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SHORT REPORT

Quality of Life Improvements with Biologic Initiation Among Subspecialist-Treated US Patients with Severe Asthma

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Purpose: Patients living with severe asthma (SA) experience multiple health-related quality of life (HRQoL) impairments. This study examined HRQoL changes after biologic treatment initiation among a large, real-world cohort of patients with SA.

Patients and methods: CHRONICLE is an ongoing observational study of subspecialist-treated adults with SA who receive biologics or maintenance systemic corticosteroids or are uncontrolled on high-dosage inhaled corticosteroids with additional controllers. Patients enrolled February 2018–February 2023 were asked to complete the St. George's Respiratory Questionnaire (SGRQ) every 6 months (total score range of 0–100 [0=best possible health], meaningful change threshold is a 4-unit reduction in the total score). Changes in SGRQ responses from 6 months before initiation to 12 to 18 months after initiation were summarized.

Results: A total of 76 patients completed the SGRQ 0 to 6 months before and 12 to 18 months after biologic initiation. The mean (SD) SGRQ total score decreased from 52.2 (20.6) to 41.9 (23.8), with improvement across the symptoms (−14.5), activity (−11.0), and impacts (−8.3) components. For specific impairments reported by ≥50% of patients before biologic initiation, fewer reported each impairment after biologic initiation; the largest reductions were for "Questions about what activities usually make you feel short of breath these days [Walking outside on level ground]" (67% to 43%), "Questions about other effects that your respiratory problems may have on you these days [I feel that I am not in control of my respiratory problems]" (55% to 34%), and "Questions about your cough and shortness of breath these days [My coughing or breathing disturbs my sleep]" (63% to 45%).

Conclusion: In this real-world cohort of adults with SA, biologic initiation was associated with meaningful improvements in asthma-related HRQoL. These data provide further insight into the burden SA places on patients and the benefits of biologic treatment.

Keywords: observational, real-world, health-related quality of life, St. George's Respiratory Questionnaire

Introduction

An estimated 5% to 10% of individuals with asthma have severe asthma (SA), which is defined by the requirement for high-dosage inhaled corticosteroids and additional controllers.[1,2] As compared with the general asthma patient population, patients with SA experience a disproportionately greater burden of symptoms, exacerbations, and treatment requirements, with a commensurate impact on health-related quality of life (HRQoL).[3,4]

Patients with persistently uncontrolled SA despite the use of high-dosage inhaled corticosteroids and additional controllers are potential candidates for biologic treatments, which have been shown to reduce asthma exacerbations and the need for oral corticosteroids (OCS) as well as to improve lung function, symptoms, and HRQoL, although specific demonstrated effects vary across biologics.[5] In their treatment preferences and goals, patients with SA may prioritize HRQoL improvements above other outcomes, including the number and severity of exacerbations.[6]

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Clinical trials and a small number of real-world studies in SA have shown improvements in HRQoL associated with biologic use.[7–15] However, the few real-world studies conducted in the US were treatment-specific and varied in design, patient population, and assessment instruments.[14,15] The impact of biologic treatments as a class on HRQoL in patients with SA in longer-term real-world settings has not been well described. Thus, the objective of this analysis was to examine changes in HRQoL after approximately 1 year of biologic treatment in a broad, real-world sample of US patients with SA.

Methods

CHRONICLE (ClinicalTrials.gov: NCT03373045) is an ongoing real-world observational study of US patients with SA per the American Thoracic Society and European Respiratory Society (ATS/ERS) definition[16] who receive biologics, maintenance systemic corticosteroids (mSCS), or are persistently uncontrolled on high-dosage inhaled corticosteroids with additional controllers. Included patients are subspecialist-treated, aged ≥ 18 years, and diagnosed with SA for at least 12 months prior to enrollment. Details regarding study design and patient recruitment have been previously published.[17]

In CHRONICLE, patients are asked to complete the self-administered 50-item St. George's Respiratory Questionnaire (SGRQ) at enrollment and subsequently every 6 months. The SGRQ is a validated instrument for evaluating the health status of patients with SA.[18,19] Scores range from 0 (best possible health) to 100 (maximum impairment), with a meaningful change threshold (MCT) of a 4-unit reduction in the total score. At the time of completion, the survey directs patients to characterize their asthma for the prior 3 months. Overall SGRQ results in the CHRONICLE population have been previously described.[20]

