**ARTICLES**

**Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial**


**Summary**

**Background** We did a randomised controlled trial to assess the benefit of maintenance infliximab therapy in patients with active Crohn’s disease who respond to a single infusion of infliximab.

**Methods** 573 patients with a score of at least 220 on the Crohn's disease activity index (CDAI) received a 5 mg/kg intravenous infusion of infliximab at week 0. After assessment of response at week 2, patients were randomly assigned repeat infusions of placebo at weeks 2 and 6 and then every 8 weeks thereafter until week 46 (group I), repeat infusions of 5 mg/kg infliximab at the same timepoints (group II), or 5 mg/kg infliximab at weeks 2 and 6 followed by 10 mg/kg (group III). The prespecified co-primary endpoints were the proportion of patients who responded at week 2 and were in remission (CDAI <150) at week 30 and the time to loss of response up to week 54 in patients who responded. Analyses of the co-primary endpoints were by intention to treat.

**Findings** 335 (58%) patients responded to a single infusion of infliximab within 2 weeks. At week 30, 23 of 110 (21%) group I patients were in remission, compared with 44 of 113 (39%) group II (p=0·003) and 50 of 112 (45%) group III (p=0·0002) patients. Thus, patients in groups II and III combined were more likely to sustain clinical remission than patients in group I (odds ratio 2·7, 95% CI 1·6–4·6). Throughout the 54-week trial, the median time to loss of response was 38 weeks (IQR 15 to >54) and more than 54 weeks (21 to >54) for groups II and III, respectively, compared with 19 weeks (10–45) for group I (p=0·002 and p=0·0002, respectively). Infliximab safety was consistent with that seen in other trials of infliximab.

**Interpretation** Patients with Crohn’s disease who respond to an initial dose of infliximab are more likely to be in remission at weeks 30 and 54, to discontinue corticosteroids, and to maintain their response for a longer period of time, if infliximab treatment is maintained every 8 weeks.

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**Introduction**

Crohn’s disease is a chronic inflammatory disorder of the gastrointestinal tract. Although mild disease can be treated with 5-aminosalicylates, many patients eventually require corticosteroids to control symptoms. Once started, acute and in particular chronic use of corticosteroids is associated with well known adverse effects. Moreover, about 45% of patients are unable to discontinue corticosteroid therapy without disease exacerbation. The purine antimetabolites and methotrexate are frequently prescribed for patients who are resistant to or dependent on corticosteroids; however, these drugs have a slow onset of action and clinical remission rates of about 40%. Clinical remission is defined by discontinuation of prednisone and a Crohn’s disease activity index (CDAI) score of 150 or less after 16 weeks for methotrexate and as a CDAI of less than 175 at 15 months for azathioprine.

Thus, there is a need for a long-term treatment that maintains clinical remission and reduces exposure to corticosteroids.

Tumour necrosis factor α (TNFα) is a proinflammatory cytokine that has an important role in the pathogenesis of Crohn’s disease. Infliximab—a chimeric anti-TNFα monoclonal antibody—binds to TNFα with high affinity, thereby neutralising its biological activity. When given as a 5 mg/kg intravenous infusion, infliximab induces remission in patients with moderately to severely active Crohn’s disease and can reduce corticosteroid requirements. Clinical experience has shown that patients can relapse after a single infusion of infliximab.

In a previous assessment of repeated administration of infliximab (four infusions of 10 mg/kg every 8 weeks) in patients with Crohn’s disease, retreatment with infliximab maintained the clinical benefit up to 8 weeks after the last infusion in nearly all patients who responded to an initial dose of treatment. However, the results were not statistically significant in that small trial. Further data from a longer study were required to establish the long-term efficacy and safety of repeated doses of infliximab in patients with Crohn’s disease who show an initial response to treatment.

