Association between T2-related co-morbidities and effectiveness of biologics in severe asthma

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Wechsler, Michael E., et al. "Association between T2-related comorbidities and effectiveness of biologics in severe asthma." American journal of respiratory and critical care medicine 209.3 (2024): 262-272.

Aim and Methods

Rationale

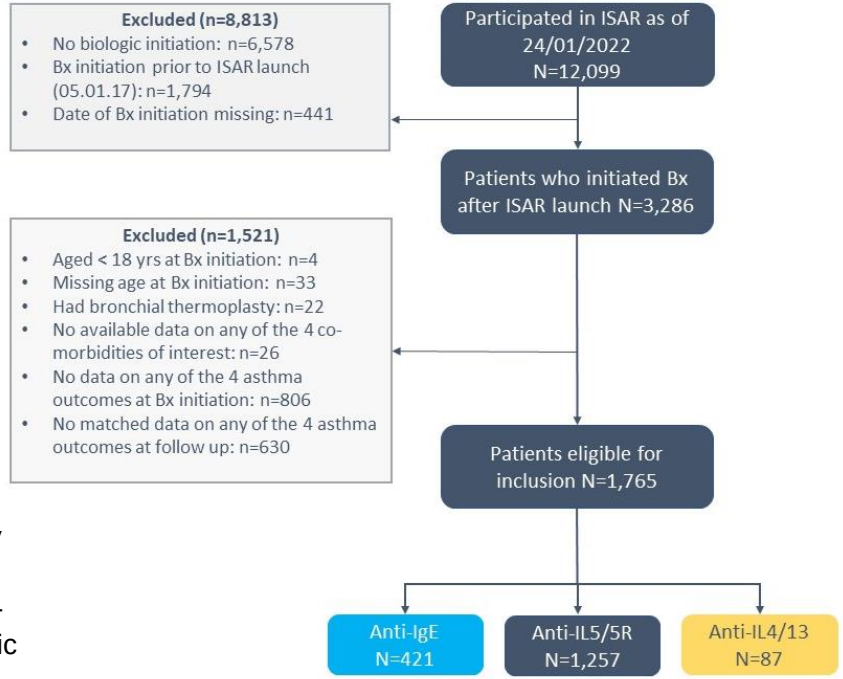
Previous studies investigating comorbidity impact on biologic effectiveness have been relatively small, of short duration, and have not compared biologic classes

Aim

To determine the association between T2-related comorbidities and biologic effectiveness in adults with severe asthma (SA)

Methods

This cohort study used ISAR data (n=21 countries, 2017-2022) to quantify pre- to post-biologic change for four outcomes (annual asthma exacerbation rate, % predicted FEV1 (ppFEV1), asthma control, and long-term oral corticosteroid daily dose [LTOCS]) in patients with/without allergic rhinitis (AR), chronic rhinosinusitis +/- nasal polyps (CRS+/-NP), NP, or eczema/atopic dermatitis (AD).



International Severe Asthma Registry data : ISAR

American Journal of Respiratory and Critical Care Medicine (AJRCCM)
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Irrespective of T2 comorbidities all groups showed improvement but greater in those with CRS+/- NP

