Exploring different composite definitions of responders and non-responders to biologic treatment for severe asthma (FULL BEAM response)
Exploring Definitions and Predictors of Severe Asthma Clinical Remission Post-Biologic in Adults (FULL BEAM remission)

ISAR FULL BEAM

Perez-de-Llano, L. et al., Am J Respir Crit Care Med 2024, https://doi.org/10.1164/rccm.202311-2192OC Scelo, G. et al., J Allergy Clin Immunol Pract. 2024 May 19:S2213-2198(24)00530-0. doi: 10.1016/j.jaip.2024.05.016.

Aims and Methods

Rationale

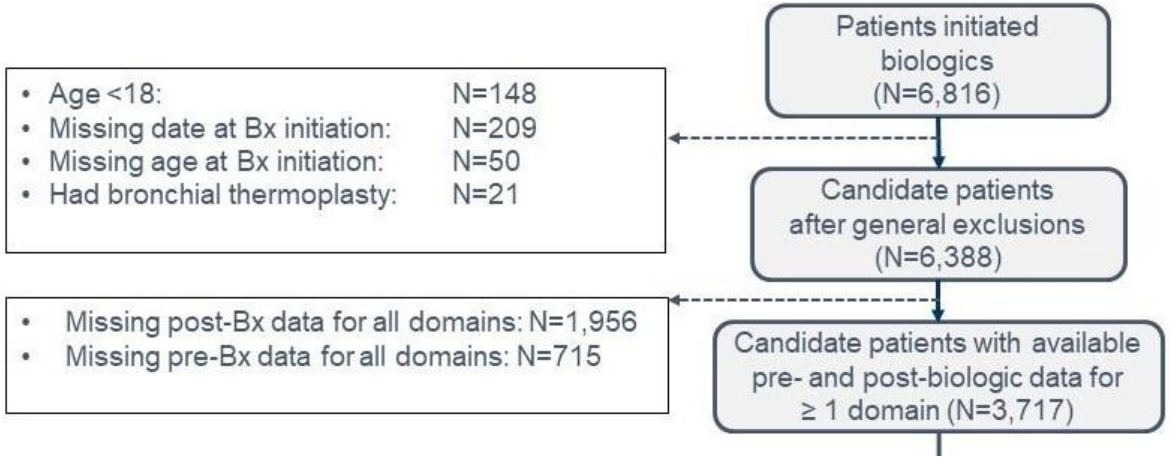
There is little agreement on definitions of real-world responders to biologic treatments for asthma and the concept of remission in severe asthma remains to be explored.

Objective

To explore composite definitions of response and remission in adults with severe asthma.

Methods

- Longitudinal cohort study across 22 countries participating in ISAR from May 2017 to January 2023
- Quantification of individual and composite definitions of response and remission at one year post-treatment using four asthma domains: exacerbation rate, asthma control, long-term oral corticosteroid (LTOCS) dose, and lung function
- Comparison of patient characteristics between response and non-response groups, and between remission and non-remission group



bx: biologics

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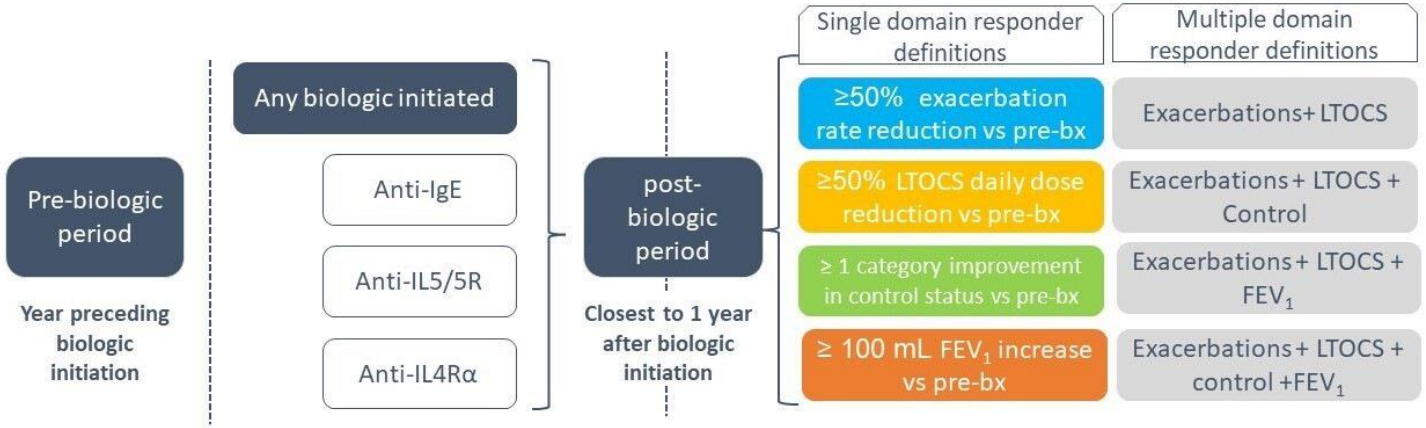
Response and remission definitions

