

disfavor celecoxib (i.e., arthritis efficacy and daily average consumption), we adopted rofecoxib data. Despite modeling this “best-case” hybrid coxib, our analysis suggests that coxibs may not be cost-effective.

Second, Mr. Loyd et al point out that our study included data from trials involving both RA and OA and that “celecoxib is mainly used to treat OA,” and in our opinion, this criticism lacks weight not only because coxibs are indeed used for both OA and RA, but also because there is no a priori reason to expect that the cost-ineffectiveness of coxibs would vary significantly by indication. The fact that coxibs were dominated in our analysis (i.e., more expensive yet less effective than alternatives) is unlikely to be overcome by subdividing data by type of arthritis.

Third, Mr. Loyd et al argue that our assumption that ASA blunts the GI safety of coxibs is not supported by robust evidence and does not comply with data from the SUCCESS study. However, our assumption is derived precisely from robust clinical evidence, including the SUCCESS study (reference 10 in our manuscript). Moreover, the largest published randomized controlled trial to date reporting clinically significant ulcer complications in patients receiving coxibs plus ASA versus NSAID plus ASA (CLASS study) (5) revealed no significant differences in complicated GI events between interventions. An error in our table (that is correct in the text itself) indicates that our assumption is based on a previously published decision analysis, that is incorrect. Mr. Loyd et al mistakenly seize on this error in their letter, but it should be quite evident that we could not have based a point estimate on a previous decision analysis, which itself does not contain any primary data. In short, there is little debate that the relative GI safety of coxibs is probably undermined by ASA. But despite this clarity, we nonetheless performed a sensitivity analysis in which we assumed no impact of ASA on relative GI safety of coxibs, and still found that coxibs are not cost-effective.

Fourth, Mr. Loyd and colleagues present a series of interlocking statements which, taken together, argue that our assumption that coxibs might promote cardiovascular adverse events is overstated. Specifically, they claim that celecoxib does not raise the risk of serious cardiovascular thrombotic events. This may be correct, but the black box warning on celecoxib issued by the Food and Drug Administration argues otherwise. More to the point, we conducted a sensitivity analysis in which we assumed no difference in cardiovascular safety between arms, and still found that coxibs are not cost-effective.

Brennan M. R. Spiegel, MD, MSHS
VA Greater Los Angeles Healthcare System
University of California Los Angeles
VA Center for Outcomes Research and Education
Los Angeles, CA

Chiun-Fang Chiou, PhD
Joshua J. Ofman, MD, MSHS
Cerner Health Insights
Beverly Hills, CA

1. Mamdani M, Rochon PA, Juurlink DN, Kopp A, Anderson GM, Naglie G, et al. Observational study of upper gastrointestinal haemorrhage in elderly patients given selective cyclooxygen-

ase-2 inhibitors or conventional nonsteroidal antiinflammatory drugs. *BMJ* 2002;325:624.

2. Watson DJ, Harper SE, Zhao PL, Quan H, Bolognese JA, Simon TJ. Gastrointestinal tolerability of the selective cyclooxygenase-2 (COX-2) inhibitor rofecoxib compared with nonselective COX-1 and COX-2 inhibitors in osteoarthritis. *Arch Intern Med* 2000;160:2998–3003.
3. Geba GP, Weaver AL, Polis AB, Dixon ME, Schnitzer TJ. Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee: a randomized trial. *JAMA* 2002;287:64–71.
4. Schnitzer TJ, Kong SX, Mitchell JH, Mavros P, Watson DJ, Pellissier JM, et al. An observational, retrospective, cohort study of dosing patterns for rofecoxib and celecoxib in the treatment of arthritis. *Clin Ther* 2003;25:3162–72.
5. Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A, et al, and the Celecoxib Long-Term Arthritis Safety Study. Gastrointestinal toxicity with celecoxib vs nonsteroidal antiinflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. *JAMA* 2000;284:1247–55.

DOI 10.1002/art.21850

Etanercept-induced granulomas: comment on the article by Phillips and Weinblatt

To the Editors:

In an article published recently in *Arthritis Care & Research*, Drs. Phillips and Weinblatt described a patient who developed pulmonary densities while receiving etanercept therapy for psoriatic arthritis (1). The lung histology showed noncaseating granulomas. The authors stated that it would be of interest to learn of other patients with a similar clinical picture.

I am aware of reports of 3 cases of lung granulomas with the histologic structure of rheumatoid nodules in etanercept-treated seropositive rheumatoid patients (2). The causal relation of these lesions to anti-tumor necrosis factor (TNF) therapy and specifically to etanercept therapy (as suggested by Drs. Phillips and Weinblatt) remains unconfirmed. This possibility, however, should be noted in light of the increased susceptibility to a variety of infections associated with TNF-blocking agents (3).

Oswaldo Hübscher, MD
CEMIC
Buenos Aires, Argentina

1. Phillips K, Weinblatt M. Granulomatous lung disease occurring during etanercept treatment. *Arthritis Rheum* 2005;53:618–20.
2. Hübscher O, Re R, Iotti R. Pulmonary rheumatoid nodules in an etanercept-treated patient [letter]. *Arthritis Rheum* 2003;48:2077–8.
3. Furst D, Breedveld F, Kalden J, Smolen J, Burmester G, Bijlsma J, et al. Updated consensus statement of biological agents, specifically TNF alpha blocking agents and IL-1ra for the treatment of rheumatic diseases, 2004. *Ann Rheum Dis* 2004;63 Suppl II:ii2–12.

