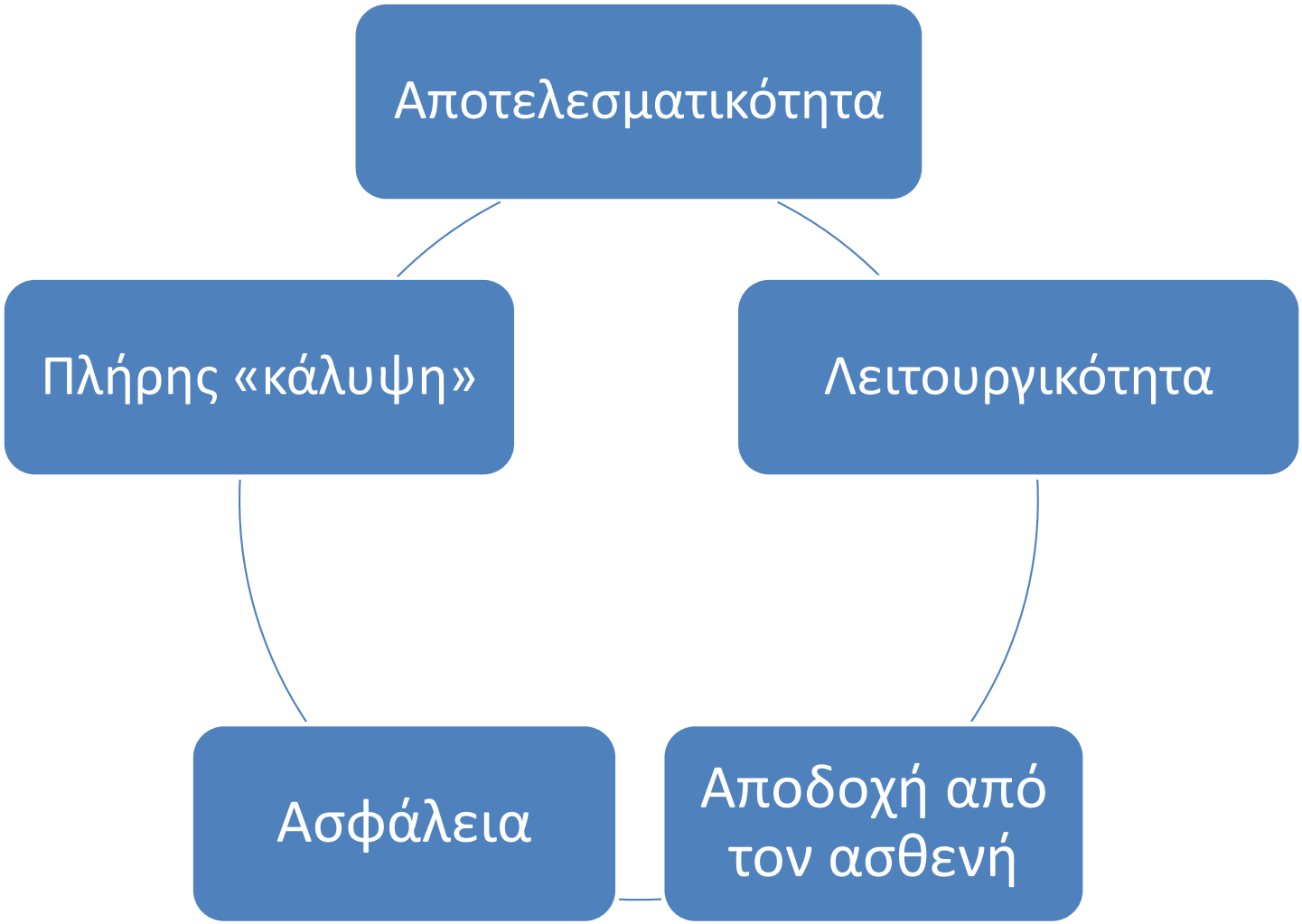
Η παραμονή στην θεραπεία στις φλεγμονώδεις αρθρίτιδες

Δημήτρης Τσερώνης
Ρευματολόγος

Παραμονή στη θεραπεία σημαίνει…



Παραμονή στη θεραπεία στην καθημερινή κλινική πράξη

- Έλεγχος της νόσου
- Αναστολή προόδου της νόσου
- Έλεγχος των συνοδών νοσημάτων
- Απουσία ανεπιθύμητων συμβαμάτων
- Ποιότητα ζωής του ασθενή

1. Degli Esposti L et al, ClinicoEconomics and Outcomes Research 2014:6; 2. Tang B et al, Clinical Therapeutics/Volume 30, Number 7, 2008; 3. Bolge S, Goren A, Tandon M, Patient Preference and Adherence 2015:9

Παραμονή στη θεραπεία & χρήση πόρων υγείας
Παράδειγμα από την Ρευματοειδή Αρθρίτιδα

Επιπλέον κόστη μη σχετιζόμενα με την φαρμακευτική δαπάνη

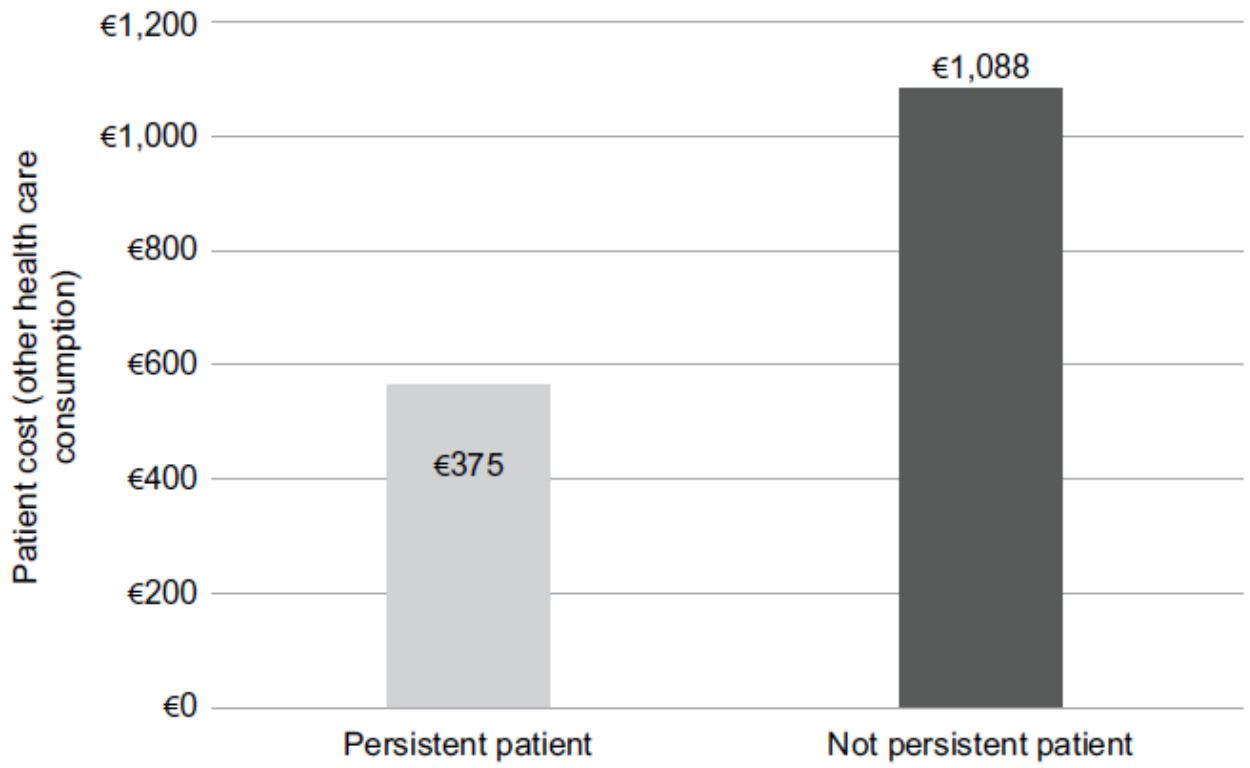


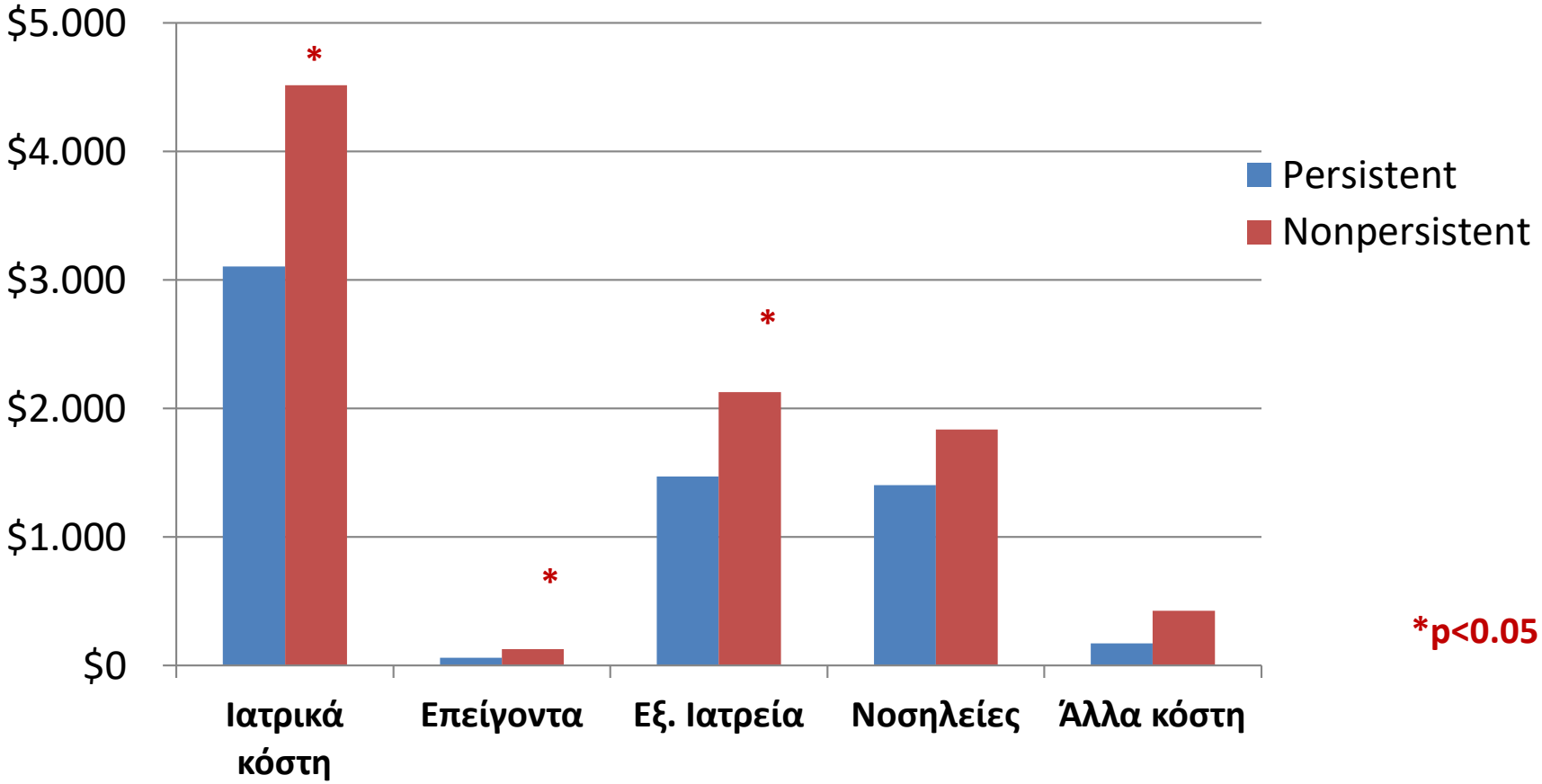
Figure 7 Costs for other health care consumption (excluding drugs).

Persistence, switch rates, drug consumption and costs of biological treatment of rheumatoid arthritis: an observational study in Italy

Clinicoecon Outcomes Res. 2017; 9: 9–17. Published online 2016 Dec 21. doi: 10.2147/CEOR.S108730

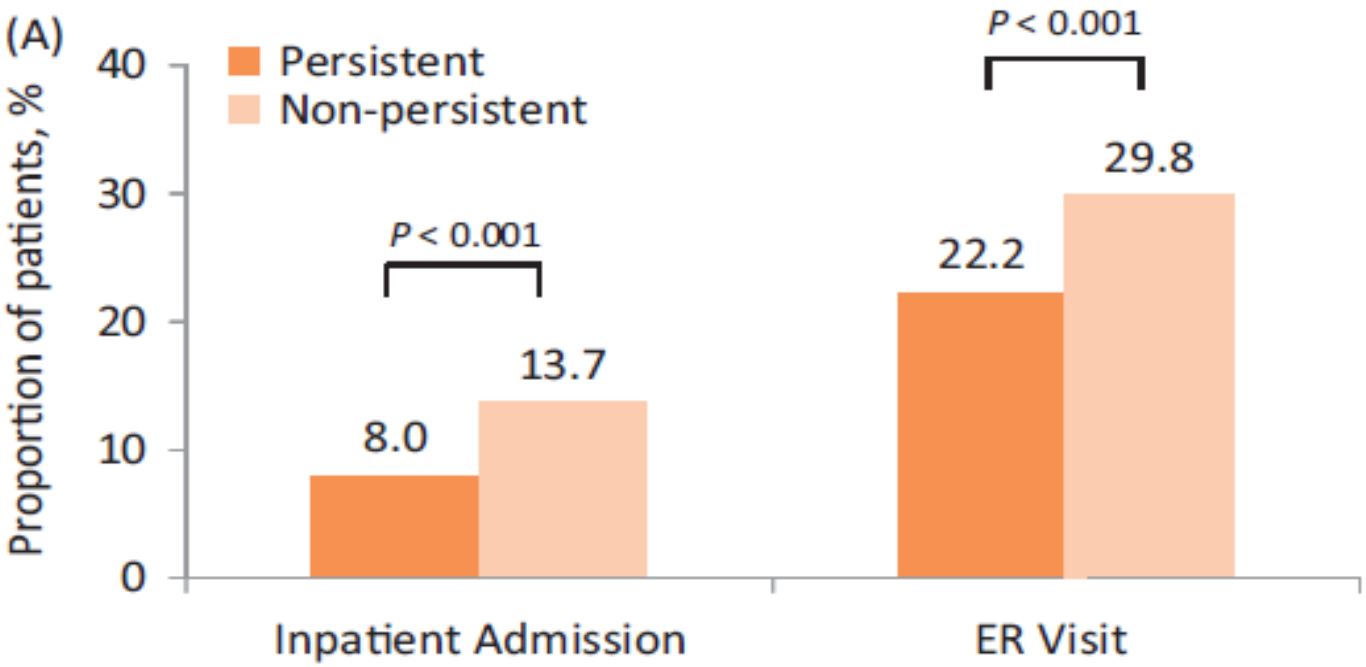
Παραμονή στη θεραπεία & χρήση πόρων υγείας
Παράδειγμα από το ΣΔ

Επίδραση της παραμονής στη θεραπεία ασθενών με διαβήτη τύπου 2 σε διάφορες πτυχές του κόστους περίθαλψης



Buysman EK, Liu F, Hammer M, Langer J. Impact of Medication Adherence and Persistence on Clinical and Economic Outcomes in Patients with Type 2 Diabetes Treated with Liraglutide: A Retrospective Cohort Study. Advances in Therapy. 2015;32(4):341-355.

