

Original article

How to prescribe antihistamines for chronic idiopathic urticaria: desloratadine daily vs PRN and quality of life

Background: Chronic idiopathic urticaria (CIU) impairs quality of life (QoL). Currently, no consensus exists regarding how second-generation H₁-antihistamines (proven to control CIU symptoms) should be taken long-term: as daily treatment or only when symptoms return (PRN). We sought to determine which regimen improves or better maintains QoL in CIU: desloratadine (DL) daily or PRN.

Methods: Subjects with CIU initially responding to DL 5 mg/day for 4 weeks were randomized for an additional 8 weeks, to DL 5 mg/day (arm 1: 'continuous', $n = 46$) or to DL only on days when urticarial wheals were present (arm 2: "PRN", $n = 60$). To ensure blinding, treatment was presented in both arms as a combination of daily treatment (arm 1: DL; arm 2: placebo), plus a "rescue" tablet (arm 1: placebo; arm 2: DL) to be taken only in case of symptoms. The main outcome measure was QoL assessed by the VQ-Dermato, a validated French QoL instrument, and the Dermatology Life Quality Index (DLQI).

Results: At 4 and 8 weeks after randomization, subjects taking continuous DL showed statistically significant improvements in VQ-Dermato Global Index score ($P = 0.001$ and $P = 0.016$, respectively) and dimension scores for daily living activity, mood state, and social functioning vs subjects taking DL PRN. Improvement in DLQI score at Week 4 was also significantly greater with continuous DL ($P = 0.001$).

Conclusion: Continuous daily therapy with DL 5 mg is a better regimen than PRN treatment to maintain or improve QoL in subjects with CIU.

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Chronic idiopathic urticaria (CIU) is a dermatologic disorder characterized by the spontaneous occurrence of erythematous wheals and intense itch (pruritus), with or without angioedema, every day or nearly every day for ≥ 6 weeks (1, 2). It affects between 0.1% and 3% of the population in the United States and Europe (3, 4).

The impact of CIU on patients' lives is often underappreciated, as disease severity assessments are traditionally based on such factors as threat to life and functional disabilities (5, 6). However, the perceptions of patients may differ significantly from those of their health care providers. The concept of health-related quality of life (QoL) refers to a patient's perception of the impact of an illness, including its treatment, on daily life (7). It encompasses physical, emotional, and social well-being and limitations of daily activities (8, 9).

The chronic discomfort, anxiety, social impairment, and other consequences of wheals and pruritus (e.g. lack of quality sleep, insomnia, irritability, and depression) and the unpredictable, relapsing nature of CIU can significantly affect patient QoL (5, 6, 10). O'Donnell et al. (8) concluded that the overall QoL impact on patients

with CIU was as severe as that reported by patients with ischemic heart disease. A more recent study found that health status (i.e. physical functioning, bodily pain, general health, and emotional well-being) and subjective satisfaction with factors such as sleep, mood, self-confidence, work, eating behavior, and resistance to stress were significantly lower in subjects with CIU compared with those with respiratory allergy (11).

Subject-reported QoL is an important outcome in clinical trials and is especially relevant when evaluating the effectiveness of CIU treatment (6, 10). With CIU, as there are no fixed lesions permitting standard measurements over time, patient perception and QoL assessment may be more meaningful to physicians in determining choice of therapy than a measure of the reduction in the number and size of transient wheals that appear in different places on the body (12).

Second-generation H₁-antihistamines are first-line treatment for CIU, based on their proven efficacy and superior safety profile compared with first-generation agents (10, 13). Desloratadine, a newer, nonsedating oral antihistamine with potent peripheral H₁-receptor

antagonism, has been shown to reduce pruritus and to improve CIU-impaired QoL in several randomized, placebo-controlled, 6-week clinical trials. Evidence of the positive effects of desloratadine on QoL can be found in a number of clinical trials that measured the drug's efficacy using the validated Dermatology Life Quality Index (DLQI) and the VQ-Dermato assessment tools – as well as in scores for total symptoms, pruritus, and number and size of wheals (14–17).

Certain guidelines recommend continuous treatment with antihistamines to achieve lasting and complete remission of lesions, followed by discontinuation of treatment (with dose tapering if necessary) (13). However, there is a lack of published data regarding the best treatment regimen to maintain therapeutic result once CIU symptoms have been controlled initially with daily continuous antihistamine treatment.

