Υπάρχουν δεδομένα διαφοροποίησης της αποτελεσματικότητας μεταξύ των TNFis ?

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ORIGINAL PAPER

Comparative efficacy and safety of biosimilar infliximab and other biological treatments in ankylosing spondylitis: systematic literature review and meta-analysis

Petra Baji · Márta Péntek · Sándor Szántó · Pál Géher · László Gulácsi · Orsolya Balogh · Valentin Brodszky

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Abstract

Objectives To compare the efficacy and safety of infliximab-biosimilar with other biological drugs for the treatment of active ankylosing spondylitis (AS).

Methods Systematic literature review for randomized controlled trials (RCTs) with adalimumab, etanercept, golimumab, infliximab and infliximab-biosimilar in AS was

agents proved to be significantly superior to placebo. Infliximab showed the highest odds ratio (OR) of 7.2 (95 % CI 3.68–13.19) compared to placebo, followed by infliximab-biosimilar with OR 6.25 (95 % CI 2.55–13.14), both assessed at week 24. No significant difference was found between infliximab-biosimilar and other biological treatments regarding their efficacy and safety.

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CTs, identified by the systematic
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point were reported for week 12
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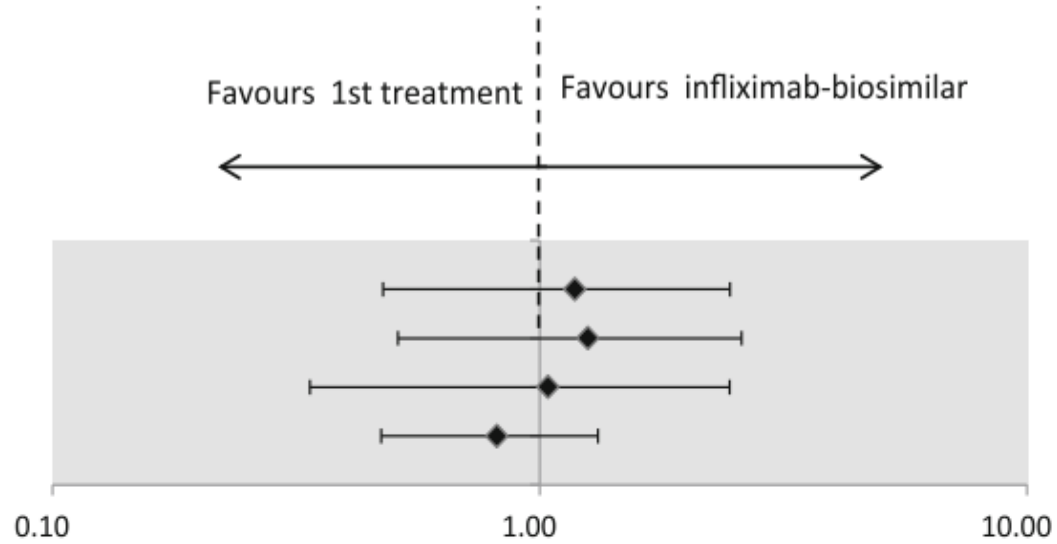
Conclusions This is the first study which includes a biosimilar drug in the meta-analysis of biological treatments in AS. The results have proven the similar efficacy and safety profile of infliximab-biosimilar treatment compared to other biologicals.

Keywords Ankylosing spondylitis · Biological drug · Biosimilar pharmaceuticals · Meta-analysis · Efficacy · Safety

