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ORIGINAL RESEARCH

Real-World Effectiveness and Safety of Single Inhaler Triple Therapy with Beclometasone/ Formoterol/ Glycopyrronium in Moderate to Severe Asthma: TriMaximize Study

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Purpose: To collect prospective data from asthma patients treated with medium- (87/5/9µg) or high-strength (172/5/9µg) extrafine single-inhaler beclometasone dipropionate/formoterol fumarate/glycopyrronium (BDP/FF/G, Trimbow®) in a real-world setting.

Patients and Methods: TriMaximize is a non-interventional, prospective, multicenter study conducted in eight European countries (enrollment: 2021–2024). The primary objective was to describe patient characteristics and therapy pathways for adult patients with moderate to severe asthma treated with BDP/FF/G for up to 36 months. Assessments included demographic/clinical characteristics, pulmonary parameters, treatment pathways, asthma control measured by asthma control test (ACT), and health-related quality of life (HrQoL) measured by Mini Asthma Quality of Life Questionnaire (Mini-AQLQ).

Results: In total, 1,445 patients (62.8% female; mean age: 57.6 years) were included. Before medium-strength BDP/FF/G initiation, 75.7% of the patients received a fixed ICS/LABA combination. Most patients starting with high-strength BDP/FF/G received fixed ICS/LABA (52.9%) or free ICS/LABA/LAMA (43.2%) combinations as prior therapy. Throughout the study, 87.1% of the patients remained on BDP/FF/G. At month 12, fewer patients (12.4%) used systemic corticosteroids (SCS) compared to baseline (33.2%). Use of rescue medication declined from 6.1 (baseline) to 3.6 puffs/week (month 12). During the first year, 79.5% of the patients experienced neither exacerbations nor used SCS. Three-component clinical remission was achieved in 45.6% (first year) and 59.3% (second/third year) of the patients. Four-component clinical remission was accomplished in 39.5% (first year) and 47.9% (second/third year). Improvements in asthma control (mean ACT change at month 12: 3.9; month 36: 4.8, $p<0.0001$) and HrQoL (mean Mini-AQLQ change at month 12: 0.8; month 36: 0.9, $p<0.0001$) exceeded the respective minimal clinically important differences. Forced expiratory volume in 1 second increased by 142 mL after 12 months ($p<0.0001$).

Conclusion: Extrafine, single-inhaler BDP/FF/G therapy was effective and safe in a routine clinical practice setting in a multinational cohort of patients with moderate to severe asthma.

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Introduction

The overall goals of asthma therapy are to minimize asthma symptoms, maximize lung function, and prevent asthma exacerbations, regardless of disease severity. Despite treatment with inhaled corticosteroids (ICS) and long-acting beta2-adrenergic agonists (LABA) treatment, 35% to 45% asthma patients remain uncontrolled.[1,2] These patients may experience significant symptoms, including, for instance, nocturnal awakenings or interference with their daily activities. To further investigate the causes of inadequate treatment outcomes, it is essential to monitor asthma patients' therapy pathways in real-world settings.

Based on the Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention report, asthma treatment should be continuously reviewed and adjusted based on clinical assessment, symptoms, patients' preferences, and side effects.[3] Treatment is escalated in a stepwise manner to control symptoms and to prevent exacerbations, according to the approach recommended by GINA.[3] While many patients achieve adequate symptom control with fixed-dose ICS/LABA combination therapy, a subset remains insufficiently controlled on dual therapy. In such cases, the addition of a long-acting muscarinic antagonist (LAMA) has been demonstrated to further improve lung function and reduce exacerbation frequency.[3] LAMA modulate bronchial muscle tone and may also mediate their effect by reducing mucus hypersecretion present in asthma.[4,5] Consequently, current clinical guidelines recommend triple therapy (ICS/LABA/LAMA) for patients that are insufficiently controlled on dual therapy (ICS/LABA). However, its effectiveness on changes in patients' symptom burden and quality of life, adherence and clinical outcomes have not been assessed in a real-world clinical setting yet.

A currently available fixed triple (ICS/LABA/LAMA) inhaler product with an, extrafine formulation is beclometasone dipropionate/formoterol fumarate/glycopyrronium (BDP/FF/G, Trimbow®, Chiesi Farmaceutici S.p.A). The rationale for using this, extrafine formulation (containing particles with mass median aerodynamic diameter of less than 2 μm) is based on its ability to deliver medication more effectively to both large and small airways, which may improve asthma control compared to standard formulations.[6–10] Inflammatory and functional changes at the level of the most peripheral airways strongly contribute to the complexity and heterogeneous manifestations of asthma.[9] This characteristic is particularly relevant for patients who remain uncontrolled despite ICS/LABA therapy, as small airway involvement is a recognized contributor to persistent symptoms.[11–15] This product is currently available as a pressurized metered dose inhaler (pMDI) in two dosage strengths - medium and high (MS: 87/5/9 μg; HS: 172/5/9 μg) – both of which were investigated in the present study.

The rationale for conducting the TriMaximize study was to address the absence of sufficient real-world evaluations concerning the usage and the clinical benefits of BDP/FF/G in asthma patients. To this end, this non-interventional multi-national study collected prospective, longitudinal data from patients with moderate to severe asthma treated with MS BDP/FF/G or HS BDP/FF/G as per its current authorized indication. Data were collected on patient characteristics and their treatment pathways upon treatment with BDP/FF/G in a real-world setting. In addition, to complement data on prior randomized trials, treatment effectiveness was assessed via various clinical parameters. Lastly, it was evaluated whether an extrafine single-inhaler triple therapy (efSITT) would lead to improved adherence and better clinical outcomes compared to previous treatments.

Material and Methods

Study Population and Design

TriMaximize is a multicenter, prospective, non-interventional study that was conducted in eight European countries (Austria, Denmark, France, Germany, Italy, Poland, Spain, and United Kingdom) at 162 sites. Depending on the country, enrolment of patients started in 2021 (Austria, Denmark, Germany, United Kingdom), 2023 (France, Spain), or 2024 (Italy, Poland). As stipulated by the protocol's inclusion/exclusion criteria, adult patients who gave written informed consent and with a confirmed diagnosis (according to physicians clinical decision) of moderate to severe asthma (with or without concomitant COPD) were enrolled. Information on the number of patients who declined participation was not

collected. Participants could be enrolled if they were prescribed a fixed combination of BDP/FF/G in either medium (MS: 87/5/9 µg) or high strength (HS: 172/5/9 µg) by their treating physician — according to the approved indication as per the current version of the Summary of Product Characteristics and independent of their study participation. This involves switching from a medium dose of ICS as previous treatment (before enrolment in the study) to MS BDP/FF/G (treatment during the study) or from a high dose of ICS as previous treatment to HS BDP/FF/G (in addition to LABA, respectively). However, HS BDP/FF/G did not become available on the market until 1.5 years after study start. Therefore, the number of enrolled patients with HS BDP/FF/G was smaller than anticipated. Patients with a previous (within 30 days before enrolment) or planned participation (during observational period) in an interventional clinical trial could not be enrolled in this study. No patient was treated with BDP/FF/G in the 12 months before the baseline examination.

During the study, follow-up observations were planned 3 months (for all countries but Spain), 6 months, 9 months (only for Germany, Poland, and the UK), and 12 months after the baseline examination taking into account local clinical practice. Patients enrolled in Germany were observed for additional two years with follow-up observations every 6 months, ie 18, 24, 30 and 36 months after baseline.

This study was conducted in accordance with the most recent version of the Declaration of Helsinki.[16] In each country, this study was approved by a responsible ethics committee. Prior to participation, all patients provided written informed consent.

This study was funded by Chiesi, which was involved in the study design, data collection, planning of statistical analyses and supervision of the report.

Study Objectives and Data

The primary objective of this study was to describe patient characteristics and therapy pathways for patients with a diagnosis of moderate to severe asthma who were treated with (MS and HS) BDP/FF/G in real world practice. Secondary objectives included the assessment of asthma control, health-related quality of life (HrQoL), treatment adherence, exacerbations, pulmonary parameters, and the use of previous and concomitant medication during the study. To this end, baseline characteristics such as demographics and medical history as well as treatment history from the 12 months before baseline were gathered from participants' medical records. During the study, participants gave information, among others, on therapy changes regarding BDP/FF/G, use of other asthma medication and rescue medication, treatment with SCS, and occurrence of exacerbation. Exacerbations which required an increased broncho-dilator rescue use for at least two days (≥ 4 puffs/day) were categorized as moderate, while those treated with SCS for a least three days or leading to an emergency room visit or hospitalization were categorized as severe.[7]

To evaluate asthma control and HrQoL, data from two validated questionnaires were utilized: the Asthma Control Test (ACT) and the short version of the Asthma Quality of Life Questionnaire (Mini-AQLQ), provided these assessments were conducted as part of routine clinical practice. The ACT questionnaire[17,18] consists of five questions with a 5-point scale concerning the patient's asthma symptom burden (score ranging from 5 to 25, with higher scores reflecting greater asthma control). An ACT score of ≥ 20 indicates well-controlled asthma, a score of 16–19 indicates partly controlled asthma, and a score of ≤ 15 indicates uncontrolled asthma. The Mini-AQLQ questionnaire assesses a patient's HrQoL and consists of 15 questions covering four domains: symptoms, activities, emotions, and environment.[19] Each item is scored from 1 (severely impaired) to 7 (not impaired at all). An overall score and four subscale scores for each domain can be calculated. The overall score and subscale scores range from 1 to 7. Patient adherence to treatment was evaluated using the 12-item Test of Adherence to Inhalers (TAI) questionnaire.[20] The questionnaire comprises ten items answered by the patient and two items answered by the patient's physician. The patient domain summary score (TAI-10 score) ranges between 10 (worst possible score) and 50 (best possible score). A TAI-10 score of 50 is considered as good adherence, a score between 46 and 49 as medium adherence, and a score of ≤ 45 reflects poor adherence. The TAI questionnaire was not used in Denmark since no validated Danish version was available.

