Abstract3

Title

SOLACE - P15-696: Canadian Humira® PoSt Marketing Observational EpidemiologicaL Study: Assessing Humira® Real-life EffeCtiveness and Impact on ModeratE to Severe Hidradenitis Suppurativa Burden of Illness and Health Care Resources Utilization

Keywords

Hidradenitis suppurativa, Humira®, adalimumab, real-life effectiveness, burden of illness, health care resource utilization

Rationale and Background

Hidradenitis suppurativa (HS) is a chronic inflammatory and systemic skin disease affecting the terminal hair follicle that presents a significant physical and psychological burden affecting patients' health-related quality of life (HR-QoL) and work productivity. The disease also greatly impacts health care resource utilization (HCRU) and costs. Although a broad range of therapeutic options are currently used to manage patients with HS, limited response and low level of evidence have been reported.

The rationale for this observational study was to determine how the efficacy of Humira®, demonstrated in pivotal trials, translated into a real-life clinical setting, by evaluating the effectiveness, impact on burden of illness, HCRU, and costs in moderate to severe HS patients. These data will be highly relevant to help health care providers and policy-makers making well-informed decisions.

This final clinical study report (CSR) includes analyses initially planned in Protocol P15-696 and an exploratory analysis, characterizing the subpopulation of HS subjects who discontinued prematurely from the study and identifying differences between

study completers and non-completers; non-completers defined as subjects who discontinued the study.

Research Question and Objectives

Primary objective:

- Assess Humira® real-life effectiveness in the management of dermatological manifestations of moderate to severe HS

Secondary objectives:

- Describe the profile and regional variation in terms of demographics, disease parameters, concurrent diseases, concomitant medication use, clinical course of HS, and management by dermatologists of Canadian patients with moderate to severe HS

- Describe the burden of illness of HS in Canada and estimate the impact of Humira® on moderate to severe HS patients in terms of physical and psychological quality of life, work productivity, HCRU, and cost

Study Design

SOLACE was a 1-year multicenter Canadian post-marketing observational study (PMOS) utilizing a prospective cohort design to assess Humira® real-life effectiveness in moderate to severe HS subjects and to estimate the impact of Humira® on subjects' burden of illness, HCRU, and costs. The study was planned to have a 2-year enrolment period (approximately), with a 1-year observational period for a total duration of 3 years. Assessments were performed during subjects' routine care visit schedule, which was at approximately 12, 24, 36, and 52 weeks after baseline.

Setting

Subject historical data up to 6-month prior to baseline visit were collected. Although there were no study-specific requirements given the observational nature of the study, data were to be collected at approximately 12, 24, 36, and 52 weeks after baseline, coinciding with the subject's routine care visit schedule.

It was anticipated that some subjects would be seen more frequently than suggested, in which case the site reviewed the subject's medical chart at the time of the visit where data was collected, to determine what, if any, information collected during the other routine care visits was appropriate for and needed to be entered into the electronic case report form (e-CRF).

Study subjects were followed for up to 52 weeks. All study data were recorded in the subject's source documentation and collected on the appropriate e-CRF. Patient-reported outcome (PRO) instruments were evaluated using self-administered questionnaires. The variables to be collected during the study were listed in the e-CRF.

Subjects and Study Size, Including Dropouts

Potential subjects were assessed for their eligibility to participate in the study using the inclusion and exclusion criteria as follows.

To be eligible for study entry, each subject must have met all of the following inclusion criteria:

1. A male or female of $\geq$ 18 years of age

2. A clinical diagnosis of moderate to severe HS according to the treating physician judgment

3. A change in ongoing therapy for any reason, but not limited to, inadequate response, intolerance, sub-optimal compliance, or subject preference. Subject was approached to participate in the study after a decision to change subject's therapy for Humira® was made by the treating physician

4. Provided written informed consent (Patient Authorization) for participation in the study

To be eligible for study entry, each subject must have not met any of the following exclusion criteria:

1. Participating in a clinical interventional study

2. Treated with Humira® or any other biologic agents for HS prior to baseline visit

3. Had any other active skin disease or condition that, in the opinion of the treating physician prohibited the subjects from participating in the study or obscured the assessment of the treatment of HS

One hundred sixty-five subjects, who provided written consent, were enrolled and formed the final study population. The enrolment period (i.e., time elapsed between first and last subject enrolled) was approximately 1.5 years. In total for the final analysis, 155 subjects were included in the safety population, and 138 subjects were included in the intent-to-treat (ITT) population.

Variables and Data Sources

Primary Variable: The proportion of subjects with moderate to severe HS treated with Humira® who achieved a clinical response using the Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 24.

