Introduction

Is It Time for a European Consensus on the Pharmacological Management of Early RA?

The past decade has greatly enhanced our understanding of rheumatoid arthritis (RA). Not only have new drug therapies become available, but this period has witnessed dramatic changes in treatment strategies as well. Evidence has shown the irreversible joint damage in RA occurs early in the disease, making a "wait and see" approach unacceptable. Thus, it appears logical to begin treatment as soon as a diagnosis of RA is confirmed, to take advantage of the "window of opportunity" to slow disease progression by treatment with disease modifying antirheumatic drugs (DMARD).

With the recommendation to initiate DMARD therapy early in the disease, it behooves us to review the clinical evidence that supports this rationale. It is assumed that what is observed with DMARD therapy in the established phase of RA will also be apparent when administered in "early" RA. Does the published literature support this assumption? Is DMARD monotherapy preferable to combination therapy in early RA? Where do corticosteroids play a role? How do the newer biologic agents fit in the armamentarium?

With the objective of the development of a consensus statement, a panel of rheumatologists convened and reviewed the available clinical publications addressing the pharmacological treatment of early RA.

Each participant was assigned a specific topic, and the peer review literature of the past 10 years was reviewed to support or challenge a draft consensus statement. Given that the treatment approach for a significant portion of this decade has been for patients not to receive a DMARD until it was "necessary," sometimes several years after onset of the disease, many trials included DMARD naïve patients, but not necessarily patients with early RA.

Our panel convened in Paris, during April of 2001, for a roundtable discussion of the draft consensus statements with regard to the pharmacological treatment of early RA and supporting evidence. The revised consensus statement and supporting evidence from the studies were presented in a satellite symposium in Prague during EULAR 2001, where the symposium attendees had the opportunity to vote as to their level of agreement with each statement. It is hoped that the clinical application of the principles set forth in this consensus statement will lead to better outcomes for patients with RA.

CONSENSUS STATEMENT OF THE PHARMACOLOGICAL MANAGEMENT OF EARLY RA

1. Early referral to a rheumatologist or a specialist experienced in treating RA is critical for diagnosis, assessment of disease status, and initiation of appropriate pharmacological therapy. Pharmacological therapy and longterm followup by rheumatologists should enhance patient outcomes.
2. The goal of treatment is rapid and sustained suppression of inflammation. When inflammation is not suppressed, damage is the inevitable consequence. Frequent sensitive assessment of outcome is required for optimal management of early RA.
3. It is recommended to initiate pharmacological treatment with an effective DMARD early in the course of the disease. The onset of action and profile of side effects differs between drugs. The availability of many effective DMARD has increased the importance for consideration of each drug's side effect profile and the tradeoff between efficacy and toxicity. Most published evidence suggests that the best outcome in early RA is obtained with sulfasalazine or methotrexate.
4. The benefit of combination therapy as the initial pharmacological intervention from the onset in early RA (excepting the selective use of steroids) has not been clinically proven in controlled trials. On the basis of available clinical evidence, step-up therapy is the strategy of choice in early RA.
5. The use of corticosteroids in early RA remains controversial. There is no evidence from clinical trials that the use of steroids in early RA will change disease activity or function, although there is some evidence that radiological progression may be retarded.
6. Sulfasalazine, because of its low potential for teratogenicity, is the drug of choice in women of childbearing years.
7. In patients who do not achieve an optimal response with initial therapy, an addition of another DMARD or biological agent may be indicated for optimal management of their disease.
8. Costs of newer agents and their longterm side effects profile will need to be balanced with therapeutic benefits.

This supplement reviews the evidence supporting these statements. The importance of early intervention with one or more DMARD that are effective yet well tolerated cannot be over-emphasized. Uncontrolled inflammation, even early in the disease, leaves an indelible mark and sets the stage for more rapid disease progression and poorer patient outcome. As results from ongoing trials with early RA become available, additional evidence will support or modify these

recommendations, e.g., the followup from the COBRA trial[1] suggests that the intensive combination treatment arm maintains the differential compared to the monotherapy arm.

No doubt the role of the biologic agents will become better defined as their longterm side effect profile is documented in followup studies. How these drugs will revise the current treatment protocol remains to be determined. While many issues remain controversial, there is one area of unanimous agreement — we are part of the most exciting era of rheumatology.

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REFERENCE

1. Landewe RB, Boers M, Verhoeven AC, et al. COBRA combination therapy in patients with early rheumatoid arthritis: long-term structural benefits of a brief intervention. Arthritis Rheum 2002;46:347-56.