1.0 Abstract

Title: Safety and Effectiveness of Adalimumab in Patients with Ankylosing Spondylitis in Routine Clinical Practice

28 January 2015

Author: Dr. med. Frank Behrens [redacted] Germany

Keywords: Adalimumab, ankylosing spondylitis, adverse events, effectiveness, disease activity

Rationale and Background: Ankylosing spondylitis (AS) has been estimated to affect up to 0.5% of adults and results in severe disability in approximately 15% of patients. 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 of AS patients in routine clinical practice in Germany.

Primary study objectives were:

- Effectiveness (as assessed by changes in Bath AS Disease Activity Index [BASDAI] and Bath AS Functional Index [BASFI] values)
- Safety (as assessed by reports of drug-related adverse events [AEs])

Secondary objectives included changes in:

- Additional disease activity parameters, including joint involvement, extraspinal manifestations, and inflammatory markers
- Patient-reported outcomes, including global disease activity, fatigue, and pain
- The percentage of patients achieving Assessment of SpondyloArthritis international Society (ASAS) improvement and partial remission criteria
- Socioeconomic parameters, including impairment in daily activities, sick leave, and hospitalization
- Concomitant medication

Exploratory analyses included:

- Patient and disease parameters influencing changes in disease activity (BASDAI) or function (BASFI) at Month 12

Study Design: Prospective, multicenter, observational (case-only) non-interventional

Setting: Routine clinical practice in Germany

Subjects and Study Size: Adult AS patients: 4681 subjects in safety set and 3756 subjects in full analysis set (FAS; used for effectiveness analyses)

Variables and Data Sources:

Key variables: BASDAI; BASFI; AEs; joint counts, extraspinal manifestations, inflammatory markers; patient-reported outcomes (global disease activity, fatigue, pain, and morning stiffness); socioeconomic outcomes (days of impairment, sick leave, and in-patient hospitalization); concomitant medication

Data sources: Case report form

Results: Adalimumab treatment was associated with reductions in mean BASDAI and BASFI scores throughout 24 months in patients who continued on therapy. Additional disease activity parameters, including the mean number of tender and swollen joints, the presence of extraspinal manifestations, mean levels of inflammatory markers, and patient-reported outcomes, including global disease activity and pain, also improved during therapy. The proportion of patients achieving ASAS improvement and partial remission criteria increased during the 24-month period. Reductions were observed in days of impairment, sick leave, and hospitalization. Positive predictors of improvements in BASDAI at month 12 included the presence of dactylitis, higher baseline BASDAI, and human leukocyte antigen (HLA) B27. The strongest predictors of improvements in function (BASFI) at Month 12 were higher baseline BASFI, employment, and presence of HLA B27. In the safety set, drug-related AEs were reported in 23.5% of patients and serious AEs (SAEs) in 3.0%. The most common category of AE by system organ class was general disorders and the most common category of SAE was surgical and medical procedures. Six deaths occurred during this study (3 patients with heart conditions and 3 patients whose cause of death was not reported). AE reports were consistent with the known adalimumab safety profile and no unexpected AEs were observed.
Discussion: Data at 24 months were available for 1698 (45.2%) subjects in the FAS; 25.9% discontinued and 28.9% 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 AS patients in Germany.
Marketing Authorisation Holder: AbbVie Ltd.
Names and Affiliations of Principal Investigators: [redacted]