JEL Classification I10 · I19

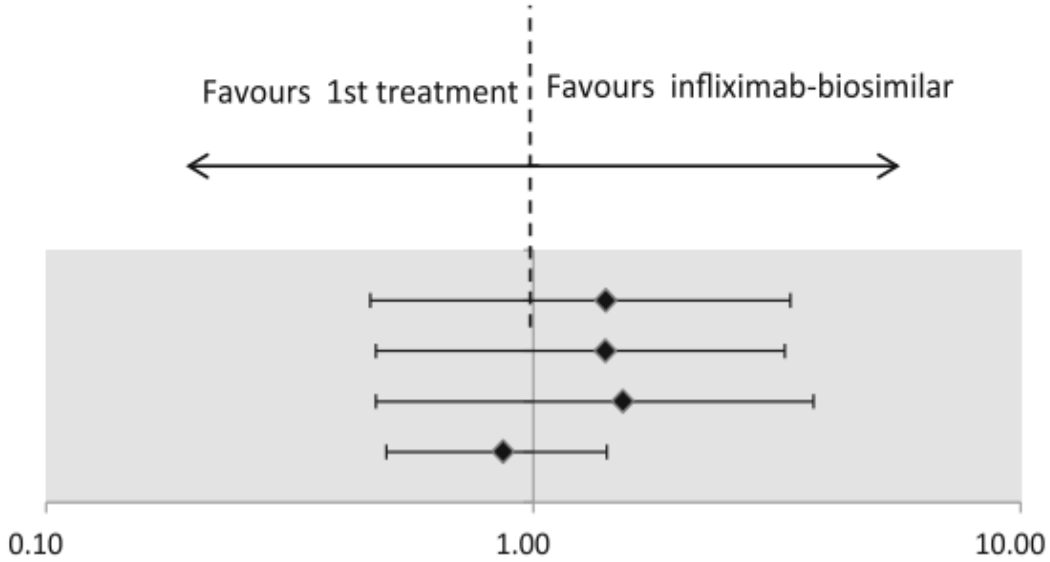
ASAS20 at week 12

Comparison	OR (95% CI)
adalimumab vs. infliximab-biosimilar	1.18 [0.48-2.46]
etanercept vs. infliximab-biosimilar	1.26 [0.51-2.6]
golimumab vs. infliximab-biosimilar	1.04 [0.34-2.46]
infliximab vs. infliximab-biosimilar	0.82 [0.47-1.32]



ASAS20 at week 24

Comparison	OR (95% CI)
adalimumab vs. infliximab-biosimilar	1.41 [0.46-3.37]
etanercept vs. infliximab-biosimilar	1.41 [0.47-3.29]
golimumab vs. infliximab-biosimilar	1.53 [0.48-3.76]
infliximab vs. infliximab-biosimilar	0.87 [0.5-1.42]



