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BRIEF REPORT

Use and Switching of Biologic Therapy in Patients with Non-Radiographic Axial Spondyloarthritis: A Patient and Provider Survey in the United States

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ABSTRACT

Introduction: The Food and Drug Administration (FDA) approved certolizumab-pegol, the first biologic for the treatment of non-radiographic axial spondyloarthritis (nr-axSpA), for use in the United States (US) in March of 2019. The objective of this study was to investigate biologic use and reasons for switching therapy among patients with nr-axSpA in the US.

Methods: This was a real-world, cross-sectional study of rheumatologists conducted in the US. Data were collected from June to August of 2018 via rheumatologist-completed patient record forms. Data from patients who had a rheumatologist-confirmed diagnosis of nr-axSpA were included in the study. Rheumatologists provided information on current medication use and reasons for switching biologics.

Results: Eighty-eight rheumatologists collected data on 495 nr-axSpA patients. Over half of nr-axSpA patients were male (53.3%), with a mean age of 44.2 years, and 69.8% of patients reported working full-time. Of the 495 nr-axSpA patients, 48.1% were receiving a biologic and no conventional synthetic disease-modifying antirheumatic drug (csDMARD), 18.4% csDMARD (no biologic), 18.2% non-steroidal anti-inflammatory drug (NSAIDs)/COX-2 (no biologic or csDMARD), 11.5% a biologic and a csDMARD, 2.0% were receiving no therapy, and 1.8% other therapy (no biologic, csDMARD, or NSAID/COX-2). Of 295 patients receiving a biologic, 77.8% were receiving their first, 13.8% their second, and 8.3% their third or more biologic. Of 74 nr-axSpA patients who switched from a previous biologic to their current biologic, rheumatologists reported that 51.4% switched due to condition worsening, 48.6% had a loss of response over time, 27.0% switched due to a lack of pain alleviation, and 25.7% of patients switched because remission was not induced.

Conclusions: This study suggests that around 60% of nr-axSpA patients were receiving biologic therapy prior to the approval of certolizumab pegol. Switching of biologics is frequent in nr-axSpA patients and is usually due to lack of efficacy, loss or response, and effort to accomplish remission.

Keywords: Biologic therapy; Non-radiographic axial spondyloarthritis; Treatment patterns

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Key Summary Points

Why carry out this study?

The purpose of this study is to investigate biologic use and reasons for switching therapy among patients with non-radiographic axial spondyloarthritis (nr-axSpA) in the United States.

What was learned from the study?

This study suggests that around 60% of nr-axSpA patients in the United States were receiving biologic therapy prior to the approval of certolizumab-pegol.

Switching of biologics is frequent in nr-axSpA patients and is usually due to lack of efficacy, loss or response, and effort to accomplish remission.

INTRODUCTION

Axial spondyloarthritis (axSpA) is an immune-mediated chronic inflammatory disease which includes two subtypes within the same disease spectrum. Patients with axSpA can be classified as ankylosing spondylitis (AS) or radiographic axSpA (r-axSpA) based upon the mNY criteria for AS [1] or the Assessment of SpondyloArthritis international Society (ASAS) criteria for r-axSpA [2]. In addition, patients can be classified as non-radiographic axial spondyloarthritis (nr-axSpA) based on ASAS criteria, which requires findings consistent with sacroiliitis on magnetic resonance imaging (MRI) per ASAS/Outcome Measures in Rheumatology (OMERACT) plus 1 spondyloarthritis (SpA) feature, or the presence of HLA B-27 plus two SpA features [2]. With the availability of MRI, the presence of signals consistent with inflammation in the axial skeleton without visible radiographic changes can be assessed [2–4].

Patients with AS and nr-axSpA have comparable clinical characteristics and burden of disease, requiring similar treatment [5]. Non-steroidal anti-inflammatory drugs (NSAIDs) are considered first-line therapy for patients with AS and nr-axSpA [6, 7]. Traditional conventional disease-modifying antirheumatic drugs (cDMARDs) such as methotrexate and sulfasalazine are not considered effective for the treatment of axSpA [7–9]. Anti-tumor necrosis factor (TNF) agents (adalimumab, etanercept, golimumab, infliximab, and certolizumab pegol) and interleukin-17 (IL-17) inhibitors (secukinumab and ixekizumab) are Food and Drug Administration (FDA)-approved therapies for patients with AS. Certolizumab pegol was approved for the treatment of nr-axSpA by the FDA in March 2019 and is currently the only approved biologic for nr-axSpA in the United States (US).

