

Día 2 - Artritis Reumatoide

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Básica: nuevo biomarcador en AR

ABSTRACT NUMBER: 0850

Single-cell RNA-seq analysis of synovial CD4+ T cells identifies a novel biomarker and therapeutic target in human rheumatoid arthritis

Akinori Murakami¹, Rinko Akamine¹, Koichi Murata¹, Kohei Nishitani¹, Hiromu Ito², Ryu Watanabe³, Takayuki Fujii¹, Takeshi Iwasaki¹, Yuki Masuo⁴, Osamu Iri¹, Shinichiro Nakamura¹, Shinichi Kuriyama¹, Yugo Morita¹, Yasuhiro Murakawa⁵, Chikashi Terao⁶, Yukinori Okada⁷, Motomu Hashimoto³, Shuichi Matsuda¹, Hideki Ueno¹ and Hiroyuki Yoshitomi¹, ¹Kyoto University, Kyoto, Japan, ²Kyoto University / Kurashiki Central Hospital, Kyoto, Japan, ³Osaka Metropolitan University, Osaka, Japan, ⁴Graduate school of medicine, Kyoto University, Kyoto, Japan, ⁵Kyoto University / RIKEN, Kyoto, Japan, ⁶RIKEN, Tokyo, Japan, ⁷The University of Tokyo / Osaka University / RIKEN, Tokyo, Japan

Con técnicas de célula única se ha identificado en el tejido sinovial un nuevo mediador inflamatorio, al que llaman **PHIF (Pathogenic Helper Inflammatory Factor)**, producido por los linfocitos T periféricos helper. Este factor activa a los monocitos y se asocia con mayor actividad de la enfermedad.

Cuando se bloquea con CRISPR, se apaga la respuesta inflamatoria.

Es decir, **PHIF podría ser una nueva diana terapéutica y biomarcador de actividad en AR.**

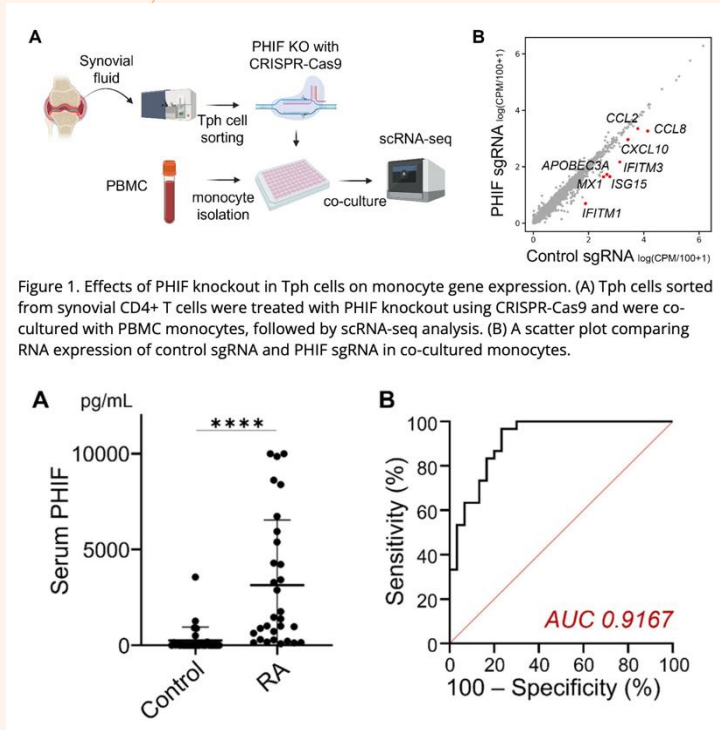


Figure 1. Effects of PHIF knockout in Tph cells on monocyte gene expression. (A) Tph cells sorted from synovial CD4+ T cells were treated with PHIF knockout using CRISPR-Cas9 and were co-cultured with PBMC monocytes, followed by scRNA-seq analysis. (B) A scatter plot comparing RNA expression of control sgRNA and PHIF sgRNA in co-cultured monocytes.