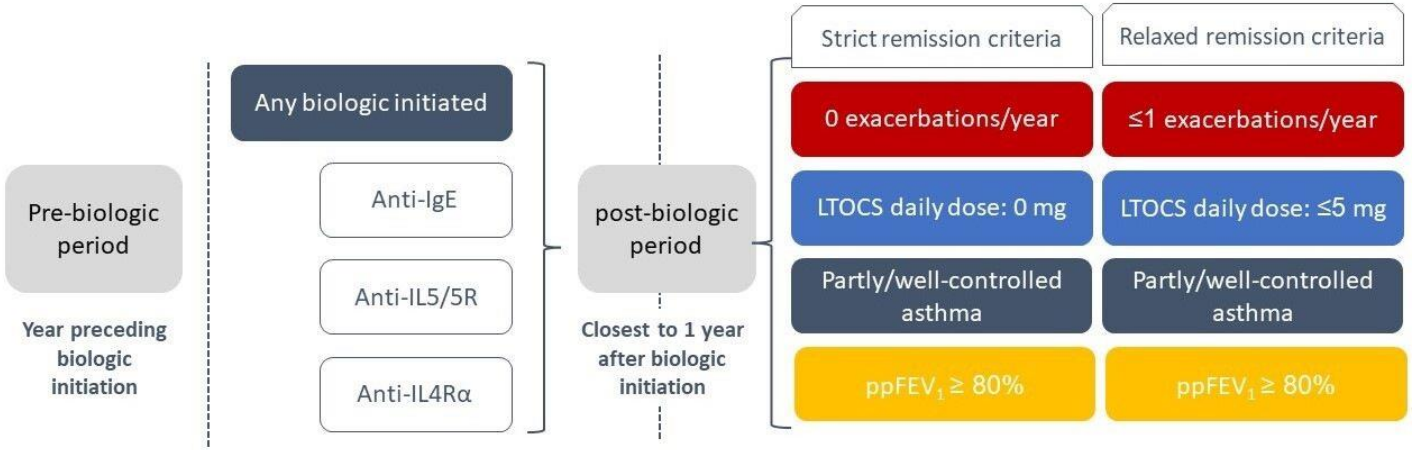
Response

Minimum impairment pre-biologic:
- Exacerbations: ≥2/year, and/or
- LTOCS: use in past year, and/or
- Asthma control: uncontrolled or partly controlled, and/or
- Lung function: <80% predicted FEV1



Remission

(No minimum impairment)



LTOCS: Long-term Oral Corticosteroids, ppFEV1: percent predicted forced expiratory volume in 1 second, anti-IgE: Anti-Immunoglobulin E, Anti-IL5: Anti-Interleukin 5, Anti-IL4Rα: Anti-Interleukin4Rα

