Demographic and Clinical Characteristics of Patients with Severe Asthma who Continued, Stopped or Switched Biologic Therapy

Andrew Menzies-Gow[1], Eileen Wang[2], Bindhu Unni[3], Marianna Alacqua[4], Mona Al-Ahmad[5], John Busby[6], Lakmini Bulathsinhala[3], Victoria Carter[3], Isha Chaudry[3], Tuck Seng Cheng[3], Borja G. Cosio[7], Neva Eleangovan[3], J. Mark FitzGerald[8], Liam G. Heaney[6], Mark Hew[9], Naeimeh Hosseini[3], David Jackson[10], Maria Kallieri[11], Désirée Larenas-Linnemann[12], Stelios Loukides[11], Njira Lugogo[13], Ruth Murray[3], Andriana Papaioannou[11], Luis Perez-de-Llano[14], Celeste Porsbjerg[15], Linda M. Rasmussen[16], Salman Siddiqui[17], Johannes Schmid[18], Trung N. Tran[4], Charlotte Ulrik[19], John W. Upham[20], David Price[3,21,22]

Affiliations
[1]*UK Severe Asthma Network and National Registry, Royal Brompton & Harefield NHS Foundation Trust, London, UK;* [2]*Division of Allergy & Clinical Immunology, Department of Medicine, National Jewish Health, Denver, CO, USA and Division of Allergy & Clinical Immunology, Department of Internal Medicine, University of Colorado Hospital, Aurora, CO, USA;* [3]*Optimum Patient Care, Cambridge, UK;* [4]*AstraZeneca, Gaithersburg, MD, USA;* [5]*Al-Rashed Allergy Center, Ministry of Health, Microbiology Department, Faculty of Medicine, Kuwait University, Kuwait;* [6]*UK Severe Asthma Network and National Registry, Queen's University Belfast, Belfast, Northern Ireland;* [7]*Son Espases University Hospital-IdISBa-Ciberes, Mallorca, Spain;* [8]*Institute for Heart and Lung Health, Vancouver, Canada;* [9]*Allergy, Asthma & Clinical Immunology Service, Alfred Health, Melbourne, Australia;* [10]*UK Severe Asthma Network and National Registry, Guy's and St Thomas' NHS Trust and Division of Asthma, Allergy & Lung Biology, King's College London, London, UK;* [11]*2nd Respiratory Medicine Department, National and Kapodistrian University of Athens Medical School, Attikon University Hospital, Athens, Greece;* [12]*Directora Centro de Excelencia en Asma y Alergia, Hospital Médica Sur, Ciudad de México, Mexico;* [13]*Department of Medicine, Division of Pulmonary and Critical Care Medicine, University of Michigan, Ann Arbor, MI, USA;* [14]*Department of Respiratory Medicine, Hospital Universitario Lucus Augusti, Lugo, Spain;* [15]*Respiratory Research Unit, Bispebjerg University Hospital, Copenhagen, Denmark;* [16]*Department of Respiratory Medicine, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark;* [17]*University of Leicester, Department of Respiratory Sciences and Infection & NIHR Leicester Biomedical Research Centre (Respiratory Theme), Leicester, UK;*[18]*University Hospital of Aarhus, Aarhus, Denmark;* [19]*Department of Respiratory Medicine, Hvidovre Hospital, Hvidovre, Denmark;* [20]*Diamantina Institute & PA-Southside Clinical Unit, The University of Queensland, Brisbane, Australia;* [21]*Observational and Pragmatic Research Institute, Singapore, Singapore;* [22]*Centre of Academic Primary Care, Division of Applied Health Sciences, University of Aberdeen, Aberdeen, UK*

INTRODUCTION: Biologics, which are monoclonal antibodies targeting molecular intermediates, provide a promising therapy for severe asthmatics. Thus, biologics have quickly become integrated into the treatment regimen of severe asthma. However, there is limited knowledge of the pattern of use of biologic therapy in current clinical practice (i.e. continue, stop, switch) and the characteristics underpinning these patterns. This study thus aimed to explore baseline clinical and demographic characteristics of a real-life severe asthma cohort according to pattern of biologic use.