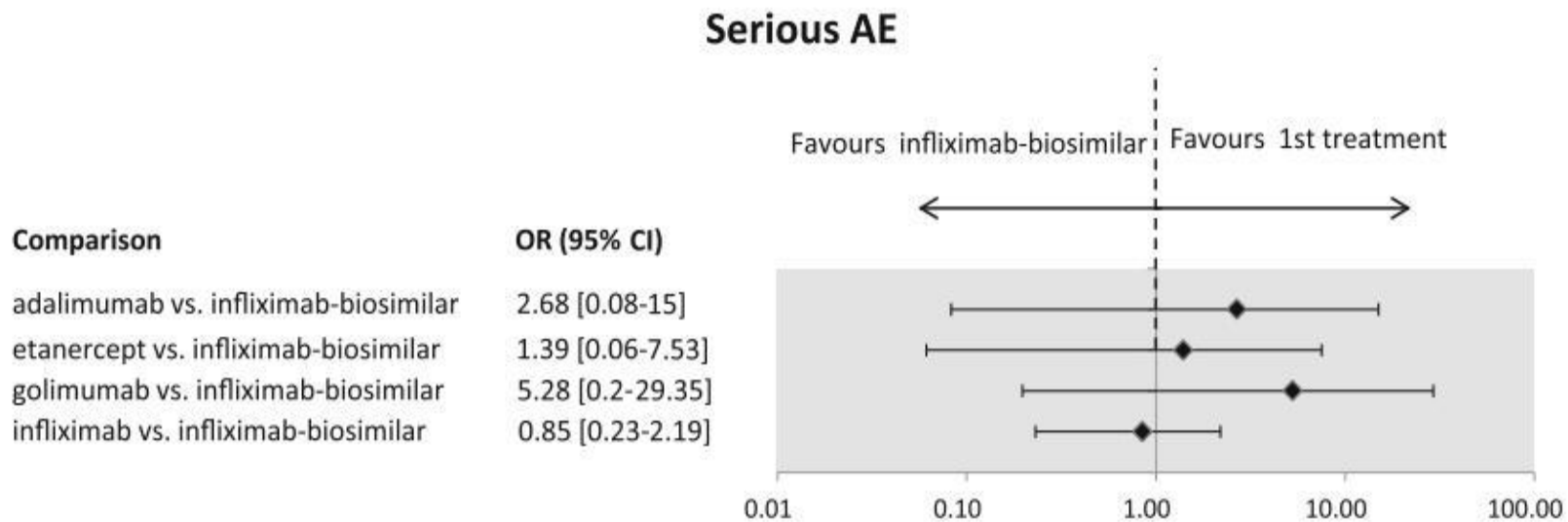


Fig. 2 The safety of infliximab-biosimilar compared to other biologicals in AS: serious adverse events (AE). Results for week 30 were available and considered for infliximab-biosimilar. Note: the Figure presents odds ratios (OR) between treatments. If the point estimate is lower than 1 then the biosimilar treatment is safer (although not necessarily statistically significantly safer). Credibility intervals provide information on whether the difference between treatments is statistically significant. If the CI contains the value 1, the difference is not statistically significant

Discussion

Our study, based on the meta-analysis of available RCTs, involving 2,395 AS patients at week 12 and 1,337 AS patients at week 24, has demonstrated that there is no significant difference in the efficacy of infliximab-biosimilar and other

Nevertheless, authors came to the same conclusion as us, namely that infliximab 5 mg/kg at 0, 2, 6 weeks was the best efficacious therapy [OR 6.53 (95 % CI 3.35, 11.61)] compared to placebo [31]. No significant differences were found between the biological treatments either.

Migliore et al. [4] compared ASAS20 response at week

EXTENDED REPORT

Drug survival on TNF inhibitors in patients with rheumatoid arthritis comparison of adalimumab, etanercept and infliximab

M Neovius,[1] E V Arkema,[1] H Olsson,[1] J K Eriksson,[1] L E Kristensen,[2] J F Simard,[1] J Askling,[1,3] for the ARTIS Study Group

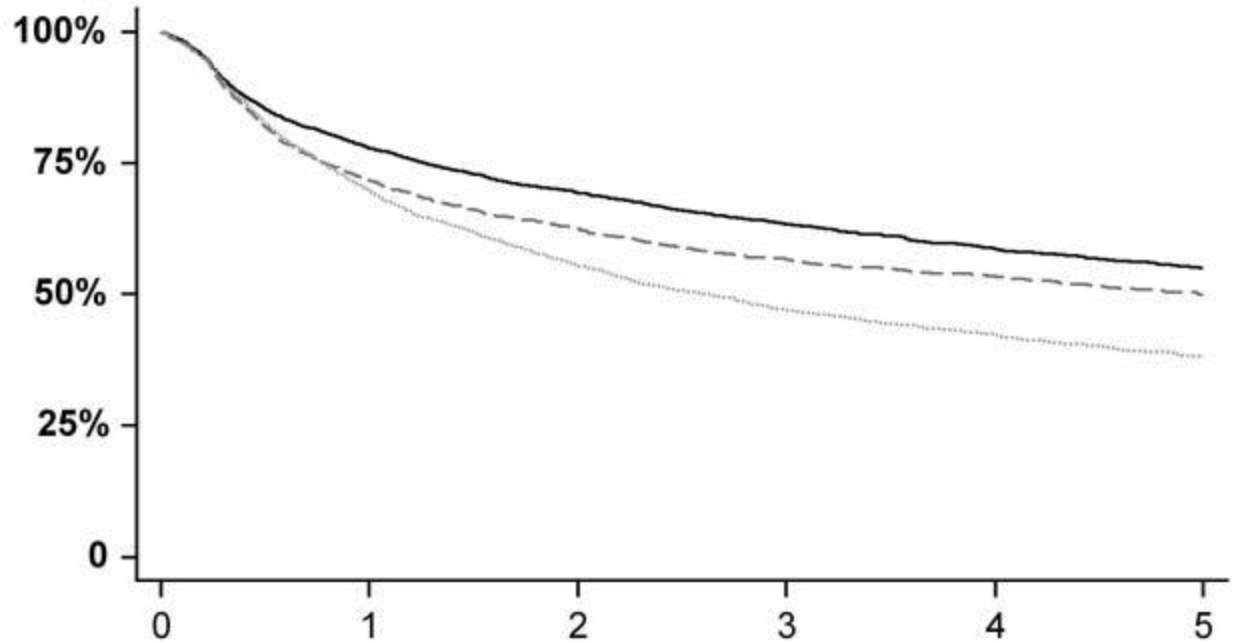
ABSTRACT

Objective To compare drug survival on adalimumab, etanercept and infliximab in patients with rheumatoid arthritis (RA).