Dieta y riesgo de AR

ABSTRACT NUMBER: 1034

Healthy Dietary Patterns and Risk of Rheumatoid Arthritis: A Systematic Review and Meta-Analysis

Elena Joerns¹, Jeffrey Sparks², Cynthia Chelf¹, Cynthia Crowson³, John Davis¹ and Vanessa Kronzer¹, ¹Mayo Clinic, Rochester, MN, ²Brigham and Women's Hospital, Boston, MA, ³Mayo Clinic, Stewartville, MN

Se incluyeron 12 estudios (casos-contróles y cohortes) con **más de 270 000 personas** hasta febrero/2025 demuestra que seguir una dieta saludable, como la mediterránea o antiinflamatoria, **reduce significativamente el riesgo de desarrollar AR.**

↓ **Riesgo de AR con dieta saludable → OR 0.54–0.84**

La evidencia, aunque observacional, es consistente y de calidad moderada.

En resumen, una **alimentación equilibrada podría ser una herramienta preventiva real** frente a la AR.

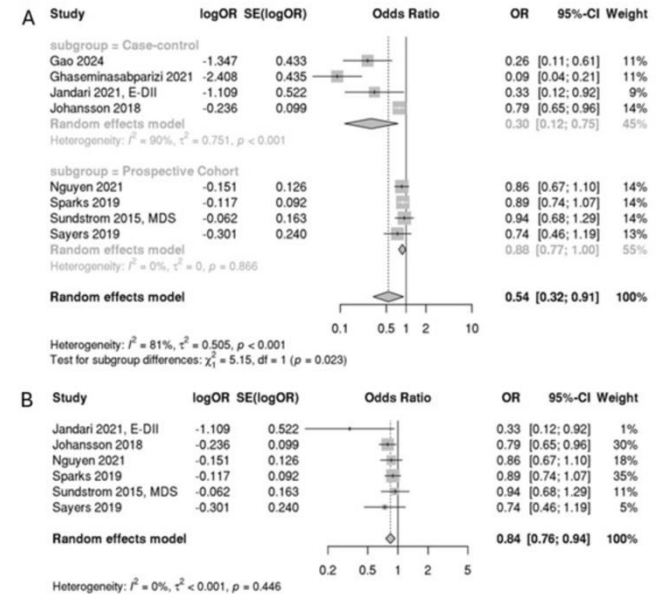


Figure 1. Association between healthy overall dietary pattern and incident RA among (A) all studies and (B) in the subset of studies with the lowest risk of bias

Prevención de AR

ABSTRACT NUMBER: 1674

A Phase 2, Randomized, Placebo-Controlled Trial of Hydroxychloroquine in Individuals At-Risk for Future Rheumatoid Arthritis

