1.0 Abstract

Title:

Effectiveness and Safety of Adalimumab in Patients with Rheumatoid Arthritis in Routine Clinical Practice

05 December 2013

Author: Dr. med. Hans-Peter Tony

[redacted]

Keywords: redacted information 03Jul2014

Adalimumab, rheumatoid arthritis, adverse events, effectiveness, disease activity

Rationale and Background:

Rheumatoid arthritis (RA) affects approximately 2.5% of adults in Germany. Non-interventional observational studies supplement clinical trials by providing data on the real-world clinical activity of therapeutic agents such as adalimumab.

Research Question and Objectives:

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

Primary study objectives were:

- Effectiveness (as assessed by changes in Disease Activity Score-28 joints [DAS28] scores and clinical remission rate)
- Safety (as assessed by reports of drug-related AEs)

Secondary objectives included changes in:

- DAS28 response as assessed by the critical difference (d_{crit}), a criterion for therapeutic response in an individual patient, and changes in disease activity classifications
- Additional disease activity parameters
- Patient-reported outcomes, including function and pain
- Socioeconomic parameters, including sick leave and hospitalization
- RA-related concomitant medication

Exploratory analyses included:

- Patient and disease parameters influencing therapeutic response at Month 6
- Subgroup analysis of DAS28 response by number of previous biologic therapies

Study Design:

Prospective, multicenter, observational (case-only) non-interventional

Setting:

Routine clinical practice in Germany

Subjects and Study Size:

Adult RA patients: 4208 subjects in safety set and 2950 subjects in full analysis set (FAS)

Variables and Data Sources:

Key variables: DAS28; AEs; patient-reported assessments of function (Funktionsfragebogen Hannover [FFbH]), global disease activity, pain, and fatigue; socioeconomic outcomes (days of impairment, sick leave, and in-patient hospitalization)

Data sources: Case report form (CRF)

Results:

Adalimumab treatment was associated with reductions in mean DAS28 and increases in clinical remission rates throughout 24 months of therapy. A therapeutic response (DAS28-d_{crit}) was achieved by 38.9% of patients at Month 3 and 61.9% at Month 24. Additional disease activity parameters, including joint counts and inflammatory markers, and patient-reported outcomes, including function and pain, also improved during therapy. Marked reductions were observed in days of impairment, sick leave, and hospitalization. Positive predictors of DAS28 response included higher baseline DAS28 and baseline MTX. The number of previous biologic agents was a negative predictor. A subgroup analysis showed that patients treated with previous biologic agents had a poorer response to adalimumab than patients with no previous biologic therapy. In the safety set, drug-related AEs were reported in 14.4% of patients and serious AEs (SAEs) in 5.8%. Four deaths occurred during the study. AE reports were consistent with the known adalimumab safety profile and no unexpected AEs were observed.

Discussion:

Data at 24 months were available for 1271 (43.1%) subjects in the FAS; 31.4% discontinued and 25.5% were lost to follow-up. Adalimumab showed consistent and sustained effectiveness throughout 24 months, although continued improvements at later time points may have been influenced by responder bias. The findings of this non-interventional study support the conclusion that adalimumab is effective and safe during long-term therapy of adult RA patients in Germany.

Marketing Authorization Holder:

AbbVie Ltd.

Names and Affiliations of Principal Investigators:

[redacted]

redacted information 03Jul2014