Methods Patients with RA (n=9139; 76% women; mean age 56 years) starting their first tumour necrosis factor (TNF) inhibitor between 2003 and 2011 were identified in the Swedish Biologics Register (ARTIS). Data were collected through 31 December 2011. Drug survival over up to 5 years of follow-up was compared overall and by period of treatment start (2003–2005/2006–2009; n=3168/4184) with adjustment for age, sex, education, period, health assessment questionnaire (HAQ), disease duration, concomitant disease modifying antirheumatic drug (DMARD) treatment and general frailty (using hospitalisation history as proxy).

characteristics of the patient population treated, both of which have changed over time.[3 4 9–11]

Previous studies from Sweden,[4] Spain,[5] Switzerland[1] and the USA[12] have shown decreasing 1-year TNFi drug survival since their introduction in the late 1990s. Danish and British data, on the other hand, showed a relatively stable TNFi discontinuation rate between 2000–2005 and 2001–2008, respectively.[3 10] During the last 10 years, characteristics of the TNFi patient population have changed, with patients today generally having lower disease activity and higher functional ability at initiation.[3 4 9–11] which in some studies have been associated with better drug survival.[1 13 14] At the same time, the penetration of TNFi treatment has increased dramatically, the number of alternative



Number at Risk (Discontinuations)

Etanercept	3892	(823)	2677	(266)	1924	(151)	1446	(94)	1027	(57)	712
Adalimumab	2349	(632)	1462	(169)	1034	(88)	766	(41)	577	(33)	418
Infliximab	2898	(824)	1730	(320)	1110	(157)	791	(74)	587	(53)	415

Adj. Hazard Ratios (95%CI)	**0-1y**	**>1-1.9y**	**2-5y**	**0-5y**
-Adalimumab vs Etanercept	1.37 (1.23-1.52)	1.18 (.97-1.44)	1.00 (.84-1.20)	**1.26 (1.16-1.37)**
-Infliximab vs Etanercept	1.48 (1.34-1.64)	2.02 (1.70-2.40)	1.70 (1.46-1.99)	**1.63 (1.51-1.77)**
-Infliximab vs Adalimumab	1.10 (.99-1.23)	1.65 (1.36-2.00)	1.67 (1.40-2.00)	**1.28 (1.18-1.40)**

EXTENDED REPORT

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

Jeffrey D Greenberg,[1] George Reed,[2] Dennis Decktor,[3] Leslie Harrold,[2] Daniel Furst,[4] Allan Gibofsky,[5] Ralph DeHoratius,[3] Mitsumasa Kishimoto,[1] Joel M Kremer,[6] on behalf of the CORRONA Investigators

ABSTRACT

Purpose To compare the effectiveness of anti-tumour necrosis factor (TNF) agents in biologically naive and 'switched' rheumatoid arthritis (RA) patients.

Methods RA patients enrolled in the CORRONA registry newly prescribed adalimumab (n=874), etanercept (n=640), or infliximab (n=728) were stratified based on previous anti-TNF use. Clinical effectiveness at 6, 12 and 24 months was examined using the modified American College of Rheumatology response criteria (mACR20/50/70) and achievement of remission (28-joint disease activity score (DAS28) and clinical disease activity index (CDAI)) in unadjusted

Despite these differences, they all block TNF, and two randomised clinical trial (RCT) meta-analyses of three commonly prescribed anti-TNF (adalimumab, etanercept and infliximab) concluded that the three anti-TNF demonstrated comparable efficacy.[1 2] However, these meta-analyses have been criticised, and their findings conflict with the results reported in two European registry studies demonstrating that adalimumab and etanercept users have better clinical responses than infliximab users.[3 4] Those reports originated from European countries with more restricted access to biological agents and dosage restrictions.

