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Effects of Systemic Corticosteroids on Blood Eosinophil Counts in Asthma:

Real-World Data

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Running head: Steroid effect on blood eosinophils in asthma

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KEYWORDS

Systemic corticosteroids, eosinophil counts, severe eosinophilic asthma, real world

ABBREVIATIONS

EMR, electronic medical record; ICD-CM, International Classification of Diseases-Clinical Modification; OCS, oral corticosteroid; RMG, Reliant Medical Group; SCS, systemic corticosteroid; SD, standard deviation.

Abstract

Introduction:

Systemic corticosteroids (SCS) are effective anti-inflammatory therapies for patients with severe or persistent asthma. SCS use reduces blood eosinophil counts; the magnitude and duration of reduction in real-world settings needs further investigation.

Objective:

To examine SCS effect on blood eosinophil counts over time among patients with asthma in a real-world setting.

Methods:

This retrospective study used Reliant Medical Group (Worcester, MA) electronic medical records between 01/2011 and 12/2015. Patients aged ≥ 12 years with ≥ 1 SCS prescription (first: index date), ≥ 1 asthma diagnosis, and ≥ 1 eosinophil count in each 12-month pre- and post-index period were included. Endpoints included SCS treatment patterns, time to SCS discontinuation and changes in index blood eosinophil counts (≥ 150 , ≥ 300 , and ≥ 400 cells/ μ L) with SCS initiation and discontinuation.

Results:

At index visit, 642 of 1,198 included patients had a blood eosinophil count ≥ 150 cells/ μ L.

After an average initial SCS prescription of 35 mg/day, mean (% change) eosinophil counts at Month 1 in the ≥ 150 , ≥ 300 , and ≥ 400 cells/ μ L subgroups decreased from index by 112 (-30%), 202

(-34%), and 290 (-36%) cells/ μ L, respectively. Of the patients with an eosinophil count ≥ 150 cells/ μ L at index, who discontinued SCS within 7, 14, or 21 days after the index date, 21%, 26%, and 25% had an eosinophil count < 150 cells/ μ L 1-month post-index, respectively.

Conclusion:

Blood eosinophil counts decreased following initiation of SCS therapy and had not returned to index levels several weeks after SCS discontinuation. The time frame of SCS discontinuation is an important consideration when identifying patients with eosinophilic asthma.

Introduction

Asthma affects 235 million people worldwide,(1) of whom around 5% are estimated to have eosinophilic asthma.(2) Eosinophilic asthma is a distinct subtype of asthma characterized by the presence of markers such as high blood or sputum eosinophil counts and, often, corticosteroid responsiveness.(3) Previously, blood eosinophil counts have been shown not to correlate well with sputum eosinophil counts; however, more recent studies have demonstrated some level of correlation.(4-6) As blood samples are easier to obtain and determine in clinical practice than sputum, blood eosinophil counts represent a more practical way to assess airway inflammation.

Oral or parenteral systemic corticosteroids (SCS) can treat acute exacerbations, reduce emergency room admission rates, and prevent exacerbation relapse.(7, 8) Acute SCS use normally lasts a few days, and doses can be much higher than in the maintenance setting.(7, 9) Some patients with more severe disease may receive SCS chronically over a period of ≥ 6 months, in addition to bursts for controlling acute events.(10)

Previous studies have demonstrated that SCS therapy reduces eosinophil counts in blood and sputum.(11-13) However, there is currently a lack of data examining the magnitude of this reduction and when eosinophil counts increase again following SCS discontinuation in real-world settings. This study examined the effect of oral SCS on blood eosinophil counts in patients with asthma in a real-world clinical practice setting.

Methods

Study design

This was a retrospective longitudinal pre-post study design based on both electronic medical records (EMRs) and claims (medical and pharmacy claims) data from the Reliant Medical Group (RMG) between January 01, 2011 and December 31, 2015. The RMG is a large private, multi-specialty group in central Massachusetts and accepts insurance plans including those from Fallon Community Health Plan, Tufts, Harvard Pilgrim, Medicaid, and Medicare. It provides comprehensive care for more than 1 million patient visits a year and has more than 300 physicians practicing in over 20 locations. Data are de-identified and comply with the patient requirements of the Health Insurance Portability and Accountability Act of the USA. The study protocol was approved by GSK prior to the start of the study (GSK ID: HO-16-16495).

The study consisted of two periods: a pre-index period of 12 months before the index date, and a post-index period of ≥ 12 months after the index date. The index date was the date of the first prescription for a SCS therapy. Patient characteristics and medical history were assessed at the index date and 12 months before the index date (pre-index period).

