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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Indacaterol acetate, Glycopyrronium bromide and Mometasone furoate (IND/GLY/MF)

inhaled corticosteroid/long-acting β2 sympathomimetic/long acting muscarinic receptor antagonist (ICS+LABA+LAMA) fixed-dose combination (FDC)

Trial Indication(s)

Asthma

Protocol Number

CQVM149BDE01

Protocol Title

Digital Adherence Monitoring of Inhalative Therapy in Real- Life Conditions

Clinical Trial Phase

Full development

Phase of Drug Development

Phase IV

Study Start/End Dates

Study Start Date: December 17, 2020 (Actual)
Primary Completion Date: January 20, 2023 (Actual)

Study Completion Date: January 20, 2023 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This study was designed as a non-interventional, multicenter, open-label, two-arm observational study for asthma patients. The study consisted of an observation phase in which patients were observed for 6 months. Patients treated with either MF/IND/GLY FDC in combination with an inhalation tracking sensor or with any other ICS+LABA+LAMA FDC approved for the treatment of asthma according to summary of product characteristics (SPC) were observed. Patients who were switched to one of the two therapy options at the time of the Baseline visit was documented to describe the potential benefit of escalating or switching therapy at the time of documentation start in terms of adherence and clinical course. The frequency of patient visits was at the discretion of the treating physician.

Centers

Germany(26)

Objectives:

Primary objective

The primary objective of this NIS was to describe the change in asthma control after 6 months from baseline under treatment with MF/IND/GLY in combination with the sensor system for inhalation tracking or under real life conditions with any other ICS+LABA+LAMA FDC.

Secondary Objectives

To describe the relationship between treatment with mometasone furoroate/indacaterol/ glycopyrronium (MF/IND/GLY) in combination with the sensor system or treatment with any other inhaled corticosteroid/long-acting β2 sympathomimetic/long acting muscarinic receptor antagonist (ICS+LABA+LAMA) fixed-dose combination (FDC) and

- the reasons for the prescription of the respective therapy

- Adherence (to medication and to the App)
- Asthma control
- lung function

under real-life conditions.

Test Product (s), Dose(s), and Mode(s) of Administration

- MF/IND/GLY Breezhaler® in combination with an electronic dose tracking system plus smartphone App and reminder notifications (Propeller Health Sensor System)
- other ICS+LABA+LAMA fixed-dose combination

Statistical Methods

The data was statistically analyzed with SAS® software. All parameters documented within this NIS were evaluated using appropriate statistical methods and reported. Analysis was based on epidemiological methods and all analysis were purely descriptive. This includes CIs or p-values, if provided. Due to the explorative nature of the analysis no alpha adjustment for multiple comparisons was performed.

Variables that are at least interval scaled were analyzed and presented in tabular form with sample statistics (number of valid values, minimum, maximum, 1st quartile, 3rd quartile, median, mean and standard deviation).

Variables that are nominal or ordinal scaled were analyzed and presented with absolute and relative frequencies.
A propensity score (PS) model was used to estimate the change in Asthma Control Test (ACT) score at 6 months compared to Baseline in the two treatment groups (MF/IND/GLY in combination with the sensor system and ICS+LABA+LAMA FDC). The PS was estimated based on a logistic PS model using the Baseline characteristics for all patients in the Analysis Set. Patients with missing data in covariates were excluded.
The treatment effect (change in ACT score at 6 months compared to Baseline) in both treatment groups was compared using Inverse Probability of Treatment Weighting (IPTW) using PS (no matching) and Prospensity Score Matching (PSM).

For adverse events, incidences are reported based on the included patient population by MedDRA System Organ Class and Preferred Term for adverse events (AEs), serious adverse events (SAEs), adverse drug reactions (ADRs), and serious adverse drug reactions.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
To participate in the study, all of the following inclusion criteria must be met:
1. Patients (m/f/d) at the age of ≥18
2. Written declaration of consent
3. Asthma diagnosis according to German Asthma Guideline NVL, 4th edition
4. Suitability for a therapy with MF/IND/GLY in combination with the sensor system or another ICS+LABA+LAMA FDC according to SPC
5. At least 6 months of inhaled therapy with ICS+LABA (high dose) or ICS+LABA+LAMA (medium or high dose) before switching or escalating asthma medication at baseline
6. Change or escalation of the asthma medication to MF/IND/GLY in combination with the sensor system or another ICS+LABA+LAMA FDC according to the therapy decision of the treating physician
7. Availability of at least one ACT value of the last 6 months before consent
8. Cohort treated with MF/IND/GLY in combination with the sensor system
- Owning an Android or iOS smartphone or tablet on which the app can be installed (via WiFi or mobile data network) and run (requires about 75 megabytes of storage space) and which is capable of establishing a Bluetooth connection to the sensor The patient must agree to activate the app, the Bluetooth connection and the mobile data connection regularly (at least once a month).
- Availability of an e-mail address

Exclusion Criteria:
To participate in the study, none of the following exclusion criteria must apply:
1. Use of a digital inhaler-coupled inhalation tracking system to support adherence in the last 3 months prior to study entry
2. Simultaneous participation in an interventional study or in another Novartis-sponsored noninterventional study
3. Asthma therapy with a biological agent, if not stable at the same dosage for at least 3 months

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Participant Flow Table

Table 10-6 Analysis sets (All patients)

	Enerzair® with sensor system (N=229) n (%)	ICS+ LAMA+LABA FDC: Enerzair® without sensor system (N=175) n (%)	ICS+ LAMA+LABA FDC: Trimbow® (N=31) n (%)	ICS+ LAMA+LABA FDC: subtotal (N=206) n (%)	Total (N=435) n (%)
Enrolled	229 (100.0)	175 (100.0)	31 (100.0)	206 (100.0)	435 (100.0)
Started to use the prescribed study medication	229 (100.0)	174 (99.4)	31 (100.0)	205 (99.5)	434 (99.8)
Included in the analysis set	222 (96.9)	172 (98.3)	31 (100.0)	203 (98.5)	425 (97.7)
Not included in the analysis set	7 (3.1)	3 (1.7)	0 (0.0)	3 (1.5)	10 (2.3)
- No study medication documented	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.2)
- Inclusion/exclusion criteria not met	7 (3.1)	3 (1.7)	0 (0.0)	3 (1.5)	10 (2.3)
Included in the safety set	210 (91.7)	159 (90.9)	28 (90.3)	187 (90.8)	397 (91.3)
Not included in the safety set	19 (8.3)	16 (9.1)	3 (9.7)	19 (9.2)	38 (8.7)
- No informed consent documented	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.2)
- No study medication documented	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.2)
- No post-Baseline data documented	19 (8.3)	16 (9.1)	3 (9.7)	19 (9.2)	38 (8.7)

