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Observational study on the efficacy of adalimumab for the treatment of ulcerative colitis and predictors of outcome

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Abstract

Background: Information on efficacy and predictors of response to adalimumab in ulcerative colitis (UC) clinical practice is limited.
Aim: Assessment of response to adalimumab and its predictors in an observational cohort study.
Methods: Retrospective cohort study based on data obtained from ENEIDA registry. All patients diagnosed with UC treated with adalimumab were included. Response to adalimumab was

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evaluated at weeks 12, 28, and 54 according to the partial Mayo score, and requirement of colectomy until end of follow-up.
Results: 48 patients with UC treated with adalimumab were included; 39 (81.3%) had previously received infliximab. Response rates at weeks 12, 28 and 54 were 70.8%, 43.2% and 35% respectively. Response to prior treatment with infliximab was the only predictive factor of response to adalimumab at week 12, which was obtained in 90% of infliximab remitters, 53.8% of responders and 33.3% of primary non-responders (p=0.01).
Colectomy was required in 11 patients (22.9%), after a mean time of 205 days. The only clinical independent predictor of colectomy was non-response to adalimumab at week 12: colectomy rates were 5/34 (14.7%) in responders and 6/14 (42.9%) in non-responders (p=0.035), time free of colectomy was significantly reduced in non-responders (p=0.01). Adalimumab withdrawal due to adverse events occurred in 4.2% of patients.
Conclusion: This study shows that adalimumab is an effective treatment in patients with UC. If used as a second anti-TNF, previous achievement of remission with the first anti-TNF predicts response, and failure to achieve response at week 12 predicts colectomy.

1. Introduction

Ulcerative colitis (UC) can be adequately treated with 5-aminosalycilic acid preparations in about half of the patients. However, those requiring corticosteroids at any point face a severe disease course over time, with high requirements of immunosuppressant treatment and colectomy[1] and high cost for the healthcare system.[2] Treatment with the anti-TNF antibody infliximab has proven effective for induction and maintenance of remission in moderate to severe UC[3] as well as in steroid refractory severe UC,[4] resulting in a reduction on the requirement for colectomies.[3] More recently the efficacy of a second anti-TNF antibody, adalimumab, a fully human IgG1, for induction and maintenance of remission in UC has been demonstrated in two phase III trials.[5,6] Addition of this drug to the limited therapeutic armamentarium available for UC expands treatment choices of anti-TNF therapy to a subcutaneous drug, which may be particularly advantageous for patients with difficult venous access, and offers an alternative for patients loosing response to infliximab.

Since the publication of the results of the first adalimumab randomized controlled trials in UC,[5] some concerns raised on the efficacy of the drug that might be related in part to dosing and in part to inclusion of a proportion of cases with previous failure to infliximab. In this regard, observational data on the use of adalimumab for treatment of UC derived from clinical practice may be relevant for positioning the drug in the therapeutic algorithm of UC. Prior observational studies suggest that adalimumab is efficacious for treatment of UC,[7–10] even in the difficult to treat population with previous failure to infliximab.

In the current observational study we analyzed the data of the Spanish inflammatory bowel disease (IBD) database on the use of adalimumab in UC previous to marketing approval. The primary objectives of the present study were to determine the efficacy of adalimumab for the induction and long term maintenance of remission in UC and to determine the need for colectomy after adalimumab treatment. Secondary objectives included the identification of predictors of clinical response to adalimumab and predictors of colectomy, based on demographic data, disease characteristics, concomitant medication and previous response to infliximab; to assess the need for dose escalation and its efficacy, and to assess adalimumab safety profile in clinical practice.

2. Patients and methods

This is a multicenter retrospective cohort study. Demographic, clinical and therapeutic data were obtained from the multicenter Spanish database of patients with IBD ENEIDA (Estudio Nacional en Enfermedad Inflamatoria intestinal sobre Determinantes genéticos y Ambientales). This project is a large prospectively maintained database that captures clinical response to IBD therapies, adverse events, and surgeries. The use of the database was approved by the ethics committee of each participating center, and the study was approved by the committee of the Spanish IBD organization (GETECCU: Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa) in 2009. All patients included in ENEIDA signed an informed consent authorizing the use of their clinical data for research purposes. For the sake of data completeness and accuracy, data on the patients included was double-checked and updated by each participating center.

Patients diagnosed with UC who had received at least one dose of adalimumab between June 2009 and May 2011, and with a minimum follow-up of 12 weeks were included. Demographic data, disease characteristics, prior and concomitant therapies, and clinical data at the time of adalimumab initiation and response, as well as adverse events were registered. Disease extent was defined according to the Montreal classification. Clinical activity was evaluated according to the Mayo score (remission defined as Mayo score ≤ 2 with no individual subscore >1; response defined as decrease in Mayo score ≥ 3 points and $\geq 30\%$ from baseline and a decrease in the rectal bleeding subscore ≥ 1 or an absolute rectal bleeding subscore of 0 or 1).[3] The partial Mayo score was used when endoscopy was not available; the criterion for remission was a score ≤ 1, and the criterion for response was the same as for the full Mayo score. The therapeutic efficacy was evaluated at weeks 12, 28, and 54. Need for colectomy at any time since the administration of the first dose was recorded.