Evaluation of SCS treatment patterns and changes in blood eosinophil counts with initiation and discontinuation of SCS therapy was performed at Months 1 and 3 in the post-index period (Figure 1a).

Patients

Patients included in this study were ≥ 12 years of age with ≥ 1 primary or secondary diagnosis of asthma, ≥ 1 SCS prescription, and ≥ 1 year of clinical activity and ≥ 1 recorded blood eosinophil count in each of the pre- and post-index periods (Figure 1a).

Patients were excluded if they had a prescription for an anti-interleukin 5 (eg, mepolizumab) therapy, or if they received chemotherapy during the pre-index period. Patient subgroup stratification was according to index blood eosinophil count (ie, the value at the index date or the value closest to the index date in the 12-month pre-index period) and comprised three non-mutually exclusive subgroups of patients with an index blood eosinophil count ≥ 150 cells/ μL , ≥ 300 cells/ μL , or ≥ 400 cells/ μL . There was no upper limit for eosinophil counts in each subgroup.

Endpoints and assessments

The primary endpoint examined the change in blood eosinophil counts between the index date and Month 1 (defined as the period within 45 days after the index date, excluding the index date itself). Blood eosinophil counts were also measured at Month 3, defined as 90 days after the index date, or within a window of 45 days before or after this day. When more than one eosinophil count was available for a patient around a specific time point in the post-index period (ie, Month 1 or Month 3), the closest value to the time point was selected.

Secondary endpoints included the assessment of SCS treatment patterns including the number of prescriptions, mean days of supply, and mean dosage and changes in blood eosinophil counts following SCS discontinuation. The definition of treatment discontinuation was either a gap of ≥ 60 days between two consecutive SCS prescriptions or between a SCS prescription and the end of the study period. A post hoc analysis of the proportion of patients with blood eosinophil counts < 150 cells/ μL at Month 1, following discontinuation of SCS therapy within 7, 14, or 21 days of the index date, was also performed.

Sample size and statistical analysis

Descriptive statistics of patient characteristics and blood eosinophil counts in the pre-index period included mean, standard deviation (SD) and median values for continuous data, and relative frequencies and proportions for categorical data. Differences between index blood eosinophil counts and post-index time points (Months 1 and 3) were calculated with a general estimating equation model accounting for correlations resulting from multiple observations between index and post-SCS time points. Time to discontinuation was evaluated using Kaplan–Meier analysis. All analyses were conducted using SAS (Cary, NC, USA) version 9.3 or later.

Results

Patient population

Of 15,839 patients identified within the database with ≥ 1 SCS prescription, 1,198 met the inclusion criteria (Figure 1b). In the overall population (N=1,198), the mean (SD) age was 54 (18.1) years, 72% of patients were female, mean (SD) body mass index was 31 (9.4) kg/m² and mean index blood eosinophil count was 215 cells/ μ L. The most frequent respiratory and allergic conditions were allergic rhinitis (21%), chronic sinusitis (11%), chronic obstructive pulmonary disease (11%), and acute sinusitis (9%) (data not shown). Overall, 556, 642, 262, and 135 patients had index blood eosinophil counts <150 , ≥ 150 , ≥ 300 , and ≥ 400 cells/ μ L, respectively (Figure 1b). Approximately, 90% of patients had their blood eosinophil count measurement before their first SCS prescription. Patients with a blood eosinophil count

<150 cells/ μ L were not included in further analyses. Patient characteristics were similar between subgroups (Table 1).

Primary endpoint – change in blood eosinophil counts with SCS initiation

Following initiation of SCS, there were significant reductions in blood eosinophil counts in all eosinophil count subgroups at all time points. In the first month of receiving SCS, reductions in mean blood eosinophil count were 112 cells/ μ L (-30%), 202 cells/ μ L (-34%), and 290 cells/ μ L (-36%) from index, in the ≥ 150 , ≥ 300 , and ≥ 400 cells/ μ L blood eosinophil counts subgroups, respectively (Figure 2). The mean time between SCS cessation and the Month 1 blood eosinophil count record was 19.0 days. Of the patients with data available for the length of SCS prescription, 32.7% were still receiving SCS treatment when their Month 1 blood eosinophil count was recorded. Absolute and percentage reductions in mean blood eosinophil counts at Month 3 were smaller than those observed at Month 1 in all subgroups (≥ 150 cells/ μ L: 65 cells/ μ L (-18%); ≥ 300 cells/ μ L: 150 cells/ μ L (-26%); ≥ 400 cells/ μ L: 246 cells/ μ L (-32%). The mean time between SCS cessation and the Month 3 blood eosinophil count record was 79.1 days; of the patients with data available, 8.1% of patients were still receiving SCS treatment when the Month 3 blood eosinophil count was recorded.

