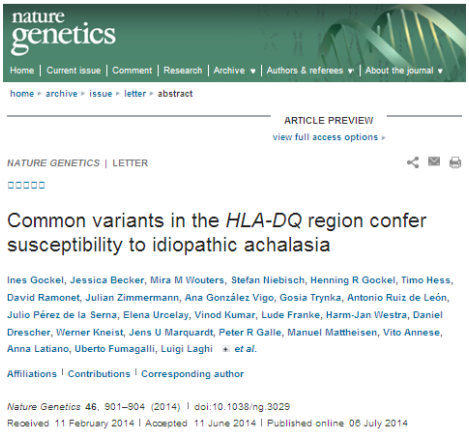
Los 10 artículos de mayor factor de impacto del 2º semestre 2014

1. Gockel, I; Becker, J; Wouters, MM; Niebisch, S; Gockel, HR; Hess, T; Ramonet, D; Zimmermann, J; **Vigo, AG**; Trynka, G; **de Leon, AR**; **de la Serna, JP**; **Urcelay, E;** Kumar, V; Franke, L; Westra, HJ; Drescher, D; Kneist, W; Marquardt, JU; Galle, PR; Mattheisen, M; Annese, V; Latiano, A; Fumagalli, U; Laghi, L; Cuomo, R; Sarnelli, G; Muller, M; Eckardt, AJ; Tack, J; Hoffmann, P; Herms, S; Mangold, E; Heilmann, S; Kiesslich, R; von Rahden, BHA; Allescher, HD; Schulz, HG; Wijmenga, C; Heneka, MT; Lang, H; Hopfner, KP; Nothen, MM; Boeckxstaens, GE; de Bakker, PIW; Knapp, M; Schumacher, J. *Common variants in the HLA-DQ region confer susceptibility to idiopathic achalasia*. NATURE GENETICS. 2014; 46 (8):901-904
   Enlace: http://www.nature.com/ng/journal/v46/n8/full/ng.3029.html


nature genetics

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NATURE GENETICS | LETTER

Common variants in the *HLA-DQ* region confer susceptibility to idiopathic achalasia

Ines Gockel, Jessica Becker, Mira M Wouters, Stefan Niebisch, Henning R Gockel, Timo Hess, David Ramonet, Julian Zimmermann, Ana González Vigo, Gosia Trynka, Antonio Ruiz de León, Julio Pérez de la Serna, Elena Urcelay, Vinod Kumar, Lude Franke, Harm-Jan Westra, Daniel Drescher, Werner Kneist, Jens U Marquardt, Peter R Galle, Manuel Mattheisen, Vito Annese, Anna Latiano, Uberto Fumagalli, Luigi Laghi ✳ *et al.*

Affiliations | Contributions | Corresponding author

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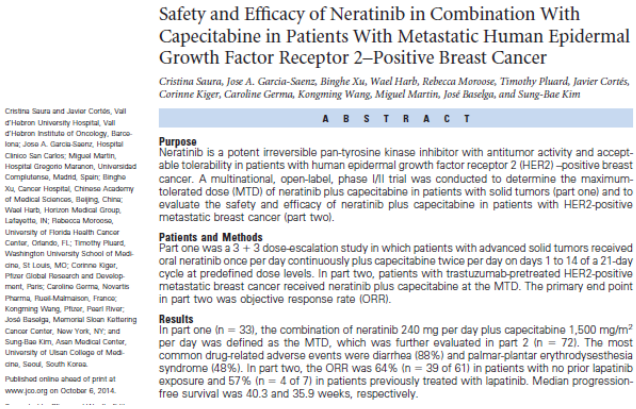
2. Saura, C; **Garcia-Saenz, JA**; Xu, BH; Harb, W; Moroose, R; Pluard, T; Cortes, J; Kiger, C; Germa, C; Wang, KM; Martin, M; Baselga, J; Kim, SB. *Safety and Efficacy of Neratinib in Combination With Capecitabine in Patients With Metastatic Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer*. JOURNAL OF CLINICAL ONCOLOGY. 2014; 32 (32):3626-
   Enlace: http://jco.ascopubs.org/content/32/32/3626.long

