Impact of pre-biologic impairment on meeting domain-specific biologic responder definitions in patients with severe asthma (BEAM)

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Aim and Methods

Rationale

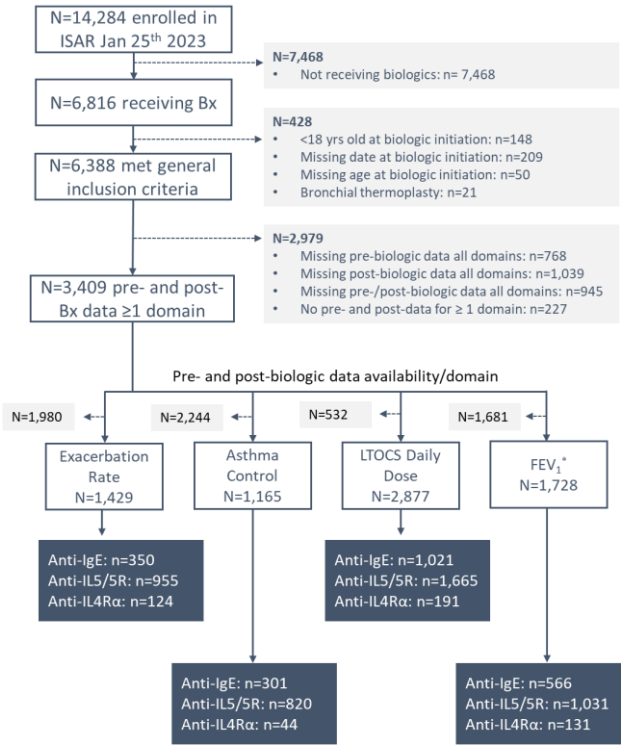
There is little agreement on clinically useful criteria for identifying real-world responders to biologic treatments for asthma.

Objective

To investigate the impact of pre-biologic impairment on meeting domain-specific biologic responder definitions in adults with severe asthma.

Methods

- Longitudinal cohort study across 22 countries participating in ISAR from May 2017 to January 2023.
- Change in four asthma domains (exacerbation rate, asthma control, long-term oral corticosteroid [LTOCS] dose, and lung function) was assessed from biologic initiation to one year post-treatment (minimum 24 weeks)
- Pre- to post-biologic changes for responders and non-responders were described along a categorical gradient for each domain derived from pre-biologic distributions (exacerbation rate: 0 to 6+/year; asthma control: well-controlled to uncontrolled; LTOCS: 0 to >30 mg/day; ppFEV1: <50 to ≥80%)



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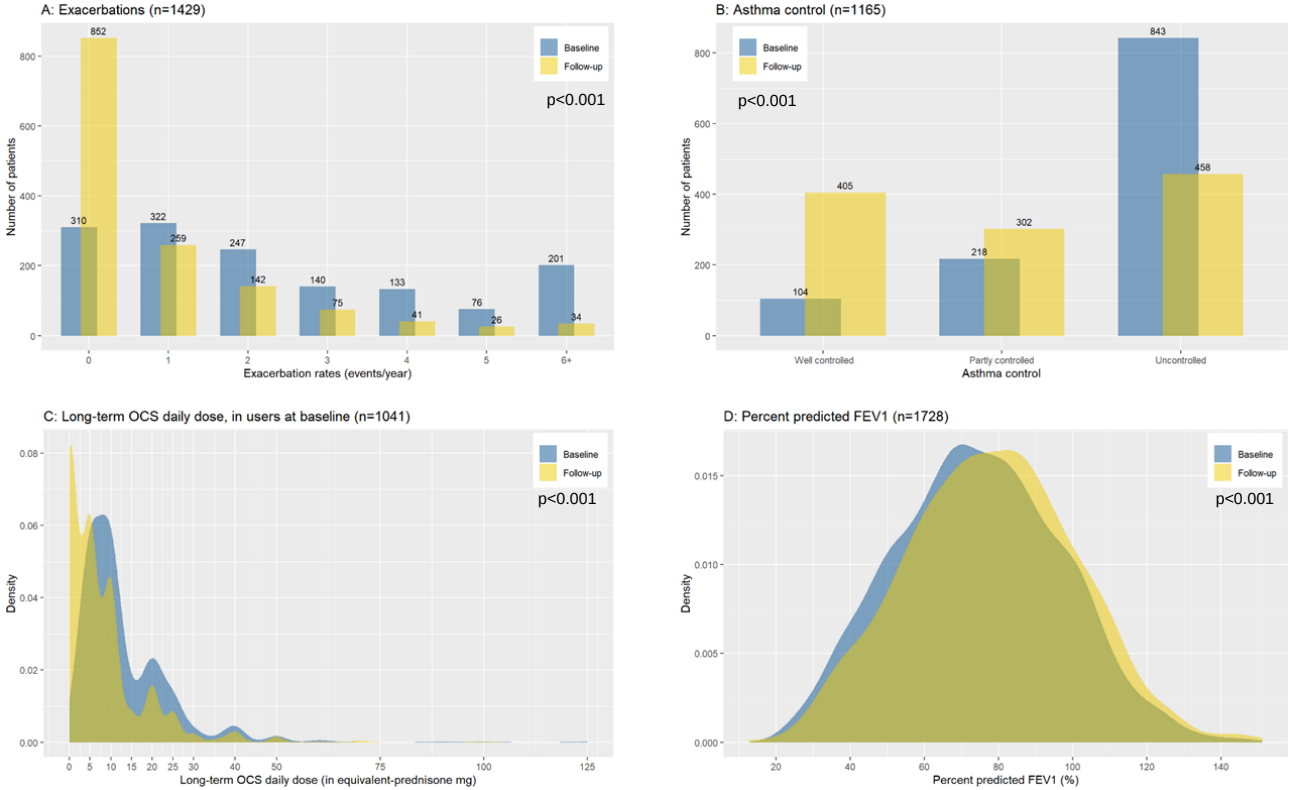
ISAR: International Severe Asthma Registry, Bx: biologic, Anti-IgE: Anti-Immunoglobulin E, Anti-IL5/5R: Anti-Interleukin 5/5R, Anti-IL4: Anti-Interleukin 4, FEV1: Forced Expiratory Volume 1 second, *both percent predicted and absolute.