This self-controlled cohort analysis of patients enrolled from February 2018 to February 2023 included patients who initiated biologic treatment after enrollment and who completed the SGRQ 0 to 6 months prior to biologic initiation and 12 to 18 months after biologic initiation. Those switching between biologics were not counted as biologic initiators. For this population, SGRQ responses were compared for the latest completion 0 to 6 months before biologic initiation and the latest completion 12 to 18 months after biologic initiation. Given the 3-month recall period for the SGRQ, the period of 12 to 18 months after biologic initiation was chosen to enable characterization of patient quality of life following approximately 1 year of biologic treatment (9 to 15 months).

Outcomes of interest were mean SGRQ scores before and after initiation of biologic treatment, and changes after initiation in specific impairments that were reported by ≥ 50% of patients before initiation. Results were reported with descriptive statistics, with means and standard deviations for continuous variables and numbers and percentages for categorical variables.

Results

Of the 4582 eligible patients, 3574 were enrolled in the CHRONICLE study from February 2018 to February 2023. Overall, 2407 patients completed the SGRQ at any point during the study, and the characteristics of those completing the SGRQ were similar to those of all enrolled patients (Table S1). The mean age for enrolled patients was 54.4 years, and patients were predominantly female (68.7%) and White (73.5%). At enrollment, and prior to patients receiving any biologics or mSCS, the mean highest blood eosinophil count (n = 1059) was 375.6 (SD: 503.3; median [IQR] 236.0 [119.6–456.8]) K/mcL, the mean highest immunoglobulin E (n = 479) was 417.5 (SD: 1026.3; median [IQR] 134.0 [43.0–362.1]) IU/mL, and the mean highest fractional exhaled nitric oxide (n = 307) was 33.0 (SD: 36.7; median [IQR] 19.0 [11.0–40.0]) ppb.

Among all enrolled patients, 225 initiated biologic treatment after enrollment. The characteristics of these patients were generally similar to all enrolled patients; however, larger percentages had ≥ 1 exacerbation during the 12 months before enrollment (68.0% vs 51.9% among all enrolled) and were uncontrolled on high-dosage ICS with additional controllers without biologics or mSCS treatment at enrollment (60.9% vs 30.2% among all enrolled) (Table 1). Of these patients, 76 completed the SGRQ 0 to 6 months before and 12 to 18 months after initiation of a biologic.

Among this evaluable population, mean (SD) SGRQ scores improved (numerically decreased) after initiation in all categories: total summary score from 52.2 (20.6) to 41.9 (23.8); symptoms component score from 64.0 (24.1) to 49.5 (24.3); activity component score from 66.3 (25.1) to 55.2 (31.7); and impacts component score from 40.3 (20.9) to 32.0 (22.7) (Figure 1).

Table 1 Characteristics for Patients Who Were Eligible, Enrolled, and Initiated Biologics After Enrollment

Characteristic	Eligible Patients (N = 4582)	All Enrolled (n = 3574)	Initiated Biologics after Enrollment (n = 225)
Age at screening, years			
Mean (SD)	54.8 (14.9)	54.4 (14.7)	53.1 (14.1)
Median (range)	56.0 (18–89)	56.0 (18–89)	54.0 (18–87)
Female, %	68.9	68.7	64.4
Race, %			
White	N/A	73.5	72.4
Black	N/A	17.6	20.0
Asian	N/A	1.8	1.8
Other[a]	N/A	3.2	2.2
Not reported	N/A	3.9	3.6
Missing	N/A	0.1	0.0
Hispanic or Latino ethnicity, %	N/A	10.0	5.8
Insurance, %			
Commercial	56.1	57.4	59.1
Medicare	24.8	23.5	21.8
Medicaid	11.1	11.2	13.8
Uninsured	1.1	1.0	1.3
Other[b]	6.8	6.9	3.6
Missing	0.1	0.1	0.4
Confirmed exacerbations per patient during 12 months before enrollment			
Mean (SD)	1.2 (1.6)	1.1 (1.6)	1.6 (1.7)
Median (range)	1.0 (0–10)	1.0 (0–10)	1.0 (0–10)
Percent with ≥1 exacerbation during 12 months before enrollment (%)	52.4	51.9	68.0
Screening/enrollment treatment class, %			
Uncontrolled on high-dose ICS/LABA only	35.1	30.2	60.9
Any monoclonal antibody	54.3	58.2	20.9
Any monoclonal antibody and mSCS	6.2	7.1	4.4
Systemic corticosteroids or immunosuppressant only	4.4	4.4	13.8

