Journal of Asthma and Allergy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

SHORT REPORT

Mortality Among Adults with Subspecialist-Treated Severe Asthma: A Descriptive Analysis from the Observational CHRONICLE Study

Njira L Lugogo[1], Jennifer Trevor[2], Joseph D Spahn[3], Reynold A Panettieri Jr[4], Donna D Carstens[3], Christopher S Ambrose[5]

[1]Department of Medicine, Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, USA; [2]Division of Pulmonary, Allergy, and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, AL, USA; [3]BioPharmaceuticals Medical, AstraZeneca, Wilmington, DE, USA; [4]Rutgers Institute for Translational Medicine and Science, The State University of New Jersey, New Brunswick, NJ, USA; [5]BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD, USA

Correspondence: Christopher S Ambrose, BioPharmaceuticals Medical, AstraZeneca, One Medimmune Way, Gaithersburg, MD, 20878, USA, Tel +1 301-398-4454, Email chris.ambrose@astrazeneca.com

Purpose: There are limited recent data assessing all-cause mortality for US patients with severe asthma. This descriptive analysis evaluated all-cause mortality in a real-world cohort of US adults with subspecialist-treated severe asthma, examining patient characteristics among those who died, physician-reported primary causes of death, and associations with treatment class.

Patients and Methods: CHRONICLE (NCT03373045) was an observational study of US adults (aged ≥18 years) with subspecialist-treated severe asthma, enrolled from February 2018 to October 2024. Patients met at least one of the following criteria: ongoing FDA-approved monoclonal antibody therapy, maintenance systemic corticosteroids (mSCS) for ≥50% of the prior year, or persistently uncontrolled asthma despite high-dosage inhaled corticosteroids and additional controllers. All-cause mortality was assessed descriptively, overall and by treatment class at time of death. Investigators reported primary causes of death and COVID-19 involvement. Treatment class exposure was calculated by the cumulative days on biologics and/or mSCS.

Results: Among 4366 enrolled patients, mean age was 54.7 years; 69.7% were female, 73.1% were White, and 18.6% were Black. Over 14,758 person-years of observation, 130 deaths occurred (3.0%), yielding a mortality of 8.8 (95% confidence interval: 7.4, 10.5) per 1000 person-years. Cardiovascular disease was the leading cause of death (25.4%), followed by cancer (13.1%) and asthma (1.5%). COVID-19 contributed to 8.5% of deaths. Observed associations for all-cause mortality ranged from 6.8 per 1000 person-years in patients who were receiving biologics without mSCS to 31.6 per 1000 person-years in those receiving mSCS without biologics.

Conclusion: US adults with subspecialist-treated severe asthma have an increased risk of all-cause mortality, especially those patients receiving mSCS. These findings highlight the importance of identifying mortality risks and limiting the use of mSCS whenever possible while supporting further research into the relationship between severe asthma and cardiovascular disease.

Keywords: asthma, death, mortality, observational study, severe

Introduction

Approximately 3–10% of people with asthma have severe disease, which can remain uncontrolled despite treatment with high-dosage inhaled corticosteroids, additional controllers, and/or systemic corticosteroids (SCS).[1,2] Multiple large cohort studies have shown that excess mortality in patients with severe asthma compared with the general asthma population is likely driven by multiple factors, including persistent uncontrolled disease with frequent exacerbations, a high comorbidity burden, and adverse effects associated with long-term SCS exposure, rather than being attributable to asthma-related death alone.[3–8] SCS sparing treatments, such as biologic therapies, have demonstrated clinically meaningful benefits, including reductions in exacerbations and SCS exposure.[9–12]

https://doi.org/10.2147/JAA.S588118
Received: 8 January 2026
Accepted: 31 March 2026
Published: 5 May 2026

A European multinational study from 2008 through 2013 reported all-cause mortality estimates of 5.2–9.5 per 1000 person-years for patients with asthma and 11.3–14.8 per 1000 person-years for patients with severe asthma.[5] The Centers for Disease Control and Prevention reported approximately 3000–4000 asthma deaths per year in the United States (US) from 2001 through 2021;[13] however, there are limited recent data assessing all-cause mortality for US patients with severe asthma.