The results of pulmonary function tests (spirometry/body plethysmography) were documented if performed as part of clinical routine, including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), peak expiratory flow (PEF), specific total airway resistance (sRtot), and the ratio of residual volume to total lung capacity (RV/TLC, a parameter assessing static hyperinflation).

Safety was evaluated throughout the study in accordance with regulatory requirements. Adverse events, special cases (eg off-label use or lack of therapeutic effect) and laboratory data were gathered in detail.

Statistical Analysis

Patients were excluded from the analysis in case of missing essential baseline characteristics (age, sex), insufficient information on prior asthma therapy, an off-label switch at BDP/FF/G initiation, or no documentation of BDP/FF/G treatment during the study.

Patients were grouped according to their BDP/FF/G treatment until the first break/discontinuation: 1) patients with MS BDP/FF/G only, 2) patients with HS BDP/FF/G only during the study. Moreover, only visits during in-label treatment with BDP/FF/G were taken into account, ie any visit with a switch from MS to HS BDP/FF/G and all subsequent visits were excluded from the analysis.

The following prior treatment groups (before start of BDP/FF/G) were defined: 1) fixed and free combinations of ICS/LABA/LAMA and 2) fixed and free combinations of ICS/LABA.

"ACT response" or "Mini-AQLQ response" was defined as a change between baseline and a follow-up visit that exceeded the respective minimal clinically important difference (MCID): ≥ 3 points for ACT or ≥ 0.5 points for Mini-AQLQ.[21] Patients were classified as "TAI-10 responders", if adherence improved from baseline to a follow-up visit, or if patients showed "good adherence" both at baseline and the follow-up visit.

The achievement of "clinical remission" was determined at the end of the 1st year and at the end of the follow-up period (2nd/3rd year): Two component clinical remission (2-CR) was defined as follows:[22] no exacerbations, no use of SCS. Three component clinical remission (3-CR) was defined as follows:[22] no exacerbations, no SCS use, ACT score ≥ 20. Four component clinical remission (4-CR) was defined as: no exacerbations, no SCS use, ACT score ≥ 20, plus one additional lung function criterion. Four different lung function criteria for 4-CR analysis were explored:[22] (1) improvement in FEV_1 or decline in FEV_1 of no more than 5 percentage points of the predicted value (ie, FEV_1 decline ≤ 5% predicted), (2) actual FEV_1 ≥ 80% of the predicted value, (3) FEV_1 decline ≤ 5% predicted or actual FEV_1 ≥ 80% of the predicted value, (4) improvement in FEV_1 by ≥ 100 mL. To ensure that clinical remission was not only achieved because of concomitant treatment with biologics, patients with an intake of biologics during the follow-up period were excluded for this analysis.

The Global Lung Initiative's (GLI) reference equations[23,24] were used to calculate the predicted values for FEV_1, FVC, and RV/TLC. Additionally, lung function parameters outside of pre-defined plausibility ranges (see Supplemental Table 1) were treated as missing values.

All variables were analyzed descriptively for the total population and also stratified by BDP/FF/G strength (MS and HS) and treatment groups. For lung function parameters and questionnaire scores, changes from baseline were calculated for each follow-up visit. Paired t-tests were used to assess the differences within groups. Categorical data was assessed using Chi-Squared-test. A p-value smaller than 5% was considered to be statistically significant.

All analyses were performed using SAS (version 9.4).

Results

Baseline Data

In total, 1,599 patients provided their written informed consent and were screened (Figure 1). The distribution of patients by country is presented in Supplemental Table 2. 154 patients were excluded due to various reasons, resulting in 1,445 patients being included in the final analysis.

Overall, 964 patients (66.7%) completed (at least) the 12-month follow-up period, and 536 patients (55.1%) participated in the additional observational period for up to two more years. Patients treated with HS BDP/FF/G participated in the study for no more than 18 months, due to the later availability of the HS formulation. Consequently, data for the time periods between month 24 (n=281) and month 36 (n=63) were only available for patients treated with MS BDP/FF/G.

On average, patients were 57.6 years of age and 62.8% were female (Table 1). Further demographics and clinical characteristics are described in Table 1.

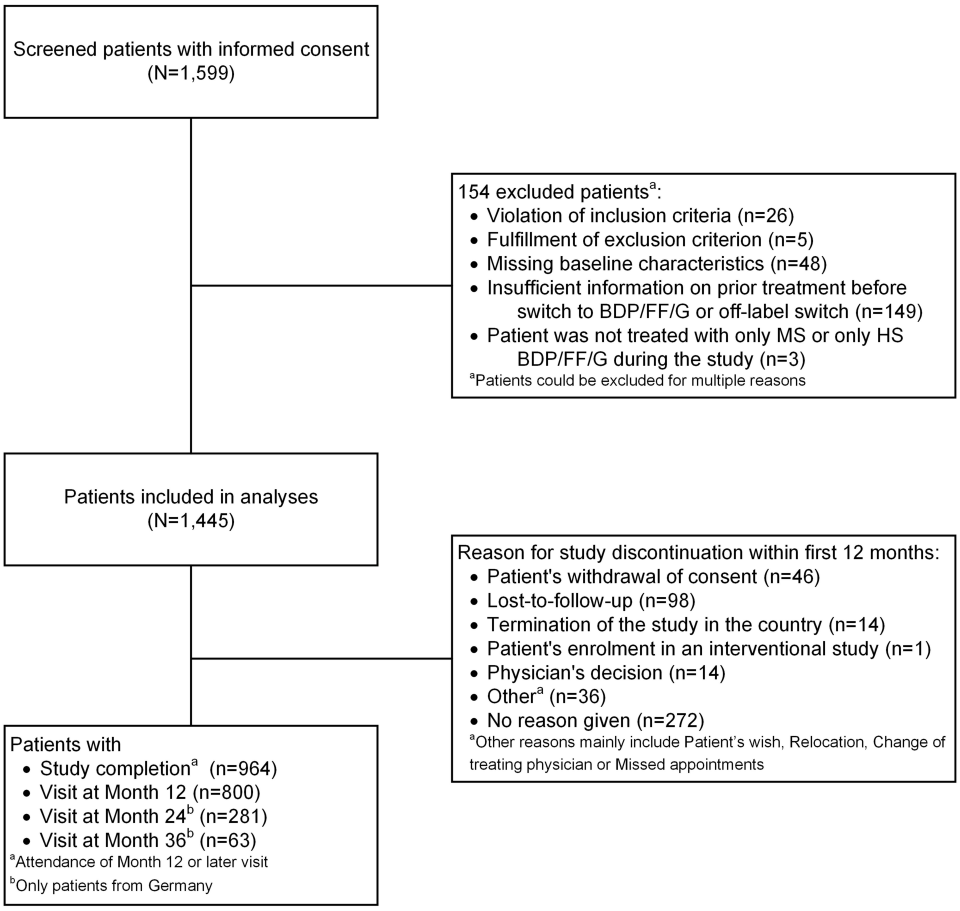

Figure 1 Patient disposition.

Treatment Pathways

Before MS BDP/FF/G initiation, 75.7% of the patients were treated with a fixed combination of MS ICS/LABA and 19.9% with a free combination of ICS/LABA/LAMA (Figure 2A). About half of the HS BDP/FF/G patients (52.9%) were treated with a fixed HS ICS/LABA combination and 43.2% with a free combination of HS ICS/LABA/LAMA before study inclusion. All patients initiated BDP/FF/G treatment at baseline. Three quarters of patients (75.0%) started BDP/FF/G treatment using MS. The most frequently documented reasons for initiation of BDP/FF/G treatment were

Table 1 Demographic and Clinical Characteristics

	MS BDP/FF/G (n=1084)	HS BDP/FF/G (n=361)	Total (n=1445)
Sex, n (%)			
Male	399 (36.8)	139 (38.5)	538 (37.2)
Female	685 (63.2)	222 (61.5)	907 (62.8)
Age* (years), mean ± SD	57.9 ± 14.8	56.4 ± 15.4	57.6 ± 15.0
BMI (kg/m^2), mean ± SD	28.8 ± 6.4	29.2 ± 6.5	28.9 ± 6.4

(*Continued*)

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Table 1 (Continued).

