APPLICATION TO EULAR STANDING COMMITTEE FOR CLINICAL AFFAIRS (ESCCA)

EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS WITH SYNTHETIC AND BIOLOGICAL DISEASE MODIFYING ANTIRHEUMATIC DRUGS

Project leaders:
Josef Smolen (Convenor), Robert Landewé (Epidemiologist).

Background
Treatment of rheumatoid arthritis (RA) has changed dramatically during the past dozen of years. New DMARDs, synthetic and biological, have emerged and are widely used today, and others will become available in the near future. In addition, and consequently, treatment strategies have changed during this time, first by requesting early referral and early institution of DMARDs, and ultimately by showing that tight control using disease activity measures and appropriate switch of treatment are highly efficacious. In addition, both the usefulness of synthetic DMARDs as well as the high efficacy of biological DMARDs, particularly TNF-inhibitors, in combination with synthetic DMARDs, especially MTX, have become fully substantiated by a multitude of clinical trials. Likewise, the role of glucocorticoids has been revisited and they have been shown to have DMARD-like activity, in particular when combined with synthetic DMARDs and at intermediate dose, while the issue of the potential superiority of combination therapy comprising only synthetic DMARDs compared to switching DMARDs requires further clarification in light of ambiguous data.

Recently, the American College of Rheumatology (ACR) has published management recommendation for RA, which may raise the impression that additional recommendations may be redundant. However, there are several reasons in support of providing EULAR recommendations, aside from the fact that most work pertaining to novel treatment strategies, disease activity assessment and new therapeutic approaches has emanated from the EULAR region. With respect to drug therapy,
important aspects are missing or overstated: (1) there is no recommendation regarding glucocorticoids in the ACR document; (2) the question of combination therapy of non-biologic DMARDs is not dealt with critically; and (3) a drug like minocycline (finding its basis in the US, but not used for RA in Europe) is positively recommended, while for example a drug like cyclosporine is not judged; and (4) switching of biologicals, particularly switching of TNF-inhibitors which is a hot topic in Europe, is not addressed at all.

With respect to follow-up of patients in clinical practice, the ACR recommendations do not make any specific suggestion regarding the optimal interval between visits. Other suggestions may be seen differently in Europe when compared to the US. Further, new biological agents may become available in the course of the preparation of these recommendations, such as tocilizumab, certolizumab and golimumab, which can be dealt with in the EULAR recommendations. Finally, it is in the core interest of EULAR and in accordance with the EULAR 2012 objectives to improve the access to care of RA patients in Europe, to provide our constituency with criteria they can act with when dealing with their governments and social security organizations, and to present ourselves as the leading organization also in this area to the EU officials.

Thus, we propose to convene a group of experienced clinicians, methodologists and patients to develop EULAR recommendations on the management of RA.

Objectives
To produce evidence-based recommendations for the management of rheumatoid arthritis with synthetic and biological DMARDs on the basis of the EULAR standard operating procedures\textsuperscript{10}.

Proposed structure
This activity will be one of the largest done hitherto by EULAR given the need to search the literature for respective evidence of nonbiologic DMARDs, biologic DMARDs and therapeutic strategies. Therefore, and in order to be inclusive, the group involved may have to be larger than usually planned for.
**Steering group**

It may be worthwhile to implement a steering group. In addition to the convenor and the epidemiologist (JS, RL), this group could consist of Ferdinand Breedveld, Maxime Dougados, Paul Emery, Pam Richards

**Panel**

Beyond the persons mentioned under steering group, the following members are suggested:

Europe: Hans Bijlsma, Gerd Burmester, Sandra Canadelo, Ernest Choy, Karel Pavelka, Jozef Rovensky, A. Filipowicz-Sosnowska, Iain McInnes, Désirée van der Heijde, Deborah Symmons, Loreto Carmona, Guido Valsecini, Juan Gomez-Reino, Emilio Martin-Mola, René Westhoven, Ronald van Vollenhoven, Alan Tyndall, Bernard Combe, Daniel Aletaha, Piet van Riel, Angela Zink, Tuulikki Sokka, Maurizio Cutolo, Cem Gabay, Tom Huizinga, Maarten DeWit, Laure Gossec, Tore Kvien, and possibly other-

From North America: Joan Bathon, Kevin Winthrop, Jeff Siegel

**Target audience**

The target audience for the recommendations are European Rheumatologists, but in addition stakeholders like European governments and social security organizations. It is hoped that this will lead to an increased knowledge and improvement of standard of care. We may consider a separate discussion about the “standard of care” in the treatment of RA, and dedicate an entire chapter to it in the report.

**Evidence-Based Structure and Methods**

At an initial meeting of the steering committee for the discussion of a systematic literature review (1962–present), the terms and definitions that are pertinent to the task will be determined and then sent to the Task Force members. The terms will then be discussed at a first task Force meeting in Zurich, together with the objectives of the endeavour, and a consensus on the appropriate glossary of terms and definitions based on the majority view of the Task Force will be obtained.
The subsequent comprehensive literature review will have to involve 2-3 fellows with specified timelines. For each of the items, the strength of evidence will be determined.

At a second meeting in Zurich, the results of the literature search will be discussed and the recommendations determined by Delphi technique and the strength of their evidence indicated.

A first draft of the Recommendations (containing Introduction, Methods and Results) will be circulated to Task Force members thereafter and a third meeting in Zurich will be held to discuss and finalise the final wording of each recommendation.

**Presentation of recommendations**

The recommendations will be presented separately for synthetic DMARDs including glucocorticoids and combination therapy, biological DMARDs and therapeutic strategies. Hopefully, the task force can also agree on an algorithm for the management of RA.

**Dissemination of the Recommendations**

The final document will be submitted for publication to the Annals of the Rheumatic Diseases as a main manuscript. It is conceivable that each of the fellows will additionally present the results of her/his search in separate manuscripts to be published in the EULAR Journal.

The recommendations should also be presented at the EULAR Congress in 2010 and subsequently at national meetings by members of the Task Force.

**Implementation of the recommendations**

The recommendations will be available at the EULAR website and sent to the national European societies for potential local implementation as standard of care. Their fulfilment can then be tested either by the national societies or by ESSCA.
Update
Depending on new insights and new therapeutic agents, the recommendations will need to be updated. It is assumed that this may be necessary every 2-5 years after their first implementation.

Financial aspects of the project
Three one day meetings in Zurich will be required, as outlined above. In addition, it would be helpful to have 3 North American participants to widen the scope of information and visibility.

The first meeting will be in February 2009, the second meeting in September 2009 and the third meeting in November/December 2009.

The costs of these meetings and of the fellows will need to be covered by EULAR, It is estimated that these costs will amount to € 80.000

It is planned to finalize the recommendations by March 2010, in time for presentation at the EULAR Congress in June 2010.

Reference List