The real-world CHRONICLE study of US adults with subspecialist-treated severe asthma has generated a large dataset that has supported multiple analyses.[14] However, no prior publications have examined all-cause mortality in detail. The current study included all patients enrolled in the CHRONICLE study between February 2018 and October 2024, providing a large cohort with sufficient follow-up to enable a detailed evaluation of mortality outcomes, including assessments of the sociodemographic and clinical characteristics of the patients who died, physician-reported primary causes of death, and associations with treatment class.

Materials and Methods

CHRONICLE (NCT03373045) was an observational study that enrolled US adults with subspecialist-treated severe asthma between February 2018 and October 2024. Eligible patients (aged ≥18 years at enrollment) were receiving care from pulmonologists or allergist-immunologists at a participating site and met ≥1 of the following criteria: (1) current use of a FDA-approved monoclonal antibody therapy for severe asthma; (2) use of maintenance SCS (mSCS) for severe asthma for at least 50% of the 12 months before enrollment; or (3) persistently uncontrolled asthma while receiving high-dosage inhaled corticosteroids and additional controllers.[14]

This descriptive analysis evaluated all-cause mortality among all enrolled CHRONICLE patients, overall and by treatment class at the time of death. Investigators reported the primary cause of death from a prespecified list and any confirmed or suspected cases of COVID-19. Free-text narratives were reviewed to determine whether deaths categorized as "other" or "unknown" could be reassigned. Treatment class exposure was calculated from the cumulative number of days patients received treatments following enrollment. To explore treatment class associations with mortality, treatment classes were defined for the ongoing receipt of biologics, receipt of mSCS (defined as SCS receipt for >30 consecutive days), combinations of these two states, and receipt of neither biologics nor mSCS.

The CHRONICLE study was performed in accordance with ethical principles consistent with the Declaration of Helsinki, the International Council for Harmonisation Good Clinical Practice guideline, guidelines for Good Pharmacoepidemiology Practices, the Health Insurance Portability and Accountability Act, and applicable legislation for observational studies. The study protocol was approved by a central institutional review board (Advarra, Columbia, MD, USA; reference number 201707165) on November 3, 2017, and was registered on ClinicalTrials.gov on December 14, 2017 (NCT03373045). All patients provided written informed consent at enrollment.

Results

Among the 4366 patients enrolled with evaluable data, the mean age at enrollment was 54.7 years (min, max: 18, 94), 69.7% were female, 73.1% were White, and 18.6% were Black (Table 1). The mean observation time per patient was 3.4 (standard deviation, 1.9) person-years; the total observation time was 14,758 person-years. Overall, 130 deaths (3.0% of patients) were reported, yielding a study mortality of 8.8 (95% confidence interval [CI]: 7.4–10.5) per 1000 person-years.

Among patients who died, the mean age at enrollment was 64.3 years (min, max: 20, 87), 59.2% were female, 79.2% were White, and 16.2% were Black. Compared with all enrolled patients, those who died were older (mean age, 64.3 years vs 54.7 years), more likely to be under the care of a pulmonologist (83.1% vs 65.1%), and more likely to have a reported diagnosis of chronic obstructive pulmonary disease in addition to asthma (29.2% vs 13.1%).

The primary cause of death was unknown in 26.9% of patients. Cardiovascular disease was the most frequent cause of death (25.4% overall; 10.8% heart failure and 14.6% other cardiovascular disease). Approximately 13.1% of patients died from cancer/malignancy (5.4% from lung cancer) and 1.5% died from asthma (Figure 1). Death with a contributory COVID-19 diagnosis was reported in 8.5% of patients (Figure 2).

Descriptively, all-cause mortality ranged from 6.8 (95% CI: 5.1, 8.8) per 1000 person-years in patients treated with biologics without mSCS to 31.6 (95% CI: 16.8, 54.0) per 1000 person-years in those treated with mSCS without