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naive patients. The adjusted OR for achieving an mACR20 response was 0.54 (95% CI 0.38 to 0.76) in first-time switchers and 0.42 (95% CI 0.23 to 0.78) in second-time switchers versus biologically naive patients at 6 months. The adjusted OR for achieving DAS28 remission were 0.29 (95% CI 0.15 to 0.58) for first-time switchers and 0.26 (95% CI 0.08 to 0.84) for second-time switchers. Persistence was higher in biologically naive patients, for whom persistence was highest with infliximab.

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.

Over the past decade, anti-tumour necrosis factor (TNF) therapies have become the most frequently

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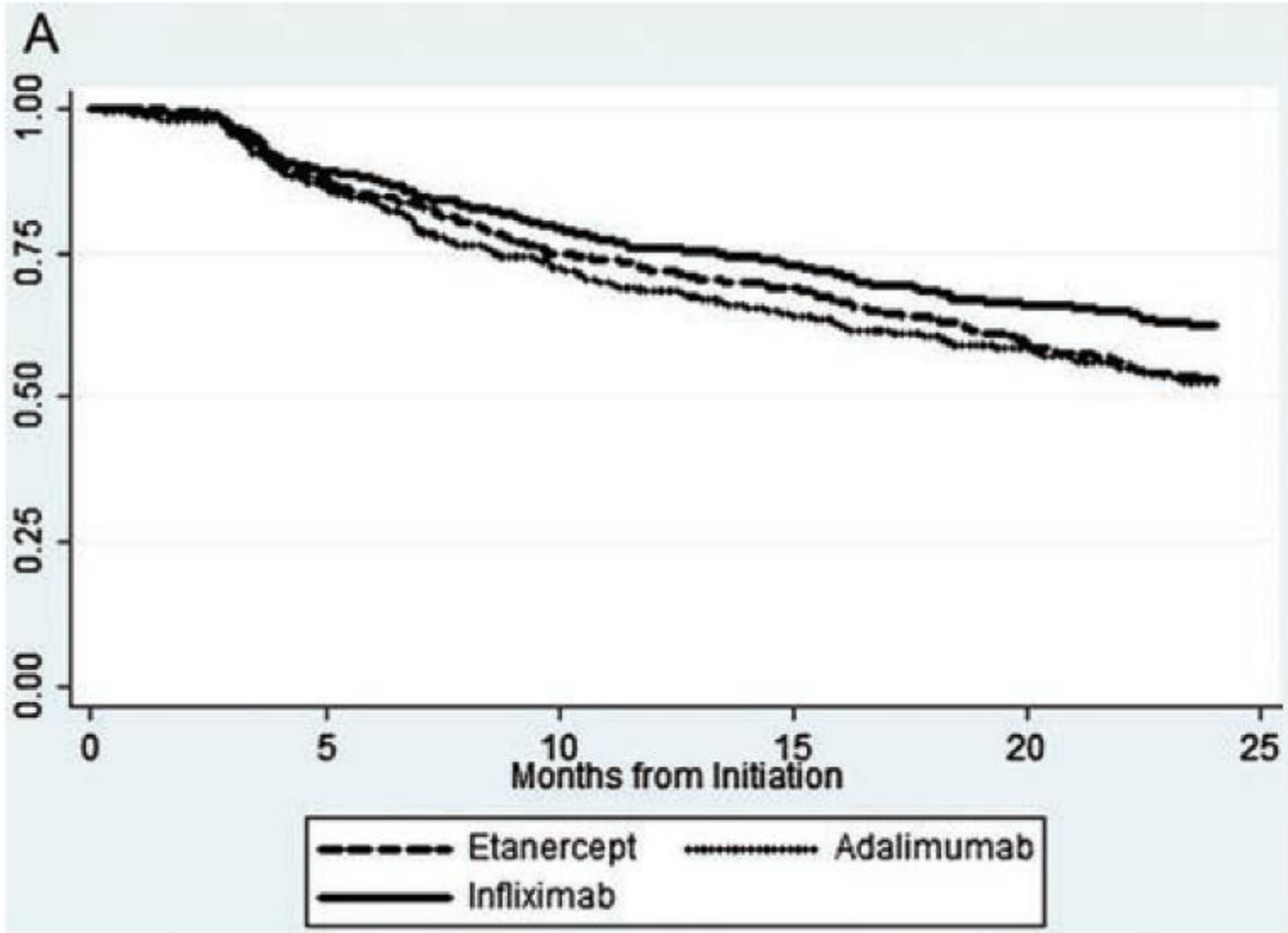
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Months from Initiation
Etanercept
Adalimumab
Infliximab

