Association of Trough Serum Infliximab to Clinical Outcome After Scheduled Maintenance Treatment for Crohn’s Disease

ELANA A. MASER, RENATA VILLELA, MARK S. SILVERBERG, and GORDON R. GREENBERG
Division of Gastroenterology, Mount Sinai Hospital, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

Background & Aims: The effect of infliximab infused at scheduled intervals on antibody formation, preinfusion trough serum concentrations of infliximab, and their clinical significance was evaluated in patients with Crohn’s disease.

Methods: Antibodies to infliximab and trough serum infliximab were measured in 105 patients with Crohn’s disease treated with 5 mg/kg infliximab for induction followed by maintenance episodic re-treatment (n = 23) or scheduled therapy at 6- to 8-week intervals (n = 82).

Results: After a median of 14 infusions (range, 2–45), 21% of patients had detectable antibodies, 25% were antibody negative, and 54% were antibody inconclusive. Antibody formation was higher after episodic compared with scheduled treatment (39% vs 16%; P = .036) and was associated with a higher rate of infusion reactions (50% vs 21%; P = .018). Ninety patients continued maintenance scheduled therapy beyond 12 months including 12 converted episodic patients, with a median follow-up of 23 months (range, 16–68 months). The rate of clinical remission was higher for patients with a detectable trough serum infliximab compared with patients in whom serum infliximab was undetectable, including those without antibodies (82% vs 6%; P < .001). A detectable trough serum infliximab was also associated with a lower C-reactive protein (2.0 vs 11.8 mg/L; P < .001) and a higher rate of endoscopic improvement (88% vs 33%; P < .001).

Concurrent immunomodulators did not alter outcomes.

Conclusions: For Crohn’s disease patients treated with scheduled maintenance infusions of infliximab, the trough serum concentration of infliximab predicts clinical outcome. Factors in addition to antibody formation, likely pharmacokinetic, modulate serum infliximab and thus the response to infliximab therapy.

Infliximab, a chimeric monoclonal IgG1 antibody that binds specifically to tumor necrosis factor-α (TNF-α) is an effective treatment for induction of remission and prevention of relapse in patients with inflammatory intestinal and/or perianal fistulizing Crohn’s disease. After a 3-dose induction regimen of 5-mg/kg infusions at 0, 2, and 6 weeks, 2 strategies have been used to maintain remission. Episodic maintenance therapy provides infliximab only on relapse, whereas scheduled maintenance therapy infliximab is administered at regular 8-week intervals. However, patients treated with episodic infusions of infliximab derive less clinical benefit from treatment than patients receiving the scheduled strategy. The improved outcome after scheduled maintenance therapy has been attributed to a lower frequency of antibody development to infliximab compared with episodic treatment, because antibody formation predicts a shorter duration of clinical response and a higher incidence of infusion reactions. Although concurrent immunomodulator therapy reduces antibody formation, whether these agents provide additional clinical benefit over treatment with scheduled infliximab therapy alone remains unclear and is currently an area of prospective study.

Scheduled maintenance infliximab treatment does not achieve complete clinical remission throughout an 8-week interval for all patients with Crohn’s disease. One plausible explanation for the incomplete treatment response to an 8-week infusion schedule is the lack of sustained suppression of TNF-α activity as a result of insufficient drug availability. The development of antibodies to infliximab is one factor associated with an undetectable concentration of serum infliximab. However, variable rates of clinical remission could also occur because of variable elimination of infliximab, independent from the formation of antibodies. Thus, more rapid clearance of infliximab would lead to reduced or absent serum levels of the drug before the end of an 8-week infusion interval. These observations suggest the trough serum infliximab concentration before the next infusion might be an important factor determining clinical outcome after infusions of infliximab, whether or not antibodies have developed. Therefore, we evaluated the effects of antibody formation and the trough serum concentration of infliximab on clinical outcome, including the duration of clinical remission, levels of C-reactive protein (CRP), and the magnitude of endoscopic improvement in patients with Crohn’s disease treated with scheduled infusions of infliximab for maintenance of remission.

