| PublisherInfo | | |
|---|---|---|
| PublisherName | : | BioMed Central |
| PublisherLocation | : | London |
| PublisherImprintName | : | BioMed Central |

# High dose chemotherapy followed by autologous stem cell transplantation in the treatment of patients with refractory RA

| ArticleInfo | | |
|---|---|---|
| ArticleID | : | 216 |
| ArticleDOI | : | 10.1186/ar-2000-66769 |
| ArticleCitationID | : | 66769 |
| ArticleSequenceNumber | : | 173 |
| ArticleCategory | : | Paper Report |
| ArticleFirstPage | : | 1 |
| ArticleLastPage | : | 3 |
| ArticleHistory | : | RegistrationDate : 2000–1–5<br>OnlineDate : 2000–1–5 |
| ArticleCopyright | : | Current Science Ltd2000 |
| ArticleGrants | : | |
| ArticleContext | : | 130753311 |

Robert Verburg,[Aff1]

Aff1 Leiden University, Netherlands

## Keywords

Autoimmune disease, cyclophosphamide, high dose chemotherapy, rheumatoid arthritis, stem cell transplantation

# Context

In recent years there has been much debate on whether high dose chemotherapy with stem cell rescue (autologous haematopoietic stem cell transplantation [ASCT]) is a potential treatment for refractory rheumatoid arthritis (RA). Intensive immunosuppressive therapy with stem cell rescue may be effective for the control of RA because the conditioning regimen may delete the relevant autoreactive lymphocyte population. Preclinical studies in rat models of autoimmune disease (polyarthritis) have demonstrated effective control of the disease process by syngeneic bone marrow transplantation (BMT) after a myeloablative preparative regimen. The reconstituting reinfused stem cells, potentially depleted of relevant autoreactive lymphocytes by T cell depletion, and the reconstituting lymphocyte population will hopefully acquire self tolerance. Several reports on patients treated with BMT for a haematological malignancy or severe aplastic anaemia and coincidental autoimmune disease support the favourable effect of BMT on autoimmune diseases. The results from the above mentioned studies have stimulated efforts to investigate the potential therapeutic effects of this treatment in RA. This study investigated the toxicity and preliminary efficacy of nonmanipulated ASCT after high dose cyclophosphamide treatment (100 mg/kg or 200 mg/kg) in eight patients with active treatment-resistant RA.

# Significant findings

Although initial positive responses were evident for both groups, 3-4 months post-therapy, recurrence of disease activity was apparent for all patients treated with 100 mg/kg. The highest dose (200 mg/kg) cyclophosphamide was effective in the control of refractory RA. One patient was in complete remission; the other three had a more than 50% reduction in tender and swollen joint count after one year. The procedure did not completely abolish disease activity. An interesting observation was that patients previously resistant to DMARDs responded well to conventional treatment when restarted.

# Comments

*This report is of particular interest because it shows not only the dose-dependent efficacy of ASCT but also that toxicity levels are acceptable and until now no patients with RA have died as a consequence of myelosuppressive therapy. However it is unlikely that RA patients are cured by this new treatment modality. Neither dose of cyclophosphamide appears to be myeloablative, but ASCT can be considered as a supportive measure in order to allow rapid recovery of haematopoiesis after intensive myelosuppression. It should be concluded that ASCT can potentially be a treatment for severe refractory RA but more extensive studies need to be conducted in order to answer the above questions.*

# Methods

Peripheral blood stem cell mobilisation was performed using filgrastim (G-CSF) with either 5 ?g/kg/day or 10 ?g/kg/day. Leukopheresis (stem cell collection) was performed on day 5 and subsequent days until the target of $2x10^6$ $CD34^+$

cells/kg was achieved. Disease-modifying antirheumatic drug(s) (DMARDs) were discontinued before treatment.

## References

1. Snowden JA, Biggs JC, Milliken S, Fuller AK, Brooks PM: A phase I/II dose escalation study of intensified cyclophosphamide and autologous blood stem cell rescue in severe, active rheumatoid arthritis. Arthritis Rheum. 2000, 42: 2286-2292.