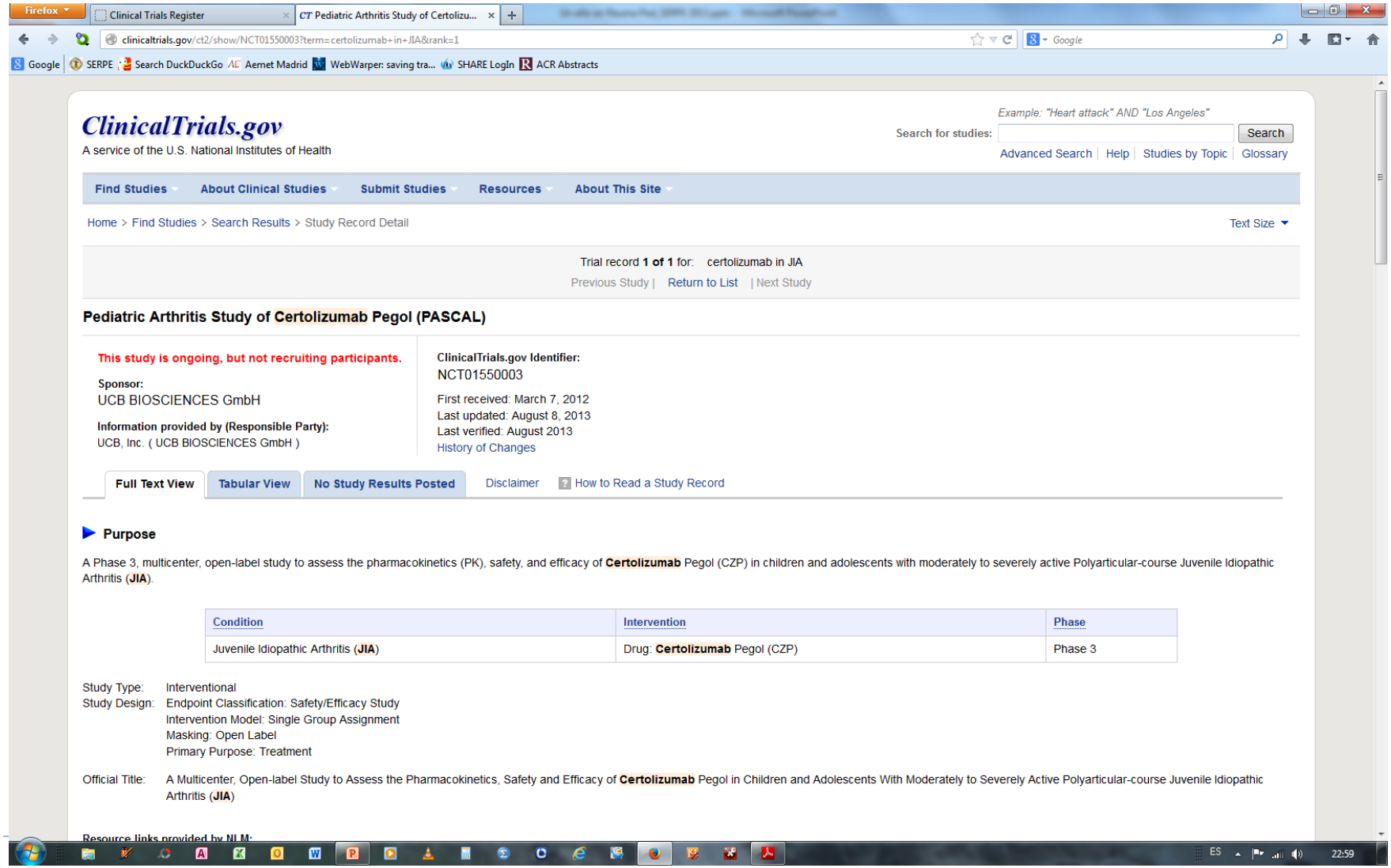
  This will be calculated as number of patients with response divided by number of patients randomized. Clinical remission while on medication for JIA is defined as inactive disease at each visit for a period of 6 months or more while on medication. Inactive disease is indicated by the presence of all of the following: no joints with active arthritis; no fever, rash, serositis, splenomegaly, hepatomegaly, or generalized lymphadenopathy attributable to juvenile idiopathic arthritis; no active uveitis (eye disease), normal erythrocyte sedimentation rate (less than 20 mm/hour) or C-reactive protein (less than 20 mm/hour); physician global assessment of disease activity indicating no active disease; and duration of morning stiffness less than 15 minutes.

Enrollment:	173
Study Start Date:	December 2010
Estimated Study Completion Date:	August 2017
Estimated Primary Completion Date:	September 2013 (Final data collection date for primary outcome measure)

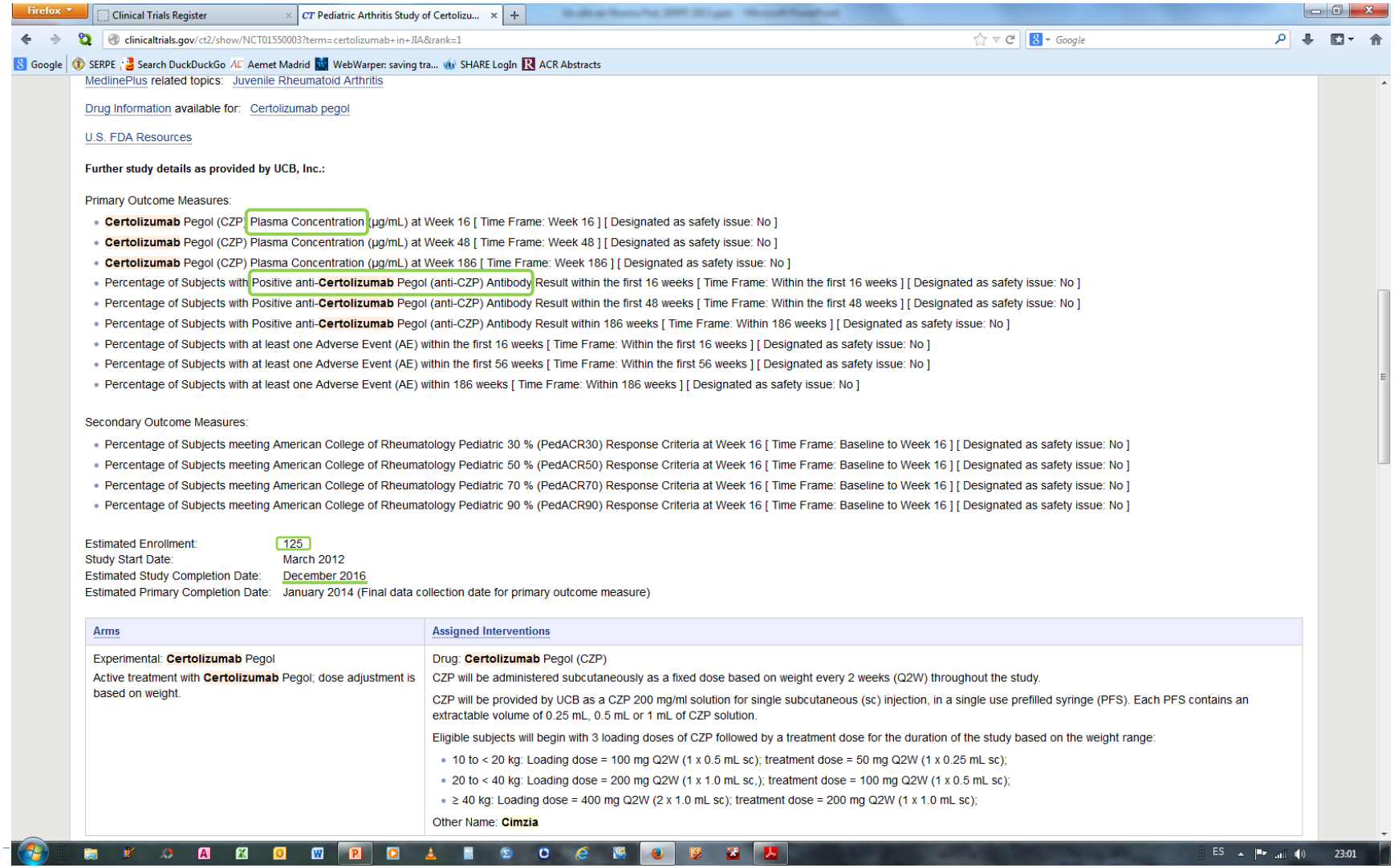
Arms	Assigned Interventions
Experimental: CNTO 148 (**Golimumab**) All patients will receive **golimumab** 30 mg per square meter every 4 weeks from Week 0 through Week 12. Patients who have a clinical response at Week 16 and who are randomly allocated to **golimumab**, will receive 30 mg per square meter every 4 weeks through Week 48. Patients will continue to receive **golimumab** 30 mg per square meter after Week 48 in a long-term extension until Week 248. All patients will receive their fixed dose of commercial methotrexate throughout the study duration.	Drug: CNTO 148 (**Golimumab**) Patients will receive subcutaneous (SC) (under the skin) injection of **golimumab** 30 mg per square meter every 4 weeks from Week 0 through Week 248. Drug: Methotrexate All patients will receive their fixed dose of commercial methotrexate (10 to 30 mg per square meter) weekly throughout the study duration.
Placebo Comparator: Placebo All patients will receive **golimumab** 30 mg per square meter every 4 weeks from Week 0 through Week 12. Patients who have a clinical response to **golimumab** at Week 16 and	Drug: Placebo Patients who have a clinical response to

ES 22:53

CERTOLIZUMAB en AIJ Poliarticular



CERTOLIZUMAB en AIJ Poliarticular



MedlinePlus related topics: Juvenile Rheumatoid Arthritis

Drug Information available for: Certolizumab pegol

U.S. FDA Resources

Further study details as provided by UCB, Inc.:

Primary Outcome Measures:

- **Certolizumab** Pegol (CZP) Plasma Concentration (µg/mL) at Week 16 [Time Frame: Week 16] [Designated as safety issue: No]
- **Certolizumab** Pegol (CZP) Plasma Concentration (µg/mL) at Week 48 [Time Frame: Week 48] [Designated as safety issue: No]
- **Certolizumab** Pegol (CZP) Plasma Concentration (µg/mL) at Week 186 [Time Frame: Week 186] [Designated as safety issue: No]
- Percentage of Subjects with Positive anti-**Certolizumab** Pegol (anti-CZP) Antibody Result within the first 16 weeks [Time Frame: Within the first 16 weeks] [Designated as safety issue: No]
- Percentage of Subjects with Positive anti-**Certolizumab** Pegol (anti-CZP) Antibody Result within the first 48 weeks [Time Frame: Within the first 48 weeks] [Designated as safety issue: No]
- Percentage of Subjects with Positive anti-**Certolizumab** Pegol (anti-CZP) Antibody Result within 186 weeks [Time Frame: Within 186 weeks] [Designated as safety issue: No]
- Percentage of Subjects with at least one Adverse Event (AE) within the first 16 weeks [Time Frame: Within the first 16 weeks] [Designated as safety issue: No]
- Percentage of Subjects with at least one Adverse Event (AE) within the first 56 weeks [Time Frame: Within the first 56 weeks] [Designated as safety issue: No]
- Percentage of Subjects with at least one Adverse Event (AE) within 186 weeks [Time Frame: Within 186 weeks] [Designated as safety issue: No]

Secondary Outcome Measures:

- Percentage of Subjects meeting American College of Rheumatology Pediatric 30 % (PedACR30) Response Criteria at Week 16 [Time Frame: Baseline to Week 16] [Designated as safety issue: No]
- Percentage of Subjects meeting American College of Rheumatology Pediatric 50 % (PedACR50) Response Criteria at Week 16 [Time Frame: Baseline to Week 16] [Designated as safety issue: No]
- Percentage of Subjects meeting American College of Rheumatology Pediatric 70 % (PedACR70) Response Criteria at Week 16 [Time Frame: Baseline to Week 16] [Designated as safety issue: No]
- Percentage of Subjects meeting American College of Rheumatology Pediatric 90 % (PedACR90) Response Criteria at Week 16 [Time Frame: Baseline to Week 16] [Designated as safety issue: No]

