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Economic Burden and Treatment Patterns of Cycling between Conventional Synthetic Disease-Modifying Antirheumatic Drugs Among Biologic-Treated Patients with Rheumatoid Arthritis

Keith A. Betts, PhD[1]; Jenny Griffith, PharmD[2]; Arijit Ganguli, PhD[2]; Nanxin Li, PhD[1]; Kevin Douglas, MD[2]; and Eric Q. Wu, PhD[1]

[1]*Analysis Group, Inc, Boston, Massachusetts; and* [2]*AbbVie Inc, Edwardsville, Illinois*

ABSTRACT

Purpose: To assess the economic outcomes and treatment patterns among patients with rheumatoid arthritis (RA) who used 1, 2, or 3 or more conventional synthetic disease-modifying antirheumatic drugs (DMARDs) before receiving a biologic therapy.

Methods: Adult patients with ≥2 RA diagnoses (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 714.xx) on different dates, ≥1 claim for a conventional synthetic DMARD, and ≥1 claim for a biologic DMARD were identified from a large commercial claims database. The initiation date of the first biologic DMARD was defined as the index date. Based on the number of distinct conventional synthetic DMARDs initiated between the first RA diagnosis and the index date, patients were classified into 3 cohorts: those who used 1, 2, or 3 or more conventional synthetic DMARDs. Baseline characteristics were measured 6 months preindex date and compared between the 3 cohorts. All-cause health care costs (in 2014 US$) were compared during the follow-up period (12 months postbiologic initiation) using multivariable gamma models adjusting for baseline characteristics. Time to discontinuation of the index biologic DMARD and time to switching to a new DMARD were compared using multivariable Cox proportional hazards models.

Findings: The 1, 2, and 3 or more conventional synthetic DMARD cohorts included 6215; 3227; and 976 patients, respectively. At baseline, patients in the 3 or more conventional synthetic DMARD cohort had the least severe RA, as indicated by the lowest claims-based index for RA severity score (1 vs 2 vs 3 or more = 6.1 vs 5.9 vs 5.8). During the study period, there was a significant association between number of conventional synthetic DMARDs and higher all-cause total health care costs (adjusted mean difference, 1 vs 2: $772; $P < 0.001$; 2 vs 3 or more: $2390; $P < 0.001$). The all-cause medical and pharmacy costs were also significantly higher with the increasing number of conventional synthetic DMARDs. Patients who cycled more conventional synthetic DMARDs were also more likely to switch treatment after biologic initiation (1 vs 2: adjusted hazard ratio = 0.89; $P = 0.005$; 2 vs 3 or more: adjusted hazard ratio = 0.89; $P = 0.087$). There were no differences in index biologic discontinuation between the 3 cohorts.

Implications: Patients with RA who cycled more conventional synthetic DMARDs had increased economic burden in the 12 months following biologic initiation and were more likely to switch therapy. These results highlight the importance of timely switching to biologic DMARDs for the treatment of RA. (*Clin Ther*. 2016;▮:▮▮▮–▮▮▮)

Key words: disease modifying antirheumatic drugs, health care costs, rheumatoid arthritis, treatment patterns.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune, chronic inflammatory disorder that affects multiple joints, such as the wrist, knuckles, knees, and ankles.[1] It is estimated to affect 0.72% of adults in the United

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States and is more common in women and elderly populations.[2] Recent evidence shows that RA imposes a significant economic burden on patients and society. The estimated annual excess direct health care costs of RA are more than $2000 per patient compared with a control cohort without RA, resulting in a total incremental expenditure of $22.3 billion (in 2008 US$) among all patients with RA in the United States.[3]

Medications are the mainstay of treatment for active RA and should start as early as possible. Conventional medication options include NSAIDs, conventional synthetic disease-modifying antirheumatic drugs (DMARDs) (eg, methotrexate), corticosteroids, and pain medications.[4] In addition, biologic DMARDs (eg, adalimumab, etanercept, infliximab) that target specific parts of the immune system have been developed and approved for the treatment of RA.[5–11]

The 2015 American College of Rheumatology (ACR) guidelines recommend using a treat-to-target strategy regardless of disease activity to achieve remission and prevent damage of the joints and loss of function.[12,13] Evidence from clinical trials suggests that the more strict the treatment aim and the more tight the control, the better the clinical outcomes and that RA patients who achieved remission, normal physical function, and radiographic inhibition have improved short-term and long-term health-related quality of life, pain, fatigue, and work-related outcomes compared with patients who did not.[14,15] The European League against Rheumatism (EULAR) guidelines emphasize tight control by recommending frequent and strict monitoring every 1 to 3 months to achieve a target of remission or low disease activity for every patient.[16]

The ACR treatment guidelines further recommend switching to a biologic DMARD, for patients with moderate or high RA disease activity after using 1 or multiple conventional synthetic DMARDs.[13] Similarly, the EULAR guidelines recommend using a biologic DMARD for patients with poor prognosis factors if the treatment goal is not achieved with the first conventional DMARD therapy.[16] A previous study[17] has shown that patients with RA who switched to a different conventional synthetic DMARD, as opposed to a biologic DMARD, after initial failure of a conventional synthetic DMARD had significantly smaller improvement in clinical outcomes measured by clinical disease activity index scores at 5, 9, and 24 months since treatment switch. In addition, patients who achieved sustained remission were found to incur less health care resource use and costs.[18] However, many patients with moderate or high RA disease activity are not treated consistently with the ACR recommendations.[19] The Consortium of Rheumatology Researchers of North America, Inc, registry[20] study recently showed that the median time between first conventional synthetic DMARD and first biologic was more than 4 years, which suggests the delay in moving patients to appropriate therapy and gaps in real-world clinical practice compared with the treat-to-target principles. Delays in receiving appropriate treatment have been shown to have significant effects on long-term patient outcomes.[21,22]

To date, no study has evaluated the real-world burden of cycling between conventional synthetic DMARDs among patients with RA. The real-world treatment patterns of biologic DMARD use after cycling between conventional synthetic DMARDs also remains unknown. The objective of the present study was to address this important knowledge gap by comparing health care costs and treatment patterns among patients with RA who cycled between different numbers of conventional synthetic DMARDs before initiating a biologic DMARD.

METHODS

Data Source

The data for our study was obtained from the Truven Health MarketScan Commercial Claims and Encounters Database and the Medicare Supplemental Database, available from January 1, 2000, to December 31, 2013. These databases contain private sector health care data from approximately 100 different insurance companies representing about 93 million covered lives. They consist of the medical claims of insured employees and their dependents, as well as Medicare-eligible retirees with employer-provided Medicare Supplemental plans from all the census regions. The databases capture person-specific enrollment history, medical services (provider and institutional), and pharmacy services. Data are de-identified and comply with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act.

Sample Selection

Adult patients with RA were included in the study if they had at least 2 RA diagnoses (International