REUMAFLORENCE 2008

Le criticità della terapia biologica

Hotel Garden Inn - Firenze - 29 novembre 2008

INQUADRAMENTO DEL PAZIENTE: QUANDO TRATTARE CON FARMACI BIOLOGICI?

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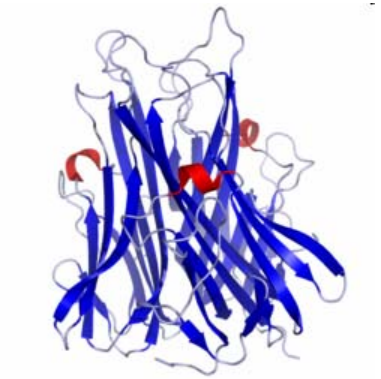
FARMACI BIOLOGICI IN REUMATOLOGIA

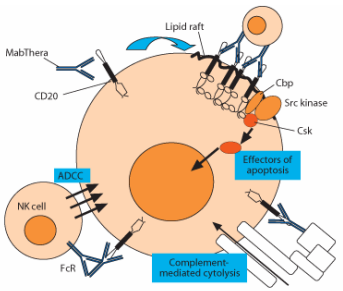
ANTI-TNFa



Infliximab
Etanercept
Adalimumab

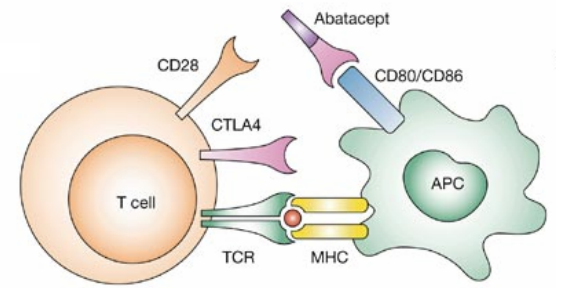
Certolizumab pegol
Golimumab

ANTI-CD20



Rituximab

CTLA4 Ig



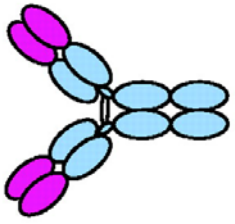
Abatacept

IL-1 Ra

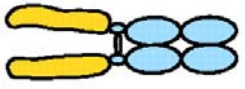
Anakinra

TNF-Recognition Domain

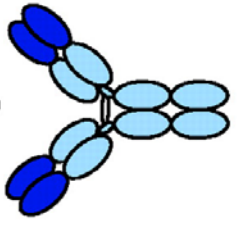
infliximab

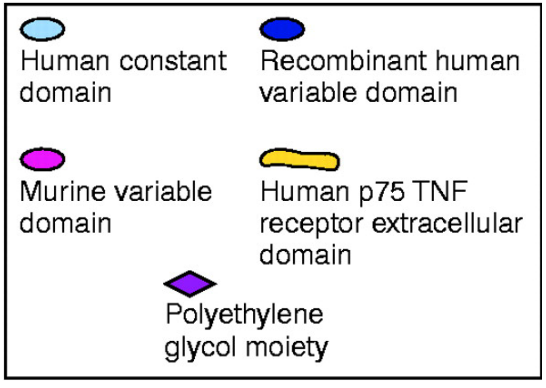


etanercept



adalimumab





Scheda tecnica Remicade

DENOMINAZIONE DEL MEDICINALE
Remicade 100 mg polvere per concentrato per soluzione per infusione.
COMPOSIZIONE QUALITATIVA E QUANTITATIVA
Ogni flaconcino contiene 100 mg di infliximab. Infliximab è un anticorpo monoclonale umano-murino chimerico IgG1prodotto con tecnologia DNA ricombinante. Dopo ricostituzione, ogni ml contiene 10 mg di infliximab.
INFORMAZIONI CLINICHE
Indicazioni terapeutiche

Artrite reumatoide
Remicade, in associazione con metotrexato, è indicato per: la riduzione dei segni e dei sintomi e il miglioramento della funzionalità in:
• pazienti con malattia in fase attiva quando la risposta ai farmaci anti-reumatici che modificano la malattia (DMARDs *disease-modifying anti-rheumatic drugs*), incluso il metotrexato, sia stata inadeguata.
• pazienti con malattia grave, in fase attiva e progressiva non trattata precedentemente con metotrexato o altri DMARDs.
In questa popolazione di pazienti è stato dimostrato, mediante valutazione radiografica, un rallentamento della progressione del danno articolare.

Malattia di Crohn negli adulti
Malattia di Crohn nei bambini
Colite ulcerosa

Spondilite anchilosante
Remicade è indicato per:
il trattamento della spondilite anchilosante grave in fase attiva in pazienti adulti che non hanno risposto in modo adeguato alle terapie convenzionali.
Artrite psoriasica
Remicade è indicato per il trattamento dell'artrite psoriasica attiva e progressiva in pazienti adulti qualora sia stata inadeguata la risposta a precedenti trattamenti con DMARD. Remicade deve essere somministrato:
- in associazione con metotrexato
- o singolarmente in pazienti che risultano intolleranti al metotrexato o per i quali esso sia controindicato Remicade ha mostrato di migliorare la funzione fisica in pazienti con artrite psoriasica e di ridurre la velocità di progressione del danno alle articolazioni periferiche, misurato con i raggi X in pazienti con sottotipi simmetrici poliarticolari della malattia.
Psoriasi

Scheda tecnica Enbrel

DENOMINAZIONE DEL MEDICINALE

Enbrel 25 mg polvere e solvente per soluzione iniettabile.

COMPOSIZIONE QUALITATIVA E QUANTITATIVA

Ciascun flaconcino contiene 25 mg di etanercept. Etanercept è una proteina di fusione del recettore umano p75 del fattore di necrosi tumorale con la frazione Fc, ottenuta tramite tecniche di DNA ricombinante attraverso un sistema mammifero di espressione in cellule ovariche di criceto Cinese (CHO).

INFORMAZIONI CLINICHE

Indicazioni terapeutiche

Artrite reumatoide

Enbrel in combinazione con metotressato è indicato per il trattamento dell'artrite reumatoide in fase attiva da moderata a grave negli adulti quando la risposta ai farmaci antireumatici modificanti la malattia metotressato incluso (a meno che controindicato), è risultata inadeguata. Enbrel può essere utilizzato in **monoterapia** in caso di intolleranza al metotressato o quando il trattamento continuo con il metotressato è inappropriato. Enbrel è anche indicato nel trattamento dell'artrite reumatoide grave, attiva e progressiva negli adulti non trattati precedentemente con metotressato. Enbrel, da solo o in combinazione con metotressato, ha dimostrato di ridurre il tasso di progressione del danno delle articolazioni, come misurato radiograficamente, e di migliorare la funzione fisica.

Artrite giovanile poliarticolare idiopatica

Trattamento dell'artrite giovanile poliarticolare idiopatica attiva in bambini e adolescenti di età comprese tra i 4 ed i 17 anni che hanno mostrato una risposta inadeguata, o che sono risultati intolleranti al metotressato. Enbrel non è stato studiato su bambini di età inferiore ai 4 anni.

Artrite psoriasica

Trattamento dell'artrite psoriasica in fase attiva e progressiva negli adulti, quando la risposta ai farmaci antireumatici modificanti la malattia è risultata inadeguata. Enbrel ha dimostrato di migliorare la funzione fisica in pazienti con artrite psoriasica, e di ridurre la velocità di progressione del danno periferico alle articolazioni come da rilevazioni ai raggi X in pazienti con sottotipi simmetrici poliarticolari della malattia.

Spondilite anchilosante

Trattamento della spondilite anchilosante severa in fase attiva negli adulti che hanno avuto una risposta inadeguata alla terapia convenzionale.

Psoriasi a placche

Scheda tecnica Humira

DENOMINAZIONE DEL MEDICINALE

Humira 40 mg soluzione iniettabile.

COMPOSIZIONE QUALITATIVA E QUANTITATIVA

Ciascun flaconcino da 0,8 ml contiene 40 mg di adalimumab. Adalimumab è un anticorpo monoclonale umano ricombinante espresso in cellule ovariche di criceto cinese (Chinese Hamster Ovary).

INFORMAZIONI CLINICHE

Indicazioni terapeutiche

Artrite reumatoide

Humira, in combinazione con metotressato, è indicato per:

• il trattamento di pazienti adulti affetti da artrite reumatoide attiva di grado da moderato a grave quando la risposta ai farmaci anti-reumatici modificanti la malattia (Disease Modifying Antirheumatic Drugs – DMARDs), compreso il metotressato, risulta inadeguata.

• il trattamento dell'artrite reumatoide grave, attiva e progressiva in adulti non precedentemente trattati con metotressato.

Humira può essere somministrato come **monoterapia** in caso di intolleranza al metotressato o quando il trattamento continuato con metotressato non è appropriato. Humira, in combinazione con metotressato, inibisce la progressione del danno strutturale, valutata radiograficamente, e migliora la funzionalità fisica.

Artrite giovanile poliarticolare idiopatica

Humira in combinazione con metotressato è indicato per il trattamento dell'artrite giovanile poliarticolare idiopatica, in adolescenti di età compresa tra 13 e 17 anni, che hanno avuto una risposta inadeguata ad uno o più farmaci anti-reumatici modificanti la malattia (DMARDs). Humira può essere somministrato come monoterapia in caso di intolleranza al metotressato o quando il trattamento continuato con metotressato non è appropriato (vedere il paragrafo 5.1).

Artrite psoriasica

Humira è indicato per il trattamento dell'artrite psoriasica attiva e progressiva in soggetti adulti quando la risposta a precedenti trattamenti con farmaci anti-reumatici modificanti la malattia (Disease Modifying Anti-rheumatic Drugs – DMARDs) è stata inadeguata. E' stato dimostrato che Humira riduce la percentuale di progressione del danno articolare periferico associato rilevato attraverso radiografie in pazienti affetti da sottogruppi poliarticolari simmetrici della malattia (vedere il paragrafo 5.1) e migliora la funzionalità fisica.

Spondilite anchilosante

Humira è indicato per il trattamento dei pazienti adulti affetti da spondilite anchilosante attiva grave in cui la risposta alla terapia convenzionale non è risultata adeguata.

Malattia di Crohn

ASAS/EULAR recommendations for the management of ankylosing spondylitis

J Zochling, D van der Heijde, R Burgos-Vargas, E Collantes, J C Davis, Jr, B Dijkmans, M Dougados, P Géher, R D Inman, M A Khan, T K Kvien, M Leirisalo-Repo, I Olivieri, K Pavelka, J Sieper, G Stucki, R D Sturrock, S van der Linden, D Wendling, H Böhm, B J van Royen and J Braun

Ann Rheum Dis 2006;65;442-452; originally published online 26 Aug 2005; doi:10.1136/ard.2005.041137

Dissemination and evaluation of the ASAS/EULAR recommendations for the management of ankylosing spondylitis: results of a study among 1507 rheumatologists

L Gossec, M Dougados, C Phillips, M Hammoudeh, K de Vlam, K Pavelka, T Pham, J Braun, J Sieper, I Olivieri, D van der Heijde, E Collantes, M Stone, T K Kvien and on behalf of ASAS (ASsessment in AS international working group)

Ann Rheum Dis 2008;67;782-788; originally published online 29 Nov 2007; doi:10.1136/ard.2007.080077

Table 2 Experts' propositions developed through three Delphi rounds—order accordi to topic (general, non-pharmacological, pharmacological, invasive, and surgical)

No	Proposition
1	Treatment of AS should be tailored according to: ● Current manifestations of the disease (axial, peripheral, entheseal, extra-articular symptoms and sig ● Level of current symptoms, clinical findings, and prognostic indicators - Disease activity/inflammation - Pain - Function, disability, handicap - Structural damage, hip involvement, spinal deformities ● General clinical status (age, sex, comorbidity, concomitant drugs)

8 There is no evidence for the efficacy of DMARDs, including sulfasalazine and methotrexate, for the treatment of axial disease. Sulfasalazine may be considered in patients with peripheral arthritis

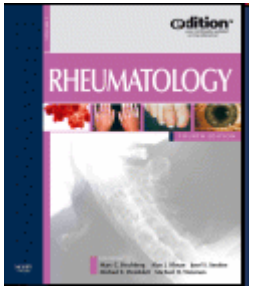
9 Anti-TNF treatment should be given to patients with persistently high disease activity despite conventional treatments according to the ASAS recommendations. There is no evidence to support the obligatory use of DMARDs before, or concomitant with, anti-TNF treatment in patients with axial disease

6	Analgesics, such as paracetamol and opioids, might be considered for pain control in patients in wh NSAIDs are insufficient, contraindicated, and/or poorly tolerated
7	Corticosteroid injections directed to the local site of musculoskeletal inflammation may be considered. use of systemic corticosteroids for axial disease is not supported by evidence
8	There is no evidence for the efficacy of DMARDs, including sulfasalazine and methotrexate, for the treatment of axial disease. Sulfasalazine may be considered in patients with peripheral arthritis
9	Anti-TNF treatment should be given to patients with persistently high disease activity despite conventio treatments according to the ASAS recommendations. There is no evidence to support the obligatory us DMARDs before, or concomitant with, anti-TNF treatment in patients with axial disease
10	Total hip arthroplasty should be considered in patients with refractory pain or disability and radiograp evidence of structural damage, independent of age. Spinal surgery—for example, corrective osteoton and stabilisation procedures, may be of value in selected patients

AS, ankylosing spondylitis; GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; DMARDs, dise modifying antirheumatic drugs; TNF, tumour necrosis factor.

ASsessment in AS international working group (ASAS)

European League Against Rheumatism (EULAR)



SPONDILITE ANCHILOSANTE

Anti-TNF-α blocking agents

The limited treatment options for AS patients discussed above mean that the demonstration of **good or very good efficacy of TNF-blockers in the treatment of patients with active AS** can be regarded as a **breakthrough in the therapy of AS**.

These drugs do not only improve signs and symptoms rapidly and in a high percentage of patients; they might even be capable of stopping bony destruction, as has already been shown in rheumatoid arthritis.