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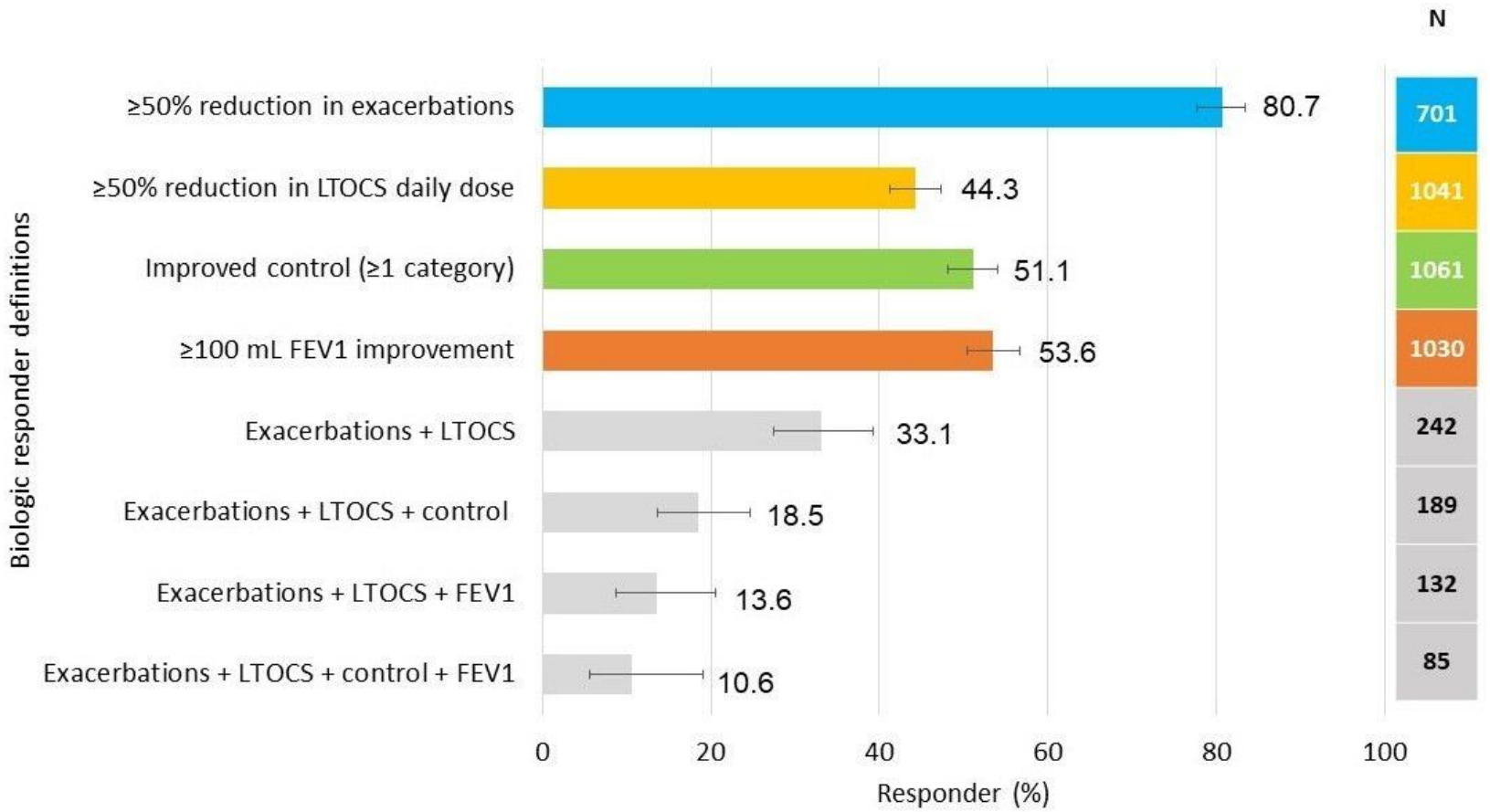
Spectrum of biologic responders, ranging from 11-80% depending upon type and number of domains used to define response



LTOCS: Long-term Oral Corticosteroids, FEV1: forced expiratory volume in 1 second.

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Patient and clinical characteristics associated with response

Pre-biologic characteristics	Trend or significant positive association with Exacerbation responders	Trend or significant positive association with LTOCS responder	Trend or significant positive association with Asthma control responder	Trend or significant positive association with Lung function responder
Responder domains	Higher exacerbation rate*	Lower exacerbation rate*	Lower exacerbation rate*	
	Lower LTOCS daily dose*	Higher LTOCS daily dose*	Lower LTOCS daily dose*	Lower LTOCS daily dose*
			Worse asthma control	
			Better lung function*	Worse lung function*
Biomarkers		Higher BEC*	Higher BEC*	Higher BEC*
				Higher FeNO*
Asthma metrics				Older asthma onset*
				Shorter asthma duration*
BMI		Lower BMI*	Lower BMI*	Lower BMI
Treatment	No theophylline	No theophylline*	No theophylline*	No theophylline*
Comorbidity profile		Sleep apnea*	No sleep apnea*	
	No osteoporosis			No osteoporosis*
		CRS*	CRS*	CRS*
		AR*	AR	AR
			NP*	NP*
	AD	AD*		