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT



Safety and Efficacy of Neratinib in Combination With Capecitabine in Patients With Metastatic Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer

Cristina Saura, Jose A. Garcia-Saenz, Binghe Xu, Wael Harb, Rebecca Moroose, Timothy Pluard, Javier Cortés, Corinne Kiger, Caroline Germa, Kongming Wang, Miguel Martin, José Baselga, and Sung-Bae Kim

ABSTRACT

Purpose
Neratinib is a potent irreversible pan-tyrosine kinase inhibitor with antitumor activity and acceptable tolerability in patients with human epidermal growth factor receptor 2 (HER2) –positive breast cancer. A multinational, open-label, phase I/II trial was conducted to determine the maximum-tolerated dose (MTD) of neratinib plus capecitabine in patients with solid tumors (part one) and to evaluate the safety and efficacy of neratinib plus capecitabine in patients with HER2-positive metastatic breast cancer (part two).

Patients and Methods
Part one was a 3 + 3 dose-escalation study in which patients with advanced solid tumors received oral neratinib once per day continuously plus capecitabine twice per day on days 1 to 14 of a 21-day cycle at predefined dose levels. In part two, patients with trastuzumab-pretreated HER2-positive metastatic breast cancer received neratinib plus capecitabine at the MTD. The primary end point in part two was objective response rate (ORR).

Results
In part one (n = 33), the combination of neratinib 240 mg per day plus capecitabine 1,500 mg/m^2 per day was defined as the MTD, which was further evaluated in part 2 (n = 72). The most common drug-related adverse events were diarrhea (88%) and palmar-plantar erythrodysesthesia syndrome (48%). In part two, the ORR was 64% (n = 39 of 61) in patients with no prior lapatinib exposure and 57% (n = 4 of 7) in patients previously treated with lapatinib. Median progression-free survival was 40.3 and 35.9 weeks, respectively.

Cristina Saura and Javier Cortés, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona; Josa A. Garcia-Saenz, Hospital Clínico San Carlos; Miguel Martín, Hospital Gregorio Maranon, Universidad Complutense, Madrid, Spain; Binghe Xu, Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; Wael Harb, Horizon Medical Group, Lafayette, IN; Rebecca Moroose, University of Florida Health Cancer Center, Orlando, FL; Timothy Pluard, Washington University School of Medicine, St Louis, MO; Corinne Kiger, Pfizer Global Research and Development, Paris; Caroline Germa, Novartis Pharma, Rueil-Malmaison, France; Kongming Wang, Pfizer, Pearl River; José Baselga, Memorial Sloan Kettering Cancer Center, New York, NY; and Sung-Bae Kim, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea.

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"El gen erb2 codifica el receptor transmembrana HER2 perteneciente a la familia receptores de factores de crecimiento (EFGR, HER2, HER3 y HER4). Este gen está sobreexpresado en el 20% de los tumores de mama y, como resultado de su acción oncogénica, los tumores tienen un comportamiento biológicamente más agresivo. Se están buscando agentes especialmente dirigidos a esta diana terapéutica que puedan modificar la historia natural de esta enfermedad.

Recientemente hemos publicado el estudio Fase I/II que ha constatado la seguridad, y también la eficacia de un nuevo agente dirigido para cáncer de mama HER2(+), neratinib, en combinación con una quimioterapia clásica, capecitabina. Este nuevo fármaco es inhibidor irreversible de la actividad tirosina-quinasa de los familia de receptores de crecimiento.

Un número importante de las pacientes incluidas en este estudio multicéntrico, han sido mujeres con cáncer de mama procedentes de nuestro hospital. Los resultados de este ensayo han permitido establecer la dosis más adecuada, que actualmente está siendo corroborada en un estudio Fase III, y que probablemente representará una oportunidad para esta población de pacientes con pronóstico tan precario."

