



Real world biologic use and switch patterns in severe asthma: data from the International Severe Asthma Registry and the US CHRONICLE Study

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Background

- With the advent of personalized medicine, biologic therapy is becoming widely used for severe asthma.
- The anti-IgE therapy omalizumab was the first biologic therapy for severe asthma. Other biologics include anti-IL5/5R (mepolizumab, reslizumab and benralizumab) and anti-IL4/13 (dupilumab) therapies.
- Despite growing evidence on the efficacy of biologics in asthma management, detailed knowledge of how biologics are actually used in real life is lacking.
- Large databases such as ISAR (international) and the CHRONICLE study (USA) enable us to study the use of biologics in severe asthma treatment.

Objectives

1. Describe biologic treatment frequency, patterns of use and reasons for biologic treatment discontinuation and switching in a real-life severe asthma cohort.
2. Identify individual patient-level factors associated with biologic stopping or switching *versus* continuation.

CHRONICLE Study (USA)



Historical cohort study

Inclusion criteria

- ≥ 18 years old at biologic initiation
- Severe asthma (GINA Step 5 or uncontrolled asthma at GINA Step 4)
- Treated with a biologic
- ≥ 6 months of follow-up after biologic initiation

All subjects were treated in countries that had access to ≥ 2 biologics. Therefore continuation, stopping, or switching of biologics was feasible.

Analyses

Demographic and clinical characteristics pre-biologic initiation

Patterns of biologic use

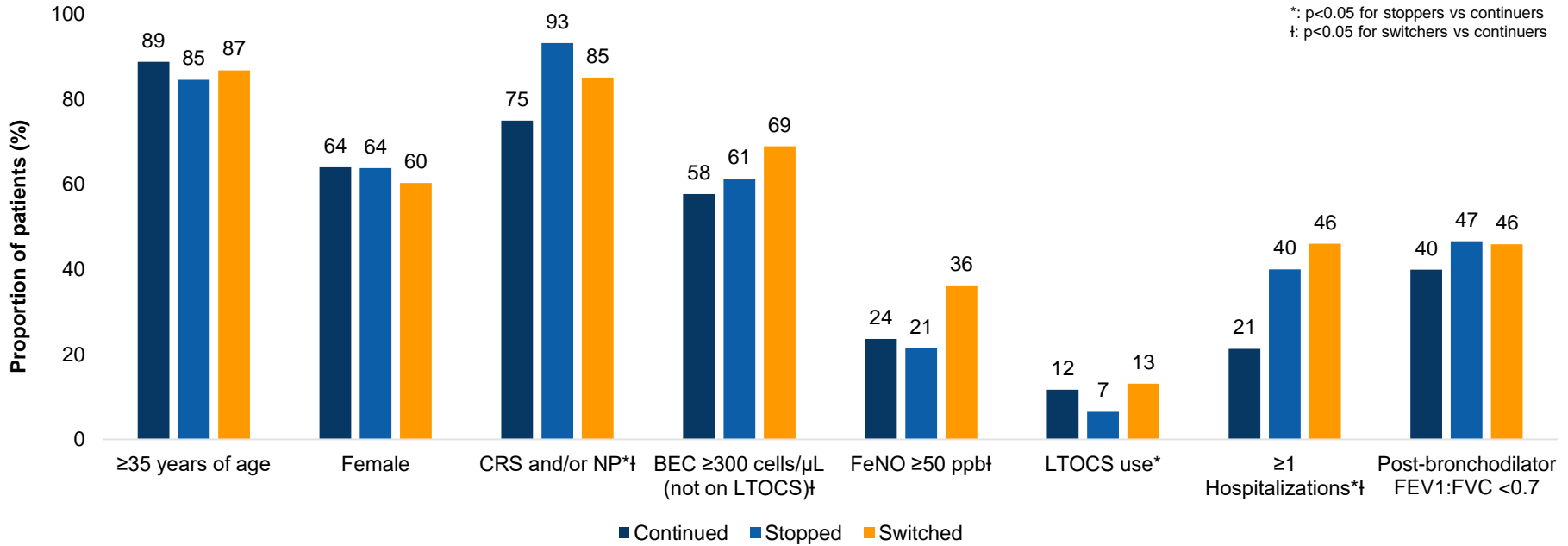
- Patterns of biologic stopping, switching and continuations
- Time to cessation of first biologic
- Switch patterns by biologic class
- Reasons for stopping or switching biologics