Secondary Variables:

- Proportion of subjects with moderate to severe HS treated with Humira® who achieved a clinical response using the HiSCR measure at Week 52

- Proportion of subjects who experienced worsening of HS by ≥ 1 Hurley Stage in ≥ 1 affected anatomic region

- Proportion of subjects who experienced flare, defined as at least 25% increase in AN count (number of abscesses + inflammatory nodules) with a minimum increase of 2 relative to baseline

- Number of days where subjects experienced HS flare-up.

- Change from baseline in Health Utility Index Mark 3 (HUI3).

- Change from baseline in Patient Global Assessment of HS (HS-PtGA).

- Change from baseline in Hospital Anxiety and Depression Scale (HADS).

- Change from baseline in Hidradenitis Suppurativa Impact Assessment (HSIA).

- Change from baseline in Hidradenitis Suppurativa Symptom Assessment (HSSA).

- Change from baseline in Female Sexual Function Index (FSFI), and International Index of Erectile Function (IIEF).

- Change from baseline in Work Productivity and Activity Impairment (WPAI: Hsu).

- Change from baseline in HCRU associated with HS.

- Distribution of subjects by management strategy employed (i.e., administration of Humira® monotherapy or in combination with other treatment modalities

including surgery and any changes in the regimen throughout the study observation period among the overall population).

- Identification of prognostic factors for HS progression and need for future surgery (i.e., primary operation, re-operation in the same anatomical area), complications (i.e., wound infection, nerve irritation, bleeding, stricture, pain) and post-operative relapse of HS).

Exploratory Variables:

- Reason for discontinuation
- Timing of study discontinuation
- Disease severity at baseline, Hurley worst stage, and International HS Severity Scoring System (IHS4)
- Demographics: age, gender, race
- Disease history: age at HS onset, years since HS onset, years since HS confirmed diagnosis
- Number of affected body area at baseline
- Number of lesions
- Presence of comorbidities, total number of comorbidities
- Number of previous treatments for HS
- Current treatment compliance up to discontinuation
- PRO instruments at baseline
- Responses by study completion

Safety Variables: Adverse events (AEs), clinical laboratory results, and physical examinations.

Given that the primary objective of this study was not to assess any safety parameters, only data spontaneously reported serious adverse events (SAEs), any non-serious event of malignancy in subjects 30 years of age and younger, whether related to study drug or not, unusual failure in efficacy, AEs leading to discontinuation of prescribed treatment under observations, and pregnancies were reported and collected.

Results

One hundred and sixty-five subjects were included in this final analysis, with 138 (83.6%) subjects included in the efficacy population (also identified as the ITT population) and 155 (93.9%) subjects included in the safety population. The main reasons for study discontinuation were withdrawal by subject (17 [37.8% of the discontinued subjects]) and lost to follow up (16 [35.6% of the discontinued subjects])

The primary endpoint – the proportion of subjects who achieved a clinical response using the HiSCR measure at Week 24 – was 68.9% (82/119 subjects; 95% confidence interval [CI]: 60.6%, 77.2%) for the ITT population. These values, obtained in a real-life setting, are slightly higher than the integrated data of HS subjects on continued HUMIRA weekly dosing reported in the PIONEER I, PIONEER II, and (open-label extension (OLE) studies; 2 Phase III multicenter trials, which enrolled 307 subjects and 326 subjects respectively, and 1 OLE study where subjects from both PIONEER I, and PIONEER II studies transitioned to (clinical response rate at Week 12: 53.5% and at Week 24: 57.6%).

The secondary endpoints that showed improvement from baseline were:

- Hurley worst stage: The proportion of subjects with Hurley worst stage II and stage III decreased from baseline compared with all timepoints, whereas the proportion of subjects with Hurley worst stage I increased from baseline compared with all timepoints.

- The number of inflammatory nodules and the AN count: The mean AN count (number of abscesses + inflammatory nodules) decreased by 8.4 at Weeks 12 and 24 and slightly more by Weeks 36 and 52/early termination (ET), with the number of inflammatory nodules contributing more to the decrease in AN count than the number of abscesses.

- Regarding the PRO instruments, significant improvement from baseline to Weeks 12, 24, 36, and 52 was shown for the HUI3 overall utility score (for all timepoints p was ≤ 0.0023), HS-PtGA (overall for all timepoints p was <0.0001), HADS (overall for all timepoints p was ≤0.0005), HSIA (overall for all timepoints p was ≤0.0001), HSSA (overall for all timepoints p was ≤0.0001). In addition, all WPAI scores improved from baseline during the study, with activity impairment, presenteeism, and work productivity loss improving slightly during the study.

