CDP571, a humanised monoclonal antibody to tumour necrosis factor $\alpha$, for moderate to severe Crohn’s disease: a randomised, double blind, placebo controlled trial


**Background:** Targeting tumour necrosis factor $\alpha$ (TNF-$\alpha$) has demonstrated efficacy in Crohn’s disease. Aim: To evaluate CDP571, a humanised antibody to TNF-$\alpha$, for treating active Crohn’s disease.

**Patients:** A total of 396 patients with moderate to severe Crohn’s disease.

**Methods:** In a 28 week, randomised, double blind, placebo controlled trial, patients received intravenous CDP571 (10 mg/kg) or placebo every eight weeks to week 24. The primary outcome measure was clinical response (a decrease in the Crohn’s disease activity index (CDAI) to $\geq 100$ points or remission (CDAI score $\leq 150$ points)) at week 28. A secondary outcome measure was clinical response (using the same definition) at week 2.

**Results:** Clinical response occurred at week 28 in 80/263 (30.4%) CDP571 patients and 31/132 (23.5%) placebo patients ($p=0.102$). Clinical response at week 2 occurred in 90/263 (34.2%) CDP571 patients and 28/132 (21.2%) placebo patients ($p=0.011$). Post hoc exploratory subgroup analysis of 159 patients with baseline C reactive protein (CRP) $>10$ mg/l demonstrated significant differences between CDP571 and placebo in clinical response rates at weeks 2 (CDP571, 50/101 (49.5%); placebo, 9/58 (15.5%); $p<0.001$) and 28 (CDP571, 29/101 (28.7%); placebo, 7/58 (12.1%); $p=0.018$). Adverse events occurred at similar frequencies in both treatment groups.

**Conclusions:** CDP571 is modestly effective for short but not long term treatment of unselected patients with moderate to severe Crohn’s disease. The clinical relevance of this short term effect is unclear. Post hoc analysis suggests both short and long term efficacy of CDP571 in patients with elevated baseline CRP ($\geq 10$ mg/l). CDP571 is well tolerated.

**Methods**

**Selection of patients**

Eligible patients, who were at least 18 years of age and had moderate to severe Crohn’s disease as defined by a score of 220–450 (inclusive) on the Crohn’s disease activity index (CDAI), took part in the trial between 18 January 2001 and 15 May 2002. The diagnosis of Crohn’s disease had been made previously based on radiological, endoscopic, or histological evidence.

Patients with any of the following were not eligible for entry into the trial: infection of a fistula (abscess) (performance of a pelvic magnetic resonance imaging scan for evaluation of an abscess was not mandatory but was at the discretion of the investigator); ulcerative colitis; bowel perforation or evidence of non-inflammatory obstruction within the six months prior to study entry (fixed stenosis at endoscopy or radiography (performance of these diagnostic evaluations was not mandatory but was at the discretion of the investigator)); obstructive symptoms due to significant mechanical obstruction within the three months prior to study entry; small bowel resection $>100$ cm and/or more than the right colon resected; a functional colostomy; or an ileostomy. Patients were also not eligible if they had: a current infection with enteric pathogens; any serious intercurrent infection or other clinically important active disease (such as renal or hepatic disease) within the three months prior to study entry; current or previous malignancy (other than carcinoma of the cervix or basal cell carcinoma successfully treated $>5$ years prior to study entry); current or previous bowel dysplasia within the five years prior to study screening (surveillance colonoscopy was not mandatory but was at the discretion of the investigator); or clinically apparent but unspecified secondary conditions.

**Abbreviations:** CDAI, Crohn’s disease activity index; CDR, complementarity determining region; CRP, C reactive protein; HACA, human antichimeric antibody; IBDQ, inflammatory bowel disease questionnaire; ITT, intention to treat; TNF-$\alpha$, tumour necrosis factor $\alpha$.
important allergies or multiple drug allergies. In addition, drug or alcohol abuse, significant abnormal haematology or biochemical values at study entry, or a history of or concurrent tuberculosis, hepatitis, or human immunodeficiency virus excluded patients from entry into the trial. Pregnant and lactating women were ineligible, as were patients who were uncooperative or unable to comply with study procedures. The institutional review board at each centre approved the study and all participants gave written informed consent.

