

Impact of Participation in the Adalimumab (Humira) Patient Support Program on Rheumatoid Arthritis Treatment Course: Results from the PASSION Study

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ABSTRACT

Introduction: Patients with rheumatoid arthritis (RA) who are treated with adalimumab (ADA) are offered a proprietary patient support program (PSP, AbbVie Care®). The main objective of this study was to examine the effectiveness of ADA on RA treatment course over time in the context of PSP utilization.

Methods: PASSION was a 78-week post-marketing observational study of RA patients with an insufficient response to ≥ 1 DMARD newly initiating ADA in routine clinical care that was conducted in Europe, Israel, Mexico, Puerto

Rico, and Australia. One prior biologic DMARD was allowed. The primary endpoint was percentage of patients achieving the minimal clinically important difference (MCID; improvement of ≥ 0.22 compared to baseline) in Health Assessment Questionnaire (HAQ) Disability Index (HAQ-DI) at week 78. Additionally, multiple clinical and patient-reported outcomes (PROs) were evaluated over time. Patients were categorized based on their participation in the PSP: ever (PSP users) vs. never (PSP non-users). Safety events were monitored throughout the study.

Results: Overall, 42.8% of PSP users achieved the MCID in HAQ-DI at week 78 (improvement of at least 0.22 compared to baseline). From 1025 enrolled, 48.7% of patients were PSP users while treated with ADA. The percentage of patients achieving MCID in the HAQ-DI was higher in PSP users vs. PSP non-users (48.1 vs. 37.8%) at week 78 ($p < 0.001$, NRI). Most of the studied clinical outcomes and PROs showed significant improvements ($p < 0.05$) from baseline to week 78 favoring PSP users over PSP non-users.

Conclusions: In patients with moderate-to-severe RA who initiated ADA, improvements in clinical, functional, and PROs were achieved in real-world settings with significantly greater improvements among PSP users in comparison with PSP non-users.

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INTRODUCTION

Rheumatoid arthritis (RA) is a common autoimmune disease that is associated with progressive disability, systemic inflammation, early death, and socioeconomic costs [1]. The prevalence of RA range from 0.4 to 1.3% [2]. The condition is characterized by joint swelling and tenderness, and, if unabated, can lead to structural damage and diminished joint function.

The treat-to-target recommendations in RA suggest that the primary treatment goal is to maximize long-term health-related quality of life [3] through early diagnosis and intervention with effective therapies. Given the chronic nature of the disease as well as the often-complex therapies administered, proper medication adherence remains crucial for ensuring optimal treatment outcomes. Despite this importance, substantial evidence exists to illustrate that treatment non-adherence is prevalent in medical care and is a rising concern to health care providers and payers, as it increases the cost of care and results in poor patient outcomes [4, 5]. In particular, medication adherence rates can be as low as 30% in patients with RA [6].

Patient support programs (PSPs), such as regular nursing services and co-pay assistance, have been proposed to educate and empower patients to handle complex and costly medications that could augment better adherence, alleviate waste, reduce cost, and improve both treatment satisfaction and outcomes [7, 8]. PSPs are intended to improve compliance and treatment outcomes through multiple methods of interaction between caregivers and patients.

PASSION was a post-marketing, multicenter, uncontrolled observational study in which patients who initiated adalimumab (ADA) received treatment according to the local product label and local standard of care, with an option to participate in elements of the offered PSP. No prospective study has previously analyzed the impact of these PSPs on functional, clinical, and patient-reported outcomes among RA patients. The main objective of the PASSION

study was to explore and describe the effectiveness of ADA on RA treatment course in the context of utilization of the PSP.

