Clinical outcomes and emergency healthcare utilization in patients with severe asthma who continued, switched or stopped biologic therapy: results from the CLEAR study

Nasloon Ali,[1,2] Stephanie Chen,[3] Trung N Tran,[3] Bill Cook,[3] Alan Altraja,[4] Arnaud Bourdin,[5] Chau-Chyun Sheu,[6,7] Ming-Ju Tsai,[6,7] Flavia C L Hoyte,[8] Anna Quinton,[9] Benjamin Emmanuel,[3] Celine Goh,[1,2] Victoria Carter,[1,2] and David Price[1,2, 10]

[1]Observational and Pragmatic Research Institute, Singapore; [2]Optimum Patient Care Global, Cambridge, UK; [3]Respiratory and Immunology, BioPharmaceuticals Medical, AstraZeneca, Gaithersburg, MD, USA; [4]Department of Pulmonary Medicine, University of Tartu and Lung Clinic, Tartu University Hospital, Tartu, Estonia; [5]PhyMedExp, University of Montpellier, CNRS, INSERM, CHU Montpellier, Montpellier, France; [6]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; [7]School of Medicine, College of Medicine, Department of Internal Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan; [8]Division of Allergy and Immunology, National Jewish Health, Denver, CO, USA; [9]BioPharmaceuticals R&D, AstraZeneca, Cambridge, UK; [10]Centre of Academic Primary Care, Division of Applied Health Sciences, University of Aberdeen, Aberdeen, UK

Title character count: 167/175 (including spaces and punctuation)

Character count: 2889/2900 (including spaces and punctuation, excluding title and authors)

No figures/tables permitted

Purpose

Biologics targeting immunoglobulin E, interleukin (IL)-4/IL-13 or IL-5/IL-5 receptor are beneficial to many patients with severe asthma. However, response to biologics varies depending on asthma phenotype, suggesting that inflammation is unaddressed in some patients. Correctly phenotyping patients is critical for selecting an appropriate biologic and for therapy success. Biomarker-based phenotyping can be challenging, which can contribute to therapy switching or stopping. This analysis compared clinical outcomes and emergency healthcare resource utilization (HCRU) in patients with severe asthma who continued, switched or stopped biologic therapy.

Methods

CLEAR was a multicenter, observational study that included adults (≥18 years old) from 23 countries enrolled in the International Severe Asthma Registry (December 2015–August 2021). Eligible patients initiated biologic therapy and had data for ≥12 months before and ≥6 months after therapy initiation. In this analysis, patients were grouped by whether they continued (used first biologic for ≥6 months), switched (discontinued first biologic <6 months after initiation and received a different biologic) or stopped (discontinued first biologic <6 months after initiation and did not receive another biologic) therapy. Propensity score matching was used to ensure comparability and adjusted for residual confounders in multivariable models. Adjusted incident rate ratios (aIRR), adjusted odds ratios (aOR) or adjusted β-coefficients (aβ) from a generalized linear model with 95% CIs were estimated to compare clinical outcomes between subgroups.

Results

Of 1859 included patients, 1116 (60.0%), 474 (25.5%) and 269 (14.5%) continued, switched and stopped biologic therapy, respectively. During the 6 months after therapy initiation, matched patients who switched or stopped therapy had a greater risk of exacerbation versus those who continued (aIRR [95% CI]: switched, 1.80 [1.48, 2.19]; stopped, 1.50 [1.16, 1.95])

and were more likely to have uncontrolled asthma (aOR [95% CI]: switched, 3.64 [2.49, 5.30]; stopped, 2.61 [1.68, 4.08]). Compared with matched patients who continued therapy, those who switched were less likely to have a reduction in long-term oral corticosteroid dose (aβ [95% CI]: −2.61 [−4.38, −0.84]) and had more HCRU (aIRR [95% CI]: hospitalization, 1.85 [1.19, 2.87]; emergency room visits, 1.85 [1.24, 2.77]).