Kevin Deane¹, Christopher Striebich², Marie Feser³, James O'Dell⁴, Judith James⁵, Jeffrey Sparks⁶, John Davis⁷, Jonathan Graf⁸, Maureen McMahon⁹, Elizabeth Solow¹⁰, Lindsay Forbess¹¹, Athan Tiliakos¹², Elena Schioppa¹³, David Fox¹⁴, Maria I. ("Maio") Danila¹⁵, Diane Horowitz¹⁶, Jonathan Kay¹⁷, Colin Strickland³, Joel Guthridge⁵, Cristina Arriens⁵, Jennifer Grossman¹⁸, Kristen Demoruelle¹⁹, Elizabeth Bemis³, Ashley Frazer-Abel³, Chelsie Fleischer²⁰, Ted Mikuls⁴, Melissa Greenleaf²¹, Kate York²², Sarah Walker²³, Lynette Keyes-Elstein²³, Margie Byron²³, Janel Fedler²⁴, Ellen Goldmuntz²⁵ and V. Michael Holers²⁶, ¹University of Colorado Denver Anschutz Medical Campus, Aurora, CO, ²University of Colorado, Aurora, CO, ³University of Colorado Anschutz Medical Campus, Aurora, CO, ⁴University of Nebraska Medical Center, Omaha, NE, ⁵Oklahoma Medical Research Foundation, Oklahoma City, OK, ⁶Brigham and Women's Hospital, Boston, MA, ⁷Mayo Clinic, Rochester, MN, ⁸UCSF, San Francisco, CA, ⁹UCLA David Geffen School of Medicine, Los Angeles, CA, ¹⁰UT Southwestern Medical Center, Dallas, TX, ¹¹Cedars-Sinai Medical Center, Los Angeles, CA, ¹²Emory University, Roswell, GA, ¹³Medical College of Georgia at Augusta University, Martinez, GA, ¹⁴University of Michigan, Dexter, MI, ¹⁵University of Alabama at Birmingham (UAB), Birmingham VA Medical Center, Birmingham, AL, ¹⁶Northwell Health, Jericho, NY, ¹⁷UMass Chan Medical School, Worcester, MA, ¹⁸UCLA, Sherman Oaks, CA, ¹⁹University of Colorado Anschutz Medical Campus, Golden, CO, ²⁰University of Colorado Denver, Aurora, CO, ²¹National Institutes of Health, Rockville, MD, ²²Rho, Inc, Durham, NC, ²³Rho, Inc., Durham, NC, ²⁴Rho, Inc., Salem, IA, ²⁵NIAD/ NIH, Washington, DC, ²⁶University of Colorado, Denver, CO

Desarrollo de AR clínica a 36 meses:
HCQ: 30.4% vs Placebo: 32.9% (p = 0.52)

HCQ no previene la AR en individuos en riesgo con anti-CCP elevado.

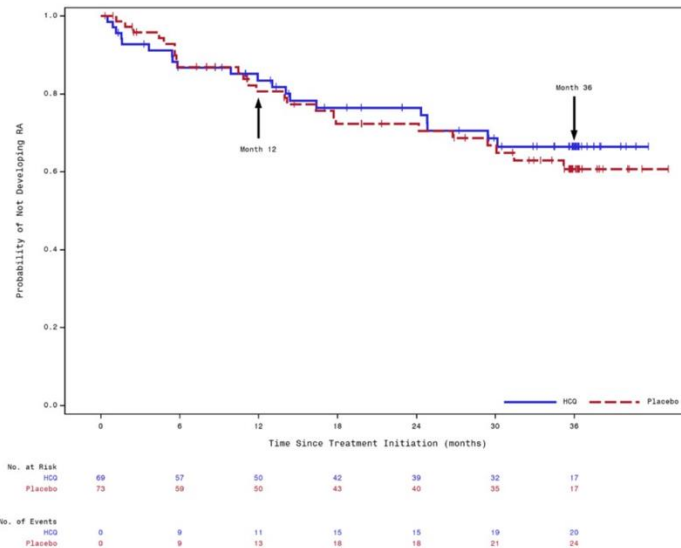


Figure. Development of clinical rheumatoid arthritis. Shown is the Kaplan-Meier based survival estimates of not developing clinical rheumatoid arthritis (clinical RA) in the modified intention-to-treat population. Tick marks indicate censored data. The number of participants at risk for development of clinical RA and the cumulative number of events in each group at each time point is given below the graph. Arrows indicate Month 12 and Month 36. In the modified intent-to-treat population, clinical RA occurred in 21 of 69 (30.4%) participants in the HCQ group and 24 of 73 (32.9%) in the placebo group. The Kaplan-Meier derived risk of clinical RA at 36 months was 0.336 with HCQ and 0.394 with placebo (difference -0.058; 95% confidence interval -0.336 to 0.220; P=0.52).

