

Rupatadine Improves Nasal Symptoms, Quality of Life (ESPRINT-15) and Severity in a Subanalysis of a Cohort of Spanish Allergic Rhinitis Patients

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■ Abstract

Background: According to current guidelines, new second-generation oral H₁-antihistamines, as well as intranasal corticosteroids (ICSs), are recommended for the treatment of allergic rhinitis (AR) in adults and children.

Objective: To assess changes in AR severity, in addition to nasal symptoms and health-related quality of life (HRQoL), after 4 weeks of treatment with rupatadine in a cohort of AR patients.

Methods: A subanalysis of a longitudinal, observational, prospective, multicenter Spanish study was carried out in spring-summer 2007. Enrolled patients had a clinical diagnosis of AR of at least 2 years' evolution, a total nasal symptom score (TNSS) of at least 5, and had not received antihistamines in the previous week or ICSs in the previous 2 weeks. HRQoL (ESPRINT-15 questionnaire), disease severity (using both the original and modified Allergic Rhinitis and its Impact on Asthma [ARIA] classifications), and nasal symptoms (TNSS) were measured at baseline and after 4 weeks of rupatadine treatment.

Results: Data from a cohort of 360 patients treated with rupatadine were analyzed (57.2% women, 42.5% with intermittent AR, 36.4% with asthma, and 61.7% with conjunctivitis). After 4 weeks of treatment, the patients showed a significantly lower mean (SD) TNSS (8.2 [1.9] vs 3.1 [2.1], $P < .001$), a significant improvement in HRQoL (3.0 [1.2] vs 1.0 [0.9], $P < .001$) and significantly reduced AR severity ($P < .0001$).

Conclusions: In addition to an improvement in nasal symptoms and HRQoL, rupatadine reduced AR severity after 4 weeks of treatment.

Key words: Allergic rhinitis. Quality of life. Severity. Oral H₁-antihistamines. Rupatadine.

■ Resumen

Introducción: Los antihistamínicos H₁ de segunda nueva generación al igual que los corticoides intranasales (CI), son altamente recomendados para el tratamiento de la rinitis alérgica (RA) en adultos y niños, de acuerdo con las actuales guías terapéuticas.

Objetivo: Valorar en una cohorte de pacientes tratados con rupatadina los cambios en la gravedad de la RA, la evolución de los síntomas nasales y su impacto en la calidad de vida de los pacientes, después de 4 semanas de tratamiento.

Métodos: Subanálisis de una cohorte de pacientes de un estudio longitudinal, observacional, prospectivo, multicéntrico realizado en España durante el periodo de la primavera-verano del 2007. Se incluyeron pacientes con el diagnóstico clínico de RA con historia previa documentada de al menos 2 años de evolución, con una puntuación de síntomas nasales (TNSS) ≥ 5 , sin tratamiento previo con antihistamínicos dentro de la semana previa o sin CI durante las 2 semanas previas. Se evaluó de forma prospectiva la calidad de vida

(cuestionario Esprint-15), la gravedad (utilizando tanto la clasificación original ARIA como la modificada) y los síntomas nasales (TNSS) después de 4 semanas de tratamiento con rupatadina.

Resultados: Se incluyeron 360 pacientes, que se trataron con rupatadina (57.2% mujeres, 42.5% con RA intermitente, 36.4% con asma y 61.7% con conjuntivitis). Tras 4 semanas, los pacientes mostraron una disminución significativa del TNSS (8.2 ± 1.9 vs. 3.1 ± 2.1 , $p < 0.001$), una mejoría significativa en la calidad de vida (Esprint-15: 3.0 ± 1.2 vs. 1.0 ± 0.9 , $p < 0.001$) y una menor gravedad de la RA ($p < 0.0001$).

Conclusión: Además de la mejoría obtenida en los síntomas nasales y la calidad de vida del paciente, el tratamiento con rupatadina ha mostrado ser capaz de mejorar la gravedad de la RA después de 4 semanas de tratamiento.