Asthma-related outcome	Allergic rhinitis		Chronic rhinosinusitis		Nasal polyposis		Eczema/atopic dermatitis	
	Ever N=761	Never N=493	Ever N=968	Never N=748	Ever N=636	Never N=1120	Ever N=243	Never N=1510
Exacerbation rates: mean (SD)	N=559	N=363	N=719	N=541	N=463	N=818	N=189	N=1092
Pre-biologics	2.24 (2.34)	2.16 (2.23)	2.65 (2.77)	3.37 (3.74)	2.88 (3.02)	3.05 (3.40)	1.97 (2.00)	3.15 (3.39)
Post-biologics	0.65 (1.21)	0.65 (1.04)	0.75 (1.25)	1.13 (1.62)	0.77 (1.21)	1.01 (1.55)	0.72 (1.35)	0.96 (0.46)
Change	**-1.59 (2.54)**	**-1.51 (2.33)**	**-1.89 (2.74)**	**-2.24 (3.51)**	**-2.11 (2.82)**	**-2.04 (3.30)**	**-1.25 (2.30)**	**-2.19 (3.22)**
p-value*	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
$ppFEV_1$: mean (SD)	N=313	N=267	N=493	N=386	N=306	N=573	N=101	N=776
Pre-biologics	76.4 (21.7)	72.2 (23.3)	75.8 (22.5)	71.0 (22.6)	76.4 (22.1)	72.2 (22.9)	73.9 (22.5)	73.6 (22.7)
Post-biologics	80.1 (22.6)	76.6 (23.2)	79.5 (23.3)	73.0 (22.1)	79.7 (23.0)	75.1 (22.8)	75.6 (21.7)	76.8 (23.1)
Change	**+3.7 (17.9)**	**+4.4 (16.0)**	**+3.8 (17.1)**	**+2.0 (17.1)**	**+3.3 (17.1)**	**+2.9 (17.1)**	**+1.7 (13.7)**	**+3.1 (17.5)**
p-value*	<0.001	<0.001	<0.001	0.023	0.001	<0.001	0.210	<0.001
Asthma control: % of uncontrolled/ partly controlled/well controlled	N=430	N=237	N=570	N=450	N=414	N=629	N=118	N=923
Pre-biologics	**65.6**/22.6/11.9	**57.8**/23.2/19.0	**65.8**/21.2/13.0	**69.6**/18.9/11.6	**65.2**/21.3/13.5	**70.3**/18.6/11.1	**71.2**/19.5/9.3	**67.8**/19.7/12.5
Post-biologics	**25.6**/31.9/42.6	**27.0**/29.1/43.9	**30.2**/26.5/43.3	**42.4**/25.3/32.2	**29.5**/24.9/45.7	**39.6**/27.2/33.2	**39.0**/33.1/28.0	**35.2**/25.4/39.4
p-value*	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
LTOCS								
Users, n (%)	283 (37.2)	202 (41.0)	445 (46.0)	383 (51.2)	312 (49.1)	543 (48.5)	243 (33.3)	772 (51.1)
LTOCS: mean daily dose in users pre-biologics (SD)	N=128	N=74	N=243	N=262	N=196	N=332	N=42	N=485
Pre-biologics	13.2 (10.9)	15.5 (15.4)	12.2 (10.0)	13.2 (10.6)	12.0 (9.3)	13.1 (10.7)	10.5 (10.1)	12.8 (10.2)
Post-biologics	11.7 (9.9)	13.9 (14.7)	10.5 (9.5)	11.0 (10.1)	9.8 (8.3)	11.4 (10.4)	8.8 (9.0)	10.9 (9.8)
Change	**-1.4 (7.6)**	**-1.6 (11.7)**	**-1.7 (6.9)**	**-2.2 (7.6)**	**-2.2 (7.2)**	**-1.7 (7.1)**	**-1.7 (8.9)**	**-1.9 (7.0)**
p-value*	0.020	0.204	<0.001	<0.001	<0.001	<0.001	0.116	<0.001

*Comparing pre- to post-biologics, using paired Wilcoxon test for exacerbations and LTOCS dose, paired t-test for $ppFEV_1$, and McNemar test (nominal symmetry test) for asthma control.

Exacerbation rates reduce (reduction shown in red) with biologics for all, regardless of presence of T2 comorbidity

ppFEV1 increases (increase shown in red) for all following biologic initiation, irrespective of comorbidity status

%of patients with uncontrolled asthma decreases significantly (shown in red) across all groups irrespective of comorbidity status, following biologic initiation

Figures in red show the **drop in mean LTOCS dose following biologic initiation, with reduction in dose achieved for all** groups irrespective of presence of T2 comorbidities

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ppFEV1: Forced expiratory volume in one second, expressed in percentage of predicted value in healthy individuals of same age, gender, and height; LTOCS: long-term oral corticosteroids.

