

# **Péntek M.: Systematic review and analysis of evidences on clinical efficacy and cost-effectiveness of biological drugs for the treatment of Ankylosing Spondylitis**

## Appendix 8.8

### Results of the health economic literature search (references and abstracts)

#### Ovid MEDLINE(R) 1946 to Present with Daily Update (7 hits)

##### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

1.

Cost per treated patient for etanercept, adalimumab, and infliximab across adult indications: a claims analysis.

Bonafede MM. Gandra SR. Watson C. Princic N. Fox KM.

Advances in Therapy. 29(3):234-48, 2012 Mar.

[Journal Article. Research Support, Non-U.S. Gov't]

UI: 22411424

**INTRODUCTION:** This paper aims to estimate the annual cost of etanercept, adalimumab, and infliximab per treated patient across adult indications using US-managed care drug use data.

**METHODS:** Adult patients who used etanercept, adalimumab, or infliximab were identified in the Thomson Reuters MarketScan Commercial Claims and Encounters Database (Thomson Reuters Healthcare, Ann Arbor, MI, USA) between January 1, 2005 and June 30, 2009. The index event was the first use of etanercept, adalimumab, or infliximab preceded by a diagnosis for rheumatoid arthritis, psoriasis, psoriatic arthritis, or ankylosing spondylitis. Patients were defined as either newly initiating or continuing tumor necrosis factor (TNF) blocker treatment based on their use during the 6 months before the index event. Annual cost per treated patient was the sum of the etanercept, adalimumab, and infliximab medication and administration costs during the 12 months following the index claim. Annual costs were calculated across all patients as well as within each indication group and patient type (new initiator or continuing).

**RESULTS:** In total, 21,652 patients met the study criteria (etanercept n = 12,065; adalimumab n = 5,685; infliximab n = 3,902); 43% of patients were new initiators. Patient characteristics were similar across treatment groups in terms of age (mean = 49, SD = 10) and gender (66% female). Across indications, the mean annual TNF-blocker cost per treated patient was \$15,345 for etanercept, \$18,046 for adalimumab, and \$24,018 for infliximab. In new initiators, the TNF-blocker cost per treated patient across indications was \$14,543 for etanercept, \$16,978 for adalimumab, and \$21,086 for infliximab; among patients continuing therapy, annual costs were \$15,836 for etanercept, \$19,457 for adalimumab, and \$25,748 for infliximab.

**CONCLUSION:** Patients on etanercept had the lowest TNF-blocker cost per treated patient for adult indications when applying actual drug use from a US-managed care population. TNF-blocker costs per treated patient on adalimumab and infliximab were approximately 18% and 57% higher than etanercept, respectively, using real-world drug use data.

Status

MEDLINE

Authors Full Name

Bonafede, Machaon M K. Gandra, Shravanthi R. Watson, Crystal. Princic, Nicole. Fox, Kathleen M. Institution

Thomson Reuters, Cambridge, MA, USA. machaon.bonafede@thomsonreuters.com

Date Created

20120321

Year of Publication

2012

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

2.

Reduction of direct and indirect costs in patients with AS receiving etanercept: results from an open-label 36-week extension of the ASCEND study in four European countries.

Moots RJ. Ostor AJ. Loft AG. Jarvinen P. Larsson P. Ekelund M. Reynolds A. Kielar D. Lindkvist RM. Qvitza S.

Rheumatology. 51(2):393-6, 2012 Feb.

[Clinical Trial, Phase IV. Journal Article. Multicenter Study. Research Support, Non-U.S. Gov't]

UI: 22210658

**OBJECTIVE:** To characterize the impact of etanercept (ETN) in AS on cost, work productivity and quality of life (QoL).

**METHODS:** A Phase 4, open-label, multi-centre (UK, Scandinavia) extension study in AS. Eligible subjects (n=84) were treated for 36-52 weeks with ETN 50mg s.c. once weekly. Analysis included direct costs (transformed out-patient and in-patient care elements), indirect costs (sick leave and lost working days), efficacy and QoL.

**RESULTS:** Annualized direct and indirect costs decreased (55.5%,  $P \leq 0.008$ ) during ETN treatment, as did out-patient and in-patient episodes (physiotherapist/physician visits,  $P=0.012$ ). Work productivity and QoL increased.

**CONCLUSION:** ETN therapy significantly reduces direct and indirect health-care costs and increases work ability and QoL in AS. Trial Registration. EUDRACT, <https://eudract.ema.europa.eu/>, 2006-001061-42.

Status

MEDLINE

Authors Full Name

Moots, Robert J. Ostor, Andrew J K. Loft, Anne G R. Jarvinen, Pentti. Larsson, Per. Ekelund, Mats. Reynolds, Alan. Kielar, Danuta. Lindkvist, Rose-Marie. Qvitza, Susanne.

Institution

Institute for Chronic Diseases and Ageing, University of Liverpool, Liverpool, UK.

r.j.moots@liverpool.ac.uk

Date Created

20120123

Year of Publication

2012

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

3.

Ankylosing spondylitis in a patient referred to physical therapy with low back pain.

Seif G. Elliott J.

Physiotherapy Theory & Practice. 28(1):63-70, 2012 Jan.

[Case Reports. Journal Article]

UI: 21721997

Low back pain (LBP) is one of the most common and costly medical conditions in the United States; various studies have reported up to 80% of the adult population will experience a significant episode of LBP sometime within their lifetime. Although many cases of LBP are related to the musculoskeletal system and appropriate for the care of the physical therapist (PT), some episodes of LBP have a systemic cause. Thus, it is the role of the PT to ensure each patient is appropriate for physical therapy intervention throughout the episode of care. When the patient's condition is not appropriate for physical therapy intervention, it is the PT's responsibility to refer the patient to other medical professions to ensure optimal patient care. The purpose of this case report is to describe a patient referred to PT who was diagnosed with ankylosing spondylitis. The patient presented initially to physical therapy with a diagnosis of LBP.

However, after several visits her symptoms were inconsistent with mechanical LBP and thus required further medical consultation.

Status

MEDLINE

Authors Full Name

Seif, Gretchen. Elliott, James.

Institution

The Medical University of South Carolina, College of Health Professions Division of Physical Therapy, Charleston, USA. seif@musc.edu

Date Created

20111122

Year of Publication

2012

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

4.

Baseline predictors of response and discontinuation of tumor necrosis factor-alpha blocking therapy in ankylosing spondylitis: a prospective longitudinal observational cohort study.

Arends S. Brouwer E. van der Veer E. Groen H. Leijnsma MK. Houtman PM. Th A Jansen TL. Kallenberg CG. Spoorenberg A.

Arthritis Research & Therapy. 13(3):R94, 2011.

[Journal Article. Research Support, Non-U.S. Gov't]

UI: 21689401

**INTRODUCTION:** Identifying ankylosing spondylitis (AS) patients who are likely to benefit from tumor necrosis factor-alpha (TNF-) blocking therapy is important, especially in view of the costs and potential side effects of these agents. Recently, the AS Disease Activity Score (ASDAS) has been developed to assess both subjective and objective aspects of AS disease activity. However, data about the predictive value of the ASDAS with respect to clinical response to TNF- blocking therapy are lacking. The aim of the present study was to identify baseline predictors of response and discontinuation of TNF- blocking therapy in AS patients in daily clinical practice.

**METHODS:** AS outpatients who started TNF- blocking therapy were included in the Groningen Leeuwarden Ankylosing Spondylitis (GLAS) study, an ongoing prospective longitudinal observational cohort study with follow-up visits according to a fixed protocol. For the present analysis, patients were excluded if they had previously received anti-TNF- treatment. Predictor analyses of response and treatment discontinuation were performed using logistic and Cox regression models, respectively.

**RESULTS:** Between November 2004 and April 2010, 220 patients started treatment with infliximab (n = 32), etanercept (n = 137), or adalimumab (n = 51). At three and six months, 68% and 63% of patients were Assessments in Ankylosing Spondylitis (ASAS)20 responders, 49% and 46% ASAS40 responders, and 49% and 50% Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)50 responders, respectively. Baseline predictors of response were younger age, male gender, higher ASDAS score, higher erythrocyte sedimentation rate (ESR) level, higher C-reactive protein (CRP) level, presence of peripheral arthritis, higher patient's global assessment of disease activity, and lower modified Schober test. In August 2010, 64% of patients were still using their TNF- blocking agent with a median follow-up of 33.1 months (range 2.4 to 68.2). Baseline predictors of discontinuation of TNF- blocking therapy were female gender, absence of peripheral arthritis, higher BASDAI, lower ESR level, and lower CRP level.

**CONCLUSIONS:** Besides younger age and male gender, objective variables such as higher inflammatory markers or ASDAS score were identified as independent baseline predictors of response and/or continuation of TNF- blocking therapy. In contrast, higher baseline BASDAI score was independently associated with treatment discontinuation. Based on these results, it seems clinically relevant to include more objective variables in the evaluation of anti-TNF- treatment.

Status

MEDLINE

Authors Full Name

Arends, Suzanne. Brouwer, Elisabeth. van der Veer, Eveline. Groen, Henk. Leijnsma, Martha K. Houtman, Pieterella M. Th A Jansen, Tim L. Kallenberg, Cees G M. Spoorenberg, Anneke.

Institution

Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands. S.Arends@reuma.umcg.nl

Other ID

Source: NLM. PMC3218909

Date Created

20111115

Year of Publication

2011

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

5.

Efficacy and safety of adalimumab treatment in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. [Review]

Poddubnyy D. Rudwaleit M.

Expert Opinion on Drug Safety. 10(4):655-73, 2011 Jul.

[Journal Article. Review]

UI: 21554150

**INTRODUCTION:** In the last couple of years, the number of patients with chronic inflammatory rheumatic diseases being treated with TNF antagonist has increased dramatically. Adalimumab, a fully human monoclonal antibody against TNF, is one of the most frequently administered TNF antagonists. Yet, unresolved issues are the long-term safety of TNF antagonists and high treatment costs. **AREAS COVERED:** The authors summarize the available data on short- and long-term efficacy and safety of adalimumab in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. The reader will find a comprehensive overview on the safety and efficacy of adalimumab for these conditions. Clinically relevant questions of adalimumab therapy are discussed. A special focus of this review is on the safety of adalimumab therapy. **EXPERT OPINION:** Adalimumab is effective and reasonably safe in the short- and long-term treatment of patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis who do not respond to the standard therapy. It inhibits radiographic progression in rheumatoid and psoriatic arthritis. Treatment with a TNF inhibitor such as adalimumab is associated with high treatment costs.

Status

MEDLINE

Authors Full Name

Poddubnyy, Denis. Rudwaleit, Martin.

Institution

Charite - Campus Benjamin Franklin, Department of Rheumatology, Hindenburgdamm 30, 12203 Berlin, Germany.

Date Created

20110613

Year of Publication

2011

#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

6.

A 3 mg/kg starting dose of infliximab in active spondyloarthritis resistant to conventional treatments is efficient, safe and lowers costs.

Tenga G. Goeb V. Lequerre T. Bacquet-Deschryver H. Daragon A. Pouplin S. Lanfant-Weybel K. Le Loet X. Dieu B. Vittecoq O.

Joint, Bone, Spine: Revue du Rhumatisme. 78(1):50-5, 2011 Jan.

[Journal Article]

UI: 20646950

**OBJECTIVE:** We assessed the efficacy, tolerance and cost of a 3 mg/kg starting dose of infliximab for ankylosing spondylitis (AS) and psoriatic arthritis (PsA).

**METHODS:** We retrospectively followed-up 45 biologic-naive consecutive patients (11 with axial AS, 24 with axial and peripheral [mixed] AS and 10 with PsA) who were treated between 2002 and 2005 with a 3 mg/kg dose of infliximab after failure of conventional therapies. The following variables were recorded: visual analog scale (VAS) scores of patient's global (G) and pain (P) assessment, duration of early morning stiffness (EMS), disease activity (BASDAI) and functional disability (BASFI). Treatment responses were assessed at 6 and 12 months using the AS assessment score (ASAS)-20% and -40% criteria and BASDAI-50.

