J Rheum Dis 2023;30(1):26-35
https://doi.org/10.4078/jrd.22.0024
pISSN: 2093-940X, eISSN: 2233-4718

Original Article

Treatment Sequence After Initiating Biologic Therapy for Patients With Rheumatoid Arthritis in Korea: A Nationwide Retrospective Cohort Study

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Objective: To evaluate treatment patterns and healthcare resource utilization (HCRU) after initiating biologic disease-modifying antirheumatic drugs (bDMARDs) in Korean patients with rheumatoid arthritis (RA).

Methods: Patients newly diagnosed with RA in 2014 were identified and followed up on using the Korean National Health Insurance Database until 2018. The initial line of therapy (LOT) or LOT1 included patients treated with conventional DMARDs (cDMARD). Patients who started a bDMARD were assigned to LOT2 bDMARD. Those who moved from a bDMARD to a Janus kinase inhibitor were assigned to LOT3. Analyzed outcomes were treatment patterns and HCRU in LOT2 bDMARD.

Results: The most prescribed initial bDMARD was a tumor necrosis factor inhibitor. Seventy-five percent of patients had changes in treatment after starting a bDMARD, such as addition/removal or switch of a DMARD, and transition to LOT3. For the first and second changes in LOT2 bDMARD, adding a cDMARD to a bDMARD was more common than switching to another bDMARD (7.98% vs. 2.93% for the first change, and 17.10% vs. 6.51% for the second change). Tocilizumab was the most common bDMARD that was switched to. Forty-eight percent of patients had at least one hospitalization after initiating bDMARDs. Of these patients, 64.3% were admitted due to RA-related reasons.

Conclusion: This real-world study provides information on treatment characteristics of RA patients in Korea after starting a bDMARD. In contrary to guidelines, cDMARD addition was more often than bDMARD switches in daily clinical practice.

Keywords: Rheumatoid arthritis, DMARD, Biologics, Health resources

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic and debilitating autoimmune condition that affects approximately 0.3% of the population of Korea [1-4]. Patients with RA commonly experience reduced mobility, long-term pain, decreased quality of life, and higher mortality risk [5-7]. Treatment options include conventional disease-modifying antirheumatic drugs (cDMARDs) such as methotrexate (MTX), biologic (b)DMARDs such as tumor necrosis factor inhibitors (TNFis), and targeted synthetic

Received June 30, 2022; **Revised** July 29, 2022; **Accepted** August 6, 2022, **Published online** August 30, 2022

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(ts)DMARDs such as Janus kinase inhibitors (JAKis) [8,9]. On initial diagnosis, cDMARDs are recommended as the first-line therapy, while bDMARDs and tsDMARDs are recommended as treatment options for patients who fail to respond to an initial course of cDMARDs [9-11]. In addition to ineffectiveness as one reason for switching treatment, other common reasons for switching treatment during either first or subsequent lines of therapy include adverse events and intolerance [9,12,13].

Evidence suggests that the prevalence of RA is increasing [4,14] and, despite a range of treatment options are available, direct and indirect economic burden of RA in Korea remains substantial. From 2012 to 2016, the number of hospitalization among patients with seropositive RA showed a 68% increase, and the average length of hospital stay increased from 12.3 days to 14.0 days [14]. Studies conducted previously have assessed therapeutic practices and healthcare resource utilization (HCRU) among Korean patients receiving cDMARDs or bDMARDs [15,16]. These showed that MTX and hydroxychloroquine were the most common cDMARDs used, while bDMARDs were used by less than 10% of patients [15]. Among patients who initiated or switched to bDMARDs, tocilizumab was the most commonly prescribed, followed by adalimumab and etanercept, although TNFis were more common for patients who were receiving bDMARDs for the first time [16]. Adalimumab was the most prescribed drug as the first bDMARD, followed by tocilizumab in a previous study using the Korean Health Insurance Review and Assessment (HIRA) Service database, yet there was no analysis regarding switching [17]. On the other hand, a Japanese population-based study showed that the most common agent that patients first switched to was tocilizumab [18]. This was also the case in a study using the Taiwan national claim database [19]. However, it is currently unclear what effect the introduction of this new treatment class has on RA treatment patterns in Korea. Therefore, the aim of this study was to use real-world data to describe updated usages of DMARDs, treatment changes, and HCRU in RA patients receiving bDMARDs in Korea.

