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The Efficacy, Tolerance and Acceptance of a New Fixed-Dose Salmeterol and Fluticasone Propionate Dry-Powder Inhaler—Salflumix Easyhaler® in COPD Patients in the Daily Clinical Practice

Zbigniew Doniec [1], Magdalena Olszanecka-Glinianowicz [2], Piotr Hantulik [3], Agnieszka Almgren-Rachtan [4] and Jerzy Chudek [5,*]

[1] Department of Pneumonology, Institute of Tuberculosis and Lung Diseases, 34-700 Rabka-Zdró, Poland
[2] Health Promotion and Obesity Management Unit, Department of Pathophysiology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, 40-751 Katowice, Poland
[3] Orion Pharma Poland Co. Ltd., 00-446 Warszawa, Poland
[4] Euromedic Medical Centre, 40-061 Katowice, Poland
[5] Department of Internal Diseases and Oncological Chemotherapy, Faculty of Medical Sciences in Katowice, Medical University of Silesia, 40-027 Katowice, Poland
* Correspondence: chj@poczta.fm

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Abstract: The efficacy of the fix-dose salmeterol/fluticasone propionate combination in chronic obstructive pulmonary disease (COPD) was only shown for the original product. This investigator-initiated study aimed to prove the efficacy and safety of Salflumix Easyhaler®, a second-entry product (dry-powder inhaler) in a real-life setting. The efficacy of the therapy was assessed in 440 COPD outpatients (36.1% classified as C&D groups according to GOLD) using the COPD assessment test (CAT) and the modified Medical Research Council (mMRC). During 86 ± 30 days, the frequency of COPD with a big and very big impact on life (CAT > 20 pts); and high scores of dyspnea (mMRC ≥ 2) decreased from 60.7% and 57.5% at I visit to 15.2% and 22.6% at III visits, respectively ($p < 0.001$). There was a greater improvement in newly diagnosed patients than those who switched from other devices due to insufficient disease control or patient dissatisfaction with the used inhaler. Patients' satisfaction was scored 3.2–3.5 in a 4 pts scale. Physicians scored the burden related to the use of Salflumix Easyhaler® as very low. Adherence exceeded 90%. This study supports effectiveness, satisfaction, and convenience with the use of this new product in COPD, and shows that ICS-containing DPI therapy is still improperly prescribed for patients with a low risk of COPD exacerbation in real-life settings.

Keywords: chronic obstructive pulmonary disease; fix-dose salmeterol/fluticasone propionate combination; generic

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a lung inflammatory disease characterized by unreversible restriction in the airflow. Inflammatory mechanisms are considered as partially preventable causes of accelerated lung aging in patients with COPD [1]. Inhaled bronchodilators (both β2-adrenergic agonists and anticholinergics) are the cornerstone of COPD therapy decreasing the frequency of exacerbations, and improving exercise capacity and health-related quality of life (HR-QoL) [2]. Inhaled corticosteroids (ICS) as anti-inflammatory drugs are recommended by GOLD guidelines in combination with a long-acting β2-adrenoceptor agonist (LABA) in moderate-to-very-severe COPD with repeated exacerbations [2].

A new generic salmeterol and fluticasone propionate fix-combination multidose predispensed dry powder inhaler (DPI), Salflumix Easyhaler® (Orion Pharma, Espoo, Finland),

was approved in 2018 in the European Union (EU) for the therapy of patients suffering from asthma or COPD. It was registered based on an open, single-center, randomized study confirming bioequivalence with the original product developed by GlaxoSmithKline, marketed in the EU as Seretide Diskus® and in the US as Advair Diskus® (patent expired in 2016). This was a pharmacokinetic four-period crossover study that compared the lung deposition and total systemic exposure of the originator and second-entry product after single-dose administration (two inhalations of 50/500 µg/inhalation strength) in 65 fasting healthy volunteers [3].