	MS BDP/FF/G (n=1084)	HS BDP/FF/G (n=361)	Total (n=1445)
Smoking status, n (%)			
Never	561 (51.8)	194 (53.7)	755 (52.2)
Current	203 (18.7)	56 (15.5)	259 (17.9)
Former	320 (29.5)	111 (30.7)	431 (29.8)
Concomitant diseases, n (%)	847 (84.1)	314 (88.7)	1161 (85.3)
Arterial hypertension	392 (39.2)	115 (33.7)	507 (37.8)
COPD	255 (25.7)	43 (12.8)	298 (22.4)
Time since diagnosis (years), mean ± SD	13.6 ± 13.6	19.7 ± 16.8	15.1 ± 14.7
GINA criteria, n (%)			
GINA step 4	913 (85.3)	166 (48.3)	1079 (76.3)
GINA step 5	157 (14.7)	178 (51.7)	335 (23.7)

Notes: The number of missing values varied between the described demographics and clinical characteristics (0–117 missing values). *Median age (interquartile range): 59 years (48–68 years).
Abbreviations: BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; BMI, Body mass index; COPD, Chronic obstructive pulmonary disease; GINA, Global Initiative for Asthma; HS, High strength; MS, Medium strength; SD, Standard deviation.

disease progression (MS BDP/FF/G: 45.8%, HS BDP/FF/G: 27.1%) and poor symptom control (MS BDP/FF/G: 42.7%, HS BDP/FF/G: 55.4%; Figure 2B).

During the 12 months before BDP/FF/G initiation, 33.2% of the patients were treated with SCS (total study population, Figure 3A). This percentage decreased after baseline until month 12 (12.4%) and 36 (13.7%; Figure 3A). In the 12 months before the study, 2.5% of the patients took biologics for an asthma-related indication, and 1.9% of the patients took biologics for another indication (Figure 3A and Supplemental Table 3). These percentages remained at a similarly low level during the study (Figure 3A). In detail, 3.7% of the patients used biologics with an asthma indication during the 12- and 36-month follow-up period, respectively. Intake of biologics for another indication was observed in 2.0% (12 months) and 2.1% (36 months) of

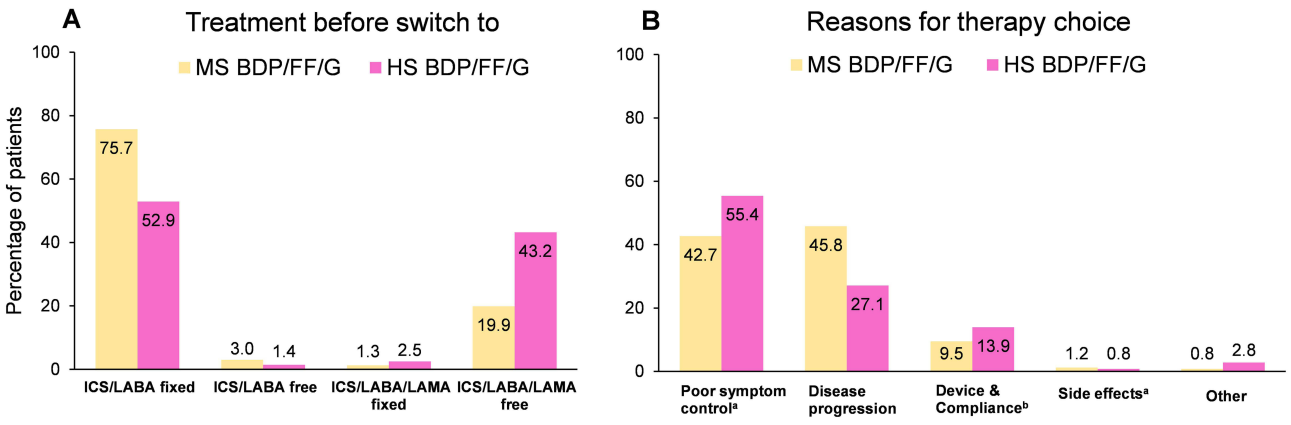

Figure 2 Treatment before switch (**A**) and reasons for therapy switch (**B**) to BDP/FF/G.
Notes: Footnote (**A**) Only switches from a prior medium ICS dose to MS BDP/FF/G during the study or from a prior high ICS dose to HS BDP/FF/G during the study were allowed. Footnote (**B**) [a]Under previous therapy, [b]Device simplification or poor compliance under previous therapy due to multiple inhalers.
Abbreviations: BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; HS, High strength; ICS, Inhaled corticosteroids; LABA, Long-acting beta2-adrenergic agonists; LAMA, Long-acting muscarinic receptor antagonist; MS, Medium strength.

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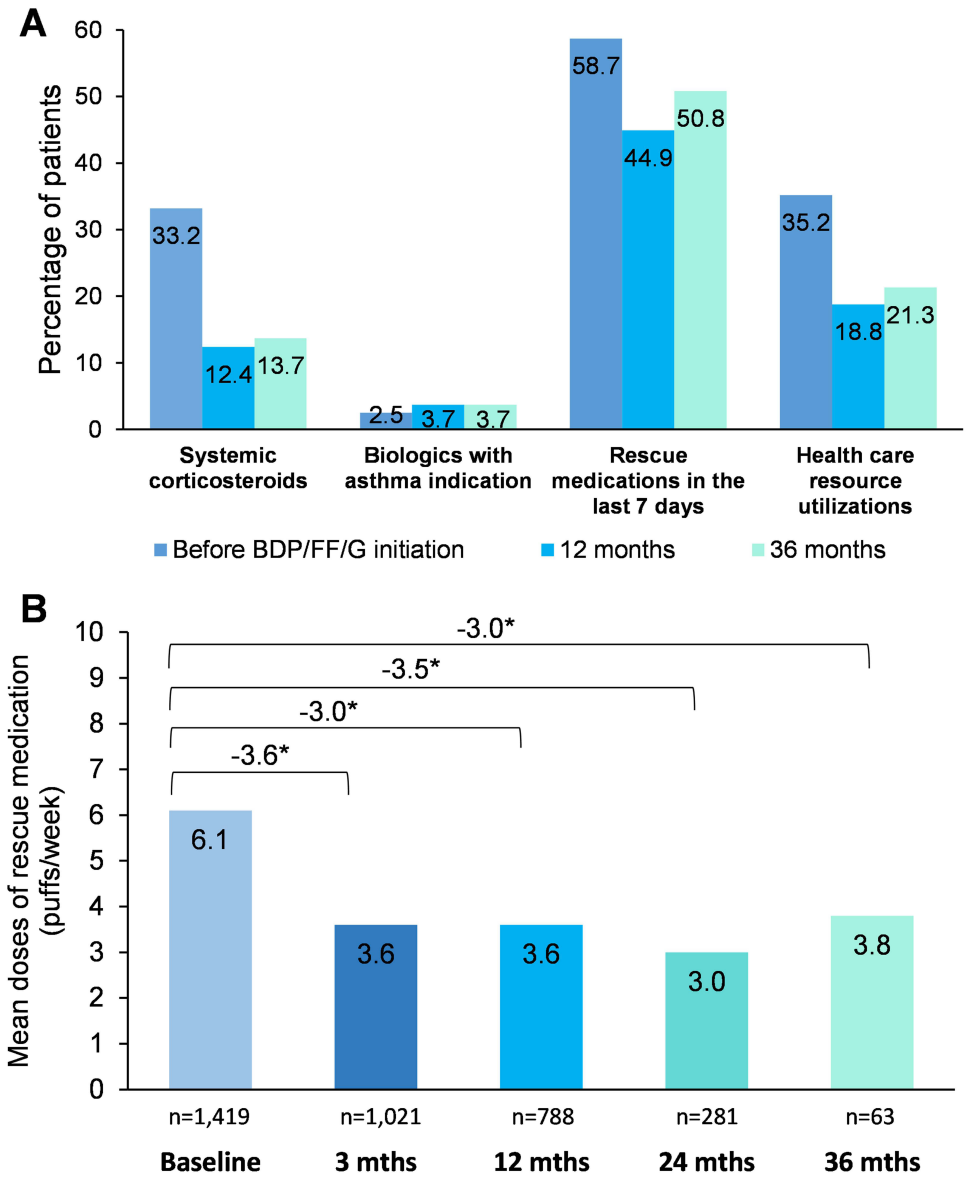

Figure 3 Asthma treatments (**A**) and mean doses of rescue medication (**B**) before first treatment with BDP/FF/G and during the study in the total study population.
Notes: Footnote (**A**) Before switch: systemic corticosteriods in last 12 months, biologics in the last 12 months, rescue medication in the last 7 days, health care resource utilization in the last 3 months. Footnote (**B**) *mean change from baseline, all p-values < 0.05.
Abbreviations: BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium.

the patients. Before and during the study, the intake of SCS and biologics for an asthma-related indication was more frequent in patients with HS than MS BDP/FF/G (Supplemental Table 3).

In the seven days before BDP/FF/G initiation, 58.7% of all patients took rescue medication (Figure 3A). At month 12 and 36, fewer patients took rescue medication in the week before the follow-up visits (month 12: 44.9%, month 36: 50.8%, Figure 3A). The number of rescue medication doses taken (puffs/week) decreased statistically significantly from 6.1 (± standard deviation, SD: 9.9, range: 0–99) at baseline to 3.6 (± 6.9, 0–56) and 3.8 (± 6.7, 0–28) after 12 and 36 months (p-value for change: <0.0001 at month 12 and 0.0393 at month 36), respectively (Figure 3B). During the 36-month follow-up period, the vast majority of the patients with an intake of rescue medication used short-acting beta2-agonist (SABA, 90.7%) and/or 9.8% of the patients used SABA in combination with a short-acting muscarinic antagonist (SAMA) as rescue medication. Additionally, 33 patients (3.2%) used ICS/LABA for symptom relief during the follow-up period.

