

1.0 Abstract

Title

Multi-country Post-Marketing Observational Study on Maintenance of Effectiveness of Adalimumab (Humira®) in Patients with Ankylosing Spondylitis and Psoriatic Arthritis

Keywords

Adalimumab, Humira®, Ankylosing Spondylitis, Psoriatic Arthritis, PMOS

Rationale and Background

Ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are the major subtypes of rheumatic diseases named as spondyloarthritis (SpAs). As data are lacking, there was a need to evaluate the current diagnostic and treatment practices in AS and PsA in Central and Eastern European Countries, with special focus on the use of conventional disease-modifying anti-rheumatic drugs (DMARDs) and biologic agents.

Clinical efficacy and safety of the recombinant, fully human, IgG1 monoclonal antibody adalimumab (Humira®) in the treatment of patients with AS or PsA have been demonstrated in several randomized, double-blind, controlled clinical trials. However, it was considered necessary to establish the long-term clinical outcomes of adalimumab therapy in routine clinical practice, in particular its sustained effectiveness, impact on extra-articular manifestations (EAMs), co-medication with non-steroidal anti-inflammatory drugs (NSAIDs) and work productivity.

The new Ankylosing Spondylitis Disease Activity Score (ASDAS) is not yet widely used in routine clinical practice, and there is a lack of clinical data in AS (and PsA) patients on adalimumab therapy, employing ASDAS as an outcome measure, particularly in comparison with the standard Bath Ankylosing Spondylitis Disease Activity Index (BASDAI).

Research Question and Objectives

The primary objective of this PMOS was to evaluate the long-term (12-month) effectiveness of treatment with adalimumab (Humira®) in patients with AS and PsA in routine clinical use in Central and Eastern European Countries.

The secondary objectives were to evaluate AS and PsA patients being routinely treated with adalimumab with regard to EAMs, functional status, the use of concomitant medication for AS and PsA, and work productivity impairment. In addition, the ASDAS (calculated by the sponsor) was to be employed in parallel with the standard BASDAI score to assess the effectiveness of adalimumab in treating axial symptoms.

Study Design

This prospective post-marketing observational study (PMOS) was performed in a multicenter, multi-country and single-arm design.

Setting

Participating countries were Czech Republic, Estonia, Hungary, Romania, Slovakia and Ukraine.

Subjects and Study Size, Including Dropouts

For 566 patients a baseline visit (V0) has been documented. 280 of these patients (49.5%) participated in Hungary, 180 (31.8%) in Romania, 40 (7.1%) in Slovakia, 30 (5.3%) in the Czech Republic, 22 (3.9%) in Estonia and 14 (2.5%) in Ukraine.

A total of 11 patients were lost to follow-up after the baseline visit and had no further entries regarding treatment with adalimumab (Humira®). These patients were excluded from the full analysis set (FAS) which accordingly comprises 555 patients. Based on the definitions from the study protocol, a total of 431 patients had axial symptoms (i.e. with a baseline value of the BASDAI > 4), therefore belong to the axial analysis set (AAS), and 148 patients had peripheral symptoms (i.e. with a baseline value of the DAS28 > 5.1), and

thus belong to the peripheral analysis set (PAS). There were 61 patients who had both axial and peripheral symptoms, (and were thus included in both data sets) and 37 patients from the FAS who did not fulfill any of the criteria for the two data sets (i.e. patients with baseline value of BASDAI ≥ 4 and DAS28 ≥ 5.1).

16.0% of the patients discontinued treatment with adalimumab (Humira®) during the study.

Variables and Data Sources

The following questionnaires were applied to assess disease activity:

- Ankylosing Spondylitis Disease Activity Index (ASDAS)
- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)
- Disease Activity Index/28 joints (DAS28)

The following questionnaires were applied to assess functionality:

- Health Assessment Questionnaire Disability Index (HAQ-DI)
- Bath Ankylosing Spondylitis Functional Index (BASFI)

For measuring of work productivity impairment the following questionnaire was used:

- Work Productivity and Activity Impairment - Specific Health Problem Questionnaire (WPAI-SHP)

Patient questionnaires have only been performed if they were part of the routine clinical practice.

Results

Treatment response was defined as a decrease in the BASDAI by at least 50% (BASDAI50) in case of axial symptoms, and as a decrease in the DAS28 by at least 1.2 in

case of peripheral symptoms. Remission in axial symptoms was defined as ASDAS < 1.3 whereas remission in peripheral symptoms was achieved with DAS28 = 2.6.

76.1% of patients with axial symptoms achieved BASDAI50 response (76.5% with AS and 73.1% with PsA). 33.6% of them achieved remission (ASDAS < 1.3) at the end of the observational period (34.3% with AS and 28.8% with PsA). 83.5% of patients with peripheral symptoms (83.3% with AS and 83.6% with PsA) achieved DAS28 response (decrease in DAS28 = 1.2) and 13.9% (11.1% with AS and 14.8% with PsA) achieved remission (DAS28 = 2.6). Clinical efficacy was also reflected by strong improvements in physical function and work-life. Adalimumab was well-tolerated; 4.7% of patients experienced a serious adverse event, and 3.6% patients experienced a serious adverse drug reaction (i.e. an event with causality assessed as at least possible). No new safety signals were detected.

Investigating the correlation between BASDAI and ASDAS demonstrated moderate to high correlation at all follow-up visits (Spearman's rank correlation coefficient of at least 0.70, except for one single case [0.68]).

Discussion

Use of adalimumab (Humira[®]) is an efficacious and well-tolerated treatment of ankylosing spondylitis and psoriatic arthritis. ASDAS was largely correlated with BASDAI and seems to be a promising novel tool.

Marketing Authorisation Holder

AbbVie Czech Republic

AbbVie Estonia

AbbVie Hungary

AbbVie Romania

AbbVie Slovakia

AbbVie Ukraine

Names and Affiliations of Principal Investigators 