This study was thus designed to determine the best strategy for prescribing antihistamines after a good initial response: continuing daily antihistamine for a few months or switching to a PRN regimen, using antihistamines only when urticarial symptoms develop.

Methods

Objectives

In patients with CIU responding to a short-term course of daily desloratadine therapy, the objective of this study was to determine whether continuing daily desloratadine treatment or switching to a PRN desloratadine regimen was the better method to maintain or improve QoL in subjects with CIU.

Subjects

Subjects aged ≥ 18 years, in general good health, and with a ≥ 6 -week history of CIU (pruritus and wheals) prior to Visit 1 were eligible for the study. Women of childbearing age had to be using an acceptable form of contraception prior to enrolment. Subjects were excluded from the study if they were pregnant or nursing, had asthma requiring chronic inhaled or systemic corticosteroids, had been injected with corticosteroids within 90 days of baseline, or had been hospitalized for CIU within 3 months before Visit 1. Treatment with investigational drugs was prohibited for 30 days before Visit 1 or for 90 days in the case of investigational antibodies for asthma or allergic rhinitis. Medications prohibited during the study included corticosteroids, antihistamines, leukotriene inhibitors, nonsteroidal anti-inflammatory drugs, tricyclic or tetracyclic antidepressants, and histamine H_2 -receptor antagonists. Additional reasons for exclusion were known hypersensitivity to desloratadine or any of its excipients, treatment with immunosuppressive drugs, clinically important systemic disease that might interfere with the evaluation of CIU or compromise subject safety, the presence of affective or intellectual disorders that might invalidate informed consent and history of noncompliance with medications or treatment protocols.

Ethics approval was obtained from the Consultant Committee for the Protection of Persons in Biomedical Research (Marseille, France), and the trial was conducted in accordance with the principles of the Declaration of Helsinki and its subsequent amend-

ments and Good Clinical Practice principles. All subjects provided written informed consent before study initiation.

Study design

This randomized, double-blind, parallel-group study was conducted in 35 centers in France. All subjects received desloratadine (Aerius; Schering-Plough, Kenilworth, NJ, USA) 5 mg once daily for 28 days (between Visits 1 and 2). Subjects responding to treatment (no or only mild overall CIU) were randomized to two arms for 2 months (between Visits 2 and 4). Subjects in arm 1 received desloratadine once daily ('continuous treatment'), and those in arm 2 received desloratadine which was to be taken only when the patients had urticarial wheals ('PRN treatment'). To ensure blinding, we could not compare a treatment given daily and a treatment only in case of symptoms. The treatment was thus presented to all patients as a double prescription: one tablet, to be taken every day in the evening, plus an additional tablet to be taken only in cases of symptoms, presented as 'rescue' treatment. In arm 1 ($n = 46$), daily treatment was desloratadine 5 mg once daily, and rescue treatment was placebo. In arm 2 ($n = 60$), daily treatment was placebo, and rescue treatment was desloratadine 5 mg. During a 2-month follow-up period (between Visits 4 and 5), all subjects received desloratadine 5 mg PRN for symptom relapse, with no scheduled daily dose (Fig. 1).

One hundred twenty-nine subjects were enrolled in the study and were included in the global population at Visit 1. Between Visits 1 and 2, three subjects withdrew prematurely (two were lost to follow-up and one withdrew for personal reasons). Among the 126 subjects in the global population at Visit 2 (prior to randomization), 15 'nonresponders' and five 'responders' were not randomized into the comparative phase due to withdrawal from the study ($n = 2$), adverse event (AE) ($n = 1$) or lack of treatment efficacy ($n = 2$), leaving 106 randomized subjects as the intent-to-treat (ITT) population. In the ITT population, eight subjects withdrew during the comparative phase with no final assessment, four had major protocol deviations, and three had missing values for the main evaluation criteria, leaving 91 subjects to comprise the per-protocol (PP) population (Fig. 2).