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In the three months before the study, 35.2% of the patients (total study population) reported an asthma-related visit/admission to health-care resource utilities (Figure 3A). During the 12- and 36-month follow-up period, health care utilization was only observed for 18.8% and 21.3% of the patients, respectively.

During the study, 187 patients (12.9% of the overall population) discontinued their initial BDP/FF/G treatment temporarily or permanently after a mean treatment duration of 161 days (MS: n = 154, 14.2%; HS: n = 33, 9.1%). Most frequently, patients (MS: n=109, 70.8%; HS: n=26, 78.8%) were transitioned to another asthma treatment (other than biologics, Figure 4). In detail, patients discontinuing MS BDP/FF/G most frequently switched to ICS/LABA (n=65, 59.6%) or a free combination of ICS/LABA/LAMA (n=25, 22.9%). The most frequent subsequent treatments among patients discontinuing HS BDP/FF/G were free combinations of ICS/LABA/LAMA (n=11, 42.3%) followed by fixed ICS/LABA/LAMA combinations (n=7, 26.9%). In total, 20 patients (10.7%) received no treatment after BDP/FF/G discontinuation. No patients on MS BDP/FF/G but three patients (9.1%) on HS BDP/FF/G switched to biologics. The occurrence of an adverse event was the most common reason for BDP/FF/G discontinuation (Total: n=85, 45.7%; MS: n=73, 47.7%; HS: n=12, 36.4%; Supplemental Figure 1). Information if the adverse events leading to discontinuation were related to treatment with BDP/FF/G was not available. Further reasons for BDP/FF/G discontinuation were disease progression (13.5%), lack of adherence (9.7%), lack of efficacy (8.6%) and good symptom control (4.8%), and other reasons (17.7%).

Exacerbations and Clinical Remission

In the 12 months before BDP/FF/G initiation, 85.0% of the patients in the total study population experienced at least one moderate exacerbation (mean number of moderate exacerbations ± SD: 1.4 ± 1.4) and 27.1% experienced at least one severe exacerbation (mean ± SD: 0.5 ± 1.1, Figure 5A). During the first year after baseline, 9.6% of patients had moderate exacerbations (mean ± SD: 0.1 ± 0.4) and 9.3% severe exacerbations (mean ± SD: 0.2 ± 0.7), respectively. Even fewer patients experienced an exacerbation in the second and third year (moderate: 7.9%, severe: 3.2%). Accordingly, statistically significant decreases in the mean number of moderate (−1.3 ± 1.5, p-value: <0.0001), severe

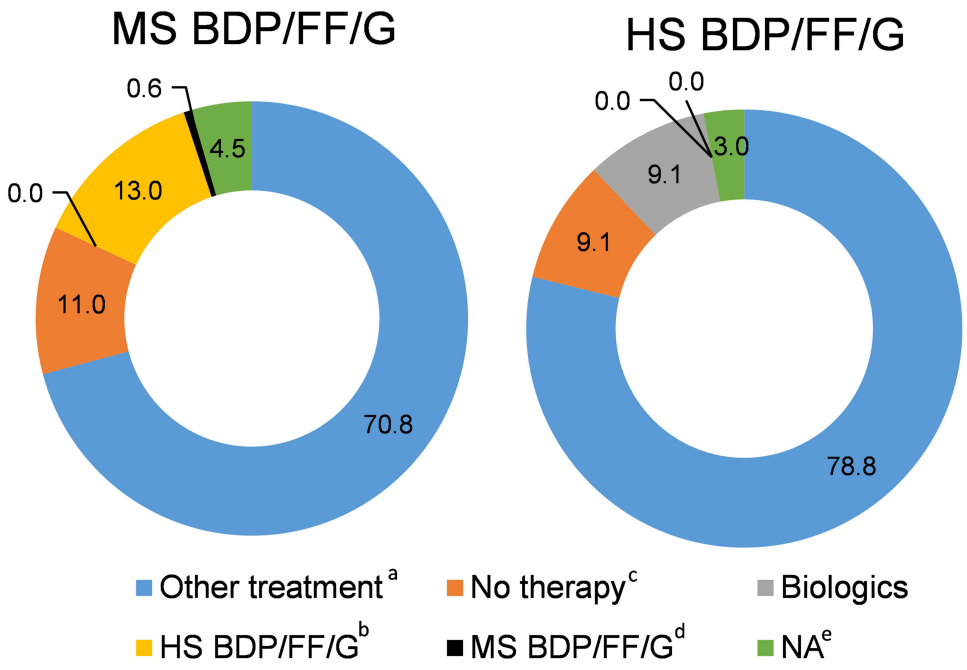

Figure 4 Treatment after first discontinuation of BDP/FF/G during the study.

Notes: Footnote: 187 patients (MS BDP/FF/G: n = 154, HS BDP/FF/G: n = 33) discontinued BBD/FF/G treatment during the study. [a]Other asthma therapy excluding biologics (eg, ICS/LABA; ICS/LABA/LAMA, free or fixed combinations); [b]Visits at/after the off-label switch from MS to HS during the study were excluded from the analyses; [c]Either no new treatment after BDP/GG/F discontinuation was documented or the information, if a new treatment was started after a (short) treatment-free period was not available; [d]MS was discontinued for 6 days and then re-started; [e]Switch cannot be determined because treatment was discontinued at last visit.

Abbreviations: BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; HS, High strength; MS, Medium strength; NA, Information not available.

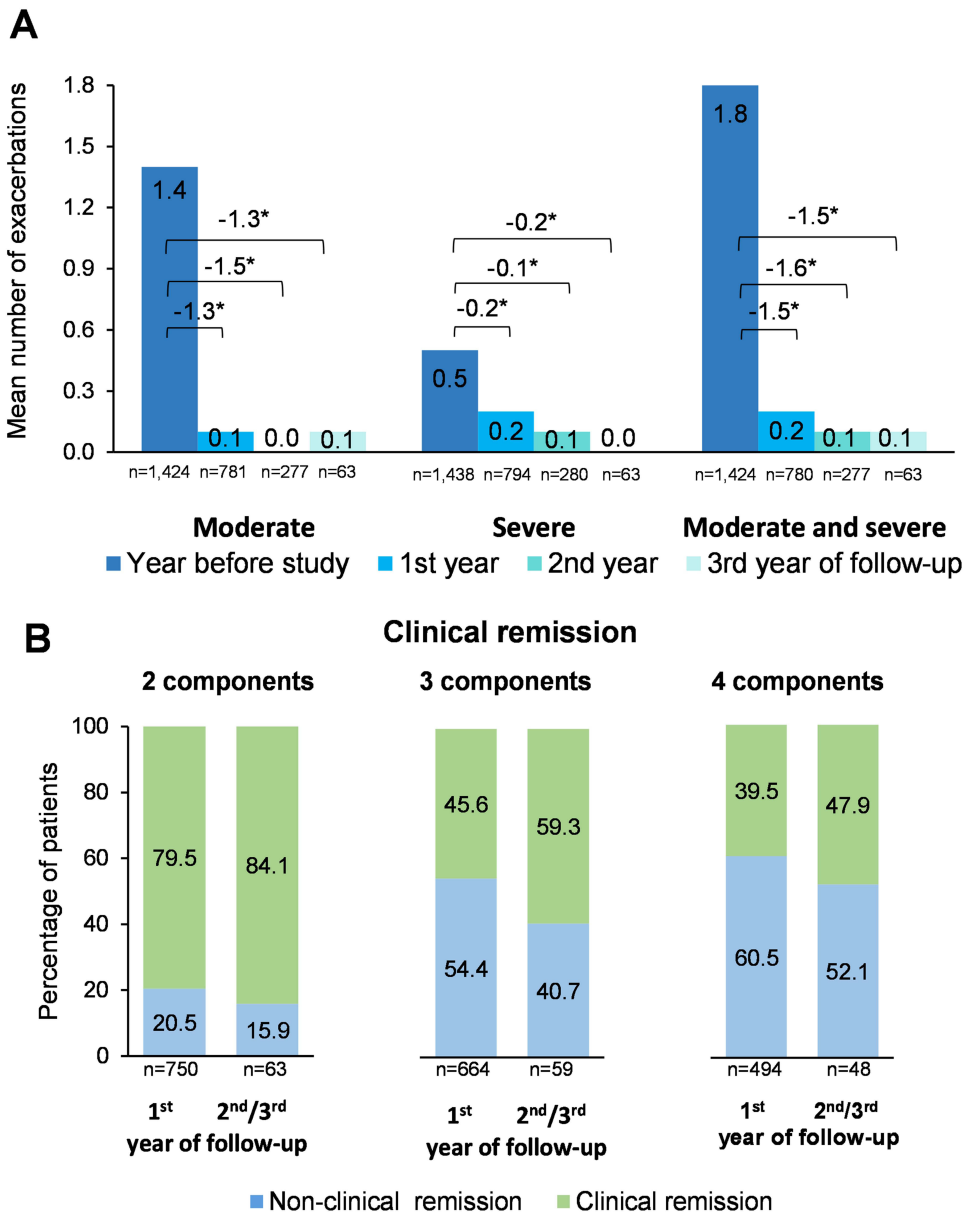

Figure 5 Mean number of exacerbations for each year of the follow-up period (**A**), and clinical remission at the end of 1st year and at the end of the follow-up period (2nd/3rd year) excluding patients with intake of biologics during the follow-up period (**B**). Footnote (**A**) Number of exacerbations within a time period could only calculated, if data were available for all visits within the respective time period; *mean change from year before study (all p-values < 0.05); changes could only be calculated if data were available for both time periods; mean exacerbations for each time period are shown based on all available data. Footnote (**B**) **2 components**: No exacerbations + No use of systemic corticosteroids, **3 components**: 2 components + ACT Score ≥ 20, **4 components**: 3 components + stable lung function (FEV_1 improvement or decline of no more than 5% of predicted). Patients with intake of biologics during the follow-up period were excluded.
Abbreviations: ACT, Asthma control test; FEV_1, Forced expiratory volume in 1 second.

