2024.11.23
Asthma school

Asthma 2024: Highlights in Basic and Clinical Research

고대안암병원 조성민

Contents

[Asthma Original Research]

CHEST

Clinical Response and Remission in Patients With Severe Asthma Treated With Biologic Therapies

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Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Severe asthma

- Remains uncontrolled
  - Despite high-dose controller therapy
  - Ruled out other causes, including lack of adherence, inadequate inhaler technique, and influence of untreated comorbidities
- 5-10% of patients with asthma
- Associated with high morbidity, loss of quality of life, and iatrogenic side effects to treatment (OCS)

Development of novel biologic therapies

- Consideration of remission as an achievable treatment target

Chest. 2024 Feb;165(2):253-266

Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Clinical Remission on Treatment	Clinical Remission off Treatment
For ≥12 months: • Sustained absence of significant asthma symptoms based on validated instrument, **and** • Optimization and stabilization of lung function, **and** • Patient and HCP agreement regarding disease remission, **and** • No use of systemic corticosteroid therapy for exacerbation treatment or long-term disease control	Same criteria maintained without asthma treatment for ≥12 months
Complete Remission on Treatment	**Complete Remission off Treatment**
Clinical remission plus the following: • Current, objective evidence of the resolution of previously documented asthma-related inflammation (eg, reduced blood or sputum eosinophil counts, FENO, and/or other relevant measures), **and** • In appropriate research settings: Current negative bronchial hyperresponsiveness	Same criteria maintained without asthma treatment for ≥12 months

Remission as a treatment outcome is clinically important

- 1) May have a better long-term prognosis in terms of a reduced risk of excessive lung function decline and future exacerbations
- 2) May have a better chance of tapering biologic therapy

A key step toward describing the longer term beneficial implications of achieving short-term remission on a biologic treatment

J Allergy Clin Immunol. 2020 Mar;145(3):757-765
Chest. 2024 Feb;165(2):253-266

Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

- **Objectives**
  - the real-life effectiveness of biologic therapy in severe asthma
  - the proportion of patients who achieve a clinical response and clinical remission
  - predictors of remission

- Danish Severe Asthma Register
  - a nationwide cohort of all patients treated with a biologic for severe asthma in Denmark
- Biologic-naive patients commencing biologic therapy
- Between January 1, 2016, and December 31, 2021

ALL BIOLOGIC THERAPIES
In the past 12 months: High dose inhaled corticosteroid corresponding to at least 1600 µg budesonide equivalent dose **AND** a second controller (LABA, LRTA or LAMA) **OR** maintenance oral corticosteroid (mOCS) at least 50% of the time
Systematic assessment with the purpose of excluding reasons for uncontrolled disease (adherence, inhalation technique, comorbidities, exposures) **AND** At least 2 exacerbations in the past 12 months or mOCS at least 50% of the time

DRUG SPECIFIC REQUIREMENTS	
Anti-IgE **(Omalizumab)**	Perennial allergy and symptoms after exposure to allergen
Anti-IL-5 /IL-5R **(Mepolizumab, Reslizumab, Benralizumab)**	Blood eosinophils >= 0.30 cells x 10^9L the past 12 months **or** Blood eosinophils >= 0.15 cells x 10^9L currently **or** Sputum eosinophils >= 3%
Anti-IL-4Rα **(Dupilumab)**	Blood eosinophils >= 0.30 cells x 10^9L the past 12 months **or** Blood eosinophils >= 0.15 cells x 10^9L currently **or** Sputum eosinophils >= 3% and/or FeNO >= 25 ppb If maintenance OCS, no requirement for increased blood eosinophils

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Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

501 patients

Clinical response

- Reduction of at least 50% in the annualized exacerbation rate if the indication was based on ≥ 2 exacerbations in the 12 months prior to treatment
- Reduction of at least 50% in the OCS dose from baseline if the indication was based on the need for mOCS

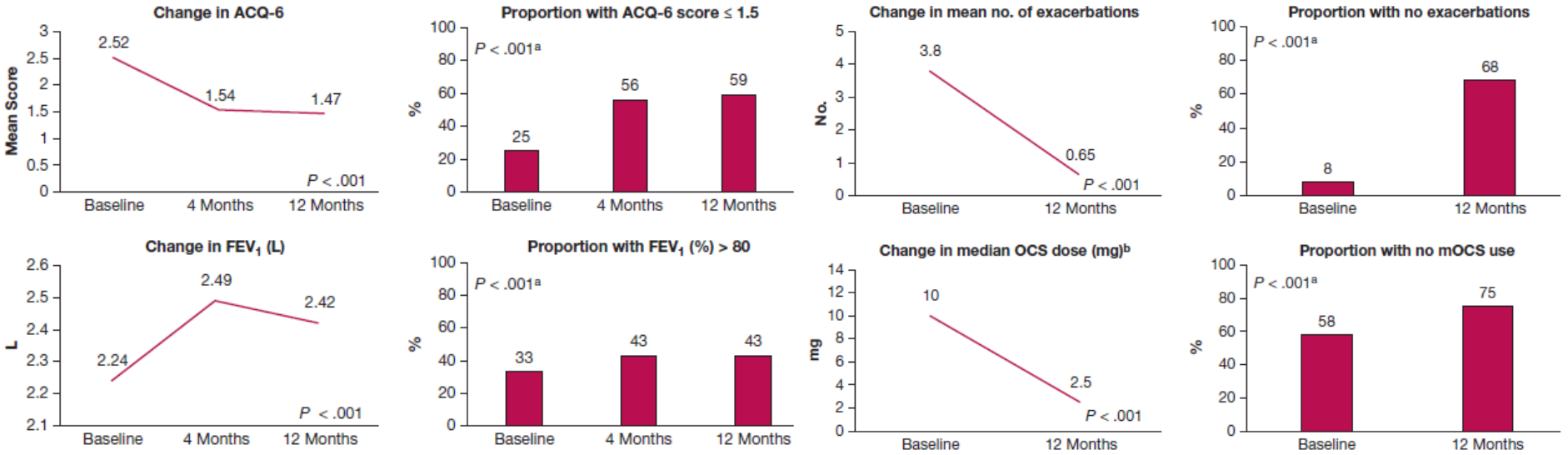
Clinical remission

- Complete absence of exacerbations and need for mOCS
- And well controlled symptoms, defined as a score on the six-question Asthma Control Questionnaire (ACQ-6) of ≤ 1.5 after 12 months of treatment
- Normalization of lung function, FEV1 > 80% of predicted value

Nonresponse

- Not fulfilling the criteria for clinical response, as well as discontinuation or switching treatment prior to 12 months

Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

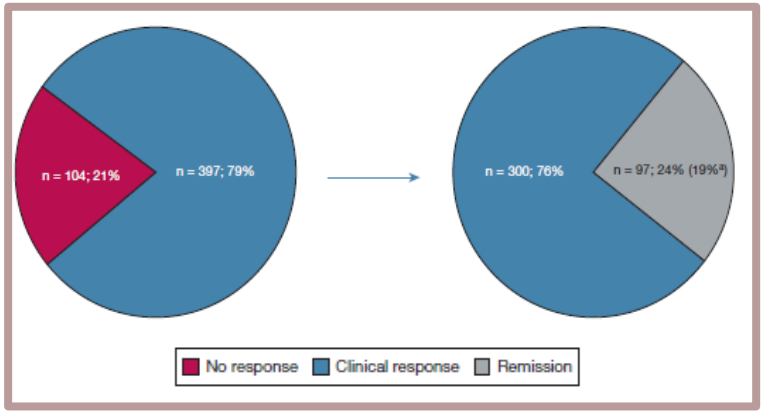


Effectiveness of biologic therapy on clinical outcomes in the DSAR

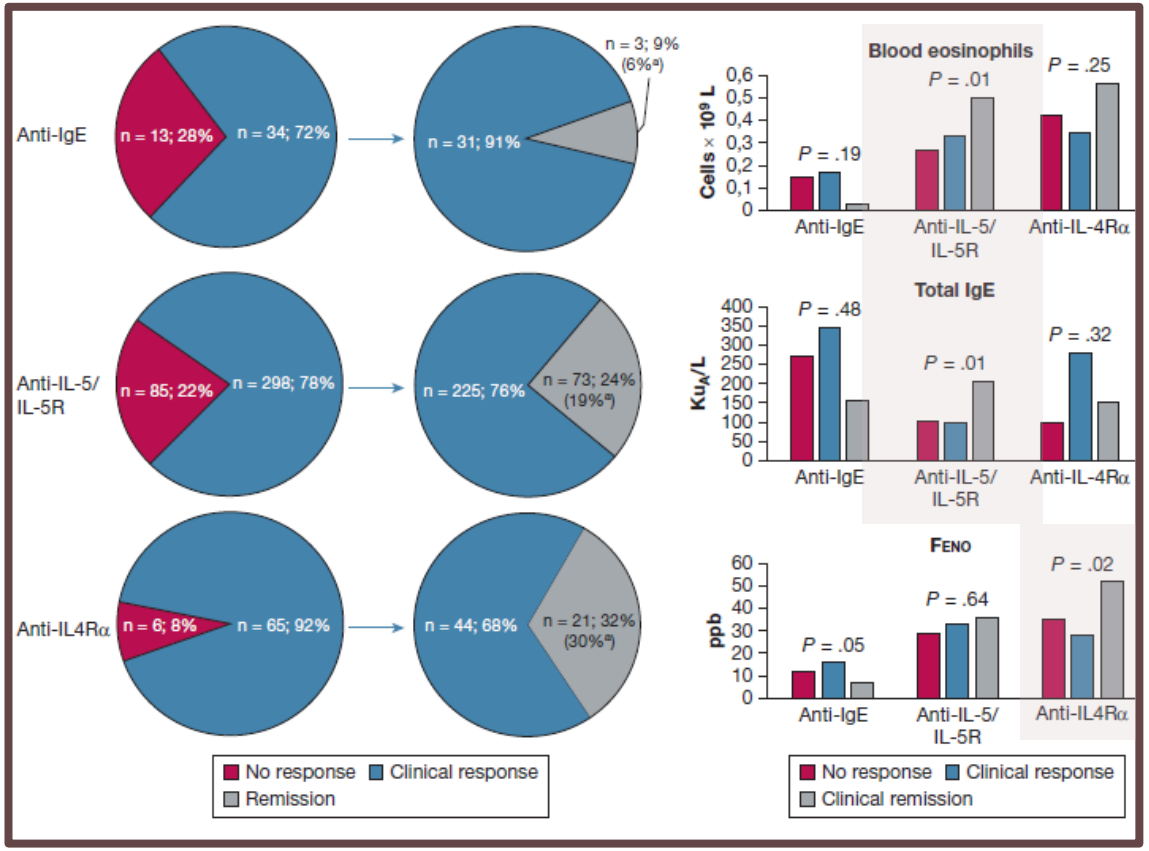
- Decreased ACQ-6 score, OCS related exacerbations, number of patients who take mOCS
- Improvement of FEV_1 (the most difficult domain to improve)

Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Response pattern and predictors of response following 12 months of treatment with biologic therapy in biologic-naive patients in the DSAR



- No response 21%
- Clinical response 79%
  - **Clinical remission 19% (24%)**



- Low remission in anti-IgE treatment
- anti-IL-5/IL-5R - higher baseline blood eosinophils and total IgE
- anti-IL-4Ra - higher fractional exhaled nitric oxide levels

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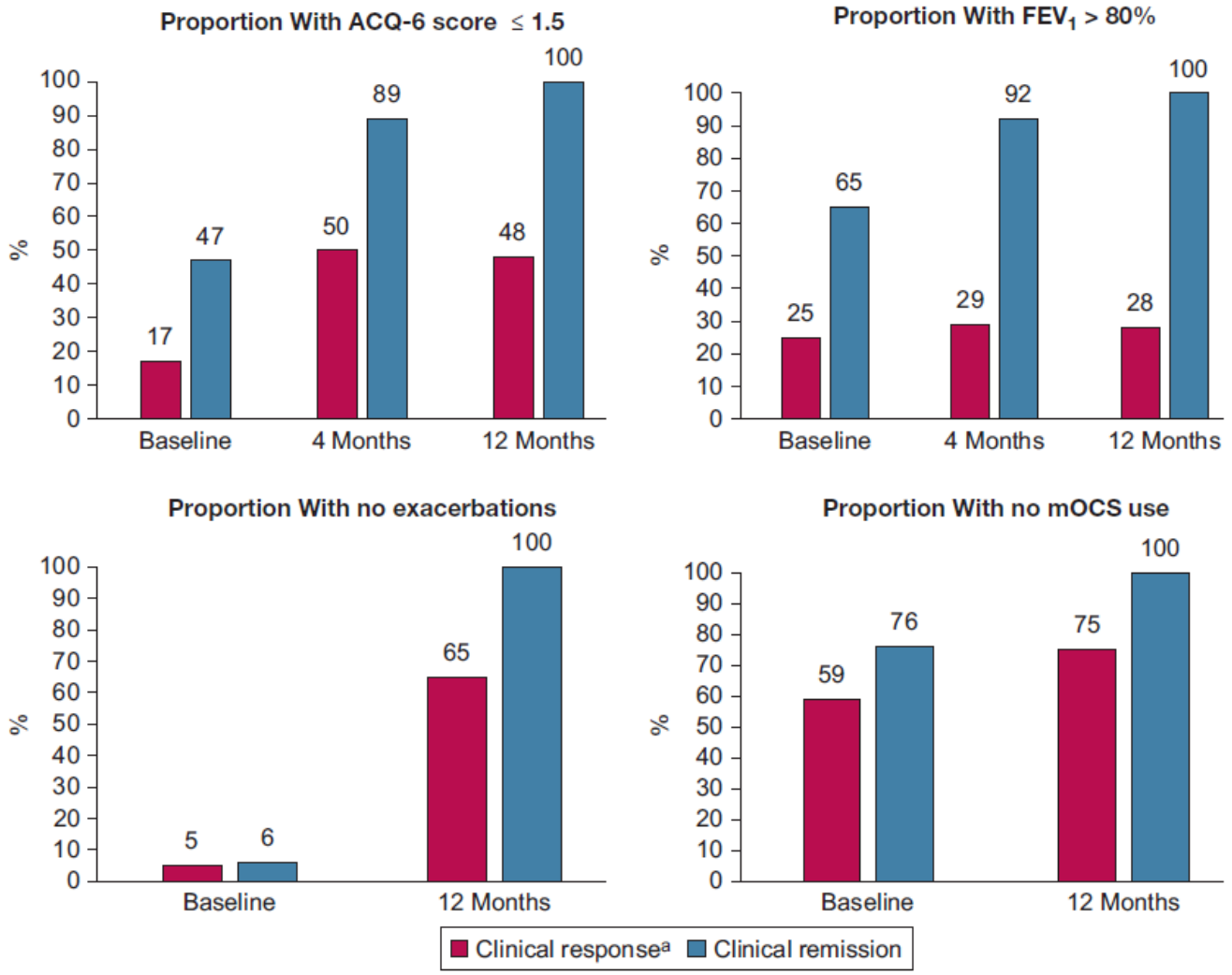
Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Temporal response in patients with clinical response and clinical remission