At Visit 1, a clinical history, including a detailed account of allergy and skin disease during the past 5 years and medications taken to treat CIU outbreaks, was taken. Both investigators and subjects evaluated the overall condition of the subjects' CIU. At Visit 2 (beginning of comparative phase), subjects who met the efficacy criteria and responded to treatment were randomized 3 : 2 by computer-generated allocation code into the two treatment arms: three subjects in the desloratadine PRN group for every two

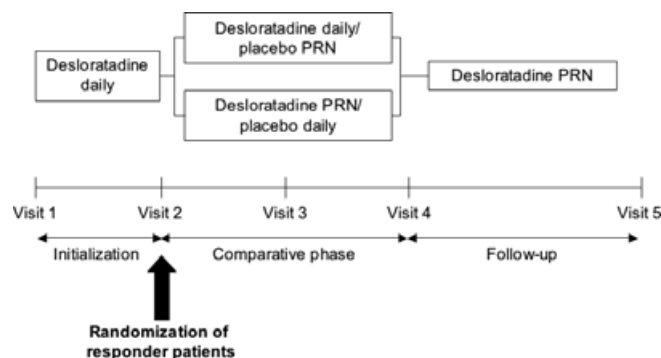


Figure 1. Study design.

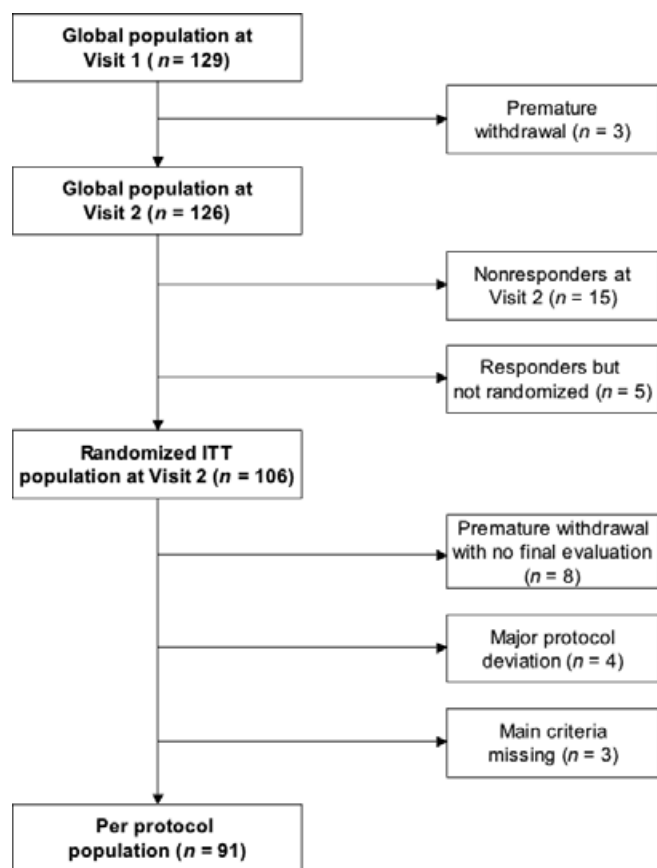


Figure 2. Flow chart of study.

subjects in the desloratadine daily treatment group. Subjects recorded pruritus severity, rescue medication usage, changes in concomitant therapies, and any health-related events in daily diaries. Beginning at Visit 4 (initiation of 2-month follow-up period), subjects noted use of desloratadine PRN. A virtual "Visit 4.1" included data from all randomized subjects who continued until Visit 4 plus subjects who withdrew from the study between Visits 2 and 4 and who had a final evaluation performed at withdrawal. Visit 5 was the last visit of the follow-up period.

Efficacy and safety assessments

The primary efficacy parameters were changes in the VQ-Dermato and DLQI scores between Visits 2 and 4. These two dermatology-specific QoL questionnaires were administered at Visits 1 through 4 to assess the effects of treatment on QoL. Both instruments have been validated in subjects with CIU (12, 18, 19). The VQ-Dermato, designed to assess QoL outcomes in French-speaking patients, measures QoL of the preceding 4 weeks (12, 19). It comprises 28 items in 7 domains: self-perception, daily living activities, mood state, social functioning, leisure activities, treatment-induced restrictions and physical discomfort (12). Questions are weighted equally, and each dimension score ranges from 0 (best QoL) to 100 (poorest QoL). An overall score (VQ-Dermato Global Index) can be calculated from the 7 domains (19).

