Title :

Efficacy of low dose Rituximab with methotrexate compared to leflunomide with methotrexate in patients with refractory rheumatoid arthritis: A randomized double blind controlled clinical trial

ABSTRACT 250

Objectives

The efficacy of low dose rituximab/methotrexate combination in refractory rheumatoid arthritis(RA) is unknown. The objective was to compare the efficacy and safety of low-dose rituximab/methotrexate *vs* leflunomide/methotrexate combination in patients with refractory RA in a tertiary care setting in Sri Lanka,

Methods

A randomized, double blind clinical trial randomized patients with a DAS>3.26 to rituximab(500mg on days1 and 15) or leflunomide(10-20mg/day) added to methotrexate(10-20 mg/week). The primary end-point was 50% improvement of ACR50 at 24 weeks. Sample size of 40 had 70% power to detect a difference. The CD3+(T cell), CD19+(B cell) and CD19+CD27+(memory B cell) counts, IgG, IgM, tetanus and pneumococcal antibody levels were measured.

Results

Baseline characteristics were comparable in the two groups. At week 24, the ACR 50 was 60% in rituximab/methotrexate vs 64 % in leflunomide/methotrexate group; p 0.79(ns). ACR20 was 85%vs 84%(p=0.93) and ACR70 was 35%vs32% (P=0.84) respectively. Serious adverse events were similar in the two groups.

Rituximab group had significant reduction in B($p< 0.001$) and memory B cells(p=0.001) with no significant change in T cells(p=0.835), tetanus(p=0.424) and pneumococcal antibody levels(p=0.09) at 24 weeks. The leflunomide group showed no significant change in B(p=0.786) or T cells($p = 0.493$) or tetanus antibody levels(p=0.338) but had significant reduction in pneumococcal antibody levels($p= 0.002$) and B memory cells($p= 0.032$)

Conclusions

Low-dose rituximab/methotrexate combination is as efficacious as leflunomide/methotrexate in refractory RA.The high responses seen in both groups have favorable cost implications for patients in developing countries. The changes in immune parameters with leflunomide are novel and need further characterization.

(Clinical Trials registration number at www.slctr.lk : SLCTR/2008/008)