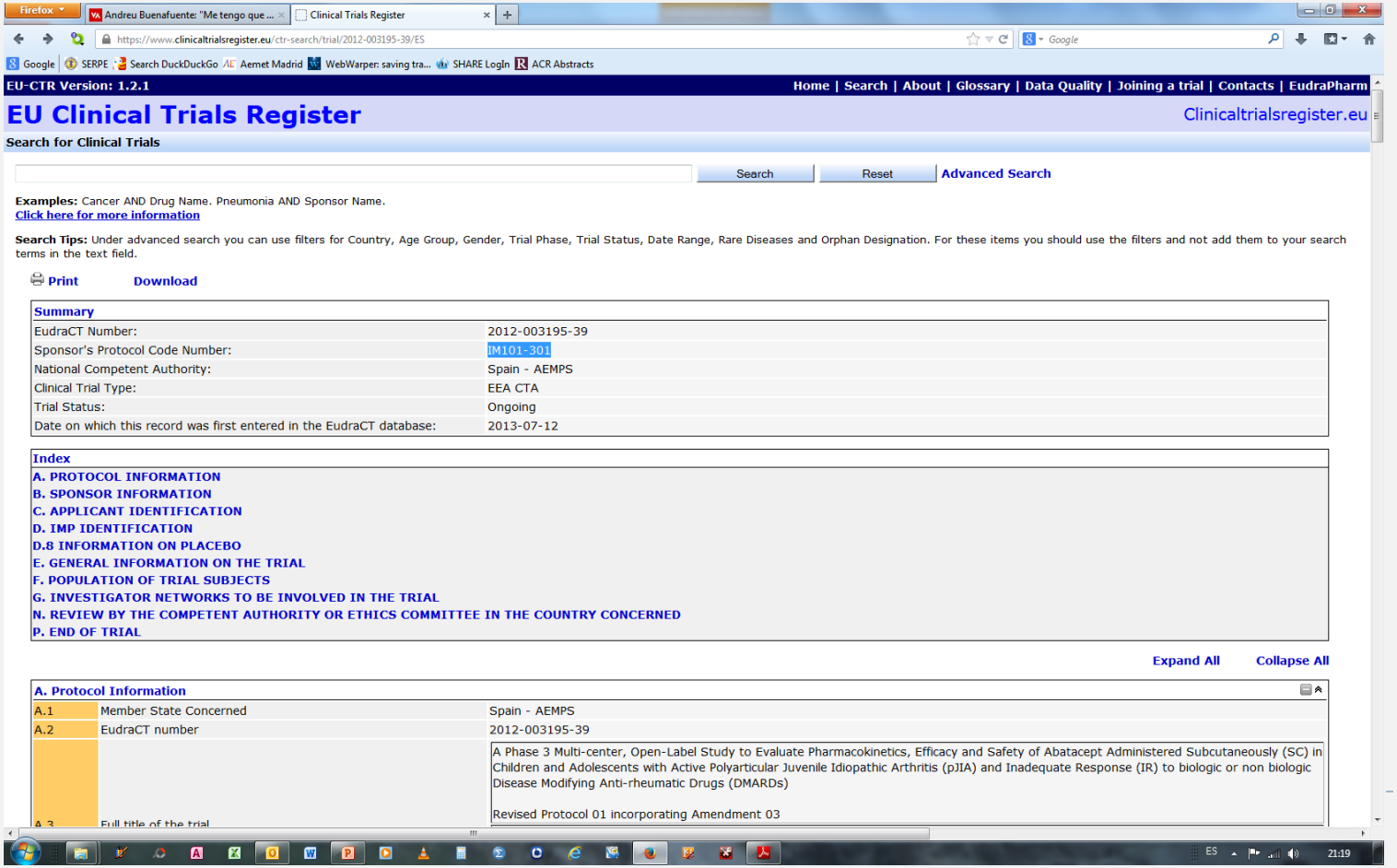
Estimated Enrollment: 125
Study Start Date: March 2012
Estimated Study Completion Date: December 2016
Estimated Primary Completion Date: January 2014 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: **Certolizumab** Pegol Active treatment with **Certolizumab** Pegol; dose adjustment is based on weight.	Drug: **Certolizumab** Pegol (CZP) CZP will be administered subcutaneously as a fixed dose based on weight every 2 weeks (Q2W) throughout the study. CZP will be provided by UCB as a CZP 200 mg/ml solution for single subcutaneous (sc) injection, in a single use prefilled syringe (PFS). Each PFS contains an extractable volume of 0.25 mL, 0.5 mL or 1 mL of CZP solution. Eligible subjects will begin with 3 loading doses of CZP followed by a treatment dose for the duration of the study based on the weight range: • 10 to < 20 kg: Loading dose = 100 mg Q2W (1 x 0.5 mL sc); treatment dose = 50 mg Q2W (1 x 0.25 mL sc); • 20 to < 40 kg: Loading dose = 200 mg Q2W (1 x 1.0 mL sc,); treatment dose = 100 mg Q2W (1 x 0.5 mL sc); • ≥ 40 kg: Loading dose = 400 mg Q2W (2 x 1.0 mL sc); treatment dose = 200 mg Q2W (1 x 1.0 mL sc); Other Name: **Cimzia**

ABATACEPT sc en AIJ Poliarticular

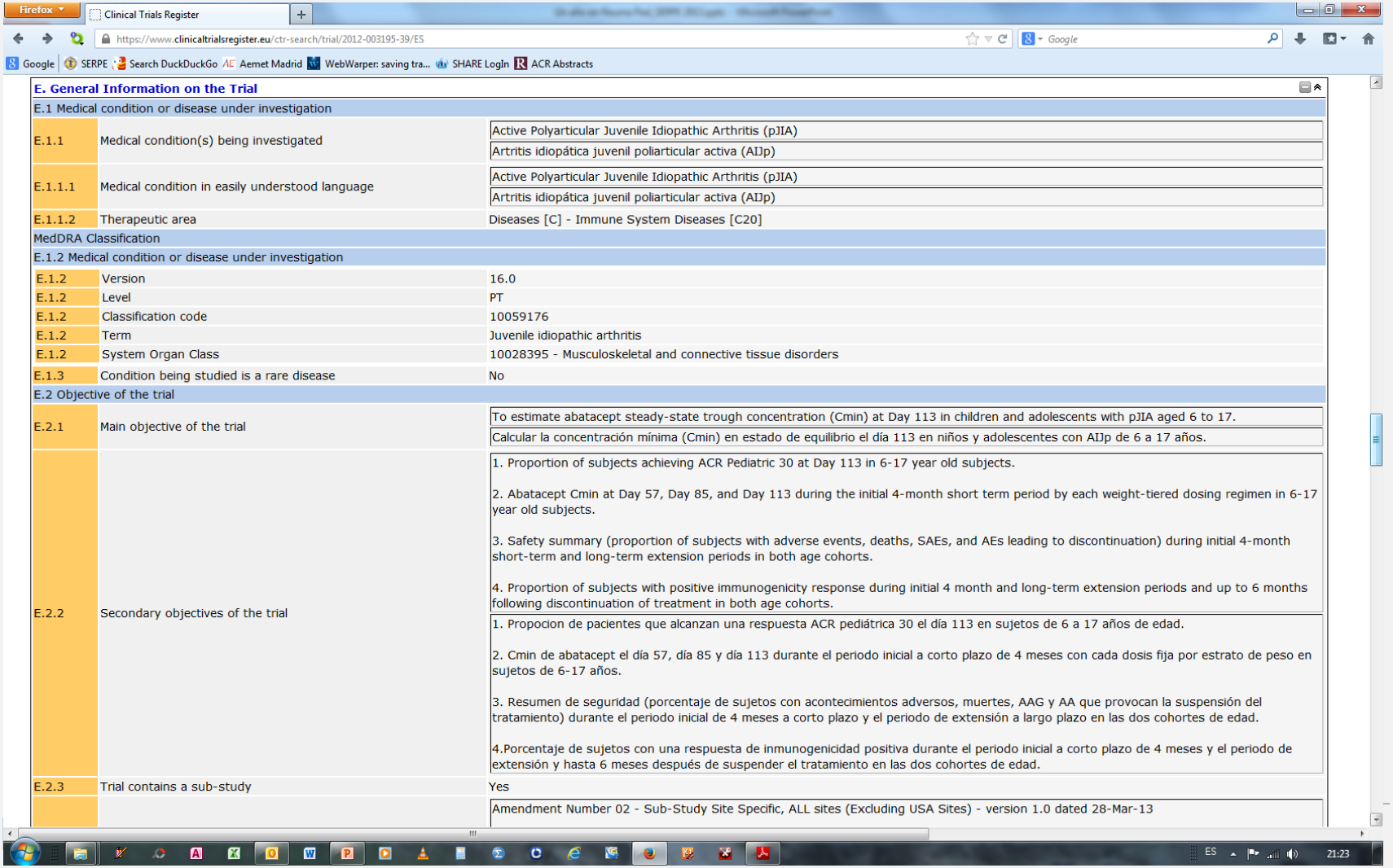
- **EudraCT Number:** 2012-003195-39. Bristol-Myers Squibb
  - Abatacept [BMS-188667]. Protocolo IM101-301 disponible en

https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-003195-39/ES



ABATACEPT sc en AIJ Poliarticular

- **EudraCT Number:** 2012-003195-39. BMS



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https://www.clinicaltrialsregister.eu/ctr-search/trial/2012-003195-39/ES

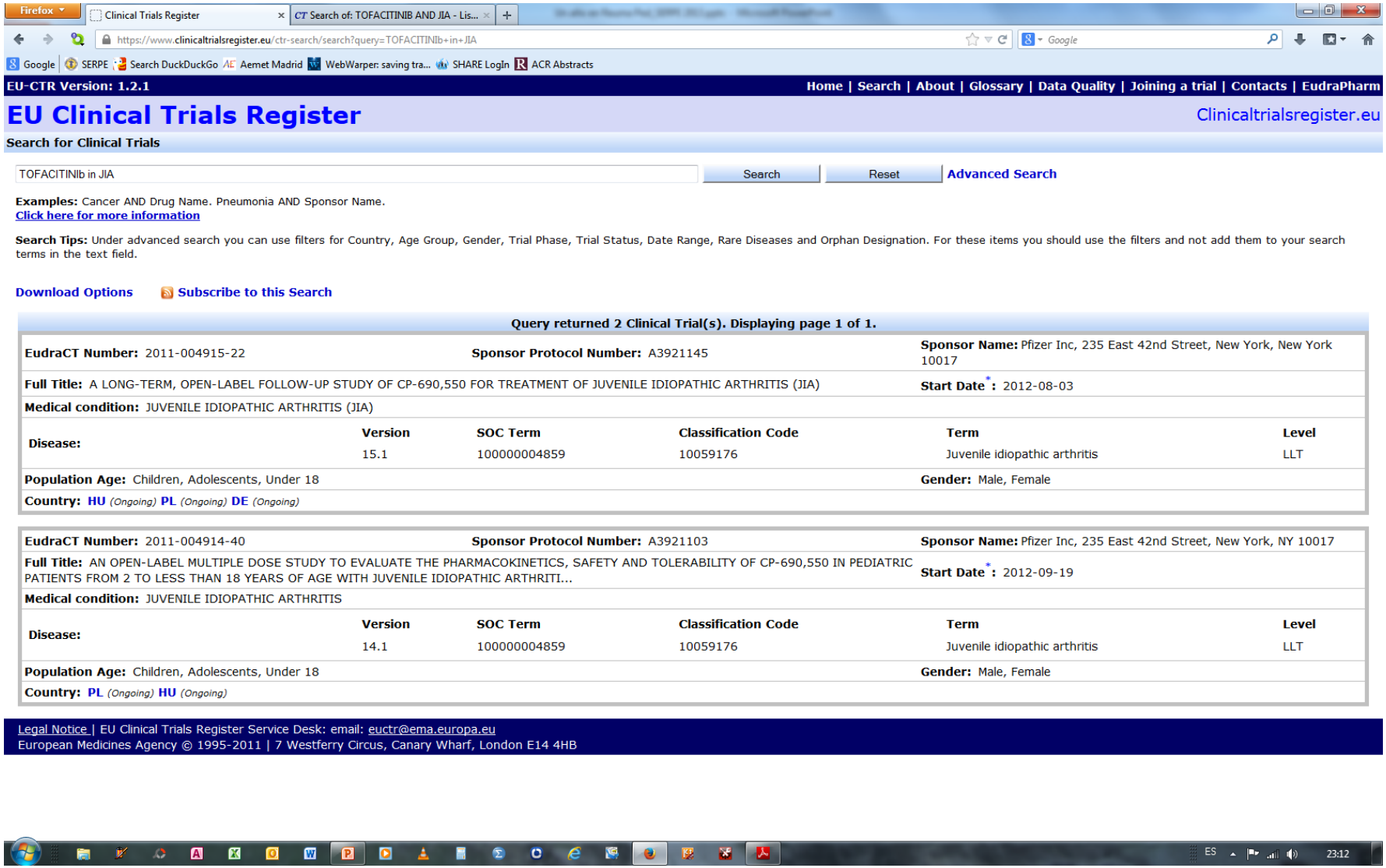
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E. General Information on the Trial

E.1 Medical condition or disease under investigation		
E.1.1	Medical condition(s) being investigated	Active Polyarticular Juvenile Idiopathic Arthritis (pJIA) Artritis idiopática juvenil poliarticular activa (AIJp)
E.1.1.1	Medical condition in easily understood language	Active Polyarticular Juvenile Idiopathic Arthritis (pJIA) Artritis idiopática juvenil poliarticular activa (AIJp)
E.1.1.2	Therapeutic area	Diseases [C] - Immune System Diseases [C20]
MedDRA Classification		
E.1.2 Medical condition or disease under investigation		
E.1.2	Version	16.0
E.1.2	Level	PT
E.1.2	Classification code	10059176
E.1.2	Term	Juvenile idiopathic arthritis
E.1.2	System Organ Class	10028395 - Musculoskeletal and connective tissue disorders
E.1.3	Condition being studied is a rare disease	No
E.2 Objective of the trial		
E.2.1	Main objective of the trial	To estimate abatacept steady-state trough concentration (Cmin) at Day 113 in children and adolescents with pJIA aged 6 to 17. Calcular la concentración mínima (Cmin) en estado de equilibrio el día 113 en niños y adolescentes con AIJp de 6 a 17 años.
E.2.2	Secondary objectives of the trial	1. Proportion of subjects achieving ACR Pediatric 30 at Day 113 in 6-17 year old subjects. 2. Abatacept Cmin at Day 57, Day 85, and Day 113 during the initial 4-month short term period by each weight-tiered dosing regimen in 6-17 year old subjects. 3. Safety summary (proportion of subjects with adverse events, deaths, SAEs, and AEs leading to discontinuation) during initial 4-month short-term and long-term extension periods in both age cohorts. 4. Proportion of subjects with positive immunogenicity response during initial 4 month and long-term extension periods and up to 6 months following discontinuation of treatment in both age cohorts. 1. Propocion de pacientes que alcanzan una respuesta ACR pediátrica 30 el día 113 en sujetos de 6 a 17 años de edad. 2. Cmin de abatacept el día 57, día 85 y día 113 durante el periodo inicial a corto plazo de 4 meses con cada dosis fija por estrato de peso en sujetos de 6-17 años. 3. Resumen de seguridad (porcentaje de sujetos con acontecimientos adversos, muertes, AAG y AA que provocan la suspensión del tratamiento) durante el periodo inicial de 4 meses a corto plazo y el periodo de extensión a largo plazo en las dos cohortes de edad. 4.Porcentaje de sujetos con una respuesta de inmunogenicidad positiva durante el periodo inicial a corto plazo de 4 meses y el periodo de extensión y hasta 6 meses después de suspender el tratamiento en las dos cohortes de edad.
E.2.3	Trial contains a sub-study	Yes
		Amendment Number 02 - Sub-Study Site Specific, ALL sites (Excluding USA Sites) - version 1.0 dated 28-Mar-13

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TOFACITINIB en AIJ Poliarticular



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EU Clinical Trials Register

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Search Tips: Under advanced search you can use filters for Country, Age Group, Gender, Trial Phase, Trial Status, Date Range, Rare Diseases and Orphan Designation. For these items you should use the filters and not add them to your search terms in the text field.