MATERIALS AND METHODS

Study design and patients

A retrospective, observational study was conducted using data obtained from the Korean HIRA reimbursement claim database. The HIRA database has healthcare claims of almost 98% of the Korean population and contains data related to patients' diagnoses, procedures, treatments, and prescription medications [20]. Patients with RA aged 18 years and older who received their first prescription for cDMARDs between January 1, 2014, and December 31, 2014 were included. They were identified as having seropositive RA (International Classification of Diseases 10th revision [ICD-10] code M05) or other RA (ICD-10 code M06), either as their main or secondary diagnosis. The index date was defined as the date of the first cDMARD prescription. Patients were excluded if they had a diagnosis of adult-onset Still's disease (M06.1) or inflammatory polyarthropathy (M06.4). Patients who had claims for any DMARD within one year preceding the index date, who had less than one year of claims data during the study period, who had received cDMARDs for another indications (including, but not limited to, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis, and lupus) were also excluded. Patients were followed up to December 31, 2018 (Supplementary Figure 1). The Institutional Review Board of the Seoul Metropolitan Government-Seoul National University Boramae Medical Center approved the study protocol (approval number: 07-2019-22). The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice Guidelines. The need for informed consent was waived as this study involved minimum risk due to its retrospective nature without using any identifiable information.

Definitions of line of therapy

A line of therapy (LOT) was defined as the period in which no additional drug classes were added to a patient's treatment regimen. Based on treatment regimens, drug classes for RA were divided into cDMARD, bDMARD, and JAKi. cDMARD included MTX, leflunomide, sulfasalazine, hydroxychloroquine, and tacrolimus. bDMARD consisted of TNFi (infliximab, adalimumab, etanercept, golimumab), and non-TNFi (tocilizumab, abatacept and rituximab). JAKi included tofacitinib and baricitinib. A switch to, or addition of, a new drug class was considered a new LOT. Therefore, LOT1 was the period in which cDMARDs were the mainstay drug of the patient's treatment regimen. Subsequently, patients who started treatment with a bDMARD or JAKi during the observational period were considered to have transitioned to LOT2 bDMARD. Patients in LOT3 were those who changed from bDMARD to JAKi or vice versa. Addition or substitution of one or more drugs belonging

to an existing or prior class, for any reason, was not considered a new LOT. A discontinued drug that was later restarted was not considered a new LOT either.

Outcomes

The following data were extracted from the HIRA database: patient baseline characteristics (including demographics, hospital type, and comorbidities), name, date, and duration of prescribed medication, and HCRU. Primary outcomes of interest consisted of two parts: 1) treatment patterns in LOT2 bDMARD, and 2) healthcare utilization (all-cause and RA-related) in LOT2 bDMARD. Treatment patterns included the most common initial and last treatment regimens, the number of changes in regimens, and regimens before transitioning to LOT3. Treatment changes within LOT2 bDMARD were defined as adding a cDMARD, switching to another bDMARD, switching from a bDMARD to cDMARD, and discontinuing all DMARDs. Patterns of the first change and the second change in treatment emphasizing on DMARD add-ons or switches, were also assessed. The initial adjustment in treatment made to the DMARD regimen after starting a bDMARD was defined as first change, and the subsequent alteration as the second. We did not list all treatment regimens but only the top three most common regimens by proportion of patients in the regimen. Additional regimens were listed if the total proportion of patients in each treatment category was <75%. Patients who were not prescribed any DMARDs within 90 days were deemed to have discontinued treatment. Any gap of <90 days between periods of prescription supply was considered a continuous treatment period. Hospitalization events were determined based on inpatient claims with length of stay ≥1 day. Multiple inpatient claims that were within one day were treated as the same episode. RA-related radiography was defined as chest X-ray, musculoskeletal X-ray, magnetic resonance imaging, or ultrasound. RA-related blood tests were defined as erythrocyte sedimentation rate and C-reactive protein test. Claims of RA-related radiography or blood tests were counted respectively. Radiography codes and blood tests codes are listed in Supplementary Table 1. All RA-related HCRU were defined to be any healthcare utilization tagged with a diagnostic code of M05 or M06 (excluding M06.1 and M06.4).

