Humanistic Burden of Refractory and Nonrefractory Chronic Idiopathic Urticaria: A Real-world Study in the United States

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ABSTRACT

Purpose: Chronic idiopathic urticaria (CIU) is a debilitating skin condition that can profoundly affect patients' quality of life. This study explored the impact of refractory and nonrefractory CIU on patients in the real-world setting in the United States.

Methods: Data were collected from the Adelphi Real World 2015 Urticaria Disease-Specific Programme. Physicians completed patient record forms (PRFs) for 4 consecutive patients consulting with nonrefractory CIU and 6 patients with refractory CIU. The PRF included information on patient characteristics, medication, and disease severity; physicians were asked about the impact of CIU on patients, and to rate their satisfaction with patients' treatment (scale, 1−7 [1 = extremely dissatisfied and 7 = extremely satisfied]). The same patients were asked to complete a patient self-completion form (PSC). This included questions regarding how CIU affected their everyday life and their satisfaction with and understanding of their condition and medications. The PSC included a number of patient-reported outcomes measures: the Dermatology Life Quality Index (scored from 0 to 30, with higher scores indicating greater impact), the Work Productivity and Activity Impairment (4 scores calculated [absenteeism, presenteeism, work productivity loss, and activity impairment], each scored from 0% to 100% after transformation, with higher scores indicating greater impairment), and the Jenkins Sleep Scale (assessed over 30 days; scored from 0 to 20, with higher scores indicating greater sleep disturbance). Completion of the PSC was voluntary.

Findings: Seventeen physicians completed a total of 184 PRFs (108 for patients with refractory CIU; 76 for those with nonrefractory CIU); 140 of these 184 patients completed a PSC form (93 with refractory CIU; 47 with nonrefractory CIU). Overall, 26% of the entire population (30% of patients with refractory CIU and 17% with nonrefractory CIU) reported that skin symptoms had a great effect on their lives (Dermatology Life Quality Index score ≥11). Sleep problems were common: mean Jenkins Sleep Scale scores were 7.8 overall (8.1 for patients with refractory CIU and 7.2 for those with nonrefractory CIU). Overall work impairment was 19% in the overall population, with similar values in refractory and nonrefractory patients (18% and 20%, respectively). Physician satisfaction with disease control was not high, with physicians reporting a mean score of 4.8 on a 7-point scale. Twenty-one percent of patients were extremely dissatisfied, very dissatisfied, or dissatisfied with their treatment, and 52% believed better control could be achieved.

Implications: : The humanistic burden of CIU is high. There is clearly a need for better management of CIU to improve outcomes for patients. (*Clin Ther.* 2019;41:205−220)

Keywords: chronic idiopathic urticaria, chronic spontaneous urticaria, quality of life, real-world evidence, refractory.

INTRODUCTION

Chronic idiopathic urticaria (CIU), also known as chronic spontaneous urticaria, is characterized by the appearance of pruritic wheals, angioedema, or both for

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>6 weeks with no identifiable trigger.[1,2] CIU affects an estimated 0.5%−1.0% of the population.[1,3] It is uncontrolled in ~50% of patients undergoing first-line treatment with approved doses of H_1-antihistamines and in 25%−33% of patients treated at higher doses.[1] Inadequately controlled patients can be treated with omalizumab as per guidelines, despite using up to 4 times the approved dose of H_1-antihistamines.[2]

Health-related quality of life (HRQoL) is impaired in patients with CIU, as considerations such as disturbed sleep, anxiety, and financial worries affect their ability to live a normal life.[4] Psychiatric comorbidities are also common in patients with CIU, particularly anxiety, depression, and somatoform disorders[1]; QoL is further compromised with such diagnoses.[5] The negative impact of CIU on patients is reflected in the results of studies showing that patients with CIU have QoL similar to those with moderate and severe psoriasis[6] and triple coronary artery disease.[7]

The impact of CIU on patients' QoL in clinical practice in the United States has not been widely investigated. The present study assessed the humanistic burden of CIU, defined as the impact of a disease on the patient's HRQoL, activities of daily living, treatment satisfaction, and adherence to treatment,[8] from the perspective of both the patients and their treating physician in the real-world clinical setting in the United States.

PATIENTS AND METHODS

Data for the present analysis were drawn from the Adelphi Real World Urticaria Disease-Specific Programme (DSP) 2015 (March−July 2015), a cross-sectional survey of physicians and patients in the real-world clinical setting. The DSP methods have been described in detail elsewhere.[9]

Board-certified physicians were recruited from across the United States. The only inclusion criteria were that participating physicians (allergists and dermatologists) were required to have been qualified for a minimum of 4 years, to be actively involved in the management of and make treatment decisions for patients with CIU, and to see at least 3 patients with CIU per month.

Patients were aged 18 to 75 years, not involved in a clinical trial, and currently receiving systemic treatment for CIU; eligibility of patients was determined by physicians based on their clinical judgment of symptoms. CIU was defined as symptoms of urticaria (hives, itching, with or without angioedema) on a continuous or intermittent basis lasting ≥6 weeks and with no known cause. The patient's disease was considered continuous if they "usually had continuous symptoms (daily or almost daily symptoms)" or intermittent if they usually had "an intermittent pattern of symptoms, with symptom-free periods lasting days or weeks." Patients with continuous CIU were classified as being symptom free if they reported no symptoms at least in the last 5 days; those with intermittent CIU were classified as symptom free if they reported no symptoms at least in the last 6 weeks.

Patients were defined as having refractory or nonrefractory disease, based on a pre-programmed research definition, to examine the characteristics of patients not responding to advanced treatment regimens. Patients were defined as having refractory CIU if they were symptomatic and on treatment step 2 or greater according to the treatment steps as defined in the Joint Task Force on Practice Parameters guidelines, which were the most recent guidelines available at the time of the analysis (Fig. 1).[10] Patients were defined as having nonrefractory CIU if they were currently asymptomatic on any treatment step or symptomatic on step 1 treatment.