Sensitivity analyses

- Prospective patients (n=2656)
- Non-US (n=1404)

Demographic and clinical characteristics of severe asthma patients before initiation of the first biologic

Pre-biologic initiation, **stoppers and switchers** were more likely to have poorer lung function and greater healthcare resource utilization than **continuers**

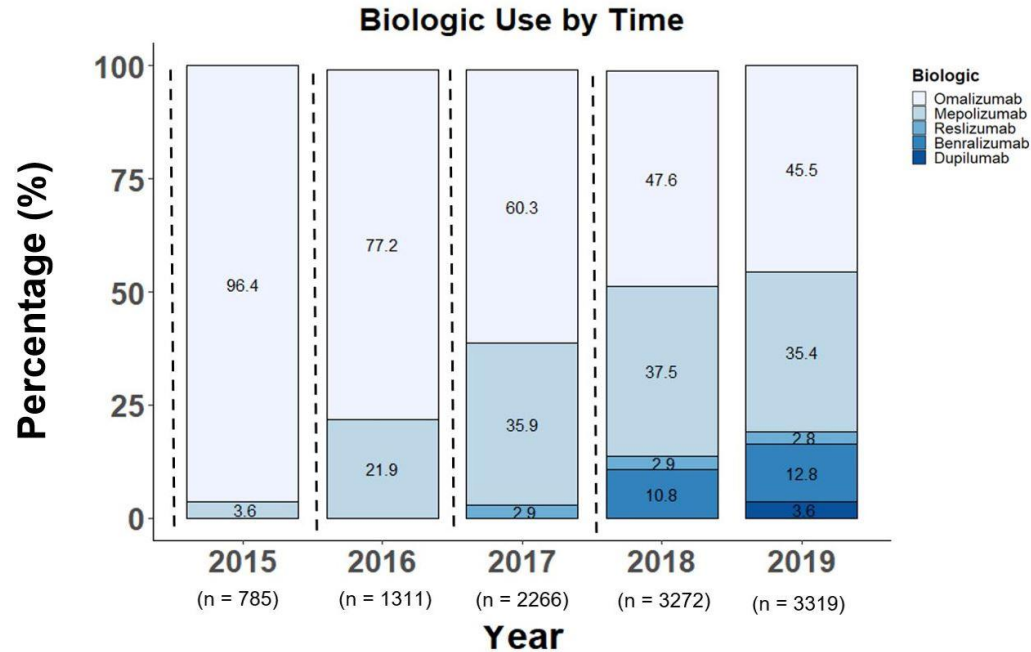


*: p<0.05 for stoppers vs continuers
†: p<0.05 for switchers vs continuers

CRS and/or NP refers to CRS with NP, eosinophilic CRS or CRS without nasal polyps.
BEC = Blood eosinophil count; CRS = Chronic rhinosinusitis; FeNO = Fractional exhaled nitric oxide; FEV1 = Forced expiratory volume in 1 second; FVC = Forced vital capacity; LTOCS = Long-term oral corticosteroids; NP = Nasal polyps
Menzies-Gow AN, Price D et al. *J Asthma Allergy* 2022;15:63-78.