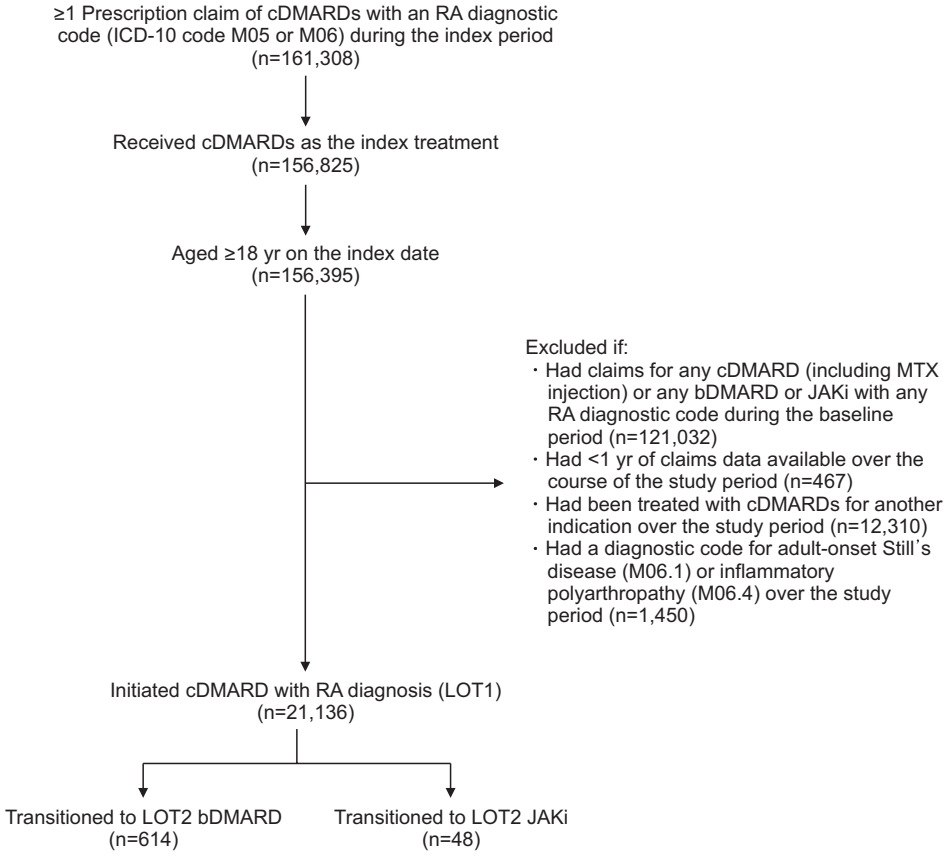

Figure 1. Flow chart of patient selection. January 1, 2014 to December 31, 2014 was designated as the index period. The index date was defined as the date of first cDMARD prescription. The baseline period was defined as 12 months before the index date. The study period was the period from index date to December 31, 2018 during which patient data were collected. bDMARD: biologic disease-modifying antirheumatic drug, cDMARD: conventional disease-modifying antirheumatic drug, ICD: International Classification of Diseases 10th revision, JAKi: Janus kinase inhibitor, RA: rheumatoid arthritis, LOT: line of treatment.