Data collection

Data were collected in full accordance with relevant legislation at the time of data collection, including the US Health Insurance Portability and Accountability Act of 1996[11] and the Health Information Technology for Economic and Clinical Health Act legislation.[12] Institutional review board ethical approval was obtained from the Western Institutional Review Board, Puyallup, WA, United States.

Physicians were asked to participate in an interview assessing their perceptions and attitudes toward the diagnosis, management, and treatment of CIU and to complete physician report forms for the next 4 patients with nonrefractory CIU and 6 patients with refractory CIU presenting to them. The physician report form collected information on patient demographic characteristics, clinical characteristics, clinical management and outcomes, and past and current medication use. The clinical impact of CIU on patients with refractory and nonrefractory CIU will be presented separately. Physicians reported how

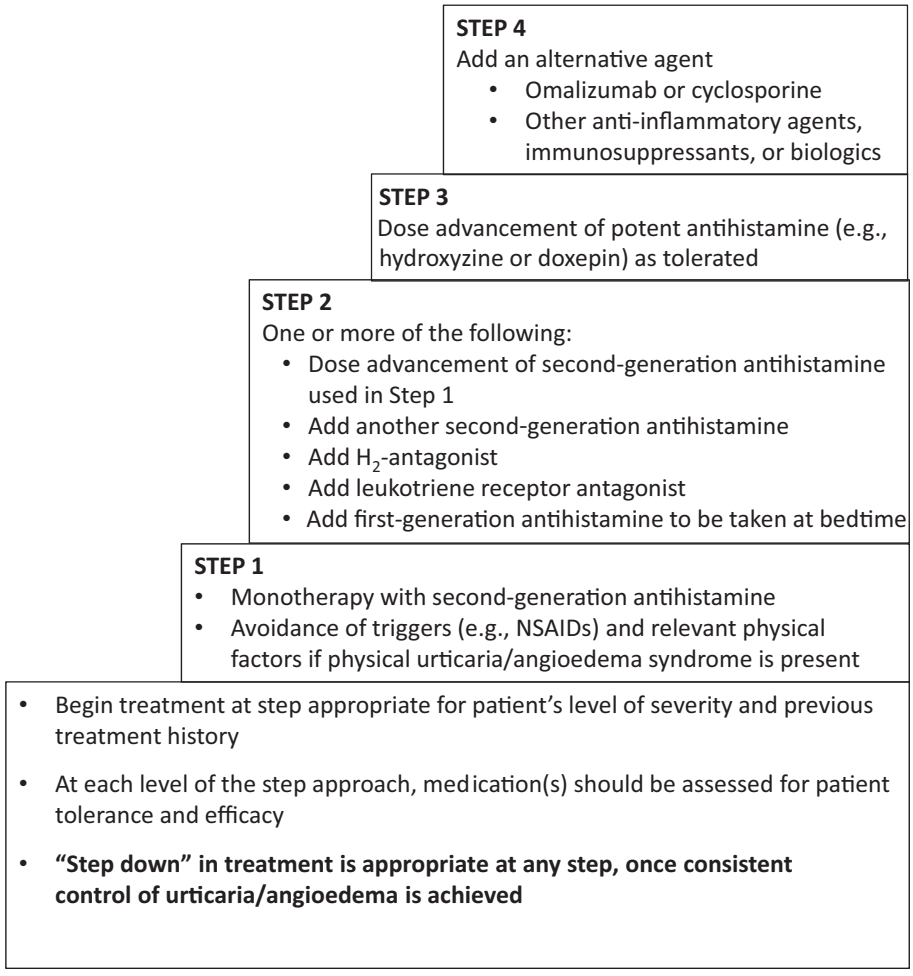

Figure 1. Step-care approach to the treatment of patients with chronic urticaria used in the definition of patients with refractory and nonrefractory disease. Reprinted from J Allergy Clin Immun, vol. 133/No. 5, J. A. Bernstein et al, The diagnosis and management of acute and chronic urticaria: 2014 update, pp 1270–7, Copyright (2014), with permission from Elsevier.

satisfied they were with the current control of the patient's CIU on a scale of 1–7, with 1 being extremely dissatisfied and 7 being extremely satisfied. Physicians also provided an assessment of the extent to which CIU affected their patients' current status, including ability to perform everyday tasks, psychological well-being, sleep, and employment. Impact was assessed on a scale of 0–10, with 0 indicating no impact and 10 indicating the worst imaginable impact.

The same patients were invited to participate using a patient self-completion form that collected information about how CIU affected their everyday life, and opinions and understanding of their medications and condition. As part of the self-completion form, patients were also asked to complete 3 validated patient-reported outcomes instruments: the Dermatology Life Quality Index (DLQI)[13,14]; the Jenkins Sleep Scale[15]; and a specific health problem version of the Work Productivity Activity Impairment (WPAI) questionnaire[16] that was adapted for use in patients with CIU. The patient self-completion form was filled out separately and confidentially, with no influence or input from anyone, including the

physician or nurse. Completion of this form was not mandatory.

The DLQI, which consists of 10 questions subdivided into 6 domains (symptoms and feelings, daily activities, leisure, work/school, personal relationships, and treatment) assesses disease activity during the past 7 days. A DLQI score is calculated on a scale of 0−30, with a higher score indicating a higher impact of the condition on the patient, with a minimal important difference of 2.24−4.[17,18]

The Jenkins Sleep Scale, which is completed by patients, is used to assess the frequency and intensity of sleep difficulties, including trouble falling asleep, wakening, trouble staying asleep, and daytime impairment over the previous 30 days. A score ranging from 0 to 20 is calculated, with a higher score indicating greater sleep disturbance.

The WPAI-CIU questionnaire was used to assess impairments in paid work and activities caused by CIU. The WPAI-CIU measures work time (hours of work) missed and work and activity impairments. Impairments were assessed, with reference to CIU, during the past 7 days. Four scores were calculated (absenteeism, presenteeism, work productivity loss, and activity impairment), each ranging from 0% to 100% after transformation, with higher scores indicating greater impairment. Impairments in work and activity were expressed as percentages of the maximum score.