Table 1 Patient Characteristics at Enrollment

Characteristic	All Enrolled (N = 4366)	Patients Who Died (n = 130)
Age at enrollment, years		
Mean (SD)	54.7 (14.6)	64.3 (13.4)
Median (min, max)	56.0 (18, 94)	67.0 (20, 87)
Female, n (%)	3041 (69.7)	77 (59.2)
Race, n (%)		
White	3190 (73.1)	103 (79.2)
Black	811 (18.6)	21 (16.2)
Asian	74 (1.7)	0
Other[a]	133 (3.0)	3 (2.3)
Not reported	154 (3.5)	3 (2.3)
Missing	4 (0.1)	0
Hispanic or Latino ethnicity, n (%)	400 (9.2)	7 (5.4)
BMI, kg/m^2		
n	3974	125
Mean (SD)	33.4 (9.0)	34.1 (9.6)
Median (min, max)	31.8 (9.1, 113.1)	33.1 (17.4, 67.5)
Residential area, n (%)		
Urban	1096 (25.1)	24 (18.5)
Rural	1166 (26.7)	36 (27.7)
Suburban	1975 (45.2)	67 (51.5)
Missing	129 (3.0)	3 (2.3)
Primary insurance, n (%)		
Commercial	2419 (55.4)	43 (33.1)
Medicaid	511 (11.7)	10 (7.7)
Medicare	1105 (25.3)	66 (50.8)
Uninsured	46 (1.1)	0
Other[b]	281 (6.5)	11 (8.4)
Missing	4 (0.1)	0
Employment status, n (%)		
Employed (full-time, part-time, or self-employed)	2102 (48.1)	21 (16.1)
Homemaker	137 (3.1)	4 (3.1)
Full-time student	90 (2.1)	0
Retired	1070 (24.5)	61 (46.9)
Disabled owing to asthma	271 (6.2)	15 (11.5)
Disabled owing to a nonasthma condition	283 (6.5)	17 (13.1)
Unemployed	269 (6.2)	7 (5.4)
Missing	144 (3.3)	5 (3.8)
Smoking history status, n (%)		
Never	2807 (64.3)	66 (50.8)
Former	1301 (29.8)	56 (43.1)
Current	257 (5.9)	8 (6.2)
Missing	1 (0.0)	0

(*Continued*)

Table 1 (Continued).

Characteristic	All Enrolled (N = 4366)	Patients Who Died (n = 130)
Subspecialist care, n (%)		
Allergist/immunologist	1524 (34.9)	22 (16.9)
Pulmonologist	2440 (55.9)	99 (76.2)
Allergist/immunologist and pulmonologist	402 (9.2)	9 (6.9)
BEC[c]		
n	1265	42
Mean (SD), cells/μL	418.9 (563.4)	441.3 (605.9)
Median (Q1, Q3), cells/μL	262.4 (121.3, 516.0)	267.5 (140.7, 501.8)
Total IgE level[c]		
n	961	12
Mean (SD), IU/mL	409.8 (1119.3)	203.4 (285.1)
Median (Q1, Q3), IU/mL	133.0 (44.0, 385.0)	53.5 (24.0, 375.5)
Respiratory comorbidities, n (%)[d]		
Allergic rhinitis	2787 (64.0)	67 (51.5)
Obstructive sleep apnea	1231 (28.3)	41 (31.5)
Chronic sinusitis/rhinosinusitis	779 (17.9)	11 (8.5)
Other	683 (15.7)	28 (21.5)
Allergy to seasonal aeroallergen[e]	625 (14.4)	17 (13.1)
Allergy to perennial aeroallergen[e]	606 (13.9)	14 (10.8)
COPD	572 (13.1)	38 (29.2)
Nasal/sinus polyps	383 (8.8)	5 (5.2)
Chronic cough	216 (5.0)	9 (6.9)
Bronchiectasis	209 (4.8)	10 (7.7)
Chronic bronchitis	167 (3.8)	5 (5.2)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)	25 (0.6)	5 (5.2)
Non-respiratory comorbidities, n (%)[d]		
Gastroesophageal reflux disease	2043 (46.9)	60 (46.2)
Hypertension	1659 (38.1)	75 (57.7)
Other	1366 (31.4)	45 (34.6)
Hypercholesterolemia/hyperlipidemia	932 (21.4)	44 (33.8)
Depression	871 (20.0)	32 (24.6)
Anxiety	823 (18.9)	37 (28.5)
Type II diabetes	675 (15.5)	36 (27.7)
Osteoarthritis or unspecified arthritis	541 (12.4)	21 (16.2)
Thyroid disease	475 (10.9)	15 (11.5)
Osteopenia/osteoporosis	342 (7.9)	16 (12.3)
Insomnia or sleep disturbance	290 (6.7)	10 (7.7)
Coronary artery disease	208 (4.8)	23 (17.7)
Congestive heart failure	186 (4.3)	17 (13.1)
Chronic kidney disease (not in renal failure)	169 (3.9)	13 (10.0)
Cardiac arrhythmia	182 (4.2)	13 (10.0)
Cataract	148 (3.4)	10 (7.7)
Valvular heart disease	87 (2.0)	7 (5.4)
Peripheral vascular disease	39 (0.9)	5 (5.2)

