Clinical Remission With Biologic Use Among US Subspecialist-Treated Patients With Severe Asthma: Results From the CHRONICLE Study

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the CHRONICLE study

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Introduction

- Severe asthma affects an estimated 5–10% of all individuals with asthma[1,2]
- A recent expert consensus proposed a framework for remission in asthma:[3]

At least 12 months of the following, with or without treatment:

- Consistent absence of significant asthma symptoms based on validated instrument; and
- Optimized and stabilized lung function; and
- Patient and provider agreement of disease remission; and
- No use of SCS therapy for treatment of exacerbations or long-term disease control

SCS, systemic corticosteroid.

Rationale and Objective

- There are limited real-world data regarding the proportion of patients with severe asthma (SA) who may achieve on-treatment clinical remission with biologic treatment
- Using a large cohort of subspecialist-treated US patients with SA enrolled in the CHRONICLE study, the objective of this analysis was to:
  - Examine the proportion of patients who achieve on-treatment clinical remission with biologic therapy
  - Examine the characteristics of patients achieving versus not achieving clinical remission or control

Study Design

- CHRONICLE (ClinicalTrials.gov identifier: NCT03373045) is an ongoing noninterventional study of US adults with severe asthma treated by allergists/immunologists or pulmonologists at participating sites
- Eligible patients must have subspecialist-diagnosed SA, as defined by European Respiratory Society/American Thoracic Society guidelines[a], for ≥ 12 months prior to enrollment
- Sites report asthma exacerbations and asthma medications, with start dates and including biologic use, for the 12 months prior to enrollment and every 6 months after enrollment
- Monthly ACT scores and 6-monthly subspecialist assessments of asthma control are also collected

[a]SA is defined as asthma that requires treatment with high dose inhaled corticosteroids plus a second controller and/or systemic corticosteroids to prevent it from becoming ‘‘uncontrolled’’ or that remains ‘‘uncontrolled’’ despite this therapy[1]

ACT, Asthma Control Test; SA, severe asthma; US, United States.

Analysis Methods

- The proportion of patients achieving clinical remission with biologic treatment was evaluated among patients enrolled between February 2018 and February 2021
- Among patients receiving biologics[a], on-treatment clinical remission was defined by:
  - The absence of SCS use in the most recent 12 months
  - A majority (> 50%) of ACT scores ≥ 20 in the most recent 6 months
  - Patient- and specialist-reported asthma control in the most recent 6 months[b]
- Lung function was not included in the analysis definition due to infrequent measurement by providers and insufficient sample
- Descriptive univariate analyses were conducted of patient characteristics for patients with and without remission

[a]Includes benralizumab, dupilumab, mepolizumab, omalizumab, and reslizumab.

[b]Patient-reported asthma control was derived from the final ACT question: "How would you rate your asthma control during the past 4 weeks?" Answers of "completely controlled" or "well-controlled" were considered patient report of asthma control. Specialist-reported asthma control was based on site report of whether they felt the patient was controlled or uncontrolled.

ACT, Asthma Control Test; SCS, systemic corticosteroid.

Results: Patient Baseline Characteristics

Characteristic		All enrolled (N = 2793)	Biologics recipients (n = 1832)
Age at first asthma diagnosis, mean (SD)		30.0 (21.5)	29.5 (21.2)
Male sex, %		31.2	33.1
BMI (kg/m^2), mean (SD)		33.2 (8.8)	32.8 (8.2)
GINA categorization of asthma control,[a] %	Well controlled	19.4	24.4
	Partly controlled	25.5	25.4
	Uncontrolled	43.7	36.6
	Unknown	11.5	13.6
Receipt of mSCS in previous 12 mo, %		12.1	11.3
Exacerbations per patient in previous 12 mo, mean (SD)		1.2 (1.6)	1.1 (1.6)
Blood eosinophil count (cells/µL), mean (SD)[a]		277.6 (386.2)	397.3 (535.6)
Total IgE level (IU/ml), mean (SD)[a]		434.9 (1094.2)	478.4 (1391.4)
Severity, n (%)	Severe	452 (9.2)	350 (10.3)
	Moderate	2116 (43.3)	1449 (42.7)
	Mild	1344 (27.5)	918 (27.1)
	Unknown/Missing	979 (20.0)	673 (19.8)

- Complete baseline characteristics have been previously reported[4,5]

Percentages may not total 100% as a result of rounding.