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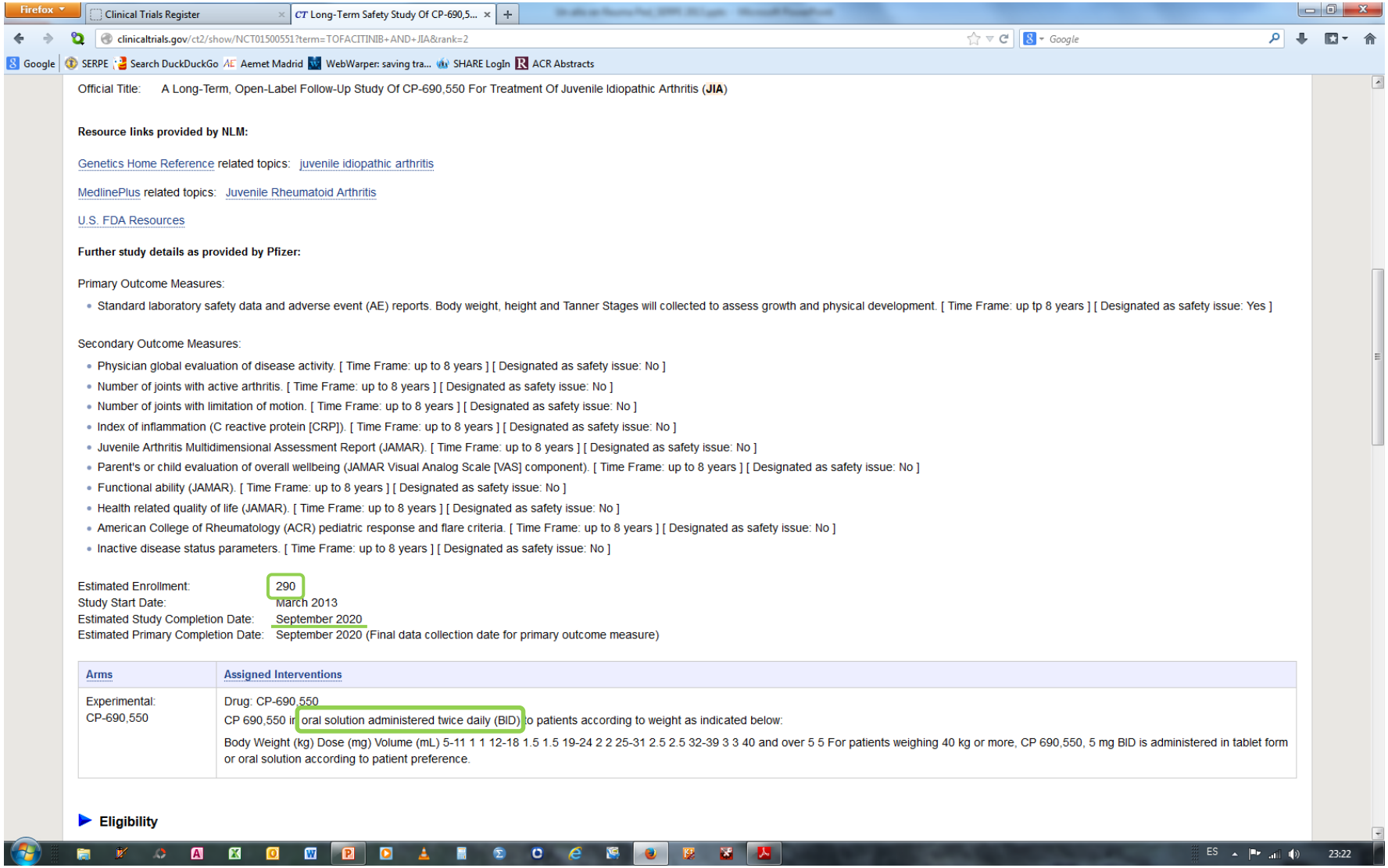
EudraCT Number: 2011-004915-22			**Sponsor Protocol Number:** A3921145		**Sponsor Name:** Pfizer Inc, 235 East 42nd Street, New York, New York 10017
Full Title: A LONG-TERM, OPEN-LABEL FOLLOW-UP STUDY OF CP-690,550 FOR TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS (JIA)					**Start Date*:** 2012-08-03
Medical condition: JUVENILE IDIOPATHIC ARTHRITIS (JIA)					
Disease:	**Version**	**SOC Term**	**Classification Code**	**Term**	**Level**
	15.1	100000004859	10059176	Juvenile idiopathic arthritis	LLT
Population Age: Children, Adolescents, Under 18					**Gender:** Male, Female
Country: HU *(Ongoing)* PL *(Ongoing)* DE *(Ongoing)*					

EudraCT Number: 2011-004914-40			**Sponsor Protocol Number:** A3921103		**Sponsor Name:** Pfizer Inc, 235 East 42nd Street, New York, NY 10017
Full Title: AN OPEN-LABEL MULTIPLE DOSE STUDY TO EVALUATE THE PHARMACOKINETICS, SAFETY AND TOLERABILITY OF CP-690,550 IN PEDIATRIC PATIENTS FROM 2 TO LESS THAN 18 YEARS OF AGE WITH JUVENILE IDIOPATHIC ARTHRITI...					**Start Date*:** 2012-09-19
Medical condition: JUVENILE IDIOPATHIC ARTHRITIS					
Disease:	**Version**	**SOC Term**	**Classification Code**	**Term**	**Level**
	14.1	100000004859	10059176	Juvenile idiopathic arthritis	LLT
Population Age: Children, Adolescents, Under 18					**Gender:** Male, Female
Country: PL *(Ongoing)* HU *(Ongoing)*					

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TOFACITINIB en AIJ Poliarticular



Official Title: A Long-Term, Open-Label Follow-Up Study Of CP-690,550 For Treatment Of Juvenile Idiopathic Arthritis (**JIA**)

Resource links provided by NLM:

Genetics Home Reference related topics: juvenile idiopathic arthritis

MedlinePlus related topics: Juvenile Rheumatoid Arthritis

U.S. FDA Resources

Further study details as provided by Pfizer:

Primary Outcome Measures:

- Standard laboratory safety data and adverse event (AE) reports. Body weight, height and Tanner Stages will collected to assess growth and physical development. [Time Frame: up tp 8 years] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- Physician global evaluation of disease activity. [Time Frame: up to 8 years] [Designated as safety issue: No]
- Number of joints with active arthritis. [Time Frame: up to 8 years] [Designated as safety issue: No]
- Number of joints with limitation of motion. [Time Frame: up to 8 years] [Designated as safety issue: No]
- Index of inflammation (C reactive protein [CRP]). [Time Frame: up to 8 years] [Designated as safety issue: No]
- Juvenile Arthritis Multidimensional Assessment Report (JAMAR). [Time Frame: up to 8 years] [Designated as safety issue: No]
- Parent's or child evaluation of overall wellbeing (JAMAR Visual Analog Scale [VAS] component). [Time Frame: up to 8 years] [Designated as safety issue: No]
- Functional ability (JAMAR). [Time Frame: up to 8 years] [Designated as safety issue: No]
- Health related quality of life (JAMAR). [Time Frame: up to 8 years] [Designated as safety issue: No]
- American College of Rheumatology (ACR) pediatric response and flare criteria. [Time Frame: up to 8 years] [Designated as safety issue: No]
- Inactive disease status parameters. [Time Frame: up to 8 years] [Designated as safety issue: No]

Estimated Enrollment: 290
Study Start Date: March 2013
Estimated Study Completion Date: September 2020
Estimated Primary Completion Date: September 2020 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: CP-690,550	Drug: CP-690,550 CP 690,550 in oral solution administered twice daily (BID) to patients according to weight as indicated below: Body Weight (kg) Dose (mg) Volume (mL) 5-11 1 1 12-18 1.5 1.5 19-24 2 2 25-31 2.5 2.5 32-39 3 3 40 and over 5 5 For patients weighing 40 kg or more, CP 690,550, 5 mg BID is administered in tablet form or oral solution according to patient preference.

Eligibility

Hospital Universitario 12 de Octubre
SaludMadrid

GUIAS CLINICAS

TRATAMIENTO de AIJ SISTÉMICA y POLIARTICULAR

ACTUALIZACIÓN GUÍA ACR AIJs

Arthritis & Rheumatism

SPECIAL ARTICLE

2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis

Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications

Sarah Ringold,[1] Pamela F. Weiss,[2] Timothy Beukelman,[3] Esi Morgan DeWitt,[4] Norman T. Ilowite,[5] Yukiko Kimura,[6] Ronald M. Laxer,[7] Daniel J. Lovell,[4] Peter A. Nigrovic,[8] Angela Byun Robinson,[9] and Richard K. Vehe[10]

Ringold S *et al*. Arthritis Rheum 2013; 65(10):2499-2512

ACTUALIZACIÓN GUÍA ACR AIJs

2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis

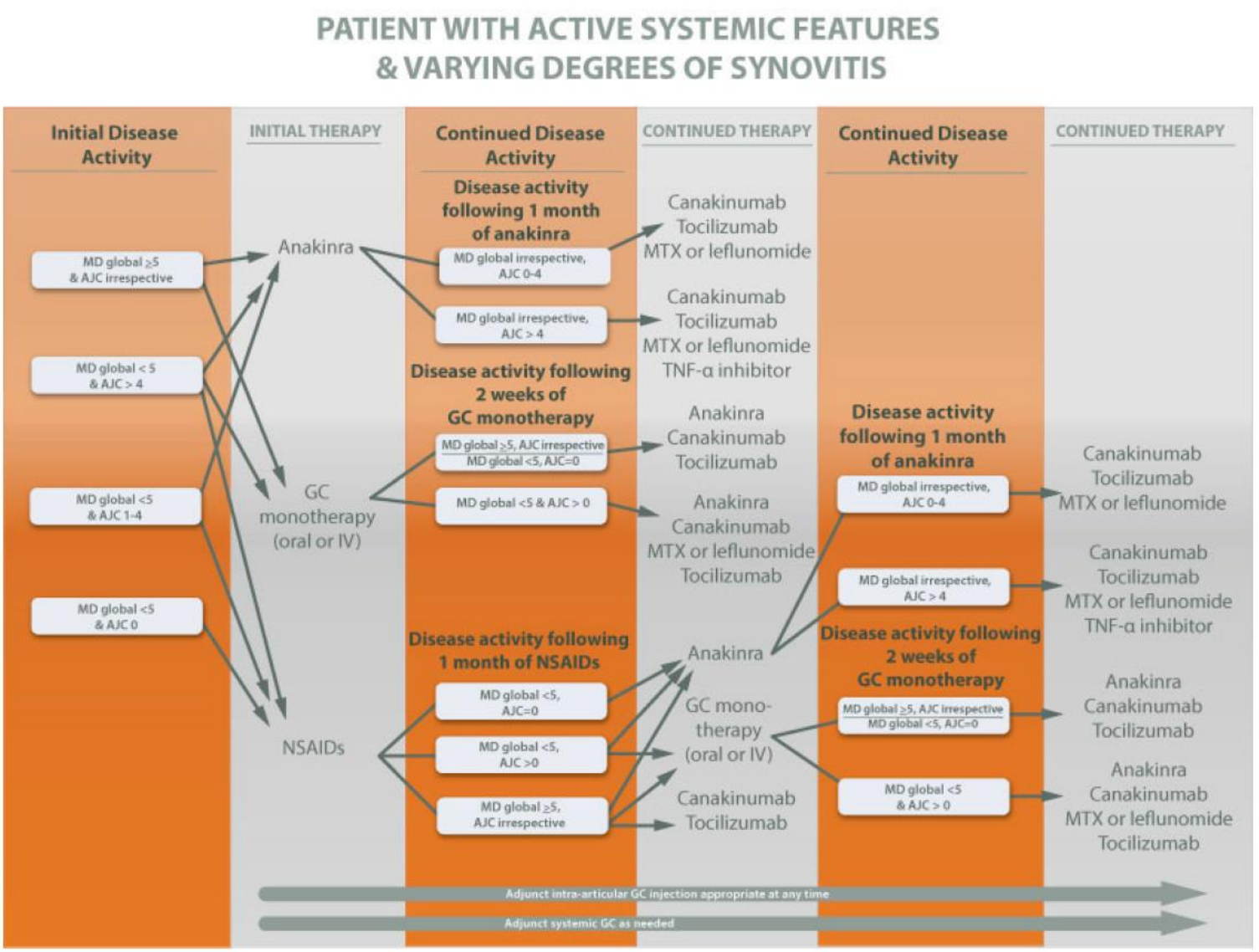
- Actualizan protocolo de tratamiento de la AIJs
  - Incluyen TCZ y CNK
  - Actualizan el tratamiento de la artritis sin síntomas sistémicos
  - Incluyen SAM
  - No es necesario repetir PPD anual

Table 1. Medications evaluated for the treatment of systemic juvenile idiopathic arthritis*

	2011 recommendations	2013 recommendations
NSAIDs†	X	X
Glucocorticoids	X	X
Methotrexate	X	X
Leflunomide	X	X
IVIG	X	X
Calcineurin inhibitors‡	X	X
TNFα inhibitors§	X	X
Abatacept	X	X
Rituximab	X	X
Anakinra	X	X
Canakinumab		X
Rilonacept		X
Tocilizumab		X