Methods

Patients

A consecutive cohort of 105 patients with refractory inflammatory and/or perianal fistulizing Crohn’s disease who initiated infliximab treatment between March 2000–February 2005 were studied. At baseline, the induction protocol for fistulizing disease was infliximab 5 mg/kg infused intravenously at 0, 2, and 6 weeks, and for inflammatory disease it was either the 3-dose induction or a single infusion at 5 mg/kg. Thereafter, 82 patients received 5 mg/kg infliximab at regular scheduled intervals of 6, 7, or 8 weeks, and 23 patients were provided infliximab on relapse of the disease. Concomitant therapy, including prednisone at a dosage of ≤15 mg/day, azathioprine (2.0–2.5 mg·kg⁻¹·day⁻¹), methotrexate (25 mg intramuscu-
larly once weekly), or antibiotics (metronizadole and/or ciprofloxacin), were administered as indicated for additional treatment of Crohn’s disease. The study was approved by the institutional Research Ethics Board, and all patients gave written informed consent.

**Evaluations**

Clinical evaluations included age, gender, disease location and duration, prior resection, smoking status, concurrent use of immunosuppressive drugs, use of prednisone, and use of antibiotics. Patients were assessed at baseline and before each infusion. Complete blood count, clinical chemistry tests (liver and renal profile), albumin, and CRP were performed at each visit. Disease activity was measured by the Harvey-Bradshaw Index (HBI).

Complete remission was defined as an HBI score ≤2, and the interval remission was defined as the percentage of time (weeks) between infusions with HBI score ≤2. Side effects were recorded including the rate of early infusion reactions. Clinically important early infusion reactions were defined as those occurring during or within 1 hour after infusion that required subsequent administration of 200-mg hydrocortisone intravenously before each infusion. Hydrocortisone was given only for a prior serious infusion reaction and not as routine prophylaxis.

Colonoscopy was performed within 2 months before the baseline infusion in all patients, and 75 patients consented to a follow-up examination, undertaken after a minimum of 6 scheduled maintenance infusions of infliximab (n = 70) or after discontinuation of infliximab (n = 5) and within 8 weeks of the sampling for antibody to infliximab and serum infliximab determinations. An endoscopic disease activity score was calculated for each examination, according to the index of Daperno et al., by one investigator (E.M.) who was blinded to the antibody to infliximab and serum infliximab concentration status of the patients. Endoscopic improvement was defined as a reduction in the follow-up endoscopic score of ≥75%, compared with baseline. Endoscopic remission was defined as disappearance of all mucosal lesions on the follow-up examination.

Patients who continued scheduled therapy beyond 52 weeks had concentrations of infliximab and antibodies against infliximab measured from a single serum sample drawn immediately before an infusion after a minimum of 6 scheduled maintenance infusions (range, 6–37 infusions), with a median interval from the baseline infusion of 88 weeks (range, 54–248 weeks), and in the event of early discontinuation, within 12 weeks (range, 7–12 weeks) after cessation of infliximab therapy. Fifteen randomly selected patients who continued scheduled therapy beyond 52 weeks had a repeat analysis on a second preinfusion serum sample drawn at least 16 weeks (range, 16–40 weeks) after the first sample. Serum infliximab and antibodies against infliximab (Prometheus Laboratories, Inc, San Diego, CA) were assessed blindly in duplicate, as described previously. Serum infliximab was measured by a microplate enzyme-linked immunosorbent assay with a cutoff value of 1.4 μg/mL; serum concentrations below the cutoff value are reported as negative. Antibodies against infliximab were measured by a microplate enzyme-linked immunosorbent assay based on the double-antigen format with a cutoff value of 1.69 μg/mL. Antibodies against infliximab were reported as negative when the concentration was <1.69 μg/mL and the serum infliximab concentration was <1.4 μg/mL and as positive when the concentration exceeded 1.69 μg/mL and the infliximab concentration was <1.4 μg/mL. An inconclusive result was reported when the serum infliximab concentration was >1.40 μg/mL, because infliximab interferes with the antibody against infliximab assay and antibody formation cannot be determined. There was complete concordance between the 2 results reported for patients who had a repeat analysis.

**Statistical Analysis**

Comparison of differences within a group was performed by using the Student paired t test for normally distributed values and the Wilcoxon signed rank test for non-normally distributed data. Differences between groups were assessed by analysis of variance (ANOVA) followed by a multiple comparisons test (Tukey test) and the Kruskal-Wallis ANOVA on ranks followed by a multiple comparisons test (Dunn’s test) when the data were not normally distributed. The χ² test was used for comparison of categorical data. Linear regression analysis was used to test the strength of association between trough serum infliximab concentration and duration of interval remission, as well as the CRP level and the magnitude of endoscopic improvement. Logistic regression was used to assess associations between a positive antibody to infliximab status and factors of interest including gender, disease location, smoking status, the indication for infliximab, induction protocol, number of infusions, use of corticosteroids, use of immunosuppressive agents, and episodic or scheduled treatment strategies. Logistic regression was also used to examine predictors of complete interval remission, endoscopic improvement of 75% or greater, and a CRP within the normal range of ≤5 mg/L after scheduled maintenance therapy, independent variables included factors of interest above, as well as the presence of antibodies to infliximab and the presence of detectable trough serum concentration of infliximab. Statistical analysis was performed by using SPSS (version 14.0; SPSS Inc, Chicago, IL). P value <.05 was considered significant.