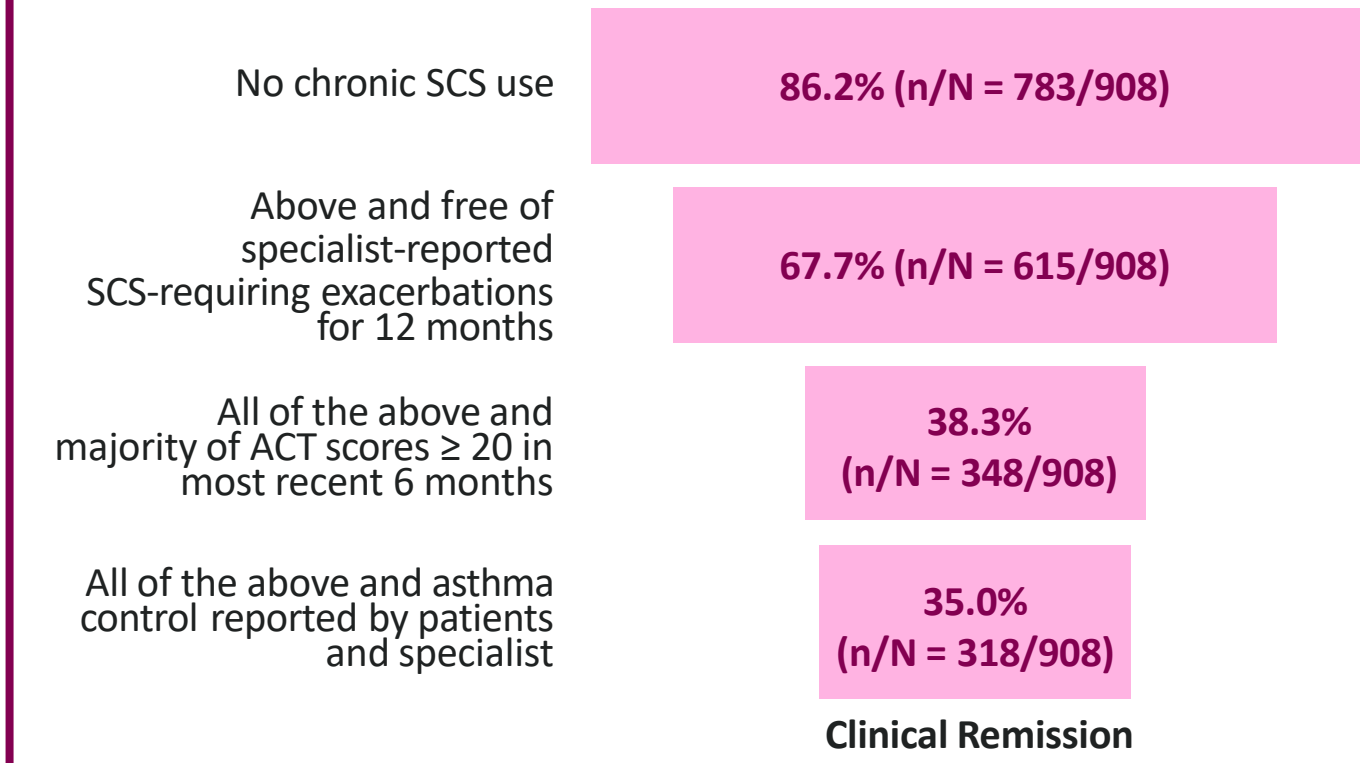
[a]Measured while patients were not receiving biologics or mSCS.

BMI, body mass index; GINA, Global Initiative for Asthma; IgE, immunoglobulin E; IU, international units; mSCS, maintenance systemic corticosteroid; SD, standard deviation.