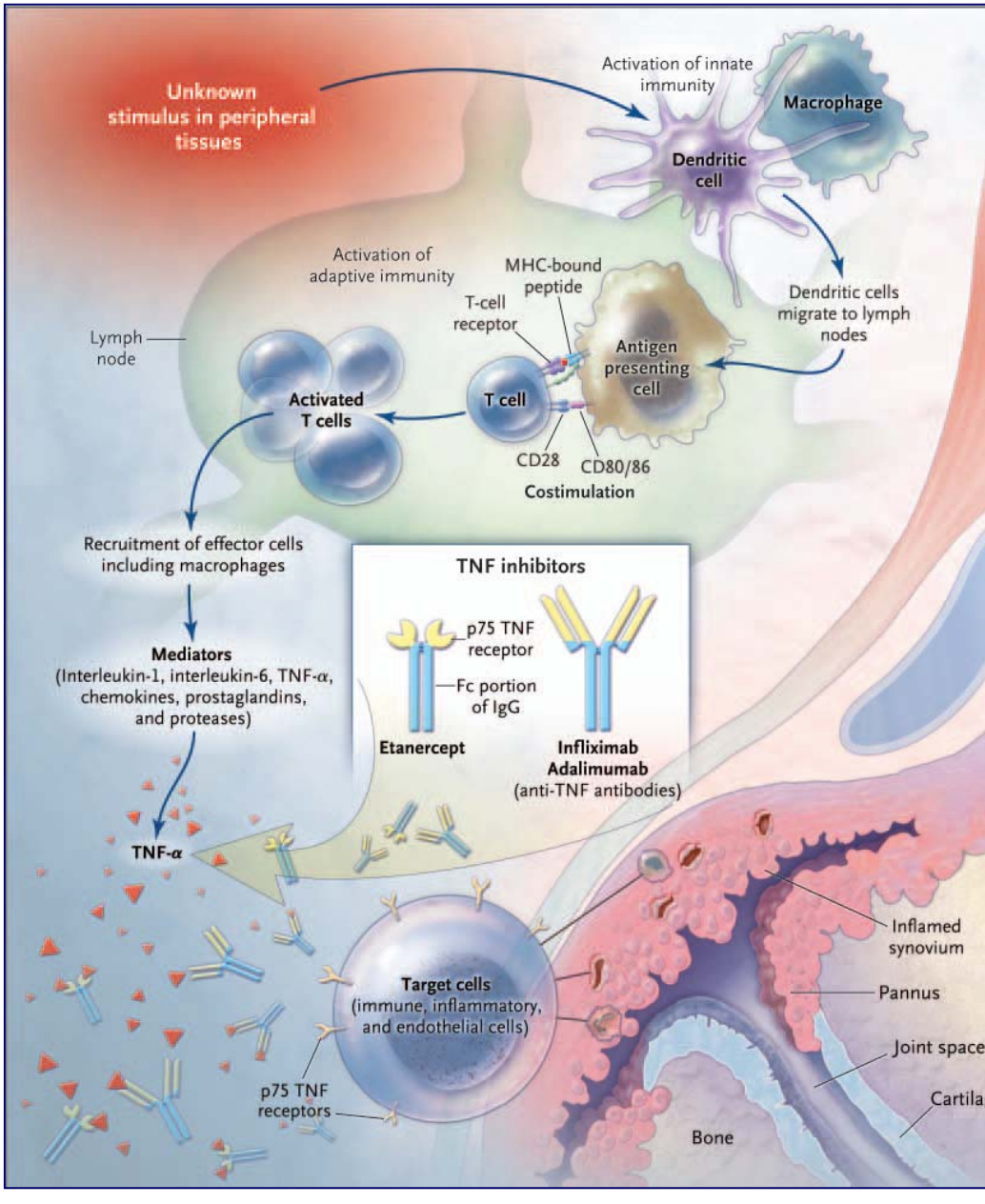
The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL THERAPEUTICS

Tumor Necrosis Factor Inhibitors for Rheumatoid Arthritis

D.L. Scott, M.D., and G.H. Kingsley, M.B., Ch.B., Ph.D.

- Infliximab
- Etanercept
- Adalimumab



ARTRITE REUMATOIDE - DEFINIZIONE

Poliartrite cronica bilaterale e simmetrica ad impronta erosiva che colpisce in modo prevalente, ma non esclusivo, le piccole articolazioni di mani e piedi.

Colpisce circa l'1% della popolazione con un rapporto ♀/♂ di 2-5:1

ARTRITE REUMATOIDE - DEFINIZIONE

Decorso clinico variabile, andando da forme lievi, autolimitantesi a forme rapidamente progressive di infiammazione multisistemica con importante morbilità e mortalità.

In molti casi l'inizio è insidioso, ma il decorso successivo è inesorabilmente progressivo.

Lee DM & Weinblatt ME. The Lancet 2001; 358: 903-911

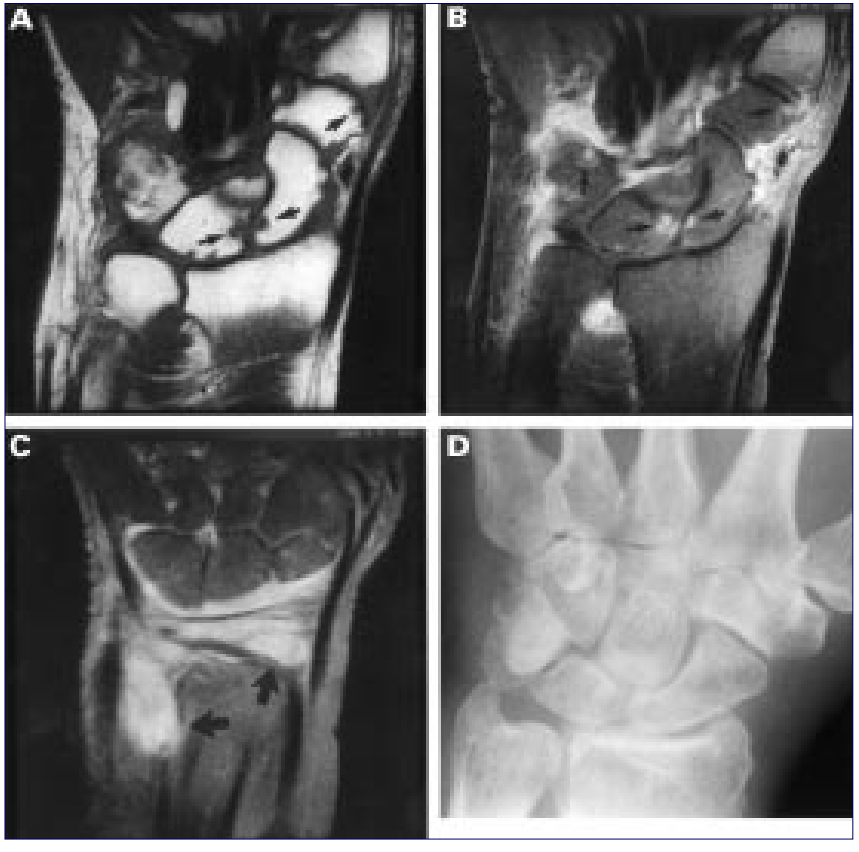
ARTRITE REUMATOIDE - DEFINIZIONE

La distruzione articolare può manifestarsi rapidamente nelle fasi precoci della malattia.

Una evidenza radiografica è presente in più del 70% dei pazienti entro i primi due anni di malattia.

Lee DM & Weinblatt ME. The Lancet 2001; 358: 903-911

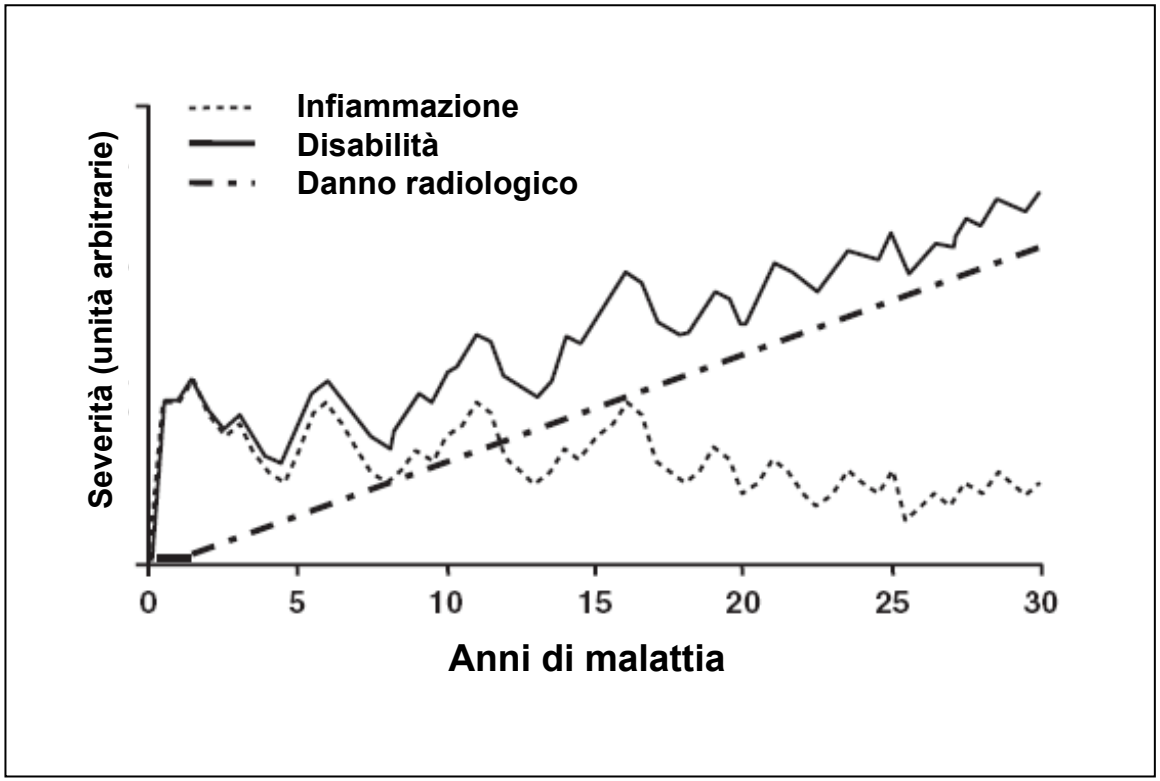
ARTRITE REUMATOIDE



Con la RM si possono identificare ipertrofia sinoviale, edema osseo e precoci erosioni già dopo quattro mesi di malattia.

*McQueen FM et al. Ann Rheum Dis 1998;**57**:350–356*

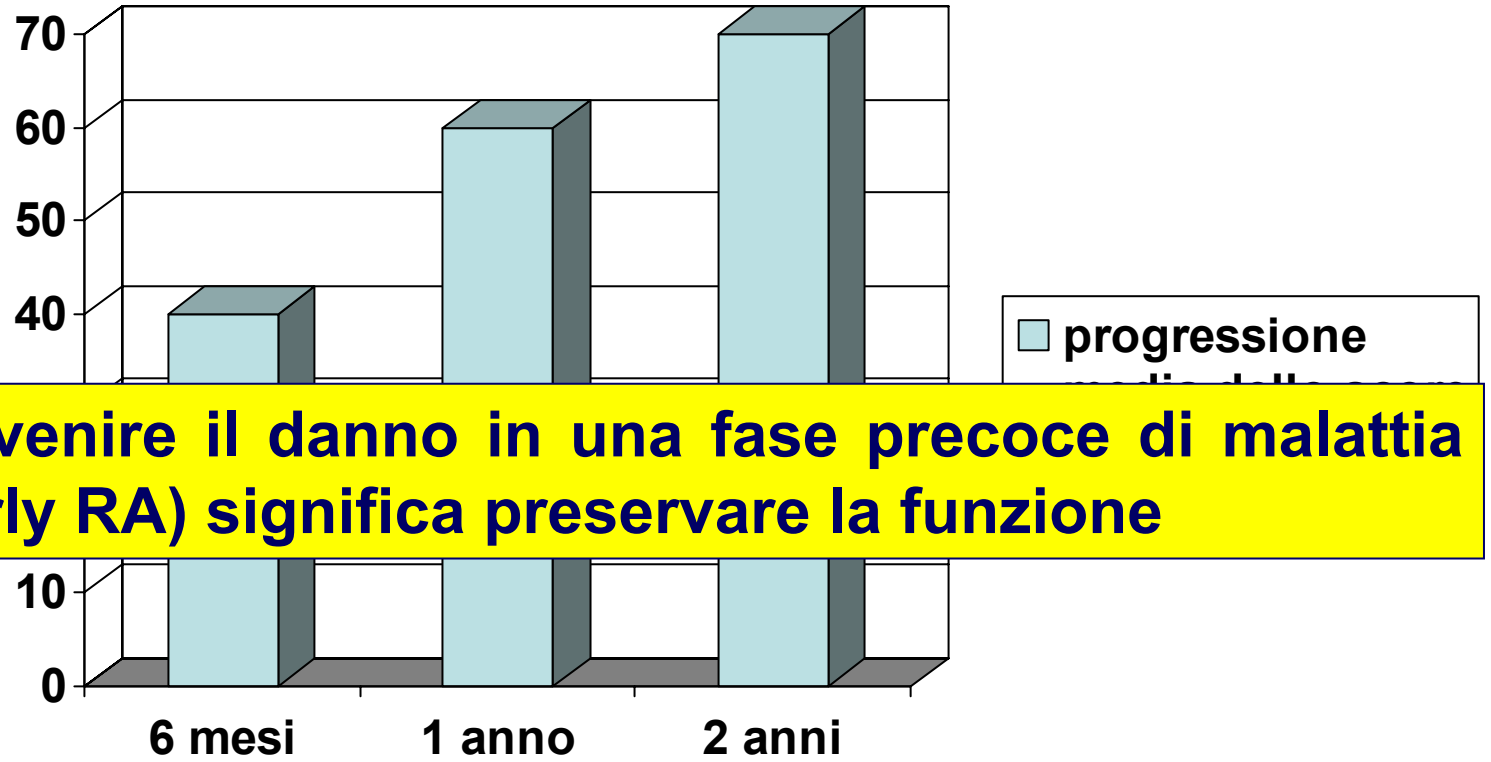
Progressione di malattia nell'artrite reumatoide



L'infiammazione costituisce il fattore che maggiormente contribuisce alla disabilità nelle fasi precoci di malattia, mentre la progressione radiologica domina la disabilità nelle fasi avanzate.

Kirwan JR. Links between radiological change, disability, and pathology in rheumatoid arthritis. J Rheumatol 2001;28:881–6

Progressione radiologica nell'artrite reumatoide



Prevenire il danno in una fase precoce di malattia (early RA) significa preservare la funzione

- I pazienti con AR hanno erosioni articolari precocemente
- Le erosioni rappresentano un danno strutturale permanente
- Il danno articolare progredisce rapidamente

Van der Heijde D. Br J Rheumatol 1995; 34 (suppll 2): 74-78

REVIEW ARTICLE

MECHANISMS OF DISEASE

FRANKLIN H. EPSTEIN, M.D., *Editor*

RHEUMATOID ARTHRITIS

Pathophysiology and Implications for Therapy

EDWARD D. HARRIS, JR., M.D.

IN 1947, a technician who had rheumatoid arthritis and who worked in the laboratory of Dr. Harry Rose at Columbia University discovered that her own serum agglutinated excessively. Dr. Rose suggested that this serologic reaction might have been caused by the arthritis. Charles Ragan, a rheumatologist, pursued this suggestion and developed the sheep-cell agglutination test,[1,2] which we know as a test for rheumatoid factor. For the first time, physicians had a key to the black box that was rheumatoid arthritis and could begin to study the immunologic abnormalities in patients with the disease. The classification of patients

agglutination in most tests for rheumatoid factor, the

subcutaneous nodules; a positive test for rheumatoid factor; and radiographic evidence of erosions, periarticular osteopenia, or both in the joints of the hand, wrist, or both.