3. Lincoff, AM; Roe, M; Aylward, P; Galla, J; Rynkiewicz, A; Guetta, V; Zelizko, M; Kleiman, N; White, H; McErlean, E; Erlinge, D; Laine, M; Ferreira, JMD; Goodman, S; Mehta, S; Atar, D; Suryapranata, H; Jensen, SE; Forster, T; **Fernandez-Ortiz, A;** Schoors, D; Radke, P; Belli, G; Brennan, D; Bell, G; Krucoff, M. *Inhibition of delta-protein kinase C by delcasertib as an adjunct to primary percutaneous coronary intervention for acute anterior ST-segment elevation myocardial infarction: results of the PROTECTION AMI Randomized Controlled Trial*. EUROPEAN HEART JOURNAL. 2014; 35 (37):2516-U171

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European Heart Journal (2014) 35, 2516–2523
doi:10.1093/eurheartj/ehu177

CLINICAL RESEARCH
Acute coronary syndromes

Inhibition of delta-protein kinase C by delcasertib as an adjunct to primary percutaneous coronary intervention for acute anterior ST-segment elevation myocardial infarction: results of the PROTECTION AMI Randomized Controlled Trial

A. Michael Lincoff[1]*, Matthew Roe[2], Philip Aylward[3], John Galla[1], Andrzej Rynkiewicz[4], Victor Guetta[5], Michael Zelizko[6], Neal Kleiman[7], Harvey White[8], Ellen McErlean[1], David Erlinge[9], Mika Laine[10], Jorge Manuel dos Santos Ferreira[11], Shaun Goodman[12], Shamir Mehta[13], Dan Atar[14], Harry Suryapranata[15], Svend Eggert Jensen[16], Tamas Forster[17], Antonio Fernandez-Ortiz[18], Danny Schoors[19], Peter Radke[20], Guido Belli[21], Danielle Brennan[1], Gregory Bell[22], and Mitchell Krucoff[2], for the PROTECTION AMI Investigators

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4. Castellano, JM; Sanz, G; Penalvo, JL; Bansilal, S; **Fernandez-Ortiz, A**; Alvarez, L; Guzman, L; Linares, JC; Garcia, F; D'Aniello, F; Arnaiz, JA; Varea, S; Martinez, F; Lorenzatti, A; Imaz, I; Sanchez-Gomez, LM; Roncaglioni, MC; Baviera, M; Smith, SC; Taubert, K; Pocock, S; Brotons, C; Farkouh, ME; Fuster, V. *A Polypill Strategy to Improve Adherence Results From the FOCUS Project*. JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY. 2014; 64 (20):2071-2082
Enlace: http://www.sciencedirect.com/science/article/pii/S0735109714059415

J Am Coll Cardiol. 2014 Nov 18-25;64(20):2071-82. doi: 10.1016/j.jacc.2014.08.021. Epub 2014 Sep 1.

A polypill strategy to improve adherence: results from the FOCUS project.

Castellano JM[1], Sanz G[2], Peñalvo JL[2], Bansilal S[3], Fernández-Ortiz A[4], Alvarez L[2], Guzmán L[5], Linares JC[5], García F[6], D'Aniello F[6], Arnáiz JA[7], Varea S[7], Martínez F[8], Lorenzatti A[8], Imaz I[9], Sánchez-Gómez LM[9], Roncaglioni MC[10], Baviera M[10], Smith SC Jr[11], Taubert K[11], Pocock S[12], Brotons C[13], Farkouh ME[14], Fuster V[15].

Author information

Abstract

BACKGROUND: Adherence to evidence-based cardiovascular (CV) medications after an acute myocardial infarction (MI) is low after the first 6 months. The use of fixed-dose combinations (FDC) has been shown to improve treatment adherence and risk factor control. However, no previous randomized trial has analyzed the impact of a polypill strategy on adherence in post-MI patients.

OBJECTIVES: The cross-sectional FOCUS (Fixed-Dose Combination Drug for Secondary Cardiovascular Prevention) study (Phase 1) aimed to elucidate factors that interfere with appropriate adherence to CV medications for secondary prevention after an acute MI. Additionally, 695 patients from Phase 1 were randomized into a controlled trial (Phase 2) to test the effect of a polypill (containing aspirin 100 mg, simvastatin 40 mg, and ramipril 2.5, 5, or 10 mg) compared with the 3 drugs given separately on adherence, blood pressure, and low-density lipoprotein cholesterol, as well as safety and tolerability over a period of 9 months of follow-up.