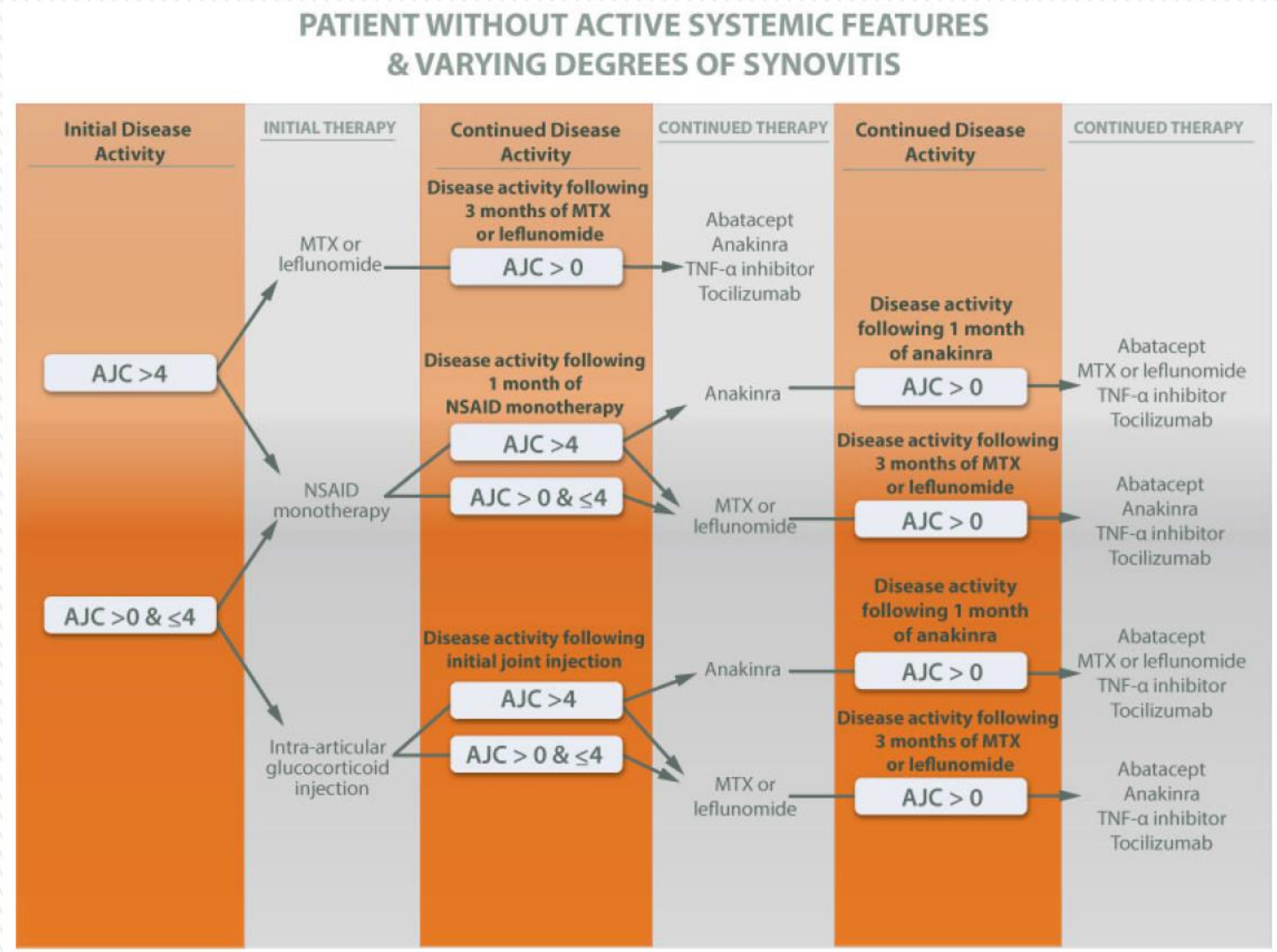
Ringold S *et al*. Arthritis Rheum 2013; 65(10):2499-2512

ACTUALIZACIÓN GUÍA ACR AIJs



Ringold S *et al*. Arthritis Rheum 2013; 65(10):2499-2512

ACTUALIZACIÓN GUÍA ACR AIJs



Ringold S *et al*. Arthritis Rheum 2013; 65(10):2499-2512

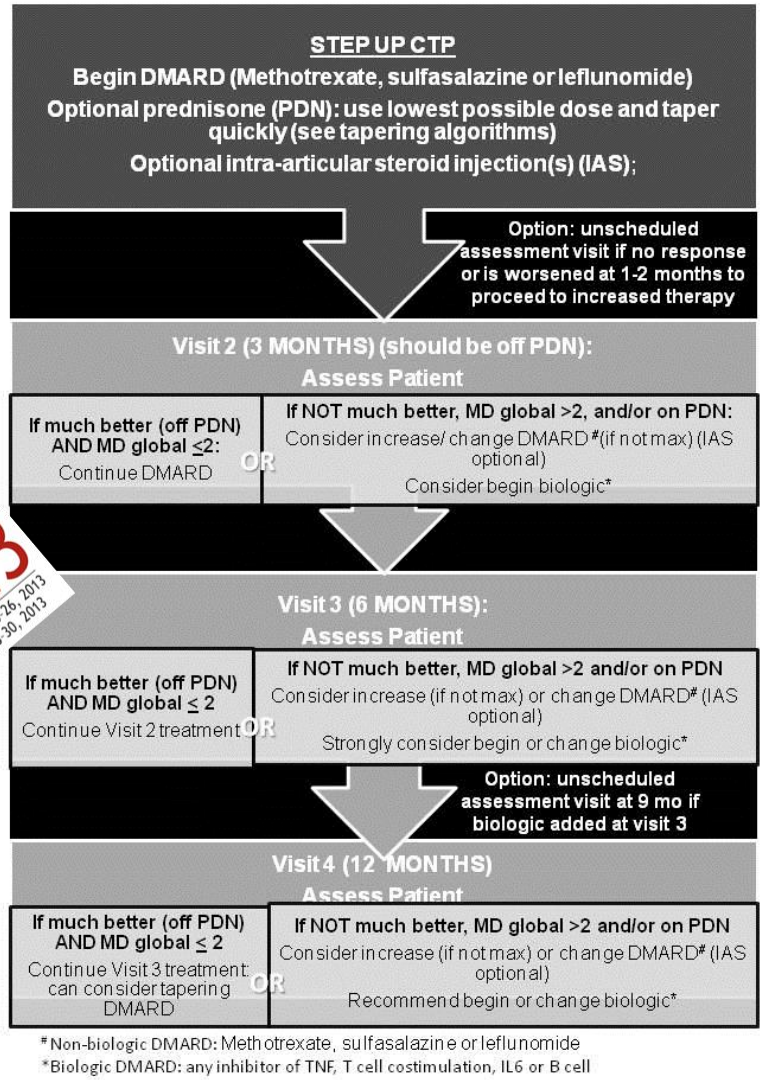
GUIA CARRA. AIJ POLI de INICIO

- Propuesta de tratamiento para los primeros 12m de AIJ Poli de inicio
- Encuesta CARRA n=230, responden 60%
- 2 reuniones consenso
- Proponen 3 algoritmos:
  - Terapia Escalonada
  - Terapia Biológica
  - Terapia Combinada precoz



Yukiko K *et al*. Abstract #277. ACR 2013 San Diego

GUIA CARRA. AIJ POLI de INICIO



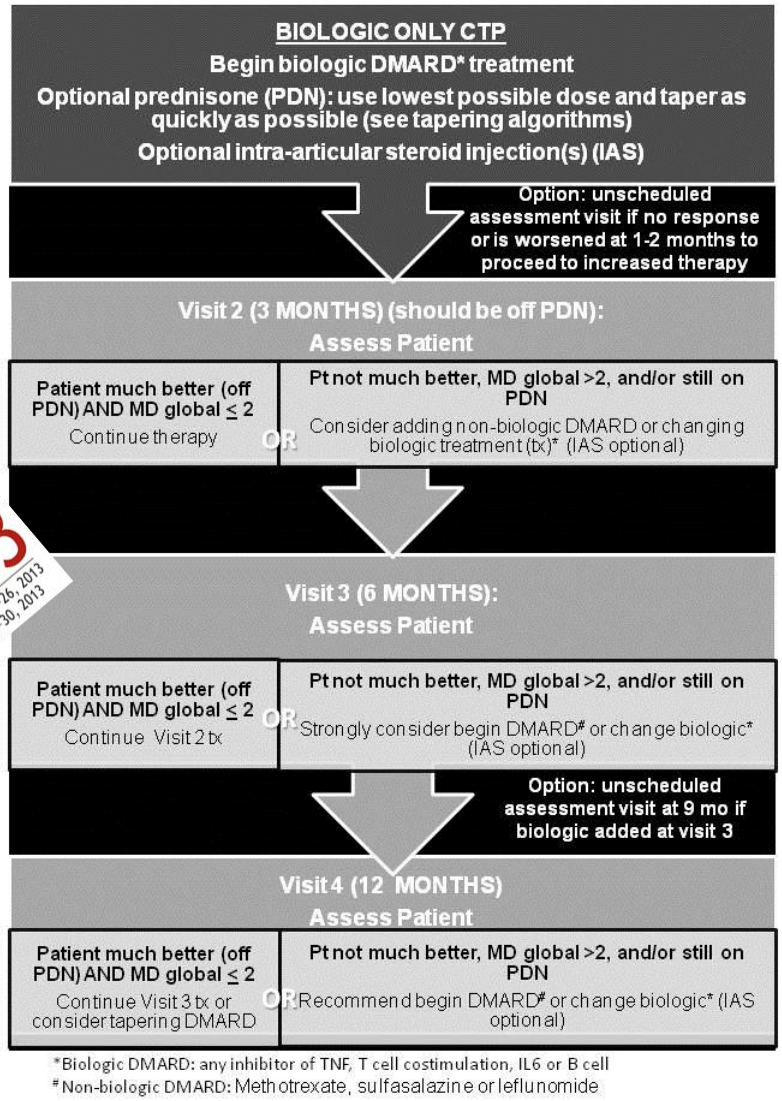
ACR/ARHP 13 Annual Meeting
San Diego
Pre-Meeting Courses: October 25-26, 2013
Scientific Sessions: October 26-30, 2013

❶ TERAPIA ESCALONADA

- **FAME** ± PDN a dosis bajas ± Infiltraciones CIA
- Modificaciones cada 3m:
  - A los 3 meses considerar aumentar dosis FAME o añadir Biológico
  - A los 6 meses repetir paso anterior, considerar muy seriamente añadir **Biológico**
  - En pacientes refractarios valorar CIA y realizar los cambios de tratamiento cada 1-2 meses

Yukiko K *et al*. Abstract #277. ACR 2013 San Diego

GUIA CARRA. AIJ POLI de INICIO

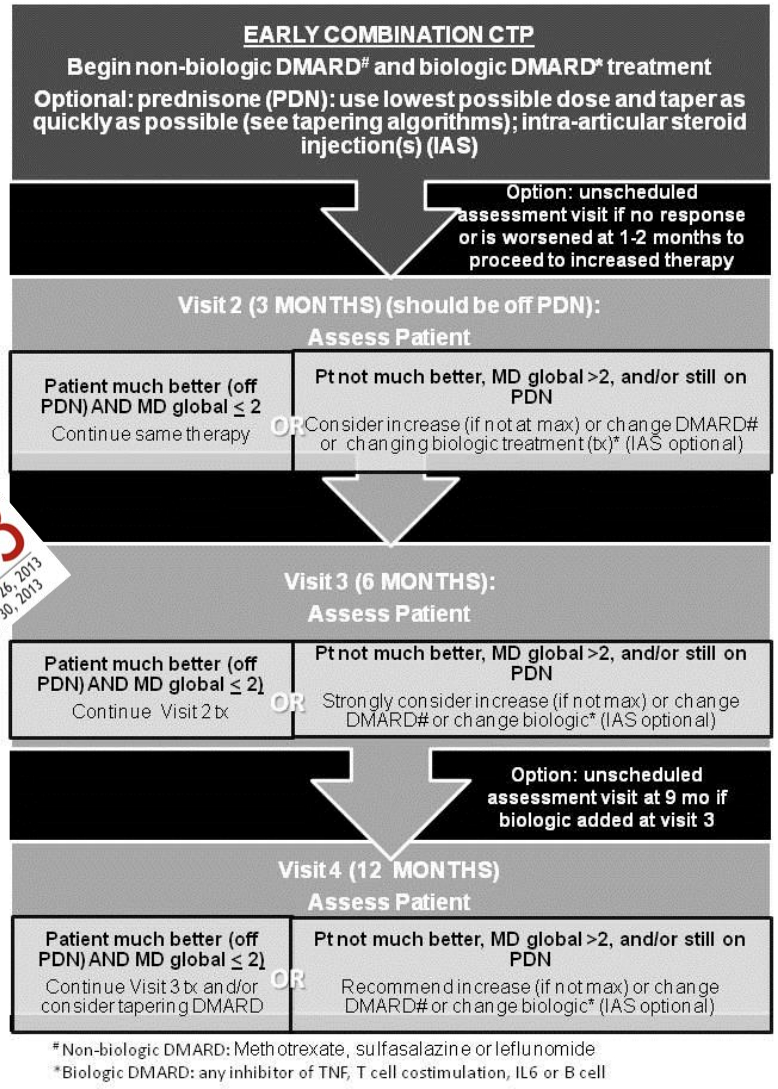


❷ TERAPIA BIOLÓGICA

- **Biológico** ± PDN a dosis bajas ± Infiltraciones CIA
- Cada 3 meses:
  - Valorar añadir FAME o cambiar de Biológico
  - Valorar infiltración CIA
  - En pacientes refractarios valorar CIA y realizar los cambios de tratamiento cada 1-2 meses

Yukiko K *et al*. Abstract #277. ACR 2013 San Diego

GUIA CARRA. AIJ POLI de INICIO



ACR/ARHP 13 Annual Meeting
San Diego
Pre-Meeting Courses: October 25-26, 2013
Scientific Sessions: October 26-30, 2013

❸ TERAPIA COMBINADA PRECOZ

- **FAME + Biológico** ± PDN ± CIA
- Cada 3 meses:
  - Maximizar dosis o cambiar FAME
  - Valorar cambiar de Biológico
  - Valorar infiltración esteroides
  - En pacientes refractarios valorar CIA y realizar los cambios de tratamiento cada 1-2 meses

Yukiko K *et al*. Abstract #277. ACR 2013 San Diego

Hospital Universitario 12 de Octubre
SaludMadrid

LUPUS ERITEMATOSO SISTÉMICO

NOVEDADES

BIOMARCADORES en LES

- **Biomarcador** se define como aquella determinación genética, biológica, bioquímica, molecular o de imagen cuyas alteraciones se correlacionan con la patogénesis o manifestaciones clínicas de la enfermedad
- Revisiones recientes

Curr Rheumatol Rep (2013) 15:312
DOI 10.1007/s11926-012-0312-0

PEDIATRIC RHEUMATOLOGY (TJA LEHMAN, SECTION EDITOR)

Use of Biomarkers in the Management of Children with Lupus

Elisabeth Binder · Monika Edelbauer

Binder E, Edelbauer M. Curr Rheumatol Rep 2013; 15:312

BIOMARCADORES en LES

Therapeutic Advances in Musculoskeletal Disease *Review*

Biomarkers in systemic lupus erythematosus: challenges and prospects for the future

Chau-Ching Liu, Amy H. Kao, Susan Manzi and Joseph M. Ahearn

- Liu CC et al. Ther Adv Musculoskel Dis 2013; 15:312

BIOMARCADORES EN LES

theclinics.com

Rheum Dis Clin N Am 39 (2013) 833–853
http://dx.doi.org/10.1016/j.rdc.2013.05.001 rheumatic.theclinics.com
0889-857X/13/$ – see front matter © 2013 Elsevier Inc. All rights reserved.