Prevención de AR

ABSTRACT NUMBER: 1678

Abatacept in individuals at risk of developing rheumatoid arthritis: results from the Arthritis Prevention in the Pre-clinical Phase of RA with Abatacept Long Term Outcomes (ALTO) Study

Andrew Cope¹, Joana Vasconcelos¹, Marianna Jasencova², Andrew Filer³, Karim Raza⁴, Sumera Qureshi¹, Maria Antonietta D'Agostino⁵, Iain McInnes⁶, Stefan Siebert⁷, John Isaacs⁷, Arthur Pratt⁸, Benjamin A. Fisher⁹, Christopher Buckley¹⁰, Paul Emery¹¹, Kulveer Mankia¹¹, Pauline Ho¹², MAYA BUCH¹³, Coziana Ciurtin¹⁴, Dirkjan van Schaardenburg¹⁵, Tom Huizinga¹⁶, René Toes¹⁶, Caroline Murphy¹ and A. Toby Prevost¹, ¹King's College London, London, United Kingdom, ²King's College London, London, ³The University of Birmingham, Birmingham, United Kingdom, ⁴University of Birmingham, Birmingham, United Kingdom, ⁵Division of Rheumatology and Clinical Immunology - Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, ⁶University of Glasgow, Glasgow, United Kingdom, ⁷Newcastle University, Newcastle upon Tyne, United Kingdom, ⁸University of Newcastle, Newcastle, United Kingdom, ⁹King's College London, London, UK; Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK, Birmingham, United Kingdom, ¹⁰University of Oxford, Oxford, United Kingdom, ¹¹University of Leeds, Leeds, England, United Kingdom, ¹²The Kellgren Centre for Rheumatology, Manchester Royal Infirmary, Manchester, United Kingdom, ¹³UNIVERSITY OF MANCHESTER, MANCHESTER, United Kingdom, ¹⁴University College London, London, ¹⁵Amsterdam UMC, Amsterdam, Netherlands, ¹⁶Leiden University Medical Center, Leiden, Netherlands

APIPPRA

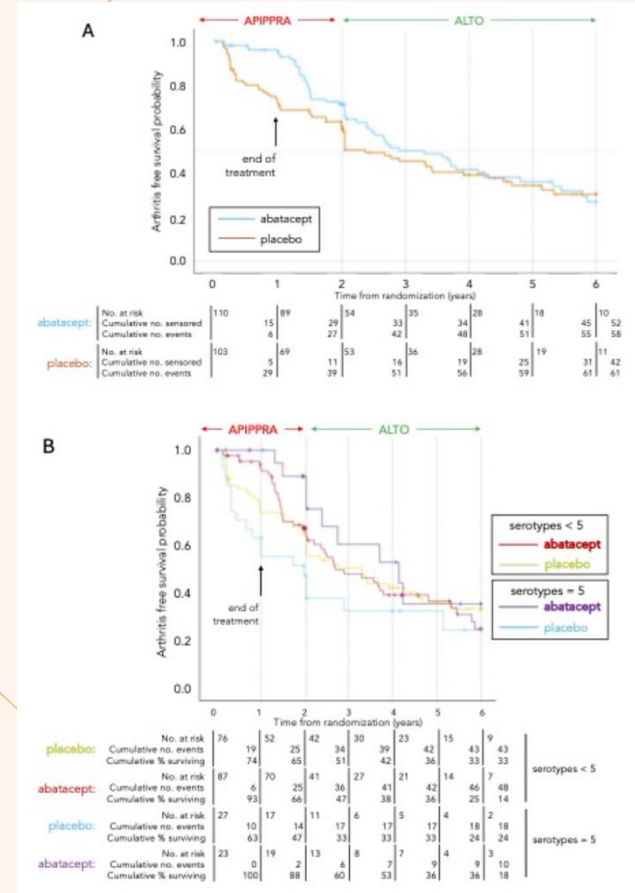


6 años

ALTO

Abatacept retrasa la progresión a AR hasta 4 años, especialmente en pacientes con respuesta autoinmune avanzada (perfil multiautoanticuerpo).