METHODS: In Phase 1, a 5-country cohort of 2,118 patients was analyzed. Patients were randomized to either the polypill or 3 drugs separately for Phase 2. Primary endpoint was adherence to the treatment measured at the final visit by the self-reported Morisky-Green questionnaire (MAQ) and pill count (patients had to meet both criteria for adherence at the in-person visit to be considered adherent).

5. Dangas, GD; Farkouh, ME; Sleeper, LA; Yang, M; Schoos, MM; **Macaya, C**; Abizaid, A; Buller, CE; Devlin, G; Rodriguez, AE; Lansky, AJ; Siami, FS; Domanski, M; Fuster, V. *Long-Term Outcome of PCI Versus CABG in Insulin and Non-Insulin-Treated Diabetic Patients.* JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY. 2014; 64 (12):1189-1197
Enlace: http://www.sciencedirect.com/science/article/pii/S0735109714045422

J Am Coll Cardiol. 2014 Sep 23;64(12):1189-97. doi: 10.1016/j.jacc.2014.06.1182.

Long-term outcome of PCI versus CABG in insulin and non-insulin-treated diabetic patients: results from the FREEDOM trial.

Dangas GD[1], Farkouh ME[2], Sleeper LA[3], Yang M[3], Schoos MM[2], Macaya C[4], Abizaid A[5], Buller CE[6], Devlin G[7], Rodriguez AE[8], Lansky AJ[9], Siami FS[3], Domanski M[2], Fuster V[2]; FREEDOM Investigators.

Author information

Abstract

BACKGROUND: The prospective, randomized FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes) trial found coronary artery bypass graft surgery (CABG) was associated with better clinical outcomes than percutaneous coronary intervention (PCI) in patients with diabetes and multivessel disease, managed with or without insulin.

OBJECTIVES: In this subgroup analysis of the FREEDOM trial, we examined the association of long-term clinical outcomes after revascularization in patients with insulin-treated diabetes mellitus (ITDM) compared with patients not treated with insulin.

METHODS: A total of 1,850 FREEDOM subjects had an index revascularization procedure performed: 956 underwent PCI with drug-eluting stents (DES), and 894 underwent CABG. A total of 602 patients (32.5%) had ITDM (PCI/DES n = 325, 34%; CABG n = 277, 31%). Subjects were classified according to ITDM versus non-ITDM, with comparison of PCI/DES versus CABG for each group. Interaction analyses were performed for treatment by diabetes mellitus (DM) status alone and for treatment by DM status by coronary lesion complexity. Analyses were performed for the primary outcome composite of death/stroke/myocardial infarction (MI) using all available follow-up data.

RESULTS: The overall 5-year event rate of death/stroke/MI was significantly higher in ITDM versus non-ITDM patients (28.7% vs. 19.5%, p < 0.001)

6. Zhang, YJ; Iqbal, J; Campos, CM; Klaveren, DV; Bourantas, CV; Dawkins, KD; Banning, AP; **Escaned, J**; de Vries, T; Morel, MA; Farooq, V; Onuma, Y; Garcia-Garcia, HM; Stone, GW; Steyerberg, EW; Mohr, FW; Serruys, PW. *Prognostic Value of Site SYNTAX Score and Rationale for Combining Anatomic and Clinical Factors in Decision Making Insights From the SYNTAX Trial*. JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY. 2014; 64 (5):423-432
   Enlace: http://www.sciencedirect.com/science/article/pii/S0735109714027442

J Am Coll Cardiol. 2014 Aug 5;64(5):423-32. doi: 10.1016/j.jacc.2014.05.022.

Prognostic value of site SYNTAX score and rationale for combining anatomic and clinical factors in decision making: insights from the SYNTAX trial.