**RESULTS:** Baseline characteristics of the 29 men and 16 women were (median [range]): G-VAS, 70 [13-100]; P-VAS, 70 [13-100]; EMS, 60 [0-180] minutes; BASDAI, 64.4 [23.9-100]; BASFI, 57.2 [3.5-98.5]. All manifestations regressed significantly ( $p < 0.0001$ ) for 39 (86.7%) and 24 (53.5%) patients at 6 and 12 months, respectively; 26 (57.8%) had achieved ASAS-20 responses at 6 months that persisted at 1 year for 20 (44.4%); 19 (42.2%) and 12 (26.7%) satisfied BASDAI 50 criteria at 6 and 12 months, respectively. Interestingly, almost 30% still received low-dose infliximab after 4 years of follow-up.

**CONCLUSION:** An initial dose of 3 mg/kg of infliximab significantly attenuated AS and PsA manifestations in >40% of the patients, making use of this dose highly advantageous in terms of safety and 33% lower cost. Copyright A 2010 Societe francaise de rhumatologie. Published by Elsevier SAS. All rights reserved.

Status

MEDLINE

Authors Full Name

Tenga, Ginette. Goeb, Vincent. Lequerre, Thierry. Bacquet-Deschryver, Helene. Daragon, Alain.

Pouplin, Sophie. Lanfant-Weybel, Karine. Le Loet, Xavier. Dieu, Bernard. Vittecoq, Olivier.  
Institution  
Department of Pharmacy, Rouen University Hospital, 76031 Rouen cedex, France.  
Date Created  
20110114  
Year of Publication  
2011

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

7.

Is the Health Utilities Index 3 valid for patients with ankylosing spondylitis?.

Gooch K. Feeny D. Wong RL. Kupper H. Pangan AL. Revicki DA. van der Heijde D.  
Value in Health. 14(1):160-5, 2011 Jan.

[Journal Article. Validation Studies]

UI: 21211498

**OBJECTIVE:** To assess the convergent and discriminative validity of the Health Utilities Index Mark 3 (HUI-3) for patients with ankylosing spondylitis (AS).

**METHODS:** Data were derived from the Adalimumab Trial evaluating Long-term efficacy and safety for Ankylosing Spondylitis (ATLAS). The study team specified 90 a priori hypotheses regarding the direction and magnitude of the expected associations between the overall and single-attribute scores of the HUI-3 and other health status and quality-of-life measures: Short Form 36 Health Survey (SF-36), Ankylosing Spondylitis Quality-of-Life Questionnaire, Bath Ankylosing Spondylitis Functional Index, Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Metrology Index, and Patient's and Physician's Global Assessments of Disease Activity. With baseline data, correlation coefficients were calculated and interpreted according to the guidelines suggested by Guyatt for negligible (0-0.19), weak (0.20-0.34), moderate (0.35-0.50), and strong (>0.5) associations. The a priori hypotheses were tested using Pearson's correlation coefficients.

**RESULTS:** A total of 315 patients with active AS were randomized and enrolled in ATLAS. The correlation coefficients between the HUI-3 scores and other health-related quality-of-life instruments confirmed 61.1% of the a priori hypotheses, with an additional 35.5% being under- or overestimated by one correlation category.

**CONCLUSION:** These results provide evidence of the cross-sectional, convergent, and discriminative validity of the HUI-3 for deriving utility scores in patients with AS. Copyright 2011 International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc. All rights reserved.  
Status

MEDLINE

Authors Full Name

Gooch, Katherine. Feeny, David. Wong, Robert L. Kupper, Hartmut. Pangan, Aileen L. Revicki, Dennis A. van der Heijde, Desiree.

Institution

Global Health Economics & Outcomes Research, Abbott Laboratories, Abbott Park, IL, USA.

katherine.gooch@abbott.com

Date Created

20110107

Year of Publication

2011

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <March 30, 2012> (3 HITS)

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

1.

The use of TNF-inhibitors in ankylosing spondylitis in Austria from 2007 to 2009 - a retrospective analysis.

Nell-Duxneuner V. Schroeder Y. Reichardt B. Bucsics A.

International Journal of Clinical Pharmacology & Therapeutics. 50(12):867-72, 2012 Dec.

[Journal Article. Research Support, Non-U.S. Gov't]

UI: 23036238

**OBJECTIVE:** The introduction of anti-tumor necrosis factor-alpha agents (TNF-inhibitors) offered new dimensions in symptom relief and alteration of disease progression for patients with Ankylosing Spondylitis (AS). In 2007, Infliximab, Etanercept and Adalimumab were approved for AS in Austria. Drug reimbursement data of 2007 were retrieved to evaluate frequency of prescription, preferred substance and data on switching therapies.

**METHODS:** Data from eight health insurance funds covering 5.4 million insured people, which corresponds to 64% of the population, was analyzed by linking two databases, combining data on therapy of individual patients and their diagnosis. For those patients on TNF-inhibitors in 2007 reimbursement data from 2008 and 2009 were obtained, respectively.

**RESULTS:** A total of 694 patients with AS on TNF inhibitors in 2007 were identified for data analysis. Yearly costs for TNF-inhibitors were highest for Adalimumab (14,399 per patient) followed by Infliximab (11,685 per patient) and Etanercept (10,184 per patient). In first-time TNF-inhibitor prescriptions, Adalimumab was prescribed most often, with a tendency towards prescription of Adalimumab and Etanercept in the younger and Infliximab in the older population. In the first year of prescription, 12% of patients already switched from the initially prescribed drug to another substance with those started on Etanercept showing the lowest switching rate. One-year drug survival in our data was highest for Etanercept with 83% still on the drug after 1 year, followed by Infliximab and then Adalimumab, while two-year drug survival was also highest for Etanercept (58%), followed by Adalimumab and then Infliximab.

**CONCLUSIONS:** Patients with Ankylosing Spondylitis starting on TNF-inhibiting therapy in Austria in 2007 were treated most often with Adalimumab, while Etanercept showed the lowest switching rate and the longest 1- and 2-year drug survival.

Status

In-Process

Authors Full Name

Nell-Duxneuner, Valerie. Schroeder, Yvonne. Reichardt, Berthold. Bucsics, Anna.

Institution

Department for Rheumatology, Heinrich Collin Strasse, Wien, Austria. valerie.nell-duxneuner@osteologie.at

Date Created

20121123

Year of Publication

2012

**EXCLUDED / NOT COST-UTILITY ANALYSIS**

2.

Clinical and economic burden of extra-articular manifestations in ankylosing spondylitis patients treated with anti-tumor necrosis factor agents.

Gao X. Wendling D. Botteman MF. Carter JA. Rao S. Cifaldi M.

Journal of Medical Economics. 15(6):1054-63, 2012.

[Journal Article. Research Support, Non-U.S. Gov't]

UI: 22563743

**OBJECTIVE:** To assess concomitant extra-articular manifestation (EAM) rates in patients with ankylosing spondylitis (AS) treated with anti-tumor necrosis factor (anti-TNF) agents and examine the economic burden of uveitis and inflammatory bowel disease (IBD) in French and German AS patients.

**METHODS:** Previous analyses of uveitis and IBD in AS patients treated with infliximab, etanercept or adalimumab were identified in PubMed/Medline (January 2000 to August 2011). A supplemental analysis incorporated more recent adalimumab clinical trial data (ATLAS [NCT00085644] and RHAPSODY

[NCT00478660]). For resource utilization/costs associated with EAMs, the search was expanded to general spondyloarthritis (SpA) conditions (i.e., AS, reactive or psoriatic arthritis, psoriatic spondylitis, IBD and undifferentiated SpA). Direct and indirect yearly costs associated with AS-associated uveitis and IBD were estimated based on interviews with French and German clinicians and literature review.

**RESULTS:** The pooled average rate of anterior uveitis (AU) flares for patients treated with anti-TNF therapy in two meta-analyses and supplemental adalimumab clinical trials was 4.9/100-patient-years (PYs). AU rates (per 100-PYs) were 3.4, 3.7 and 5.7 for infliximab ( $p=0.26$  vs etanercept;  $p=0.86$  vs adalimumab), adalimumab ( $p=0.033$  vs etanercept) and etanercept, respectively. IBD flares (per 100-PYs) were 0.2 for infliximab ( $p<0.001$  vs etanercept;  $p=0.18$  vs adalimumab), 0.63 for adalimumab ( $p=0.009$  vs etanercept) and 2.2 for etanercept. No studies assessing EAM-associated resource utilization or costs in AS patients were found. Direct medical costs associated with IBD treatment ranged from 483 (Germany) to 6443 (France). Clinician-estimated AS-related uveitis direct medical costs were 1410 (Germany) and 1812 (France).

**CONCLUSIONS:** Clinical data synthesis demonstrated significantly lower AU flare rates with adalimumab vs etanercept and significantly lower IBD rates with both adalimumab and infliximab vs etanercept. Economic analysis indicated substantial costs associated with AU and IBD flares secondary to AS in France and Germany. Future economic evaluations of anti-TNF agents should incorporate EAMs and subsequent treatment costs. Limitations include restricted availability of randomized, placebo-controlled clinical trial data, inclusion of data from open-label studies, lack of real-world (i.e., non-trial-based) EAM rates and a lack of EAM-specific direct and indirect costs with which to compare the results presented herein.

Status

In-Process

Authors Full Name

Gao, Xin. Wendling, Daniel. Botteman, Marc F. Carter, John A. Rao, Sumati. Cifaldi, Mary.

Institution

Pharmerit North America, LLC Bethesda, MD, USA.

Date Created

20121119

Year of Publication

2012

### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

3.

Pharmacoeconomics of adalimumab for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and Crohn's disease.

Gladman DD. Brown RE.

Expert Review of Pharmacoeconomics & Outcomes Research. 8(2):111-25, 2008 Apr.

[Journal Article]

UI: 20528400

Adalimumab is a monoclonal antibody that inhibits TNF, an osteogenic cytokine involved in the pathogenesis of chronic, disabling inflammatory diseases. Adalimumab is indicated for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and Crohn's disease. It alleviates the symptoms of these diseases, prevents disease progression in some patients and, in the case of Crohn's disease, induces and maintains remission. Compared with traditional disease-modifying antirheumatic drugs that offer significantly less benefit, adalimumab is much more costly. However, most studies to date demonstrate the cost-effectiveness of adalimumab treatment. Cost-effectiveness data for newer indications of adalimumab, including ankylosing spondylitis and Crohn's disease, are needed. As longer term data for adalimumab become available, the cost-effectiveness data will have greater precision.

Status

PubMed-not-MEDLINE

Authors Full Name

Gladman, Dafna D. Brown, Ruth E.

Institution

Centre for Prognosis Studies in The Rheumatic Diseases, University Health Network, Toronto Western Hospital, 399 Bathurst St. 1E-410B, Toronto, ON M5T 2S8, Canada. dafna.gladman@utoronto.ca.

Date Created

20100610

Year of Publication

2008

## Web of knowledge (39 hits)

### EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU Nell-Duxneuner, V  
Schroeder, Y  
Reichardt, B  
Bucsics, A

AF Nell-Duxneuner, Valerie  
Schroeder, Yvonne  
Reichardt, Berthold  
Bucsics, Anna

TI The use of TNF-inhibitors in ankylosing spondylitis in Austria from 2007 to 2009-a retrospective analysis

### SO INTERNATIONAL JOURNAL OF CLINICAL PHARMACOLOGY AND THERAPEUTICS

AB Objective: The introduction of anti-tumor necrosis factor-alpha agents (TNF-inhibitors) offered new dimensions in symptom relief and alteration of disease progression for patients with Ankylosing Spondylitis (AS). In 2007, infliximab, etanercept and adalimumab were approved for AS in Austria. Drug reimbursement data of 2007 were retrieved to evaluate frequency of prescription, preferred substance and data on switching therapies. Methods: Data from eight health insurance funds covering 5.4 million insured people, which corresponds to 64% of the population, was analyzed by linking two databases, combining data on therapy of individual patients and their diagnosis. For those patients on TNF-inhibitors in 2007 reimbursement data from 2008 and 2009 were obtained, respectively. Results: A total of 694 patients with AS on TNF-inhibitors in 2007 were identified for data analysis. Yearly costs for TNF-inhibitors were highest for adalimumab (14,399 E per patient) followed by infliximab (11,685 per patient) and etanercept (10,184 E per patient). In first-time TNF-inhibitor prescriptions, adalimumab was prescribed most often, with a tendency towards prescription of adalimumab and etanercept in the younger and infliximab in the older population. In the first year of prescription, 12% of patients already switched from the initially prescribed drug to another substance with those started on etanercept showing the lowest switching rate. One-year drug survival in our data was highest for etanercept with 83% still on the drug after 1 year, followed by infliximab and then adalimumab, while two-year drug survival was also highest for etanercept (58%), followed by adalimumab and then infliximab. Conclusions: Patients with Ankylosing Spondylitis starting on TNF-inhibiting therapy in Austria in 2007 were treated most often with adalimumab, while etanercept showed the lowest switching rate and the longest 1- and 2-year drug survival.