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Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Baseline Predictors of Clinical Remission After 12 Months of Biologic Therapy Analyzed in a Multivariate Logistic Regression Model With Remission as the Outcome

Predictors	OR (95% CI)	*P* Value
Sex		.13
Male	1.57 (0.88-2.83)	
Female	1.00 (Reference)	
BMI (kg/m^2) (1 unit increase)	0.92 (0.86-0.99)	.02
Duration of disease (1 y increase)	0.98 (0.97-0.99)	.047
Blood eosinophil count (doubling concentration)	1.18 (0.98-1.42)	.09
FENO (doubling concentration)	1.02 (0.81-1.27)	.88

Lower BMI

- obesity as an unmanaged comorbidity negatively affects asthma control
- may be associated with reduced steroid responsiveness

Duration of disease

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Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

ASTHMA ■

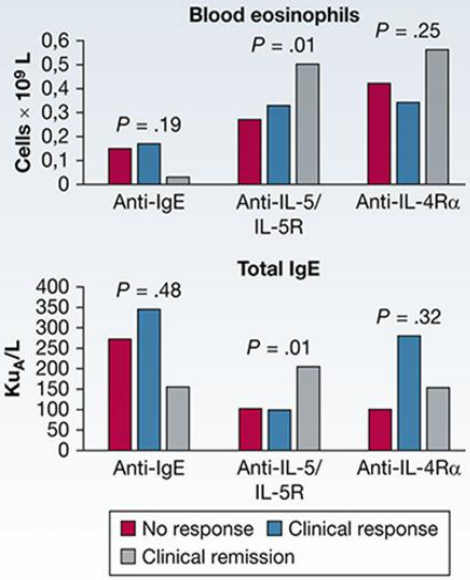
How Many Patients With Severe Asthma Treated With Biologic Therapy Achieve Clinical Remission and What Predicts Response?

CHEST

STUDY DESIGN

- Observational cohort study of 500 Danish patients with asthma over 12 months
- **Definitions**
  - **Clinical response:** ≥50% reduction in exacerbations AND/OR ≥50% reduction in oral corticosteroids (OCS)
  - **Clinical remission:** Cessation of exacerbations and OCS use AND normalization of lung function and improved asthma questionnaire

RESULTS



21% HAD NO RESPONSE

79% HAD A CLINICAL RESPONSE

19% HAD CLINICAL REMISSION

Baseline biomarkers predicted remission for each drug class (FeNO not pictured)

- Almost **one in five** patients with severe asthma achieve remission following treatment with biologic therapy
- Remission was predicted by shorter disease **duration at time of treatment initiation and lower BMI**
  - Early intervention is important for achieving optimal results
- **Clinical remission** is an achievable treatment goal in adult patients with severe asthma

Chest. 2024 Feb;165(2):253-266

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

ORIGINAL ARTICLE

Asthma and Lower Airway Disease

Plasma protein signatures of adult asthma

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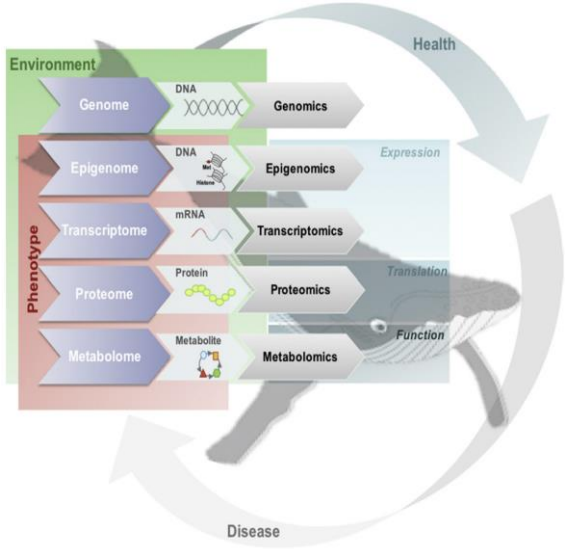
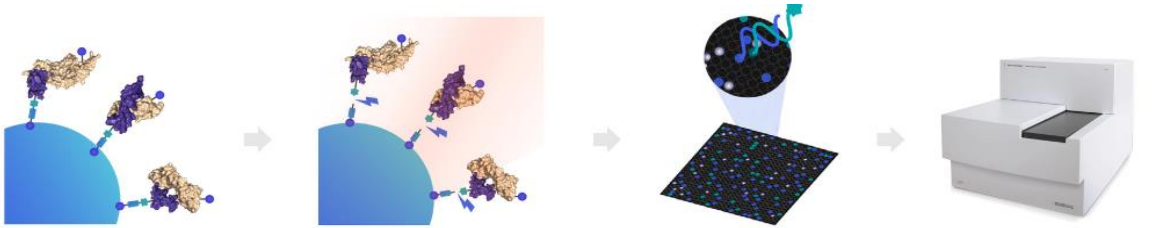
Plasma protein signatures of adult asthma

Proteomics

- the study of the proteome
- How protein quantities, modifications, and structures change during development and in response to internal or external stimuli
- Proteomic-based approaches for biomarker investigation
  - Better understand pathways affected in a disease
  - Identify individuals at a high risk of developing the disease
  - Identify individuals who are most likely to respond to specific treatment





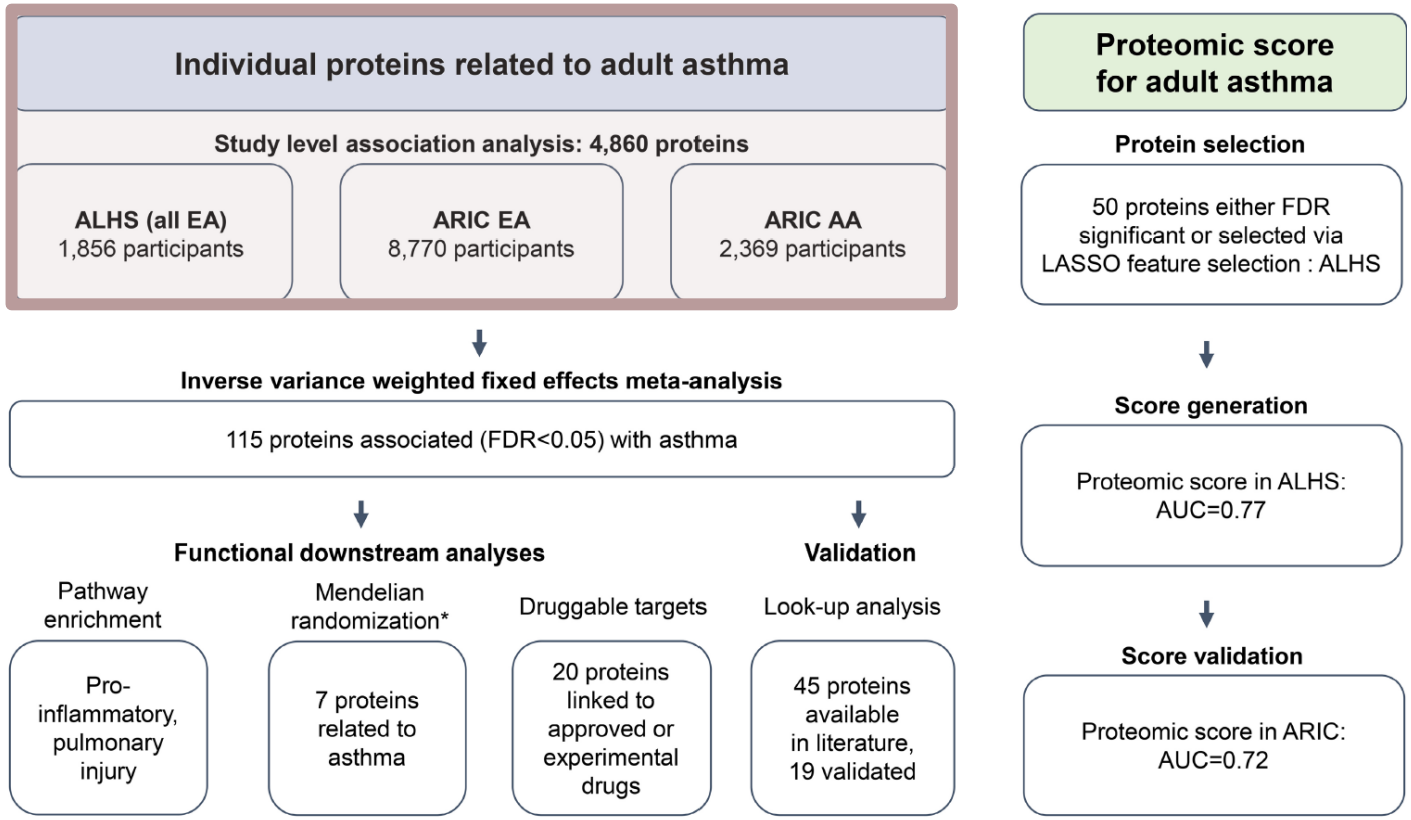
SOMAScan V4 (5K) assay

- Aptamers - synthetically designed to bind a specific human protein or protein complex with high specificity
- RFU (relative fluorescence units) - a semi-quantitative measure of protein abundance

Allergy. 2024 Mar;79(3):643-655

Plasma protein signatures of adult asthma

- **Objectives**
  - To identify plasma proteomic signatures of asthma

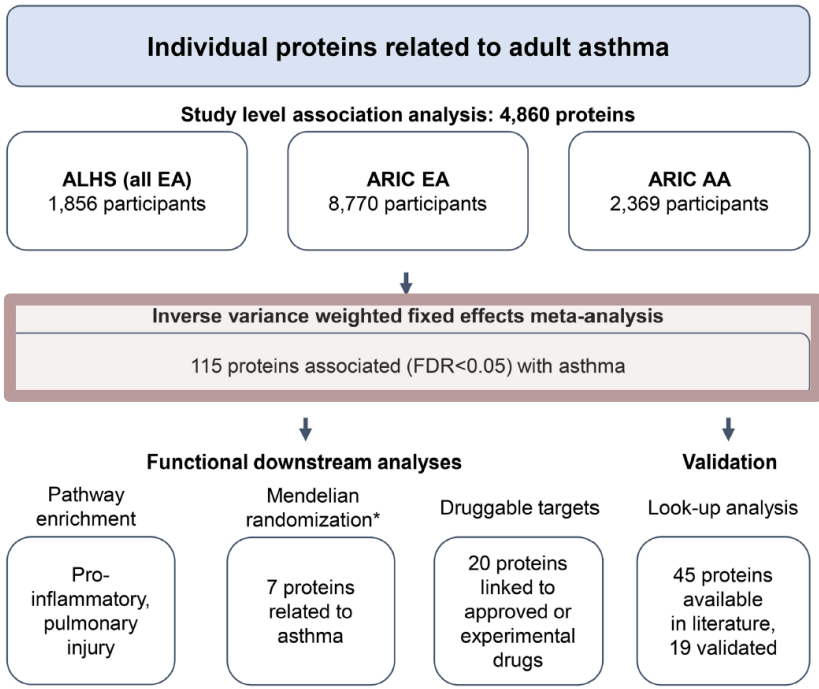


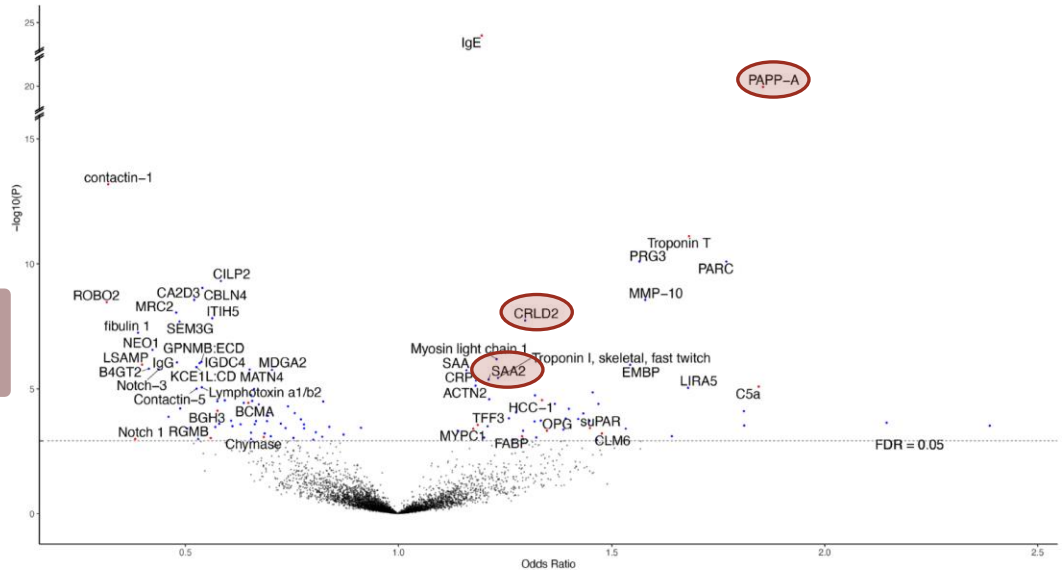
n = 12,995, 1,231 asthma vs. 11,764 Control