Παραμονή στη θεραπεία & χρήση πόρων υγείας
Παράδειγμα από την πολλαπλή σκλήρυνση



Για τους ασθενείς που παραμένουν στη θεραπεία

- 50% λιγότερες εισαγωγές στο νοσοκομείο
- 35% λιγότερες προσελεύσεις στα επείγοντα

Thomas NP et al. J Med Econ. 2016;19(5):497-505

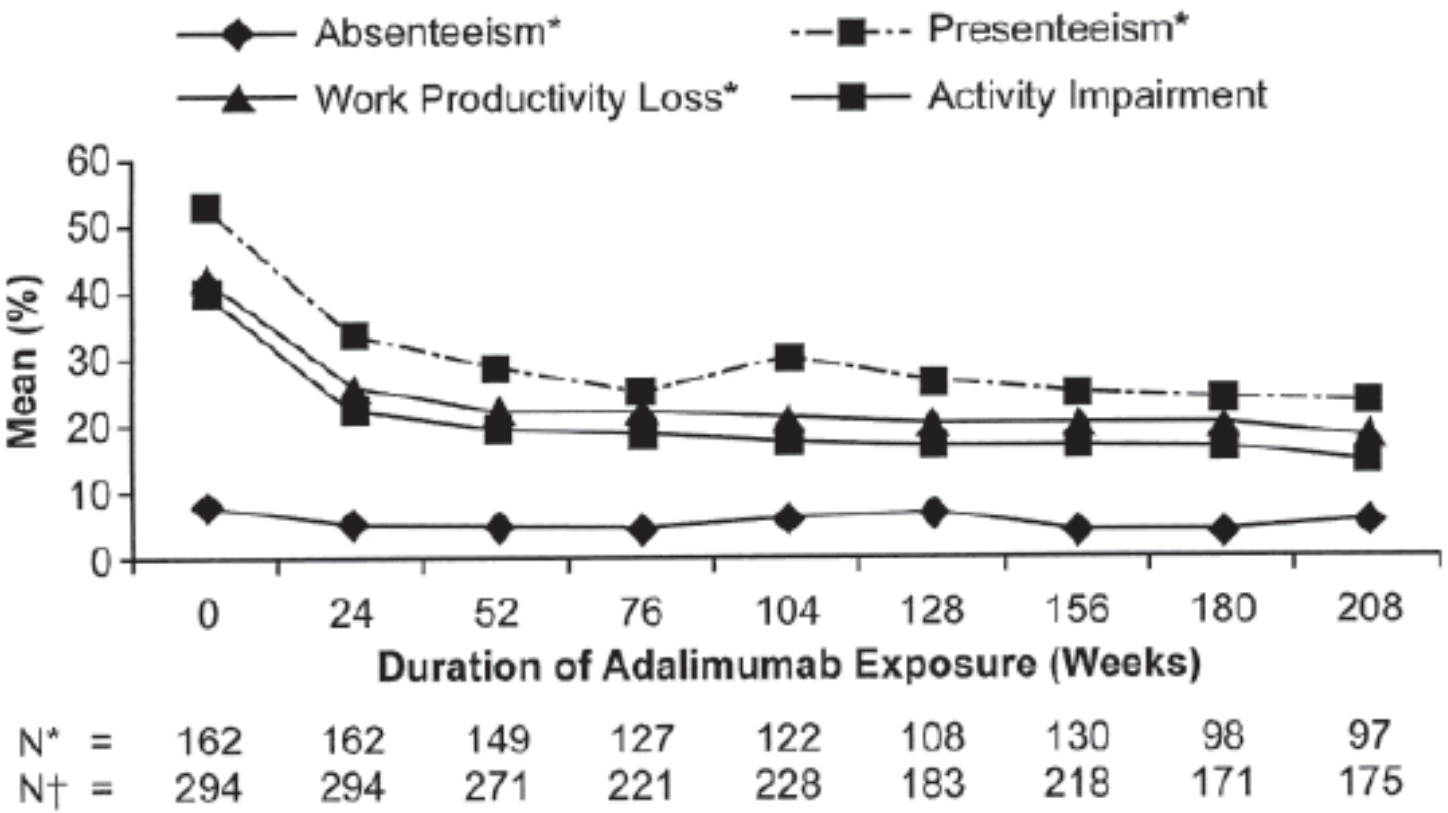
Παραμονή στη βιολογική θεραπεία ασθενών με ρευματικά νοσήματα…*value for money ?*

Ασθενείς με >80% παραμονή vs. <80% παραμονή

- Υψηλότερο φαρμακευτικό κόστος
- **60% μείωση** του μη φαρμακευτικού κόστους (επισκέψεις στο γιατρό, εξετάσεις, εισαγωγή στο νοσοκομείο, νοσηλείες κλπ)
- Χαμηλότερη συννοσηρότητα
- Υψηλότερη ποιότητα ζωής του ασθενή (intangible costs)

1. Degli Esposti L et al, ClinicoEconomics and Outcomes Research 2014;6:401-7 2. Tang B et al, Clin Ther. 2008;30:1375–1384

Επίδραση της παραμονής στην θεραπείας στην ικανότητα για εργασία



J Rheumatol. 2010;37:385-92

Σχετίζεται η παραμονή στην θεραπεία με τον θεραπευτικό μας στόχο ;

Efficacy VS effectiveness?

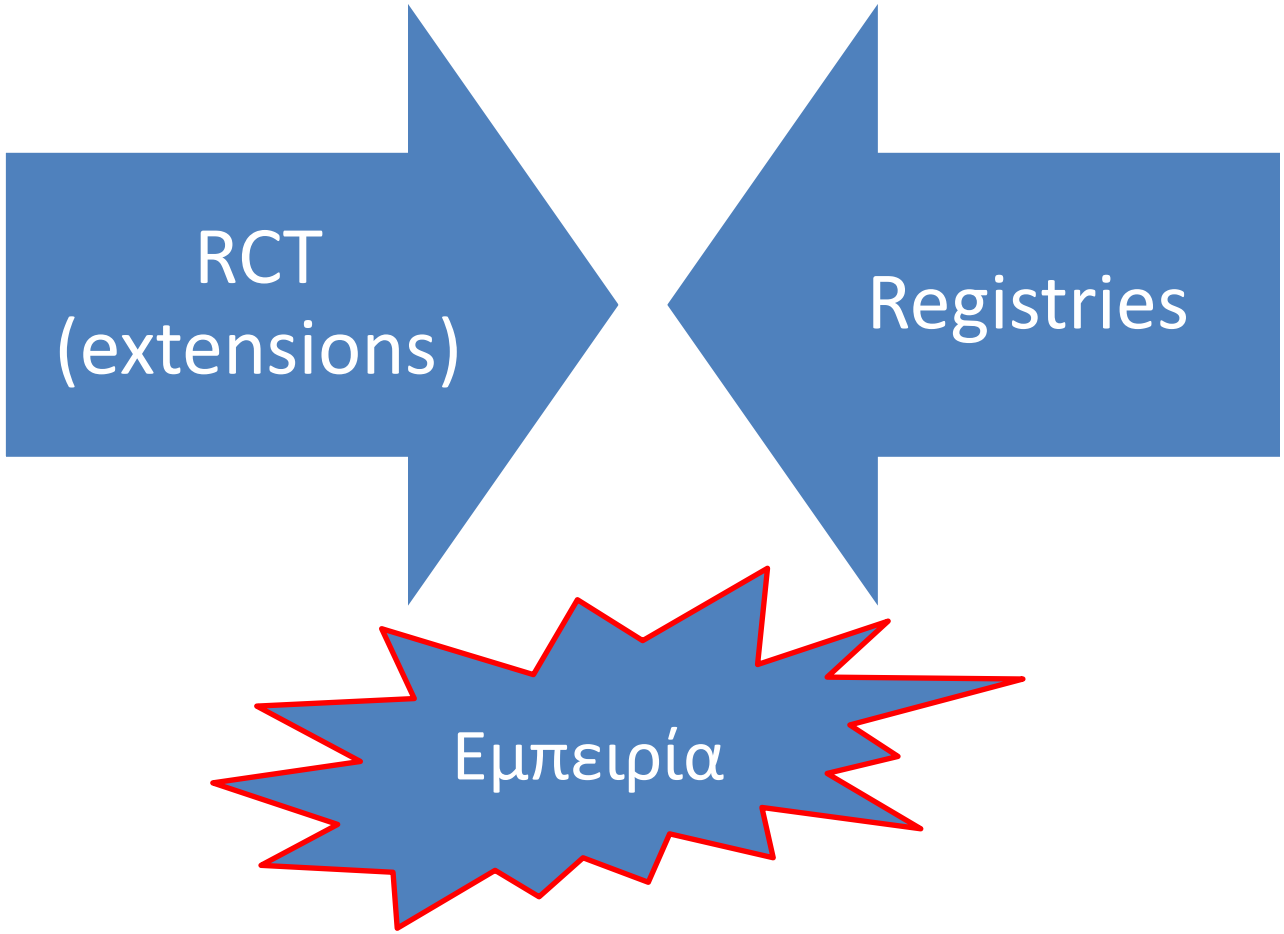
- Efficacy=ανταπόκριση σε συγκεκριμένους δείκτες στις κλινικές μελέτες.

- Effectiveness=αποτελεσματικότητα του φαρμάκου στην κλινική πράξη

Οι αντι-TNF έχουν αποδείξει efficacy στις κλινικές μελέτες, το **effectiveness** τους όμως στην κλινική πράξη **εξαρτάται από την παραμονή στη θεραπεία**[1,2]

1. Degli Esposti L et al, ClinicoEconomics and Outcomes Research 2014:6; 2. Tang B et al, Clinical Therapeutics/Volume 30, Number 7, 2008

Παραμονή στη θεραπεία: *πόθεν έσχες ;*



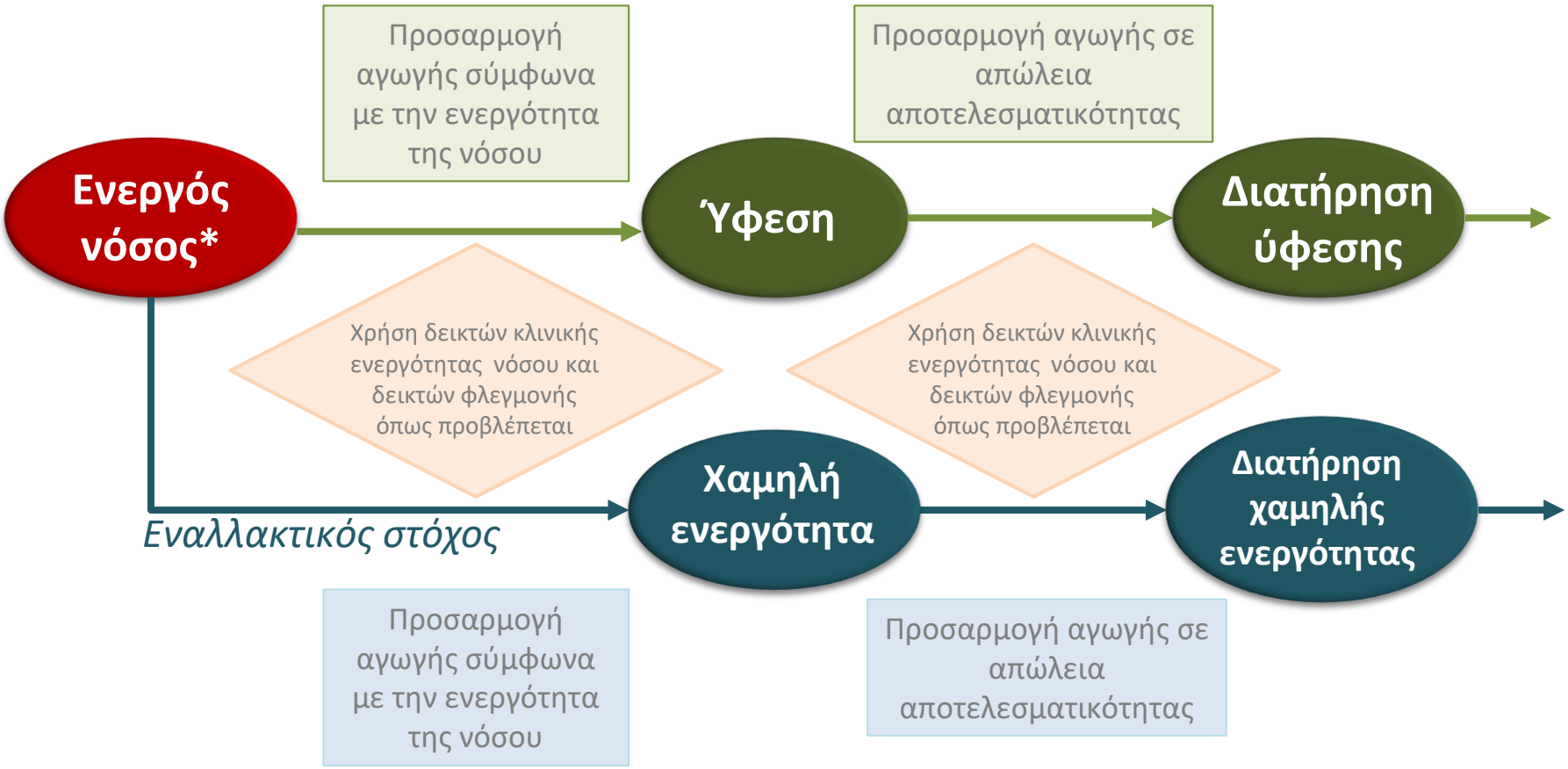
Παραμονή στην θεραπεία με infliximab

Σχετίζεται η ταχύτητα δράσης με την παραμονή?