TC 0

Z9 0

SN 0946-1965

PD DEC

PY 2012

VL 50

IS 12

BP 867

EP 872

DI 10.5414/CP201707

UT WOS:000313595100003

ER

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### EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU van der Burg, LRA  
ter Wee, MM  
Boonen, A

AF van der Burg, Lennart R. A.  
ter Wee, Marieke M.  
Boonen, Annelies

TI Effect of biological therapy on work participation in patients with ankylosing spondylitis: a systematic review

SO ANNALS OF THE RHEUMATIC DISEASES

AB Objectives To review systematically the effect of biological treatment in patients with ankylosing spondylitis (AS) on three work outcomes: work status, absence from paid work and at-work productivity. Methods A systematic literature search was performed (Pubmed, Embase, Cochrane Library) to identify relevant articles. Risk of bias of included studies was assessed using the Cochrane guidelines for cohorts and randomised controlled trials (RCTs). Data were extracted using a self-composed data extraction form. Owing to extensive interstudy heterogeneity, narrative summaries were used to present the data. Results Nine studies were included (six uncontrolled cohorts, one population-controlled cohort and two RCTs) that reported on 39 comparisons. Overall, 961 patients were treated with three different tumour necrosis factor a inhibitors (etanercept, infliximab, adalimumab). For presenteeism and absence from work, most comparisons showed improvement in favour of biological agents, but not all comparisons were statistically significant and they usually concerned before-after analyses. For work status, changes were less often positive, but studies dealt with patients with longstanding AS, lacked power and had a relatively short follow-up. Conclusions Although trends towards beneficial effects of biological agents in longstanding AS were seen on all work outcomes, the methodological limitations in the studies included hampers clear conclusions. Since the majority of studies were (extensions of) controlled trials, the generalisability of the effect of biological agents on work participation in real life should be further studied in larger (population-controlled) studies. The effect of biological agents in patients with early disease has not yet been examined.

TC 0

Z9 0

SN 0003-4967

PD DEC

PY 2012

VL 71

IS 12

BP 1924

EP 1933

DI 10.1136/annrheumdis-2012-201914

UT WOS:000310701300006

ER

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**EXCLUDED / ABSTRACT**

PT J

AU Marcellusi, A  
Botteman, MF  
Rao, S  
Cifaldi, M  
Solem, CT  
Gitto, L  
Giannantoni, P  
Mennini, FS

AF Marcellusi, A.  
Botteman, M. F.  
Rao, S.  
Cifaldi, M.  
Solem, C. T.  
Gitto, L.  
Giannantoni, P.  
Mennini, F. S.

TI COST EFFECTIVENESS OF ADALIMUMAB VERSUS GOLIMUMAB AND PLACEBO IN  
ANKYLOSING SPONDYLITIS IN ITALY

SO VALUE IN HEALTH

TC 0

Z9 0

SN 1098-3015

PD NOV

PY 2012

VL 15

IS 7

BP A444

EP A444

UT WOS:000312411100882

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Rachid, B  
El Zorkany, B  
Youseif, E  
Tikly, M

AF Rachid, Bahiri  
El Zorkany, Bassel  
Youseif, Ehab  
Tikly, Mohammed

TI Early diagnosis and treatment of ankylosing spondylitis in Africa and the Middle East

SO CLINICAL RHEUMATOLOGY

AB Ankylosing spondylitis (AS) is the prototype for spondyloarthritis primarily affecting young men. Geographic and ethnic variations exist in the prevalence and severity of AS and relate to the wide disparity in the frequency of human leukocyte antigen (HLA)-B27, a major genetic risk factor. The strength of the disease association with HLA-B27 is lower in most Arab populations (25-75 %) than in Western European populations (> 90 %), and there is no association in sub-Saharan Africa, where the prevalence of HLA-B27 is < 1 %. Other epidemiologic differences between European and African populations are the apparent later age at presentation in sub-Saharan Africa, and the high rate of spondyloarthropathies associated with human immunodeficiency virus infection. Diagnosis of AS is often delayed 8-10 years; potential reasons for the delay in Africa and the Middle East include low awareness among physicians and patients, the requirement for radiographic evidence of sacroiliitis for diagnosis, and limited access to magnetic resonance imaging in some countries. Treatment should be initiated early to prevent or reduce skeletal deformity and physical

disability. Nonsteroidal anti-inflammatory drugs are effective first-line treatment and anti-tumor necrosis factor-alpha drugs are indicated for patients who have an inadequate response to first-line therapy. In Africa and the Middle East, such treatments may be precluded either by cost or contraindicated because of the high prevalence of latent tuberculosis infection. Research is sorely needed to develop cost-effective tools to diagnose AS early as well as effective, inexpensive, and safe treatments for these developing regions.

TC 0

Z9 0

SN 0770-3198

PD NOV

PY 2012

VL 31

IS 11

BP 1633

EP 1639

DI 10.1007/s10067-012-2058-5

UT WOS:000310379500016

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Goh, L  
Samanta, A

AF Goh, Leslie  
Samanta, Ash

TI Update on biologic therapies in ankylosing spondylitis: a literature review

SO INTERNATIONAL JOURNAL OF RHEUMATIC DISEASES

AB Aim The present paper aims to review the recent advances in diagnosis and management of ankylosing spondylitis (AS). Method Medline and abstracts submitted to the recent European League Against Rheumatism (EULAR) congress were searched to obtain quality-controlled information on the management of AS. Results The use of magnetic resonance imaging (MRI) allows the diagnosis of AS to be made in the pre-radiographic stage. The Assessment in Spondylarthritis International Society recommendations for the management of AS have been modified so that patients with non-radiographic spondyloarthritis (SpA) can now be considered for biological therapy. The older anti-tumour necrosis factor (TNF) continued to be

effective in longer-term studies. Studies with longer duration of follow-up have shown that some patients with pre-radiographic SpA entered into prolonged drug-free remission. It is likely that in the foreseeable future, more AS patients will be treated with biological therapies at an earlier stage of the disease. New biologic therapies, golimumab and secukinumab, are looking promising in improving the signs and symptoms of AS, at least in the short-term. Conclusion Longer-term studies of AS patients treated with infliximab, etanercept and adalimumab continued to show a good clinical response. There is a need for more long-term studies to examine the longitudinal efficacy of golimumab and secukinumab in AS.

TC 0

Z9 0

SN 1756-1841

PD OCT

PY 2012

VL 15

IS 5

BP 445

EP 454

DI 10.1111/j.1756-185X.2012.01765.x

UT WOS:000310077300017

ER

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**EXCLUDED / NOT AS**

PT J

AU Chastek, B  
Fox, KM  
Watson, C  
Gandra, SR

AF Chastek, Benjamin  
Fox, Kathleen M.  
Watson, Crystal  
Gandra, Shravanthi R.

TI Etanercept and Adalimumab Treatment Patterns in Psoriatic Arthritis Patients Enrolled in a Commercial Health Plan

SO ADVANCES IN THERAPY

AB Treatment patterns, including persistence, gaps in therapy, switching, and discontinuation, were examined in patients with psoriatic arthritis (PsA) who received the tumor necrosis factor (TNF)-blockers etanercept or adalimumab.

This retrospective study utilized administrative claims data from a United States commercial health plan. Adults (age 18-64 years) with PsA who started therapy with etanercept or adalimumab as index therapy between January 1, 2006 and December 31, 2008 were included in the analysis. Patients were continuously enrolled in the health plan for at least 6 months before and at least 12 months after the start of index therapy. Initial TNF-blocker dose and rates of therapy persistence (continuous use of index medication without a gap of at least 60 days), therapy gaps, and discontinuation (gap in therapy of at least 60 days) were estimated. Those who discontinued were further classified as: (1) discontinued all biologic therapy, (2) restarted index medication, (3) switched to another biologic therapy, or (4) other.

A total of 346 patients with PsA (202 etanercept, 144 adalimumab) were eligible. Most (90.6% etanercept; 88.9% adalimumab) started index therapy at the labeled dose. Persistence with index therapy for 12 months was observed in 50% of patients on etanercept and 45% of patients on adalimumab ( $P = 0.37$ ). Patients on etanercept had a longer duration of persistence (434 vs. 353 days;  $P = 0.02$ ), more pauses of at least 7 days (4.7 vs. 3.5;  $P = 0.004$ ), and a longer mean pause length (48.6 vs. 29.3 days;  $P = 0.01$ ) than patients on adalimumab. Of patients who discontinued (24.8% etanercept; 35.1% adalimumab), 46.4% and 41.5% restarted etanercept and adalimumab, respectively; 24.8% and 35.1% discontinued all TNF-blockers; 20.0% and 19.2% switched to another biologic; and 8.8% and 4.3% had other therapy changes.

Approximately half of PsA patients were persistent on their index TNF-blocker for 12 months. Pauses in therapy and therapy discontinuation were common, but more than 40% of patients restarted their index TNF-blocker after discontinuation.

TC 0

Z9 0

SN 0741-238X

PD AUG

PY 2012

VL 29

IS 8

BP 691

EP 697

DI 10.1007/s12325-012-0039-3

UT WOS:000308038700004

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Kobayashi, S  
Harigai, M  
Mozaffarian, N  
Pangan, AL  
Sharma, S  
Brown, LS  
Miyasaka, N

AF Kobayashi, Shigeto  
Harigai, Masayoshi  
Mozaffarian, Neelufar  
Pangan, Aileen L.  
Sharma, Shringi  
Brown, L. Steven  
Miyasaka, Nobuyuki

TI A multicenter, open-label, efficacy, pharmacokinetic, and safety study of adalimumab in Japanese patients with ankylosing spondylitis

SO MODERN RHEUMATOLOGY

AB We evaluated the efficacy, pharmacokinetics, and safety of adalimumab in Japanese patients with active ankylosing spondylitis (AS) who had an inadequate response to, or who were intolerant of, treatment with a parts per thousand yen1 nonsteroidal anti-inflammatory drugs (NSAIDs). This phase 3, multicenter, open-label trial assessed the percentage of patients with a 20% response in the Assessment of SpondyloArthritis international society working group criteria (ASAS20) at week 12 as the primary endpoint. Secondary outcome measures included assessments of disease activity, clinical response, functionality, and spinal mobility at weeks 12 and 60. Serum trough adalimumab concentrations were summarized using descriptive statistics. The adverse event profile was summarized for patients who received at least one dose of the study drug during the assessment period. At week 12, 73.2% (30/41) achieved an ASAS20 response and nearly 40% met ASAS partial remission criteria; proportions were maintained after up to 60 weeks of therapy. Mean adalimumab concentrations reached steady-state between weeks 12 and 20. Adalimumab was generally safe and well tolerated, with approximately 90% of adverse events considered to be mild. These results support the use of adalimumab as a safe and effective therapy for Japanese patients with active AS.