The primary goal of treating patients with nr-axSpA is to maximize long-term health-related quality of life (HRQoL) through control of symptoms and inflammation, prevention of progressive structural damage, preservation of function and social participation [7]. This study was conducted to assess levels of biologic use and reasons for switching among patients with nr-axSpA in the US prior to the approval of the first biologic for this indication.

METHODS

This study employed a cross-sectional survey design, and the survey methodology was implemented as previously described [10]. Rheumatologists in the US that provided consultation for ≥ 10 axSpA patients per month were eligible to participate and were recruited via publicly available physician lists. A geographically representative sample of eligible rheumatologists ($n = 88$) was achieved. Rheumatologists completed patient record forms which included patient demographic and treatment pattern data for the next five consecutive nr-axSpA patients they consulted with. Data from 495 patient records were provided. Rheumatologists also provided reasons why they prescribed or discontinued a specific medication. For patients records to be included in the survey, patients were required to have a

rheumatologist-confirmed diagnosis of nr-axSpA.

All questionnaires used in the survey were reviewed and approved by Western Institutional Review Board (IRB). Patients provided consent for de-identified and aggregated reporting of research findings. Data were de-identified according to the Health Insurance Portability and Accountability Act (HIPAA) regulations before receipt by Adelphi Real World. Data were collected from June to August 2018.

Clinical Characteristics and Outcome Measures

Each rheumatologist completed patient record forms which included patient demographics (sex, age, body mass index (BMI), employment status), disease status (defined as improving, stable, unstable, and deteriorating), remission status, clinical characteristics, and current treatment patterns. The physician global assessment was completed by the rheumatologist with a 0 indicating best and a 100 indicating worst possible. Rheumatologists also indicated their reasons for prescribing biologics and their reasons for switching patients to a different biologic.

Statistical Analyses

Descriptive analyses of patient demographics, clinical characteristics, treatment patterns, and reasons for discontinuation were conducted. Categorical variables were analyzed by frequency counts and percentages, with Chi-square tests used for subgroup analyses. Continuous variables were analyzed by mean [standard deviation (SD)], with two-sample *t* tests used for subgroup analyses.

RESULTS

Demographics

A total of 495 nr-axSpA patients were included in this study. Overall, 53.3% (n = 264) of nr-axSpA patients were male, had a mean age of 44.2 years, mean BMI of 27.1, and 77.7% were employed either full-time or part-time (Table 1). Rheumatologists reported that the majority of nr-axSpA patients' current disease status was considered stable or improving (86.5%), and 40.7% were in remission. The mean physician's global assessment was 31.1 for nr-axSpA patients.

Medication Use

More than half (59.6%) of nr-axSpA patients were currently receiving a biologic, with 47.4% receiving adalimumab, followed by etanercept (22.5%), infliximab (12.1%), certolizumab pegol (6.9%), golimumab (5.5%), and secukinumab (5.5%). Overall, 48.1% (n = 238) were receiving a biologic as monotherapy and 11.5% (n = 57) were receiving a biologic in combination with a cDMARD (Table 1). In addition, 18.4% (n = 91) of nr-axSpA patients were receiving a cDMARD without a biologic, 18.2% (n = 90) were receiving a NSAID/ cyclooxygenase-2 inhibitor (Cox-2), and 2.0% (n = 10) were not receiving any type of medication. Of the patients receiving a biologic, the majority (77.8%; n = 224) were receiving their first biologic (Fig. 1).

Factors that Influence Choice of a Biologic

For most patients (92.7%), rheumatologists reported that strong overall efficacy was one of the main reasons why they prescribed the current biologic to their nr-axSpA patient (Table 2). For over half of patients, rheumatologists also indicated that familiarity with the drug (67.2%), fast onset of action (55.5%), inhibiting disease progression (53.8%), sustained pain relief (51.8%), and good overall safety profile (50.8%) were reasons they prescribed current biologics.