Statistically significant improvements were observed from pre- to post-biologic initiation for all asthma outcome domains assessed



FEV1: forced expiratory volume in one second; OCS: oral corticosteroid

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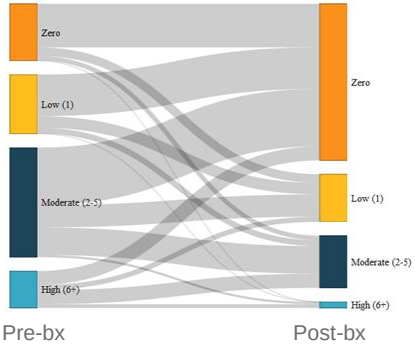
Responders to biologics increased with greater pre-biologic impairment:

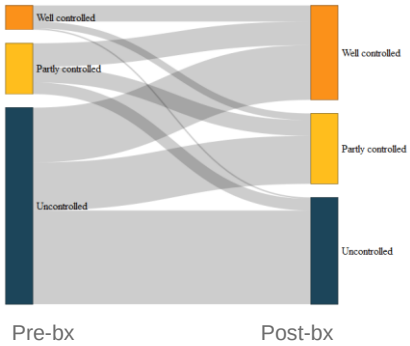
Increasing from 70.2 to 90.0% for exacerbation rate, 46.3 to 52.3% for asthma control, 31.1 to 58.5% for LTOCS daily dose, and 35.8 to 50.6% for ppFEV1

Exacerbations



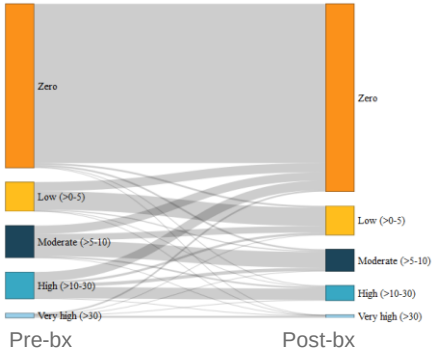
Pre-biologic exacerbation number/yr	Post-biologic status		
	Worsened	Unchanged	Improved
	N (% of patients)		
Zero: 0/yr (n=310)	73 (23.5)	237 (76.5)	NA
Low: 1/yr (n=322)	33 (10.2)	63 (19.6)	226 (70.2)
Moderate: 2-5/yr (n=596)	12 (2.0)	150 (25.2)	434 (72.8)
High: 6+/yr (n=201)	NA	20 (10.0)	181 (90.0)