* p<0.05

LTOCS: Long-term Oral Corticosteroids, BMI: Body Mass Index, AD: Atopic Dermatitis, AR: Allergic Rhinitis, CRS: Chronic Rhinosinusitis, BEC: Blood Eosinophil Count, NP: Nasal Polyps, FeNO: Fractional Exhaled Nitric Oxide

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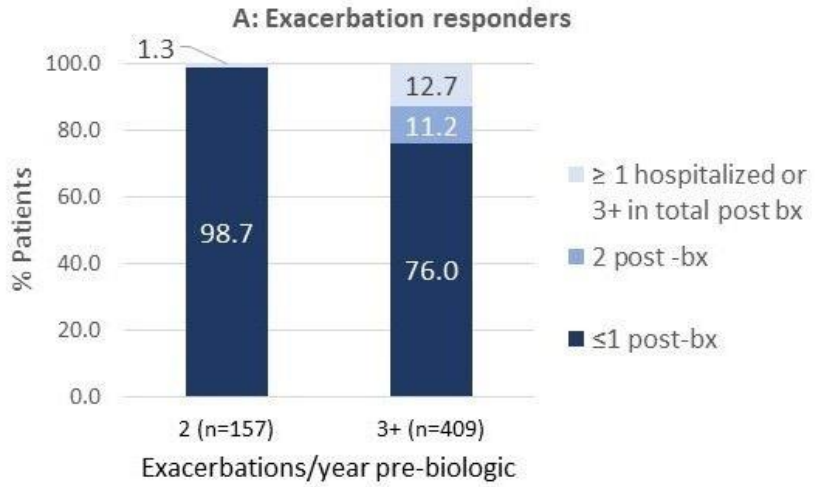
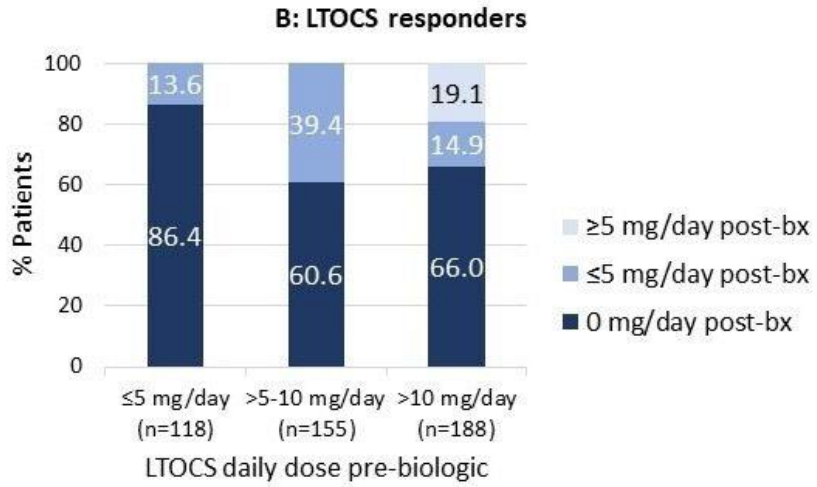
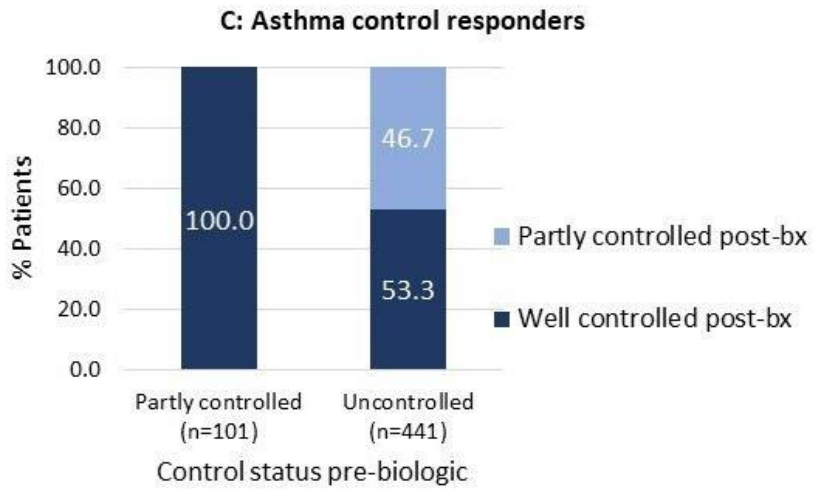
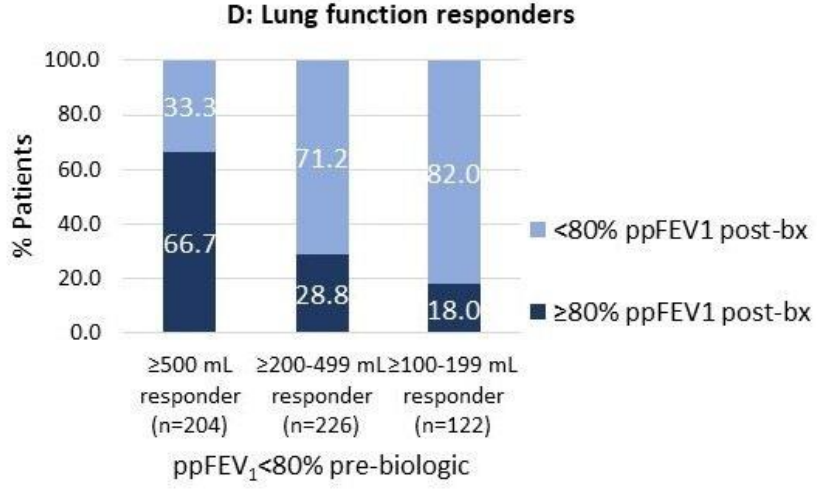
Residual impairments in responders by pre-biologic levels of impairment