METHODS

Patients and Study Design

This was a post-marketing, multicenter, observational study of patients treated with ADA according to the local product label and local standard of care and having access to their country's PSP. The study enrolled adult patients with a diagnosis of moderate-to-severe RA who have had insufficient response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Prior treatment with one biologic DMARD other than ADA was allowed. Patients were recruited at participating sites in Australia, Belgium, Czech Republic, France, Germany, Greece, Israel, Mexico, Netherlands, Portugal, Puerto Rico, Slovakia, Switzerland, and the United Kingdom. The study duration was up to 78 weeks. Patients could prematurely stop the study participation at any time without prejudice. All patients in the study were offered the option to enroll in the PSP. Offered PSP consisted of various elements such as starter pack, injection guide, and educational material regarding life with RA and ADA such as patient booklet or DVD about the disease, call centers (in and outbound)/hotline, nursing services (scheduling a visit at the patients home/pharmacy/doctor's office) that were available in all participating countries while provision for refill reminders, e-mail communications, newsletters, support groups, home medication delivery, and financial assistance varied between participating countries. Patients that were enrolled in the study and treated per standard of care were a priori categorized based on their participation in the PSP: ever (PSP users) vs. never (PSP non-users) and outcomes were compared after adjusting for corresponding baseline values. The study protocol was approved by the responsible ethics committees and internal review boards at each study site and the study was done in compliance with the Declaration of Helsinki of 1964, Good Clinical Practice guidelines, and

applicable local regulations. Informed consent was obtained from all patients.

Study Outcomes

The primary endpoint (as observed) was the percentage of patients achieving minimal clinically important difference (MCID) in the Health Assessment Questionnaire Disability Index (HAQ-DI) at week 78 (improvement of at least 0.22 in HAQ-DI compared to baseline). The secondary endpoint of treatment effectiveness was the percentage of patients achieving MCID in HAQ-DI at weeks 24 and 52. Additional secondary parameters assessed included: (1) changes in 28-joint Disease Activity Score (DAS28); (2) changes in Simplified Disease Activity Index (SDAI); (3) changes in Clinical Disease Activity Index (CDAI); and (4) ACR 20/50/70 responses rates.

Health Outcomes Assessments

HAQ-DI Scores

HAQ is a self-reported patient-oriented outcome measure. The Disability Index of HAQ is calculated as the mean of eight category scores (range, 0–3). The eight category scores are averaged to produce an overall HAQ-DI score. The overall HAQ-DI score is on a scale of 0–3, zero indicating no disability and 3 indicating complete disability [9]. HAQ-DI was measured at baseline and weeks 24, 52, and 78 and expressed as mean change from baseline.

Work Productivity and Activity Impairment (WPAI)

The WPAI questionnaire consists of six questions that ask patients to identify the number of hours missed from work and usual activities, as well as the degree to which work or regular daily activities were limited over the past 7 days. The questionnaire yields four scores: (1) percentage of work time missed because of ill health (absenteeism), (2) percentage impairment while working due to ill health (presenteeism), (3) percentage activity impairment due to ill health (activity impairment), and (4) an overall percentage work impairment score due to health

problems (work productivity loss). WPAI was measured at baseline and weeks 24, 52, and 78 and expressed as mean change from baseline [10].

Compliance Questionnaire Rheumatology (CQR)

The CQR is a self-report measure consisting of 19 four-point Likert scale statements ranging from 1 (do not agree at all) to 4 (agree very much). The total score is calculated by summing all 19 items and subtracting 19 from the total and dividing by 0.57 [11]. The total score ranges between 0 (complete non-compliance) and 100 (perfect compliance). CQR was measured at baseline and weeks 24, 52, and 78 and expressed as mean change from baseline.

Treatment Satisfaction Questionnaire for Medication (TSQM)

The TSQM is a 14-item questionnaire designed as a general measure of treatment satisfaction with medication. The TSQM items cover four domains, corresponding to distinct aspects related to the satisfaction of patients with their treatment (effectiveness; side effects; convenience and global satisfaction). A score can be obtained for each sub-domain by summing of the corresponding items transformed on a 0–100 scale; higher values indicate higher satisfaction, better perceived effectiveness, lower burden associated to side effects, better convenience. TSQM was measured at baseline and weeks 24, 52, and 78 and expressed as mean change from baseline [12].

