1.0 Abstract

Title

A Post-Marketing Observational Study to Determine the Effectiveness and Patient Satisfaction with Adalimumab (Humira®) Treatment in Patients with Rheumatoid Arthritis (RA) (PASSION)

Keywords

Humira; adult; rheumatoid arthritis; observational; patient support program

Rationale and Background

In clinical practice, patients who start adalimumab (Humira®) are treated per local product label, are advised of the potential benefits and risks of adalimumab by their physicians, are instructed in injection techniques, and are offered access to Patient Support Programs (PSPs), where available. Before Study P12-072, no prospective study had been conducted to analyze the impact of the PSP utilization on adalimumab treatment effectiveness and patient satisfaction.

Research Question and Objectives

Study P12-072 was a non-confirmatory observational study to evaluate the effectiveness of adalimumab on RA treatment course and patient satisfaction over time in context with PSP utilization.

Study Design

Study P12-072 was a post-marketing, multi-center, uncontrolled observational study conducted according to a single arm design with all patients utilizing commercial adalimumab subcutaneously every other week or as allowed per local product label and having access to their country's adalimumab PSP. The study was designed to explore and describe the effectiveness of adalimumab on RA treatment course and patient satisfaction over time in context of PSP utilization. For Study P12-072, the

core elements of the PSP that were offered to all participating patients were call centers (in and outbound)/hotlines, nursing services, starter packs, provision of educational materials (print and digital) regarding RA and adalimumab, and injection guides. Other elements of the PSP which varied between countries included (but were not limited to) refill reminders, email contacts, support groups, and newsletters.

Setting

There were to be approximately 150 to 200 sites in approximately 16 countries outside the United States (US). It was expected that approximately 150 to 200 rheumatologists from various ex-US countries (including Puerto Rico) would participate in the study based on the available eligible patient population and the sites' ability to conduct this observational study. The participating physicians were to be representative of the rheumatologists who prescribe adalimumab for patients with RA.

Subjects and Study Size, Including Dropouts

Patients eligible for enrollment were to be representative of the population in which adalimumab is used to treat RA. The study population was to be adult patients (≥ 18 years of age) with a diagnosis of moderate to severe RA who had an insufficient response to 1 or more disease-modifying anti-rheumatic drugs (DMARDs) and not more than 1 prior biologic DMARD, and who met the requirements per the local label for treatment with adalimumab. Prior treatment with adalimumab was not allowed. Patients were to have been prescribed adalimumab based on current clinical practice criteria without taking participation in the study into account, with the first dose corresponding to the Enrollment/Baseline visit. Approximately 1,000 patients with moderately to severely active RA who had an insufficient response to 1 or more DMARDs and fulfilled the study eligibility criteria were to be enrolled.

A patient was eligible for study participation if he/she met the following criteria:

1. Male or female aged at least 18 years who had been newly prescribed adalimumab therapy according to the local product label, with the first dose corresponding to the Enrollment/Baseline visit.
2. Patient with a diagnosis of moderate to severe RA, who had insufficient response to 1 or more DMARDs, and had a prescription of adalimumab according to the local regulations.
3. Patients should have been evaluated for tuberculosis (TB) exposure/risk factors for active and latent TB (per local requirements and according to the local product label).
4. Patients must have been able and willing to provide written authorization to disclose and use personal health information (and informed consent where applicable) and comply with the requirements of this study protocol as well as agree to data being collected and provided to AbbVie.

A patient was not eligible for study participation if he/she met any of the following criteria:

1. Patients should not have been enrolled if they could not be treated in accordance with the local adalimumab product label.
2. Patients had been treated with > 1 prior biologic DMARD for RA. Any prior treatment with adalimumab was prohibited.

Variables and Data Sources

The outcome parameters for effectiveness of adalimumab treatment in combination with various elements of PSPs over time included:

- Primary endpoint: percentage of patients achieving Minimal Clinically Important Difference (MCID) in Health Assessment Questionnaire Disability Index (HAQ-DI) at Week 78 (MCID is improvement of at least 0.22 in HAQ-DI compared to Baseline).