Zhang YJ[1], Iqbal J[2], Campos CM[2], Klaveren DV[3], Bourantas CV[2], Dawkins KD[4], Banning AP[5], Escaned J[6], de Vries T[7], Morel MA[7], Farooq V[2], Onuma Y[2], Garcia-Garcia HM[2], Stone GW[8], Steyerberg EW[3], Mohr FW[9], Serruys PW[10].

Author information

Abstract

BACKGROUND: The results of SYNTAX trial have been reported based on "corelab" calculated SS (cSS). It has been shown that reproducibility of SS is better among the core laboratory technicians than interventional cardiologists. Thus, the prognostic value and clinical implication of the "site" SYNTAX SS (sSS) remain unknown.

OBJECTIVES: The study sought to evaluate the prognostic value and clinical implication of the sSS after percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery in the randomized SYNTAX trial.

METHODS: The sSS was calculated by the site investigators before randomization in the SYNTAX trial. New tertiles based on the sSS were defined with low (0 to 19), intermediate (20 to 27), and high (≥28) scores. The clinical endpoints were compared between PCI and CABG by Kaplan-Meier estimates, log-rank comparison, and Cox regression analyses using the new tertiles. The sSS-based SS II was calculated and its predictive performance was evaluated.

RESULTS: The mean difference in cSS and sSS is 3.8 ± 11.2, with a mean absolute difference of 8.9 ± 7.8. In the overall cohort, using sSS there was a higher incidence of major adverse cardiac and cerebrovascular events (MACCE) at 5-year follow-up in the PCI group for low (31.9% vs. 24.5%; r

7. Spelman, T; Gray, O; Trojano, M; Petersen, T; Izquierdo, G; Lugaresi, A; Hupperts, R; Bergamaschi, R; Duquette, P; Grammond, P; Giuliani, G; Boz, C; Verheul, F; **Oreja-Guevara, C;** Barnett, M; Grand'Maison, F; Rio, ME; Lechner-Scott, J; Van Pesch, V; Bolanos, RF; Flechter, S; Den Braber-Moerland, L; Iuliano, G; Amato, MP; Slee, M; Cristiano, E; Saladino, ML; Paine, M; Vella, N; Kasa, K; Deri, N; Herbert, J; Moore, F; Petkovska-Boskova, T; Alroughani, R; Savino, A; Shaw, C; Vucic, S; Santiago, V; Bacile, EA; Skromne, E; Poehlau, D; Cabrera-Gomez, JA; Lucas, R; Butzkueven, H. *Seasonal Variation of Relapse Rate in Multiple Sclerosis is Latitude Dependent.* ANNALS OF NEUROLOGY. 2014; 76 (6):880-890
   Enlace: http://onlinelibrary.wiley.com/doi/10.1002/ana.24287/pdf

Ann Neurol. 2014 Dec;76(6):880-90. doi: 10.1002/ana.24287. Epub 2014 Oct 20.

Seasonal variation of relapse rate in multiple sclerosis is latitude dependent.

Spelman T[1], Gray O, Trojano M, Petersen T, Izquierdo G, Lugaresi A, Hupperts R, Bergamaschi R, Duquette P, Grammond P, Giuliani G, Boz C, Verheul F, Oreja-Guevara C, Barnett M, Grand'Maison F, Edite Rio M, Lechner-Scott J, Van Pesch V, Fernandez Bolanos R, Flechter S, Den Braber-Moerland L, Iuliano G, Amato MP, Slee M, Cristiano E, Saladino ML, Paine M, Vella N, Kasa K, Deri N, Herbert J, Moore F, Petkovska-Boskova T, Alroughani R, Savino A, Shaw C, Vucic S, Santiago V, Bacile EA, Skromne E, Poehlau D, Cabrera-Gomez JA, Lucas R, Butzkueven H.

Author information

Abstract

OBJECTIVE: Previous studies assessing seasonal variation of relapse onset in multiple sclerosis have had conflicting results. Small relapse numbers, differing diagnostic criteria, and single region studies limit the generalizability of prior results. The aim of this study was to determine whether there is a temporal variation in onset of relapses in both hemispheres and to determine whether seasonal peak relapse probability varies with latitude.