(−0.2 ± 0.9, p-value: <0.0001) and total exacerbations (−1.5 ± 1.6, p-value: <0.0001) were observed in the first year after baseline (Figure 5A). Similar decreases in the number of moderate, severe and total exacerbations were detected in the second and third study year.

In the year before baseline, patients in the MS BDP/FF/G group had on average slightly more moderate exacerbations (1.4 ± 1.3) but fewer severe exacerbations (0.4 ± 0.9) than patients in the HS BDP/FF/G group (moderate: 1.3 ± 1.7, severe: 0.8 ± 1.3; Supplemental Table 4). After 12 months, patients treated with MS BDP/FF/G showed statistically significant decreases in both moderate (−1.4 ± 1.5) and severe (−0.2 ± 0.8) annualized exacerbations (p-values < 0.0001). For patients treated with HS

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BDP/FF/G, the reduction in exacerbations were slightly smaller but still statistically significant (moderate exacerbations: −0.9 ± 1.1, severe exacerbations: −0.4 ± 1.1, p-values < 0.0001; Supplemental Table 5).

Twelve months after initiating treatment with BDP/FF/G, 79.5% of patients (without additional biologic therapy) achieved 2-CR. Furthermore, 45.6% met the criteria for 3-CR, while 39.5% achieved 4-CR (no SCS use, no exacerbations, ACT score ≥ 20, and stable lung function, defined as an improvement in FEV_1 or decline no more than 5% of predicted value compared to baseline; Figure 5B). In the following two years of treatment with BDP/FF/G, the proportion of patients with 2-CR increased to 84.1%, with 3-CR to 59.3% and with 4-CR to 47.9%. The proportion of patients in clinical remission using alternative criteria for a stable or normal lung function is described in Supplemental Table 6.

Scores and Treatment Adherence

At baseline, based on ACT, 20.0% of the patients in the total study population were "controlled", 24.6% were "partly controlled", and 55.4% were "uncontrolled" (Figure 6A). The mean baseline ACT was 14.9 (± SD: 4.8). During the study, the percentage of patients with adequate asthma control increased to 46.3% at month 3, to 52.8% at month 12, and to 59.3% at month 36 (Figure 6A). The mean changes in ACT score from baseline exceeded the MCID of 3 points[25] at each follow-up visit (3 months: 3.3 ± 4.7, p-value: < 0.0001; 12 months: 3.9 ± 4.9, p-value: < 0.0001; 24 months: 3.9 ± 4.3, p-value: < 0.0001; 36 months: 4.8 ± 4.7 p-value: < 0.0001). Overall, 60.8% of the patients met or exceeded the MCID of 3 points for ACT after 12 months and were classified as "responders" (Figure 6A, footnote). This percentage remained constant after 24 (62.4%) and 36 months (67.9%). At baseline, the mean ACT was 14.9 ± 4.7 in patients treated with MS and 15.1 ± 5.0 in patients treated with HS BDP/FF/G during the study. Both treatment groups (MS and HS BDP/FF/G) showed similar, statistically significant improvements (p-values < 0.0001) in asthma control (Figure 6B). In detail, the mean change in ACT score was 4.0 ± 4.8 after 12 months, 3.9 ± 4.3 after 24 months, and 4.8 ± 4.7 after 36 months (p-values< 0.0001) in MS BDP/FF/G patients. In HS BDP/FF/G patients, a mean change in ACT of 3.6 ± 5.4 after 12 months and of 5.3 ± 5.7 after 18 months was observed (p-values< 0.0001). At each visit, the percentage of ACT responders was similar in both treatment groups (Figure 6B, footnote). With respect to the patients' prior treatment, the mean baseline ACT was slightly higher in patients with prior ICS/LABA/LAMA (15.4 ± 5.1) than in patients with ICS/LABA treatment (14.8 ± 4.6). Statistically significant improvements in asthma control were observed in both prior treatment groups (Figure 6C). However, changes in ACT and the percentage of ACT responders were slightly lower in patients with ICS/LABA/LAMA in comparison to patients with ICS/LABA as prior treatment (Figure 6C, footnote).

At baseline, the mean Mini-AQLQ total score was 4.2 ± 1.2 and 7.1% of the patients showed no impairment in HrQoL (ie, Mini-AQLQ score ≥ 6). Within the study period, 26.1% of the patients showed no impairments in HrQoL after 12 months and 25.5% after 36 months. Mean changes from baseline met or exceeded the MCID of 0.5 points at all analyzed visits (3 months: 0.7 ± 1.0, 12 months: 0.8 ± 1.1, 24 months: 0.8 ± 1.0, 36 months: 0.9 ± 1.0, Figure 7A). Accordingly, the majority of the patients were Mini-AQLQ responders at each follow-up visit (Figure 7A, footnote). In general, sub-scores for symptoms, environment, emotions, and activity also showed mean improvements of ≥ 0.5 points at each follow-up visit. Evaluating MS and HS BDP/FF/G treatment groups, similar results were observed (Figure 7B). At each visit, mean improvements of ≥ 0.5 points in the total score and the sub-scores were observed in MS and HS BDP/FF/G patients. Accordingly, more than half of the patients with MS and HS BDP/FF/G were Mini-AQLQ responders (Figure 7B, footnote). With respect to the patients' prior treatment, average improvements in the Mini-AQLQ total score exceeding the MCID were seen in patients with prior ICS/LABA/LAMA and ICS/LABA treatments (Figure 7C). Also in the sub-scores most mean changes exceeded the MCID of 0.5 points in both prior treatment groups (except for the sub-scores for environment, which did not reach the MCID for the group with prior ICS/LABA/LAMA treatment). The percentage of patients showing Mini-AQLQ response was higher in patients with ICS/LABA compared to patients with ICS/LABA/LAMA as prior treatment (Figure 7C, footnote).

At baseline, the mean TAI-10 score was 47.0 and improved statistically significantly after 3 months (p-value <0.0001), 12 months (p-value < 0.0001), and 24 months (p-value: 0.0009) compared to baseline, but not at 36 months (p-value: 0.1116, Figure 8A). At baseline, 45.7% of the patients showed good, 28.6% moderate, and 25.8% poor treatment adherence (Supplemental Table 7). The percentage of patients with good adherence increased to 54.1% at month 12 and remained approximately at 50% at later visits. The percentage of patients with moderate adherence remained rather stable during the follow-up period (range: 19.5% at month 24 to 27.6% at month 3). At month 12, 20.1%

