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ORIGINAL RESEARCH

Satisfaction and quality of life of allergic patients following sublingual five-grass pollen tablet immunotherapy in Spain

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Abstract

Background: Five-grass pollen tablet is an effective and well-tolerated therapy for patients with allergic rhinoconjunctivitis (ARC). This trial sought to determine the satisfaction and health-related quality of life (HRQoL) of patients undergoing this treatment.

Methods: This was a cross-sectional, multicentre, observational, naturalistic study, following a discontinuous pre- and co-seasonal five-grass pollen regimen over two seasons in Spain (2012, 2013). The HRQoL of the patients was measured with the specific Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) for adults, adolescent (AdolRQLQ), or paediatric (PRQLQ) patients. Treatment satisfaction was assessed by the Satisfaction Scale for Patients Receiving Allergen Immunotherapy (ESPIA) questionnaire. Patients/investigators were surveyed on beliefs and attitudes towards the five-grass pollen tablet. ARC evolution according to allergic rhinitis and its impact on asthma (ARIA) criteria and treatment adherence were evaluated.

Results: Among the 591 ARC patients included, the mean (SD) HRQoL scores were 1.40 (1.1) in adults, 1.33 (1.1) in adolescents, and 1.15 (1.1) in children, indicating low levels of impairment (scale 0–6). ESPIA answers showed high levels of satisfaction, with an average score of 69.2 (scale 0–100). According to ARIA criteria, 88.2% of patients reported improvement of ARC. Moreover, this was accompanied by a reduced use of symptomatic medication. Adherence to treatment was estimated at 96.8%. In general, both patients and specialists exhibited a positive attitude towards five-grass pollen tablet treatment.

Conclusion: ARC patients treated with five-grass pollen tablet showed favourable levels of HRQoL and treatment satisfaction, with concomitant improvements in ARC and symptomatic medication use, which translated into high levels of treatment adherence and a positive attitude towards five-grass pollen tablet.

Keywords: sublingual immunotherapy, pollen, rhinitis allergic seasonal, conjunctivitis allergic, health-related quality of life, patient satisfaction, symptom improvement, cross-sectional study.

Citation

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Introduction

Allergic rhinoconjunctivitis (ARC) is considered a significant health problem, which is estimated to affect approximately 23% of adult population in Spain [1]. It is a major risk factor for the development of comorbidities including asthma, associated with sleep and mood disturbances, and has been shown to impair daily activities and performance at work or school, exerting a negative impact on patient's health-related quality of life (HRQoL) [2,3]. Allergen-specific immunotherapy (AIT) is the only etiologic treatment for ARC [4]. Although traditional pharmacotherapy is widely used, this approach only targets the symptoms of the condition [5,6]. AIT is recommended for patients with moderate-to-severe ARC who have not responded to symptomatic pharmacotherapy [4]. Traditional AIT, which is administered by subcutaneous injections (SCIT), typically every month for 3–5 years, has shown notable efficacy in several trials [7–12].

Orally administered once-daily sublingual five-grass pollen tablet immunotherapy (five-grass pollen tablet; Oralair®) is an alternative form of AIT, which has proven efficacy, with a more favourable safety and tolerability profile than SCIT [11]. The active constituents in five-grass pollen tablet comprises purified and calibrated freeze-dried extract of pollen from sweet vernal grass (*Anthoxanthum odoratum*), cocksfoot/orchard grass (*Dactylis glomerata*), perennial rye grass (*Lolium perenne*), meadow grass (*Poa pratensis*), and timothy grass (*Phleum pratense*) [13]. Inclusion of these five components (rather than one) better mimics the exposure profile in Europe, sensitization conditions, and the polysensitization of allergic patients across the continent [14,15].

Recent studies indicate that five-grass pollen tablet exhibits a positive influence on the patient's HRQoL, largely reflecting symptom improvement and a reduction in the use of symptomatic medication [16–20]. To further investigate these findings, this observational study was specifically conducted to assess the level of treatment satisfaction and HRQoL with five-grass pollen tablet in patients with grass-pollen-related ARC.

Methods

Patients and study design

This was a cross-sectional, observational, multicentre, naturalistic study conducted in Spain. Patients aged ≥6 years with moderate-to-severe ARC to grass pollen uncontrolled with symptomatic treatment, who had received five-grass pollen tablet in a discontinuous pre- and co-seasonal regimen (before and during the previous grass-pollen season, principally Spring/Summer) were eligible for participation. Patients who had received any other form of AIT or those who were unable to comply with the trial protocol were excluded. Written informed consent was obtained from participating patients, their parents, or legal representatives. Moreover, the study was approved by the Research Ethics Committee at the Hospital Universitario de La Princesa (Madrid).

Eligible patients were identified from clinical records and attended a single clinic visit during which demographics, medical, and treatment history were confirmed. Patients were then required to complete self-administered questionnaires (if necessary with the help of parents or caregivers) to evaluate HRQoL, treatment satisfaction, and attitude towards medication. Symptom severity was evaluated retrospectively. Physician demographics were also recorded, and physician attitude towards medication was evaluated by self-administered questionnaire. Analyses were conducted separately for the previous 2012 and 2013 pollen seasons.

Assessments

HRQoL: HRQoL was evaluated using validated age-specific instruments [21–24]. Adult patients (≥18 years of age) completed the Spanish version of the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) [21–24], consisting of 28 items distributed in 7 dimensions (activity limitations, sleep disturbances, general problems, practical problems, nose symptoms, eye symptoms, and emotional function). Adolescents aged 12–17 years were asked to complete the Spanish adolescent RQLQ (AdolRQLQ) [22], consisting of 25 items distributed in 6 dimensions (activity limitation, nasal symptoms, eye symptoms, practical problems, non-hay fever symptoms, and emotional function); whereas, patients under 12 years of age completed the paediatric RQLQ (PRQLQ) [24], which consists of 23 items distributed in 5 dimensions (nose symptoms, eye symptoms, practical problems, activity limitation, and other symptoms). In all three questionnaires, each item was scored from 0 (not impaired at all) to 6 (severely impaired).

Treatment satisfaction: To determine the level of satisfaction with five-grass pollen tablet, adult patients were asked to complete the Satisfaction Scale for Patients Receiving Allergen Immunotherapy (ESPIA) questionnaire [25], comprising 16 items specifically designed for patients treated with AIT. Overall satisfaction in this validated instrument is graded from 0 to 100 (100 denoting the highest level of satisfaction). Psychometric properties of the (unvalidated) paediatric version of the ESPIA questionnaire were also evaluated in an exploratory analysis.