Secondary endpoints – treatment patterns

Based on the first SCS prescription post-index, the mean (SD) daily dose of SCS was 35 mg (22.2), 36 mg (22.7), and 35 mg (11.7) for the ≥ 150 cells/ μ L, ≥ 300 cells/ μ L, and ≥ 400 cells/ μ L subgroups, respectively. Across all subgroups, 12–13% of patients had at least one SCS prescription within 30 days of the blood eosinophil count recorded at the Month 3 time point. By virtue of the study design, the temporal association between SCS and blood

eosinophil count is greatest up to 1-month post-SCS initiation. For these patients, the mean (SD) daily SCS doses were 35 mg (17.0), 32 mg (12.5), and 37 mg (12.0) in the ≥ 150 cells/ μ L, ≥ 300 cells/ μ L, and ≥ 400 cells/ μ L subgroups respectively.

Secondary endpoints – change in eosinophil counts following discontinuation of SCS therapy

To further investigate the association between SCS therapy and blood eosinophil count, we examined continued SCS therapy as a possible explanation for eosinophil reductions. The proportion of patients using SCS therapy reduced within the first 30 days post-index date (Kaplan–Meier rate of persistent patients: 14%). After 90 days, 3% of patients remained on SCS therapy, suggesting that this subset of patients were chronic users of SCS (Figure 3).

Across all patients, the median time to SCS discontinuation was 10 days (interquartile range: 5–14). Following SCS discontinuation, mean blood eosinophil counts increased for each subgroup but remained 70–229 cells/ μ L below index at Month 1 and 32–177 cells/ μ L below index at Month 3 (Figure 4).

The percentage increase in mean blood eosinophil counts between Month 1 and Month 3 were 54%, 32%, and 28% in the ≥ 150 cells/ μ L, ≥ 300 cells/ μ L, and ≥ 400 cells/ μ L patient subgroups, respectively. Finally, post hoc analyses of patients with an index blood eosinophil count ≥ 150 cell/ μ L who discontinued SCS therapy within 7, 14, or 21 days from the index date, showed that 21%, 26%, and 25% still had an eosinophil count < 150 cell/ μ L 1-month post-index (Figure 5).

Discussion

This study provides insights into the effect of SCS therapy on blood eosinophil counts over time in patients with asthma and index blood eosinophil counts ≥ 150 cells/ μL in a real-world setting. A reduction in index blood eosinophil counts was seen within the first month of observation following SCS initiation, and cessation of SCS resulted in an increase in blood eosinophil counts towards pre-index levels to rise. One month after SCS initiation, over one-fifth of patients with an index blood eosinophil count ≥ 150 cell/ μL had a count < 150 cell/ μL , regardless of the length of SCS treatment within Month 1. Moreover, 3 months after cessation of SCS, mean blood eosinophil counts in all subgroups were still lower than the measurements taken in the pre-index period.

It is unclear whether blood eosinophil counts at Month 3 continue to remain lower than at index due to a continued effect of SCS initiated at the index date. A small percent of the population (13%) had a SCS prescription within 30 days prior to the Month 3 time point, suggesting few patients remained on therapy for longer than 1 month. However, as data for patients across multiple time points could not be obtained, it is not possible to know if blood eosinophil counts were reduced due to continued SCS use by a small proportion of patients at Month 3, residual effects of the initial prescription or other factors not captured in this study.

Following SCS discontinuation, mean blood eosinophil counts returned to near index levels by Month 3 in the ≥ 150 cells/ μL subgroup. In contrast, although blood eosinophil counts in the ≥ 400 cells/ μL subgroup increased at a similar rate, these remained proportionally lower compared with index levels than the other two subgroups at Month 3. A previous study by

Casciano *et al.* demonstrated that patients with high blood eosinophil counts had an increased risk of severe exacerbations leading to hospital admissions.(14) As SCS is indicated for the treatment of severe exacerbations, patients with high blood eosinophil counts may be more likely to be chronic or high-dose SCS users compared with patients with lower eosinophil thresholds.(9)