Severe asthma patients with CRS / NP benefit from biologics to a greater extent than patients without: exacerbations

Biomarker independent

Adjusting for **BEC had no impact on the estimate** for exacerbations for patients with CRS +/- NP (rate ratio = 0.77, 95% CI: 0.65, 0.91, p=0.002)

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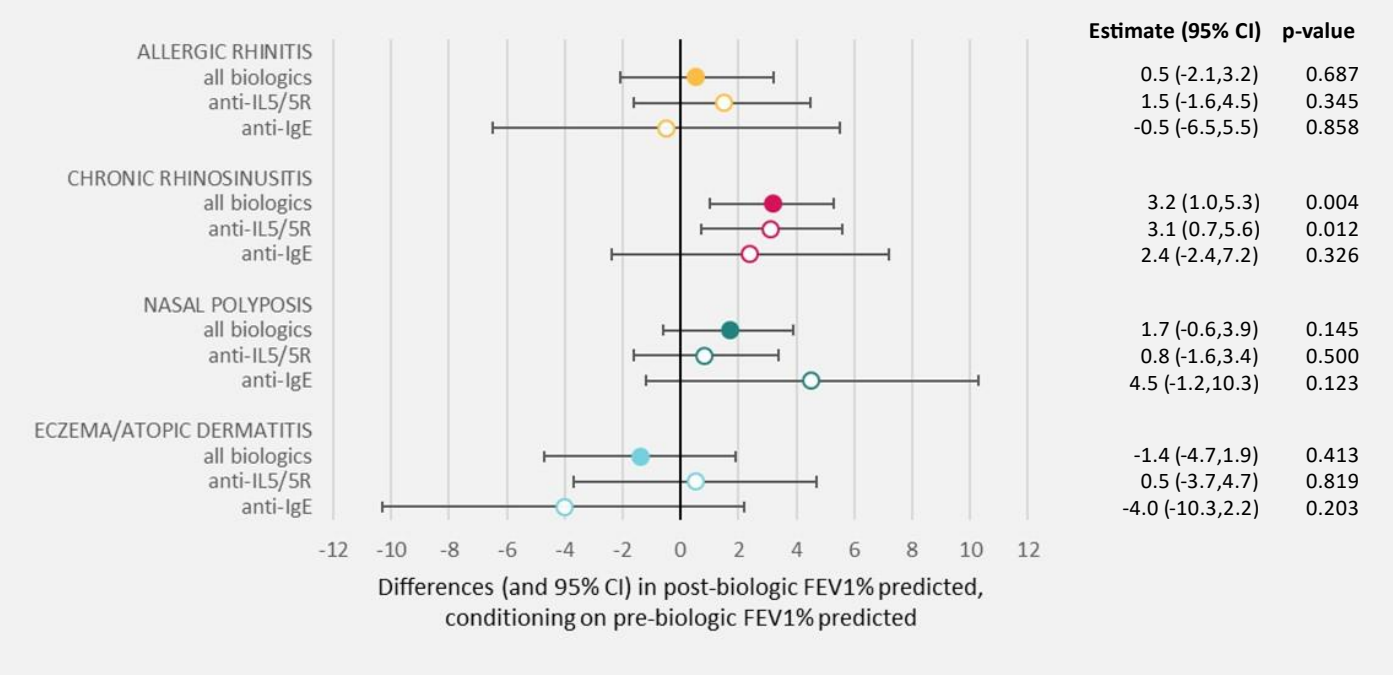
BEC: Blood Eosinophil Count, CRS: Chronic rhinosinusitis; NP: Nasal polyposis; 95% CI: 95% confidence interval.

Severe asthma patients with CRS / NP benefit from biologics to a greater extent than patients without: lung function