In the ACCENT I trial, we aimed to assess the efficacy and safety of repeated infusions of infliximab in patients who improved after an initial infusion. Our hypothesis was that maintenance infliximab treatment is a more effective intervention than a single infusion. Secondary objectives included the assessment of infliximab’s corticosteroid-sparing effects and safety in a large number of patients.
Patients and methods

Patients

This multicentre, randomised, double-blind trial was carried out at 55 sites in North America, Europe, and Israel. Recruitment of patients took place from Feb 26, 1999, to Jan 24, 2000. For the prespecified 30-week endpoint analysis, the last completed visit was on Aug 30, 2000. For results up to 54 weeks, the last completed visit was on March 15, 2001. The protocol was approved by the institutional review boards at participating sites. Written informed consent was obtained from all patients.

Eligible patients had Crohn’s disease of at least 3 months’ duration with a score on the CDAI\(^\text{17}\) between 220 and 400. Patients receiving the following treatments were eligible: 5-aminosalicylates or antibiotics (if the dose remained constant for 4 weeks before the screening visit); corticosteroids (prednisone, prednisolone, or budesonide) at the equivalent of 40 mg per day of prednisone or less (stable dose for 3 weeks); azathioprine and 6-mercaptopurine (stable dose for 8 weeks); or methotrexate (stable dose for 6 weeks). Patients not receiving medical therapy had to have discontinued treatment for at least 4 weeks before screening. Patients were excluded from the study if they had received previous treatment with infliximab or any other agent targeted at TNF.

Procedures

Patients were screened for eligibility 2 weeks before enrolment. At week 0, all eligible patients received a 5 mg/kg intravenous infusion of infliximab. 2 weeks later, patients were assessed for a response to treatment as defined by a decrease in CDAI score of 70 points or more from the baseline value and at least a 25% reduction in the total score. Patients were randomly assigned subsequent infusions, at weeks 2 and 6 and every 8 weeks thereafter until week 46, of placebo (group I), 5 mg/kg infliximab (group II), or 5 mg/kg infliximab at weeks 2 and 6 followed by 10 mg/kg thereafter (group III).

The prespecified co-primary efficacy endpoints were the proportion of week-2 responders in clinical remission at week 30, and the time to loss of response up to week 54 among week-2 responders. The findings presented here address the primary objective of this study, which was to assess the benefit of infliximab maintenance treatment in patients with an initial early (within 2 weeks) response to a single infliximab infusion.

Taking variability between sites and effects of concomitant medications into account, allocation of patients to a treatment group was done with an adaptive stratified design with investigational site and duration of continuous exposure to corticosteroids (<1 year; >1 year; no corticosteroids and no other Crohn’s disease medications; no corticosteroids but other Crohn’s disease medications) as the strata. Since there were 55 investigative sites from North America, Europe, and Israel involved in the study, an adaptive randomisation procedure was used to allocate patients centrally to treatment based on the current balance of treatment groups within each stratum. An interactive voice-response system was used. A pharmacist prepared the infusion (infliximab [Remicade] or an identically appearing placebo, both from Centocor, Malvern, PA, USA). Neither the patients nor study investigators were aware of the treatment assignment.

Patients were assessed at weeks 0, 2, 6, 10, 14, 22, 30, 38, 46, and 54. At each visit, adverse events were prospectively collected by direct questioning of patients by primary investigators or site coordinators, and samples for clinical laboratory assessments and the patient’s CDAI scores were obtained. Health-related quality of life was mainly assessed by the inflammatory-bowel-disease questionnaire (IBDQ).\(^\text{18}\) Blood samples for measurement of infliximab concentrations were collected immediately before each infusion and at the end of the infusion at weeks 0, 22, and 46.

For reasons other than lack of efficacy or loss of response, patients originally assigned to groups I, II, and III, respectively. Worsening was defined by: (1) an increase in CDAI of at least 70 points from the qualifying score with a total score of at least 175, (2) an increase in CDAI of 35% or more from the baseline value, or (3) the introduction of a new treatment for active Crohn’s disease. Patients and physicians remained unaware of the treatment assignment. All data obtained after episodic retreatment were included in the safety analyses but not in the efficacy analyses.