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Baseline Characteristics

Table 10-4 Demography (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Gender, n (%)					
Male	104 (46.8)	85 (49.4)	11 (35.5)	96 (47.3)	200 (47.1)
Female	118 (53.2)	87 (50.6)	20 (64.5)	107 (52.7)	225 (52.9)
Ethnicity, n (%)					
Caucasian	221 (99.5)	166 (96.5)	31 (100.0)	197 (97.0)	418 (98.4)
Black	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.2)
Asian	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (0.5)	5 (2.9)	0 (0.0)	5 (2.5)	6 (1.4)
Employment status, n (%)					
Full-time employee	97 (43.7)	70 (40.7)	12 (38.7)	82 (40.4)	179 (42.1)
Part-time employee	8 (3.6)	6 (3.5)	1 (3.2)	7 (3.4)	15 (3.5)
Self-employed	6 (2.7)	2 (1.2)	0 (0.0)	2 (1.0)	8 (1.9)
In vocational training	4 (1.8)	3 (1.7)	0 (0.0)	3 (1.5)	7 (1.6)
School student	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Student	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
Retired person	53 (23.9)	45 (26.2)	11 (35.5)	56 (27.6)	109 (25.6)
Pensioner	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
In parental leave	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.2)
Unemployed	11 (5.0)	6 (3.5)	1 (3.2)	7 (3.4)	18 (4.2)
Not specified	37 (16.7)	38 (22.1)	6 (19.4)	44 (21.7)	81 (19.1)
Life situation, n (%)					
Living alone	29 (13.1)	17 (9.9)	1 (3.2)	18 (8.9)	47 (11.1)
Living in a partnership	117 (52.7)	87 (50.6)	22 (71.0)	109 (53.7)	226 (53.2)
Not specified	76 (34.2)	68 (39.5)	8 (25.8)	76 (37.4)	152 (35.8)
Education, n (%)					
No graduation	29 (13.1)	0 (0.0)	0 (0.0)	0 (0.0)	29 (6.8)
Primary/ lower secondary school leaving certificate	28 (12.6)	12 (7.0)	0 (0.0)	12 (5.9)	40 (9.4)
Secondary school leaving certificate	35 (15.8)	27 (15.7)	12 (38.7)	39 (19.2)	74 (17.4)
General qualification for university entrance	17 (7.7)	11 (6.4)	3 (9.7)	14 (6.9)	31 (7.3)
Completed vocational training	32 (14.4)	58 (33.7)	6 (19.4)	64 (31.5)	96 (22.6)

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	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
University (of applied sciences) degree	11 (5.0)	8 (4.7)	1 (3.2)	9 (4.4)	20 (4.7)
Not specified	70 (31.5)	56 (32.6)	9 (29.0)	65 (32.0)	135 (31.8)
Smoke status, n (%)					
Non-smoker	103 (46.4)	88 (51.2)	14 (45.2)	102 (50.2)	205 (48.2)
Ex-smoker	70 (31.5)	47 (27.3)	10 (32.3)	57 (28.1)	127 (29.9)
Smoker	47 (21.2)	32 (18.6)	6 (19.4)	38 (18.7)	85 (20.0)
Not specified	2 (0.9)	5 (2.9)	1 (3.2)	6 (3.0)	8 (1.9)
Influenza vaccination, n (%)					
No	54 (24.3)	71 (41.3)	15 (48.4)	86 (42.4)	140 (32.9)
Yes	83 (37.4)	43 (25.0)	7 (22.6)	50 (24.6)	133 (31.3)
Unknown	85 (38.3)	58 (33.7)	9 (29.0)	67 (33.0)	152 (35.8)
Pneumococcal vaccination, n (%)					
No	58 (26.1)	69 (40.1)	10 (32.3)	79 (38.9)	137 (32.2)
Yes	83 (37.4)	40 (23.3)	9 (29.0)	49 (24.1)	132 (31.1)
Unknown	81 (36.5)	63 (36.6)	12 (38.7)	75 (36.9)	156 (36.7)
Age (years)					
n	222	172	31	203	425
Mean	52.4	55.0	56.9	55.3	53.8
Standard deviation	15.3	14.7	14.6	14.7	15.1
Minimum	19.0	21.0	20.0	20.0	19.0
1st quartile	43.0	44.0	51.0	44.0	43.0
Median	54.0	56.0	58.0	57.0	55.0
3rd quartile	63.0	67.0	66.0	67.0	65.0
Maximum	83.0	81.0	86.0	86.0	86.0
Height (cm)					
n	222	172	31	203	425
Mean	171.5	170.8	166.7	170.2	170.9
Standard deviation	9.8	9.8	8.7	9.7	9.8
Minimum	152.0	148.0	153.0	148.0	148.0
1st quartile	164.0	163.0	160.0	162.0	163.0
Median	171.0	170.0	167.0	170.0	170.0
3rd quartile	178.0	178.0	170.0	178.0	178.0
Maximum	197.0	194.0	187.0	194.0	197.0
Weight (kg)					
n	222	172	31	203	425

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Mean	84.7	82.7	78.8	82.1	83.5
Standard deviation	21.7	18.9	17.7	18.7	20.4
Minimum	43.0	45.0	55.0	45.0	43.0
1st quartile	70.0	69.0	69.0	69.0	70.0
Median	82.0	80.5	74.0	80.0	81.0
3rd quartile	96.0	91.5	87.0	90.0	93.0
Maximum	205.0	150.0	152.0	152.0	205.0
Body mass index (BMI) (kg/m²)					
n	222	172	31	203	425
Mean	28.7	28.3	28.4	28.4	28.6
Standard deviation	6.7	6.2	6.0	6.1	6.4
Minimum	16.6	18.3	19.9	18.3	16.6
1st quartile	24.2	24.1	24.2	24.2	24.2
Median	27.9	27.1	27.4	27.1	27.5
3rd quartile	31.6	31.5	31.3	31.5	31.5
Maximum	59.9	55.5	49.6	55.5	59.9

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Table 10-5 Apps used for asthma therapy support at Baseline by treatment groups (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Patients using Apps for asthma therapy support, n (%)					
No	148 (66.7)	172 (100.0)	31 (100.0)	203 (100.0)	351 (82.6)
Yes	74 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	74 (17.4)
Functions used from the Apps for asthma therapy support, n (%)					
Inhalation diary	15 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	15 (3.5)
Symptom diary	15 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	15 (3.5)
Recording the use of on-demand medication	5 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)
Reminder function	56 (25.2)	0 (0.0)	0 (0.0)	0 (0.0)	56 (13.2)
Sharing the data with the attending physician	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
Information on disease management (e.g. tips in case of asthma attack, health tips)	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
Support in handling the inhaler	4 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.9)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Note: multiple answers possible for "Functions used from the Apps for asthma therapy support".

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Primary Outcome Result(s)

1. Change from Baseline in asthma control test (ACT) score

Table 10-7 Change in ACT score at 6 months compared to Baseline (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Change in ACT score at 6 months compared to Baseline					
n	151	124	24	148	299
Mean	3.0	4.3	3.3	4.1	3.5
Standard deviation	4.0	5.2	2.8	4.9	4.5
Minimum	-10.0	-9.0	-3.0	-9.0	-10.0
1st quartile	1.0	1.0	1.5	1.0	1.0
Median	3.0	4.0	3.0	4.0	3.0
3rd quartile	5.0	8.0	5.0	7.0	6.0
Maximum	14.0	18.0	9.0	18.0	18.0

Note: Positive values represent an increase in asthma control after treatment. Negative values represent a decrease in asthma control after treatment.

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Table 10-8 Change in ACT score at 6 months compared to Baseline by subgroup ACT score ≥ 20 before the study inclusion (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Change in ACT score at 6 months compared to Baseline for patients with ACT score ≥ 20 before the study inclusion					
n	49	26	3	29	78
Mean	0.7	2.5	5.7	2.8	1.5
Standard deviation	3.8	4.7	3.1	4.6	4.2
Minimum	-10.0	-9.0	3.0	-9.0	-10.0
1st quartile	0.0	0.0	3.0	0.0	0.0
Median	0.0	2.0	5.0	2.0	1.0

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
3rd quartile	2.0	5.0	9.0	5.0	3.0
Maximum	11.0	13.0	9.0	13.0	13.0
Change in ACT score at 6 months compared to Baseline for patients with ACT score < 20 before the study inclusion					
n	102	98	21	119	221
Mean	4.1	4.7	3.0	4.4	4.3
Standard deviation	3.6	5.2	2.7	4.9	4.3
Minimum	-10.0	-9.0	-3.0	-9.0	-10.0
1st quartile	2.0	1.0	1.0	1.0	2.0
Median	4.0	5.0	3.0	4.0	4.0
3rd quartile	6.0	8.0	5.0	7.0	7.0
Maximum	14.0	18.0	7.0	18.0	18.0

Note: Positive values represent an increase in asthma control after treatment. Negative values represent a decrease in asthma control after treatment.

