

SUPPLEMENTARY INFORMATION

Characteristics of Patients with COPD Initiating

Budesonide/Glycopyrronium/Formoterol or Other Triple Therapies in Japan: A Real-World Healthcare Claims Database Study (MITOS-AURA)

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12 **Table S1.** Respiratory antibiotic list

Antibiotic substance name			
• Amoxicillin hydrate	• Cefaclor	• Cefteram pivoxil	• Josamycin
• Amoxicillin hydrate/potassium clavulanate	• Cefalexin	• Ceftributen hydrate	• Josamycin propionate
• Ampicillin hydrate	• Cefatrizine propylene glycolate	• Cefuroxime axetil	• Lincomycin hydrochloride hydrate
• Ampicillin hydrate/cloxacillin sodium hydrate	• Cefcapene pivoxil hydrochloride hydrate	• Clarithromycin	• Piperacillin sodium
• Ampicillin sodium	• Cefdinir	• Clindamycin hydrochloride	• Rokitamycin
• Ampicillin sodium/cloxacillin sodium hydrate	• Cefditoren pivoxil	• Clindamycin phosphate	• Roxithromycin
• Ampicillin sodium/sulbactam sodium	• Cefixime hydrate	• Erythromycin	• Spiramycin acetate
• Aspoxicillin hydrate	• Cefotiam hexetil hydrochloride	• Erythromycin ethylsuccinate	• Sultamicillin tosilate hydrate
• Azithromycin hydrate	• Cefpodoxime proxetil	• Erythromycin lactobionate	• Tazobactam sodium/piperacillin sodium
• Bacampicillin hydrochloride	• Cefroxadine hydrate	• Erythromycin stearate	

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14 **Table S2.** Baseline demographic characteristics by BGF cohort subgroups

	Early BGF adopters (N = 636)				Contemporary BGF users (N = 2558)			
	BGF as first triple therapy (N = 401)	BGF as first triple therapy (naive) (N = 187)	BGF as first triple therapy (step-up) (N = 214)	Switch to BGF (N = 235)	BGF as first triple therapy (N = 1466)	BGF as first triple therapy (naive) (N = 572)	BGF as first triple therapy (step-up) (N = 894)	Switch to BGF (N = 1092)
Age at index, mean (SD), years	74.6 (9.7)	74.4 (9.7)	74.7 (9.8)	72.2 (10.2)	73.8 (9.9)	74.8 (9.2)	73.2 (10.2)	72.2 (10.3)
Age category at index, n (%)								
40–59 years	31 (7.7)	11 (5.9)	20 (9.3)	25 (10.6)	134 (9.1)	42 (7.3)	92 (10.3)	128 (11.7)
60–64 years	23 (5.7)	14 (7.5)	9 (4.2)	17 (7.2)	84 (5.7)	24 (4.2)	60 (6.7)	83 (7.6)
65–69 years	42 (10.5)	24 (12.8)	18 (8.4)	43 (18.3)	178 (12.1)	68 (11.9)	110 (12.3)	138 (12.6)
70–74 years	79 (19.7)	36 (19.3)	43 (20.1)	42 (17.9)	302 (20.6)	124 (21.7)	178 (19.9)	241 (22.1)
≥75 years	226 (56.4)	102 (54.5)	124 (57.9)	108 (46.0)	768 (52.4)	314 (54.9)	454 (50.8)	502 (46.0)
Sex, n (%)								
Female patients	100 (24.9)	44 (23.5)	56 (26.2)	63 (26.8)	383 (26.1)	127 (22.2)	256 (28.6)	321 (29.4)
Male patients	301 (75.1)	143 (76.5)	158 (73.8)	172 (73.2)	1083 (73.9)	445 (77.8)	638 (71.4)	771 (70.6)

Index year, <i>n</i> (%)								
2019	145 (36.2)	53 (28.3)	92 (43.0)	129 (54.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2020	256 (63.8)	134 (71.7)	122 (57.0)	106 (45.1)	500 (34.1)	176 (30.8)	324 (36.2)	430 (39.4)
2021	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	966 (65.9)	396 (69.2)	570 (63.8)	662 (60.6)

15 *BGF* budesonide/glycopyrronium/formoterol fumarate dihydrate, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *MITT* multiple-inhaler triple therapy,

