Improvements in patient-reported outcomes: A prospective, non-interventional study with aclidinium bromide for treatment of COPD

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KEYWORDS
Aclidinium bromide; COPD; Morning symptoms; Quality of life; Non-interventional study

Summary
Background: The inhaled long-acting muscarinic antagonist aclidinium bromide has been shown to significantly improve lung function parameters and symptom severity in patients with COPD in randomised placebo- and active-controlled clinical studies. To obtain a comprehensive view of the treatment effects, patient-reported outcomes were investigated in a real-life COPD population in routine clinical practice in Austria.

Methods: Multicentre, prospective, non-interventional study in patients with COPD who were newly initiated on treatment with Eklira® Genuair® (aclidinium bromide; recommended dose 400 µg twice daily) as first-line or add-on therapy. Patients were either treatment naïve or switched from other COPD medications. Health-related quality of life by means of the COPD Assessment Test™ (CAT) and symptom-related variables were evaluated at the first visit (baseline) and after approximately 12 weeks of treatment. Features of the inhaler were assessed by patients and physicians at the follow-up visit.

Results: A total of 795 COPD patients (56% male; median age: 64 years) were enrolled and treated. During the observational period, the proportion of patients with at least moderate nighttime symptoms, early-morning symptoms, and limitations in morning activities decreased from 45.0% to 21.4%, from 57.7% to 26.0%, and from 49.9% to 25.3%, respectively. All improvements from baseline in symptom severity and activity limitation were statistically significant (p < 0.0001, all tests). The mean (±SD) frequency of nocturnal awakenings decreased from 1.2 (±1.4) to 0.7 (±1.2) times per night (p < 0.0001). Quality of life improved significantly

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in patients treated with aclidinium bromide over 3 months compared to baseline ($p < 0.0001$; mean CAT total score: $18.5 \pm 7.5$ vs. $13.8 \pm 7.3$). Up to 90% of the patients and up to 91% of the physicians assessed individual features of the inhaler as ‘very good’ or ‘good’. Aclidinium bromide was well tolerated; 6.9% of the patients reported adverse drug reactions, none of which were serious.

Conclusions: This non-interventional study indicated beneficial effects of Eklira® Genuair® in the treatment of COPD with regard to nighttime and early-morning symptoms, limitation of morning activities, and quality of life under routine conditions. The acceptance of the inhaler device was high, which is a prerequisite to ensure adherence in long-term therapy.

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### Methods

#### Study design and treatment

This was a multicentre, prospective, non-interventional study (Austrian National Eklira® Evaluation and Documentation, A NEED), designed in accordance with the recommendations given in the Scientific Guidance for the Conduct of Non-interventional Studies by the Austrian Federal Office for Safety in Healthcare and the principles of the Declaration of Helsinki. The study was conducted between March 2013 and April 2014 with the participation of 62 respiratory physicians in Austria. The Austrian Federal Office for Safety in Healthcare was notified about the conduct of this non-interventional study before the start of the observational period. Ethical approval for this study was obtained from the Ethics Committee of the City of Vienna. All patients gave written informed consent to the documentation and processing of their pseudonymised data. Eklira® Genuair® (Almirall S.A., Barcelona, Spain) was administered according to the specifications given in the summary of product characteristics (Eklira® Genuair® 322 µg inhalation powder). The recommended dose is 322 µg aclidinium (corresponding to 400 µg aclidinium bromide metered-dose) twice daily. Study-related data were documented on standardised forms at the start of the observational period (baseline visit, V1) and at a follow-up visit (V2), scheduled approximately 12 weeks after the start of treatment as per routine clinical practice.