Concomitant medications

Patients receiving prednisone/prednisolone for ≥4 weeks at a stable dose (maximum allowed dose 20 mg/day for ≥2 weeks) were eligible for entry into the trial. Similarly, patients receiving budesonide for ≥4 weeks at a stable dose (maximum allowed dose 6 mg) for ≥2 weeks could also be enrolled into the study. Patients treated with parenteral corticosteroids or corticosteroids within four weeks and those in whom corticosteroid treatment was discontinued within two weeks were not eligible. Treatment with azathioprine or 6-mercaptopurine at a stable dose for ≥16 weeks, or methotrexate at a stable dose for 12 weeks, was permitted. Patients who discontinued these agents within the four weeks prior to study entry were ineligible. Receipt of sulphasalazine, mesalamine, or balsalazide at a stable dose for ≥12 weeks was permitted, as was antibiotic treatment for Crohn’s disease at a stable dose for ≥8 weeks (provided that the patient agreed to continue the antibiotic during screening and throughout the 28 week trial). Patients who had received sodium cromoglycate, mycophenolate, or cyclosporin within four weeks of study commencement were excluded, as were those who had been treated with more than four doses of opioid containing analgesics or non-steroidal anti-inflammatory drugs (including cyclooxygenase 1 and 2 inhibitors) within two weeks. Taking certain opioids (loperamide, diphenoxylate, codeine) for the control of diarrhoea was permitted during the seven days before each visit. At each visit, a

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 132)</th>
<th>CDP571 (n = 263)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease site (n (%))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileum</td>
<td>25 (18.9)</td>
<td>45 (17.1)</td>
</tr>
<tr>
<td>Ileocolon</td>
<td>71 (53.8)</td>
<td>145 (55.1)</td>
</tr>
<tr>
<td>Colon</td>
<td>35 (26.5)</td>
<td>72 (27.4)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Fistula (n (%))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Open or draining perianal</td>
<td>26 (19.7)</td>
<td>60 (22.8)</td>
</tr>
<tr>
<td>or abdominal enterocutaneous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>fistula</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous intestinal resection (n (%))</td>
<td>43 (32.4)</td>
<td>106 (40.3)</td>
</tr>
<tr>
<td>CDAI score (mean (SD))</td>
<td>301 (61)</td>
<td>297 (63)</td>
</tr>
<tr>
<td>IBDD score (mean (SD))</td>
<td>124 (28)</td>
<td>129 (29)</td>
</tr>
<tr>
<td>CRP concentration (mg/l)</td>
<td>7.5 (5.6–10.0)</td>
<td>6.7 (5.5–8.0)</td>
</tr>
<tr>
<td>Concomitant medications (n (%))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids (includes budesonide)</td>
<td>54 (40.9)</td>
<td>109 (41.4)</td>
</tr>
<tr>
<td>Azathioprine or 6-mercaptopurine</td>
<td>36 (27.3)</td>
<td>81 (30.8)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>4 (3.0)</td>
<td>9 (3.4)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>18 (13.6)</td>
<td>39 (14.8)</td>
</tr>
<tr>
<td>5-Aminosalicylates*</td>
<td>76 (57.6)</td>
<td>157 (59.7)</td>
</tr>
<tr>
<td>One or more of 1, 2, or 3</td>
<td>77 (58.3)</td>
<td>154 (58.6)</td>
</tr>
<tr>
<td>One or more of 1, 2, 3, or 4</td>
<td>82 (62.1)</td>
<td>160 (60.8)</td>
</tr>
<tr>
<td>Past anti-TNF-α therapy (n (%))</td>
<td>28 (21.2)</td>
<td>63 (24.0)</td>
</tr>
</tbody>
</table>