16 *SD* standard deviation

17 **Table S3.** Baseline clinical characteristics by BGF cohort subgroups

	Early BGF adopters (N = 636)				Contemporary BGF users (N = 2558)			
	BGF as first triple therapy (N = 401)	BGF as first triple therapy (naive) (N = 187)	BGF as first triple therapy (step-up) (N = 214)	Switch to BGF (N = 235)	BGF as first triple therapy (N = 1466)	BGF as first triple therapy (naive) (N = 572)	BGF as first triple therapy (step-up) (N = 894)	Switch to BGF (N = 1092)
Body mass index at index, mean (SD), kg/m ²	22.3 (4.3)	22.1 (4.7)	22.5 (4)	21.3 (3.9)	22 (4.5)	21.9 (4.3)	22.1 (4.6)	21.9 (4.3)
Smoking status, n (%)								
Unknown/missing	249 (62.1)	121 (64.7)	128 (59.8)	156 (66.4)	1006 (68.6)	384 (67.1)	622 (69.6)	756 (69.2)
Non-smoker	46 (11.5)	25 (13.4)	21 (9.8)	23 (9.8)	133 (9.1)	56 (9.8)	77 (8.6)	97 (8.9)
Smoker	106 (26.4)	41 (21.9)	65 (30.4)	56 (23.8)	327 (22.3)	132 (23.1)	195 (21.8)	239 (21.9)
Specific COPD diagnosis (pre-index period), n (%)								
J41.x (Simple and mucopurulent chronic bronchitis)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (0.2%)	1 (0.2%)	2 (0.2%)	5 (0.5%)
J42 (Unspecified chronic bronchitis)	122 (30.4%)	47 (25.1%)	75 (35%)	107 (45.5%)	531 (36.2%)	177 (30.9%)	354 (39.6%)	468 (42.9%)

J43.x (Emphysema)	121 (30.2%)	50 (26.7%)	71 (33.2%)	66 (28.1%)	427 (29.1%)	152 (26.6%)	275 (30.8%)	366 (33.5%)
J44.x (Other COPD)	301 (75.1)	134 (71.7)	167 (78.0)	200 (85.1)	1079 (73.6%)	406 (71.0%)	673 (75.3%)	883 (80.9%)
J44.0 (COPD with [acute] lower respiratory infection)	6 (1.5)	2 (1.1)	4 (1.9)	2 (0.9)	12 (0.8%)	6 (1%)	6 (0.7%)	12 (1.1%)
J44.1 (COPD with [acute] exacerbation)	41 (10.2)	10 (5.3)	31 (14.5)	34 (14.5)	115 (7.8%)	37 (6.5%)	78 (8.7%)	162 (14.8%)
J44.9 (COPD, unspecified)	284 (70.8)	128 (68.4)	156 (72.9)	197 (83.8)	1037 (70.7%)	384 (67.1%)	653 (73.0%)	865 (79.2%)
Asthma + COPD overlap (pre-index period), <i>n</i> (%) ^a	243 (60.6)	93 (49.7)	150 (70.1)	221 (94.0)	923 (63.0)	278 (48.6)	645 (72.1)	975 (89.3)
Patients with moderate or severe COPD exacerbations, <i>n</i> (%)	52 (13.0)	8 (4.3)	44 (20.6)	64 (27.2)	158 (10.8)	28 (4.9)	130 (14.5)	207 (19)
Patients with moderate exacerbations, <i>n</i> (%)	26 (6.5)	3 (1.6)	23 (10.7)	42 (17.9)	103 (7.0)	17 (3.0)	86 (9.6)	127 (11.6)
Patients with severe exacerbations, <i>n</i> (%)	28 (7)	5 (2.7)	23 (10.7)	28 (11.9)	62 (4.2)	11 (1.9)	51 (5.7)	94 (8.6)

18 ^aUsing ICD-10 codes J45 and J46, and MDV code 8850253

19 *BGF* budesonide/glycopyrronium/formoterol fumarate dihydrate, *COPD* chronic obstructive pulmonary disease, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol,

20 *MITT* multiple-inhaler triple therapy, *SD* standard deviation

21 **Table S4.** Baseline multimorbidity (reported in >5% of any main cohort) during the 12-month pre-index period by BGF cohort subgroups