- The Agricultural Lung Health Study (ALHS)
- Atherosclerosis Risk in Communities (ARIC)

Allergy. 2024 Mar;79(3):643-655

Plasma protein signatures of adult asthma





Associations between plasma proteins and current asthma

- 51 – positive associations
- 64 – negative associations

PAPP-A (Pappalysin-1)

- more abundant in asthma cases and positively associated with asthma severity
- Biomarker of airway remodeling

CRLD2 (Cysteine-rich secretory protein LCCL domain-containing 2)

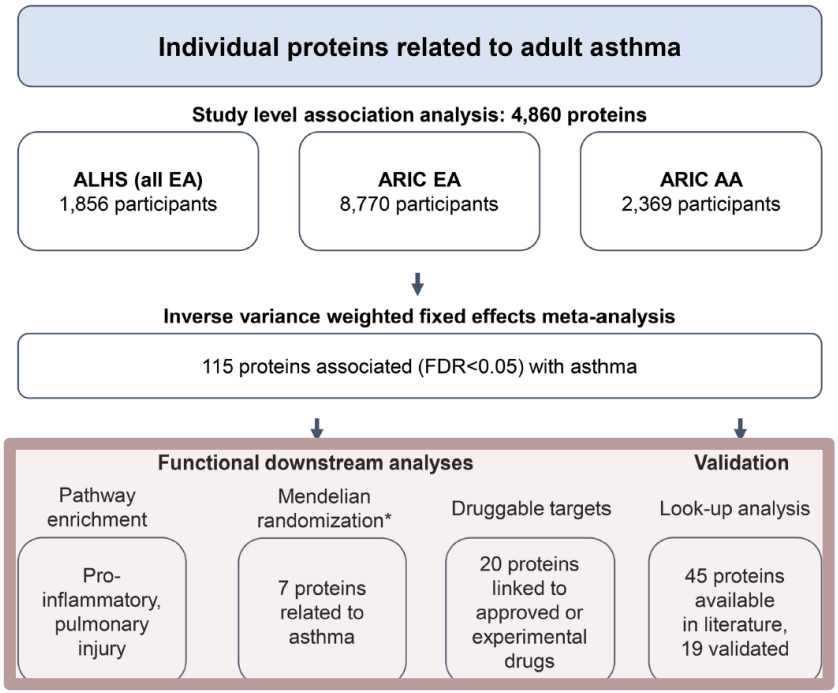
- Glucocorticoid response

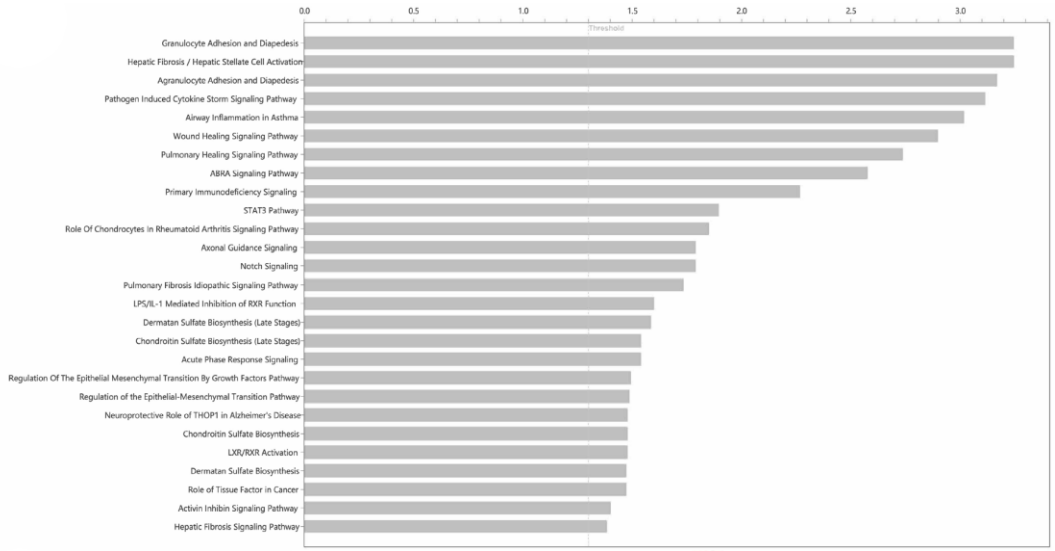
SAA1 (Serum amyloid A-1)

- consistent with asthma promoting upregulation of circulating pro-inflammatory mediators in addition to airway-specific changes

Allergy. 2024 Mar;79(3):643-655

Plasma protein signatures of adult asthma



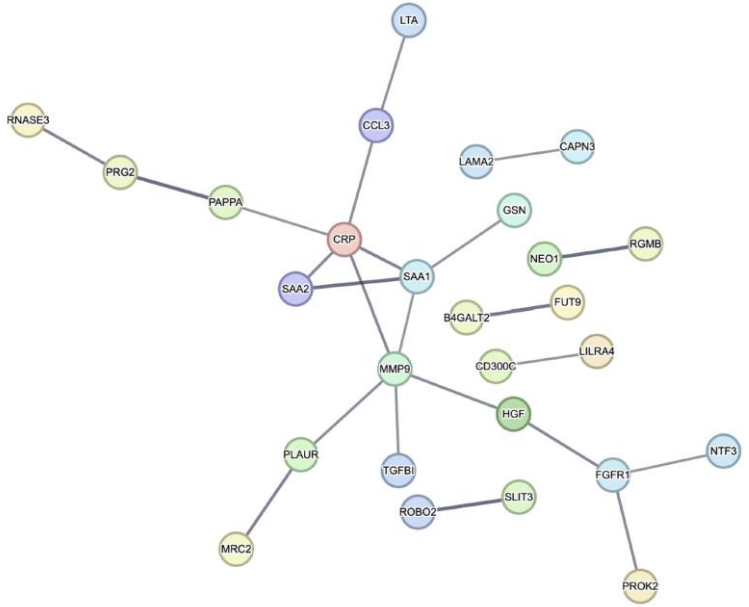


Functionally enriched pathways among proteins related to asthma

- Adhesion and diapedesis of granulocytes
- Pulmonary healing
- Airway inflammation

Network of functional associations between proteins

- acute phase response
- pulmonary injury-related signaling
- epithelial-mesenchymal transition - plays an important role in airway remodeling in asthma



Allergy. 2024 Mar;79(3):643-655.

Plasma protein signatures of adult asthma

Proteomic score for adult asthma

Protein selection

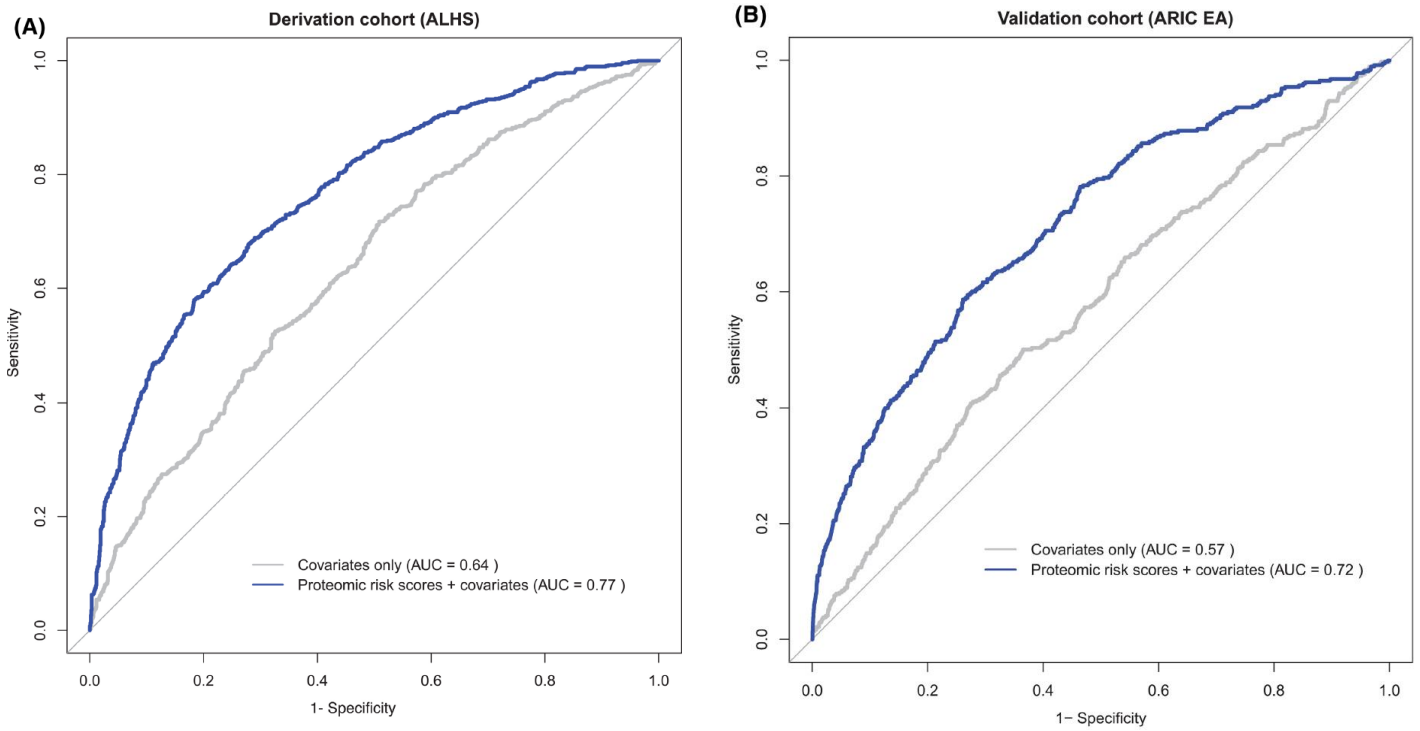
50 proteins either FDR significant or selected via LASSO feature selection : ALHS

Score generation

Proteomic score in ALHS: AUC=0.77

Score validation

Proteomic score in ARIC: AUC=0.72

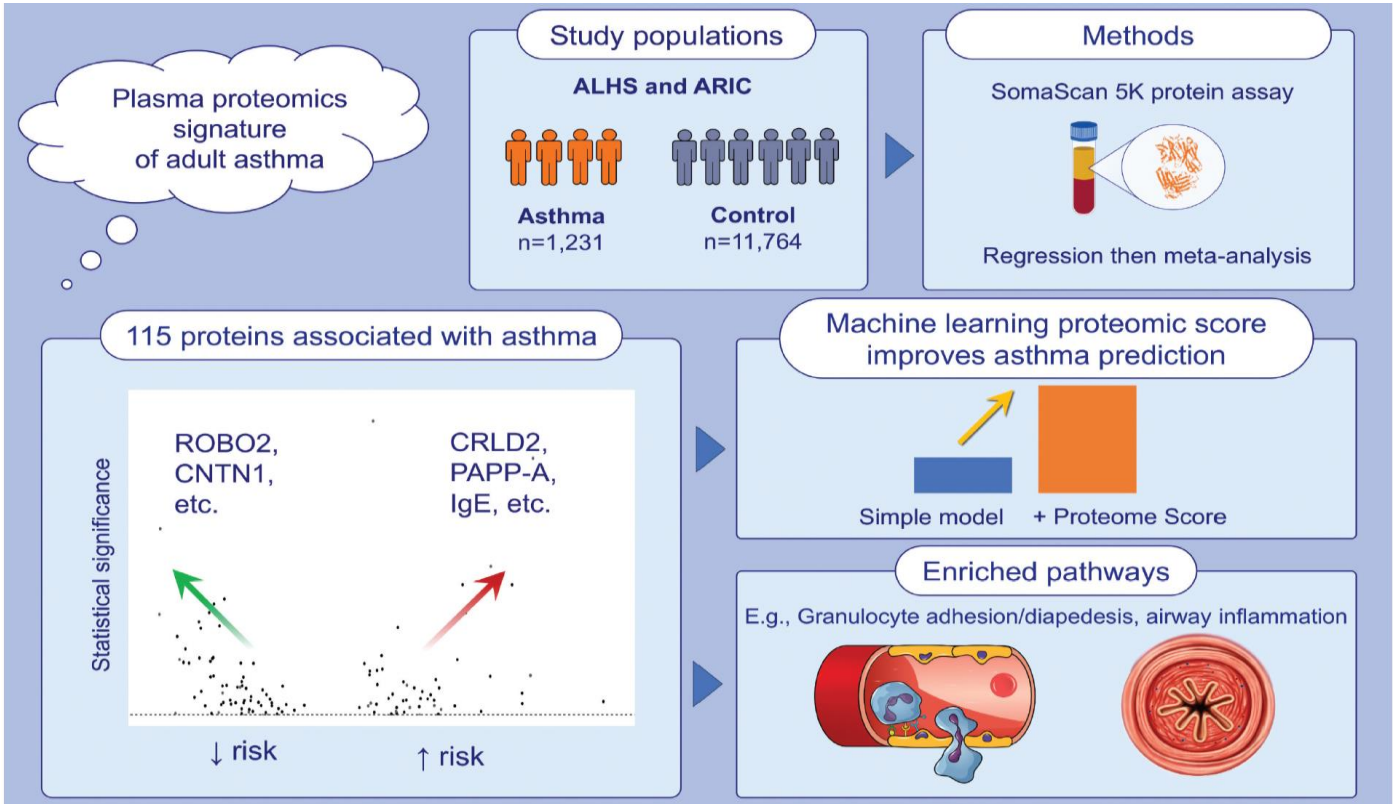


Performance of proteomic score in derivation (ALHS) and validation (ARIC) cohorts