Palabras clave: Rinitis alérgica. Calidad de vida. Gravedad. Antihistaminicos H_1 . Rupatadina.

Introduction

According to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines [1], the management of allergic rhinitis (AR) encompasses allergen avoidance, patient education, pharmacotherapy, and allergen-specific immunotherapy. With regard to pharmacotherapy, ARIA recommends intranasal and new second-generation H_1 -antihistamines for all levels of severity of intermittent and persistent AR. In the case of nasal congestion or moderate to severe persistent disease, an intranasal corticosteroid (ICS) is also recommended [2].

Bousquet et al [3] have found that patients with moderate to severe seasonal AR treated by general practitioners, using their own criteria of severity and treating as they do in daily clinical practice, showed a significantly lower improvement in AR symptoms and in quality of life compared to those treated according to guidelines.

AR is associated with impaired social life, sleep, school, and work. It is well known that the health-related quality of life (HRQoL) of patients can be altered by the severity and duration of rhinitis. The extent to which disease-associated problems affect HRQoL should be assessed using specific AR tools. Indeed, the fact that specific tools facilitate this measurement may be ignored by patients and health care professionals [4], and generic instruments may be not sensitive enough to detect changes in these aspects [5]. The ESPRINT-15 questionnaire (EsQ-15) is a Spanish validated specific instrument to assess HRQoL in AR; it is particularly recommended for use in Spanish-speaking populations [6,7].

Rupatadine is a new second-generation H_1 -antihistamine, with an additional anti-platelet activating factor effect, that is approved and marketed for the treatment of AR and urticaria in adults and adolescents (aged ≥ 12 years) [8]. Rupatadine has been shown to be effective in the treatment of seasonal, perennial and persistent AR [9-11], with a fast onset of action [12] and a very good long-term safety profile [13].

The current study subanalyzes a cohort of patients treated only with rupatadine from a prospective, multicenter, observational, longitudinal study. The aim was to evaluate the treatment response in patients with AR in terms of changes in nasal symptoms, HRQoL (EsQ-15), and disease severity.

Patients and Methods

Patients

Once the selection criteria had been verified, each investigator was able to include up to 5 outpatients with AR in the study. Eligible patients, aged 18 years or older, were categorized as having intermittent or persistent, mild, or moderate to severe AR according to the original ARIA classification [1]. Furthermore, a new criterion to discriminate moderate and severe AR from moderate/severe AR was investigated [14]. The total nasal symptom score (TNSS) rated 4 symptoms (nasal obstruction, nasal itching, sneezing, and rhinorrhea) on a Likert scale from absent (0) to severe (3). Patients with a TNSS of 5 or higher, not treated with antihistamines in the previous week or with topical ICSs in the previous 2 weeks, were included in the study. Patients with comorbidities such as asthma or conjunctivitis were also included. The study was approved by the ethics committee at Hospital Clinic de Barcelona.

Study Design

A prospective, multicenter, observational, longitudinal study was designed with the aim of evaluating treatment response in patients with AR in terms of changes in HRQoL, symptoms, and severity. Patients with a diagnosis of AR were enrolled between April and July 2007. The study was conducted by allergologists and ear-nose-throat (ENT) specialists practicing in primary health services and hospitals throughout Spain. Physicians enrolled a maximum of 5 consecutive AR patients who were treated as usual in daily clinical practice.

Sociodemographic data (age, gender, race, education level), clinical history of AR (intermittent/persistent), time since diagnosis, and comorbidities were collected during the initial visit. At the baseline visit and after 4 weeks, clinical data relating to AR symptoms (TNSS), severity, and HRQoL (using the EsQ-15) were recorded. Therapeutic management was recorded retrospectively at the end of the follow-up (4 weeks of treatment). Patients were only considered for the analysis if they completed the evaluation at both baseline and after treatment.

Outcome Measures

Assessment of AR Nasal Symptoms. Patients evaluated the intensity of nasal symptoms (rhinorrhea, nasal itching, nasal obstruction, and sneezing) using a 4-point Likert scale from 0 to 3 (0=no symptom, 1=mild, 2=moderate, 3=severe). The TNSS was obtained from the sum of all 4 individual symptom scores, with a total possible score ranging from 0 (no symptoms) to 12 (maximum symptom intensity).