Patients receiving corticosteroids were to maintain a stable dose until week 6, after which a defined tapering schedule was started if the patient’s condition had improved. Patients who entered the trial receiving corticosteroid doses of more than 20 mg per day prednisone equivalent had their treatment tapered at a maximum rate of 5 mg per week; the maximum rate for patients receiving 20 mg per day prednisone equivalent or less was 2.5 mg per week. Aminosalicylates and immunomodulators were maintained at a constant dose.

All study participants were included in the safety analysis. Blood samples were collected to determine the presence of antinuclear antibodies (ANA) at weeks 0, 10, 30, and 54. Samples positive for ANA were tested for anti-double-stranded-DNA antibodies (anti-dsDNA). The criterion for a positive anti-dsDNA result was the presence of an ANA titre of 1:40 or more and a positive result on the Crithidia assay. The Crithidia assay provides ready access to non-nuclear dsDNA. Samples for determination of antibodies to infliximab were obtained at weeks 0, 10, 14, 22, and 54. During episodic retreatment, samples were drawn specifically to test for antibodies to infliximab before each episodic retreatment infusion. Patients were also tested at study termination.

Statistical analysis

The main objective of the study was to assess the efficacy and safety of infliximab maintenance treatment in patients responding to a single infliximab infusion. Efficacy was assessed as the continued benefit provided by the maintenance treatment. For this purpose, the primary endpoint of this study was designed as the time to loss of response up to and including week 54 among week-2 responders, as defined by a CDAI of at least 175, a CDAI increase of at least 35%, and a CDAI at least 70 points from the qualifying score with a total score of at least 175, (2) an increase in CDAI of 35% or more from the baseline value, or (3) the introduction of a new treatment for active Crohn’s disease. Patients and physicians remained unaware of the treatment assignment. All data obtained after episodic retreatment were included in the safety analyses but not in the efficacy analyses.

Patients who crossed over to episodic infliximab retreatment, who received a drug not allowed by the protocol, who had surgery for Crohn’s disease, or who discontinued follow-up due to lack of efficacy or loss of response were judged to have failed treatment, irrespective of the CDAI score. Patients who discontinued the study for reasons other than lack of efficacy or loss of response...
and those with missing CDAI scores were censored in the analysis of time to loss of response up to week 54. These patients were treated as not in clinical response or clinical remission for other analyses.

In the primary analysis at week 30, a χ² test compared the proportion of patients in remission at week 30 among the treatment groups. A p value of 0·01 was set to define significance. The analysis of the time to loss of response up to week 54 was done with the log-rank test for grouped data. Time to loss of response was defined as the week of assessment corresponding to the earliest occurrence of loss of response, as defined above. The median time to loss of response was obtained by interpolation between the two visits between which 50% of patients had a loss of response. The α level of 0·04 was used for the week 54 co-primary endpoint analysis. Nominal two-sided p values with an α of 0·05 were reported for secondary analyses.

A χ² test was also used to calculate the proportion of patients who were in remission and not receiving corticosteroid therapy and the proportion of patients who responded according to the previously described criterion. The consistency of treatment benefit was examined for the primary endpoint (the proportions of patients in remission in subgroups by odds ratios, with 95% CIs calculated from a logistic regression. Subgroups were defined by demographic features, geographic location, baseline disease characteristics, and concomitant medications at baseline. Analysis of variance based on ranks was used to compare the median CDAI, IBDQ, and C-reactive protein values at predefined study visits. To be conservative about patients’ status in this comparison, the closest previous value was carried forward for patients treated with a protocol-prohibited medication or dose because of lack of efficacy or loss of response, for those who had Crohn’s-disease-related surgery, for those who crossed over to episodic retreatment, and for those who discontinued regularly scheduled follow-up.