ARC frequency and severity: ARC was classified as persistent or intermittent in frequency and as mild or moderate-to-severe ARC, according to the Allergic Rhinitis and its Impact on Asthma (ARIA) criteria [26]. Typical symptoms associated to ARC (sneezing, rhinorrhoea, nasal itching, nasal congestion, ocular itching, and tearing) were classified as mild, moderate, or severe, according to the Center for Drug Evaluation and Research guidelines [27]. Both ARC severity and associated symptoms

before and after five-grass pollen tablet were assessed retrospectively, based on the data retrieved from the clinical records of the patients.

Patients survey on beliefs and attitudes towards five-grass pollen tablet: All patients were asked to complete a descriptive survey, specifically designed for this study, which included 17 questions/statements divided in three sections, aimed at assessing the following aspects of five-grass pollen tablet therapy: beliefs/attitudes, effectiveness/security, and compliance/adherence. The section on compliance and adherence included the Spanish version of the validated Haynes–Sackett questionnaire [28]. Compliance was estimated as the difference between prescriptions written and collected (%); whereas, adherence was calculated as the proportion of tablets returned unused (%).

Investigators attitude towards five-grass pollen tablet: Investigator beliefs and attitudes to five-grass pollen tablet were assessed by a self-administered questionnaire, specifically designed for this study, before patient recruitment. The clinical practice of investigators in relation to five-grass pollen tablet was assessed by determining their level of agreement with each of 10 statements scored from 1 (totally agree) to 5 (totally disagree). The factors that investigators typically consider when prescribing five-grass pollen tablet were evaluated in 19 statements scored again from 1 (always) to 5 (never). The preferences of investigators for oral (five-grass pollen tablet) compared to other routes of administration were determined by the number and percentage of investigators answering 'better', 'equal', or 'worse'. In addition, the investigators were asked about the primary advantages and disadvantages of the five-grass pollen tablet and their level of adherence with treatment guidelines.

Statistics: Statistical analyses were performed using the SAS system version 9.2 (SAS Institute Inc., Cary, NC, USA). Data were stratified by patient age (6–11 years, 12–17 years, and 18–80 years). Baseline demographics were summarized descriptively. The correlation between sociodemographic and clinical variables with the level of satisfaction and HRQoL was analysed using the ANOVA test (categorical variables) or the Pearson and Spearman correlation coefficients (continuous variables). A significance level of 0.05 was used in all comparisons between groups. A descriptive analysis of the answers to the questionnaire on beliefs and attitudes towards five-grass pollen tablet was conducted. Likert-type answers were described as percentage of patients in each category. The global level of satisfaction of patients with five-grass pollen tablet was described as a continuous variable in a 0–100 scale.

Results

A total of 591 evaluable patients with moderate-to-severe ARC participated in this observational study, who were treated with five-grass pollen tablet over two seasons.

Among the participants, 116 (19.6%) were children aged 6–11 years, 87 (14.7%) were adolescents aged 12–17 years, and 388 (65.7%) were adults. Table 1 presents the most relevant sociodemographic and clinical data. Among the 46 patients (7.8%) who discontinued the treatment prematurely, the most common reason was clinical improvement (33.3%), followed by adverse reactions (15.6%).

HRQoL

The mean (SD) scores of RQLQ, AdolRQLQ, and PRQLQ were 1.40 (1.1) in adults, 1.33 (1.1) in adolescents, and 1.15 (1.1) in children, respectively (Figure 1), indicating low levels of impairment. Of note, 26.5% of the patients exhibited scores between 0 and 0.5 (denoting no symptoms). Regarding the dimensions included in the questionnaires, the differences on daily activities impairment emerge across different ages; older patients exhibited higher levels of impairment and practical problems ($p<0.005$). Higher scores from HRQoL questionnaires were associated with the following: work or school impairment, presence of troublesome symptoms during treatment, taking other allergy medication, difficulties to get to places with presence of grass pollen, and increased medication taken for allergy since starting five-grass pollen tablet ($p<0.05$). As expected, the scores were inversely related to the level of satisfaction of patients with five-grass pollen tablet ($p<0.0001$).

Treatment satisfaction

Adult patients showed a high level of satisfaction following five-grass pollen tablet treatment, as shown by an ESPIA questionnaire mean (SD) score of 69.2 (23.7) (Figure 2). High levels of satisfaction were also recorded for those dimensions related to cost–benefit balance and general satisfaction with five-grass pollen tablet; mean (SD) scores were 68.6 (28.4) and 75.4 (25.9), respectively. Data for adolescent and paediatric patients were evaluated in an exploratory analysis, because the questionnaire used had not been validated. Nevertheless, the results showed reasonable correlation with those in the adult population (data not shown).

ARC frequency and severity

ARC followed a more favourable clinical course after the five-grass pollen tablet treatment. Symptoms transitioned from being persistent to intermittent for 60.9% of patients; whereas, the severity of ARC was reduced from severe or moderate to mild in 49.1% of patients. Improvements were recorded for all the ARIA measures across all age groups, reaching statistical significance for the reduction in impairment of daily living activities (Figure 3). These outcomes were reflected in a statistically significant reduction in the use of medications for symptomatic relief; specifically for systemic antihistamines, topical antihistamines, and nasal corticosteroids (Figure 3).

