Evidence for treating rheumatoid arthritis to target: results of a systematic literature search update

We read with interest a recent paper by Stoffer et al on treat to target (T2T) evidence for rheumatoid arthritis (RA) published in the current issue of the journal.

The systematic literature review provided newer evidence by building on the existing 2010 T2T recommendations for RA. Based on this paper, the 2014 recommendation update was also published in the same issue. We congratulate the authors for performing thorough evidence summary. However, we would like to share a few concerns pertaining to the present paper.

The authors comment in their results section regarding the cost-effectiveness of the T2T strategy depending on a paper by Vermeer et al.

Methotrexate monotherapy, when applied to patients with RA naïve to combination synthetic disease modifying anti rheumatic therapy (csDMARD), affords a disease activity score (DAS28)-based remission in 20%–25% patients with similar results for most biological therapies except for rituximab (inhibition of joint damage and improved clinical outcomes with rituximab plus methotrexate in early active rheumatoid arthritis (IMAGE) trial). On the other hand, ACR20 and 50 responses are much better (around 60% and 50%, respectively) with methotrexate alone and again similar to biological monotherapy in the same group. The picture is strikingly different for DMARD inadequate responders (DMARDIR) or for biological failure failures. When we talk about T2T for RA, the scenario of early and prolonged introduction of biological agents in a significant proportion of patients is inevitable.

In the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry, as quoted by the authors, a step-up strategy from initial methotrexate monotherapy to csDMARD to anti-tumour necrosis factor (TNF) therapy (TNFi) was compared against usual care with DAS-based T2T, which demonstrated incremental cost-effectiveness ratio (ICER) of €3591 per patient in remission. From individual subcomponents, it is clear (table 3 of the said article) that TNFi bear the highest burden of cost.

In contrast, a recent systematic review reported that, in DMARD-naïve population, ICERs of TNFi in comparison with csDMARDs ranged from €39 000–€1 273 000/quality adjusted life year (QALY) with infliximab having the highest ICER; going up to 12 000–708 000 for TNFi in DMARDIR; abatacept and tocilizumab had rather low ICER of approximately €40 000 and €20 000/QALY, respectively; and in TNFi inadequate responders, rituximab was associated with the lowest ICERS ranging from €26 000–€48 000/QALY.

Willingness to pay (WTP) is an important consideration in measuring cost-effectiveness. Herein lies the difficulties faced in India and likewise other low-middle-income countries. Even in the Western world, there is no consensus on WTP question; the National Institute for Health and Care Excellence published a threshold of €24 000–€35 000/QALY in UK. With this threshold, biological therapies fail cost-effectiveness measures in DMARD naïve. In DMARDIR population, TNFi fail cost-effectiveness measures. Rituximab is the only notable consistent exception.

Is this WTP threshold practicable at all in the Indian scenario, in particular and Southeast Asia in general? There are no WTP guidelines in vogue in India and if we consider the WHO recommendation of cost-effectiveness for low-middle-income countries, at 3X gross domestic product (GDP) per capita, WTP comes to €4333.20. The difference in WTP capacity is overwhelming. Therefore, we believe that the claim of cost-effectiveness of T2T strategy, in a significant proportion brought about by biological therapy, is only partially true and may fall flat in the context of low/middle-income countries.

Government agencies and large international umbrella bodies need to play more proactive role. Intuitively, the cheapest effective biological therapy made available by national governmental functions can really be the long-term viable solution, given that the public health implication of RA is far from negligible. A similar advancement was made between the Government of India and Gilead Pharmaceuticals, Foster City, CA, USA mediated through the WHO for preferential pricing and cost reduction for AmBisome for the treatment of Indian patients with visceral leishmaniasis.

Time is ripe for the international bodies such as American College of Rheumatology (ACR) or European League Against Rheumatism (EULAR) to incorporate the issues of cost-effectiveness in just light and consider seriously the advocacy of incorporation of strategic management plan for RA in the national guidelines.

Rudra Prosad Goswami, Kaushik Basu, Shyamashis Das, Sumantro Mondal, Parasar Ghosh, Akalendu Ghosh
Department of Rheumatology, Institute of Post Graduate Medical Education and Research, Kolkata, India.

Correspondence to Dr Rudra Prosad Goswami, Abhyudoy Housing, Flat 18/14, ECIP, Ph IV, Type B, EM Bypass, Kolkata 700107, West Bengal, India; rudra.goswami@gmail.com

Competing interests None declared.

Provenance and peer review Not commissioned; internally peer reviewed.

Received 28 December 2015
Revised 6 March 2016
Accepted 7 March 2016
Published Online First 29 March 2016

http://dx.doi.org/10.1136/annrheumdis-2015-209094


REFERENCES