Asthma Control



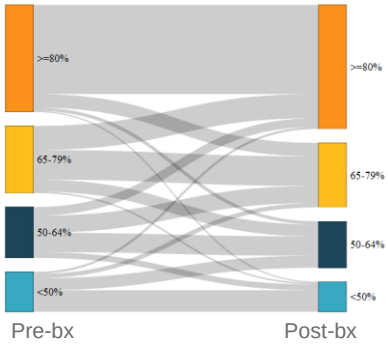
Pre-biologic control status	Post-biologic status		
	Worsened	Unchanged	Improved
	N (% of patients)		
Well controlled (n=104)	35 (33.7)	69 (66.3)	NA
Partly controlled (n=218)	50 (22.9)	67 (30.7)	101 (46.3)
Uncontrolled (n=843)	NA	402 (47.7)	441 (52.3)

LTOCS daily dose



Pre-biologic daily LTOCS dose, mg	Post-biologic status		
	Worsened	Unchanged	Improved
	N (% of patients)		
Zero: 0mg (n=1,836)	53 (2.9)	1,783 (97.1)	NA
Low: >0-5mg (n=328)	20 (6.1)	206 (62.8)	102 (31.1)
Moderate: >5-10mg (n=360)	19 (5.3)	175 (48.6)	166 (46.1)
High: >10-30mg (n=300)	5 (1.7)	127 (42.3)	168 (56.0)
Very high: >30mg (n=53)	NA	22 (41.5)	31 (58.5)

% predicted FEV1



Pre-biologic ppFEV1	Post-biologic status		
	Worsened	Unchanged	Improved
	N (% of patients)		
≥80% (n=698)	117 (16.8)	581 (83.2)	NA
65-79% (n=438)	88 (20.1)	193 (44.1)	157 (35.8)
50-64% (n=332)	38 (11.4)	126 (38.0)	168 (50.6)
<50% (n=260)	NA	140 (53.8)	120 (46.2)

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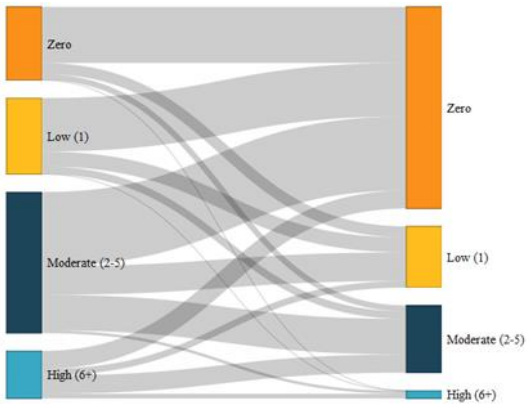
Bx: biologic, ppFEV1: percent predicted Forced Expiratory Volume 1 second, LTOCS: Long-term Oral Corticosteroid, NA: Not Applicable

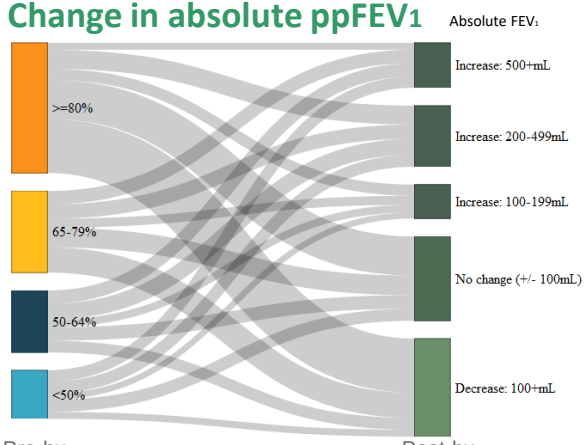
Even those with low pre-biologic impairment, who would be actively excluded from RCTs investigating biologic efficacy, exhibited clinically meaningful post-biologic improvement

Exacerbations



Pre-biologic exacerbation number/yr	Post-biologic status		
	Worsened	Unchanged	Improved
	N (% of patients)		
Zero: 0/yr (n=310)	73 (23.5)	237 (76.5)	NA
Low: 1/yr (n=322)	33 (10.2)	63 (19.6)	226 (70.2)
Moderate: 2-5/yr (n=596)	12 (2.0)	150 (25.2)	434 (72.8)
High: 6+/yr (n=201)	NA	20 (10.0)	181 (90.0)

Change in absolute ppFEV1



ppFEV1 at baseline	Post-biologic status				
	dec. 100+mL	No change	inc. 100-199mL	inc. 200-499mL	inc. 500+mL
	N (% of patients)				
≥80% (n=698)	290 (41.5)	210 (30.1)	60 (8.6)	101 (14.5)	37 (5.3)
65-79% (n=438)	136 (31.1)	105 (24.0)	48 (11.0)	77 (17.6)	72 (16.4)
50-64% (n=332)	63 (18.9)	72 (21.7)	41 (12.3)	85 (25.6)	71 (21.4)
<50% (n=260)	37 (14.2)	65 (25.0)	33 (12.7)	64 (24.6)	61 (23.5)