The sensitivity of blood eosinophil counts to changes in SCS as demonstrated in the current study is in agreement with previous studies that showed SCS decrease eosinophil counts in patients with severe eosinophilic asthma.(11, 12) Furthermore, in a small clinical study, blood eosinophil counts were shown to reflect the clinical response of acute exacerbations to corticosteroid treatment.(17) In a post hoc analysis of the SIRUS randomized controlled trial in steroid-dependent patients with severe eosinophilic asthma, the effect of oral corticosteroids (OCS) on blood eosinophil counts was assessed. Following a median daily prednisone dose of 10 mg, and average prednisone adjustment of 2.5 mg during the trials' optimization phase of up to 8 weeks, patients who increased OCS dose (N=31) demonstrated blood eosinophil count reductions from 330 cells/ μ L to 200 cells/ μ L.(18, 19) In contrast, those who decreased their OCS dose (N=60) demonstrated blood eosinophil count increases from 220 cells/ μ L to 310 cells/ μ L.(19) Although patients included in SIRIUS were receiving maintenance SCS treatment, the percentage change in blood eosinophil counts observed over the optimization phase, (39% reduction) is consistent with the findings in our study, where an approximate 34% reduction in blood eosinophils was observed between index and Month 1. This effect should be considered when making clinical assessments of blood eosinophil counts after recent SCS treatment.

Thresholds of blood eosinophil counts can vary across asthma severity. However, a combination of clinical markers is essential in determining the importance and interpretation of blood eosinophil counts in patients with severe asthma. For example, in a post hoc analysis of the DREAM study, which enrolled patients with severe asthma both OCS-dependent and non-dependent, patients had similar median blood eosinophil counts (280–290 cells/ μ L) after a mean OCS dose of 17 mg/day.(15, 16)

The utility of a single measure of blood eosinophil count of ≥ 150 cells/ μ L over time to identify patients with severe eosinophilic asthma has been reported.(20) In the post hoc analysis of the MENSA study, 85% of patients remained ≥ 150 cells/ μ L over the subsequent 56 weeks post-screening. Measuring blood eosinophil counts two, three, or four times at an interval of 4 weeks modestly improved the accuracy of predicting patients with ≥ 150 cells/ μ L to 88%, 88%, and 89%, respectively. We applied the findings from the MENSA post hoc analysis to the current study by using the single closest measurement to the Month 1 or Month 3 time points, within a window of 45 days before or after these time points.

Limitations of this study were due to the real-world study design, which included a lack of consistent measurements for individual patients across time points and small patient numbers in stratified subgroups. This limitation is intrinsic to the use of administrative datasets.(21) The analysis did not account for the degree of disease severity, did not assess chronic users of SCS and did not examine the possible impact of high-dose inhaled steroid therapy on blood eosinophil counts. Other factors that could influence the blood eosinophil results include diurnal variability and sensitivity to external factors (eg, allergen exposure in allergic individuals). Additionally, as treatment patterns were derived from EMR prescription information, there were no patient adherence data. Given that the RMG dataset only included patients from the state of Massachusetts, further studies are needed to validate the results in this study in relation to generalizability to a broader patient population.

The pre-post design used in this study avoids the need to identify a comparable control group and related biases, and the problems associated with unobserved and uncontrollable confounders. The repeated blood eosinophil count measurements enabled analysis of SCS exposure across various cohorts and time periods. Finally, the use of data from a real-world setting makes the results relevant to the clinical management of patients with asthma who are prescribed SCS.

Conclusion

The results from this real-world study highlight the importance of the temporal relationship between SCS administration and blood eosinophil counts in patients with eosinophilic asthma. As anticipated, there was a progressive decrease in blood eosinophil counts

following the administration of SCS therapy and weeks after SCS discontinuation, blood eosinophil counts had not returned to index levels. As SCS reduces blood eosinophil counts, the time frame of SCS discontinuation is an important consideration when identifying patients with eosinophilic asthma.

Author contributions

M-HL and MSD contributed to the study concept and design and were involved in data acquisition. CB and BH contributed to the study concept and design. GG, DL, and SS were involved in data acquisition. All authors were involved in the data analysis and interpretation, preparation and review of the manuscript, and approved the final version to be submitted.

Disclosure statements

HO, J-PL, CB, and BH are GSK employees and hold stocks/shares. M-HL, MSD, GG, and DL are employees of Analysis Group, Inc., a consulting company that has received research funds from GSK. SS is an employee of RMG Research Department, which has received research funds from GSK.

Role of the funding source

This study was funded by GSK (HO-16-16495). GSK employees contributed to the study design, analysis and interpretation of data, the writing of the manuscript and the approval of the final version to be submitted. The decision to submit for publication was that of the authors alone. The sponsor did not place any restrictions on access to the data or on the

statements made in the manuscript. The authors had full access to all the data in the study and had final responsibility to submit for publication.

