1.0 Abstract

Title

HUMIRA Special Investigation (Long-term Treatment in Patients with Non-infectious Intermediate-, Posterior-, or Pan-uveitis)

Keywords

Non-infectious Intermediate-, Posterior-, or Pan-uveitis , Tumor Necrosis Factor (TNF) Blockers, Adalimumab , Humira, real world

Rationale and Background

Rationale

Details of the rationale can be found in the protocol (Annex 1, page 69, Protocol Section 7.2).

Humira (adalimumab) was approved for treatment of Non-infectious Intermediate-, Posterior-, or Pan-uveitis on Sep 2016 and was launched to the market on the same day in Japan.

When the Humira (adalimumab) was approved, PMDA indicated that “The applicant is required to develop and appropriately implement a risk management plan.” as the approval condition for the indication.

This study evaluated appropriate use of this regimen as described in the J-RMP which was to collect data on the safety and effectiveness of Humira in daily practice.

Background

In general, the Pharmaceuticals and Medical Devices Agency (PMDA) requires pharmaceutical companies to collect data on the safety and effectiveness of a drug in routine daily practice of an approved new drug/indication.

Research Question and Objectives

To evaluate the long- term safety and effectiveness of adalimumab in patients with Non-infectious Intermediate-, Posterior-, or Pan-uveitis in daily practice in Japan.

Primary endpoints

- Incidence of adverse drug reactions (ADR)

Secondary endpoints

✓ Safety endpoints

- Incidence of serious adverse event (SAE)

✓ Effectiveness endpoints

- Overall improvement
- Uveitis flares
- Amount of steroids used
- Change in AC cell grade (SUN criteria)
- Change in Vitreous Haze grade (NEISUN criteria)
- Change in Visual acuity
- Change in VFQ-25 score
- Factors that may affect the effectiveness

Study Design

This was a Single-arm, multi-center, prospective cohort study.

This PMOS was conducted in accordance with GPSP, ministerial ordinance of MHLW of Japan.

Setting

Study Period

✓ Registration period

From 11 Oct 2016 to 30 Jun 2018

✓ Study period

From 11 Oct 2016 to 30 Jun 2020

Investigative Sites

After a MR explains details of the purpose and methods of the study to participating physicians in medical sites where Humira would be used, a written agreement was finalized between AbbVie GK and each participating institution.

Study medication

Humira was prescribed to patients as per Japan label by a physician with sufficient knowledge and experience in the treatment of ophthalmological disease.

The recommended subcutaneous injection for Uveitis is an initial dose of 80 mg followed by 40 mg given after one week, starting 40 mg every other week at 2 weeks after the second dose.

Observation Period

For each patient, the observation for safety and effectiveness evaluation started from the enrollment which is beginning of the treatment with Humira. And the observation period is from the start of treatment to up to the following time point.

- ✓ Safety: 52 weeks, Occurrence of malignancy: 104 weeks
- ✓ Effectiveness: 52 weeks

Subjects and Study Size, Including Dropouts

Subjects

Patients who are prescribed Humira (adalimumab) for the treatment of Non-infectious Intermediate-, Posterior-, or Pan-uveitis in daily practice

Inclusion Criteria

Patients who meet the following inclusion criteria can be included this study.

- ✓ Patients who are diagnosed with Non-infectious Intermediate-, Posterior-, or Pan-uveitis
- ✓ Patients who give informed consent to participate this study before starting Humira (adalimumab) treatment

Exclusion Criteria

- ✓ Patients who have been previously treated with adalimumab

Study Size

250 patients

Variables and Data Sources

Variables

1) Patient demographics and characteristics
2) Previous drug treatment

3) Previous non-drug treatment including surgery

4) Treatment with Humira

5) Concomitant drug treatment

6) Concomitant non-drug treatment

7) Effectiveness

8) AEs

9) Malignant tumor: follow up

Data Sources

The original data source for this study was medical records retained by medical institutions participating in this study. Physicians completed registration form and case report form prepared by AbbVie.

For some survey questions, such as those listed below, the information provided in CRF was the original data source.

- ✓ Observations
- ✓ assessments

Results

60 sites of these sites enrolled patients into the study. Recruitment period was from 11 Oct 2016 to 30 Jun 2018.

A total of 259 patients were enrolled in this study. The CRF were collected from 256 patients. 5 patients of whom were excluded from the safety analysis set because of the exclusion criteria or registration criteria violation/ineligible cases, therefore 251

patients were included in the final safety analysis set. Of the 251 patients in the safety analysis set, 5 were excluded from the effectiveness analysis set, therefore 246 patients were included in the final effectiveness analysis set.

Safety

The cumulative rate of ADRs was 18.73% (47/251) in this study. The rates of ADRs from the previous clinical trials submitted for approval (M10-877 [4)], M10-880 [2)], M11-327 [3)]) was 69.8% (324/464) [1)], and the rates of ADRs in this study was comparable with previous Humira trials.

The cumulative rates of AEs were 27.89% (70/251) and the rates of SAEs was 9.56% (24/251). There were 30 different SAE, among which "Herpes Zoster" and "Tuberculosis" each accounted 0.80% (2/251), and "Disseminated tuberculosis", "Pyelonephritis", "Tuberculoma of central nervous system", "Pneumonia bacterial", "Colon cancer", "Breast cancer female", "Thyroiditis subacute", "Diabetes mellitus inadequate control", "Personality change", "Putamen haemorrhage", "Macular oedema", "Interstitial lung disease", "Dermatitis", "Drug eruption", "Toxic skin eruption", and "Polymyalgia rheumatica" each accounted 0.40% (1/251), only 24 patients were observed with SAE.

The safety results of this study were consistent to the currently documented safety profile of Humira, as described in the label.

Effectiveness

Overall improvement rate was 95.1% (234/246).

The patient characteristics with significant differences in effective rates were "Number of flares (left eye) " and "Presence / absence of pretreatment drug (biologics) ". The amount of corticosteroid use was slightly higher in this study compare to the clinical trial, however the tendency of the reduction from the start of administration was similar. In addition, the proportion of subjects without new active inflammatory

chorioretinal or inflammatory retinal vascular lesions was equivalent to that in the registrational clinical trial.

These results indicated that Humira used for chronic Non-infectious Intermediate-, Posterior-, or Pan-uveitis has been shown to be highly effective in the real world.

Conclusion

The results of this observational study support the safety and effectiveness of Humira used for patients with Non-infectious Intermediate-, Posterior-, or Pan-uveitis in routine daily practice in Japan. The safety results of this study were consistent to the currently documented safety profile of the product, as described in the label. Humira used for Non-infectious Intermediate-, Posterior-, or Pan-uveitis has been shown to be highly effective in the real world.

Marketing Authorization Holder(s)

AbbVie GK

3-1-21 Shibaura, Minato-ku, Tokyo 108-0023, Japan

+81-3-4577-1111

Names and Affiliations of Principal Investigators

Not applicable