Beliefs about Medicines Questionnaire (BMQ)

The BMQ is a measure of beliefs about medicines in general, and one specific medicine (ADA in this study). It consists of two subscales: necessity and concern. Final scores as estimated using recorded answers on a five-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. Higher scores indicate stronger perceptions of the concerns and necessity of ADA. The BMQ questionnaire was measured at baseline and week 78 and expressed as mean change from baseline [13].

Patient Activation Measure (PAM)—13

Patient's expectations regarding PSP and health management was measured by the Patient Activation Measure (PAM-13), which is a 13-item instrument that assesses self-reported knowledge, skills, and confidence for self-management [14]. Items are scored on a five-point scale. The sum of these scores is converted in a 0–100 point scale. Based on validated cut-off points, the four levels of activation were determined. A higher level refers to higher activations scores. Patients in level 1 are often passive and lack confidence for self-management resulting in low self-management engagement. Patients in level 2 become aware that they should be involved in their care, although there remain gaps in knowledge and skills. Patients in level 3 gain confidence for self-management and start to take action. The fourth, and highest, level of activation includes patients who have adopted new behaviors and are challenged to maintain these behaviors over time. Therefore, patients with higher levels of activation are considered better self-managers. The PAM-13 was measured at baseline and week 78.

Safety

All treatment-emergent serious adverse events (SAEs), treatment emergent adverse events (TEAEs) leading to premature discontinuation, non-serious treatment-emergent events of malignancy in patients 30 years of age and younger were collected. Additionally, spontaneously reported non-serious TEAEs were included in the safety evaluation. AEs were tabulated using the Medical Dictionary for Regulatory Activities (MedDRA) version 18.1 system organ class and preferred terms.

Statistical Analysis

Sample Size Determination

Sample size calculation of this study was based on the estimation precision approach. A total of 700 patients were needed to estimate the 95% confidence interval with 3.7% precision (confidence band width of 7.4%). With an estimated dropout rate of 30%, approximately 1000

patients should be enrolled into this study to maintain the precision of 0.037. This sample size was considered sufficient to meet the objectives of this post-marketing, uncontrolled, observational study with approximately 150–200 participating sites in 14 countries.

The intent-to-treat (ITT) population consisted of all enrolled patients who have taken at least one dose of ADA. The primary endpoint of percentage of patients achieving MCID in HAQ-DI at week 78 vs. baseline was compared between PSP users and PSP non-users. Patient information was summarized using descriptive statistics, continuous variables were compared by analysis of variance, and discrete variables were analyzed using χ^2 tests. Clinically relevant secondary outcomes were compared between PSP users and PSP non-users. Non-responder imputation (NRI) was used for response rate variables and last-observation carried forward (LOCF) for continuous variables, as appropriate. For continuous variables, the mean and standard deviation are presented.

Safety analysis was performed on the intent-to-treat population, which included all patients who received at least one dose of ADA. Serious AEs were summarized descriptively. AEs were presented as events per 100 patient-years (100 PY). All statistical tests were two-sided at a significance level of 0.05; analyses were performed by the study sponsor using SAS software (SAS Institute Inc., Cary, NC).

RESULTS

Patient Characteristics

A total of 1025 patients were included in the ITT population (ITT). Of these, 499 (48.7%) patients were PSP users and 526 (51.3%) were PSP non-users. The majority of patients were female (77.1%) and white (88.1%); 17.8% patients were treated with one prior biologic DMARD. Mean patient age at baseline was 54.3 years, and mean duration of RA was 7.8 years. There was a statistically significantly higher percentage of patients with prior biologic exposure among PSP non-users compared to PSP users group (24.0 vs. 11.2%, $p < 0.001$) at baseline.

Additionally, PSP users had more severe disease compared to PSP non-users, as evidenced by significantly higher TJC ($p = 0.01$), SJC ($p = 0.007$), DAS28 (CRP) ($p = 0.007$), HAQ-DI ($p = 0.045$), and SDAI ($p = 0.005$) at baseline (Table 1). Discontinuation rates were lower among PSP users versus PSP non-users (25.5 vs. 41.6%, $p < 0.001$). Lack of efficacy was the most common reason cited for study discontinuation in both groups (PSP users: 13.2%; PSP non-users: 19.4%) (Table 2).