The efficacy of salmeterol and fluticasone propionate combined therapy was shown in a randomized, double-blind TORCH (towards a revolution in COPD health) trial [4]. This study showed a trend towards improved survival in patients receiving fix-dose combination therapy compared to non-users of ICS and LABA. In addition, there was a significant reduction in rates of exacerbation and forced expiratory volume in one second (FEV1) decline among those treated with the fix-dose combination therapy with moderate-to-severe COPD [4,5]. The combined therapy was associated with an increased risk of non-fatal pneumonia [6], not overweighing the clear clinical benefits.

Salflumix Easyhaler® differs from the original product and other salmeterol and fluticasone propionate generics by the drug delivery system of Easyhaler®, developed by Orion Pharma (Espoo, Finland). This high resistance DPI system offers greater consistency of drug delivery during inhalation sufficiently forceful to de-aggregate the drug powdered into breathable-sized particles [7]. Contrary metered dose inhalers (MDIs) are considered less dependent on a patient's ability to produce airflow than DPIs are; however, patients may have difficulties in coordinating device activation and inhalation, which can be overcome with the use of a spacer (a valved holding chamber) [8]. Of note, hydrofluorocarbons (HFCs) as MDIs propellants are greenhouse gases with a high global warming potential [9]. Therefore, the use of MDIs has environmental consequences.

Since Salflumix Easyhaler® launching in Poland in 2018, it was the first study assessing the efficacy and safety of this medical product. This study aimed to assess firstly, effectiveness and secondly, tolerance of Salflumix Easyhaler® when given as a first ICS/LABA combination in already treated and newly diagnosed patients with COPD in real-life settings. In addition, this study assessed patients' satisfaction, errors, and burden related to its use, adherence, as well as physicians' perception of this product's overall use.

2. Materials and Methods

It was a post-authorization, non-interventional, multicenter, investigator-initiated study—IIS (EU PAS 36156) of the Salflumix Easyhaler® (Orion Pharma, Espoo, Finland) used in everyday clinical practice, involving outpatients with COPD, carried out between July 2020 and May 2021. In this prospective study, 220 pulmonologists (study investigators) enrolled 440 patients, assessed during 3 subsequent appointments with approximately 6-week intervals. The inclusion criteria for COPD patients were: adult patient with COPD and recently initiated (from 2 to 8 weeks) therapy with Salflumix Easyhaler® as a first fixed-dose DPI. This IIS did not meet the criterion of a medical experiment; therefore, not requiring a bioethical committee. Only anonymized data were processed during the implementation of the project.

The project was supported by an observational card. The collected set of data included the diagnosis and control of COPD (according to GOLD 2020 criteria [6]); the modified Medical Research Council (mMRC) scale; prescribed Salflumix Easyhaler® dose and COPD co-medication, comorbidities, and their pharmacotherapy; reported patients' satisfaction; adherence and AEs (with eventual relation to the assessed DPI). In addition, physicians scored efficacy, application, the burden of treatment, and adverse drug reactions (ADRs) related to the assessed DPI. Changes in the prescribed doses of salmeterol and fluticasone propionate during the study conduct were reported. Assessments were repeated at subsequent doctor's appointments.

During the initial visit, patients were reinstructed with the appropriate application of Salflumix Easyhaler®, and the patient information leaflet was used to address reported difficulties with the usage of the DPI.

2.1. Assessment Tools

The study implemented standardized and validated tools assessing changes in COPD burden (COPD assessment test—CAT, modified Medical Research Council scale—mMRC), and subjective scales for inhalation therapy scoring.

CAT is a questionnaire for people with COPD designed to measure the impact of COPD on a patient's life and how this changes over time. It is a preferred measure of the symptomatic impact of COPD in clinical assessment schemes since 2013, included in the GOLD 2000 guidelines [2].

The mMRC was used as a simple and standardized method of categorizing disabilities related to COPD [10]. In this questionnaire, a patient selects a grade on a 5-point scale (rating of 0–4) that describes everyday situations or activity levels provoking breathlessness and impairment.