To make a diagnosis of rheumatoid arthritis, at least the first four symptoms must have been present for six or more weeks. These new criteria demonstrate 91 to 94 percent sensitivity and 89 percent specificity for the diagnosis of rheumatoid arthritis, as compared with that of rheumatic disease unrelated to rheumatoid arthritis in control subjects.[7] It is worth emphasizing that the diagnosis of rheumatoid arthritis should not be made on the basis of these criteria alone if another systemic disease associated with arthritis is definitely present. The conditions most likely to be confused with early-onset rheumatoid arthritis include systemic lupus erythematosus, psoriatic arthritis and other seronegative spondyloarthropathies, mixed connective-tissue disease, Reiter's syndrome, polymyalgia rheumatica, and Sjögren's syndrome with polyarthritis.

To treat patients with rheumatoid arthritis more effectively, it is essential to determine the pathobiologic phase of the disease (Table 1). The following sections correlate the disease's pathobiologic, clinical,

options available in 1990 will be contrasted with those

(Harris E.D., Jr.: "Rheumatoid Arthritis. Pathophysiology and Implicatios for Therapy". - N Engl J Med: 322, 1277-1289, 1990)

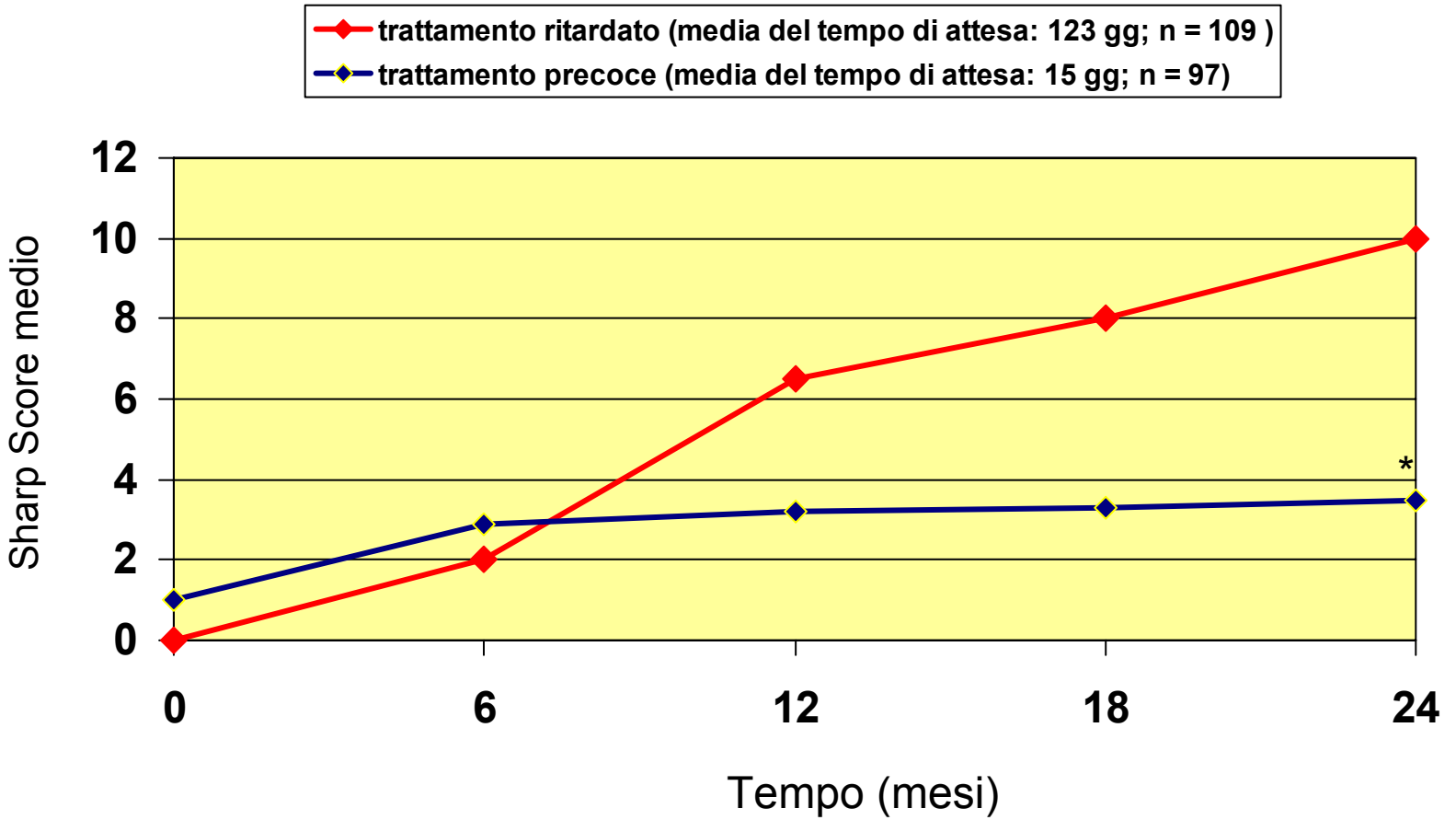
Table 1. The Stages of Rheumatoid Arthritis.

STAGE	PATHOLOGIC PROCESS	SYMPTOMS	PHYSICAL SIGNS	RADIOGRAPHIC CHANGES*
1	Presentation of antigen to T cells	Probably none	—	—
2	T-cell proliferation B-cell proliferation Angiogenesis in synovial membrane	Malaise, mild joint stiffness and swelling	Swelling of small joints of hands or wrists, or pain in hands, wrists, knees, and feet	None
3	Accumulation of neutrophils in synovial fluid Synovial-cell proliferation without polarization or invasion of cartilage	Joint pain and swelling, morning stiffness, malaise and weakness	Warm, swollen joints, excess synovial fluid, soft-tissue proliferation within joints, pain and limitation of motion, rheumatoid nodules	Soft-tissue swelling
4				
5	joints	phalangeal joints)	complications	

tion of articular cartilage. It follows that effective therapy must be instituted during stages 2 and 3 if the irreversible loss of articular cartilage is to be prevented.

*MRI denotes magnetic resonance imaging.

Trattamento precoce con DMARDs



(*) p < 0.05 vs gruppo a trattamento ritardato

Lard LR et al. Am J Med 2001; 111: 446-51

ARTHRITIS & RHEUMATISM
Vol. 46, No. 2, February 2002, pp 347–356
DOI 10.1002/art.10083

Published by Wiley-Liss, Inc.

COBRA Combination Therapy in Patients With Early Rheumatoid Arthritis

Long-Term Structural Benefits of a Brief Intervention

Robert B. M. Landewé,[1] Maarten Boers,[2] Arco C. Verhoeven,[1] Rene Westhovens,[3] Mart A. F. J. van de Laar,[4] Harry M. Markusse,[5] J. Christiaan van Denderen,[6] Marie Louise Westedt,[7] Andre J. Peeters,[8] Ben A. C. Dijkmans,[2] Piet Jacobs,[9] Annelies Boonen,[1] Désirée M. F. M. van der Heijde,[1] and Sjef van der Linden[1]

Objective. **The Combinatietherapie Bij Reumatoide Artritis (COBRA) trial demonstrated that step-down combination therapy with prednisolone, methotrexate, and sulfasalazine (SSZ) was superior to SSZ monotherapy for suppressing disease activity and radiologic progression of rheumatoid arthritis (RA). The current study was conducted to investigate whether the benefits of COBRA therapy were sustained over time, and to determine which baseline factors could predict outcome.**

Methods. **All patients had participated in the 56-week COBRA trial. During followup, they were seen by their own rheumatologists and were also assessed regularly by study nurses; no treatment protocol was specified. Disease activity, radiologic damage, and functional ability were the primary outcome domains. Two independent assessors scored radiographs in sequence according to the Sharp/van der Heijde method. Outcomes were analyzed by generalized estimating equations on the basis of intent-to-treat, starting with data obtained at the last visit of the COBRA trial (56 weeks after baseline).**

Results. **At the beginning of followup, patients in the COBRA group had a significantly lower mean time-averaged 28-joint disease activity score (DAS28) and a significantly lower median radiologic damage (Sharp) score compared with those in the SSZ monotherapy group. The functional ability score (Health Assessment Questionnaire [HAQ]) was similar in both groups. During the 4–5 year followup period, the time-averaged DAS28 decreased 0.17 points per year in the SSZ group and 0.07 in the COBRA group. The Sharp progression rate was 8.6 points per year in the SSZ group and 5.6 in the COBRA group. After adjustment for differences in treatment and disease activity during followup, the between-group difference in the rate of radiologic progression was 3.7 points per year. The HAQ score did not change significantly over time. Independent baseline predictors of radiologic progression over time (apart from treatment allocation) were rheumatoid factor positivity, Sharp score, and DAS28.**

Conclusion. **An initial 6-month cycle of intensive combination treatment that includes high-dose corticosteroids results in sustained suppression of the rate of radiologic progression in patients with early RA, independent of subsequent antirheumatic therapy.**

ARTHRITIS & RHEUMATISM
Vol. 46, No. 4, April 2002, pp 894–898
DOI 10.1002/art.10135

Delay to Institution of Therapy and Induction of Remission Using Single-Drug or Combination–Disease-Modifying Antirheumatic Drug Therapy in Early Rheumatoid Arthritis

Timo Möttönen,[1] Pekka Hannonen,[2] Markku Korpela,[3] Martti Nissilä,[4] Hannu Kautiainen,[4] Jorma Ilonen,[5] Leena Laasonen,[6] Oili Kaipiainen-Seppänen,[7] Per Franzen,[8] Tapani Helve,[6] Juhani Koski,[9] Marianne Gripenberg-Gahmberg,[8] Riitta Myllykangas-Luosujärvi,[7] and Marjatta Leirisalo-Repo,[6] for the FIN-RACo Trial Group

Objective. To study the impacts of 1) the delay from the onset of symptoms to the institution of disease-modifying antirheumatic drug (DMARD) therapy, 2) two treatment strategies (treatment with a combination of DMARDs or with a single drug), and 3) the presence of HLA–DRB1 alleles (shared epitope) on the prediction of disease remission after 2 years in patients with early rheumatoid arthritis (RA).

Methods. In the FIN-RACo (FINnish Rheumatoid Arthritis Combination therapy) trial, 195 patients with recent-onset RA (median duration 6 months) were randomly assigned to receive either 1) a combination of DMARDs (sulfasalazine, methotrexate, hydroxychloroquine, and prednisolone) or 2) a single DMARD with or without prednisolone. The presence of a shared epitope was tested for in 165 of the 178 patients completing the study. The additional variables of age, sex, presence of rheumatoid factor, number of fulfilled American College of Rheumatology criteria for the classification of RA, and length of delay from onset of symptoms to institution of therapy were entered into a logistic regression model to determine the significant predictors for remission at 2 years.

Results. The delay to therapy (cut point of 4 months) was the only significant predictor for remission in patients treated using the single-DMARD strategy, while no variable was a significant predictor for remission in those treated using the combination-DMARD strategy. The frequency of achieving remission in the combination-DMARD group after 2 years was similar in patients with short (0–4 months) and long (>4 months) delay periods (11 of 26 patients and 22 of 53 patients, respectively [~42% in each group]), while the corresponding frequencies in the single-DMARD group were 8 of 23 patients (35%) and 7 of 63 patients (11%) ($P = 0.021$). The presence of a shared epitope was not related to the induction of remission.

Conclusion. The delay of a few months from the onset of symptoms to institution of therapy decreases the ability of the traditional single-drug strategy to induce remission in early RA.

DIAGN

RAP-RA

(Resistant Aggressive Progressive-Rheumatoid Arthritis)

TOIDE

ARD ONLINE

EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)

B Combe, R Landewe, C Lukas, H D Bolosiu, F Breedveld, M Dougados, P Emery, G Ferraccioli, J M W Hazes, L Klareskog, K Machold, E Martin-Mola, H Nielsen, A Silman, J Smolen and H Yazici

Ann Rheum Dis 2007;66;34-45; originally published online 5 Jan 2006; doi:10.1136/ard.2005.044354

RAP - RA

Se durata > 4 mesi e presenza di fattori di aggressività e progressione:

- Presenza di fattore reumatoide IgM or IgA
- Elevati livelli di VES e PCR
- Numero di articolazioni tumefatte > 9
- Precoce evidenza radiologica di erosioni
- Presenza di antiocorpi anti-CCP
- Presenza dei HLADRB1*0401 e DRB1*0404

Recommendation 4

ARD ONLINE

EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)

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Ann Rheum Dis 2007;66;34-45; originally published online 5 Jan 2006; doi:10.1136/ard.2005.044354

Recommendation 5

Patients at risk of developing persistent and/or erosive arthritis should be started with DMARDs as early as possible even if they do not yet fulfil established classification criteria for inflammatory rheumatological diseases.