ELSEVIER

Biomarkers and Updates on Pediatrics Lupus Nephritis

Michael Bennett, PhD[a], Hermine I. Brunner, MD, MSc[b,*]

Bennett M, Brunner HI. Rheum Dis Clin N Am 2013; 39:833-53

TERAPIA BIOLÓGICA en LES

Current Opinion in Pharmacology

New biologic therapy for systemic lupus erythematosus

Hui Jen Ding[1,2] and Caroline Gordon[1,3]

Ding HJ, Gordon C. Curr Opin Pharmacol 2013; 13:405-12

TERAPIA BIOLÓGICA en LES

summary of biologics already in use and in development for the treatment of SLE

Group	Subgroup	Target	Mechanism of action	Type	Name	Current phase
Cell-targeted therapy	B-cells	CD20	B-cell depletion	Chimeric mAb	Rituximab	III
		CD20	B cell modulation	Synthetic peptide (SMIP)	SBI-087	I
		CD22	B-cell depletion	Humanised mAb	Epratuzumab	III
		Soluble BLyS	B-cell modulation	Fully human mAb	Belimumab	IV
		Soluble and membrane BLyS	B-cell modulation	Fully human mAb	Tabalumab (LY2127399)	III
		Soluble and membrane BLyS	B-cell modulation	Peptibody	Blisibimod (A-623)	II
		BLyS and APRIL receptors	B-cell modulation	Receptor fusion protein	Atacicept	II
	T-cells	T-cells	T-cell modulation	Spliceosomal p140 peptide	Lupuzor	II
Co-stimulatory modulation	T-cells	B7-RP1	T cell modulation	Fully human mAb	AMG-557	I
	T-cells	CD28/80	T-cell modulation	Recombinant Ig fusion protein	Abatacept	III
Cytokine inhibition	IL	IL-6 receptor	IL-6 receptor blockade	Humanised mAb	Tocilizumab	I
		IL-6	IL-6 blockade	Fully human mAb	Sirukumab (CNTO 136)	II
	IFN	IFNα	Inhibition of IFNα pathway	Fully human mAb	Sifalimumab (MEDI-545)	II
		IFNα	Inhibition of IFNα pathway	Humanised mAb	Rontalizumab	I/II
		IFNα	Neutralisation of IFNα	Humanised mAb	AGS 009	
		IFNα	Induction of anti-IFNα antibodies	Kinoid (vaccine)	IFNα-kinoid	I/II
		IFNγ	Inhibition of IFNγ	Humanised mAb	Fontolizumab (AMG 811)	I
	TNFa	Soluble and membrane TNFα	TNFα inhibitor	Chimeric mAb	Infliximab	Open-label

Ding HJ, Gordon C. Curr Opin Pharmacol 2013; 13:405-12

RITUXIMAB en LES

Lupus

Rituximab in systemic lupus erythematosus: an updated systematic review and meta-analysis

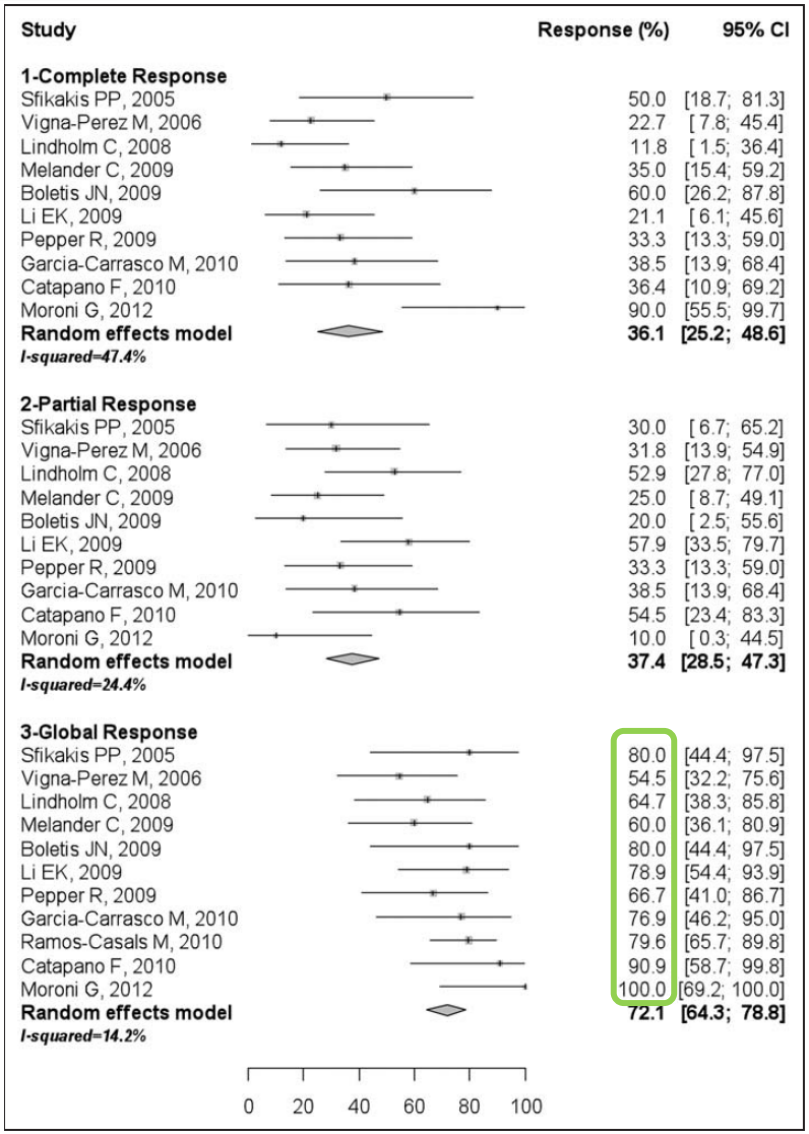
B Duxbury[1], C Combescure[2] and C Chizzolini[3]

- Revisión sistemática y meta-análisis de RTX en LES
- 30 estudios con un total de 1,243 pacientes
- Respuesta se analiza mediante BILAG y SLEDAI obteniendo diferentes resultados
- Heterogeneidad definiciones, tratamientos y formas clínicas
- Discrepancia en efectividad de RTX entre estudios controlados y observacionales

Duxbury B *et al*. Lupus 2013 Oct 17, Epub

RITUXIMAB en LES

RENAL



Duxbury B *et al*. Lupus 2013 Oct 17, Epub

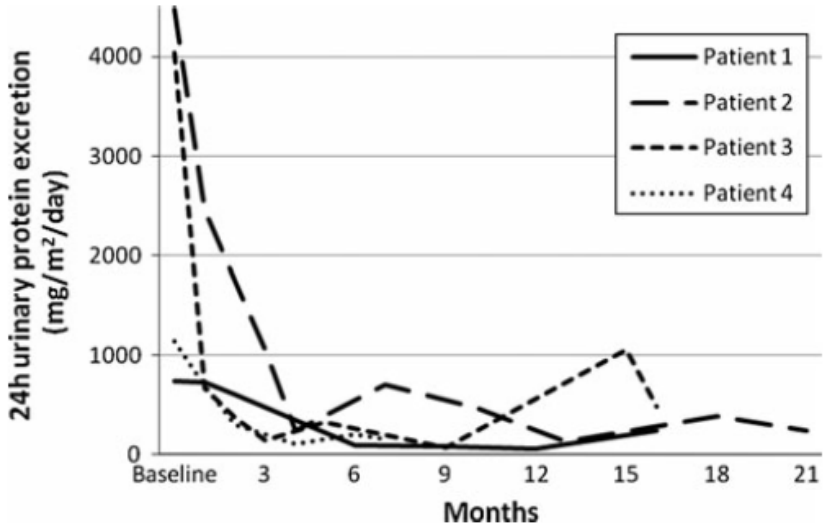
RITUXIMAB EN LES

Rheumatol Int (2013) 33:809–813
DOI 10.1007/s00296-011-2239-6

SHORT COMMUNICATION

Safety and efficacy of Rituximab in refractory pediatric systemic lupus erythematosus nephritis: a single-center experience of Northern Greece

Maria Trachana · Artemis Koutsonikoli · Evagelia Farmaki · Nikoleta Printza · Vasiliki Tzimouli · Fotios Papachristou



Trachana M *et al*. Rheumatol Int 2013; 33:809-13

RTX Y MMF SIN ESTEROIDES EN LES

Annals of the
RHEUMATIC DISEASES
The EULAR Journal

Clinical and epidemiological research

EXTENDED REPORT

Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids

Marie B Condon,[1] Damien Ashby,[1] Ruth J Pepper,[1] H Terence Cook,[1,2] Jeremy B Levy,[1] Megan Griffith,[1] Tom D Cairns,[1] Liz Lightstone[1,2,3]

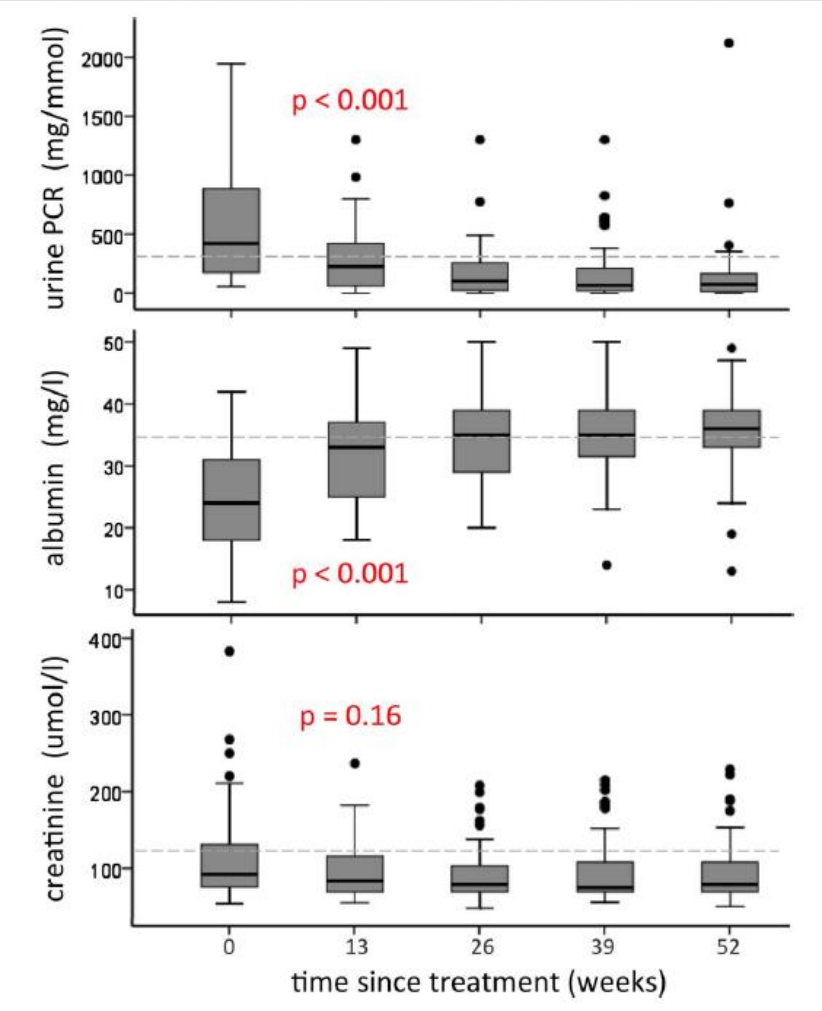
Condon MB *et al*. Ann Rheum Dis 2013; 72:1280-6

RTX y MMF SIN ESTEROIDES en LES

- Protocolo de tratamiento:
  - RTX [1g] y MPIV [500 mg] los días 1 y 15 [en total 2 dosis]
  - Mantenimiento con MMF 500 mg/12 hr [máx 3,000 mg/d]
- Definen la **remisión renal** como elevaciones de la creatinina sérica no superiores al 15% de la normal
- Consideran **remisión bioquímica completa** cuando el cociente albúmina/creatinina es <50 mg/mmol y **parcial** cuando es mayor pero en rango no nefrótico y con reducciones >50% de la inicial
- Incluyen a 50 pacientes
  - 40% clase IV activa o IV+V
  - 44% clase V pura

Condon MB *et al*. Ann Rheum Dis 2013; 72:1280-6

RTX Y MMF SIN ESTEROIDES EN LES



- 45/50 [90%] en remisión BQ tras mediana de 37 sem
  - Completa en 36 [72%]
  - Parcial en 9 [18%]
- 12 recaídas renales en 11 pacientes [22%]: 8 estaban en remisión completa y 4 en parcial
- 6/50 [12%] recaídas sistémicas
- 9/50 [18%] EAs que implicaron ingresos, en 5 por infecciones

Condon MB *et al*. Ann Rheum Dis 2013; 72:1280-6

TERAPIA ANTI-IFNα en LES

available at www.sciencedirect.com

Clinical Immunology

www.elsevier.com/locate/yclim

ELSEVIER

REVIEW

Anti-interferon alpha treatment in SLE

Kyriakos A. Kirou*, Elena Gkrouzman

Kirou KA, Gkrouzman E. Clin Immunol 2013; 148:303-12

TERAPIA ANTI-IFNα en LES

Agent	Type	Company	Phase of testing for SLE
anti-IFNα and anti-IFNAR strategies			
Sifalimumab	Fully human anti-IFNα IgG1 mAb	MedImmune	Phase II SC trial announced; other phase II pending
Rontalizumab	Humanized anti-IFNα IgG1 mAb	Genentech	Phase II results announced
AGS-009	Humanized anti-IFNα IgG4 mAb	Argos Therapeutics	Phase I results published
MEDI-546	Fully human anti-IFNα receptor subunit 1 (IFNAR1) mAb	MedImmune	Phase II ongoing
IFNα-Kinoid	Active immunotherapy to induce host humoral polyclonal anti-IFNα response	Neovacs	Phase I/II results published
pDC inhibitors			
CPG-52364	Selective TLR7/8/9 antagonist, quinazoline derivative	Pfizer	Phase I in healthy volunteers completed
IMO-8400	Synthetic oligonucleotide TLR7/8/9 antagonist	Idera Pharmaceuticals	Phase I trial planned
DV-1179	Bifunctional inhibitor of TLR7/9	Dynavax/GlaxoSmithKline	Phase I in healthy volunteers completed