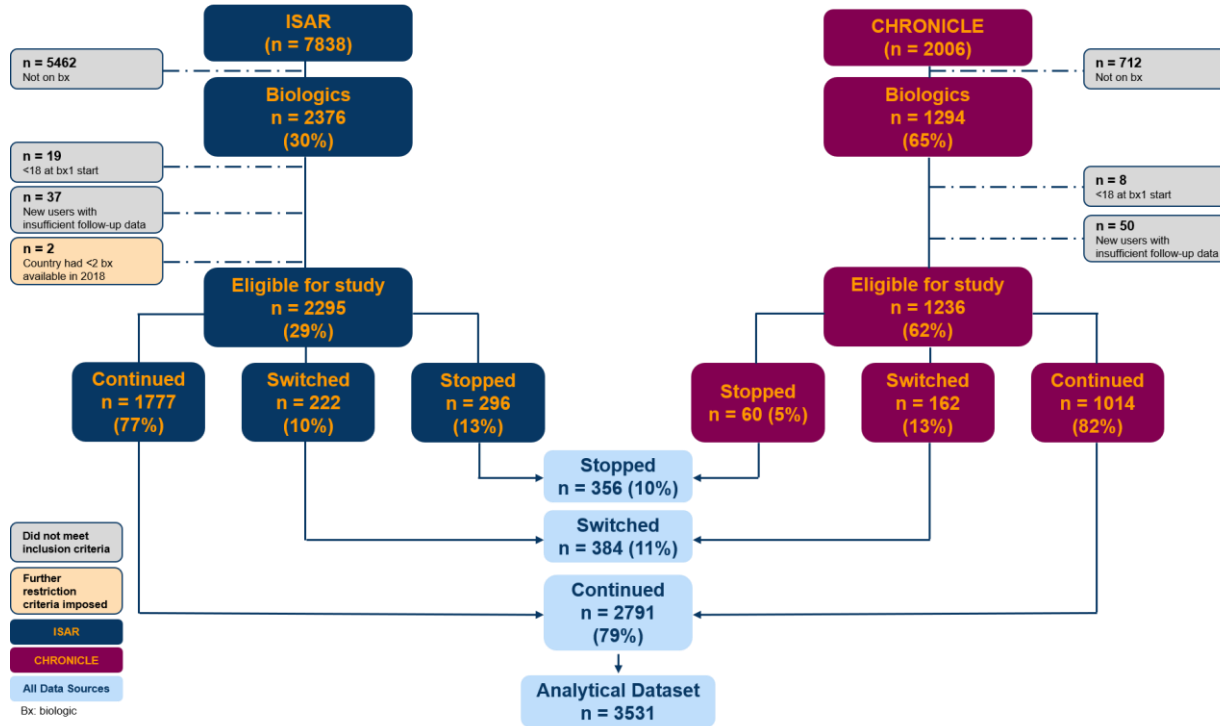
Patterns of biologic use over time by biologic class

Over time, the proportional use of **Anti-IgE therapy** ↓ while that of **Anti-IL5/5R therapies** ↑.