Subjective patients' satisfaction with the use of Salflumix Easyhaler® was scored as: not sufficient, satisfactory, good, and very good.

Physicians' subjective assessment of the current inhalation therapy with Salflumix Easyhaler® was based on questions concerning 4 domains: its efficacy, application of DPI—Salflumix Easyhaler®, the burden of treatment, and ADRs. The questions are presented in the result section) Answers were provided on a linear scale from 1 to 7, where: strongly disagree (1), neutral (4), and strongly agree (7).

2.2. Data Analysis

The efficacy of therapy was scored as the percentage of patients obtaining a small and an average impact of COPD on life (CAT $\leq$ 20 points), and those with at least 2 points decrease since the initial assessment. In addition, effectiveness was analysed as the percentage of patients without high scores of dyspnea (mMRC $\geq$ 2 points) at the subsequent visits.

Patients obtaining $\leq$2 points in the MAQ (medication adherence questionnaire) were scored as compliant with the use of Salflumix Easyhaler®.

Safety data (reported AEs during the study conduct) were analyzed by the pharmacovigilance team, addressing their relation to the use of Salflumix Easyhaler®.

2.3. Study Flow

Seven patients were lost to follow up and two stopped the treatment (0.45% of all enrolled). Finally, nine subjects were excluded from the analysis of the efficacy of COPD management. The safety data were calculated for all the enrolled patients (N = 440).

2.4. Statistical Analysis

Analyses were performed using the STATISTICA 11.0 PL (TIBCO, Palo Alto, CA, USA). Data were expressed as mean values with standard deviations or percentages. The χ^2 test, χ^2 for trend, and ANOVA were used as appropriate to compare variables within the group and subgroups. A *t*-test was used to compare differences in variability of the continuous variables between subgroups. A "*p*" value < 0.05 was scored as statistically significant.

3. Results

3.1. Study Group Characteristics

There were 440 patients with COPD (mean age 63.6 $\pm$ 11.5 years). One-hundred-seventy-three (39.3%) of them were newly diagnosed. According to the ABCD classification, patients with a high risk of exacerbation (C&D) constituted 36.1% of the study group, and 46.9% of the subgroup was switched to Salflumix Easyhaler®. Within the last 12 months, a history of disease exacerbation was noted at 67.7% and hospitalization in 13.9% of the whole group (Table 1).

Table 1. Characteristics of 440 COPD, newly diagnosed, and switched that recently commenced therapy with Salflumix Easyhaler®.