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References

1. World Health Organization. Chronic Respiratory Disease: Asthma.
<http://www.who.int/respiratory/asthma/scope/en/> (accessed July 2017)
2. de Groot JC, ten Brinke A, Bel EHD. Management of the patient with eosinophilic asthma: a new era begins. *ERJ Open Research*. 2015;1(1).
3. Walford HH, Doherty TA. Diagnosis and management of eosinophilic asthma: a US perspective. *J Asthma Allergy*. 2014;7:53–65.
4. Wagener AH, de Nijs SB, Lutter R, Sousa AR, Weersink EJ, Bel EH, et al. External validation of blood eosinophils, FE(NO) and serum periostin as surrogates for sputum eosinophils in asthma. *Thorax*. 2015;70(2):115–20.
5. Ortega H, Katz L, Gunsoy N, Keene O, Yancey S. Blood eosinophil counts predict treatment response in patients with severe eosinophilic asthma. *J Allergy Clin Immunol*. 2015;136(3):825–6.
6. Bacci E, Cianchetti S, Ruocco L, Bartoli ML, Carnevali S, Dente FL, et al. Comparison between eosinophilic markers in induced sputum and blood in asthmatic patients. *Clin Exp Allergy*. 1998;28(10):1237-43.
7. Alangari AA. Corticosteroids in the treatment of acute asthma. *Ann Thorac Med*. 2014;9(4):187–92.
8. Rowe BH, Spooner C, Ducharme F, Bretzlaff J, Bota G. Early emergency department treatment of acute asthma with systemic corticosteroids. *Cochrane Database of Systematic Reviews*. 2001(1).

9. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. Web link: <http://ginasthma.org/2017-gina-report-global-strategy-for-asthma-management-and-prevention/> Last accessed 13 July 2017.
10. Lefebvre P, Duh MS, Lafeuille MH, Gozalo L, Desai U, Robitaille MN, et al. Burden of systemic glucocorticoid-related complications in severe asthma. *Curr Med Res Opin.* 2017;33(1):57–65.
11. Lassalle P, Sergeant M, Delneste Y, Gosset P, Wallaert B, Zandecki M, et al. Levels of soluble IL-2 receptor in plasma from asthmatics. Correlations with blood eosinophilia, lung function, and corticosteroid therapy. *Clin Exper Immunol.* 1992;87(2):266–71.
12. Sakae TM, Maurici R, Trevisol DJ, Pizzichini MM, Pizzichini E. Effects of prednisone on eosinophilic bronchitis in asthma: a systematic review and meta-analysis. *Jornal Brasileiro de Pneumologia.* 2014;40(5):552–63.
13. Prazma C BE, Barnes N, Price R, Albers F, Yancey S. Steroid Sparing Response with Mepolizumab: Durability of Steroid Reduction in Severe Asthma. *The Journal of Allergy and Clinical Immunology.* 2016;137(2):Supplement, AB16.
14. Casciano J, Krishnan JA, Small MB, Buck PO, Gopalan G, Li C, et al. Burden of asthma with elevated blood eosinophil levels. *BMC Pulm Med.* 2016;16(1):100.
15. Pavord ID, Korn S, Howarth P, Bleecker ER, Buhl R, Keene ON, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. *Lancet.* 2012;380(9842):651–9.
16. Prazma CM, Wenzel S, Barnes N, Douglass JA, Hartley BF, Ortega H. Characterisation of an OCS-dependent severe asthma population treated with mepolizumab. *Thorax.* 2014;69(12):1141–2.
17. Baigelman W, Chodosh S, Pizzuto D, Cupples LA. Sputum and blood eosinophils during corticosteroid treatment of acute exacerbations of asthma. *Am J Med.* 1983;75(6):929–36.

18. Bel EH, Wenzel SE, Thompson PJ, Prazma CM, Keene ON, Yancey SW, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371(13):1189–97.
19. Prazma C BE, Price R, Bradford E, Albers FC, Yancey S. Oral Corticosteroid Dose Modulation in Severe Asthma: Impact on Peripheral Blood Eosinophil Count. *American Journal of Respiratory and Critical Care Medicine*. 2017(195):A1363.
20. Ortega H, Gleich G, Mayer B, Yancey S. Reproducibility of a Single Blood Eosinophil Measurement as a Biomarker in Severe Eosinophilic Asthma. *Ann Am Thorac Soc*. 2015;12(12):1896–7.
21. Aaron SD, Vandemheen KL, FitzGerald JM, Ainslie M, Gupta S, Lemiere C, et al. Reevaluation of Diagnosis in Adults With Physician-Diagnosed Asthma. *JAMA*. 2017;317(3):269-79.