Incidence of adverse events were tabulated by treatment groups. Incidences of serious adverse events and infections requiring antimicrobial treatment were determined for patients who received only a single infusion of infliximab and compared against respective incidences among patients who received several infliximab infusions. Assuming that 60% of patients responded at week 2 and were therefore included in the primary efficacy analysis, a sample size of 170 per treatment group provided approximately 95% power to detect a significant treatment effect in remission rate at week 30, with a two-sided χ² test at an α level of 0·01. This sample size also provided approximately 90% power to detect a significant treatment effect in the time to loss of response up to week 54, with a two-sided log-rank test for grouped data at an α level of 0·04.

**Role of the funding source**
This study was designed by a committee composed of Centocor staff members and the ACCENT Steering Committee members. Centocor staff collected data from all clinical sites to create the clinical database. Centocor staff members and members of the ACCENT Steering Committee analysed and interpreted the data, wrote the paper, and agreed to submit it for publication. The principal investigators approved the content of the paper before submission.

**Results**
Patients’ disposition, baseline characteristics, and previous or concomitant medication
Of 580 patients enrolled, 573 patients at 55 study centres (40 North America, 13 Europe, and two Israel) were started on infliximab 5 mg/kg; 335 (58%) were responders at week 2. These 335 responders were randomly assigned placebo (group I, 110 patients), the 5 mg/kg maintenance regimen (group II, 113 patients), or the 10 mg/kg maintenance regimen (group III, 112 patients) and were assessed in the predefined primary efficacy analyses (figure 1). The 573 patients comprised 239 (42%) men and 334 (58%) women with a median age of 35 years (range
18–76). Baseline characteristics of the week-2 responders compared with non-responders were similar with the exception of Crohn’s disease duration, previous segmental resections, and C-reactive protein concentration (table 1).

124 (22%) patients had discontinued maintenance study treatment by week 54. Among all patients, the proportions of patients who discontinued study treatment (and did not cross over) were similar across groups I, II, and III (38 [20%], 49 [26%], and 37 [19%], respectively). Within group I, the most common reason for discontinuing study treatment was lack of efficacy (23 [12%]); in groups II and III, the most common reasons for discontinuation were adverse event (38 [10%]) and lack of efficacy (31 [8%]), respectively. Further details of adverse events leading to discontinuation of study treatment among all patients are provided under safety results.

### Efficacy

Throughout follow-up, patients assigned continued active treatment showed a greater therapeutic benefit than patients retreated with placebo. At week 30 (figure 2), the proportion of week-2 responders in remission was higher in both group II and group III (44 [39%] and 50 [45%], respectively) than in group I (23 [21%]). Thus, patients in groups II and III combined were more likely to be in clinical remission at 30 weeks than patients in group I (odds ratio 2·7, 95% CI 1·6–4·6). The difference in remission rates between groups II or III and group I was seen as early as week 10 (2·0, 1·3–3·2) and was sustained thereafter. Similar results were seen at week 54 (figure 2).

No difference in the rate of remission was present between groups II and III at week 30 (1·3, 0·74–2·20) or week 54 (1·58, 0·90–2·80). A similar pattern of clinical response was observed at weeks 30 and 54 (figure 2).

Patients in groups II and III had a significantly longer time to loss of response than patients in group I (p=0·0002). The median time to loss of response was 46 weeks (IQR 17 to >54) in groups II and III combined compared with 19 weeks (10–45) in group I. When compared separately, patients in both groups II and III had a significantly longer time to loss of response than patients in group I (median 38 weeks [15 to >54], p=0·002, and >54 weeks [21 to >54], p=0·0002, respectively).

At week 54, about three times as many patients (32 [29%] vs 9 [6%]; odds ratio 4·2, 95% CI 1·5–11·5) in groups II and III combined had discontinued corticosteroids while in clinical remission compared with patients in group I (p=0·004). The median corticosteroid doses over time up to week 54 are shown in figure 3. The median corticosteroid dose was reduced more rapidly in groups II and III (0 mg per day by week 22) than in group I (10 mg per day at week 22).