- The benefit of adding the proteome score to a covariates-only prediction model is reflected by the improved performance

Allergy. 2024 Mar;79(3):643-655

Plasma protein signatures of adult asthma



- **The first large-scale proteomics study, identified**
  - **Over 100 plasma proteins associated with asthma**
  - **Novel proteins that could inform development of diagnostic biomarkers and therapeutic targets in asthma**

Allergy. 2024 Mar;79(3):643-655

[Asthma Original Research]

CHEST

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

Dennis Thomas, PhD; Vanessa M. McDonald, PhD; Sean Stevens, MBiostat; Melissa Baraket, PhD; Sandra Hodge, PhD; Alan James, PhD; Christine Jenkins, MD; Guy B. Marks, PhD; Matthew Peters, MD; Paul N. Reynolds, MD, PhD; John W. Upham, PhD; Ian A. Yang, PhD; and Peter G. Gibson, DMed

Chest. 2024 Aug;166(2):262-270

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

Remission of Asthma

- Clinical remission
  - no symptoms or exacerbations for a specific period
- Complete (Pathophysiological) remission
  - normal lung function, airway responsiveness and/or inflammatory markers
  - Persistence of airway hyperresponsiveness and/or airway inflammation is found in most adults with clinical remission of asthma

Special Series

Consensus of an American College of Allergy, Asthma, and Immunology, American Academy of Allergy, Asthma, and Immunology, and American Thoracic Society workgroup on definition of clinical remission in asthma on treatment

Table 1
Asthma Clinical Remission on Treatment Criteria

All the following criteria must be met over a 12-mo period and may be applied to those receiving monoclonal antibody therapy (biologic) for asthma:
1. **NO** exacerbations requiring a physician visit, emergency care, hospitalization, and/or systemic corticosteroid for asthma (ie, oral, injectable).
2. **NO** missed work or school over a 12-mo period due to asthma-related symptoms.
3. Stable and optimized pulmonary function results on all occasions, when measured over a 12-mo period, with ≥2 measurements during the y.
4. Continued use of controller therapies (ICS, ICS/LABA, leukotriene receptor antagonist) ONLY at low-medium dose of ICS, or less, as defined by most recent GINA strategy.
5. ACT >20, AirQ <2, ACQ <0.75 on all occasions measured in the previous 12-mo period, with ≥2 measurements during the y.
6. Symptoms requiring 1-time reliever therapy (SABA, ICS-SABA, ICS-LABA) no more than once a mo.

GINA 2024

Ann Allergy Asthma Immunol. 2023 Dec;131(6):782-785

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

Macrolide in management of asthma

- GINA 2024, Step 5

Azithromycin

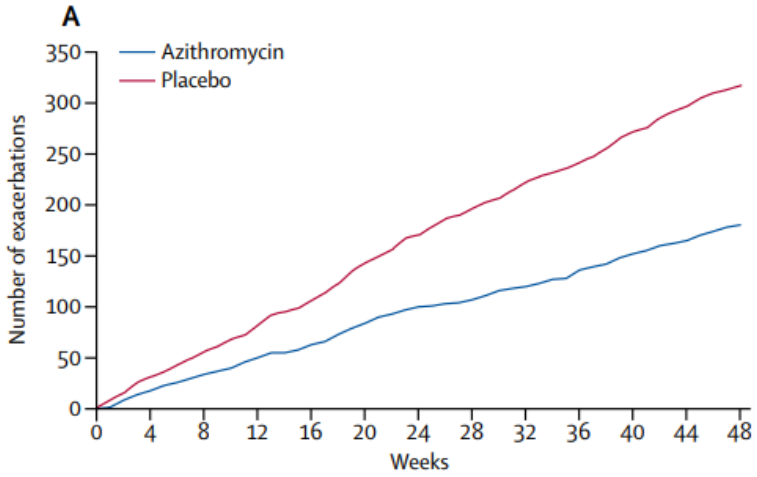
Add-on azithromycin (three times a week) can be considered after specialist referral for adult patients with persistent symptomatic asthma despite high-dose ICS-LABA. Before considering add-on azithromycin, sputum should be checked for atypical mycobacteria, ECG should be checked for long QTc (and re-checked after a month on treatment), and the risk of increasing antimicrobial resistance should be considered.[372] Diarrhea is more common with azithromycin 500 mg 3 times per week.[373] Treatment for at least 6 months is suggested, as a clear benefit was not seen by 3 months in the clinical trials.[373,374] The evidence for this recommendation includes a meta-analysis of two clinical trials[373,374] in adults with persistent asthma symptoms that found reduced asthma exacerbations among those taking medium or high-dose ICS-LABA who had either an eosinophilic or non-eosinophilic profile and in those taking high-dose ICS-LABA (Evidence B).[375] The option of add-on azithromycin for adults is recommended only after specialist consultation because of the potential for development of antibiotic resistance at the patient or population level.[373]

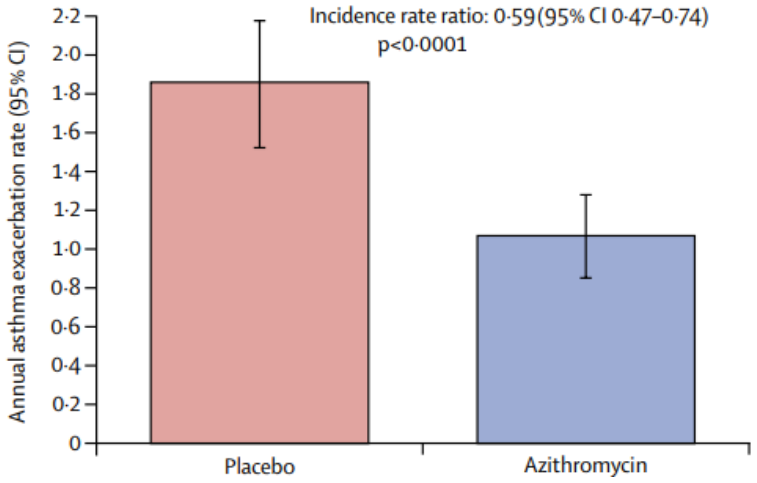
Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

- Randomised, double-blind, placebo controlled parallel group trial
- Azithromycin 500 mg or placebo three times per week for 48 weeks
- Between June 12, 2009, and Jan 31, 2015
- **Azithromycin group (n = 213) vs. Placebo group (n = 207)**





- **Benefit of add-on azithromycin in reducing asthma exacerbations in adults with uncontrolled asthma who are taking maintenance inhaled corticosteroid and a long-acting bronchodilator**
- **Azithromycin might be a useful add-on therapy in persistent asthma.**

Lancet. 2017 Aug 12;390(10095):659-668;
Chest. 2024 Aug;166(2):262-270

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

- **Objectives**
  - Evaluation of the efficacy of long-term azithromycin in achieving remission in patients with persistent uncontrolled asthma

- **335 participants**
  - Azithromycin (n = 168) vs Placebo (n = 167)

- **Inflammation subcategories**
  - Eosinophilic — sputum eosinophil count > 3% and neutrophil level < 61%
  - Neutrophilic — sputum neutrophil level > 61% and eosinophil count < 3%
  - Paucigranulocytic — sputum eosinophil count < 3% and neutrophil level < 61%

Zero exacerbations + zero oral corticosteroids during the previous 6 months at 12 months	**Primary remission (Clinical remission)**	**Secondary remission**	**Complete remission**
5-item Asthma Control Questionnaire score ≤ 1 at 12 months			
Lung function criteria - Optimization: Postbronchodilator FEV1 ≥ 80% or - Stabilization: Postbronchodilator FEV1 ≤ 5% decline from baseline			
Sputum eosinophil count < 3%			

Chest. 2024 Aug;166(2):262-270

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

TABLE 2] Remission Analysis

	Remission Criteria	Placebo		Azithromycin		*P* Value
		No.[a]	No. (%)[b]	No.[a]	No. (%)[b]	
1	ACQ-5 score ≤ 1 at 12 mo	167	87 (52.1)	168	103 (61.3)	.089
2	No exacerbations in the last 6 mo	167	116 (69.5)	168	134 (79.8)	.030
3	No maintenance OCS use in last 6 mo	167	162 (97.0)	168	163 (97.0)	.99
	Clinical remission	167	65 (38.9)	168	85 (50.6)	**.032**
4	Postbronchodilator FEV_1 ≥ 80% or ≤ 5% decline from baseline	124	109 (87.9)	126	109 (86.5)	.74
	Clinical remission plus lung function criteria	124	46 (37.1)	126	64 (50.8)	**.029**
5	Sputum eosinophil count < 3%	167	74 (44.3)	168	72 (42.9)	.79
	Complete remission	124	17 (13.7)	126	29 (23.0)	.058

Chest. 2024 Aug;166(2):262-270

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

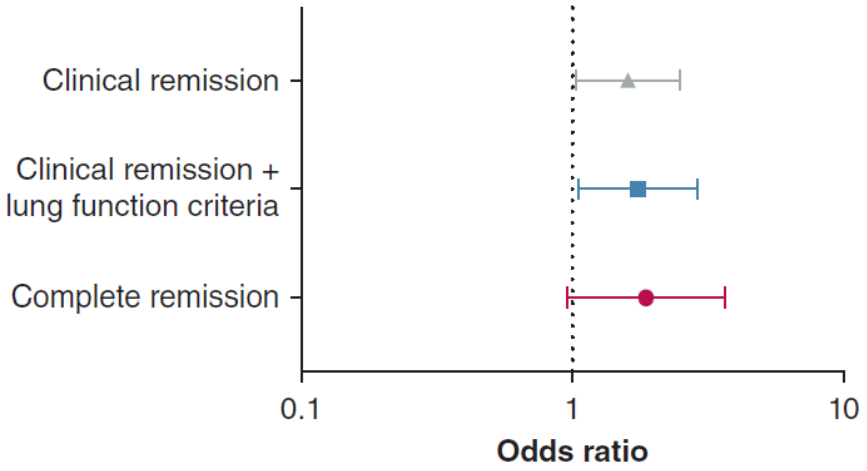
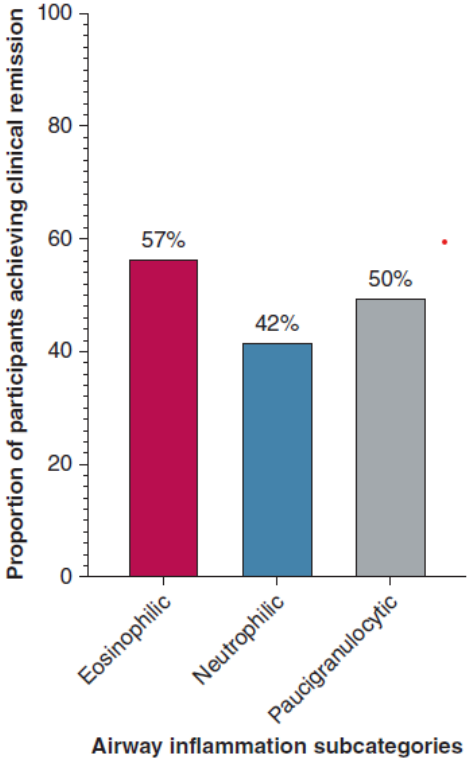


Figure 2 – *Placebo vs azithromycin: the odds of achieving various categories of remission (ORs and 95% CIs are displayed). The scale of the x axis is log10.*



Azithromycin arm compared with placebo

- Higher proportion achieved clinical remission, clinical remission,
- plus lung function criteria and complete remission

Clinical remission

- One-half of the population
- Eosinophilic (57%), Neutrophilic (42%), and Paucigranulocytic (50%)

Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma

- A Secondary Analysis of a Randomized, Double-Anonymized, Placebo-Controlled Trial

- **The first study to**
  - Evaluate the efficacy of a macrolide to induce asthma remission in patients with asthma
  - Demonstrate that remission can be achieved in noneosinophilic asthma

- **Azithromycin**
  - Low cost oral therapy
  - Concerns – potential for antimicrobial resistance and side-effects (cardiac, sensory, GI effects)

- **Weakness**
  - The post hoc nature of this analysis
  - Definition of remission

- **Adults with persistent symptomatic asthma achieved a higher remission rate when treated with azithromycin**
- **Remission on treatment may be an achievable treatment target in severe asthma**
  - **Even in noneosinophilic asthma**

Chest. 2024 Aug;166(2):262-270

DOI: 10.1111/all.16146

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

ORIGINAL ARTICLE

Asthma and Lower Airway Disease

The effects of inhaled corticosteroids on healthy airways

Emanuele Marchi[1] | Timothy S. C. Hinks[1] | Matthew Richardson[2] | Latifa Khalfaoui[2] | Fiona A. Symon[2] | Poojitha Rajasekar[3] | Rachel Clifford[3] | Beverley Hargadon[2] | Cary D. Austin[4] | Julia L. MacIsaac[5] | Michael S. Kobor[5] | Salman Siddiqui[2] | Jordan S. Mar[4] | Joseph R. Arron[4] | David F. Choy[4] | Peter Bradding[2]