Study Outcomes

The study met its primary endpoint with 72.1% (as observed) and 42.8% (NRI) of patients achieving the MCID in HAQ-DI at week 78. A higher proportion of PSP users than non-users achieved the MCID in HAQ-DI (48.1 vs. 37.8%; $p < 0.001$, NRI) at week 78 (Fig. 1). Differences in the proportions of patients achieving the HAQ-DI MCID between PSP users and non-users were apparent at weeks 24 and 52 [52.3 vs.

Table 1 Baseline demographics and disease characteristics

Characteristic	PSP users, $N = 499$	PSP non-users, $N = 526$
Age (years)	54.4 ± 13.2	54.2 ± 13.4
Female, n (%)	380 (76.2)	410 (77.9)
White, n (%)*	419 (84.0)	484 (92.0)
Duration of RA, (years)	8.2 ± 8.8	7.5 ± 8.1
Prior biologic DMARD, n (%)*	56 (11.2)	126 (24.0)
HAQ-DI	1.55 ± 0.7	1.44 ± 0.7
TJC 28*	13.0 ± 7.7	11.6 ± 7.0
SJC 28*	9.1 ± 6.1	8.0 ± 5.5
CRP (mg/l)*	28.1 ± 63.6	15.5 ± 24.4
DAS28 (CRP) (range 0–10)*	5.4 ± 1.2	5.2 ± 1.1
DAS28 (ESR) (range 1–10)*	5.7 ± 1.3	5.5 ± 1.3
SDAI*	37.3 ± 16.3	34.0 ± 13.9
CDAI	34.4 ± 14.4	32.3 ± 13.2
PaGA of disease activity	63.4 ± 22.2	62.4 ± 22.9
PhGA of disease activity	62.6 ± 20.9	64.7 ± 18.5
PAM-13 scores	60.7 ± 15.3	58.9 ± 14.6
BMQ		
Necessity scale*	4.24 ± 0.7	4.11 ± 0.7
Concern scale	3.01 ± 0.9	3.04 ± 0.8

All values are mean ± standard deviation, unless otherwise indicated. * significantly different at $p < 0.05$

PSP patient support program; RA rheumatoid arthritis, DMARD (biologic) disease-modifying antirheumatic drug, DAS28 28-joint disease activity score, CRP C-reactive protein, ESR erythrocyte sedimentation rate, SDAI simple disease activity index, CDAI clinical disease activity index, TIC 28 tender joint count for 28 joints, SIC 28 swollen joint count for 28 joints, HAQ-DI health assessment questionnaire-disability index, PaGA parents global assessment, PhGA physician global assessment, PAM patient activation measure, BMQ beliefs about medicines questionnaire

Table 2 All reasons for study discontinuation by PSP utilization category

Subject disposition	PSP users, N = 499	PSP non-users, N = 526
Discontinued (%)***	127 (25.5)	219 (41.6)
Adverse event	22 (4.4)	30 (5.7)
Withdrew consent	13 (2.6)	24 (4.6)
Lost to follow-up	17 (3.4)	29 (5.5)
Serious adverse events	10 (2.0)	14 (2.7)
Lack of efficacy	66 (13.2)	102 (19.4)
Other	16 (3.2)	35 (6.7)

