Association between T2-related comorbidities and effectiveness of biologics in adult patients from the International Severe Asthma Registry

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Introduction

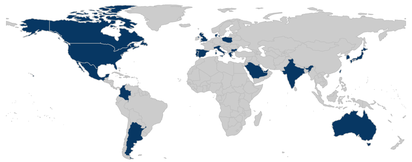
- T2-related comorbidities are common in patients with severe asthma, particularly allergic rhinitis (AR), chronic rhinosinusitis (CRS), nasal polyposis (NP), and eczema/atopic dermatitis (AD).
- These comorbidities are known to be associated with worse asthma-related outcomes but whether they impact the effectiveness of biologics is understudied.

Aim

- To determine the association between T2-related comorbidities and effectiveness of biologics in adult patients with severe asthma.

Materials and methods

- **Data source:** adult patients with severe asthma who initiated biologics from 21 countries contributing to ISAR



- **4 comorbidity variables:**
  - AR, CRS (with or without NP), NP, and AD
  - Presence assessed by physicians during routine clinical care
- **4 asthma-related outcome variables:**
  - **Asthma exacerbations** (events/year), **percent predicted FEV$_1$** (ppFEV$_1$)*, **asthma control** (GINA categories), and **long-term oral corticosteroid (LTOCS) daily dose**
  - Pre-biologic assessment: closest to biologic initiation
  - Post-biologic assessment: as close as available to 1-year post-biologic initiation (minimum 24 weeks of follow-up required)

*Post-bronchodilator if available, pre-bronchodilator otherwise

- **Study population**
  - **Patients prospectively enrolled in ISAR (since 1 May 2017)** with required available data as of 24 January 2022
  - **1765 eligible patients** who initiated:
    - Anti-immunoglobulin E (IgE): n=421
    - Anti–interleukin-5 (IL-5)/5 receptor (5R): n=1257
    - Anti–interleukin (IL)-4/13: n=87
- **Statistical analysis**
  - Comparison of pre- to post-biologic differences for each outcome between patients with and without (reference group) the comorbidity of interest
  - Multivariable models adjusting for age, sex, and pre-biologic values:
    - Negative binomial regressions (exacerbation rates)
    - Multiple linear regressions (lung function and LTOCS)
    - Logistic regressions (asthma control)
  - All types of biologics together, and in patients initiating anti-IgE and anti–IL-5/5R separately. Separate analysis in patients initiating anti–IL-4/13 not conducted due to low numbers
  - Two-sided comparisons

Table. Study population baseline characteristics

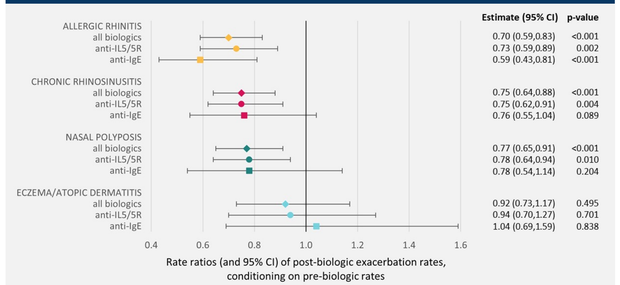
Characteristics	Total N=1765	Anti–IL-5/5R N=1257	Anti-IgE N=421
Gender: Women, n (%)	1070 (60.6)	754 (60.0)	257 (61.0)
Age: Median (Q1, Q3)	55 (45, 63)	56 (48, 64)	51 (39, 60)
Exacerbations 3+/year, n (%)	n=1651 686 (41.6)	n=1183 553 (46.7)	n=384 121 (31.5)
ppFEV$_1$ <80%, n (%)	n=1488 916 (61.6)	n=1076 668 (62.1)	n=335 202 (60.3)
Asthma control Uncontrolled, n (%)	n=1338 875 (65.4)	n=980 664 (67.8)	n=298 178 (59.7)
LTOCS use Yes, n (%)	n=1765 860 (48.7)	n=1257 687 (54.7)	n=421 149 (35.4)
AR Ever, n (%)	n=1727 1,287 (74.5)	n=1228 900 (73.3)	n=412 310 (75.2)
CRS Ever, n (%)	n=1716 968 (56.4)	n=1220 739 (60.6)	n=410 179 (43.7)
NP Ever, n (%)	n=1756 636 (36.2)	n=1251 504 (40.3)	n=419 97 (23.2)
AD Ever, n (%)	n=1753 243 (13.9)	n=1249 144 (11.5)	n=417 71 (17.0)

