

1.0 Abstract

Title

Physical activity in patients with rheumatoid arthritis treated with adalimumab in routine clinical practice

Pace - Multi-country, Multi-center, Post-marketing Observational Study in Routine Clinical Use in Central and Eastern Europe

Keywords

Humira®, adalimumab, rheumatoid arthritis, observational, physical function

Rationale and Background

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease where pain and joint damage, resulting in increasing functional disability, and attendant comorbidities, particularly in the cardiovascular system, hamper patients' quality of life, and may cause socioeconomic decline and premature mortality. Reduced quality of life (QOL), as compared with healthy individuals is even more pronounced for RA patients who do not participate in regular physical activity. Research illustrates the importance of physical activity for patients with RA: several treatment trials have demonstrated that physical activity has positive impacts upon pain, disease activity and functional status.

Although physical activity has positive impacts upon pain, disease activity and functional status in patients with RA and the fact that even dynamic forms of exercise are generally safe for RA patients, they remain less physically active than the general population. Despite the extensive research on the effects of biologic therapy on RA outcomes, little is known about possible improvement in physical activity.

Clinical remission in RA has become an increasingly attainable goal with the introduction of biologic therapy, targeting specific cytokines, such as tumor necrosis factor α (TNF α). Further, as compared with classical disease modifying anti-rheumatic drugs (DMARDs), biologic agents have demonstrated greater potency in suppressing signs and symptoms, inhibiting structural damage, improving physical function, quality of life and workability outcomes in patients with RA.

Very little is known about physical activity in patients on biologic therapy. It could be hypothesized that improved control of RA signs and symptoms, better physical function and inhibition of structural damage all make the ground for an increased

physical activity in patients treated with biologic agents after inadequate response to conventional DMARDs. Adalimumab is the biologic agent which demonstrated unsurpassed efficacy in improving physical function, as well as short- and long-term work productivity outcomes in patients with RA, therefore adalimumab is a good candidate biologic agent to evaluate the impact on physical activity in RA.

Research Question and Objectives

The primary objective of this study was to evaluate physical activity and its changes in patients with rheumatoid arthritis (RA) who were treated with adalimumab therapy in clinical practice. Physical activity and its changes were investigated by the use of the Short QUestionnaire to ASsess Health-enhancing physical activity (SQUASH).

The secondary objectives of this study in RA patients on adalimumab therapy were:

- to assess changes in RA disease activity (based on DAS28 index),
- to determine percentages of patients in clinical disease remission (DAS28 < 2.6) and low disease activity state (LDAS, DAS28 < 3.2),
- to assess changes in physical function (based on HAQ-DI),
- to evaluate the relationship between disease activity, physical function and physical activity,
- to analyze the influence of certain sociodemographic factors (age, gender, education and occupation) on physical activity.

Study Design

This post-marketing observational study (PMOS) was performed in a prospective, multi-country, multi-center, and single-arm approach. There were not more than five target visits: one at baseline (V0), and four follow-up visits 3, 6, 9 and 12 months after baseline (V1, V2, V3, and V4).

Setting

Participating countries were Bosnia and Herzegovina, Estonia, Hungary, Romania, Russia, Serbia and Ukraine.

Subjects and Study Size, Including Dropouts

For 462 patients, a V0 visit was documented. Of these patients, 15 (3.2%) participated in Bosnia and Herzegovina, 11 (2.4%) in Estonia, 221 (47.8%) in Hungary, 120 (26.0%) in Romania, 4 (0.9%) in Serbia, 90 (19.5%) in Russia and 1 (0.2%) in Ukraine.

For 2 patients, adalimumab (Humira®) treatment was not documented within this study. These patients were excluded from the main analysis set (MAS) which comprised 460 patients.

In total, 146 MAS patients dropped out before the end of study. Of these, 121 discontinued treatment with adalimumab and 25 were lost to follow-up.

Variables and Data Sources

The following questionnaires were used within this study:

- The Short QUEStionnaire to ASsess Health-enhancing physical activity (SQUASH) to assess the individual habitual activity level
- The Disease Activity Index / 28 joints (DAS28) to assess disease activity
- The Health Assessment Questionnaire - Disability Index (HAQ-DI) to assess functionality.

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

Results

Physical activity improved considerably throughout the study as assessed by the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH) questionnaire. Mean total score of SQUASH increased from 4747.8 at V0 to 5611.9 at V4-LOCF (mean increase of 870.0). The influence of sociodemographic factors on physical activity appeared to be negligible. In accordance with improvements in physical activity, disease activity (DAS28) decreased from 6.1 (V0) to 3.3 at V4-LOCF (mean change of -2.9). Over the course of the study the physical functional capacity of subjects improved, as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI). The average HAQ-DI score decreased from 1.6 at V0 to 0.9 at V4-LOCF, which relates to a mean change of -0.7 at V4-LOCF. The rate of patients being permanently work disabled showed a minor decrease (from 22.0% at V0 to 17.4% at V4).

Overall, 35 SAEs occurred in 32 patients (7.0%), the majority of which were classified as moderately severe (26, 74.3%). Seven SAEs (20%) were evaluated as severe, out of which four (aspartate aminotransferase increased, alanine aminotransferase increased, lung adenocarcinoma and pancreatic carcinoma) were classified as being related to adalimumab (Humira®) with reasonable possibility.

Overall, 21 (60.0%) SAEs were considered to be related to adalimumab with reasonable possibility. No new safety signals were detected.

Discussion

Adalimumab (Humira®) was an effective and well-tolerated treatment of RA. Effectiveness is reflected by improvements in disease activity, habitual physical activity, physical functional capacity, and workability.

Obviously, data gathered in this observational study is of a lower evidence level than data retrieved from randomized clinical trials. The effectiveness data of adalimumab (Humira®) on disease activity and physical function in this study was comparable to previously published studies. The safety profile of adalimumab (Humira®) in this study was in alignment with the established safety profile of the drug.

Marketing Authorisation Holder(s)

AbbVie Bosnia and Herzegovina

AbbVie Estonia

AbbVie Hungary

AbbVie Romania

AbbVie Russia

AbbVie Serbia

AbbVie Ukraine

Names and Affiliations of Principal Investigators

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