Notes: [a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other. [b]Includes other government insurance and Other. [c]BEC and IgE level are reported at enrollment for those not receiving biologics or SCS within 30 days of testing. [d]Respiratory and nonrespiratory comorbidities are reported for those occurring in at least 5% of the patients who died. [e]Confirmed by testing (skin prick or specific IgE).

Abbreviations: BEC, blood eosinophil count; BMI, body mass index; COPD, chronic obstructive pulmonary disease; IgE, immunoglobulin E; SCS, systemic corticosteroids; max, maximum; min, minimum; Q1, first quartile; Q3, third quartile; SD, standard deviation.

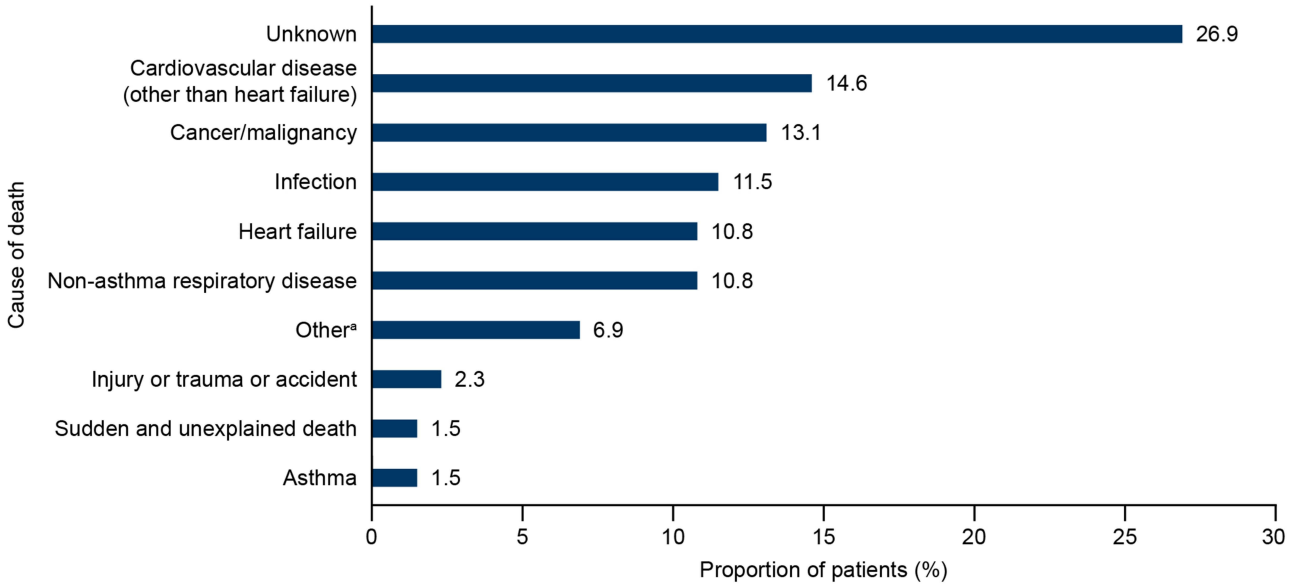

Figure 1 Primary causes of death in patients with severe asthma among those who died (n = 130).
Notes: [a]Other includes organ failure, hypokalemia or malnutrition, hemophagocytic lymphohistiocytosis, gastric perforation, dementia or Alzheimer's, chronic kidney disease, accidental tramadol overdose, sepsis, and severe hypoglycemia (each reported in 1 patient).