	All Patients [N = 440]	Newly Diagnosed [N = 173]	Switched [N = 267]	*p*
Sex:				
Women [N; %]	174; 39.5	72; 41.6	102; 38.2	0.47
Men [N; %]	266; 60.5	101; 58.4	165; 61.8	
Age [years]	63.6 ± 11.5	60.0 ± 11.1	66.1 ± 11.1	<0.001
>65 years old [N; %]	214; 48.6	59; 34.1	155; 58.1	<0.001
Place of residence:				
City [N; %]	296; 67.3	124; 71.7	172; 64.4	0.11
Village [N; %]	144; 32.7	49; 28.3	95; 35.6	
Education:				
Primary [N; %]	75; 17.0	22; 12.7	53; 19.9	<0.001
Vocational [N; %]	176; 40.0	54; 31.2	122; 45.7	
Secondary [N; %]	144; 32.7	74; 42.8	70; 26.2	
Higher [N; %]	45; 10.2	23; 13.3	22; 8.2	
Professional activity:				
Intellectual worker [N; %]	109; 24.8	58; 33.5	51; 19.1	<0.001
Physical worker [N; %]	116; 26.4	55; 31.8	61; 22.8	
Unemployed [N; %]	8; 1.8	5; 2.9	3; 1.1	
Pension or retired [N; %]	207; 47.0	55; 31.8	152; 56.9	
ABCD GOLD 2020 classification:				
Group A [N; %]	120; 27.3	74; 42.8	46; 17.2	<0.001
Group B [N; %]	161; 36.6	65; 37.6	96; 36.0	
Group C [N; %]	78; 17.7	25; 14.5	53; 19.9	
Group D [N; %]	81; 18.4	9; 5.2	72; 27.0	
COPD exacerbations in the last 12 months [N; %]	298; 67.7	96; 55.5	202; 75.7	<0.001
The number of exacerbations per patient [N]	2.0 ± 1.5	1.7 ± 1.0	2.2 ± 1.6	0.003
Hospitalization for COPD in the last 12 months [N; %]	61; 13.9	20; 11.6	41; 15.4	0.26
The number of hospitalizations per patient [N]	1.3 ± 0.9	1.2 ± 0.4	1.4 ± 1.0	0.44
Indication to switch to Salflumix Easyhaler®:				
Insufficient control of the disease [N; %]	-	-	182; 68.2	-
Patients' dissatisfaction from the previous device [N; %]	-	-	85; 31.8	-
Dose of Salflumix Easyhaler®:				
50/250 µg twice daily [N; %]	169; 38.4	81; 46.8	88; 33.0	0.004
50/500 µg twice daily [N; %]	271; 61.6	92; 53.2	179; 67.0	
Duration of Salflumix Easyhaler® use:				
2–4 weeks [N; %]	398; 90.5	162; 93.6	236; 88.4	0.07
5–8 weeks [N; %]	42; 9.5	11; 6.4	31; 11.6	
Other currently used medication for COPD [N; %]	175; 39.8	42; 24.3	133; 49.8	<0.001
Comorbidity:				
Hypertension [N; %]	122; 27.7	35; 20.2	87; 32.6	<0.01
Coronary artery disease [N; %]	33; 7.5	6; 3.5	27; 10.1	0.01
Heart failure [N; %]	16; 3.6	4; 2.3	12; 4.5	0.23
Heart arrhythmias [N; %]	12; 2.7	4; 2.3	8; 3.0	0.67
Past stroke [N; %]	3; 0.7	1; 0.6	2; 0.7	0.83
Type 2 diabetes [N; %]	40; 9.1	14; 8.1	26; 9.7	0.56
Cancer [N; %]	3; 0.7	0	3; 1.1	-

Before the initial visit, patients were using Salflumix Easyhaler® twice daily for 2 to over 8 weeks. A larger dose (50 µg + 500 µg) was prescribed in 61.6% of all the patients, 53.2 newly diagnosed, and 67.0% switched to Salflumix Easyhaler®. Other medications for COPD were used by 39.8% of the patients (mostly switched to Salflumix Easyhaler®), including anticholinergics (ipratropium bromide or tiotropium bromide) and short-acting beta-2 agonists (salbutamol) as the most frequently prescribed medications.

Insufficient disease control was reported as a twice more frequent cause to switch to Salflumix Easyhaler® than patients' dissatisfaction with a previously used inhaler (Table 1).

3.2. Efficacy

The analysis covered 86 ± 30 days of Salflumix Easyhaler® exposure from the first to the third visit. At the first visit, 0.7% of patients had a small (CAT < 10 pts) and 38.6% had an average (CAT 10–20 pts) impact of the disease on life. Salflumix Easyhaler® use decreased the impact of the disease on life. The percentage of patients with a small and an average impact of the disease on life increased to 18.5% and 66.3%, respectively, on the third visit (Table 2). In parallel, the frequency of the disease with a big and very big impact on life (CAT > 20 pts) decreased from 60.7% at the first visit to 15.2% at the third visit. Concordantly, the percentage of subjects with high scores of dyspnea (mMRC ≥ 2) decreased from 57.5% to 22.6% ($p < 0.001$). In addition, the frequency of exacerbations from the previous visit decreased from the 8.4% reported on the second visit to 4.2% on the third visit ($p < 0.01$). From the first to the third visit, any exacerbation was reported in 45 patients (10.2%)—allowing for a rough estimation of the exacerbation rate during 12 months at 43.2% (by multiplying by a factor of 4.24 obtained by dividing 365 days by 86). Hospitalizations due to COPD exacerbation were rare (Table 2).