Results: Patients Achieving Clinical Remission

- There were 908 patients with biologic use[a] for ≥ 12 months and complete data
  - 67.7% (n = 615) had no SCS use in the most recent 12 months for exacerbations or chronic treatment
  - 318 (35.0%) had at least 50% of monthly ACT scores ≥ 20 and had patient- and specialist-reported asthma control in the most recent 6 months in addition to no SCS use

Proportion of patients who met cumulative criteria for clinical remission



[a]Breakdown of biologic use was as follows: benralizumab (22.5%), mepolizumab (19.4%), omalizumab (46.5%), reslizumab (2.2%), and dupilumab (15.4%).

ACT, Asthma Control Test; HCP, healthcare provider; SCS, systemic corticosteroid.

Results: Patient Characteristics Associated with Remission

Characteristic		Clinical remission	
		Yes (n = 318)	No (n = 590)
Age at first asthma diagnosis, mean (SD)		30.9 (21.2)	28.8 (20.8)
Male sex, n (%)		116 (36.5)	166 (28.1)
BMI (kg/m^2), mean (SD)		31.2 (7.6)	33.4 (8.4)
Race, %	White	85.5	81.2
	Black	10.7	14.1
	Other[a]	2.5	3.0
	Not reported/missing	1.3	1.7
Ethnicity, %	Hispanic or Latino	4.1	5.4
	Not Hispanic or Latino	95.9	94.6
Smoking history, %	Never	69.5	68.8
	Former	28.0	26.3
	Current	2.5	4.9
	Missing	0	0

- More patients who achieved clinical remission were male and White than those who did not achieve remission
- On average, patients who achieved clinical remission had a lower BMI than those who did not

Percentages may not total 100% as a result of rounding.

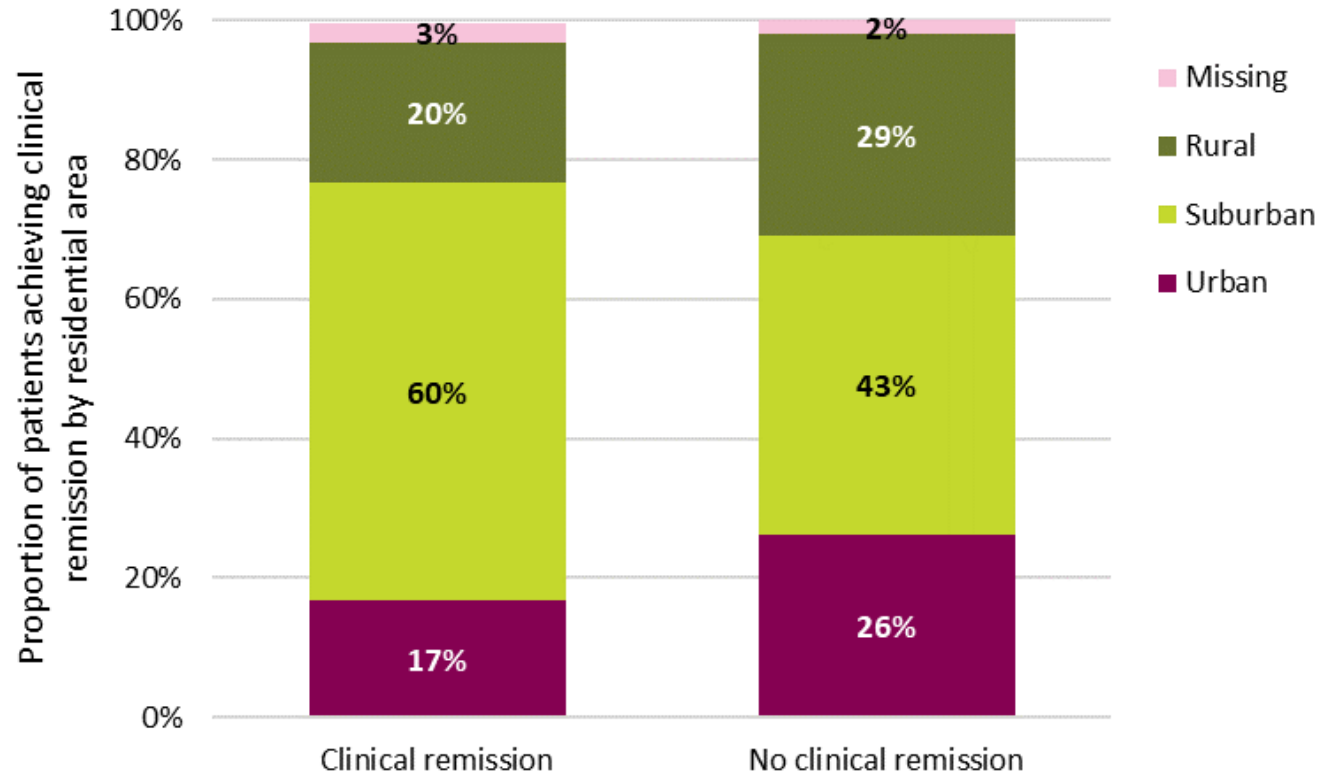
[a]Other includes Asian, American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander.

