1.0 Abstract

Title: Real-World Outcome of Adalimumab on Rheumatoid Arthritis Patients in Taiwan

Keywords: Adalimumab, Rheumatoid Arthritis, HCRU, WPAI

Rationale and background:
Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease associated with a substantial comorbidity burden. Patients with RA have poorer survival experience and can lead to the deterioration of their health-related quality of life (HRQoL).

Given the requirement to keep a balance between effectiveness and cost containment to ensure that the available health resources are used in a cost-effective manner, there is an increasing demand for real-world evidence (RWE) from policy makers, regulators, providers and payers in the region to optimize spending and patient outcomes.

So far, there are no prospective study data available regarding adalimumab's impact on patients' quality of life (QoL) and healthcare resource utilization (HCRU) in Taiwan.

The goal of this study is to determine the QoL, HCRU and costs of the patients care in subjects with RA who are treated with adalimumab in Taiwan.

Research question and objectives:
The objective of this study is to assess the impact of adalimumab on HRQoL and work productivity in patients with RA in Taiwan.

Study design:
This is a prospective observational study involving 100 subjects enrolled at seven different sites and observed for 12-week baseline and 24 weeks after initiation to assess the effect of adalimumab on HRQoL and work productivity in patients with RA in Taiwan.

To assess health and disability outcomes, the HAQ-DI at baseline, Week 12 and Week 24 after treatment initiation with adalimumab will be collected. In addition, other PROs of work activity and well-being, including the WPAI, EQ-5D, and SF-36, will also be collected.

Setting:
Clinical settings are preferred by the participating rheumatologist.

Subjects and study size, including dropouts:
100 patients diagnosed with RA are enrolled at seven different sites in Taiwan.

Inclusion Criteria:
Patients meeting all of the following inclusion criteria at baseline were included:

1. Subject has a diagnosis of RA as defined by the 1987 revised American College of Rheumatology (ACR) classification criteria and/or the ACR/the European League against Rheumatism (EULAR) 2010 classification criteria (any duration since diagnosis)
2. Male or female subjects ≥ 18 years of age (local definition according to adalimumab label) who is in compliance with eligibility for adalimumab based on the local label
3. Patients with moderate to severe RA defined as Disease Activity Score in 28 Joints (DAS28) (erythrocyte sedimentation rate) or DAS28 (C-reactive protein) >3.2
4. Biologically treatment naïve and initiated adalimumab at baseline visit
5. Availability of clinical data of the previous 12 weeks prior to baseline
6. Ability to self-complete patient questionnaires
7. Subject must be able and willing to provide written informed consent and comply with the requirements of this study protocol

Exclusion Criteria:
Patients meeting any of the following exclusion criteria at baseline were excluded:

1. Patients who are pregnant or breast feeding at enrolment or wish to become pregnant in the next 24 weeks
2. Participation in any RA-related clinical trial at the time of enrolment, at baseline or at any point during the past 24 weeks prior to baseline
3. Patients, who in the clinician's view, may not be able to accurately report their QoL or prior resource utilization
4. Patients, who in the clinician's view, may not be able to adhere to adalimumab therapy over 24 weeks

Variables and data sources:
Primary Variable

- Change in HAQ-DI score at week 24 from baseline

Secondary Variable

- Change in other PROs (SF-36 domain scales, EQ-5D Index, Work Productivity and Activity Impairment Questionnaire [WPAI]) from baseline to weeks 12 and 24
- Change in HAQ-DI score at week 12 from baseline
- Number and percent of patients achieving a clinically meaningful improvement on the HAQ-DI, from baseline to weeks 12 and 24
- Healthcare resource utilization (HCRU) at baseline, 12 and 24 weeks

Exploratory Variable

- Difference of the change in HAQ-DI score from baseline to 24 weeks between as observed population and withdrawal population
- Change in patient satisfaction questions from baseline to weeks 12 and 24
- Patient's impression of change at weeks 12 and 24 from baseline
- Association between disease severity and PROs
- Association between change in disease severity and change in PROs

Case Report Forms (CRFs) and patient questionnaires (PROs)
Collection of data includes but not limited to subject demographics, clinical history, comorbidities, spontaneous adverse events (AEs), and concomitant medications. The following questionnaires will be utilized to collect data directly from participating subjects:

- EQ-5D
- SF-36
- HAQ-DI
- WPAI
- HCRU
- Patient Global Impression of Change (PGIC)
- Patient Treatment Satisfaction Questions

Results:

- **Patient Demographics**
  Mean average of age in RA patients were about 54 years old (SD ± 12.2) with majority of patients in age group of 45-54 and 55-64 years. Only 5% were RA elderly patients (75+ years old). The majority of RA patients in Taiwan were female (87%).