διακοπή θεραπείας– διατήρηση αποτελεσματικότητας ?

Δεδομένα διατήρησης της θεραπείας στις φλεγμονώδης αρθρίτιδες (Registry-data)

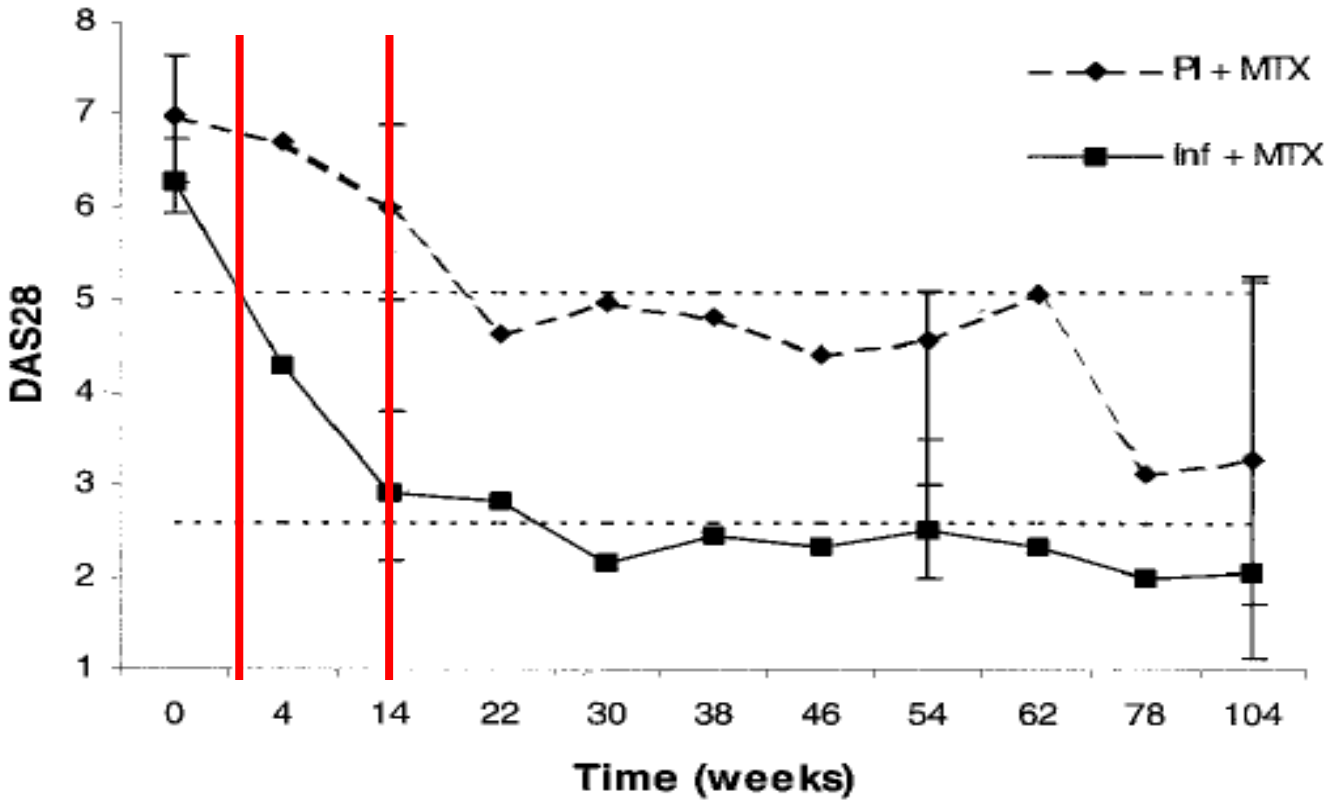
Η γρήγορη επίτευξη της ύφεσης σχετίζεται με αυξημένη διατήρηση του θεραπευτικού αποτελέσματος (T2T)



** Ρευματοειδής αρθρίτιδα, Αγκυλοποιητική σπονδυλαρθρίτιδα, Περιφερική αρθρίτιδα, Ψωριασική αρθρίτιδα*

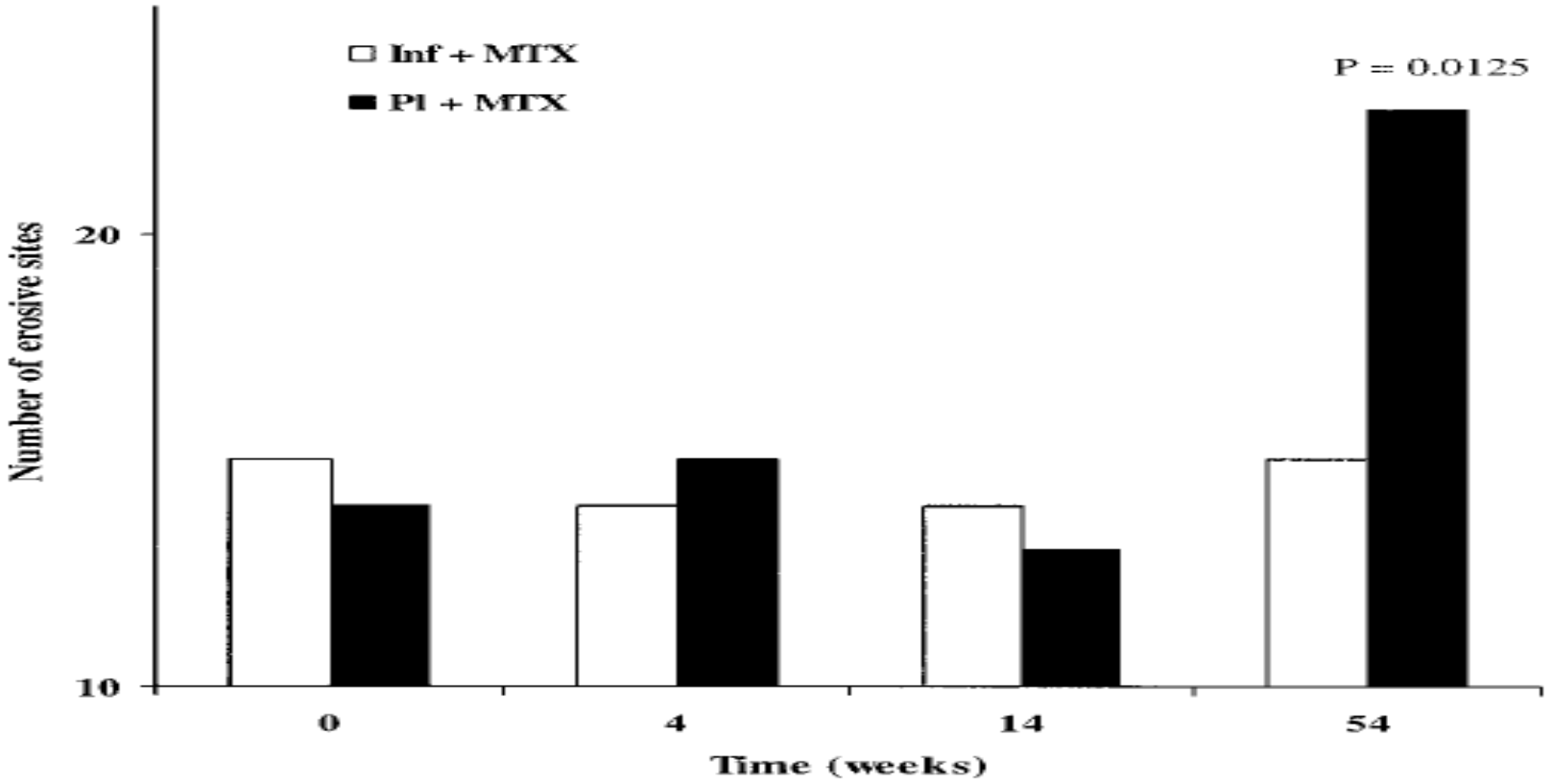
Smolen JS. Ann Rheum Dis 2013;0:1–11

Η ταχύτητα δράσης σχετίζεται με την διατήρηση της θεραπευτικής απάντησης



Quinn MA 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. *Arthritis Rheum 2005,*52:27-35.

Η «γρήγορη» ένταξη σε infliximab είναι δείκτης καλής πρόγνωσης



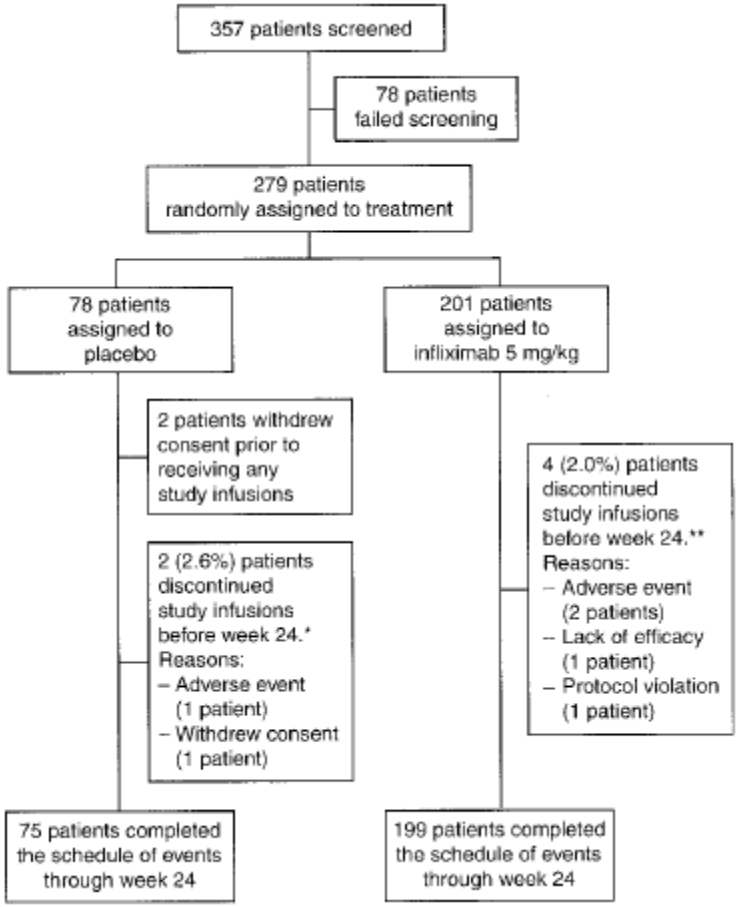
Quinn MA et al. Very early treatment with infliximab in addition to methotrexate in early, poor-prognosis rheumatoid arthritis reduces magnetic resonance imaging evidence of synovitis and damage, with sustained benefit after infliximab withdrawal. *Arthritis Rheum 2005,*52:27-35.

