1.0 Abstract

Title

PMOS: HUM04-28. A five-year, post marketing observational study to follow-up patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis who are treated with HUMIRA® (adalimumab) (ProAct).

Keywords

Rheumatoid Arthritis/Psoriatic Arthritis/Ankylosing Spondylitis, HUMIRA® (adalimumab therapy), safety, efficacy.

Rationale and Background

HUMIRA® (adalimumab), a recombinant full-length immunoglobulin, is the first member of a new class of tumour necrosis factor (TNF) antibody compounds, developed to contain exclusively human sequences with a very high affinity for human TNF. It is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA), active and progressive psoriatic arthritis (PsA), and active ankylosing spondylitis (AS), when the response to conventional therapy has been inadequate. To ensure maximum efficacy in RA and PsA, HUMIRA® (adalimumab) is given in combination with methotrexate (MTX)/other disease-modifying anti-rheumatic drugs (DMARDs) or can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. In AS, Humira is given in monotherapy.

Upon initiation of this study, HUMIRA® (adalimumab) had generally been well tolerated and had demonstrated therapeutic efficacy. It had also shown sustained efficacy in open-label long term studies [1-5], however the data related to patients treated for 4 and 5 years were still limited. Therefore, this follow-up observation study was planned for 5 years and focused on safety information as well as maintenance of efficacy parameters for HUMIRA® (adalimumab) during normal clinical practice.

Research Question and Objectives

The objectives of this study were to observe and assess the long-term use, safety, and efficacy of HUMIRA® (adalimumab) as prescribed by the rheumatologist in a normal clinical setting and in accordance with the terms of the European marketing authorization.

Study Design

This is a multicenter, uncontrolled observational study of RA, PsA, and AS patients in whom HUMIRA® (adalimumab) was prescribed at the time of entry following normal clinical practice, and treated with or without other anti-rheumatic treatments prior to enrollment. RA patients were included as from the start of the study (2004). Subsequent amendments allowed inclusion of PsA patients (2005) and AS patients (2006). Due to a change in the reimbursement criteria for RA, DAS28 was collected as from 2010 on for RA patients.

The total observation period was approximately 5 years, with routine visits at baseline and afterwards preferably after 3, 6, 9, 12, 18, 24, 30, 36, 42, 48, 54, and 60 months.

Setting

As many patients as were willing to participate in this follow-up study were to be enrolled.

Patient data were collected during routine visits at baseline and afterwards preferentially after 3, 6, 9, 12, 18, 24, 30, 36, 42, 48, 54, and 60 months.

Subjects and Study Size, Including Dropouts

Five thousand nine hundred and forty (5940) patients, 2845 RA patients, 1128 PsA patients of which 198 with oligoarticular PsA, and 1967 AS patients, were enrolled till 21 December 2012. The last study visit took place on 11 January 2018.

Variables and Data Sources

- Demographic data.
- Disease activity.
- Clinical examination.
- Concomitant medication.
- (Serious)Adverse events.

Results

Five thousand nine hundred and forty (5940) patients, 2845 RA patients, 1128 PsA patients of which 198 with oligoarticular PsA, and 1967 AS patients, were enrolled till 21 December 2012. The last study visit took place on 11 January 2018.

Twenty (20) patients were younger than 18 years old, 9 RA patients, 1 PsA patient, and 10 AS patients. These patients were not considered in the statistical analysis.

Among the 5920 remaining patients 2836 had RA, 1127 PsA of which 197 oligoarticular PsA, and 1957 AS.

The average study duration for RA patients was 2.8 years (SD: 2.0) ranging between 0 and 10 years, for PsA patients it was 3.0 years (SD: 2.0) ranging between 0 and 9 years, and for AS patients it was 2.9 years (SD: 2.0) ranging between 0 and 8 years.

Onset data

On average, RA patients were 56.6 years of age (SD: 13.0, Range: [18.9; 88.7]), PsA patients 49.5 years (SD: 12.4, Range: [18.1; 88.9]), and AS patients 43.6 years (SD: 12.5, Range: [18.0; 82.0]).

In the RA group, 2004 patients (71.8%) were female and 787 (28.2%) male. In the PsA group, these were 523 (46.9%) females and 591 (53.1%) males, while in the AS group these were 903 patients (46.6%) females and 1033 (53.4%) males.

In the RA group, 2378 patients (83.8%) were anti-TNF-naïve and 458 (16.2%) anti-TNF- experienced. This was the case for 947 patients (84.0%) and 180 (16.0%) patients in the PsA group, while in the AS group there were 1570 anti-TNF-naïve patients (80.2%) and 387 anti-TNF- experienced patients (19.8%), respectively. The following concomitant medications were used:

- Steroids: 1273 RA patients (44.9%), 189 PSA patients (16.8%), and 148 AS patients (7.6%)
- NSAIDs: 1132 RA patients (39.9%), 474 PsA patients (42.0%), and 1031 AS patients (52.7%)
- DMARDs: 2060 RA patients (72.6%), 684 PsA patients (60.7%), and 344 AS patients (17.6%)

Follow-up data

The average adalimumab treatment duration was 2.8 years±2.0 (Range: [0.0; 10.4]) for RA patients, for PsA patients it was 3.0 years± 2.0 (Range: [0.0; 8.5]), and for AS patients 2.9 years± 2.0 (Range [0.0; 8.3]).

Physician's assessment of disease activity

The disease activity as assessed by the physician decreased during the study as illustrated by a decrease in the average VAS at baseline from 58.5 mm to 24.6 mm at Month 3, reaching 12.1 mm at Month 60 in RA patients. A similar decrease was observed in PSA patients: From 54.6 mm to 18.9 mm at Month 3, reaching 10.2 mm at Month 60 as well as in AS patients: From 59.2 mm to 19.9 mm, reaching 9.7 mm, respectively.

Clinical evaluations (HAQ% and DAS28)

In RA patients, physical function (HAQ%, calculated according to the Belgian reimbursement criteria) improved during the study from an average at baseline of 47.8% to 27.0% at Month 3, reaching 19.9% at Month 60. A similar decrease was observed in PSA patients: From 41.0% to 20.5% at Month 3, reaching 14.6% at Month 60 as well as in AS patients: From 40.8% to 16.5%, reaching 11.4%, respectively.

In RA patients, disease activity decreased during the study as illustrated by a decrease in the average DAS28 score at baseline from 5.04 to 3.19 at Month 3, reaching 2.52 at Month 60.

At baseline, 16 RA patients (4.2%) were in remission (DAS28<2.6) while at Month 60 this was the case for 187 patients (56.0%).

Adverse events

In total, 5416 adverse events were recorded in 1792 patients (30.3%), 3302 events were reported for 976 patients (34.4%) in the RA group, 860 events for 323 patients (28.7%) in the PsA group, and 1254 events for 493 patients (25.2%) in the AS group.

SAEs were observed in 560 RA patients (19.8%), 164 PsA patients (14.6%), and 210 AS patients (10.7%). Fatal events were reported in 42 RA patients (1.48%), in 4 PsA patients (0.35%), and in 9 AS patients (0.46%).

Discussion

In this observational study a marked improvement of the disease activity and physical function was seen in patients with RA (DAS 28, HAQ%), PsA (TJC, SJC, HAQ%) and AS (BASDAI, HAQ%). The biggest improvements were seen in the first 3 months of treatment.

These results are consistent with previously published long term efficacy data in RA, PsA and AS patients.

The safety profile observed in this study was similar to that observed in clinical trials of adalimumab for the treatment of RA, PsA and AS.

Marketing Authorisation Holder(s)

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