TC 0

Z9 0

SN 1439-7595

PD AUG

PY 2012

VL 22

IS 4

BP 589

EP 597

DI 10.1007/s10165-011-0557-x

UT WOS:000307515100014

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Moghimi, J  
Sheikhvatan, M  
Semnani, V

AF Moghimi, Jamileh  
Sheikhvatan, Mehrdad  
Semnani, Vahid

TI The use of low-dose etanercept as an alternative therapy for treatment of ankylosing spondylitis: a case series

SO RHEUMATOLOGY INTERNATIONAL

AB During recent decades, biological medications play a crucial role for treating rheumatologic disorders and thus are strongly recommended for initial treatment of ankylosing spondylitis. However, because of high cost of biological drugs, the use of these drugs has been limited. In current series, we tried to assess safety of low-dose etanercept as a common usable biological drug in patients with ankylosing spondylitis. In a case-series study, 4 men with ankylosing spondylitis were treated with low-dose Etanercept (25 mg/2 weeks) plus methotrexate (10 mg/week). Safety was assessed by measuring rate of differences in severity of clinical manifestations and level of C-reactive protein (CRP). After the completion of treatment with low-dose etanercept, inflammatory low back pain and morning stiffness was reduced lower than 30 min in all patients. Only one patient had baseline high serum ESR and positive CRP that was changed to negative following treatment protocol. At one-year follow-up, all participants continued their regular treatment regimen with the etanercept survival rate 100%. Neither side effects related to drug nor clinical complications were observed within the follow-up period. Our findings suggest that low-dose etanercept (25 mg/2 weeks) has an acceptable safety and effectiveness profile in individuals with ankylosing spondylitis and can be good alternative instead of conventional therapy with etanercept (25 mg two times per week).

TC 3

Z9 3

SN 0172-8172

PD AUG

PY 2012

VL 32

IS 8

BP 2271

EP 2274

DI 10.1007/s00296-011-1920-0

UT WOS:000306827500007

ER

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**EXCLUDED / NOT AS**

PT J

AU Cortesi, PA  
Scalone, L  
D'Angiolella, L  
Belisari, A  
Fusco, F  
Oivieri, I  
Mantovani, LG

AF Cortesi, P. A.  
Scalone, L.  
D'Angiolella, L.  
Belisari, A.  
Fusco, F.  
Oivieri, I.  
Mantovani, L. G.

TI Systematic literature review on economic implications and pharmaco-economic issues of psoriatic arthritis

SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY

AB The introduction of anti tumour necrosis factors- $\alpha$  (TNF- $\alpha$ ) agents has greatly advanced the management of psoriatic arthritis (PsA). Functional disability in patients with PsA may result in significant impairment of Quality of Life (QoL), psychosocial disability and productivity loss. Although many patients respond adequately to methotrexate and other therapies, in patients who have incomplete responses, anti TNF- $\alpha$  agents reduce inflammation and minimise joints damage, increasing functional capacity and QoL, and decreasing the progression rate of structural damage in peripheral joints. Because of the high costs associated to anti TNF- $\alpha$  agents therapy, an increasing number of economic evaluations have been performed over the last few years, and several cost-of-illness and cost-effectiveness studies have been published concerning use of anti TNF- $\alpha$  agents in management of PsA. We performed a systematic literature review to better understand the pharmaco-economic perspective of PsA. The pharmaco-economic studies analysed have demonstrated the high socioeconomic burden of PsA and that TNF- $\alpha$  blockers treatment options provide value for money in the musculoskeletal and cutaneous manifestations of psoriatic disease.

TC 7

Z9 7

SN 0392-856X

PD JUL-AUG

PY 2012

VL 30

IS 4

SU 73

BP S126

EP S131

UT WOS:000310828700023

ER

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**EXCLUDED / ABSTRACT**

PT J

AU Avila-Ribeiro, P  
Vieira-Sousa, E  
Canhao, H  
Fonseca, JE

AF Avila-Ribeiro, P.  
Vieira-Sousa, E.  
Canhao, H.  
Fonseca, J. E.

TI TAPERING INFLIXIMAB IN ANKYLOSING SPONDYLITIS: CAN WE REDUCE COSTS?

SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY

TC 0

Z9 0

SN 0392-856X

PD JUL-AUG

PY 2012

VL 30

IS 4

BP 644

EP 644

UT WOS:000308897200193

ER

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**EXCLUDED / REVIEW**

PT J

AU Kirchhoff, TD  
Mittendorf, T  
Schmidt, RE  
Jablonka, A  
Merkesdal, S

AF Kirchhoff, Timm D.  
Mittendorf, Thomas  
Schmidt, Reinhold E.  
Jablonka, Alexandra  
Merkesdal, Sonja

TI Cost-effectiveness of TNF-alpha inhibition in active ankylosing spondylitis: a systematic appraisal of the literature

**SO EXPERT REVIEW OF PHARMACOECONOMICS & OUTCOMES RESEARCH**

AB Ankylosing spondylitis (AS) is the most frequent prototype of spondyloarthritides. Substantial direct costs and productivity losses often arise in young patients. Currently, tumor necrosis factor (TNF) inhibitors are the only approved therapy escalation when usual care (physiotherapy and NSAIDs) proves to be insufficient. Owing to their high medication costs, TNF inhibitors are a target of cost-effectiveness analyses. There is consistent evidence regarding the use of TNF inhibitors according to recommendations in patients with active AS finding TNF inhibitors to be cost effective from a societal perspective. However, there are relevant uncertainties (discontinuation rate and progression rate) in the long-term estimates of the cost-effectiveness analyses analyzed. Whether TNF inhibitors are cost effective from an insurance perspective in the long run will have to be addressed by models based on observational data.

TC 0

Z9 0

SN 1473-7167

PD JUN

PY 2012

VL 12

IS 3

BP 307

EP 317

DI 10.1586/ERP.12.19

UT WOS:000307938600015

ER

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**EXCLUDED / NOT AS**

PT J

AU Reynolds, A  
Koenig, AS  
Bananis, E  
Singh, A

AF Reynolds, Alan  
Koenig, Andrew S.  
Bananis, Eustratios  
Singh, Amitabh

TI When is switching warranted among biologic therapies in rheumatoid arthritis?

SO EXPERT REVIEW OF PHARMACOECONOMICS & OUTCOMES RESEARCH

AB Switching among biologic therapies is common practice in patients with rheumatoid arthritis who have an inadequate response or intolerable adverse events. Evidence from observational studies and association guidelines supports the use of sequential biologic therapy for these reasons. Owing to recent economic pressures on healthcare budgets, patients with rheumatoid arthritis who are well controlled on and tolerant of their current biologic therapy may be switched to alternative biologics, despite limited evidence supporting this practice. Clinical research and experience suggest that TNF antagonists are not interchangeable, as meaningful differences have been observed in their efficacy and safety profiles. Additional research is needed to assess the risk: benefit ratio of specific sequences of biologic therapies and the validity of switching biologic therapies for nonclinical purposes.

TC 0

Z9 0

SN 1473-7167

PD JUN

PY 2012

VL 12

IS 3

BP 319

EP 333

DI 10.1586/ERP.12.27

UT WOS:000307938600016

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Reveille, JD  
Ximenes, A  
Ward, MM

AF Reveille, John D.  
Ximenes, Antonio  
Ward, Michael M.

TI Economic Considerations of the Treatment of Ankylosing Spondylitis

SO AMERICAN JOURNAL OF THE MEDICAL SCIENCES

CT 9th Annual Research and Education Meeting of Spondyloarthritis Research and Treatment Network (SPARTAN)

CY JUL 29-30, 2011

CL Portland, OR

AB Ankylosing spondylitis (AS) is associated with both significant direct and indirect costs, which vary by country, and have generally increased dramatically since the introduction of anti-tumor necrosis factor therapy. The cost-effectiveness of biologic agents is controversial, although cost-effectiveness studies need to consider the potential impact of anti-tumor necrosis factor treatments on work ability. Alternatives to reduce costs associated with biologics have been examined, including on-demand dosing and lower dose alternatives. Other treatment measures, such as total hip arthroplasty and physical therapy, are also effective in reducing pain and improving function in patients with AS, although the optimal type or combination of physical therapy treatment modalities, the optimal frequency and duration of treatment and whether therapy

is equally effective in stable disease and uncontrolled AS need to be determined. No studies have examined differences in patient outcomes based on subspecialty care. Establishing an evidence base for these questions would help inform policy decisions to design the most cost-effective measures to treat AS.

TC 0

Z9 0

SN 0002-9629

PD MAY

PY 2012

VL 343

IS 5

BP 371

EP 374

DI 10.1097/MAJ.0b013e3182514093

UT WOS:000303667300009

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Arends, S  
van der Veer, E  
Kallenberg, CGM  
Brouwer, E  
Spoorenberg, A

AF Arends, Suzanne  
van der Veer, Eveline  
Kallenberg, Cees G. M.  
Brouwer, Elisabeth  
Spoorenberg, Anneke

TI Baseline predictors of response to TNF-alpha blocking therapy in ankylosing spondylitis

SO CURRENT OPINION IN RHEUMATOLOGY

AB Purpose of review

Identifying the characteristics of patients with ankylosing spondylitis (AS) before start of treatment which are able to predict a beneficial response to tumor necrosis factor-alpha (TNF-alpha) blocking therapy is

relevant, especially in view of the high costs and potential side-effects of these agents. This review provides an overview of clinical trials and observational studies investigating baseline predictors of response after 3-6 months of TNF-alpha blocking therapy and baseline predictors of long-term anti-TNF-alpha treatment continuation in AS.

#### Recent findings

In multiple studies, increased acute phase reactants, higher disease activity, higher functional status, younger age, and HLA-B27 positivity were identified as independent baseline predictors of achieving clinical response to TNF-alpha blocking therapy. Increased acute phase reactants, presence of peripheral arthritis, and male sex were repeatedly identified as independent baseline predictors of anti-TNF-alpha treatment continuation.

#### Summary

Several studies using multivariate analyses identified comparable baseline predictors of response and/or continuation of TNF-alpha blocking therapy. The single predictors identified have, at best, moderate capacity to predict treatment response in the individual patient. The development of a prediction model may lead to a more robust instrument to support physicians in decision making on TNF-alpha blocking therapy in AS in daily clinical practice.

TC 1

Z9 1

SN 1040-8711

PD MAY

PY 2012

VL 24

IS 3

BP 290

EP 298

DI 10.1097/BOR.0b013e32835257c5

UT WOS:000302231200007

ER

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### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Rafia, R

Ara, R

Packham, J

Haywood, K

Healey, E

AF Rafia, R.  
Ara, R.  
Packham, J.  
Haywood, K.  
Healey, E.

TI Healthcare costs and productivity losses directly attributable to ankylosing spondylitis

SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY

AB Objective

To describe the healthcare resource use and productivity losses associated with patients with ankylosing spondylitis (AS) and explore the relationship between disease severity and total costs.

Methods

A cross-sectional postal survey was conducted on a sample of 1,000 patients with AS randomly selected from registries at 10 secondary care rheumatology centres in the UK. Information on demographic characteristics, disease and functional activity, healthcare use and work status (presenteeism and absenteeism) during the previous three months was collected. The relationship between disease severity and total costs was explored using a two-part regression model, controlling for age, gender and disease duration and validated on respondents (n=470) of the second round of the survey.

Results

Respondents at baseline (n=612) covered the full spectrum of AS, had a mean BASDAI of 4.6 and 55.3% of individuals scored at least 4 on the BASDAI scale. The mean (median) three month total cost was (£)2,802 ((£)1,160). Both physical function and disease activity were significant predictors of total costs. Mean (median) three month total costs for patients with BASDAI <4, 4-6 and >6 were (£)1,331 ((£)502), (£)2,790 ((£)1,281) and (£)4,840 ((£)5,017) respectively. Direct National Health Service funded healthcare costs contributed to just 15% of total costs while unemployment, absenteeism from work and reduced productivity at work accounted for 63.2%, 1.4% and 19.0% of total costs, respectively.

Conclusion

This study shows that direct healthcare costs alone do not describe the total costs associated with AS and that productivity losses associated with AS are considerable.

TC 1

Z9 1

SN 0392-856X

PD MAR-APR

PY 2012

VL 30

IS 2

BP 246

EP 253

UT WOS:000303905800017

ER

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## EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU Bonafede, MMK

Gandra, SR

Watson, C

Princic, N

Fox, KM

AF Bonafede, Machaon M. K.

Gandra, Shrvanathi R.