The DLQI measures QoL during the preceding 7 days and comprises 10 equally weighted items that evaluate the impact of dermatologic diseases on itchiness/soreness/pain, embarrassment,

interference with shopping, choice of clothing, social leisure, difficulty with sports, difficulty with work or study, problems with partner, sexual difficulties, and problems at home due to treatment (18). Individual items are scored on a scale of 0 (least impairment) to 3 (worst impairment), with the total DLQI score ranging from 0 to 30 (higher score indicating greater QoL impairment) (18). For this study, a validated French translation of the DLQI was used.

Secondary efficacy parameters for the randomization period (Visits 2–4) included average use of rescue (PRN) desloratadine or placebo, change in pruritus symptoms and in overall condition of CIU, discontinuations due to treatment failure, investigator's assessment of response to therapy, and quality of disease control. In a separate assessment, both investigators and subjects used the following scale to evaluate CIU overall condition: 0 = none (no signs/symptoms were evident), 1 = mild (signs/symptoms were clearly present but minimal awareness; easily tolerated), 2 = moderate (definite awareness of signs/symptoms; bothersome but tolerable), and 3 = severe (signs/symptoms were hard to tolerate; interfered with activities of daily living and/or sleeping). Responders were subjects with a score of 0 or 1. The evaluation of overall condition included the entire time period since the preceding visit or the 7 days before the first evaluation. Daily pruritus severity was scored in subject diaries as no, light, moderate, or severe pruritus. Investigators assessed response to therapy at Visits 2 and 4, based on the subjects' condition at the time of evaluation compared with their condition prior to starting treatment. A 5-point scale that ranged from 1 = complete relief to 5 = treatment failure was utilized. Secondary efficacy parameters for the follow-up period (Visits 4–5) included disease-free period after 3 months of daily treatment (from time of onset of first pruritus outbreak), the percentage of subjects free of symptoms 2 months after Visit 4, and average desloratadine rescue intake (time between Visit 4 and first date subject noted desloratadine rescue intake in diary).

At each visit after Visit 1, investigators questioned and/or examined subjects for evidence of AEs. The safety population included all subjects who received the study drug beginning at Visit 1.

Statistical analyses

For the randomized, comparative phase of the study (Visit 2–4), both the ITT and PP populations were analyzed. The ITT population included all subjects randomized at Visit 2; the PP population included all subjects randomized at Visit 2 for whom a final evaluation was performed and who had no major protocol deviations between Visits 2 and 4. The changes in scores between visits for the PP population were standardized with the following formulas to take into account the different levels of QoL at randomization:

$$\Delta = \frac{VQDERM_4 - VQDERM_2}{VQDERM_2} \quad \text{and}$$

$$\Delta = \frac{VQDERM_3 - VQDERM_2}{VQDERM_2}$$

$VQDERM_2$ = VQ-Dermato score at Visit 2; $VQDERM_3$ = VQ-Dermato score at Visit 3; $VQDERM_4$ = VQ-Dermato score at Visit 4.

Data for significant improvements in the DLQI score were obtained using formulas similar to those used for the VQ-Dermato:

$$\Delta = \frac{DLQI_4 - DLQI_2}{DLQI_2} \quad \text{and} \quad \Delta = \frac{DLQI_3 - DLQI_2}{DLQI_2}$$

DLQI₂ = DLQI score at Visit 2; DLQI₃ = DLQI score at Visit 3; DLQI₄ = DLQI score at Visit 4.

Data were analyzed using SAS software (version 8.2). For all tests, the α risk was set to 0.05, and a 2-sided approach was used. For multiple testing, Bonferroni's corrections were performed. Qualitative variables were frequency, percentage, and 95% confidence interval (CI), and quantitative data were described by mean $\pm$ standard deviation (SD) and 95% CI.

Changes from Visit 2 to Visit 4 in VQ-Dermato and DLQI scores, the overall condition of CIU, pruritus symptoms, and the investigator's assessment of response to therapy were assessed using the Mann-Whitney test. A Student's *t* test was used to compare average PRN medication use and average treatment consumption between Visits 2 and 5 among treatment groups. The percentage of symptom-free subjects 2 months after Visit 4, quality of disease control, and discontinuations due to treatment failure were compared between groups using the Chi-square test. Finally, the disease-free period after 3 months of daily treatment was estimated using the Kaplan-Meier method, and between-group comparisons were made using the log-rank test.

