Pharmacoeconomic considerations in the treatment of psoriatic arthritis

In recent years, we have witnessed remarkable advances in the therapeutic approach to patients with various rheumatic diseases. Perhaps most notable has been the introduction of biological agents, particularly inhibitors of the key pro-inflammatory cytokine tumour necrosis factor-α (TNF-α). Initially, TNF-inhibitors were tested in patients with refractory, severe, established rheumatoid arthritis (RA). Data from many trials conclusively proved that in addition to dramatically improving the signs and symptoms of the disease, TNF-inhibitor therapy also enhanced functional status and quality of life and attenuated the progression of radiographic joint damage [1]. The remarkable success achieved by these agents has ‘raised the bar’ for the goals of therapy for RA. Currently, debate surrounds how best to define disease remission; until recently, such a goal was much more hypothetical than tangible. Following upon their success in refractory RA, TNF-inhibitors have been studied and proven to be highly effective in patients with early RA as well as in those with a variety of other autoimmune conditions, most notably psoriatic arthritis (PsA), ankylosing spondylitis and psoriasis. In PsA, treatment with TNF-inhibitors has been shown to attain the same breadth of positive outcomes as previously observed in RA. Thus, patients experience prominent reduction in the signs and symptoms of peripheral arthritis, important improvement in functional status and quality of life and near complete attenuation of the progression of radiographic joint damage [2]. Moreover, treatment has resulted in important improvements in clinical manifestations highly characteristic of PsA, including skin psoriasis, enthesitis and dactylitis [3].

The tremendous excitement regarding the clinical efficacy of novel biological therapies has been somewhat tempered by cost considerations [4]. Because the acquisition costs of TNF-inhibitors far exceed those of traditional therapies including the so-called disease-modifying antirheumatic drugs (DMARDs) such as methotrexate, their use in the clinic has almost certainly been less than it would have been if these costs were lower. In addition, there has been a growing interest in pharmacoeconomic analyses of newer antirheumatic therapies in order to help estimate their ‘value.’ In the setting of escalating healthcare expenditures around the globe, such assessments are certainly germane. Indeed, pharmacoeconomic analyses are an integral part of the licensing of new therapies in a number of countries, including the UK, Canada and Australia. In order to be useful, pharmacoeconomic analyses must employ a comprehensive approach. They need to consider not only the acquisition cost of the medications themselves but also the direct and indirect costs of the disease being treated. There is an abundance of data clearly showing that RA is a serious, progressive condition that can be associated with tremendous morbidity and functional disability [5]. A key correlate of functional disability is work disability. Thus, uncontrolled RA is expensive, with costs that vary directly with the severity and activity of disease [6]. A key implication of this data is that a therapy that was highly effective in improving clinical status, albeit at a relatively high cost, might still have an incremental cost-effectiveness within the range of generally accepted medical interventions. In RA, a number of analyses of the cost-efficacy of TNF-inhibitors have been conducted. Interestingly, independent assessments of the three available agents (etanercept, infliximab and adalimumab) have arrived at very similar estimates of the cost-efficacy of these agents in RA; that is, approximately US $30 000 per quality adjusted life year (QALY) gained as a result of the treatment [7]. Because of the chronic nature of the disease, the potential subjectivity of some of the outcome assessments and other factors, these analyses are not without their critics [8]. Nevertheless, it is crucial that pharmacoeconomic assessments be performed in rheumatology as in all areas of medicine. Additional studies, for example those looking at alterations in the work status of RA patients related to specific therapeutic approaches, have been performed, and will help define the potential justification for the use of newer agents in RA patients [9, 10].

As the use of novel therapies expands to other rheumatic conditions, even those with semblance to RA, it is critical that specific pharmacoeconomic analyses be performed in each distinct condition. Bansback and colleagues [11] report the results of their pharmacoeconomic analysis of the TNF-inhibitor etanercept in PsA. The authors utilized a measure of functional status, the HAQ score, and modelled changes in HAQ for a cohort of patients over time using data from published interventional studies. The correlation between HAQ and utility was assessed specifically in a group of PsA patients. Functional status was transformed into utilities for the various transition states that defined the level of response to treatment in terms of QALYs gained and cost-effectiveness estimated. The authors populated their analysis assuming patients had failed treatment with two individual DMARDs (methotrexate and sulfasalazine) before entering the analysis, in keeping with guidelines developed by the British Society of Rheumatology for the use of TNF-inhibitors in PsA. Over 10yr of treatment, as compared with treatment with combination methotrexate and ciclosporin or leflunomide, the authors found a cost of approximately £30 000 per QALY gained for using the TNF-inhibitor etanercept. This pharmacoeconomic analysis has a number of strengths. The authors chose a time horizon of reasonable length, given the chronic nature of the disease. Wherever possible, actual data from clinical trials were used, supplemented by observational data from a local cohort of patients. The assumptions made appeared to be conservative, and sensitivity analyses were appropriately performed. Limitations to the analysis largely arise from a paucity of relevant long-term data that is PsA specific. While this analysis focused on a single drug, the authors are appropriately even-handed as regards the presumed implications of this analysis for other macromolecule TNF-inhibitors. Because many pharmacoeconomic analyses are supported by the companies that produce the drugs being assessed, methodological transparency and a lack of bias are crucial.