Watson, Crystal

Princic, Nicole

Fox, Kathleen M.

TI Cost per Treated Patient for Etanercept, Adalimumab, and Infliximab Across Adult Indications: a Claims Analysis

SO ADVANCES IN THERAPY

AB Introduction: This paper aims to estimate the annual cost of etanercept, adalimumab, and infliximab per treated patient across adult indications using US-managed care drug use data.

Methods: Adult patients who used etanercept, adalimumab, or infliximab were identified in the Thomson Reuters MarketScan (R) Commercial Claims and Encounters Database (Thomson Reuters Healthcare, Ann Arbor, MI, USA) between January 1, 2005 and June 30, 2009. The index event was the first use of etanercept, adalimumab, or infliximab preceded by a diagnosis for rheumatoid arthritis, psoriasis, psoriatic arthritis, or ankylosing spondylitis. Patients were defined as either newly initiating or continuing tumor necrosis factor (TNF) blocker treatment based on their use during the 6 months before the index event. Annual cost per treated patient was the sum of the etanercept, adalimumab, and infliximab medication and administration costs during the 12 months following the index claim. Annual costs were calculated across all patients as well as within each indication group and patient type (new initiator or continuing).

Results: In total, 21,652 patients met the study criteria (etanercept n = 12,065; adalimumab n = 5,685; infliximab n = 3,902); 43% of patients were new initiators. Patient characteristics were similar across treatment groups in terms of age (mean = 49, SD = 10) and gender (66% female). Across indications, the mean annual TNF-blocker cost per treated patient was \$15,345 for etanercept, \$18,046 for adalimumab, and \$24,018 for infliximab. In new initiators, the TNF-blocker cost per treated patient across indications was \$14,543 for etanercept, \$16,978 for adalimumab, and \$21,086 for infliximab; among patients continuing therapy, annual costs were \$15,836 for etanercept, \$19,457 for adalimumab, and \$25,748 for infliximab.

Conclusion: Patients on etanercept had the lowest TNF-blocker cost per treated patient for adult indications when applying actual drug use from a US-managed care population. TNF-blocker costs per treated patient on adalimumab and infliximab were approximately 18% and 57% higher than etanercept, respectively, using real-world drug use data.

TC 2

Z9 2

SN 0741-238X

PD MAR

PY 2012

VL 29

IS 3

BP 234

EP 248

DI 10.1007/s12325-012-0007-y

UT WOS:000303446600004

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Moots, RJ

Ostor, AJK

Loft, AGR

Jarvinen, P

Larsson, P

Ekelund, M

Reynolds, A

Kielar, D

Lindkvist, RM

Qvitza, S

AF Moots, Robert J.

Ostor, Andrew J. K.

Loft, Anne G. R.

Jarvinen, Pentti

Larsson, Per

Ekelund, Mats

Reynolds, Alan

Kielar, Danuta

Lindkvist, Rose-Marie

Qvitza, Susanne

TI Reduction of direct and indirect costs in patients with AS receiving etanercept: results from an open-label 36-week extension of the ASCEND study in four European countries

SO RHEUMATOLOGY

AB Objective. To characterize the impact of etanercept (ETN) in AS on cost, work productivity and quality of life (QoL).

Methods. A Phase 4, open-label, multi-centre (UK, Scandinavia) extension study in AS. Eligible subjects (n = 84) were treated for 36-52 weeks with ETN 50 mg s.c. once weekly. Analysis included direct costs (transformed out-patient and in-patient care elements), indirect costs (sick leave and lost working days), efficacy and QoL.

Results. Annualized direct and indirect costs decreased (55.5%, P 0.008) during ETN treatment, as did out-patient and in-patient episodes (physiotherapist/physician visits, P = 0.012). Work productivity and QoL increased.

Conclusion. ETN therapy significantly reduces direct and indirect health-care costs and increases work ability and QoL in AS.

TC 2

Z9 2

SN 1462-0324

PD FEB

PY 2012

VL 51

IS 2

BP 393

EP 396

DI 10.1093/rheumatology/ker404

UT WOS:000299415600028

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU ter Wee, MM

Lems, WF

Usan, H

Gulpen, A

Boonen, A

AF ter Wee, M. M.

Lems, W. F.

Usan, H.

Gulpen, A.

Boonen, A.

TI The effect of biological agents on work participation in rheumatoid arthritis patients: a systematic review

SO ANNALS OF THE RHEUMATIC DISEASES

AB This study reviewed the effect of biological agents on participation in paid work among patients with rheumatoid arthritis (RA). A systematic literature search was performed to identify published articles reporting the effect of biological agents on employment status, sick leave and/or presenteeism. The quality of included articles was assessed according to the guidelines as proposed by the Dutch Cochrane Centre. Narrative summaries were used to present the data separately for randomised controlled trials (RCTs) as well as controlled and uncontrolled cohort studies. 19 studies (six uncontrolled cohorts, seven controlled cohorts and six RCTs) were included, in which 11 259 patients were treated with biological agents. Employment status improved in four out of 13 studies, absence from work in all 10 studies and presenteeism in seven out of nine studies that reported this outcome. For absenteeism and presenteeism the statistical significance of change or difference was not always provided and results within studies were sometimes conflicting when using different time frames or alternative outcomes. The large heterogeneity in terms of population, design, analyses and most important in outcome measures limits interpretation of the data. RCTs as well as cohort studies showed positive results of biological agents on both absenteeism and presenteeism compared with other disease-modifying antirheumatic drugs (DMARD), continuing the failing DMARD, the general population or the situation before the start of biological agents. The effect on employment status was more conflicting, but 50% of studies that addressed patients with early methotrexate-naive RA showed a positive result on employment status.

TC 5

Z9 5

SN 0003-4967

PD FEB

PY 2012

VL 71

IS 2

BP 161

EP 171

DI 10.1136/ard.2011.154583

UT WOS:000298681800002

ER

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**EXCLUDED / REVIEW**

PT J

AU Gaujoux-Viala, C  
Fautrel, B

AF Gaujoux-Viala, Cecile  
Fautrel, Bruno

TI Cost Effectiveness of Therapeutic Interventions in Ankylosing Spondylitis A Critical and Systematic Review

SO PHARMACOECONOMICS

AB Objectives: This report reviews the cost effectiveness of different therapeutic interventions used in the treatment of ankylosing spondylitis (AS).

Methods: We performed a systematic search of the databases MEDLINE via PubMed, EMBASE and the Cochrane Library and used hand-searching to identify articles on cost effectiveness of therapies for adult patients with AS published up to November 2010.

Results: Of 135 articles, 13 studies were analysed. Two articles were on physical therapies, one article was on NSAIDs and ten articles were on tumour necrosis factor (TNF) inhibitors (infliximab = 6, etanercept = 2, infliximab and etanercept = 1 and adalimumab = 1). Of the latter, no article directly compared TNF inhibitors. Articles showed substantial heterogeneity in methodological approaches and thus results, which prevented us from any extensive comparison, data pooling or meta-analysis. The incremental cost-effectiveness ratio (ICER) for spa-exercise treatment was \$7465 (95% CI 3294, 14 686) per QALY. The ICERs for infliximab, etanercept and adalimumab were \$5307-237010, \$29 815-123 761 and \$7344-33 303 per QALY, respectively.

Conclusions: Modelling treatment strategies in chronic relapsing diseases such as AS presents specific challenges, as reflected in the variation in the cost-effectiveness results reported. Although quite variable, the cost-effectiveness ratios for AS therapies remain within an acceptable range.

TC 0

Z9 0

SN 1170-7690

PY 2012

VL 30

IS 12

BP 1145

EP 1156

UT WOS:000312041400004

ER

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## EXCLUDED / NOT AS

PT J

AU Chimenti, MS

Perricone, C  
Graceffa, D  
Di Muzio, G  
Ballanti, E  
Guarino, MD  
Conigliaro, P  
Greco, E  
Kroegler, B  
Perricone, R

AF Chimenti, M. S.

Perricone, C.  
Graceffa, D.  
Di Muzio, G.  
Ballanti, E.  
Guarino, M. D.  
Conigliaro, P.  
Greco, E.  
Kroegler, B.  
Perricone, R.

TI Complement system in psoriatic arthritis: a useful marker in response prediction and monitoring of anti-TNF treatment

## SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY

AB Objective

Treatment with anti-TNF agents is well established in psoriatic arthritis (PsA). Anti-TNF agents are capable of modulating complement activity in vitro but there are no data on the in vivo effect. Anti-TNF have high costs and potential risks, thus, there is an urgent need for accurate predictors of response. We aimed at studying the usefulness of erythrocyte-sedimentation rate (ESR), C-reactive protein (CRP), and complement for response prediction and monitoring of anti-TNF treatment in PsA patients.

Methods

Fifty-five patients were included consecutively before starting etanercept or adalimumab. ESR, CRP, plasma complement C3, C4, and C3 and B cleavage fragments were evaluated at baseline and after 22 weeks of anti-TNF treatment. Disease activity was measured with DAS28 and response to therapy with EULAR criteria. Complement was evaluated at baseline in 30 healthy subjects as well.

Results

At baseline, C3 and C4 levels were significantly higher than in controls (C3 126.9 +/- 22 vs. 110 +/- 25 mg/dl,  $p=0.000002$ ; C4 31.2 +/- 9.2 vs. 22.7 +/- 8.3 mg/dl,  $p=0.0003$ ). After anti-TNF therapy, C3 and C4 levels were significantly reduced to normalization ( $p=0.0009$  and  $0.0005$ , respectively) and ESR, CRP and DAS28 showed a significant reduction ( $p=0.002$ ,  $0.004$  and  $0.0001$ , respectively). Split products of C3 and B were not observed at baseline and after 22 weeks. Higher baseline C3 levels were associated with EULAR non-response ( $p=0.011$ ).

Conclusion

PsA patients with moderate to severe disease show elevated C3 and C4 levels, reverted by anti-TNF treatment. High C3 may be considered a hallmark of inflammation and C3 revealed the highest predictive

value for response to anti-TNF.

TC 0

Z9 0

SN 0392-856X

PD JAN-FEB

PY 2012

VL 30

IS 1

BP 23

EP 30

UT WOS:000301814600004

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Sushma, K  
Vijayalakshmi, MA  
Krishnan, V  
Satheeshkumar, PK

AF Sushma, Krishnan  
Vijayalakshmi, Mookambeswaran A.  
Krishnan, Venkataraman  
Satheeshkumar, Padikara Kutty

TI Cloning, expression, purification and characterization of a single chain variable fragment specific to tumor necrosis factor alpha in Escherichia coli

SO JOURNAL OF BIOTECHNOLOGY

AB Anti TNF-alpha molecules have been used as therapeutic agents in a variety of human diseases such as Rheumatoid arthritis, Ankylosing spondylitis, Chron's diseases, Psoriasis, etc., where high levels of TNF-alpha plays a destructive role. The limitations of the present TNF-alpha inhibitors in terms of size, tissue penetration and immunogenicity, etc., provoked the search for small anti TNF-alpha molecules. In the present study, a single chain variable fragment (ScFv) construct was made from a monoclonal antibody of the class IgG raised against TNF-alpha was used. The anti TNF-alpha ScFv was well expressed as soluble form in Escherichia coli BL21 (DE3), which was purified to homogeneity by commercial methacrylate monolith-convective interaction media (CIM) supports using two different chemistries, immobilized metal

affinity chromatography (IMAC) with copper ions followed by anion exchange chromatography. The anti TNF-alpha ScFv found to be inhibiting the TNF-alpha mediated cytotoxicity in MCF-7 cells with an IC(50) of 8 mu g. Data presented here are promising and encouraging to further optimize anti TNF-alpha ScFv production in larger scale with higher recovery at a cheaper price for therapeutic purposes. (C) 2011 Elsevier B. V. All rights reserved.

TC 3

Z9 3

SN 0168-1656

PD DEC 20

PY 2011

VL 156

IS 4

SI SI

BP 238

EP 244

DI 10.1016/j.jbiotec.2011.06.039

UT WOS:000298144700002

ER

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## INCLUDED

PT J

AU An, TD

Boonen, A

van de Laar, MAFJ

Franke, AC

Severens, JL

AF An Tran-Duy

Boonen, Annelies

van de Laar, Mart A. F. J.