Table 10-9 Change in ACT score at 6 months compared to Baseline by subgroup Asthma pre-medication before the study inclusion (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Change in ACT score at 6 months compared to Baseline for patients treated with ICS+LABA (high-dose) before the study inclusion					

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
n	48	59	16	75	123
Mean	3.4	4.7	2.8	4.3	4.0
Standard deviation	5.0	5.1	3.1	4.8	4.9
Minimum	-10.0	-9.0	-3.0	-9.0	-10.0
1st quartile	1.0	1.0	1.0	1.0	1.0
Median	4.0	5.0	2.0	4.0	4.0
3rd quartile	6.0	8.0	5.0	8.0	7.0
Maximum	14.0	14.0	9.0	14.0	14.0
Change in ACT score at 6 months compared to Baseline for patients treated with ICS+LAMA+LABA (medium-dose or high-dose) before the study inclusion					
n	102	63	8	71	173
Mean	2.7	3.6	4.3	3.6	3.1
Standard deviation	3.3	5.1	1.8	4.8	4.0
Minimum	-10.0	-9.0	2.0	-9.0	-10.0
1st quartile	1.0	-1.0	3.0	0.0	1.0
Median	2.0	3.0	4.0	3.0	3.0
3rd quartile	5.0	7.0	5.5	7.0	5.0
Maximum	13.0	18.0	7.0	18.0	18.0

Note: Positive values represent an increase in asthma control after treatment. Negative values represent a decrease in asthma control after treatment.

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Table 10-10 Change in ACT score at 6 months compared to Baseline by asthma control assessed with ACT score before the study inclusion (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Change in ACT score at 6 months compared to Baseline for patients with controlled asthma (ACT score ≥ 20) before the study inclusion					
n	49	26	3	29	78
Mean	0.7	2.5	5.7	2.8	1.5
Standard deviation	3.8	4.7	3.1	4.6	4.2
Minimum	-10.0	-9.0	3.0	-9.0	-10.0
1st quartile	0.0	0.0	3.0	0.0	0.0
Median	0.0	2.0	5.0	2.0	1.0
3rd quartile	2.0	5.0	9.0	5.0	3.0
Maximum	11.0	13.0	9.0	13.0	13.0
Change in ACT score at 6 months compared to Baseline for patients with partially controlled asthma (16 ≤ ACT score ≤ 19) before the study inclusion					
n	52	40	6	46	98
Mean	2.8	4.1	2.5	3.9	3.3
Standard deviation	3.3	5.1	2.3	4.9	4.1
Minimum	-10.0	-8.0	1.0	-8.0	-10.0
1st quartile	1.0	0.5	1.0	1.0	1.0
Median	2.0	4.5	2.0	3.0	2.0
3rd quartile	4.0	7.0	2.0	7.0	5.0
Maximum	13.0	18.0	7.0	18.0	18.0

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Change in ACT score at 6 months compared to Baseline for patients with uncontrolled asthma (ACT score ≤ 15) before the study inclusion					
n	50	58	15	73	123
Mean	5.4	5.2	3.1	4.8	5.0
Standard deviation	3.5	5.2	2.9	4.9	4.4
Minimum	-5.0	-9.0	-3.0	-9.0	-9.0
1st quartile	3.0	2.0	1.0	2.0	2.0
Median	5.0	5.5	4.0	5.0	5.0
3rd quartile	7.0	8.0	5.0	8.0	8.0
Maximum	14.0	16.0	7.0	16.0	16.0

Note: Positive values represent an increase in asthma control after treatment. Negative values represent a decrease in asthma control after treatment.

Secondary Outcome Result(s)

1. Description of reasons for prescribing MF/IND/GLY plus sensor or triple FDC as indicated by the physician

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Table 10-11 Main reason for prescribing the treatment (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Main reason for prescribing the treatment from the physician's perspective, n (%)					
Patient is not adequately controlled on current medication	145 (65.3)	124 (72.1)	22 (71.0)	146 (71.9)	291 (68.5)
Switch from free combination to fixed-dose combination	47 (21.2)	28 (16.3)	7 (22.6)	35 (17.2)	82 (19.3)
Patient has difficulty handling previous inhalers	1 (0.5)	2 (1.2)	1 (3.2)	3 (1.5)	4 (0.9)
Preference for new inhaler	7 (3.2)	11 (6.4)	0 (0.0)	11 (5.4)	18 (4.2)
Preference for the active ingredients	3 (1.4)	7 (4.1)	0 (0.0)	7 (3.4)	10 (2.4)
Digital support*	14 (6.3)	-	-	-	14 (3.3)
Adherence support*	5 (2.3)	-	-	-	5 (1.2)
Other reason	0 (0.0)	0 (0.0)	1 (3.2)	1 (0.5)	1 (0.2)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)

Main reason for prescribing the treatment from the patient's perspective, n (%)					
Patient is not adequately controlled on current medication	130 (58.6)	113 (65.7)	19 (61.3)	132 (65.0)	262 (61.6)
Switch from free combination to fixed-dose combination	45 (20.3)	22 (12.8)	10 (32.3)	32 (15.8)	77 (18.1)
Patient has difficulty handling previous inhalers	1 (0.5)	3 (1.7)	0 (0.0)	3 (1.5)	4 (0.9)
Preference for new inhaler	13 (5.9)	27 (15.7)	1 (3.2)	28 (13.8)	41 (9.6)
Preference for the active ingredients	4 (1.8)	6 (3.5)	0 (0.0)	6 (3.0)	10 (2.4)
Digital support*	24 (10.8)	-	-	-	24 (5.6)
Adherence support*	5 (2.3)	-	-	-	5 (1.2)
Other reason	0 (0.0)	1 (0.6)	1 (3.2)	2 (1.0)	2 (0.5)

(*) Only collected for patients treated with MF/IND/GLY in combination with the sensor system.

2. Description of patient characteristics at baseline

   Please see baseline characteristics section

3. Percentage of patients showing an improvement in self-reported test adherence to inhalers (TAI) questionnaire

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Table 10-13 Development of adherence according to TAI (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Development of adherence according to TAI at 3 months (visit 2) compared to Baseline, n (%)					
From non-adherent to adherent	7 (4.2)	12 (9.5)	1 (4.0)	13 (8.6)	20 (6.3)
From non-adherent to moderately adherent	9 (5.5)	10 (7.9)	1 (4.0)	11 (7.3)	20 (6.3)
From moderately adherent to adherent	17 (10.3)	21 (16.7)	4 (16.0)	25 (16.6)	42 (13.3)
No improvement in adherence	132 (80.0)	83 (65.9)	19 (76.0)	102 (67.5)	234 (74.1)
Missing	57	46	6	52	109
Development of adherence according to TAI at 6 months (visit 3) compared to Baseline, n (%)					
From non-adherent to adherent	8 (5.4)	8 (6.7)	1 (4.2)	9 (6.3)	17 (5.8)
From non-adherent to moderately adherent	8 (5.4)	11 (9.2)	1 (4.2)	12 (8.3)	20 (6.9)
From moderately adherent to adherent	17 (11.6)	17 (14.2)	6 (25.0)	23 (16.0)	40 (13.7)
No improvement in adherence	114 (77.6)	84 (70.0)	16 (66.7)	100 (69.4)	214 (73.5)
Missing	75	52	7	59	134

Note: Non-adherent: TAI ≤ 45; Moderately adherent: 46 ≤ TAI ≤ 49; Adherent: TAI = 50.