### Introduction

Chronic obstructive pulmonary disease (COPD) can have a major impact on the quality of life of affected patients. As the condition progresses, the burden and severity of symptoms increase over time and gradually limit physical activities in daily life. This may lead into a downward spiral of muscle wasting and deterioration of the patients’ physical condition [1], which further decreases the capacity to cope with activities of daily living. Withdrawal from social life, low self-esteem, anxiety and depression are negative psychosocial and emotional consequences [2–4]. COPD symptoms such as dyspnoea (shortness of breath) are generally worse in the morning than at other times of the day, interfering with basic self-care tasks and routine activities [5]. Especially patients with severe COPD also suffer from nighttime symptoms and sleep deprivation, which is associated with a wide range of health problems [6–8]. Thus, an important goal in COPD management, which is also stressed in the current GOLD guideline [9], is the alleviation of symptoms to improve exercise tolerance, physical and mental well-being, and quality of life. In addition to traditional parameters of lung function, patient-reported outcomes, including burden of symptoms, activity limitation and health-related quality of life, have become pivotal in the assessment of the effectiveness of interventions for COPD [10].

Pharmacotherapy for COPD relies mainly on inhaled medications. Aclidinium bromide is an inhaled long-acting muscarinic antagonist approved in Europe and the United States of America, among other countries, for maintenance treatment of COPD. It has been shown to exert bronchodilatory efficacy over 24 h using a twice-daily regimen [11,14]. Placebo- and active-controlled clinical Phase III studies with twice-daily aclidinium bromide in patients with moderate-to-severe COPD demonstrated significant improvements in the severity of early-morning and nighttime symptoms [12–15]. Clinically meaningful improvements in health status were maintained over a 52-week period [15,16].

Adherence to treatment and the correct use of the inhaler device are essential for therapeutic success. Factors that may affect adherence to inhaled COPD medication include perceived treatment effects on symptoms, cognitive function, complexity of treatment regimens, and convenience and ease of use of inhaler devices [17]. Aclidinium bromide (Eklira®) is delivered by the Genuair® multidose dry powder inhaler, which is equipped with a dose indicator and mechanisms for providing feedback on correct inhalation and prevention of accidental double-dosing. In a clinical study, a substantial number of patients with moderate or severe COPD was able to properly use the Genuair® inhaler for optimal inhalations [18].

To gain more knowledge on the quality of life and burden of symptoms in patients treated with Eklira® Genuair® for COPD in a real-life setting, a non-interventional study using patient-reported outcome measures, including severity of early-morning and nighttime symptoms, was performed. Patient satisfaction with the therapy and the handling of the Genuair® inhaler were also captured. This article reports the first real-life data on patient-reported assessments of COPD therapy with Eklira® Genuair®.
Study population

Adults (≥40 years of age) with a diagnosis of COPD who were newly initiated on treatment with Eklira® Genuair®, either as initial therapy, as part of a therapy switch, or as an add-on therapy, could be included by participating physicians. The diagnosis of COPD was established as per clinical routine without study specific requirements, in compliance with the non-interventional nature of this investigation. Therapy decisions had to be made by the physicians independently from considering a patient’s inclusion into the study. Pregnant or breast-feeding women and patients with contraindications to Eklira® Genuair®, including known hypersensitivity against aclidinium bromide, atropine or any of its derivatives, hereditary problems of galactose intolerance, lactase deficiency, or glucose-galactose malabsorption were not eligible for inclusion.

Assessments

Health-related quality of life was assessed by using the German version of the COPD Assessment Test™ (CAT) [19]. Patients were asked to complete the CAT questionnaire at the baseline and follow-up visit. At both visits, patients were also asked to indicate the frequency of nocturnal awakenings due to COPD and to evaluate the severity of their nighttime and early-morning COPD symptoms and the degree of impairment in their morning activities on 5-point Likert scales (no, mild, moderate, severe, very severe symptoms/impairment), corresponding to scores from 0 to 4. At the end of the observational period (follow-up visit), physicians and patients evaluated the features of the inhaler (including handling, comfort, ease of use, grip) on a 4-point Likert scale (very good, good, moderate, poor). Willingness to continue treatment with Eklira® Genuair® or repeat its prescription and the respective reasons for continuation were also documented at the follow-up visit. During the entire study period, patients were monitored for adverse events (AEs).