AR Severity. The number of impaired severity items (sleep, daily activities/sport/leisure, work/school performance, and troublesome symptoms) allows the grading of AR severity according to the original ARIA classification as "mild" (no affected item) or "moderate/severe" (1 or more items are affected). A modified ARIA severity classification (m-ARIA), proposed by Valero et al [14], was also used. The m-ARIA classification discriminates between moderate and severe and defines AR severity as mild (no affected item), moderate (1 to 3 affected items), or severe (all 4 affected items).

Quality of Life. HRQoL was assessed using the EsQ-15 [7]. This AR-specific questionnaire is a shorter version of ESPRINT-28 [6]. The EsQ-15 contains 15 items grouped into 4 dimensions: symptoms (5 items), activities of daily living (3 items), sleep disturbances (3 items), psychological impact (3 items), and 1 general question. All items are scored on a 7-point Likert scale, ranging from 0 (minimum impact on HRQoL) to 6 (maximum impact on HRQoL). The 15 items provide an overall score on a 5-point scale (0=excellent, 1=very good, 2=good, 3=not too bad, 4=bad).

Statistical Analysis

The descriptive analysis set included patients who provided the necessary data to assess the main variable: HRQoL of life measured by the EsQ-15 (at least 3 of the 5 dimensions without any missing items). The comparative analysis set included patients with an overall EsQ-15 score at baseline and at the final visit.

Baseline characteristics of patients were described using aggregate and dispersion measures for continuous variables, while percentages and confidence intervals were used for categorical variables.

Comparisons were carried out between baseline and after 4 weeks of treatment. These analyses were conducted using paired bilateral *t* tests (if normal distribution was confirmed by Kolmogorov-Smirnov and homogeneity tests) or equivalent nonparametric tests (Wilcoxon test) for continuous variables. Proportions were compared using the χ^2 test or the Fisher exact test for contemporary data and the McNemar test for evolutionary data. *P* values of less than .05 were considered statistically significant. Statistics were generated using a standard statistical package (SPSS for Windows, version 13.0, SPSS Inc, Chicago, Illinois, USA).

Results

Sample Description

The entire observational study was conducted in a cohort of 707 patients with AR. Data from 360 patients who had

undergone treatment with rupatadine were selected for the current subanalysis. Sociodemographic and clinical characteristics, as well as AR duration (intermittent, persistent) and comorbidities (asthma, conjunctivitis) are described in Table 1.

Nasal Symptoms

After 4 weeks of treatment, there was a significant improvement in the TNSS, as well as in each individual symptom ($P<.001$) (Table 2). The majority of patients (88.3%) showed improvement in the TNSS.

AR Severity

After 4 weeks of treatment, patients showed a significant decrease in AR severity according to the original ARIA classification. There was a significant ($P<.0001$) increase in the proportion of patients with mild AR and a decrease in the number of those with moderate/severe AR (Table 2).

According to the m-ARIA classification, improved discrimination between moderate and severe AR categories was also detected ($P<.0001$). After 4 weeks of treatment, the proportion of patients classified as mild, moderate, or severe was 60.6%, 35.8%, and 3.6%, respectively (Figure 1). Figure 2 shows the proportion of patients in each severity category from baseline to follow-up.

Table 1. Baseline Characteristics of Cohort of Spanish Patients (n=360) with Allergic Rhinitis (AR) Treated With Rupatadine.