METHODS: The international MSBase Registry was utilized to analyze seasonal relapse onset distribution by hemisphere and latitudinal location. All analyses were weighted for the patient number contributed by each center. A sine regression model was used to model relapse onset and ultraviolet radiation (UVR) seasonality. Linear regression was used to investigate associations of latitude and lag between UVR trough and subsequent relapse peak.

RESULTS: A total of 32,762 relapses from 9,811 patients across 30 countries were analyzed. Relapse onset followed an annual cyclical sinusoidal pattern with peaks in early spring and troughs in autumn in both hemispheres. Every 10° of latitude away from the equator was associated with a

"En este artículo se confirma la relación de los efectos ambientales con la probabilidad y frecuencia de tener brotes de esclerosis múltiple. Es un estudio muy grande multicéntrico en el que participaron alrededor de 10.000 pacientes de 20 países diferentes.

Se confirma una asociación significativa de probabilidad de brote con respecto a la estación en el hemisferio norte y aunque un poco menos significativa también esa probabilidad en el hemisferio sur. Es la primera vez que se demuestra que hay una relación estadística entre la disminución de las radiaciones ultravioletas y el aumento significativo de brotes en los distintos países y además esto es dependiente de la latitud; aumentando el incremento de brotes en latitudes más altas. Las personas viviendo en latitudes más altas tienen menos niveles de vitamina D, y reciben menos radiaciones ultravioletas en todas las estaciones del año pero alcanzan un mínimo del nivel de vitamina D (y de radiaciones ultravioleta) en primavera y en invierno y antes que las personas que viven cerca del ecuador. El mayor aumento de número de brotes es principalmente al inicio de la primavera. "

8. Villar, LM; Casanova, B; Ouamara, N; Comabella, M; Jalili, F; Leppert, D; de Andres, C; Izquierdo, G; **Arroyo, R**; Avsar, T; Lapin, SV; Johnson, T; Montalban, X; Fernandez, O; **Alvarez-Lafuente, R;** Masterman, D; Garcia-Sanchez, MI; Coret, F; Siva, A; Evdoshenko, E; Alvarez-Cermeno, JC; Bar-Or, A. *Immunoglobulin M Oligoclonal Bands: Biomarker of Targetable Inflammation in Primary Progressive Multiple Sclerosis.* ANNALS OF NEUROLOGY. 2014; 76 (2):231-240
Enlace: http://onlinelibrary.wiley.com/doi/10.1002/ana.24190/abstract

Ann Neurol. 2014 Aug;76(2):231-40. doi: 10.1002/ana.24190. Epub 2014 Jul 2.

Immunoglobulin M oligoclonal bands: biomarker of targetable inflammation in primary progressive multiple sclerosis.

Villar LM[1], Casanova B, Ouamara N, Comabella M, Jalili F, Leppert D, de Andrés C, Izquierdo G, Arroyo R, Avşar T, Lapin SV, Johnson T, Montalbán X, Fernández O, Álvarez-Lafuente R, Masterman D, García-Sánchez MI, Coret F, Siva A, Evdoshenko E, Álvarez-Cermeño JC, Bar-Or A.

Author information

Abstract

OBJECTIVE: To identify a biomarker distinguishing patients who, despite a primary progressive multiple sclerosis (PPMS) clinical course, may nonetheless benefit from immune therapy.

METHODS: The presence or absence of both immunoglobulin (Ig) G and IgM oligoclonal bands (OCB) was blindly examined in paired cerebrospinal fluid (CSF) and serum samples from a large PPMS patient cohort, and related to clinical and imaging evidence of focal inflammatory disease activity.

RESULTS: Using both cross-sectional samples and serial sampling in a subgroup of patients followed prospectively as part of the placebo-controlled OLYMPUS study of rituximab in PPMS, we found that the presence of CSF-restricted IgM OCB (but not of IgG OCB) is associated with an active inflammatory disease phenotype in PPMS patients. This finding was confirmed in an independent, multicenter validation cohort.

INTERPRETATION: The presence of CSF IgM OCB may be a biomarker for a subset of PPMS patients with more active inflammatory disease, who may benefit from immune-directed treatments.