**Results**

**Patients**

Baseline characteristics of the 105 patients are shown in Table 1. The indication for infliximab was inflammatory disease in 66 patients and inflammatory disease associated with perianal fistulizing disease in 39 patients. Thirty-one patients received concurrent immunosuppressive therapy (azathioprine or methotrexate). After infliximab induction treatment, 82 patients received scheduled maintenance infliximab therapy at a maximum interval of 8 weeks, and 23 patients received episodic infliximab on relapse of the disease.

**Antibodies to Infliximab**

After a median of 14 infusions (range, 2–45), 22 patients (21%) had detectable antibodies, 26 patients (25%) were antibody negative, and 57 patients (54%) were antibody inconclusive. Of the 22 patients with antibody development, 17 patients (77%) had a titer of 8.0 μg/mL or greater. The incidence of antibody formation for patients exposed to episodic treatment was higher compared with patients who received scheduled therapy at regular intervals (39% vs 16%; P = .036) (Figure 1A).

Patients who received concurrent immunomodulators tended toward a lower incidence of antibody formation (10% vs...
The development of antibodies to infliximab was reduced only by a scheduled maintenance treatment strategy (odds ratio, 0.23; 95% confidence interval, 0.08–0.73; Figure 1B). In a logistic regression analysis of factors that could potentially influence antibody formation including gender, disease location, smoking status, the indication for infliximab, induction protocol, number of infusions, use of prednisone, use of immunomodulators, and maintenance treatment regimen, the development of antibodies to infliximab was reduced only by a scheduled maintenance treatment strategy (odds ratio, 0.23; 95% confidence interval, 0.08–0.73; P = .012).

Twenty-eight patients (27%) had early infusion reactions. The incidence of infusion reactions was higher in patients with antibody formation compared with patients who were antibody negative or antibody inconclusive (50% vs 21%; odds ratio, 3.6; 95% confidence interval, 1.3–9.6; P = .018). Immunomodulators did not alter the incidence of infusion reactions (29% vs 28%; P = .89).

**Outcome of Infliximab Therapy at 52 Weeks**

Of the 105 patients, 15 patients discontinued infliximab before 52-week follow-up after a median of 3 infusions (range, 2–5). The reasons for discontinuation were bowel obstruction requiring surgery (n = 4), perianal fistulizing disease requiring surgery (n = 1), infusion reaction (n = 3), mandibular osteomyelitis (n = 1), pregnancy (n = 2), and lack of insurance (n = 4). Of the 15 patients discontinuing infliximab before 52 weeks, 1 patient (1%) was antibody inconclusive, 4 patients (4%) were antibody positive, and 10 patients (10%) were antibody negative.

Ninety patients continued scheduled maintenance treatment for 52 weeks or longer, of whom 12 patients were converted from episodic therapy to scheduled treatment after their first maintenance infusion. The median follow-up period was 23 months (range, 16–68 months). Of the 90 patients receiving scheduled maintenance infliximab, 57 patients (63%) were antibody inconclusive with a detectable serum trough concentration of infliximab (median, 5.4 μg/mL; range, 2.0–11.7 μg/mL), and 33 patients had undetectable serum infliximab, of whom 18 patients (20%) were antibody positive, and 15 patients (17%) were antibody negative. The median trough serum infliximab was not different between patients receiving infliximab infusions at intervals of 6 or 7 weeks and intervals of 8 weeks (6.7 vs 5.2 μg/mL; P = .13) and did not differ for inconclusive patients treated with concurrent immunomodulator (azathioprine or methotrexate) therapy to episodic and scheduled treatment strategies.

**Figure 1.** Incidence of antibodies to infliximab. (A) Total cohort (n = 105), after episodic (n = 23) and scheduled (n = 82) treatment strategies. (B) In the presence and absence of concurrent immunomodulator (azathioprine or methotrexate) therapy to episodic and scheduled treatment strategies.