Concetto di "*window of opportunity*"

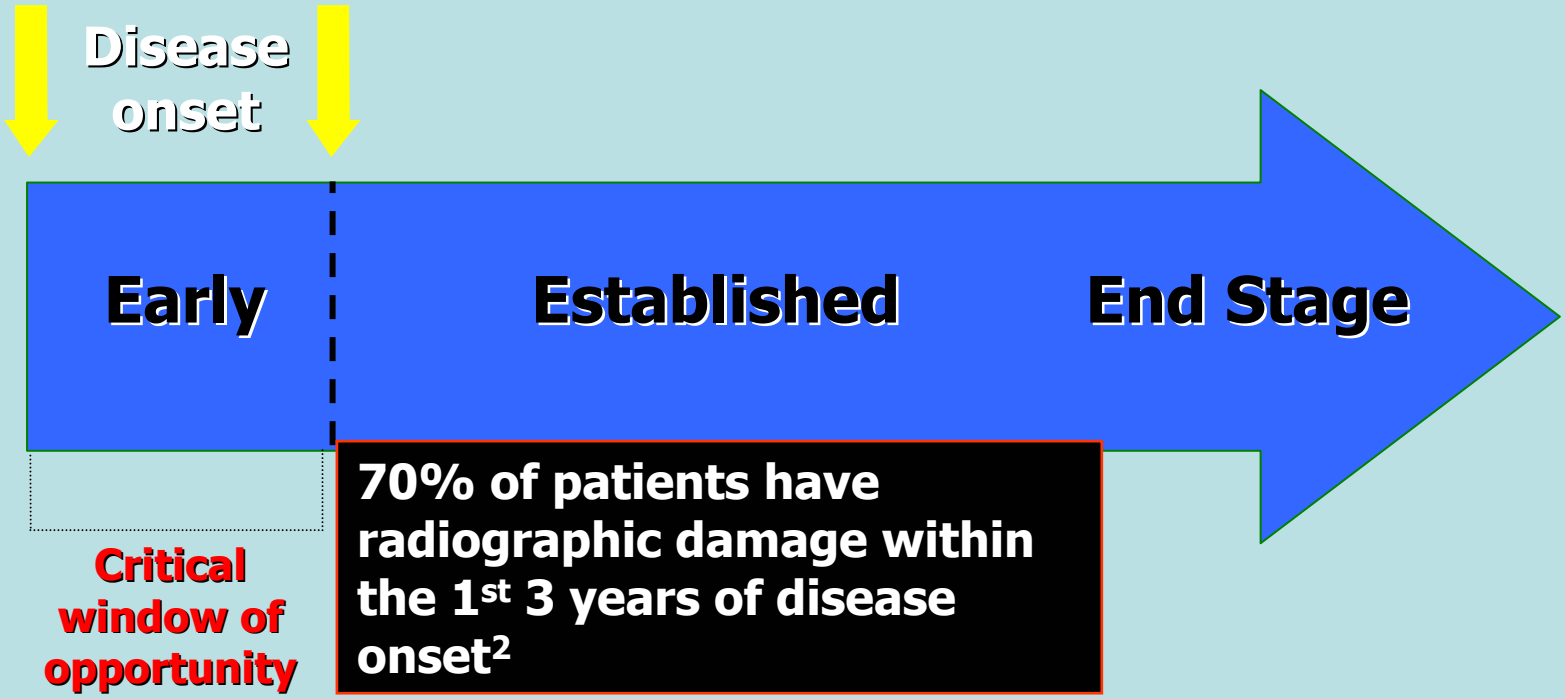
Una metanalisi: *Anderson JJ, Wells G, et al. Arthritis Rheum 2000;43:22–9*

Sei RCTs:
Van der Heide A, Jacobs JW, et al. Ann Intern Med 1996;124:699–707
Buckland-Wright JC, Clarke GS, et al. J Rheumatol 1993;20:243–7
Tsakonas E, Fitzgerald AA, et al. J Rheumatol 2000;27:623–9
Egsmose C, Lund B, et al. J Rheumatol 1995;22:2208–13
Mottonen T, Hannonen P, et al. Arthritis Rheum 2002;46:894–8
Choy EH, Scott DL, et al. Clin Exp Rheumatol 2002;20:351–8

ACR Recommendations: Early Aggressive Treatment of RA

"Successful treatment to limit joint damage and functional loss requires early diagnosis and timely initiation of disease modifying agent. The goal of treatment is to arrest the disease and achieve remission."[1]

American College of Rheumatology (ACR)
Ad Hoc Committee on Clinical Guidelines



1. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines *Arthritis Rheum.* 2002;46:328-346.
2. van der Heijde DM. *Br J Rheumatol.* 1995;10:435-453.

MTX:

Rau R, Herborn G, Menninger H, Sangha O. Radiographic outcome after three years of patients with early erosive rheumatoid arthritis treated with intramuscular methotrexate or parenteral gold. Extension of a one-year double-blind study in 174 patients. Rheumatology (Oxford). 2002 Feb;41(2):196-204.

Sharp JT, Strand V, Leung H, Hurley F, Loew-Friedrich I. Treatment with leflunomide slows radiographic progression of rheumatoid arthritis: results from three randomized controlled trials of leflunomide in patients with active rheumatoid arthritis. Leflunomide Rheumatoid Arthritis Investigators Group. Arthritis Rheum 2000;43:495–505.

F. Atzeni, P. Sarzi-Puttini. Artrite reumatoide all'esordio. Early rheumatoid arthritis. Reumatismo, 2007; 59(2):100-117

B Combe, R Landewe, C Lukas, H D Bolosiu, F Breedveld, M Dougados, P Emery, G Ferraccioli, J M W Hazes, L Klareskog, K Machold, E Martin-Mola, H Nielsen, A Silman, J Smolen, H Yazici. EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2007;66:34–45. doi: 10.1136/ard.2005.044354

SSZ:

Hannonen P, Mottenen T, Hakola M, Oka M. Sulfasalazine in early rheumatoid arthritis: a 48 week double-blind, prospective, placebo-controlled study. Arthritis Rheum 1993; 36: 1501-9.

The Australian Multicentre clinical trial group. Sulfasalazine in early RA. J Rheumatol 1992; 19: 1672-7.

CSA:

Van den Borne BE, Landewe RB, The HS, Breedveld FC, Dijkmans BA. Low dose cyclosporin in early rheumatoid arthritis: effective and safe after two years of therapy when compared to chloroquine. Scand J Rheumatol 1996; 25: 307-16.

LNF:

Sharp JT, Strand V, Leung H, Hurley F, Loew-Friedrich I. Treatment with leflunomide slows radiographic progression of rheumatoid arthritis: results from three randomized controlled trials of leflunomide in patients with active rheumatoid arthritis. Leflunomide Rheumatoid Arthritis Investigators Group. Arthritis Rheum 2000; 43:495–505

Smolen JS, Kalden JK, Scott DL, Rozman B, Kvien TK, Larsen A,et al. Efficacy and safety of leflunomide compared with placebo and sulphasalazine in active rheumatoid arthritis: a double-blind, randomised, multicentre trial. Lancet 1999; 353: 259-66.

Strand V, Cohen S, Schiff M, Weaver A, Fleisch R, Cannon G, et al. for the Leflunomide Rheumatoid Arthritis nvestigators group. Treatment of active rheumatoid arthritis with leflunomide compared with placebo and methotrexate. Arch Intern Med 1999; 159: 2542-50.

ARD ONLINE

EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)

B Combe, R Landewe, C Lukas, H D Bolosiu, F Breedveld, M Dougados, P Emery, G Ferraccioli, J M W Hazes, L Klareskog, K Machold, E Martin-Mola, H Nielsen, A Silman, J Smolen and H Yazici

Ann Rheum Dis 2007;66;34-45; originally published online 5 Jan 2006; doi:10.1136/ard.2005.044354

Recommendation 9

Among the DMARDs, methotrexate is considered the anchor drug and should be used first in patients at risk of developing persistent disease.

Il metotressato è pressoché sovrapponibile in termini di efficacia ai farmaci anti-TNF alfa in monoterapia in pazienti con early (durata inferiore a tre anni) severe rheumatoid arthritis

- *Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, Keystone EC, et al. A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. N Engl J Med 2000;343:1586–93.*

- *Breedveld FC, Kavanaugh AF, Cohen SB, Pavelka K, van Vollenhoven R, Perez JL, et al. Early treatment of rheumatoid arthritis with adalumimab plus methotrexate vs adalumimab alone or methotrexate alone: the PREMIER study. Arthritis Rheum 2006;54:26–37.*

RCTs hanno dimostrato una maggiore efficacia dell'associazione farmaci anti-TNF + metotressato rispetto alla monoterapia.

- *Klareskog L, van der Heijde D, de Jager JP, Gough A, Kalden J, Malaise M, et al. Therapeutic effect of the combination of **etanercept** and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial. Lancet 2004;363:675–81. (**STUDIO TEMPO**)*

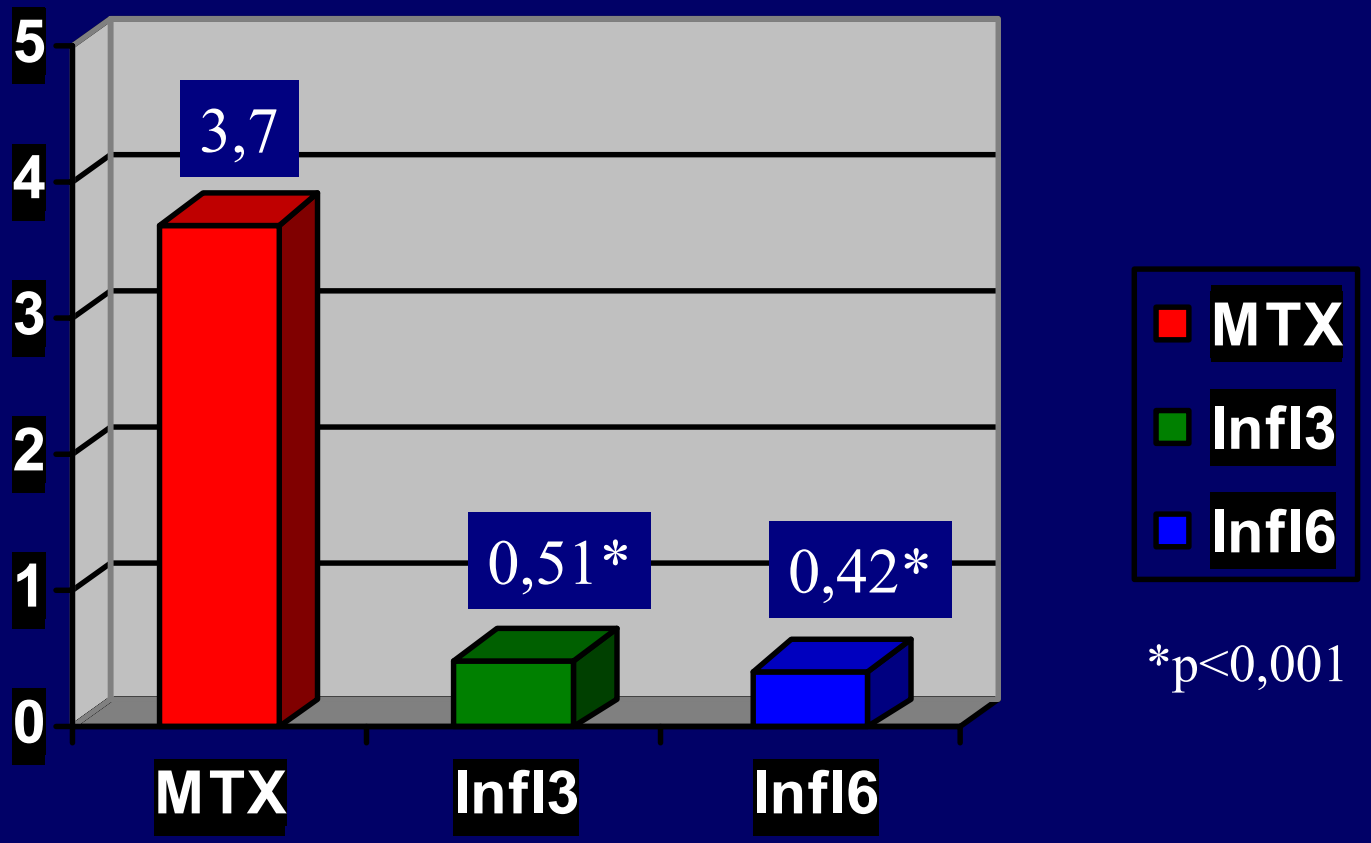
- *Breedveld FC, Kavanaugh AF, Cohen SB, Pavelka K, van Vollenhoven R, Perez JL, et al. Early treatment of rheumatoid arthritis with **adalumimab** plus methotrexate vs adalumimab alone or methotrexate alone: the **PREMIER study**. Arthritis Rheum 2006;54:26–37.*

- *St Clair EW, van der Heijde DM, Smolen JS, Maini RN, Bathon JM, Emery P, et al. Combination of **infliximab** and methotrexate therapy for early rheumatoid arthritis: a randomized, controlled trial. Arthritis Rheum 2004;50:3432–43. (**STUDIO ASPIRE**)*

- *Quinn MA, Conaghan PG, O'Connor PJ, Karim Z, Greenstein A, Brown A, et al. Very early treatment with **infliximab** in addition to methotrexate in early, poor-prognosis rheumatoid arthritis reduces magnetic resonance imaging evidence of synovitis and damage, with sustained benefit after infliximab withdrawal: results from a twelve-month randomized, double-blind, placebo controlled trial. Arthritis Rheum 2005;52:27–35.*

Studio ASPIRE
ENDPOINT primario - Risultati radiografici

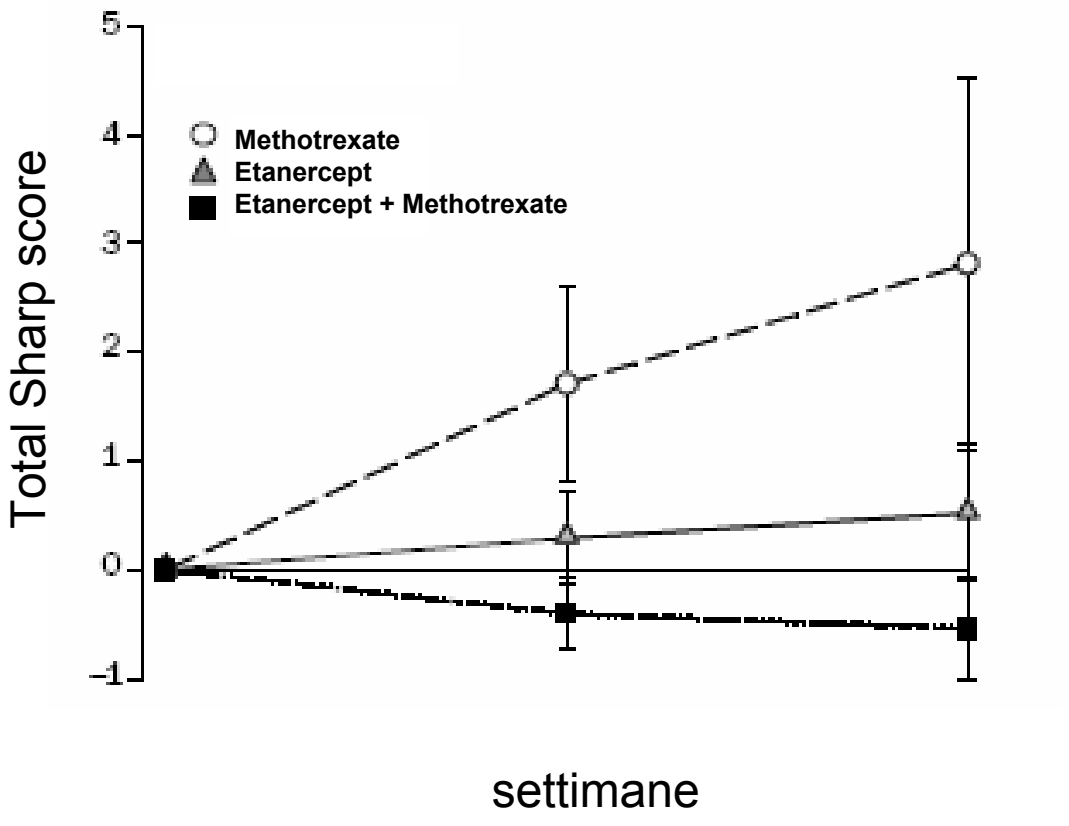
Variazione del VdH modif Sharp score a 54 wks



*p<0,001

St Clair EW, van der Heijde DM, Smolen JS, Maini RN, Bathon JM, Emery P, et al. Combination of ***infliximab*** and methotrexate therapy fo