*Mesalamine, sulphasalazine, and 5-ASA.
Outcomes and statistical analysis

The intention to treat (ITT) population included all patients who were evaluated at the screening and baseline visits and who received at least one dose of study medication. The primary efficacy variable was the percentage of patients who showed clinical response (a decrease in CDAI score of ≥100 points from baseline or remission (CDAI score ≤150)) at week 28. The major secondary efficacy variable was the percentage of patients who showed clinical response at week 2. Other secondary efficacy variables included: (1) percentage of patients who showed a clinical response at weeks 4, 8, 12, 16, and 24; (2) percentage of patients who were in clinical disease remission (CDAI score ≤150) at weeks 2, 4, 8, 12, 16, 24, and 28; (3) percentage of patients who showed a decrease in CDAI score of ≥70 points at weeks 2, 4, 8, 12, 16, 24, and 28; (4) CDAI and IBDQ scores at weeks 2, 4, 8, 12 (CDP571 only), 16, 24, and 28; (5) percentage of patients in the subgroup with fistulae who showed closure of at least 50% and 100% of fistulae at any visit and on two consecutive visits over a six week period, closure being defined as no drainage on gentle compression; and (6) CRP concentrations at weeks 4, 8, 16, and 28. Safety endpoints were: (1) adverse events; (2) laboratory data; and (3) the presence of antibodies to CDP571 at weeks 0, 8, 16, and 24. A post hoc exploratory analysis was performed to test the hypothesis that elevated baseline CRP concentration (CRP ≥10 mg/l) might be a predictor of response to CDP571, as measured by the percentage of patients who showed clinical response. We also performed exploratory comparisons to determine the impact of concomitant therapy with azathioprine or 6-mercaptopurine, concomitant therapy with corticosteroids, and past therapy with infliximab on the percentage of patients who showed clinical response at weeks 2, 4, 8, 12, 16, 24, and 28.

The percentages of patients who showed a clinical response (decrease in CDAI score of ≥100 points or achieved remission (CDAI ≤150)), a decrease in CDAI score of ≥70 points (secondary end point), or who were in clinical disease remission (CDAI score ≤150) at weeks 2, 4, 8, 12, 16, 24, and 28 were summarised and compared between treatment groups using the Mantel-Haenszel test, adjusting for steroid and/or immunosuppressant and/or antibiotic use. CDAI scores, IBDQ scores, and CRP concentrations were summarised at weeks 2 (CDAI, IBDQ only), 4, 8, 12 (CDP571 only), 16, 24 (CDP571 and IBDQ only), and 28, compared with baseline values, and presented graphically. Of the subgroup of patients with fistulae, the percentage showing closure of at
All statistical tests were two sided and p values carried forward approach was not used for these analyses. Scores, IBDQ scores, and CRP values, data for patients who were performed with Fisher’s exact test. For analyses of CDAI concomitant therapy with corticosteroids, and antecedent ant therapy with azathioprine or 6-mercaptopurine, concomitant therapy with corticosteroids, and antecedent therapy with infliximab on the percentage of patients who showed clinical response at weeks 2, 4, 8, 12, 16, 24, and 28 were performed with Fisher’s exact test. For analyses of CDAI scores, IBDQ scores, and CRP values, data for patients who were lost to follow up or who withdrew from the study because of deterioration in their condition or adverse events were censored at the time of the last study visit (a last value carried forward approach was not used for these analyses). All statistical tests were two sided and p values <0.05 were considered statistically significant.

Sample size
We estimated that 256 patients were needed in the CDP571 group and 128 patients in the placebo group in order to have 90% power to detect a true difference in the proportion of patients who achieved clinical response (reduced their CDAI score by ≥100 points or achieved remission (CDAI score ≤150)) at week 28, assuming a true difference of 12.5% and a placebo rate of 7%. We planned to recruit a total of 384 patients.

