

1.0 **Abstract**

Title

Humira® for Subcutaneous Injection Special Investigation (All-case survey) in
Patients with Juvenile idiopathic arthritis

Keywords

Adalimumab, Juvenile idiopathic arthritis

Rationale and Background

This postmarketing surveillance of Humira for Subcutaneous Injection (generic name: adalimumab [recombinant]) was conducted to clarify the following with regard to the treatment of juvenile idiopathic arthritis (JIA) affecting multiple joints with Humira. This postmarketing observational study (PMOS) was required by the Pharmaceuticals and Medical Device Agency (PMDA), as the approval conditions for JIA. Because the number of clinical trial subjects in Japan is very limited, the background information of patients using Humira should be kept track of by conducting a use-results survey in all cases until data for a certain number of cases are accumulated after marketing, and data on the safety and effectiveness of Humira should be obtained early and necessary measures for the proper use of Humira should be taken.

Research Question and Objectives

To assess the safety and effectiveness of adalimumab on JIA

Study Design

This was an all-case survey, single-arm, multi-center, prospective cohort study (Post-Marketing Observational Study). The observation period for each subject was 24 weeks, and follow-up period was 2 years.

Setting

This study was conducted for all sites which used Humira for JIA from July 2011 to February 2016 in Japan. The registration period of subjects was the same.

Subjects and Study Size, Including Dropouts

Subjects

Inclusion Criteria

All patients with Juvenile idiopathic arthritis who were not responding well to conventional therapy and received Humira were enrolled in the survey

Exclusion Criteria

- Contraindications according to the Package Insert
- Patients who have serious infections
- Patients who have tuberculosis
- Patients with a history of hypersensitivity to any ingredient of Humira
- Patients who have demyelinating disease or with a history of demyelinating disease
- Patients who have congestive cardiac failure

Study Size

Target sample size: 100 patients

Actual sample size: 368 patients

Immediately after the approval of JIA as an indication for treatment with Humira, all patients who received Humira for the treatment of JIA affecting multiple joints were registered, and the data for the first 100 patients were tabulated and analyzed, and the results reported to the regulatory authority. Registration of patients was continued

until the authority concludes its final evaluation. The actual sample size was 368 patients because this surveillance was conducted for all-case survey as the condition for approval of JIA under the direction of the authorities.

Variables and Data Sources

Variables

Effectiveness

DAS28, Serum Matrix metalloprotease-3 level, Anti-cyclic citrullinated peptide antibody, Physician Global Assessment (Visual Analog Scale)

Safety

Adverse events, Adverse drug reactions, Height, Weight

Data Sources

Data sources in this study are from institute's medical chart. Participant physicians in this study transcribe the data from medical chart to Case Report Form (CRF) which AbbVie prepares.

Results

A total of 375 patients were registered. Case report forms (CRFs) were retrieved from 368 patients, and could not be retrieved from 7 patients. Among the 368 patients with retrieved CRFs, 356 patients were eligible for safety analysis, and 205 patients were eligible for effectiveness analysis in at least one item of effectiveness evaluation after start treatment.

Effectiveness

The changes of the DAS28-4/ESR and DAS28-4/CRP scores from baseline were statistically significant among 128 patients and 175 patients at Week 24 and the scores

significantly improved. The change of the anti-cyclic citrullinated peptides antibodies score from baseline was statistically significant in 39 patients at Week 24 and scores significantly improved. In the changes of other effectiveness indexes (Physician Global Assessment (VAS), Serum Matrix metalloprotease-3 level), scores significantly improved at all time points from Week 4 to Week 24 compared to those before start of treatment.

Safety

239 adverse events were observed in 129 patients in the safety analysis set, and the incidence rate of adverse events was 36.2% (129/356). 27 serious adverse events were observed in 17 patients, and the incidence rate of serious adverse events was 4.8% (17/356).

174 adverse drug reactions were observed in 106 patients in the safety analysis set, and the incidence rate of adverse drug reactions was 29.8% (106/356). 15 serious adverse drug reactions were observed in 12 patients and the incidence rate of serious adverse drug reactions was 3.4% (12/356).

And Humira had no adverse impact on patients' growth in height and weight.

Discussion

No new safety and efficacy issues were found and thus taking any specific actions is considered unnecessary.

Marketing Authorization Holder(s)

AbbVie GK


Names and Affiliations of Principal Investigators

Not applicable