El beneficio no se mantiene en todos más allá de 4-5 años, lo que sugiere que **no previene permanentemente la enfermedad, pero modula su curso.**



Resultados clínicos en AR

n = 675 pacientes
Seguimiento medio: 217 ± 9,8 meses (~18 años)

ABSTRACT NUMBER: 1679

Does First-Line b- or tsDMARDs Choice Influence Progression to Difficult-to-Treat Rheumatoid arthritis? Insights from our longitudinal RA UCLouvain Brussels cohort

Cécile VAN MULLEM¹, Francesco NATALUCCI¹, Stéphanie DIERCKX¹, Aleksandra AVRAMOVSKA¹, Tatiana SOKOLOVA² and Patrick Durez¹, ¹Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Belgium, ²Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCLouvain) – Institut de Recherche Expérimentale et Clinique (IREC), Rheumatology, Brussels, Brussels Hoofdstedelijk Gewest, Belgium

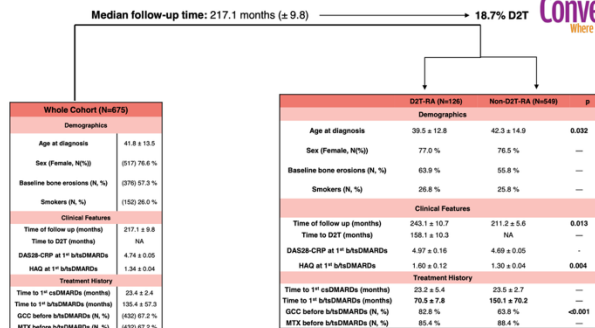
18.8% desarrolló 2DT-AR

Los factores que más predicen la progresión son:

- mayor severidad inicial,
 - uso previo de corticoides,
 - inflamación persistente,
- más que la elección del biológico inicial

Estos resultados sugieren que **la gravedad intrínseca y la inflamación persistente son los verdaderos motores de la refractariedad**

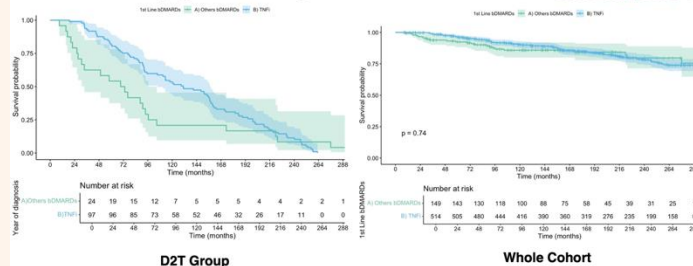
Results/1



27/10/2025 ACR Convergence 2025

Results/4

Risk of D2T-RA progression according to 1st line bDMARDs



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Resultados clínicos en AR

ABSTRACT NUMBER: 1677

First line anti-TNF therapy in early rheumatoid arthritis is associated with a lower frequency of difficult-to-treat disease at five years and better long-term outcomes compared with usual care

Task Toyoda¹, Kerem Abacar¹, Farag Shuweihdi², Megan Sheridan³, Jacqueline Nam³, Ai Lyn Tan⁴, Lesley-Anne Bissell³, Paul Emery⁵ and Kulveer Mankia⁵, ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, England, United Kingdom, ²Dental Translational and Clinical Research Unit, School of Medicine, University of Leeds, Leeds, England, United Kingdom, ³Leeds Teaching Hospitals NHS Trust, Leeds, England, United Kingdom, ⁴NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds; Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, England, United Kingdom, ⁵University of Leeds, Leeds, England, United Kingdom