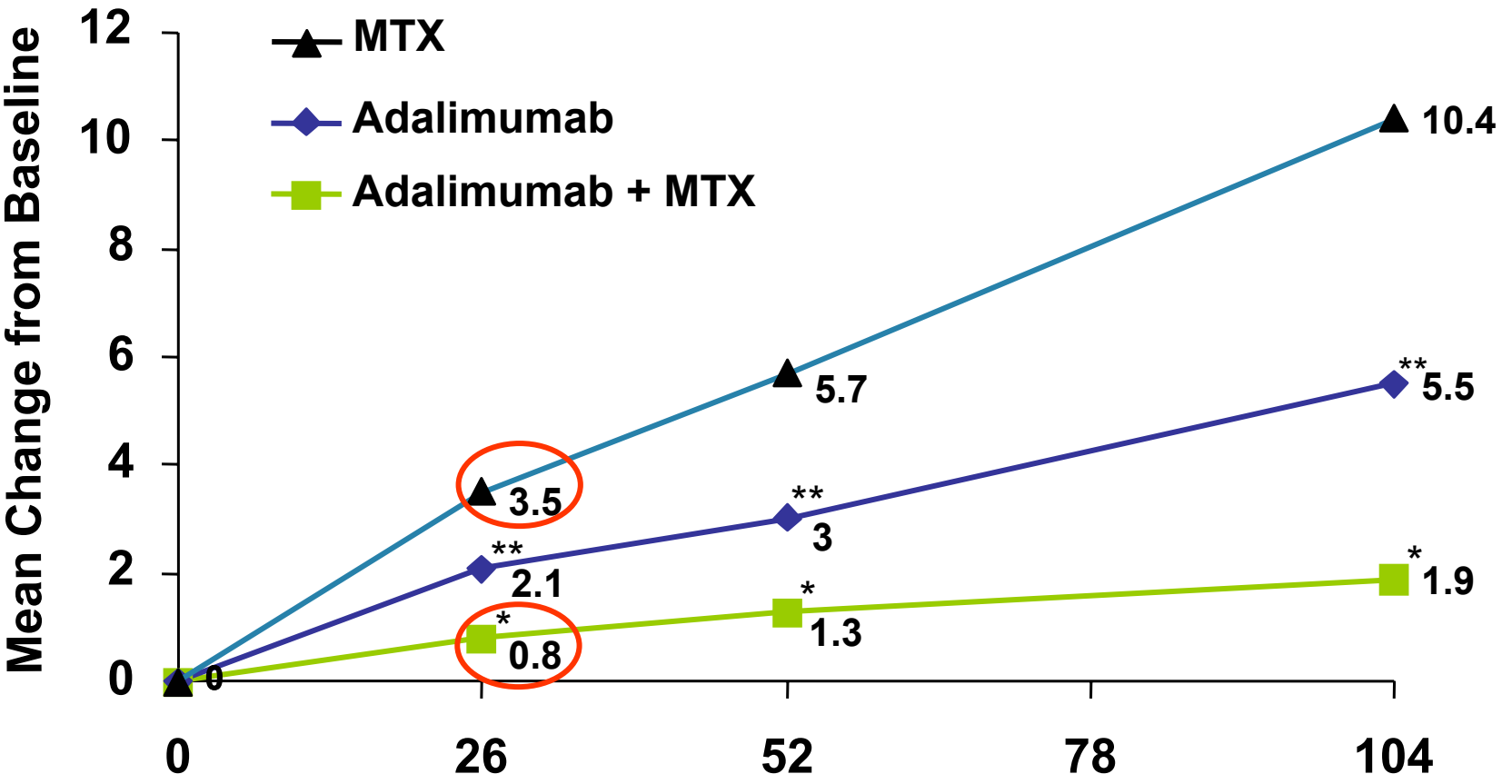
STUDIO TEMPO



•*Klareskog L, van der Heijde D, et al. Lancet 2004;363:675–81*

STUDIO PREMIER

Inhibition of Disease Progression – Total Sharp Score

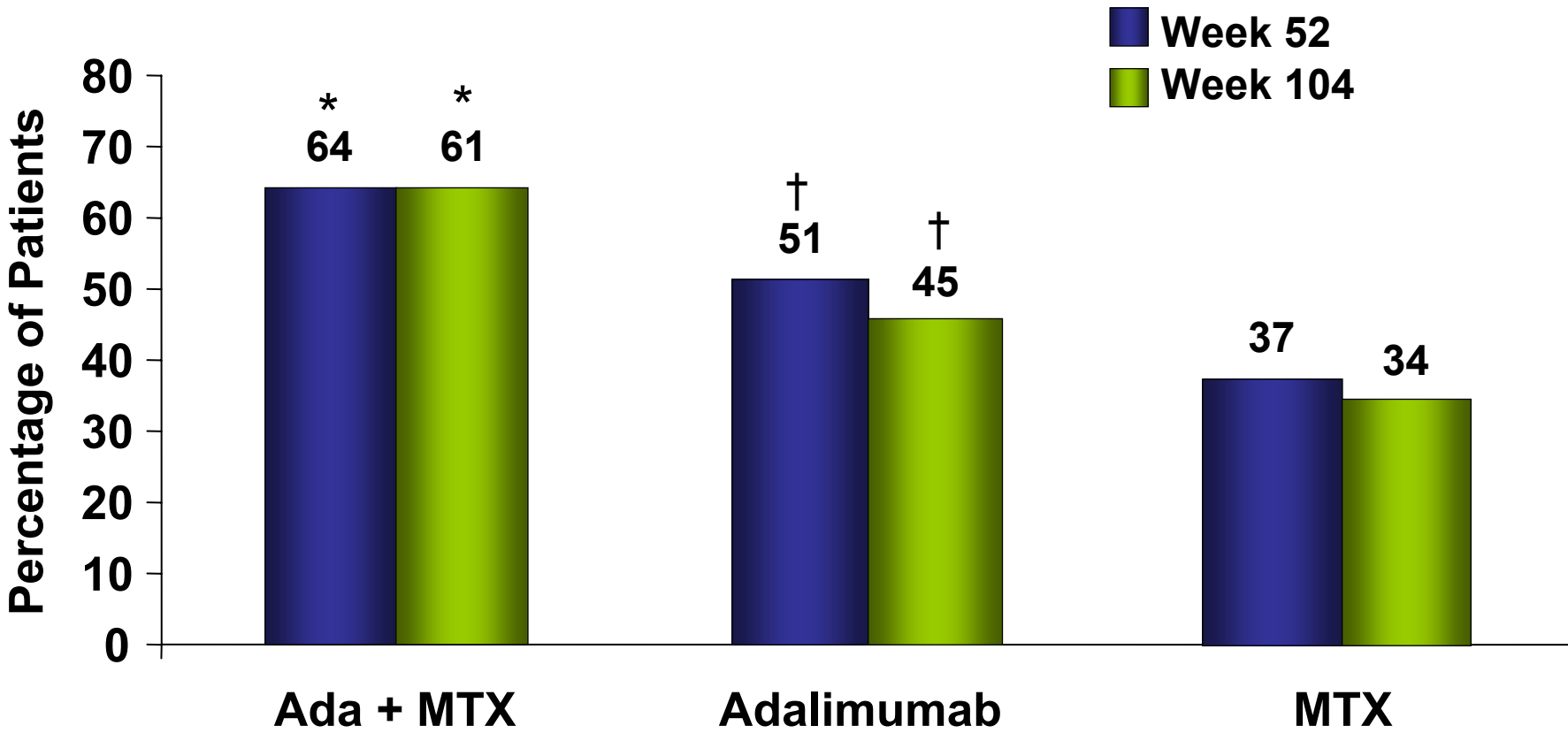


*p<0.001 for HUMIRA + MTX vs MTX alone and HUMIRA alone; **p<0.001 for HUMIRA vs MTX alone

Breedveld FC, et al. Arthritis Rheum 2006;54:26–37

STUDIO PREMIER

Percentage of Patients With no Radiographic Progression



*p<0.01 for adalimumab + MTX vs MTX alone and adalimumab alone; †p<0.01 for adalimumab vs MTX
ΔTSS ≤0.5

Breedveld FC, et al. Arthritis Rheum 2006;54:26–37

L’obiettivo terapeutico attuale è quello di ottenere la remissione dei sintomi allo scopo di prevenire il danno strutturale e la disabilità nel lungo temine.

ARTHRITIS & RHEUMATISM
Vol. 46, No. 2, February 2002, pp 347–356
DOI 10.1002/art.10083

Published by Wiley-Liss, Inc.

COBRA Combination Therapy in Patients With Early Rheumatoid Arthritis

Long-Term Structural Benefits of a Brief Intervention

Una **associazione di methotrexate e sulfasalazina** con **dosi elevate di steroidi** in una strategia terapeutica *step-down* ha determinato effetti protratti nel tempo sulla progressione radiologica, in confronto ad una monoterapia con sulfasalazina in 155 pazienti con early rheumatoid arthritis.

• *Landewe RB, Boers M, Verhoeven AC, Westhovens R, van de Laar MA, Markusse HM, et al. COBRA combination therapy in patients with early rheumatoid arthritis: long-term structural benefits of a brief intervention. Arthritis Rheum 2002; 46:347–56*

• *Boers M, Verhoeven AC, Markusse HM, van de Laar MA, Westhovens R, vanDenderen JC, et al. Randomised comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. Lancet 1997;350:309–18.*

ARTHRITIS & RHEUMATISM
Vol. 46, No. 4, April 2002, pp 894–898
DOI 10.1002/art.10135

Delay to Institution of Therapy and Induction of Remission Using Single-Drug or Combination–Disease-Modifying Antirheumatic Drug Therapy in Early Rheumatoid Arthritis

FIN-RACo study

197 pazienti con AR iniziata entro i precedenti due anni erano randomizzati a ricevere o un regime a quattro farmaci con methotrexate, sulfasalazina, idrossiclorochina e prednisolone (5 mg/d) oppure un singolo DMARD.

Dopo 18 mesi, una maggiore percentuale di pazienti nel *gruppo combination therapy* era in remissione.
Dopo 5 anni il *gruppo combination* aveva dimostrato una minore progressione radiologica e una minore disabilità.

Korpela M, Laasonen L, Hannonen P, Kautiainen H, Leirisalo-Repo M, Hakala M, et al. Retardation of joint damage in patients with early rheumatoid arthritis by initial aggressive treatment with disease-modifying antirheumatic drugs: five-year experience from the FIN-RACo study. Arthritis Rheum 2004;50:2072–81.

• *Mottonen T, Hannonen P, Leirisalo-Repo M, Nissila M, Kautiainen H, Korpela M, et al. Comparison of combination therapy with single-drug therapy in early rheumatoid arthritis: a randomised trial. FIN-RACo trial group. Lancet 1999;353:1568–73.*

• *Puolakka K, Kautiainen H, Mottonen T, Hannonen P, Korpela M, Julkunen H, etal. Impact of initial aggressive drug treatment with a combination of disease modifying antirheumatic drugs on the development of work disability in early rheumatoid arthritis: a five-year randomized followup trial. Arthritis Rheum 2004;50:55–62.*

Agenti TNF bloccanti
(in combinazione con methotrexate versus methotrexate in monoterapia) nella *early rheumatoid arthritis*

Un intervento intensivo e precoce nel corso di una artrite persistente, ma comunque di durata inferiore a tre anni, è determinante nel **rallentare in maniera significativa la progressione radiologica nel lungo termine** nell'aumentare la percentuale di individui in stato di remissione clinica.

• *Breedveld FC, Kavanaugh AF, Cohen SB, Pavelka K, van Vollenhoven R, Perez JL, et al. Early treatment of rheumatoid arthritis with **adalumimab** plus methotrexate vs adalumimab alone or methotrexate alone: the **PREMIER study**. Arthritis Rheum 2006;54:26–37.*

• *St Clair EW, van der Heijde DM, Smolen JS, Maini RN, Bathon JM, Emery P, et al. Combination of **infliximab** and methotrexate therapy for early rheumatoid arthritis: a randomized, controlled trial. Arthritis Rheum 2004;50:3432–43 (**STUDIO ASPIRE**)*

• *Quinn MA, Conaghan PG, O'Connor PJ, Karim Z, Greenstein A, Brown A, et al. Very early treatment with **infliximab** in addition to methotrexate in early, poor-prognosis rheumatoid arthritis reduces magnetic resonance imaging evidence of synovitis and damage, with sustained benefit after infliximab withdrawal: results from a twelve-month randomized, double-blind, placebocontrolled trial. Arthritis Rheum 2005;52:27–35.*

*Genovese MC, Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, et al. **Etanercept** versus methotrexate in patients with early rheumatoid arthritis: two-year radiographic and clinical outcomes. Arthritis Rheum 2002;46:1443–50 (**estensione Enbrel ERA (early rheumatoid arthritis) trial**).*

Agenti TNF bloccanti
(in combinazione con methotrexate versus methotrexate in monoterapia)
nella *established rheumatoid arthritis*

La terapia biologica in associazione con methotrexate ha dimostrato una efficacia superiore sia **clinica** che **radiologica** rispetto alla monoterapia.