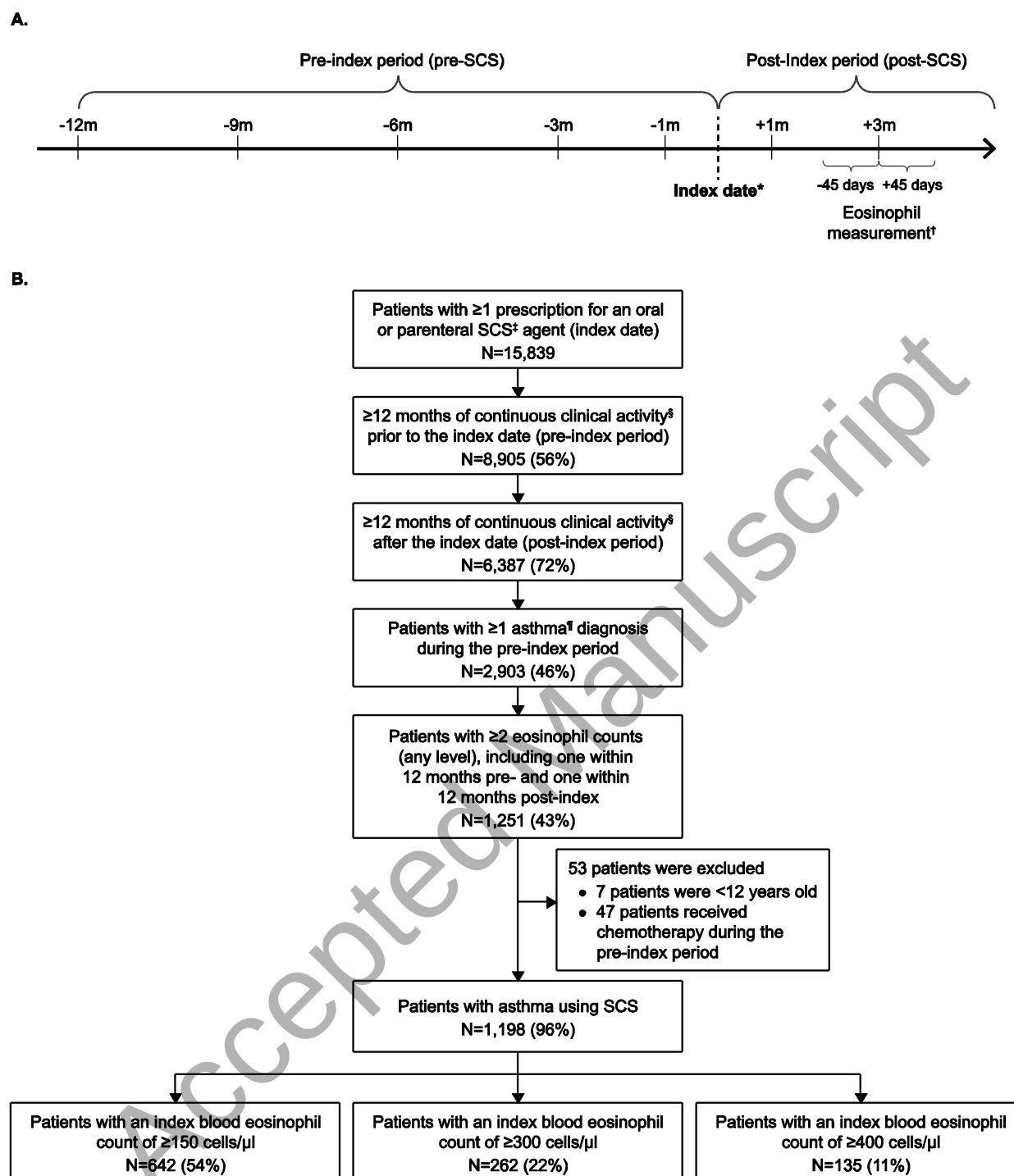


Figure 1. A) Overview of study design and **B)** Patient selection and disposition.

SCS, systemic corticosteroid.