Patients provided written informed consent for use of their anonymized and aggregated data for research and publication in scientific journals. Data were collected by a third-party fieldwork agency in such a way that patients and physicians could not be identified directly; all data were aggregated and de-identified before receipt.

Statistical Analysis

The DSP is a research program conducted with no a priori hypotheses specified. Data were analyzed by using descriptive statistics. Continuous variables are reported with means and SDs; categorical variables are reported with frequency and percentage. Comparisons of the cohorts with refractory versus nonrefractory disease were performed for all data points other than basic patient demographic characteristics, using bivariate analysis. Differences between patient types were assessed by using Mann−Whitney *U* tests for continuous variables or categorical variables with ordered responses, Fisher's exact tests for dichotomized variables, and Pearson's χ^2 tests for categorical variables with >2 categories. The significance level was set at 5%; all tests were 2-sided.

Owing to incomplete data, a level of missingness was expected across variables. The level of missingness was reported for each variable being analyzed. Formal sample size calculations were not applied to the DSP at the time of sampling. Had such calculations been used, a sample size of 64 patients in each group would have been required to detect an effect size of 0.5 in a nonspecified outcome variable between 2 groups of patients, with no adjustment for covariates (power of 80%; $P = 0.05$). Results obtained by analysis on <64 patients in each group should be interpreted with this knowledge.

All statistical analyses were performed by using Stata software release 14 (StataCorp LLC, College Station, Texas).

RESULTS

A total of 17 physicians (15 allergists and 2 dermatologists) participated in the physician interview, fewer than originally specified in the study protocol (70 allergists and 30 dermatologists). Recruitment was lower than planned, and physicians were therefore asked to include more patients than the protocol-specified 6 patients with refractory CIU and 4 with nonrefractory CIU. Physicians were predominantly male (13 men and 4 women) and office-only based (13 hospital based and 4 office based). Physicians completed a total of 184 patient record forms (median, 10 per physician; range, 2−35): 108 for patients with refractory CIU (median, 6 per physician; range, 0−19) and 76 for patients with nonrefractory CIU (median, 4 per physician; range, 0−23).

In total, 140 patients completed the patient self-completion form: 93 had refractory CIU and 47 had nonrefractory CIU. Patient demographic and clinical characteristics are reported in Table I. Patients had a median age of 48.5 years (refractory CIU, 47.5 years; nonrefractory CIU, 50 years), and 86% were female (refractory CIU, 87%; nonrefractory CIU, 84%). The mean time since a diagnosis of CIU was 2.6 years (refractory CIU, 2.6 years; nonrefractory CIU, 2.6 years). Disease was classified as mild in 52% of patients, moderate in 35% of patients, and severe in

Table I. Demographic and clinical characteristics of patients with refractory and nonrefractory chronic idiopathic urticaria (CIU).

Characteristic	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)
Age, y			
No. of missing entries	0	0	0
Mean (SD)	47.7 (15.3)	48.0 (14.2)	47.3 (16.8)
Median	48.5	47.5	50.0
Interquartile range	35.5–60.0	38.5–60.0	31.5–60.0
Sex			
No. of missing entries	0	0	0
Male	26 (14%)	14 (13%)	12 (16%)
Female	158 (86%)	94 (87%)	64 (84%)
BMI, kg/m^2			
No. of missing entries	1	0	1
Mean	29.8	30.6	28.7
SD	7.2	7.7	6.4
Employment status			
No. of missing entries	28	11	17
Working full-time	88 (56%)	58 (60%)	30 (51%)
Working part-time	7 (4%)	3 (3%)	4 (7%)
Student	6 (4%)	2 (2%)	4 (7%)
Unemployed	9 (6%)	8 (8%)	1 (2%)
Homemaker	19 (12%)	10 (10%)	9 (15%)
Retired	27 (17%)	16 (16%)	11 (19%)
Time since diagnosis, mean (SD), y	2.6 (5.1)	2.6 (5.6)	2.6 (4.5)
Current disease severity			
No. of missing entries	3	2	1
Mild	95 (52%)	48 (45%)	47 (63%)
Moderate	64 (35%)	42 (40%)	22 (29%)
Severe	22 (12%)	16 (15%)	6 (8%)

BMI = body mass index.

12% of patients. The incidence of severe disease was more common in patients with refractory CIU than in those with nonrefractory CIU (15% vs 8%, respectively).

Humanistic Impact of CIU

Patient-reported Impact of CIU

The mean total DLQI score for the overall population was 6.3; the mean total score was higher in patients with refractory versus nonrefractory disease CIU (7.0 vs 5.0, respectively; $P = 0.0222$). Skin symptoms had a very large or extremely large effect on the lives of 26% of patients overall (30% of patients with refractory CIU and 17% of patients with nonrefractory CIU; $P = 0.0639$), as reflected by DLQI scores $\geq$11; 60% of patients overall (56% of patients with refractory disease and 67% of those with nonrefractory disease) had DLQI scores $\leq$5, indicating that their disease had a small effect or no effect on their life (Table II). DLQI domains affected to a greater extent in patients with refractory versus nonrefractory disease were those relating to itching, pain and stinging skin, and impact on the clothes patients wore (Fig. 2). Mean scores for the patient-

Table II. Humanistic impact of chronic idiopathic urticaria (CIU) in patients with refractory and nonrefractory CIU.