Table 2. Changes in the control of COPD during 3 visits (86 ± 30 days) in patients treated with Salflumix Easyhaler®.

	VISIT			
	I	**II**	**III**	**χ^2/ANOVA**
	[N = 440]	**[N = 439]**	**[N = 433]**	***p* Value**
Salflumix Easyhaler@ dose:				
50/250 µg twice daily [N; %]	169; 38.4	210; 47.8	219; 50.6	<0.001
50/500 µg twice daily [N; %]	271; 61.6	229; 52.2	214; 49.4	<0.001
COPD assessment test (CAT) [pts]	21.5 ± 5.3	16.1 ± 5.6	14.5 ± 5.2	<0.001
At least 2 pts decrease [N; %]	-	336; 76.5	377; 87.1	<0.001
Little impact on life (< 10 pts) [N; %]	3; 0.7	60; 13.7	80; 18.5	<0.001
Average impact on life (10-20 pts) [N; %]	170; 38.6	282; 64.2	287; 66.3	
Big impact on life (21-30 pts) [N; %]	248; 56.4	97; 22.1	66; 15.2	
Very big impact on life (> 30 pts) [N; %]	19; 4.3	0	0	
COPD exacerbation [N; %]		37; 8.4	18; 4.2	-
Hospitalizations due to exacerbation [N; %]		3; 0.7	0	-
Modified Medical Research Council (mMRC) scale [pts]	1.6 ± 1.0	1.1 ± 1.0	0.8 ± 0.9	<0.001
mMRC < 2 pts [N; %]	187; 42.5	294; 67.0	335; 77.4	<0.001
mMRC ≥ 2 pts [N; %]	253; 57.5	145; 33.0	98; 22.6	<0.001
Compliance—MAQ ≤ 2 pts [N; %]	411; 93.4	436; 99.3	433; 100	0.08

COPD—chronic obstructive pulmonary disease; MAQ—medication adherence questionnaire; mMRC—modified Medical Research Council scale.

During the study period, the prescription of larger doses of Salflumix Easyhaler® was steadily decreasing from 61.6% to 49.4% ($p < 0.001$)—Table 2.

A greater percentage of patients with a big and very big impact on life (CAT > 20 pts) was found among those receiving large drug doses than in those with a small or an average impact on life (64.2% for 50 µg + 500 µg vs. 55.0% for 50 µg + 250 µg; $p = 0.06$).

In the subgroup analysis, a big and very big impact on life (CAT > 20 pts) at the first visit was more frequent in patients previously treated for COPD than in newly diagnosed ones (69.8% vs. 50.9%; $p < 0.001$), corresponding to a greater percentage of individuals with high scores of dyspnea (mMRC $\geq$ 2) among those previously treated (68.6% vs. 43.9%)—Table 2.

During the study period, a decrease in the impact of COPD on life was observed in both subgroups (Figure 1). At the third visit, only 19.9% of previously treated subjects and 9.4% of newly diagnosed reported a big impact of the disease on life, with no patients reporting a very big impact of the disease on life. In parallel, the percentage of subjects with high scores of dyspnea (mMRC $\geq$ 2) decreased from 69.8% to 27.8% ($p < 0.001$) in previously treated subjects and from 50.9% to 11.8% ($p < 0.001$) in newly diagnosed patients.