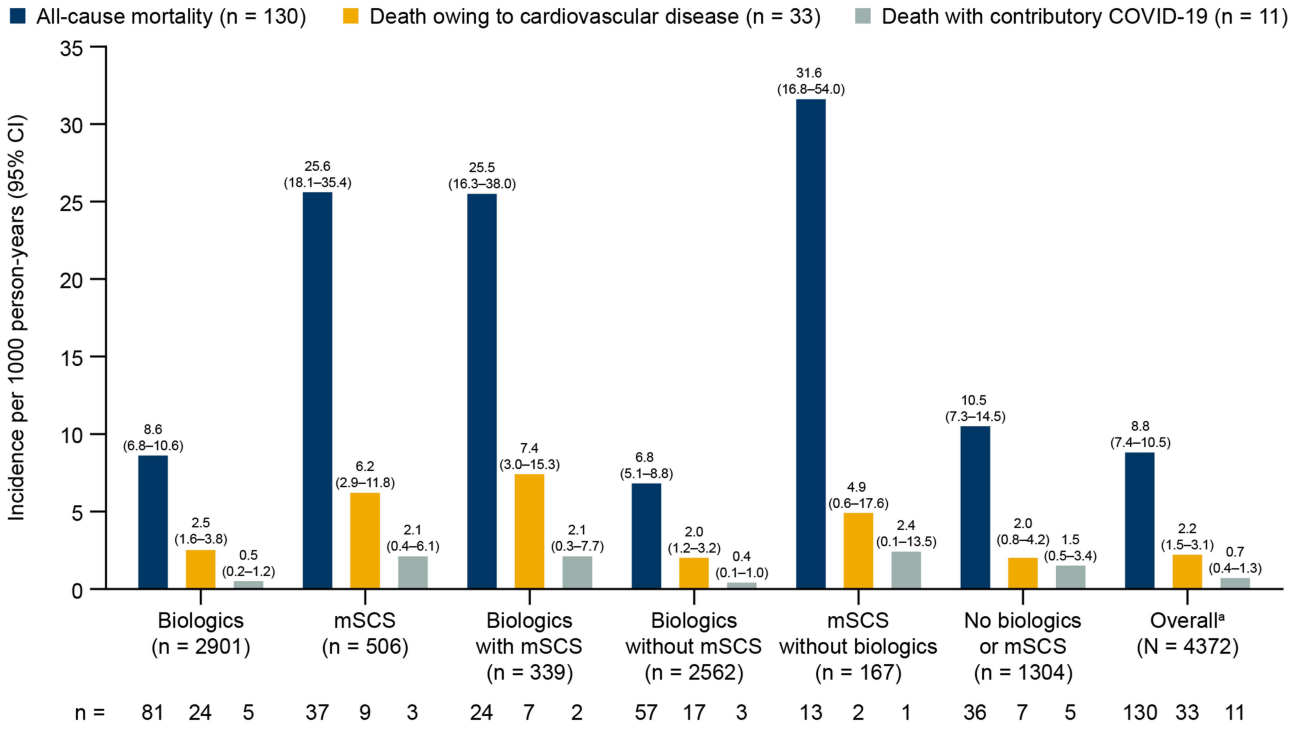

Figure 2 Mortality (per 1000 person-years) by treatment class at time of death.
Notes: [a]Population denominator includes all patients enrolled. The biologics and mSCS groups were not mutually exclusive; patients receiving both treatments were counted in each group.
Abbreviations: CI, confidence interval; mSCS, maintenance systemic corticosteroids.

https://doi.org/10.2147/JAA.S588118

biologics. Patients treated with mSCS had the highest mortality owing to cardiovascular disease and contributory COVID-19 (Figure 2).

Discussion

Although asthma-related mortality in severe asthma is rare, patients with severe asthma have an increased risk of all-cause mortality compared with the general asthma population. An observational study in France reported a 2.35-fold elevated risk of all-cause mortality among patients with severe asthma compared with a matched general population.[7] Among the present cohort of US adults with subspecialist-treated severe asthma, all-cause mortality (8.8 per 1000 person-years) was lower than estimates for adults with severe asthma from Europe from 2008 through 2013. However, the European study was completed approximately a decade earlier than the present study (ie, before most currently available biologic therapies for asthma were approved), enrolled approximately 3-fold more current smokers, and included adults who were not receiving subspecialist care for their severe asthma.[5]