*** Statistically significant at $p < 0.001$. Each patient could have >1 reasons for discontinuation

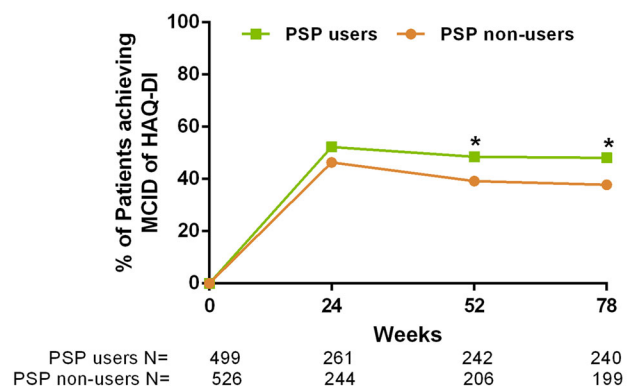
46.4% ($p = 0.058$) and 48.5 vs. 39.2% ($p = 0.003$)]. Significant improvements from baseline to week 78 overtime were observed in PSP users vs. PSP non-users in HAQ-DI (-0.53 vs. -0.39 ; $p = 0.011$), DAS28(CRP) (-2.33 vs. -1.97 ; $p = 0.018$), SDAI (-24.5 vs. -19.8 ; $p = 0.001$), and CDAI (-22.66 vs. -18.55 ; $p = 0.002$) (Fig. 2). The proportion of patients in the ITT population achieving ACR 20/50/70 response rates increased over time (observed data). A statistically significantly higher proportion of PSP users achieved ACR 20/50/70 response rates than PSP non-users at week 78 (Fig. 2).

Fig. 1 Percentage of patients achieving MCID in HAQ-DI overtime

Compared to PSP non-users, PSP users had significantly lower activity impairment as measured by WPAI at all measured time points (Table 3). No statistically significant differences were observed in the other three domains of WPAI. Numerical improvement in the favor of PSP users was observed for the CQR at all measured time points (Table 3). Higher convenience and global satisfaction (TSQM) were demonstrated at all measured time points, numerical improvement was observed in the effectiveness domain at weeks 24 and 52 and became significant at week 78 ($p = 0.011$) (Table 3). Compared to the PSP users, PSP non-users had statistically significant improvement from baseline at week 78 in the BMQ necessity scale ($p = 0.019$), but not the BMQ concern scale (Table 3). The percentage of patients that demonstrated improvement in PAM-13 levels was significantly higher among PSP users vs. PSP non-users (35.7 vs. 28.1%, $p = 0.01$). Additionally, compared to PSP users, PSP non-users had significantly higher percentage of patients that started at PAM-13 level 4 at baseline and remained at level 4 until week 78 of ADA treatment (64.5 vs. 53.8%, $p = 0.028$).