Sociodemographic Characteristics	
Age, mean (SD), years	36.3 (13.1)
Sex, % (No.)	
Female	57.2 (206)
Male	42.8 (154)
Education level, % (No.)	
Less than compulsory education	4.4 (16)
Finalized compulsory education	21.9 (79)
Finalized secondary education	40.0 (144)
Finalized higher education	33.1 (119)
Unknown	0.6 (2)
Geographical origin, % (No.)	
Africa	1.1 (4)
Latin America	4.4 (16)
Member states of the European Union (EU)	93.9 (338)
European nonmember states of EU	0.6 (2)
Clinical characteristics of AR	
Years since AR diagnosed, mean (SD)	7.2 (6.0)
Type of AR (according to ARIA guidelines ^a), % (No.)	
Persistent	57.5 (207)
Intermittent	42.5 (153)
Comorbidities, % (No.)	
Asthma	36.4 (131)
Conjunctivitis	61.7 (222)
Not reported	1.9 (7)

^aAllergic Rhinitis and its Impact on Asthma guidelines [1].

Table 2. Changes in Allergic Rhinitis (AR) Clinical Status After 4 Weeks of Treatment With Rupatadine^a

Outcome Measures	Baseline	After 4 Weeks	P Value
TNSS, mean (SD) global score	8.2 (1.8)	3.1 (2.1)	<.0001
Rhinorrhea	2.1 (0.7)	0.8 (0.7)	<.0001
Nasal itching	1.9 (0.7)	0.7 (0.7)	<.0001
Nasal obstruction	2.1 (0.8)	0.9 (0.7)	<.0001
Sneezing	2.0 (0.7)	0.7 (0.7)	<.0001
TNSS, symptoms intensity, % (No.)			
Very mild symptoms (0-2 points)	0.0 (0)	10.3 (37)	<.0001
Mild symptoms (3-6 points)	0.0 (0)	68.2 (245)	
Moderate symptoms (7-9 points)	63.9 (230)	19.2 (69)	
Severe symptoms (10-12 points)	36.1 (130)	2.2 (8)	

Abbreviation: TNSS, total nasal symptom score.

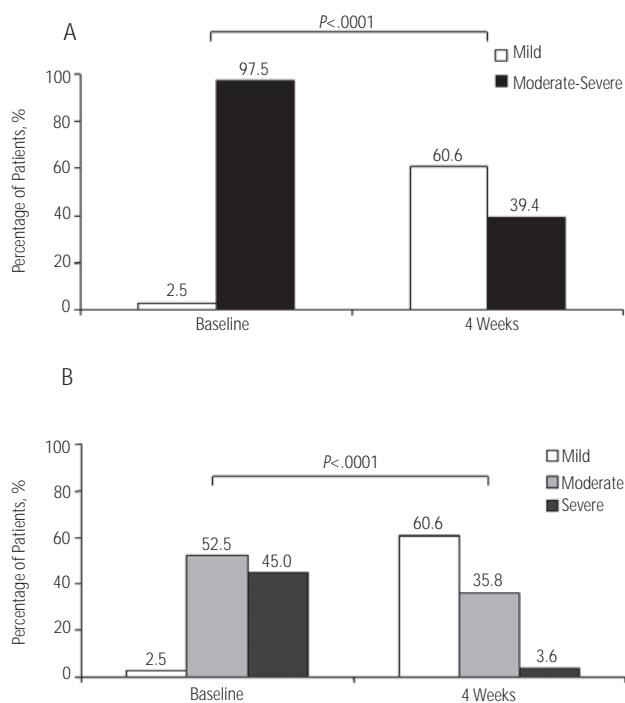
^aNo. of patients, 360

Figure 1. Change in severity of allergic rhinitis from baseline after 4 weeks of rupertadine treatment using both the original (A, 2 categories) [1] and modified (B, 3 categories) [14] Allergic Rhinitis and its Impact on Asthma severity classifications.

When data were analyzed according to the duration of AR (intermittent, persistent), improvement of severity from baseline after 4 weeks of treatment with rupertadine was also strong and significant ($P < .001$) (Table 3).

Quality of Life

With regard to HRQoL, the EsQ-15 global score decreased significantly ($P < .001$) from baseline to 4 weeks of rupertadine treatment. All EsQ-15 dimensions (symptoms, activities of daily living, sleep, psychological impairment, and general health) also showed significant improvements ($P < .001$) after 4 weeks of treatment (Table 4).