Median CDAI scores (figure 4) were at or near remission levels for all three treatment groups at week 2. The proportions of patients who maintained a clinical remission at every visit from week 14 to week 54 were 11% (12/110), 25% (28/113), and 33% (37/112) for group I, group II, and group III, respectively. An analogous pattern of improvement was seen for IBDQ (figure 4).

### Pharmacokinetics

In group I patients who received only a single dose of 5 mg/kg infliximab, concentrations of infliximab in serum were undetectable in more than 50% of patients by week 14. In patients who received maintenance infliximab infusions (groups II and III), the trough concentrations of drug remained relatively constant up to week 54. From week 22 onwards, higher trough concentrations were seen in group III than in group II, as would be expected. Median trough infliximab concentrations in patients positive for antibody to infliximab were significantly higher than in patients negative for antibody to infliximab (median 0·8 [0·4–2·3] vs 0·1 [0·0–0·4], p=0·0002).

### Safety

Adverse events leading to discontinuation of study treatment were adverse event (38 [10%]) and lack of efficacy (23 [20%], 49 [26%], and 37 [19%], respectively). Within group I, the most common reason for discontinuing study treatment was lack of efficacy (23 [12%]); in groups II and III, the most common reasons for discontinuation were adverse event (38 [10%]) and lack of efficacy (31 [8%]), respectively. Further details of adverse events leading to discontinuation of study treatment among all patients are provided under safety results.

### Baseline characteristics

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Race</th>
<th>All patients (n=573)</th>
<th>Week-2 responders (n=335)</th>
<th>Week-2 non-responders (n=238)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>549 (96%)</td>
<td>315 (94%)</td>
<td>234 (98%)</td>
</tr>
<tr>
<td>Black</td>
<td>12 (2%)</td>
<td>10 (3%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Asian</td>
<td>5 (1%)</td>
<td>4 (1%)</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>7 (1%)</td>
<td>6 (2%)</td>
<td>1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35 (28–46)</td>
<td>35 (27–46)</td>
<td>37 (30–46)</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>7·9 (3·9–14·7)</td>
<td>7·5 (3·7–14·2)</td>
<td>9·3 (4·6–15·3)</td>
</tr>
<tr>
<td>Involved intestinal area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileum</td>
<td>137/568 (24%)</td>
<td>74/331 (22%)</td>
<td>63/237 (27%)</td>
</tr>
<tr>
<td>Colon</td>
<td>109/568 (19%)</td>
<td>74/331 (22%)</td>
<td>35/237 (15%)</td>
</tr>
<tr>
<td>Ileum and colon</td>
<td>32/568 (57%)</td>
<td>183/331 (55%)</td>
<td>139/237 (59%)</td>
</tr>
<tr>
<td>Gastroduodenum</td>
<td>43/573 (8%)</td>
<td>24/335 (7%)</td>
<td>19/238 (7%)</td>
</tr>
<tr>
<td>Previous segmental resection(s)</td>
<td>291/573 (51%)</td>
<td>148/335 (44%)</td>
<td>143/238 (60%)</td>
</tr>
<tr>
<td>CDAI*, median (IQR)</td>
<td>297 (260–342)</td>
<td>299 (264–342)</td>
<td>291 (249–340)</td>
</tr>
<tr>
<td>IBIDQ, median (IQR)</td>
<td>127 (110–147)</td>
<td>129 (114–147)</td>
<td>125 (106–145)</td>
</tr>
<tr>
<td>C-reactive protein concentration (mg/dL), median (IQR)</td>
<td>0·8 (0·4–2·3)</td>
<td>1·1 (0·4–2·8)</td>
<td>0·6 (0·4–1·5)</td>
</tr>
<tr>
<td>Patients with concomitant medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S-aminosalicylates</td>
<td>288 (50%)</td>
<td>159 (47%)</td>
<td>129 (54%)</td>
</tr>
<tr>
<td>Sulfasalazine and azathioprine</td>
<td>144 (29%)</td>
<td>81 (24%)</td>
<td>63 (27%)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>23 (4%)</td>
<td>10 (3%)</td>
<td>13 (6%)</td>
</tr>
<tr>
<td>Patients with concomitant corticosteroids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>293 (51%)</td>
<td>175 (52%)</td>
<td>118 (50%)</td>
</tr>
<tr>
<td>&gt;20 mg per day</td>
<td>93 (16%)</td>
<td>61 (18%)</td>
<td>32 (13%)</td>
</tr>
</tbody>
</table>

