## 1.0            Abstract

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

**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 Korea.

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 Korea.

**Research question and objectives:**
The objective of this non-interventional, observational study is to assess the effect of adalimumab on HRQoL and work productivity in patients with RA in Korea.

**Study design:**
This is a prospective observational study involving 91 subjects enrolled at nine different sites and are observed for 12-week baseline and 24 weeks after initiation to assess the effect of adalimumab on health-related QoL and work productivity in patients with RA in Korea.

To assess health and disability outcomes, the health assessment questionnaire disability index (HAQ-DI) will be assessed at baseline, Week 12 and Week 24 after treatment initiation with adalimumab. In addition, other PROs of work activity and well-being, including the WPAI, EuroQol 5 dimension (EQ-5D), and Short Form 36- Item Health Survey (SF-36), will also be assessed. In addition, the health care resource utilization will be collected.

**Setting:**
Clinical settings are preferred by the participating rheumatologist.

**Subjects and study size, including dropouts:**
91 patients diagnosed with RA are enrolled at nine different sites in Korea.

**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 subject $\geq$ 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 24 weeks from the 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
• 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

Additional Secondary Variable
• Changes in the disease severity and PROs from baseline to 24 weeks

Exploratory Variable
• Change in patient satisfaction questions from baseline to weeks 12 and 24

**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**

  The mean age of overall RA patients was 55.7 (SD ±13.3) years, with the majority 37.4% (n= 34) 55-64 years. 5.5% (n=5) were 75+ years old , the majority 70.3% of RA patients were female (n=64) and under national/public insurance 65.9% (n=60)

- **Clinical Characteristics at Baseline**

  The mean DAS28 at baseline was 6.1 (SD ±1.0), with majority 93.4% (n=85) of patients within the category of high disease activity. 25.3% (n=23) of RA patients suffered from comorbidities, including 9.9% diabetes (n=9), 5.5%, chronic pulmonary diseases    (n=5), and 4.4% cerebrovascular diseases (n=4)

- **HAQ-DI at Weeks 12 and 24 after Initiation of Adalimumab**

  Mean change from baseline in HAQ-DI was statistically significant at both 12 weeks (p<0.0001) and 24 weeks (p<0.0001), with the HAQ-DI scores improving from -0.46 (SD ±0.6) at 12 weeks to -0.67 (SD ±0.67) at 24 weeks. Clinical improvement in HAQ-DI, defined as improvement from baseline greater than -0.22, was achieved in 65.8% (n=52) and 77.5% (n=55) patients at Week 12 and Week 24, respectively

- **Change in SF-36 Domain Scales at Weeks 12 and 24 after Initiation of Adalimumab**

  The mean change from baseline in PCS-T score improved from 6.56 (SD ±6.98) at 12 weeks to 9.51 (SD ±7.77) at 24 weeks. Mean change from baseline in MCS T-score improved from 5.26 (SD ±11.62) at 12 weeks to 6.63 (SD ±12.31) at 24 weeks

- **Change in EQ-5D-3L Index at Weeks 12 and 24 after Initiation of Adalimumab**

  Mean change from baseline in EQ-5D-3L index score was statistically significant at 12 weeks (0.15, SD ±0.24); p<0.0001) and at 24 weeks (0.18, SD ±0.25); p<0.0001)

- **Change in WPAI at Weeks 12 and 24 after Initiation of Adalimumab**

  Significant mean change in percentage overall work impairment of -0.19 (SD ±0.32) and -0.25 (SD ±0.31) was observed at 12 weeks and 24 weeks, respectively (p≤0.01). The mean change from baseline in percentage of activity impairment was -0.15 (SD ±0.31) at 12 weeks and -0.25 (SD ±0.34) at 24 weeks

- **Patient Satisfaction Questions at Weeks 12 and 24 after Initiation of Adalimumab**

  Approximately 42% (n=30), 38% (n=27), 46.5% (n=33), 45% (n=33) patients rated "very satisfied" at 24 weeks and 10% (n=9), 34.2% (n=27), 34.2% (n=27). 40%, at 12 weeks on how the RA treatment with adalimumab improved morning stiffness in and around their joints, improved their mobility,

improved the ability to perform daily living requiring fine motor skills and overall RA treatment respectively.

- **Patients' Global Impression of Change at Weeks 12 and 24 after Initiation of Adalimumab**

Approximately 13% (n=10) at 12 weeks and 18% (n=13) at 24 weeks of the RA patients felt "very much better". However, 32% (n=25) of RA patients felt "much better" at 12 weeks since initiation of adalimumab whereas 45% (n=32) felt "much better" after 24 weeks. Around 13% (n=10) patient felt there was "no change" at 12 weeks after the initiation of adalimumab, whereas only 4% felt "no change" at 24 weeks.

- **Post-Index Healthcare Resource Utilization**

Overall 99% of patients consulted more than one healthcare professional. Majority of the patients (99%; n=87) visited a rheumatologist. Overall, 77% (n=67) of patients received more than one procedure. Blood samples (69%; n=61) and urine test (40%; n=35) were most common procedures received by patients.

Around 82% patients used disease-modifying antirheumatic drugs (DMARDs), which mainly consisted of methotrexate (66%) or leflunomide (27%). 73% patients used NSAID; mainly naproxen (14%) and indomethacin (14%). None of the patients received surgeries. Only three patients had more than one hospitalization.

- **Associations between Disease Severity and PROs at Baseline**

Association on disease severity was observed with MCS T-score (p=0.030), EQ-5D-3L index (p=0.032), and percentage of activity impairment (p=0.026) on change in DAS28 at 12 weeks. Only the PCS T-score showed a significant association with change in DAS28 at 24 weeks (p=0.004)

- **Summary of GLM - Modifying Effects on Changes in PROs**

Mild liver diseases were found to be significantly associated with change in PCS T-score (p=0.028) and EQ-5D-3L index score (p=0.038) at 24 weeks, while diabetes was significantly associated with change in PCS T-score at 12 weeks (p=0.032). Presence of peptic ulcer disease had a significant impact on the change in EQ-5D-3L index score at 24 weeks (p=0.003).

No statistically significant association was found for the other dependent variables with any change in PROs reported across different instruments.

**Adverse events**

A total of 12 patients reported adverse events. Six patients experienced serious adverse events including aggravation of joint pain, arthritis, herniated lumbar disc, spinal stenosis, and bacterial pneumonia. Six patients experienced adverse events including rash, rash on injection site, bacterial pneumonia, rosacea, skin rash and skin redness with itching

No patients died during the study.

**Conclusion**

The current study for Korea demonstrate that adalimumab was effective in producing clinically important and statistically significant reductions in the signs and symptoms of disease at 12 and 24 weeks, as validated across different PRO instruments.

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