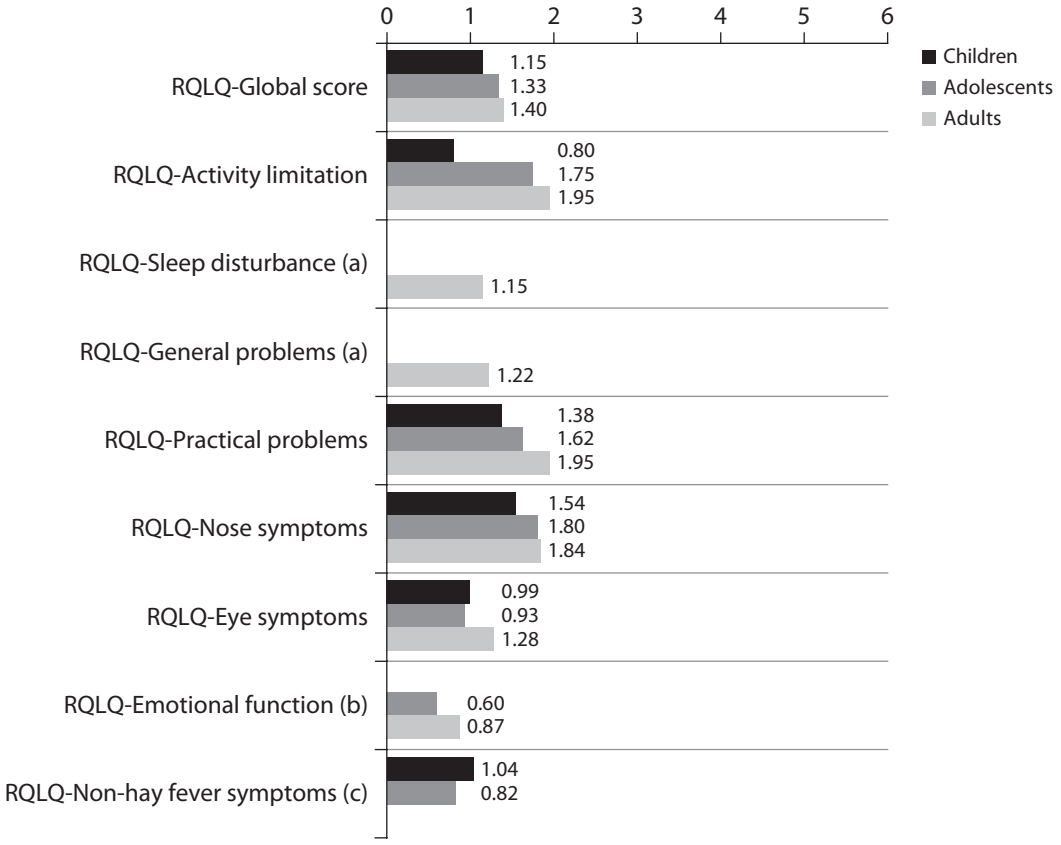
Table 1. Socio-demographic and clinical data of patients included in the study.

Variable		Children (6–11)	Adolescents (12–17)	Adults (≥18)	Total	*p*-value
Age	n	116†	87†	388†	591†	<0.0001
	Average (SD)	9.0 (1.5)	14.5 (1.8)	33.9 (11.2)	26.2 (14.2)	
Gender	Male	75 (64.7%)	54 (62.1%)	194 (50.0%)	323 (54.7%)	0.0067
Habitat	Rural (<10,000 pop.)	11 (9.5%)	10 (11.5%)	51 (13.2%)	72 (12.2%)	0.4199
	Semi-urban (>10,000-<30,000 pop.)	11 (9.5%)	7 (8.0%)	50 (13.0%)	68 (11.5%)	
	Urban (>30,000-<200,000 pop.)	68 (58.6%)	48 (55.2%)	184 (47.7%)	300 (50.9%)	
	Metropolitan (>200,000 pop.)	26 (22.4%)	22 (25.3%)	101 (26.2%)	149 (25.3%)	
Level of education	No formal education	6 (9.4%)	-	4 (1.1%)	10 (2.0%)	<0.0001
	Primary education	57 (89.1%)	20 (30.8%)	52 (14.0%)	129 (25.8%)	
	Secondary education	1 (1.6%)	43 (66.2%)	139 (37.5%)	183 (36.6%)	
	University education		2 (3.1%)	176 (47.4%)	178 (35.6%)	
Employment status	Unemployed			23 (6.2%)	23 (4.7%)	<0.0001
	Self-employed			37 (10.0%)	37 (7.5%)	
	Employed by other			210 (56.9%)	210 (42.5%)	
	Unable to work			1 (0.3%)	1 (0.2%)	
	Pensioner			10 (2.7%)	10 (2.0%)	
	Housework			18 (4.9%)	18 (3.6%)	
	Student	58 (100.0%)	67 (100.0%)	70 (19.0%)	195 (39.5%)	
Duration of ARC	Average (SD) years	3.9 (2.0)	5.9 (3.3)	10.4 (8.7)	8.45 (7.7)	<0.0001
Diagnosis method	Skin prick-test	115 (99.1%)	87 (100.0%)	385 (99.2%)	587 (99.3%)	0.7027
	Specific classic IgE	71 (61.2%)	45 (51.7%)	181 (46.6%)	297 (50.3%)	0.0217
	Molecular diagnosis	27 (23.3%)	25 (28.7%)	89 (22.9%)	141 (23.9%)	0.5113
	Other	3 (2.6%)	1 (1.1%)	12 (3.1%)	16 (2.7%)	0.5984
Comorbidities	Yes	94 (81.0%)	66 (75.9%)	263 (67.8%)	423 (71.6%)	0.0134
	Asthma	72 (62.1%)	54 (62.1%)	206 (53.1%)	332 (56.2%)	0.1129
	Sinusitis	4 (3.4%)	2 (2.3%)	23 (5.9%)	29 (4.9%)	0.2640
	Nasal polyposis	1 (0.9%)		2 (0.5%)	3 (0.5%)	0.6932
	Medium otitis	5 (4.3%)	1 (1.1%)	6 (1.5%)	12 (2.0%)	0.1475
	Eczema	13 (11.2%)	3 (3.4%)	19 (4.9%)	35 (5.9%)	0.0235
	Urticaria	2 (1.7%)	6 (6.9%)	12 (3.1%)	20 (3.4%)	0.1130
	Atopic dermatitis	32 (27.6%)	10 (11.5%)	25 (6.4%)	67 (11.3%)	<0.0001
	Headache	5 (4.3%)	5 (5.7%)	36 (9.3%)	46 (7.8%)	0.1604
	Food allergy	15 (12.9%)	8 (9.2%)	44 (11.3%)	67 (11.3%)	0.7081
	Drugs allergy		1 (1.1%)	16 (4.1%)	17 (2.9%)	0.0383
	Other	5 (4.3%)	1 (1.1%)	14 (3.6%)	20 (3.4%)	0.4290

† Total evaluated unless specified otherwise.
SD=standard deviation.

Symptoms exhibited after the five-grass pollen tablet were similar across all ages, sneezing (71.3%) being the most common, followed by rhinorrhoea (66.5%) and nasal itching (64.1%). A general reduction in the intensity of symptoms was reported after five-grass pollen tablet (Figure 4). These results were similar irrespective of the sensitization status. Only 15 patients (2.5%) showed no improvement in the ARIA criteria, ARC symptoms, or use of symptomatic medication.

Figure 1. Mean score from patients' RQLQ by dimension after treatment with five-grass pollen tablet.



(a) Dimensions not included in the AdolRQLQ or the PRQLQ.
(b) Dimensions not included in the PRQLQ.
(c) Dimensions not included in the adults RQLQ Mean score from patients RQLQ questionnaire by dimensions after five-grass pollen tablet treatment.
AdolRQLQ=Rhinoconjunctivitis Quality of Life Questionnaire for adolescent patients; PRQLQ= Rhinoconjunctivitis Quality of Life Questionnaire for pediatric patients; RQLQ=Rhinoconjunctivitis Quality of Life Questionnaire for adult patients.

