Utilization and Adherence Patterns of Subcutaneously Administered Anti–Tumor Necrosis Factor Treatment Among Rheumatoid Arthritis Patients

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ABSTRACT

Background: Adherence to therapy is a key requirement underlying achievement of clinical outcomes in randomized controlled drug registration trials. In postmarketing studies, comparison of adherence among therapies can become more complicated when drug dosing and administration schedules differ or when methods used to measure adherence are not consistently applied.

Objective: The objective of this exploratory study was to investigate a broad range of utilization and adherence outcomes associated with subcutaneous biologic treatments for rheumatoid arthritis (RA).

Methods: Adult patients (aged ≥18 years) exhibiting ≥2 claims with an RA diagnosis (code 714.x), at least 24 months of continuous medical and pharmacy eligibility, and 30-day supplies of adalimumab, etanercept, or golimumab were selected from the Optum Insight Clinformatics database. Adherence and utilization measures were calculated and compared across treatment groups.

Results: A total of 1532 adalimumab, 2099 etanercept, and 261 golimumab patients met inclusion criteria. Compared with both adalimumab and etanercept patients, golimumab patients were significantly more likely to have a medication possession ratio of ≥0.80 (82% vs 71% vs 62%; $P < 0.001$) and significantly less likely to have ≥4 late medication refills (6.9% vs 17.7% vs 26.1%; $P < 0.001$ for all). Etanercept patients had significantly greater refill intervals (37.7 vs 34.9 and 35.1 days) and had the lowest proportion of adherent fills (70% vs 77% and 75%) compared with both golimumab and adalimumab patients ($P < 0.001$ for all). Bivariate effects were reproduced in multivariate models that controlled for treatment duration.

Conclusions: A number of statistically significant medication adherence differences were observed among golimumab, adalimumab, and etanercept patients in treatment for RA. Overall, golimumab patients appeared to be the most adherent group. Findings may be partially attributable to golimumab patients' likely increased disease severity, their prior experience with biologic medication, or golimumab's once-monthly dosing schedule, which requires fewer administrations than both adalimumab and etanercept. (*Clin Ther*. 2014;36:737–747)

Key words: adalimumab, adherence, claims data, etanercept, golimumab, pharmacoeconomic.

Rheumatoid arthritis (RA) is an autoimmune disease that affects 1% of the global population and is characterized by an inflammation of the joints and surrounding tissues.[1] During the past decade, the treatment of RA has improved significantly with the development of a variety of biologic agents targeting tumor necrosis factor (TNF).[2] As a result, the use of these agents has significantly increased as either monotherapy or combination therapy with nonbiologic disease-modifying antirheumatic drugs (DMARDs).[3] Despite increased utilization, patient adherence to biologic agent use remains unclear.[4]

Adherence, typically defined as the degree to which a medication is taken as prescribed, encompasses dosage, timing, and frequency.[5] A number of recent reviews have highlighted the inconsistent reporting of adherence to biologic treatments,[4,6,7]

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obfuscating any attempt to evaluate and compare the real-world cost or clinical benefits of these agents. For example, one investigation of biologic-treated Medicaid enrollees defined 1-year adherence as a proportion of days covered (PDC) of ≥80%, which resulted in 1-year adherence rates of 11% for anakinra patients, 32% for etanercept patients, and 43% for infliximab patients.[8] Similarly, another investigation measured adherence using the medication possession ratio (MPR) of ≥80% but reported much higher rates of adherence: 63% for new etanercept patients and 65% for new adalimumab patients.[9] Brocq et al[10] focused on 1-year drug continuation rates and reported rates of 87% for etanercept users, 83% for adalimumab users, and 68% for infliximab users. As these results indicate, current estimates of biologic therapy adherence vary considerably across methods, ranging from 11% to 87%, which can be directly attributable to a lack of uniformity in defining and calculating specific adherence outcomes. An analysis examining a broader range of treatment measures related to patient adherence may serve to ameliorate this issue.

Adalimumab,[11] etanercept,[12] and golimumab[13] are 3 anti-TNF biologic agents currently approved for the treatment of RA. Each of these medications is administered via subcutaneous injection and has been reported to be effective in the treatment of RA,[14–17] although each has a unique formulation and dosing schedule. The purpose of this exploratory study was to investigate a number of utilization measures associated with adalimumab, etanercept, and golimumab treatment, including dosing, refill intervals, and multiple proxies of adherence, and to compare findings across treatment groups.

METHODS

Sample Selection

Study data were derived from the Optum Insight Clinformatics database of insured individuals. Data were completely void of identifying information. Medical, pharmacy, and laboratory claims for members with a rheumatic disease diagnosis during quarter 4 of calendar year 2005 through quarter 1 of 2012 were studied. Figure 1 details the study inclusion and exclusion criteria and the sample size remaining after each exclusion criterion imposition. To be eligible for this study, members were required to receive treatment with a biologic during the case finding window: January 1, 2009 through March 31, 2011. Members were retained for analyses if their most recent biologic on record was either adalimumab, etanercept, or golimumab, with the earliest fill for that particular biologic serving as the study index date. Members treated with certolizumab were initially considered to be included in this study, although they were eventually excluded due to underrepresentation relative to other groups (n = 80 [3% of final sample]). This approach ensured that representation of patients was maximized for biologics such as golimumab, which indicated a lower overall prevalence in the data set. All members were required to have at least 2 years of continuous eligibility: 1 year before and 1 year after the index date. Members were also required to have at least 2 claims for rheumatoid arthritis (code 714.x) within 1 year of the index date and no diagnoses of ankylosing spondylitis (code 720.x) or psoriatic arthritis (code 696.x) within that same period. All members must have been at least 18 years of age, and women must not have been pregnant at any time during the study. In addition, members with a comorbid diagnosis of Crohn disease (code 555.x) were excluded because this is an approved indication for adalimumab.[11] Because most patients received 30-day supplies of medication (68%), to minimize artifacts, only those members with 30-day supply fills of their index medication across their episode of care were maintained for final analyses. After the imposition of all inclusion and exclusion criteria, the final sample size was 3892 (n = 1532 for the adalimumab group, n = 2099 for the etanercept group, and n = 261 for the golimumab group).

Measures

Patient demographic characteristics were summarized from the membership table and included age, sex, geographic region of residence, insurance line of business, and type of benefit plan. In addition, the Charlson Comorbidity Index, an overall measure of health,[18] was calculated during the 1-year preindex period, as were the rates for a variety of other comorbidities of interest. Prior biologic utilization during the 1-year preindex period was also calculated.

The following section outlines the primary treatment outcomes, which were calculated for all