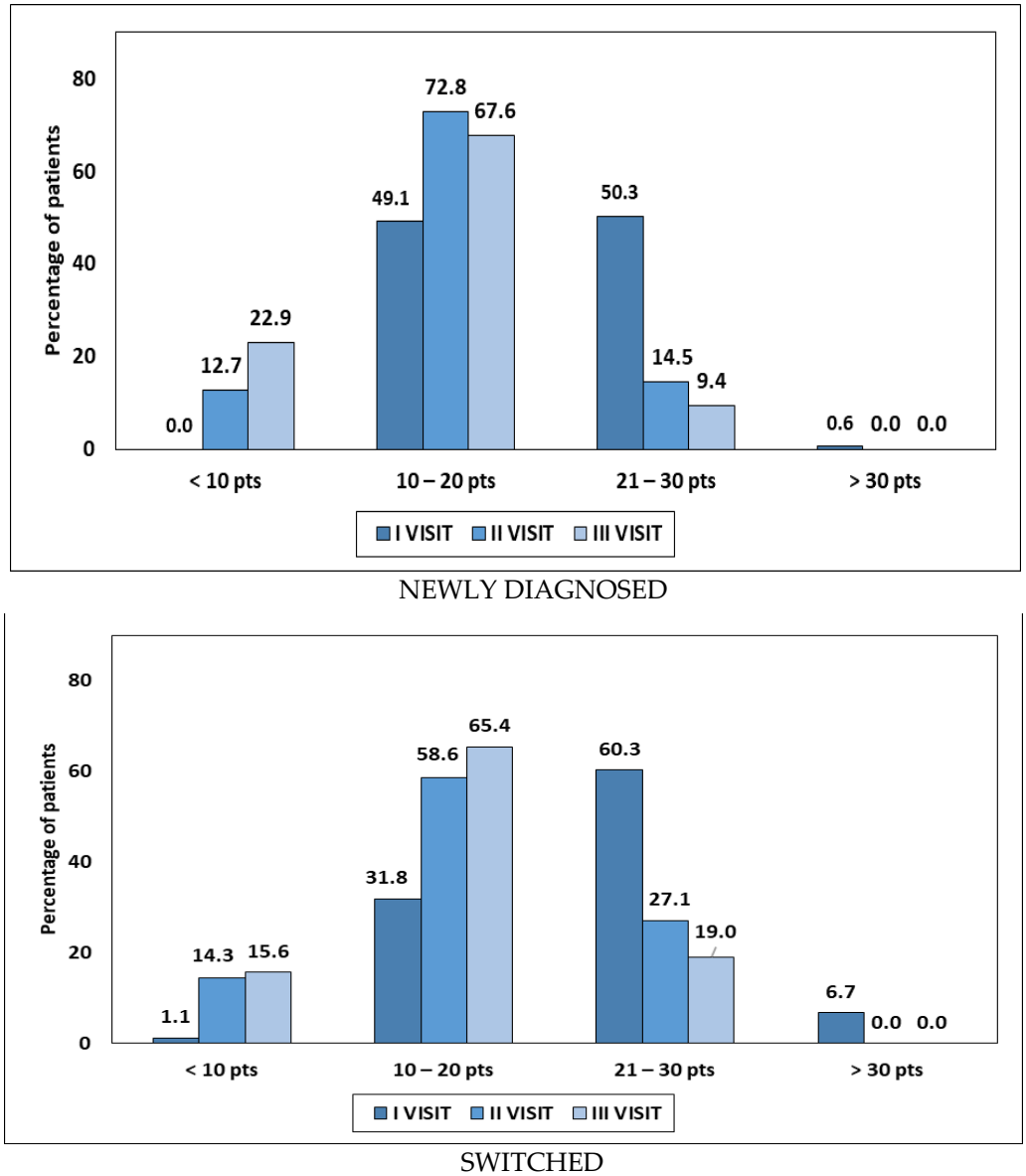

Figure 1. COPD assessment test (CAT) obtained across 3 visits in the subgroups of newly diagnosed and switched from other inhalators ($p < 0.001$; χ^2 for trend).

3.3. Subjective Patients' Satisfaction

An average subjective patient satisfaction with the use of the assessed DPI was scored for 3.2 ± 0.7 pts and was improving with time. On the third visit, it was scored 3.5 ± 0.6 pts. No difference between newly diagnosed and switched COPD patients was noted (data not shown).