Patients survey on beliefs and attitudes towards five-grass pollen tablet

The results of the patient survey on beliefs and attitudes towards the five-grass pollen tablet revealed generally positive opinions relating to the prior use of this therapy (Figure 5). For instance, 91.2% of patients considered that taking the five-grass pollen tablet a few months before and during the pollen season was essential for controlling the allergy symptoms during that season; 46.2% agreed that five-grass pollen tablet had not led to the requirement of other allergy medication; and only 14.9% of patients believed that, in order to prevent allergy symptoms, five-grass pollen tablet should be taken permanently. In terms of effectiveness, 58.2% claimed to have no issues with going to places with grasses and 78.6% claimed they would need to take the five-grass pollen tablet again the following year to prevent ARC symptoms.

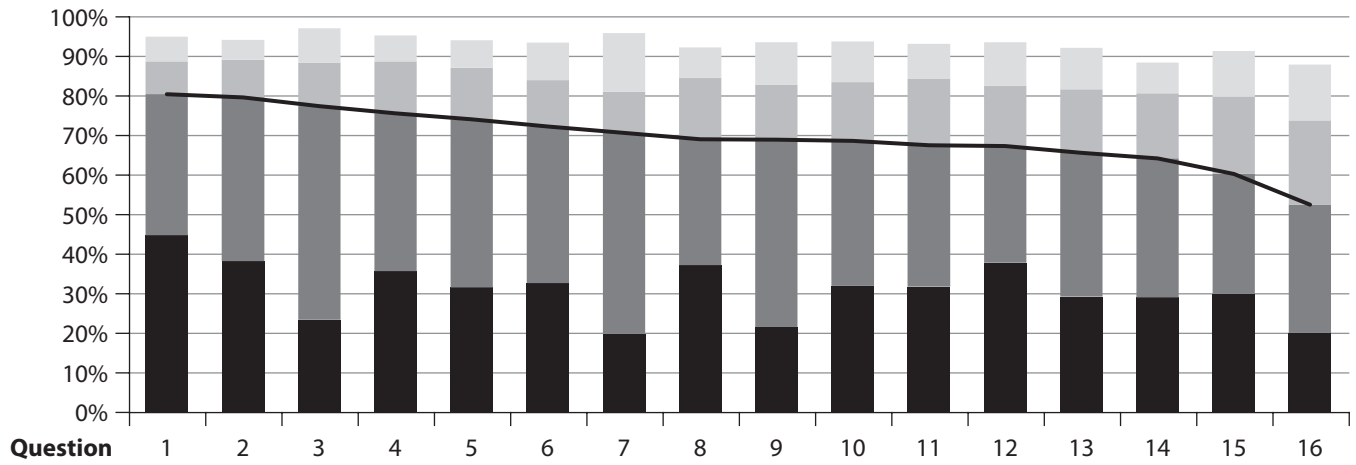
The overall mean (SD) level of satisfaction with the five-grass pollen tablet, on a scale of 0 (lowest) to 10 (highest), was 7.5 (2.4), indicating a high level of satisfaction with the agent (Figure 5).

Estimates of patient compliance and adherence were high; 93.3% of patients were calculated to be compliant to the prescribed regimen, and 96.8% of patients had good treatment adherence. In relation to compliance, 25.1% of patients stated that they had difficulties to take the tablets; whereas, only 27.5% of patients claimed that they had not forgotten to take any tablet, and 34% forgot to take five or more tablets.

Investigators attitude towards five-grass pollen tablet

A total of 154 investigators completed the online survey on beliefs and attitudes towards the five-grass pollen tablet.

Figure 2. Frequency of agreement of patients with the ESPIA questionnaire in adult patients[a].



Question

1. Since being vaccinated for my allergy, I have fewer symptoms
2. My vaccine works
3. Thanks to the vaccine, I am less dependent on carrying other medication (pills, inhalers, etc)
4. My vaccine works faster than I expected
5. Thanks to the vaccine, I no longer avoid things or places that caused my allergy
6. My vaccine helps me to perform my daily activities
7. Since being vaccinated, I can go anywhere with my family and friends
8. Thanks to the vaccine, I can work or study better
9. Since being vaccinated, I enjoy outdoor activities more
10. Since being vaccinated, I don't find myself in uncomfortable or compromising situations caused by my allergy
11. Since being vaccinated, I have gained in quality of life
12. The good performance of my vaccine compensates for all the things I have to do to get it (visits, prescriptions, leave, etc)
13. The good performance of my vaccine compensates for the financial burden it involves
14. The good performance of my vaccine compensates for the discomforts it may cause me
15. In general, I am satisfied with my allergy vaccine
16. In general, I would recommend this vaccine treatment to other people

(a) This English language version has not been subject to the standard process of translation–back translation in accordance with the recommendations of the specialized bibliography. It is merely a free translation included here for informational purposes only.
ESPIA=Satisfaction Scale for Patients Receiving Allergen Immunotherapy.

The level of agreement of investigators with statements regarding general clinical management of ARC, factors to be considered when prescribing five-grass pollen tablet, and treatment guidelines followed are detailed in Figure 6. Of note, 89.0% of investigators believed that five-grass pollen tablet could prevent the occurrence of asthma, and 81.1% considered that the patients showed good treatment compliance. In general, the investigators considered the five-grass pollen tablet to be better than other AIT across nearly all measures. More than half of the investigators rated the five-grass pollen tablet as being more favourable owing to ease of administration (86.4%), safety and risk of adverse reactions (62.3%), and tolerability (59.7%) (Figure 7). In contrast, 72.7% of the investigators considered the five-grass pollen tablet to be disadvantaged by its higher cost (Figure 7). Nevertheless, 86.4% of the physicians claimed that they would take five-grass pollen tablet if they suffered ARC related to grass pollen.