Results

Baseline characteristics

In the global population at Visit 1 (*N* = 129), the mean age was 43.6 ± 13.7 years, 63.6% of subjects were female, and 69% had a CIU duration of <5 years. Nearly 52% were treated with antihistamines; 53.5% had moderate CIU, and 21.7% of subjects had severe CIU. Compared with the randomized population (*n* = 106) at Visit 2, nonresponders (*n* = 15) were older, had a longer duration and greater severity of CIU, and were less likely to have been treated with antihistamines.

At Visit 1, the 2 randomized treatment groups in the ITT population were comparable in demographic and clinical characteristics (Table 1). There were no statistically significant differences between the two groups for the scores of any individual item on the VQ-Dermato or the DLQI at Visit 1.

Efficacy analyses

VQ-Dermato. In the ITT population, daily desloratadine therapy led to statistically significant improvements in the

VQ-Dermato Global Index score at Visits 3, 4, and 4.1 compared with desloratadine PRN: *P* = 0.001 at Visit 3, *P* = 0.016 at Visit 4, and *P* = 0.034 at Visit 4.1 (Fig. 3). Results for the PP population are shown in Table 2.

The QoL dimensions with a statistically significant difference in favor of desloratadine daily vs desloratadine PRN at Visits 3 and 4 were daily living activity (*P* = 0.005 and *P* = 0.007, respectively), mood state (*P* = 0.003 and *P* = 0.005, respectively), and social functioning (*P* = 0.040 and *P* = 0.044, respectively). A similar significant difference was noted at Visit 3 for physical discomfort (*P* = 0.002) (Fig. 4). Results in the PP population were similar to those in the ITT population for Visits 3 and 4, except for physical discomfort, for which no significant difference appeared between groups at Visit 4.

DLQI. In the ITT population, significant improvements in the DLQI score were seen in the desloratadine daily group vs the desloratadine PRN group at Visit 3 (*P* = 0.001). This difference was not significant at Visit 4 (Table 3). Similar observations were noted for the PP population (Table 2);

Secondary efficacy analyses during the randomized treatment period (2 months between Visits 2 and 4). Subjects taking desloratadine daily had a significantly lower mean number of days with moderate or severe pruritus (than those taking desloratadine PRN [6.3 ± 9.6 vs 12.7 ± 13.3 days, respectively; *P* = 0.012)). The CIU score increased (worsened) in the desloratadine PRN group by 0.23 ± 0.7 and remained unchanged in the desloratadine daily group, but this difference was not statistically significant. Treatment failure (measured by use of prohibited medications) was reported in two subjects in the desloratadine PRN group but in no subject in the desloratadine daily group. At Visit 4, there was a trend toward more subjects given desloratadine daily achieving complete relief [*n* = 21; 52.5% (95% CI: 36.1–68.5%)] than those given desloratadine PRN [*n* = 16; 30.8% (95% CI: 18.7–45.1%; *P* = 0.097)]. More subjects receiving desloratadine PRN (*n* = 51; 87.9%) chose to use rescue medication (desloratadine or

Table 1. Demographic and clinical characteristics of the ITT population at Visit 1

	Placebo daily/desloratadine PRN (<i>n</i> = 60)	Desloratadine daily/placebo PRN (<i>n</i> = 46)	Total population (<i>n</i> = 106)
Mean age, years (SD)	44.4 ($\pm$ 14.3)	41.1 ($\pm$ 12.4)	43.0 ($\pm$ 13.6); <i>P</i> = 0.21
Male/female	18/42	20/26	38/68; <i>P</i> = 0.16
Mean weight, kg (SD)	68.7 ($\pm$ 13.9)	73.5 ($\pm$ 14.3)	70.8 ($\pm$ 14.2)
Mean height, cm (SD)	166.5 ($\pm$ 8.8)	168.7 ($\pm$ 9.6)	167.5 ($\pm$ 9.2)
Mean CIU duration, months (SD)	50.3 ($\pm$ 80.6)	54.9 ($\pm$ 77.3)	52.3 ($\pm$ 78.9); <i>P</i> = 0.768
Subjects taking antihistamines (%)	35 (58.3)	24 (52.2)	59 (55.7)
Mean CIU score (SD)	1.9 ($\pm$ 0.8)	1.9 ($\pm$ 0.8)	1.9 ($\pm$ 0.8); <i>P</i> = 0.694
DLQI score (SD)	6.1 ($\pm$ 4.5)	5.1 ($\pm$ 4.5)	NA; <i>P</i> = NS