BMI, body mass index; SD, standard deviation.

Results: Remission by Residential Area

- Suburban residence was more prevalent among clinical remission achievers than nonachievers (60% vs 43%)

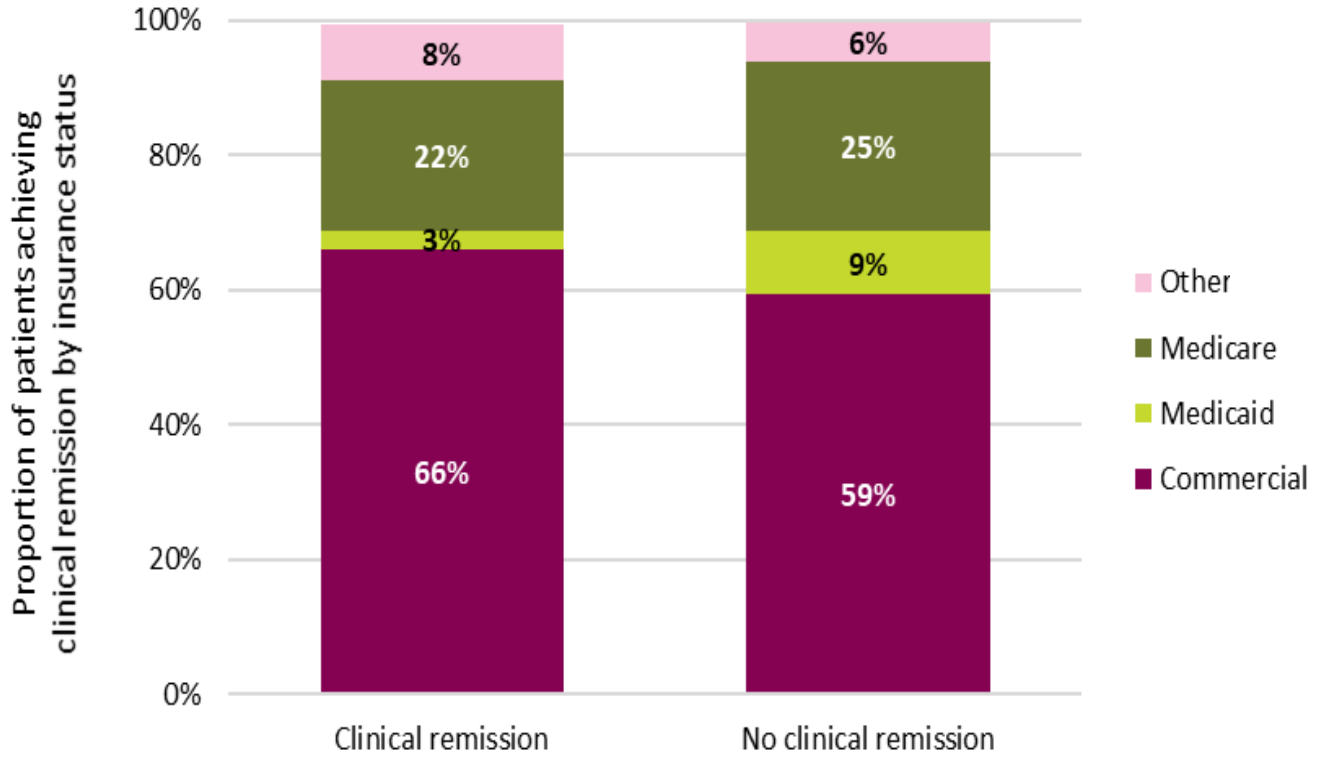
Baseline characteristics of patients who achieved clinical remission and those who did not by residential area