RESULTS
Four hundred and eighty seven patients were screened, of whom 396 were randomised. The number of patients randomised in each country was as follows: Australia 85 (21.5%), Bulgaria 14 (3.5%), Canada 44 (11.1%), Czech Republic 28 (7.1%), Hungary 42 (10.6%), Poland 38 (9.6%), and the USA 145 (36.6%). Of the 396 randomised patients, 133 received placebo and 263 received CDP571. One patient was randomised to receive CDP571 but actually received placebo; this patient was included in the placebo group for the safety population and in the CDP571 group for the other analyses. No post baseline efficacy data were obtained for one of the patients and the remaining 395 patients comprised the ITT population. Baseline characteristics of the two groups of patients were similar (table 1). The disposition of participating patients is shown in fig 1.

Clinical effectiveness
The percentage of patients who had a clinical response (decrease in CDAI score of ≥70 points at weeks 2, 4, 8, 12, 16, 24, and 28) was not significantly higher in patients treated with CDP571 (80/263; 30.4%) than in those who received placebo (31/132, 23.5%; p = 0.102). However, at week 2 (major secondary end point) and week 4 (secondary end point) there were significant differences in clinical response rates in favour of CDP571 (fig 2). At week 2, clinical response occurred in 90/263 (34.2%) CDP571 patients and 28/132 (21.2%) placebo patients (p = 0.011). There were no differences in clinical response between the treatment groups at weeks 8, 12, 16, and 24. The percentages of patients who achieved clinical remission (CDAI score ≤150) at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were similar in the two treatment groups (table 2). The percentages of patients who achieved a decrease in CDAI score of ≥70 points at weeks 2 and 4 (secondary end points) were significantly higher in patients treated with CDP571 compared with patients treated with placebo but there were no significant differences at weeks 8, 12, 16, 24, and 28 (secondary end points) (table 2). Mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 but these differences were not significant (fig 3A). The mean IBDQ scores at weeks 2, 4, 8, 16, 24, and 28 (secondary end points) were higher in patients treated with CDP571 but lower in those who received placebo (fig 3B). The mean CRP values at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3C). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3D). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3E). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3F). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3G). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3H). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3I). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3J). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3K). The mean CDAI scores at weeks 2, 4, 8, 12, 16, 24, and 28 (secondary end points) were lower in patients treated with CDP571 compared with patients treated with placebo but these differences were not significant (fig 3L).
any visit, closure of at least 50% of fistulae for any two consecutive visits over six weeks, closure of 100% of fistulae at any visit, and closure of 100% of fistula for any two consecutive visits over six weeks (secondary end points) were similar in the two treatment groups (table 2). Based on the confidence intervals, the geometric mean CRP concentrations at weeks 4 and 28 (secondary end points) were lower in patients treated with CDP571 than in placebo treated patients (fig 3C).

Exploratory comparisons were made to determine the impact of an elevated baseline CRP concentration (>10 mg/l), concomitant therapy with azathioprine or 6-mercaptopurine, concomitant therapy with corticosteroids, and antecedent therapy with infliximab on the percentage of patients who showed a clinical response (decrease in CDAI score of >100 points or who achieved remission (CDAI ≤150)) at weeks 2, 4, 8, 12, 16, 24, and 28. Concomitant therapy with azathioprine or 6-mercaptopurine, concomitant therapy with corticosteroids, and antecedent therapy with infliximab did not influence the percentage of patients who showed a clinical response at weeks 2, 4, 8, 12, 16, 24, and 28 (data not shown). There were no significant differences in the outcomes for any of the primary or secondary end points according to the stratification criteria (concomitant therapy with at least one of: corticosteroids, azathioprine, 6-mercaptopurine, methotrexate, or antibiotics). Likewise, multivariate analyses identified no interactions between the treatment response and any of the baseline characteristics of the patients.