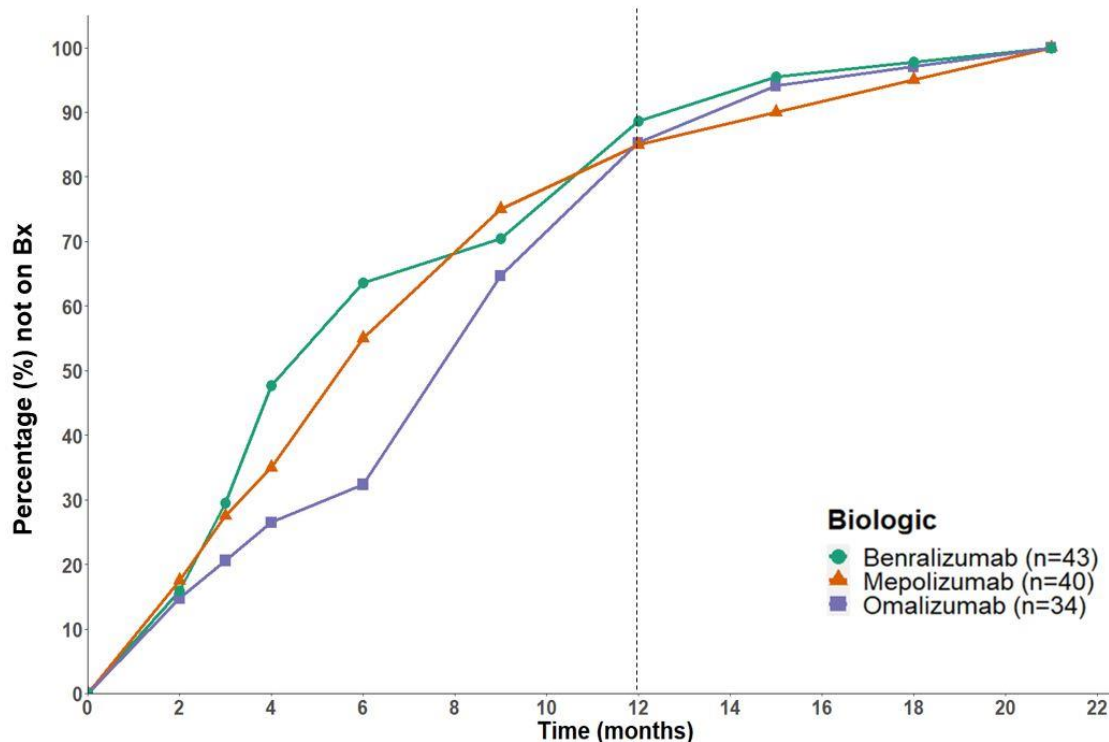


Patterns of biologic use in patients with severe asthma

79% of patients **continued** their first biologic for at least 6 months while **10.2% stopped** and **10.8% switched** during follow ups.

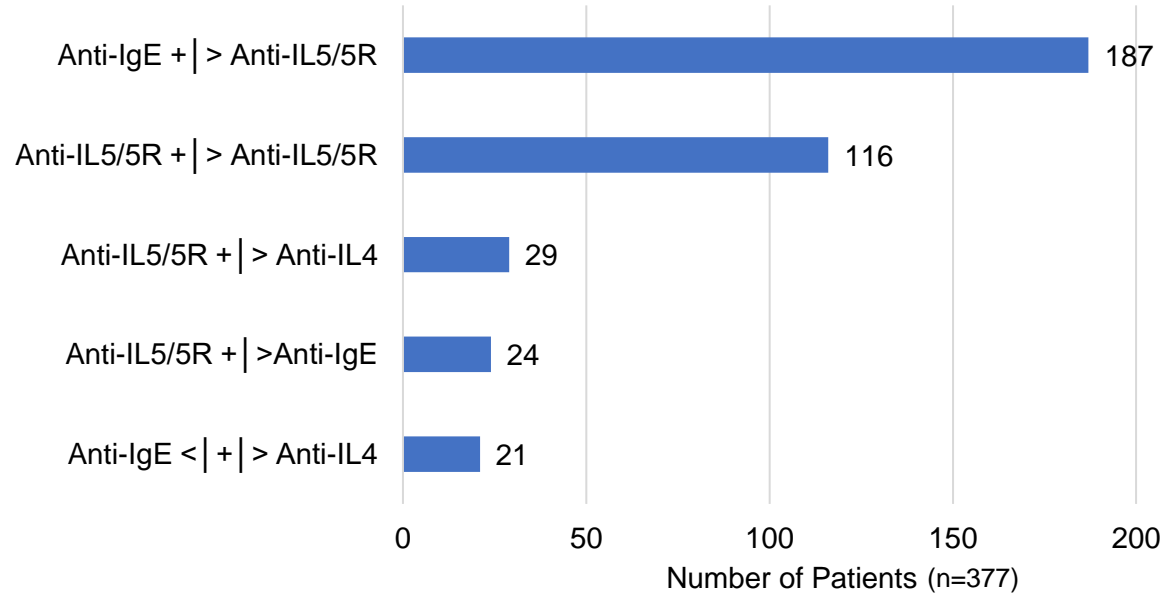


Most patients stopped their first biologic within 12 months. The time patients received their initial biologic varied for those who switched.