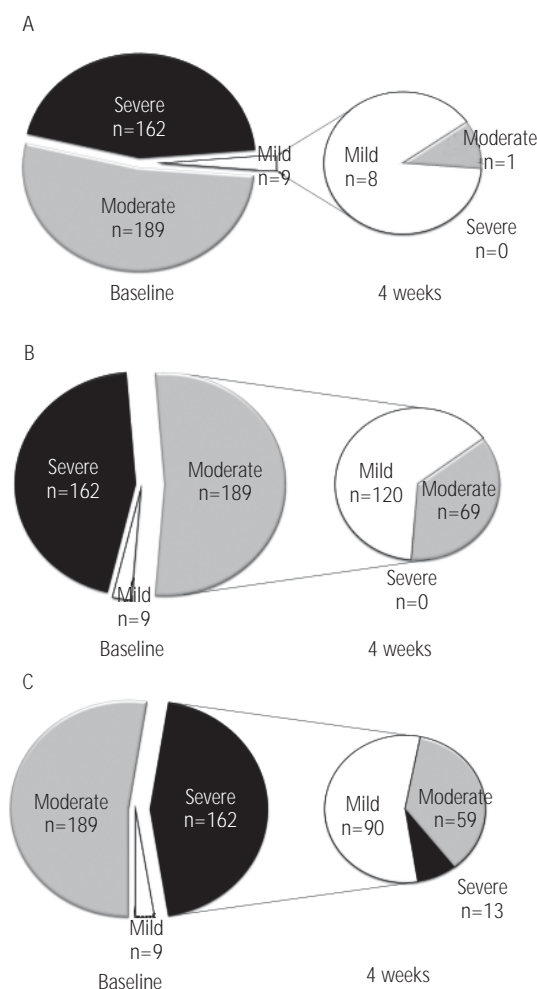


Figure 2. Allocation of the proportion of patients in each category: mild (A), moderate (B), and severe (C), using the modified Allergic Rhinitis and its Impact on Asthma severity classification [14] at baseline and after 4 weeks of rupertadine treatment.

Table 3. Improvement in Allergic Rhinitis (AR) Severity According to the Modified Allergic Rhinitis and its Impact on Asthma Classification on Symptom Duration

Patients With Intermittent AR					
	Baseline		4 Weeks of Treatment		P Value ^a
	No.	%	No.	%	
Mild	6	3.9	95	62.7	<.0001
Moderate	99	64.7	48	31.4	
Severe	48	31.4	9	5.9	
Total	153	100	153	100	

Patients With Persistent AR					
	Baseline		4 Weeks of Treatment		P Value ^a
	No.	%	No.	%	
Mild	3	1.4	122	59.5	<.0001
Moderate	90	43.5	81	39.1	
Severe	114	55.1	4	1.9	
Total	207	100	207	100	

^aAnalysis between categories was performed with χ^2 .

Table 4. Improvement in ESPRINT-15 Dimension Scores in Allergic Rhinitis Patients (n=360) Treated With Rupatadine for 4 Weeks^a

	Baseline	After 4 Weeks	P Value
Global score	3.0 (1.2)	1.0 (0.9)	<.0001
Symptoms	3.4 (1.1)	1.2 (1.0)	<.0001
Daily Activities	2.9 (1.3)	1.0 (1.1)	<.0001
Sleep	2.8 (1.6)	1.0 (1.1)	<.0001
Psychological Impact	3.0 (1.5)	1.0 (1.1)	<.0001

^aScores are shown as mean (SD).

Discussion

In the present study, we have shown that rupatadine treatment, used in daily clinical practice by allergologists and ENT specialists, markedly improved the control of nasal symptoms, severity of disease, and HRQoL in a cohort of AR outpatients evaluated in a prospective, observational study.