3.4. Compliance

The compliance rate increased from 93.4% to 100% across the visits (Table 2), without a difference between the previously treated and newly diagnosed patients (data not shown).

3.5. Physician Assessment of Salflumix Easyhaler® Therapy

The therapy of COPD with the evaluated DPI was scored as effective (5.8 ± 1.1 pts), not generating technical problems (6.0 ± 1.1 pts) and burden (6.0 ± 1.1 pts.) for the patients, and rarely ADRs at the first assessment. The scores were increased during reassessments (Table 3).

Table 3. Patients' and physicians' assessment of the use of Salflumix Easyhaler@.

	VISIT			ANOVA	
	I	II	III	*p* Values	
	[N = 440]	[N = 439]	[N = 433]	II vs. I	III vs. I
Patient's satisfaction with use of the DPI [pts]	3.2 ± 0.7	3.4 ± 0.7	3.5 ± 0.6	<0.001	<0.001
Physician's assessment [pts]:					
The applied therapy is effective.	5.8 ± 1.1	6.0 ± 0.9	6.4 ± 0.8	<0.001	<0.001
The patient has no problems with the correct use of the inhaler [pts].	6.0 ± 1.1	6.2 ± 0.9	6.5 ± 0.7	0.001	<0.001
The treatment does not affect the patient's feeling of being burdened with treatment [pts].	6.0 ± 1.1	6.2 ± 0.9	6.4 ± 0.8	0.01	<0.001
Treatment-related AEs are rare [pts].	6.2 ± 1.0	6.3 ± 0.9	6.5 ± 0.9	0.33	<0.001

AEs—adverse events; DPI—dry powder inhaler.

3.6. Adverse Events Assessed as Related to Salflumix Easyhaler®

Only one of the AEs of throat irritation, assessed as related to the use of the evaluated DPI, was reported. Two patients discontinued the treatment, one due to the occurrence of AEs and the second due to clinical improvement with no feeling of the need for therapy continuation.

4. Discussion

The performed IIS shows that COPD patients prescribed with the second entry product—Salflumix Easyhaler®, a new DPI on the Polish market—achieved clinical improvement in the daily clinical settings. The study enrolled both newly diagnosed and recently switching from other devices, mostly due to the therapy's ineffectiveness. During the 86 days period of therapy, the percentage of patients with a big and very big impact on life (CAT > 20 pts) decreased from 60.7% to 15.2% at the third visit, and a significant improvement (at least 2 pts decrease in CAT) was noted in 87.1% of the study cohort. Concordantly, the percentage of subjects with high scores of dyspnea (mMRC $\geq$ 2) decreased from 57.5% to 22.6%. Exacerbations from the first to the third visit were reported in 10.2% of patients.

It is hard to compare the obtained data with the TORCH trial [4]. Our study was designed to analyze survival and FEV1 decline. Moreover, the analysis of the reduction in the rate of exacerbation is difficult due to the short period of follow-up. Proportionally converting the frequency of exacerbations from 86 days to a year, we may suppose a

reduction rate from 67.7% during the last 12 months prior to the initiation of the therapy with Salflumix Easyhaler® to approximately 43.2% during its use.

The decreasing frequency of exacerbation was reflected by the increased percentage of patients with CAT ≤20 pts during the subsequent visits. This supports the efficacy of Salflumix Easyhaler®. Concordantly, as much as 87.1% of the study patients had a significant decrease in the CAT score (at least 2 pts). We also used the mMRC dyspnea scale as widely used to assess symptom burden in COPD, showing a decline in the percentage of patients with dyspnea (mMRC ≥ 2) to 22.6% at the third visit. The observed improvement was caused mostly by the escalation of therapy. The analysis of the effect of DPI substitution was not possible among the patients who switched from the other inhalers as data concerning prescribed doses of inhaled medications before the commencement of Salflumix Easyhaler® were not collected.