*Lipsky PE, van der Heijde DM, St Clair EW, Furst DE, Breedveld FC, Kalden JR, et al. **Infliximab** and methotrexate in the treatment of rheumatoid arthritis. **A**nti- **T**umor Necrosis Factor **T**rial in **R**heumatoid **A**rthritis with **C**oncomitant **T**herapy Study Group. N Engl J Med 2000;343:1594–602 (**ATTRACT study**).*

*• Klareskog L, van der Heijde D, de Jager JP, Gough A, Kalden J, Malaise M, et al. Therapeutic effect of the combination of **etanercept** and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial. Lancet 2004;363:675–81 (**TEMPO study**).*

*• Keystone EC, Kavanaugh AF, Sharp JT, Tannenbaum H, Hua Y, Teoh LS, et al. Radiographic, clinical, and functional outcomes of treatment with **adalimumab** (a human anti-tumor necrosis factor monoclonal antibody) in patients with active rheumatoid arthritis receiving concomitant methotrexate therapy: a randomized, placebo-controlled, 52-week trial. Arthritis Rheum 2004;50:1400–11 (**DE019 study**)*

PETER E. LIPSKY, M.D., DESIREE M.F.M. VAN DER HEIJDE, M.D., E. WILLIAM ST. CLAIR, M.D., DANIEL E. FURST, M.D., FERDINAND C. BREEDVELD, M.D., JOACHIM R. KALDEN, M.D., JOSEF S. SMOLEN, M.D., MICHAEL WEISMAN, M.D., PAUL EMERY, M.D., MARC FELDMANN, M.B., B.S., PH.D., GREGORY R. HARRIMAN, M.D., AND RAVINDER N. MAINI, F.R.C.P., FOR THE ANTI–TUMOR NECROSIS FACTOR TRIAL IN RHEUMATOID ARTHRITIS WITH CONCOMITANT THERAPY STUDY GROUP

TABLE 4. EFFECT OF 54 WEEKS OF TREATMENT ON JOINT DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS.*

VARIABLE	METHOTREXATE PLUS PLACEBO (N=64)	3 mg OF INFLIXIMAB/kg EVERY 8 WK PLUS METHOTREXATE (N=71)	3 mg OF INFLIXIMAB/kg EVERY 4 WK PLUS METHOTREXATE (N=71)	10 mg OF INFLIXIMAB/kg EVERY 8 WK PLUS METHOTREXATE (N=77)	10 mg OF INFLIXIMAB/kg EVERY 4 WK PLUS METHOTREXATE (N=66)
Radiographic score					
Total score (increase or decrease from base line)	7.0±10.3	1.3±6.0	1.6±8.5	0.2±3.6	−0.7±3.8
P value		<0.001	<0.001	<0.001	<0.001
Erosion score (increase or decrease from base line)	4.0±7.9	0.2±2.9	0.3±4.7	0.2±2.9	−0.7±3.0
P value		<0.001	<0.001	<0.001	<0.001
Joint-space–narrowing score (increase from base line)	2.9±4.2	1.1±4.4	0.7±4.3	0.0±3.1	0.0±2.5
P value		<0.001	<0.001	<0.001	<0.001
Major progression (% of patients)	31	8	13	1	0
P value		<0.001	<0.001	<0.001	<0.001
Improvement (% of patients)	14	44	48	39	55
P value		<0.001	<0.001	<0.001	<0.001
Clinical response†					
No. of patients	14	35	36	48	44
Total radiographic score (increase from base line)	6.0±8.7	1.5±7.2	0.7±5.5	0.1±3.8	1.4±4.0
P value		0.017	0.009	0.006	<0.001
No clinical response†					
No. of patients	50	36	35	29	22
Total radiographic score (increase from base line)	7.2±10.8	1.1±4.7	2.6±10.7	0.2±3.4	0.7±3.2
P value		<0.001	<0.001	<0.001	0.002
Duration of disease ≤3 yr					
No. of patients	14	15	16	17	4
Total radiographic score (increase or decrease from base line)	9.1±7.7	0.4±4.5	−1.1±6.4	0.6±2.7	0.3±3.3
P value		<0.001	<0.001	<0.001	0.007

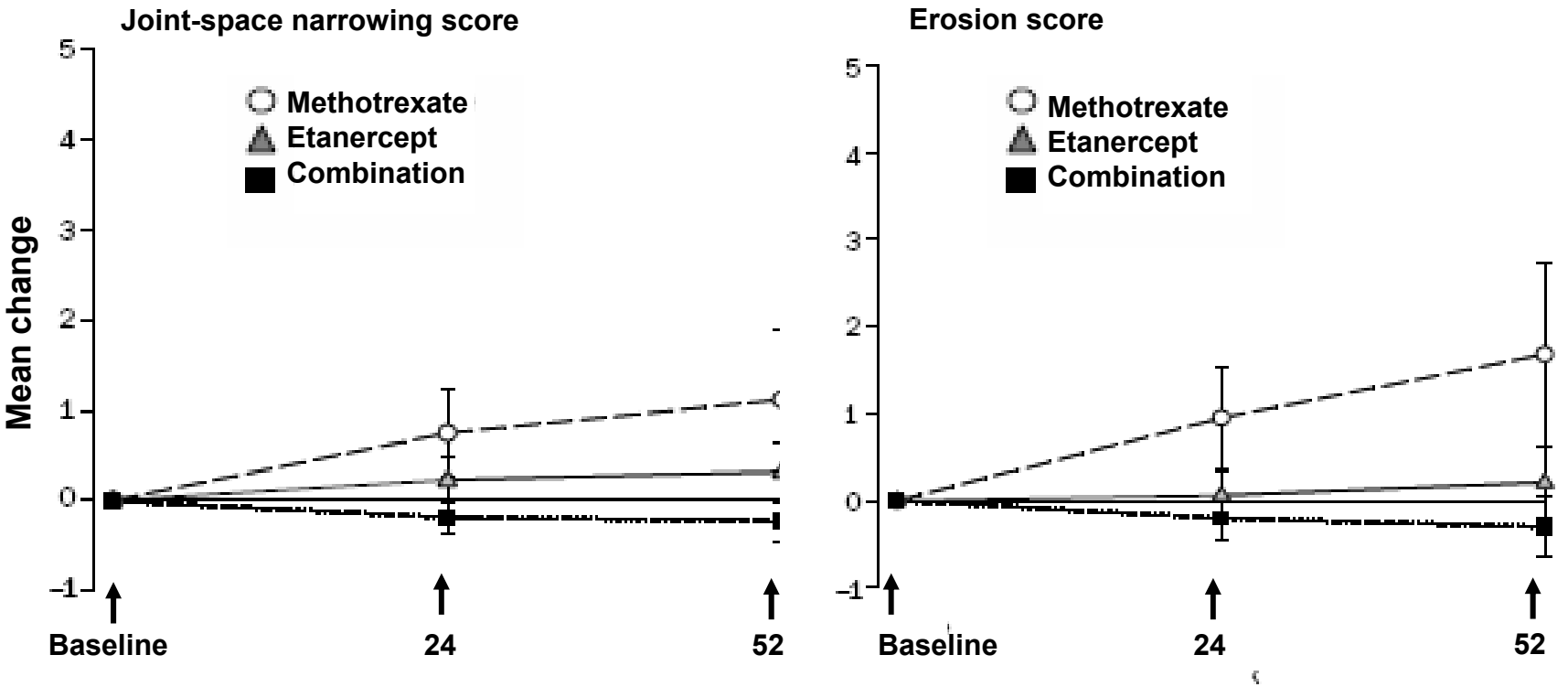
*Plus–minus values are means ±SD. Joint damage was assessed radiographically with use of the van der Heijde modification of the Sharp scoring system. Total scores can range from 0 to 440. Scores on the erosion subscale used can range from 0 to 280, and scores on the joint-space–narrowing subscale can range from 0 to 160. Higher scores indicate more articular damage. P values are for the comparison with the group given methotrexate and placebo.

†A clinical response was defined as an improvement of at least 20 percent according to the criteria of the American College of Rheumatology (ACR 20).

THE LANCET – Vol 363 – February 28, 2004

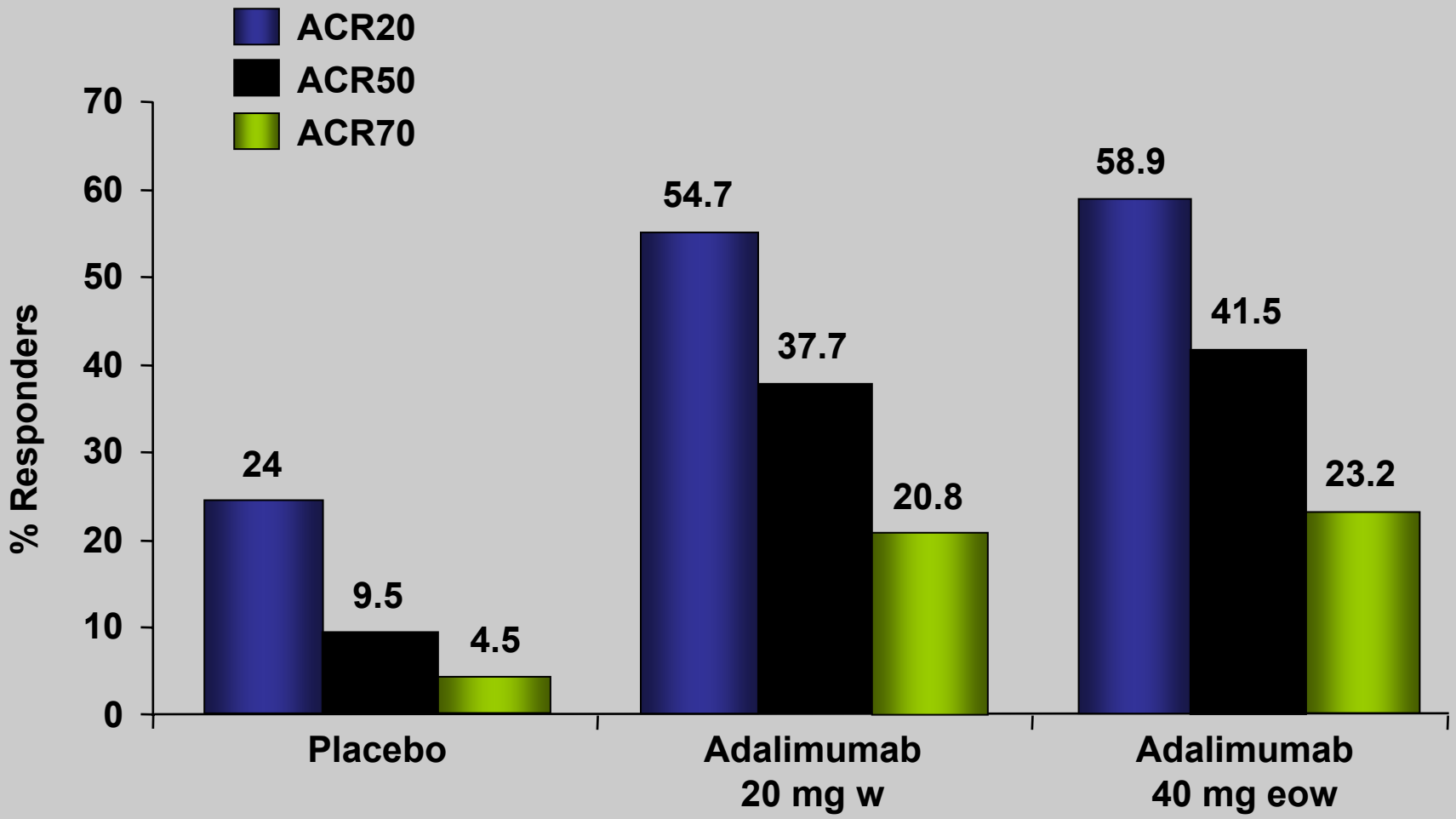
Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial

*Lars Klareskog, Désirée van der Heijde, Julien P de Jager, Andrew Gough, Joachim Kalden, Michel Malaise, Emilio Martín Mola, Karel Pavelka, Jacques Sany, Lucas Settas, Joseph Wajdula, Ronald Pedersen, Saeed Fatenejad, Marie Sanda, for the TEMPO (Trial of Etanercept and Methotrexate with Radiographic Patient Outcomes) study investigators**



DE019

ACR20/50/70 Response at 52 Weeks

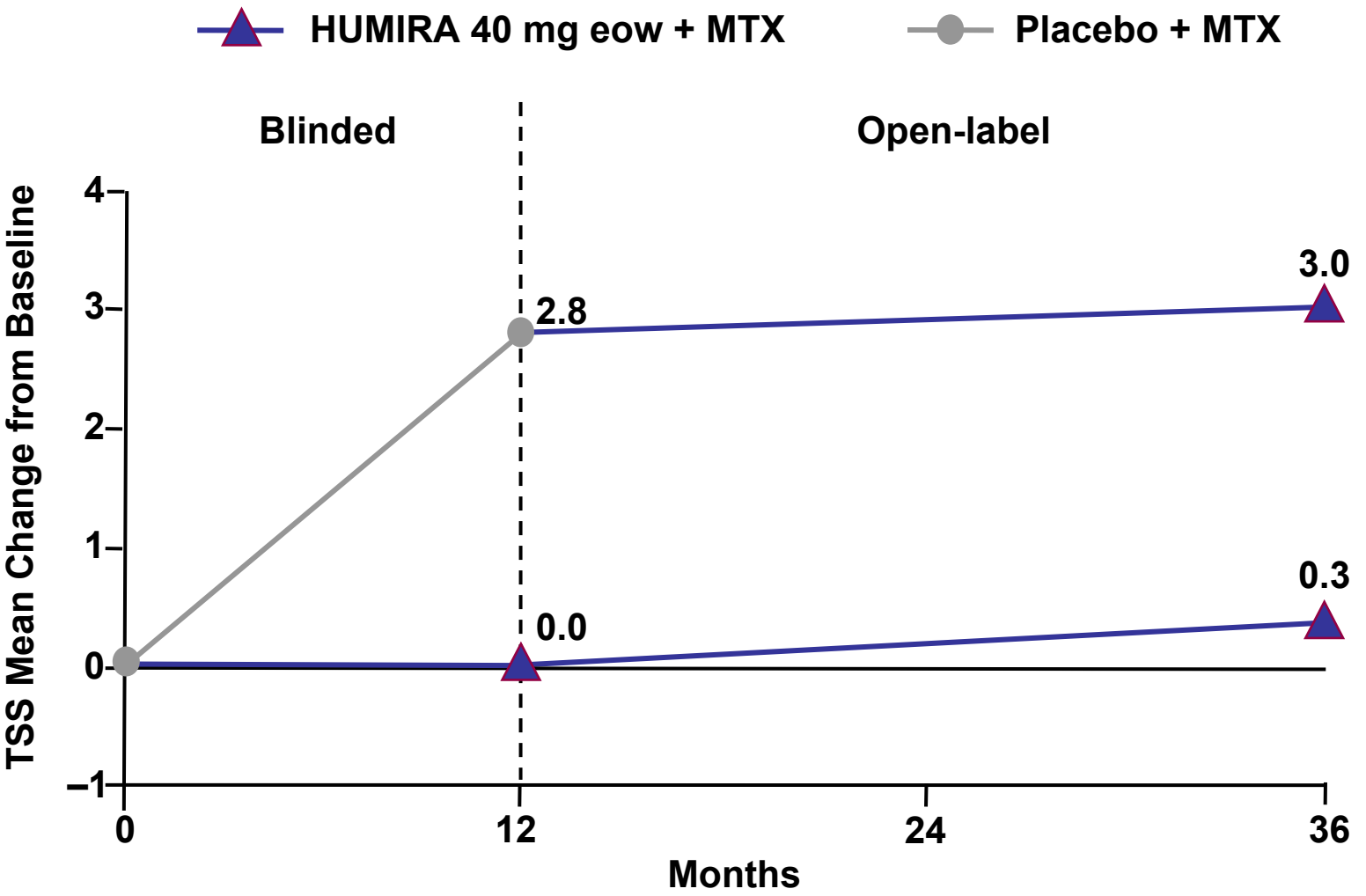


All values $P \leq 0.001$ vs placebo

Keystone EC, et al. Arthritis Rheum. 2004;50:1400–11

DE019

Maintenance of Inhibition of Disease Progression



Keystone EC, et al. Ann Rheum Dis 2005;64(suppl):S419. Abstract SAT0034

Clinical and Radiographic Outcomes of Four Different Treatment Strategies in Patients With Early Rheumatoid Arthritis (the BeSt Study)

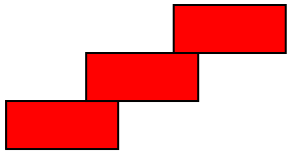
Y. P. M. Goekoop-Ruiterman, J. K. de Vries-Bouwstra, C. F. Allaart, D. van Zeben, P. J. S. M. Kerstens, J. M. W. Hazes, A. H. Zwinderman, H. K. Ronday, K. H. Han, M. L. Westedt, A. H. Gerards, J. H. L. M. van Groenendael, W. F. Lems, M. V. van Krugten, F. C. Breedveld, and B. A. C. Dijkmans

ARTHRITIS & RHEUMATISM 2005; 52(11):3381–90

Vengono confrontate quattro strategie di trattamento nella ***early rheumatoid arthritis***, rappresentate da un regime *progressive step-up*, una monoterapia sequenziale, una strategia *triple step-down* includente methotrexate, sulfasalazina e prednisone a dose elevata, e infine infliximab più methotrexate.