Adverse events
The two treatment groups were similar with regard to the percentages of patients with: any adverse event; serious adverse events; adverse events leading to withdrawal from the study; severe adverse events; adverse events probably related to the study medication; and adverse events definitely related to the study medication (table 3). The most common (75%) adverse events were generally similar between the two treatment groups (table 3). The percentage of patients with infusion reactions (defined as adverse events occurring within two hours of the start of the study medication infusion) was greater in patients treated with CDP571 (20.5%) compared with placebo (10.5%) (table 3). The percentage of patients with infections was the same in the two treatment groups (29.3%) (table 3). One patient in the placebo group developed adenocarcinoma, with the rectum being the most likely primary site. One patient in the CDP571 group developed cervical cancer. This was discovered incidentally (CIN stage II) and was considered to be unrelated to the study drug. No patient developed tuberculosis or opportunistic infections, and no patient died from any cause in either treatment group during the study. The frequency of anti-idiotypic antibodies to CDP571 was (10.9%) 27/247 in the CDP571 treatment group. The frequency of these antibodies was (4.7%) 4/86 in patients treated with CDP571 who received concomitant antimetabolite therapy compared with (14.3%) 23/161 in those who did not receive these drugs. There were no clinically significant changes in laboratory values in either treatment group.

Figure 3 Mean scores or values at each study visit, according to treatment group. (A) Crohn’s disease activity index (CDAI) scores; (B) inflammatory bowel disease questionnaire (IBDQ) scores; and (C) C reactive protein (CRP) values (geometric means). Error bars represent SD values (A, B) or 95% confidence intervals (C).
Figure 4  Percentages of patients with Crohn’s disease at each study visit who experienced a clinical response (decrease in Crohn’s disease activity index (CDAI) score >100 points or who achieved clinical remission (CDAI score <150 points)) according to baseline C reactive protein (CRP) concentration. (A) Patients with a baseline CRP concentration >10 mg/l; (B) patients with a baseline CRP <=10 mg/l.

Table 3  Adverse events in the two treatment groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>No of patients (%)</th>
<th>CDP571 (n = 133)</th>
<th>Placebo (n = 263)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with adverse events</td>
<td>96 (72.2)</td>
<td>200 (76.0)</td>
<td></td>
</tr>
<tr>
<td>Patients with serious adverse events</td>
<td>18 (13.5)</td>
<td>27 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Patients with adverse events leading to withdrawal</td>
<td>26 (19.5)</td>
<td>37 (14.1)</td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Patients with severe adverse events</td>
<td>22 (16.5)</td>
<td>46 (17.5)</td>
<td></td>
</tr>
<tr>
<td>Patients with probably drug related adverse events</td>
<td>3 (2.3)</td>
<td>17 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Patients with definitely drug related adverse events</td>
<td>1 (0.8)</td>
<td>8 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Adverse events occurring in &gt;=5% of patients in at least one of the treatment groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>39 (29.3)</td>
<td>77 (29.3)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>20 (15.0)</td>
<td>32 (12.2)</td>
<td></td>
</tr>
<tr>
<td>Crohn’s disease aggravated</td>
<td>14 (10.5)</td>
<td>22 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>8 (6.0)</td>
<td>20 (7.6)</td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>7 (5.3)</td>
<td>19 (7.2)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6 (4.5)</td>
<td>17 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>8 (6.0)</td>
<td>13 (4.9)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>10 (7.5)</td>
<td>10 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>7 (5.3)</td>
<td>10 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>8 (6.0)</td>
<td>7 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Patients with adverse events occurring within 2 hours of the start of the infusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>14 (10.5)</td>
<td>54 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>0 (0)</td>
<td>7 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (0.8)</td>
<td>5 (1.9)</td>
<td></td>
</tr>
<tr>
<td>Dermatitis</td>
<td>0 (0)</td>
<td>4 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>4 (3.0)</td>
<td>2 (0.8)</td>
<td></td>
</tr>
</tbody>
</table>
CDP571 for moderate to severe Crohn’s disease