Condition, <i>n</i> (%)	Early BGF adopters (<i>N</i> = 636)				Contemporary BGF users (<i>N</i> = 2558)			
	BGF as first triple therapy (<i>N</i> = 401)	BGF as first triple therapy (naïve) (<i>N</i> = 187)	BGF as first triple therapy (step-up) (<i>N</i> = 214)	Switch to BGF (<i>N</i> = 235)	BGF as first triple therapy (<i>N</i> = 1466)	BGF as first triple therapy (naïve) (<i>N</i> = 572)	BGF as first triple therapy (step-up) (<i>N</i> = 894)	Switch to BGF (<i>N</i> = 1092)
Any	342 (85.3)	155 (82.9)	187 (87.4)	205 (87.2)	1186 (80.9)	461 (80.6)	725 (81.1)	904 (82.8)
Cardiac arrhythmias	77 (19.2)	31 (16.6)	46 (21.5)	40 (17.0)	303 (20.7)	105 (18.4)	198 (22.1)	196 (17.9)
Congestive heart failure	118 (29.4)	49 (26.2)	69 (32.2)	63 (26.8)	429 (29.3)	152 (26.6)	277 (31)	333 (30.5)
Deficiency anemia	51 (12.7)	26 (13.9)	25 (11.7)	25 (10.6)	161 (11.0)	64 (11.2)	97 (10.9)	92 (8.4)
Depression	25 (6.2)	10 (5.3)	15 (7.0)	20 (8.5)	101 (6.9)	32 (5.6)	69 (7.7)	74 (6.8)
Diabetes, complicated	23 (5.7)	10 (5.3)	13 (6.1)	6 (2.6)	89 (6.1)	34 (5.9)	55 (6.2)	78 (7.1)
Diabetes, uncomplicated	70 (17.5)	38 (20.3)	32 (15.0)	57 (24.3)	198 (13.5)	61 (10.7)	137 (15.3)	143 (13.1)
Fluid and electrolyte disorders	65 (16.2)	26 (13.9)	39 (18.2)	38 (16.2)	242 (16.5)	86 (15.0)	156 (17.4)	185 (16.9)
Hypertension, uncomplicated	193 (48.1)	73 (39.0)	120 (56.1)	118 (50.2)	709 (48.4)	255 (44.6)	454 (50.8)	559 (51.2)

Liver disease	62 (15.5)	30 (16.0)	32 (15.0)	39 (16.6)	228 (15.6)	97 (17.0)	131 (14.7)	178 (16.3)
Metastatic cancer	21 (5.2)	6 (3.2)	15 (7.0)	13 (5.5)	79 (5.4)	34 (5.9)	45 (5.0)	38 (3.5)
Other neurological disorders	16 (4.0)	8 (4.3)	8 (3.7)	18 (7.7)	58 (4.0)	21 (3.7)	37 (4.1)	34 (3.1)
Peptic ulcer disease, excluding bleeding	81 (20.2)	39 (20.9)	42 (19.6)	68 (28.9)	306 (20.9)	101 (17.7)	205 (22.9)	277 (25.4)
Peripheral vascular disorders	55 (13.7)	24 (12.8)	31 (14.5)	23 (9.8)	206 (14.1)	80 (14.0)	126 (14.1)	120 (11.0)
Renal failure	34 (8.5)	15 (8.0)	19 (8.9)	10 (4.3)	118 (8.0)	47 (8.2)	71 (7.9)	77 (7.1)
Rheumatoid arthritis/collagen vascular diseases	33 (8.2)	15 (8.0)	18 (8.4)	27 (11.5)	113 (7.7)	32 (5.6)	81 (9.1)	67 (6.1)
Solid tumor without metastasis	108 (26.9)	51 (27.3)	57 (26.6)	61 (26.0)	420 (28.6)	176 (30.8)	244 (27.3)	248 (22.7)
Solid tumor without metastasis (lung cancer)	51 (12.7)	22 (11.8)	29 (13.6)	31 (13.2)	190 (13.0)	78 (13.6)	112 (12.5)	97 (8.9)
Valvular disease	29 (7.2)	17 (9.1)	12 (5.6)	14 (6.0)	128 (8.7)	49 (8.6)	79 (8.8)	57 (5.2)