Results: Remission by Insurance Status

- Compared with patients who did not achieve remission, a greater proportion of those who achieved clinical remission had commercial insurance

Baseline characteristics of patients who achieved clinical remission and those who did not by insurance status[a,b]



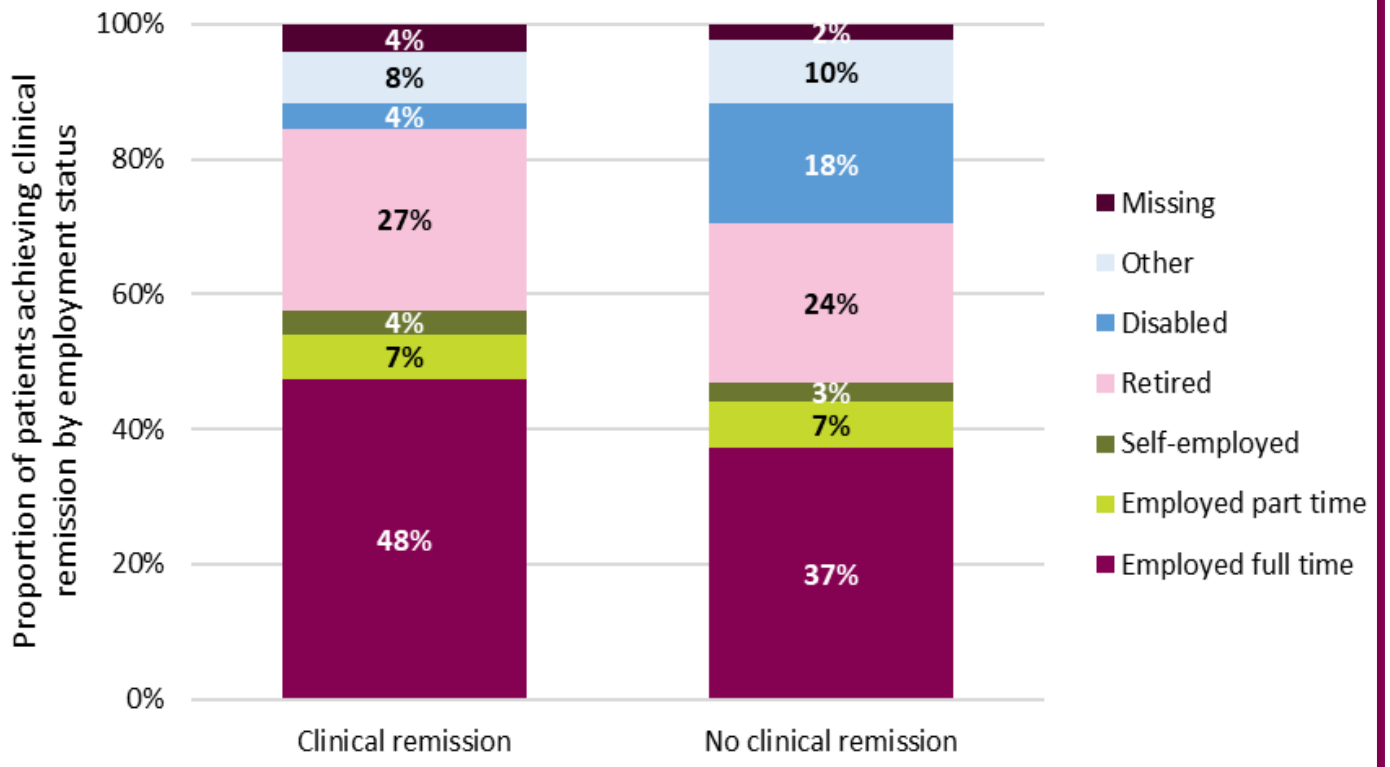
[a]Less than 1% of patients with clinical remission or no clinical remission were uninsured or had missing data.

[b]Other includes other government insurance.