Notes: [a]Includes Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other. [b]Other insurance including other government insurance.
Abbreviations: ICS, inhaled corticosteroids; LABA, long-acting beta-agonist; mSCS, maintenance systemic corticosteroids; SD, standard deviation.

For specific impairments reported by ≥ 50% of patients before biologic initiation, fewer patients reported each impairment after biologic initiation (Figure 2). The most frequently reported impairments before and after initiation were "Questions about what activities usually make you feel short of breath these days [Playing sports or other physical activities]" (93% to 82%), followed by "Questions about what activities usually make you feel short of breath these days [Walking up hills]" (92% to 86%), and "My breathing makes it difficult to do things such as very heavy manual work, ride a bike, run, swim fast, or play competitive sports" (91% to 83%). The impairments with the largest after-initiation differences were for "Questions about what activities usually make you feel short of breath these days [Walking outside on level ground]" (−24%) followed by "Questions about other effects that your respiratory problems may have on you these days [I feel that I am not in control of my respiratory problems]" (−21%), and "Questions about your cough and shortness of breath these days [My coughing or breathing disturbs my sleep]" (−19%).

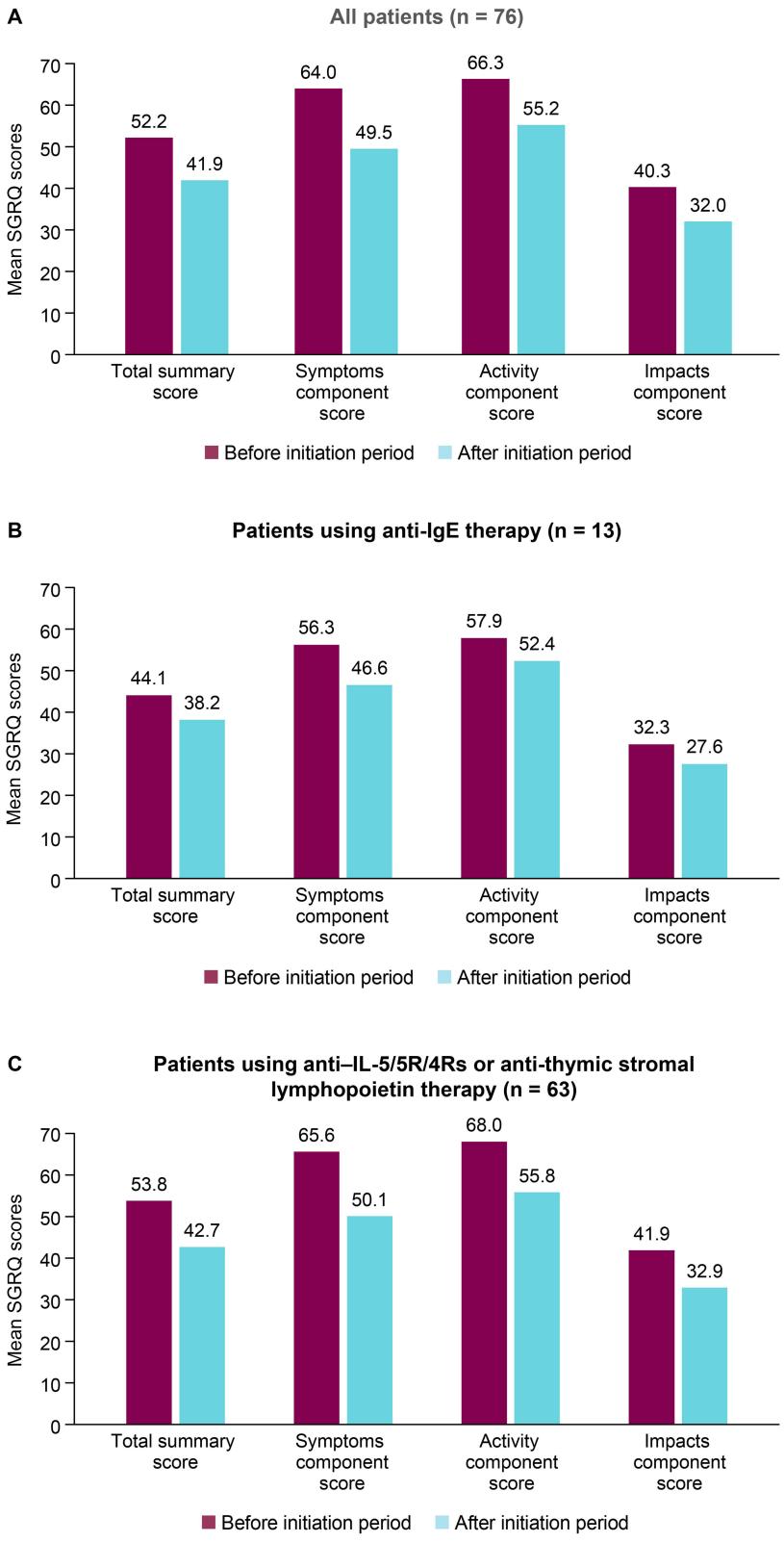

Figure 1 SGRQ scores 6 months before and 12 to 18 months after initiation of biologics. (**A**) All patients (n = 76). (**B**) Patients using anti-IgE therapy (n = 13). (**C**) Patients using anti–IL-5/5R/4Rs or anti-thymic stromal lymphopoietin therapy (n = 63).
Abbreviations: IgE, immunoglobulin E; IL, interleukin; SGRQ, St. George's Respiratory Questionnaire.