A clear improvement from baseline was observed in the TNSS, and each of the individual symptoms, evaluated after 4 weeks of rupatadine treatment. Some studies have reported that the change in TNSS can be considered clinically relevant when patients have an improvement of symptoms of 40% [15,16]. In our study, the baseline TNSS score was around 8 and a change in score of 3 or more can be considered to be clinically relevant since, in randomized, placebo-controlled clinical trials, a TNSS reduction of 20% to 35% has been observed in placebo groups, whereas a 40% or 50% reduction in TNSS has been observed in active groups [15,16]. The magnitude of the improvement with rupatadine was even higher (62%) in comparison with baseline values.

Another clinically relevant finding from our study is the improvement of AR severity according to the ARIA classification. We assessed AR severity using a modified ARIA (m-ARIA) classification, differentiating between moderate and severe rhinitis and, therefore, including the new criterion proposed by Valero et al [14]. Using the original ARIA classification, the magnitude of improvement in AR severity was 58.3%; when the m-ARIA classification was used, this improvement reached 74.7%. In addition, after 4 weeks of rupatadine treatment, only 3.6% of patients remained in the severe category and could be considered uncontrolled patients, whereas 96.4% of patients were classified as having mild or moderate AR post-treatment. These findings reinforce the need to discriminate between the 2 different severity grades, moderate/severe, based on the original ARIA classification [17,18].

Furthermore, we analyzed changes in AR severity according to the duration of AR (intermittent vs persistent). It is interesting to note the high percentage of patients who were categorized at baseline as severe in both types of AR: 31.4% with intermittent AR and 55.1% with persistent AR.

These values are higher than those previously reported, where 10% to 20% of patients were considered to be uncontrolled [16]. A possible reason for this discrepancy is that the majority of outpatients in our study were treated by specialists, whereas other authors enrolled patients from primary care.

Allergic disorders usually have a significant impact on a patient's QoL. In particular, allergic symptoms of respiratory origin can worsen many aspects of the daily routine because they not only affect functional capabilities but also lead to an impairment of mental, social, and emotional abilities [2]. One of the strengths of the present study was that the administered HRQoL questionnaire, the EsQ-15, is a specifically developed instrument that takes into account the concerns of Spanish-speaking patients with AR [6]. The EsQ-15 was developed to provide an instrument which would be suitable for use in a variety of contexts, including real clinical practice and observational studies [7]. The current study is the first application of this questionnaire in a cohort of patients followed prospectively. After 4 weeks of follow-up, patients treated with rupatadine showed an improved perception of their HRQoL according to the EsQ-15. Significant improvements were reported in all dimensions: symptoms, daily activities, sleep, and psychological impact. Finally, these findings, which indicate a better health status after treatment with rupatadine, are clearly observed by means of the normal distribution of responses obtained in the last item of this questionnaire.

Some limitations may exist in this cohort study. We used a prospective study design with the aim of replicating real clinical practice. There were no exclusion criteria, as is usually the situation in clinical trials, because we wanted to analyze the entire range of patients typically seen by allergologists or ENT specialists. Furthermore, treatment was administered by specialists according to normal clinical practice. To date, the benefit of this approach has only been evaluated with the cohort of patients receiving rupatadine [19].

In summary, the present study is the first to evaluate changes in AR severity during pharmacological treatment, with the aim of mimicking routine clinical practice in Spanish AR patients. The cohort of patients treated with rupatadine showed a clear and important improvement in nasal symptoms, disease severity, and HRQoL (assessed using the AR-specific EsQ-15). Finally, we should take into account the fact that the newly proposed AR severity categorization could help clinicians to classify populations of patients into a more accurately defined severity status, and to develop more focused disease-management strategies based on controlled and uncontrolled AR.

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Conflicts of Interests

Dr A.Valero was recently an investigator, speaker and/or advisor for MSD, Uriach, ESTEVE, Chiesi, GSK, FAES, UCB. Dr J Bartra was recently an investigator, speaker and/or advisor for FAES, UCB, and MSD. Dr A del Cubillo was recently an investigator, speaker, and/or advisor for URIACH, FAES, MSD, GSK, and ALK-ABELLO. Dr J. Mullol has been a member of national and international scientific advisory boards, received grants for research projects, and performed clinical trials for Boehringer-Ingelheim, FAES, GSK, Hartington Pharmaceuticals, MSD, Novartis, Schering Plough, Stallergenes, UCB, and Uriach SA. Dr I. Izquierdo is an employee in the medical department of J.Uriach & Cia, S.A. Mr J. Giralt is an employee of the statistical department of J.Uriach & Cia, S.A.