Patterns of biologic switches for patients with severe asthma

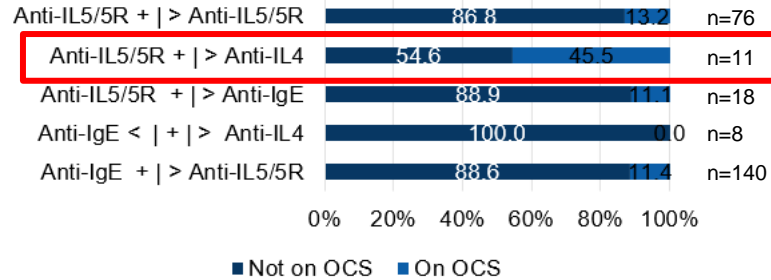
Of patients who stopped or switched their first biologic, the most common **first switch** was from **omalizumab** to (or, rarely, combined with) an **anti-IL-5/5R**.



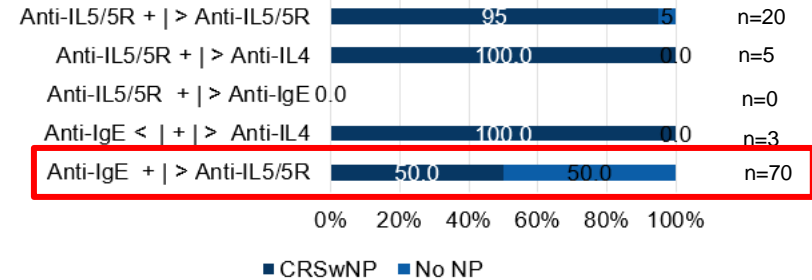
Patterns are mutually exclusive; | : or, < , > : sequence of switch; +: add-on use

Patterns of biologic switches by age, LTOCS use, age of asthma onset and presence of nasal polyps