ITT, intent-to-treat; SD, standard deviation; CIU, chronic idiopathic urticaria; DLQI, Dermatology Life Quality Index; NA, not available; NS, not significant.

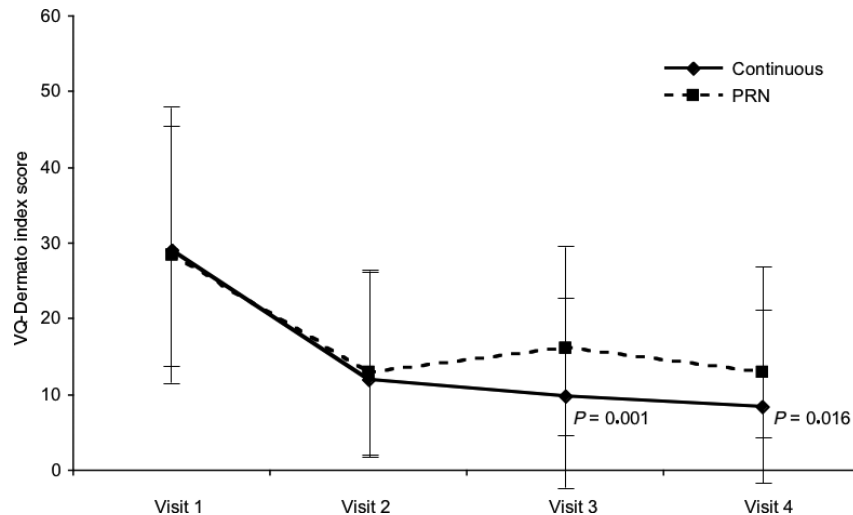


Figure 3. Change in VQ-Dermato Global Index score (arithmetic mean) in the ITT population.

placebo) during randomized treatment than those receiving desloratadine daily [$n = 28$; 63.6% ($P = 0.005$)].

Secondary efficacy analyses during the follow-up period (2 months between Visits 4 and 5). There was no statistically significant difference in the median time to onset of the first moderate or severe pruritus event between subjects given desloratadine PRN (4 days) and subjects given desloratadine daily (3 days). Between Visits 4 and 5, when all subjects received desloratadine only for symptom relapse, the CIU score decreased (improved) in the group that had previously received desloratadine PRN (-0.22 ± 0.62) and increased (worsened) in the group that had previously received desloratadine daily (0.21 ± 1.13 ; $P = 0.037$). Among the ITT population, 77.2% of subjects ($n = 68$), including 71.4% ($n = 35$) in the PRN group and 84.6% ($n = 33$) in the daily group took desloratadine rescue medication during the follow-up period. The median time to rescue-desloratadine intake was 2 days for both groups.

Table 2. Change from baseline in the VQ-Dermato and DLQI scores in the PP population

Score	Desloratadine daily/placebo PRN	Desloratadine PRN/placebo daily	P
VQ-Dermato			
Visit 3	-0.1 ± 1.0 ($n = 32$)	0.7 ± 2.1 ($n = 44$)	0.001
Visit 4	-0.06 ± 1.4 ($n = 31$)	0.52 ± 3.1 ($n = 45$)	0.048
Visit 4.1	0.08 ± 1.6 ($n = 33$)	0.52 ± 3.1 ($n = 44$)	0.08
DLQI			
Visit 3	-0.23 ± 0.9 ($n = 22$)	0.87 ± 1.8 ($n = 33$)	0.002
Visit 4	0.02 ± 1.1 ($n = 21$)	0.34 ± 1.41 ($n = 36$)	NS
Visit 4.1	-0.004 ± 1.07 ($n = 24$)	0.34 ± 1.4 ($n = 33$)	NS

DLQI, Dermatology Life Quality Index; PP, per-protocol; NS, not significant.