The effects of inhaled corticosteroids on healthy airways

Inhaled corticosteroid (ICS)

- modulate the expression of many molecular pathways at the level of gene transcription through direct DNA-binding or via inhibition of pro-inflammatory transcription factor binding
  - upregulation of anti-inflammatory molecules, β-adrenoceptors
  - suppression of pro-inflammatory genes

In severe asthma, ICS is relatively ineffective even at high doses and the mechanisms behind corticosteroid insensitivity are poorly understood

Hypothesis	**- Gene expression data in severe asthma will be more interpretable if we can delineate the effects of high-dose ICS**
Aim	**- To understand transcriptional consequences of ICS therapy without the confounding effects due to disease-related processes**

Allergy. 2024 Jul;79(7):1831-1843

The effects of inhaled corticosteroids on healthy airways

- **Objectives**
  - To investigate the effects of ICS on gene expression in healthy airways, without confounding caused by changes in disease-related genes and disease-related alterations in ICS responsiveness

Randomized, open-labelled, bronchoscopy study

30 participants

- **(i) fluticasone propionate 500 mcg b.i.d. via Accuhaler (Diskus) daily for 4 weeks (n = 20)**
- **(ii) no treatment (observation) for 4 weeks (n = 10)**

Bronchoscopy performed at

- **Baseline prior to the start of treatment/observation**
- **The end of Week 4**

The primary endpoint

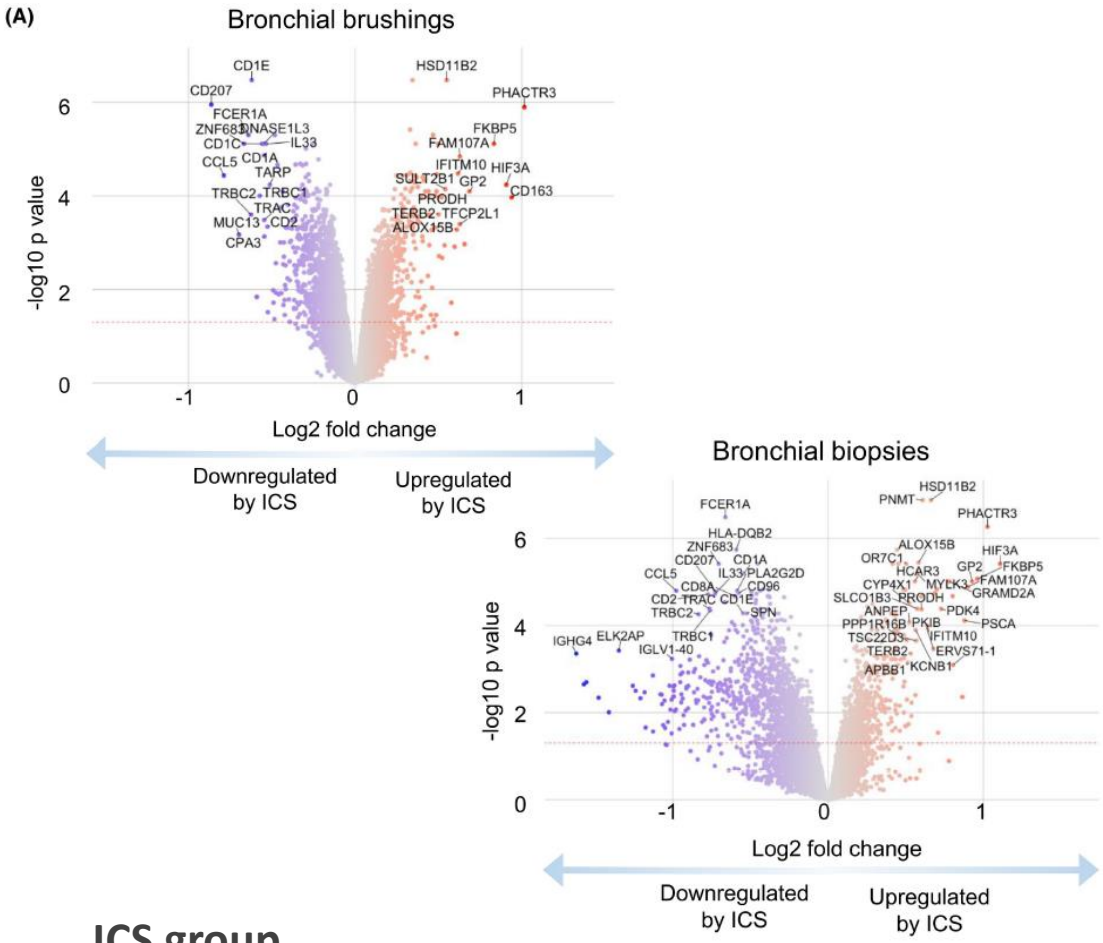
- **corticosteroid-inducible gene expression pattern in healthy airways**

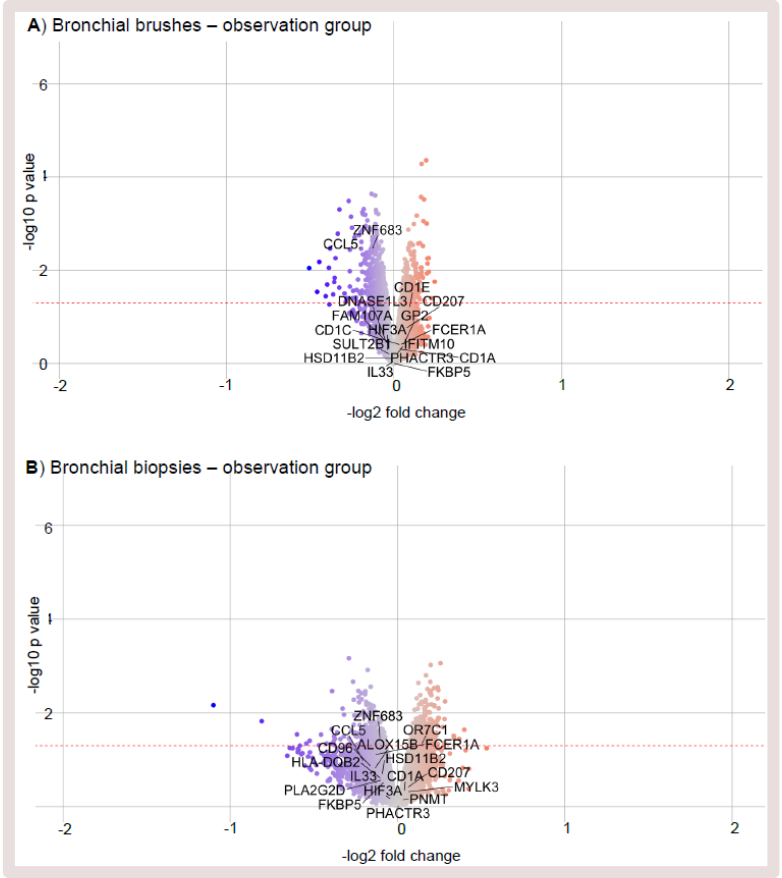
Secondary endpoints

- **the relative change from baseline in airway cellularity**

Allergy. 2024 Jul;79(7):1831-1843

The effects of inhaled corticosteroids on healthy airways





ICS group

- Upregulation - 72 genes in brushings / 53 genes in biopsies
- Downregulation- 82 genes in brushings / 416 genes in biopsies

Observation group

- No significant changes in gene expression observed

Allergy. 2024 Jul;79(7):1831-1843

The effects of inhaled corticosteroids on healthy airways

	Bronchial brushes			Bronchial biopsies					
Gene	Baseline read count	Log2 fold change	FDR *p* value	Baseline read count	Log2 fold change	FDR *p* value	Mean of FDR *p* values	Comments and aliases	Functional role
PHACTR3	497	3.59	1.43E-41	325	3.28	4.29E-38	2.14E-38	Phosphatase and Actin Regulator 3; associated with the nuclear scaffold in proliferating cells.	Cytoskeletal changes
HSD11B2	468	1.89	3.22E-41	392	1.81	9.88E-37	4.94E-37	Hydroxysteroid 11-β Dehydrogenase 2: converts cortisol to cortisone, prevents mineralocorticoid receptor activation.	Steroid metabolism
FKBP5	3336	1.88	2.17E-27	5029	1.67	3.14E-20	1.57E-20	Regulates corticosteroid sensitivity; asthma susceptibility gene.	Steroid metabolism
FAM107A	3486	1.45	6.14E-22	3657	1.60	4.02E-17	2.01E-17	Family With Sequence Similarity 107 Member A; role in Actin and microtubule organization.	Cytoskeletal changes
HIF3A	584	3.18	4.42E-17	990	2.67	5.35E-21	2.21E-17	Hypoxia Inducible Factor 3 Subunit α; canonical sensor of hypoxia.	Hypoxic sensing
MYLK3	476	1.10	1.19E-40	490	1.47	6.54E-17	3.27E-17	Myosin Light Chain Kinase 3; Immune response to CCR3 signalling in eosinophils, regulates smooth muscle contraction.	Smooth muscle/immune
GP2	341	2.48	1.26E-15	286	3.12	9.81E-28	6.29E-16	Glycoprotein 2; binds pathogens such as enterobacteria.	Innate immune
SULT2B1	1706	1.38	3.05E-17	1199	1.44	2.01E-15	1.02E-15	Hydroxysteroid Sulfotransferase 2; catalyses the sulphate conjugation hormones.	Steroid metabolism
GRAMD2A	2452	1.15	5.37E-24	2309	1.38	2.69E-15	1.35E-15	GRAM Domain Containing 2A; organization of endoplasmic reticulum-plasma membrane contact sites.	Cellular metabolism
SYT8	503	1.12	2.93E-15	470	1.13	2.37E-22	1.46E-15	Synaptotagmin 8; regulate exocytosis of hormones and in intracellular organelles.	Steroid metabolism
SLCO1B3	124	1.94	1.69E-17	111	2.27	5.11E-14	2.55E-14	Solute Carrier Organic Anion Transporter 1B3; transports conjugated steroids, leukotrienes, prostaglandins.	Steroid metabolism
HCAR2	4673	1.10	9.06E-20	3361	1.22	1.15E-13	5.73E-14	Niacin Receptor 1; receptor for niacin and mediates neutrophil apoptosis and anti-inflammatory effect of butyrate.	Anti-inflammatory
PSCA	23,905	1.21	9.32E-14	13,008	1.87	3.83E-14	6.58E-14	Prostate stem cell antigen; may regulate cell proliferation.	Cell proliferation
TFCP2L1	3228	1.38	2.76E-13	4849	1.40	1.64E-16	1.38E-13	Transcription corepressor activity and probably Wnt/β-catenin signalling.	Cell proliferation
PRODH	5268	1.20	5.53E-14	4754	1.10	8.22E-13	4.39E-13	Proline Dehydrogenase 1; catalyses proline catabolism.	Cellular metabolism
TSC22D3	7099	1.12	1.19E-17	8967	1.14	1.55E-12	7.73E-13	Glucocorticoid-Induced Leucine Zipper; mediates anti-inflammatory effects of glucocorticoids in macrophages.	Anti-inflammatory
IFITM10	1872	1.55	4.46E-22	1816	1.23	3.71E-11	1.86E-11	IFITM family functions include controlling cell proliferation and	Cell proliferation
ANPEP	2159	1.16	4.30E-14	1707	1.02	6.28E-11			
KCNB1	602	1.03	1.83E-15	662	1.28	6.63E-10			
GNMT	704	1.28	2.24E-12	548	1.10	1.97E-07			

Upregulated differentially expressed genes

- Steroid metabolism (HSD11B2, FKBP5, SULT2B1, SYT8, SLCO1B3)
- Cellular proliferation (PSCA, TFCP2L1, IFITM10, ANPEP)
- Cellular metabolism (GRAMD2A, PRODH, GNMT)
- Cytoskeletal changes (PHACTR3, FAM107A)