**Table 1.** Baseline Patient Characteristics

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Values are median and range.
antibody-negative patients who had an undetectable serum infliximab concentration (66% vs 67%; \( P = .62 \)) and were shorter than the median duration of remission of 100% for antibody-inconclusive patients with a detectable serum infliximab concentration (\( P < .001 \); Figure 2A). Median CRP for antibody-positive patients and antibody-negative patients showed similar above normal elevations (14.1 vs 13.7 mg/L; \( P = .72 \)) and were higher compared with the normal median CRP of 2.1 mg/L for antibody-inconclusive patients (\( P < .001 \); Figure 2B). The magnitude of endoscopic improvement from baseline also was not different between antibody-positive patients and antibody-negative patients (25% vs 7%; \( P = .43 \)) and was significantly less than the endoscopic improvement of 89% for antibody-inconclusive patients (\( P < .001 \); Figure 2C).

A higher proportion of antibody-positive patients and antibody-negative patients discontinued infliximab therapy before 52 weeks compared with antibody-inconclusive patients (29% vs 2%; odds ratio, 23.1; 95% confidence interval, 2.9–183.2; \( P < .001 \)). Compared with patients who continued infliximab beyond 52 weeks, discontinued patients had a shorter median duration of remission (50% vs 100%; \( P < .001 \)), a higher median CRP (16.1 vs 3.5 mg/L; \( P = .003 \)), and lesser endoscopic improvement from baseline (−29% vs 64%; \( P < .001 \)).

**Relationship of Outcome to Serum Infliximab**

For the 105 patients evaluated, a positive relationship was found between the serum concentration of infliximab and the interval clinical remission (\( R^2 = 0.61; P < .001 \); Figure 3A). There also was an inverse relationship between the serum concentration of infliximab and CRP (\( R^2 = 0.26; P < .001 \); Figure 3B) and a positive relationship between the serum concentration of infliximab and the change in endoscopic score from baseline (\( R^2 = 0.46; P < .001 \); Figure 3C).

Further evaluation of the 90 patients who continued scheduled maintenance infliximab beyond 52 weeks identified a strong association between clinical outcome and the preinfusion trough serum concentration of serum infliximab. A higher proportion of patients with a detectable trough serum infliximab concentration achieved complete interval clinical remission compared with patients in whom the trough serum infliximab was undetectable (82% vs 6%; \( P < .001 \); Figure 4A). The median serum CRP level was lower for patients with a detectable trough serum infliximab (2.0 vs 11.8 mg/L; \( P < .001 \)), and a higher proportion of patients achieved a normal CRP (76% vs 32%; \( P < .001 \); Figure 4B). A higher proportion of patients with a detectable trough serum infliximab exhibited endoscopic improvement of 75% or greater (88% vs 33%; \( P < .001 \); Figure 4C) and complete endoscopic remission (47% vs 19%; \( P = .03 \)).

Concurrent immunomodulator therapy compared with infliximab treatment alone did not alter the proportion of patients who achieved complete interval remission (\( P = .49 \)), a normal CRP (\( P = .16 \)), and endoscopic improvement (\( P = .59 \)). Logistic regression was used to analyze factors that could potentially influence outcome after scheduled maintenance therapy, including gender, disease location, smoking status, indication for infliximab, number of infusions, use of corticosteroids, use of immunomodulators, the presence of antibodies to infliximab, and a detectable trough serum concentration of infliximab. Only a detectable trough serum concentration of infliximab was a significant positive predictor for complete interval remission (odds ratio, 38.1; 95% confidence interval, \( P < .001 \)).

**Figure 2.** Clinical outcomes according to antibody to infliximab status (n = 105). (A) Duration of interval clinical remission defined as the percentage of time (weeks) between infusions with HBI score of 2 or less. (B) Serum CRP. (C) Endoscopic improvement defined as the percentage change in endoscopic score from the baseline to the follow-up evaluation. The box represents the 25th–75th percentiles, the whiskers correspond to the 5th–95th percentiles, and the solid line within boxes are median values. Antibody inconclusive vs antibody positive and antibody negative, \( P < .001 \); antibody positive vs antibody negative, \( P = \text{NS} \).
9.1–60.5; \( P < .001 \), a normal CRP (odds ratio, 8.3; 95% confidence interval, 2.6–26.9; \( P < .001 \), and endoscopic improvement of \( \geq 75\% \) (odds ratio, 22.6; 95% confidence interval, 4.1–124.1; \( P < .001 \)).