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Table 10-14 Development of adherence according to TAI by subgroup "patients with medication-treated chronic disease beside asthma" (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Patients with medication-treated chronic disease besides asthma, n (%)					
Yes	77 (34.7)	78 (45.3)	15 (48.4)	93 (45.8)	170 (40.0)
No or unknown	145 (65.3)	94 (54.7)	16 (51.6)	110 (54.2)	255 (60.0)
Development of adherence according to TAI at 3 months (visit 2) compared to Baseline for patients with medication-treated chronic disease, n (%)					
From non-adherent to adherent	1 (2.1)	4 (6.7)	0 (0.0)	4 (5.6)	5 (4.2)
From non-adherent to moderately adherent	2 (4.2)	6 (10.0)	0 (0.0)	6 (8.3)	8 (6.7)
From moderately adherent to adherent	10 (20.8)	11 (18.3)	2 (16.7)	13 (18.1)	23 (19.2)
No improvement in adherence	35 (72.9)	39 (65.0)	10 (83.3)	49 (68.1)	84 (70.0)
Missing	29	18	3	21	50
Development of adherence according to TAI at 6 months (visit 3) compared to Baseline for patients with medication-treated chronic disease, n (%)					
From non-adherent to adherent	1 (2.6)	4 (7.5)	0 (0.0)	4 (6.3)	5 (4.9)
From non-adherent to moderately adherent	2 (5.1)	4 (7.5)	0 (0.0)	4 (6.3)	6 (5.8)

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	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
From moderately adherent to adherent	9 (23.1)	8 (15.1)	3 (27.3)	11 (17.2)	20 (19.4)
No improvement in adherence	27 (69.2)	37 (69.8)	8 (72.7)	45 (70.3)	72 (69.9)
Missing	38	25	4	29	67
Development of adherence according to TAI at 3 months (visit 2) compared to Baseline for patients without[1] medication-treated chronic disease, n (%)					
From non-adherent to adherent	6 (5.1)	8 (12.1)	1 (7.7)	9 (11.4)	15 (7.7)
From non-adherent to moderately adherent	7 (6.0)	4 (6.1)	1 (7.7)	5 (6.3)	12 (6.1)
From moderately adherent to adherent	7 (6.0)	10 (15.2)	2 (15.4)	12 (15.2)	19 (9.7)
No improvement in adherence	97 (82.9)	44 (66.7)	9 (69.2)	53 (67.1)	150 (76.5)
Missing	28	28	3	31	59
Development of adherence according to TAI at 6 months (visit 3) compared to Baseline for patients without[1] medication-treated chronic disease, n (%)					
From non-adherent to adherent	7 (6.5)	4 (6.0)	1 (7.7)	5 (6.3)	12 (6.4)
From non-adherent to moderately adherent	6 (5.6)	7 (10.4)	1 (7.7)	8 (10.0)	14 (7.4)
From moderately adherent to adherent	8 (7.4)	9 (13.4)	3 (23.1)	12 (15.0)	20 (10.6)
No improvement in adherence	87 (80.6)	47 (70.1)	8 (61.5)	55 (68.8)	142 (75.5)
Missing	37	27	3	30	67

Note: Non-adherent: TAI ≤ 45; Moderately adherent: 46 ≤ TAI ≤ 49; Adherent: TAI = 50.
[1] No medication-treated chronic disease besides asthma or unknown

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Table 10-15 Development of adherence according to TAI by subgroup "age of patient" (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Age group, n (%)					
< 55 years	114 (51.4)	80 (46.5)	11 (35.5)	91 (44.8)	205 (48.2)
≥ 55 years	108 (48.6)	92 (53.5)	20 (64.5)	112 (55.2)	220 (51.8)
Development of adherence according to TAI at 3 months (visit 2) compared to Baseline for patients ≥ 55 years at study inclusion, n (%)					
From non-adherent to adherent	2 (2.3)	4 (5.8)	1 (5.9)	5 (5.8)	7 (4.1)
From non-adherent to moderately adherent	0 (0.0)	6 (8.7)	0 (0.0)	6 (7.0)	6 (3.5)
From moderately adherent to adherent	6 (7.0)	14 (20.3)	3 (17.6)	17 (19.8)	23 (13.4)
No improvement in adherence	78 (90.7)	45 (65.2)	13 (76.5)	58 (67.4)	136 (79.1)
Missing	22	23	3	26	48
Development of adherence according to TAI at 6 months (visit 3) compared to Baseline for patients ≥ 55 years at study inclusion, n (%)					
From non-adherent to adherent	2 (2.6)	4 (6.3)	1 (6.3)	5 (6.3)	7 (4.5)
From non-adherent to moderately adherent	0 (0.0)	5 (7.8)	0 (0.0)	5 (6.3)	5 (3.2)
From moderately adherent to adherent	4 (5.3)	12 (18.8)	4 (25.0)	16 (20.0)	20 (12.8)
No improvement in adherence	70 (92.1)	43 (67.2)	11 (68.8)	54 (67.5)	124 (79.5)
Missing	32	28	4	32	64

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	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Development of adherence according to TAI at 3 months (visit 2) compared to Baseline for patients < 55 years at study inclusion, n (%)					
From non-adherent to adherent	5 (6.3)	8 (14.0)	0 (0.0)	8 (12.3)	13 (9.0)
From non-adherent to moderately adherent	9 (11.4)	4 (7.0)	1 (12.5)	5 (7.7)	14 (9.7)
From moderately adherent to adherent	11 (13.9)	7 (12.3)	1 (12.5)	8 (12.3)	19 (13.2)
No improvement in adherence	54 (68.4)	38 (66.7)	6 (75.0)	44 (67.7)	98 (68.1)
Missing	35	23	3	26	61
Development of adherence according to TAI at 6 months (visit 3) compared to Baseline for patients < 55 years at study inclusion, n (%)					
From non-adherent to adherent	6 (8.5)	4 (7.1)	0 (0.0)	4 (6.3)	10 (7.4)
From non-adherent to moderately adherent	8 (11.3)	6 (10.7)	1 (12.5)	7 (10.9)	15 (11.1)
From moderately adherent to adherent	13 (18.3)	5 (8.9)	2 (25.0)	7 (10.9)	20 (14.8)
No improvement in adherence	44 (62.0)	41 (73.2)	5 (62.5)	46 (71.9)	90 (66.7)
Missing	43	24	3	27	70

Note: Non-adherent: TAI ≤ 45; Moderately adherent: 46 ≤ TAI ≤ 49; Adherent: TAI = 50.

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4. Course of adherence

Table 14-16 Course of adherence according to TAI over 6 months (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
TAI Score at visit 1					
n	211	172	31	203	414
Mean	45.5	47.1	48.6	47.3	46.4
Standard deviation	4.4	4.6	2.6	4.4	4.5
Minimum	28.0	19.0	38.0	19.0	19.0
1st quartile	42.0	46.0	48.0	46.0	43.0
Median	46.0	49.0	50.0	49.0	48.0
3rd quartile	50.0	50.0	50.0	50.0	50.0
Maximum	50.0	50.0	50.0	50.0	50.0
TAI Score at visit 2					
n	170	126	25	151	321
Mean	44.4	48.5	49.4	48.6	46.4
Standard deviation	5.9	3.1	1.2	2.9	5.2
Minimum	29.0	35.0	46.0	35.0	29.0
1st quartile	39.0	48.0	49.0	48.0	42.0
Median	47.0	50.0	50.0	50.0	49.0
3rd quartile	50.0	50.0	50.0	50.0	50.0
Maximum	50.0	50.0	50.0	50.0	50.0
TAI Score at visit 3					
n	154	120	24	144	298
Mean	44.3	48.0	49.5	48.2	46.2
Standard deviation	6.5	3.5	1.1	3.3	5.6
Minimum	20.0	33.0	46.0	33.0	20.0
1st quartile	39.0	47.5	50.0	48.0	43.0
Median	48.0	50.0	50.0	50.0	49.0
3rd quartile	50.0	50.0	50.0	50.0	50.0
Maximum	50.0	50.0	50.0	50.0	50.0

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
TAI Score at last visit					
n	189	143	26	169	358
Mean	44.3	48.1	49.6	48.3	46.2
Standard deviation	6.5	3.5	1.1	3.3	5.6
Minimum	20.0	33.0	46.0	33.0	20.0
1st quartile	39.0	48.0	50.0	49.0	43.0
Median	48.0	50.0	50.0	50.0	50.0
3rd quartile	50.0	50.0	50.0	50.0	50.0
Maximum	50.0	50.0	50.0	50.0	50.0

Note: Non-adherent: TAI ≤ 45; Moderately adherent: 46 ≤ TAI ≤ 49; Adherent: TAI = 50.