References

1. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001;108(Suppl 5):S147-334.
2. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, Zuberbier T, Baena-Cagnani CE, Canonica GW, van Weel C, Agache I, Ait-Khaled N, Bachert C, Blaiss MS, Bonini S, Boulet LP, Bousquet PJ, Camargos P, Carlsen KH, Chen Y, Custovic A, Dahl R, Demoly P, Douagui H, Durham SR, van Wijk RG, Kalayci O, Kaliner MA, Kim YY, Kowalski ML, Kuna P, Le LT, Lemiere C, Li J, Lockey RF, Mavale-Manuel S, Meltzer EO, Mohammad Y, Mullol J, Naclerio R, O'Hehir RE, Ohta K, Ouedraogo S, Palkonen S, Papadopoulos N, Passalacqua G, Pawankar R, Popov TA, Rabe KF, Rosado-Pinto J, Scadding GK, Simons FE, Toskala E, Valovirta E, van Cauwenberge P, Wang DY, Wickman M, Yawn BP, Yorgancioglu A, Yusuf OM, Zar H, Annesi-Maesano I, Bateman ED, Ben Kheder A, Boakye DA, Bouchard J, Burney P, Busse WW, Chan-Yeung M, Chavannes NH, Chuchalin A, Dolen WK, Emuzyte R, Grouse L, Humbert M, Jackson C, Johnston SL, Keith PK, Kemp JP, Klossek JM, Larenas-Linnemann D, Lipworth B, Malo JL, Marshall GD, Naspitz C, Nekam K, Niggemann B, Nizankowska-Mogilnicka E, Okamoto Y, Orru MP, Potter P, Price D, Stoloff SW, Vandenplas O, Viegi G, Williams D; World Health Organization; GA(2)LEN; AllerGen. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*. 2008;63(Suppl 86):8-160.
3. Bousquet J, Lund VJ, Van Cauwenberge P, Bremard-Oury C, Mounedji N, Stevens MT, El-Akkad T. Implementation of guidelines for seasonal allergic rhinitis: a randomized controlled trial. *Allergy*. 2003;58(8):733-41.
4. Spector SL, Nicklas RA, Chapman JA, Bernstein IL, Berger WE, Blessing-Moore J, Dykewicz MS, Fineman SM, Lee RE, Li JT, Portnoy JM, Schuller DE, Lang D, Tilles SA; Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma, and Immunology; American College of Allergy, Asthma, and Immunology; Joint Council of Allergy, Asthma, and Immunology. Symptom severity assessment of allergic rhinitis: part 1. *Ann Allergy Asthma Immunol*. 2003;91(2):105-14.