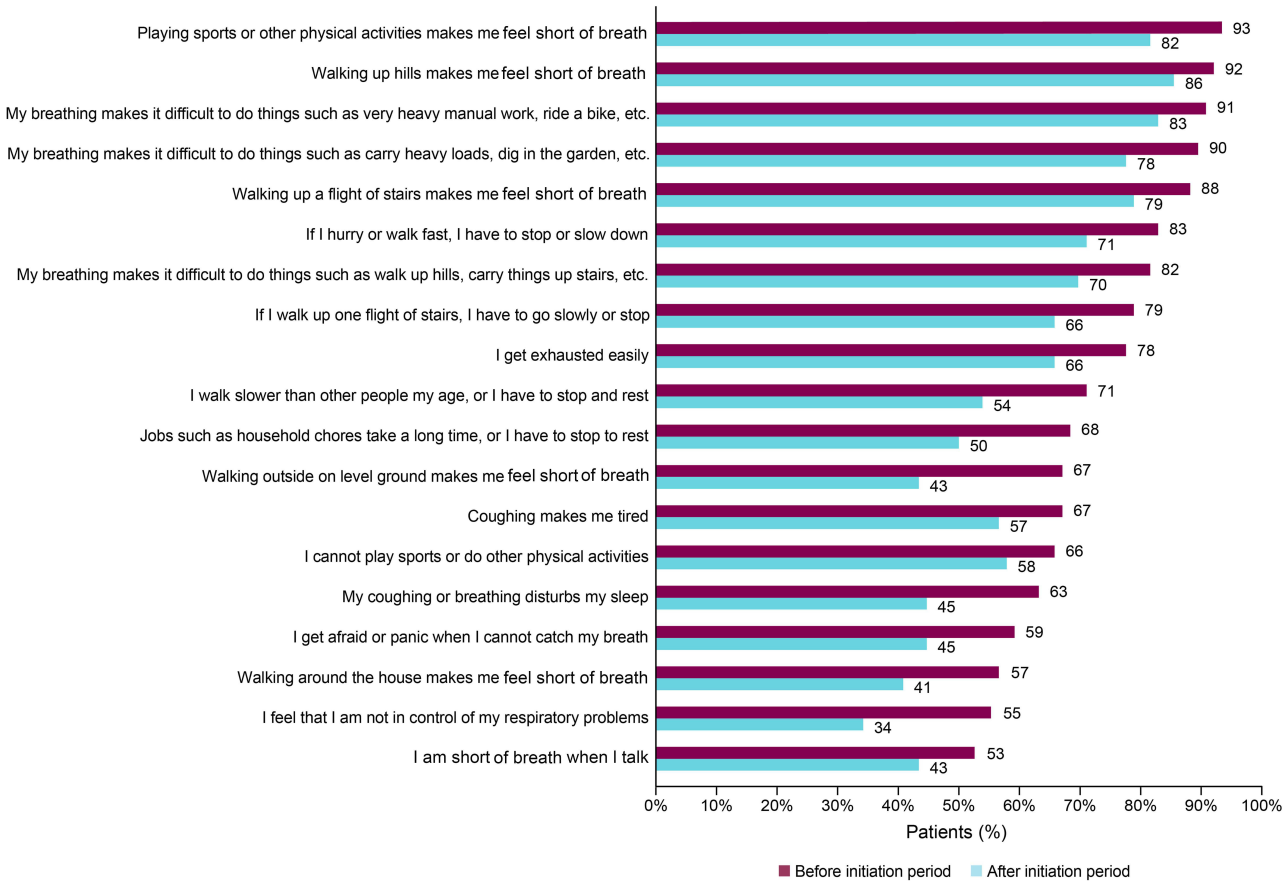

Figure 2 Specific impairments reported by patients 6 months before and 12 to 18 months after initiation of biologics, from greatest to least improvement (n = 76). Results limited to those specific impairments reported by ≥ 50% of patients before biologic initiation.

Discussion

This analysis is the first class-level contemporary characterization of HRQoL changes among US subspecialist-treated patients with SA who initiated biologics. Results generally align with the results of randomized, placebo-controlled studies, as well as real-world studies of individual biologics that have observed improved HRQoL among patients with SA following treatment initiation.[11,21,22] The findings also add to the growing body of data supporting the usefulness of the SGRQ for characterizing the real-world HRQoL status of patients with SA.[20,23] The numerous specific impairments captured by the SGRQ enable a robust characterization of the many ways in which HRQoL specifically improves among real-world patients with SA who initiate biologics. The largest improvements were in shortness of breath associated with walking on level ground, feeling in control of their disease, and sleep disturbances. As might be expected, there were smaller absolute improvements in the percentage of patients reporting impairments with more strenuous activities, such as shortness of breath with walking up hills, inability to play sports or do other physical activities, and difficulty with heavy manual work. It is possible that greater improvements with these more strenuous activities might require more time on biologic treatment as well as physical reconditioning efforts by patients and health care professionals.[24]