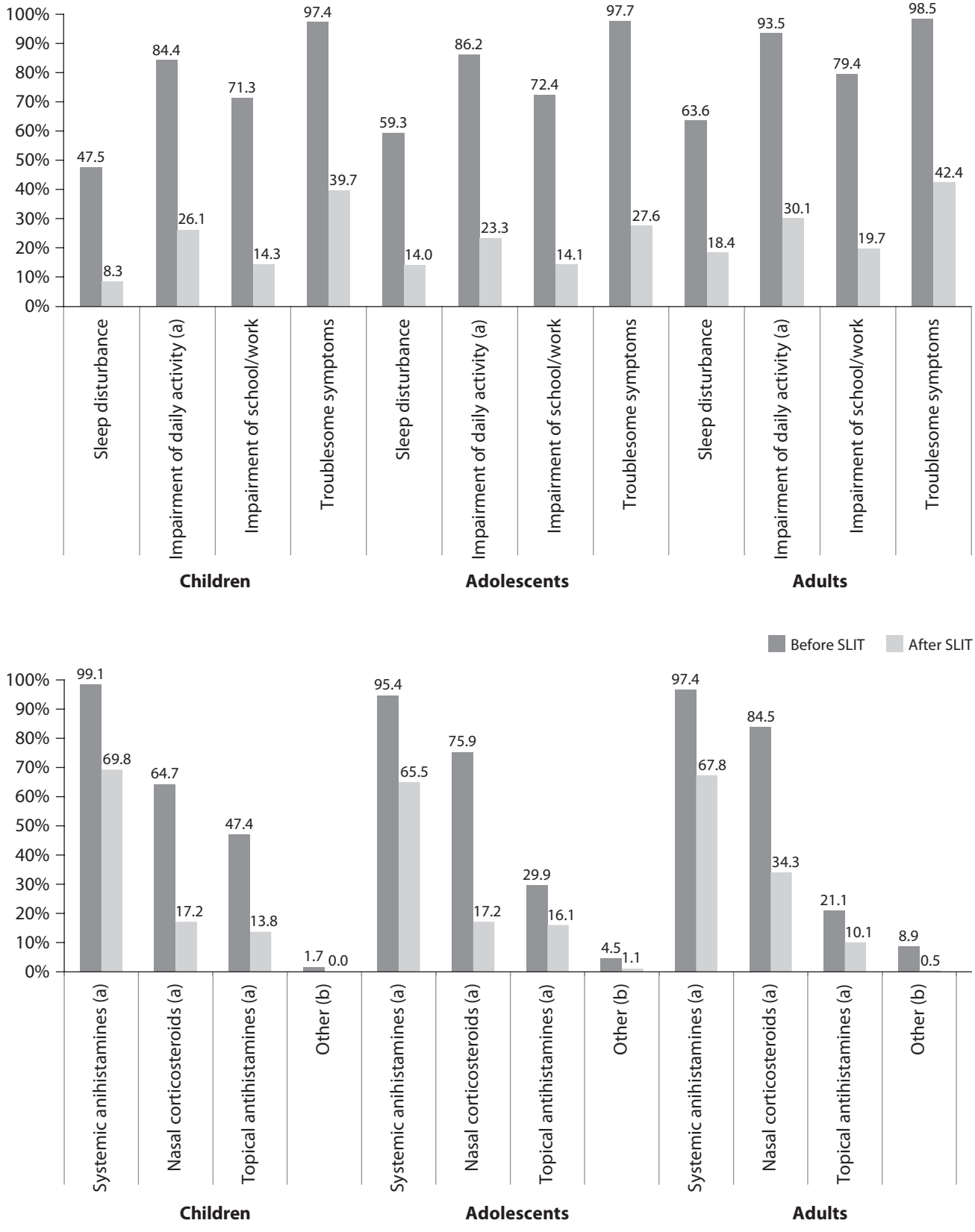
Safety

Overall, 29.1% of the patients experienced at least one adverse event when taking five-grass pollen tablet, the most common adverse events being oral pruritus (32.5%), followed by throat irritation (18.1%), ear pruritus (12.4%), tongue swelling (11.2%), and mouth swelling (9.2%). Treatment withdrawal owing to adverse events was recorded for 4% of patients, and none was due to severe adverse reactions.

Discussion

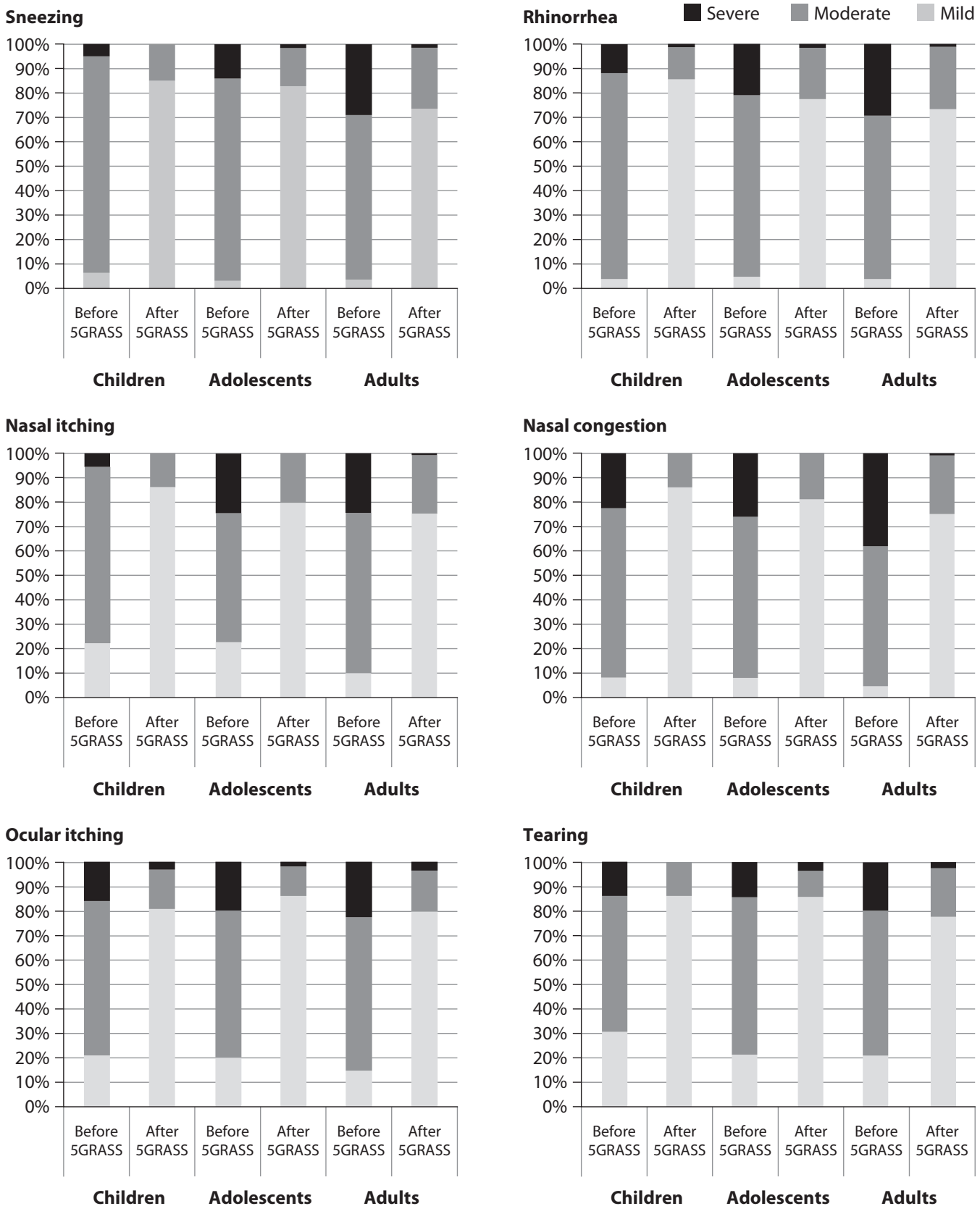
Controlled clinical studies have demonstrated the efficacy of five-grass pollen tablet in terms of symptom control and a reduced need for additional medication to provide symptom relief [16–20]. However, ARC also exhibits a significant negative impact on other patient outcomes, including HRQoL and