DOI 10.1002/art.21851

Reply

To the Editors:

We would like to thank Dr. Hübscher for bringing to our attention his report of the development of pulmonary nod-

ules in a patient with rheumatoid arthritis treated with etanercept (Hubscher O, Re R, Iotti R. Pulmonary rheumatoid nodules in an etanercept-treated patient [letter]. *Arthritis Rheum* 2003;48:2077–8). It would be of interest to know whether the pulmonary nodules resolved in his patient when the anti-TNF treatment was discontinued. We reported a patient who developed bilateral reticular nodular interstitial disease with biopsy evidence of culture negative noncaseating granulomas while receiving etanercept therapy for psoriatic arthritis. These granulomas resolved with discontinuation of etanercept therapy and have not recurred with the addition of adalimumab therapy.

These cases highlight the importance of reporting adverse events to the US Food and Drug Administration (FDA) through the MedWatch system (FDA Safety Information and Adverse Event Reporting Program available at URL: <http://www.fda.gov/medwatch/>). It is only through a voluntary reporting system that we will be able to identify rare events that occur with drug therapy. It will be of interest to know whether other clinicians have observed similar granulomatous culture-negative reactions in patients receiving anti-TNF therapy.

Michael E. Weinblatt, MD
Brigham and Women's Hospital
Boston, MA
Kristine Phillips, MD, PhD
University of Michigan School of Medicine
Ann Arbor, MI

DOI 10.1002/art.21860

A rheumatologist's perspective on musculoskeletal ultrasound in rheumatology: comment on the editorial by Roemer et al

To the Editors:

A recent editorial by 3 eminent musculoskeletal radiologists on the use of musculoskeletal ultrasound (MSUS) in rheumatology correctly highlights the important role that MSUS can play in improving the diagnosis of synovitis, enthesitis, and bony erosions and in guiding local therapy to the benefit of rheumatology patients (1). The editorial also concludes that rheumatologists and radiologists should engage in the development of MSUS by “cooperation and constant communication between the specialties.” We are in full support of these concepts as we enjoy working with our musculoskeletal radiology colleagues, both in our clinical rheumatologic practice, and also in the implementation of national and European MSUS training and research projects. However, this editorial makes a number of strident statements that are unfortunately not correct and that are not helpful in achieving good relations and collaboration between radiologists and rheumatologists in the development of MSUS.

Despite adopting a moderate tone towards the end of the editorial, the authors argue firmly against the practice of MSUS by rheumatologists. One of the principal arguments

against training rheumatologists in MSUS is on the grounds that this will lead to inappropriate or self referral of patients for MSUS. They cite the example from other specialties where the impact of the availability of a number of radiographic procedures in primary care led to a higher use of all imaging modalities when compared with physicians who referred to radiologists (2). There are numerous other explanations for this, which include higher patient acceptability for immediate on-site scanning and the fact that a superior working knowledge by physicians of an imaging modality may lead to a greater use of this modality. Indeed the authors of the study quoted eventually concluded that “it is not possible to determine which group of physicians uses imaging more appropriately” (2). Roemer et al then go on to argue that the radiologist is uniquely placed as a “gatekeeper” to “guard patients against greedy self referral” by rheumatologists and they cite the presence of radiologists as providing a “heavier focus on patient care.” This is a very unfortunate and extremely inappropriate misconception that does not respect the decency or professionalism of clinical rheumatologists in how they manage their patients, nor does it reflect the reality of working practices between rheumatologists and radiologists.

In all of our rheumatologic practices, we are trained to routinely select from a wide number of imaging modalities including plain radiography, MSUS, computed tomography (CT), magnetic resonance imaging (MRI), and nuclear medicine to achieve better assessment and diagnosis in our patients. We have not noted that our own radiology colleagues feel it necessary to act as gatekeepers in restricting these activities, and in the minority of cases when we are unsure of the optimal imaging option to perform, we routinely seek the advice of our radiology colleagues. Indeed in the financial model in which they seek to stake out the moral high ground for themselves, there is equal incentive for the radiologist to proceed with inappropriately referred imaging for financial reward. Rheumatologists could equally perform unnecessary procedures (such as joint injection, and the prescription and supervision of unnecessary long-term medications such as anti-tumor necrosis therapy) solely for financial reward, something of which there is absolutely no evidence. We believe that the professional training of both radiologists and rheumatologists renders them equally capable of acting responsibly in the patient's best interests and regret that our radiology colleagues would express an alternative point of view, and worse, that it should be published unchallenged in a leading rheumatology journal. The authors go on to state that radiologists “will choose the most cost-efficient modality to query a rheumatologic disease.” This statement ignores the predominant use of MRI over MSUS for musculoskeletal imaging in the US, in contrast to the wider use of more cost-effective MSUS in musculoskeletal disease in Europe where clinicians have been involved in performing MSUS for over a decade.

We firmly believe that both rheumatologists and radiologists will continue to perform MSUS in the future, and that each speciality has specific advantages over the other in training in MSUS. The advantages of a rheumatologist performing MSUS are not discussed in the editorial, al-