*First prescription of SCS agent; [†] eosinophil measurement for the 3-month time point was ± 45 days; [‡]SCS agents identified by Generic Product Identifier class of 22; [§]clinical activity defined as the period between the first and last record in the electronic medical records database. These data were collected for 12 months before the index date and 12 months after, but this study focused on the first 3 months after the index date; [¶]asthma diagnosis identified by the International Classification of Diseases (ICD)-9-Clinical Modification (CM) code: 493.xx and ICD-10-CM code: J45.xx

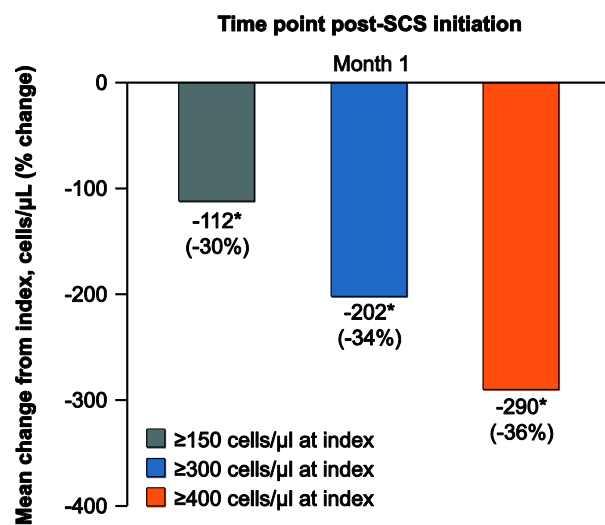


Figure 2. Mean change in blood eosinophil count from index

SCS, systemic corticosteroid.

* Statistical significant difference (P -value < 0.05) based on generalized estimating equation model adjusting for correlations between index and post observations.

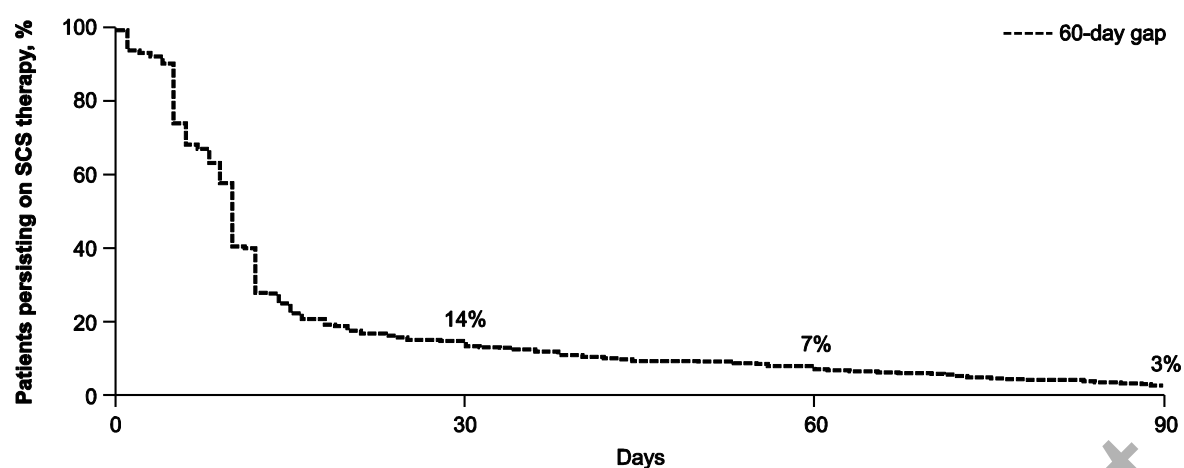


Figure 3. Proportion of patients* with an index blood eosinophil count of ≥ 150 cell/ μ L remaining on SCS therapy over time.

SCS, systemic corticosteroid.

*Patient data were only included when information regarding the number of days of prescription supply was available.

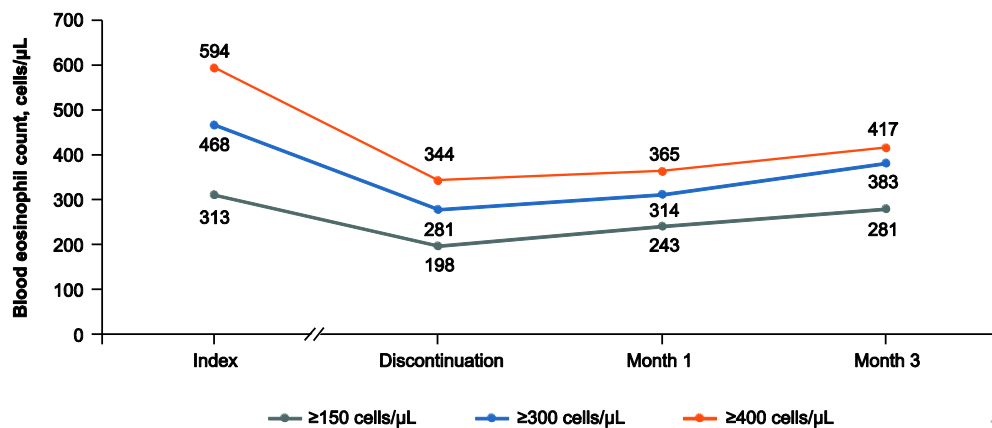


Figure 4. Changes in mean blood eosinophil count at discontinuation and post-discontinuation of SCS.