**Discussion**

Infliximab is now an established treatment for patients with refractory Crohn’s disease.\(^2,4\) However, Crohn’s disease is a chronic illness that frequently requires long-term treatment, and understanding why some patients derive less benefit with infliximab is an important focus for investigation. Our results showed for Crohn’s disease patients receiving maintenance infusions of infliximab treatment at scheduled intervals, the proportion of patients who obtained clinical benefit was similar for antibody-positive patients and antibody-negative patients, which was less than observed for antibody-inconclusive patients. The favorable clinical outcome for antibody-inconclusive patients related directly to detectable trough serum concentrations of infliximab including longer duration of interval clinical remission, lower levels of CRP, and greater endoscopic improvement. The rates of clinical and endoscopic remission were significantly reduced for patients with an undetectable trough serum infliximab, whether or not antibodies to infliximab were present. Together, these observations suggest an important relationship between clinical outcome and the trough serum concentration of infliximab that is not solely influenced by the effects of antibody formation.

Antibody formation was associated with a shorter duration of remission, as previously reported for Crohn’s disease patients treated with infliximab.\(^7\) However, a similar clinical outcome was observed for antibody-negative patients, also characterized by undetectable trough levels of serum infliximab. Thus, in the context of clinical outcome the presence of antibodies might be a surrogate marker for the effects of absent serum infliximab. The ACCENT I trial suggested a similar conclusion, with results showing a trend toward a higher rate of clinical remission for antibody-inconclusive patients relative to antibody-positive and antibody-negative patients. Although this outcome was attributed to higher serum infliximab concentrations for the antibody-inconclusive patients, serum infliximab levels were not fully reported.\(^2,6,12\) More definitive support for a relationship between trough serum infliximab and clinical remission is provided from a pharmacokinetic analysis of data from the EXPRESS trial, a multicenter, maintenance study of patients with psoriasis, all of whom were treated with infliximab at scheduled 8-week intervals.\(^13\) In this trial, patients with detectable preinfusion serum infliximab concentrations maintained a 75% improvement of the psoriasis area and severity index during 50 weeks of evaluation, whereas patients with undetectable serum infliximab, including those without antibodies, were less likely to maintain response.\(^13\)

Overall, 21% of patients in our study developed antibodies to infliximab. However, the 39% incidence of antibody formation for patients exposed to episodic treatment was significantly higher compared with 16% for those receiving scheduled therapy. Antibody formation was also associated with an increased incidence of infusion reactions. In ACCENT-1, antibody formation also was higher for patients receiving episodic infliximab and was associated with a higher incidence of infusion reactions.\(^2,6\) The highest reported overall incidence of antibody development to infliximab of 61% reported by Baert et al\(^7\) was likely related to a study cohort composed only of patients receiving episodic re-treatment. Together, these observations further support a treatment strategy of scheduled infliximab at regular intervals to be less immunogenic than episodic on-demand infliximab treatments.

![Figure 3](image-url)
Maintenance episodic infliximab treatment compared with scheduled therapy is associated with lower rates of clinical remission and endoscopic mucosal healing, reflecting, in part, the higher incidence of antibody formation.\(^5,14\) However, a maintenance strategy of regular scheduled infliximab also affords a greater likelihood for sustained serum concentrations of infliximab between infusions. Our results support and extend the clinical utility of regular scheduled infliximab for Crohn’s disease by showing detectable preinfusion trough concentrations of serum infliximab lead to higher rates of clinical and endoscopic remission, as well as normal CRP. Elevations of CRP are associated with moderate to severe clinical symptoms of disease activity and endoscopic evidence of active inflammation.\(^15\) Although the implications of endoscopic remission to clinical remission and long-term outcome of patients with Crohn’s disease are not firmly established,\(^16\) prevention of recurrent intestinal ulceration is likely to improve clinical well-being and reduce fibrostenotic obstructive complications.

Considerable variability in the trough concentration of serum infliximab between patients has been reported after 24 weeks of scheduled treatment; although within patients, levels remain relatively constant over time at a fixed infliximab dose and regular 8-week infusion interval.\(^9,13\) We found similar variations in the trough serum infliximab beyond 52 weeks of scheduled treatment. Moreover, median serum infliximab concentrations were not different for patients treated at intervals of 6–7 weeks compared with 8-week intervals. These findings suggest individual differences in the clearance of infliximab from the circulation, with more rapid elimination in some patients. Although one contributing factor is the development of antibodies to infliximab, 25% of our patientsexhibited an undetectable trough serum infliximab concentration without detectable antibodies, similar to previous experience.\(^6,13,17\) Thus, antibodies to infliximab are not the only explanation for elimination of infliximab from the circulation. Metabolic factors also are likely to contribute to a variable and more rapid elimination of infliximab and, therefore, diminished clinical benefit.