LTOCS: Long-term Oral Corticosteroids, ppFEV1: percent predicted forced expiratory volume in 1 second, bx: biologics

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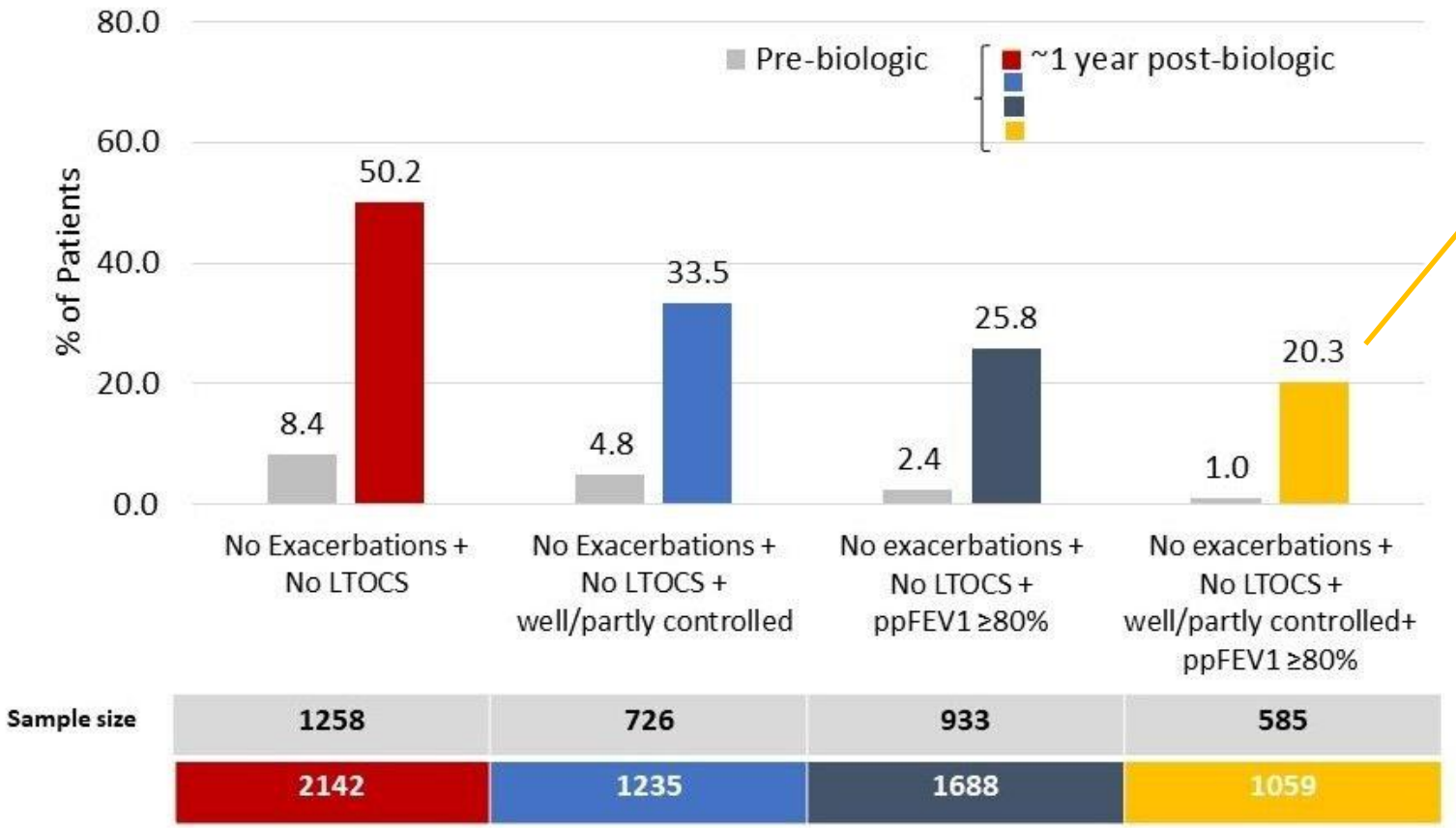
Proportion of patients in remission by different definitions