Reasons for Switching to a Different Biologic

Of 295 nr-axSpA patients receiving a biologic, 25.1% (n = 74) were receiving either their second or third biologic. Rheumatologists provided reasons why these patients were switched to a different biologic. The most frequently reported reasons were due to condition

Table 1 Patient demographics and medication use of Nr-axSpA patients

	Nr-axSpA patients (n = 495)
Sex	
Male	264 (53.3%)
Female	231 (46.7%)
Age, mean	44.2
Ethnic, origin	
White/Caucasian	394 (79.6%)
African American	34 (6.9%)
Native American	2 (0.4%)
Asian	13 (2.6%)
Middle Eastern	5 (1.0%)
Mixed Race	12 (2.4%)
Other	0 (0.0%)
Hispanic/Latino	35 (7.1%)
BMI (kg/m^2), mean	27.1
Smoking status*	
Current smoker	53 (11.6%)
Ex-smoker	91 (19.9%)
Never smoked	313 (68.5%)
Employment status**	
Full-time	344 (69.8%)
Part-time	39 (7.9%)
Homemaker	37 (7.5%)
Student	14 (2.8%)
Unemployed	20 (4.1%)
Retired	35 (7.1%)
Long-term sick leave	4 (0.8%)
Disease status	
Improving	153 (30.9%)
Stable	275 (55.6%)
Unstable	40 (8.1%)
Deteriorating	27 (5.5%)
In remission	189 (40.7%)
Physician's global assessment***, mean	31.1
Time since diagnosis, months, mean	46.2
Medication	
Biologic without cDMARD	238 (48.1%)
Biologic and cDMARD	57 (11.5%)
cDMARD	91 (18.4%)
NSAID/Cox-2	90 (18.2%)
No medication	10 (2.0%)
Duration of current biologic therapy****, months, mean	20.5

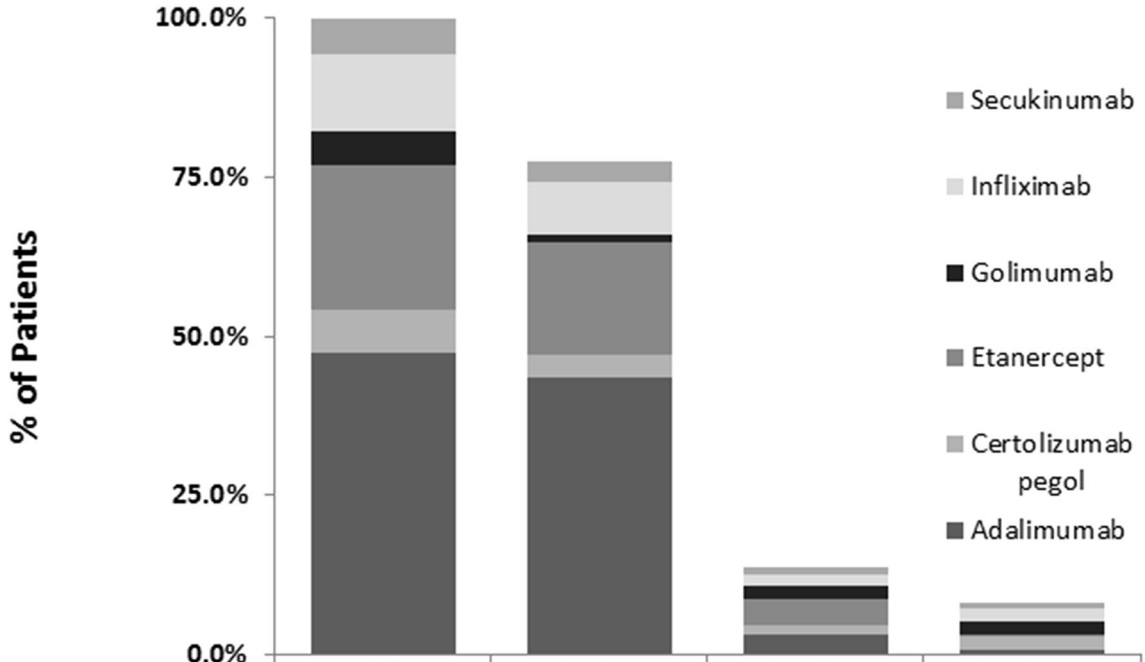
*Smoking status: n = 457
**Employment status: n = 493
***Physician's global assessment: n = 75
****Duration of current biologic therapy: n = 307

worsening (51.4%), followed by secondary lack of efficacy (48.6%), lack of alleviation of pain (27.0%), and remission not being induced (26.0%) (Fig. 2). Primary lack of efficacy, remission not being maintained, and patients requesting a change in therapy were each reported for 14.9% of patients as to why they were being switched to a different biologic.