Table 1. Patient baseline demographics and characteristics at the index date

Variable	LOT2 bDMARD (n=614)
Female	455 (74.1)
Age (yr)	51.6±13.3
Insurance type	
National health insurance	592 (96.4)
Medical aid	22 (3.6)
Hospital type*	
Tertiary referral center	260 (42.3)
General hospital	189 (30.8)
Community hospital	76 (12.4)
Clinics	89 (14.5)
Rheumatology specialty	398 (64.8)
Charlson comorbidities	
Myocardial infarction	1 (0.2)
Congestive heart failure	10 (1.6)
Peripheral vascular disease	55 (9.0)
Cerebrovascular disease	31 (5.1)
Dementia	11 (1.8)
Chronic pulmonary disease	165 (26.9)
Rheumatic disease	401 (65.3)
Peptic ulcer disease	159 (25.9)
Mild liver disease	117 (19.1)
Moderate liver disease	0 (0)
Diabetes without chronic complication	96 (15.6)
Diabetes with chronic complication	36 (5.9)
Hemiplegia or paraplegia	1 (0.2)
Renal disease	9 (1.5)
Any malignancy including lymphoma and leukemia, except malignant neoplasm of skin	20 (3.3)
Metastatic solid tumor	1 (0.2)
HIV/AIDS	0 (0)
Specific comorbidities	
Diabetes	106 (17.3)
Hypertension	135 (22.0)
Dyslipidemia	193 (31.4)
Multiple sclerosis	0 (0)
Narrow angle glaucoma	2 (0.3)
Neurogenic bladder	20 (3.3)
Urinary or gastric retention	273 (44.5)
Urinary retention	0 (0)
Gastric retention	273 (44.5)
Ischemic heart disease	30 (4.9)
Restrictive/interstitial lung disease	11 (1.8)
Osteoporosis	106 (17.3)
Tuberculosis and latent tuberculosis	5 (0.8)
Non-tuberculosis mycobacteria infection	2 (0.3)
Hepatitis B	12 (2.0)
Hepatitis C	1 (0.2)
Thyroid disease	135 (22.0)
Charlson comorbidities index score ≥2	325 (52.9)

Values are presented as number (%) or mean±standard deviation. bDMARD: biologic disease-modifying antirheumatic drug, HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome, LOT: line of treatment. *In Korea, tertiary referral centers are the largest hospitals with the greatest number of specialist services; general hospitals and community hospitals are smaller with fewer departments. Clinics provide primary care services.

Statistical analyses

This study provides descriptive data on the treatment pattern in patients with RA. Outcomes were summarized using mean±standard deviation (SD) or number (percentage [%]). Kaplan–Meier plots were used to describe time to treatment changes; 1) discontinuation and 2) the start of LOT3. The first date of each LOT for each patient was defined as month 0. HCRU was analyzed as resource use per patient per year, including only patients who used that type of healthcare resource.

RESULTS

Patient characteristics

Of the 161,308 patients who had at least one prescription claim of cDMARDs with a RA diagnostic code (M05 or M06, excluding M06.1 and M06.4) in 2014, 21,136 initiated cDMARD (LOT1 population) (Figure 1). Most of these patients (68.9%, n=14,571) had a diagnostic code of M06 alone; 28.9% (n=6,106) had a diagnostic code of M05 alone, and 2.2% (n=459) had both M05 and M06 codes. Of initial cDMARD-treated patients (LOT1), 662 (3.1%) transitioned to LOT2 within five years. Of these LOT2 patients, 614 (92.7%) commenced bDMARD treatment (LOT2 bDMARD) and 48 (7.3%) were treated with JAKi (LOT2 JAKi). Common regimens just before initiating a bDMARD or JAKi were MTX+leflunomide (n=113, 17.1%), MTX+hydroxychloroquine (n=96, 14.5%), MTX monotherapy (n=82, 12.4%), MTX+hydroxychloroquine+sulfasalazine (n=75, 11.3%), MTX+tacrolimus (n=48, 7.3%) and hydroxychloroquine monotherapy (n=38, 5.7%). Due to the relatively small number of patients transitioned to LOT2 JAKi, only evaluated the LOT2 bDMARD in the following analysis.

Baseline characteristics of patients transitioned to LOT2 bDMARD are summarized in Table 1. The mean±SD age at the index date was 51.6±13.3 years and 74.1% were females. Only twenty-three (3.7%) patients who initiated bDMARD had a diagnostic code of M06 alone. Approximately two-thirds of patients who started bDMARD treatment were followed by a rheumatologist. Main comorbidities were dyslipidemia, chronic pulmonary disease, peptic ulcer disease, hypertension and thyroid disease (Table 1).