Ταχύτατη βελτίωση – ύφεση νόσου

Efficacy and Safety of Infliximab in Patients With Ankylosing Spondylitis

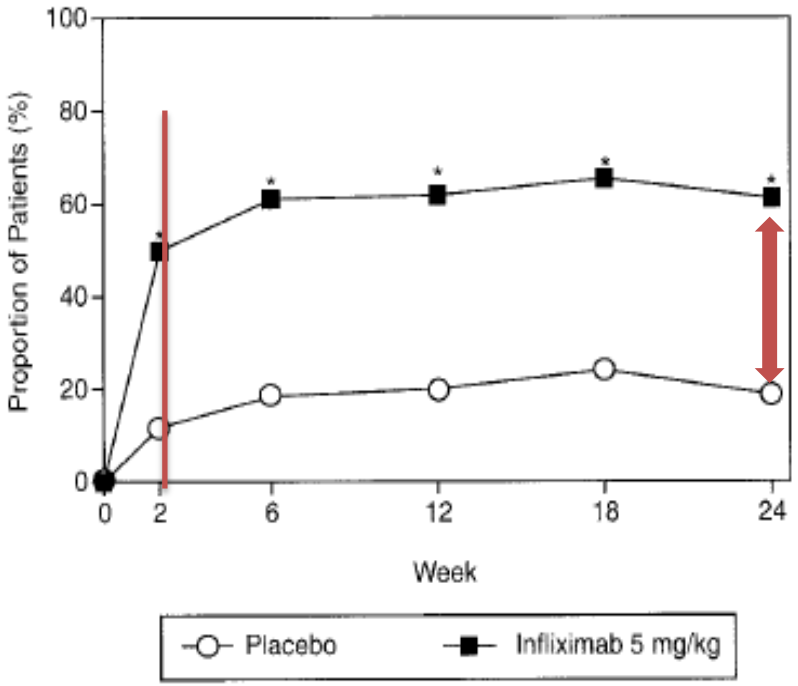
Results of a Randomized, Placebo-Controlled Trial (ASSERT)

Désirée van der Heijde,[1] Ben Dijkmans,[2] Piet Geusens,[3] Joachim Sieper,[4] Kimberly DeWoody,[5] Paul Williamson,[5] Jürgen Braun,[6] and the Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy Study Group

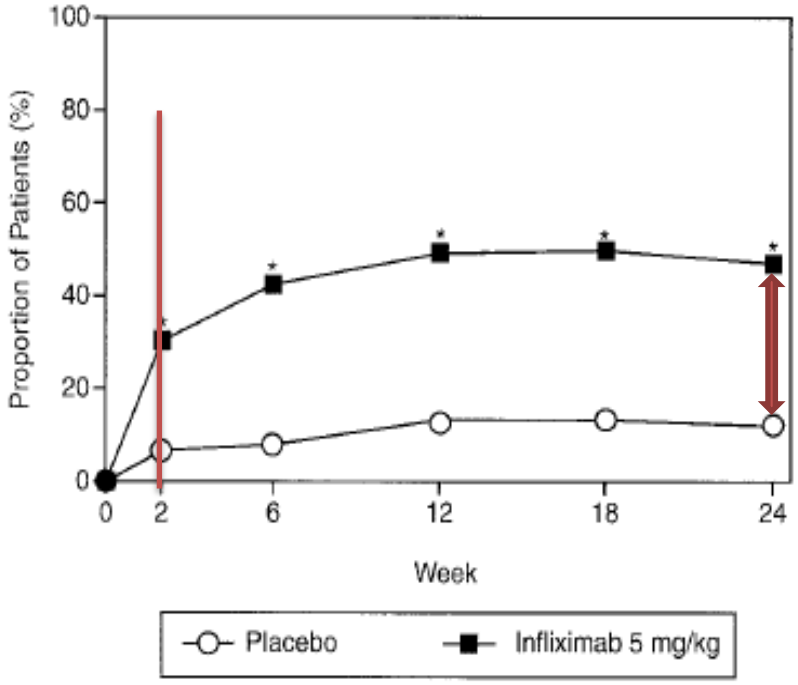


Van der Heijde et al. Efficacy and Safety of Infliximab in Patients With Ankylosing Spondylitis Results of a Randomized, Placebo-Controlled Trial Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy Study Group (***ASSERT***) *Arthritis Rheum 2005, 52:582-591*

Ταχύτατη βελτίωση + διατήρηση ύφεσης νόσου



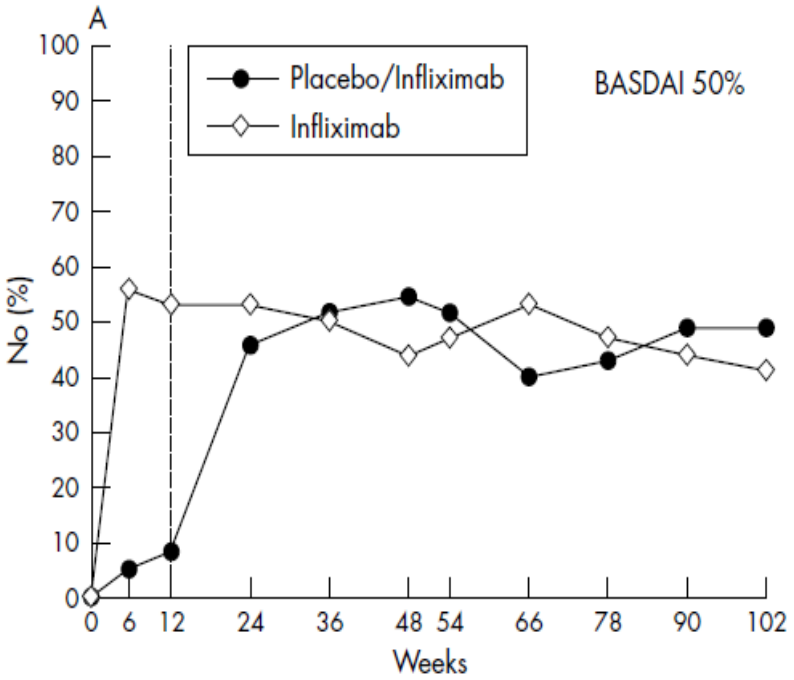
ASAS 20

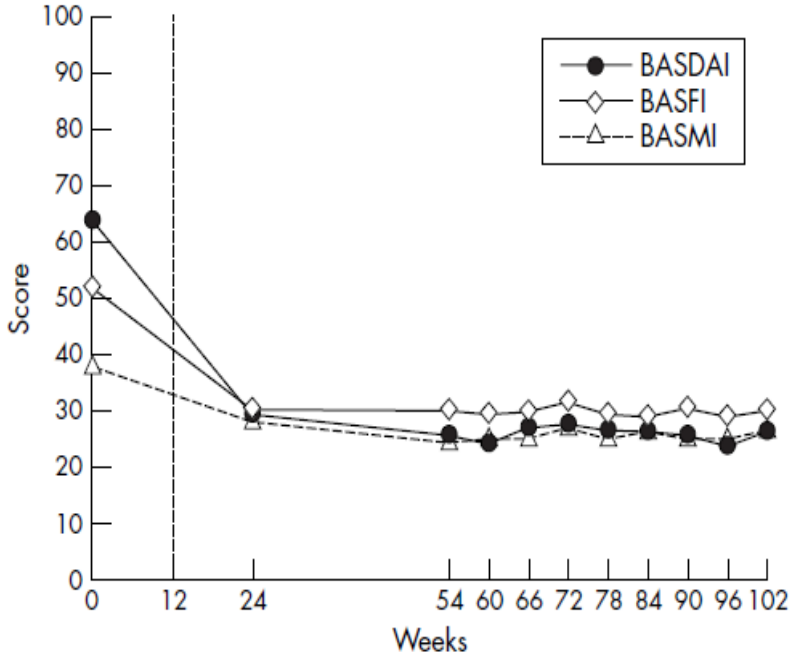


ASAS 40

Van der Heijde et al. Efficacy and Safety of Infliximab in Patients With Ankylosing Spondylitis Results of a Randomized, Placebo-Controlled Trial Ankylosing Spondylitis Study for the Evaluation of Recombinant Infliximab Therapy Study Group (***ASSERT***) *Arthritis Rheum 2005, 52:582-591*

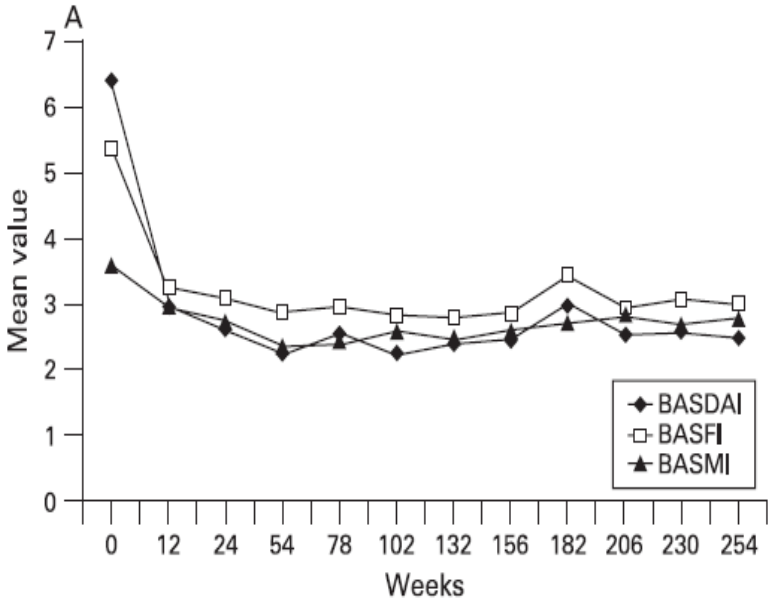
Μετά από 2 έτη…

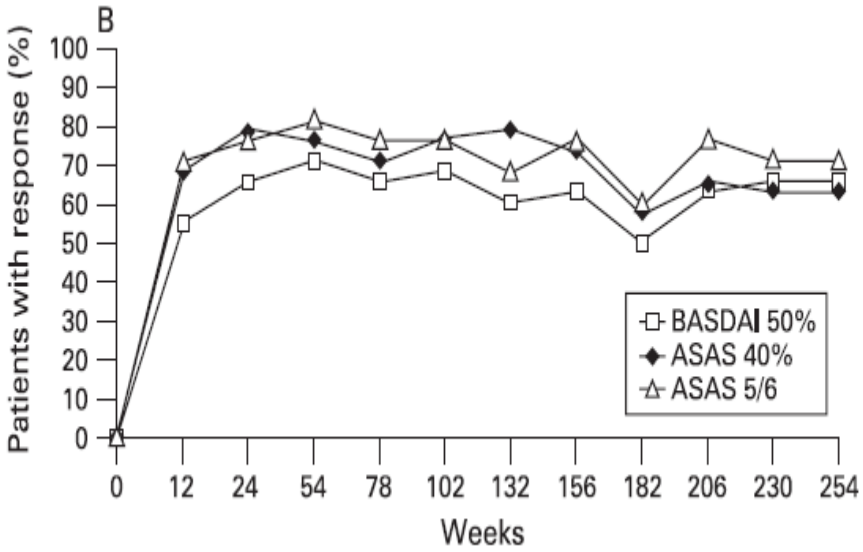




Braun J, Brandt J, Listing J et al. Two year maintenance of efficacy and safety of infliximab in the treatment of ankylosing spondylitis Ann Rheum Dis 2005;64:229–234

Μετά από 5 έτη…





Braun et al. Persistent clinical efficacy and safety of anti-tumour necrosis factor a therapy with infliximab in patients with ankylosing spondylitis over 5 years: evidence for different types of response Ann Rheum Dis 2008;67:340–345

Πώς τα πήγαν στα 5 έτη όσοι ολοκλήρωσαν;

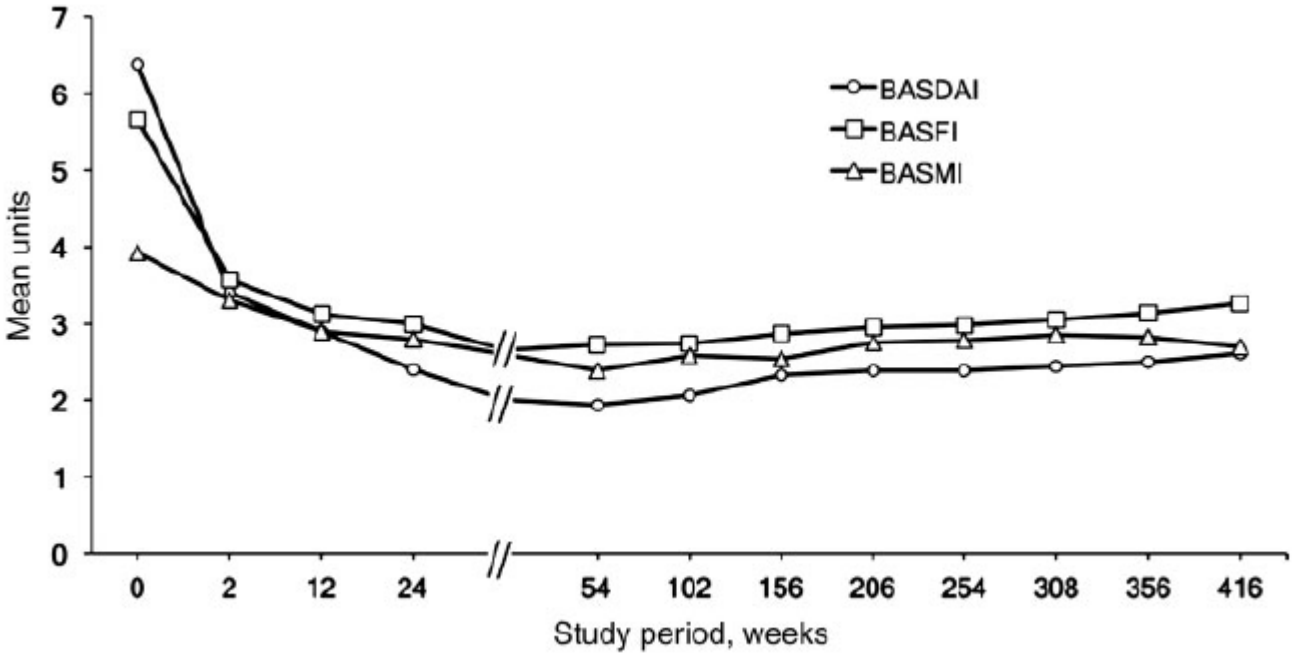
Table 2 Longitudinal analysis of disease status for all 38 completers for assessment of the prevalence of similar clinical status at week 12 and other follow-up time points of the study

	12 weeks (95% CI)	At all time points of follow-up	At 90% of the time points (95% CI)	At 80% of the time points of follow-up (95% CI)
Partial remission	7 (18.4%) (9.2 to 33.4)	3/7	5/7 (71.4%) (35.9 to 91.8)	6/7 (85.7%) (48.7 to 97.4)
BASDAI<3	21 (55.3%) (39.7 to 69.9)	12/21	16/21 (76.2%) (54.9 to 89.4)	19/21 (90.5%) (71.1 to 97.3)
BASFI<3	24 (63.2%) (47.3 to 76.6)	14/24	17/24 (70.8%) (50.8 to 85.1)	17/24 (70.9%) (50.8 to 85.1)
No arthritis	33 (86.8%) (72.7 to 94.2)	24/33	31/33 (93.9%) (80.4 to 98.3)	32/33 (97.0%) (84.7 to 99.5)
No enthesitis	29 (76.3%) (60.8 to 87.0)	14/29	25/29 (86.2%) (69.4 to 94.5)	25/29 (86.2%) (69.4 to 94.5)
No arthritis/enthesitis	28 (73.7%) (58.0 to 85.0)	14/28	22/28 (78.6%) (60.5 to 89.8)	23/28 (82.1%) (64.4 to 92.1)
BASDAI/global assessment <4	25 (65.8%) (49.9 to 78.8)	12/25	20/25 (80.0%) (60.9 to 91.1)	21/25 (84.0%) (65.3 to 93.6)
CRP ⩽6 mg/l	34 (89.5%) (75.9 to 95.8)	8/34	23/34 (67.6%) (50.8 to 80.9)	27/34 (79.4%) (63.2 to 89.7)

Numbers are n of patients, numbers in brackets are % of patients.