Humanistic Factor	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)	P*
Patient-reported				
DLQI†				
No. of missing entries	48	18	30	
Mean (SD)	6.3 (6.6)	7.0 (6.6)	5.0 (6.6)	0.0222
DLQI effect on patient's life, no. (%)				0.0639
No. of missing entries	48	18	30	
No effect (score, 0—1)	45 (33)	25 (28)	20 (44)	
Small effect (score, 2—5)	36 (26)	25 (28)	11 (24)	
Moderate effect (score, 6—10)	20 (15)	13 (14)	7 (15)	
Very large effect (score, 11—20)	29 (21)	23 (26)	6 (13)	
Extremely large effect (score, 21—30)	6 (4)	4 (4)	2 (4)	
Jenkins Sleep Evaluation questionnaire‡				
No. of missing entries	54	21	33	
Mean (SD)	7.8 (5.1)	8.1 (4.8)	7.2 (5.6)	0.2167
Physician-reported§				
Assessment of patient's current status for…				
…impairment in ability to perform everyday tasks/usual activities				0.0068
No. of missing entries	13	8	5	
Mean (SD)	2.9 (2.4)	3.3 (2.4)	2.3 (2.2)	
…impairment in physical ability to take part in sports/leisure activities				0.0064
No. of missing entries	14	8	6	
Mean (SD)	2.8 (2.5)	3.2 (2.5)	2.2 (2.3)	
…interference with personal/sexual relationships				0.0310
No. of missing entries	22	12	10	
Mean (SD)	2.6 (2.5)	3.0 (2.7)	2.1 (2.2)	
…avoidance of social interactions				0.0183
No. of missing entries	16	8	8	
Mean (SD)	2.6 (2.5)	3.0 (2.5)	2.1 (2.3)	
…impact of psychological well-being, including anxiety and stress				<0.0001
No. of missing entries	14	9	5	
Mean (SD)	3.4 (2.6)	4.1 (2.6)	2.4 (2.4)	
…impairment on sleep				<0.0001
No. of missing entries	14	9	5	
Mean (SD)	3.3 (3.0)	4.2 (3.2)	2.1 (2.3)	

Table II. (*Continued*)

Humanistic Factor	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)	P*
…impact on employment/studying				0.2424
No. of missing entries	21	14	7	
Mean (SD)	2.5 (2.6)	2.7 (2.7)	2.1 (2.4)	

DLQI = Dermatology Life Quality Index.
* Comparison of refractory and nonrefractory CIU (Mann–Whitney *U* test).
† During the last 7 days; range, 0–30.
‡ During the last 30 days; range, 0–20.
§ On a scale of 0–10, where 0 = none and 10 = worst imaginable.

reported Jenkins Sleep Scale were moderate (7.8 for the overall population, 8.1 for refractory CIU, and 7.2 for nonrefractory CIU [$P = 0.2167$], equivalent to 4–7 disturbed nights per month) (Table II and Fig. 3).

Physician-reported Impact of CIU

The aspects most affected by CIU, as rated by the physician, were psychological well-being (including anxiety and stress) and sleep (Table II). Physicians scored sleep impairment at 3.3 in the overall population, with a greater degree of impairment in patients with refractory CIU (score, 4.2 vs 2.1 for patients with nonrefractory CIU; $P < 0.0001$). Psychological well-being was scored at 3.4 overall; physicians judged patients with refractory CIU to be affected to a greater extent than those with nonrefractory CIU (scores 4.1 and 2.4; $P < 0.0001$).

Impact of CIU on Employment

The proportion of patients in employment was 61% of patients overall (63% of those with refractory CIU and 58% of those with nonrefractory CIU). Overall work impairment, as measured by using the WPAI, was 19% in the overall population, with similar values in refractory and nonrefractory patients (18% and 20%, respectively; $P = 0.9643$) (Table III). Overall impairment of activities of daily living was 24% overall (25% in patients with refractory CIU and 20% in patients with nonrefractory CIU; $P = 0.2378$).

Symptoms and Medication Use

Overall, 39% of patients (41% with refractory CIU and 35% with nonrefractory CIU; $P = 0.1683$) rarely or never consulted a health care professional during symptomatic periods (Table IV). Most patients (60%) experienced warning signs before a symptomatic period (61% with refractory disease and 59% with nonrefractory disease; $P > 0.999$). These symptoms ranged from itching to abnormal heartbeat. Overall, 37% of patients responded by altering the medication they took (31% with refractory disease and 50% with nonrefractory disease; $P = 0.2330$).

Patients also reported altering their medication under other circumstances, with 31% overall not taking their medication when symptoms were under control (33% and 26% of patients with refractory and nonrefractory CIU, respectively; $P = 0.5286$) and 34% increasing the dose or frequency of their medication (40% and 18%; $P = 0.0223$). Overall, however, 84% of patients rarely or never forgot to take their medication (85% and 84% of patients with refractory and nonrefractory CIU, respectively; $P = 0.2266$) (Table IV).

Patients generally believed that their physician had clearly explained their CIU and how their medication controlled their CIU (Fig. 4). Patients were generally keen to ask for and try new treatments as they became available. In general, patients' attitudes to their condition were similar, regardless of whether they had refractory disease.

Satisfaction With Treatment

Patient-reported Satisfaction With Treatment

Overall, 21% of patients were extremely dissatisfied, very dissatisfied, or dissatisfied with their treatment, and 52% believed better control could be achieved (Table V). Patients rated their satisfaction