Statistical analysis

Statistical analysis was based on all patients who were treated with Eklira® Genuair® and for whom any study-related data were documented. A sample size of 1000 patients was considered representative to determine the proportion of patients with an improvement in quality of life based on the CAT with a maximal confidence interval of ±3.1% (95% confidence level; N = 400,000, i.e. 5% of the adult Austrian population) with a minimum number of 384 patients needed to draw meaningful conclusions. Data were checked for plausibility before analysis. Missing data were not imputed. All data were summarised descriptively, and exploratory tests were performed using the statistical software package SAS® version 9.1.3 (SAS Institute Inc., Cary, North Carolina, USA). Adverse events were classified using the MedDRA coding system (version 16.1). Mean, standard deviation, median, range, and upper and lower quartiles were calculated for continuous variables; absolute and relative frequencies were computed for categorical variables. Percentages relate to the total analysis population if not stated otherwise. Changes from baseline in CAT scores, symptom severity scores, nocturnal awakenings, and morning activity limitation scores were analysed in patients with respective data available at both study visits; statistical significance was assessed by the Wilcoxon signed rank test. Differences between subgroups (patients with newly diagnosed COPD vs. patients with previously known COPD) were tested by using the Wilcoxon rank sum test. All tests were performed at the 5% level of significance.

Results

Patient baseline characteristics

A total of 795 patients with a median age of 64 years were enrolled and treated with Eklira® Genuair®. Three of the patients were younger than 40 years of age, but were not excluded from data analysis due to the non-interventional character of the study. Demographic data are summarised in Table 1. 80% of the patients had a history of smoking (current or former smokers), with ex-smokers having quit smoking between 1 month and 47 years ago (median: 6.5 years; N = 279). COPD diagnosis had been established in 489 patients (61.5%) a median of 7 years prior to the study; 250 patients (31.4%) were newly diagnosed with COPD. For 56 patients (7.0%), the time of diagnosis was not available.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total population</th>
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<td>Age (years), mean (±SD)</td>
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<tr>
<td>Height (cm), mean (±SD)</td>
<td>170.3 (±8.7)</td>
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<tr>
<td>Smoking status, n (%)</td>
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<tr>
<td>Ex-smoker</td>
<td>290 (36)</td>
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<tr>
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<tr>
<td>History of COPD, n (%)</td>
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<tr>
<td>Newly diagnosed</td>
<td>250 (31)</td>
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<tr>
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<tr>
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<tr>
<td>Cardiovascular disorders</td>
<td>316 (40)</td>
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<tr>
<td>Metabolic and nutritional disorders</td>
<td>149 (19)</td>
</tr>
<tr>
<td>Other respiratory tract disorders</td>
<td>41 (5)</td>
</tr>
</tbody>
</table>

COPD = chronic obstructive pulmonary disease; SD = standard deviation.

a Calculated for patients with previously known COPD (N = 489).

b Most common disease categories (≥5%).
The most frequently prescribed COPD medications prior to commencing the therapy with Eklira® Genuair® were fixed combinations of inhaled corticosteroids (ICS) and long acting β2-agonists (LABA) with 47.2%, followed by inhaled short acting β2-agonists (SABA) with 42.5%, anticholinergics (long-acting and short acting muscarinic receptor antagonists) with 38.6%, LABA (12.1%), ICS (10.8%), xanthine derivatives (9.1%), leukotriene antagonists (3.5%), and other (3.0%).

**Treatment with Eklira® Genuair®**

The mean (±SD) duration of the observational period (baseline to follow-up visit) was 12.2 (±5.0) weeks (N = 733). Three hundred thirty nine patients (42.6%) received Eklira® Genuair® as initial therapy, 193 patients (24.3%) were switched from other COPD medications, i.e. mainly tiotropium bromide (188 patients, 23.6%), and 171 patients (21.5%) received Eklira® Genuair® as add-on therapy. No information on the type of Eklira® Genuair® therapy was provided for 23 patients (3.0%) and multiple answers were given for 69 patients (8.7%).

