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Letter to the Editor

Long-term infliximab therapy is needed for sustained steroid-free remission in patients with ulcerative colitis

Florence Le Roy¹, MD, Laurent Siproudhis^{1,2}, MD-PhD, Jean-François Bretagne¹, MD-PhD, Guillaume Bouguen^{1,2}, MD-PhD

¹ Gastroenterology Unit, CHU Pontchaillou, University of Rennes 1, France

² INSERM U991, University of Rennes 1, France

³ Functional Digestive Disorders Unit, CHU Pontchaillou, University of Rennes 1, France

Correspondence to:

Guillaume Bouguen

Service des Maladies de l'Appareil Digestif

2 rue Henri le Guillou

35033 Rennes Cedex, FRANCE

Telephone (0033)-2-99-28-43-17 / Fax (0033)-2-99-28-41-89

Email: guillaume.bouguen@free.fr

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Dear Editor,

Data on the long-term efficacy of infliximab (IFX) in ulcerative colitis (UC) are scarce and there is limited evidence especially on sustained steroid-free remission and outcomes after IFX withdrawal. The ability of IFX to modify the course of the disease in the long-term, such as decreasing the need for surgery, remains questionable.¹ After 10 to 24 months of follow-up, retrospective studies report heterogeneous remission rates for UC between 17% and 90%.²⁻⁴ This wide range of remission may be due to the duration of IFX exposure, therefore affecting outcomes after IFX discontinuation. In small cohorts of 4 to 51 patients in remission, the rate of relapse following IFX discontinuation ranged from 0% to 59% after 6.5 months to 4.5 years of follow-up.^{2,5} This rate of relapse leads to difficult decision-making regarding maintenance therapy with IFX.

We reviewed the medical charts of 100 patients treated with IFX for UC in a single gastroenterology unit between 2005 and 2012. Clinical remission was defined as a partial Mayo score of 2 points or lower, without bleeding; response, by a decrease of 2 points; and relapse, by an increase of 2 points. Survival curves were estimated by the Kaplan–Meier method and compared using the log rank statistic. A Cox proportional hazards regression model was used to assess independent predictors of each event. Seventeen of the 100 patients were treated for acute, severe UC (refractory to intravenous steroids); 83, for steroid dependency or secondary to immunosuppressive therapy failure. In total, 52% of patients had concomitant immunosuppressive therapy at baseline.

After a median duration follow-up of 55.1 months (IQR, 35.2-74.4), 35% of patients underwent surgery (median time from IFX initiation: 9.4 months). CRP>6 mg/L at week 6 was the only independent factor associated with colectomy (HR=3.43, 95%CI, 1.17-10.9; p=0.023). Sixty-four patients (64%) reached clinical remission after a median time of 20 weeks following IFX initiation (IQR, 6.5-47), and 28/64 (44%) relapsed during follow-up. The cumulative probabilities of sustained clinical remission at 1, 3 and 5 years were 74, 52 and 39%, respectively. Based on standard clinical and biological parameters at IFX initiation and on the short-term outcomes, the independent factors associated with sustained clinical remission were: duration of IFX therapy >1 year (HR=2.61, 95%CI, 1.05-7.01; p=0.03), leukocyte count<10,000/mm³ (HR=2.18, 95%CI, 1.02-4.77; p=0.04) and platelet count<400,000/mm³ (HR=2.77, 95%CI, 1.18-6.46; p=0.02) at IFX initiation. Severe acute colitis at baseline did not influence long-term outcomes.

Finally, IFX was discontinued in 38/64 patients because of steroid-free clinical remission. After a median follow-up of 54 months (IQR, 25.4-64.5) following IFX withdrawal, 4/38 patients underwent colectomy (10%), 24 relapsed (63.2%), and 14 remained in clinical remission (36.8%). The cumulative probabilities of relapse after IFX discontinuation were 24%, 61% and 81% at 1, 3 and 5 years, respectively (Figure 1). Based on univariate and multivariate analyses, age<21 years at diagnosis (HR=12, 95%CI, 2.77-58.24; p=0.001) and a platelet count>400,000/mm³ at IFX withdrawal (HR=6.68, 95%CI 1.55-30.82; p=0.011) were associated with relapse. Continuous use of thiopurines following IFX withdrawal did not modify patient outcome and was not

associated with sustained clinical remission ($p=0.29$) or relapse ($p=0.61$) or with disease extent and disease severity at baseline.

In conclusion, after a 5-year follow-up IFX discontinuation in UC patients led to a high rate of relapse and was inversely associated with sustained remission. In our series, one-third of patients underwent colectomy, one-third relapsed and only one-third experienced a sustained clinical remission. These results support the use of long-term IFX maintenance therapy in these patients.

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Figure Legend

Figure 1: Cumulative probabilities of relapse after infliximab discontinuation in ulcerative colitis patients in steroid-free clinical remission.

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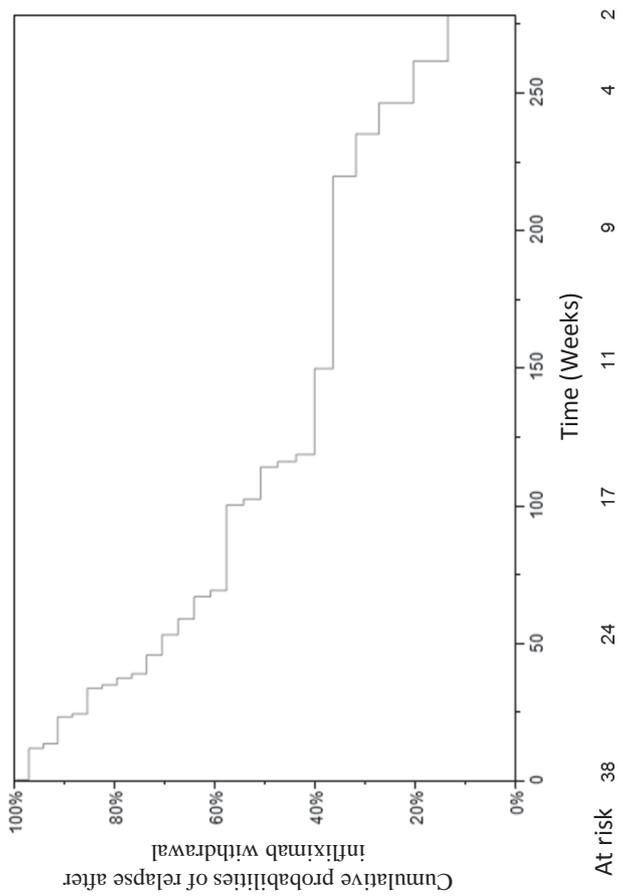


Fig. 1