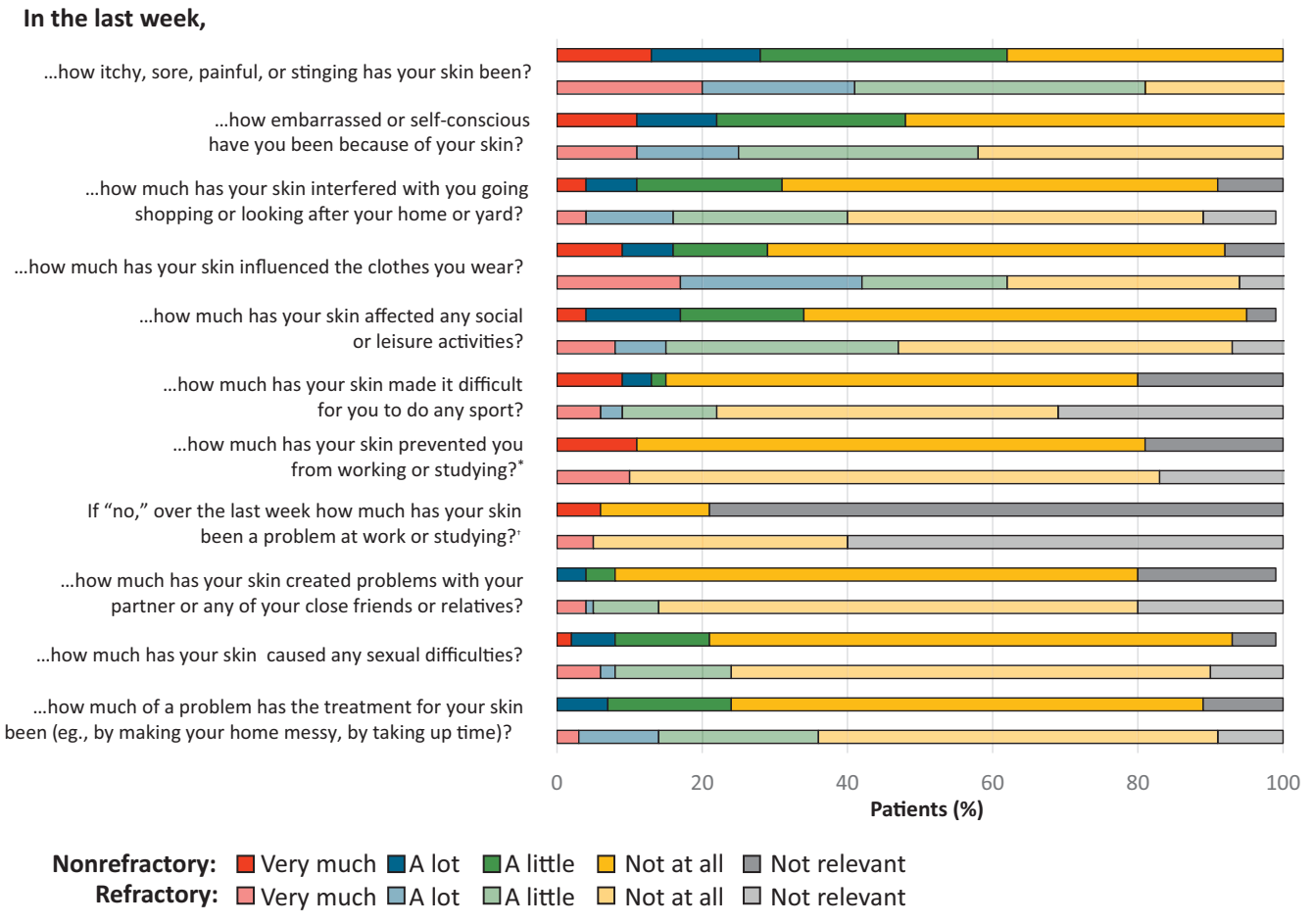

Figure. 2. Impact of chronic idiopathic urticaria on aspects of daily living in the past 7 days, measured by using the Dermatology Quality of Life questionnaire. *Responses were yes, no, or not relevant. †Responses were a lot, a little, not at all, or not relevant.

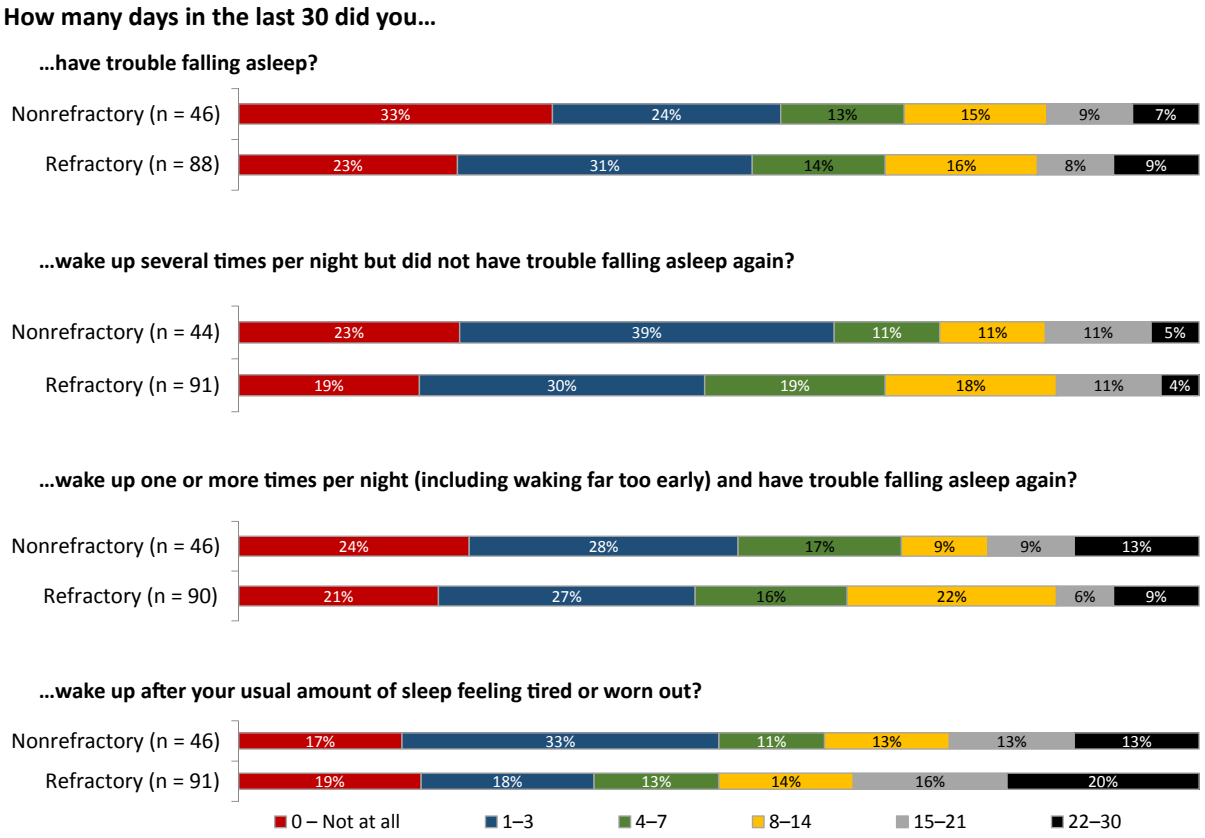

Figure 3. Impact of chronic idiopathic urticaria on sleep patterns over the past 30 days, assessed using the Jenkins Sleep Evaluation Questionnaire. Data are patients with response.