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24 **Table S5.** Number of prior exacerbations during the 12-month pre-index baseline period by cohort

	Early BGF adopters (N = 636)	Contemporary BGF users (N = 2558)	FF/UMEC/VI users (N = 11,179)	MITT users (N = 5931)
Moderate/severe exacerbations, n (%)				
0	520 (81.8)	2193 (85.7)	9712 (86.9)	5098 (86.0)
1	73 (11.5)	246 (9.6)	1072 (9.6)	633 (10.7)
2	29 (4.6)	65 (2.5)	236 (2.1)	138 (2.3)
≥3	14 (2.2)	54 (2.1)	159 (1.4)	62 (1.0)
Moderate exacerbations, n (%)				
0	568 (89.3)	2328 (91.0)	10,245 (91.6)	5454 (92.0)
1	41 (6.4)	151 (5.9)	635 (5.7)	354 (6.0)
2	19 (3.0)	43 (1.7)	178 (1.6)	78 (1.3)
≥3	8 (1.3)	36 (1.4)	121 (1.1)	45 (0.8)
Severe exacerbations, n (%)				
0	580 (91.2)	2402 (93.9)	10,586 (94.7)	5548 (93.5)
1	39 (6.1)	126 (4.9)	516 (4.6)	322 (5.4)
2	13 (2.0)	19 (0.7)	61 (0.5)	49 (0.8)
≥3	4 (0.6)	11 (0.4)	16 (0.1)	12 (0.2)

25 *BGF* budesonide/glycopyrronium/formoterol fumarate dihydrate, *FF/UMEC/VI* fluticasone furoate/umeclidinium/vilanterol, *MITT* multiple-inhaler triple therapy

26 **Table S6.** Types of wards of hospital admission during the 12-month pre-index baseline period (occurring in >0.5% of any cohort) by cohort

	Early BGF adopters (N = 636)	Contemporary BGF users (N = 2558)	FF/UMEC/VI users (N = 11,179)	MITT users (N = 5931)
Patients with ≥ 1 hospitalization	282	898	3822	2548
Types of wards of admission, <i>n</i> (%)				
Internal Medicine	82 (29.1)	210 (23.4)	986 (25.8)	845 (33.2)
Pulmonary Medicine	64 (22.7)	238 (26.5)	793 (20.7)	436 (17.1)
Pulmonology	30 (10.6)	77 (8.6)	352 (9.2)	190 (7.5)
Cardiovascular Medicine	25 (8.9)	61 (6.8)	276 (7.2)	182 (7.1)
General Surgery	12 (4.3)	61 (6.8)	243 (6.4)	192 (7.5)
Gastroenterological Internal Medicine	10 (3.5)	57 (6.3)	233 (6.1)	127 (5.0)
Orthopedics	19 (6.7)	46 (5.1)	197 (5.2)	155 (6.1)
Cardiology	8 (2.8)	55 (6.1)	197 (5.2)	120 (4.7)
Urology	9 (3.2)	48 (5.3)	177 (4.6)	107 (4.2)
Respiratory Surgery	10 (3.5)	27 (3.0)	139 (3.6)	83 (3.3)
Gastrointestinal Medicine	10 (3.5)	34 (3.8)	129 (3.4)	67 (2.6)

Ophthalmology	5 (1.8)	25 (2.8)	126 (3.3)	48 (1.9)
Neurosurgery	9 (3.2)	26 (2.9)	77 (2.0)	40 (1.6)
Cardiovascular Surgery	4 (1.4)	11 (1.2)	60 (1.6)	44 (1.7)
Nephrology	4 (1.4)	23 (2.6)	50 (1.3)	42 (1.6)
Neurology	2 (0.7)	11 (1.2)	52 (1.4)	36 (1.4)
General Medicine	4 (1.4)	5 (0.6)	55 (1.4)	38 (1.5)
Otorhinolaryngology	4 (1.4)	4 (0.4)	47 (1.2)	31 (1.2)
Emergency Medicine	4 (1.4)	8 (0.9)	27 (0.7)	24 (0.9)

27 *BGF* budesonide/glycopyrronium/formoterol fumarate dihydrate, *FF/UMEC/VI* fluticasone furoate/umeclidinium, *MITT* multiple-inhaler triple therapy