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**“Reply to letter by Dr Oresland: Ulcerative colitis:  
failed tacrolimus – infliximab or surgery;”**

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**“Reply to letter by Dr Oresland: Ulcerative colitis: failed  
tacrolimus – infliximab or surgery?”**

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Oreslands surgical comments concerning our study as well as essentially all trials on pharmacological therapy in IBD are well taken. We agree that the current medical armamentarium suffers from the lack of long term solutions. We also share his concern that unremitting efforts with the sequential use of different immunosuppressives may render patients more susceptible to infections and increase perioperative risks if the proper timing of a surgical intervention is missed. The one out of four remission rate following infliximab upon tacrolimus failure is clearly unsatisfactory. Moreover, a significant fraction of the approximate quarter of patients responding to infliximab following tacrolimus failure may well have to be operated ultimately in the further course of disease. However, being physicians, we have to take into account patients preferences when discussing treatment options and in general patients' preference is to retain their colon until all other options have failed.

As a matter of fact, Oresland's view is the *ex post* view. The trial was undertaken to test the possibility that a substantial proportion of patients refractory to tacrolimus would benefit from a TNF-antibody. This sequence of treatments, if the clinical conditions allows, makes good sense since the half-life of tacrolimus is much shorter and, after stopping, the risk of a combined and likely additive immunosuppression would be minimized. This is different when applying infliximab with its long half-life first and ciclosporine second, resulting in severe infectious complications due to triple or quadruple immunosuppression (1). Unfortunately, *ex post* it appears that the tacrolimus refractory cohort is a negative selection and as a rule exhibits cross-refractoriness to anti TNF, although the mechanisms of action are quite different. Therefore we have emphasized in the final sentence of our report that "the risks and benefits (of immunosuppression) have to be weighed carefully against the risks and benefits of proctocolectomy" (2). Therefore, the trial was justified to help estimate the potential benefit versus risk of infliximab following tacrolimus and the benefit turned out to be limited.

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- 1) Maser EA, Deconda D, Lichtiger S, Ullman T, Present DH, Kornbluth A. Cyclosporine and infliximab as rescue therapy for each other in patients with steroid-refractory ulcerative colitis. *Clin Gastroenterol Hepatol*. 2008 Oct;6(10):1112-6
- 2) Herrlinger KR, Barthel DN, Schmidt KJ, Büning J, Barthel CS, Wehkamp J, Stange EF, Fellermann K. Infliximab as rescue medication for patients with severe ulcerative/indeterminate colitis refractory to tacrolimus. *Aliment Pharmacol Ther*. 2010 May;31(9):1036-41

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- 1) Oresland T. Ulcerative colitis: failed tacrolimus – infliximab or surgery? (letter) *Aliment Pharmacol Ther* 2010; in press.
- 2) Herrlinger KR, Barthel DN, Schmidt KJ, Büning J, Barthel CS, Wehkamp J, Stange EF, Fellermann K. Infliximab as rescue medication for patients with severe ulcerative/indeterminate colitis refractory to tacrolimus. *Aliment Pharmacol Ther.* 2010 May;31(9):1036-41
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