Safety

No serious AEs occurred during the study period. Among the global population ($N = 129$), 41 subjects (31.8%) reported at least one AE. Among the randomized population, 35 subjects (33%) – 19 in the desloratadine PRN group and 16 in the desloratadine daily group – experienced AEs. The most frequent AEs reported among the randomized population were nasopharyngitis (6.7%) and headache (5.7%). Adverse events prompted three withdrawals from the study prior to randomization (one for 'aggravated condition' considered unlikely due to study drug; one for malaise/dizziness, nausea, fatigue, and decreased vigilance; and one for weight gain, both considered probably related to study drug).

Discussion

Most therapeutic CIU trials have studied short-term efficacy, and no evidence-based information about the best way to use antihistamines in the long-term management of this chronic disease had been previously published. This study is the first to assess how the second-generation antihistamine desloratadine should be administered over the long-term course of chronic CIU. These results, although limited to desloratadine, may be applicable to other second-generation antihistamines; however, differences in the pharmacology of various antihistamines may lead to results different from those of the current study (20, 21).

Our study is also the second controlled trial to use QoL as the main outcome measure (22). Quality-of-life measures are particularly relevant in assessing the results of CIU treatment because they provide a comprehensive evaluation of the impact of the disease and its treatment

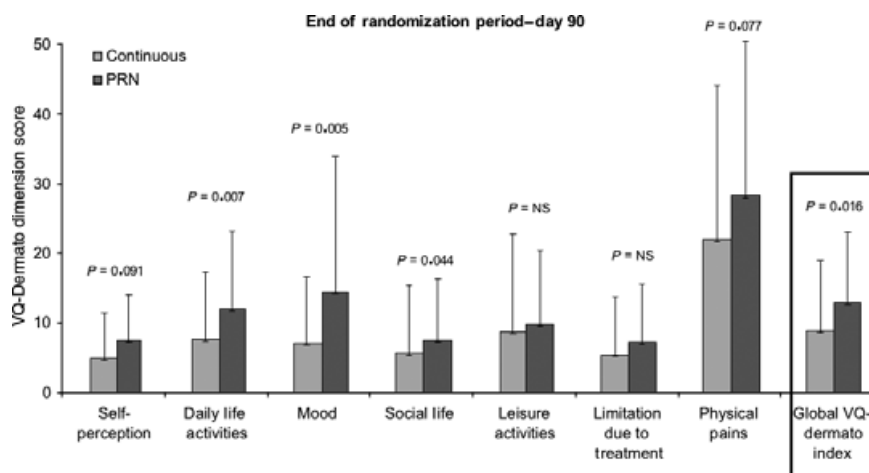


Figure 4. Comparison of VQ-Dermato dimension scores between the desloratadine daily and desloratadine PRN treatment groups at the end of randomization period (Visit 4).

from the patient's perspective. New guidelines from the dermatology section of the European Academy of Allergy and Clinical Immunology and the Global Allergy and Asthma European Network note that health-related QoL should be used as a primary outcome measure in clinical trials (10). An increasing amount of clinical evidence has shown that from the patient's perspective, the negative impact of CIU on QoL is similar to or greater than that of other, more severe, chronic dermatologic disorders, such as psoriasis and atopic dermatitis (5, 6, 8, 11, 19).

General measures of health status and health-related QoL (e.g. the Nottingham Health Profile and the Medical Outcomes Study Short Form 36) are useful for comparing QoL impairment across different conditions, but they do not address areas of relevance to particular diseases (6, 12). Disease-specific QoL instruments are more sensitive to changes and are therefore more useful in evaluating the impact of treatments (6). The psychometric properties of QoL instruments are intrinsic to the language and culture of the populations in which they were created and validated (6). The choice of an instrument for a given purpose in a specific population is a key issue. Therefore, we used two instruments specific for skin disorders, a French translation of the DLQI and the VQ-Dermato, which was validated in a French population.

