

1.0 Abstract

Title

HUMIRA® 40 mg Syringe 0.8 mL for Subcutaneous Injection Protocol for Special investigation on Long-Term administration Ulcerative Colitis

Keywords

Adalimumab, Ulcerative Colitis

Rationale and Background

Background

It was indicated that administration of Humira at 160 mg (Week 0)/80 mg (Week 2)/40 mg (from Week 4 onward) improves disease activity and Quality of Life (QOL) in Japanese patients with moderate to severe ulcerative colitis. This postmarketing observational study (PMOS) was requested by the Pharmaceuticals and Medical Device Agency (PMDA), as part of the approval for the ulcerative colitis indication.

Rationale

The purpose of this study was to examine the safety and efficacy of Humira in Japanese patients with moderate to severe ulcerative colitis under the condition of daily medical care.

Research Questions and Objectives

This investigation was conducted to obtain the following information regarding the use of Humira 40 mg Syringe 0.8 mL for Subcutaneous Injection in patients with Ulcerative Colitis.

1. Unknown adverse reactions (in particular, clinically significant)
2. Incidence and conditions of occurrence of adverse reactions in clinical practice
3. Factors likely to affect the safety and effectiveness

Key Survey Items in Safety

Infection, tuberculosis, malignant tumor, injection site reaction, autoimmune disease, pancytopenia, demyelinating disorders, congestive cardiac failure, and interstitial pneumonia. For enteral infection, the cause (virus or bacteria) will be examined.

Primary Endpoints

1. Number of patients with adverse events [Time Frame: Up to Week 52]
Number of patients with adverse events with evaluation beginning upon administration of Humira

Secondary Endpoints

1. Full Mayo score [Time Frame: Up to Week 52]
2. Partial Mayo score [Time Frame: Up to Week 52]
3. C-reactive Protein [Time Frame: Up to Week 52]
4. Mayo endoscopic sub-score [Time Frame: Up to Week 52]

Study Design

Patients are observed for a period of 52 weeks after administration of Humira was started (even though the treatment is continued even after 52nd week, the CRF was completed at the time point of Week 52). All patients were enrolled in the surveillance upon agency request, not only adults per the approved indication. For

patients who were lost to follow up during the observation period, their last available data prior to study discontinuation were included in the analysis.

Subjects and Study Size, Including Dropouts

Subjects

Patients with moderate to severe active ulcerative colitis (only when ineffectively treated with the existing medications) who were prescribed Humira were surveyed.

Study Size

Planned number of the sample size: 1500 (Actual number enrolled was: 1621)

Inclusion Criteria

Patients with moderate to severe active ulcerative colitis (only when ineffectively treated with the existing medications) who were prescribed Humira were surveyed.

Surveillance Schedule

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

1. Duration of the survey: July 2013 to March 2018
2. Duration of enrollment: July 2013 to July 2016

Variables and Data Sources

Patient characteristics, hospitalization, treatment, drug use, clinical indices and AEs were collected through CRF forms.

Results

Safety

A total of 1621 patients were enrolled. Among the enrolled patients, case report forms were not collected from 28 patients, and there were 1593 patients whose data in case report forms were assessable. 1523 patients were handled as the safety analysis set after 70 patients ("safety assessment impossible") were excluded from the 1593 patients for whom case report forms were attained. Among 1523 patients included in the safety analysis set, 408 adverse reactions were noted in 276 patients, and the percentage of patients who experienced adverse reactions was 18.12%.

Common adverse reactions by system organ class of adverse reactions (MedDRA SOC: ≥ 25 patients) and their incidence rates were "infections and infestations" (6.04%, 92/1523), "skin and subcutaneous tissue disorders" (4.01%, 61/1523), "gastrointestinal disorders" (2.95%, 45/1523), "respiratory, thoracic and mediastinal disorders" (2.43%, 37/1523), "general disorders and administration site conditions" (2.04%, 31/1523), and "Lab test" (1.84%, 28/1523).

Common adverse reactions by preferred term (MedDRA PT: ≥ 10 cases) and their incidence rates were "nasopharyngitis" (1.58%, 24/1523), "rash" (1.38%, 21/1523), "colitis ulcerative" (1.31%, 20/1523), "pyrexia"/"upper respiratory tract inflammation" (0.85%, 13/1523 each), "C-reactive protein increase" (0.72%, 11/1523), and "arthralgia" (0.66%, 10/1523).

Possible factors having an impact on the occurrence of adverse reactions were examined. As a result, there was no factor requiring special actions. Important investigation items did not exhibit any new risk.

Efficacy

1241 patients were handled as the efficacy analysis set after 282 patients ("efficacy assessment impossible") were excluded from the 1523 patients who made up the

safety analysis set. Among 1241 patients of the efficacy analysis set, the general improvement rate was effective or better in 864 patients (69.6%).

Possible factors having an impact on the efficacy were examined. As a result, there was no factor requiring special actions.

Discussion

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

Marketing Authorization Holder(s)

AbbVie GK


Names and Affiliations of Principal Investigators

Not applicable.