I due gruppi con un trattamento iniziale intensivo (combination e gruppo infliximab) hanno dimostrato una più rapida risposta clinica e un migliore outcome radiografico rispetto alla monoterapia sequenziale e al gruppo step-up DMARD therapy.

TREATMENT STRATEGIES



Sequential monotherapy

n=126

MTX 15mg

↓

MTX 25mg

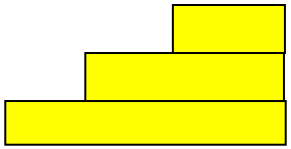
↓

SSA

↓

leflunomide

↓



Step-up combination

n=121

MTX 15mg

↓

MTX 25mg

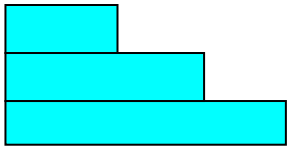
↓

MTX+SSA

↓

MTX+SSA+HCQ

↓



Combination + prednisone

n=133

MTX 7.5mg+SSA +pred 60→7.5mg

↓

MTX 25mg+SSA+ pred 7.5mg

↓

MTX+CSA+pred

↓

MTX+infliximab

↓

Combination + infliximab

n=128

MTX25mg+ infliximab 3mg/kg

↓

↓

↓

↓

MTX 25mg+ infliximab 10mg/kg

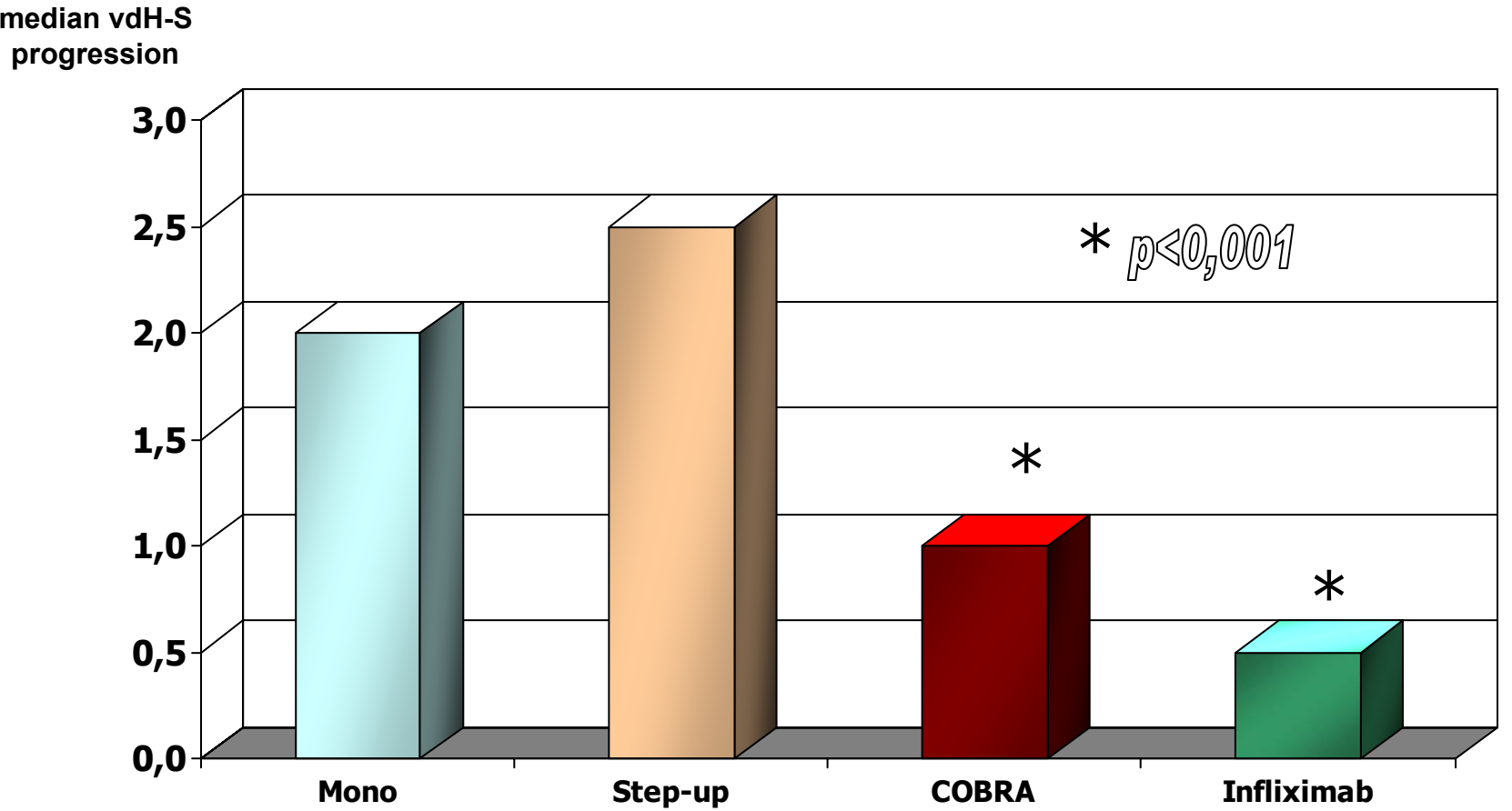
↓

SSA

↓

Arthritis & Rheumatism 2005; 52(11):3381–90

PREVENTION OF RADIOGRAPHIC PROGRESSION



Arthritis & Rheumatism 2005; 52(11):3381–90

La remissione clinica dell'artrite reumatoide è un obiettivo realisticamente raggiungibile.

Studio **TICORA**: risposta clinica a 18 mesi

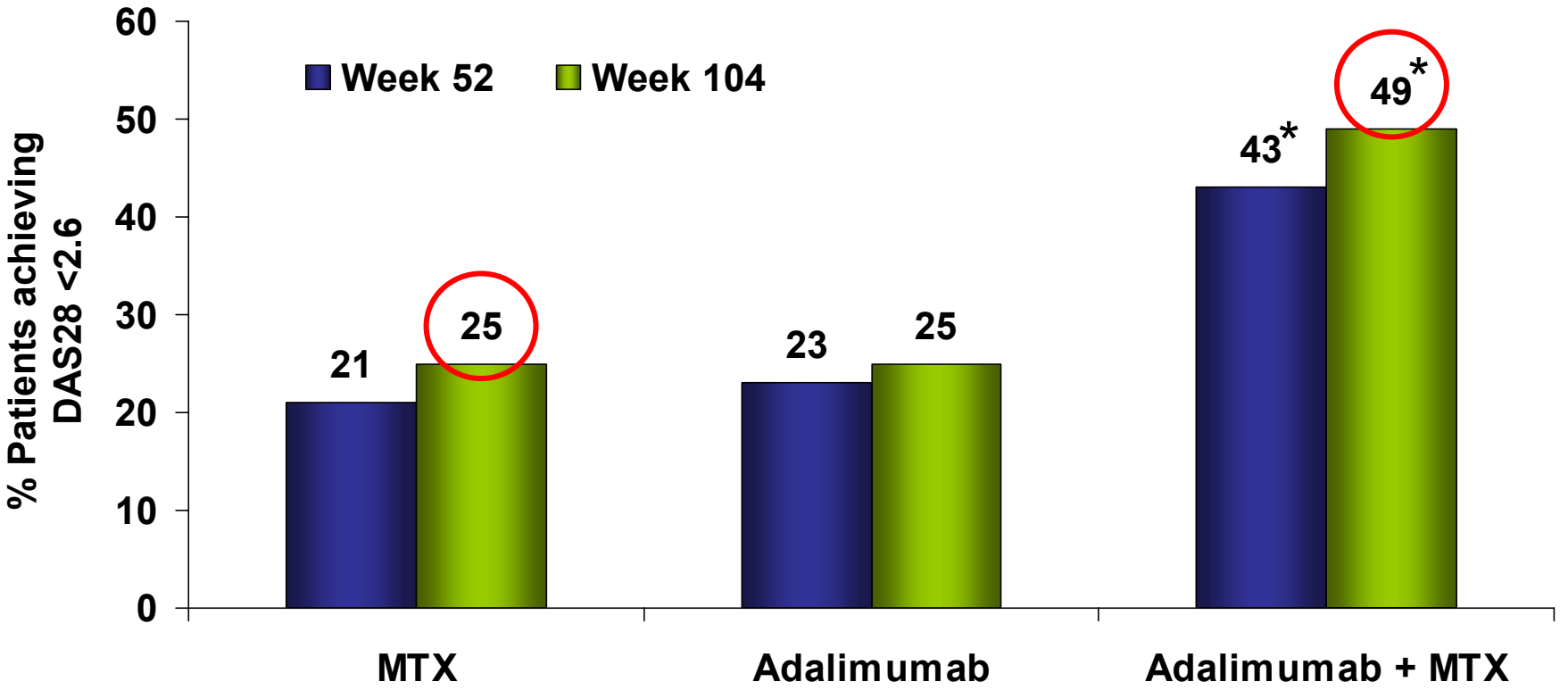
	Gruppo trattamento intensivo (n = 55) (%)	Gruppo trattamento di routine (n = 55) (%)	OR IC 95%
Risposta EULAR	80	44	3,6 (1,5-6,7)*
Remissione DAS	65	16	9,6 (3,8-24,3)*
ACR 20	89	64	4,0 (1,5-10,5)*
ACR 50	82	45	4,9 (2,1-11,4)*
ACR 70	70	18	9,5 (3,9-23,0)*

* $p < 0,001$

*Grigor C, Capell H, Stirling A, McMahon AD, Lock P, Vallance R, et al. Effect of a treatment strategy of **ti**ght **co**ntrol for **r**heumatoid **a**rthritis (the **TICORA study**): a single-blind randomised controlled trial. Lancet 2004;364:263–9*