"Entre los pacientes diagnosticados de esclerosis múltiple (EM), podemos distinguir, fundamentalmente, tres formas clínicas: recurrente-remitente (RR), secundaria progresiva (SP) y primariamente progresiva (PP). Aproximadamente un 20% de los pacientes con EM está diagnosticado de EMPP. En los últimos años hemos asistido a la llegada de un número importante de fármacos capaces de modificar el curso de la enfermedad, si bien todos ellos están únicamente indicados para pacientes con formas clínicas EMRR (EMSP en algunos casos), pero no se ha aprobado todavía ningún fármaco que nos permita tratar a los pacientes diagnosticados de EMPP. La relevancia de este estudio estriba en que hemos identificado un biomarcador, la presencia de bandas oligoclonales IgM, que nos permitiría distinguir, dentro de los pacientes EMPP, aquellos con un perfil inflamatorio más activo y que por tanto podrían beneficiarse de algunas de las terapias aprobadas para los pacientes con EMRR"

9. **Jimenez-Quevedo, P**; **Gonzalez-Ferrer, JJ**; Sabate, M; Garcia-Moll, X; Delgado-Bolton, R; **Llorente, L**; **Bernardo, E**; **Ortega-Pozzi, A**; **Hernandez-Antolin, R**; Alfonso, F; **Gonzalo, N**; **Escaned, J**; **Banuelos, C**; Regueiro, A; Marin, P; **Fernandez-Ortiz, A**; Das Neves, B; **del Trigo, M**; **Fernandez, C**; Tejerina, T; Redondo, S; **Garcia, E**; **Macaya, C**. *Selected CD133(+) Progenitor Cells to Promote Angiogenesis in Patients With Refractory Angina Final Results of the PROGENITOR Randomized Trial.* CIRCULATION RESEARCH. 2014; 115 (11):950
Enlace: http://circres.ahajournals.org/content/115/11/950.long

Circ Res. 2014 Nov 7;115(11):950-60. doi: 10.1161/CIRCRESAHA.115.303463. Epub 2014 Sep 17.

Selected CD133⁺ progenitor cells to promote angiogenesis in patients with refractory angina: final results of the PROGENITOR randomized trial.

Jimenez-Quevedo P[1], Gonzalez-Ferrer JJ[2], Sabate M[2], Garcia-Moll X[2], Delgado-Bolton R[2], Llorente L[2], Bernardo E[2], Ortega-Pozzi A[2], Hernandez-Antolin R[2], Alfonso F[2], Gonzalo N[2], Escaned J[2], Bañuelos C[2], Regueiro A[2], Marin P[2], Fernandez-Ortiz A[2], Neves BD[2], Del Trigo M[2], Fernandez C[2], Tejerina T[2], Redondo S[2], Garcia E[2], Macaya C[2].

⊕ Author information

Abstract

RATIONALE: Refractory angina constitutes a clinical problem.

OBJECTIVE: The aim of this study was to assess the safety and the feasibility of transendocardial injection of CD133(+) cells to foster angiogenesis in patients with refractory angina.

METHODS AND RESULTS: In this randomized, double-blinded, multicenter controlled trial, eligible patients were treated with granulocyte colony-stimulating factor, underwent an apheresis and electromechanical mapping, and were randomized to receive treatment with CD133(+) cells or no treatment. The primary end point was the safety of transendocardial injection of CD133(+) cells, as measured by the occurrence of major adverse cardiac and cerebrovascular event at 6 months. Secondary end points analyzed the efficacy. Twenty-eight patients were included (n=19 treatment; n=9 control). At 6 months, 1 patient in each group had ventricular fibrillation and 1 patient in each group died. One patient (treatment group) had a cardiac tamponade during mapping. There were no significant differences between groups with respect to efficacy parameters; however, the comparison within groups showed a significant improvement in the number of angina episodes per month (median absolute difference, -8.5 [95%

