Switch to adalimumab in patients with Crohn's disease controlled by maintenance infliximab: prospective randomised SWITCH trial.

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Gut. 2012 Feb;61(2):229-34.

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Introduction

Infliximab (IFX) and adalimumab (ADA) are both effective in inducing and maintaining clinical and endoscopic remission in Crohn's disease (CD) (1). In the ACCENT 1 trial, patients who underwent IFX administration as maintenance therapy were more likely to sustain clinical remission until week 54 (28% and 38% for 5 mg/kg and 10 mg/kg) compared with placebo (14%, p=0.007 and <0.001) (2). In the CHARM trial a greater percentage of patients who received ADA (36% and 41% for administration every other week or weekly) were in clinical remission at week 56 compared with placebo (12%, p< 0.001) (3). Similar results emerged from the CLASSIC II trial, in which 79% (ADA administration every other week) and 83% (ADA administration weekly) of patients were in remission at week 56 compared with 44% of patients receiving placebo (p<0.05) (4). Switch to ADA has been evaluated in patients presenting with loss of response or intolerance to IFX. In this patient population ADA induced remission in 21% of patients compared with 7% in the placebo group (p<0.05), representing a valid alternative in case loss of response or intolerance to IFX occur (5). For practical and economical reasons, switch from intravenous (IFX) to subcutaneous (ADA) administration has entered clinical practice and is being frequently requested by patients, who usually prefer self-administration at home.

What is this paper about?

The SWITCH trial is an interesting open label randomized controlled single centre trial prospectively evaluating the impact of elective switching of patients with CD well controlled with intravenous IFX to subcutaneous ADA. CD patients with ongoing response to IFX in stable clinical remission (Crohn's Disease Activity Index, CDAI, <200) for at least 6 months were recruited. Seventy-three patients were randomized to continue IFX 5 mg/kg at the same interval than before randomization (37 patients) or to switch to ADA 80 mg at inclusion and 40 mg every other week (36 patients) for one year. Dose optimisation or short courses of steroids were allowed in case of disease flare. If complete loss of response or intolerance occurred, patients were allowed to cross over to the alternative treatment arm.

The study aimed to evaluate patients' preference for ADA over IFX as well as the proportion of patients requiring rescue therapy or discontinuation of therapy after switching.

As expected, throughout the study most patients preferred ADA over IFX considering different items such as efficacy, administration, side effects and daily activities. 17 patients in the ADA group (47%) required dose intensification or early termination because of loss of response or intolerance, compared with only 6 patients in the IFX group (16%, p=0.003).

ADA dose optimisation and return to IFX were successful strategies in most patients (8/10), who became intolerant or lost response to ADA. Cross-over to ADA was successful in the patients, who lost tolerance to IFX. All serious adverse events occurred in patients randomised to ADA and were related to complicated CD.

Conclusion

This study shows that approximately one third of patients who switched to ADA returned to IFX within one year. In case of intolerance or loss of response to ADA, return to IFX was a successful management strategy. ADA was less tolerated compared with IFX but this is probably due to the fact that only patients with a long maintained response (and tolerance) to IFX entered the study. In conclusion, switch to another anti-TNF agent should not be counselled for practical reasons alone, but only in case of loss of tolerance or response to the current anti-TNF agent. Given the small number of approved biological agents in CD, therapy optimisation still remains the best strategy.

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