- **Clinical Characteristics**
  Mean average DAS28 was found to be 6.3 (SD ± 0.9), with majority of patients comprising of high disease activity (91%). 22% of RA patients suffering from comorbidities with a majority including diabetes, peptic ulcer disease and peripheral vascular disease.

- **Change in HAQ-DI at Weeks 12 and 24 after Initiation of Adalimumab**
  Mean change from baseline in HAQ-DI scores were -0.34 (SD ± 0 59) at week 12 and -0.44 (SD ± 0.46) at week 24 ($p=0.0002$ and $p<0.0001$, respectively). Clinical improvement in HAQ-DI, defined as improvement from baseline greater than -0.22, was achieved in 60.42% patients at week 12 and 59.57% patients at week 24.

- **Change in SF-36 Domain Scales at Weeks 12 and 24 after Initiation of Adalimumab**
  Mean change from baseline in PCS-T score improved from 5.72 at 12 weeks to 8.09 (SD ± 5.78) at 24 weeks ($p<0.001$ vs baseline, respectively). Mean change from baseline in MCS-T score improved from 3.67 (SD ± 7.94) at 12 weeks to 5.85 at 24 weeks ($p<0.001$ vs baseline, respectively).

- **Change in EQ-5D-3L Index at Weeks 12 and 24 after Initiation of Adalimumab**
  Mean changes from baseline in the EQ-3L index were 0.23 (SD ± 0.3) at 12 weeks and 0.33 (SD ± 0.38) at 24 weeks ($p<0.001$, respectively).

- **Change in WPAI at Weeks 12 and 24 after Initiation of Adalimumab**
  Significant mean changes from baseline in percentage of overall work impairment at 24 weeks (-0.19) (SD ± 0.23) was comparable to the change at 12 weeks (-0.18) (SD ± 0 23). Changes from baseline in percentage of activity impairment at 24 weeks improved to -0.24 (SD ± 0.25) compared with -0.14 (SD ± 0.22) at 12 weeks.

- **Patient Satisfaction Questions at Weeks 12 and 24 after Initiation of Adalimumab**
  Approximately 18%, 20%, 22%, 24% at week 12 and 41%, 46%, 47%, 48% at week 24 of patients rated "very satisfied" on how RA treatment with adalimumab improved morning stiffness in and around the joints, improved mobility, improved the ability to perform daily living requiring fine motor skills and satisfaction with RA treatment overall, respectively, demonstrating improvement in all domains.

  More patients felt "somewhat satisfied" at week 12 than week 24 (63% vs 40%, respectively) on how RA treatment improved mobility. Higher number of patients were "somewhat satisfied" at week 12 compared to 24 weeks (55% vs 35%). The improvement in overall satisfaction domain is demonstrated by the shift from replies in the category of "somewhat satisfied" at week 12 compared to week 24 (56% vs 38%, respectively).

- **Patients' Global Impression of Change at Weeks 12 and 24 after Initiation of Adalimumab**
  None (0%) of the RA patients felt "very much better" at 12 weeks from baseline however approximately 12% patients felt "very much better" at 24 weeks. Approximately 43% of RA patients felt "much better" 12 weeks after the initiation of adalimumab whereas 59% felt "much better" after 24 weeks. Around 9% patient felt there was "no change" at 12 weeks after the initiation of adalimumab, whereas only 6% felt "no change" at 24 weeks.

- **Post-Index Healthcare Resource Utilization**
  Overall 99% of patients consulted more than one healthcare professional. The majority of patients (around 97%) visited a rheumatologist. 95% of patients received more than one procedure. Blood samples (87%) and chest X-ray (27%) were most common procedures received by patients.

  Around 96% of patients used disease-modifying antirheumatic drugs (DMARDs), mainly methotrexate (84%), hydroxychloroquine (57%), and sulfasalazine (36%). 73% of patients used anti-inflammatory drugs (NSAIDs), mainly celecoxib (30%); steroids were used by 57% of patients.

  None of the patients received surgeries. Only one patient had more than one hospitalization.

- **Associations between Disease Severity and PROs at Baseline**
  There was no significant association of disease severity with changes in other PROs.

- **GLM - Modifying Effects on Changes in PROs**
  Diabetes was significantly correlated with changes in HAQ-DI, EQ-5D-3L index, and WPAI percentage activity impairment scores at both 24 weeks and 12 weeks after the initiation of adalimumab. Peptic ulcer disease also showed a significant correlation with PCS T-score at 24 weeks (p=0.034) and 12 weeks (p=0.031).

Discussion
The results of the present study for Taiwan demonstrate that adalimumab was effective in producing clinically important and statistically significant reductions in the signs and symptoms of disease at 24 weeks. These findings in the Taiwanese patients can be further validated in other Asian population, when the results from similar studies currently underway in China and Korea are available.

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