The observed improvement in the mean SGRQ total score (−10.2) is clinically meaningful, at more than twice the MCT of a 4-point reduction. This observed improvement is generally consistent with changes observed at similar timepoints in clinical trials. In the ANDHI trial of benralizumab in severe eosinophilic asthma, Harrison et al[9] reported a least squares mean change in SGRQ total score at 24 weeks from baseline of −23.1 with treatment compared to −14.9 with placebo; improvement was evident at week 4 but continued through week 24. In the MUSCA trial of mepolizumab among patients with severe eosinophilic asthma, Chupp et al[13] reported a least squares mean change in SGRQ total score

at 24 weeks from baseline of −15.6 with treatment versus −7.9 with placebo. At 52 weeks in the NAVIGATOR trial of tezepelumab in severe asthma of all phenotypes, there was a least squares mean improvement in SGRQ total score of −21.9 with treatment compared to −15.9 with placebo, with greater improvements from baseline and compared to placebo in patients with higher eosinophil counts.[25] These studies demonstrated larger improvements from baseline than those observed in the CHRONICLE cohort. This difference is expected as clinical trials require patients to have a recent history of multiple exacerbations, reduced lung function, and poorly controlled asthma symptoms at enrollment. As a result, patients participating in clinical trials are likely to have worse HRQoL at baseline, and greater improvements over time would be expected with treatment.