Treatment regimens in LOT2 bDMARD

The most common initial treatment regimen among bDMARD-treated patients in LOT2 bDMARD was adalimumab+MTX (98/614, 16.0%), followed by etanercept+MTX (72/614, 11.7%) and tocilizumab+MTX (68/614, 11.1%) (Figure 2). The last prescribed regimen in LOT2 bDMARD (including patients transitioned to LOT3) was similar to the first, with the top three last regimens being adalimumab+MTX (69/614, 11.2%), tocilizumab+MTX (69/614, 11.2%), and etanercept+MTX (56/614, 9.1%) (Figure 2). In addition, glucocorticoids (96.4%), NSAIDs (97.6%), and other analgesics (81.8%) were commonly prescribed. Opioids such as tramadol were less prescribed (31.1%).

Treatment changes in LOT2 bDMARD

In LOT2 bDMARD, 458/614 (74.6%) had at least one change in the treatment regimen during LOT2, including switching, add-ons, and discontinuation of DMARDs or transition to LOT3. The median number of changes in treatment was 2, but over 35.0% of patients had four or more changes. The overall treatment pattern did not change when patients who discontinued DMARDs were excluded (n=457); the proportion of patients that changed (switched or added DMARDs, or transitioned to LOT3) treatment was 76.4% (n=349), and the median number of changes in LOT2 was 2.

One hundred twenty-nine (21.0%) patients switched or added a DMARD as their first change in treatment. Adding a cDMARD was the most common (8.3%), while only 2.9% of patients switched to another bDMARD (Table 2). The most common add-on cDMARD was MTX (n=30, 58.8%), followed by hydroxychloroquine (n=11, 21.6%), and leflunomide (n=8, 15.7%). On the other hand, 7.0% of patients switched from

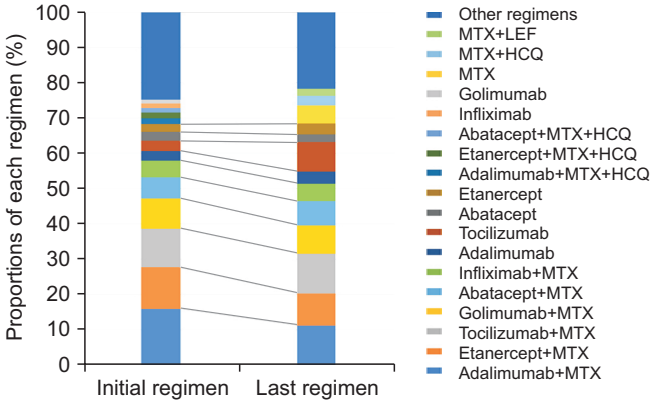

Figure 2. Common initial and last treatment regimens in LOT2 bDMARD (n=614). LOT: line of therapy, bDMARD: biologic disease-modifying antirheumatic drug, MTX: methotrexate, LEF: leflunomide, HCQ: hydroxychloroquine.

Table 2. Most common* first and second treatment changes (add-on or switch) during LOT2

Treatment regimen	LOT2 bDMARD (n=614)	
	First change (n=129)	Second change (n=276)
Patients with switches		
Switch to cDMARD†	43 (7.0)	26 (4.2)
Switch to another bDMARD†	18 (2.9)	40 (6.5)
Patients with add-on medication		
Addition of a cDMARD‡	49 (78.0)	105 (17.1)
Addition of a bDMARD‡	0 (0.0)	54 (8.8)

Values are presented as number (%). LOT: line of treatment, bDMARD: biologic disease-modifying antirheumatic drug, cDMARD: conventional disease-modifying antirheumatic drug. *Most common includes at least the top three regimens by proportion of patients in each regimen. Additional regimens were listed if the proportion of patients receiving each treatment change category was below 75%. †For bDMARDs, the top 5 for first switch and top 6 for second switch are included in the proportion shown. Percentages given as a proportion of all patients in LOT2 bDMARD. ‡For bDMARDs, the top 3 for first add-on and top 5 for second add-on are included in the proportion shown. Percentages given as a proportion of all patients in LOT2 bDMARD.