- **70% of patients with only 1 exacerbation per year improved to zero exacerbations**
- **28% of patients with ppFEV1≥80% improved by ≥100mL FEV1**

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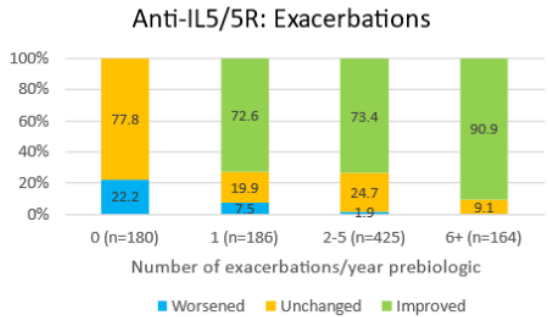
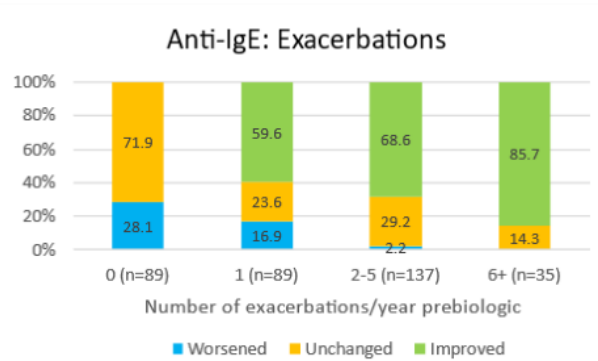
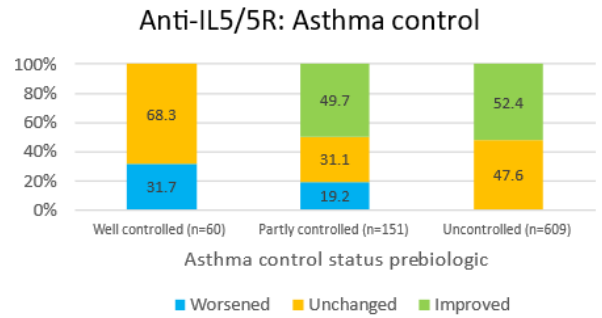
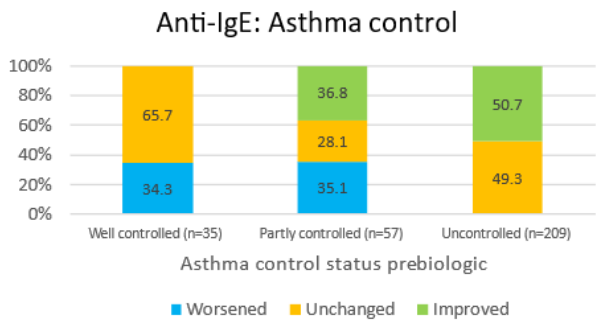
Proportion of patients showing improvement post-biologic tended to be greater for anti–IL-5/5R compared to anti-IgE, irrespective of the degree of pre-biologic impairment

Post-biologic status (worsened, unchanged, improved) according to pre-biologic impairment and biologic class for the asthma outcome domains exacerbation rate and asthma control









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Anti-IgE: Anti-Immunoglobulin E, Anti-IL5/5R: Anti-Interleukin 5/5R

Summary

BEAM: Improvement across all domains, ↑with greater pre-biologic disease, but meaningful change even with ↓ pre-biologic impairment

Statistically significant improvements were observed from pre- to post-biologic treatment **for all asthma outcome domains** assessed

The proportion of patients showing **improvement post-biologic tended to be greater for anti–IL-5/5R** compared to anti-IgE for exacerbation, asthma control, and ppFEV1 domains irrespective of pre-biologic impairment

Those with **greater disease burden pre-biologic therapy tended to have a greater magnitude of effect** for each domain assessed

Even those with low pre-biologic impairment, who would be actively excluded from RCTs investigating the efficacy of biologics, exhibited **clinically meaningful post-biologic improvement**

A **multi-dimensional approach** to define and assess biologic responders and response needed

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Anti-IgE: Anti-Immunoglobulin E, Anti-IL5/5R: Anti-Interleukin 5/5R, RCT: Randomized Controlled Trial, ppFEV1: percent predicted Forced Expiratory Volume 1 second,