The relatively large reduction in the proportion of patients reporting cough- or breathing-related sleep disturbances is notable, as sleep disturbances are highly prevalent among patients with SA and have been independently associated with reduced quality of life and poorer asthma control.[26] Likewise, the considerable reduction in reported feelings of not being in control of one's respiratory problems is an important treatment consideration, given that anxiety and depression are highly prevalent among patients with SA and associated with poorer health status and asthma control.[27] Moreover, the results for specific impairments show large proportions of patients reporting limitations of high-exertion activities, which suggests such impairments have a notable impact on quality of life and should be considered in individual treatment decisions. Patients with asthma, especially those with SA, perceive worse physical HRQoL than mental HRQoL.[28]

Patients living with SA may prioritize specific and individualized HRQoL improvements, such as sleep disturbances or high-exertional activities, over improvements in other outcomes in their treatment preferences. Understanding such preferences has been identified as a key factor in patient-centered approaches to shared decision-making.[6] Shared decision-making has been shown to improve adherence and outcomes such as asthma control and lung function, as well as asthma-related HRQoL, among patients with poorly controlled asthma.[29] The present study findings may help physicians structure individualized discussions regarding specific aspects of HRQoL and their implications for treatment options. Additionally, these results underscore the value of biologic treatment for SA and highlight the importance of screening uncontrolled patients with SA for biologic eligibility.

Limitations

General limitations of the CHRONICLE study have been previously described[17]; they include inherent limitations of descriptive analysis, differences in standard of care policies across study sites, and lack of randomized site selection. Moreover, CHRONICLE is limited to US adults with SA receiving subspecialist care and may not be generalizable to the broader SA population in the US or globally. Despite having a large sample for the CHRONICLE study overall, the inclusion requirements of initiating a biologic after enrollment and completing the SGRQ during certain time intervals before and after enrollment meant that the analysis sample was relatively small. This analysis is limited in that it only included patients who completed the SGRQ, and those who did not complete it could have had more poorly controlled asthma, which may have led to underestimation of overall HRQoL burden. In addition, CHRONICLE uses the SGRQ exclusively to characterize HRQoL, so comparisons with other instruments were not possible. Lastly, HRQoL scales, including the SGRQ, have been shown to overestimate HRQoL in patients with frequent exposure to corticosteroids and underestimate the benefits of corticosteroid-sparing agents,[30] as they do not account for the adverse effects of extended systemic corticosteroid exposure. Any adverse effects associated with biologic use or improvement in inflammatory comorbidities from biologic use would also affect the evaluation of HRQoL in patients with SA.

Conclusions

In this real-world cohort of US patients with SA, the initiation of biologic treatment was associated with clinically meaningful improvements in asthma-related HRQoL. These data provide further insight into the burden SA places on patients as well as the benefits of biologic treatment and suggest providers should prioritize HRQoL in SA treatment decisions. Health care professionals can use these data to inform shared decision-making discussions with patients. Among patients with SA and decreased HRQoL, the potential for improvements with biologics should be considered in treatment decisions for eligible patients.

Abbreviations

HRQoL, health-related quality of life; ICS, inhaled corticosteroids; LABA, long-acting beta agonists; MCT, meaningful change threshold; mSCS, maintenance systemic corticosteroids; OCS, oral corticosteroids; SA, severe asthma; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire.

Data Sharing Statement

CHRONICLE is an ongoing study; individual de-identified participant data cannot be shared until the study concludes. The full study protocol is available upon request of the corresponding author. Individuals who were or were not involved in the study may submit publication proposals to the study's Publication Steering Committee by contacting the corresponding author.

Ethics Approval and Informed Consent

The CHRONICLE study protocol received central institutional review board (Advarra, Columbia, MD) approval on November 3, 2017, and was registered on ClinicalTrials.gov on December 14, 2017 (NCT03373045). A signed informed consent form is obtained at enrollment for study participation and to acquire medical records from other providers, including pharmacy records.

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