**Patient-perceived severity of nighttime and early-morning symptoms**

Nighttime COPD symptoms were reported by 561 patients (70.6%) at the baseline visit and by 405 patients (50.9%) at the follow-up visit (Fig. 1). The proportion of patients with nighttime symptoms of at least moderate intensity decreased between baseline and follow-up visit from 45.0% to 21.4% (moderate: 30.3% to 16.5%; severe: 11.3% to 3.9%; very severe symptoms: 3.4% to 1.0%).

Early-morning COPD symptoms were reported at base-line by most patients (N = 729, 91.7%), and at the follow-up visit by 598 patients (75.2%) (Fig. 1). The proportion of patients with early-morning symptoms of at least moderate intensity decreased during the observational period from 57.7% to 26.0% (moderate: 42.4% to 21.3%; severe: 12.1% to 3.5%; very severe symptoms: 3.3% to 1.3%). Shortness of breath and cough were the predominant symptoms in the morning, affecting 648 (81.5%) and 642 (80.8%) patients at baseline. A decrease in the prevalence of symptoms of at least moderate intensity was observed at the follow-up visit for all analysed symptoms (Fig. 1).

Mean improvements from baseline in the severity of nighttime and early-morning symptoms (any symptom, shortness of breath, cough, difficulties clearing the lung, wheezing) were statistically significant in the total population and all examined subgroups (p < 0.0001 all tests, Fig. 2). The comparison between subgroups showed significantly greater improvements in symptom severity in patients newly diagnosed with COPD than in patients with previously known COPD (p ≤ 0.047; Fig. 2).

**Impact of COPD on morning activities**

At the baseline visit, 397 patients (49.9%) were at least moderately impaired in the performance of their morning activities due to COPD, 298 patients (37.5%) were mildly impaired, and 96 patients (12.1%) were not impaired (no information was provided for 4 patients). At the follow-up visit, 201 patients (25.3%) experienced at least moderate activity limitation; 338 patients (42.5%) were mildly and 191 patients (24.0%) not impaired in their morning activities (data were missing for 65 patients). The mean reduction in the limitation of morning activities was statistically significant from baseline in the total population as well as in all examined subgroups (p < 0.0001 all tests; Fig. 3). The reduction was more pronounced in newly diagnosed patients compared to patients with previously known COPD (p < 0.0001; Fig. 3).

**Nocturnal awakenings**

The mean (±SD) frequency of nocturnal awakenings due to COPD decreased between baseline and follow-up visit from 1.2 (±1.4) times per night (N = 695) to 0.7 (±1.2) times per night (N = 647). The improvement was statistically significant (mean ± SD: -0.46 ± 1.09; N = 612; p < 0.0001). Statistically significant reductions in the frequency of nocturnal awakenings were also seen in all examined

![Figure 1](image-url)  
**Figure 1** Prevalence (% patients) of nighttime and early-morning COPD symptoms (any symptom), and individual morning symptoms at baseline (V1) and after approximately 3 months (V2) by symptom severity. Percentages relate to the total number of study patients (N = 795).
subgroups: newly diagnosed patients (mean \( \pm \)SD: 0.55 \( \pm \)0.99; N = 184; \( p < 0.0001 \)), patients with previously known COPD (mean \( \pm \)SD: 0.38 \( \pm \)1.13; N = 388; \( p < 0.0001 \)), and patients switched from tiotropium bromide (mean \( \pm \)SD: 0.20 \( \pm \)1.01; N = 150; \( p = 0.0099 \)).

Health-related quality of life (COPD Assessment Test)

The mean (\( \pm \)SD) CAT total score decreased statistically significantly from 18.5 (\( \pm \)7.5) at baseline to 13.8 (\( \pm \)7.3) points at the follow-up visit (\( p < 0.0001 \); Fig. 4).

