INFLIXIMAB IN STEROID DEPENDENT CROHN'S DISEASE PATIENTS TREATED WITH AZATHIOPRINE OR 6-MERCAPTOPURINE: A RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL

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Aim. To evaluate the usefulness of infliximab combined with azathioprine (AZA) or 6-mercaptopurine (6MP) to achieve clinical remission without steroids in steroid-dependent Crohn's disease (CD) patients.
Methods. CD patients who had an active disease despite prednisone (>= 10 mg/d) given for more than 6 months were eligible for the trial. All the patients were treated with AZA (2-3 mg/kg/d) or 6MP (1-1.5 mg/kg/d); they were stratified as follows: stratum 1 (AZA failure), patients receiving AZA/6MP at a stable dose for at least 6 months and disease still active (CDAI > 150) at inclusion; stratum 2 (naive), patients not yet treated with AZA/6MP. In each stratum, patients were randomized per center to receive either 3 infusions of infliximab (5 mg/kg) at day 0, week 2 and week 6, or 3 infusions of placebo. During the 24 weeks of the study, if a clinical remission was achieved (CDAI less than 150), steroids were tapered according to a standardized scheme; in patients who experienced a relapse, the dose of steroids was increased until a new remission was achieved, and then tapered. The primary end-point was remission off steroids at week 24. Secondary end-points were remission without steroids at week 12, treatment failure due to steroid resistance, cumulative dose of steroids at week 24 and a side-effect steroid score.
Results. At the 22 centers participating to the trial, 115 patients (63F, age: 30+/-11 yrs) were randomized, 56 in AZA failure stratum and 59 in the naive stratum. Disease location was colon (36%), small bowel (14%) or both (50%); active perianal lesions were present in 22%. At inclusion, CDAI was 189+/-96 (mean+/-SD), median duration of steroid treatment was 15 months, and median dose of prednisone was 30 mg/d. In the stratum 1, median duration of AZA/6MP treatment was 24 months. Fifty-seven patients were allocated to infliximab and 58 to placebo infusions. The percentage of remission off steroids was higher in the infliximab group than in the placebo group at week 12 (75% vs 38%; P<0.001) and at week 24 (57% vs 29%; P=0.003). There was no significant difference in infliximab efficacy between the two strata (P>0.10). Treatment failure due to steroid resistance were also less common in the infliximab group (5% vs 23% for placebo, P=0.01). Cumulative dose of steroids was lower in the infliximab group (1489 ± 1458 vs 1826 ± 1605 mg, P= 0.002). Median side-effect steroid score was not different in the two groups at week 12 and week 24. Severe adverse events occurred in 5% and 7% of patients in the infliximab and placebo groups, respectively. Follow-up at 48 weeks will be available in September 2003.
Conclusion. Infliximab combined witrh AZA/6MP is more effective that AZA/6MP alone in steroid-dependent patients. This strategy may be effective even if AZA/6MP has previously failed to allow steroid withdrawal.

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