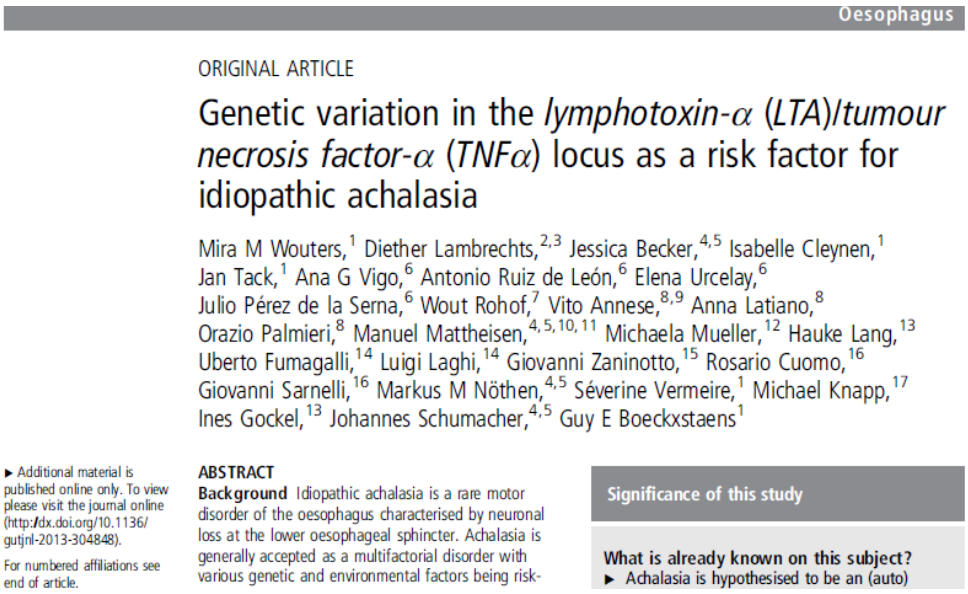
"La importancia de nuestro estudio radica en que es el primer estudio a nivel mundial que evalúa la seguridad y la factibilidad de la implantación de este subtipo de células progenitoras CD133+ en el contexto clínico de la angina refractaría. Además a diferencia de otros estudios con estas células las aislamos de la sangre periférica mediante estimulación medular y posteriormente realización de aféresis.
Otro aspecto importante es el método de administración que consiste en la inyección transendocardica con el sistema NOGA. Se trata de una tecnología que nos permite saber en tiempo real exactamente donde estamos inyectando las células

en el ventrículo a través de un catéter que se introduce por la arteria femoral. Existen solo 3 centros en España que dispongan de esta tecnología.

Por último es importante resaltar que es un estudio no financiado por la industria.

Con respecto a los resultados confirmamos que es seguro y factible inyectar estas células y existen resultados prometedores en términos de eficacia que serán la base de un estudio a gran escala que confirme resultados."

10. Wouters, MM; Lambrechts, D; Becker, J; Cleynen, I; Tack, J; **Vigo, AG**; **de Leon, AR**; **Urcelay, E**; **de la Serna, JP**; Rohof, W; Annese, V; Latiano, A; Palmieri, O; Mattheisen, M; Mueller, M; Lang, H; Fumagalli, U; Laghi, L; Zaninotto, G; Cuomo, R; Sarnelli, G; Nothen, MM; Vermeire, S; Knapp, M; Gockel, I; Schumacher, J; Boeckxstaens, GE. **Genetic variation in the lymphotoxin-alpha (LTA)/tumour necrosis factor-alpha (TNF alpha) locus as a risk factor for idiopathic achalasia.** GUT. 2014; 63 (9):1401-1409
Enlace: http://gut.bmj.com/content/63/9/1401.full.pdf+html



Oesophagus

ORIGINAL ARTICLE

Genetic variation in the *lymphotoxin-α (LTA)/tumour necrosis factor-α (TNFα)* locus as a risk factor for idiopathic achalasia

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ABSTRACT

Background Idiopathic achalasia is a rare motor disorder of the oesophagus characterised by neuronal loss at the lower oesophageal sphincter. Achalasia is generally accepted as a multifactorial disorder with various genetic and environmental factors being risk-

Significance of this study

What is already known on this subject?

▸ Achalasia is hypothesised to be an (auto)