DISCUSSION

We found CDP571 to be effective for inducing a short term clinical response at weeks 2 and 4 (secondary end points) in unselected patients with moderate to severe Crohn’s disease. However, the clinical relevance of this short term response, which was not maintained through to week 28 (primary end point), is unclear. This lack of sustained efficacy in the overall study patient population was confirmed by failure to achieve statistical significance for most other secondary end points. Thus although CDP571 can induce a modest short term clinical response, it does not appear to be suitable for the long term treatment of unselected patients with moderate to severe Crohn’s disease. It should however be borne in mind that this study was concerned with acute treatment of patients with Crohn’s disease and a primary end point based on the results at week 28 may not be the most appropriate end point in such an instance.

Post hoc exploratory analysis was performed to determine whether patients with elevated baseline CRP concentrations had greater rates of clinical response than the overall patient population. Among these selected patients with elevated baseline CRP (>10 mg/l), the rates of clinical response in CDP571 treated patients were significantly greater than in the placebo treated group at weeks 2, 12, 16, 24, and 28 (with a trend towards statistical significance at week 4). There were no significant differences in clinical response rates between the treatment groups throughout the 28 week study for patients in whom the baseline CRP concentration was <10 mg/l. Interestingly, a feature of this analysis is the lower placebo response in patients with CRP >10 mg/l compared with those in whom baseline concentrations of this protein were not elevated. It is possible that patients with higher levels of CRP may be less likely to exhibit spontaneous improvement.

Analysis of the adverse events associated with the administration of CDP571 showed that it was well tolerated. Indeed, combining the results of the trial described here with five other published studies11–13 17 18 gives a total of 960 patients with Crohn’s disease who have been treated with either CDP571 or placebo. The combined safety data from these six studies, as well as those from two open label extension studies, shows CDP571 to have a favourable safety profile similar to the results of this study (Celltech, Slough, UK, data on file). In addition, CDP571 appears to have a relatively low immunogenicity profile. The frequency of antidrug antibodies to CDP571 (10.9%) compares favourably with results that have been reported for infliximab, where as many as 60% of retreated patients have developed antibodies.1 6 7 These contrasting results demonstrate the benefits of using a “humanised” anti-TNF-α antibody.

In conclusion, CDP571 is modestly effective for short but not long term treatment of unselected patients with moderate to severe Crohn’s disease. The clinical relevance of this short term effect is unclear. Subgroup analysis suggests both short and long term efficacy of CDP571 in selected patients with elevated baseline CRP (>10 mg/l). CDP571 is well tolerated.

ACKNOWLEDGEMENT

Supported by a research grant from Celltech, Slough, UK.

Authors’ affiliations

W J Sandborn, Mayo Clinic, Rochester, Minnesota, USA
B G Feagan, University of Western Ontario, London, Ontario, Canada
G Radford-Smith, Royal Brisbane Hospital, Herston, Queensland, Australia
A Kovacs, Peterfy Hospital, Budapest, Hungary

R Enns, St Paul’s Hospital, University of British Columbia, Vancouver, British Columbia, Canada
A Innes, J Patel, Celltech Research and Development, Slough, UK

Conflicts of interest: W Sandborn and B Feagan have served as consultants for Celltech. A Innes is an employee of Celltech. J Patel is a former employee of Celltech.

