

1.0 Abstract

Title: A 2-year HRQL observational study evaluating the effect of treatment with adalimumab on Work Productivity and Sleep in patients with rheumatic diseases in Greece.

05 March 2015

Author: Kyriakos Tarantinos

Keywords: Adalimumab (Humira®), HRQL, rheumatic diseases, work productivity, sleep.

Rationale and Background:

Work Productivity is improved in patients with inflammatory rheumatic diseases after treatment with TNF antagonists, especially adalimumab. There are no data for Work Productivity in PsA and limited data exist for Sleep disturbance in patients treated with adalimumab. Since there are no data for Work productivity and Sleep disturbance in Greek patients with rheumatic diseases (RA, PsA and AS) the effect of treatment with adalimumab will be assessed.

Research Question and Objectives: Rheumatoid arthritis (RA) is an inflammatory disorder with a reported prevalence of approximately 1% of the population.¹ RA is characterized by a progressive inflammatory synovitis with joint swelling and tenderness. Psoriatic Arthritis (PsA) is an inflammatory musculoskeletal disorder associated with psoriasis. Ankylosing Spondylitis (AS) is a chronic inflammatory disease of the axial skeleton, large peripheral joints and entheses. Due to the early onset and long-term nature of the functional disability, the lifetime costs and socioeconomic impairment for subjects with active AS are likely to be high. Working ability is reduced in patients with RA and AS resulting in a very high economic cost and patient-reported Work Productivity loss is associated with signs and symptoms of these diseases. On the other hand data on PsA effect on Work productivity are lacking. Inflammatory rheumatic diseases (RA, PsA and AS) are also associated with sleep disturbances and sleep is an important concern in these patients. Treatment with TNF inhibitors and especially adalimumab has shown to improve work productivity in patients with rheumatic diseases.

The primary objective was the evaluation of the mean change of activity impairment as measured by the WPAI GHP instrument in patients with inflammatory rheumatic diseases such as RA, PsA and AS treated with adalimumab over a period of two years. Work Productivity and Activity Impairment Questionnaire General Health (WPAI GH) gives information about the effect of symptoms and health problems due to RA, PsA and AS on the ability to work and perform regular activities. The WPAI-GH outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity.

The secondary objectives were to assess the effect of adalimumab at 3, 6, 12, 18 and 24 months of treatment in specific work and sleep scale scorings in patients with rheumatic diseases.

Study Design: This is a multi-center, uncontrolled prospective observational study of patients who at the time of entry had a moderate to severe rheumatic disease (RA, PsA, AS) and who were subsequently prescribed adalimumab following normal clinical practice and according to the current Summary of Product Characteristics (SmPC), with or without other anti-rheumatic treatments, prior to enrollment in this study.

Setting: A total of 80 investigators, hospital based and Private Practitioners across Greece enrolled patients with rheumatic diseases in the present study. The study period was between 17 March 2011 (First Patient First Dose) and 28 July 2014 (Last Patient Last Dose).

Subjects and Study Size: 500 patients were enrolled with a mean (\pm SD) age of 52.5 (\pm 14.8) years; 57.8% were females. Out of the 500 participants, 79 (15.8%) did not complete the study for various reasons, the most common of which was "Lack of efficacy/exacerbation" (31.6%) and "Lost to follow-up" (29.1%).

Variables and Data Sources:

Key variables: Demographic data/ Personal interviews, medical files

Medical history data/Personal interviews, medical files

PPD test/IgRAs, CXR/diagnosis/comments

DMARDs/concomitant medications/other biological agents

Comorbidities/concomitant medications

Safety parameters (AEs/SAEs)

Efficacy parameters/laboratory examinations

WPAI GH questionnaire considering 169 employed subjects which examined three parameters over the working population: work time missed, impairment at work, overall work productivity loss and one parameter over the entire population (500 subjects) about overall activity impairment. A higher score sustained a greater loss of productivity at work and daily activities.

Medical Outcome Study (MOS) questionnaire which examined sleep initiation, maintenance, respiratory problems, quantity, perceived adequacy and somnolence. A higher score stands for a worse outcome.

Data sources: Case report form

Results: Adalimumab over the study period of 24 months showed a decrease in the mean value of the four outcomes of the study (work time missed, impairment while working, overall work impairment and activity impairment due to health) compared to baseline values indicating a lowering in the impact of the disease to subjects' activities and an overall improvement in their ability to work. The percentage of Rheumatoid Arthritis patients with painful and swollen joints decreased over the study period. In subjects with Ankylosing Spondylitis, there was a high correlation between the improvement in BASDAI score indexes and the improvement in overall work impairment due to health index. The results of the same four indices in each of the three diseases suggest that the level of initial impairment and the effect of treatment at month 24 is comparable across patients with each of the three diseases. Regarding the MOS-SLEEP scale, an overall improvement in the quality of sleep was observed in patients with RA, AS and PsA. A gradual decrease in the mean value of sleep problems index was also recorded. Also, a statistically significant lower mean value in sleep problems index was observed in the subgroup of subjects with PsA, indicating the lower impact of PsA in sleep quality.

In terms of the Adverse Events reported during the study, 94 (18.8%) experienced at least one Adverse Event (AE). The total number of AEs reported was 191, out of which 158 (17% of study population) were Non-Serious and 33 (2.8% of study population) were Serious. Out of the 191 AEs, 121 were assessed as related to study drug treatment. The most frequent Serious related AE reported in the study was Pyrexia, an AE which is labeled according to the Summary of Product Characteristics. During this study no emerging safety issue arose.

Discussion: Data at 24 months were available for 421 (84.2%) subjects with 11 (2.2%) dropouts. Adalimumab showed to improve both work productivity and overall sleep quality in Greek patients with rheumatic diseases in a 2 year follow up study, although continued improvements at later time points may have been influenced by responder bias. The findings of this observational study support the conclusion that adalimumab is improving Work Productivity and Sleep in patients with rheumatic diseases in Greece.

Marketing Authorization Holder: AbbVie Ltd.

Names and Affiliations of Principal Investigators: [REDACTED]