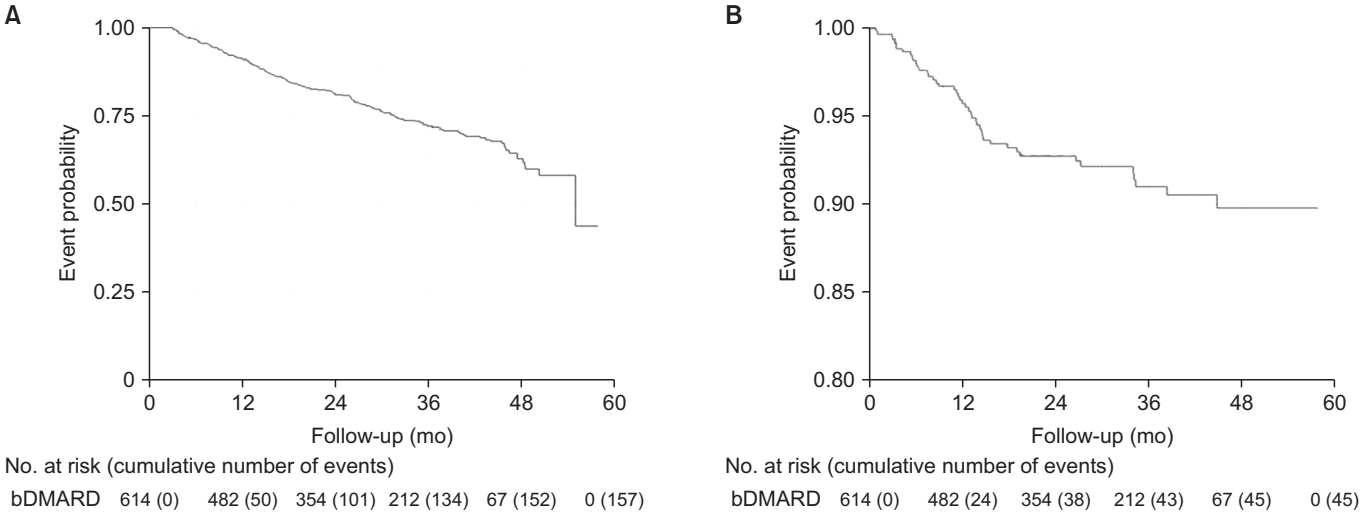

Figure 3. Kaplan–Meier plots showing (A) time point of discontinuing all DMARDs in LOT2 bDMARD and (B) the entry point to LOT3 from LOT2 bDMARD. The first date of the LOT2 period is depicted as 0 on the X-axis. DMARDs: biologic disease-modifying antirheumatic drugs, LOT: line of therapy, bDMARD: biologic disease-modifying antirheumatic drug.

bDMARD to a cDMARD as their first change in treatment. More patients (n=276) switched or added a DMARD during the second change in treatment. Again, adding a cDMARD was more common than switching to another bDMARD (17.1% vs. 6.5%, respectively). The most common add-on cDMARD was MTX (n=83, 42.3%), while the most common bDMARD that patients switched to was tocilizumab (n=14, 17.5%). In the second change of LOT2 period, about 9% of patients resumed a bDMARD after switching to cDMARD (Table 2).

Discontinuation and transition to LOT3

During LOT2, 157 (25.6%) patients receiving a bDMARD discontinued all DMARD treatment (Figure 3A). Forty-five (7.3%) bDMARD users transitioned to LOT3 (JAKi treatment) during the 5-year follow-up. Among patients who transitioned to LOT3, approximately half (24/45, 53.3%) of them did so within the first year (Figure 3B). Common regimens in LOT2 bDMARD just before transitioning to LOT3 were adalimumab with MTX (7/45, 15.6%), abatacept with MTX (6/45, 13.3%), golimumab with MTX (4/45, 8.9%), and tocilizumab (4/45, 8.9%).

Healthcare resource utilization during LOT2

Proportions of patients with all-cause and RA-related hos-

pitalizations during LOT2 were 48.4% and 31.1%, respectively (Table 3). The mean±SD length of hospital stay was 11.5±19.6 days, with RA-related hospital stays being longer than all-cause-related hospital stay (16.8 days). Only 1.0% of patients visited the emergency room (ER) for RA-related reasons, while 30.9% of patients visited the ER for any reason. The mean±SD number of outpatient visits per person per year was 32.8±27.2 for all-cause-related visits, and 2.8±4.2 for RA-related visits. Physiotherapy was only used in 2.6% of patients.