Abbreviations: AD, eczema/atopic dermatitis; AR, allergic rhinitis; CRS, chronic rhinosinusitis; LTOCS, long-term oral corticosteroids; NP, nasal polyposis; ppFEV$_1$, percent predicted forced expiratory volume in 1 second

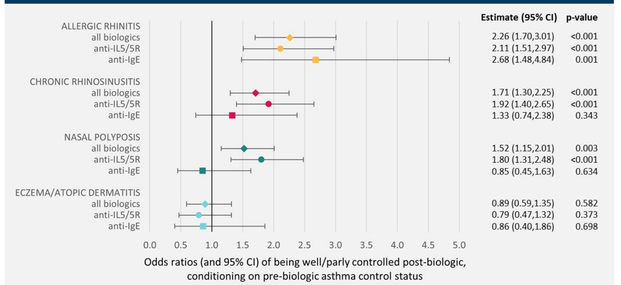
Results

- At 1-year post-biologic initiation, patients had improved from baseline in all outcomes, irrespective of comorbidity status
- However, patients with T2-related comorbidities had greater improvements in exacerbations, ppFEV$_1$, and asthma control
- The association varied by comorbidity, outcome assessed, and biologic class

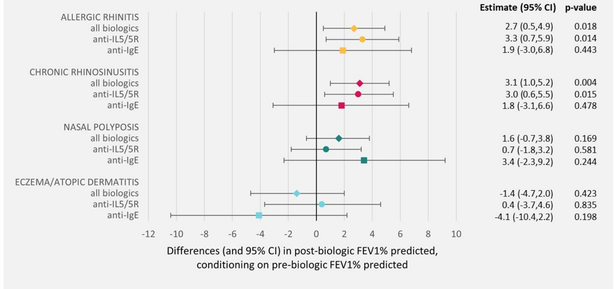
Exacerbations



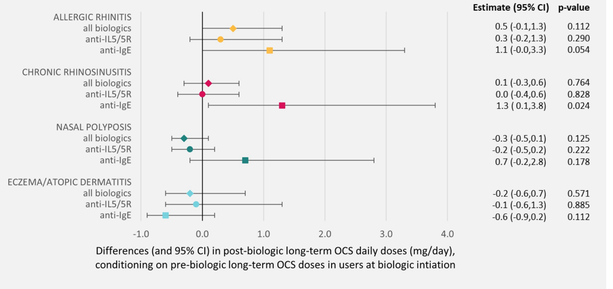
Asthma control



Lung function (ppFEV$_1$)



Long-term OCS daily dose



Abbreviations: CI, confidence interval; FEV1, forced expiratory volume in 1 second; IgE, immunoglobulin E; IL5/5R, interleukin-5/5 receptor; OCS, oral corticosteroids; ppFEV$_1$, percent predicted forced expiratory volume in 1 second

Conclusions

- **Patients with severe asthma with a T2, upper airway-related comorbidity might benefit from biologic therapy to a greater extent than patients without, likely as these comorbidities are proxies for T2-asthma, the target of anti-T2 biologics**
- **Greater improvements in exacerbations and asthma control were observed in presence of CRS, NP, and AR; greater improvements in lung function were observed in presence of CRS and AR**
- **No association detected with AD**
- **Our results highlight the importance of systemic evaluation for comorbidities and a multidisciplinary approach to their management in patients with severe asthma**

Acknowledgements

Writing, editorial support, and/or formatting assistance in the development of this poster was provided by Andrea Lim, BSc (Hons) and Joash Tan, BSc (Hons), of the Observational and Pragmatic Research Institute, Singapore, which was funded by AstraZeneca.

Disclosures

This study was conducted by the Observational and Pragmatic Research Institute (OPRI) Pte Ltd and was partially funded by Optimum Patient Care Global and AstraZeneca Ltd. No funding was received by the Observational & Pragmatic Research Institute Pte Ltd (OPRI) for its contribution. **Presenter's conflict of interest disclosure**: Michael E. Wechsler's full COI disclosure can be found in "COI disclosures".

Additional COI disclosures

Electronic copy of the poster

Poster presented at American Thoracic Society 119th International Conference: May 19-24, 2023; Washington, DC