APPENDIX

INVESTIGATORS

Australia

1. Brett Jones, Division of Medicine, the Liverpool Hospital, Liverpool, NSW, Australia
2. Peter Gibson, Department of Medicine, Royal Melbourne Hospital, Parkville, Victoria, Australia
3. Bill Connell, St Vincent’s Hospital Melbourne, Fitzroy, Victoria, Australia
4. Graham Radford-Smith, Department of Gastroenterology, Royal Brisbane Hospital, Herston, Queensland, Australia
5. Timothy Florin, Mater Misericordiae Hospital, South Brisbane, Queensland, Australia
6. Peter Bampton, Flinders Medical Center, Bedford Park, South Australia, Australia
7. Stephen Riordan, Prince of Wales Hospital, Randwick, New South Wales, Australia
8. Doug Taupin, the Canberra Hospital, Garran, Australian Capital Territory, Australia
9. Andrew Hallam, Peninsula Specialist Centre, Kippa-Ring, Queensland, Australia
10. John Masson, Department of Endoscopy, Townsville General Hospital, Townsville, Australia
11. Ian Lawrance, Fremantle Hospital, Fremantle, Western Australia, Australia
12. Grant Phelps, Ballarat Gastroenterology, Ballarat, Victoria, Australia
13. Peter Katelaris, Concord Repatriation Hospital, Concord, New South Wales, Australia

Bulgaria

1. Z Krastev, Clinic of Gastroenterology, Medical University-Sofia, Sofia, Bulgaria
2. S Stoynov, DUB “Tzarita Ioana” Sofia, Bulgaria

Canada

1. Jeffrey Baker, St Michael’s Hospital, Toronto, ON, Canada
2. Charles Bernstein, Health Sciences Centre, Winnipeg, MB, Canada
3. Laurington DaCosta, Hotel-Dieu Hospital, Kingston, ON, Canada
4. Robert Enns, St Paul’s Hospital, Vancouver, BC, Canada
5. Brian Feagan and James Gregor, London Health Sciences Centre, London, ON, Canada
6. David A Lloyd, St Joseph’s Health Care London, London, ON, Canada
7. Lloyd Sutherland, University of Calgary, Health Science Centre, Calgary, AB, Canada