Franke, Angelinus C.

Severens, Johan L.

TI A discrete event modelling framework for simulation of long-term outcomes of sequential treatment strategies for ankylosing spondylitis

SO ANNALS OF THE RHEUMATIC DISEASES

**AB Objective** To develop a modelling framework which can simulate long-term quality of life, societal costs and cost-effectiveness as affected by sequential drug treatment strategies for ankylosing spondylitis (AS). **Methods** Discrete event simulation paradigm was selected for model development. Drug efficacy was modelled as changes in disease activity (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)) and functional status (Bath Ankylosing Spondylitis Functional Index (BASFI)), which were linked to costs and health utility using statistical models fitted based on an observational AS cohort. Published clinical data were used to estimate drug efficacy and time to events. Two strategies were compared: (1) five available nonsteroidal anti-inflammatory drugs (strategy 1) and (2) same as strategy 1 plus two tumour necrosis factor alpha inhibitors (strategy 2). 13 000 patients were followed up individually until death. For probability sensitivity analysis, Monte Carlo simulations were performed with 1000 sets of parameters sampled from the appropriate probability distributions.

**Results** The models successfully generated valid data on treatments, BASDAI, BASFI, utility, quality-adjusted life years (QALYs) and costs at time points with intervals of 1-3 months during the simulation length of 70 years. Incremental cost per QALY gained in strategy 2 compared with strategy 1 was (sic)35 186. At a willingness-to-pay threshold of (sic)80 000, it was 99.9% certain that strategy 2 was cost-effective.

**Conclusions** The modelling framework provides great flexibility to implement complex algorithms representing treatment selection, disease progression and changes in costs and utilities over time of patients with AS. Results obtained from the simulation are plausible.

TC 0

Z9 0

SN 0003-4967

PD DEC

PY 2011

VL 70

IS 12

BP 2111

EP 2118

DI 10.1136/annrheumdis-2011-200333

UT WOS:000297571900009

ER

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**EXCLUDED / ABSTRACT**

PT J

AU Farrell, J  
Muszbek, N  
Sheppard, O  
Chaudhary, M  
Naci, H  
Kachroo, S

AF Farrell, J.  
Muszbek, N.  
Sheppard, O.  
Chaudhary, M.  
Naci, H.  
Kachroo, S.

TI THE LONG TERM COST-EFFECTIVENESS OF GOLIMUMAB FOR THE TREATMENT OF SEVERE,  
ACTIVE ANKYLOSING SPONDYLITIS IN ADULTS WHO HAVE RESPONDED INADEQUATELY  
TO CONVENTIONAL THERAPY

SO VALUE IN HEALTH

TC 0

Z9 0

SN 1098-3015

PD NOV

PY 2011

VL 14

IS 7

BP A311

EP A311

UT WOS:000299107100407

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Jacobs, P  
Bissonnette, R  
Guenther, LC

AF Jacobs, Philip  
Bissonnette, Robert  
Guenther, Lyn C.

TI Socioeconomic Burden of Immune-Mediated Inflammatory Diseases - Focusing on Work Productivity and Disability

SO JOURNAL OF RHEUMATOLOGY

AB Chronic disabling conditions, such as immune-mediated inflammatory diseases (IMID), adversely affect patients in terms of physical suffering and pain, impaired function, and diminished quality of life. These persistent relapsing diseases have a significant influence on individual employment status and work-related productivity. In addition to the significant burden on patients and their families, IMID represent a sizable burden to society due to high healthcare and non-healthcare related costs. Non-healthcare related, or indirect, costs primarily associated with decreased work productivity, disability payments, and early retirements are typically greater contributors than direct healthcare costs to the total costs associated with IMID. This article discusses the socioeconomic impact of several IMID, including rheumatoid arthritis, inflammatory bowel disease, ankylosing spondylitis, and psoriasis. (J Rheumatol 2011;38 Suppl 88:55-61; doi:10.3899/jrheum.110901)

TC 2

Z9 2

SN 0315-162X

PD NOV

PY 2011

VL 38

SU 88

BP 55

EP 61

DI 10.3899/jrheum.110901

UT WOS:000297564000010

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Braun, ADJ  
Braun, J  
Inman, RD

van der Heijde, D  
Hsu, B  
Tandon, N  
Han, CL

AF Braun, Atul Deodhar J.  
Braun, J.  
Inman, R. D.  
van der Heijde, Desiree  
Hsu, Benjamin  
Tandon, Neeta  
Han, Chenglong

TI Cost Per Placebo Adjusted Response of Golimumab, Adalimumab, and Etanercept in Patients with Active Ankylosing Spondylitis

SO ARTHRITIS AND RHEUMATISM

CT 75th Annual Scientific Meeting of the American-College-of-Rheumatology/46th Annual Scientific Meeting of the Association-of-Rheumatology-Health-Professionals

CY NOV 04-09, 2011

CL Chicago, IL

SP Amer Coll Rheumatol, Assoc Rheumatol Hlth Professionals

TC 0

Z9 0

SN 0004-3591

PD OCT

PY 2011

VL 63

IS 10

SU S

MA 922

BP S362

EP S362

UT WOS:000297621501117

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU D'Angelo, S  
Palazzi, C  
Cantini, F  
Lubrano, E  
Marchesoni, A  
Mathieu, A  
Salvarani, C  
Scarpa, R  
Spadaro, A  
Olivieri, I

AF D'Angelo, S.  
Palazzi, C.  
Cantini, F.  
Lubrano, E.  
Marchesoni, A.  
Mathieu, A.  
Salvarani, C.  
Scarpa, R.  
Spadaro, A.  
Olivieri, I.

TI Etanercept in spondyloarthropathies. Part II: safety and pharmacoeconomic issues

**SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY**

AB Etanercept (ETN) and other anti-TNF-alpha agents have revolutionised the management of spondyloarthropathies (SpA). With the increasingly widespread and prolonged use of these drugs an assessment of their long-term safety is extremely important. An additional concern regarding biological agents is their higher costs compared with conventional drugs. We examined safety data regarding ETN from clinical reports, clinical trials, review articles, databases and registries. In addition, evidence was reviewed about the cost effectiveness of ETN in the treatment of patients with SpA. Our review suggests that ETN is well tolerated as long-term, continuous treatment of SpA with a favourable risk-benefit ratio maintained from 4 to 5 years. Diversity in structure and mode of action could explain some differences in the safety profile of ETN with respect to the other anti-TNF agents. In particular, ETN is less immunogenic and is less likely to induce tuberculosis re-activation than the other TNE-alpha antagonists. Although ETN is considerably more expensive than conventional therapy, it reduces direct and indirect costs associated to SpA by improving disease activity and quality of life. Recent pharmacoeconomic studies have demonstrated its cost-effectiveness in the treatment of SpA.

RI 

D'Angelo, Salvatore	H-9010-2012
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TC 1

Z9 2

SN 0392-856X

PD SEP-OCT

PY 2011

VL 29

IS 5

BP 865

EP 870

UT WOS:000297192600019

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Lee, TW  
Singh, R  
Fedorak, RN

AF Lee, T. W.  
Singh, R.  
Fedorak, R. N.

TI A one-hour infusion of infliximab during maintenance therapy is safe and well tolerated: a prospective cohort study

SO ALIMENTARY PHARMACOLOGY & THERAPEUTICS

AB Background

Infliximab is a chimeric monoclonal antibody to tumour necrosis factor alpha (TNF alpha) with efficacy in inducing and maintaining remission of inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis and psoriasis. Infliximab is generally administered over 2 h with a further 1-h postinfusion observation. This time interval has substantial impact on healthcare resources and is costly in terms of patient's time away from work.

Aim

To examine the safety and tolerability of a 1-h, relative to a 2-h maintenance of infusion of infliximab, and to determine the effect of corticosteroid premedication and concurrent immunosuppressor use on infusion reaction rates.

Method

A prospective cohort study with variable follow-up duration of 2165 consecutive infliximab infusions in 415 patients during 2009 was conducted. Diagnosis, infusion episode number, infusion rate, premedication, concurrent immunosuppressor therapy, the nature and the outcome of infusion reactions were examined.

Results

The majority of infusions (74%) were for management of inflammatory bowel disease. Infusion reactions

clustered within the first eight infusions with subsequent sporadic reactions. The infusion reaction incidence rate per 1000 person days in 274 1-h infusions from 54 patients and 1356 2-h infusions from 256 patients were 0.08 and 0.28 respectively ( $P = 0.07$ ). Poisson regression model confirmed that the concurrent use of immunosuppressor therapy was associated with a lower infusion reaction rate, whereas corticosteroid premedication was not.

TC 0

Z9 0

SN 0269-2813

PD JUL 15

PY 2011

VL 34

IS 2

BP 181

EP 187

DI 10.1111/j.1365-2036.2011.04699.x

UT WOS:000292152300006

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Poddubnyy, D  
Rudwaleit, M

AF Poddubnyy, Denis  
Rudwaleit, Martin

TI Efficacy and safety of adalimumab treatment in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis

SO EXPERT OPINION ON DRUG SAFETY

AB Introduction: In the last couple of years, the number of patients with chronic inflammatory rheumatic diseases being treated with TNF alpha antagonist has increased dramatically. Adalimumab, a fully human monoclonal antibody against TNF alpha, is one of the most frequently administered TNF alpha antagonists. Yet, unresolved issues are the long-term safety of TNF alpha antagonists and high treatment costs. Areas covered: The authors summarize the available data on short- and long-term efficacy and safety of adalimumab in the treatment of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis. The

reader will find a comprehensive overview on the safety and efficacy of adalimumab for these conditions. Clinically relevant questions of adalimumab therapy are discussed. A special focus of this review is on the safety of adalimumab therapy.

Expert opinion: Adalimumab is effective and reasonably safe in the short- and long-term treatment of patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis who do not respond to the standard therapy. It inhibits radiographic progression in rheumatoid and psoriatic arthritis. Treatment with a TNF alpha inhibitor such as adalimumab is associated with high treatment costs.

TC 0

Z9 0

SN 1474-0338

PD JUL

PY 2011

VL 10

IS 4

BP 655

EP 673

DI 10.1517/14740338.2011.581661

UT WOS:000291533800015

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Zhang, SL

Li, Y

Deng, XH

Huang, F

AF Zhang, Shengli

Li, Yan

Deng, Xiaohu

Huang, Feng

TI Similarities and differences between spondyloarthritis in Asia and other parts of the world

SO CURRENT OPINION IN RHEUMATOLOGY

AB Purpose of review

Spondyloarthritis (SpA) is a group of diverse interrelated inflammatory arthritides, which share multiple clinical features as well as common genetic predisposing factors. Ankylosing spondylitis (AS) is regarded as the most typical subtype. The purpose of this article is to review relevant studies conducted in Asia and other parts of the world, which may open a window to a better understanding of the epidemiology, clinical feature, diagnosis, and management of this condition.

Recent findings

The prevalence, clinical feature, diagnosis, and therapy of SpA and its correlation with HLA-B27 in Asia are generally similar to other parts of the world. NSAIDs form the cornerstone of the treatment for AS. The new treatment options with tumor necrosis factor (TNF)-alpha blocking agents seem a breakthrough for patients with SpA refractory to conventional treatment. Recent results showed that thalidomide was an effective, well tolerated, and economic option for refractory AS patients, especially in maintaining disease remission after etanercept or infliximab treatment was discontinued.

Summary

The similarities between spondyloarthritis in Asia and other parts of the world are major and the differences are minor. Because of the major socioeconomic burden and poor access to expensive means of treatment of SpA in Asia, the rheumatologists and physicians in Asia are working hard to look for effective but cheaper alternatively regimens for refractory SpA patients. Thalidomide may be a potentially effective option for patients who cannot afford biologicals in undeveloped areas.