Figure 3. Presence of alterations related to ARC following ARIA criteria (top) and use of other pharmacological treatment (bottom) before and after treatment with five-grass pollen tablet.



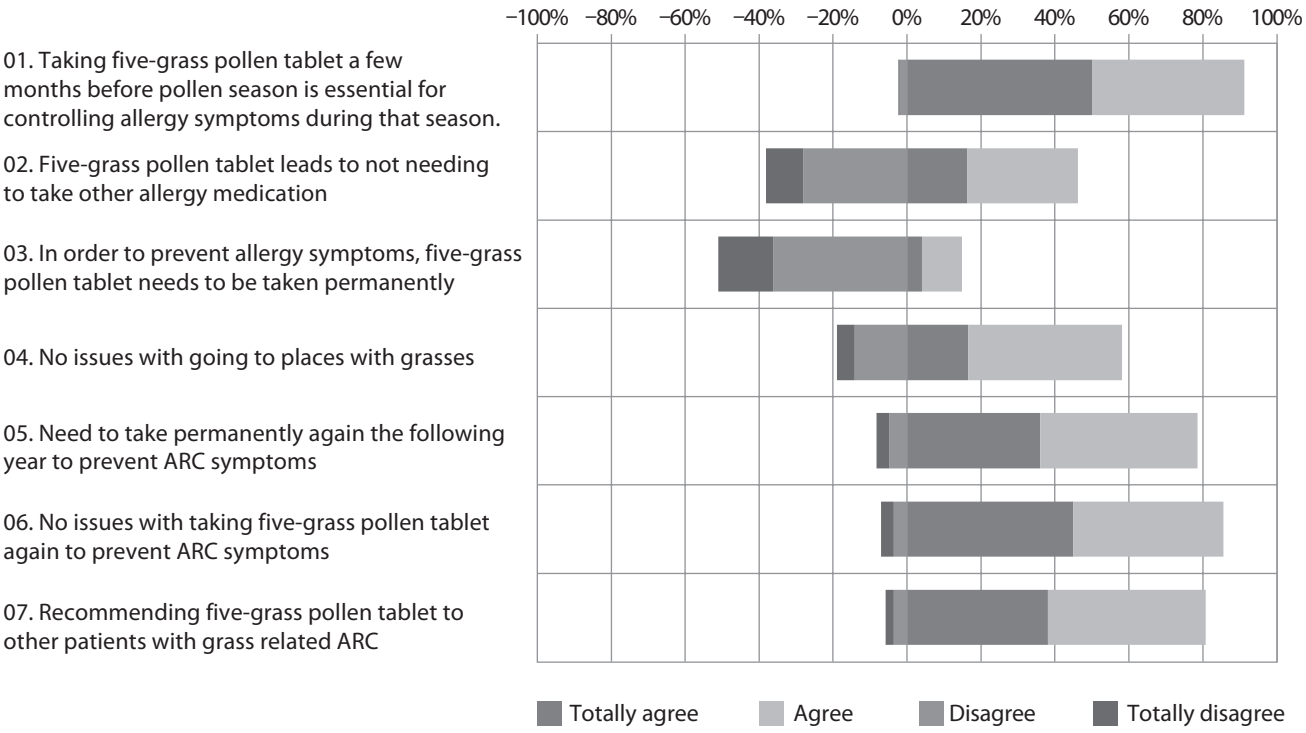
(a) Statistically significant reduction ($p<0.05$). (b) Systemic corticosteroids, nasal descongestants and oral descongestants. ARC=Allergic rhinoconjunctivitis; ARIA=Allergic Rhinitis and its Impact on Asthma; SLIT=Sub-lingual immunotherapy (five-grass pollen tablet).

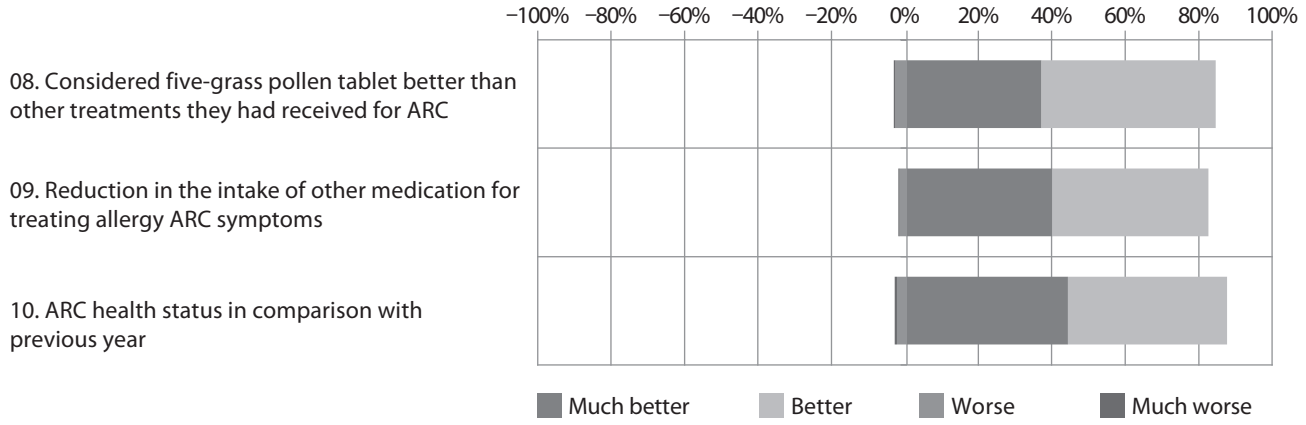
Figure 4. Symptom intensity before and after treatment with five-grass pollen tablet.