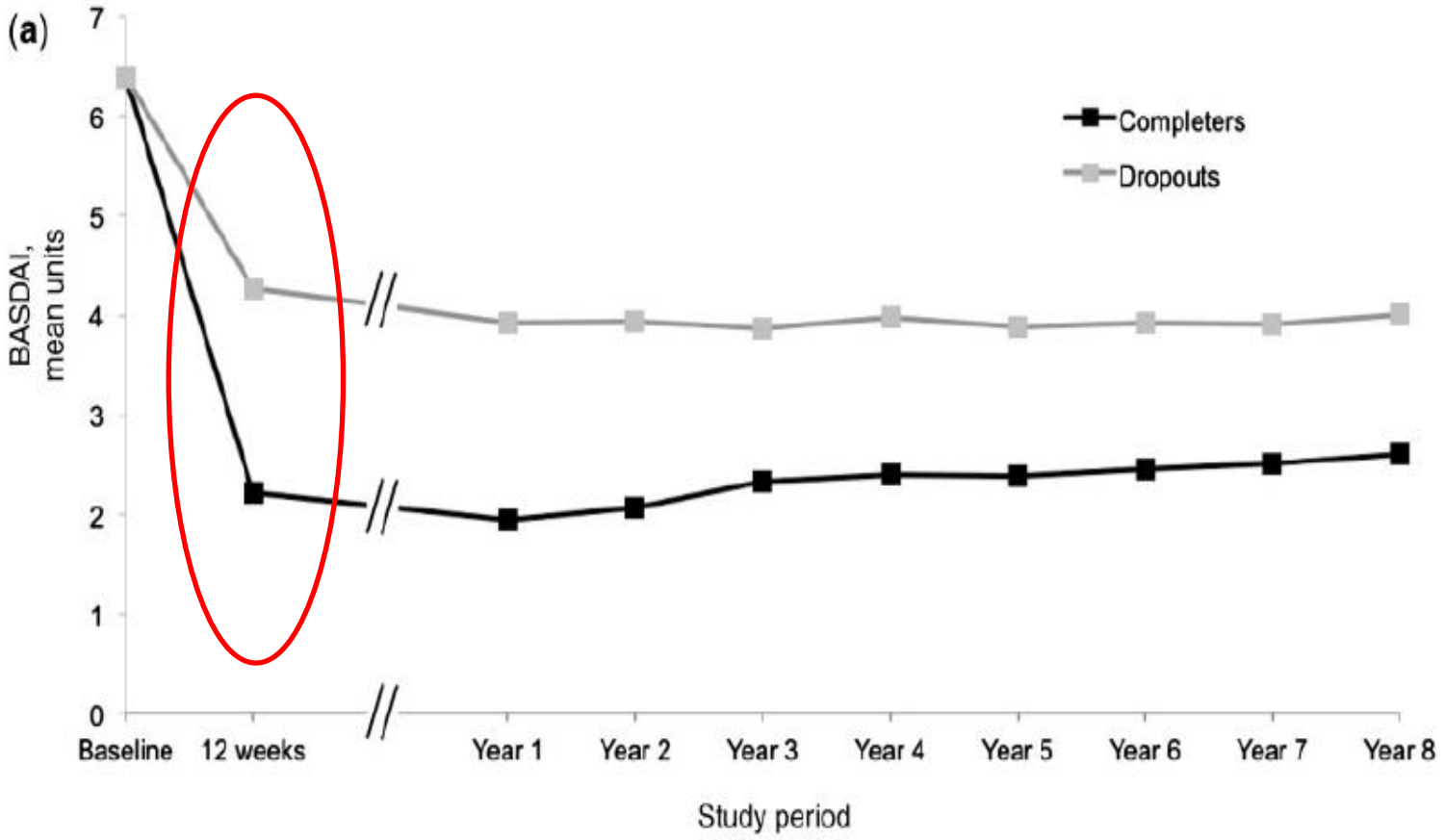
Braun et al. Persistent clinical efficacy and safety of anti-tumour necrosis factor a therapy with infliximab in patients with ankylosing spondylitis over 5 years: evidence for different types of response Ann Rheum Dis 2008;67:340–345

Παραμονή στη θεραπεία και αποτελεσματικότητα



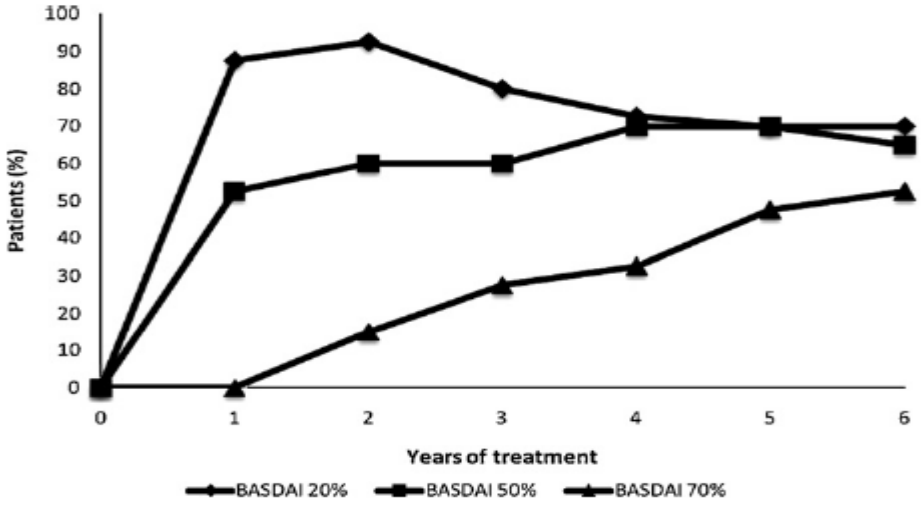
Baraliakos X. et al. Persistent clinical efficacy and safety of infliximab in ankylosing spondylitis after 8 years—early clinical response predicts long-term outcome
Rheumatology 2011;50:16901699

Παραμονή στη θεραπεία και αποτελεσματικότητα



Baraliakos X. et al. Persistent clinical efficacy and safety of infliximab in ankylosing spondylitis after 8 years—early clinical response predicts long-term outcome
Rheumatology 2011;50:16901699

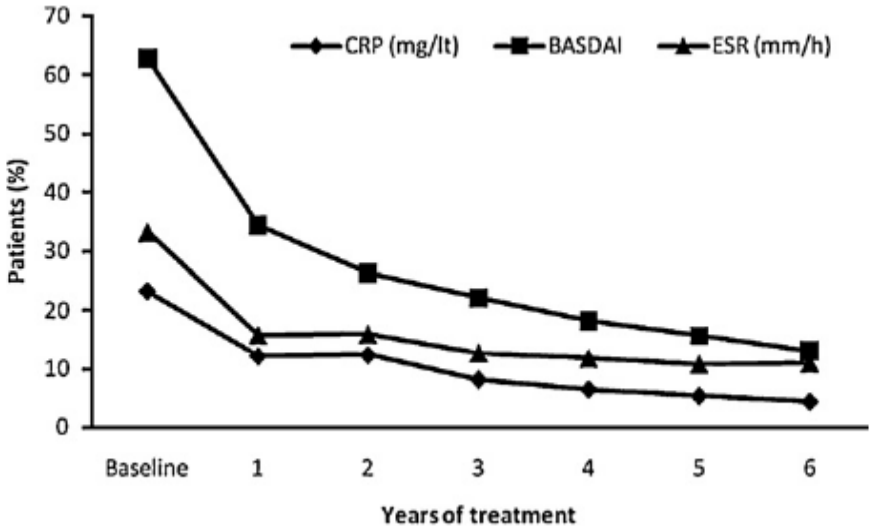
Στον ελληνικό χώρο…



Assessment of response for clinical and laboratory parameters after 6 years of treatment.

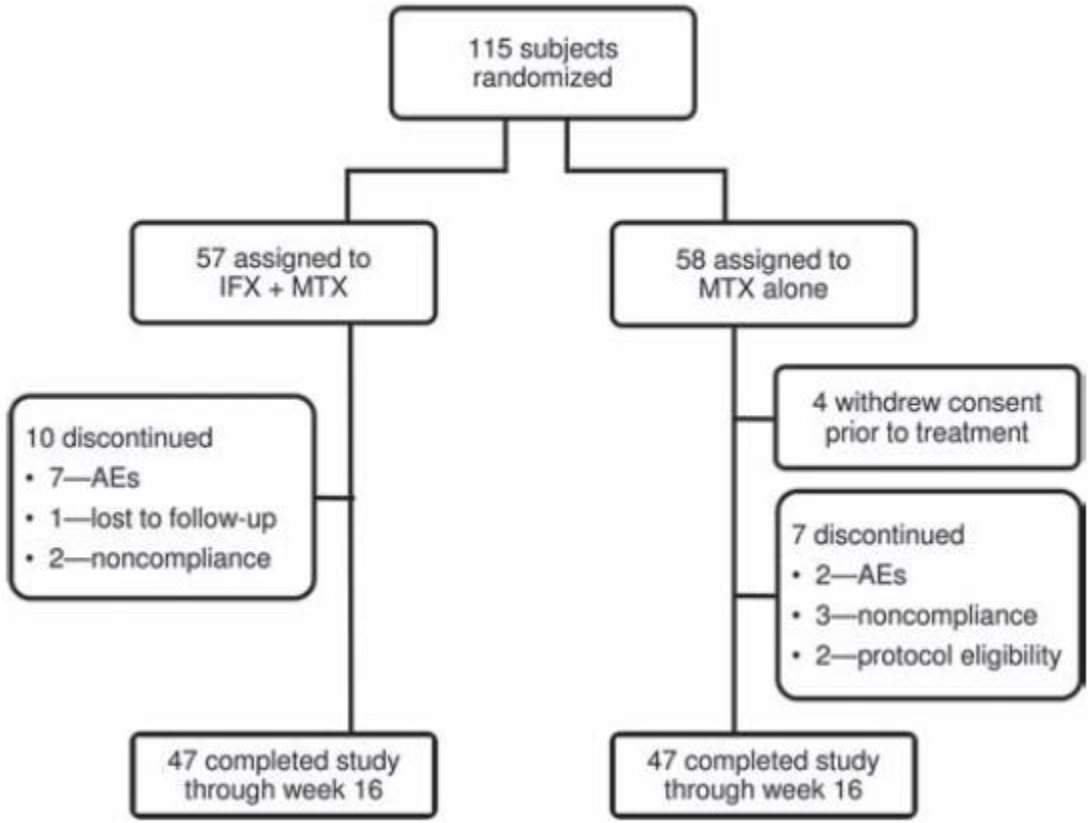
Parameter[a]	Baseline	6th year
Global disease assessment		
Patient (0–10 cm)	7.8 (1.2)	1.38 (0.8)
Physician (0–10 cm)	7.6 (1.1)	1.67 (0.8)
BASDAI	6.28 (1.1)	1.5 (1.0)
CRP (mg/l)	23.2 (19.2)	6.0 (5.3)
ESR (mm/1 h)	33.2 (18.2)	11.0 (6.2)
Hematocrit	41.4 (2.7)	46.0 (2.2)
Hemoglobin	13.4 (2.0)	15.1 (0.8)

6 έτη παρακολούθησης



1. Venetsanopoulou AI, Voulgari PV, Alamanos Y, et al. Persistent clinical responseof infliximab treatment, over a 4-year period in ankylosing spondylitis. Rheumatol Int 2007;27:935–9.
2. Saougou I, Markatseli TE ,Voulgari PV , Drosos AA. Maintained clinical response of infliximab treatment in ankylosing spondylitis: A 6-year long-term study Joint Bone Spine 2010, 77: 325-329

Infliximab- treat to target in PsA?