Allergy. 2024 Jul;79(7):1831-1843

The effects of inhaled corticosteroids on healthy airways

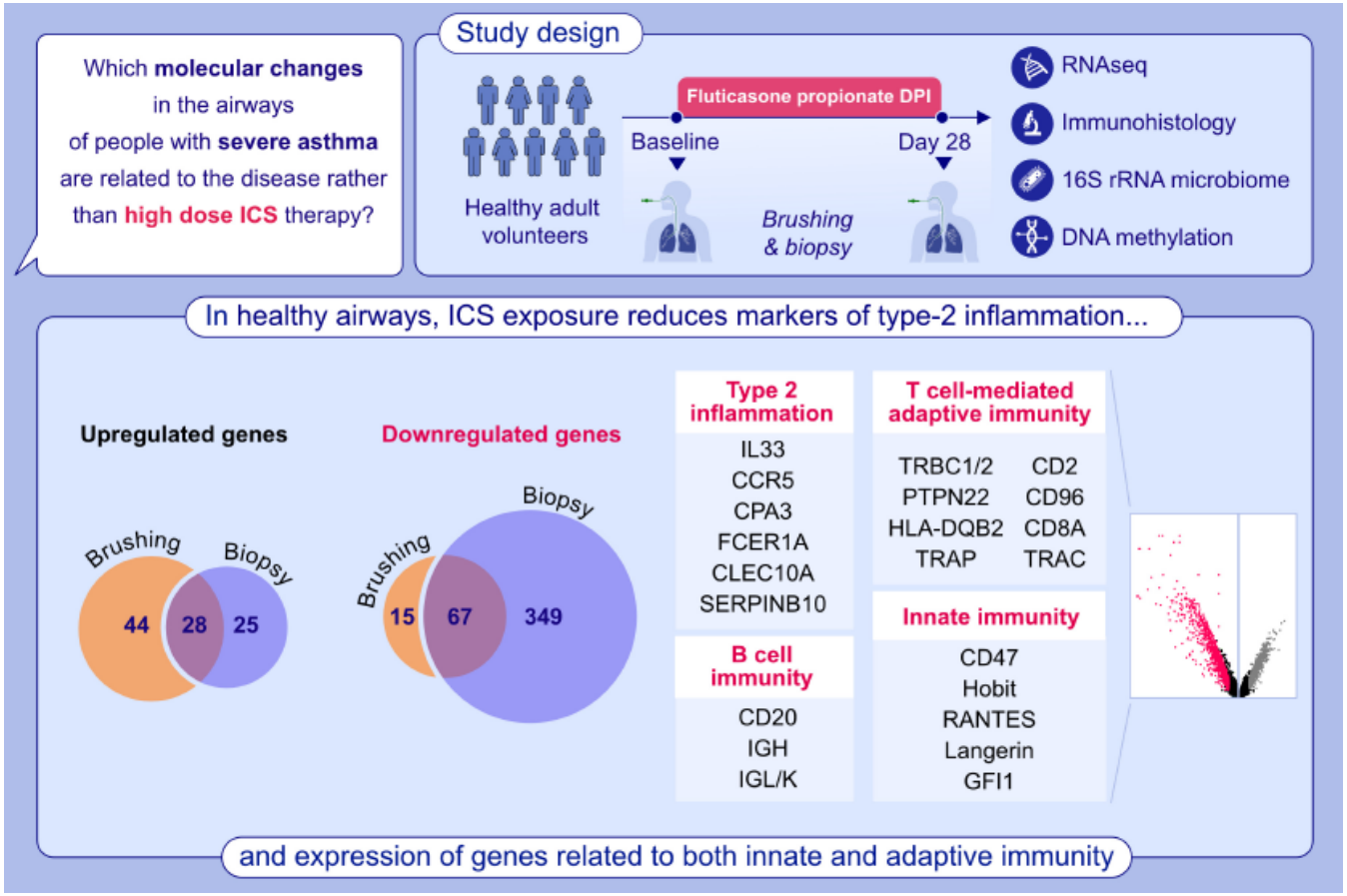
	Bronchial brushes			Bronchial biopsies					
Gene	Baseline read count	Log2 fold change	FDR *p* value	Baseline read count	Log2 fold change	FDR *p* value	Mean of FDR *p* values	Comments and aliases	Functional role
FCER1A	144	−2.78	2.15E-24	228	−2.25	6.93E-29	1.08E-24	High affinity IgE receptor; expressed on airway mast cells and dendritic cells.	Type 2 immunity
ZNF683	136	−3.33	2.31E-23	131	−3.06	1.32E-20	6.62E-21	Hobit; transcription factor promoting tissue residency in innate and adaptive lymphocytes.	Adaptive immunity
CD207	169	−3.78	3.05E-23	144	−2.90	4.24E-18	2.12E-18	Langerin; C-type lectin with mannose binding specificity, involved in nonclassical antigen-processing.	Antigen presentation
CCL5	1133	−2.39	1.21E-15	1233	−2.15	2.67E-16	7.37E-16	RANTES; chemoattractant for monocytes, memory T helper cells and eosinophils.	Adaptive immunity
IL33	3885	−1.20	2.18E-22	6985	−1.24	3.70E-15	1.85E-15	Interleukin 33; airway epithelial cell alarmin which acts via ST2 to promote type-2 responses.	Type 2 immunity
CD96	253	−1.62	1.31E-12	399	−1.64	3.49E-14	6.71E-13	TACTILE (T cell activation, increased late expression); involved in adhesion of T and NK cells to target cells.	Cell mediated immunity
TARP	100	−2.50	7.30E-15	112	−1.90	3.18E-10	1.59E-10	TCR Gamma Alternate Reading Frame Protein.	T cell adaptive immunity
TRBC1	353	−2.33	3.39E-10	540	−2.07	3.65E-13	1.70E-10	T-cell receptor Beta constant chain 1.	T cell adaptive immunity
TRBC2	463	−2.41	7.16E-10	741	−2.07	2.98E-13	3.58E-10	T-cell receptor Beta constant chain 2.	T cell adaptive immunity
PTPN22	165	−1.26	1.43E-09	243	−1.52	5.76E-11	7.42E-10	Protein Tyrosine Phosphatase Non-Receptor Type 22. Regulates Treg frequency and T-cell motility.	T cell adaptive immunity
TRAC	539	−1.92	3.37E-09	764	−1.84	4.48E-13	1.68E-09	T-cell receptor Alpha constant chain.	T cell adaptive immunity
CPA3	228	−2.26	7.00E-09	913	−1.98	1.51E-09	4.26E-09	Carboxypeptidase A3: mast cell-specific peptidase located in secretory granules.	Type 2 immunity
CD2	566	−1.87	1.23E-08	732	−1.87	8.60E-14	6.14E-09	Lymphocyte Function Antigen 2; T and NK cell marker and co-stimulatory	T cell adaptive immunity
CLEC10A	135	−1.71	1.82E-08	199					
SERPINB10	287	−1.18	1.82E-08	350					
CD8A	516	−1.55	6.40E-07	611					
GFI1	133	−1.06	1.73E-06	177					
HLA-DQB2	798	−1.01	9.52E-06	640					
CCR5	295	−1.42	9.97E-05	426					
PTPN7	248	−1.32	0.0003	312					

Downregulated differentially expressed genes

- T2-driven inflammation (FCER1A, CPA3, IL33, CLEC10A, SERPINB10, CCR5)
- T cell-mediated adaptive immunity (TARP, TRBC1, TRBC2, PTPN22, TRAC, CD2, CD8A, HLA-DQB2, CD96, PTPN7)
- Innate or adaptive immunity (ZNF683, CCL5, CD207, GFI1)
  - B-cell function and immumunoglobulin production (JCHAIN)
  - protective innate immunity (CD48, CD163)
  - mast cell proteases (TPSB1, TPSAB1, CPA3)
  - beta chain of the high affinity IgE receptor (MS4A2)
  - prostaglandin D2 synthase (PTGDS1)

Allergy. 2024 Jul;79(7):1831-1843

The effects of inhaled corticosteroids on healthy airways



- **Strengths**
  - Evaluated activity of ICS in healthy airways
  - → Removal of the confounding that might occur due to disease-related changes in gene expression or inherent ICS responsiveness
- **Limitation**
  - 4 weeks of ICS → might not fully representative of longer term therapy

Allergy. 2024 Jul;79(7):1831-1843

The effects of inhaled corticosteroids on healthy airways

- **T2-driven inflammation**
  - The most significantly downregulated
  - T2 immunity exhibits many host-protective functions, including maintaining metabolic homeostasis, suppressing excessive T1 inflammation, maintenance of barrier defense and regulation of tissue regeneration
  - the ability of ICS to downregulate this extensive set of T2-related genes implies that homeostasis in health involves a low level of T2 signalling in the airway mucosa that is very sensitive to ICS
- **Innate and adaptive immunity**
  - Known immunosuppressive effects of corticosteroids
  - Reproducible dose-dependent increased pneumonia risk in people using ICS
- **No upregulation of IL-17 signature after 4 weeks of ICS treatment**
  - IL-17-dependent signalling in asthma may be disease-dependent rather than ICS-dependent

- **The effects of inhaled corticosteroids on healthy airways are poorly defined**
- **In healthy airways, 4-week ICS exposure reduces gene expression related to**
  - **markers of type-2 inflammation**
  - **both innate and adaptive immunity**

Chest. 2024 Aug;166(2):262-270

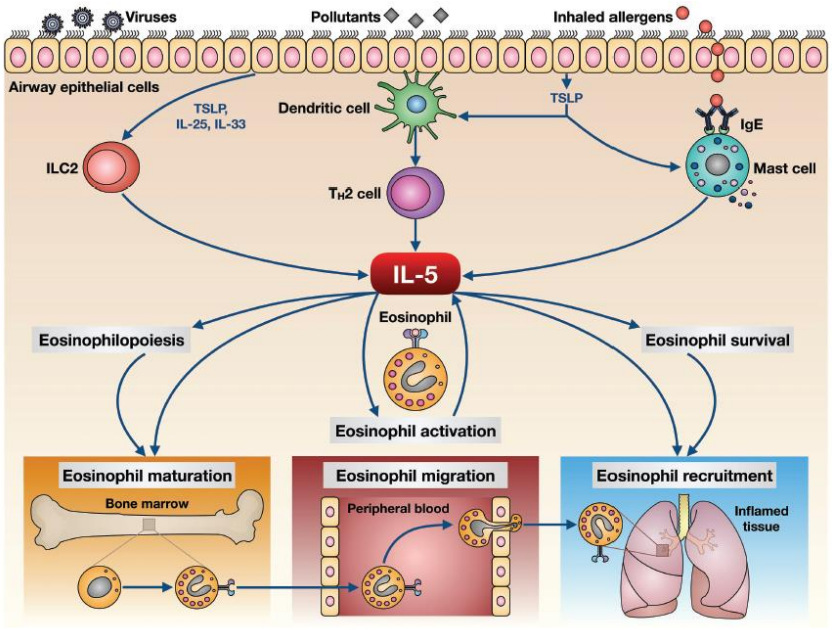
The NEW ENGLAND JOURNAL of MEDICINE

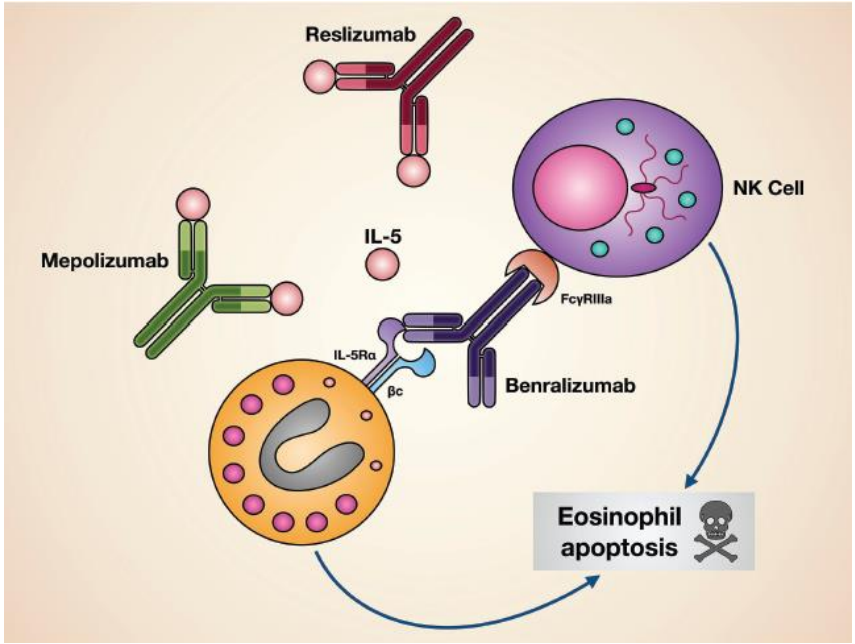
ORIGINAL ARTICLE

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

David J. Jackson, Ph.D., Michael E. Wechsler, M.D., Daniel J. Jackson, M.D., David Bernstein, M.D., Stephanie Korn, M.D., Ph.D., Paul E. Pfeffer, Ph.D., Ruchong Chen, M.D., Ph.D., Junpei Saito, M.D., Ph.D., Gustavo de Luíz Martinez, M.D., Lucyna Dymek, M.D., Ph.D., Loretta Jacques, Ph.D., Nicholas Bird, M.Sc., Stein Schalkwijk, Pharm.D., Ph.D., Douglas Smith, M.B.A., Peter Howarth, D.M., and Ian D. Pavord, D.M., F.Med.Sci., for the SWIFT-1 and SWIFT-2 Investigators*

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype





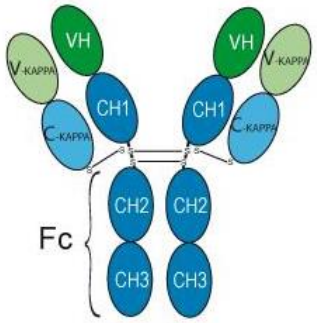
- **Interleukin-5 is responsible for the growth and differentiation, recruitment, activation, and survival of eosinophils, and influences the activity of a range of other inflammatory and structural airway cells.**

Front Physiol 2019; 10: 1514.
N Engl J Med. 2024 Sep 9.