Kirou KA, Gkrouzman E. Clin Immunol 2013; 148:303-12

TERAPIA ANTI-IFNα en LES

Arthritis & Rheumatism

Sifalimumab, a Human Anti–Interferon-α Monoclonal Antibody, in Systemic Lupus Erythematosus

A Phase I Randomized, Controlled, Dose-Escalation Study

Michelle Petri,[1] Daniel J. Wallace,[2] Alberto Spindler,[3] Vishala Chindalore,[4] Kenneth Kalunian,[5] Eduardo Mysler,[6] C. Michael Neuwelt,[7] Gabriel Robbie,[8] Wendy I. White,[8] Brandon W. Higgs,[8] Yihong Yao,[8] Liangwei Wang,[8] Dominique Ethgen,[†] and Warren Greth[8]

Petri M *et al*. Arthritis Rheum 2013; 65:1011-21

LES. CALIDAD ASISTENCIAL

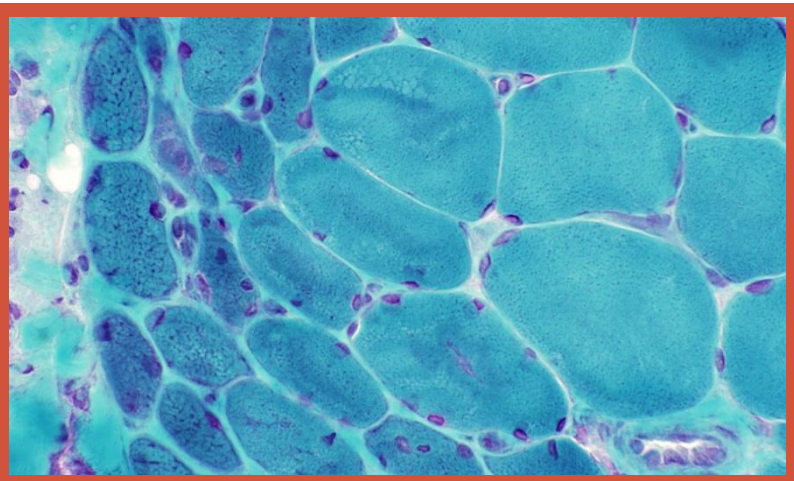
Arthritis Care & Research

ORIGINAL ARTICLE

International Consensus for Provisions of Quality-Driven Care in Childhood-Onset Systemic Lupus Erythematosus

MATTHEW C. HOLLANDER,[1] JESSICA M. SAGE,[2] ALEXANDRIA J. GREENLER,[2] JOSHUA PENDL,[2] TADEJ AVCIN,[3] GRACIELA ESPADA,[4] MICHAEL W. BERESFORD,[5] MICHAEL HENRICKSON,[2] TSZ-LEUNG LEE,[6] MARILYNN PUNARO,[7] JENNIFER HUGGINS,[2] ANNE M. STEVENS,[1] MARISA S. KLEIN-GITELMAN,[8] AND HERMINE I. BRUNNER[2]

- Hollander MC *et al*. Arthritis Res Ther 2013 Sep; 65:1416-23



DERMATOMIOSITIS JUVENIL

NOVEDADES

DMJ. Bases genéticas



Genome-wide Association Study of Dermatomyositis Reveals Genetic Overlap with other Autoimmune Disorders

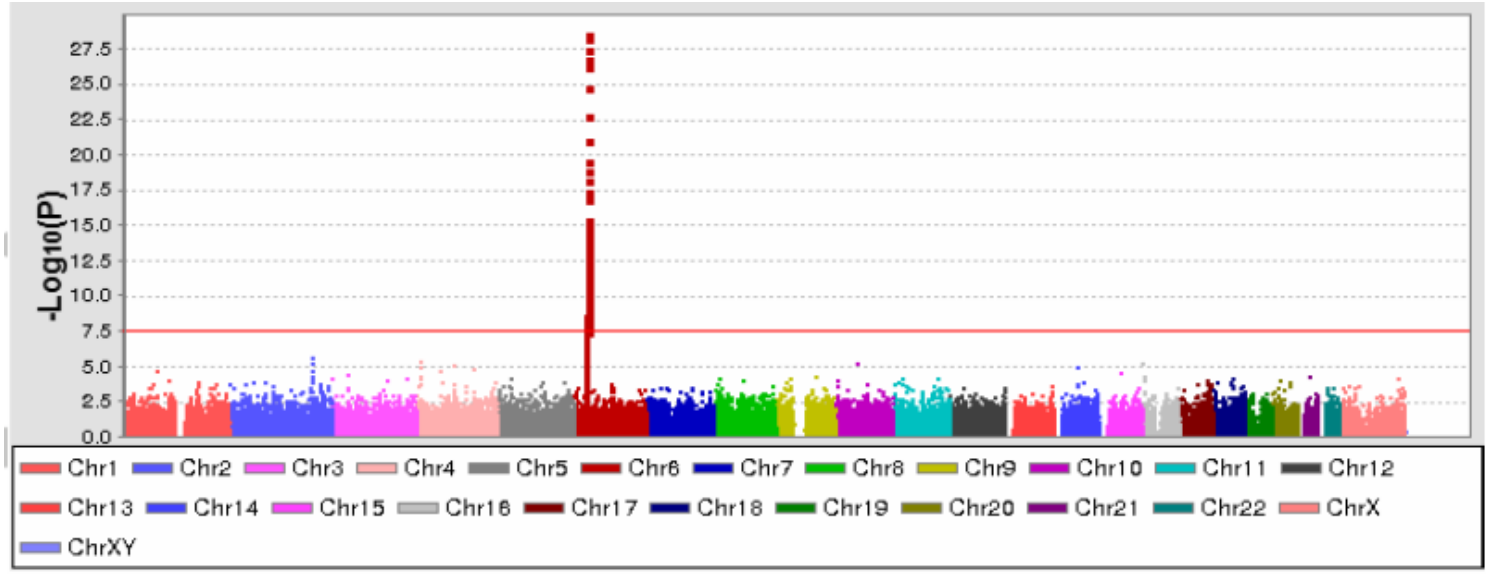
*Frederick W. Miller,[1] *Robert G. Cooper,[2] Jiri Vencovsky,[3] Lisa G. Rider,[1] Katalin Danko,[4] Lucy R. Wedderburn,[5] Ingrid E. Lundberg,[6] Lauren M. Pachman,[7] Ann M. Reed,[8] Steven R. Ytterberg,[8] Leonid Padyukov,[6] Albert Selva-O'Callaghan,[9]

- Estudio de Asociación de Genoma Completo [GWAS] en 1,178 pacientes [705 con DM y 473 con DMJ] y 4,724 controles
- 80 SNPs [Polimorfismos de un solo nucleótido] en la región HLA y 141 SNPs fuera de ella

Miller FW *et al*. Arthritis Rheum Epub 2013 Aug 27. doi 10.1002/art.38137

DMJ. Bases genéticas

- La región HLA es la principal región genética asociada a DM
- Describen 3 nuevos asociados con DMJ pend validación:
  - PLCL1 [Phospholipase C-like 1]
  - BLK [B lymphoid tyrosine kinase] → Presente en LES, AR, SSc y SS
  - CCL21 [Chemokine C-C motif ligand 21]



- Miller FW *et al*. Arthritis Rheum Epub 2013 Aug 27. doi 10.1002/art.38137

DMJ. PDN *vs* PDN+CsA *vs* PDN+MTX

- **[EULAR 2013] [OP0059] A RANDOMIZED TRIAL IN NEW ONSET JUVENILE DERMATOMYOSITIS: PREDNISONE VS PREDNISONE PLUS CYCLOSPORINE VS PREDNISONE PLUS MTX**
- n=138 pacientes
  - 59%♀ [81]
  - Edad media 7,4 años [Q1-Q3 1,1-15,4]
  - Duración de la enfermedad: mediana 2,8 meses
- 3 brazos de Tto. Respuesta a los 6 meses:
  - PDN 52,2%
  - PDN+CsA 67,4%
  - PDN+MTX 73,9% (p 0,08)



DMJ. PDN *vs* PDN+CsA *vs* PDN+MTX

- **[EULAR 2013] [OP0059] A RANDOMIZED TRIAL IN NEW ONSET JUVENILE DERMATOMYOSITIS: PREDNISONE VS PREDNISONE PLUS CYCLOSPORINE VS PREDNISONE PLUS MTX**
- Tiempo transcurrido hasta la remisión
  - Más corto con las combinaciones que con PDN solamente
- Efectos adversos más frecuentes con CsA que con MTX:
  - PDN 20,7%
  - PDN+CsA 51,1%
  - PDN+MTX 28,3%



DMJ. Actividad según RM

Annals of the
RHEUMATIC DISEASES
The EULAR Journal

ARD Online First, published on May 1, 2013 as 10.1136/annrheumdis-2012-202915
Clinical and epidemiological research

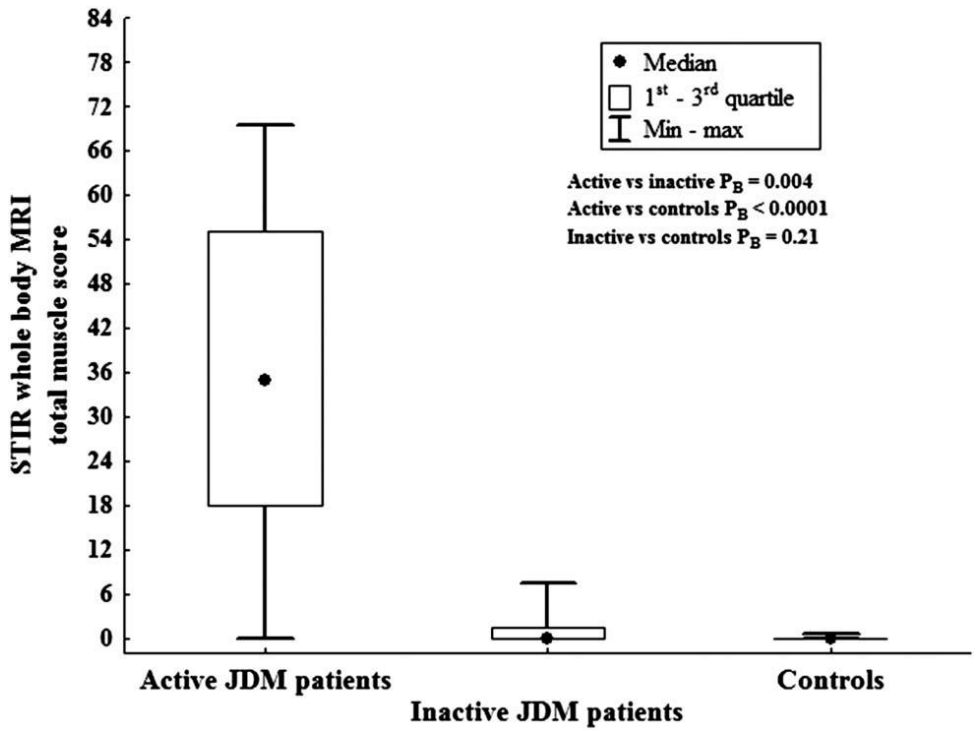
EXTENDED REPORT

Whole-body MRI in the assessment of disease activity in juvenile dermatomyositis

Clara Malattia,[1,2] Maria Beatrice Damasio,[3] Annalisa Madeo,[1] Angela Pistorio,[4] Anna Providenti,[1] Silvia Pederzoli,[1] Stefania Viola,[1] Antonella Buoncompagni,[1] Chiara Mattiuz,[3] Agnese Beltramo,[1] Alessandro Consolaro,[1] Angelo Ravelli,[1,2] Nicolino Ruperto,[1] Paolo Picco,[1] Gian Michele Magnano,[3] Alberto Martini[1,2]

Malattia C *et al*. Ann Rheum Dis Epub May 2013. doi 10.1136/annrheumdis-2012-202915

DMJ. Actividad según RM



- Detecta inflamación muscular subclínica
- Detecta afectación subcutánea y miofascial
- Buena correlación con MMT [r_s=-0,84] y cMAS [rs=-0,81]
- Buena concordancia inter-observador

Malattia C *et al*. Ann Rheum Dis Epub May 2013. doi 10.1136/annrheumdis-2012-202915

RM y PRONÓSTICO DMJ

- Patrones y evolución a los 3 meses:
  - "Parcheado": Mejoran 10/13 [77%]
  - "Difuso": Mejora 1/8 [12.5%]
- El patrón en la RM puede permitir detectar de forma precoz pacientes que precisarán un tratamiento más agresivo

PReS-FINAL-2129 WHOLE-BODY VERSUS LOCALIZED MAGNETIC RESONANCE IMAGING IN THE ASSESSMENT OF JUVENILE DERMATOMYOSITIS

Annalisa Madeo 1,*, Maria Beatrice Damasio 2, Marta Dellepiane 1, Anna Providenti 1, Diliana Beleva 1, Antonella Buoncompagni 1, Agnese Beltramo 1, Nicolino Ruperto 1, Alberto Martini 1, Clara Malattia 1

PReS paediatric rheumatology european society

RTX EN DMJ REFRACTARIA

Arthritis & Rheumatism

Rituximab in the Treatment of Refractory Adult and Juvenile Dermatomyositis and Adult Polymyositis