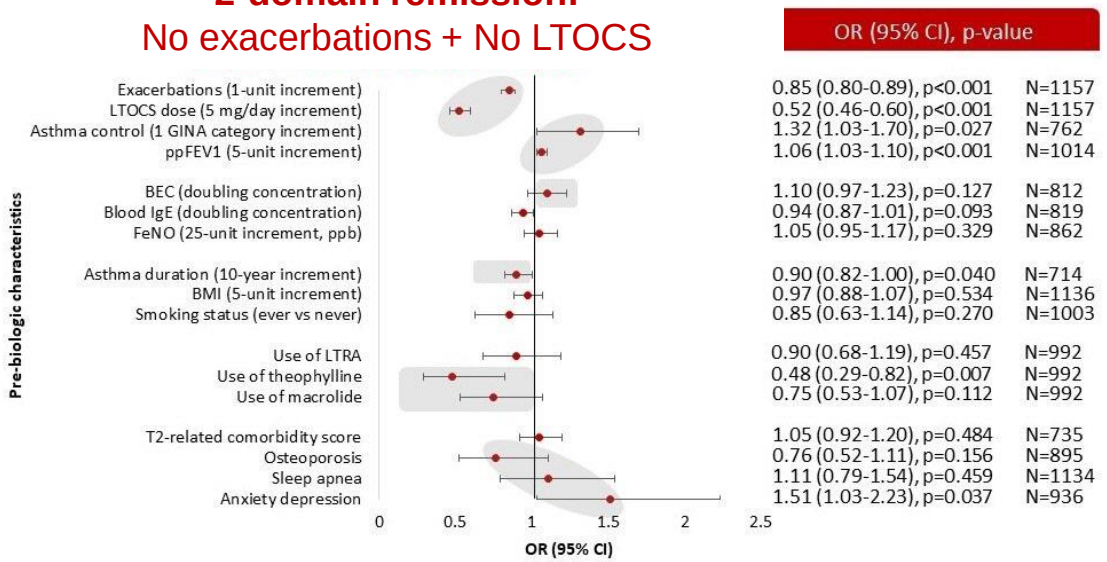
1 in 5 patients meet remission criteria in all 4 domains

LTOCS: Long-term Oral Corticosteroids, ppFEV1: percent predicted forced expiratory volume in 1 second

