

MabThera® (rituximab) in rheumatoid arthritis

Introduction

Early treatment with biologic therapy in rheumatoid arthritis (RA) is critical to achieve minimum disease progression and remission, the ultimate treatment goal in this currently incurable disease. However, disease progression and response to treatment vary greatly between patients. At least one-third of RA patients do not respond to tumour necrosis factor (TNF) inhibitor therapy, owing to inadequate efficacy, intolerance or compliance problems.¹ In addition, 69-88 percent of RA patients fail to achieve remission after one year of treatment with TNF inhibitor agents.^{2,3}

MabThera (rituximab) represents a proven treatment option for patients who experience inadequate response or intolerance to TNF inhibitor therapy.⁴ MabThera is a selective B cell targeted therapy which interferes with the inflammatory cascade of RA, inhibiting the series of reactions that lead to synovial inflammation, cartilage loss, bone erosion and joint damage.⁵ MabThera may work when TNF inhibitors do not as it is a completely different class of treatment, targeting a different part of the inflammatory cascade.

B cell vs anti-TNF cycling

For those patients who do not respond to initial TNF inhibitor therapy, MabThera offers a superior clinical response over a second TNF inhibitor.⁶ A recent head-to-head study investigating the efficacy of MabThera compared with cycling between TNF inhibitors in patients who have not responded to at least one TNF inhibitor therapy suggests that using MabThera is a more effective strategy to control disease activity than using an alternative TNF inhibitor.⁶ These findings are further supported by data showing MabThera offers significant improvements in DAS28* scores compared with alternative TNF inhibitor therapy.⁷

Inhibition of Joint Damage

RA patients begin to suffer progressive, permanent joint damage early on in their disease, long before the onset of visible changes, such as joint deformity and disability. Within the first two years, up to 70% of people with RA have radiographic evidence of joint damage.⁸ The ability to slow disease progression and prevent joint damage is a major treatment goal. In patients who have experienced an inadequate response or intolerance to treatment with one or more TNF inhibitors⁹, MabThera is the only biologic proven to suppress RA radiographic progression.

In the REFLEX (Randomised Evaluation of Long-term Efficacy of rituXimab in rheumatoid arthritis) study, joint damage progression was delayed after only one

* Disease Activity Score

course of MabThera.⁹ X-ray evidence at 56 weeks showed that the progression of bone erosions and narrowing of joint spaces in patients treated with MabThera were reduced by more than 50 % compared to patients receiving methotrexate alone.⁹

Continued analysis of this data showed that this treatment effect was maintained over two years in patients who had not responded to previous treatment with TNF inhibitors.¹⁰

Response rates and repeat treatment

Administered as just two 1000mg infusions two weeks apart, MabThera is unique among RA therapies offering patients an unprecedented duration of response of at least six months with each treatment course. It has also been shown to maintain or improve response with each repeat course of treatment, with more patients reaching DAS28 low disease activity and remission criteria with each further course of treatment.¹¹

However, timely repeat treatment before a patient's disease activity flares is important to maximise treatment response. Findings from a recent study show that systematic monitoring of DAS28 scores can optimise repeat treatment timing with MabThera. This strategy offers an opportunity to further reduce disease activity with a second course of treatment.⁶

Improvements in health-related quality of life

Patients' measures of success such as improvements of daily function or quality of life have played an increasingly important role in evaluating treatment efficacy.¹² Recently published study data from the REFLEX study show that MabThera provides significant improvements and sustained effects on nearly every tested measure of health related quality of life, symptoms, and function, both mental and physical. Consequently, MabThera meaningfully improves patients' perceptions of their disease, offering them greater freedom and an improved quality of life.¹³

For more information and images of MabThera, B cell therapy and RA, please visit www.mabthera-ra.com

References:

- ¹ Lawrence RC, Helmick CG *et al.* Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum* 1998;41:778-99
- ² Remicade ASPIRE St.Clair *et al.* *Arthritis Rheum* 2004;50:3432-3443
- ³ Enbrel TEMPO van der Heijde *et al.* *Ann Rheum Dis* 2005; 64:1582-7
- ⁴ Cohen SB, Emery P *et al.* Rituximab for rheumatoid arthritis refractory to anti-tumor necrosis factor therapy. *Arthritis Rheum* 2006;54:2793-806
- ⁵ Panayi GS. *Rheumatology* 2005; 44(Suppl 2): 3-7
- ⁶ Finckh A, Ciurea A, *et al.* B cell depletion may be more effective than switching to an alternative anti-tumor necrosis factor agent in rheumatoid arthritis patients with inadequate response to anti-tumor necrosis factor agents. *Arthritis Rheum* 2007;56:1417-23
- ⁷ A. Finckh, A. Ciurea, L. Brulhart *et al.* Which subgroup of RA patients benefit most from switching to rituximab versus alternative anti-TNF agents after previous failure to anti-TNF agent? Abstract # tbc, EULAR 2008
- ⁸ O'Dell JR. *N Engl J Med* 2004; 350: 2591-2602
- ⁹ Keystone E, *et al.* *Arthritis Rheum* 2006; 65(Suppl. II): 58
- ¹⁰ Stan Cohen, E. Keystone, M. Genovese *et al.* Continued Inhibition of Structural Damage in Rheumatoid Arthritis Patients Treated With Rituximab at 2 Years: REFLEX Study. Abstract THU0167, EULAR 2008
- ¹¹ Keystone E, Fleischmann R *et al.* Safety and efficacy of additional courses of rituximab in patients with active rheumatoid arthritis. *Arthritis Rheum* 2007;56:3896-908
- ¹² Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. *Ann Intern Med.* Jan 1 1994;120(1):26-34
- ¹³ E Keystone, GR Burmester, R Furie *et al.* Improvement in Patient-Reported Outcomes in the REFLEX Trial of Rituximab in Patients with Severe Rheumatoid Arthritis Refractory to Anti-Tumor Necrosis Factor Therapy. *Arthritis Care & Research* (in press)

