1.0 Abstract

Title: Post-marketing Observational Study to Evaluate the Safety and Efficacy of HUMIRA (Adalimumab SC) for the Treatment of Moderate to Severe Crohn's Disease in Daily Clinical Practice

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Keywords

Adalimumab, Crohn's disease, observational study, Crohn's Disease Activity Index, Short Inflammatory Bowel Disease Questionnaire

Rationale and Background

Crohn's disease (CD), a chronic intestinal inflammatory disorder associated with increased morbidity and mortality and reduced health-related quality of life (HRQOL), affects approximately 0.3% of the German population. Adalimumab was approved for use in patients with CD in Europe in 2007. The goal of this study was to document the effectiveness and safety of adalimumab as used in daily clinical practice to treat adult German patients with CD.

Research Question and Objectives

The research question in this study was whether the effectiveness and safety of adalimumab was maintained during long-term therapy of patients with CD in routine clinical practice in Germany.

Primary study objectives were to evaluate:

- Effectiveness in reducing disease activity as assessed by the Crohn's Disease Activity Index (CDAI)
- Effectiveness in improving HRQOL as assessed by the Short Inflammatory Bowel Disease Questionnaire (SIBDQ)
- Safety as assessed by reports of adverse events (AEs)

Secondary objectives included changes in the Harvey-Bradshaw Index (HBI), inflammatory markers, and socioeconomic outcomes. Exploratory regression analyses were conducted to determine predictors of response to therapy at Month 12.

Study Design

This study was a 60-month prospective, multicenter, observational study of adalimumab in adult patients with CD who resided in Germany. Visits were scheduled every 3 months for the first year and every 6 months thereafter. Patients continued in the study for a maximum of 60 months or until discontinuation from adalimumab therapy.

Setting

Patients for this study were enrolled by 319 clinicians throughout Germany, primarily gastroenterologists. Patients were seen during regular visits for routine clinical care.

Subjects and Study Size, Including Dropouts

The safety set consisted of 4107 patients who received at least one dose of adalimumab. The full analysis set (FAS) consisted of 1621 patients with adequate data to evaluate adalimumab effectiveness. At 60 months, 263 patients (6.4%) remained in the safety set and 79 (4.9%) in the FAS. Approximately 65% of patients who discontinued were lost to follow-up for unknown reasons.

Variables and Data Sources

Case report forms were the primary data source. Key effectiveness variables included CDAI, SIBDQ, HBI, inflammatory markers, and socioeconomic outcomes.

Results

Adalimumab treatment was associated with marked reductions in disease activity and improvements in HRQOL in the FAS. Beneficial effects were observed at the earliest visit (Month 3) and maintained for 60 months in patients remaining on therapy. Improvements were also observed in inflammatory markers and socioeconomic outcomes. Higher disease activity at baseline was a positive predictor of therapeutic response at Month 12, while negative predictors included smoking, age, use of 5-aminosalicylic acid/sulfasalazine at baseline, and number of CD-related operations. In the safety set, 16.7% of patients experienced an AE and 13.34% experienced a serious AE (SAE). The most common AE by system organ class was infections and infestations and the most common SAE was gastrointestinal disorders, mostly related to CD complications. Two deaths were reported during the study. AE reports were consistent with the known adalimumab safety profile and no new safety signals were observed.

Discussion

Adalimumab was effective in reducing CD symptoms and generally safe and well-tolerated during up to 60 months of therapy. Study limitations include the high discontinuation rate and the potential for responder bias. This observational study supports the conclusion that adalimumab is effective and safe during long-term routine care of adult patients with CD in Germany.

Marketing Authorisation Holder(s)

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