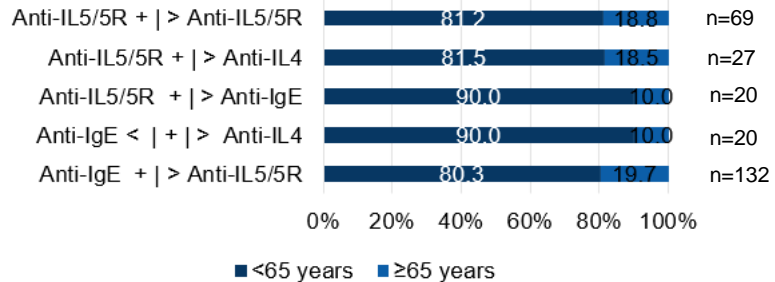
Long-term OCS use



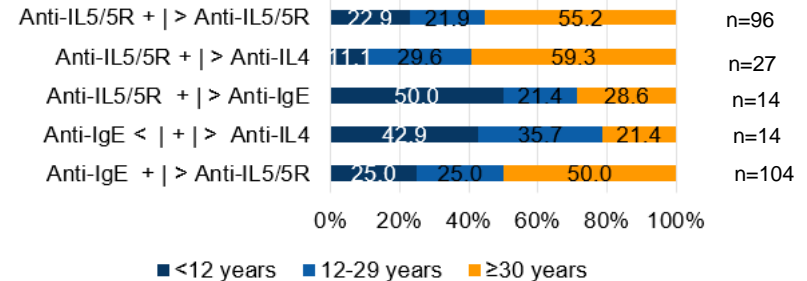
Presence of nasal polyps



Age



Age of asthma onset

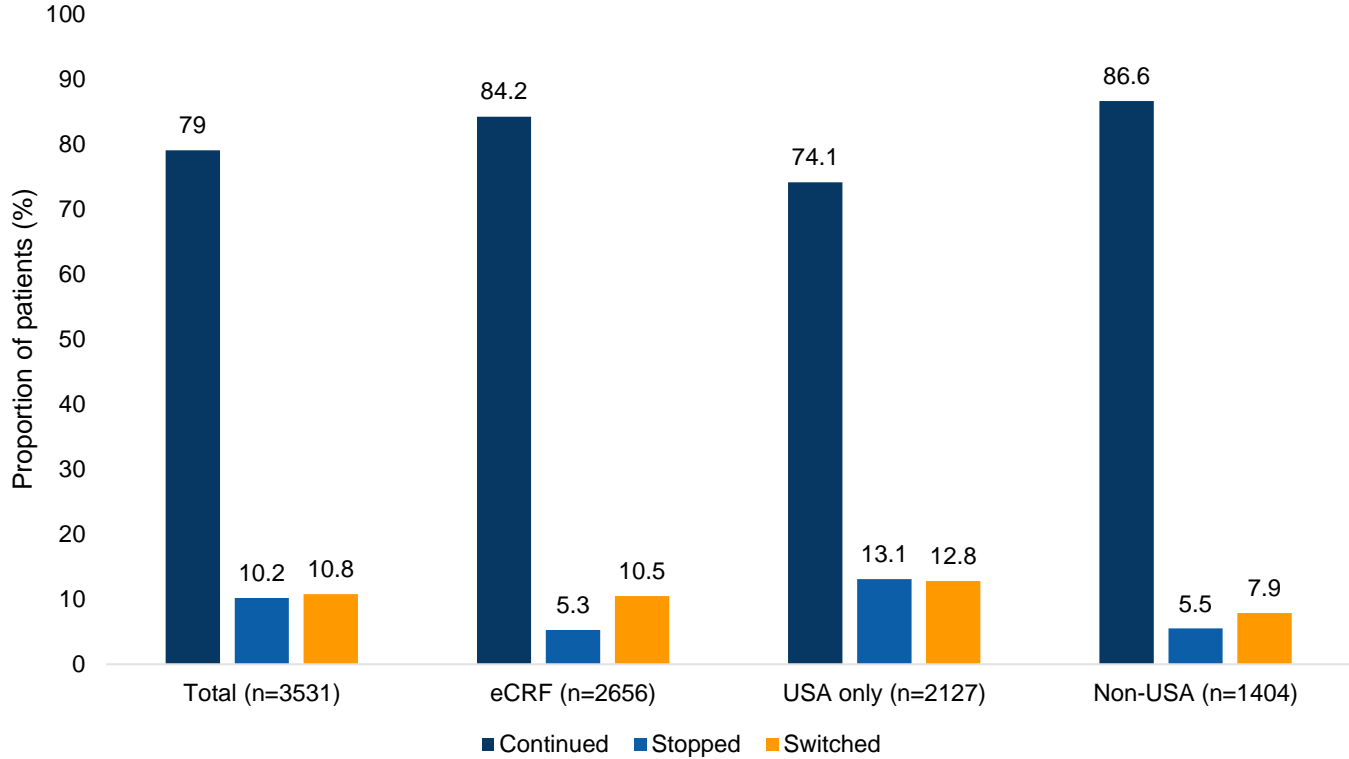


Reasons a patient stopped or switched their first-prescribed biologic

The most commonly cited reasons for stopping or switching a biologic were **insufficient clinical efficacy** and **adverse outcomes**.

Reason	Stopped (n=139)	Switched (n=280)
Reason available n (%)	113	183
Insufficient Clinical Efficacy	72 (63.7%)	158 (86.3%)
Potential Adverse Outcomes	18 (15.9%)	14 (7.7%)
Biologic Access Restriction	8 (7.1%)	5 (2.7%)
Patient Preference	4 (3.5%)	3 (1.6%)
Other	12 (10.6%)	11 (6.0%)

Sensitivity analyses of prospective and non-US patients: Patterns of biologic use