TNFi produces more DMARD-free remission



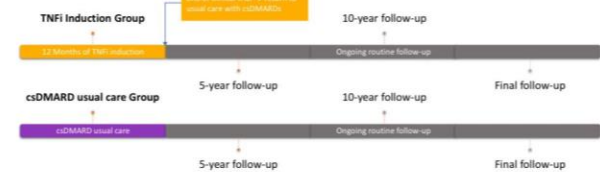
% (n)	5 years, n=342			10 years, n=302			Final follow-up, n=342		
	csDMARD	TNFi induction	OR (95% CI) p-value	csDMARD	TNFi induction	OR (95% CI) p-value	csDMARD	TNFi induction	OR (95% CI) p-value
DMARD-free remission	6% (14)	13% (15)	2.25 (1.06-5.07) 0.049	10% (21)	13% (12)	1.46 (0.64-3.33) 0.369	7% (16)	14% (16)	2.54 (1.14-5.64) 0.023
Escalation to one bDMARD only	15% (35)	23% (26)	1.71 (0.93-3.15) 0.086	13% (26)	28% (26)	2.63 (1.32-5.25) 0.006	15% (33)	29% (33)	2.55 (1.35-4.82) 0.004
Failure of one MoA of bDMARD	15% (35)	5% (6)	1.09 (0.28-3.12) 0.886	14% (29)	10% (9)	0.69 (0.29-1.65) 0.403	12% (27)	11% (12)	0.86 (0.28-1.95) 0.720
csDMARD only*	66% (151)	58% (66)	—	53% (110)	44% (41)	—	51% (117)	39% (44)	—

RA: rheumatoid arthritis, csDMARD: conventional synthetic disease-modifying anti-rheumatic drug, TNFi: tumour necrosis factor inhibitor, OR: odds ratio, bDMARD: biologic disease-modifying anti-rheumatic drug, MoA: mechanism of action

*Reference category for multinomial logistic regression

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Study Design



- Patient recruitment was from 2006-2015
- Follow-up was until May 2025

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Menos enfermedad difícil de tratar → 0.9% vs 7% a 5 años (OR 0.11).

Más remisión sostenida → >60% mantenida hasta 10 años (OR 1.9).

Más remisión libre de fármacos → 13% vs 6% (OR 2.25).

Retrasa la necesidad de nuevos biológicos → +11 meses de tiempo hasta escalada.

Beneficio coste-efectivo con biosimilares → Apoya reconsiderar el algoritmo terapéutico inicial.

Medidas de estilo de vida

ABSTRACT NUMBER: 1327

Systematic Review of Mobility in Rheumatoid Arthritis with Digitally Measured Objective Assessment

Anna fishbein¹, Rachel Lawson², Veleka Allen¹, Xiaozhong Zhang³, Laura Chambre⁴, Stephen Ruhmel¹, Sophie Wilhelm¹, Fredric Marrache⁵, Maria Wiekowski¹, Markus Kohlmann⁶ and Jeffrey Curtis⁷, ¹Sanofi, Morristown, NJ, ²Sanofi, Earley, United Kingdom, ³Sanofi, Chengdu, China (People's Republic), ⁴Sanofi, Cambridge, MA, ⁵Sanofi, Gentilly, France, ⁶Sanofi, Frankfurt, Germany, ⁷University of Alabama at Birmingham, Birmingham, AL

Movilidad en AR medida digitalmente
Revisión sistemática (105 estudios)

◆ **Tecnologías usadas:** Acelerómetros (51%), monitores de actividad, pedómetros, smartwatches.

◆ **Hallazgos clave:**

- 9–10 h/día de sedentarismo.
- Solo 5–17% cumplen las guías de actividad física.
- Mayor actividad = menor fatiga y mejor calidad de vida.
- Patrón diario: rigidez matutina → menor actividad matinal.

◆ **Factores asociados:**

- ↓ Actividad ↔ ↑ actividad inflamatoria.
- Remisión ↔ ↑ movilidad y bienestar.