METHODS: This retrospective cohort study included patient-level data from 11 countries (Bulgaria, Canada, Denmark, Greece, Italy, Japan, Kuwait, South Korea, Spain, UK and USA) in the International Severe Asthma Registry (ISAR) between January 2015 – September 2019. This study includes adult severe asthma patients on biologics: Omalizumab (Anti-Immunoglobulin E); Dupilumab (Anti-interleukin 4 receptor alpha); Mepolizumab, Reslizumab and Benralizumab (Anti-interleukin 5/interleukin-5 receptor). Biologic utilization was categorised as: i) continued (i.e. use of 1 biologic for ≥6 months, with no indication of biologic therapy end); ii) switched (i.e. users receiving >1 biologic, ; iii) stopped (i.e. individuals on 1 biologic who discontinued). The distribution of baseline (closest to biologic initiation) demographic and clinical characteristics was described for each of these three biologic utilisation groups. Global statistical tests (Chi-squared, Fisher's exact, ANOVA, Welch-ANOVA, Kruskal-Wallis), as appropriate, were used to determine significant differences in distributions of these characteristics.

RESULTS: Of the 2,208 ISAR patients on biologic therapy, 1664 (75.4%), 298 (13.5%) and 209 (9.5%), respectively, continued, stopped or switched biologic. Age of asthma onset and smoking status were not significantly different by pattern of biologic use. Compared to continuing patients, stoppers were less likely to have nasal polyps, allergic rhinitis or eczema, while switchers had the highest prevalence of chronic rhinosinusitis (Table 1). Moreover, switchers had the highest health resource utilisation, maintenance OCS use and biomarker counts. The highest proportion of patients with fixed airway obstruction (FEV1/FVC <0.7) were in the stop group.

CONCLUSION: These results suggest that biologic switchers or discontinuers might have significantly different prevalence of comorbidities, higher health resource utilisation, as well as more impaired lung function than biologic continuers. As these results provide an overview of the potential differences in demographic and clinical characteristics among ISAR patients with different biologic utilisation patterns, the next analytical step is to leverage these results to examine the predictors of continuing, switching or stopping biologics.

Table 1: Baseline clinical and demographic characteristics of study participants, stratified by biologic utilisation pattern

Variable, N (%)*	Continued (N= 1664)	Stopped (N=298)	Switched (N=209)	p-value
Age				
Mean (SD)	*54.2 (14.6)*	*53.6 (15.9)*	*51.5 (15.4)*	0.047[@]
Comorbidities				
Nasal Polyps	**1543**	**296**	**193**	<0.001[$]
Yes	376 (24.4)	25 (8.5)	33 (17.1)	
Chronic Rhinosinusitis	**1231**	**263**	**160**	0.001[$]
Yes	520 (42.2)	108 (41.1)	91 (56.9)	
Allergic Rhinitis	**1122**	**262**	**158**	<0.001[$]
Yes	429 (38.2)	30 (11.5)	40 (25.3)	
Eczema	**1380**	**275**	**185**	0.035[$]
Yes	76 (5.5)	5 (1.8)	10 (5.4)	
Exacerbations	**890**	**120**	**109**	<0.001[$]
0	280 (31.5)	14 (11.7)	7 (6.4)	
1 − 3	313 (35.2)	24 (20.0)	35 (32.1)	
≥4	297 (33.4)	82 (68.3)	67 (61.5)	
Health care resource				
Invasive ventilation	**927**	**64**	**75**	0.002[#]
≥2	14 (1.5)	3 (4.7)	1 (1.3)	
Hospitalisation	**929**	**69**	**87**	<0.001[$]
≥2	61 (6.6)	17 (24.6)	22 (25.3)	
Emergency department	**810**	**71**	**86**	<0.001[$]
≥2	131 (16.2)	19 (26.8)	33 (38.4)	
Biomarkers				
IgE	**1104**	**152**	**150**	0.49[$]
≥400	389 (35.2)	44 (29.0)	58 (38.7)	
Blood eosinophil count	**1277**	**254**	**198**	0.01[$]
≥0.3	887 (69.5)	184 (72.4)	160 (80.8)	
Fractionally exhaled NO	**926**	**125**	**125**	0.004[$]
Intermediate − High (≥25)	596 (64.4)	82 (65.6)	99 (79.2)	
Lung Function				
Post BD FEV1/FVC Ratio	**746**	**102**	**89**	0.008[$]
<0.7	239 (32.0)	48 (47.1)	34 (38.2)	
Maintenance OCS	369 (22.2)	68 (22.8)	63 (30.1)	0.036[$]

*Refers to number non-missing for each characteristic, and proportion exhibiting characteristic divided by number non-missing; **p-values are from global [#]Fisher's exact test, [$]Chi-square, [@]ANOVA tests, which compare the proportions/mean of all 3 groups against each other**