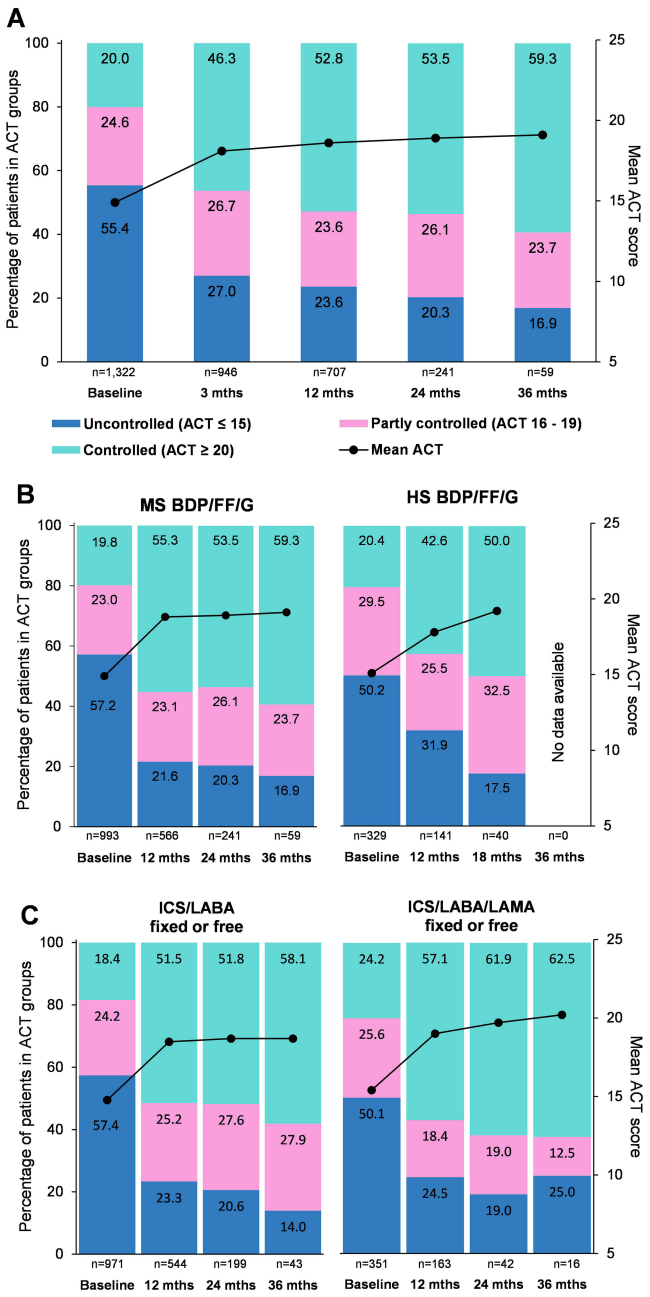

Figure 6 Asthma control assessed by ACT score in (**A**) the total study population, (**B**) patients with MS and HS BDP/FF/G, and (**C**) patients with ICS/LABA and ICS/LABA/LAMA as prior treatment. Footnote (**A**) **ACT responders (MCID of 3 points met or exceeded)**: 3 mths: 54.1%, 12 mths: 60.8%, 24 mths: 62.4%, 36 mths: 67.9%. Footnote (**B**) **ACT responders MS**: 3 mths: 55.4%, 12 mths: 61.3%, 24 mths: 62.4%, 36 mths: 67.9%. **ACT responders HS**: 3 mths: 47.8%, 12 mths: 60.8%, 18 mths: 64.1%. Footnote (**C**) **ACT responders ICS/LABA**: 3 mths: 57.6%, 12 mths: 62.9%, 24 mths: 66.1%, 36 mths: 81.0%. **ACT responders ICS/LABA/LAMA**: 3 mths: 41.8%, 12 mths: 53.7%, 24 mths: 42.9%, 36 mths: 28.6%.

Notes: For the total population as well as for all subgroups, there was a statistically significant improvement (p-value < 0.01) from baseline to each follow-up visit in ACT score.

Abbreviations: ACT, Asthma control test; BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; HS, High strength; ICS, Inhaled corticosteroids; LABA, Long-acting beta2-adrenergic agonists; LAMA, Long-acting muscarinic receptor antagonist; MS, Medium strength.

of the patients showed poor adherence. This percentage increased to 31.0% at month 24 and 27.3% at month 36. Accordingly, 63.5% of the patients were TAI-10 responders at month 12, 56.6% at month 24, and 59.3% at month 36 (Figure 8A, footnote). On average, the TAI-10 score at baseline was higher (signifying better adherence) in the HS (48.2) than in the MS BDP/FF/G group (46.7, Figure 8B). Statistically significant improvements in the TAI-10 score were observed in MS BDP/FF/G patients at month 12 (mean change: 1.0, p-value < 0.0001) and month 24 (mean change: 1.0, p-value: 0.0009) and in those with HS BDP/FF/G at month 18 (mean change: 1.1, p-value: 0.0089). In general, the

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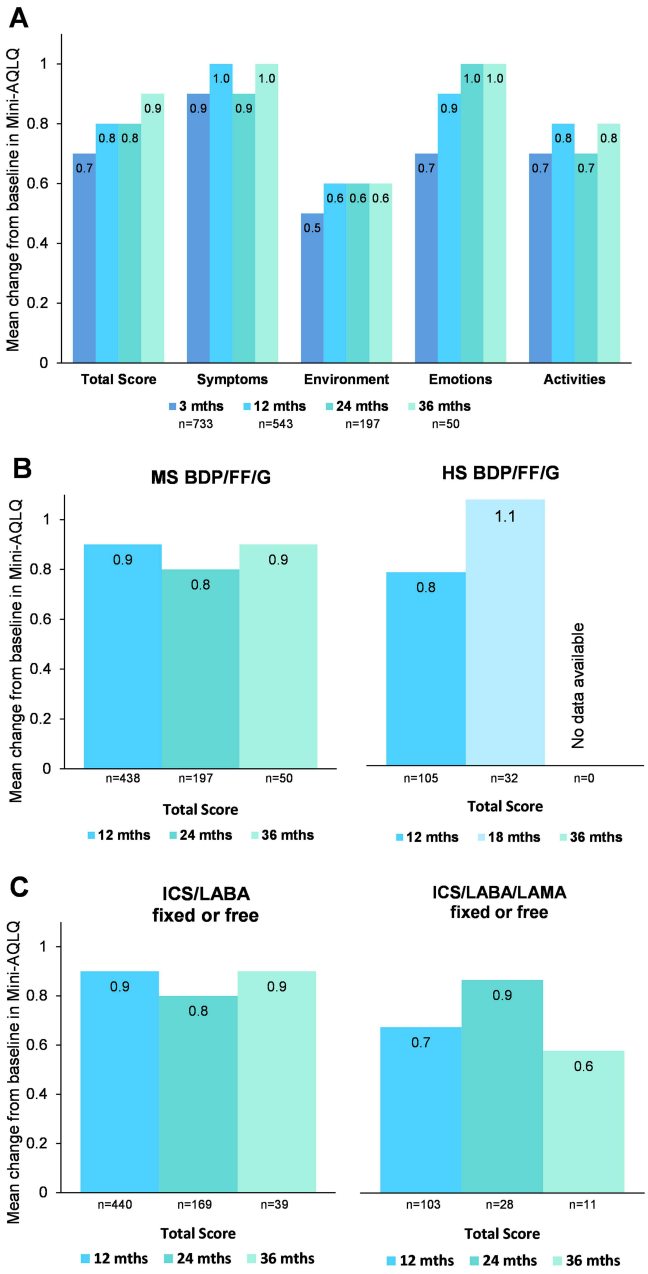

Figure 7 Change in impairment of HrQoL assessed by Mini-AQLQ in (**A**) the total study population, (**B**) patients with MS and HS BDP/FF/G, and (**C**) patients with ICS/LABA and ICS/LABA/LAMA as prior treatment. Footnote (**A**) **Mini-AQLQ responders** (MCID of 0.5 points for total score met or exceeded): 3 mths: 52.9%, 12 mths: 61.5%, 24 mths: 60.4%, 36 mths: 64.0%. Footnote (**B**) **Mini-AQLQ responders MS**: 3 mths: 53.2%, 12 mths: 62.3%, 24 mths: 60.4%, 36 mths: 64.0%. **Mini-AQLQ responders HS**: 3 mths: 51.6%, 12 mths: 58.1%, 18 mths: 65.6%. Footnote (**C**) **Mini-AQLQ responders ICS/LABA**: 3 mths: 54.9%, 12 mths: 62.3%, 24 mths: 59.8%, 36 mths: 66.7%. **Mini-AQLQ responders ICS/LABA/LAMA**: 3 mths: 44.7%, 12 mths: 58.3%, 24 mths: 64.3%, 36 mths: 54.4%.
Notes: All mean changes (except for change in total score after 36 mths in patients with ICS/LABA/LAMA fixed or free) were statistically significant (p-value < 0.01).
Abbreviations: BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; HS, High strength; ICS, Inhaled corticosteroids; LABA, Long-acting beta2-adrenergic agonists; LAMA, Long-acting muscarinic receptor antagonist; Mini-AQLQ, Short version of the Asthma Quality of Life Questionnaire; MS, Medium strength.

percentage of TAI-10 responders was higher in HS than in MS BDP/FF/G patients (Figure 8B, footnote). At each visit, the mean TAI-10 score was slightly higher in patients with prior ICS/LABA/LAMA compared to those with prior ICS/LABA treatment (Figure 8C). Improvements in TAI-10 score were seen irrespective of the patients' prior treatment, but they were only statistically significant in patients with prior ICS/LABA treatment at month 12 (mean change: 1.0, p-value: < 0.0001) and month 24 (mean change: 1.1, p-value: 0.0014). More patients with prior ICS/LABA/LAMA treatment were TAI-10 responders at each visit (3 months: 72.2%, 12 months: 75.8%, 24 months: 75.0%, 36 months:

