COPD Patients Initiating Roflumilast in Sweden, Germany and the United States: Findings from the Roflumilast PASS study

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RATIONALE

Roflumilast is an oral selective phosphodiesterase-4 inhibitor indicated for the treatment of severe chronic obstructive pulmonary disease (COPD) patients associated with chronic bronchitis and a history of exacerbations. A post-authorisation safety study (PASS) with focus primarily on 5-year all-cause mortality as primary outcome is ongoing in Sweden, Germany and the United States (US) (EU PAS register number: EUPAS6553).

OBJECTIVES

The objective of this *post hoc* sub-analysis was to describe and compare comorbidities, COPD drug treatment, healthcare utilization and moderate exacerbations in COPD patients exposed and unexposed to roflumilast, using real-life data from healthcare registries in the three countries.

METHODS

COPD patients aged 40 years and above were identified during 2011–2013 in Sweden, 2010–2011 in Germany and 2011 in the US. Patients exposed to roflumilast were described at the time of treatment initiation and compared to the unexposed background COPD population at a fixed date. *A moderate exacerbation* was defined as acute use of systemic corticosteroids and/or systemic antibiotics during 12 months and *triple therapy* as a dispensation of long-acting muscarinic antagonist, long-acting β_2-agonist and inhaled corticosteroid during 4 months prior to date of comparison.

ACKNOWLEDGEMENTS

Funding

- The study was sponsored by Takeda; sponsorship for the study is being transferred to AstraZeneca; the sponsor was not involved in the analysis of the results

The permission to use the data was granted from:

- The Swedish National Board of Health and Welfare (Socialstyrelsen 26.11.2013) and by the Ethics Committee in Stockholm (diary number 2013/1412-31/2)
- The Statutory Health Insurances contributing data to GePaRD and their responsible authorities

We thank all data sources for contributing the underlying data for these analyses

Authors VM, JM, PK and FH are employed by EPID Research, which is a contract research organization that performs commissioned pharmacoepidemiological studies and thus its employees have been and currently are working in collaboration with several pharmaceutical companies including Takeda Development Centre Europe. Authors NW, BK, TS and EG are employed by Leibniz Institute for Prevention Research and Epidemiology BIPS GmbH, which performs commissioned pharmacoepidemiological studies and thus its employees have been and currently are working in collaboration with several pharmaceutical companies including Takeda Development Centre Europe. Authors WM, CK and EK are employed by Quintiles, which is a contract research organization that performs commissioned pharmacoepidemiological studies and thus its employees have been and currently are working in collaboration with several pharmaceutical companies including Takeda Development Centre Europe. GJ has participated in the steering committee by Takeda for this study and served on advisory boards arranged by Astra Zeneca, Novo Nordisk and Novartis.

REFERENCES

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RESULTS

In Sweden, Germany and the US, 3,257, 5,084 and 2,269 patients starting roflumilast treatment were identified (Table 1). The mean ages (years) were 70.9, 67.4 and 71.2 among exposed and 71.3, 63.9 and 70.9 among unexposed, respectively.

In Sweden, Germany and the US the percentage of patients with COPD hospitalizations was 32.9, 29.8, 21.6 in roflumilast exposed and 5.0, 1.8, 2.5 in unexposed (Table 2).

Table 1. Number of patients starting roflumilast by study year

Year	SWE	GER	US
2010	-	1,480	-
2011	1,304	3,604	2,269
2012	1,217	-	-
2013	736	-	-
TOTAL	3,257	5,084	2,269

Table 2. Visits to healthcare and use of antibiotics or corticosteroids within 1 year prior to baseline*

		SWE		GER		US	
Study variables		Exposed N=3,257	Unexposed N=168,204	Exposed N=5,084	Unexposed N=772,716	Exposed N=2,269	Unexposed N=605,360
Hospitalizations for any cause	*0*	50.4	68.3	45.3	70.5	54.7	73.0
	1-2	28.8	22.8	36.5	23.4	38.7	23.1
	≥3	20.8	8.9	18.3	6.1	6.6	3.9
Other respiratory disease related hospitalizations	*0*	88.9	95.6	93.5	98.4	94.1	98.7
	1-2	9.9	4.2	6.2	1.6	5.6	1.3
	≥3	1.1	2.9	0.2	0.0	0.3	0.1
Hospitalizations due to COPD	*0*	67.1	95.0	70.2	98.2	78.4	97.5
	1-2	21.1	4.3	24.4	1.7	19.8	2.4
	≥3	11.7	0.7	5.3	0.1	1.8	0.1
Chronic use of corticosteroids	-	9.9	2.7	11.0	0.8	11.1	2.0
Chronic use of antibiotics	-	0.7	0.2	0.0	0.0	1.3	0.3
Moderate exacerbations • Non chronic use of corticosteroids • Non chronic use of antibiotics	*0*	14.7	51.5	19.0	72.1	25.2	41.9
	1-2	21.6	30.3	28.3	19.6	20.6	34.4
	3-5	27.4	5.1	29.3	6.3	22.0	17.2
	≥6	36.2	5.1	23.3	1.9	32.1	6.5

***The prevalence of healthcare visits and use of antibiotics or corticosteroids is summarized with percentages (%). Underscored values denote standardized difference of more than 0.1, which has been taken to indicate the imbalance between groups[1]. The total amount of patients is given in the header of each column.**

In Sweden, Germany and the US the prevalence (%) of moderate exacerbations was 85.3, 81.0, 74.8 in exposed and 48.5, 27.9, 58.1 in unexposed (Table 2), and the percentage on triple therapy was 65.3, 53.6, 48.4 in exposed and 17.6, 3.8, 6.9 in unexposed (Table 4), in the three countries respectively.

