

Real-world Impact of Adherence to ICS/LABAs on Asthma Outcomes in the US

Abstract A1605; Session TP015: Updates in Adherence and Treatment of Lung Disease

Carlyne M. Averell¹, François Laliberté², Guillaume Germain², Sean D. MacKnight², David J. Stadel¹, Mei S. Duh³, Amy Guisinger¹, Matthew D. Rousculp¹

¹GSK, Research Triangle Park, NC, USA; ²Groupes d'analyse, Ltée, Montréal, QC, Canada; ³Analysis Group, Inc., Boston, MA, USA

Aims

- Asthma treatment guidelines highlight the importance of medication adherence in asthma management and control.^{1,2} Previous studies have reported associations between improved adherence with fluticasone propionate/salmeterol and improved asthma outcomes.^{3,4} However, limited real-world information exists on the association of adherence and outcomes in patients using other inhaled corticosteroid/long-acting beta agonists (ICS/LABAs).
- The objective of this study was to evaluate the association between adherence to fixed-dose ICS/LABAs and outcomes among patients with asthma.

Methods

- This retrospective observational study was conducted using the IQVIA PharMetrics Plus database in asthma patients initiating fixed-dose ICS/LABA between January 1, 2014 and March 31, 2019. The index date was the first ICS/LABA dispensing date. The 12-month pre-index period was the baseline, and patients had ≥6 months follow-up post-index.

Key Inclusion Criteria	Key Exclusion Criteria
<ul style="list-style-type: none"> ≥2 pharmacy claims for fixed-dose ICS/LABA during January 1, 2014 to March 31, 2019 Index date = first dispensing date ≥18 years of age at index date ≥12 months of continuous enrollment prior to index date (baseline period) ≥6 months follow-up (follow-up spanned from index to: a switch to a non-ICS/LABA controller or triple therapy, end of eligibility, or end of data) ≥2 asthma diagnoses during baseline or on index date 	<ul style="list-style-type: none"> ≥1 diagnosis of chronic obstructive pulmonary disease (COPD) or asthma/COPD overlap syndrome during baseline or follow-up ≥1 pharmacy claim for a long-acting muscarinic antagonist (LAMA) medication during baseline or on index date ≥1 diagnosis for acute respiratory failure or cystic fibrosis during baseline or on index date ≥1 diagnosis of lung cancer, bronchiectasis, alpha 1 antitrypsin deficiency, or lung transplant during baseline or follow-up

Study Outcomes



- Outcomes were assessed beginning in the second quarter, as the rate per-patient-per-quarter (PPQ), and the proportion of patients with ≥1 event for: asthma-related overall and severe exacerbations, short-acting beta agonist (SABA) and oral corticosteroid (OCS) use, asthma-related healthcare resource use (HRU) and medical healthcare costs.
- Overall asthma-related exacerbations were defined as an asthma-related inpatient (IP) visit or emergency department (ED) visit (i.e., severe exacerbation), or an asthma-related outpatient (OP) visit with a systemic or OCS dispensing within ± 5 days.

Statistical Analysis

- Adherence to ICS/LABAs was measured by the **proportion of days covered (PDC)** in each complete quarter of follow-up as continuous and dichotomous (adherent: PDC ≥0.80; non-adherent: PDC <0.80) measures. PDC was calculated for each quarter by dividing the number of days on therapy (based on filled prescriptions) by 90 (duration of quarter in days).
- Regression models were used to evaluate associations (odds ratios [ORs] and rate ratios [RRs]) between adherence in each quarter and outcomes in the subsequent quarter, controlling for repeated measures (generalized estimating equations, GEE) and baseline characteristics.

References
 1. Global Initiative for Asthma (GINA). 2020 GINA Report. 2020
 2. National Heart, Lung, and Blood Institute (NHLBI). Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. 2020
 3. Delea TE, et al. *Curr Med Res Opin*. 2008;24(12):3435-3442
 4. Ismaili A, et al. *Curr Med Res Opin*. 2014;30(7):1417-1424

Results

A total of 50,037 patients met all study eligibility criteria. Baseline patient characteristics, overall and stratified by adherence in the first and second quarters of follow-up, are shown in **Table 1**. Overall, mean age of all patients was 45.3 years, 64% were female, and mean follow-up time was 23.3 months.