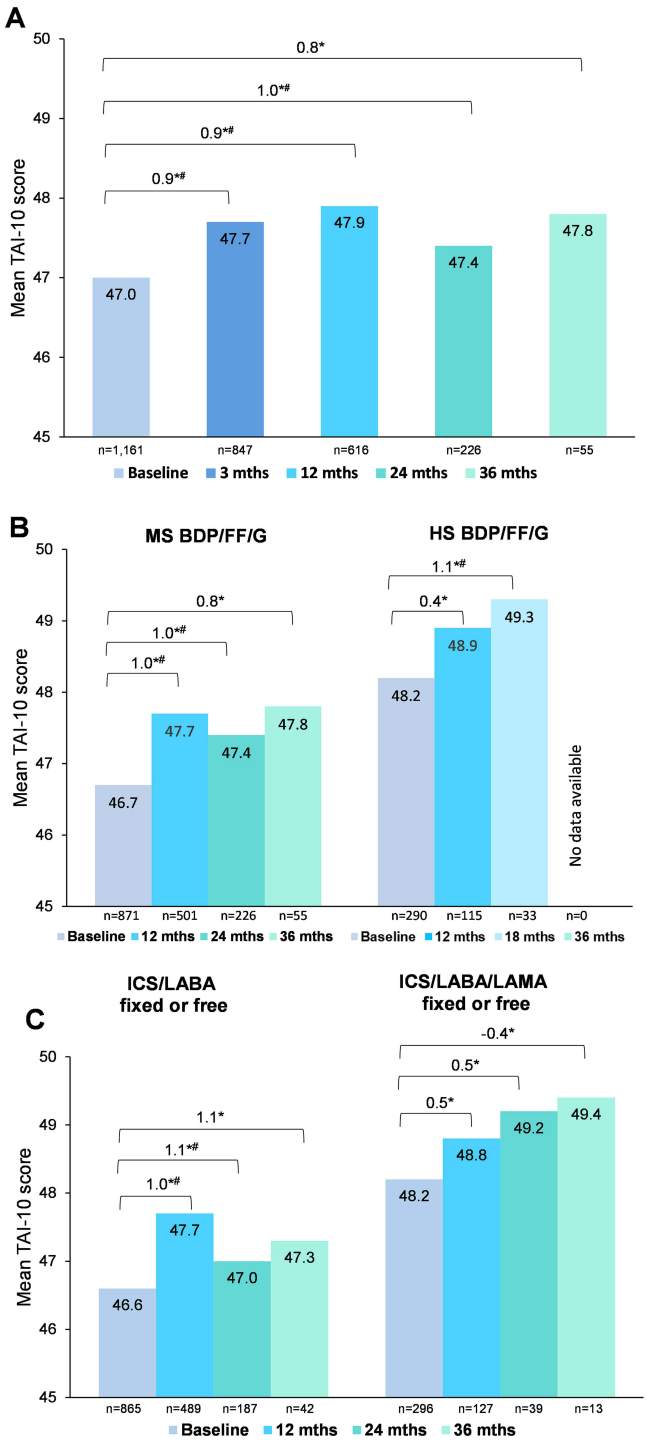

Figure 8 Treatment adherence in (**A**) the total study population, (**B**) patients with MS and HS BDP/FF/G, and (**C**) patients with ICS/LABA and ICS/LABA/LAMA as prior treatment. Footnote (**A**) **TAI-10 responders**[a]: 3 mths: 62.5%, 12 mths: 63.5%, 24 mths: 56.6%, 36 mths: 59.3%. Footnote (**B**) **TAI-10 responders MS**: 3 mths: 60.5%, 12 mths: 59.7%, 24 mths: 56.6%, 36 mths: 59.3%. **TAI-10 responders HS**: 3 mths: 72.7%, 12 mths: 80.4%, 18 mths: 78.8%. Footnote (**C**) **TAI-10 responders ICS/LABA**: 3 mths: 60.1%, 12 mths: 60.3%, 24 mths: 53.0%, 36 mths: 54.8%. **TAI-10 responders ICS/LABA/LAMA**: 3 mths: 72.2%, 12 mths: 75.8%, 24 mths: 75.0%, 36 mths: 75.0%.
Notes: *mean change from baseline; changes could only be calculated if data were available for both the baseline and follow-up visit; mean scores for each time point are shown based on all available data, #p-value < 0.05. The TAI-10 score is calculated as sum over the ten items answered by the patient. [a]Achievement of a higher adherence category at follow-up visit in comparison to baseline, ie change from poor (TAI-10 score < 45) to medium (46–49) or poor to good (50) or medium to good, or maintenance of good adherence.
Abbreviations: BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; HS, High strength; ICS, Inhaled corticosteroids; LABA, long-acting beta2-adrenergic agonists; LAMA, Long-acting muscarinic receptor antagonist; MS, Medium strength; TAI, Test of adherence to inhalers.

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75.0%), than those with prior ICS/LABA treatment (3 months: 60.1%, 12 months: 60.3%, 24 months: 53.0%, 36 months: 54.8%; Figure 8C, footnote).

Lung Function

Baseline values for each lung function parameter in the total population as well as in patients treated either with MS or HS BDP/FF/G are given in Supplemental Table 8. In general, all parameters of spirometry and body plethysmography improved statistically significantly after 3 months and 12 months (Table 2). On average, FEV_1 increased by 153 mL and

Table 2 Changes From Baseline with 95% Confidence Intervals for Parameters of Spirometry and Body Plethysmography

	Time Points	Mean Change from Baseline	95% CI	N	Missing
FEV_1 (mL)	3 months	153	[123; 183]	719	93
	12 months	142	[106; 178]	590	68
	24 months	51	[−15; 117]	231	27
	36 months	20	[−130; 171]	51	6
$FEV_1\%_{\text{ of pred}}$ (percentage points)	3 months	5.33	[4.35; 6.31]	713	99
	12 months	4.90	[3.73; 6.06]	583	75
	24 months	2.42	[0.30; 4.55]	229	29
	36 months	2.62	[−2.26; 7.50]	50	7
PEF (mL/s)	3 months	387	[303; 470]	595	217
	12 months	345	[245; 445]	480	178
	24 months	206	[32; 380]	183	75
	36 months	92	[−178; 363]	44	13
$FVC_{\%\text{ of pred}}$ (percentage points)	3 months	4.56	[3.63; 5.50]	730	82
	12 months	3.56	[2.43; 4.69]	588	70
	24 months	2.04	[−0.05; 4.13]	221	37
	36 months	0.69	[−2.58; 3.97]	51	6
$RV/TLC_{\%\text{ of pred}}$ (percentage points)	3 months	−6.90	[−10.21; −3.59]	503	309
	12 months	−8.85	[−12.54; −5.16]	385	273
	24 months	−11.18	[−18.07; −4.29]	150	108
	36 months	−13.18	[−25.20; −1.16]	40	17
$sRtot_{\%\text{ of pred}}$ (percentage points)	3 months	−28.18	[−40.49; −15.86]	469	343
	12 months	−32.74	[−43.76; −21.72]	351	307
	24 months	−38.24	[−65.12; −11.35]	138	120
	36 months	−32.74	[−71.97; 6.50]	25	32

Abbreviations: % of pred, Percentage of predicted; BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/ glycopyrronium; CI, Confidence interval; FVC, Forced vital capacity; FEV_1, Forced expiratory volume in 1 second; HS, High strength; MS, Medium strength; PEF, Peak expiratory flow; RV/TLC, Ratio of residual volume to total lung capacity; SD, Standard deviation; sRtot, Specific total airway resistance.

142 mL until month 3 and 12 (MCID: 100 mL),[26,27] respectively. For most parameters, changes were less pronounced 24 and 36 months after baseline. The number of patients with available lung function data, especially 36 months after baseline, decreased (n < 55). Changes in lung function parameters were slightly more pronounced in patients treated with HS than in patients with MS BDP/FF/G, except for sRtot (Supplemental Table 9).

Safety

During the observational period of 36 months, 1,214 adverse events (AE) were observed in 512 patients (35.4% of total, Supplemental Table 10). For the majority of AEs, patients recovered or were recovering (87.6%). Five patients died. Four deaths were not related to BDP/FF/G (hepatic cancer, hemoptysis, urosepsis). For one fatal event, the cause of death was not available but a possible relationship to BDP/FF/G was stated. 160 patients (11.1%) showed 283 adverse drug reactions (ADRs) related to BDP/FF/G. The majority of ADRs were classified as respiratory, thoracic, and mediastinal disorders (n = 83), with cough being the most frequently reported event.

In total, 49 ADRs were serious (26 patients), 17 of which were respiratory, thoracic, and mediastinal disorders. No patient was treated with BDP/FF/G in the 12 months before the baseline examination.

Discussion

The TriMaximize study is the largest, multi-national, non-interventional study in a routine clinical practice setting on the effectiveness, the usage patterns, and the safety of a fixed, extrafine BDP/FF/G triple therapy in asthma patients, so far. During an extended observational time of up to three years, the patients' disease burden improved significantly, including decrease of annual exacerbations, the need for rescue medication and concomitant oral steroid therapy. This was accompanied by improved asthma control (as measured by the ACT) and a decrease in the utilization of healthcare resources. In addition, TriMaximize provides for the first time remission data of inhaled BDP/FF/G triple therapy in a real-life setting. Therefore, the real-world data collected in this study provide important support for the results of prior clinical trials on the treatment of asthma patients with BDP/FF/G.[28]

Patient Pathways

Most of the patients starting BDP/FF/G with the medium dosage strength (MS) were treated with a fixed dual ICS/LABA therapy, which is in line with GINA step 4, before study start.[3] Patients starting BDP/FF/G with the high dosage strength (HS) were treated to a similar extent with a fixed ICS/LABA combination (GINA 4), or a free triple combination of ICS/LABA/LAMA before study start (GINA 5).[3] In line with the previously reported benefits of transitioning from free triple to extrafine single-inhaler triple therapy (efSITT),[29–32] many patients in this study underwent such a transition.

Due to potentially differing prescribing patterns in clinical practice, some of which may have categorically favored the medium strength formulation over the high strength, and because the HS formulation was available approximately 1.5 years after the study had started, comparatively fewer HS patients could be enrolled.