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

Depemokimab (GSK3511294)

- ultra-long-acting biologic therapy with enhanced binding affinity for IL-5
- binds to the same epitope as mepolizumab
- 6-month dosing intervals



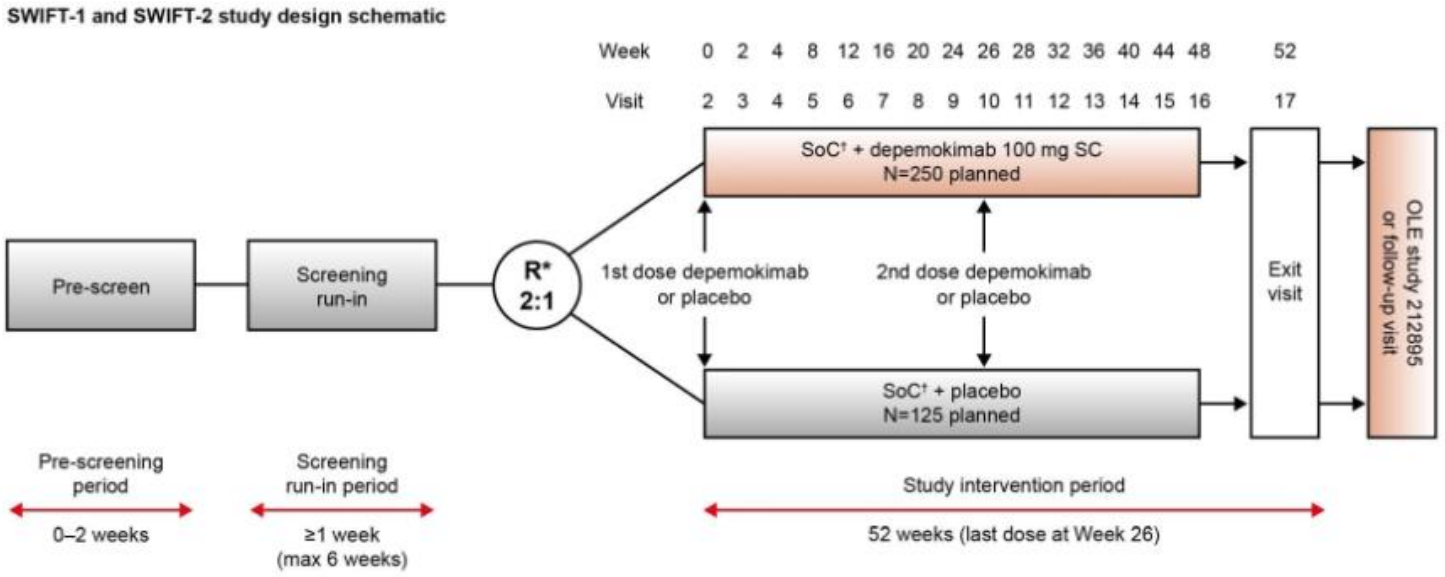
- In a cell-based in vitro assay
  - 29-fold increase in IL-5 potency versus mepolizumab
  - 2-fold reduction in clearance compared with mepolizumab
  - 30-fold greater IL-5 binding affinity than mepolizumab
  - Return to 50% of the maximal blood eosinophil suppression effect was observed at around day 169 post-dose for GSK3511294 (1 mg/kg) and day 29 for mepolizumab (1 mg/kg)

Br J Clin Pharmacol. 2022;88:702–712.
N Engl J Med. 2024 Sep 9.

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

Phase 3A SWIFT-1, SWIFT-2

- **Multicenter, randomized, double-blind, placebo-controlled trials**
- **Eligibility criteria**
  - At least 12 years, Asthma diagnosis at least 2 years earlier
  - **Blood eosinophil count**
    - at least 300 cells during the previous1 year
    - count of at least 150 cells at screening
  - Regular treatment with medium- or high-dose inhaled glucocorticoids in the previous 1 year
  - Current treatment with at least one additional controller for at least 3 months
  - **History of at least two exacerbations resulting in the administration of systemic glucocorticoids in the previous 1 year**



Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

- **Objectives**
  - to investigate the efficacy and safety of depemokimab as an adjunctive treatment to standard care for patients who had severe asthma with an eosinophilic phenotype

Phase 3A SWIFT-1, SWIFT-2

- **The primary end point**
  - **the annualized rate of exacerbations during a 52-week period**

- **The secondary end points - the change from baseline to week 52**
  - St. George's Respiratory Questionnaire
  - Asthma Control Questionnaire–5
  - Prebronchodilator FEV1
  - Scores on the asthma nightly and daily symptom diaries
  - the annualized rate of exacerbations resulting in hospitalization or an emergency department visit during a 52-week

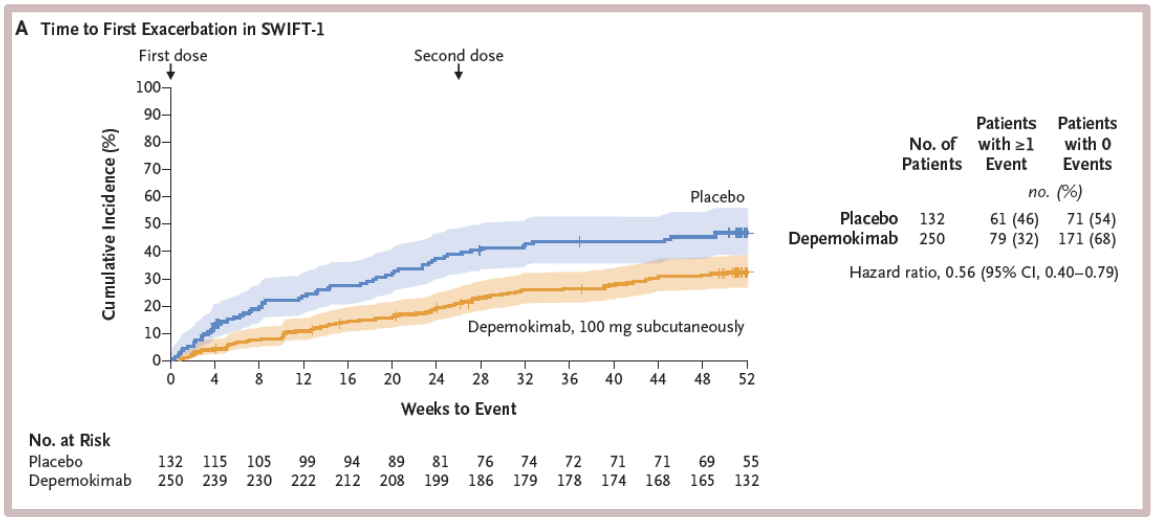
- **Safety end points**
  - Occurrence of adverse events, serious adverse events, and adverse events of special interest

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

Table 2. Summary of Primary and Secondary End Points.*

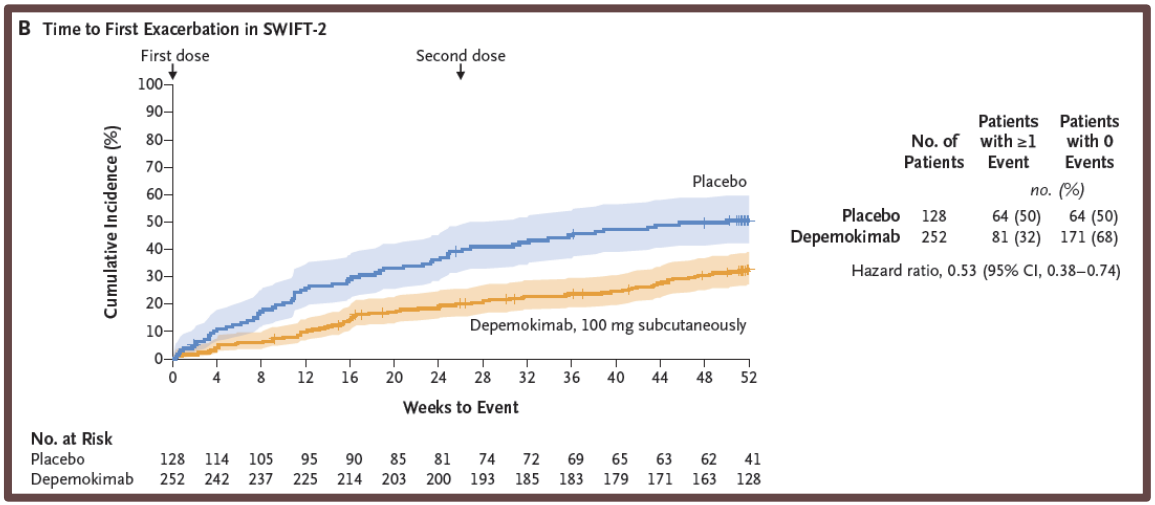
End Point	SWIFT-1			SWIFT-2		
	Depemokimab (N=250)	Placebo (N=132)	P Value†	Depemokimab (N=252)	Placebo (N=128)	P Value†
Primary end point						
Annualized rate of exacerbations at 52 wk (95% CI)	0.46 (0.36 to 0.58)	1.11 (0.86 to 1.43)	<0.001	0.56 (0.44 to 0.70)	1.08 (0.83 to 1.41)	<0.001
Rate ratio (95% CI)	0.42 (0.30 to 0.59)			0.52 (0.36 to 0.73)		
Percent between-group difference in annual rate (95% CI)	58 (41 to 70)			48 (27 to 64)		
No. of exacerbations‡	120	150		153	167	
Secondary end points						
Change from baseline in SGRQ score at 52 wk§	−13.03±1.11	−9.67±1.54	0.08	−14.80±1.04	−12.49±1.46	0.20
Treatment difference (95% CI)	−3.36 (−7.11 to 0.39)			−2.31 (−5.84 to 1.23)		
Change from baseline in ACQ-5 score at 52 wk¶	−0.82±0.07	−0.77±0.09		−0.81±0.07	−0.70±0.09	
Treatment difference (95% CI)	−0.04 (−0.27 to 0.18)			−0.11 (−0.33 to 0.11)		
Change from baseline in prebronchodilator FEV_1 at 52 wk — liter	0.16±0.03	0.16±0.04		0.24±0.03	0.18±0.04	
Treatment difference (95% CI)	−0.01 (−0.089 to 0.088)			0.06 (−0.04 to 0.15)		
Change from baseline in asthma nightly symptom diary at 52 wk‖	−1.39±0.12	−1.30±0.17		−1.18±0.09	−0.97±0.13	
Treatment difference (95% CI)	−0.09 (−0.50 to 0.31)			−0.21 (−0.52 to 0.09)		
Change from baseline in asthma daily symptom diary at 52 wk‖	−1.33±0.10	−1.25±0.14		−1.13±0.08	−0.93±0.11	
Treatment difference (95% CI)	−0.08 (−0.42 to 0.26)			−0.21 (−0.48 to 0.07)		

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype



SWIFT-1

- Depemokimab
  - 81 patients with 124 events (32%)
  - Exacerbation event over the 52-week trial of 32%
- Placebo
  - 61 patients with 151 events (46%)
  - Exacerbation event over the 52-week trial of 47%



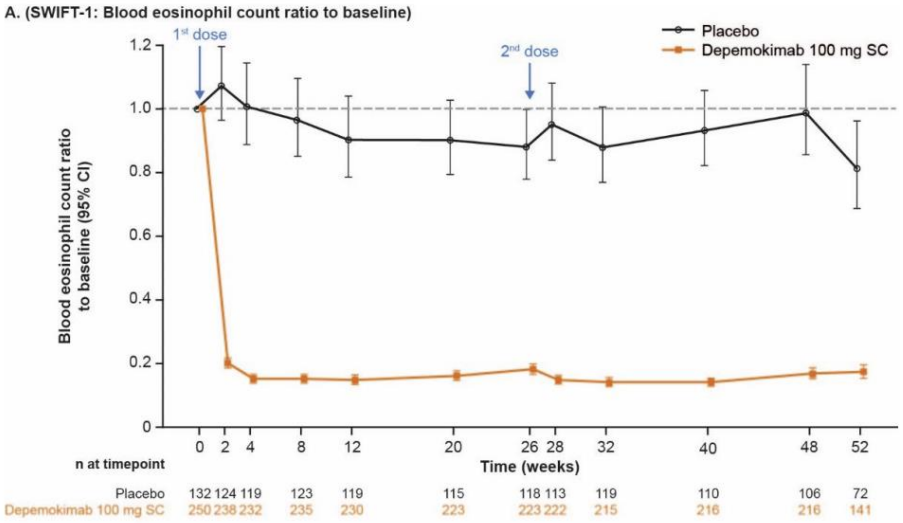
SWIFT-2

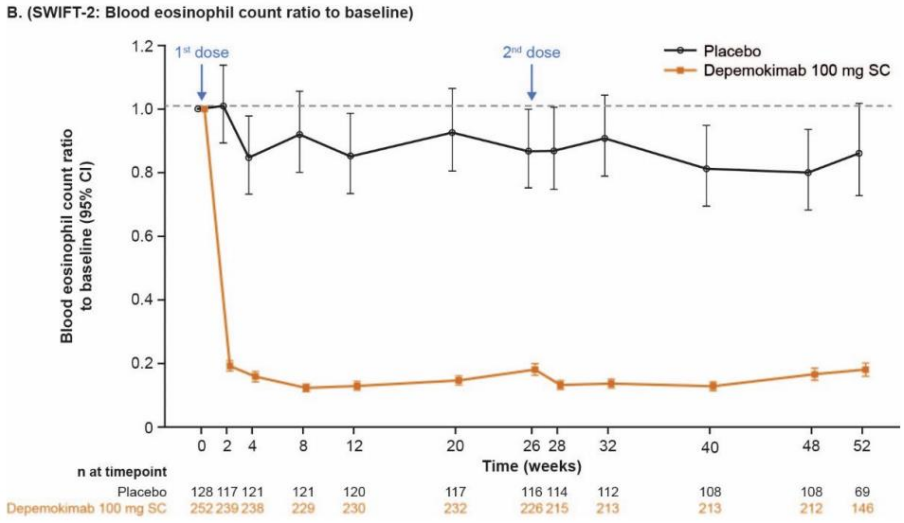
- Depemokimab
  - 81 patients with 159 events (32%)
  - Exacerbation event over the 52-week trial of 33%
- Placebo
  - 64 patients with 167 events (50%)
  - Exacerbation event over the 52-week trial of 51%

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

Table 3. Adverse Events.