IBDQ=inflammatory bowel disease questionnaire (values can range from 32 to 224). *On final clinical data review, 13 enrolled patients had baseline Crohn’s disease activity index (CDAI) >220. For nine of these patients, CDAI as calculated by investigator was >=220. Remaining four patients were protocol violators.
Antibodies to infliximab

Up to week 54, 442 patients were assessed for the presence of antibodies to infliximab (table 2). The presence of infliximab in the serum is known to interfere with the interpretation of the analyses for antibodies to infliximab. Results for patients who were not positive for antibodies to infliximab but who had detectable concentrations of infliximab after their last infusion were classified as inconclusive. In this assessment, 64 of 442 (14%) patients developed antibodies to infliximab: 41 (28%) in group I, 14 (9%) in group II, and nine (6%) group III. Close to half the patients (46%) had inconclusive test results for antibodies to infliximab due to the detection of infliximab in the serum, which could compete for the detection of antibodies to infliximab in the immunoassay used. Antibody titres were similar across all treatment groups, and only three patients had a titre greater than 1:40.

Four (6%) of the 64 patients receiving steroids at baseline in combination with immunomodulators were lower than in patients who had negative or inconclusive test results.

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Four (6%) of the 64 patients receiving steroids at baseline in combination with immunomodulators were lower than in patients who had negative or inconclusive test results.
week-2 responders

*p=NS (group II vs group I), p=0·001 (group III vs group I). **p=0·015 (group II vs group I). ||p=0·060 (group II vs group I). ¶p=0·050 (group II vs group I). ‡p=0·001 (group II vs group I). §p=0·0001 (group II vs group I). ¶¶p=0·001 (group II vs group I). ‡‡p=0·013 (group II vs group I). ‡‡p=0·0001 (group II vs group I). ‡‡p=0·015 (group II vs group I). |p|=0·0076 (group II vs group I). |p|=0·0060 (group II vs group I). |p|=0·0001 (group II vs group I). ‡‡p=0·0015 (group II vs group I). ‡‡p=0·0001 (group II vs group I). ‡‡p=0·015 (group II vs group I). ‡‡p=0·0001 (group II vs group I).

Developed antibodies to infliximab. By contrast, 17% (26/154) of patients receiving steroids alone, and 18% (27/154) of patients receiving neither corticosteroids nor immunomodulators developed antibodies to infliximab.

Safety

Safety data for all 573 treated patients are reported according to the actual treatment received. Since some patients in each group received episodic treatment, a number of patients in group I received several infusions of infliximab. Total exposure to infliximab for each group is presented in table 3. Headache, abdominal pain, and upper respiratory tract infection (URTI) were reported in 61 of 993 (6%) patients. Like symptoms were similar among treatment groups.

Figure 4: Median CDAI and IBDQ scores to week 54 among week-2 responders

Table 2: Incidence of infusion reactions during infliximab infusions by antibodies to infliximab status up to week 54

<table>
<thead>
<tr>
<th>Positive*</th>
<th>Negative†</th>
<th>Inconclusive‡</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evaluative patients with appropriate samples§</td>
<td>64 (14%)</td>
<td>173 (40%)</td>
<td>205 (46%)</td>
</tr>
</tbody>
</table>