Interestingly, during the three years of observation in the study, only 12.9% of the patients changed their initial BDP/FF/G treatment regimen. In patients who discontinued their BDP/FF/G treatment, the majority among the MS BDP/FF/G patients switched back to ICS/LABA, whereas the majority among the HS BDP/FF/G patients switched to another triple therapy. With respect to the return to dual therapy (ICS/LABA) it seems plausible that the triple therapy was used during a foreseeable phase of increased symptoms, such as during allergy season, and was then de-escalated (which is also in line with the minimum effective treatment according to GINA).[3]

Importantly, the proportion of patients using SCS and rescue medications decreased from baseline. Although most patients were switched to BDP/FF/G due to disease progression and poor symptom control, the reliance on both SCS and rescue medications declined. This finding is particularly significant, as GINA guidelines recommend using add-on low-dose oral corticosteroids only as a last resort because of their serious short- and long-term side effects.[3] Additionally, SABAs should no longer be the preferred reliever treatment, as regular use is associated with adverse outcomes such as airway hyperresponsiveness, reduced bronchodilator responsiveness, increased allergic inflammation, and elevated eosinophil levels.[33,34] Overuse of SABAs is also linked to higher rates of exacerbations, creating a harmful cycle that must be broken to ensure safe and sustained asthma control.[35]

Effectiveness

Upon initiating BDP/FF/G, many patients experienced a fast and significant improvement regarding exacerbations, lung function and symptoms that were mostly maintained over the entire study duration. In addition, significant and clinically relevant improvements in symptom control, health-related quality of life, and treatment adherence were observed, as measured by ACT, Mini-AQLQ, and TAI, respectively.

Improvements and clinical stability were seen in patients switching from ICS/LABA to triple therapy, which was an expected observation. These results are in line with the recommendations outlined in the GINA report which advises that patients with uncontrolled asthma on ICS/LABA should be escalated to a triple therapy with additional LAMA.[3] The triple therapy was shown to be an efficient therapy in these patients causing lower economic burden on the healthcare system than alternative treatments such as biologics.[3,36,37] The cost-effectiveness stems from reduced hospitalization rates, fewer exacerbations, and decreased reliance on emergency care, making it a more sustainable option for managing moderate to severe disease in broader patient populations.

Remarkably, patients who were pretreated with the same drug-class combination, ie a free or another fixed triple combination of ICS/LABA/LAMA, experienced clinically significant improvements in asthma control and HrQoL. The reason is possibly threefold, based on the transition to a fixed single-inhaler triple therapy and to an extrafine formulation of the combination. On one side, the use of a fixed single-inhaler triple therapy may improve adherence and reduce healthcare resource utilization as has been previously reported.[29–32] Notably, adherence was higher in patients treated with HS BDP/FF/G. Since the HS group comprised patients with more severe exacerbations, they may have derived greater benefit from the therapy, which likely contributed to improved adherence. This perceived benefit is also reflected in quality of life measures, with a 1.1-point increase at 18 months – twice the MCID – on the Mini-AQLQ questionnaire.

On the other side, it is well documented that extrafine aerosols (ie, particles with mass median aerodynamic diameter of less than 2 μm) can effectively reach the peripheral lung areas and, as a result, the small airways.[38–40] This is of relevance as small airway involvement has been shown to be present in all stages of asthma, particularly in its severe stages.[15] Pilot studies indicate that extrafine BDP/FF/G improves lung function as seen in small and large airway parameters.[41,42]

And thirdly, ex-vivo asthma models demonstrate that beclometasone, formoterol, and glycopyrronium produce a synergistic bronchorelaxant effect.[43] Across multiple concentration combinations, administered at 100:6:12.5 combination ratio, the observed airway smooth-muscle relaxation exceeded the predicted additive response ($p<0.05$), confirming a robust synergistic bronchodilator interaction.The outcomes pertaining to lung function further support the effectiveness of BDP/FF/G, with regard to large and small airway function. Notably, improvements in airflow obstruction (FEV_1) or hyperinflation (RV/TLC), particularly in the first year after treatment start, were observed. In comparison to baseline, we observed improvements in the first year and stable lung function parameters during the second and third year of the study. The slight deterioration in the second and third year may be attributed to the known progressive decline in lung function seen in the natural course of asthma over time.[44] Even in healthy individuals, the yearly decline of FEV_1 is approximately 25 mL.[45] Although reduced, use of SABA as rescue medication was not completely discontinued, despite the caveats outlined in the recent GINA recommendations. Irrespective of the considerable differences between patient populations in the Phase 3 trials, the less controlled setting of a real-world study in comparison to randomized clinical trials and the differences in the applied statistical methods, the results are largely consistent with those of the clinical trials TRIMARAN and TRIGGER.[28]

Remission as a general treatment goal in asthma has recently been introduced in the literature[46] and in various national guidelines.[47] All guidelines agree on 3-CR criteria (no exacerbations, no use of SCS, good asthma control).[47] In contrast, lung function criteria chosen for 4-CR definitions differ substantially between the studies[48] and are still debated (stable, improved or normal lung function criteria are currently used).[22] While there is increasing data on remission rates in patients treated with biologics, there is currently little information on remission rates in patients treated with single inhaler triple therapies only. In a post-hoc analysis of randomized controlled studies (TRIMARAN and TRIGGER), more patients achieved clinical remission on triple treatment with BDP/FF/G as compared to BDP/FF.[49] We show, for the first time, that 3-CR can be achieved in a real world setting in > 40% of the patients after one year of BDP/FF/G treatment,

and in nearly 60% after 3 years of treatment. In addition, we provide the more rigorous 4-CR data, with various lung function criteria discussed in the literature.[22] Irrespective of the lung function criterion chosen, at least one out of four patients achieved 4-CR in our study. Thus, we show that clinical remission is a realistic goal in patients moderate-to-severe asthma treated with BDP/FF/G single inhaler treatment.

Safety

Use of BDP/FF/G appeared to be safe, all reported ADRs (283 ADRs in 11.1% of patients) were in accordance with the summary of product characteristics of BDP/FF/G. No new safety signal was detected.

Strengths and Limitations

This is the first large, multi-national real-world study on the routine use of a fixed, extrafine formulation of BDP/FF/G in asthma patients with a particularly long follow-up of up to three years. The effectiveness data seem to be particularly robust, as the assessed parameters remained stable over the course of the study. The effectiveness was assessed via a particularly wide range of outcome parameters, including clinical parameters and validated scores with available MCIDs (Mini-AQLQ, ACT). The inclusion of lung function parameters, especially body plethysmography, provided a valuable addition to complement the outcomes of the clinical scores.

The study's shortcomings are largely those inherent of any large-scale observational study, including the expected types of bias (eg selection bias, attrition bias). The inclusion of a large number of sites introduces heterogeneity in clinical practices, data quality, and documentation standards, which may not be fully accounted for. Data were collected for clinical and administrative purposes, which may result in misclassification, missing data, and variable outcome ascertainment. For instance, some inconsistencies in lung function data at the later visits may be biased due to drop-outs, eg patients with better lung function discontinuing study participation. Follow-up data on the second and third year was derived only from Germany resulting in smaller sample sizes at these time points, which may have impacted statistical significance. As national cohorts varied in size, country-level representativeness must be considered to be limited. Furthermore, the data were obtained from patients in European countries only. As factors such as environmental conditions, genetic predispositions, and healthcare practices can vary globally and may influence asthma outcomes, further research in diverse geographic and demographic settings is needed to confirm the generalizability of our results. Remaining exacerbations may relate to disease severity, comorbidities (COPD, in particular), or individual variability, which were beyond the scope of this study. Future research should focus on predictors of response and long-term outcomes in broader populations. Direct comparability between this study and the clinical trials is naturally limited due to distinct differences in the study design and statistical analysis strategy. Furthermore, the real-world cohort in this study was more diverse in terms of higher disease burden and comorbidities than the cohort in the clinical trials, which had more stringent eligibility criteria.[28]

Conclusions

TriMaximize outcomes showed that BDP/FF/G therapy is effective and safe as a single inhaler treatment in a routine clinical practice setting in an international cohort of patients with moderate to severe asthma over three years. Patients experienced a fast and stable improvement in terms of exacerbations, asthma symptoms, decreased need of rescue medication and oral corticosteroid therapy, and they gained better control of their airways disease. For the first time, TriMaximize provides prospective remission data in asthma patients on inhaled BDP/FF/G triple therapy in a real-world setting.

Abbreviations

ACT, Asthma control test; BDP/FF/G, Beclometasone dipropionate/formoterol fumarate/glycopyrronium; BMI, Body mass index; COPD, Chronic obstructive pulmonary disease; CR, Clinical remission; FEV_1, Forced expiratory volume in one second; FVC, Forced vital capacity; HS, High strength; HrQoL, Health-related quality of life; IC, Inspiratory capacity; ICS, Inhaled corticosteroid; LABA, Long-acting beta2-adrenergic agonist; LAMA, Long-acting muscarinic antagonist; Mini-AQLQ, Mini asthma quality of life questionnaire; MS, Medium strength; PEF, Peak expiratory flow;

RV/TLC, Residual volume to total lung capacity; SCS, Systemic corticosteroids; sRtot, Specific total airway resistance; TAI, Test of adherence to inhalers.

Data Sharing Statement

The data analysed in this study are available from the corresponding author Dr. Gessner upon reasonable request.

Ethics Statement

The study was approved by the following ethics committees: Austria: Ethic committee of Vienna, EK 21-126-VK-NIS; Denmark: The Research Ethics Committees, 21004536; France: Comité de protection des personnes Sud-Est VI, 22.02880.000118; Germany: Sächsische Landesärztekammer, EK-BR-124/20-1; Italy: Comitato Etico Territoriale – Ligura, 51/202; Poland: Komisja Bioetyczna Przy Uniwersytecie Medycznym W Lodzi, RNN/237/23/KE; Spain: Hospital De La Santa Creu I Sant Pau, 22/357 (R-EOM); UK: NHS/ HRA and Health and Care Research Wales, 294788).

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Collaborators

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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