Furthermore, all individual CAT item scores decreased significantly from baseline (\( p < 0.0001 \)), with the largest mean improvement in the item 'breathless when walking up a hill or one flight of stairs' (Table 2). The subgroup analysis showed significant improvements from baseline in the CAT total score and each item score in all examined subgroups (\( p < 0.0001 \) all tests; total score: Fig. 4; item scores: results not shown). The improvement in the CAT total score was statistically significantly greater in patients with newly diagnosed COPD than in patients with previously known COPD (\( p < 0.0001 \); Fig. 4); similar results were obtained for the item scores (\( p < 0.0115 \); results not shown), with the exception of 'cough' (\( p = 0.3300 \)).

**Figure 2**  Change from baseline in symptom severity scores (nighttime, early-morning, and individual morning symptoms rated on 5-point scales from 0 = 'no symptom' to 4 = 'very severe'). Data are presented as mean and SD (error bar). Sample size ranges: N = 701–724 (total population); N = 216–223 (newly diagnosed COPD); N = 433–450 (previously known COPD); N = 167–170 (switched from tiotropium bromide). \( \ast p < 0.0001 \) for baseline versus follow-up after approximately 12 weeks (change from baseline); \( \dagger p < 0.0001 \), \( \ddagger p < 0.05 \) for newly diagnosed COPD versus previously known COPD.

**Figure 3**  Change from baseline in limitation of morning activity score (impairment of morning activities rated on a 5-point scale from 0 = 'no impairment' to 4 = 'very severe'). Data are presented as mean and SD (error bar). Sample sizes: N = 727 (total population); N = 223 (newly diagnosed COPD); N = 451 (previously known COPD); N = 172 (switched from tiotropium bromide). \( \ast p < 0.0001 \) for baseline versus follow-up after approximately 12 weeks (change from baseline); \( \dagger p < 0.0001 \) for newly diagnosed COPD versus previously known COPD.

**Figure 4**  Change from baseline in CAT total scores (score range: 0–40, higher scores represent a more severe impact of COPD on a patient’s life). Data are presented as mean and SD (error bar). Sample sizes: N = 710 (total population); N = 218 (newly diagnosed COPD); N = 440 (previously known COPD); N = 165 (switched from tiotropium bromide). \( \ast p < 0.0001 \) for baseline versus follow-up after approximately 12 weeks (change from baseline); \( \dagger p < 0.0001 \) for newly diagnosed COPD versus previously known COPD. MCID = minimal clinically important difference.
A clinically relevant improvement in the total CAT score by at least 2 points (minimal clinically important difference) in patients with complete CAT data available was observed in 75.2% of 710 patients of the total population, in 74.4% of 281 female patients, in 76.5% of 400 male patients, in 83.0% of 218 patients newly diagnosed with COPD, in 72.3% of 440 patients with previously known COPD, and in 61.8% of 165 patients who were switched from tiotropium bromide.

The number of patients who stated that COPD had a high or very high impact on their daily life (CAT score ≥ 21) decreased from 271 (38.2%) to 123 (17.3%), whereas the number of patients who reported a low or medium impact (score < 21) increased from 439 (61.8%) to 587 (82.7%).

### Discussion

This is the first report of a real-life experience with Eklira<sup>®</sup> Genuair<sup>®</sup> in daily clinical practice. Demographic data of the real-life population were similar to those of the patients in clinical phase III studies with aclidinium bromide [12–14,16]. However, these clinical studies were performed in patients with moderate-to-severe COPD and a smoking history of > 10 pack years, whereas the severity of COPD was not investigated in the real-life population of this study and smoking history was not a selection criterion. The seemingly high proportion of non-smokers in this study is not surprising in the light of recent publications on the prevalence of airflow obstruction among non-smokers. There is increasing evidence that approximately every fourth to third person with COPD has never smoked [20–22]. Approximately one third of the study patients were newly diagnosed with COPD, i.e. treatment-naive with regard to this disease, and approximately one out of four patients were switched from form tiotropium bromide, another long-acting muscarinic antagonist. In clinical studies with aclidinium bromide, a similar proportion of patients, i.e. 26–30%, had received tiotropium bromide prior to entering the study [12–14,16]. The results of this non-interventional study indicate that after approximately 3 months of treatment with Eklira<sup>®</sup> Genuair<sup>®</sup>, the severity of COPD-related nighttime and early-morning symptoms was significantly reduced under the conditions of daily clinical practice. Thus, our results support the findings of clinical studies showing that aclidinium bromide statistically significantly reduced the severity of nighttime and early-morning symptoms over 6- and 12-weeks of treatment compared to placebo [13,14].