Arthritis Care & Research
Vol. 66, No. 3, March 2014, pp 464–472
DOI 10.1002/acr.22151

ORIGINAL ARTICLE

Comparative Effectiveness of Anti–Tumor Necrosis Factor Drugs on Health-Related Quality of Life Among Patients With Inflammatory Arthritis

JIAN SHENG CHEN,[1] JOANNA MAKOVEY,[1] MARISSA LASSERE,[2] RACHELLE BUCHBINDER,[3] AND LYN M. MARCH[1]

Objective. To compare the relative effectiveness of anti–tumor necrosis factor (anti-TNF) therapies on health-related quality of life (HRQOL) by inflammatory arthritis types.

Methods. Patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA) who had anti-TNF therapy (etanercept, adalimumab, or infliximab) in the Australian Rheumatology Association Database during 2001–2011 were assessed using the Medical Outcomes Study Short Form 36 (SF-36), Assessment of Quality of Life (AQoL), and Health Assessment Questionnaire (HAQ) disability index (DI) on a biannual basis. Linear regression was used for the analysis; the lack of independence in outcomes for multiple assessments in the same patient was taken into account using generalized estimating equations.

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Results. There were 18,119 assessments (first-time drug use n = 12,274, subsequent use n = 3,098, and no use n = 2,747) provided by 3,033 patients (2,240 RA, 507 AS, and 286 PsA patients) with the anti-TNF therapies. The effects of subsequent use versus first-time use were reduced on the SF-36 physical component summary, AQoL, and HAQ DI scores among RA patients. After adjusting for therapy order, calendar year, sex, age, smoking status, and various medication uses, the 3 anti-TNF preparations had similar effects on the HRQOL measures for patients with RA, AS, or PsA. However, differences between anti-TNF therapies were observed in the AQoL score among PsA patients (infliximab versus etanercept: −0.06 [95% confidence interval (95% CI) −0.12, −0.004]) and in the SF-36 mental component summary score among RA patients (adalimumab versus etanercept: −1.17 [95% CI −1.88, −0.46]).

Conclusion. This study revealed similar effectiveness of etanercept, adalimumab, and infliximab on the HRQOL measures among Australians with RA, AS, and PsA.

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ORIGINAL RESEARCH

Anti-tumor necrosis factor (TNF) drugs for the treatment of psoriatic arthritis: an indirect comparison meta-analysis

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Eric Druyts[2]
J Antonio Aviña-Zubieta[3,4]
Edward J Mills[1,2]

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Objective: To evaluate the comparative effectiveness of available tumor necrosis factor-α inhibitors (anti-TNFs) for the management of psoriatic arthritis (PsA) in patients with an inadequate response to disease-modifying antirheumatic drugs (DMARDs).

Methods: We used an exhaustive search strategy covering randomized clinical trials, systematic reviews and health technology assessments (HTA) published on anti-TNFs for PsA. We performed indirect comparisons of the available anti-TNFs (adalimumab, etanercept, golimumab, and infliximab) measuring relative risks (RR) for the psoriatic arthritis response criteria (PsARC), mean differences (MDs) for improvements from baseline for the Health Assessment Questionnaire

response, golimumab yielded the highest RR and etanercept the second highest; adalimumab and infliximab both yielded notably smaller RRs. For HAQ improvement, etanercept and infliximab yielded the largest MD among PsARC responders. For PsARC nonresponders, etanercept, infliximab, and golimumab yielded similar MDs, and adalimumab a notably lower MD. For PASI improvement, infliximab yielded the largest MD and golimumab the second largest, while etanercept yielded the smallest MD. In some instances, the estimated magnitudes of effect were notably different from the estimates of previous HTA indirect comparisons.

Conclusion: There is insufficient statistical evidence to demonstrate differences in effectiveness between available anti-TNFs for PsA. Effect estimates seem sensitive to the analytic approach, and this uncertainty should be taken into account in future economic evaluations.

Keywords: anti-tumour necrosis factor drugs, biologic DMARDs, indirect comparison meta-analysis, psoriatic arthritis, health assessment questionnaire, psoriatic arthritis response criteria, psoriasis area and severity index


THE END