DISCUSSION

This study provides real-world evidence on the medication use and the reasons why nr-axSpA patients switch biologic therapy in the US. At the time of the study, over half (59.6%) of nr-axSpA patients were prescribed biologic therapy even though there was not an FDA-approved biologic for nr-axSpA during the time the study was conducted.

The treatment landscape for nr-axSpA has changed with the emergence of biologic agents. NSAIDs are still considered first-line



	All (n=289)	1st line (n=225)	2nd line (n=40)	3rd line + (n=24)
Secukinumab	5.5%	3.1%	1.4%	1.0%
Infliximab	12.1%	8.3%	1.7%	2.1%
Golimumab	5.5%	1.4%	2.1%	2.1%
Etanercept	22.5%	17.6%	4.2%	0.3%
Certolizumab pegol	6.9%	3.5%	1.4%	2.1%
Adalimumab	47.4%	43.6%	3.1%	0.7%

Fig. 1 Line of biologic therapy among Nr-axSpA patients

pharmacological treatment for nr-axSpA [11], however biologics may be effective for patients that do not respond to NSAIDs. Biologics are considered for treating nr-axSpA patients with objective signs of inflammation, defined as active inflammation seen on MRI or elevated C-reactive protein (CRP) levels or patients who do not respond to NSAID therapy [6]. Currently, certolizumab pegol is the only FDA-approved biologic for nr-axSpA in the US. However, agents directed at the IL-17 pathway, such as ixekizumab [12–14] and secukinumab [15–17] have also proven to be effective in both AS and nr-axSpA.

Patient symptoms often drive the initiation and choice of treatment. In this study, we found that in addition to strong overall efficacy and safety, that fast onset of action, sustained pain relief, reduced fatigue, and maintaining the patients' ability to perform daily activities were factors that influenced rheumatologists' treatment choices for their nr-axSpA patients. Lack of alleviation of pain, the condition worsening, and remission not being maintained were also reasons why rheumatologists switch nr-axSpA patients to a different biologic.

Some limitations of this study should be considered. Rheumatologists were required to include patients who had a diagnosis of nr-axSpA in their medical records, but this may not necessarily have included patients who fulfilled the formal classification criteria or clinical test results, so misclassification could exist. Additionally, this study does not capture data from

Table 2 Rheumatologists' reasons for choosing a specific biologic therapy

Reasons for choice, *n* (%)	***n* = 299**
Strong overall efficacy	277 (92.6%)
Familiarity/experience with drug	201 (67.2%)
Fast onset of action	166 (55.5%)
Inhibits disease progression	161 (53.8%)
Sustained pain relief	155 (51.8%)
Good overall safety profile	152 (50.8%)
Achieves low disease activity	144 (48.2%)
Efficacious in treating joint symptoms	139 (46.5%)
Convincing efficacy data in clinical trials	133 (44.5%)
Maintains patients' ability to perform daily tasks/activities	129 (43.1%)
Achieves clinical remission	128 (42.8%)
Control of acute episode/flares	123 (41.1%)
Included in local/national formulary	122 (40.8%)
Strong efficacy as monotherapy	112 (37.5%)
Achieves consistent efficacy over time	106 (35.5%)
Reduces fatigue	97 (32.4%)
Has a reasonable cost-effectiveness ratio	76 (25.4%)
Method of delivery is acceptable to the patient	76 (25.4%)
Allows reduction in steroid use	75 (25.1%)
Improves patients' mood/outlook	72 (24.1%)
Low out of pocket cost/affordability for patients	71 (23.7%)
Specifically to address enthesitis	58 (19.4%)
Delays onset of SI joint involvement	58 (19.4%)
Delays or prevents the progression of the condition to AS/radiographic disease	53 (17.7%)
Suitability for patients with CV risk	29 (9.7%)
No black box warning concerns	10 (3.3%)

patients who are not under the care of a rheumatologist. Drug unresponsiveness and disease status was determined by the rheumatologist and we did not collect information regarding which parameters were used to make these clinical decisions. Despite these limitations, this study provides a pragmatic overview of real-world treatment patterns of consulting nr-axSpA patients in the United States prior to the FDA approval of a biologic treatment for nr-axSpA patients. These analyses also provide insight into the factors that impact biologic choice and biologic switching among rheumatologists in the United States.