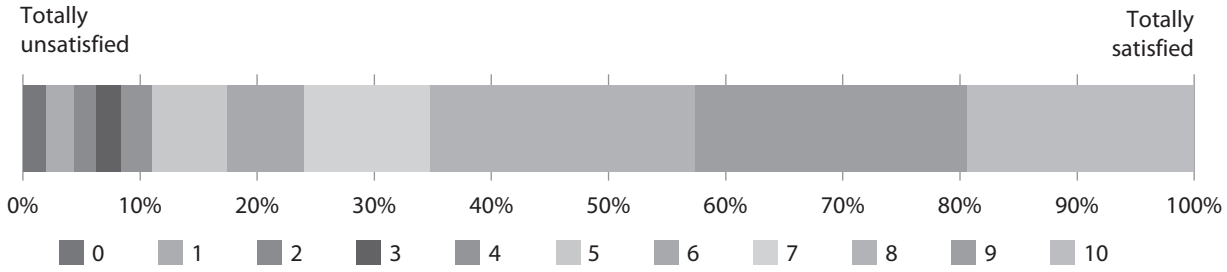


5GRASS=Five-grass pollen tablet.

Figure 5. Results from the patient survey on beliefs and attitudes towards five-grass pollen tablet[a].







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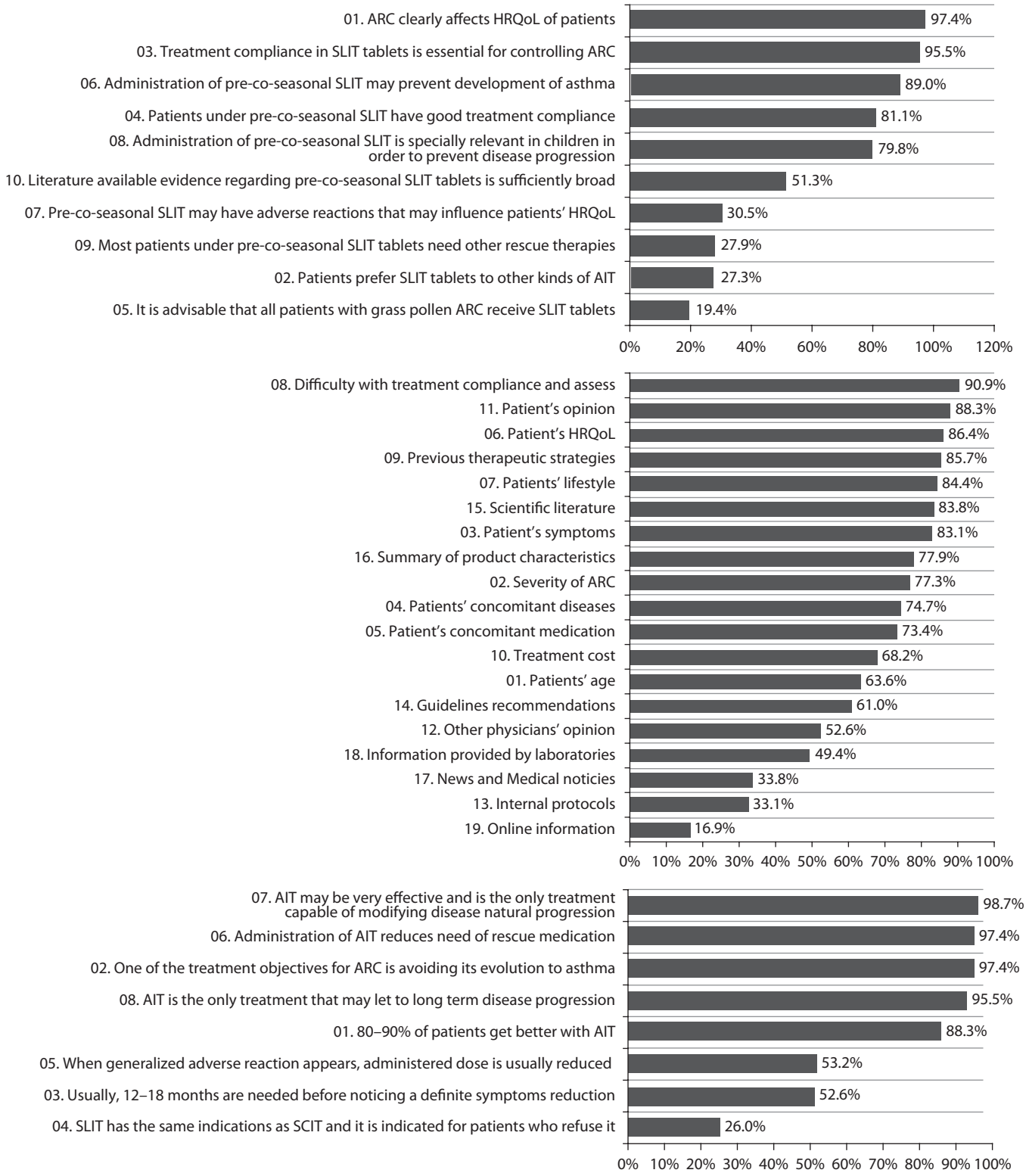
ARC=Allergic rhinoconjunctivitis.

Figure 6. Level of agreement with investigators with statements included in the survey. General clinical management of ARC (top), factors considered always and almost always when prescribing five-grass pollen tablet (middle) and agreement with general ARC guidelines (bottom)[a].



