1.0 Abstract

Title

Post-marketing observational study to evaluate the effect of HUMIRA (adalimumab) treatment with AbbVie's patient support program on patient reported outcomes and health resource utilization in inflammatory arthritis, psoriasis and inflammatory bowel diseases in Hungary in a real-life setting: The VALUE study

Keywords

Humira, adalimumab, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease, ulcerative colitis, observational study, patient support program, adherence, health-related quality of life, healthcare resource utilization, disease activity, treatment satisfaction, workability

Rationale and Background

Patient support program (PSP) services, such as nursing services, medication management and counseling and co-pay assistance, have been shown to have a positive impact on medication adherence, clinical and humanistic outcomes, and on reducing the healthcare utilization and costs associated with the management of immune mediated inflammatory diseases. AbbVie offered an array of services as part of a patient support program, called AbbVie Care to individuals prescribed HUMIRA (adalimumab) in the past years. The purpose of AbbVie Care program is to provide educational resources that aim to help patients understand their health condition and disease management (e.g., lifestyle – exercise or diet), but also help them understand how to administer the product safely and be empowered to stay on track with their prescribed treatment plan, all with the goal of maximizing patient outcomes.

Although several randomized, controlled studies conducted with HUMIRA (adalimumab) report the effect of the drug in various immune-mediated inflammatory diseases (IMIDs), at the time of study initiation there were very limited data are available on the effect of HUMIRA (adalimumab) in combination with AbbVie Care PSP on functional health and wellbeing globally and no clinical and observational data were available on this subject in Hungary.

Research Question and Objectives

The aim of VALUE study (NCT02750800) was to evaluate the effect of HUMIRA (adalimumab) plus AbbVie Care PSP in patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), psoriasis (Ps), Crohn's disease (CD) and ulcerative colitis (UC) in the routine clinical setting in Hungary.

The primary objective was to evaluate the impact of HUMIRA (adalimumab) therapy plus AbbVie Care on patient functional health and wellbeing as measured by SF-36v2 PCS in patients with RA, AS, PsA, Ps, CD and UC.
Secondary objectives were:

- To evaluate the impact of HUMIRA (adalimumab) therapy plus AbbVie Care on general and disease specific quality of life (QoL), health resource utilization, treatment satisfaction, satisfaction with information provided by AbbVie Care, medication adherence, disease activity and work productivity.
- To define relationship between patient-reported outcomes and patient socio-demographics (age, gender, work status), diagnosis and patient types.
- Evaluate the effect of exposure to AbbVie Care on other selected patient reported outcomes.

Study Design

This study was conducted in a prospective, open label, multicenter, observational cohort setting. There were five target visits: baseline visit at enrollment and four follow-up visits 3, 6, 9 and 12 months after baseline.

Setting

This study was conducted in altogether 26 different (rheumatology, dermatology or gastroenterology) biological therapy centers in 17 individual Hungarian health care institutions. HUMIRA (adalimumab) was prescribed in the usual manner in accordance with the terms of the local marketing authorization and professional and reimbursement guidelines with regards to dose, population and indication.

Subjects and Study Size, Including Dropouts

The full analysis dataset (FAS) consisted of 412 patients. All patients entered in the study were enrolled in the AbbVie Care PSP program.

Six subgroups were defined by their diagnosis. 76 (18.4%) patients comprised the ankylosing spondylitis (AS) group, 62 (15.0%) the Crohn's disease (CD) group, 69 (16.7%) patients the psoriasis (Ps) group, 75 (18.2%) patients the psoriatic arthritis (PsA) group, 67 (16.3%) patients the rheumatoid arthritis (RA) group and 63 (15.3%) patients the ulcerative colitis (UC) group. In total, 98 patients dropped out before the end of the study. Of these, 18 dropped out because of AE/SAE, 12 were lost to follow-up, 12 were patient requests and 53 were investigator decision without further explanation collected. In three cases reason of drop-out was not provided.

Variables and Data Sources

The primary data sources were the patient documentation in medical records and patient questionnaires.

The following questionnaires were applied for all patients at each visit: SF-36v2, EQ-5D-5L, WPAI-SHP, MMAS-4, SIMS, TSQM-1.4, irrespective of the diagnosis.

The following disease specific outcome measures were administered at each visit:

- **Quality of life measures:** SIBDQ in CD or UC, DLQI in Ps and PsA; ASQoL in AS and axial PsA patients.
- **Disease activity measures**: $DAS28_{ESR}$ in RA and peripheral PsA, $ASDAS_{ESR}$ in AS axial PsA, PASI in Ps, CDAI in CD and pMayo in UC patients.

Results

General quality of life measures showed improvement in the patients' quality of life. The primary endpoint of the study, the SF-36v2 Physical component score (PCS) showed statistically significant ($p \leq 0.05$) increase in all indications from baseline (V0) to 12 months (V4), corresponding to an improvement in HRQoL. The mean change from baseline to study end was 9.43±10,224 for the FAS. No statistical comparisons, only descriptive analysis have been performed for the remaining outcome measures to define statistical significance in change from baseline to study end. The mean changes per indication were as follows: AS: 11.02 ± 10.239, CD: 7.63 ± 9.512, PS: 4.38 ± 9.135, PsA: 12.26 ± 10.734, RA: 11.81 ± 10.830, UC: 9.02 ± 8.652. The mean SF-36v2 Mental component score (MCS) increased in all indications in somewhat smaller degree from baseline (V0) to 12 months (V4), with the mean changes per indication as follows: AS: 9.63 ± 13.314, CD: 10.60 ± 15.868, PS: 6.61 ± 13.246, PsA: 8.54 ± 12.627, RA: 5.99 ± 11.856, UC: 11.50 ± 15.350.