Table 3. Change from baseline in the DLQI score in the ITT population

DLQI score	Desloratadine daily/placebo PRN	Desloratadine PRN/placebo daily	P
Visit 1	5.1 ± 4.5 (n = 46)	6.1 ± 4.5 (n = 60)	NS
Visit 2	2.0 ± 3.2 (n = 46)	2.3 ± 2.7 (n = 59)	NS
Visit 3	1.9 ± 3.8 (n = 42)	3.3 ± 3.3 (n = 55)	0.001
Visit 4	1.9 ± 3.3 (n = 40)	2.2 ± 2.3 (n = 51)	NS
Last evaluation visit	2.1 ± 3.7 (n = 43)	2.2 ± 2.3 (n = 51)	NS

DLQI, Dermatology Life Quality Index; ITT, intent-to-treat; NS, not significant.

Second-generation H₁-antihistamines such as desloratadine have proven efficacy in reducing the CIU symptoms of pruritus and wheal and flare. In three randomized, placebo-controlled studies, daily treatment with desloratadine 5 mg significantly reduced the detrimental impact of CIU on daily activities and sleep (14–16). This in turn led to improved QoL, as measured by the DLQI (14, 15, 17) or a 5-question shortened version of the DLQI (23). Increased QoL in CIU has also been demonstrated with other second-generation antihistamines (22, 24, 25). However, most therapeutic trials using H₁-antihistamines have only addressed short-term efficacy, even though CIU is a chronic disease which has to be managed over the long-term. Our study was designed to provide health care providers with information adapted for the chronic nature of CIU.

In this study, there was a significant advantage of daily treatment of CIU with desloratadine over PRN usage in maintaining the QoL benefit achieved after an initial month of daily desloratadine treatment indeed at the end of the first month of randomized treatment the advantage was demonstrated in terms of changes in the VQ-Dermato Global Index scores and in several individual dimension scores (i.e. daily living activity, mood state, social functioning, and physical discomfort). The differences were still significant at the end of the second month. The DLQI results confirmed these findings, although the difference detected by the DLQI at the end of the first month was no longer significant at the end of the second month of randomized treatment.

Second-generation antihistamines offer an advantage to physicians and patients concerned with improving overall QoL. These agents have a lower propensity to cross the blood-brain barrier, and, therefore, some such as desloratadine, have rates of somnolence and anticholinergic effects similar to that of placebo. In our study, only one subject withdrew for reasons of decreased vigilance possibly as a result of desloratadine treatment. However,

the most frequently reported AEs were nasopharyngitis and headache, which did not prompt withdrawal from the study. No severe AEs or deaths were reported.

For reasons of considerable initial improvement in both VQ-Dermato and DLQI scores after the first month of treatment (randomization), no major improvements were expected after randomization; only decreases, maintenance, or slight improvements in QoL were expected to occur. However, both instruments showed statistically significant differences in scores in the desloratadine daily treatment group vs the desloratadine PRN group. The benefit at Visits 4 and 4.1 was significant only with the VQ-Dermato, which showed that this instrument was more sensitive to minor changes in QoL than the DLQI.

The VQ-Dermato is the first reliable dermatology-specific QoL instrument generated and validated in France (12). The DLQI was generated and validated in the United Kingdom; its French translation has been cross-validated. The higher sensitivity of the VQ-Dermato may be because it was developed and validated in the culture and population in which the current trial was conducted, in addition to its greater number of questions.

The superiority of desloratadine daily treatment, as shown by the two QoL instruments, was confirmed by the results of secondary analyses using other criteria. Subjects in the daily treatment group experienced fewer days with moderate or severe pruritus, had a higher percentage of complete relief at the end of the randomized treatment period, and were less likely to use rescue medication.

After Visit 4, when all subjects took desloratadine PRN, there was an apparently paradoxical worsening of QoL in those who had taken desloratadine daily vs an improvement in those who had taken desloratadine PRN. This may be explained by the fact that a subject's estimation of his QoL is relative to his previous status. In subjects previously under continuous treatment, taking a medication PRN can be viewed as a worsening compared with the previous better control of CIU, while subjects already under a PRN regimen may tend to adapt better to incomplete disease control results over time.

Conclusion

This randomized study of desloratadine, with QoL as a main outcome measure, demonstrated that once control of CIU symptoms is obtained with daily treatment, continuous therapy (whether or not the patient is showing symptoms) preserves patient QoL better over the long term as compared with than PRN treatment only given only at symptom flare-up. The results provide useful therapeutic information to help physicians manage their patients with CIU.

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