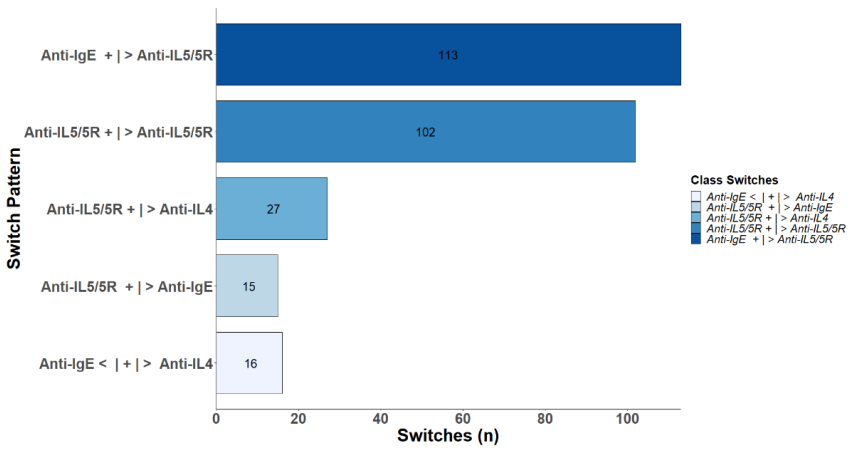
eCRF = Electronic case report form; US = United States
Menzies-Gow AN, Price D et al. *J Asthma Allergy* 2022;15:63-78.

Sensitivity analyses of prospective and non-US patients: Patterns of first biologic switch

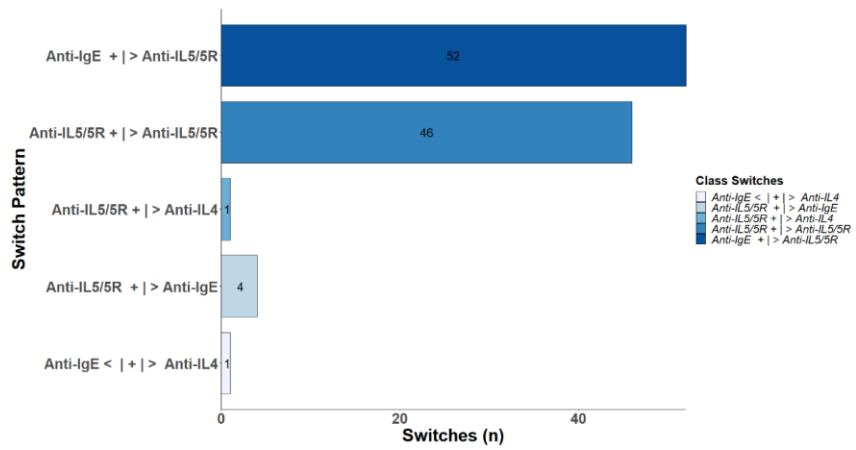


Like in the overall population, the most common first switch in prospective and non-US patients was from **omalizumab to an anti-IL5/5R therapy**.

eCRF data only (n=273)



Non-US data only (n=104)



eCRF = Electronic case report form; IgE = Immunoglobulin E; IL4 = Interleukin 4; IL5/5R = Interleukin 5/5 receptor; US = United States
 Menzies-Gow AN, Price D et al. *J Asthma Allergy* 2022;15:63-78.



Conclusions

- **Omalizumab was the most common initial biologic in 2015 (88.2%) and benralizumab in 2019 (29.6%)**
- **79% of patients continued treatment with their first biologic, 10.2% stopped and 10.8% switched**
 - Most patients stopped their first biologic within 12 months
- **The most frequent first switch was from omalizumab to an anti-IL5/5R therapy (49.6%)**
 - The most common subsequent switch was from one anti-IL5/5R to another (44.4%)
- **Most frequent reasons for stopping/switching were insufficient efficacy and adverse effects**
 - Stoppers and switchers were more likely to have poorer lung function and greater healthcare resource utilization than continuers
- **The SUNNIE study's description of real-life patterns of continuing, stopping, or switching biologics enhances our understanding of global biologic use**
 - Prospective studies involving structured switching criteria could ascertain optimal strategies to identify patients who may benefit from switching

Acknowledgements

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- Registration of the ISAR database with the European Union Electronic Register of Post-Authorization studies was also undertaken (ENCEPP/DSPP/23720). ISAR has ethical approval from the Anonymised Data Ethics Protocols and Transparency (ADEPT) committee (ADEPT0218). All data collection sites in the International Severe Asthma Registry (ISAR) have obtained regulatory agreement in compliance with specific data transfer laws, country-specific legislation, and relevant ethical boards and organizations.