Table 1. Baseline Demographics and Clinical Characteristics

Characteristics	All Patients (N = 50,037)	PDC from 1-3 months (N = 15,028)			PDC from 4-6 months (N = 9,395)		
		Adherent PDC ≥0.80 (N = 35,009)	Non-adherent PDC <0.80 (N = 15,028)	Std. Diff. (%)	Adherent PDC ≥0.80 (N = 9,395)	Non-adherent PDC <0.80 (N = 40,642)	Std. Diff. (%)
Observation period (months), mean (SD)	23.3 (12.7)	21.8 (12.3)	23.9 (12.8)	17.3	20.8 (11.9)	23.8 (12.8)	24.7
Age, mean (SD)	45.3 (13.5)	47.2 (13.2)	44.5 (13.5)	20.2	47.4 (13.1)	44.8 (13.5)	19.2
Female, n (%)	32,063 (64.1)	9,486 (63.1)	22,577 (64.5)	2.8	5,815 (61.9)	26,248 (64.6)	5.6
Quan-CGI score, mean (SD)	1.18 (0.90)	1.22 (0.93)	1.16 (0.88)	7.3	1.23 (0.93)	1.16 (0.89)	7.2
Asthma-related comorbidities, n (%)							
Allergic rhinitis	20,128 (40.2)	6,531 (43.5)	13,597 (38.8)	9.4	4,194 (44.6)	15,934 (39.2)	11.0
Sinusitis	14,696 (29.4)	4,361 (29.0)	10,335 (29.5)	1.1	2,802 (29.8)	11,894 (29.3)	1.2
GERD	10,127 (20.2)	3,422 (22.8)	6,705 (19.2)	8.9	2,187 (23.3)	7,940 (19.5)	9.1
Depression	8,680 (17.3)	2,630 (17.5)	6,050 (17.3)	0.6	1,654 (17.6)	7,026 (17.3)	0.8
Obesity	8,521 (17.0)	2,625 (17.5)	5,896 (16.8)	1.7	1,638 (17.4)	6,883 (16.9)	1.3
Medications, n (%)							
Leukotriene modifiers	15,063 (30.1)	5,131 (34.1)	9,932 (28.4)	12.5	3,313 (35.3)	11,750 (28.9)	13.6
ICS	9,518 (19.0)	3,728 (24.8)	5,790 (16.5)	20.4	2,673 (28.5)	6,845 (16.8)	27.7
SABA (≥1 canister)	34,723 (69.4)	10,599 (70.5)	24,124 (68.9)	3.5	6,820 (72.6)	27,903 (68.7)	8.6
OCS (≥1 dispensing)	27,106 (54.2)	8,213 (54.7)	18,893 (54.0)	1.4	5,153 (54.8)	21,953 (54.0)	1.7
Asthma-related exacerbations, n (%)							
Overall	13,752 (27.5)	4,102 (27.3)	9,650 (27.6)	0.6	2,578 (27.4)	11,174 (27.5)	0.1
IP/ED-defined	4,444 (8.9)	1,219 (8.1)	3,225 (9.2)	3.9	729 (7.8)	3,715 (9.1)	5.0
Asthma-related HRU, mean (SD)							
Hospitalizations	0.02 (0.13)	0.02 (0.13)	0.01 (0.13)	0.8	0.02 (0.13)	0.02 (0.13)	0.3
ED visits	0.10 (0.41)	0.09 (0.37)	0.10 (0.43)	4.5	0.08 (0.34)	0.10 (0.42)	5.7
OP visits	1.27 (2.32)	1.38 (2.21)	1.22 (2.37)	7.2	1.41 (2.14)	1.23 (2.36)	8.0

Abbreviations: CGI, Charlson comorbidity index; CI, confidence interval; ED, emergency department; GEE, generalized estimating equations; GERD, gastroesophageal reflux disease; HRU, healthcare resource use; ICS, inhaled corticosteroid; IP, inpatient; LABA, long-acting β₂ agonist; OCS, oral corticosteroid; OP, outpatient; OR, odds ratio; PDC, proportion of days covered; PPQ, per patient per quarter; RR, rate ratio; SABA, short-acting β₂ agonist; SD, standard deviation; std. diff., standardized difference.

Compared to non-adherent patients, adherent patients were significantly less likely to experience any asthma exacerbation or severe exacerbation, and had significantly lower rates of severe exacerbations, but similar rates of overall exacerbations (**Table 2**).

Table 2. Impact of ICS/LABA Adherence on Asthma Exacerbations

Asthma-related exacerbations, PPPQ	≥ 1 Exacerbation		Number of Exacerbations	
	Adjusted OR (95% CI) ¹	P-value	Adjusted RR (95% CI) ¹	P-value
Overall exacerbations				
Continuous PDC (per 20%)	0.961 (0.949, 0.973)	<0.001	0.998 (0.988, 1.009)	0.739
PDC ≥0.80	0.942 (0.890, 0.998)	0.041	0.993 (0.945, 1.044)	0.783
IP/ED-defined (severe) exacerbations				
Continuous PDC (per 20%)	0.952 (0.930, 0.975)	<0.001	0.951 (0.929, 0.974)	<0.001
PDC ≥0.80	0.778 (0.691, 0.877)	<0.001	0.792 (0.702, 0.893)	<0.001

¹ Estimates were derived from multivariable GEE models, which control for repeated measures using PDC data from the initial quarter of follow-up and outcomes from the subsequent quarter of follow-up, and so on. Odds ratios were obtained from models using log link and binomial distribution, while rate ratios were derived from models using log link and Poisson distribution. Adjusted models controlled for baseline covariates with a 10% std. diff. between adherent (PDC ≥0.80) and non-adherent (PDC <0.80) patients in the first or second quarters, as well as Quan-CGI, baseline HRU, and baseline healthcare costs.