The mean EQ-5D-5L index score increased in all indications from baseline (V0) to 12 months (V4), with mean changes per indications: AS: 0.185 ± 0.175, CD: 0.169 ± 0.194, PS: 0.084 ± 0.143, PsA: 0.203 ± 0.182, RA: 0.152 ± 0.186, UC: 0.123 ± 0.144. Similarly, the mean EQ-5D-5L visual analog score (VAS) increased in all indications from baseline (V0) to 12 months (V4). Disease area specific quality of life improved from baseline to month 12 in all indications.

With regards to the satisfaction with medication administered, the mean TSQM-1.4 global satisfaction subdomain, effectiveness subdomain and convenience subdomain scores increased in all indications showing improvement in the satisfaction, whereas the side effect subdomain increased in all indications except for Ps patients, where a slight decrease have been observed.

Concerning the satisfaction with information about medicines, the mean SIMS score and its sub scores Action and usage and Potential problems of medication showed increase in the full analysis set between V0 and V4.

The self-reported adherence improved throughout the study as measured by MMAS-4 in the FAS population showing some differences in different diagnosis groups. The mean MMAS-4 score increased AS, Ps, RA and UC indications corresponding to improved self-reported medication adherence, whereas decreased in CD and PsA.

The workability of the patients enrolled to the study improved throughout the follow up period. The mean WPAI-SH presenteeism domain decreased in all indications indicating improved workability while working. The mean WPAI-SH absenteeism domain decreased in all indications, indicating a decrease in the work time missed due to the respective IMID. The mean WPAI-SH TAI domain decreased in all indications, indicating an improvement in the general (non-work) activity impairment due to the respective IMID. The mean WPAI-SH TWPI domain decreased in all indications, indicating a reduction in the overall work impairment due to the respective IMID.

The improvement in SF-36v2 PCS score showed significant association ($p \leq 0.05$) with lower baseline age (<40 years vs 40-64 years) and baseline employment status (working for payment), as well as with patient type (being demanding or non-coping vs denying) and diagnosis (having AS, PsA, UC vs Ps). Both the improvement in EQ-5D-5L index score and TSQM1.4 Global satisfaction score showed significant association with the baseline employment status (working for payment; $p = 0.002$ and $p = 0.036$, respectively), in addition, EQ-5D-5L VAS score mean change from baseline was significantly higher in bio naïve patients ($p \leq 0.05$). The improvement in MMAS-4 score showed significant association with diagnosis (having AS, Ps or UC vs CD, $p \leq 0.05$). Finally, the improvement in WPAI-SH TAI showed statistically significant association ($p \leq 0.05$) with Ps diagnosis. Disease duration (time from diagnosis), gender and presence of any comorbidity were not identified as independent explanatory factors for the outcome measures analysed.

Healthcare resource utilization improved as well. The mean number of hospital admission, hospital inpatient days, outpatient visits, sick leave episodes and sick leave days decreased in all indications according to the performed descriptive analysis without any formal statistical comparisons.

Disease activity decreased in all indications comparing baseline and study end values. In the UC cohort statistically significant inverse correlation was observed between SIBDQ and pMayo scores ($r= -0.453$, $p=0.002$). Statistically significant correlation was also observed between DLQI and PASI scores ($r=0.323$, $p=0.016$) in the Ps cohort.

98.6% of completer dataset remained in the PSP program till study end. When evaluating the AbbVie Care program at the last study visit, 56.5% of responders (n=317) deemed the program as “very good” and 40.5% as “good”, indicating a general satisfaction with the program. The different elements of the program were evaluated as “very good” or “good” by more than 90% of the responders. 98.0% of the responders would recommend the program for other patients. To assess the effect of the different length of PSP exposures on patient outcomes was not possible because of the low number of patients who discontinued the PSP before the study end and therefore had shorter PSP exposure than the length of the observational period.

No new HUMIRA (adalimumab) safety signal was detected in the study.

Discussion

The results of VALUE study showed that HUMIRA (adalimumab) treatment combined with patient support program AbbVie Care produced improvements in health-related quality of life, treatment satisfaction, satisfaction with information provided on medication, self-reported medication adherence, workability and health resource utilization and was also associated with high drug persistence in the treatment of the selected immune mediated inflammatory diseases in Hungary. Improvements were observed in disease activity measures as well. Moreover, participants were highly satisfied with the patient support program. HUMIRA (adalimumab) was well-tolerated and no new safety signals were detected Due to the lack of a control, non-PSP arm, the real impact of AbbVie Care is difficult to quantify, nonetheless VALUE study's results seem to confirm previous published research demonstrating the benefits associated with AbbVie PSP program in various IMIDs.

Marketing Authorisation Holder(s)

AbbVie Deutschland GmbH & Co. [redacted]

Names and Affiliations of Principal Investigators

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