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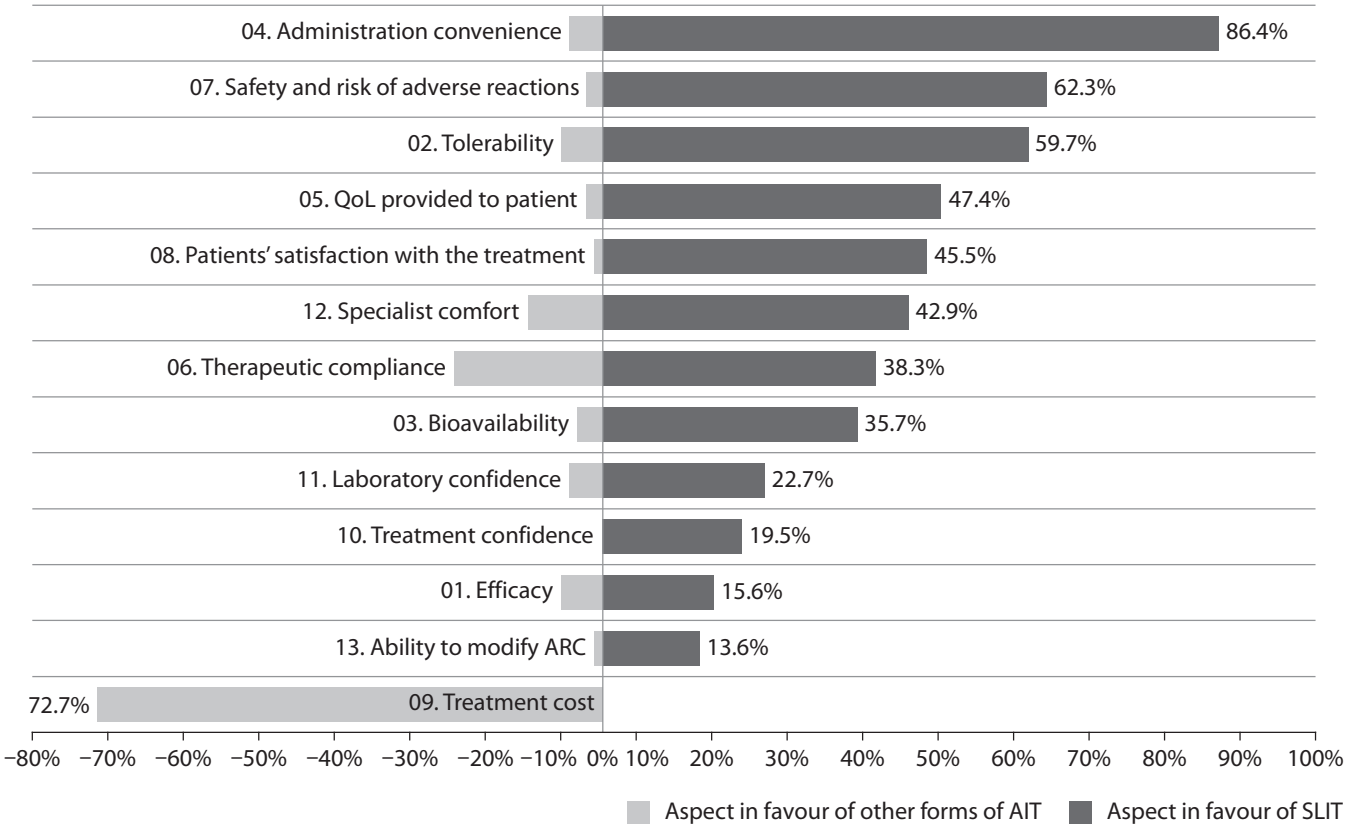
AIT=Allergen immunotherapy; ARC=Allergic rhinoconjunctivitis; HRQoL=Health related quality of life; SCIT=Sub-cutaneous immunotherapy; SLIT=Sub-lingual immunotherapy (five-grass pollen tablet).

Figure 7. Aspects of five-grass pollen tablet that investigators consider better or worse in comparison with AIT[a].



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AIT=Allergen-specific immunotherapy; SLIT=Sub-lingual immunotherapy (five-grass pollen tablet).

productivity [2,29], which are also positively modified with five-grass pollen tablet treatment [16–20]. We confirm this and add new findings in relation to five-grass pollen tablet through our novel naturalistic study, conducted over two seasons in a wide age range of patients with grass-pollen-related ARC.

In this study, self-reported scores for HRQoL showed generally low levels of impairment across all age groups, with approximately a quarter of patients reporting scores denoting no symptoms. These low levels of HRQoL scores are consistent with the findings of a randomized, double-blind, placebo-controlled clinical trial conducted in Spain, where patients experienced an improvement in HRQoL and low levels of impairment following sublingual immunotherapy with grass plus olive pollen extract, after completing the treatment [30]. Similarly, our HRQoL outcomes corroborated those from investigations with five-grass pollen tablet performed in other countries, where patients with pollen-related ARC evaluated HRQoL using RQLQ [31–33]. Furthermore, our results extend the apparent beneficial effects of five-grass pollen tablet on HRQoL from the adult patient population to adolescents and children. In general, answers to the ESPIA questionnaire indicated a high level of satisfaction in all dimensions among adult patients previously treated with the five-grass pollen tablet, with similar results reported for adolescents and children in an exploratory analysis. These findings further corroborate high levels of satisfaction from prior observational studies of patients with grass-pollen ARC treated with the five-grass pollen tablet, across a variety of age groups including children [34–37]. Underpinning these findings, our study showed a more favourable clinical course of the condition following five-grass pollen tablet treatment, with 60.9% of patients experiencing less frequent symptoms, when evaluations were made using ARIA criteria. A significant improvement in daily living activities was particularly noteworthy, as was the significant reduction in the use of most-used symptomatic medications.

Overall, the above pattern of positive outcomes was recorded in this study, also translated into high levels of treatment adherence (96.8%) and compliance (93.3%). Patient and physician opinions on the utility of the five-grass pollen tablet were also positive. Patients, generally, reported high levels of satisfaction with the agent, and considered it to exhibit a positive impact on their condition. These findings were in line

with the opinions of physicians, who believed that five-grass pollen tablet exhibited a clear positive effect on the HRQoL of the patients. In addition, most physicians claimed that they would use five-grass pollen tablet treatment themselves for ARC.

Although this study was not designed to evaluate safety, adverse drug reactions were generally infrequent, rarely resulted in withdrawal, and no adverse event was of a serious nature.

Strengths of the study include the use of age- and disease-specific validated instruments to evaluate HRQOL and adult patient satisfaction, the use of standardized criteria to assess disease dimensions, and the employment of specific instruments designed for this study to evaluate patient and physician opinions on therapy. Provided the seasonal nature of ACR, we also conducted this investigation to cover two different pollen seasons (2012, 2013), with data collection afterwards. These periods covered the main pollen season in Europe, which typically occurs between March and July, with minor variations occurring with changes in latitude [14]. The limitations of this study were its retrospective design, involving one-visit evaluation, and the subjective nature of the self-reported survey data collected. The selection of investigators and lack of both a centralized laboratory and intensive monitoring, among others, may also have hampered the internal validity. However, the sites and investigators for this study were selected to ensure a fair representation of the Spanish territory.

In conclusion, this observational, naturalistic study in ARC patients, treated with the five-grass pollen tablet, showed favourable levels of HRQoL and treatment satisfaction, with concomitant improvements in ARC and symptomatic medication use, which translated into high levels of treatment adherence and a positive attitude towards the five-grass pollen tablet.

Contributions: Stallergenes was responsible for the study design, collection, analysis and interpretation of data, and writing the manuscript. All authors contributed by data acquisition, critical appraisal of the manuscript, and approval of the final version of the manuscript. All authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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