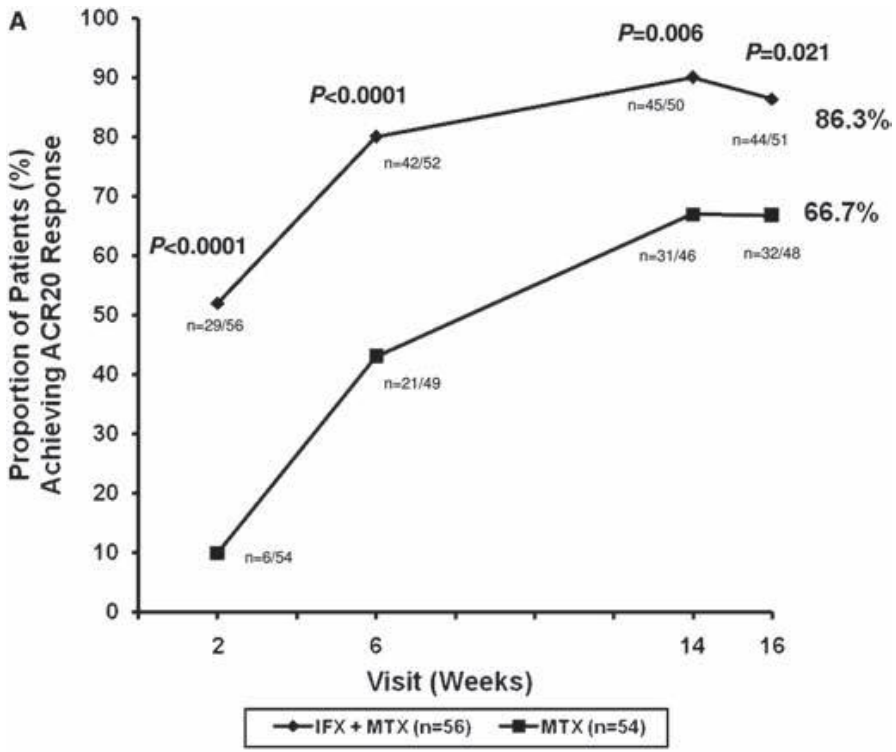


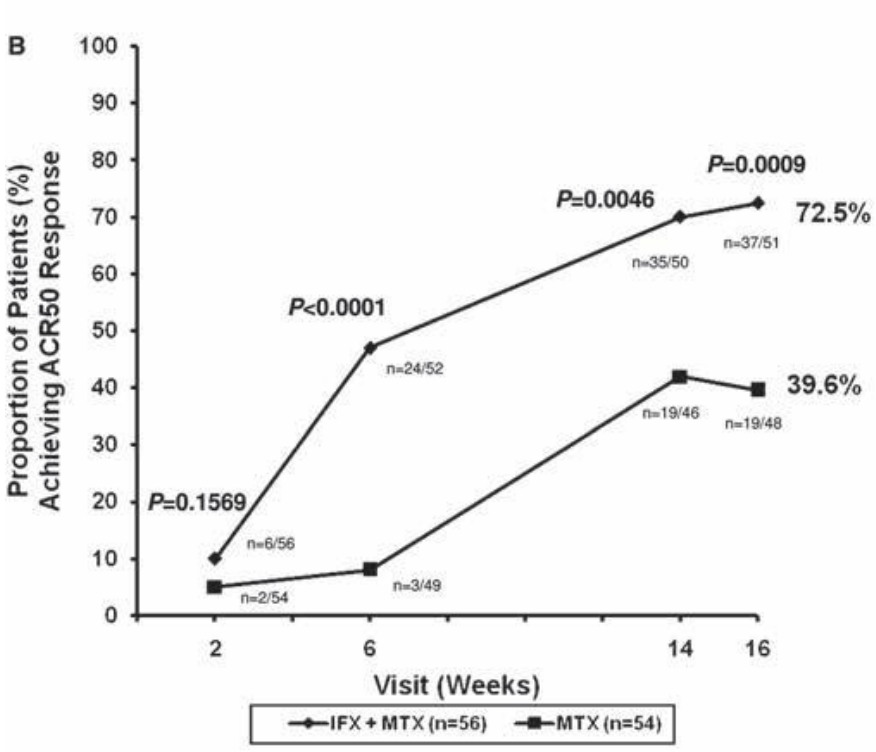
RESPOND Study

DMARD Naive Patients

Baranauskaite As et al. Infl iximab plus methotrexate is superior to methotrexate alone in the treatment of psoriatic arthritis in methotrexate-naive patients: the **RESPOND** study
Ann Rheum Dis 2012;71:541–548

Η «γρήγορη» ένταξη σε infliximab μειώνει την ενεργότητα της νόσου

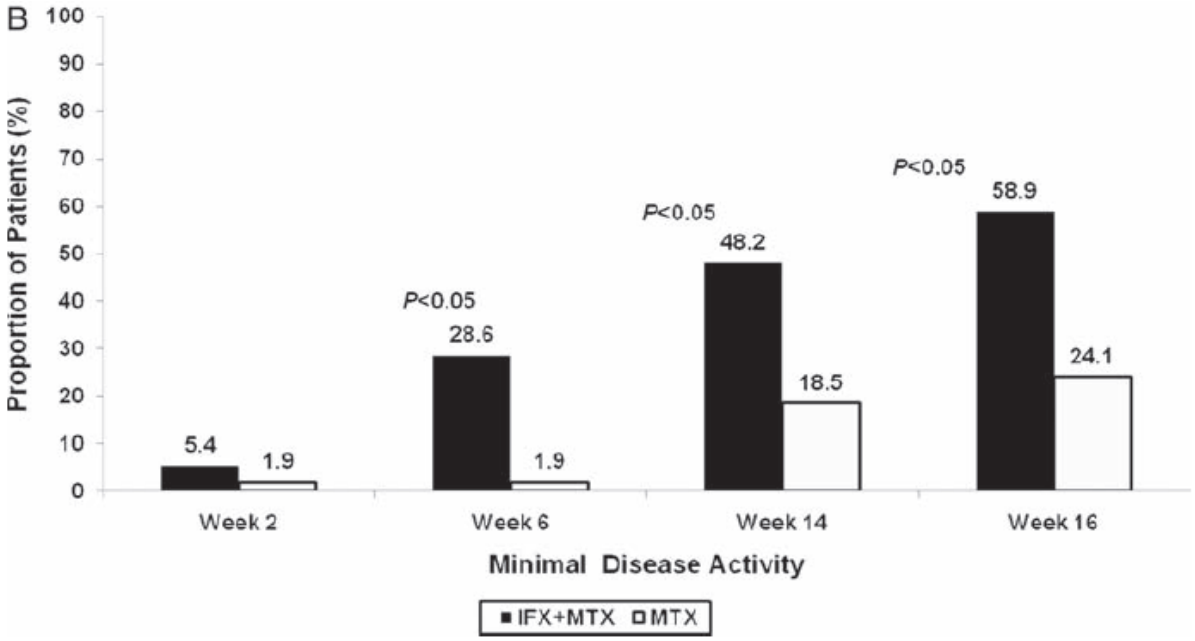




Baranauskaite As et al. Infl iximab plus methotrexate is superior to methotrexate alone in the treatment of psoriatic arthritis in methotrexate-naive patients: the **RESPOND** study
Ann Rheum Dis 2012;71:541–548

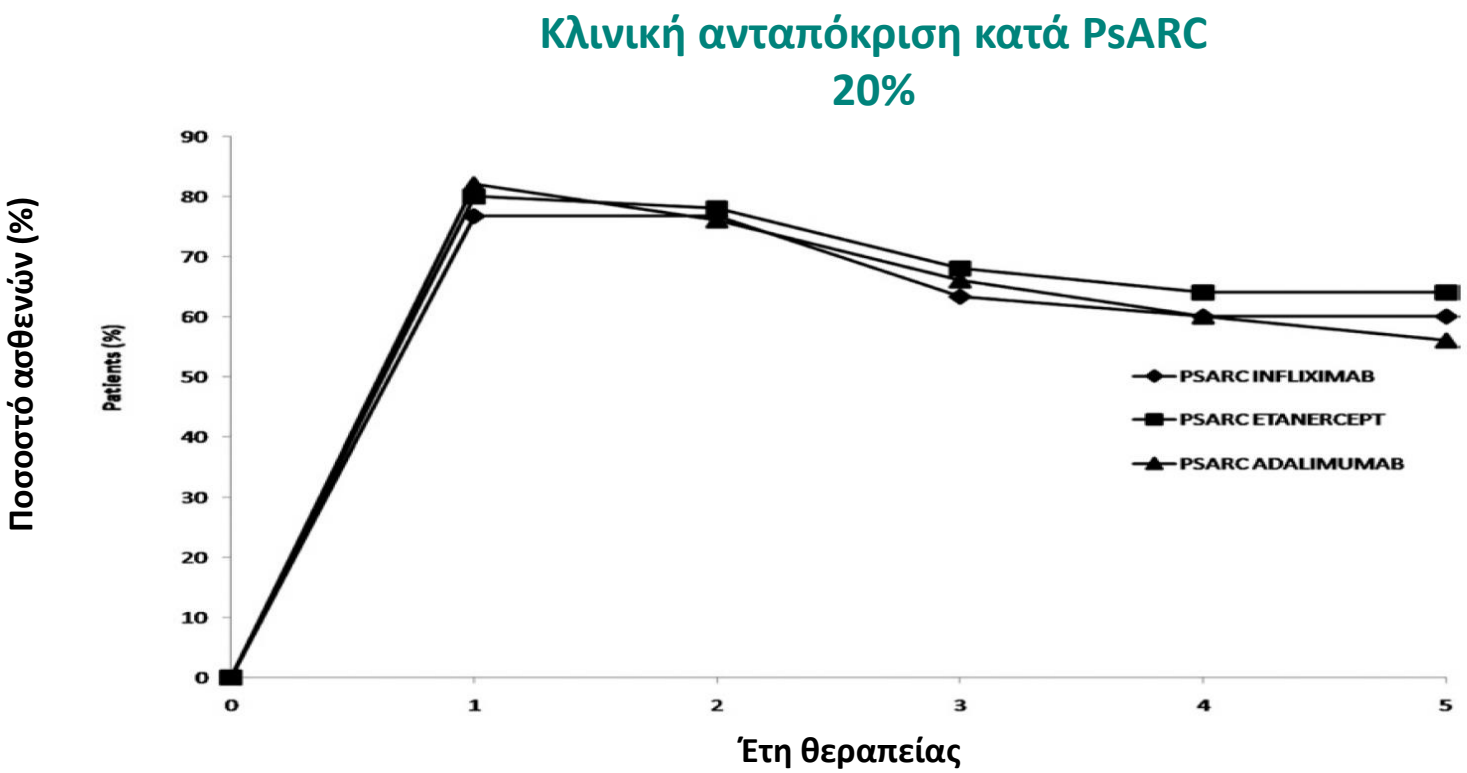
Ταχεία επίτευξη Minimal Disease Activity

ACR domain	Infliximab plus methotrexate (n=56)	Methotrexate (n=54)	p Value
Swollen joint count, median change*	–11.0	–9.0	0.0016
Tender joint count, median change*	–14.0	–9.5	0.0007
Subject's pain assessment,† mean change±SD (mm)	–45.8±26.4	–23.1±20.0	<0.0001
Subject's GAD,† mean change±SD (mm)	–43.0±24.2	–24.1±22.7	<0.0001
Evaluator's GAD,† mean change±SD (mm)	–47.4±18.3	–30.6±21.6	<0.0001
HAQ–DI, mean change±SD	–0.99±0.72	–0.56±0.72	0.0041
CRP, median change (mg/l)	–12.0	–5.8	0.0026
ESR, median change (s)	–12.0	–8.0	0.0023



Baranauskaite As et al. Infl iximab plus methotrexate is superior to methotrexate alone in the treatment of psoriatic arthritis in methotrexate-naive patients: the **RESPOND** study
Ann Rheum Dis 2012;71:541–548

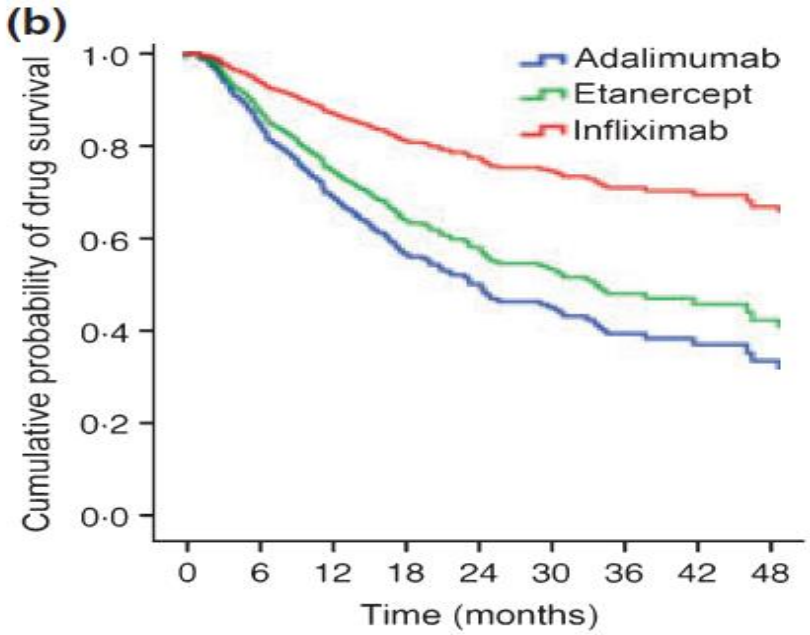
Ελληνική εμπειρία: μακροχρόνια αποτελεσματικότητα αντι TNF θεραπειών στη ΨΑ



Saougou I, et al. Seminars Arthr Rheum 2010

DERMBIO: Μητρώο ασθενών με ψωρίαση υπό anti-TNFα θεραπεία

Ποσοστό παραμονής ασθενών στη θεραπεία με anti-TNFα παράγοντες στα 4 έτη (n=747)



70% με Infliximab

40% με Etanercept

40% με Adalimumab

Hazard ratios (HRs) for factors determining drug survival were calculated by logistic regression.

Τα αποτελέσματα που παρουσιάζονται προέρχονται από μητρώα ασθενών και όχι από τυχαιοποιημένη μελέτη άμεσης σύγκρισης των θεραπευτικών παραγόντων, επομένως δεν υποδεικνύουν σύγκριση μεταξύ αυτών.
R. Gniadecki et al. Adherence to treatment with biologics in patients with psoriasis

Gniadecki R, et al. Br J Dermatol. 2011 May;164(5):1091-6.