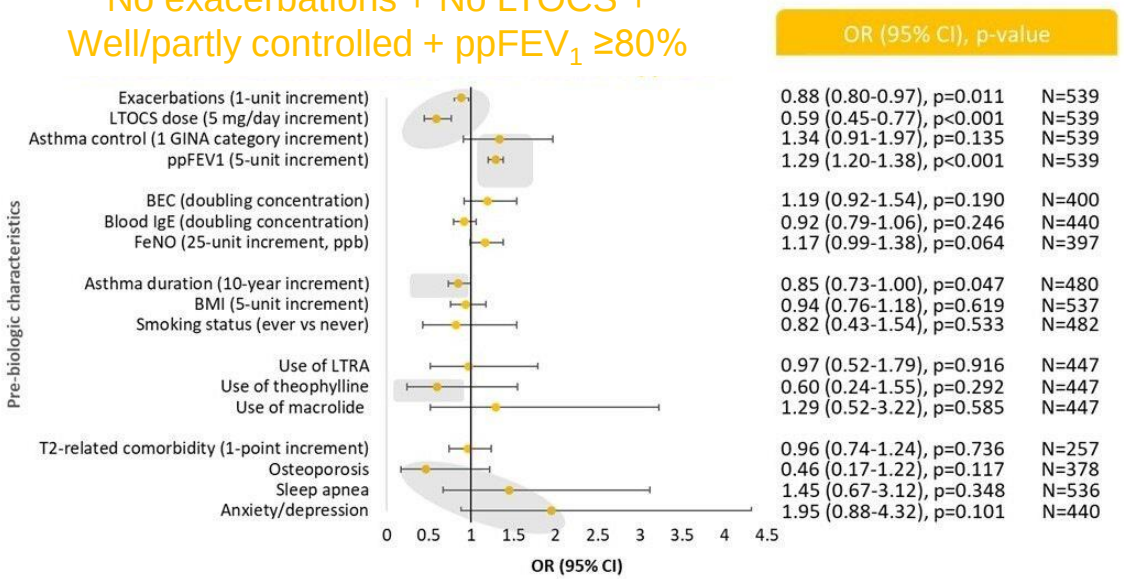
Perez-de-Llano, L. et al., Am J Respir Crit Care Med 2024, https://doi.org/10.1164/rccm.202311-2192OC

Patients with less severe disease and shorter duration of asthma pre-biologic have a better chance of achieving clinical remission post-biologic

2-domain remission:
No exacerbations + No LTOCS



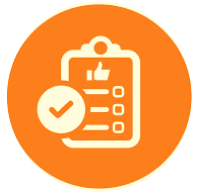
4-domain remission:
No exacerbations + No LTOCS + Well/partly controlled + ppFEV$_1$ ≥80%



LTOCS: Long-term Oral Corticosteroids, ppFEV1: percent predicted forced expiratory volume in 1 second, GINA: Global Initiave for Asthma, BMI: Body Mass Index, T2: Type 2, BEC: Blood Eosinophil Count, NP: Nasal Polyps, FeNO: Fractional Exhaled Nitric Oxide, IgE: Immunoglobulin E, LTRA: Leukotriene Receptor Antagonist

Perez-de-Llano, L. et al., Am J Respir Crit Care Med 2024, https://doi.org/10.1164/rccm.202311-2192OC

FULL BEAM Response summary:
High response does not mean remission
Need for flexible interpretation of response to biologics



Large proportion of responders (80% of patients reduced exacerbations by at least 50%), however residual impairment observed in responders

Responses and their predictors vary according to the outcome assessed

Greater pre-biologic impairment is associated with a better response for all outcomes assessed. However, a shorter asthma duration is associated only with a better lung function response

Flexible interpretation to biologic response is needed, considering the degree of pre-biologic impairment and identification of characteristics (such as asthma duration) that can affect the response, to formulate a personalized likelihood of response

LTOCS: Long-Term Oral Cortocosteroids, ppFEV1: percent predicted Forced Expiratory Volume in 1 second

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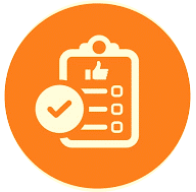
FULL BEAM Remission summary:

Greater chance of remission if less severe impairment and shorter asthma duration at initiation of biologics



Only 20% of patients reached the strictest remission definition (no exacerbation, no LTOCS, well/partly controlled, and ppFEV1 >=80%)

Patients with less severe disease and shorter duration of asthma pre-biologic-initiation had a better chance of achieving remission post-biologic
The odds of achieving 4-domain remission decreased by 15% for every additional 10-years asthma duration

These results highlight the need to consider earlier intervention with biologics for patients with severe asthma prior to significant and irreversible lung function impairment

Since remission is more likely to occur if targeted earlier in the asthma life cycle, a paradigm shift away from targeting response in those with more severe asthma, towards the promotion of remission in those with less severe disease but at risk of developing severe asthma is needed

LTOCS: Long-Term Oral Corticosteroids, ppFEV1: percent predicted Forced Expiratory Volume in 1 second

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