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Table 14-17 Course of adherence over 6 months according to inhalation tracking App/ diary data (Analysis set)

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Week 1 after Baseline (%)					
n	100	1	-	1	101
Mean	81.1	100.0	-	100.0	81.2
Standard deviation	27.3	-	-	-	27.2
Minimum	29.0	100.0	-	100.0	29.0
1st quartile	50.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 2 after Baseline (%)					
n	101	1	-	1	102
Mean	81.5	100.0	-	100.0	81.7
Standard deviation	27.1	-	-	-	27.1
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 3 after Baseline (%)					
n	103	1	-	1	104
Mean	82.9	100.0	-	100.0	83.0
Standard deviation	25.6	-	-	-	25.6
Minimum	29.0	100.0	-	100.0	29.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 4 after Baseline (%)					
n	104	1	-	1	105
Mean	83.7	100.0	-	100.0	83.8
Standard deviation	25.3	-	-	-	25.2
Minimum	14.0	100.0	-	100.0	14.0

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 5 after Baseline (%)					
n	102	1	-	1	103
Mean	81.1	100.0	-	100.0	81.3
Standard deviation	28.3	-	-	-	28.2
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 6 after Baseline (%)					
n	102	1	-	1	103
Mean	82.7	100.0	-	100.0	82.8
Standard deviation	26.2	-	-	-	26.1
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 7 after Baseline (%)					
n	102	1	-	1	103
Mean	81.3	100.0	-	100.0	81.5
Standard deviation	27.4	-	-	-	27.4
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 8 after Baseline (%)					
n	104	1	-	1	105
Mean	83.5	100.0	-	100.0	83.7

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Standard deviation	26.1	-	-	-	26.1
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 9 after Baseline (%)					
n	106	1	-	1	107
Mean	83.3	100.0	-	100.0	83.5
Standard deviation	26.2	-	-	-	26.1
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 10 after Baseline (%)					
n	105	1	-	1	106
Mean	82.6	100.0	-	100.0	82.8
Standard deviation	27.0	-	-	-	26.9
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 11 after Baseline (%)					
n	104	1	-	1	105
Mean	83.0	100.0	-	100.0	83.2
Standard deviation	26.1	-	-	-	26.0
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 12 after Baseline (%)					

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	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
n	102	1	-	1	103
Mean	81.9	100.0	-	100.0	82.0
Standard deviation	27.8	-	-	-	27.7
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 13 after Baseline (%)					
n	92	1	-	1	93
Mean	83.3	100.0	-	100.0	83.5
Standard deviation	27.6	-	-	-	27.5
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	71.5	100.0	-	100.0	86.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 14 after Baseline (%)					
n	86	1	-	1	87
Mean	82.1	100.0	-	100.0	82.3
Standard deviation	27.2	-	-	-	27.1
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 15 after Baseline (%)					
n	80	1	-	1	81
Mean	81.1	86.0	-	86.0	81.2
Standard deviation	27.6	-	-	-	27.4
Minimum	14.0	86.0	-	86.0	14.0
1st quartile	57.0	86.0	-	86.0	57.0
Median	100.0	86.0	-	86.0	100.0
3rd quartile	100.0	86.0	-	86.0	100.0

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Maximum	100.0	86.0	-	86.0	100.0
Week 16 after Baseline (%)					
n	80	1	-	1	81
Mean	81.5	100.0	-	100.0	81.7
Standard deviation	28.5	-	-	-	28.4
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	57.0	100.0	-	100.0	57.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 17 after Baseline (%)					
n	77	1	-	1	78
Mean	83.2	100.0	-	100.0	83.4
Standard deviation	28.5	-	-	-	28.4
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	86.0	100.0	-	100.0	86.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 18 after Baseline (%)					
n	77	1	-	1	78
Mean	82.2	100.0	-	100.0	82.5
Standard deviation	29.1	-	-	-	29.0
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	71.0	100.0	-	100.0	71.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 19 after Baseline (%)					
n	74	1	-	1	75
Mean	84.4	100.0	-	100.0	84.6
Standard deviation	26.9	-	-	-	26.8
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	86.0	100.0	-	100.0	86.0

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 20 after Baseline (%)					
n	74	1	-	1	75
Mean	85.2	86.0	-	86.0	85.2
Standard deviation	27.8	-	-	-	27.6
Minimum	0.0	86.0	-	86.0	0.0
1st quartile	86.0	86.0	-	86.0	86.0
Median	100.0	86.0	-	86.0	100.0
3rd quartile	100.0	86.0	-	86.0	100.0
Maximum	100.0	86.0	-	86.0	100.0
Week 21 after Baseline (%)					
n	72	1	-	1	73
Mean	84.4	86.0	-	86.0	84.4
Standard deviation	27.1	-	-	-	26.9
Minimum	0.0	86.0	-	86.0	0.0
1st quartile	86.0	86.0	-	86.0	86.0
Median	100.0	86.0	-	86.0	100.0
3rd quartile	100.0	86.0	-	86.0	100.0
Maximum	100.0	86.0	-	86.0	100.0
Week 22 after Baseline (%)					
n	69	1	-	1	70
Mean	86.8	100.0	-	100.0	87.0
Standard deviation	27.0	-	-	-	26.8
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	86.0	100.0	-	100.0	86.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 23 after Baseline (%)					
n	68	1	-	1	69
Mean	88.3	100.0	-	100.0	88.4
Standard deviation	23.6	-	-	-	23.5

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	86.0	100.0	-	100.0	86.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 24 after Baseline (%)					
n	67	1	-	1	68
Mean	87.9	100.0	-	100.0	88.1
Standard deviation	25.0	-	-	-	24.8
Minimum	0.0	100.0	-	100.0	0.0
1st quartile	86.0	100.0	-	100.0	86.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 25 after Baseline (%)					
n	60	1	-	1	61
Mean	86.7	100.0	-	100.0	86.9
Standard deviation	26.9	-	-	-	26.7
Minimum	14.0	100.0	-	100.0	14.0
1st quartile	93.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 26 after Baseline (%)					
n	48	1	-	1	49
Mean	88.4	71.0	-	71.0	88.1
Standard deviation	24.5	-	-	-	24.4
Minimum	14.0	71.0	-	71.0	14.0
1st quartile	100.0	71.0	-	71.0	100.0
Median	100.0	71.0	-	71.0	100.0
3rd quartile	100.0	71.0	-	71.0	100.0
Maximum	100.0	71.0	-	71.0	100.0
Week 27 after Baseline (%)					
n	35	1	-	1	36

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Mean	89.4	71.0	-	71.0	88.9
Standard deviation	21.4	-	-	-	21.3
Minimum	29.0	71.0	-	71.0	29.0
1st quartile	86.0	71.0	-	71.0	86.0
Median	100.0	71.0	-	71.0	100.0
3rd quartile	100.0	71.0	-	71.0	100.0
Maximum	100.0	71.0	-	71.0	100.0
Week 28 after Baseline (%)					
n	22	1	-	1	23
Mean	94.8	100.0	-	100.0	95.0
Standard deviation	15.0	-	-	-	14.7
Minimum	43.0	100.0	-	100.0	43.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 29 after Baseline (%)					
n	14	1	-	1	15
Mean	89.9	100.0	-	100.0	90.5
Standard deviation	23.3	-	-	-	22.6
Minimum	29.0	100.0	-	100.0	29.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 30 after Baseline (%)					
n	11	1	-	1	12
Mean	88.4	100.0	-	100.0	89.3
Standard deviation	23.7	-	-	-	22.8
Minimum	29.0	100.0	-	100.0	29.0
1st quartile	86.0	100.0	-	100.0	93.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0