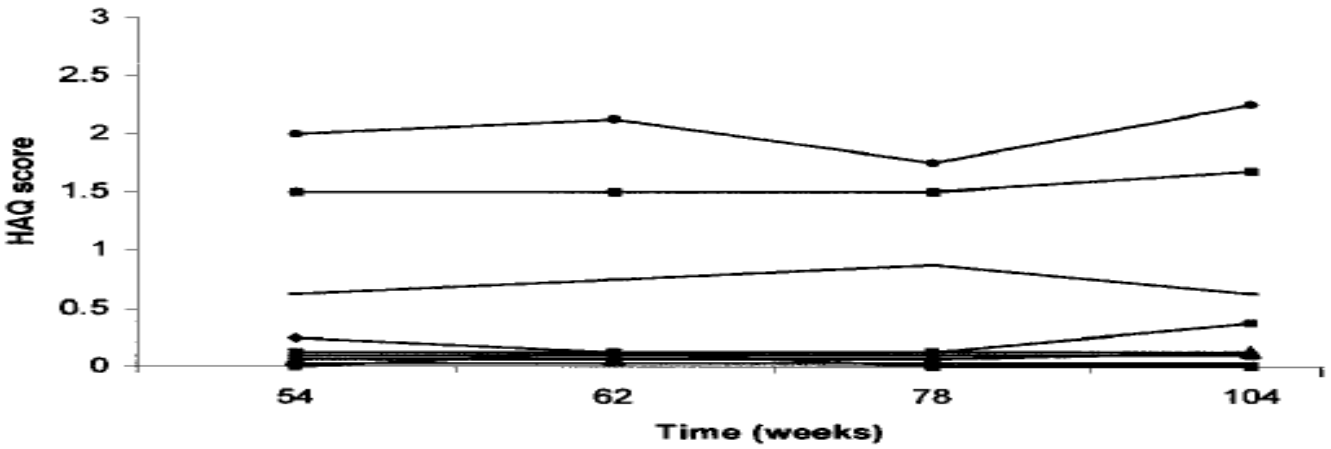
Πώς ερμηνεύεται το μεγαλύτερο ποσοστό παραμονής στη θεραπεία με Infliximab;

- Γρήγορο αποτέλεσμα
- Το ποσοστό ΑΕ είναι παρόμοιο με τις υπόλοιπες anti-TNFa βιολογικές θεραπείες και χαμηλό
- Η ενδοφλέβια χορήγηση εξασφαλίζει υψηλότερη συμμόρφωση
- Η δόση του Infliximab προσαρμόζεται στο σωματικό βάρος του κάθε ασθενούς (5mg/kg)

Gniadecki R, et al. Br J Dermatol. 2011 May;164(5):1091-6.

Αποσυρση , επαναχορήγηση …. Τι γίνεται με το θεραπευτικο αποτέλεσμα?

Μετά τη διακοπή;



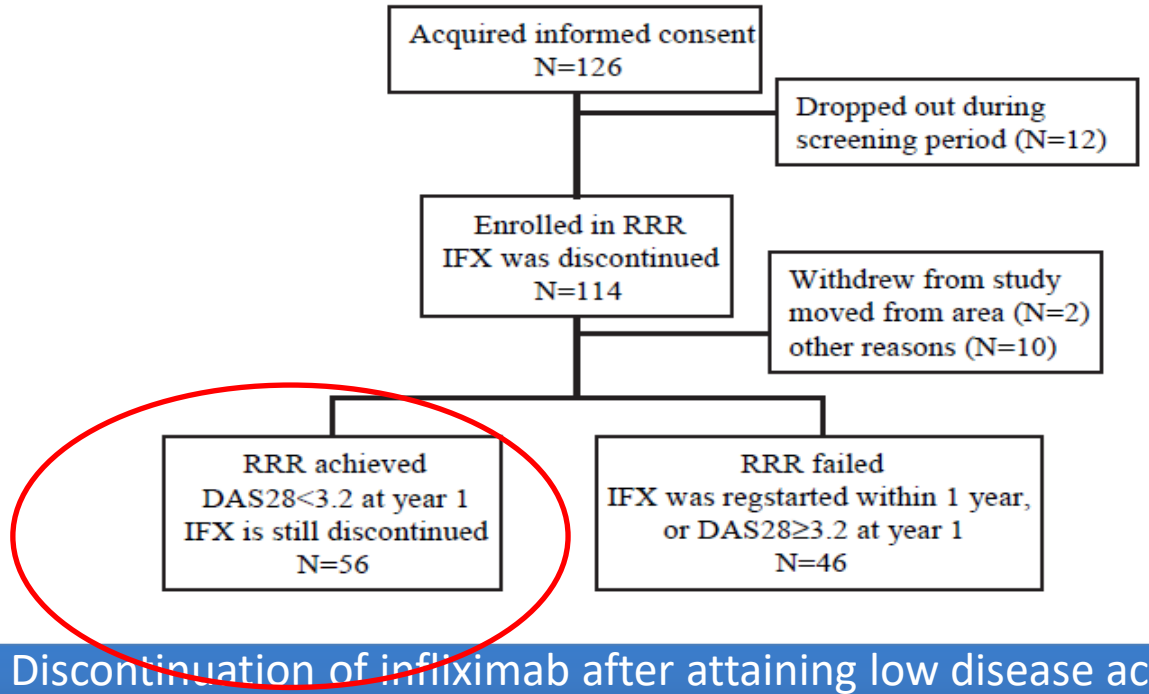
Ένα χρόνο μετά τη διακοπή του infliximab διατήρηση του «καλού» αποτελέσματος

Quinn MA 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. *Arthritis Rheum 2005*,52:27-35

RRR (…ζωή χωρίς το infliximab)

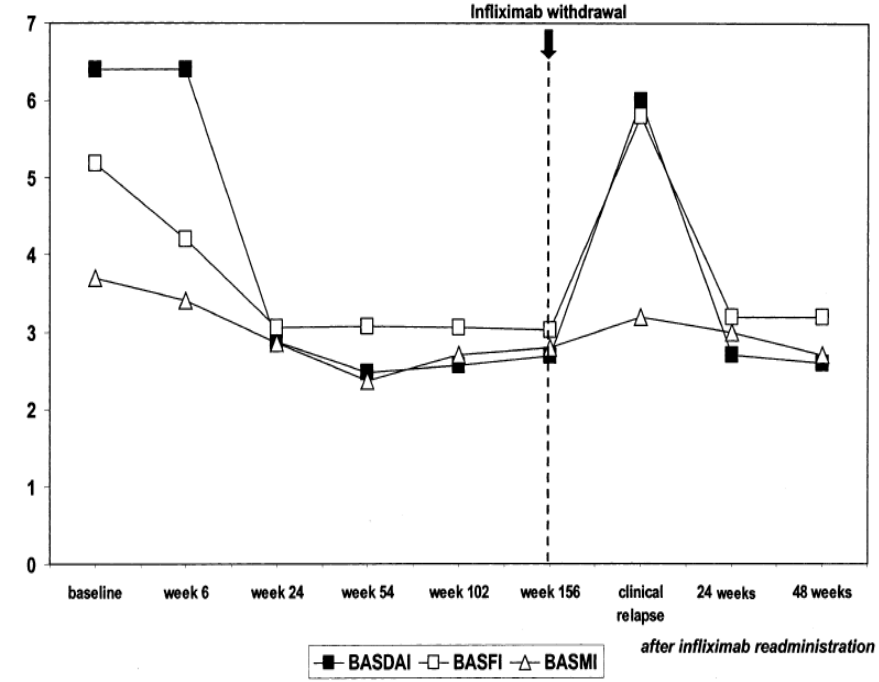
Discontinuation of infliximab after attaining low disease activity in patients with rheumatoid arthritis: RRR (remission induction by Remicade in RA) study

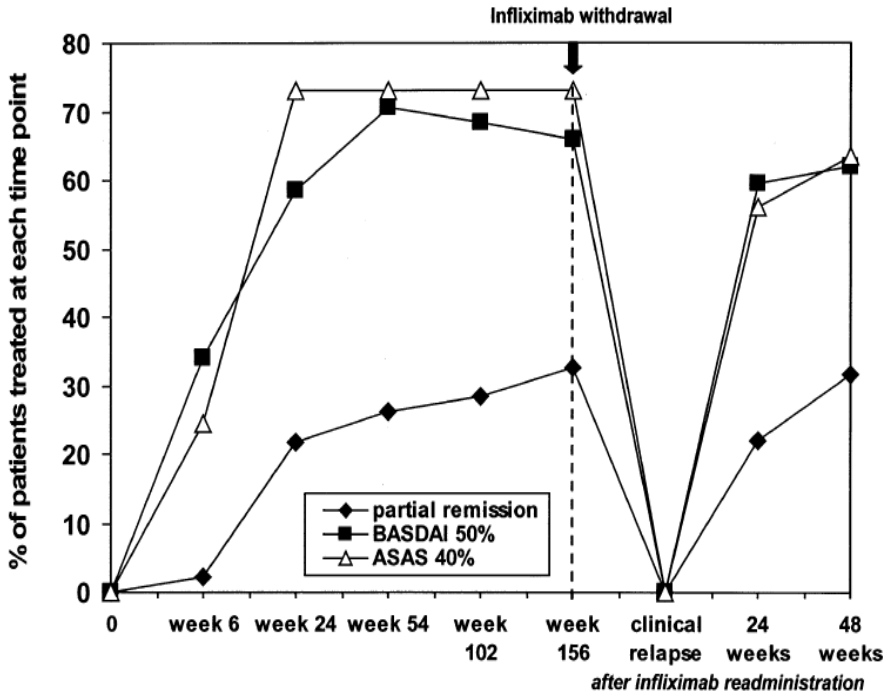
Y Tanaka,[1] T Takeuchi,[2] T Mimori,[3] K Saito,[1] M Nawata,[1] H Kameda,[4] T Nojima,[3] N Miyasaka,[5] T Koike[6]; for the RRR study investigators



Y Tanaka et al. Discontinuation of infliximab after attaining low disease activity in patients with rheumatoid arthritis: RRR (remission induction by Remicade in RA) study *Ann Rheum Dis 2010;69:1286–1291*

Απόσυρση και επαναχορήγηση





CONCLUSION:

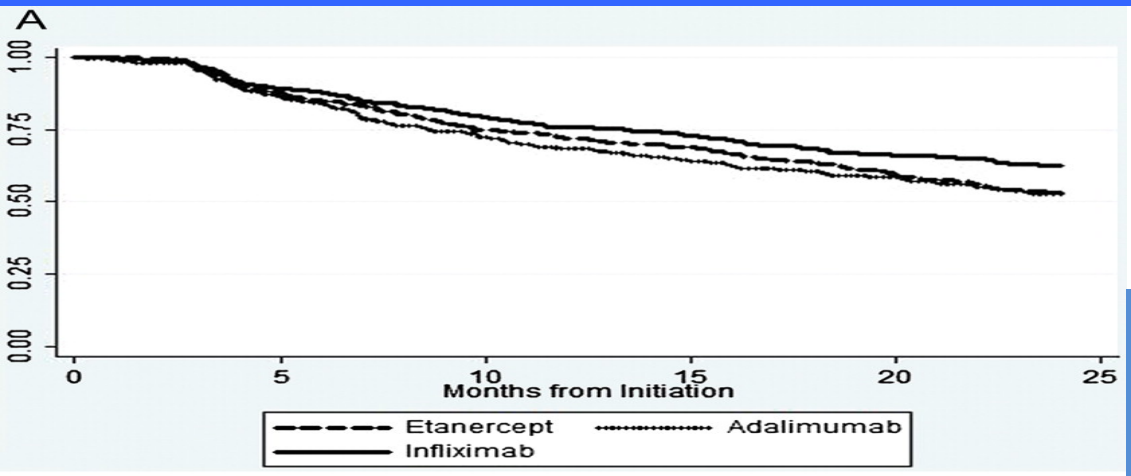
Readministration of infliximab after discontinuation of longterm treatment was generally safe and efficacious. Ongoing remission after discontinuation was rare. There was only one patient with relevant adverse events. ATI were detected only in this patient, but there was no correlation to clinical data. Formation of ATI seems to be rare after longterm infliximab therapy in AS

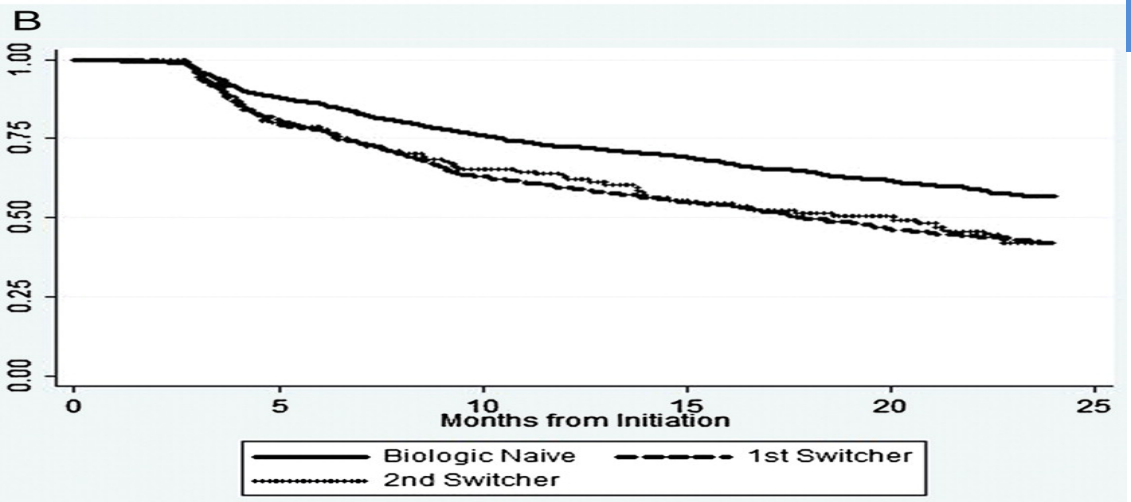
Baraliakos X. et al. Safety and Efficacy of Readministration of Infliximab After Longterm Continuous Therapy and Withdrawal in Patients with AS. *J Rheumatol 2007;34:510–15*

Μητρώα καταγραφής…..(registry data)

Τα αποτελέσματα που παρουσιάζονται στα μητρώα ασθενών είναι αποτέλεσμα καταγραφής και όχι από τυχαιοποιημένές μελετές άμεσης σύγκρισης μεταξύ των θεραπευτικών παραγόντων, επομένως δεν υποδεικνύουν σύγκριση μεταξύ αυτών

ΜΗΤΡΩΑ ΚΑΤΑΓΡΑΦΗΣ (Corrona USA)





A comparative effectiveness study of adalimumab, etanercept and infliximab in biologically naive and switched rheumatoid arthritis patients: results from the US CORRONA registry

Conclusions No differences in rates of drug response or remission were observed among the three anti-TNF. Infliximab was associated with greater persistence in biologically naive patients. Response, remission and persistence outcomes were diminished for patients who switched anti-TNF.