Czech Republic

1. Petr Zdenek, 1st Internal Clinic-Gastroenterology, Faculty Hospital, Lochotin, Czech Republic

www.gutjnl.com
REFERENCES


USA

1. Stephen J Bickston, University of Virginia Health System, Charlottesville, VA, USA

2. Jeffery Breiter, Center for Medical Research LLC, Manchester, CT, USA

3. Florian Cortese, Mercury Street Medical Group, Butte, MT, USA

4. Lance DeFrancisco, Altoona, PA, USA

5. Willem de Villiers, Internal Medicine and GI, UK Chandler Medical Center, Lexington, KY, USA

Poland

1. Krzysztof Marlicz, Department of Gastroenterology, Pomeranian Medical Academy, Szczecin, Poland

2. Jan Dzienszewski, Gastroenterology Clinic, Brodnicki Hospital, Warsaw, Poland

3. Grazyna Rydzewska, Gastroenterology Clinic, Central Clinical Hospital of Ministry of Internal Affairs, Warsaw, Poland

4. Leszek Paradowski, Department of Gastroenterology, Medical Academy, Wroclaw, Poland

5. Krzysztof Linke, Internal Diseases Institute, Poznan, Poland

6. Józef Bogdal, Department of Gastroenterology, Collegium Medicum of the Jagiellonian University, Cracow, Poland

7. Andrzej Krysiewski, Institute of Internal Medicine, Medical Academy of Gdansk, Gdansk, Poland

8. Professor Krasnodelbski, Surgery Gastroenterology Department, Warsaw, Poland

Hungary

1. Miklos Udvardy, University Clinic (Debrecen), Debrecen, Hungary

2. Tamas Zagoni, I Medical Department, Semmelweis University, Szentkiralyi, Budapest, Hungary

3. Janos Lonovics, I Medical Department, Szent Gyorgyi Albert University, Szeged, Hungary

4. Gyorgy Nagy, II Medical Department, BAZ County Hospital, Miskolc, Hungary

5. Laszlo Lakatos, I Medical Department, Veszprem County Hospital, Veszprem, Hungary

6. Agota Kovacs, Peterfy Hospital, I Internal Medicine Department, Budapest, Hungary

Czech Republic

1. Josef Hajek, Internal Clinic B, Internal Department 3, Pardubice, Czech Republic

2. Miroslava Volfova, Faculty Hospital Hradec Králové, Hradec Králové, Czech Republic

3. Ivan Gregar, Faculty Hospital-Internal Clinic, Olomouc, Czech Republic

4. Milan Lukas, General Faculty Hospital, Prague, Czech Republic

5. Willem de Villiers, Internal Medicine and GI, UK Faculty Hospital-Internal Clinic, Olomouc, Czech Republic

6. Jiri Stehlík, Gastroenterology, Internal Clinic, Masaryk’s Hospital, Ústí nad Lbem, Czech Republic

7. Miroslav Zavoral, Central Military Hospital, Internal Department of Internal Medicine, Prague, Czech Republic

8. Libor Gabalec, District Hospital Ústí nad Orlicí, Department of Internal Medicine, Ústí nad Orlicí, Czech Republic

9. Milan Lukas, IV Internal Clinic Gastroenterology, General Faculty Hospital, Prague, Czech Republic

10. Mark Griffin, Gastroenterology Specialties, Lincoln, NE, USA

11. Stephen B Hanauer, University of Chicago, Chicago, IL, USA

12. Robert Hardli, Chevy Chase Clinical Research, Chevy Chase, MD, USA

13. William R Harlan, Asheville Gastroenterology Associates, Asheville, NC, USA

14. Gary R Lichtenstein, University of Pennsylvania Hospital, Philadelphia, PA, USA

15. Donald C Lipkis, Institute of Healthcare Assessment, San Diego, CA, USA

16. Gregory Mula, New Orleans Clinical Trial Management, Covington, LA, USA

17. Frederick Opper, Hanover Med Spec PA, Wilmington, NC, USA

18. Daniel Pambianco, Charlottesville Medical Research, Charlottesville, VA, USA

19. William Priebt, Tacoma Digestive Disease Research, Tacoma, WA, USA

20. Ron Pruitt, Nashville Medical Research Institute, Nashville, TN, USA

21. Michael Safidi, Consultants for Clinical Research, Cincinnati, OH, USA


23. David Stanton, Community Clinical Trials, Orange, CA, USA

24. Douglas Wolf, Atlanta Gastroenterology Associates, Atlanta, GA, USA
EDITOR’S QUIZ: GI SNAPSHOT

Robin Spiller, Editor

Large abdominal mass in Crohn’s disease

Clinical presentation
A 49 year old male patient with a 23 year history of Crohn’s disease was admitted to our hospital for the appearance of an abdominal mass in the right upper quadrant of the abdomen. He reported the occurrence of abdominal distension and fullness for two weeks. Two years before he underwent ileocolic resection and six months later surgical treatment of a perianal localisation of his Crohn’s disease.

At admission, a large abdominal mass was found on physical examination. Pain was absent. Routine blood examination did not reveal abnormal values. Tumoral marker levels, including CEA and CA 19.9, were negative.

An abdominal ultrasound revealed a large (13 cm in diameter) right upper quadrant mass. A computerised tomography scan showed a bulky abdominal neoplasm, with sharp tumour margins and homogeneous density before and after intravenous contrast delivery.

Question
A small bowel radiography was also performed (fig 1). What is the diagnosis?

See page 1503 for answer

This case is submitted by:

M Caricato, F Ausania, D Borzomati, S Valeri, R Coppola
Department of Surgery, Campus Bio-Medico University, Rome, Italy

A Verzì
Department of Surgical Pathology, Campus Bio-Medico University, Rome, Italy

G Tonini
Department of Oncology, Campus Bio-Medico University, Rome, Italy

Figure 1 Small bowel radiography.

Correspondence to: Dr M Caricato, Department of Surgery, Campus Bio-Medico University, Via Longoni 47, 00155 Rome, Italy; m.caricato@unicampus.it

doi: 10.1136/gut.2003.035956