Previous studies have shown higher asthma-related mortality in non-Hispanic Black patients with asthma in the US than non-Hispanic White patients.[13] However, in the subspecialist-treated population enrolled in the CHRONICLE study, the proportion of deaths reported in Black patients was consistent with their representation in the enrolled study population. Previous studies have reported that Black patients may be less likely than White patients to receive subspecialist care for their asthma, a disparity that may reconcile these observations.[15,16]

The high percentage of deaths attributed to cardiovascular disease in the overall cohort is consistent with previous findings that patients with asthma have a high risk of cardiovascular events, likely owing to increased systemic inflammation, enhanced coagulation activation, and SCS toxicity.[17–25] Patients with asthma have been reported to have a 32% increased risk of cardiovascular disease and a 25% increased risk of cardiovascular disease-related mortality compared with people without asthma.[25]

Consistent with previous studies outside of the US, mortality was highest in patients receiving mSCS and was lowest among those receiving biologics without mSCS.[19–21] Studies in Denmark, Korea, Sweden, and the United Kingdom have shown that adults with asthma receiving oral corticosteroids (OCS) or mSCS had a greater risk of all-cause mortality than those not receiving corticosteroids, with dose-dependent effects.[19–21,23] Long-term OCS treatment for asthma is associated with multiple comorbidities, including hypercholesterolemia, hypertension, coronary heart disease, heart failure, cancer, and diabetes.[19,26] In CHRONICLE, mortality due to cardiovascular disease and respiratory disease was increased among patients receiving mSCS compared with those receiving biologics. The increased incidence of death with contributory COVID-19 in patients receiving mSCS aligns with findings that patients with uncontrolled asthma requiring OCS have an increased risk of COVID-19-related death.[27,28] However, comparisons across treatment classes should be interpreted with caution because those receiving mSCS are likely to represent a patient population with more severe baseline disease characteristics.

Limitations of the CHRONICLE study have been described previously[14] and include differences in standards of care across study sites and the descriptive nature of the analyses. The CHRONICLE study included adults with severe asthma in the US receiving subspecialist care, which may limit the generalizability of the findings to the broader severe asthma population. Owing to the observational study design, causal effects of treatment class on mortality could not be assessed. Treatment class exposure was calculated based on the cumulative number of days patients received each treatment following enrollment, and deaths were attributed to the treatment classes at the time of death, which may have introduced misclassification bias. The lack of multivariate adjustment means that disease severity and comorbidities may have confounded these descriptive results. Despite these limitations, the study provides valuable insights into real-world mortality risk among patients with severe asthma. Further adjusted or prospective analyses would help confirm the impact of treatment class on mortality.

Conclusion

This study confirms an increased risk of mortality in US adults with subspecialist-treated severe asthma, including among those treated with mSCS. These findings can help to identify mortality risks in patients with severe asthma and support future investigations into relationships between severe asthma and fatal cardiovascular disease.

Abbreviations

CI, confidence interval; COVID-19, coronavirus disease 2019; mSCS, maintenance SCS; OCS, oral corticosteroids; SCS, systemic corticosteroids; SD, standard deviation.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. Individuals who were or were not involved in the CHRONICLE study may submit publication proposals to the study's Publication Steering Committee by contacting the corresponding author.

Ethical Approval and Informed Consent

The CHRONICLE study was performed in accordance with ethical principles consistent with the Declaration of Helsinki, the International Council for Harmonisation Good Clinical Practice guideline, guidelines for Good Pharmacoepidemiology Practices, the Health Insurance Portability and Accountability Act, and applicable legislation for observational studies. The study protocol was approved by a central institutional review board (Advarra, Columbia, MD, USA; reference number 201707165) on November 3, 2017, and was registered on ClinicalTrials.gov on December 14, 2017 (NCT03373045). All patients provided written informed consent at enrollment.

Acknowledgments

Medical writing support was provided by Sarah Shires, PhD, of Oxford PharmaGenesis, Inc. (Newtown, PA, United States), and Elizabeth Gandhi, PhD, of Oxford PharmaGenesis (Cambridge, UK), which was in accordance with Good Publication Practice (GPP 2022) and was funded by AstraZeneca, Wilmington, DE, United States. Abstracts reporting interim analyses of mortality outcomes from the CHRONICLE study have been presented as an oral presentation at the American College of Chest Physicians (CHEST) Annual Meeting, October 8–11, 2023, Honolulu, HI, United States (Lugogo NL et al. *Chest*. 2023;164:A18–A22) and as a poster at the American Thoracic Society (ATS) International Conference; May 17–22, 2024; San Diego, CA, USA (Lugogo NL et al. *Am J Respir Crit Care Med.* 2024;209:A5250).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

The CHRONICLE study (ClinicalTrials.gov identifier: NCT03373045) is funded by AstraZeneca.