TC 0

Z9 2

SN 1040-8711

PD JUL

PY 2011

VL 23

IS 4

BP 334

EP 338

DI 10.1097/BOR.0b013e32834640a9

UT WOS:000291244200003

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Machado, J  
Moncada, JC

Pineda, R

AF Machado, Jorge  
Carlos Moncada, Juan  
Pineda, Ricardo

TI Profile of use of anti tumor necrosis factor in Colombian patients

SO BIOMEDICA

AB Introduction. Tumor necrosis factor-alpha antagonists (anti-TNF alpha) have shown an increasing consumption and generate a significant economic burden on health systems.

Objectives. The prescribing patterns of tumor necrosis factor-alpha antagonists were determined in a patient population associated with the Sistema General de Seguridad Social en Salud in Colombia.

Materials and methods. A descriptive observational study was conducted in 316 patients with respect to use of tumor necrosis factor-alpha antagonists during a treatment period from January 2008 to June 2009. The database examined contained indications of use, inclusion criteria to medication, duration of illness, co-morbidities and adverse reactions. The data were retrieved from the clinical histories. Student's t test was used for the comparison of quantitative variables, and the chi-square test was used to establish associations between categorical variables and multivariate analysis were used.

Results. Mean age was 44.6 +/- 13.9 years; 63.9% of participants were female. Of the 316 patients, 17.1% received monotherapy. The order of prescription drugs was as follows: adalimumab (37.3%), infliximab (37.3%) and etanercept (25.4%), all were prescribed in appropriately defined daily doses. Co-medication drugs most frequently prescribed were: disease-modifying anti-rheumatic (82.9%), NSAIDs (29.1%), omeprazole (22.5%), antihypertensives (21.2%), folic acid (19.9%) calcium plus vitamin D (9.8%), calcitriol (6.0%). 10.4% of patients had a record of some adverse drug reaction. The average cost of therapy per patient per year was US\$23,464.

Conclusions. Anti-TNF alpha are being used at recommended doses, particularly in rheumatoid arthritis and in combination with other anti-rheumatic drugs. The direct cost of therapy was high for the country's health system.

TC 0

Z9 0

SN 0120-4157

PD JUN

PY 2011

VL 31

IS 2

BP 250

EP 257

UT WOS:000295570100013

ER

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## EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU Kwakernaak, AJ  
Houtman, PM  
Weel, JFL  
Spoorenberg, JPL  
Jansen, TLTA

AF Kwakernaak, Arjan J.  
Houtman, Pieternella M.  
Weel, Jan F. L.  
Spoorenberg, Johanna P. L.  
Jansen, Tim L. T. A.

TI A comparison of an interferon-gamma release assay and tuberculin skin test in refractory inflammatory disease patients screened for latent tuberculosis prior to the initiation of a first tumor necrosis factor alpha inhibitor

## SO CLINICAL RHEUMATOLOGY

AB Treatment with TNF alpha inhibitors increases risk of reactivating a latent tuberculosis infection (LTBI). Therefore screening, prior to therapy with TNF alpha inhibitors, has been recommended, even in low-endemic areas such as well-developed Western Europe countries. We evaluated interferon-gamma release assay (IGRA), as opposed to tuberculin skin test (TST), for detection of LTBI in refractory inflammatory disease patients prior to the initiation of a first TNF alpha inhibitor. In addition, we evaluated the impact of impaired cellular immunity on IGRA. Patients starting on TNF alpha inhibition were screened for LTBI by TST and IGRA (Quantiferon-TB Gold). Data on tuberculosis exposure and Bacillus Calmette-Guérin (BCG) vaccination were obtained. Cellular immunity was assessed by CD4(+) T lymphocyte cell count. Nine out of 56 patients (16.1%) tested positive for LTBI. A concordant positive result was present in three patients with a medical history of tuberculosis exposure. Six patients with discordant test results had either: (1) a negative TST and positive IGRA in combination with a medical history of tuberculosis exposure (n = 1) or (2) a positive TST and negative IGRA in combination with BCG vaccination (n = 3) or a medical history of tuberculosis exposure (n = 2). CD4(+) T lymphocyte cell counts were within normal limits, and no indeterminate results of IGRA were present. IGRA appears reliable for confirming TST and excluding a false positive TST (due to prior BCG vaccination) in this Dutch series of patients. In addition, IGRA may detect one additional case of LTBI out of 56 patients that would otherwise be missed using solely TST. Immune suppression appears not to result significantly in lower CD4(+) T lymphocyte cell counts and indeterminate results of IGRA, despite systemic corticosteroid treatment in half of the patients. Confirmation in larger studies, including assessment of cost-effectiveness, is required.

TC 4

Z9 4

SN 0770-3198

PD APR

PY 2011

VL 30

IS 4

BP 505

EP 510

DI 10.1007/s10067-010-1550-z

UT WOS:000288709100008

ER

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**EXCLUDED / NOT AS**

PT J

AU Mewar, D  
Wilson, AG

AF Mewar, Devesh  
Wilson, Anthony G.

TI Treatment of rheumatoid arthritis with tumour necrosis factor inhibitors

SO BRITISH JOURNAL OF PHARMACOLOGY

AB Advances in our understanding of the key mediators of chronic inflammation and tissue damage characteristic of rheumatoid arthritis (RA) have resulted in the development of novel therapies primarily targeting pro-inflammatory cytokines. Inhibitors of tumour necrosis factor (TNF) are the most widely used of the biological therapies at present with five different agents currently available; four are based on monoclonal anti-TNF antibodies and a soluble TNF receptor-Fc fusion protein. Long-term use of these molecules has proven to be highly effective in the majority of patients; however, around one-third have a suboptimal response potentially leading to further cartilage and bone damage, furthermore these agents are expensive compared with conventional therapies such as methotrexate. Many recent studies have attempted to identify therapeutic response biomarkers of TNF inhibitors which could be used to improve therapeutic targeting. The presence of rheumatoid factor and anti-cyclic citullinated protein antibodies, present in around 65% of RA patients, are associated with a poorer response to anti-TNF agents. Poorer response is also associated with levels of C-reactive protein and cartilage degradation product at initiation of treatment. Intriguingly, genetic studies of variants of TNF and of genes encoding members of the Toll-like receptors, nuclear factor-kappa B and p38 mitogen-activated protein kinase signalling families have been associated with response to individual anti-TNF agents. Continued advances in technologies such as ultra high throughput sequencing and proteomics should facilitate the discovery of additional biomarkers of response to anti-TNF resulting in improved disease control and quality of life for RA patients and reduced costs for healthcare funders.

TC 13

Z9 14

SN 0007-1188

PD FEB

PY 2011

VL 162

IS 4

BP 785

EP 791

DI 10.1111/j.1476-5381.2010.01099.x

UT WOS:000286473000001

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Arends, S  
Brouwer, E  
van der Veer, E  
Groen, H  
Leijnsma, MK  
Houtman, PM  
Jansen, TLTA  
Kallenberg, CGM  
Spoorenberg, A

AF Arends, Suzanne  
Brouwer, Elisabeth  
van der Veer, Eveline  
Groen, Henk  
Leijnsma, Martha K.  
Houtman, Pieterella M.  
Jansen, Tim L. Th A.  
Kallenberg, Cees G. M.  
Spoorenberg, Anneke

TI Baseline predictors of response and discontinuation of tumor necrosis factor-alpha blocking therapy in ankylosing spondylitis: a prospective longitudinal observational cohort study

SO ARTHRITIS RESEARCH & THERAPY

**AB Introduction:** Identifying ankylosing spondylitis (AS) patients who are likely to benefit from tumor necrosis factor-alpha (TNF-alpha) blocking therapy is important, especially in view of the costs and potential side effects of these agents. Recently, the AS Disease Activity Score (ASDAS) has been developed to assess both subjective and objective aspects of AS disease activity. However, data about the predictive value of the ASDAS with respect to clinical response to TNF-alpha blocking therapy are lacking. The aim of the present study was to identify baseline predictors of response and discontinuation of TNF-alpha blocking therapy in AS patients in daily clinical practice.

**Methods:** AS outpatients who started TNF-alpha blocking therapy were included in the Groningen Leeuwarden Ankylosing Spondylitis (GLAS) study, an ongoing prospective longitudinal observational cohort study with follow-up visits according to a fixed protocol. For the present analysis, patients were excluded if they had previously received anti-TNF-alpha treatment. Predictor analyses of response and treatment discontinuation were performed using logistic and Cox regression models, respectively.

**Results:** Between November 2004 and April 2010, 220 patients started treatment with infliximab (n = 32), etanercept (n = 137), or adalimumab (n = 51). At three and six months, 68% and 63% of patients were Assessments in Ankylosing Spondylitis (ASAS) 20 responders, 49% and 46% ASAS40 responders, and 49% and 50% Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)50 responders, respectively. Baseline predictors of response were younger age, male gender, higher ASDAS score, higher erythrocyte sedimentation rate (ESR) level, higher C-reactive protein (CRP) level, presence of peripheral arthritis, higher patient's global assessment of disease activity, and lower modified Schober test. In August 2010, 64% of patients were still using their TNF-alpha blocking agent with a median follow-up of 33.1 months (range 2.4 to 68.2). Baseline predictors of discontinuation of TNF-alpha blocking therapy were female gender, absence of peripheral arthritis, higher BASDAI, lower ESR level, and lower CRP level.

**Conclusions:** Besides younger age and male gender, objective variables such as higher inflammatory markers or ASDAS score were identified as independent baseline predictors of response and/or continuation of TNF-alpha blocking therapy. In contrast, higher baseline BASDAI score was independently associated with treatment discontinuation. Based on these results, it seems clinically relevant to include more objective variables in the evaluation of anti-TNF-alpha treatment.

RI 

Groen, Henk	B-2163-2013
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TC 8

Z9 10

SN 1478-6354

PY 2011

VL 13

IS 3

AR R94

DI 10.1186/ar3369

UT WOS:000297149700025

ER

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## EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU Moots, RJ  
Haraoui, B  
Matucci-Cerinic, M  
van Riel, PLCM  
Kekow, J  
Schaefferbeke, T  
Davis, A  
Tedeschi, MA  
Freundlich, B  
Chang, DJ  
Singh, A

AF Moots, R. J.  
Haraoui, B.  
Matucci-Cerinic, M.  
van Riel, P. L. C. M.  
Kekow, J.  
Schaefferbeke, T.  
Davis, A.  
Tedeschi, M. A.  
Freundlich, B.  
Chang, D. J.  
Singh, A.

TI Differences in biologic dose-escalation, non-biologic and steroid intensification among three anti-TNF agents: evidence from clinical practice

## SO CLINICAL AND EXPERIMENTAL RHEUMATOLOGY

### AB Objectives

To evaluate prevalence of dose escalation among RA patients in normal clinical practice treated with etanercept, adalimumab or infliximab and to estimate its economic impact.

#### Methods

A retrospective observational study of 739 patients with RA receiving continuous treatment with etanercept (n=319), adalimumab (n=313) or infliximab (n=107) for 18 months. Dose escalation, intensification of concomitant DMARDs and risk of dose escalation were evaluated, as well as costs.

#### Results

Significantly more patients prescribed adalimumab (10%,  $p<0.001$ ) or infliximab (35%,  $p<0.001$ ) experienced dose escalation compared with patients treated with etanercept (3%). DMARD or steroid dose adjustment, when added as criteria of escalation, occurred more often among patients treated with adalimumab (28%;  $p=0.022$ ) or infliximab (47%;  $p<0.001$ ) than those prescribed etanercept (19%). Independent of confounding covariates, hazard of dose escalation was significantly higher for either infliximab (28.1-fold) or adalimumab (4.9-fold) relative to etanercept. Escalation among subjects treated with either infliximab or adalimumab incurred statistically significant increases in total cost of care compared with non-escalators whereas such differences observed for subjects treated with etanercept were not significant.

#### Conclusions

Patients receiving monoclonal antibody therapies, adalimumab or infliximab, had significantly higher rates

of dose escalation than patients receiving the soluble TNF receptor, etanercept, and related costs were higher.

