Role of adalimumab in the treatment of early rheumatoid arthritis

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ABSTRACT

Adalimumab, a recent addition to the therapeutic armamentarium in rheumatoid arthritis (RA), has been evaluated in patients with early RA. The DE019 study, a double blind randomized placebo controlled trial of adalimumab given 20 mg once a week or 40 mg every other week demonstrated both clinical and radiographic efficacy. A subset analysis of patients with early disease revealed that early treatment with adalimumab may be more efficacious than therapy later in the course of disease, particularly with regard to radiographic progression. The findings support early aggressive intervention in RA.

Introduction

As outlined in previous chapters, accumulated data supports the use of aggressive therapy early in the course of RA. A recent addition to the therapeutic armamentarium in RA, adalimumab (Humira®), has also been evaluated in patients with early RA.

Adalimumab is a fully human IgG1 monoclonal antibody with high specificity for TNF. In late DMARD-refractory disease adalimumab has been demonstrated to induce substantial improvement in signs and symptoms of disease with significant inhibition of progression of joint damage when used alone or in combination with MTX (1-5).

Materials and methods

In the DE019 adalimumab study, adalimumab given subcutaneously in a dose of 20 mg once a week or 40 mg every other week in combination with MTX was evaluated in a 52-week, double blind, randomized, placebo (MTX alone) controlled trial in combination with methotrexate in 618 patients with an inadequate response to methotrexate (6). Inclusion criteria included age 18 years or older and a diagnosis of RA according to the ACR criteria. Patients had to have 6 swollen and 9 tender joints as well as a CRP > 1 mg/dl. They had to have been on MTX for 3 months, and taking a stable dose of 12.5 mg to 25 mg/day for 4 weeks prior to baseline. They had to be rheumatoid factor positive or have at least 1 joint erosion on radiographs of the hands and feet. If patients were receiving prednisone their dose had to be stable for 4 weeks prior to baseline.

Results

Analysis of baseline characteristics of the patient population revealed that patients had severe disease on study entry. Recently, a subset analysis of the clinical and radiographic response to adalimumab in the DE019 study was carried out in patients with early (< 2 years duration) and late disease (> 2 years duration) (7). Seventy-four of the 618 patients enrolling in the DE019 study had early disease (55 receiving adalimumab and 19 receiving placebo) while for patients with late disease, 363 received adalimumab and 181 received placebo. When given in a dose of 40 mg every other week adalimumab resulted in ACR 20, 50 and 70 responses of 70%, 59%, and 41% respectively in patients with early RA compared to patients with late disease, i.e. 62%, 36%, and 18%, respectively. HAQ improved by 0.79 units in patients with early RA compared with 0.57 units in patients with late disease. Twenty-five percent of patients with early disease had no tender joints while 38% had a zero HAQ compared to 9% and 15% respectively for patients with late disease. For both early and late disease patients receiving adalimumab in combination with MTX, mean changes from baseline in the erosion score, joint space narrowing and the modified total Sharp x-ray score were comparable and less than for those receiving MTX alone. The results suggest that early treatment with adalimumab may be
more efficacious than therapy later in the course of disease. A study is currently in progress to investigate the initiation of combination adalimumab and MTX versus monotherapy with adalimumab or MTX in early RA.

Conclusion
In summary, evidence has been presented that therapy in RA with adalimumab may be more beneficial in patients with early disease. This data supports the findings from other studies that early aggressive intervention in RA affords the opportunity for better outcomes.

References
6. KEYSTONE EC, KAVANAUGH A, SHARP J et al.: Adalimumab (D2E7), a fully human anti-TNFα monoclonal antibody inhibits the progression of structural joint damage in patients with active RA despite concomitant methotrexate therapy. *Arthritis Rheum* 2002; 9; 205.