With regards to the perception that patients have about their chronic respiratory symptoms, with the implementation of the CAT questionnaire PROs have been classified as a relevant measure with impact on disease, directly affecting physical activity, quality of life generally, and prognosis. From randomized clinical trials there is evidence on association and correlation of COPD symptom perception and FEV<sub>1</sub>, however it might need dedicated clinical research in this respect to establish such a correlation, which is not within the scope of this investigation. The study also indicates a high perceived symptom burden among patients with COPD. Unspecified nighttime symptoms were frequently reported by the study patients, i.e. by 71% prior to treatment with Eklira<sup>®</sup> Genuair<sup>®</sup> and by 51% at the end of the observation (data were missing for 1% and 9%, respectively). Data on the prevalence of nighttime symptoms are scarce in the literature. A cross-sectional European survey in 2807 patients with COPD showed that sleep was disturbed in 78% of the patients [7]. It has to be noted that a standardised definition of nighttime symptoms or a clear distinction from sleep disturbance is not available in COPD [8], which limits the comparability between studies. The survey also showed that the presence of COPD-related nighttime symptoms increased the risk for early-morning
symptoms and was associated with reduced health-related quality of life [7]. Recent analyses also linked sleep disturbance with COPD exacerbations and mortality [23]. However, the impact of COPD-related symptoms on sleep and morning activities of affected patients seemed to be considerably underestimated by physicians [7]. Our study supports the notion that nighttime symptoms are common in COPD patients and need to be taken into account when considering treatment options. Still, nighttime symptoms and sleep disturbances are not adequately addressed in current management guidelines for COPD [8].

Early-morning symptoms were experienced by most patients (92%) prior to starting the therapy with Eklira® Genuair®. Other real-life studies have reported lower prevalence of morning symptoms, i.e. 57% of 133 patients or 40% of 1489 patients with COPD, respectively [24,25]. A possible explanation for the high proportion of patients with early-morning symptoms in our study may be the fact that 31% of the study population were newly diagnosed with COPD and untreated at study start; thus, COPD-related symptoms, if probably only of mild intensity, may have been more frequent among these patients than among already treated patients. A higher burden of symptoms in newly diagnosed patients may also explain the observations drawn from the exploratory subgroup analyses, which suggest that patients with newly diagnosed COPD, i.e. patients who had not been previously treated for COPD, may benefit more from treatment with Eklira® Genuair® than patients with a history of COPD (and presumably previous treatment). Nevertheless, statistically significant improvements in the severity of early-morning and nighttime symptoms (as well as in the frequency of nocturnal awakenings, limitation of morning activities, and quality of life as assessed by the CAT) were also seen in patients with previously known COPD and in patients switched from tiotropium bromide to Eklira® Genuair®.

The impact of early-morning COPD symptoms on health status and daily life may be substantial. Presence of morning symptoms has been shown to increase the risk of COPD exacerbations, increase the number of days absent from work, and impair the performance of activities in the morning and throughout the day [25,26]. Treatment with aclidinium bromide over 6 weeks significantly reduced the COPD-related impairment of morning activities in a clinical study population [14]. Our data support a beneficial treatment effect on the ability to perform morning activities in a real-world population, as significant improvements in activity limitation were seen under treatment with Eklira® Genuair®.