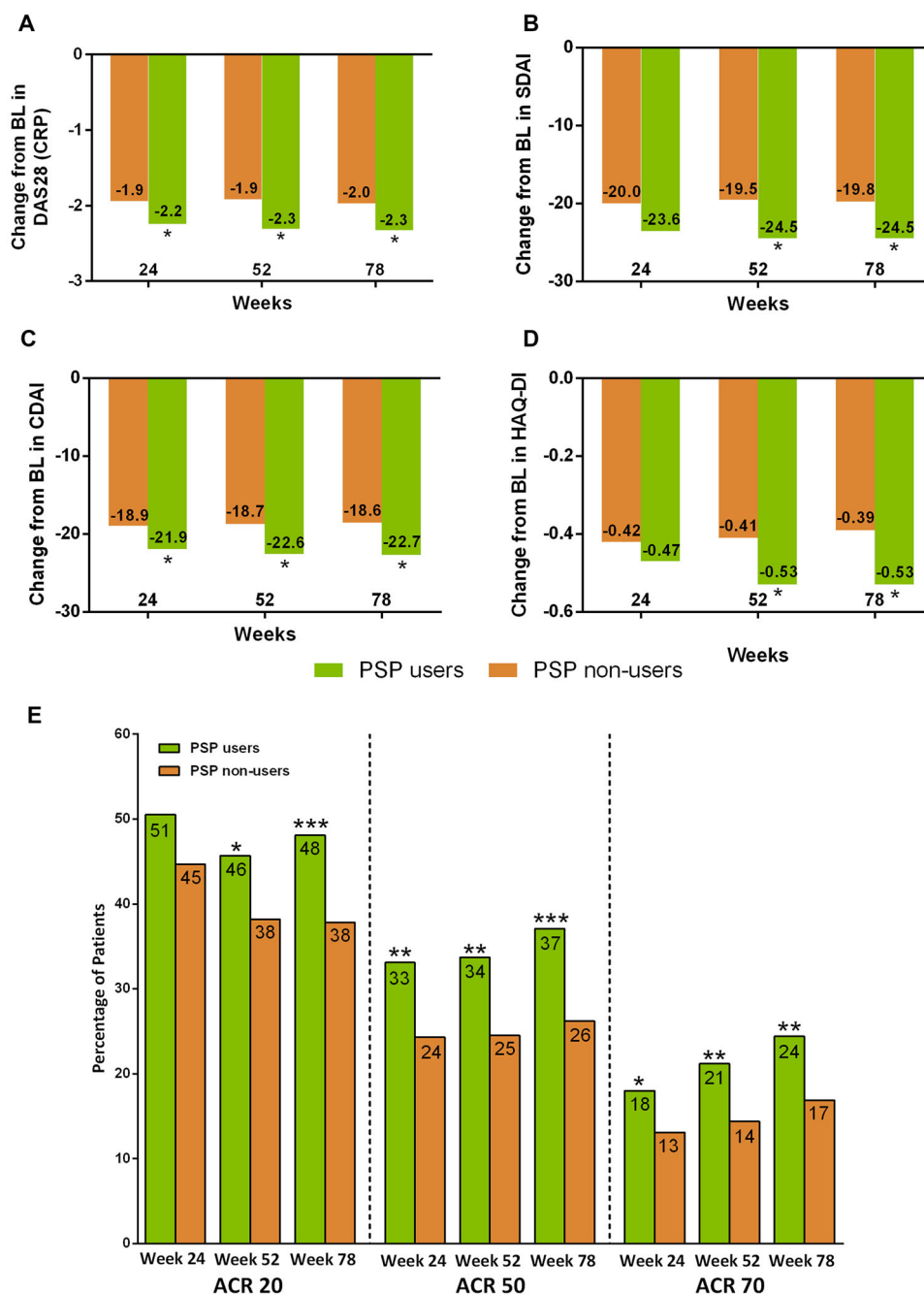
Safety

The incidence of AEs (10.6 E/100-PY) was comparable to the known safety profile of ADA across approved indications (Table 4). Infections were reported in 58 (5.7%) patients and



* $P < 0.05$, Non Responder Imputation. Differences in the HAQ-DI in MCID changes over time are adjusted for the baseline differences. HAQ-DI= health assessment questionnaire disability index, MCID=minimum clinically important difference.

Fig. 2 Changes from baseline in DAS28 (CRP) (a), SDAI (b), CDAI (c), HAQ-DI (d), and ACR response rates[#] (e) over time between PSP users and PSP non-users



* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Data represented by LOCF imputation. [#]Data represented by NRI. LOCF=last observation carried forward, NRI=non-responder imputation. Differences in each of the outcome measures over time between the PSP users and PSP non-users are adjusted for their respective baseline scores.

serious infections were reported in 30 (2.9%) patients. The most common infections included pneumonia (0.9%), appendicitis (0.2%), salpingo-oophoritis (0.2%), and urinary tract

infections (0.2%). One patient (<0.1%) reported an opportunistic infection (non-serious mild bronchopulmonary aspergillosis). Three deaths were reported during the study: (1) due

Table 3 Patient-reported outcomes by PSP utilization category

Patient-reported outcomes	24 weeks		52 weeks		78 weeks	
	PSP users	PSP non-users	PSP users	PSP non-users	PSP users	PSP non-users
WPAI						
Absenteeism	-2.32 (149)	-5.43 (138)	-2.80 (152)	-5.18 (147)	-5.71 (156)	-8.17 (151)
Presenteeism	-18.68 (167)	-17.06 (163)	-18.34 (169)	-17.08 (168)	-19.07 (172)	-17.75 (173)
Work productivity loss	-17.55 (148)	-18.17 (137)	-17.77 (152)	-16.69 (147)	-22.28 (156)	-19.94 (151)
Activity impairment	-23.90* (474)	-20.11 (458)	-25.06* (478)	-20.97 (466)	-26.42* (478)	-20.56 (468)
CQR	2.44 (488)	2.01 (458)	2.39 (490)	1.99 (466)	2.30 (490)	1.80 (467)
TSQM						
Convenience	6.67* (387)	3.85 (269)	7.38* (413)	4.77 (292)	7.23* (422)	4.76 (300)
Effectiveness	14.56 (368)	14.29 (262)	16.06 (392)	15.41 (286)	16.24* (401)	13.62 (294)
Side effects	8.21 (367)	8.10 (246)	8.09 (393)	8.55 (274)	8.37 (403)	8.25 (284)
Global satisfaction	11.44* (383)	10.85 (267)	12.53* (408)	11.12 (292)	11.68* (417)	9.87 (300)
BMQ						
Necessity	NC	NC	NC	NC	-0.03* (409)	-0.04 (362)
Concern	NC	NC	NC	NC	-0.12	-0.17 (361)
PAM-13, %	NC	NC	NC	NC	35.7 (499)	28.1 (526)