→ **Conclusión:** La monitorización digital cuantifica de forma precisa el impacto funcional de la AR y abre la puerta al uso de **biomarcadores digitales de actividad y fatiga**.

Medidas de estilo de vida

ABSTRACT NUMBER: 1374

AZD1163, a Novel Bispecific Human Antibody Targeting PAD2/4 Enzymes Responsible for Generating Citrullinated Protein Auto-antigens in Rheumatoid Arthritis, Demonstrates Dose-dependent Inhibition of Systemic PAD Activity in Healthy Volunteers

Susanne Prothon¹, Jacob Leander¹, Ulla Seppälä¹, Eduard Molins², Mia Collins¹, Nicholas White³, Ivonne Puente¹, Andre Santa Maria¹, Gary Sims⁴, David Han⁵, Obada Al Hamdan⁶, Ronald Goldwater⁷, Emon Khan⁸ and David Close⁹, ¹AstraZeneca, Gothenburg, Sweden, ²AstraZeneca, Barcelona, Spain, ³AstraZeneca, Cambridge, United Kingdom, ⁴AstraZeneca, Gaithersburg, ⁵Parexel, Los Angeles, ⁶Parexel, Berlin, Germany, ⁷Parexel, Baltimore, ⁸BioPharmaceuticals R&D, Late Respiratory and Immunology, AstraZeneca, Academy House, Cambridge, United Kingdom, ⁹AstraZeneca, Royston, United Kingdom

Fase I en voluntarios sanos, n=83

Objetivo: Evaluar seguridad, farmacocinética y efecto inhibitor de AZD1163 sobre actividad PAD.

◆ **Resultados principales:**

- Bien tolerado, sin señales de toxicidad relevantes
- Vida media 38 días, biodisponibilidad 65%
- Inhibición >95% de actividad PAD2/4 (confirmada ex vivo)
- Baja inmunogenicidad (ADA 6.7%)

◆ **Conclusión:** Primera molécula capaz de bloquear la citrulinación patológica de manera segura.

👉 *Possible terapia preventiva o muy temprana en AR.*

Comorbilidades: RCV

ABSTRACT NUMBER: 1334

Cardiac Biomarkers and Prediction of Major Cardiovascular Events in Rheumatoid Arthritis: Results from the ESPOIR Cohort

manon Iesturgie¹, Fiona Oudart¹, Anne Cauvet², Virginie Gonzalez², Bruno Fautrel³, Arnaud Constantin⁴, Nathalie Rincheval⁵, Yannick Allanore⁶ and Jérôme Avouac⁷,
¹INSERM U¹⁰¹⁶, Paris, France, ²INSERMU¹⁰¹⁶, Paris, France, ³Sorbonne Université - APHP, Department of Rheumatology, Hôpital Pitié-Salpêtrière, Inserm UMRS 1136_5, PARIS, France, Paris, France, ⁴Hôpital Pierre-Paul Riquet, CHU Purpan, Toulouse, France, ⁵Institut de Recherche Clinique EA²⁴¹⁵, Université de Montpellier, Département de Statistiques, Montpellier, France, ⁶Université Paris Cité, Paris, France, ⁷Hôpital Cochin, AP-HP Centre - Université Paris Cité, Paris, France

Cohorte ESPOIR (n=559; 76% mujeres, edad media 49 años, DAS28=5.26).

- Seguimiento medio: **11 años**.
- Medición basal de:
 - **hs-cTnT** (lesión miocárdica subclínica).
 - **ST2** (marcador de fibrosis e inflamación cardíaca).
- Eventos principales: infarto, ictus o muerte cardiovascular.

→ Los pacientes con niveles elevados de hs-cTnT o ST2 al inicio presentaron entre 2 y 3 veces más riesgo de infarto, ictus o muerte cardiovascular. **La combinación de ambos biomarcadores mejoró la predicción más allá de la PCR y de los factores clásicos, mostrando su potencial para estratificar RCV en la práctica clínica.**