with how their treatment helped their symptoms, how quickly their treatment worked, how well they tolerated their treatment, and how effective their treatment was at reducing the frequency of urticaria at a mean score of 7.1, 6.6, 8.1, and 6.6, respectively, on a scale of 1−10, where 10 indicated extremely satisfied. In general, more patients with refractory CIU were dissatisfied with their treatment than those with nonrefractory CIU (25% vs 14%, respectively; $P = 0.0239$), although similar proportions of both groups believed better control could be achieved (54% and 49% of patients; $P = 0.7069$). Patients with refractory CIU were less satisfied than those with nonrefractory CIU with how their treatment helped their symptoms (satisfaction scores of 6.8 and 7.8 for refractory and nonrefractory disease, respectively; $P = 0.0481$), how well they tolerated their treatment (scores of 7.7 and 8.8; $P = 0.0347$), and perceived efficacy of treatment at reducing the frequency of symptomatic periods (scores of 6.1 and 7.5; $P = 0.0098$) (Fig. 5).

Physician-reported Satisfaction With Treatment

Satisfaction with disease control was not high, with physicians reporting an overall mean score of 4.8 on a scale of 1−7, where 1 was extremely dissatisfied and 7 was extremely satisfied. Satisfaction with treatment was lower for patients with refractory disease (4.3 vs 5.6 for patients with nonrefractory disease; $P < 0.0001$) (Table V). Physicians believed better disease control was possible for 57% of patients overall. This was higher for patients with refractory versus nonrefractory CIU (74% vs 32%, respectively; $P < 0.0001$).

Table III. Work impairment and activity limitation due to chronic idiopathic urticaria (CIU) in patients with refractory and nonrefractory CIU assessed by using the Work Productivity Assessment Index.

CIU-related Impairment in the Last 7 Days, %	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)	P*
Overall work impairment				0.9643
No. of missing entries	107	58	49	
Mean	18.7	17.7	20.4	
SD	22.8	21.0	26.2	
Work time missed				0.5955
No. of missing entries	106	58	48	
Mean	3.4	2.0	5.9	
SD	12.8	6.3	19.6	
Impairment while working				0.9419
No. of missing entries	107	58	49	
Mean	17.4	16.6	18.9	
SD	21.4	19.3	25.0	
Activity impairment				0.2378
No. of missing entries	45	16	29	
Mean	23.5	25.4	19.8	
SD	29.5	30.0	28.2	

* Comparison of refractory and nonrefractory CIU (Mann–Whitney *U* test).

DISCUSSION

The signs and symptoms of CIU can vary considerably over time, but when symptomatic, CIU can affect the HRQoL of patients with refractory and nonrefractory disease. The present study assessed the humanistic burden of CIU from the perspective of both the patient and their treating physician in the real-world clinical setting.

A substantial proportion of the study patients reported that various aspects of their lives were affected very much or a lot by their CIU; the most affected DLQI domains related to the physical symptoms and ability to lead a normal life. Although the physician-reported prevalence of symptoms was similar in patients with refractory and nonrefractory disease, patients with refractory disease reported a greater impact of symptoms on their QoL, as reflected by their DLQI scores (7.0 and 5.0, respectively, for patients with refractory and nonrefractory CIU). These scores were somewhat lower than the baseline DLQI scores of 9.64 and 9.32 reported in patients with CIU in 2 Phase III studies assessing the impact of treatment with fexofenadine[17] and those reported in the ASSURE-CSU (Assessment of the Economic and Humanistic Burden of Chronic Spontaneous/Idiopathic Urticaria Patients) real-world study.[19] This is likely due to the different characteristics of patients in the 2 studies. The DLQI has been used to compare the effects of CIU with other skin diseases in a Brazilian population; patients with CIU in this study had greater QoL impairment than patients with psoriasis, basal cell carcinoma, or acne (DLQI scores of 13.5 vs 10.3, 8.5, and 7.4, respectively).[20]

CIU and its symptoms affected patients' sleep, as reported by patients using the Jenkins Sleep Scale scores and physicians using their clinical judgment. The patient-reported impact of CIU on sleep was similar in those with refractory and nonrefractory disease, in contrast to the physician-reported assessment of impact of CIU on sleep, which was significantly greater in patients with refractory disease. Other studies have shown that CIU affects sleep quality and quantity, with subsequent effects on

Table IV. Symptoms and medication use for patients with chronic idiopathic urticaria (CIU). Unless otherwise indicated, values are no. (%).

Factors	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)	P*
When you have an urticaria symptomatic period, how often do you make an appointment to see your doctor about your urticaria?				0.1683†
No. of missing entries	86	44	42	
Every time	19 (19)	8 (13)	11 (32)	
Most times	16 (16)	12 (19)	4 (12)	
Sometimes	25 (26)	18 (28)	7 (21)	
Rarely	34 (35)	23 (36)	11 (32)	
Never	4 (4)	3 (5)	1 (3)	
Do you experience "warning signals" before a symptomatic period of urticaria symptoms?				>0.999‡
No. of missing entries	91	49	42	
Yes	56 (60)	36 (61)	20 (59)	
No	37 (40)	23 (39)	14 (41)	
When you notice "warning signals," do you change what medication you take in attempt to prevent the symptoms?				0.2330‡
No. of missing entries	130	72	58	
Yes	20 (37)	11 (31)	9 (50)	
No	34 (63)	25 (69)	9 (50)	
When you feel like your urticaria is under control, do you sometimes stop taking your medication?				0.5286‡
No. of missing entries	64	26	38	
Yes	37 (31)	27 (33)	10 (26)	
No	83 (69)	55 (67)	28 (74)	
Do you ever increase the dose/frequency of your medication?				0.0223‡
No. of missing entries	62	24	38	
Yes	41 (34)	34 (40)	7 (18)	
No	81 (66)	50 (60)	31 (82)	
How often do you just forget to take your urticaria medication?				0.2266§
No. of missing entries	62	24	38	
Never	67 (55)	42 (50)	25 (66)	
Rarely	36 (30)	29 (35)	7 (18)	
Sometimes	13 (11)	10 (12)	3 (8)	
Usually	3 (2)	1 (1)	2 (5)	
All the time	3 (2)	2 (2)	1 (3)	
Warning symptoms experienced				
No. of missing entries	128	72	56	
Itching sensation	55 (98)	35 (97)	20 (100)	>0.999‡
Painful/burning sensation	27 (48)	16 (44)	11 (55)	0.5785‡
Redness of the face	16 (29)	12 (33)	4 (20)	0.3646‡
Abnormal heartbeat	11 (20)	8 (22)	3 (15)	0.7284‡
Difficulty breathing	9 (16)	6 (17)	3 (15)	>0.999‡
Feeling faint/dizzy	7 (13)	6 (17)	1 (5)	0.4016‡