Results: Remission by Employment Status

- Those achieving clinical remission were more likely to be employed full-time compared to those who did not (48% vs. 37%)
- Work disability was more prevalent among patients who did not achieve clinical remission compared to people who did (18% vs 4%)

Baseline characteristics of patients who achieved clinical remission and those who did not by employment status[a]



[a]Other includes homemakers, full-time students, or unemployed.

Discussion: Summary of Current Findings

- In a real-world population, nearly 7 in 10 patients with severe asthma who had ≥ 12 months of biologic use did not have exacerbations or require treatment with SCS
- More than 1 in 3 patients met criteria for on-treatment clinical remission as defined by:
  - The absence of SCS use in the most recent 12 months; and
  - A majority (> 50%) of ACT scores ≥ 20 in the most recent 6 months; and
  - Patient- and specialist-reported asthma control in the most recent 6 months
- Limitations of this analysis are that lung function was not evaluated due to limited data, and associations between individual biologics and remission were not explored due to significant selection bias across individual biologics
- More patients who achieved clinical remission were male, White, had commercial insurance, lived in a suburban area, and were employed full-time than those who did not achieve remission

SCS, systemic corticosteroid.

Discussion: Other Studies of On-Treatment Clinical Remission in SA with Biologic Use

- A post-hoc analysis of three Phase III trials (SIROCCO/CALIMA and ZONDA) found that a greater proportion of benralizumab recipients achieved clinical remission at 12 months compared with placebo recipients (14.5% vs. 7.7% and 22.5% vs. 7.5%, respectively)[6]
  - Over 75% of all patients receiving benralizumab met ≥ 2 composite remission components, out of a possible 4 total components
  - Further, approximately half of all patients met ≥ 3 composite remission components
- Similarly, a post-hoc analysis using data from a Phase III trial (LIBERTY ASTHMA QUEST) found that a greater proportion of dupilumab recipients achieved clinical remission at 12 months compared with placebo recipients (20.1% vs. 4.6%)[7]
- An important caveat is that definitions of clinical remission have varied across studies
- Overall, on-treatment clinical remission is an important disease management goal and may be facilitated by the introduction of biologic treatments

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Disclosures and Acknowledgements

- Disclosures
  - Bradley E. Chipps: Advisory boards, consultant, and speaker – AstraZeneca, Boehringer Ingelheim, Genentech, GSK, Novartis, Regeneron, Sanofi
  - Njira Lugogo: Consulting fees for advisory board participation from Amgen, AstraZeneca, Genentech, GSK, Novartis, Regeneron, Sanofi, and Teva; honoraria for non-speakers' bureau presentations from GSK and AstraZeneca; and travel support from AstraZeneca; her institution received research support from Amgen, AstraZeneca, Avillion, Gossamer Bio, Genentech, GSK, Regeneron, Sanofi, and Teva
  - Warner Carr: Speaker – AstraZeneca, Teva, Boehringer Ingelheim, Regeneron, and Sanofi; Consultant – AstraZeneca, Teva, Boehringer Ingelheim, Regeneron, Sanofi, Circassia, CSL Behring, Genentech, GSK, Horizon Pharma, Kaleo, Viatris, Pfizer, Takeda, Meda, Baxalta, Novartis, Greer Laboratories, Alcon Laboratories, Bausch Health, Grifols, Optinose, Aerocrine
  - Eduardo Genofre, Frank Trudo, and Christopher S. Ambrose: Employees and shareholders – AstraZeneca
  - The CHRONICLE study protocol received central institutional review board (Advarra, Columbia, MD) approval on November 3, 2017. Patients completed written informed consent. The CHRONICLE study is being performed according to ethical principles consistent with the Declaration of Helsinki, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Clinical Practices, Good Pharmacoepidemiology Practices, the Health Insurance Portability and Accountability Act (HIPAA), and applicable legislation for observational studies
- Acknowledgements

  - Medical writing services were provided by Casey Demko, MS, of Oxford PharmaGenesis Inc. (Newtown, PA, USA), which were in accordance with Good Publication Practice (GPP3) and funded by AstraZeneca (Gaithersburg, MD, USA)
  - Portions of this research post were presented at the American Academy of Allergy, Asthma & Immunology Annual Meeting, February 25–28, 2022, Phoenix, AZ