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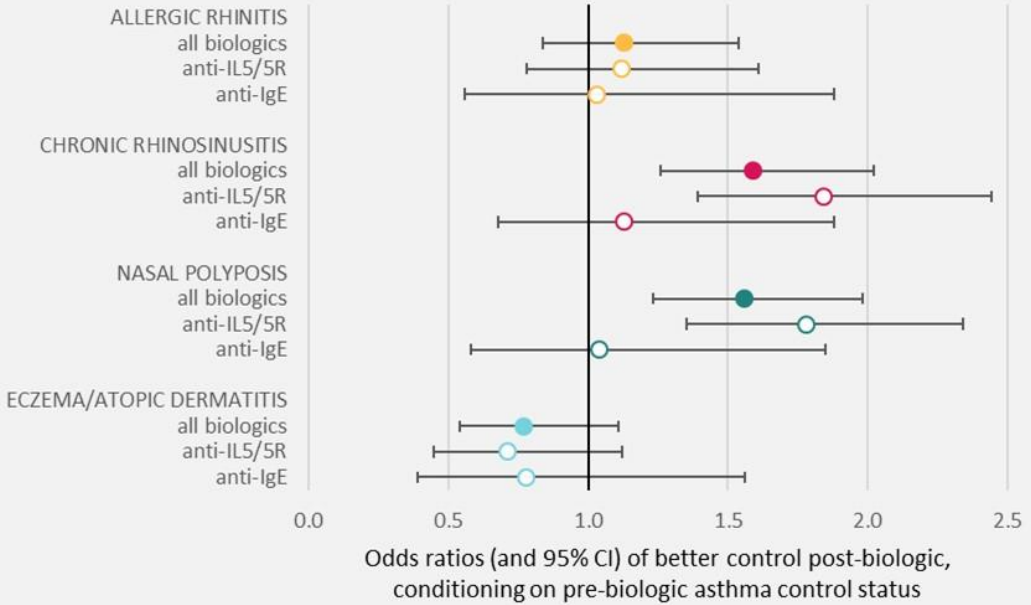
CRS: Chronic rhinosinusitis; FEV1% predicted: : Forced expiratory volume in one second, expressed in percentage of predicted value in healthy individuals of same age, gender, and height; NP: Nasal polyposis; 95% CI: 95% confidence interval.

Severe asthma patients with CRS / NP benefit from biologics to a greater extent than patients without: asthma control



	Estimate (95% CI)	p-value
ALLERGIC RHINITIS		
all biologics	1.13 (0.84,1.54)	0.416
anti-IL5/5R	1.12 (0.78,1.61)	0.542
anti-IgE	1.03 (0.56,1.88)	0.922
CHRONIC RHINOSINUSITIS		
all biologics	1.59 (1.26,2.02)	<0.001
anti-IL5/5R	1.84 (1.39,2.44)	<0.001
anti-IgE	1.13 (0.68,1.88)	0.628
NASAL POLYPOSIS		
all biologics	1.56 (1.23,1.98)	<0.001
anti-IL5/5R	1.78 (1.35,2.34)	<0.001
anti-IgE	1.04 (0.58,1.85)	0.907
ECZEMA/ATOPIC DERMATITIS		
all biologics	0.77 (0.54,1.11)	0.159
anti-IL5/5R	0.71 (0.45,1.12)	0.140
anti-IgE	0.78 (0.39,1.56)	0.482

Biomarker independent

Although attenuated, **association for asthma control trends in patients with NP remain when adjusting for BEC** (odds ratio=1.37, 95% CI: 1.06-1.77), p=0.015)

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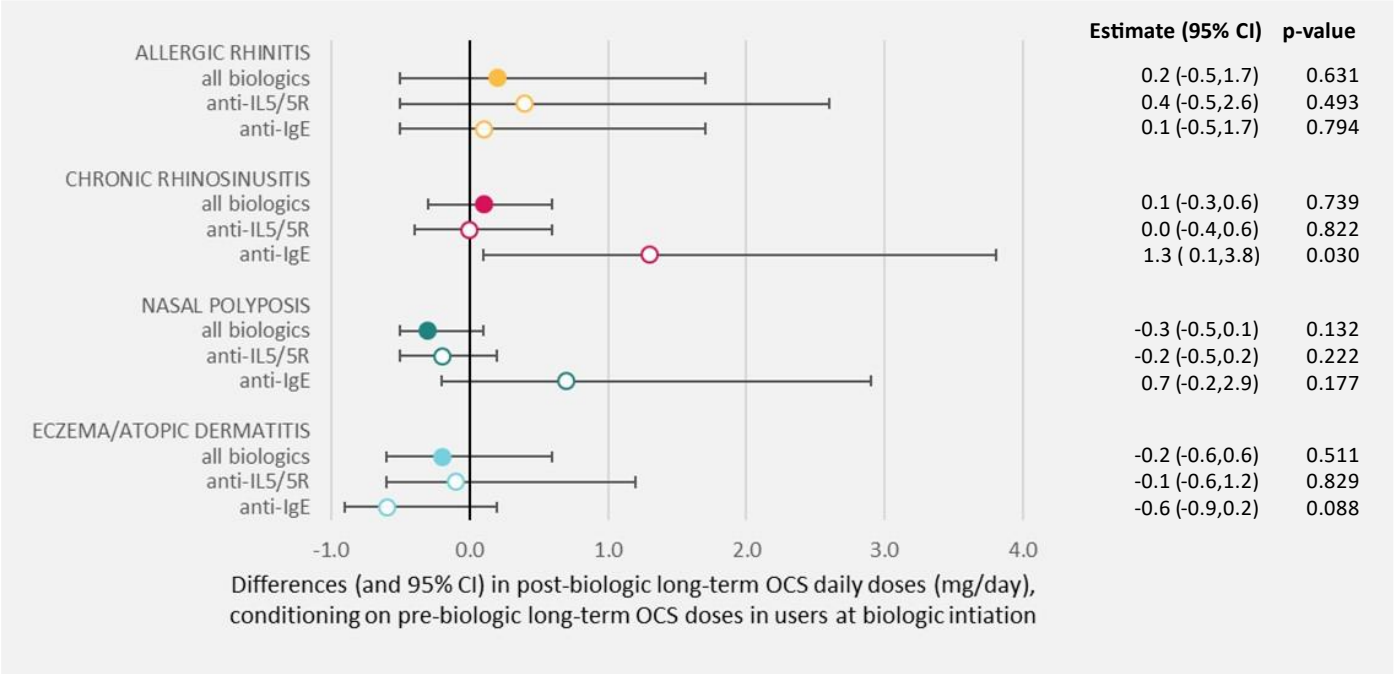
BEC: Blood Eosinophil Count, CRS: Chronic rhinosinusitis; NP: Nasal polyposis; 95% CI: 95% confidence interval.