Table 4. Baseline COPD drug treatment within 4 months prior to roflumilast initiation*

	SWE		GER		US	
COPD treatment	Exposed N=3,257	Unexposed N=168,204	Exposed N=5,084	Unexposed N=772,716	Exposed N=2,269	Unexposed N=605,360
No COPD medication[I]	2.9	43.0	4.5	69.0	7.6	55.8
SAMA and/or SABA only[I]	3.0	4.5	3.0	4.4	6.1	8.5
Monotherapy[I]	9.2	18.5	11.0	9.5	13.9	14.7
Double therapy[I]	19.6	16.5	27.8	13.2	24.0	14.0
Triple therapy[I]	65.3	17.6	53.6	3.8	48.4	6.9
Oxygen use	5.4	0.5	N/A	N/A	50.2	11.1

Abbreviations: SAMA, inhaled short-acting muscarinic antagonist; SABA, inhaled short-acting β_2-agonist; ICS, inhaled corticosteroid; LAMA, long-acting muscarinic antagonist; LABA, long-acting β_2-agonist; N/A, not available.
***Baseline COPD drug treatment is summarized with percentages (%). Underscored values denote standardized difference of more than 0.1, which has been taken to indicate the imbalance between groups[1]. The total amount of patients is given in the header of each column.**
[I]COPD drug treatment is defined by 5 categories: no treatment, short-acting drug, monotherapy (LABA or LAMA or ICS (+/- SAMA or SABA)), double therapy ((LABA and LAMA) or (LABA and ICS) or (LAMA and ICS) (+/- SAMA or SABA)) and triple therapy (LABA and LAMA and ICS (+/- SAMA or SABA)); each patient contributes only to one cell (except oxygen use)

In all three countries roflumilast exposed patients had higher prevalence of asthma, emphysema, pneumonia/influenza and osteoporosis than unexposed patients. The burden of respiratory and cardiovascular diseases was highest in the US followed by Germany and Sweden (Table 3).

Table 3. Baseline comorbidities*

	SWE		GER**		US	
Comorbidities	Exposed N=3,257	Unexposed N=168,204	Exposed N=5,084	Unexposed N=772,716	Exposed N=2,269	Unexposed N=605,360
Asthma[I]	24.2	14.7	46.1	23.9	50.9	27.2
Emphysema[I]	12.5	3.2	42.2	6.6	49.4	15.6
Pneumonia/influenza[II]	10.5	4.3	9.5	5.1	33.8	12.6
Coronary heart disease[I]	22.0	22.4	27.4	20.4	68.8	57.3
Hip fracture[II]	0.7	1.1	0.8	0.9	1.2	1.5
Inflammatory bowel disease[I]	1.6	1.8	1.4	1.2	1.3	1.9
Diverticulitis[II]	0.9	0.9	9.1	8.5	11.6	11.0
Osteoporosis[II]	16.2	7.0	23.1	11.9	16.8	12.2
Arterial hypertension[I]	39.5	41.0	66.7	58.5	85.3	82.4
Hyperlipidemia[I]	10.5	13.4	39.5	41.2	77.9	76.3
Atrial fibrillation[I]	12.2	15.4	11.0	7.7	41.2	33.7
Deep vein thrombosis[II]	0.4	0.5	2.6	2.2	2.8	2.1
Mood disorder[I]	42.0	39.6	26.0	24.0	8.9	8.4
Psychosis[I]	4.6	7.5	1.2	1.7	4.4	4.5
Anxiety disorders[II]	1.3	1.2	15.5	15.0	18.8	12.7
Hyperthyroidism[II]	0.5	0.4	5.7	4.5	1.7	1.3
Parkinson's disease[I]	6.5	6.0	0.2	0.3	1.6	1.9
Smoking[I]	13.4	8.6	N/A	N/A	58.4	35.9
Multiple sclerosis[I]	0.2	0.3	0.2	0.4	0.5	0.4
Lupus erythematosus[I]	0.2	0.3	0.1	0.1	0.7	0.6
Cirrhosis[I]	0.3	0.4	0.6	0.6	0.1	0.1

Abbreviations: N/A, not available
***The prevalence of baseline comorbidities is summarized with percentages (%). Underscored values denote standardized difference of more than 0.1, which has been taken to indicate the imbalance between groups[1]. The total amount of patients is given in the header of each column.**
****In Germany comorbidities are evaluated during one year prior to baseline only.**
[I]Baseline comorbidities defined any time before baseline (not valid for Germany).
[II]Baseline comorbidities defined one year before baseline.

CONCLUSIONS

In Sweden, Germany and the US, roflumilast-initiating patients represent the more severe end of the COPD disease spectrum, with more comorbidities, more moderate exacerbations and higher use of healthcare resources. The disease severity as well as the need for new treatment options is reflected in the number of patients on triple therapy who initiated roflumilast. The prevalence of baseline comorbidities differed noticeably across countries, but such variation could arise from differences in study registers or in country-specific diagnostic criteria.

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