1.0 Abstract

Title

Humira® 40mg Syringe 0.8mL Subcutaneous Injection. Special Investigation in patients with Intestinal Behcet's disease

Keywords

Adalimumab, Behcet's disease

Rationale and Background

<Background>

Adalimumab is expected effective for the treatment of intestinal Behcet's disease judged from the report that patients maintained endoscopic and histological remission under adalimumab monotherapy even in 22 months after switch from concomitant therapy with infliximab and immuneregulator which alleviated intestinal Behcet's disease.

<Rationale>

This survey was performed as a total survey in Japanese patients with intestinal Behcet's disease for the purpose of verifying the safety and efficacy of Humira in usual clinical practice.

The sponsor was instructed by the Pharmaceuticals and Medical Devices Agency (PMDA) to perform a total survey for the purpose of verifying the safety and efficacy of adalimumab in the patients with intestinal Behcet's disease in actual clinical use, since the clinical study substantiated the safety and efficacy but was performed in a limited number of patients.

Research Questions and Objectives

A specified use-results survey of HUMIRA® 40 mg Syringe 0.8 mL for Subcutaneous Injection (Nonproprietary name: Adalimumab (recombinant)" was performed for the purpose of obtaining the following information in Japanese patients with intestinal Behcet's disease.

(Primary Endpoints)

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

< Key survey items in safety>

Infection, tuberculosis, malignant tumor, administration site reaction, autoimmune disease, pancytopenia, demyelinating disorders, congestive cardiac failure, and interstitial pneumonia

(Secondary Endpoints)

4. Efficacy measured by overall evaluation of gastrointestinal symptoms, evaluation of gastrointestinal symptoms of Behcet's disease, evaluation of main symptoms of Behcet's disease, evaluation of secondary symptoms of Behcet's disease, degree of improvement of endoscopic findings, and CRP
5. Factors likely to affect the efficacy

Study Design

The observation period of the survey was 156 weeks at the longest and segmented to 52 weeks, 104 weeks, and 156 weeks depending on the treatment stage. The observation period differed from patient to patient because of the need to recover CRFs from all patients registered during the re-examination period (4 years) and submit the report to PMDA.

Subjects and Study Size, Including Dropouts

<Subjects>

Japanese patients with intestinal Behcet's disease.

<Study Size>

Number of sample size : No decided

<Inclusion Criteria>

Patients receiving Humira® for the treatment of Behcet's disease after the approval of the indication are to be all enrolled.

The survey was performed in the patients with intestinal Behcet's disease (not sufficiently responsive to existing therapies, e.g. steroids, immunomodulator), who were treatable with Humira® (Also refer to "Precautions relating to the indications").

<Exclusion Criteria>

Patients included in "Contraindication" in the package insert

1. Patients with serious infection (sepsis etc.) [Symptomatic worsening may occur.]
2. Patients with active tuberculosis [Symptomatic worsening may occur.]
3. Patients with a history of hypersensitivity to any of the ingredients of HUMIRA
4. Patients with a current or past history of demyelinating disorder (multiple sclerosis, etc.) [Symptomatic relapse or worsening may occur.]
5. Patients with congestive heart failure [Symptomatic worsening may occur.]

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

Duration of the survey: 16MAY2013to 15MAY2017

Duration of registration: 16MAY2013to 15AUG2015

Variables and Data Sources

Patient characteristics, hospitalization, oxygen inhalation or artificial respiratory support, treatment, drug use, and AEs were collected through CRF forms.

Results

- Safety

  There were 200 cases of ADRs reported among 120 of the 462 patients included in the safety analysis population; the incidence rate of ADRs was 25.97% (120/462 patients). The incidence rate of AE was 35.71%(165/462 patients). This incidence rate of ADRs and AE was lower than that reported by the time of approval (ADRs :70.00%, 14/20 patients AEs : 100.00%,20/20 patients).

The most common ADRs (by MedDRA PT: 5 or more cases) and their incidence rates were as follows: “pyrexia”, 2.60% (12/462 patients); “C-reactive protein increased”, 1.95% (9/462 patients); “nasopharyngitis”, 1.73% (8/462 patients); “pneumonia”, 1.52% (7/462 patients); and “Behcet's syndrome”, 1.08% (5/462 patients). There were 69 cases of serious ADRs reported among 51 patients and the incidence rate of serious ADRs was 11.04% (51/462 patients). The most common serious ADRs (by MedDRA PT: 3 or more cases) and their incidence rates were as follows: “pyrexia”, 1.30% (6/462 patients); “pneumonia”, 1.08% (5/462 patients); “Behcet’s syndrome”, 0.72% (4/462 patients); and “sepsis”, 0.65% (3/462 patients).

- Efficacy

Among the 333 patients included in the efficacy analysis population, there were 324 patients whose global improvement rating was “effective” or “markedly effective”; the efficacy rate was 84.6% (324/383 patients).

Discussion

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

Marketing Authorization Holder(s)

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Names and Affiliations of Principal Investigators

Not applicable.