The proportion of subjects who experienced flare during the study varied from 3.3% (4/122 subjects) to 6.7% (8/119 subjects). No trends were observed over time and among the Canadian regions. These values, obtained in a real-life setting, are lower than results reported in the integrated data of PIONEER I and PIONEER II studies (9.8% at Week 12 and 12.3% overall, N= 316).

Assessing prognostic factors, the logistic regression analysis confirmed that males have a significantly higher probability, approximately 4 times the odds for females, of a clinical response at Week 24 (female vs. male odds ratio = 0.242; 95% CI: 0.074, 0.791; p = 0.0189). A comparison of the age at disease onset indicated that the odds of a clinical response at Week 24 decreased by 5% with each additional year (age at disease onset odds ratio = 0.954; 95% CI: 0.914, 0.995; p = 0.0278)

Regarding HCRU related to HS care, the most frequently reported sought-after care for HS was a visit to a primary care physician followed by a visit to other health care, for a mean number of visits per month of ≤ 0.1 overall for all timepoints (0.31≤ standard deviation [SD] ≤0.62) and between 0.1 and 0.2 overall for all timepoints, respectively. The mean number of visits were low (0.0 to 0.1 for all timepoints) for: dermatologist, surgeon, psychologist, hospital ER, use of ambulance service. There were no reported visits to a nurse practitioner and for complementary therapy.

The exploratory analysis showed that:

- As per the IHS4 scoring system, the proportion of subjects with severe HS who achieved a clinical response slightly increased from Week 24 (69.9% [58/83] subjects) to Week 52/ET (75.9% [66/87] subjects).

- Disease status:

  - Proportionally, slightly more subjects with severe HS were completers (71.7% [86/120] subjects) than non-completers (62.8% [27/43] subjects)

  - Proportionally, more subjects with Hurley worst stage II were completers (71.7% [86/120] subjects) than non-completers (53.5% [23/43] subjects)

The primary objective of this study was not to assess safety parameters. The key safety data collected were as follows:

- The median time in trial was 365.0 days (range: 33 – 531 days), and the median treatment duration was 349.0 days (range: 1 – 456 days).

- No deaths were reported during the study.

- There were no reports of malignancy, including in subjects 30 years of age and younger during the study (as per protocol safety variable).

- Three (1.9%) subjects experienced serious treatment emergent adverse events (TEAEs) that were assessed by the Investigator to be reasonably possibly related to Humira®: 1 (0.6%) subject experienced a serious and severe soft tissue infection; 1 (0.6%) subject experienced a serious and severe myelitis that led to treatment discontinuation, and 1 (0.6%) subject experienced a serious and severe anal abscess.

- One subject (0.6%) experienced 3 severe TEAEs (arthritis, depression, and urticaria) that led to discontinuation and that were assessed by the Investigator to be reasonably possibly related to Humira®.

- The most commonly experienced comorbidity was obesity (between 59.1% and 64.0% of subjects during the study) followed by depression (between 27.8% and 35.5% of subjects during the study).

- Mean changes from baseline to each analysis visits in laboratory parameters, vital signs, and physical examination values were clinically unremarkable.

Discussion

SOLACE was a 1-year multicenter Canadian PMOS utilizing a prospective cohort design to assess Humira® real-life effectiveness in moderate to severe HS patients and to estimate the impact of Humira® on patients' burden of illness, HCRU, and costs.

This final CSR includes analyses initially planned in Protocol P15-696 and an exploratory analysis, characterizing the subpopulation of HS subjects who discontinued prematurely from the study and identifying differences between study completers and non-completers.

Assessing real-life effectiveness, this study represented an external validity to previous study using Humira® in HS patients (PIONEER I, PIONEER II, and OLE studies). Results from this study are comparable to results from other studies using Humira® for patients with HS, where such a treatment led to an increase in HiSCR and a decrease in the number of lesions.

In conclusion, from Week 12 to Week 52, Humira®, used in a real-life setting, was effective at decreasing the number of inflammatory lesions associated with HS, with more than 60% of the subjects achieving the HiSCR. A decrease in HS severity was

shown using the Hurley worst stage, with proportionally less subjects assessed as stages II and III, and more subjects assessed as stage I at all timepoints compared with baseline. Thus, the treatment with Humira® contributed to reducing the physical and psychological burden of illness associated with HS, as assessed with PRO instruments. The safety profile was consistent with the known safety profile of Humira®, and no new signal or unexpected trend was identified for the patient population.

Marketing Authorisation Holder(s)

AbbVie Corporation

Names and Affiliations of Principal Investigators

The study investigators were from 23 Canadian centres, as listed below.