Shortness of breath was the most common early-morning symptom of COPD in our study and has previously been linked to performance of daily activities and quality of life in patients with COPD [27,28]. Alleviating breathing symptoms may help to increase physical activity and improve health status and quality of life. In line with the observed improvements in symptom severity, the results of the CAT indicate that the impact of COPD on the patients’ lives was significantly reduced during the observational period. After approximately 3 months, 75% of the patients achieved clinically important improvements in the CAT total score, indicating meaningful improvements in their health status. In clinical studies, clinically important improvements in health status and quality of life were seen after 3 months of treatment with aclidinium bromide in approximately 43–49% of the patients [13,16]. The higher proportion of patients with clinically important improvements in this study may be explained by the differences in study population, i.e. a considerable number of patients with newly diagnosed COPD. Although a different tool for the assessment of quality of life and health status was used in clinical studies, i.e. the gold standard Saint George’s Respiratory Questionnaire (SGRQ), the CAT correlates very well with the SGRQ and is preferred in daily practice as it is shorter and less complicated [19,29].

Adherence to treatment is critical in COPD and is influenced by many factors, including patient satisfaction with the handling and features of the inhaler [30]. The results of the patient evaluation of the therapy with Eklira® Genuair® showed that between 60% and 72% of the patients considered the individual inhaler attributes as ‘very good’. In a study indicating patient preference in favour of the Genuair® versus the HandiHaler® inhalation device [31], the proportions of patients who were very satisfied with specific inhaler attributes were smaller (35–54%). The feedback mechanism to indicate correct inhalation was the lowest rated feature in the comparative study, but was the second highest rated attribute in our study; however, ‘ease of dose preparation’ and ‘ease of use’ were highly rated in both studies. Overall, the results indicated high patient satisfaction, which was also reflected in the high proportion of patients willing to continue the therapy with Eklira® Genuair®. Whether a high level of treatment satisfaction translates into good adherence to Eklira® Genuair® needs to be investigated in future studies.

The monitoring for ADRs during the current study indicated good tolerability of aclidinium bromide in a predominantly elderly population. Throat irritation, which is not labelled for Eklira® Genuair®, was reported by 4 patients and may have been caused by the powder inhalation. Overall, our safety data are in line with the safety and tolerability profile of aclidinium bromide reported in clinical 6-week and 12-week studies [13,14]. The limitations of this study are those associated with its observational and non-interventional character, including the lack of a comparator group. Approximately one out of four patients used Eklira® Genuair® as add-on therapy. The use of concomitant medications for COPD may have led to an underestimation in observed treatment effects in these patients as compared to monotherapy use of aclidinium bromide. Selection bias due to loss-to-follow-up cannot be excluded, as the reasons for missed follow-up visits were not documented. However, even if only patients with more severe disease had discontinued the study prematurely, this would not have changed the general trend towards improved symptom severity, because the drop-out rate was low (approximately 8%). Although we used patient-administered questionnaires to measure quality of life as well as symptom prevalence and severity, recall bias may not have been an issue, as patients were capturing their actual condition.

Conclusion

This non-interventional study indicated significant reductions in the frequency of nocturnal awakenings due to COPD, the
severity of nighttime and early-morning symptoms, and the limitation of morning activities, as well as clinically relevant improvements in health-related quality of life under treatment with Eklira® Genuair® in a real-life population with COPD. Beneficial treatment effects were seen in patients with newly diagnosed COPD as well as in patients with a history of COPD or previously treated with another long-acting muscarinic antagonist, although improvements in the patient-reported outcomes were greater in newly diagnosed patients than in patients with previously known COPD. Based on the results of the patients’ therapy assessment and willingness to continue the treatment with Eklira® Genuair® (118), the level of patient satisfaction was high. Taken together, this study supports the usefulness of Eklira® Genuair® for the treatment of COPD in daily clinical practice.

Conflict of interest

Katharina Marth has no conflict of interest.

Elisabeth Schuller is an employee of Almirall GmbH, the study was funded by Almirall GmbH.

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