(*continued on next page*)

Table IV. (*Continued*)

Factors	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)	*P**
Feeling sick	6 (11)	4 (11)	2 (10)	>0.999‡
Other	6 (11)	3 (8)	3 (15)	0.6553‡

* Comparison of refractory and nonrefractory CIU.
† Mann–Whitney *U* test.
‡ Fisher's exact test.
§ Pearson's χ^2 test.

QoL and patient well-being.[6,19] In an analysis of National Health and Wellness Survey data, patients with chronic urticaria reported higher rates of sleep problems than patients with psoriasis, including those with severe psoriasis,[6] whereas sleep was one of the domains most affected in the ASSURE-CSU study.[19] Indeed, improving sleep quality has been highlighted as an unmet need in CIU.[1]

CIU had a notable impact on productivity in patients in the present study, as previously reported.[19,21] Absenteeism and presenteeism have been shown to be higher in patients with chronic

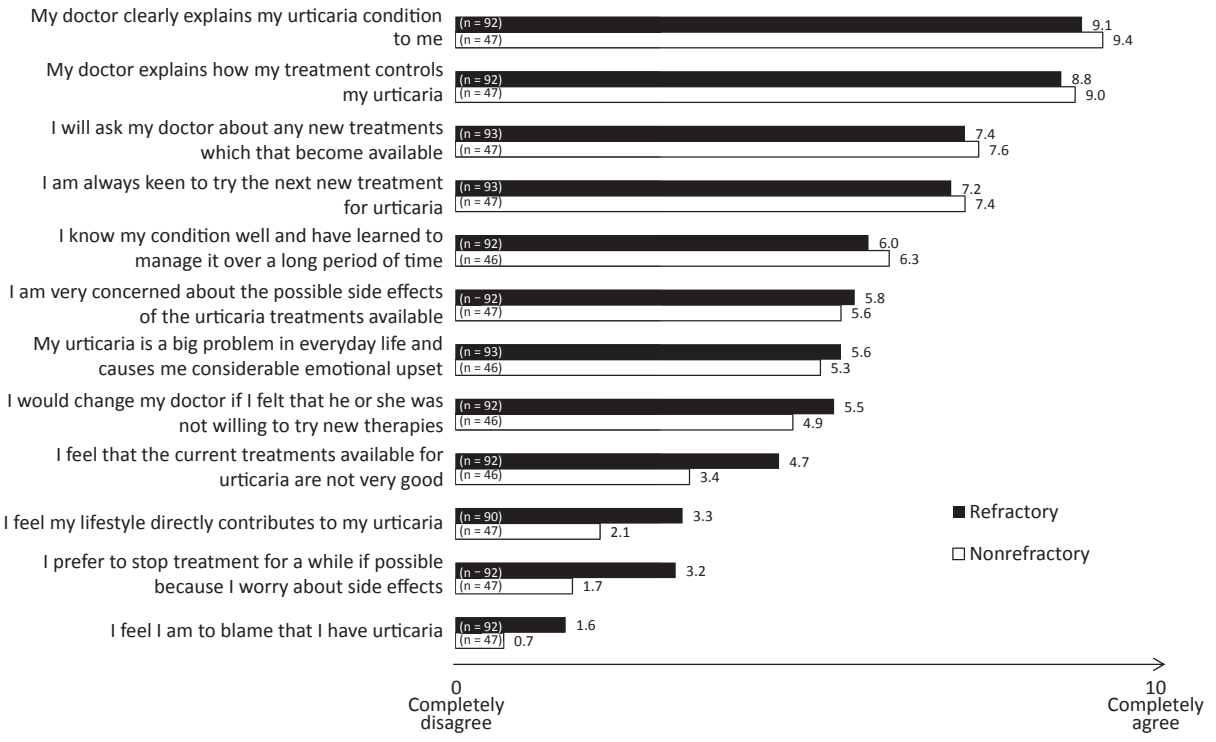

Figure 4. Patient attitudes to their chronic idiopathic urticaria. Patients responded to a series of questions, assessing attitudes to various aspects of their chronic idiopathic urticaria, scoring each one on a scale from 0 to 10, where 0 was complete disagreement and 10 was complete agreement with the statement. Values are mean scores.

Table V. Satisfaction with treatment for chronic idiopathic urticaria (CIU). Unless otherwise indicated, values are no. (%).

Variable	All Patients (N = 184)	Refractory CIU (n = 108)	Nonrefractory CIU (n = 76)	P*
Patient-reported				
Satisfaction with current control of CIU				0.0239†
No. of missing entries	60	27	33	
Extremely dissatisfied	4 (3)	4 (5)	0	
Very dissatisfied	5 (4)	4 (5)	1 (2)	
Dissatisfied	17 (14)	12 (15)	5 (12)	
Neither satisfied nor dissatisfied	22 (18)	14 (17)	8 (19)	
Satisfied	20 (16)	14 (17)	6 (14)	
Very satisfied	27 (22)	21 (26)	6 (14)	
Extremely satisfied	29 (23)	12 (15)	17 (40)	
Do you think…				0.7069‡
No. of missing entries	59	26	33	
…this is the best control that can be achieved?	60 (48)	38 (46)	22 (51)	
…better control can be achieved?	65 (52)	44 (54)	21 (49)	
Physician-reported				
Satisfaction with treatment§				<0.0001†
No. of missing entries	0	0	0	
Mean (SD)	4.8 (1.8)	4.3 (1.7)	5.6 (1.7)	
Do you think…				<0.0001‡
No. of missing entries	0	0	0	
…this is the best control that can be achieved?	80 (43)	28 (26)	52 (68)	
…better control can be achieved?	104 (57)	80 (74)	24 (32)	