5. Guyatt GH, King DR, Feeny DH, Stubbings D, Goldstein RS. Generic and specific measurement of health-related quality of life in a clinical trial of respiratory rehabilitation. *J Clin Epidemiol.* 1999;52(3):187-92.
6. ESPRINT Study Group and Investigators. Development and validation of a new Spanish instrument to measure health-related quality of life in patients with allergic rhinitis: the ESPRINT questionnaire. *Value Health.* 2007;10(6):466-77.
7. Valero A, Alonso J, Antépara I, Bar E, Colas C, del Cuvillo A, Ferrer M, Herdman M, Martí-Guadaño E, Monclús L, Navarro-Pulido AM, Sastre J, Izquierdo I, Mullol J. Health-related quality of life in allergic rhinitis: comparing the short form ESPRINT-15 and MiniRQLQ questionnaires. *Allergy.* 2007;62:1372-8.
8. Keam SJ, Plosker GL. Rupatadine: a review of its use in the management of allergic disorders. *Drug.* 2007;67(3):457-74.
9. Guadaño EM, Serra Batlles J, Meseguer J, Castillo JA, de Molina M, Valero A, Picado C. Rupatadine 10 mg and ebastine 10 mg in seasonal allergic rhinitis: a comparison study. *Allergy.* 2004;59(7):766-71.
10. Kowalski ML, Jukiewicz D, Kruszewski-J, Nowak D, Zietkowski Z, Spicakova M, Vernerova E, Seberova E, Klenha K, Izquierdo I. Rupatadine 10 and 20 mg are effective and safe in the treatment of perennial allergic rhinitis after 4 weeks of treatment: A randomized, double-blind, controlled trial with loratadine and placebo. *Therapy.* 2009;6(3):417-25.
11. Fantin S, Maspero J, Bisbal C, Agache I, Donado E, García O, Arnáiz A, De la Cruz G, Pérez I, Izquierdo I. A 12-week placebo-controlled study of rupatadine 10 mg once daily compared with cetirizine 10 mg once daily, in the treatment of persistent allergic rhinitis. *Allergy.* 2008;63(7):924-31.
12. Stübner P, Horak F, Zieglmayer R, Arnaiz E, Leuratti C, Pérez I, Izquierdo I. Effects of rupatadine vs placebo on allergen-induced symptoms in patients exposed to aeroallergens in the Vienna Challenge Chamber. *Ann Allergy Asthma Immunol.* 2006;96(1):37-44.
13. Valero A, de la Torre F, Castillo JA, Rivas P, del Cuvillo A, Antépara I, Borja J, Donado E, Mola O, Izquierdo I. Safety of rupatadine administered over a period of 1 year in the treatment of persistent allergic rhinitis: a multicentre, open-label study in Spain. *Drug Saf.* 2009;32(1):33-42.
14. Valero A, Ferrer M, Sastre J, Navarro AM, Monclús L, Martí-Guadaño E, Herdman M, Dávila I, Del Cuvillo A, Colás C, Baró E, Antépara I, Alonso J, Mullol J. A new criterion by which to discriminate between patients with moderate allergic rhinitis and patients with severe allergic rhinitis based on the Allergic Rhinitis and its Impact on Asthma severity items. *J Allergy Clin Immunol.* 2007;120(2):359-65.
15. Bousquet JP, Combescure C, Klossek JM, Daures JP, Bousquet J. Changes in visual analog scale score in a pragmatic randomized cluster trial of allergic rhinitis. *J Allergy Clin Immunol.* 2009;123:1349-54.
16. Bousquet JP, Bachert C, Canonica GW, Csale TB, Mullol M, Klossek JM, Daures JP, Bousquet J. Uncontrolled allergic rhinitis during treatment and its impact on quality of life: a cluster randomized trial. *J Allergy Clin Immunol.* 2010;126(3):666-8.e1-5.
17. Valero A, Baró E, Sastre J, Navarro-Pulido AM, Izquierdo I, Martí-Guadaño E, Ferrer, Dávila I, del Cuvillo A, Colas C, Antépara I, Alonso J, Mullol J. Reference Values For Facilitating the Interpretation of the ESPRINT-15 Questionnaire (Spanish Version). *J Investig Allergol Clin Immunol.* 2009;19(5):396-403.
18. Valero A, M Ferrer, E Baró, J Sastre, AM Navarro, E Martí-Guadaño, I Dávila, A del Cuvillo, C Colás, I Antépara, J Alonso, O Mola, I Izquierdo, J Mullol. Discrimination between moderate and severe disease may be used in patients with either treated or untreated allergic rhinitis. *Allergy.* 2010;65:1609-13.
19. Bartra J, Mullol J, de Castellar R, del Cuvillo A, Navarro A, Torrents A, Mola O, Izquierdo I. Rupatadine improves disease severity and quality of life in a cohort of allergic rhinitis patients assessed using the ESPRINT-15 quality of life questionnaire. *Allergy.* 2009;64 (suppl 90):450-51.

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