Pharmacokinetic models of infliximab treatment indicate that higher trough serum concentrations of infliximab might be achieved by shortening the infusion interval or increasing the dose of infliximab.\(^9\) Of the two strategies, shortening the infusion interval by 2 weeks increases the trough level of infliximab more than raising the dose of infliximab by 100 mg and would incur a lesser drug cost. A shorter infusion interval might, therefore, be the preferred strategy for dose modification to increase the preinfusion serum infliximab and improve clinical outcome. An additional therapeutic approach is the coadministration of methotrexate to infliximab because the rate of disappearance of infliximab is slower among patients who are taking methotrexate than those who are receiving infliximab alone.\(^18\) The mechanism underlying this action of methotrexate is unclear, but it is independent of effects on antibody formation. Trough serum concentrations of infliximab in our study were similar for patients treated with immunomodulators compared with infliximab alone, but the proportion of patients receiving methotrexate was too small to draw conclusions regarding effects on infliximab concentrations.

Although immunomodulator therapy reduced formation of antibodies to infliximab, the treatment effect was significant only for patients exposed to episodic infusions of infliximab. For patients receiving regular scheduled infliximab treatment,

![Figure 4. Clinical outcomes after scheduled maintenance therapy beyond 52 weeks according to the presence and absence of a detectable trough serum infliximab concentration (n = 90). Proportion of patients with (A) complete interval clinical remission defined as an HBI score 2 or less between infusions of infliximab. (B) Serum CRP within the normal range defined as 5 mg/L or less. (C) Endoscopic improvement defined as a reduction in the follow-up endoscopic score from baseline of 75% or greater.](image-url)
the impact of immunomodulators on antibody development was minimal, and concurrent immunomodulator therapy provided no additional clinical benefit. In ACCENT-1, patients who were treated only with scheduled infliximab at regular 8-week intervals and received immunomodulators also did not appear to derive a significant reduction of antibody formation or an improved rate of clinical remission. However, 2 prospective trials have been initiated for Crohn’s disease patients treated with scheduled maintenance infliximab to independently evaluate concurrent administration of methotrexate or azathioprine and ascertain the potential for increased toxicity against any gain in clinical benefit. Intravenous hydrocortisone premedication before an infliximab infusion is an additional approach that reduces but does not eliminate antibody formation, but this strategy does not impact on rates of clinical remission or the incidence of infusion reactions.

Limitations of our study include the inability to reliably exclude low titer antibodies in antibody-inconclusive patients. However, in the ACCENT-1 trial only 2.5% of patients with an antibody-inconclusive status proved to be antibody-positive 26 weeks after their last infusion. Moreover, even in the presence of low titer antibodies in an inconclusive patient, detectable infliximab implies antibody saturation and further supports serum infliximab as the dominant of the two factors relating to outcome. We also found 2 antibody-positive patients receiving maintenance regular scheduled therapy achieved complete clinical and endoscopic remission. Previous studies have similarly shown an antibody-positive status does not entirely preclude a clinical response to infliximab. These findings suggest factors in addition to the trough serum concentration of infliximab might influence clinical outcome. On the other hand, characterization of the antibody(s) to infliximab measured by the double-antigen technique used in our study has not been described. It remains conceivable that more than 1 antibody is generated to infliximab with different affinities and regions of binding to the drug that, in turn, cause variable effects on the clinical response to infliximab.

In summary, for patients with Crohn’s disease treated with scheduled infusions of infliximab, a detectable trough concentration of serum infliximab concentration is associated with higher rates of clinical remission and endoscopic improvement and lower levels of CRP. These outcome parameters were not improved further by concurrent therapy with immunomodulators. Factors in addition to antibody formation, likely pharmacokinetic, modulate serum concentrations of infliximab and thus influence clinical benefit. Whether scheduled maintenance infusions of infliximab shorter than an interval of 8 weeks improve clinical outcome by increasing the proportion of patients with detectable preinfusion serum concentrations of infliximab warrants prospective evaluation.

References


Address requests for reprints to: G. R. Greenberg, MD, Mount Sinai Hospital, 445-600 University Avenue, Toronto, Ontario, Canada MSG 1X5. e-mail: ggreenberg@mtsinai.on.ca; fax: (416) 586-4802.

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