TC 8

Z9 10

SN 0392-856X

PD JAN-FEB

PY 2011

VL 29

IS 1

BP 26

EP 34

UT WOS:000288292000005

ER

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#### **EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Aikawa, NE

Twardowsky, AD

de Carvalho, JF

Silva, CA

Silva, ILAFE

Ribeiro, ACD

Saad, CGS

Moraes, JCB

de Toledo, RA

Bonfa, E

AF Aikawa, Nadia Emi

Twardowsky, Aline de Oliveira

de Carvalho, Jozelio Freire

Silva, Clovis A.

Avelino Franca e Silva, Ivan Leonardo

de Medeiros Ribeiro, Ana Cristina

Schain Saad, Carla Goncalves

Bertacini Moraes, Julio Cesar

de Toledo, Roberto Acayaba

Bonfa, Eloisa

TI Intestinal microsporidiosis: a hidden risk in rheumatic disease patients undergoing anti-tumor necrosis factor therapy combined with disease-modifying anti-rheumatic drugs?

SO CLINICS

AB OBJECTIVE: Immunosuppressed patients are at risk of microsporidiosis, and this parasitosis has an increased rate of dissemination in this population. Our objective was to evaluate the presence of microsporidiosis and other intestinal parasites in rheumatic disease patients undergoing anti-tumor necrosis factor/disease-modifying anti-rheumatic drug treatment.

METHODS: Ninety-eight patients (47 with rheumatoid arthritis, 31 with ankylosing spondylitis and 11 with psoriatic arthritis) and 92 healthy control patients were enrolled in the study. Three stool samples and cultures were collected from each subject.

RESULTS: The frequency of microsporidia was significantly higher in rheumatic disease patients than in control subjects (36 vs. 4%, respectively;  $p < 0.0001$ ), as well as in those with rheumatic diseases (32 vs. 4%, respectively;  $p < 0.0001$ ), ankylosing spondylitis (45 vs. 4%, respectively;  $p < 0.0001$ ) and psoriatic arthritis (40 vs. 4%, respectively;  $p < 0.0001$ ), despite a similar social-economic class distribution in both the patient and control groups ( $p = 0.1153$ ). Of note, concomitant fecal leukocytes were observed in the majority of the microsporidia-positive patients (79.5%). Approximately 80% of the patients had gastrointestinal symptoms, such as diarrhea (26%), abdominal pain (31%) and weight loss (5%), although the frequencies of these symptoms were comparable in patients with and without this infection ( $p > 0.05$ ). Rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis disease activity parameters were comparable in both groups ( $p > 0.05$ ). The duration of anti-tumor necrosis factor/disease-modifying anti-rheumatic drugs and glucocorticoid use were also similar in both groups.

CONCLUSION: We have documented that microsporidiosis with intestinal mucosa disruption is frequent in patients undergoing concomitant anti-tumor necrosis factor/disease-modifying anti-rheumatic drug therapy. Impaired host defenses due to the combination of the underlying disease and the immunosuppressive therapy is the most likely explanation for this finding, and this increased susceptibility reinforces the need for the investigation of microsporidia and implementation of treatment strategies in this population.

RI 

Bonfa, Eloisa	B-8438-2012
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TC 2

Z9 2

SN 1807-5932

PY 2011

VL 66

IS 7

BP 1171

EP 1175

DI 10.1590/S1807-59322011000700008

UT WOS:000294436800008

## EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU Tenga, G  
Goeb, V  
Lequerre, T  
Bacquet-Deschryver, H  
Daragon, A  
Pouplin, S  
Lanfant-Weybel, K  
Le Loet, X  
Dieu, B  
Vittecoq, O

AF Tenga, Ginette  
Goeb, Vincent  
Lequerre, Thierry  
Bacquet-Deschryver, Helene  
Daragon, Alain  
Pouplin, Sophie  
Lanfant-Weybel, Karine  
Le Loet, Xavier  
Dieu, Bernard  
Vittecoq, Olivier

TI A 3 mg/kg starting dose of infliximab in active spondyloarthritis resistant to conventional treatments is efficient, safe and lowers costs

SO JOINT BONE SPINE

AB Objective: We assessed the efficacy, tolerance and cost of a 3 mg/kg starting dose of infliximab for ankylosing spondylitis (AS) and psoriatic arthritis (PsA).

Methods: We retrospectively followed-up 45 biologic-naïve consecutive patients (11 with axial AS, 24 with axial and peripheral [mixed] AS and 10 with PsA) who were treated between 2002 and 2005 with a 3 mg/kg dose of infliximab after failure of conventional therapies. The following variables were recorded: visual analog scale (VAS) scores of patient's global (G) and pain (P) assessment, duration of early morning stiffness (EMS), disease activity (BASDAI) and functional disability (BASFI). Treatment responses were assessed at 6 and 12 months using the AS assessment score (ASAS)-20% and -40% criteria and BASDAI-50.

Results: Baseline characteristics of the 29 men and 16 women were (median [range]): G-VAS, 70 [13-100]; P-VAS, 70 [13-100]; EMS, 60 [0-180] minutes; BASDAI, 64.4 [23.9-100]; BASFI, 57.2 [3.5-98.5]. All manifestations regressed significantly ( $p < 0.0001$ ) for 39 (86.7%) and 24 (53.5%) patients at 6 and 12 months, respectively; 26 (57.8%) had achieved ASAS-20 responses at 6 months that persisted at 1 year for 20 (44.4%); 19 (42.2%) and 12 (26.7%) satisfied BASDAI 50 criteria at 6 and 12 months, respectively. Interestingly, almost 30% still received low-dose infliximab after 4 years of follow-up.

Conclusion: An initial dose of 3 mg/kg of infliximab significantly attenuated AS and PsA manifestations in >40% of the patients, making use of this dose highly advantageous in terms of safety and 33% lower cost.

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TC 2

Z9 2

SN 1297-319X

PD JAN

PY 2011

VL 78

IS 1

BP 50

EP 55

DI 10.1016/j.jbspin.2010.04.017

UT WOS:000286136400011

ER

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**EXCLUDED / NOT COST-UTILITY ANALYSIS**

PT J

AU Gooch, K  
Feeny, D  
Wong, RL  
Kupper, H  
Pangan, AL  
Revicki, DA  
van der Heijde, D

AF Gooch, Katherine  
Feeny, David  
Wong, Robert L.  
Kupper, Hartmut  
Pangan, Aileen L.  
Revicki, Dennis A.  
van der Heijde, Desiree

TI Is the Health Utilities Index 3 valid for patients with ankylosing spondylitis?

SO VALUE IN HEALTH

AB Objective: To assess the convergent and discriminative validity of the Health Utilities Index Mark 3 (HUI-3) for patients with ankylosing spondylitis (AS).

Methods: Data were derived from the Adalimumab Trial evaluating Long-term efficacy and safety for Ankylosing Spondylitis (ATLAS). The study team specified 90 a priori hypotheses regarding the direction and magnitude of the expected associations between the overall and single-attribute scores of the HUI-3 and other health status and quality-of-life measures: Short Form 36 Health Survey (SF-36), Ankylosing Spondylitis Quality-of-Life Questionnaire, Bath Ankylosing Spondylitis Functional Index, Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Metrology Index, and Patient's and Physician's Global Assessments of Disease Activity. With baseline data, correlation coefficients were calculated and interpreted according to the guidelines suggested by Guyatt for negligible (0-0.19), weak (0.20-0.34), moderate (0.35-0.50), and strong (>0.5) associations. The a priori hypotheses were tested using Pearson's correlation coefficients.

Results: A total of 315 patients with active AS were randomized and enrolled in ATLAS. The correlation coefficients between the HUI-3 scores and other health-related quality-of-life instruments confirmed 61.1% of the a priori hypotheses, with an additional 35.5% being under-or overestimated by one correlation category.

Conclusion: These results provide evidence of the cross-sectional, convergent, and discriminative validity of the HUI-3 for deriving utility scores in patients with AS. Copyright (C) 2011, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

TC 1

Z9 1

SN 1098-3015

PD JAN-FEB

PY 2011

VL 14

IS 1

BP 160

EP 165

DI 10.1016/j.jval.2010.10.012

UT WOS:000299039700019

ER

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#### EXCLUDED / NOT COST-UTILITY ANALYSIS

PT J

AU Strombeck, B  
Englund, M  
Bremaner, A

Jacobsson, LTH  
Kedza, L  
Kobelt, G  
Petersson, IF

AF Strombeck, Britta  
Englund, Martin  
Bremander, Ann  
Jacobsson, Lennart T. H.  
Kedza, Ljuba  
Kobelt, Gisela  
Petersson, Ingemar F.

TI Cost of Illness from the Public Payers' Perspective in Patients with Ankylosing Spondylitis in Rheumatological Care

SO JOURNAL OF RHEUMATOLOGY

AB Objective. To estimate the incremental costs to public payers for patients with ankylosing spondylitis (AS) of working age compared with reference subjects from the general population.  
Methods. We investigated total costs for 3 years (2005-2007) in 116 outpatients under 66 years of age with AS attending rheumatological care in Malmo, Sweden. Mean (SD) age was 46 (11) years and mean (SD) disease duration was 24 (11) years. Two subjects per AS patient matched for age, sex, and residential area were selected from the Population Register to serve as a reference group. We retrieved data concerning sick leave, prescription drugs, and healthcare consumption from Swedish health-cost registers by the unique personal identification numbers.  
Results. The mean total cost for the 3-year period 2005-2007 was US \$37,095 (SD \$30,091) for patients with AS, and \$11,071 (SD \$22,340) for the reference group. The mean indirect cost was \$19,618 and \$5905, respectively. Mean cost for healthcare was \$8998 for the AS patients and \$4187 for the reference subjects, and mean cost for drugs was \$8479 and \$979, respectively. The patients with AS treated with biological therapy constituted 80% of the total drug cost, but just 40% of the cost for disability pension.  
Conclusion. Patients with AS had 3-fold increase in costs compared to reference subjects from the general population, and the drug costs were almost 10 times as high. Production losses (indirect cost) represented more than half of total cost (53%). (First Release August 15 2010; J Rheumatol 2010;37:2348-55: doi:10.3899/jrheum.100099)

RI 

Englund, Martin	J-7245-2012
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TC 2

Z9 2

SN 0315-162X

PD NOV

PY 2010

VL 37

IS 11

BP 2348

EP 2355

DI 10.3899/jrheum.100099

UT WOS:000284301900026

ER

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**INCLUDED**

PT J

AU Neilson, AR  
Sieper, J  
Deeg, M

AF Neilson, Aileen R.  
Sieper, Joachim  
Deeg, Maria

TI Cost-effectiveness of etanercept in patients with severe ankylosing spondylitis in Germany

SO RHEUMATOLOGY

AB Methods. A mathematical model previously applied to the UK was adapted using resource use and cost data (for 2007) from the national database of the German Collaborative Arthritis Centres. Social health insurance (SHI) and societal perspectives were analysed. Assumptions on initial response and changes in health-related quality of life were based on Phase III randomized controlled trials. Initial treatment response according to British Society for Rheumatology guidelines were assumed as a conservative estimate in the German context. Long-term disease progression was based on the available literature. Incremental cost-effectiveness ratios (ICERs) were expressed as euros/quality-adjusted life year (QALY), for a cohort of 1000 patients over 25 years. Sensitivity analyses explored uncertainty in results.  
Results. In the base case, ETN plus usual care (including NSAIDs) yielded 1475 more QALYs at an additional cost of euro80 827 668 (SHI) or euro32 657 590 (societal) leading to an ICER of euro54 815/QALY and euro22 147/QALY, respectively. Over a shorter time horizon of 10 years, the ICERs were euro59 006 and euro29 815 for SHI and societal viewpoints, respectively. Assumptions having the largest impact on results included withdrawal rates from ETN, quality of life, disease costs and initial response.  
Conclusions. Cost-effectiveness for ETN in patients with severe AS in Germany differs according to the cost perspective. Study estimates were higher than in the UK but comparable with reported cost-effectiveness of anti-TNF treatments in patients with RA in Germany.

TC 5

Z9 5

SN 1462-0324

PD NOV

PY 2010

VL 49

IS 11

BP 2122

EP 2134

DI [10.1093/rheumatology/keq222](https://doi.org/10.1093/rheumatology/keq222)

UT WOS:000283120300019

ER

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EF