1.0 Abstract

Title

An extended observational study (P12-707: HOPEFUL III Study) of follow-up survey (P12-069: HOPEFUL II study) of the study of adalimumab (D2E7) for prevention of joint destruction in patients with rheumatoid arthritis in Japan (M06-859)

Keywords

Adalimumab, Rheumatoid Arthritis, Effectiveness, Safety

Rationale and Background

Adalimumab is a fully human tumor necrosis factor (TNF)-alpha monoclonal antibody preparation and was approved in Japan for treatment of rheumatoid arthritis (RA) in patients showing an inadequate response to conventional therapy in April 2008.

An increasingly important question from physicians and patients in the new of effective treatment of RA with anti-TNF agents is the ability to decrease or stop therapy in patients who have maintained response over a period of time, especially in patients who began anti-TNF treatment early in their disease. An additional issue is the cost of the biologic treatment to the patient or to the payer, and the effect of this on the ability to maintain treatment. In Japan, most of the patients must pay 30% co-payment of their medical costs, which may limit long term treatment.

Therefore, it is of great interest to both physicians and patients to gain the following information:

The possibility to stop adalimumab treatment when a patient has maintained a long-term response. The OPTIMA study (AbbVie Inc.) was conducted to study this situation, however, there is no such Japanese data yet.

The ability to maintain the inhibition of progression in joint destruction of under long-term adalimumab treatment. The PREMIER study gave an answer to this question in other populations, but there is no such Japanese data yet.

Research Question and Objectives

The objectives of this Observational study are follows.

Main Objective:

To determine the ability to maintain response after discontinuation of adalimumab treatment.

- In patients who discontinue treatment with adalimumab after sustained low disease activity,* the proportion of patients who experience disease flare (DAS28-CRP > 3.2) during the first year after discontinuation of adalimumab (first year of biologic-free period) will be assessed.
  * Defined as DAS28-CRP < 3.2 at Week 46 and 52 of the HOPEFUL I.

Secondary Objective:

Determine radiographic progression in patients participating in the study, including the proportion of the patients who display minimal progression (change in TSS of less than 0.5 Units).

Study Design

This Post Marketing Observational Study will be conducted in a two-arm, multicenter format.

Inclusion criteria is that the Japanese patients with RA who have continued the 1-year observational period of HOPEFUL II study, provided informed consent to participate in this HOPEFUL III study. Patients who use biological agents other than

adalimumab in the HOPEFUL II observational period will be excluded from the HOPEFUL III study.

Setting

This PMOS study was conducted in Japan, and the durations of the survey and registration periods were as follows:

Duration of the survey: March 2011 to December 2014

Duration of registration: April 2011 to December 2012.

Subjects and Study Size, Including Dropouts

For this post-marketing observational study no sample size calculation was performed.

The background of the following target sample size refers to the anticipated number of patient who may complete HOPEFUL II Study.

1. Target sample size: Approximately 125.
2. Rationale for sample size: The number of patients to complete HOPEFUL II study is approximately 140. Informed consent rate from HOPEFUL II through HOPEFUL III is 90%.

Variables and Data Sources

Information was collected at the different time points as follows:

Discontinuation of participation from the HOPEFUL III study, adalimumab treatment, concomitant drug information, including disease-modifying antirheumatic drugs (DMARDs), glucocorticoids and others, effectiveness evaluation (Disease Activity Score 28 [DAS-28], Matrix metalloprotease-3 [MMP-3], x-ray findings for hands and feet and Health Assessment Questionnaire [HAQ]), and adverse events were collected by paper-based CRF every 1 year after completion of the HOPEFUL II.

Effectiveness analysis was performed on the data obtained during the HOPEFUL I to HOPEFUL III. Safety analysis was performed on the data from the patients who treated adalimumab during the HOPEFUL III.

Results

Baseline Characteristics

This study is extended study of the HOPEFUL II. Then, baseline characteristics were summarized at Week 0 of the HOPEFUL II. Of the 172 patients, 82.0% (141/172) were female. The patients had a mean ± SD age of 55.8 ± 12.8 years at administration and a mean body weight of 56.45 ± 9.84 kg. Mean disease duration was 1.332 ± 1.463 years. 58.1% (100/172) and 77.9% (134/172) of the patients were rheumatoid factor positive and anti-cyclic citrullinated peptide antibody positive, respectively. Additionally, 100% (172/172) and 66.9% (115/172) of the patients were concomitantly treated with methotrexate and corticosteroids, respectively.

Effectiveness

77 patients who achieved DAS28-CRP < 3.2 at Week 46 and 52 of the HOPEFUL I were discontinued adalimumab treatment at Week 0 of the HOPEFUL II. 71.4% (55/77) of the patients who discontinued adalimumab treatment were maintained sustained low disease activity for 1 year. After 2 years (104 weeks; after 1 year in HOPEFUL III) and 3 years (156 weeks; after 2 year in HOPEFUL III) of ADA discontinuation, 58.4% (45/77) and 45.5% (35/77) of the patients maintained DAS28-CRP < 3.2 without disease flare.

Safety

101 patients who treated adalimumab at least once during the HOPEFUL III were in the safety analysis set. 31 ADRs were reported by 18 patients (17.82% [18/101]) and 3 serious ADRs were reported by 2 patients (1.98% [2/101]).

Discussion

For 1 year, more than 70% of the patients who discontinued adalimumab maintained sustained low disease activity without disease flare. No new safety signals were identified from the patients who were treated with adalimumab.

Marketing Authorisation Holder(s)

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Names and Affiliations of Principal Investigators

Not applicable.