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# The dosage of infliximab in the treatment of ankylosing spondylitis: Dollars and sense

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## ABSTRACT

*While it seems clear that anti-TNF treatments do improve the clinical condition of patients with ankylosing spondylitis, there is some evidence that doses much smaller than those formally studied in controlled trials may also be very effective, and we would recommend that this aspect be pursued given the overall costs involved.*

It seems clear that TNF antagonists are effective, at least over a one-year term, in relieving signs and symptoms in patients with AS and other spondyloarthropathies (1, 2). They reduce laboratory and MRI correlates of inflammation, i.e. gadolinium uptake and marrow inflammation (3), but whether they have any effect on the longer term radiologic progression is currently unclear, and given the generally slow nature of this progression the question may never be answered. In the treatment of rheumatoid arthritis the dosage is now standardized, and although some patients have been reported to respond better, at least to Infliximab, in a higher dose, the initial dose normally is 3 mg/kg every 8 weeks (after a loading course). Indeed, the ATTRACT study (4) – the pivotal trial in rheumatoid arthritis patients with concomitant methotrexate – showed surprisingly little overall dose response, at least in terms of ACR 20 percent responders. The initial studies reported in spondyloarthropathies, in general, extrapolated the dosage used for the related inflammatory bowel disease, 5 mg/kg, and used it every 6 weeks. There is no doubt that this is effective (1), but our experience is that a much lower dose is also effective. The published open data from Edmonton show an impressive BASDAI response to a 3 mg/kg dose, generally rounded up to the nearest 100 mg (3). We have now treated with this regime 24 patients in Edmonton and 14

in Guadalajara, Mexico. The response of this group has been excellent. Indeed, it was our joint impression that the results in AS, assessed by overall responses, were even better than those seen in RA. It seems important to assess the dose formally as, given the cost implications quite apart from other issues, we should surely be using the lowest dose that is effective in controlling symptoms. A recent publication also suggests that in spondyloarthritis in general a lower dose of 5 mg/kg q 14 weeks may suffice (5).

In Edmonton we have 11 patients still receiving 3 mg/kg (6 at 200 and 5 at 300 mg per infusion), and 3 receiving 5 mg/kg, all q 8 weeks. In addition, 4 discontinued with adverse events (1 reactivation of osteomyelitis, 1 anaphylaxis, and 2 less severe infusion reactions), together with 4 for lack of efficacy. Two others moved and are now lost to follow up.

The Mexican group comprises 14 patients. All received 3 mg/kg, some were rounded down, 11 received 200 mg and 3 received 300 mg (mean weight 72.5 kg). Eleven patients have now had treatment discontinued with no return of disease over a mean of 12 weeks. None were discontinued because of side effects. In the whole group 17/25 have been successfully treated with 200 mg per infusion. For a 66 kg individual 3 mg/kg amounts to 200 mg. It appears that some rounding down is feasible with AS, and that 200 mg can be successfully used even for a 75 kg patient. For maintenance q 8 weeks, this dose requires 6 ampoules during a 6 month period, whereas using Class A evidence, i.e. placebo controlled clinical trials, a dose of 5 mg/kg q 6 weeks would have to be recommended for the 75 or even the 65 kg patient. This would require 16 ampoules, increasing the cost by some US\$ 12,000 approximately.

This therefore is a plea for further dose ranging studies so that we can possibly reduce the cost barriers of this very effective therapeutic approach.

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