DISCUSSION

This claim database study describes the prescribing patterns, treatment practices, and HCRU among patients initiating bDMARDs for RA in Korea. Adalimumab, etanercept, and tocilizumab were the three most commonly prescribed initial bDMARDs, consistent with previously published data [4,16]. During bDMARD treatment, adding a cDMARD to a bDMARD was more common than switching to another bDMARD in clinical practice. MTX was the most frequently added cDMARD to a bDMARD, whereas tocilizumab was the most common one that bDMARD patients switched to. Regarding HCRU during bDMARD treatment, almost half of RA patients were at least once admitted to the hospital and one-third visited the ER. The proportion of RA-related HCRU among all-cause HCRU was quite low after bDMARD initiation.

Given that most treatment changes occurred during the first year after starting a bDMARD, aside from treatment related adverse events, a great deal of changes might be due to inadequate response to the initial bDMARD. The 2019 European League Against Rheumatism (EULAR) and 2021 American College of Rheumatology (ACR) guidelines recommend switching to a different bDMARD or JAKi for patients who do not meet the treatment target after 3 to 6 months of bDMARD or JAKi therapy [10,11]. The 2020 Korean guidelines to RA management also recommend to switch if a patient does not achieve an adequate response to the first bDMARD or tsDMARD [21]. However, our study demonstrated higher rates of add-on of cDMARD to bDMARD than switching to another bDMARD. This might be attributable to the following factors: 1) expectancy of increased efficacy on adding a cDMARD, 2) convenience of adding cDMARD therapy, 3) patient's characteristics such as age, socioeconomic status, and comorbidities, and 4) HIRA restrictions on switching back to a bDMARD once it is used. In a previous study, older age and having inflammatory bowel disease were associated with a lower likelihood of switching to another bD-

Table 3. Healthcare resource utilization during LOT2

Variable	LOT2 bDMARD (n=614)
Hospitalizations	
All cause	
Patients	297 (48.4)
No. per person per year	0.8 (0.2, 19.2)
LOS per hospitalization, days	11.5±19.6
RA-related	
Patients	191 (31.1)
No. per person per year	0.8 (0.2, 11.3)
LOS per hospitalization, days	16.8±38.7
ER visits	
All cause	
Patients	190 (30.9)
No. per person per year	0.7 (0.2, 11.0)
RA-related	
Patients	6 (1.0)
No. per person per year	0.4 (0.3, 1.0)
Outpatient visits	
All cause	
Patients	609 (99.2)
No. per person per year	25.5 (3.1, 365.3)
RA-related	
Patients	278 (45.3)
No. per person per year	1.1 (0.2, 30.1)
RA-related radiology visits	
Patients	93 (15.1)
No. per person per year	0.5 (0.2, 12.2)
RA-related blood tests	
Patients	118 (19.2)
No. per person per year	0.9 (0.2, 8.8)
RA-related physiotherapy/rehabilitation visits	
Patients	16 (2.6)
No. per person per year	1.0 (0.2, 23.4)
RA-related surgical procedures	
Patients	29 (4.7)
No. per person per year	0.4 (0.2, 2.6)

Values are presented as number (%), median (min, max)*, or mean±standard deviation. LOT: line of treatment, bDMARD: biologic disease-modifying antirheumatic drug, LOS: length of stay, ER: emergency room, RA: rheumatoid arthritis. *Median no. of events per year calculated for patients with at least one event.

MARD in patients with RA [22]. In addition, the literature does not point out that an ill-timed switch in inadequate responders would generally result in poor disease control or a diminished quality of life in patients. Moreover, cDMARD add-on was again more common than switching bDMARDs in the next change of treatment, implying that adding a cDMARD to bDMARD after initiating a biologic therapy is a general practice in Korea.

Our analyses also showed that few patients transitioned from bDMARD therapy to JAKi. This low switch rate to JAKi may indicate that once patients are treated with bDMARDs, they tend to continue therapy within the group of bDMARDs. A previous study showed that among RA patients who switched their first-line bDMARD, 77.0% of patients switched to a different bDMARD instead of a JAKi [23]. Furthermore, that study showed that 64.7% and 23.5% of patients made the second switch to a bDMARD or a JAKi, respectively [23]. In our study, tofacitinib was the only JAKi with data that we could look into. Baricitinib and upadacitinib were approved in Korea in 2017 and 2020, respectively [15]. Additional studies are needed to properly analyze LOT3 (bDMARD to JAKi) data in the future.