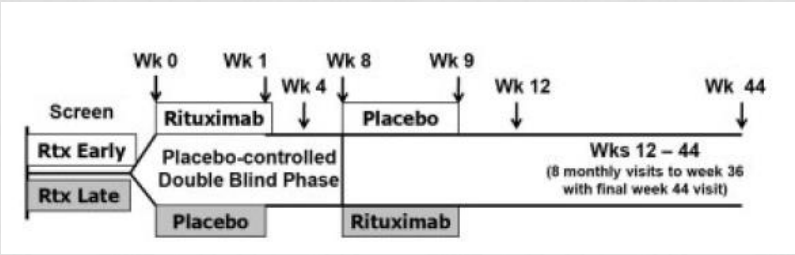
A Randomized, Placebo-Phase Trial

Chester V. Oddis,[1] Ann M. Reed,[2] Rohit Aggarwal,[1] Lisa G. Rider,[3] Dana P. Ascherman,[4] Marc C. Levesque,[1] Richard J. Barohn,[5] Brian M. Feldman,[6] Michael O. Harris-Love,[7] Diane C. Koontz,[1] Noreen Fertig,[1] Stephanie S. Kelley,[1] Sherrie L. Pryber,[8] Frederick W. Miller,[3] Howard E. Rockette,[1] and the RIM Study Group

Oddis CV *et al*. Arthritis Rheum 2013; 65:314-24

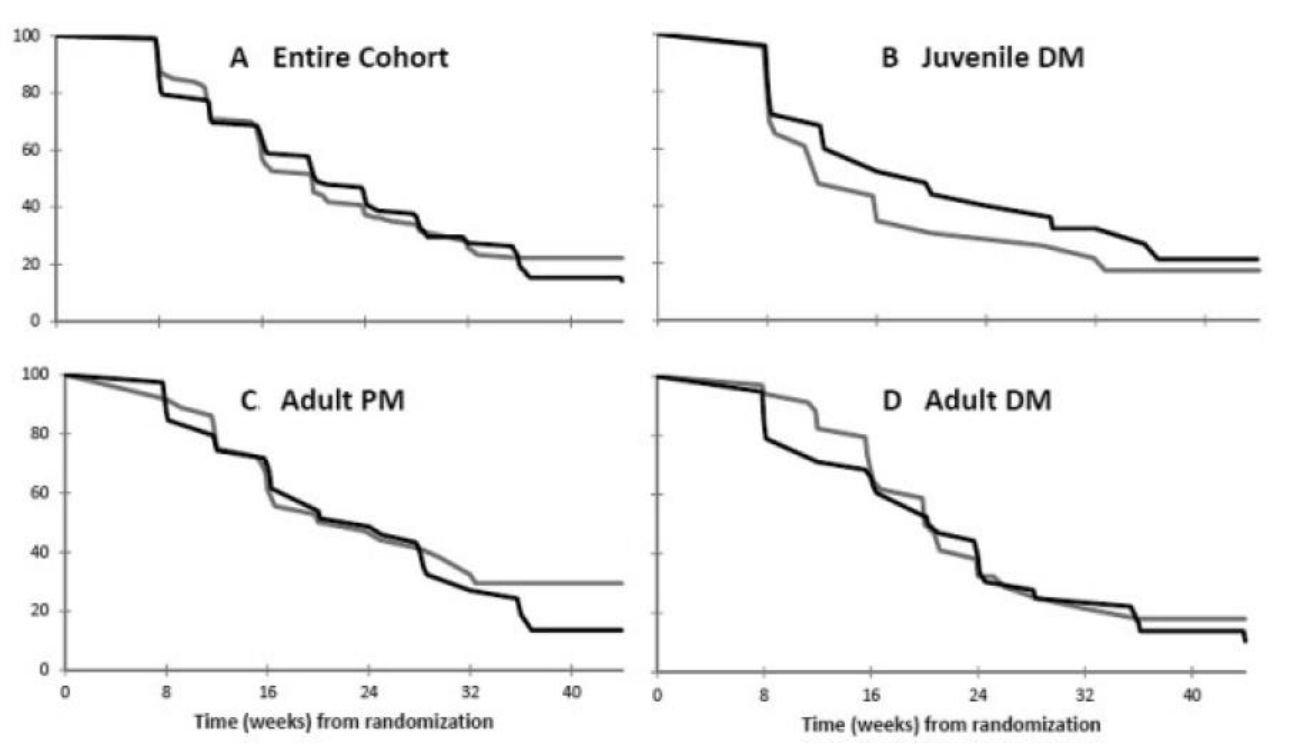
RTX EN DMJ REFRACTARIA

- Estudian a 200 pacientes con MII:
  - 76 Polimiositis
  - 76 Dermatomiositis
  - 48 DMJ
- A 93 se les administra RTX precozmente
- 102 reciben RTX de forma tardía [después de 8ª sem]
- Dosificación de RTX
  - Niños con SC <1,5 m^2: 575 mg/m^2 @ sem 0 y 1 u 8 y 9
  - Niños y Adultos con SC> 1,5 m^2: 750 mg/m^2 @ sem 0 y 1 u 8 y 9



Oddis CV *et al*. Arthritis Rheum 2013; 65:314-24

RTX EN DMJ REFRACTARIA



Tiempo hasta alcanzar la mejoría

- 83% mejoran a la semana 44
- No encuentran diferencias entre los grupos
- A las 8 sem mejora un 20% MMT:
  - 15% RTX
  - 20,6% PBO

Oddis CV *et al*. Arthritis Rheum 2013; 65:314-24

DMJ. CRITERIOS INACTIVIDAD

Annals of the
RHEUMATIC DISEASES
The EULAR Journal

Clinical and epidemiological research

EXTENDED REPORT

The PRINTO criteria for clinically inactive disease in juvenile dermatomyositis

Dragana Lazarevic,[1] Angela Pistorio,[2] Elena Palmisani,[1] Paivi Miettunen,[1] Angelo Ravelli,[1,3] Clarissa Pilkington,[4] Nico M Wulffraat,[5] Clara Malattia,[3] Stella Maris Garay,[6] Michael Hofer,[7] Pierre Quartier,[8] Pavla Dolezalova,[9] Inmaculada Calvo Penades,[10] Virginia P L Ferriani,[11] Gerd Ganser,[12] Ozgur Kasapcopur,[13] Jose Antonio Melo-Gomes,[14] Ann M Reed,[15] Malgorzata Wierzbowska,[16] Lisa G Rider,[17] Alberto Martini,[1-3] Nicolino Ruperto[1]; for the Paediatric Rheumatology International Trials Organisation (PRINTO)

Lazarevic D *et al*. Ann Rheum Dis 2013; 72:686-93

DMJ. CRITERIOS INACTIVIDAD

Inactive disease criteria	Reference sample, patients off therapy (N=38)	Comparison sample, active patients (N=76)	Sensitivity	Specificity	Cohen's κ
Top criteria derived by the Study Steering Committee					
C1: 3 of 4 (CPK ≤150, CMAS ≥48, MMT ≥78, MD-GLOVAS ≤0.2)	30/31	0/76	0.97	1.0	0.98
C2: 3 of 4 (aldolase ≤6, CMAS ≥48, MMT ≥78, MD-GLOVAS ≤0.2)	29/30	0/75	0.97	1.0	0.98
C3: 3 of 4 (CPK ≤150, CMAS ≥48, MMT ≥78, MYOACT ≤0.2)	31/33	0/76	0.94	1.0	0.96
C4: 3 of 4 (LDH ≤150, CMAS ≥48, MMT ≥78, MD-GLOVAS ≤0.2)	31/33	0/76	0.94	1.0	0.96
C5: 3 of 4 (CPK ≤150, CMAS ≥48, MMT=80, MD-GLOVAS ≤0.2)	30/32	0/76	0.94	1.0	0.95
C6: 3 of 4 (LDH ≤150 and ALT ≤35, CMAS ≥48, MMT ≥78, MD-GLOVAS ≤0.2)	30/32	0/75	0.94	1.0	0.95

Lazarevic D *et al*. Ann Rheum Dis 2013; 72:686-93

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ESCLERODERMIA

VALORACIÓN de la GRAVEDAD en EsS JUVENIL

Arthritis & Rheumatism

A Preliminary Disease Severity Score for Juvenile Systemic Sclerosis

Francesco La Torre,[1] Giorgia Martini,[1] Ricardo Russo,[2] Maria Marta Katsicas,[2] Fabrizia Corona,[3] Giuseppina Calcagno,[4] Fernanda Falcini,[5] Fabio Vittadello,[1] and Francesco Zulian[1]

La Torre F *et al*. Arthritis Rheum 2012 Dec; 64:4143-50

VALORACIÓN de la GRAVEDAD en EsS JUVENIL

Organ system	Components of the severity index
General	Body mass index
	Hemoglobin
Vascular	Raynaud's phenomenon requiring vasodilators
	Number of digital scars
	Number of ulcers/gangrene
Cutaneous	Modified Rodnan skin thickness score
Osteoarticular	Arthritis
	Limited range of motion
	Tendon friction rubs
Muscular	Childhood Myositis Assessment Scale
Gastrointestinal	Symptoms of gastroesophageal reflux
	Abnormal esophageal transit
	Malabsorption
Respiratory	Forced vital capacity
	Diffusing capacity for carbon monoxide
	Pulmonary artery systolic pressure by Doppler echocardiography
	Standard chest radiography
	High-resolution computed tomography of the chest
Cardiac	Electrocardiogram
	Echocardiogram
	Clinical signs of congestive heart failure
Renal	Creatinine clearance (glomerular filtration rate)

La Torre F *et al*. Arthritis Rheum 2012 Dec; 64:4143-50

VALORACIÓN de la GRAVEDAD en EsS JUVENIL

Juvenile Systemic Sclerosis Severity Score*

	0 (normal)	1 (mild)	2 (moderate)	3 (severe)	4 (end-stage)	Maximum possible score
General†	BMI ≥ baseline Hgb >11.5 gm/dl	BMI < 1st centile Hgb 10–11.4 gm/dl	BMI < 2nd centile Hgb 9–9.9 gm/dl	BMI < 3rd centile Hgb 7–8.9 gm/dl	BMI < 4th centile Hgb <7 gm/dl	4
Vascular	No Raynaud's	Raynaud's requiring vasodilators	Digital tip scars	Digital tip ulcerations	Digital gangrene	4
Skin	MRSS 0	MRSS 1–14	MRSS 15–29	MRSS 30–39	MRSS >40	4
Osteoarticular‡	No articular involvement		Presence of limited range of motion		Presence of arthritis and/or tendon friction rub	2
Muscle‡	Normal proximal muscle strength	CMAS 39–51	CMAS 26–38	CMAS 13–25	CMAS 0–12	2
GI†	Normal results of proximal GI tract investigations	GI symptoms Distal esophageal hypomotility GERD on 24-hour Ph-metry or scintiscan	Medium and/or high esophageal hypomotility	Malabsorption syndrome	Hyperalimentation	4
Respiratory§	DLco >80% FVC >80% Normal HRCT sPAP <30 mm Hg	DLco 70–79% FVC 70–79% Ground glass changes on HRCT sPAP 31–45 mm Hg	DLco 50–69% FVC 50–69% Honeycomb changes on HRCT sPAP 46–75 mm Hg	DLco <50% FVC <50% Fibrosis on radiography sPAP >75 mm Hg	O_2 dependence	8
Cardiac§	Normal EKG LVEF >50%	EKG conduction defect LVEF 45–49%	Arrhythmia LVEF 40–44%	Arrhythmia requiring treatment LVEF 30–39%	Congestive heart failure LVEF <30%	8
Renal¶	GFR >90 ml/minute	GFR 75–89 ml/minute	GFR 50–74 ml/minute	GFR 10–49 ml/minute	End-stage renal failure	4

La Torre F *et al*. Arthritis Rheum 2012 Dec; 64:4143-50

CAPILAROSCOPIA

RHEUMATOLOGY

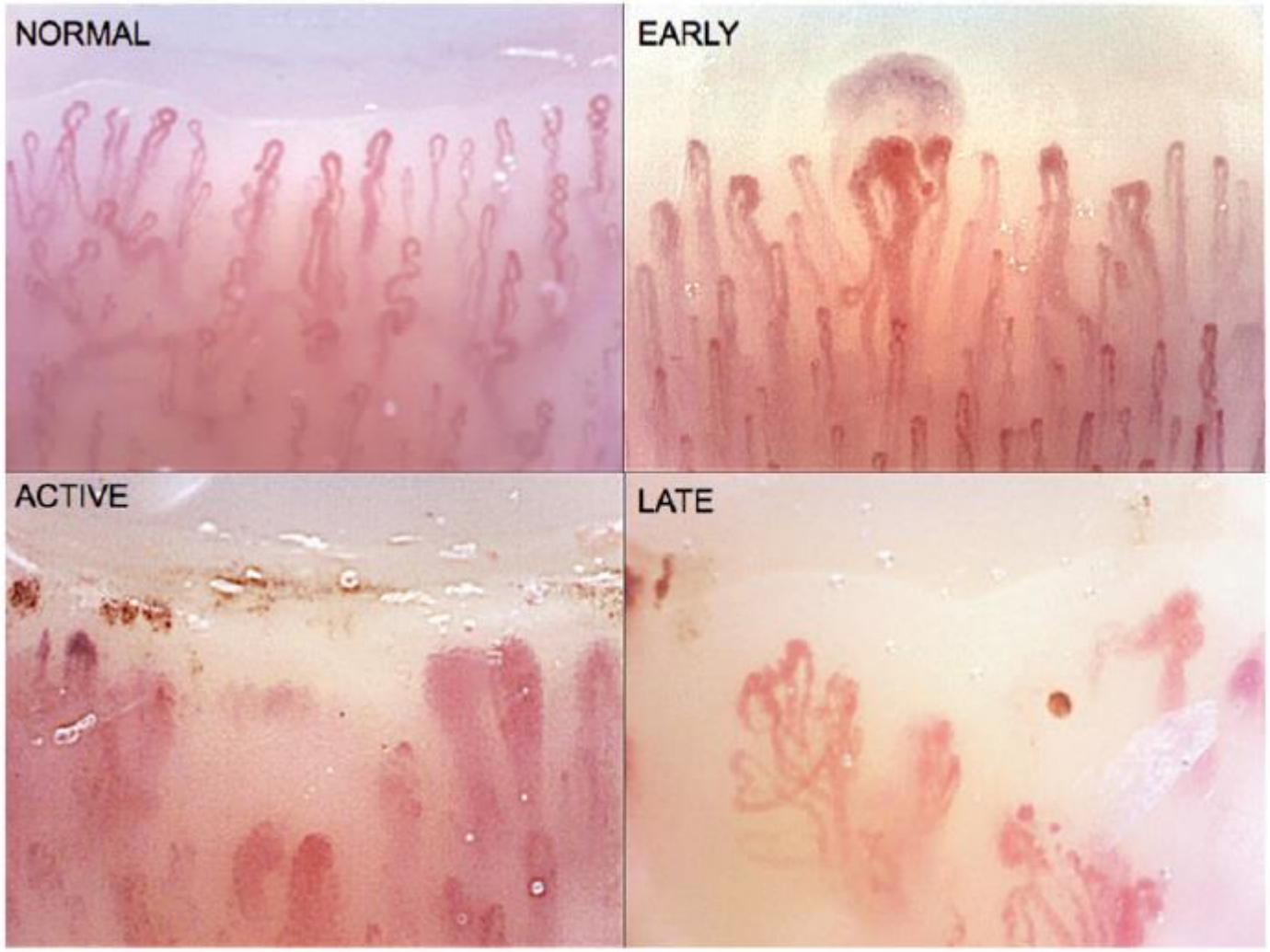
Review

State of the art on nailfold capillaroscopy: a reliable diagnostic tool and putative biomarker in rheumatology?