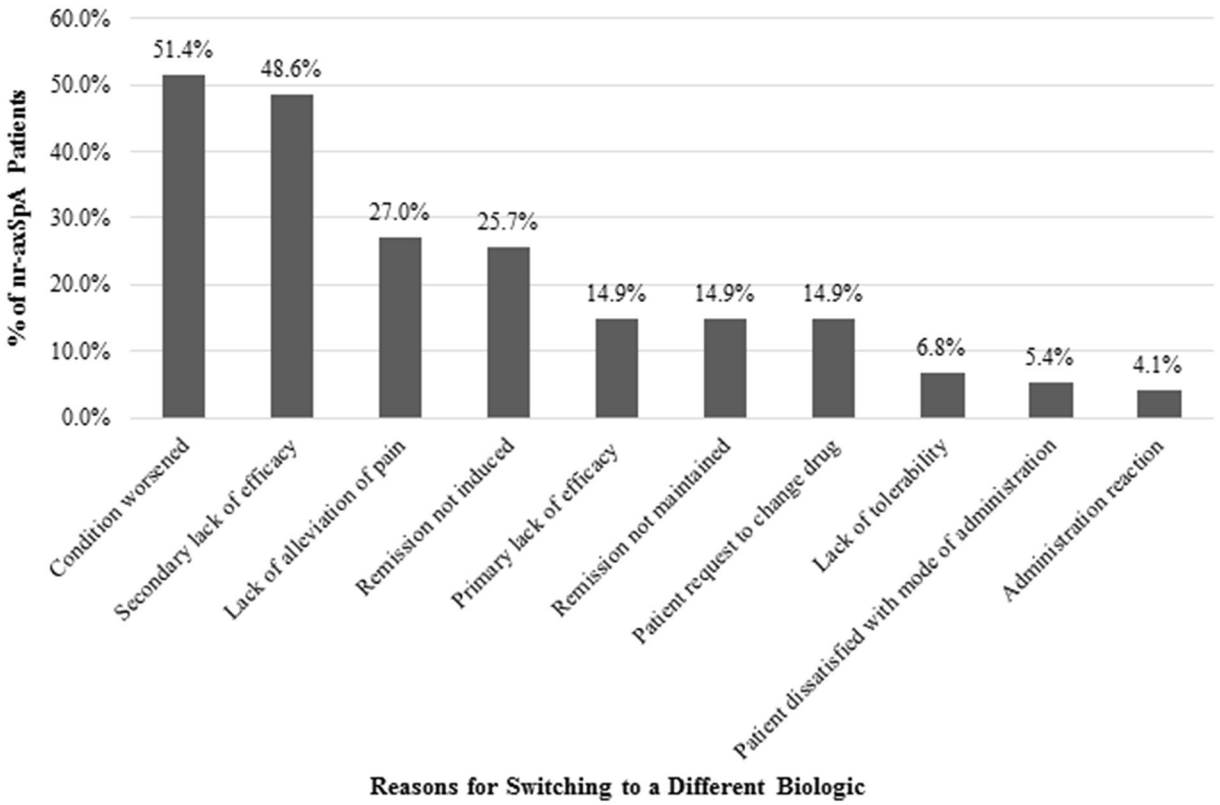


Fig. 2 Top ten reasons that rheumatologists switched Nr-axSpA patients to a different biologic (n = 74)

CONCLUSIONS

This study suggests that around 60% of nr-axSpA patients were receiving biologic therapy prior to the approval of certolizumab pegol. Switching of biologics is frequent in nr-axSpA patients and is usually due to lack of efficacy, loss or response, and effort to accomplish remission.

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Compliance with Ethics Guidelines. All questionnaires used in the survey were reviewed and approved by Western Institutional Review Board (IRB). Patients provided consent for de-identified and aggregated reporting of research findings. Data were de-identified according to the Health Insurance Portability and Accountability Act (HIPAA) regulations before receipt by Adelphi Real World.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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