PREMIER

Remission by DAS28 <2.6

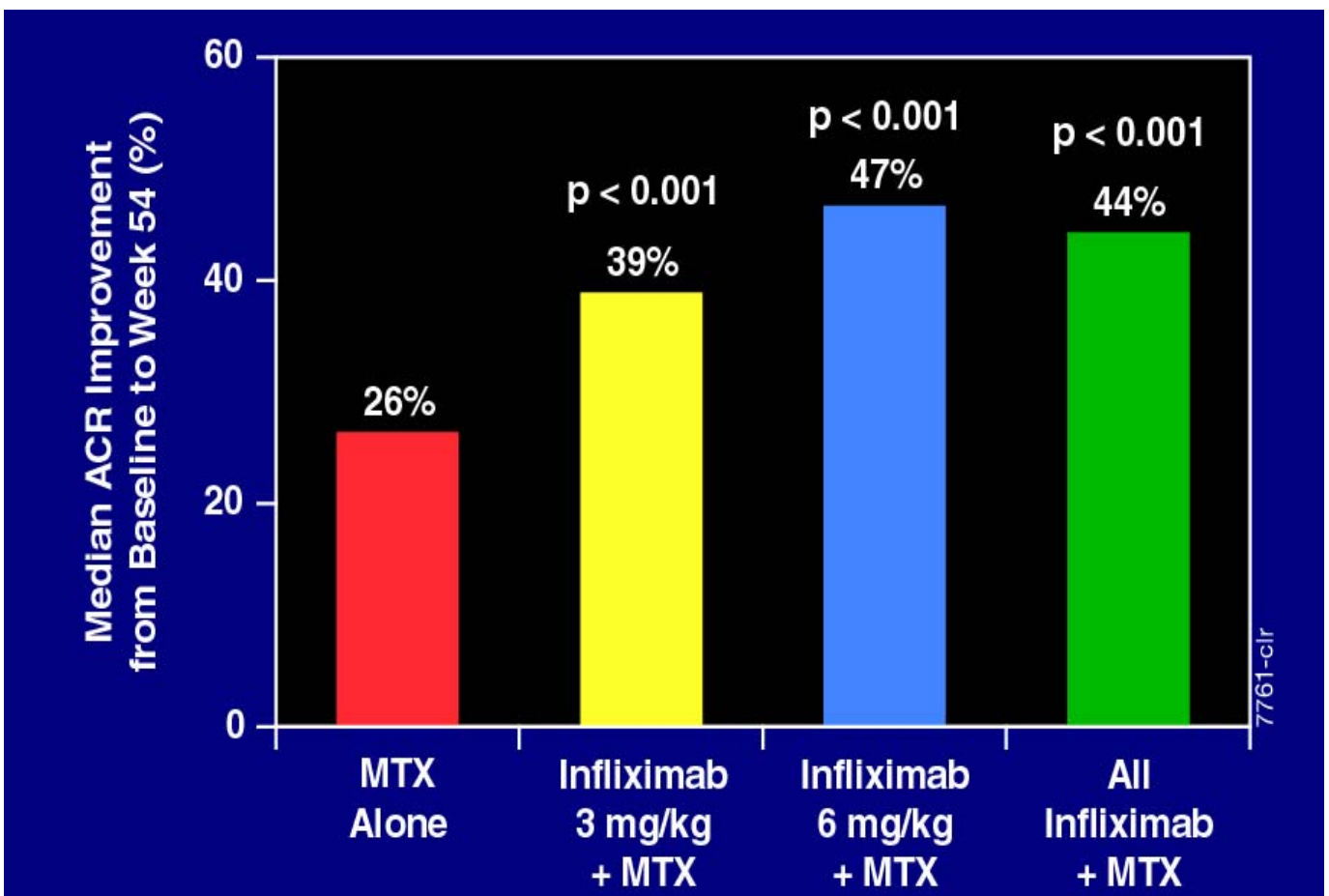


*p<0.001 for adalimumab + MTX vs MTX alone and adalimumab alone

Breedveld FC, et al. Arthritis Rheum 2006;54:26–37

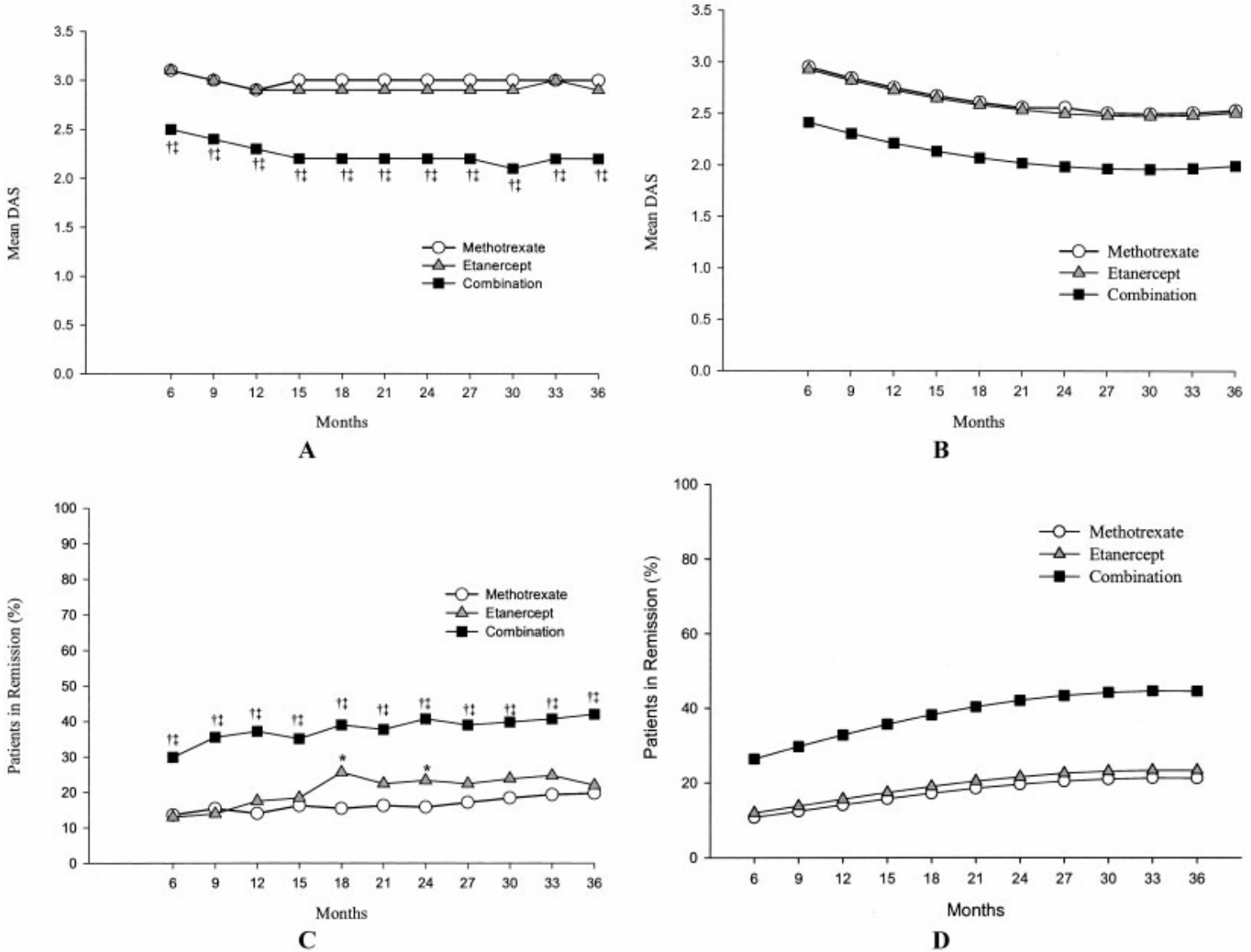
Signs and Symptoms
Primary Endpoint: ACR-N at Week 54

*St Clair EW, van der Heijde DM, Smolen JS, Maini RN, Bathon JM, Emery P, et al. Combination of **infliximab** and methotrexate therapy for early rheumatoid arthritis: a randomized, controlled trial. Arthritis Rheum 2004;50:3432–43*



ne **ACR-N** is defined as the minimum of the following 3 items: the percentage change from baseline in the number of tender joints, the percentage change from baseline i e number of swollen joints, and the median of the percentage change from baseline for the patient's global assessment, physician's global assessment, pain, disability, an

D. van der Heijde, L. Klareskog, R. Landewé, G. A. W. Bruyn, A. Cantagrel, P. Durez, G. Herrero-Beaumont, Y. Molad, C. Codreanu, G. Valentini, R. Zahora, R. Pedersen, D. MacPeek, J. Wajdula, and S. Fatenejad, for the **TEMPO Study** Investigators. Disease Remission and Sustained Halting of Radiographic Progression With Combination Etanercept and Methotrexate in Patients With Rheumatoid Arthritis. ARTHRITIS & RHEUMATISM Vol. 56, No. 12, December 2007, pp 3928–3939



Disease Activity Score (**DAS**) and **DAS remission over time**. **A e C:** univariate. **B e D:** multivariate analysis.

Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, double-blind, parallel treatment trial

Paul Emery, Ferdinand C Breedveld, Stephen Hall, Patrick Durez, David J Chang, Deborah Robertson, Amitabh Singh, Ronald D Pedersen, Andrew S Koenig, Bruce Freundlich

Lancet 2008; 372: 375–82

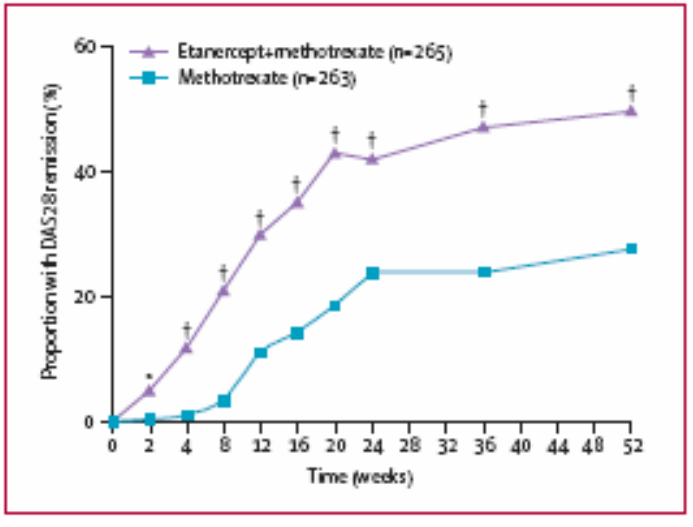


Figure 2: DAS28 remission over 52 weeks of treatment
A significant difference in the proportion of patients in DAS28 remission was seen in week 2 and persisted for the study period. *p=0·002. †p<0·0001.

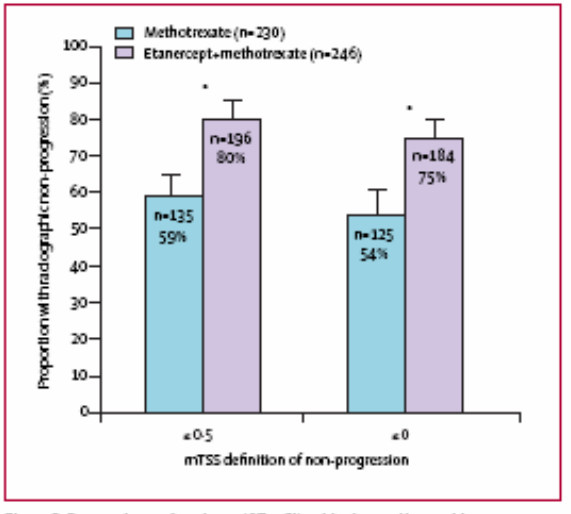


Figure 3: Proportions of patients (95% CI) achieving radiographic non-progression at week 52
*p<0·0001.

CONCLUSIONI

• I farmaci anti-TNFα in associazione al metotressato si sono rivelati farmaci molto efficaci nel trattamento dell'artrite reumatoide nelle sue fasi evolutive risultando superiori ai tradizionali DMARDs impiegati in monoterapia o in combinazione, o quanto meno di pari efficacia però con effetto superiore sulla progressione radiologica.

• I farmaci anti-TNFa hanno dimostrato di rallentare la progressione radiologica della malattia.

• I farmaci anti-TNFa migliorano la qualità di vita dei pazienti riducendone in modo significativo la disabilità.

• Esitono studi convincenti circa il loro impiego nell'artrite reumatoide early.

Sulla base delle attuali conoscenze sulla patogenesi della malattia esiste un razionale terapeutico secondo il quale **i farmaci anti-TNFa dovrebbero essere usati non appena si pone diagnosi di artrite reumatoide nella sua variante progressiva e aggressiva**.

Ma la realtà sul campo è questa o un po' diversa?

Caso 1.
Paziente con storia di AR stabilizzata erosiva, in fase florida nonostante varie terapie di fondo. Cosa fare?

Anti-TNFα

Caso 2.
AR di vecchia data, classica. Sufficientemente controllata dal MTX 10 mg/sett.. La malattia si riacutizza e ci accorgiamo che la paziente assume MTX ogni 15 giorni → si richiedono esami preparatori per anti-TNF, ma nel contempo si riordina la terapia (aumento della dose del MTX da 10 a 15 mg una volta alla settimana). Controllo a 3 settimane: la paziente afferma di sentirsi bene. Obiettivamente solo calor e lieve tumor a carico della caviglia sinistra e ginocchio destro. All'esame Rx non vi è evidenza di progressione radiologica. DAS28 è passato da 5,4 a 3,0. Cosa fare?

Due possibilità:
mantenere questa scelta terapeutica o passare agli anti-TNF?

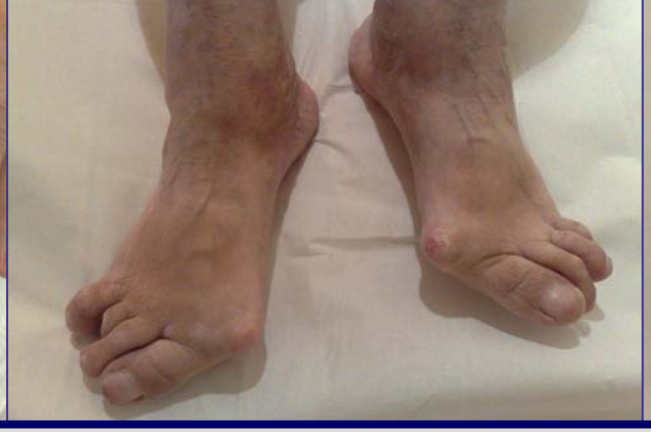
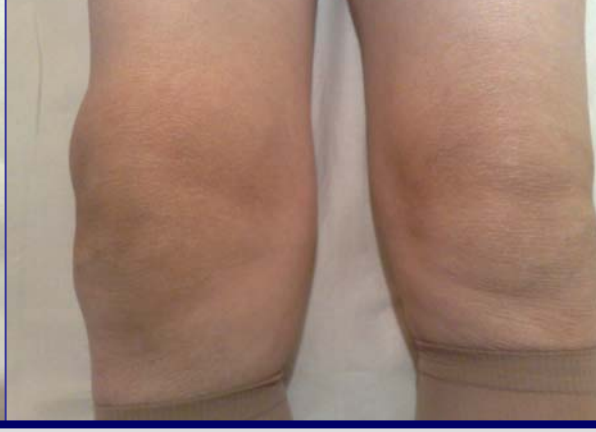
Caso 3.
Paziente con AR all'esordio in terapia con MTX con RM prima e dopo (un anno) con qualche geode in più, ma indici di flogosi normali, qualità di vita sostanzialmente buona.

Cosa fare?

Aggiungere un secondo DMARDs o dare un anti-TNFα?

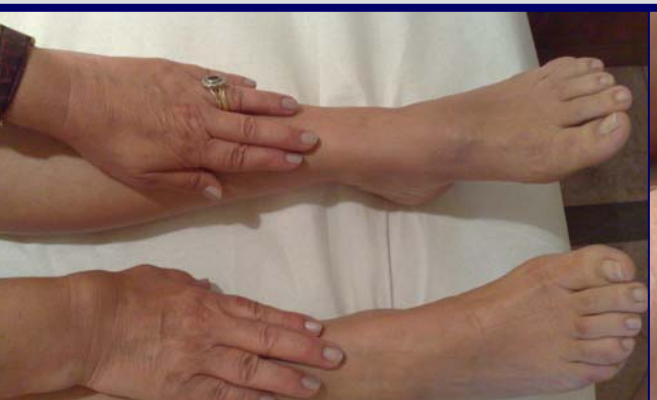
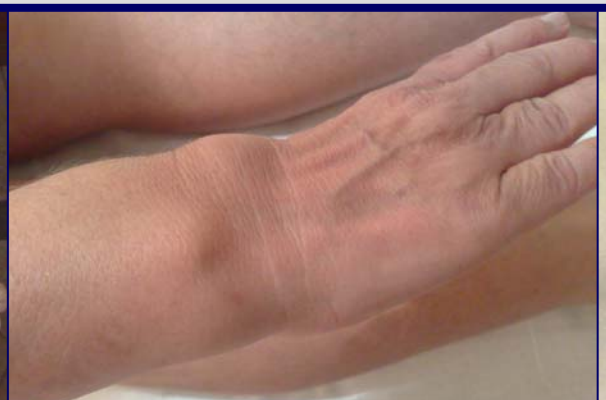
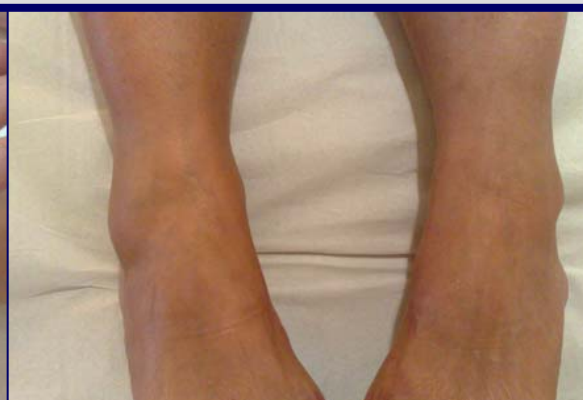
Caso 4.
Situazione clinica simile alla precedente. Oligoartrite di polso, scarsa o assente attività flogistica, ma chiara dimostrazione di progressione radiologica alla RM.
Che fare?

?

due casi simili di AR classica stabilizzata, ma a basso grado di attività (P. A. di anni 6

Che fare?
Mantenere MTX e LNM
o passare ad un anti-TNFa?

Pierre-Auguste Renoir

Nasce a Limoges nel 1841.

Dal 1898 comincia ad avvertire i primi sintomi di una grave malattia reumatica.

Nonostante l'artrite gli renda difficoltoso l'uso delle mani, continua a dipingere.
Insiste anche nella scultura. Ma non potendo lavorare da solo, dal 1913 si fa aiutare dall'artista catalano Richard Guino.

Muore nel 1919 a Cagnes-sur Mer.

GRAZIE PER LA VOSTRA ATTENZIONE

Bagnante che si pettina. 1911.
National Gallery. Londra

Le baigneuses. 1918-1919.
Musée d'Orsay. Parigi

Fare diagnosi di AR è difficile nelle fasi precoci della malattia

(***Arnett FC*** *et al: "The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis". Arthritis Rheum 1988, 31: 315-324*)