Maurizio Cutolo[1] and Vanessa Smith[2]

Cutolo M, Smith V. Rheumatology 2013; 52:1933-40

CAPILAROSCOPIA



Cutolo M, Smith V. Rheumatology 2013; 52:1933-40

CRIBADO de HT PULMONAR en EsS

The Journal of Rheumatology

Combination of Echocardiographic and Pulmonary Function Test Measures Improves Sensitivity for Diagnosis of Systemic Sclerosis-associated Pulmonary Arterial Hypertension: Analysis of 2 Cohorts

Heather Gladue, Virginia Steen, Yannick Allanore, Rajeev Saggar, Rajan Saggar, Paul Maranian, Veronica J. Berrocal, Jerome Avouac, Christophe Meune, Mona Trivedi, and Dinesh Khanna

- Gladue H *et al*. J Rheumatol 2013 Oct; 40:1706-11

CRIBADO de HT PULMONAR en EsS

- 2 cohortes de pacientes [206+141] con Escl. sistémica
- Detectan >95% HTP mediante la combinación de:
  - Ecografía transtorácica [presión sistólica estimada del VD]
  - Pruebas de función respiratoria [Capacidad Vital Forzada/Test de difusión de CO]

Multivariate logistic regression for association with pulmonary arterial hypertension (PAH).

	OR (95% CI)	p
Age	1.04 (0.996, 1.09)	0.07
SSc disease duration	0.99 (0.93, 1.05)	0.78
ACA	1.54 (0.53, 4.42)	0.43
ATA	0.53 (0.16, 1.79)	0.31
eRVSP > 40 mm Hg	29.34 (11.26, 76.41)	< 0.001
FVC%/DLCO% ≥ 1.6	2.98 (1.16, 7.66)	0.02

ACA: anti-centromere antibody; ATA: anti-topoisomerase antibody; eRVSP: estimated right ventricular systolic pressure; FVC%/DLCO%: forced vital capacity/DLCO percent predicted ratio.

- Gladue H *et al*. J Rheumatol 2013 Oct; 40:1706-11

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AUTOINFLAMATORIAS

INDICE ACTIVIDAD AUTOINFLAMATORIAS

Annals of the RHEUMATIC DISEASES The EULAR Journal

Clinical and epidemiological research

EXTENDED REPORT

Validation of the Auto-Inflammatory Diseases Activity Index (AIDAI) for hereditary recurrent fever syndromes

Maryam Piram,[1] Isabelle Koné-Paut,[1] Helen J Lachmann,[2] Joost Frenkel,[3] Seza Ozen,[4] Jasmin Kuemmerle-Deschner,[5] Silvia Stojanov,[6] Anna Simon,[7] Martina Finetti,[8] Maria Pia Sormani,[9] Alberto Martini,[8,10] Marco Gattorno,[8] Nicolino Ruperto,[8] on the behalf of EUROFEVER, EUROTRAPS and the Paediatric Rheumatology International Trials Organisation (PRINTO) networks

Piram M *et al*. Ann Rheum Dis 2013 Sep Epub. doi:10.1136/annrheumdis-2013-203666

AIDAI

- Recoge 12 síntomas que se evalúan como Sí/No [0 / 1]
- Mismo rendimiento con escala semicuantitativa [0 a 3 según intensidad de los síntomas] que dicotómica
- Cada día 1línea, suma al mes 12 x 31=372

ID:			Age:			Month:					Year:		
Autoinflammatory diseases related symptoms today													
Days	Fever ≥38°C (100.4°F) (a)	Overall symptoms (b)	Abdo-minal pain (c)	Nausea/ vomiting (d)	Diar-rhoea (e)	Head-aches (f)	Chest pain (g)	Painful nodes (h)	Arthr-algia or Myalgia (i)	Swelling of the joints (j)	Eyes manife-stations (k)	Skin rash (l)	Pain relief drugs taken
Scored as:	0/1	0/1Yes/No	0/1Yes/ No	0/1Yes/ No	0/1Yes/ No	0/1Yes/ No	0/1Yes/ No	0/1Yes/ No	0/1Yes/ No	0/1Yes/ No	0/1Yes/N o	0/1Yes/ No	
1													
2													
3													
...													
31													

Piram M *et al*. Ann Rheum Dis 2013 Sep Epub. doi:10.1136/annrheumdis-2013-203666

NUEVA ENTIDAD

blood

Regular Article

A novel syndrome of congenital sideroblastic anemia, B-cell immunodeficiency, periodic fevers, and developmental delay (SIFD)

Daniel H. Wiseman,[1] Alison May,[2] Stephen Jolles,[3] Philip Connor,[4] Colin Powell,[5] Matthew M. Heeney,[6] Patricia J. Giardina,[7] Robert J. Klaassen,[8] Pranesh Chakraborty,[8] Michael T. Geraghty,[8] Nathalie Major-Cook,[8] Caroline Kannengiesser,[9,10] Isabelle Thuret,[11] Alexis A. Thompson,[12] Laura Marques,[13] Stephen Hughes,[14] Denise K. Bonney,[1] Sylvia S. Bottomley,[15] Mark D. Fleming,[16] and Robert F. Wynn[1]

- Describen 12 casos con anemia sideroblástica [Hb 7,1 g/dL], episodios recurrentes de fiebre [5-7d c/3-4 sem], ↑↑ RFA y síntomas GI de inicio a los 2 meses de vida [mediana]
- Analíticamente sideroblastos con anemia microcítica, panhipogammaglobulinemia y linfopenia B
- Asocia retraso del desarrollo, convulsiones y sordera

Wiseman DH *et al*. Blood 2013; 122:112-23

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TRAPS. REGISTRO EUROFEVER

Annals of the RHEUMATIC DISEASES The EULAR Journal

Clinical and epidemiological research

EXTENDED REPORT

The phenotype of TNF receptor-associated autoinflammatory syndrome (TRAPS) at presentation: a series of 158 cases from the Eurofever/EUROTRAPS international registry

H J Lachmann,[1] R Papa,[2] K Gerhold,[3] L Obici,[4] I Touitou,[5] L Cantarini,[6] J Frenkel,[7] J Anton,[8] I Kone-Paut,[9] M Cattalini,[10] B Bader-Meunier,[11] A Insalaco,[12] V Hentgen,[13] R Merino,[14] C Modesto,[15] N Toplak,[16] R Berendes,[17] S Ozen,[18] R Cimaz,[19] A Jansson,[20] P A Brogan,[21] P N Hawkins,[1] N Ruperto,[2] A Martini,[22] P Woo,[21] M Gattorno,[2] for the Paediatric Rheumatology International Trials Organisation (PRINTO), the EUROTRAPS and the Eurofever Project

Lachmann HJ *et al*. Ann Rheum Dis 2013 Aug Epub; doi: 10.1136/annrheumdis-2013-204184

REGISTRO EUROFEVER

Annals of the RHEUMATIC DISEASES The EULAR Journal

Clinical and epidemiological research

EXTENDED REPORT

Treatment of autoinflammatory diseases: results from the Eurofever Registry and a literature review

Nienke ter Haar,[1] Helen Lachmann,[2] Seza Özen,[3] Pat Woo,[4] Yosef Uziel,[5] Consuelo Modesto,[6] Isabelle Koné-Paut,[7] Luca Cantarini,[8] Antonella Insalaco,[9] Bénédicte Neven,[10] Michael Hofer,[11] Donato Rigante,[12] Sulaiman Al-Mayouf,[13] Isabelle Touitou,[14] Romina Gallizzi,[15] Efimia Papadopoulou-Alataki,[16] Silvana Martino,[17] Jasmin Kuemmerle-Deschner,[18] Laura Obici,[19] Nicolae Iagaru,[20] Anna Simon,[21] Susan Nielsen,[22] Alberto Martini,[23] Nicolino Ruperto,[24] Marco Gattorno,[24*] Joost Frenkel,[1*] Paediatric Rheumatology International Trials Organisation (PRINTO) and the Eurofever/Eurotraps Projects

Ter Haar N *et al*. Ann Rheum Dis 2013; 72:678-85

REGISTRO EUROFEVER

- Tratamiento de elección
  - Colchicina para FMF
  - Bloqueo de IL1 para DIRA y CAPS
  - Corticoides a demanda para PFAPA, MKD y TRAPS
  - Pacientes con TRAPS se pueden beneficiar de terapia anti TNFα [respuesta clínica incompleta]
  - Pacientes con FMF, MKD, TRAPS o PAPA se pueden beneficiar de bloqueo de IL1

Ter Haar N *et al*. Ann Rheum Dis 2013; 72:678-85



VACUNACIONES

EN REUMATOLOGÍA PEDIÁTRICA

ESTADO VACUNAL en AIJ

RHEUMATOLOGY

Vaccination coverage in children with juvenile idiopathic arthritis followed at a paediatric tertiary care centre

Marie-Paule Morin[1], Caroline Quach[2], Élise Fortin[2] and Gaëlle Chédeville[1]

- Revisan cartilla vacunal de 200 pacientes con AIJ consecutivos
- Evalúan % con vacunas completas según programa de Canadá
  - 52% a los 2,5 años [DTP 99%, Sarampión 58%]
  - Ultima visita media 11,4 años 61% [DTP 80%, Sarampión 83%]
- Garantizar completar las vacunas cuando la AIJ lo permita

Morin MP *et al*. Rheumatology 2012; 51:2046-50

TRIPLE VÍRICA y AIJ

JAMA®
The Journal of the American Medical Association

ORIGINAL CONTRIBUTION

Effects of the Live Attenuated Measles-Mumps-Rubella Booster Vaccination on Disease Activity in Patients With Juvenile Idiopathic Arthritis

A Randomized Trial

Marloes W. Heijstek, MD
Sylvia Kamphuis, MD, PhD
Wineke Armbrust, MD
Joost Swart, MD
Simone Gorter, MD
Lara D. de Vries, MD
Gaby P. Smits, MSc
Pieter G. van Gageldonk, BASc
Guy A. M. Berbers, PhD
Nico M. Wulffraat, MD, PhD

Heijstek MW *et al*. JAMA 2013; 309:2449-56

TRIPLE VÍRICA y AIJ

- Estudio multicéntrico Holandés sobre 137 pacientes
- 68 se aleatorizan a recibir SRP y 69 no se vacunan [control]
- Utilizan virus vivo atenuado
  - 60 en tto. con MTX y 15 con biológicos [ETN o ANA]
  - Interrumpen biológicos 5 vidas medias antes de SRP
  - Esperan 1 mes después de bolo de MPIV
- No observan variaciones en la actividad de la enfermedad valorada mediante JADAS-27
- Títulos más altos en vacunados que en controles
  - Sarampión 100% vs 92%
  - Paperas 97% vs 81%
  - Rubéola 100% vs 94%

Heijstek MW *et al*. JAMA 2013; 309:2449-56

VAG y AIJ

PEDIATRIC RHEUMATOLOGY

RESEARCH Open Access

Prospective surveillance study of acute respiratory infections, influenza-like illness and seasonal influenza vaccine in a cohort of juvenile idiopathic arthritis patients

Luciana M Carvalho[1*], Flávia E de Paula[2], Rodrigo V D Silvestre[3], Luciana R Roberti[1], Eurico Arruda[2], Wyller A Mello[3] and Virginia P L Ferriani[1]

VAG y AIJ

- Vigilancia de la gripe en 2 temporadas respiratorias [n=61 y 63]
  - 72% y 41% presentaron IVRS cada temporada
  - **Tasa de incidencia** 7,6 y 3,9 por 1,000 niño-días ~ a sanos
  - **20% de las recaídas** [10/50] de AIJ se asociaron con IVRS
- Inmunogenicidad de VAG en niños con AIJ [n=44]
  - 70% recibía MTX o LEF
  - 11% seguía tratamiento con anti TNFs
  - Respuesta a la VAG inalterada independientemente de forma clínica o tratamiento
  - Pacientes con anti TNFs presentaban menor tasa de seroconversión a H1N1 [60%] comparado con otras cepas H3/N2 [100%] o B/Florida [80%]

Carvalho LM *et al*. Pediatr Rheumatol Online J 2013; 11:10

PAPILOMAVIRUS & LES

Annals of the RHEUMATIC DISEASES The EULAR Journal

Clinical and epidemiological research

EXTENDED REPORT

Immunogenicity and safety of a quadrivalent human papillomavirus vaccine in patients with systemic lupus erythematosus: a case–control study

Chi Chiu Mok, Ling Yin Ho, Lai Shan Fong, Chi Hung To

- Inmunogenicidad vacuna anti VPH cuadrivalente en 50 pacientes con LES [≥74%] y 50 controles [≥93%]
- 70% PDN, 66% HCQ, 48% AZA, 18% MMF

Mok CC *et al*. Ann Rheum Dis 2013; 72:659-64

VACUNAS y ENF. REUMATICAS

nature REVIEWS RHEUMATOLOGY

REVIEWS

Vaccinations in juvenile chronic inflammatory diseases: an update

Clovis A. Silva, Nadia E. Aikawa and Eloisa Bonfa

Silva CA *et al*. Nat Rev Rheumatol 2013; 9:532-43

GRACIAS