Of note, in only 5.2% of highly symptomatic, newly diagnosed patients at a high risk of future exacerbations (GOLD D), ICS/LABA should be considered as initial therapy, according to the current GOLD strategy [2]. Our finding supports previous evidence that ICS-containing DPI therapy is prescribed for patients across all GOLD classes in real-life settings [11]. Such overuse of ICS-containing therapy may expose to the unnecessary risk of pneumonia. Older age (>65 years old), low FEV1 (<50% of the predicted value), higher dose, and long-time ICS use were identified as the risk factors in one of the most recent meta-analyses [12]. In our study, one-third of patients had an increased risk related to an older age.

An increased risk of non-fatal pneumonia was shown over a decade ago in the registration study of the fix-dose combination therapy with salmeterol and fluticasone propionate [6]. Surprisingly in our study, no episode of pneumonia related to the use of Salflumix Easyhaler® was reported. However, this does not entitle the conclusion that the second-entry product does not increase the risk of pneumonia. It is rather a problem of reporting methodology and probably the perception of infections by doctors as related not only to the nature of the disease *per se*, but also, at least partially, to the therapy. As a consequence, the incidence of pneumonia (bronchopneumonia) in real-life registries is much lower than in clinical trials [13]. The problem to capture pneumonia events also exists in COPD trials. More stringent criteria for pneumonia diagnosis results in lower reported incidence rates of the disease [14]. We also cannot exclude that the lack of episodes of pneumonia during a relatively short period of observation was affected by the increased sanitary restrictions preventing the spreading of various infections during the COVID-19 pandemic when this study was carried out.

An important issue is the correct use of DPIs by COPD patients. Of note, Salflumix Easyhaler® was favorably rated both by patients and their physicians, regardless of previous use of other devices. In the opinion of pulmonologists, this DPI generates neither technical problems, nor a burden for the majority of patients. Moreover, in the previous clinical studies, the correct use of Easyhaler® was less dependent on patients' hand-breath coordination than on pressurized metered-dose inhalers [7]. In addition, higher consistency of drug dose delivery was shown in comparison to the other DPIs [15], which could translate into the high treatment efficacy and over 90% adherence observed in our study.

Study Limitations

The lack of FEV1 tracking by spirometry and a short period of Salflumix Easyhaler® use should be mentioned as the main study limitations for the assessment of the efficacy. The study questionnaire included the possibility to enter FEV1 measures during all three visits; however, less than 20% of patients had more than one measurement precluding the performance of the analysis in everyday clinical practice. The GOLD guidelines recommend spirometry reassessment not less than once a year during the follow-up of COPD patients; however, the COVID-19 pandemic could cause an even lower frequency of assessments. In addition, we neither assessed HR-QoL, nor collected data concerning the doses for previously used inhalers. We would like to acknowledge that the study was performed

during the COVID-19 pandemic with sanitary restrictions, which might affect the rates of varied infections, including pneumonia.

5. Conclusions

This study supports effectiveness, satisfaction, and convenience with the use of this new product in COPD, and shows that ICS-containing DPI therapy is still improperly prescribed for patients with a low risk of COPD exacerbation in real-life settings.

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Institutional Review Board Statement: According to the local regulations confirmed in the opinion of the legal office, the monitoring of efficacy and safety of registered drugs used in line with the summary of product characteristics does not require the permission of the bioethics committee. Information on post-authorization studies that are not clinical trials (i.e., outside the scope of Directive 2001/20/EC) should be registered in the EU PAS provided by the European Medicines Agency (EMA). The registration number: EU PAS 36156.

Informed Consent Statement: Consent for the collection and the use of anonymized data was obtained from each study participant.

Data Availability Statement: The datasets are available from the EUROMEDIC on a reasonable request (agnieszka@euromedic.edu.pl).

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Conflicts of Interest: Z.D. and M.O.-G. as medical consultants received honorariums for the study design. A.A.-R. is the Director of the Department of Pharmacovigilance. J.C. received an honorarium for data analysis and manuscript drafting. An Orion Pharma representative (PH) the Director of Medical Affairs, didn't received honorarium for the study participation.

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