Data are mean change from baseline (n) unless otherwise indicated. * $p < 0.05$. *NC* not collected. Data represented by LOCF imputation for intent-to-treat population for WPAI (work productivity and activity impairment), CQR (compliance questionnaire for rheumatology), and TSQM (treatment satisfaction questionnaire for medications). Data represented as observed for BMQ (beliefs about medicines questionnaire). Data represented by NRI for PAM (patient activation measure)-13. Data represented as observed for BMQ. Results are adjusted for baseline WPAI, CQR, TSQM, and BMQ. *LOCF* last observation carried forward, *NRI* non-responder imputation

to cerebral B cell non-Hodgkin's lymphoma (with deglutition and respiratory insufficiency), which was assessed by investigator as probably not related to ADA; (2) bile duct stone and metastases to liver (primary source of metastasis was unknown and the event assessed by investigator as probably related to ADA); and (3) esophageal hemorrhage caused by esophageal varices and hepatic cirrhosis caused by alcoholism (event assessed by investigator as probably not related to ADA). Eight patients

(0.8%) experienced malignancies (one event of adenocarcinoma of colon, one event of B-cell lymphoma, three events of breast cancer, one event of metastatic lung adenocarcinoma, and one event of liver metastases). No melanoma was reported. One event (<0.1%) of demyelination was reported. No events of active or latent tuberculosis or oral candidiasis were reported. Seventy-five (7.3%) patients prematurely discontinued from study participation due to AEs.

Table 4 Overview of treatment of emergent adverse events

Adverse event (AE)	Adalimumab <i>N</i> = 1025 <i>n</i> (%)	Adalimumab <i>N</i> = 1025 PYs = 1251.8 E (E/IOOPYS)
Any AE	174 (17.0)	322 (25.7)
Serious AE	97 (9.5)	133 (10.6)
Severe AE	53 (5.2)	75 (6.0)
AE leading to discontinuation of study drug	75 (7.3)	103 (8.2)
Serious infections	30 (2.9)	33 (2.6)
Opportunistic infections (excluding oral candidiasis and TB)	1 (<0.1)	1 (<0.1)
Tuberculosis (active, latent)	0	0
Malignancies	8 (0.8)	8 (0.6)
AE leading to death	3 (0.3)*	4 (0.3)

* Three deaths (1) cerebral B-cell non-Hodgkin lymphoma, (2) bile duct stone and metastases to liver, and (3) esophageal hemorrhage and hepatic cirrhosis

DISCUSSION

The main purpose of the study was to provide information on the clinical, functional, and patient-reported outcomes in a real-life practice setting among RA patients that initiated ADA and were offered to participate in the PSP. To our knowledge, PASSION is the first prospective study to show a significant improvement in treatment and patient-reported outcomes in moderate to severe RA patients participating in PSP. Results from this post-marketing observational multinational study showed that patients with moderate to severe RA who initiated ADA and enrolled in the PSP achieved an overall greater improvement in clinical, functional, and patient-reported outcomes as compared to the patients who initiated ADA without participation in the PSP. A higher percentage of patients using elements of the PSP achieved the primary endpoint of MCID in HAQ-DI as compared to the PSP non-users. After adjusting for the baseline differences, the secondary endpoint of clinical effectiveness, the percentage of patients achieving MCID in HAQ-DI at weeks 24 and 52 showed numerical improvement at week 24 and significant improvement at week 52 in