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	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
Week 31 after Baseline (%)					
n	8	1	-	1	9
Mean	91.1	100.0	-	100.0	92.1
Standard deviation	20.1	-	-	-	19.0
Minimum	43.0	100.0	-	100.0	43.0
1st quartile	93.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 32 after Baseline (%)					
n	5	1	-	1	6
Mean	97.2	100.0	-	100.0	97.7
Standard deviation	6.3	-	-	-	5.7
Minimum	86.0	100.0	-	100.0	86.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 33 after Baseline (%)					
n	3	1	-	1	4
Mean	95.3	100.0	-	100.0	96.5
Standard deviation	8.1	-	-	-	7.0
Minimum	86.0	100.0	-	100.0	86.0
1st quartile	86.0	100.0	-	100.0	93.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 34 after Baseline (%)					
n	2	1	-	1	3
Mean	100.0	100.0	-	100.0	100.0
Standard deviation	0.0	-	-	-	0.0
Minimum	100.0	100.0	-	100.0	100.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0

	Enerzair® with sensor system * (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal ** (N=203)	Total (N=425)
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 35 after Baseline (%)					
n	1	1	-	1	2
Mean	100.0	100.0	-	100.0	100.0
Standard deviation	-	-	-	-	0.0
Minimum	100.0	100.0	-	100.0	100.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 36 after Baseline (%)					
n	1	1	-	1	2
Mean	100.0	100.0	-	100.0	100.0
Standard deviation	-	-	-	-	0.0
Minimum	100.0	100.0	-	100.0	100.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0
Week 37 after Baseline (%)					
n	1	1	-	1	2
Mean	100.0	100.0	-	100.0	100.0
Standard deviation	-	-	-	-	0.0
Minimum	100.0	100.0	-	100.0	100.0
1st quartile	100.0	100.0	-	100.0	100.0
Median	100.0	100.0	-	100.0	100.0
3rd quartile	100.0	100.0	-	100.0	100.0
Maximum	100.0	100.0	-	100.0	100.0

Note: App data on adherence were collected from all patients treated with MF/IND/GLY in combination with sensor system,
diary data on adherence were collected from all patients treated with ICS+LAMA+LABA FDC.
The App data were recorded automatically, the diary data were entered manually.
To make the comparison of adherence between App and diary data easier, results from the diary data on adherence were converted and shown in percent.
(*) Total number of patients treated with MF/IND/GLY in combination with sensor system
(**) Total number of patients treated with ICS+LAMA+LABA FDC

5. Percentage of days with adherence to treatment in the subgroup receiving MF/IND/GLY plus sensor

Table 10-16 Percentage of days with adherent medication use over 6 months – only for treatment group MF/IND/GLY in combination with sensor system

Analysis set for patients in treatment group Enerzair® with sensor system	
	Total * (N=222)
Percentage of days with adherent medication use over 6 months (%)	
n	110
Mean	77.5
Standard deviation	26.4
Minimum	24.4
1st quartile	49.0
Median	95.9
3rd quartile	100.0
Maximum	100.0

(*) Total number of patients treated with MF/IND/GLY in combination with sensor system

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Table 10-17 Course of the App usage according to patient's indication – only for treatment group MF/IND/GLY in combination with sensor system

Analysis set for patients in treatment group Enerzair® with sensor system	Visit 2 * (N=183)	Visit 3 * (N=169)
App usage at least once per week		
No	9 (4.9)	14 (8.3)
Yes	148 (80.9)	124 (73.4)
Unknown	26 (14.2)	31 (18.3)
App usage only on certain days (e.g. not on weekends)		
No	101 (68.2)	84 (67.7)
Yes	30 (20.3)	34 (27.4)
Unknown	17 (11.5)	6 (4.8)
Missing	35	45
How many days per week on average has the patient used the App since the last visit?		
Once a week	7 (4.7)	6 (4.8)
2 to 4 times a week	74 (50.0)	69 (55.6)
5 to 7 times a week	53 (35.8)	43 (34.7)
Unsystematic use	3 (2.0)	1 (0.8)

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Analysis set for patients in treatment group Enerzair® with sensor system	Visit 2 * (N=183)	Visit 3 * (N=169)
Unknown	11 (7.4)	5 (4.0)
Missing	35	45
How often did the patient use the App?		
Never	5 (55.6)	5 (35.7)
Only at the beginning after the last visit	2 (22.2)	1 (7.1)
Only at the end of the time between visits	0 (0.0)	0 (0.0)
Use of App only during clinical deterioration	0 (0.0)	0 (0.0)
Use of App not during vacation	0 (0.0)	0 (0.0)
Irregular use due to other circumstances	1 (11.1)	4 (28.6)
Unknown	1 (11.1)	4 (28.6)
Missing	174	155
Time period of the App usage		
Less than one week	0 (0.0)	1 (100.0)
Up to 2 weeks	2 (100.0)	0 (0.0)
Up to 5 weeks	0 (0.0)	0 (0.0)
Up to 8 weeks	0 (0.0)	0 (0.0)
Up to 11 weeks	0 (0.0)	0 (0.0)
Unknown	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)
Missing	181	168
Reason for irregular App use according to physician's assessment		
Good asthma control	0 (0.0)	2 (14.3)
No motivation for self-engagement	2 (22.2)	4 (28.6)
Other reason	7 (77.8)	8 (57.1)
Missing	174	155

(*) Total number of patients treated with 'MF/IND/GLY in combination with sensor system' for whom th e respective visit is documented

6. Clinically relevant improvement in ACT score: Proportion of patients showing clinically relevant improvement in ACT score of 3 points at 6 months

Table 10-19 Effect description on asthma control according to ACT scores at Baseline and after 6 months (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+ LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+ LABA FDC: Trimbow® (N=31)	ICS+LAMA+ LABA FDC: subtotal (N=203)	Total (N=425)
Patients showing clinically relevant improvement in ACT score after 6 months					
Yes	76 (50.3)	74 (59.7)	14 (58.3)	88 (59.5)	164 (54.8)
No	75 (49.7)	50 (40.3)	10 (41.7)	60 (40.5)	135 (45.2)
Missing	71	48	7	55	126
ACT scores of patients at Baseline and after 6 months					
< 19 at Baseline and < 19 after 6 months	26 (17.2)	42 (33.9)	12 (50.0)	54 (36.5)	80 (26.8)
< 19 at Baseline and ≥ 19 after 6 months	70 (46.4)	55 (44.4)	9 (37.5)	64 (43.2)	134 (44.8)
≥ 19 at Baseline and < 19 after 6 months	7 (4.6)	4 (3.2)	0 (0.0)	4 (2.7)	11 (3.7)
≥ 19 at Baseline and ≥ 19 after 6 months	48 (31.8)	23 (18.5)	3 (12.5)	26 (17.6)	74 (24.7)
Missing value at Baseline or after 6 months	71	48	7	55	126

Note: Clinically relevant improvement for a patient means that the ACT score from this patient at visit 3 is at least 3 points higher than the ACT score at Baseline.

7. Percentage of patients with an ACT score <19

Please see table above (Table 10-19)

8. Course of lung function trough Forced Expiratory Volume in one second (FEV1)

Table 10-20 Course of lung function (FEV_1) over 6 months compared to Baseline (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
FEV_1 at visit 1 (L/S)					
n	221	169	30	199	420
Mean	2.32	2.29	1.73	2.20	2.27
Standard deviation	0.82	0.86	0.71	0.86	0.84
Minimum	0.80	0.82	0.71	0.71	0.71
1st quartile	1.70	1.59	1.13	1.51	1.59
Median	2.26	2.17	1.63	2.14	2.21
3rd quartile	2.77	2.84	2.27	2.71	2.76
Maximum	5.22	4.59	3.46	4.59	5.22
FEV_1 at visit 2 (L/S)					
n	180	132	25	157	337
Mean	2.46	2.35	1.83	2.27	2.37
Standard deviation	0.80	0.89	0.74	0.89	0.85
Minimum	0.67	0.82	0.75	0.75	0.67
1st quartile	1.86	1.62	1.23	1.57	1.73
Median	2.38	2.28	1.67	2.21	2.31
3rd quartile	2.94	2.85	2.27	2.81	2.86
Maximum	5.44	4.79	3.53	4.79	5.44
FEV_1 at visit 3 (L/S)					
n	167	122	22	144	311
Mean	2.44	2.41	1.84	2.32	2.39
Standard deviation	0.86	0.92	0.70	0.91	0.88
Minimum	0.70	0.80	0.85	0.80	0.70
1st quartile	1.82	1.60	1.25	1.55	1.67
Median	2.41	2.39	1.57	2.22	2.35
3rd quartile	2.90	2.97	2.49	2.89	2.90
Maximum	5.44	4.88	3.44	4.88	5.44