- Secondary endpoint: percentage of patients achieving MCID in HAQ-DI at Weeks 12, 24, 36, 52, 64 (improvement of at least 0.22 in HAQ-DI compared to Baseline).
- Other effectiveness parameters: Changes in Disease Activity Score-28 (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), American College of Rheumatology response rates (ACR 20/50/70) and European League Against Rheumatism (EULAR) moderate and good responses.
- Health outcomes assessments including HAQ-DI, Work Productivity and Activity Impairment (WPAI), Compliance Questionnaire Rheumatology (CQR), and Treatment Satisfaction Questionnaire for Medication (TSQM) scores.
- Expectation regarding PSP and health management via Patient Activation Measure (PAM-13).
- Change in patient perceptions as measured by the Beliefs about Medicines Questionnaire (BMQ).
- Utilization and satisfaction with PSP as measured by PSP utilization and satisfaction assessments.

Safety variables: Treatment-emergent serious adverse events (SAEs), treatment-emergent adverse events (TEAEs) leading to discontinuation, non-serious treatment-emergent events of malignancy in patients 30 years of age and younger, and spontaneously reported treatment-emergent non-serious adverse events (AEs).

Results

One thousand and thirty-six patients were enrolled in the study and 1025 patients across sites in 14 countries were analyzed in this report as the intent-to-treat (ITT) population, which was defined as patients who received at least 1 dose of adalimumab. Of the 1025 patients, 499 were PSP users.

The percentage of patients in the ITT population achieving MCID in HAQ-DI at Week 78 was 72.1% using the as observed analysis. Using the non-responder

imputation (NRI) analysis, a statistically significantly greater proportion of PSP users than PSP non-users achieved MCID in HAQ-DI at Week 78.

Evaluating the secondary effectiveness measure, the percentage of patients in the ITT population achieving MCID in HAQ-DI increased from Week 12 (60.9%) to Week 64 (73.7%) using the as observed analysis. The proportion of patients achieving MCID in HAQ-DI was higher for PSP users than PSP non-users at Weeks 12, 24, 36, 52, and 64 using NRI analysis. For all patients taking adalimumab in this study, improvement over time was seen for DAS28 (erythrocyte sedimentation rate [ESR]), DAS28 (C-reactive protein [CRP]), ACR 20/50/70 response rates, SDAI, CDAI, and health outcomes assessments including WPAI, TSQM, CQR, PAM-13, and BMQ. In terms of EULAR response, EULAR good responders (calculated both using ESR-based DAS28 and CRP-based DAS28) increased over time while the percentage of EULAR moderate responders decreased. PSP satisfaction, only assessed for PSP users, was rated as very good/fully applies or good/applies in the majority of PSP satisfaction assessment items. PSP users had greater improvements from Baseline than PSP non-users at Week 78 in DAS28 (CRP), SDAI, CDAI, WPAI, TSQM responses, and PAM-13. A larger proportion of PSP users achieved ACR 20/50/70 response rates than PSP non-users at Week 78.

The protocol required that all SAEs, non-serious events of malignancy in patients 30 years of age or younger, and AEs leading to discontinuation of study be actively solicited. The safety profile of adalimumab which has over 4.6 million patient-years of post-marketing exposure is well-established; non-serious events were not actively solicited as these events were not likely to contribute to the further understanding of the safety profile of the product. Any non-serious AEs were collected as spontaneous reports if AbbVie was notified. No new safety signals were observed in this study. Adalimumab was well-tolerated in the treatment of subjects with RA. Three patients died, 17% experienced at least 1 TEAE, and 9.5% experienced at least 1 SAE. Most patients had TEAEs that were probably not related or not related to adalimumab and mild to moderate in severity, as assessed by the Investigator. A total of 7.3% of

patients discontinued from the study due to a TEAE. No events of treatment-emergent TB were reported, and 8 treatment-emergent events of malignancies in 8 patients were reported. No clinically meaningful changes in laboratory and vital signs were observed during the study.

Discussion

Study P12-072 showed that patients with moderate to severe RA taking adalimumab showed improvement in effectiveness measures and health outcome assessments. Per NRI analysis, patients who enrolled in the AbbVie PSP for adalimumab achieved overall better improvement in effectiveness measures and health outcomes assessments as compared to patients who initiated adalimumab without participation in a PSP. No new safety signals were identified with adalimumab treatment for RA. The results from this study indicate that the AbbVie PSP for adalimumab may have a positive effect on clinical, functional, and humanistic outcomes. The improvements in outcomes of the patients observed in this study may be due to the role of AbbVie's PSP in improving the persistence and/or adherence of adalimumab in patients with RA.

Marketing Authorisation Holder

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