favor of PSP users vs. PSP non-users. Significant improvements of 26, 15, 19, and 18% from baseline to week 78 were observed in PSP users over PSP non-users in HAQ-DI, DAS28 (CRP), SDAI, and CDAI, respectively, (Fig. 2a–d) and superior response rates in ACR 20/50/70 responses were observed at weeks 52 and 78. PSP users performed significantly better than PSP non-users at weeks 24, 52, and 78, except for ACR 20 response rate at week 24, when PSP users performed numerically better than PSP non-users (Fig. 2e). It should also be noted that the ADA discontinuation rate was significantly lower among PSP users (25.5%) as compared to the PSP non-users (41.9%), suggesting that PSP participation may have an impact on ADA treatment persistence (Table 2).

In this post-marketing observational study, no new safety signals were identified with ADA treatment for RA [15, 16]. Few events identified as risks with anti-TNF therapy were observed, and no active/latent tuberculosis was reported. Three deaths and eight events of malignancies were reported [15].

PSP users reported significant improvements in outcomes during 78 weeks of initiated ADA treatment in managing their health and gained

skills and confidence to do so as evidenced by higher PAM-13 levels compared to the PSP non-users. Additionally, PSP users had significantly lower activity impairment (WPAI), improved convenience and global satisfaction (TSQM), and felt lower necessity for prescribed medication (BMQ) in comparison to the PSP non-users. Only numerical improvement in the favor of PSP users was observed for CQR.

The majority of the PSPs fall into one of three categories with the following objectives: (1) to support patients and help them take their medications as prescribed (compliance/adherence); (2) to help patients understand their condition and provide advice on managing disease, e.g., lifestyle (exercise or diet), disease education; (3) to provide a service or financial assistance or reimbursement support for patients also known as patient assistance programs. A recent systematic review of the published literature by Burudpakdee et al. demonstrated that across inflammatory and immunologic diseases PSPs significantly improve adherence and persistence [17]. Research led by Lorig et al. showed that health education for self-management in patients with chronic arthritis had sustained health benefits while reducing health care costs [18]. Similarly, Barlow et al. demonstrated that patients who participated in the arthritis support management program acquired substantial and prolonged benefits in terms of perceived ability to manage arthritis, reduction in pain, and improved psychological well-being [19]. Esselens et al. also observed that patients who participated in an outpatient RA care program that provided multidisciplinary care with immediate access to different health professionals had higher remission rates and were able to better preserve functionality and general health status compared with patients who received standard care provided by a rheumatologist [20].

As in any observational study, only observed confounders were accounted for, hence the findings of the study should be interpreted with the caution of unobserved confounding. Additionally, the study only collected data on study discontinuation rates and not on discontinuation of ADA; therefore no conclusions about drug adherence/persistence can be made from

the current analysis. However, previously published studies on AbbVie's PSP have reported improvements in adherence/persistence of ADA among PSP users [21].

CONCLUSIONS

The results from the PASSION study demonstrated that patients with moderate-to-severe RA who initiated ADA and participated in the PSP achieved an overall significantly greater improvement in clinical, functional, and patient-reported outcomes when compared to patients who did not participate in the PSP while treated with ADA. No new safety signals were identified with ADA treatment. As this was a post-marketing observational study, only limited safety data were collected. This study indicates that participation in a PSP can have a positive effect on clinical and quality of life outcomes in RA patients such as physical functioning, treatment satisfaction, and activities impairment and may also have an impact on the treatment persistence and adherence.

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Compliance with Ethics Guidelines. The study protocol was approved by the responsible ethics committees and internal review boards at each study site and the study was done in compliance with the Declaration of Helsinki of 1964, Good Clinical Practice guidelines, and applicable local regulations. Informed consent was obtained from all patients.

Data Availability. Qualified researchers may request access to the study data sets from AbbVie via the process defined on AbbVie.com, under Clinical Trial Data and Information Sharing.

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