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	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
FEV_1 at last visit (L/S)					
n	186	138	23	161	347
Mean	2.46	2.40	1.86	2.32	2.40
Standard deviation	0.85	0.91	0.69	0.90	0.88
Minimum	0.70	0.80	0.85	0.80	0.70
1st quartile	1.83	1.60	1.25	1.57	1.71
Median	2.41	2.35	1.60	2.26	2.35
3rd quartile	2.98	2.97	2.49	2.86	2.94
Maximum	5.44	4.88	3.44	4.88	5.44
Change of FEV_1 at 6 months compared to Baseline (L/S)					
n	166	121	22	143	309
Mean	0.15	0.15	0.08	0.14	0.15
Standard deviation	0.41	0.36	0.19	0.34	0.38
Minimum	-0.87	-1.20	-0.38	-1.20	-1.20
1st quartile	-0.04	-0.02	-0.01	-0.02	-0.02
Median	0.08	0.16	0.03	0.14	0.12
3rd quartile	0.26	0.29	0.17	0.26	0.26
Maximum	3.63	1.72	0.69	1.72	3.63

Change of FEV_1 was calculated using FEV_1 at 6 months − FEV_1 at Baseline.

9. Course of forced vital capacity (FVC)

Table 10-21 Course of lung function (FVC) over 6 months compared to Baseline (Analysis set)

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
FVC at visit 1 (L)					
n	219	165	30	195	414
Mean	3.2	3.1	2.4	3.0	3.1
Standard deviation	1.0	1.1	0.8	1.1	1.0
Minimum	1.3	1.2	1.4	1.2	1.2
1st quartile	2.4	2.4	1.8	2.2	2.3
Median	3.0	3.0	2.2	2.9	3.0
3rd quartile	3.9	3.8	3.0	3.7	3.8
Maximum	6.8	5.9	4.6	5.9	6.8
FVC at visit 2 (L)					
n	180	131	25	156	336
Mean	3.3	3.2	2.5	3.1	3.2
Standard deviation	1.0	1.1	0.9	1.1	1.0
Minimum	1.5	1.0	1.3	1.0	1.0
1st quartile	2.5	2.4	1.9	2.3	2.4
Median	3.1	3.0	2.4	3.0	3.1
3rd quartile	4.0	3.9	3.2	3.8	3.9
Maximum	7.3	6.4	4.5	6.4	7.3
FVC at visit 3 (L)					
n	167	122	22	144	311
Mean	3.3	3.2	2.6	3.1	3.2
Standard deviation	1.1	1.1	0.9	1.1	1.1
Minimum	1.4	0.8	1.5	0.8	0.8
1st quartile	2.4	2.4	1.8	2.3	2.3

	Enerzair® with sensor system (N=222)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=172)	ICS+LAMA+LABA FDC: Trimbow® (N=31)	ICS+LAMA+LABA FDC: subtotal (N=203)	Total (N=425)
Median	3.2	3.1	2.6	3.0	3.0
3rd quartile	4.0	4.0	3.4	4.0	4.0
Maximum	6.9	5.5	4.3	5.5	6.9
FVC at last visit (L)					
n	186	138	23	161	347
Mean	3.3	3.2	2.6	3.1	3.2
Standard deviation	1.1	1.1	0.9	1.1	1.1
Minimum	1.4	0.8	1.5	0.8	0.8
1st quartile	2.4	2.4	1.8	2.3	2.4
Median	3.3	3.0	2.6	3.0	3.1
3rd quartile	4.0	4.0	3.4	4.0	4.0
Maximum	6.9	6.4	4.3	6.4	6.9
Change of FVC at 6 months compared to Baseline (L)					
n	164	117	22	139	303
Mean	0.1	0.1	0.2	0.1	0.1
Standard deviation	0.5	0.4	0.4	0.4	0.4
Minimum	-1.0	-1.4	-0.3	-1.4	-1.4
1st quartile	-0.1	-0.1	-0.1	-0.1	-0.1
Median	0.1	0.1	0.1	0.1	0.1
3rd quartile	0.3	0.3	0.3	0.3	0.3
Maximum	2.8	1.2	1.0	1.2	2.8

Change of FVC was calculated using FVC at 6 months − FVC at Baseline.

10. Adverse events

Please see the safety section

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

No data identified.

Safety Results

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Table 10-30 Overview of patients with adverse events (Safety Set)

Number of patients with at least one event of the following types:	Enerzair® with sensor system (N=210) n (%) [95% CI]	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%) [95% CI]	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%) [95% CI]	ICS+LAMA+LABA FDC: subtotal (N=187) n (%) [95% CI]	Total (N=397) n (%) [95% CI]
Adverse event	62 (29.5) [23.4 - 36.2]	44 (27.7) [20.9 - 35.3]	7 (25.0) [10.7 - 44.9]	51 (27.3) [21.0 - 34.3]	113 (28.5) [24.1 - 33.2]
Adverse event with suspected relationship to respective study medication (ADR)	22 (10.5) [6.7 - 15.4]	17 (10.7) [6.4 - 16.6]	4 (14.3) [4.0 - 32.7]	21 (11.2) [7.1 - 16.7]	43 (10.8) [8.0 - 14.3]
Adverse event with suspected relationship to sensor or Propeller-App	8 (3.8) [1.7 - 7.4]	N.A.	N.A.	N.A.	8 (2.0) [0.9 - 3.9]
Adverse event with suspected relationship to COVID-19	3 (1.4) [0.3 - 4.1]	3 (1.9) [0.4 - 5.4]	0 (0.0) [0.0 - 12.3]	3 (1.6) [0.3 - 4.6]	6 (1.5) [0.6 - 3.3]
Adverse event leading to discontinuation of study medication	25 (11.9) [7.9 - 17.1]	20 (12.6) [7.9 - 18.8]	3 (10.7) [2.3 - 28.2]	23 (12.3) [8.0 - 17.9]	48 (12.1) [9.1 - 15.7]
Serious adverse event	3 (1.4) [0.3 - 4.1]	2 (1.3) [0.2 - 4.5]	0 (0.0) [0.0 - 12.3]	2 (1.1) [0.1 - 3.8]	5 (1.3) [0.4 - 2.9]
Serious adverse event with suspected relationship to respective study medication	0 (0.0) [0.0 - 1.7]	0 (0.0) [0.0 - 2.3]	0 (0.0) [0.0 - 12.3]	0 (0.0) [0.0 - 2.0]	0 (0.0) [0.0 - 0.9]
Serious adverse event with suspected relationship to sensor or Propeller-App	0 (0.0) [0.0 - 1.7]	N.A.	N.A.	N.A.	0 (0.0) [0.0 - 0.9]
Serious adverse event with suspected relationship to COVID-19	1 (0.5) [0.0 - 2.6]	0 (0.0) [0.0 - 2.3]	0 (0.0) [0.0 - 12.3]	0 (0.0) [0.0 - 2.0]	1 (0.3) [0.0 - 1.4]
Serious adverse event leading to discontinuation of study medication	1 (0.5) [0.0 - 2.6]	0 (0.0) [0.0 - 2.3]	0 (0.0) [0.0 - 12.3]	0 (0.0) [0.0 - 2.0]	1 (0.3) [0.0 - 1.4]

Data source: eCRF data were reconciled with the ARGUS data base of Novartis Safety Department at the final closure of the database.
Definition of Safety Set: Patients with post-Baseline data (either post-Baseline visit or any information on AE page) and for whom the date of initiation of study medication use was entered in the eCRF during the study.