* Comparison of refractory and nonrefractory CIU.
† Mann–Whitney *U* test.
‡ Fisher's exact test.
§ On a scale of 1–7, where 1 = extremely dissatisfied and 7 = extremely satisfied.

urticaria than in matched control subjects.[21,22] Although levels of absenteeism and presenteeism for patients with refractory and nonrefractory disease in the present study were lower than data published to date,[19] the overall work impairment of 19% observed in the present study is a considerable burden for patients and society. Effective control of CIU symptoms has the potential therefore to improve productivity in this patient population.

Almost one half of the patients were not satisfied by their treatment, suggesting a remaining unmet need across all patients with CIU and raising the question of whether expectations are too low among patients with CIU. In contrast, most physicians in this study were unsatisfied with the current control of the patient's condition, particularly for those with refractory CIU, for whom 75% of physicians believed better control could be achieved. The reasons for this discordance are currently unknown, but others have reported that patient satisfaction tends to be related to the impact of their condition on daily functioning, whereas physicians tend to consider a wider range of clinical outcomes when measuring satisfaction with treatments for systemic lupus erythematosus.[23] Patients may not understand the treatment and management options available to

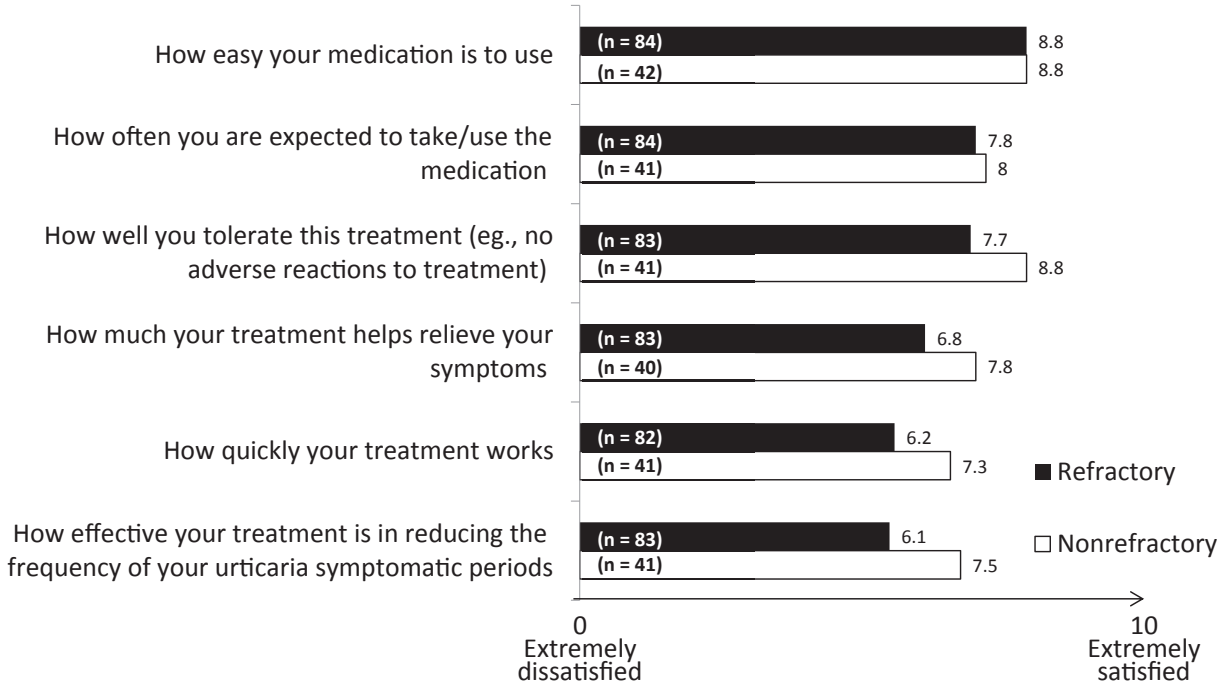

Figure 5. Patient satisfaction with treatment. Patients responded to a series of questions, assessing satisfaction with various aspects of their chronic idiopathic urticaria treatment, scoring each one on a scale from 0 to 10, where 0 was complete dissatisfaction and 10 was complete satisfaction. Values are means.

them, an issue that could be addressed by improving communication with their physician.

Our findings must be considered in light of some potential limitations. This analysis was of a relatively small sample, with a limited number of respondents for some variables. Because patients were recruited when they presented to their physician, under- and over-representation of various patient groups is possible. Although the impact of CIU seems to be lower for the various outcomes studied than suggested by the results of other real-world studies, our findings are nonetheless an important indicator that the burden of CIU is not negligible and should be considered an unmet need in this patient population. However, our findings may not be generalizable to the broader CIU population in the United States.

CONCLUSIONS

The present analysis has shown that the humanistic burden of CIU is considerable in patients with refractory and nonrefractory disease; patients with refractory CIU seem to experience a greater impact of their condition than those with nonrefractory disease. There is clearly a need for improved treatment and communication between patients and physicians, which may lead to better outcomes and satisfaction with treatment.

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Mr. Hoskin was responsible for the design of the study, analysis and interpretation of data, drafting, and revising the work; Dr. Ortiz was responsible for the analysis and interpretation of data, and drafting and revising the work; and Drs. Paknis and Kavati were responsible for interpretation of data and drafting and revising the work. All authors approved the final draft and agree to be accountable for all aspects of the work.

CONFLICTS OF INTEREST

Mr. Hoskin is employed by Adelphi Real World. Drs. Ortiz, Paknis, and Kavati are employees of Novartis Pharmaceuticals Corporation and own stock or stock options. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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