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Longitudinal Treatment Patterns and Associated Outcomes in Patients With Newly Diagnosed Systemic Lupus Erythematosus

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ABSTRACT

Purpose: The treatment of systemic lupus erythematosus (SLE) is complex, with a wide range of drugs commonly prescribed. The aims of this study were to identify longitudinal treatment patterns in patients with incident SLE and to estimate the associations of treatment patterns with clinical and economic outcomes.

Methods: This retrospective, observational cohort study used a US managed care claims database to identify patients with newly diagnosed SLE and 4-year treatment follow-up. Patients were aged ≥18 years, with continuous medical and pharmacy benefits for 12 months before and 48 months after the index date (first medical claim with a diagnosis of SLE). Longitudinal treatment patterns were grouped using a k-means cluster analysis. Therapies were included in the cluster analysis if the mean number of prescriptions in each year was ≥0.05. Clinical and economic outcomes were compared across clusters using multivariate regression analyses.

Findings: Data from 1611 patients with incident SLE were analyzed (91.4% women; mean [SD] age, 44.5 [9.5] years; 56.2% managed primarily by a specialist). Hydroxychloroquine and corticosteroids were the most commonly prescribed therapies; methotrexate, azathioprine, and mycophenolate mofetil also met the criteria for inclusion in the cluster analysis. Ten treatment clusters were identified; the most common was minimally treated patients (42.8%). Hydroxychloroquine monotherapy, corticosteroid monotherapy, and corticosteroid/hydroxychloroquine combination therapy were received by 34.0%, 11.2%, and 7.8% of patients, respectively. Methotrexate or azathioprine with a corticosteroid/hydroxychloroquine were received by 4.2% of patients. Changes in therapy, except discontinuations, were rare. Compared with the minimally treated cluster, those that received corticosteroid monotherapy (mean dose, >12.0 mg/d) had poorer clinical and economic outcomes; the hydroxychloroquine-monotherapy cluster had similar or better outcomes; and patients who received a corticosteroid/hydroxychloroquine with or without methotrexate or azathioprine demonstrated outcomes that were poorer but that appeared better than those with corticosteroid monotherapy. SLE-related visits with a nonspecialist were common (~45%) and remained unchanged over time despite better clinical and economic outcomes associated with specialist visits.

Implications: This study utilized cluster analysis, an unsupervised machine-learning method, to systematically discern treatment patterns over 4 years and to estimate outcomes associated with the identified treatment patterns. The results suggest that minimal treatment is the most common approach in patients with newly diagnosed SLE. Clinical and economic outcomes are poorest with corticosteroid monotherapy but may improve with the addition of hydroxychloroquine and/or an immunosuppressive agent. A large proportion of SLE care is provided by nonspecialists despite the potential benefits of involving

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Key words: clinical outcomes, cluster analysis, economic outcomes, systemic lupus erythematosus, treatment patterns.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of unknown etiology, with diverse clinical manifestations. In the United States, SLE affects an estimated 161,000 to 322,000 adults, with a ~10-fold higher prevalence in women than in men.[1] The course of the disease is largely unpredictable, and no cure has been developed. However, in recent years, improvements in medical care have led to improved patient survival.[2]

Although hydroxychloroquine and belimumab are approved for the treatment of SLE,[3–5] other standard therapies include NSAIDs, corticosteroids, immunosuppressive/immunomodulatory agents (including methotrexate, azathioprine, and mycophenolate mofetil [MMF]), and biologics (eg, rituximab).[6–15] SLE therapies can provide clinical benefit; however, they are also associated with significant toxicities. Long-term use of high-dose corticosteroids can cause substantial morbidity, including osteoporosis and fractures, Cushingoid appearance and weight gain, hyperglycemia/diabetes, cardiovascular disease, and/or immunosuppression.[16] Immunosuppressants are associated with a high risk for adverse events (AEs), including infections, hematologic toxicities, and gastrointestinal events.[17] AEs associated with the biologics include infusion-related reactions and an increased risk for infection.[18,19] Therefore, the risk–benefit profile is paramount when considering SLE treatment options.

The evidence describing treatment patterns and the factors that affect a clinician's choice of therapy are limited; however, previous studies have found associations with race,[20] age at diagnosis,[20] duration of disease,[21] specialization of the treating physician,[21–24] and disease activity and damage scores.[20] Furthermore, a patient's symptoms and organ involvement should also affect the choice of therapy.[25]

SLE has a substantial economic impact in terms of the direct costs of medical treatment and the indirect costs associated with the loss of productivity.[26,27] In the United States, a mean direct annual cost of US $12,643 has been reported, with acute care hospitalizations accounting for 49% of this cost.[26]

This study aimed to identify the longitudinal patterns of drug treatment in patients with incident SLE in a large, commercially insured population in the United States and to estimate how different treatment patterns are associated with clinical and economic outcomes, including SLE severity, SLE flares, and health care resource utilization and costs.

PATIENTS AND METHODS

This retrospective, observational cohort study followed for 4 years the treatment of a cohort with incident SLE, using the MarketScan commercial claims database (Truven Health Analytics, Ann Arbor, Michigan). The individuals included in this database are representative of individuals with employer-sponsored insurance, including employees and their covered spouses and dependents, in the United States.[28] The database contains deidentified, individual-level data from inpatient and outpatient visits and outpatient prescription drug experience, compliant with the Health Insurance Portability and Accountability Act.

Patients

Patients with newly diagnosed SLE were identified based on a previously published algorithm used for studying the prevalence and incidence of SLE using managed care claims data.[29] The *index date* was the earliest date of a medical claim with a diagnosis of SLE (*International Classification of Diseases, Ninth Revision–Clinical Modification* diagnostic code 710.0x), between January 1, 2002, and December 31, 2008. Patients were aged ≥18 years at index, with continuous medical and pharmacy benefits for 12 months before index and for 48 months after index. Patients were excluded if SLE was diagnosed during the 12 months before index. Eligible patients had, during the first 12 months after index, at least 1 SLE-related inpatient claim or at least 2 SLE-related visits (a minimum of 30 days apart) to an office or emergency department (ED). At least 1 SLE diagnosis at index or during the 12 months after index must have been made by a rheumatologist, dermatologist, nephrologist, or neurologist. Between 12 and 48 months after index, at least 1 additional SLE diagnosis was required to ensure that the identified patients were SLE cases.