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Table 10-31 Summary of patients with adverse events (Safety Set)

MedDRA SOC MedDRA PT	Enerzair® with sensor system (N=210) n (%)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%)	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%)	ICS+LAMA+LABA FDC: subtotal (N=187) n (%)	Total (N=397) n (%)
Patients with at least one adverse event *	62 (29.5)	44 (27.7)	7 (25.0)	51 (27.3)	113 (28.5)
Blood and lymphatic system disorders	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Hypereosinophilic syndrome	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Cardiac disorders	2 (1.0)	1 (0.6)	0 (0.0)	1 (0.5)	3 (0.8)
Cardiac ventricular thrombosis	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Myocardial infarction	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Right ventricular failure	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Tachycardia	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Gastrointestinal disorders	1 (0.5)	1 (0.6)	1 (3.6)	2 (1.1)	3 (0.8)
Abdominal pain upper	0 (0.0)	0 (0.0)	1 (3.6)	1 (0.5)	1 (0.3)
Nausea	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
General disorders and administration site conditions	8 (3.8)	8 (5.0)	1 (3.6)	9 (4.8)	17 (4.3)
Chest discomfort	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Chest pain	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Drug ineffective	4 (1.9)	8 (5.0)	1 (3.6)	9 (4.8)	13 (3.3)
Fatigue	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
General physical health deterioration	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

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MedDRA SOC MedDRA PT	Enerzair® with sensor system (N=210) n (%)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%)	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%)	ICS+LAMA+LABA FDC: subtotal (N=187) n (%)	Total (N=397) n (%)
Immune system disorders	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
Anaphylactic shock	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Mite allergy	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Infections and infestations	15 (7.1)	9 (5.7)	0 (0.0)	9 (4.8)	24 (6.0)
Bronchitis	1 (0.5)	2 (1.3)	0 (0.0)	2 (1.1)	3 (0.8)
COVID-19	5 (2.4)	5 (3.1)	0 (0.0)	5 (2.7)	10 (2.5)
Cystitis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Erysipelas	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Fungal infection	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Infection	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
Infective exacerbation of asthma	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Nasopharyngitis	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Oral candidiasis	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Sinusitis	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Wound infection	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Injury, poisoning and procedural complications	1 (0.5)	3 (1.9)	0 (0.0)	3 (1.6)	4 (1.0)
Device difficult to use	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Device use issue	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Fall	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Joint injury	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Rib fracture	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)

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MedDRA SOC MedDRA PT	Enerzair® with sensor system (N=210) n (%)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%)	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%)	ICS+LAMA+LABA FDC: subtotal (N=187) n (%)	Total (N=397) n (%)
Investigations	4 (1.9)	2 (1.3)	0 (0.0)	2 (1.1)	6 (1.5)
Forced expiratory volume decreased	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
Forced vital capacity decreased	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
Fractional exhaled nitric oxide increased	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Pulmonary function test decreased	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Weight increased	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Musculoskeletal and connective tissue disorders	3 (1.4)	2 (1.3)	0 (0.0)	2 (1.1)	5 (1.3)
Foot deformity	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Muscle spasms	2 (1.0)	1 (0.6)	0 (0.0)	1 (0.5)	3 (0.8)
Musculoskeletal discomfort	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Nervous system disorders	4 (1.9)	4 (2.5)	1 (3.6)	5 (2.7)	9 (2.3)
Disturbance in attention	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Headache	3 (1.4)	3 (1.9)	0 (0.0)	3 (1.6)	6 (1.5)
Tremor	1 (0.5)	0 (0.0)	1 (3.6)	1 (0.5)	2 (0.5)
Product issues	8 (3.8)	1 (0.6)	0 (0.0)	1 (0.5)	9 (2.3)
Device wireless communication issue	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Product quality issue	7 (3.3)	1 (0.6)	0 (0.0)	1 (0.5)	8 (2.0)

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MedDRA SOC MedDRA PT	Enerzair® with sensor system (N=210) n (%)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%)	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%)	ICS+LAMA+LABA FDC: subtotal (N=187) n (%)	Total (N=397) n (%)
Renal and urinary disorders	0 (0.0)	2 (1.3)	0 (0.0)	2 (1.1)	2 (0.5)
Dysuria	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Urinary retention	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Respiratory, thoracic and mediastinal disorders	34 (16.2)	21 (13.2)	5 (17.9)	26 (13.9)	60 (15.1)
Aphonia	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Asthma	13 (6.2)	7 (4.4)	3 (10.7)	10 (5.3)	23 (5.8)
Chronic obstructive pulmonary disease	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Cough	9 (4.3)	5 (3.1)	1 (3.6)	6 (3.2)	15 (3.8)
Dysphonia	3 (1.4)	2 (1.3)	1 (3.6)	3 (1.6)	6 (1.5)
Dyspnoea	7 (3.3)	5 (3.1)	1 (3.6)	6 (3.2)	13 (3.3)
Dyspnoea exertional	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Lower respiratory tract congestion	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Nasal polyps	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Obstructive sleep apnoea syndrome	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Oropharyngeal pain	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Pharyngeal paraesthesia	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Productive cough	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Rales	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Respiratory failure	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Sleep apnoea syndrome	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Sputum discoloured	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Throat irritation	2 (1.0)	1 (0.6)	0 (0.0)	1 (0.5)	3 (0.8)

MedDRA SOC MedDRA PT	Enerzair® with sensor system (N=210) n (%)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%)	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%)	ICS+LAMA+LABA FDC: subtotal (N=187) n (%)	Total (N=397) n (%)
Skin and subcutaneous tissue disorders	2 (1.0)	2 (1.3)	0 (0.0)	2 (1.1)	4 (1.0)
Pruritus	0 (0.0)	2 (1.3)	0 (0.0)	2 (1.1)	2 (0.5)
Rash	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Social circumstances	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Patient dissatisfaction with device	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)

(*) A patient was counted only once in the respective system organ class and/or the preferred term.

All-Cause Mortality

There was no death in this study.

Serious Adverse Events

Table 14-23 Summary of patients with serious adverse events (Safety set (SAF))

MedDRA primary system organ class MedDRA preferred term	Enerzair® with sensor system (N=210) n (%)	ICS+LAMA+LABA FDC: Enerzair® without sensor system (N=159) n (%)	ICS+LAMA+LABA FDC: Trimbow® (N=28) n (%)	ICS+LAMA+LABA FDC: subtotal (N=187) n (%)	Total (N=397) n (%)
Patients with at least one serious adverse event *	**3 (1.4)**	**2 (1.3)**	**0 (0.0)**	**2 (1.1)**	**5 (1.3)**
Cardiac disorders	**1 (0.5)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (0.3)**
Myocardial infarction	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Infections and infestations	**2 (1.0)**	**2 (1.3)**	**0 (0.0)**	**2 (1.1)**	**4 (1.0)**
COVID-19	1 (0.5)	1 (0.6)	0 (0.0)	1 (0.5)	2 (0.5)
Erysipelas	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.5)	1 (0.3)
Wound infection	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Respiratory, thoracic and mediastinal disorders	**1 (0.5)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**1 (0.3)**
Chronic obstructive pulmonary disease	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Respiratory failure	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

(*) A patient is counted only once in the respective system organ class and/or the preferred term.

Other Relevant Findings

Not applicable

Conclusion:

Overall, this NIS provides useful data on asthma control under treatment with MF/IND/GLY in combination with the sensor system for inhalation tracking or with any other ICS+LABA+LAMA FDC in real life conditions. Improvement in asthma

control was achieved at 6 months in both study groups with higher mean change in ACT score and adherence was observed in ICS+LABA+LAMA FDC group compared to MF/IND/GLY group. Similar results were observed when the change in ACT score and adherence was analyzed by subgroups. This study also supports the potential benefit of sensor system which shows higher adherence through inhalation tracking, reminder notifications, and patient activation.

Date of Clinical Trial Report

12 Sep 2023