Certainly, regarding peripheral arthritis, PsA has similarities to RA. It may be appropriate to consider issues in pharmacoeconomic analyses for PsA that have emerged from assessments...
in RA. For example, it has relatively recently become appreciated that the extent of radiological progression in PsA may be comparable with that of RA [12]. Progressive radiographic damage does correlate with functional disability, and costs related to such damage will have been at least partly accounted for in pharmacoeconomic assessments based on functional status. However, joint damage itself may require expensive orthopaedic interventions. If highly effective therapies such as the TNF-inhibitors attenuate the progression of joint damage to such an extent that they obviate the need for such procedures, this should favourably impact their cost-efficacy. Similar considerations arise for indirect costs. When the indirect costs saved by effective therapy are separately added to assessments of TNF-inhibitors, their cost per QALY improves significantly [7]. However, because function itself closely correlates with work status, this could be considered ‘double dipping’. Failure costs, or the costs of treatments other than those being measured that are necessary to control disease, are infrequently included in pharmacoeconomic studies. In RA, patients effectively treated with TNF-inhibitors might reduce or eliminate their use of non-steroidal anti-inflammatory drugs (NSAIDs), analgesics and prednisolone. While the acquisition costs of such drugs may not be a large total cost, in combination with the costs to diagnose and treat the adverse effects potentially associated with their chronic use, can be considerable [13]. Perhaps most important, in RA the costs of disease are skewed, with the greatest costs being generated by those patients with the most severe, active disease [6, 14, 15]. Therefore, if effective therapies are focused on such patients, and therapy is continued only for those in whom it induces significant improvement, then the cost-effectiveness of this treatment would actually be greater than that estimated from assessments of groups of patients who had more heterogeneous disease activity and responses to treatment. This would presumably be the case in PsA as well.

PsA does have important distinctions from RA that bear upon pharmacoeconomic considerations. Thus, in addition to peripheral arthritis, patients can have clinically important involvement in their entheses and tendon sheaths, their skin and in their axial skeleton. While enthesitis, dactylitis and spinal arthritis may be captured to some extent from an economic standpoint using the HAQ, this has not been fully delineated. Similarly, important changes in skin psoriasis may not be adequately reflected in changes in the HAQ. Therefore, therapies such as the TNF-inhibitors that are very effective at improving these other prominent manifestations of PsA may have a more favourable cost-efficacy than that achieved by analyses focused on peripheral arthritis. Compared with RA patients, those with PsA tend to be younger and more often male. Therefore, patients are more likely to be in their prime working years, which has implications for those pharmacoeconomic assessments using the human capital approach. Finally, it might be argued that there is an even greater unmet need for the newer therapies in PsA patients than is there in RA, particularly if dermatological and spinal involvement are taken into account.

So what are the implications of the results of the assessment reported elsewhere in this journal; does treatment with a TNF-inhibitor provide ‘value’ in the treatment of PsA? The answer is a definite ‘perhaps’, as such discussions inevitably evolve from scientific towards political considerations. Certainly, physicians empathize with their patients and wish that newer therapies might be less expensive. In the case of the TNF-inhibitors, the anticipated introduction of additional agents combined with the impact of market forces may indeed help lower their costs. However, even at current cost levels, a number of widely accepted and widely utilized medical interventions have costs per QALY that exceed what was reported by Bansback and colleagues [11] for TNF-inhibitor therapy in PsA [4]. To believe that this would then imply that the use of TNF-inhibitors in PsA is therefore guaranteed requires a level of political and bureaucratic naivities few clinicians possess. Rather, it highlights the necessity for healthcare providers to become advocates for their patients with rheumatic diseases, so that highly effective therapies might be appropriately utilized for our patients. For this, it will be crucial to have cost-effectiveness and other economic analyses performed specifically in the conditions for which newer therapies are being considered [16–18].

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