Conclusions

Overall, 40% of patients switched or stopped biologic therapy. These patients experienced worse clinical outcomes and more HCRU than those who continued biologic therapy.

Clinical implications

Patients who continued biologic therapy had better clinical outcomes than those who switched or stopped, suggesting the importance of selecting the right initial biologic for continual therapy. Biologics targeting multiple inflammatory pathways may address the limitations of phenotyping, which may reduce therapy stopping or switching.

Funding

This study was funded by AstraZeneca. The International Severe Asthma Registry is jointly funded by Optimum Patient Care Global and AstraZeneca.

Acknowledgments

Medical writing support was provided by Madeleine Wynn, MRes, of PharmaGenesis London, London, UK, with funding from AstraZeneca.

Disclosures

Nasloon Ali, Celine Goh and **Victoria Carter** are employees of Optimum Patient Care Global, a co-funder of the International Severe Asthma Registry. **Stephanie Chen, Trung N Tran, Bill Cook, Anna Quinton** and **Benjamin Emmanuel** are employees of AstraZeneca

and may own stock or stock options in AstraZeneca. **Alan Altraja** has received lecture fees from AstraZeneca, Berlin-Chemie Menarini, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, MSD, Norameda, Novartis, Orion, Sanofi, Teva Pharmaceuticals and Zentiva; has received sponsorships from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, MSD, Norameda, Novartis and Teva Pharmaceuticals; and has been a member of advisory boards for AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Sanofi and Teva Pharmaceuticals. **Arnaud Bourdin** has received grants from AstraZeneca, Boehringer Ingelheim, Cephalon-Teva, GlaxoSmithKline, Novartis and Sanofi-Regeneron; has provided consultancy for Actelion, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, MedinCell, Merck, Novartis, Roche and Sanofi-Regeneron; and has acted as an investigator or co-investigator for trials sponsored by Actelion, AstraZeneca, Boehringer Ingelheim, Chiesi, Galapagos, GlaxoSmithKline, Merck, Novartis, Roche, Sanofi-Regeneron and Vertex Pharmaceuticals. **Chau-Chyun Sheu** has received speaker fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis and Pfizer, and has acted as an investigator for trials sponsored by Aridis Pharmaceuticals, AstraZeneca, Bristol Myers Squibb, Galapagos, Horizon Therapeutics, Insmed, Novartis, Roche, Sanofi-Regeneron and Shionogi. **Ming-Ju Tsai** has received grants from Boehringer Ingelheim and has received honoraria for lectures from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis and Orient EuroPharma. **Flavia C L Hoyte** has received honoraria from AstraZeneca for serving on advisory boards; has received speaker fees from GlaxoSmithKline; has participated in research with Genentech, Sanofi and Teva Pharmaceuticals, for which her institution has been renumerated; and her family owns stock in Amgen, Johnson & Johnson, Merck and Pfizer. **David Price** has advisory board membership with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia Pharmaceuticals, Mundipharma, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals, Thermo Fisher Scientific and Viatris; has consultancy agreements with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Mundipharma, Novartis, Pfizer, Teva Pharmaceuticals, Theravance Biopharma and Viatris; has received grants and unrestricted funding for

investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia Pharmaceuticals, Mundipharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals, Theravance Biopharma, UK National Health Service and Viatris; has received payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Mundipharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Sanofi Genzyme, Teva Pharmaceuticals and Viatris; has received payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Circassia Pharmaceuticals, Mundipharma, Novartis, Teva Pharmaceuticals and Thermo Fisher Scientific; has received funding for patient enrollment or completion of research from Novartis; has stock or stock options with AKL Research and Development Ltd, which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Global Ltd (Australia and UK) and 74% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); owns a 5% shareholding in Timestamp, which develops adherence monitoring technology; is a peer reviewer for *Health Technology Assessment* and grant committees of the UK Efficacy and Mechanism Evaluation Programme; and was an expert witness for GlaxoSmithKline.