No additional benefit observed in terms of LTOCS dose reduction



	Estimate (95% CI)	p-value
ALLERGIC RHINITIS		
all biologics	0.2 (-0.5,1.7)	0.631
anti-IL5/5R	0.4 (-0.5,2.6)	0.493
anti-IgE	0.1 (-0.5,1.7)	0.794
CHRONIC RHINOSINUSITIS		
all biologics	0.1 (-0.3,0.6)	0.739
anti-IL5/5R	0.0 (-0.4,0.6)	0.822
anti-IgE	1.3 (0.1,3.8)	0.030
NASAL POLYPOSIS		
all biologics	-0.3 (-0.5,0.1)	0.132
anti-IL5/5R	-0.2 (-0.5,0.2)	0.222
anti-IgE	0.7 (-0.2,2.9)	0.177
ECZEMA/ATOPIC DERMATITIS		
all biologics	-0.2 (-0.6,0.6)	0.511
anti-IL5/5R	-0.1 (-0.6,1.2)	0.829
anti-IgE	-0.6 (-0.9,0.2)	0.088

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95% CI: 95% confidence interval.

PRISM II Summary

The power of biologics to improve severe asthma outcomes in patients with T2 comorbidities

Association between T2-related co-morbidities and effectiveness of biologics in severe asthma

Where

ISAR Global Study

21 countries + 1765 severe asthma patients

Who

With/without AR, CRS+/-NP NP, or AD

Initiated on anti–IL-5/5R, anti-IgE,or anti–IL-4/13

What

Pre and post biologic change in:

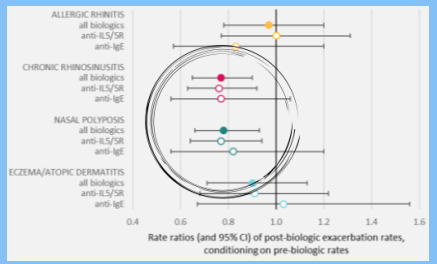
Annual exacerbation rate,

% predicted FEV1

asthma control

LTOCS daily dose

Results



- Biologics led to **improvements in all four asthma outcomes irrespective of comorbidity status**
- **Comorbid CRS+/-NP : 23% fewer exacerbations, 59% higher odds of better post-biologic control**

- Similar estimates for those with comorbid NP
- **Independent of biomarker** profile
- **AR and AD conversely were not predictive** of treatment effect

Practice change

✓ **CRS +/- NP key components in predicting successful treatment with biologics**

✓ **Systematic evaluation for comorbidities + multidisciplinary collaboration vital** in achieving optimal outcomes in severe asthma care

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AR: allergic rhinitis, CRS+/-NP: chronic rhinosinusitis +/- nasal polyps , AD: eczema/atopic dermatitis, LTOCS: Long term Oral Corticosteroids