1.0 Abstract

Title

Effectiveness of adalimumab in moderate to severe **H**idr**A**denitis **S**uppu**R**ativa patients - a **M**ulti c**O**u**N**tr**Y** study in real life setting - HARMONY Study

Keywords

Hidradenitis suppurativa, Adalimumab, Humira

Rationale and Background

Hidradenitis Suppurativa (HS) is a chronic, inflammatory, recurrent, debilitating skin disease that usually presents after puberty as recurrent inflamed tender subcutaneous nodules in the apocrine gland-bearing areas of the body, most commonly in the armpits, groin and anogenital regions. HS lesions result in scarring, create sinus tracts and often produce an unpleasant odor and recurrent discharge. HS impairs both physical and emotional aspects of an individual's quality of life and is known to be associated with several comorbidities. It is considered difficult to treat and until recently, no approved therapies existed and a broad range of therapeutic options were used in managing patients with HS, with very limited response and with very limited evidence.

Adalimumab (Humira®) is a fully human IgG monoclonal antibody which targets TNF-α and is administered subcutaneously. It is approved for the treatment of various diseases such as moderate to severe plaque psoriasis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis and juvenile idiopathic arthritis. Adalimumab has been shown to be safe and effective in three randomized controlled clinical trials with strict inclusion and exclusion criteria and has gained European Medicines Agency (EMA) approval for the use in moderate to severe HS.

The rationale of this observational study is to determine how the efficacy and safety of adalimumab as demonstrated in pivotal trials translates into real world everyday clinical settings, evaluating its effectiveness and patient reported outcome. Effectiveness trials typically have limited exclusion criteria and involve the broader patient populations in routine clinical practice, treated per local label, which might include patients with significant comorbid conditions and could be used to model and disseminate best practices. This observational study is the first effectiveness research examining adalimumab used according to the local label, under real world conditions in the clinical practice patient population.

Research Question and Objectives

The primary objective of the study was to estimate the effectiveness of adalimumab treatment on disease severity at 12 weeks.

The secondary objectives of this observational study were:

- To estimate the effectiveness of adalimumab treatment on disease severity at 24, 36, and 52 weeks
- To estimate the impact of adalimumab treatment on patients' quality of life, level of pain and psychological affect in the overall population as well as in the subpopulations (with and without comorbidities) over a period of 52 weeks
- To estimate the impact of adalimumab treatment on patients' work productivity and resource utilization associated with HS, in the overall population as well as in the subpopulations (with and without comorbidities) over a period of 52 weeks
- To describe treatment practices over the study period

Study Design

This is a prospective, multi-country, post marketing observational study (PMOS) of HS patients receiving adalimumab treatment according to routine clinical practice. It was planned to be conducted in approximately 12 countries.

The study population comprises adult patients who were diagnosed with moderate to severe HS and who have not been treated with adalimumab prior to the baseline visit. The decision to treat with adalimumab had to be made by the physician in accordance with the local label prior to any decision to approach the patient to participate in this study.

The study consists of 5 visits: one baseline visit (V1) and four follow-up visits approximately 12, 24, 36 and 52 weeks after baseline (V2, V3, V4, and V5).

Setting

In this analysis, the following countries were included: Austria, Belgium, Switzerland, Czech Republic, Great Britain, Greece, Hungary, Ireland, Israel, Lebanon, and Slovenia.

Subjects and Study Size, Including Dropouts

In total, 231 patients were enrolled in the study. 201 of these patients fulfilled all selection criteria and had data for at least one follow-up visit. Thus, these patients were included in full analysis set (FAS). The COMPLETER analysis set consists of 103 of the FAS patients who did not discontinue adalimumab during the study.

Variables and Data Sources

Data were to be documented on case report forms (CRFs). In addition, patients were asked to complete the following questionnaires at the visits prior to any other study-related assessment: The Patient Health Questionnaire (PHQ-9), Dermatology Life Quality Index (DLQI), Work Productivity and Activity Impairment - HS (WPAI-HS), Euro Quality of Life 5 Dimensions (EQ-5D), and a numeric rating scale (NRS) for Patient's Global Assessment of Skin Pain.

Site characteristics were collected on a site information form.

Results

Patients were enrolled from 59 sites in 11 countries in Europa and the Middle East. The majority of participating sites were university hospitals (61%), followed by public hospitals (44.1%) and private practices (3.4%).

At week 12 more than two thirds (70.2%) of the patients achieved HiSCR. This rate was maintained until end of the study, when 72.1% achieved HiSCR.

Consistently, patient reported outcomes improved under treatment with adalimumab (between baseline and week 52 [LOCF]): depression (PHQ-9), disability and psychosocial impairment in dermatological disorders (DLQI), health status (EQ-5D-3L, utility index and VAS), absenteeism and total work productivity in employed patients and total activity in all patients (WPAI), skin pain (worst and mean) (NRS).

27 SAEs were documented in this study, which occurred in 23 patients. 8 SAEs had a causal relationship (“reasonable possibility”) with adalimumab. One patient who was on adalimumab for 3 months died during the study; this patient experienced three SAEs (PTs: bladder cancer, metastases to liver, liver function test abnormal). The investigator assessed the relationship to adalimumab as reasonably possible.

Discussion

Study results yield a comprehensive and detailed picture of the demographic characteristics of an international patient population diagnosed HS.

Notably, many study patients suffered from HS for several years and were still classified as Hurley stage III or II at baseline. Thus, long-term disease management was clearly unsatisfactory for many patients, which is even more conspicuous in light of the fact that 67.8% of sites reported following international treatment guidelines. Therefore, verifying the extent to which guideline recommendations were observed could be worthwhile. Additional causes for insufficient treatment may include lack of access to optimal healthcare specialist, or poor compliance.

Under treatment with adalimumab, more than two thirds achieved HiSCR, i.e. patients experienced a fast and effective improvement. This rate was then also maintained over a year until the final visit at 52 weeks.

The clinical benefit was supported by observed improvements in most assessed PROs, including improvement in depression, disability and psychosocial impairment, pain and workability.

In this study, only serious adverse events (SAEs) and any serious or non-serious malignancies in patients 30 years of age and younger had to be documented and reported. Thus, no comprehensive safety evaluation can be performed. Based on the data obtained, no new safety signals or unexpected trends were identified.

In summary, results of this study confirm effectiveness of adalimumab in treatment of HS. Patient-relevance was confirmed by the observed statistically significant improvements in most assessed PROs.

Marketing Authorization Holder(s)

AbbVie Ltd.