Disclosure

N.L.L.: consultant – AbbVie, Amgen, Apogee, AstraZeneca, Avillion, Foresee, Genentech, GSK, Niox, Novartis, Regeneron Pharmaceuticals, Sanofi, and Teva; fees for nonspeaker bureau presentations – AstraZeneca, GSK, Regeneron Pharmaceuticals, Sanofi, and Teva; travel support – AstraZeneca, GSK, Regeneron Pharmaceuticals, Sanofi, and Teva; her institution received research support from Amgen, AstraZeneca, Avillion, Bellus, Evidera, Genentech, Gossamer Bio, GSK, Janssen, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi, and Teva; she is also an honorary faculty member of the Observational and Pragmatic Research Institute (OPRI) but does not receive compensation for this role. She is also a data and safety monitoring board member for Incyte. J.T.: consultant and advisory boards – AstraZeneca. J.D.S.: employee and shareholder – AstraZeneca. R.A.P.Jr: advisory boards and grant support – AstraZeneca, Genentech, Novartis, Sanofi, and Regeneron Pharmaceuticals. D.D.C.: employee and shareholder – AstraZeneca. C.S.A.: employee and shareholder – AstraZeneca. The authors report no other conflicts of interest in this work.

References

1. Global Initiative for Asthma. Global strategy for asthma management and prevention. 2024. Available from: www.ginasthma.org. Accessed June 25, 2025.
2. Chung KF, Wenzel SE, Brozek JL, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014;43(2):343–373. doi:10.1183/09031936.00202013
3. Bourdin A, Fabry-Vendrand C, Ostinelli J, et al. The burden of severe asthma in France: a case-control study using a medical claims database. *J Allergy Clin Immunol Pract*. 2019;7(5):1477–1487. doi:10.1016/j.jaip.2018.12.029
4. Choi H, Lee H, Ryu J, et al. Bronchiectasis and increased mortality in patients with corticosteroid-dependent severe asthma: a nationwide population study. *Ther Adv Respir Dis*. 2020;14:1753466620963030. doi:10.1177/1753466620963030
5. Engelkes M, de Ridder MA, Svensson E, et al. Multinational cohort study of mortality in patients with asthma and severe asthma. *Respir Med*. 2020;165:105919. doi:10.1016/j.rmed.2020.105919
6. Kankaanranta H, Viinanen A, Klavus A, et al. Burden of asthma by severity and exacerbation frequency among adult patients naive to biologic asthma therapy: a Finnish cohort study. *J Allergy Clin Immunol Glob*. 2025;4(2):100453. doi:10.1016/j.jacig.2025.100453
7. Roche N, Garcia G, de Larrard A, et al. Real-life impact of uncontrolled severe asthma on mortality and healthcare use in adolescents and adults: findings from the retrospective, observational RESONANCE study in France. *BMJ Open*. 2022;12(8):e060160. doi:10.1136/bmjopen-2021-060160
8. Tupper OD, Ulrik CS. Long-term predictors of severe exacerbations and mortality in a cohort of well-characterised adults with asthma. *Respir Res*. 2021;22(1):269. doi:10.1186/s12931-021-01864-z
9. Bel EH, Wenzel SE, Thompson PJ, et al. Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma. *N Engl J Med*. 2014;371(13):1189–1197. doi:10.1056/NEJMoa1403291
10. Jackson DJ, Lugogo NL, Gurnell M, et al. Oral corticosteroid reduction and discontinuation in adults with corticosteroid-dependent, severe, uncontrolled asthma treated with tezepelumab (WAYFINDER): a multicentre, single-arm, phase 3b trial. *Lancet Respir Med*. 2026;14(2):129–140. doi:10.1016/S2213-2600(25)00359-5
11. Nair P, Wenzel S, Rabe KF, et al. Oral glucocorticoid-sparing effect of benralizumab in severe asthma. *N Engl J Med*. 2017;376(25):2448–2458. doi:10.1056/NEJMoa1703501
12. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. *N Engl J Med*. 2018;378(26):2475–2485. doi:10.1056/NEJMoa1804093
13. Centers for Disease Control and Prevention (CDC) National Center for Health Statistics. AsthmaStats: asthma as the underlying cause of death. 2023. Available from: https://www.cdc.gov/asthma/asthma_stats/asthma-deaths_2001-2021.html. Accessed January 24, 2025.
14. Ambrose CS, Chipps BE, Moore WC, et al. The CHRONICLE study of US adults with subspecialist-treated severe asthma: objectives, design, and initial results. *Pragmatic Obs Res*. 2020;11:77–90. doi:10.2147/por.s251120
15. Carr T, Tkacz J, Chung Y, et al. Gaps in care among uncontrolled severe asthma patients in the United States. *J Allergy Clin Immunol Pract*. 2024;12(7):1775–1782e1772. doi:10.1016/j.jaip.2024.03.018
16. Zoratti EM, Havstad S, Rodriguez J, Robens-Paradise Y, Lafata JE, McCarthy B. Health service use by African Americans and Caucasians with asthma in a managed care setting. *Am J Respir Crit Care Med*. 1998;158(2):371–377. doi:10.1164/ajrccm.158.2.9608039
17. Adrish M, Hanania NA. Asthma and cardiovascular disease: a bidirectional association? *Respirology*. 2023;28(3):217–219. doi:10.1111/resp.14468
18. Choi HG, Kwon MJ, Kim JH, et al. Association between asthma and cardiovascular diseases: a longitudinal follow-up study using a national health screening cohort. *World Allergy Organ J*. 2024;17(6):100907. doi:10.1016/j.waojou.2024.100907
19. Ekstrom M, Nwaru BI, Hasvold P, Wiklund F, Telg G, Janson C. Oral corticosteroid use, morbidity and mortality in asthma: a nationwide prospective cohort study in Sweden. *Allergy*. 2019;74(11):2181–2190. doi:10.1111/all.13874
20. Lee H, Ryu J, Nam E, et al. Increased mortality in patients with corticosteroid-dependent asthma: a nationwide population-based study. *Eur Respir J*. 2019;54(5):1900804. doi:10.1183/13993003.00804-2019
21. Skov IR, Madsen H, Henriksen DP, Andersen JH, Pottegard A, Davidsen JR. Low-dose oral corticosteroids in asthma associates with increased morbidity and mortality. *Eur Respir J*. 2022;60(3):2103054. doi:10.1183/13993003.03054-2021
22. Tattersall MC, Guo M, Korcarz CE, et al. Asthma predicts cardiovascular disease events: the multi-ethnic study of atherosclerosis. *Arterioscler Thromb Vasc Biol*. 2015;35(6):1520–1525. doi:10.1161/ATVBAHA.115.305452
23. Xu X, Tran TN, Golam S, Carter V, Price DB. Systemic corticosteroid dose–response effects in asthma: an observational cohort study. *ERJ Open Res*. 2025;11(1):00172–02024. doi:10.1183/23120541.00172-2024
24. Yu S, Lee SC, Hong JH, Han CH, Park SC, Jung JY. Cardiovascular and cerebrovascular mortality in patients with preceding asthma exacerbation. *Respirology*. 2023;28(3):281–286. doi:10.1111/resp.14444
25. Zhang B, Li ZF, An ZY, et al. Association between asthma and all-cause mortality and cardiovascular disease morbidity and mortality: a meta-analysis of cohort studies. *Front Cardiovasc Med*. 2022;9:861798. doi:10.3389/fcvm.2022.861798
26. Bleecker ER, Menzies-Gow AN, Price DB, et al. Systematic literature review of systemic corticosteroid use for asthma management. *Am J Respir Crit Care Med*. 2020;201(3):276–293. doi:10.1164/rccm.201904-0903SO
27. Global Initiative for Asthma. Pocket guide for asthma management and prevention for adults, adolescents and children 6–11 years. 2023. Available from: https://ginasthma.org/wp-content/uploads/2023/07/GINA-2023-Pocket-Guide-WMS.pdf. Accessed February 1, 2025.
28. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*. 2020;584(7821):430–436. doi:10.1038/s41586-020-2521-4