ΜΗΤΡΩΑ ΚΑΤΑΓΡΑΦΗΣ (Corrona USA)

Table 5 The unadjusted persistence rates and adjusted likelihood of drug discontinuation based on anti-TNFα switching status*

	Persistence rate			
	12 months (95% CI)	24 months (95% CI)	Adjusted HR (95% CI)	p Value
TNF inhibitor switching status				
Biologically naive (referent)	72% (70% to 75%)	57% (54% to 60%)	1	
First switchers	60% (55% to 64%)	42% (37% to 47%)	1.42 (1.22 to 1.67)	<0.001
Second switchers	63% (54% to 70%)	42% (33% to 51%)	1.35 (1.03 to 1.76)	0.028
Interdrug comparisons				
Biologically naive				
Infliximab (referent)	76% (72% to 80%)	63% (58% to 67%)	1	
Adalimumab	68% (64% to 73%)	53% (47% to 58%)	1.42 (1.12 to 1.80)	0.004
Etanercept	72% (68% to 76%)	53% (48% to 59%)	1.27 (1.00 to 1.61)	0.047
First switchers				
Infliximab (referent)	65% (56% to 72%)	43% (34% to 52%)	1	
Adalimumab	57% (51% to 62%)	42% (35% to 48%)	1.14 (0.84 to 1.55)	NS
Etanercept	60% (50% to 68%)	41% (31% to 50%)	1.01(0.71 to 1.44)	NS

*Results are presented as HR with 95% CI in parentheses; the models adjusted for age, gender, patient and provider assessments of disease activity, self-reported disability, comorbidity, methotrexate use and year of anti-TNF initiation.
NS, not significant; TNF, tumour necrosis factor.

ΜΗΤΡΩΑ ΚΑΤΑΓΡΑΦΗΣ (BSRBR - UK)

TABLE 2. Details of drug discontinuation prior to first 6 month follow-up[a]

Reason	All (3223)	Etanercept (1413)	Infliximab (1810)
Any reason	614 (19.1)	264 (18.7)	350 (19.3)
Inefficacy	270 (8.4)	118 (8.4)	152 (8.4)
Adverse event	295 (9.2)	129 (9.1)	166 (9.2)
Other	41 (1.3)	12 (0.9)	29 (1.6)
Unknown	8 (0.3)	5 (0.4)	3 (0.2)

[a]Observed differences between etanercept and infliximab are not statistically significant.

TABLE 3. EULAR response after 6 months of therapy[a]

EULAR response	Overall (3223)	Etanercept (1413)	Infliximab (1810)
Good	584 (18.1)	245 (17.3)	339 (18.7)
Moderate	1602 (49.7)	727 (51.5)	875 (48.3)
None	1037 (32.2)	441 (31.2)	596 (32.9)
Remission	292 (8.6)	120 (8.0)	172 (9.0)

[a]Observed differences between etanercept and infliximab are not statistically significant.

ΜΗΤΡΩΑ ΚΑΤΑΓΡΑΦΗΣ (DREAM - Neatherlands)

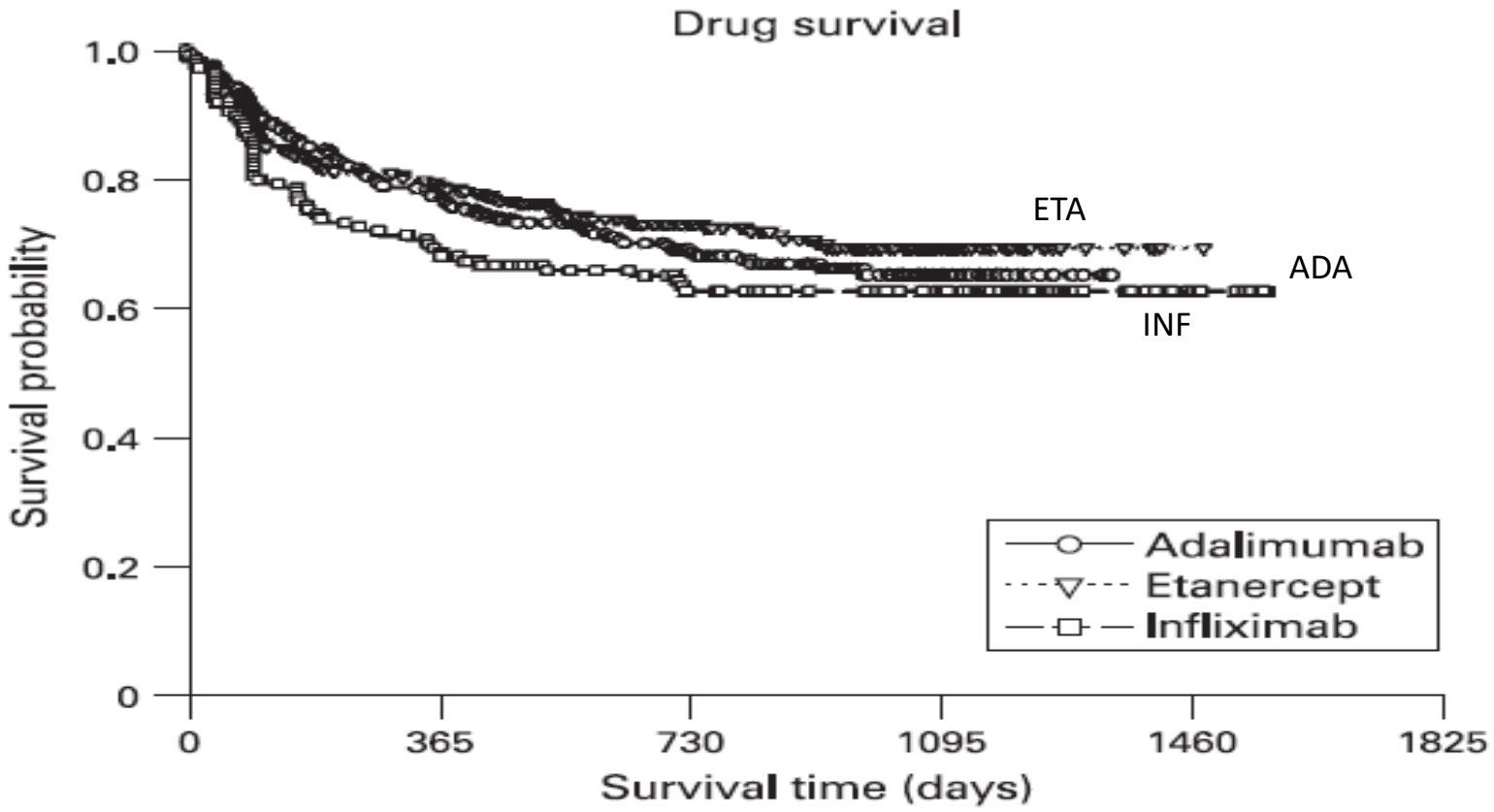


Figure 1 drug survival in the three treatment groups.

ΜΗΤΡΩΑ ΚΑΤΑΓΡΑΦΗΣ (DREAM - Neatherlands)

Table 2 Co-medication used and changes within 12 months

	Concomitant use	Dose decrease	Discontinuation	Dose increase
DMARD				
Adalimumab (n = 267)	231 (87%)	67 (29%)	63 (27%)	9 (4%)
Etanercept (n = 289)	225 (78%)	52 (23%)	61 (27%)	12 (5%)
Infliximab (n = 151)	128 (85%)	22 (17%)	35 (27%)	7 (6%)
p Value	0.02	0.039	0.999	0.712
Prednisone, oral				
Adalimumab (n = 267)	78 (29%)	13 (17%)	15 (19%)	3 (4%)
Etanercept (n = 289)	115 (40%)	19 (16%)	27 (23%)	5 (4%)
Infliximab (n = 151)	44 (29%)	4 (9%)	9 (20%)	3 (7%)
p Value	0.018	0.803	0.470	0.733
Prednisone*				
Adalimumab (n = 267)	31 (12%)			
Etanercept (n = 289)	51 (18%)			
Infliximab (n = 151)	28 (19%)			
p Value	0.076			

*Intra-articular or intramuscular.
DMARD, disease-modifying antirheumatic drug.

Συγχορήγηση με Μεθοτρεξάτη και παραμονή..

Treatment persistence with adalimumab, etanercept, or infliximab in combination with methotrexate and the effects on health care costs in patients with rheumatoid arthritis.[3]

CONCLUSIONS:
In this population of patients with RA, overall treatment persistence was high, with patients treated with infliximab + MTX having significantly higher persistence compared with those treated with adalimumab + MTX or etanercept + MTX.

The role of methotrexate co-medication in TNF-inhibitor treatment in patients with psoriatic arthritis: results from 440 patients included in the NOR-DMARD study.[1]

CONCLUSIONS:
We found similar responses to TNFi in patients with and without concomitant MTX, but drug survival was superior in patients receiving co-medication. The effect of MTX on drug survival was most prominent in patients receiving IFX. Smoking at baseline and use of TNFi as monotherapy were identified as independent predictors of drug discontinuation.

Tumour necrosis factor inhibitor monotherapy vs combination with MTX in the treatment of PsA: a systematic review of the literature.[2]

CONCLUSION:
Available evidence on the efficacy and safety of TNF inhibitor monotherapy vs add-on MTX therapy shows little or no improvement with combination therapy, although the use of concomitant MTX appears to prolong TNF inhibitor drug survival of mAb TNF inhibitors. Registries and observational studies have the potential to fill some of the knowledge gaps in this area

1.Fagerli KM1, Lie E, van der Heijde D, Heiberg MS, Lexberg AS, Rødevand E, Kalstad S, Mikkelsen K, Kvien TK
Ann Rheum Dis. 2014 Jan;73(1):132-7. doi: 10.1136/annrheumdis-2012-202347. Epub 2013 Jan 3

2.Behrens F1, Cañete JD2, Olivieri I2, van Kuijk AW2, McHugh N2, Combe B
Rheumatology (Oxford). 2015 May;54(5):915-26. doi: 10.1093/rheumatology/keu415. Epub 2014 Oct 27

3. Degli Esposti L et al, ClinicoEconomics and Outcomes Research 2014;6:401-7 2. Tang B et al, Clin Ther. 2008;30:1375–1384

Adverse effects (ARTIS-Sweden)

Table 2 Discontinuations, person-years and incidence rates over up to 5 years of follow-up in Swedish patients with rheumatoid arthritis starting their first TNFi between 2003 and 2011

	Etanercept (n=3892)	Adalimumab (n=2349)	Infliximab (n=2898)	Total (n=9139)
Observation years	9259	5131	5808	20 198
Discontinuations, n (%)	1391 (100%)	963 (100%)	1470 (100%)	3782 (100%)
Lack/loss of efficacy*	710 (51%)	476 (49%)	738 (52%)	1924 (51%)
Adverse event	474 (34%)	349 (36%)	525 (37%)	1348 (36%)
Other	207 (15%)	138 (14%)	165 (12%)	510 (13%)
Discontinuation causes not counted as events, n (%)				
Pregnancy	59 (1.5%)	15 (0.6%)	12 (0.4%)	86 (0.9%)
Remission†	44 (1.1%)	53 (2.3%)	50 (1.7%)	147 (1.6%)
Death	31 (0.8%)	30 (1.3%)	35 (1.2%)	96 (1.1%)
Incidence per 100 person-years	15	19	25	19
1 year drug survival				
Observation years, sum	2355	1349	1667	5371
Discontinuations, n	671	517	668	1856
%	26%	34%	36%	31%

*As decided by treating physician or patient (standardised failure definition NOT used).
†Note: These numbers represent patients who have *discontinued* TNFi therapy due to remission. Patients in remission *continuing* therapy do not contribute to these numbers.
TNF, tumour necrosis factor; TNFi, TNF inhibitor.

Take home notes…

- η παραμονή στην θεραπεία είναι εξαιρετικής σημασίας στην διαχείριση χρόνιων νοσημάτων
- η παραμονή στην θεραπεία είναι δείκτης αξιολόγησης της επίτευξης του θεραπευτικού μας στόχου στην καθημέρα κλινική πράξη
- θετική σχέση κόστους - όφελος στους ασθενείς με αυξημένη παραμονή στην θεραπευτική προσέγγιση
- Η ταχύτητα δράσης σχετίζεται με την παραμονή στην θεραπεία