SCS, systemic corticosteroid.

The index value is the value at the index date or the value closest to the index date in the 12-month pre-index period. The Month 1 and Month 3 post-discontinuation values are the closest to the time point within a window of 45 days after the index date for Month 1, and a window of ± 45 days around the Month 3 time point.

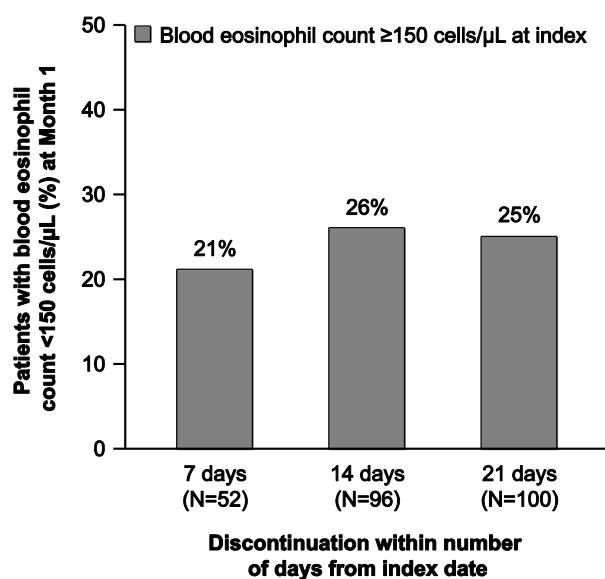


Figure 5. Proportion of patients with an index blood eosinophil count ≥ 150 cells/ μ L with a count < 150 cells/ μ L at Month 1 following SCS discontinuation within 7, 14, and 21 days of the index date.

SCS, systemic corticosteroid.

Baseline value is the closest measure in the baseline period to or at index date; Value at 1 month is the closest to the Month 1 time point after discontinuation and within a window of 45 days after the index date.

Table 1. Patient demographics and clinical characteristics.

	Blood eosinophil count in patients with asthma*		
	≥150 cells/μL (N=642)	≥300 cells/μL (N=262)	≥400 cells/μL (N=135)
Age at index date, years, mean (SD)	56 (18.0)	55 (19.8)	55 (20.0)
Female, n (%)	441 (69)	175 (67)	88 (65)
Insurance type, n (%)			
Commercial	227 (35)	98 (37)	51 (38)
Medicare	190 (30)	82 (31)	42 (31)
Medicaid	79 (12)	26 (10)	11 (8)
Unknown	146 (23)	56 (21)	31 (23)
Index blood eosinophil count*			
Eosinophil count, cells/μL, mean (SD)	333 (434.7)	511 (638.9)	680 (857.2)
From measure to index date, days, mean (SD)	124 (109.4)	120 (105.1)	112 (104.2)
Body mass index[†]			
Number of patients, n (%)	625 (97)	256 (98)	131 (97)
Body mass index, kg/m ² , mean (SD)	31 (9.1)	31 (8.8)	30 (8.6)
Quan-Charlson comorbidity index, mean (SD)	2 (1.8)	2 (1.7)	2 (1.8)
Comorbidities[†], n (%)			
Upper respiratory and allergic			
- Allergic rhinitis	138 (22)	62 (24)	35 (26)
- Chronic sinusitis	69 (11)	29 (11)	20 (15)
- Chronic obstructive pulmonary disease	75 (12)	21 (8)	10 (7)
- Acute sinusitis	49 (8)	20 (8)	8 (6)
- Nasal polyps	9 (1)	7 (3)	4 (3)
Systemic and infections			
- Cardiovascular disease	357 (56)	139 (53)	72 (53)
- Bacterial infection‡	226 (35)	78 (30)	31 (23)
- Respiratory infections‡	197 (31)	73 (28)	39 (29)
- Diabetes	158 (25)	65 (25)	32 (24)

SD, standard deviation.

*The index value is the value at the index date or the value closest to the index date in the 12-month pre-index period; [†]assessed within the 12-month pre-index period; [‡]some

respiratory infections may be bacterial infections but the overlap between these two groups was not analyzed.

Other comorbidities with a frequency of $\leq 1.5\%$ included atopic dermatitis, Crohn's disease, eosinophilic esophagitis, eosinophilic granulomatosis with polyangiitis, hypereosinophilic syndrome, multiple sclerosis, those in the respiratory and intrathoracic system, rheumatoid arthritis, and systemic lupus erythematosus.

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