*Includes all patients with appropriate samples who had at least one positive sample at any time. †Includes all patients with appropriate samples who had a negative sample after last assessment, excluding patients who were positive. ‡Includes all patients with appropriate samples who had an inconclusive sample (sample with detectable infliximab concentration) after last assessment, excluding those who were positive. §Patients with appropriate samples either had antibodies to infliximab at some time after first infusion or had one or more samples obtained after last infusion.
Steroid-associated complications are well known, yet many benefits. Hence, patients thought previously to be immunomodulators in this setting provided important unmet need. Of the patients who participated in ACCENT I had failed to achieve remission, and 18% had experienced serious adverse events and infections were similar between those who received only a single infliximab infusion and those who received several infliximab infusions. Two patients died of sepsis—one in association with an exacerbation of Crohn’s disease with bowel obstruction and treated with partial bowel resection of the inflamed bowel.

The risk-benefit ratio for patients at high risk of infection should be considered before starting infliximab therapy. In particular, the development of a case of tuberculosis is a cause for concern. Since becoming widely available in 1998, infliximab has been given to about 175,000 patients, and 101 cases of tuberculosis have been reported (62 patients with rheumatoid arthritis, 21 with Crohn’s disease, four with other diagnoses, and 14 with unknown diagnoses). Thus, despite the absence of controlled data, there might be an association between infliximab treatment and reactivation of tuberculosis. This potential risk should be considered before starting infliximab therapy. In particular, the development of a case of tuberculosis is a cause for concern. Since becoming widely available in 1998, infliximab has been given to about 175,000 patients, and 101 cases of tuberculosis have been reported (62 patients with rheumatoid arthritis, 21 with Crohn’s disease, four with other diagnoses, and 14 with unknown diagnoses). Thus, despite the absence of controlled data, there might be an association between infliximab treatment and reactivation of tuberculosis. This potential risk should be considered before starting infliximab therapy.

Close to half the patients had inconclusive test results for tuberculosis. Such ambiguity results from the ongoing presence of infliximab in the serum, which competes with antibodies to infliximab in the ELISA used. The risk-benefit ratio for patients at high risk of infection should be considered before starting infliximab therapy. In particular, the development of a case of tuberculosis is a cause for concern. Since becoming widely available in 1998, infliximab has been given to about 175,000 patients, and 101 cases of tuberculosis have been reported (62 patients with rheumatoid arthritis, 21 with Crohn’s disease, four with other diagnoses, and 14 with unknown diagnoses). Thus, despite the absence of controlled data, there might be an association between infliximab treatment and reactivation of tuberculosis. This potential risk should be considered before starting infliximab therapy. In particular, the development of a case of tuberculosis is a cause for concern. Since becoming widely available in 1998, infliximab has been given to about 175,000 patients, and 101 cases of tuberculosis have been reported (62 patients with rheumatoid arthritis, 21 with Crohn’s disease, four with other diagnoses, and 14 with unknown diagnoses). Thus, despite the absence of controlled data, there might be an association between infliximab treatment and reactivation of tuberculosis. This potential risk should be considered before starting infliximab therapy. In particular, the development of a case of tuberculosis is a cause for concern. Since becoming widely available in 1998, infliximab has been given to about 175,000 patients, and 101 cases of tuberculosis have been reported (62 patients with rheumatoid arthritis, 21 with Crohn’s disease, four with other diagnoses, and 14 with unknown diagnoses). Thus, despite the absence of controlled data, there might be an association between infliximab treatment and reactivation of tuberculosis. This potential risk should be considered before starting infliximab therapy. In particular, the development of a case of tuberculosis is a cause for concern. Since becoming widely available in 1998, infliximab has been given to about 175,000 patients, and 101 cases of tuberculosis have been reported (62 patients with rheumatoid arthritis, 21 with Crohn’s disease, four with other diagnoses, and 14 with unknown diagnoses). Thus, despite the absence of controlled data, there might be an association between infliximab treatment and reactivation of tuberculosis. This potential risk should be considered before starting infliximab therapy.

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