We discovered increased HCRU for non-RA-related causes in bDMARD-treated patients, such as the number of hospitalizations, emergency room, and outpatient visits. Patients treated with bDMARD had a number of comorbidities, including chronic lung disease and cardiovascular disease, which might have led to an increased HCRU for non-RA-related causes. The mean number of hospitalizations was 1.8 per person per year, which was higher than the rate reported in a previous study from Korea (0.1 per person per year in 2016 among patients with seropositive RA) [14]. However, the number of RA-related outpatient visits was substantially lower in our study (2.8 per person per year) than in the previous Korean study (7.5 per person per year in 2016 among patients with seropositive RA) [14]. This inconsistency might reflect differences in patient inclusion criteria and methodology or disparity in patient populations. Disease activity might be better controlled among bDMARD-treated patients in our study than in the overall population of patients with RA.

A key strength of our study was the use of a large database of healthcare claims, covering nearly the whole Korean population. In addition, to the best of our knowledge, this is the first study in Korea to provide information on treatment changes for patients with RA after initiating a bDMARD, covering switching as well as add-on cDMARDs, in a real-world setting. This study also has several limitations. First, there were about twice as many patients in the LOT1 population with the diagnostic code M06 alone as there were with the M05 alone, suggesting that many patients with the M06 code may not actually have RA. Patients who had a diagnostic code of M06 might have an autoimmune disease such as inflammatory bowel disease or uveitis misclassified as seronegative RA. However, only a small percentage of cases which entered LOT2 were coded as M06. Second, the diagnosis registered in the HIRA database might be the disease linked to the highest reimbursement. Thus, at times it might not represent the status or severity of RA in each subject. Third, due to the limited information available using a claim database, there may be unidentified confounding variables such as disease activity, RA-related medications, and reasons for treatment changes. Methodologic limitations of the study were associated with the calculation of HCRU, which was done using the number of events over the treatment duration. As per the exclusion criteria, we analyzed cases that included ≥1 year of post-index data. This might have introduced a survivor bias. However, the impact of this bias is likely to be small as only 467 (0.3%) of the 156,395 patients who met the inclusion criteria were excluded based on this criterion. On the other hand, a 1-year washout period might be insufficient for an incident case. However, most patients with RA experience flare within months after discontinuing all DMARDs treatment. Thus, a 1-year washout period for any DMARD prescription appeared to be sufficient for our study subjects. Finally, the study duration was limited by the 5-year threshold for data storage in the HIRA database.

CONCLUSION

In conclusion, TNFi plus MTX was the most common regimen first prescribed to RA patients who commenced bDMARD. Over 35% of patients had four or more changes in the DMARD regimen after starting a bDMARD. Adding a cDMARD was more common than switching to another bDMARD or JAKi in terms of escalating therapy, and switchers were most prescribed tocilizumab. These findings present key information to develop future Korean guidelines for biologic therapy in RA.

SUPPLEMENTARY DATA

Supplementary data can be found with this article online at https://doi.org/10.4078/jrd.22.0024.

FUNDING

This research was initiated and funded by Astellas Pharma Inc. Medical writing support was provided by Rhian Harper Owen, PhD, and Iona Easthope, DPhil, of Cello Health MedErgy (Europe), funded by Astellas Pharma Inc.

ACKNOWLEDGMENTS

We acknowledge Elvira Lansang, MD and Budiwan Sumarsono, MD, MSc, from Astellas Pharma Singapore for their valuable input.

CONFLICT OF INTEREST

SK is an employee of Astellas Pharma Singapore Pte. Ltd. MS is an employee of Astellas Pharma Europe B.V. JLC is a consultant for Astellas Pharma Singapore Pte. Ltd. MJK, JWP, SL and KS have nothing to disclose.

AUTHOR CONTRIBUTIONS

JWP, SK, MS, JLC, and KS conceived the work. MS and JLC performed data curation. MJK, SKL, SK, MS, and JLC performed formal analysis. SK and KS performed funding acquisitions. MJK wrote the original draft. JWP, YJ, MS, JLC and KS reviewed and edited the manuscript.

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