Adherent patients were significantly less likely to have an ED visit per quarter than non-adherent patients, and had significantly lower odds of hospitalization per 20% increase in adherence, though the difference between adherent and non-adherent patients was non-significant. However, adherent patients were significantly more likely to have an OP visit per quarter than non-adherent patients (**Table 3**).

Table 3. Impact of ICS/LABA Adherence on Asthma-related HRU

Asthma-related HRU, PPPQ	≥ 1 Visit		Number of Visits	
	Adjusted OR (95% CI) ¹	P-value	Adjusted RR (95% CI) ¹	P-value
Hospitalizations				
Continuous PDC (per 20%)	0.930 (0.881, 0.982)	0.009	0.930 (0.881, 0.982)	0.009
PDC ≥0.80	0.824 (0.638, 1.063)	0.136	0.811 (0.629, 1.045)	0.105
ED visits				
Continuous PDC (per 20%)	0.953 (0.929, 0.978)	<0.001	0.951 (0.926, 0.976)	<0.001
PDC ≥0.80	0.775 (0.680, 0.883)	<0.001	0.785 (0.683, 0.901)	<0.001
OP visits				
Continuous PDC (per 20%)	1.058 (1.052, 1.065)	<0.001	1.050 (1.043, 1.057)	<0.001
PDC ≥0.80	1.187 (1.154, 1.221)	<0.001	1.137 (1.102, 1.174)	<0.001

¹ Estimates were derived from multivariable GEE models, which control for repeated measures using PDC data from the initial quarter of follow-up and outcomes from the subsequent quarter of follow-up, and so on. Odds ratios were obtained from models using log link and binomial distribution, while rate ratios were derived from models using log link and Poisson distribution. Adjusted models controlled for baseline covariates with a 10% std. diff. between adherent (PDC ≥0.80) and non-adherent (PDC <0.80) patients in the first or second quarters, as well as Quan-CGI, baseline HRU, and baseline healthcare costs.

The odds of SABA and OCS use were significantly lower per 20% increase in adherence, though the differences between adherent and non-adherent patients were not statistically significant (**Table 4**).

Table 4. Impact of ICS/LABA Adherence on SABA and OCS Use

Medication use, PPPQ	≥ 1 Dispensing		Number of Canisters or Dispensings	
	Adjusted OR (95% CI) ¹	P-value	Adjusted RR (95% CI) ¹	P-value
SABA use				
Continuous PDC (per 20%)	0.991 (0.985, 0.996)	0.001	1.000 (0.995, 1.006)	0.867
PDC ≥0.80	0.991 (0.966, 1.017)	0.490	1.048 (1.025, 1.072)	<0.001
OCS use				
Continuous PDC (per 20%)	0.988 (0.982, 0.995)	<0.001	0.993 (0.987, 0.999)	0.023
PDC ≥0.80	0.982 (0.954, 1.011)	0.215	1.007 (0.979, 1.035)	0.635

¹ Estimates were derived from GEE models. Adjusted models controlled for baseline covariates with a 10% std. diff. between adherent (PDC ≥0.80) and non-adherent (PDC <0.80) patients in the first or second quarters, and Quan-CGI, baseline HRU, healthcare costs.

Total medical, hospitalization, and ED visit costs were significantly lower per 20% increase in adherence, though the difference between adherent and non-adherent patients was significant only for ED costs (**Table 5**).

Table 5. Impact of ICS/LABA Adherence on Asthma-related Costs¹

Asthma-related costs, \$US 2019, PPPQ	Cost Difference	
	Adjusted (95% CI) ²	P-value
Total medical costs		
Continuous PDC (per 20%)	-39.62 (-70.60, -12.49)	0.006
PDC ≥0.80	-77.27 (-174.89, 25.63)	0.134
Hospitalization costs		
Continuous PDC (per 20%)	-31.93 (-58.96, -6.83)	0.010
PDC ≥0.80	-50.93 (-134.30, 48.18)	0.282
ED visit costs		
Continuous PDC (per 20%)	-2.74 (-4.06, -1.49)	<0.001
PDC ≥0.80	-6.57 (-13.65, -3.72)	<0.001
OP visit costs		
Continuous PDC (per 20%)	-1.34 (-15.25, 11.26)	0.801
PDC ≥0.80	-25.61 (-82.94, 27.54)	0.316

¹ Among patients with asthma-related medical costs in a given quarter.
² Estimates were derived from GEE models. Cost differences were obtained from models using identity link and normal distribution.

Conclusions

Real-world adherence to ICS/LABAs among asthma patients was associated with reduced overall and severe exacerbations, rescue medication use, healthcare resource use, and medical costs.

Disclosures

- This study was funded by GlaxoSmithKline (GSK ID HO-19-19562).
- CMA, DJS and MDR are GSK employees and hold GSK shares; AG is a research assistant at GSK. FL, GG, SGM, and MSD are employees of Analysis Group, Inc., a consulting company that received research funds from GSK to conduct this study.

Presented at the American Thoracic Society Annual Meeting, Virtual, May 14–19, 2021

Scan the QR code or click on <https://doi.org/10.1177/08850666211014351> to access a downloadable version of this poster, a version that has been formatted for online viewing, and the associated audio recording.