Event	SWIFT-1		SWIFT-2	
	Depemokimab (N=250)	Placebo (N=132)	Depemokimab (N=251)	Placebo (N=129)*
Any adverse event — no. (%)	183 (73)	97 (73)	180 (72)	101 (78)
Related to depemokimab or placebo†	8 (3)	5 (4)	11 (4)	1 (1)
Leading to permanent discontinuation or withdrawal from trial	3 (1)	2 (2)	2 (1)	1 (1)
Leading to dose interruption or delay	1 (<1)	0	0	0
Serious adverse event — no. (%)‡	15 (6)	22 (17)	19 (8)	13 (10)





- **Rapid and sustained reductions in the blood eosinophil count, 83% and 82% reduction**

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

- **Limitation**
  - Initiated during the coronavirus disease 2019 pandemic
  - Conducted across multiple regions, with a corresponding potential for variability in standard care
  - Did not evaluate the level of exhaled nitric oxide
  - Did not collect earlier data regarding exposure to biologic therapy or the rationale for not continuing such therapy

- **Depemokimab, ultra-long-acting anti-IL-5 biologic therapy**
  - **Significant reductions in the annual rate of exacerbations**
  - **Acceptable safety profile**

- **A potential advance in patient quality of life**
  - **a reduced dosing frequency - associated with a lower patient-reported treatment burden**
  - **an expected reduction in health care use**

Original Article

Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma

Wansu Chen, PhD, MS[a], Eric J. Puttock, PhD[a], Michael Schatz, MD[b,c], William Crawford, MD[d], William M. Vollmer, PhD[e], Fagen Xie, PhD[a], Stanley Xu, PhD[a], Eva Lustigova, MPH[a], and Robert S. Zeiger, MD, PhD[b,c] *Pasadena, San Diego, and Harbor City, Calif; and Portland, Ore*

Allergy Clin Immunol Pract. 2024 Oct;12(10):2705-2716.e6

Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma

Asthma severity

- However, the retrospective definition of mild asthma as 'easy to treat' is less useful, as patients with few interval symptoms can have exacerbations triggered by external factors such as viral infections or allergen exposure, and the treatment that was historically regarded as the lowest intensity – short-acting beta$_2$ agonist (SABA) alone – actually *increases* the risk of exacerbations.
- 'Mild asthma' is a retrospective label, so it cannot be used to decide which patients are suitable to receive Step 1 or Step 2 treatment.
- In clinical practice and in the general community, the term 'mild asthma' is often used to mean infrequent or mild symptoms, and it is often assumed that these patients are not at risk and do not need ICS-containing treatment.
- For these reasons, GINA suggests that the term 'mild asthma' should generally be avoided in clinical practice if possible or, if used, qualified with a reminder that patients with infrequent symptoms can still have severe or fatal exacerbations, and that this risk is substantially reduced with ICS-containing treatment.
- GINA is continuing to engage in stakeholder discussions about the definition of mild asthma, to obtain agreement about the implications for clinical practice and clinical research of the changes in knowledge about asthma pathophysiology and treatment since the current definition of asthma severity was published.

- 50 to 75% of the asthma population, however, likely to be underestimated
- 30 to 40% of asthma exacerbations requiring emergency consultation

→ **Relatively little attention has been paid to risk factors for AAEs in this population**

GINA 2024

Allergy Clin Immunol Pract. 2024 Oct;12(10):2705-2716.e6

Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma

- **Objectives**
  - To investigate prevalence of future asthma exacerbation among patients with mild asthma and identify risk factors associated with acute asthma exacerbations among these patients

Multiethnic health plan enrollees of Kaiser Permanente Southern California (KPSC)

- Integrated health care system throughout the Southern California region
- for more than 4.8 million patients across 15 medical centers and approximately 250 medical office

199,010 patients

TABLE I. Definition of mild asthma (all criteria were met)

1	An asthma-coded visit (ICD-9: 493; ICD-10: J45) on t_0 at any care settings
2	Age 18-85 y at t_0
3	≤1 asthma controller dispensing in baseline window. Inhaled corticosteroid/long-acting β-agonist inhaler was considered as one controller.
4	≤2 canisters of short-acting β-agonist dispensed in baseline window
5	No more than 1 acute asthma exacerbation in baseline window
6	No asthma hospitalization in baseline window
7	No encounter diagnosis of chronic obstructive pulmonary disease, reactive airways dysfunction syndrome, cystic fibrosis, HIV infection, immune deficiency, active immunosuppressive treatment, transplantation of major organs, or respiratory, intrathoracic, laryngeal, or breast cancer (Table E1 lists ICD codes) in baseline window
8	Enrolled in health plan in baseline window and in 1 y after t_0

Exclusion

- More than two SABA canisters per year (equivalent to 400 or more puffs/y or 2 uses/wk)
- Two or more asthma exacerbations per year

Acute Asthma Exacerbation (AAE)

- (1) a hospitalization, emergency department (ED) visit or hospital-based observation with a principal discharge diagnosis of asthma or wheezing
- (2) other specific respiratory conditions being the principal or primary diagnosis with either (acute) exacerbation or status asthmaticus being the secondary (non-principal or primary) diagnosis in the 12 months after t0 (index date)

Allergy Clin Immunol Pract. 2024 Oct;12(10):2705-2716.e6

Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma

6.5% of AAE

Patient characteristics	Patients with future AE (n = 12,913)	Patients without future AE (n = 186,097)	Total (n = 199,010)
Age, y (mean [SD])	46.1 (17.3)	43.5 (17.8)	43.6 (17.8)
Female	69.8%	63.6%	64.0%
Body mass index			
Mean (SD)	31.9 (7.8)	30.1 (7.3)	30.2 (7.4)
Normal/underweight	18.2%	26.1%	25.6%
Overweight	27.7%	30.4%	30.3%
Obese	54.0%	43.4%	44.1%
Unknown	0.1%	0.1%	0.1%
Exercise ≥ 1 d/wk	52.3%	56.0%	55.8%

Patient characteristics	Patients with future asthma exacerbation (n = 12,913)	Patients without future asthma exacerbation (n = 186,097)	Total (n = 199,010)
Short-acting β-agonist canisters, n			
0	40.6%	51.5%	50.8%
1	45.7%	41.5%	41.8%
2	13.7%	7.0%	7.4%
Controller dispensing, n			
0	63.2%	76.3%	75.4%
1	36.8%	23.7%	24.6%
Type of controller			
None	63.2%	76.3%	75.4%
Inhaled corticosteroids	24.7%	17.0%	17.5%
Inhaled corticosteroids/long-acting β-agonists	9.2%	4.6%	4.9%
Long-acting muscarinic antagonists	0.1%	0.1%	0.1%
LM	2.8%	2.0%	2.1%

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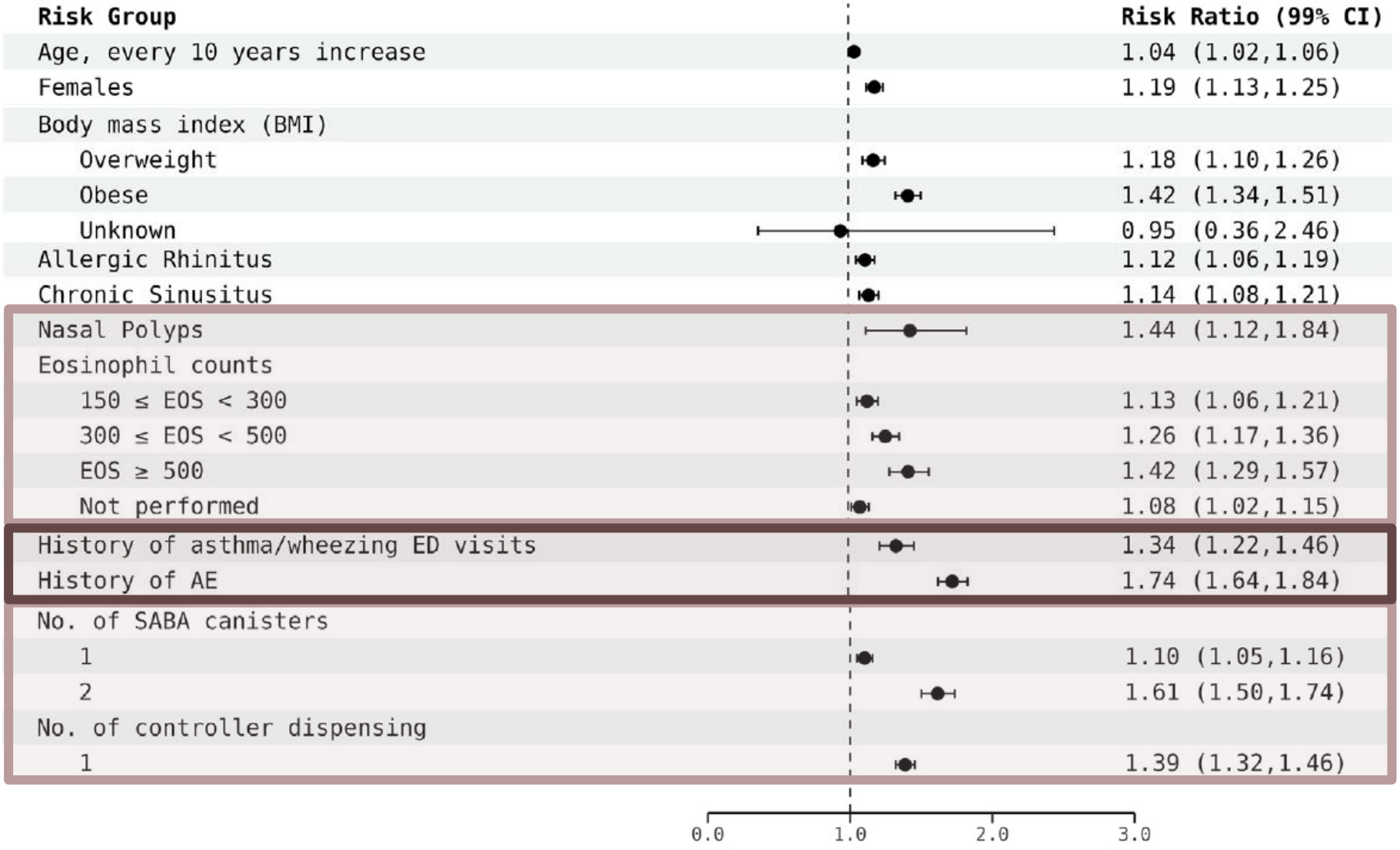
Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma



Allergy Clin Immunol Pract. 2024 Oct;12(10):2705-2716.e6

Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma

Strengths

- administrative data-driven approach, a comprehensive list of potential risk factors, and the large sample size

Limitations

- Limited potential risk factors such as asthma symptoms, activities, emotions, and patient attitudes toward asthma medications
- Cannot exclude the possibility that some of these patients had clinical characteristics consistent with more severe asthma
- Cannot determine the use of or adherence to prescribed medication
- Lung function and biological asthma markers (FeNO, IgE..) not included

- **Population-based disease management strategies for asthma should be expanded to patients with mild asthma**
- **Many of the risk factors identified for patients with mild asthma overlap with those previously reported for moderate and severe asthma**
- **Even patients with mild asthma should be assessed for asthma exacerbation risk, and effective interventions are needed for high-risk individuals**

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Take home message

- **Clinical Response and Remission in Patients With Severe Asthma Treated With Biologic Therapies**
  - Targeted biologic therapies provided an opportunity to consider remission as a new treatment goal

- **Plasma protein signatures of adult asthma**
  - Identification of plasma proteins may inform development of diagnostic biomarkers and therapeutic targets in asthma

- **Effect of Azithromycin on Asthma Remission in Adults With Persistent Uncontrolled Asthma**
  - The possibility of achieving asthma remission using long-term azithromycin and in noneosinophilic asthma.

Take home message

- **The effects of inhaled corticosteroids on healthy airways**
  - Type 2 signalling in the airway mucosa is sensitive to ICS

- **Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype**
  - Ultra-long-acting biologic therapy with enhanced binding affinity for interleukin-5, with 6 months dosing intervals.

- **Risk Factors for Acute Asthma Exacerbations in Adults With Mild Asthma**
  - Management strategies for asthma should be expanded to include people with mild asthma in addition to those with moderate to severe disease

Thank You For Your Attention

Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Baseline Variable	No Response (n = 104)	Clinical Response (Including Patients With Clinical Remission) (n = 397)	*P* Value
Medication use			
Budesonide equivalent dose, μg	1,600 (600-1,600)	1,600 (800-1,600)	.59
mOCS	65 (63)	146 (37)	< .001
mOCS dose, mg	10.00 (5.00-10.00)	10.00 (5.00-12.50)	.26
Symptom control			
ACQ-6 score	2.59 ± 1.21	2.50 ± 1.22	.59
ACQ-6 score ≤ 1.5	16 (24)	75 (25)	.86
Exacerbations in the past 12 mo	2.90 ± 2.85	4.01 ± 2.82	< .001
Inflammatory markers			
Blood eosinophils, cells × 10^9/L	0.25 (0.13-0.56)	0.39 (0.15-0.64)	.14
Blood eosinophils ≥ 0.3 10^9/L	42 (44)	222 (59)	.01

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Clinical Response and remission in Patients with Severe asthma treated with Biologic therapies

Baseline Variable	Clinical Response (Excluding Patients With Clinical Remission) (n = 300)	Clinical Remission (n = 97)	*P* Value
Female	162 (54)	37 (38)	.01
BMI, kg/m^2	28 ± 6	26 ± 4	.001
Duration of disease, y	23 ± 19	18 ± 17	.02
Duration of disease ≥ 10 y	158 (67)	41 (51)	.01
Age at asthma onset, y	33 ± 21	38 ± 21	.04
Medication use			
Budesonide equivalent dose, μg	1,600 (800-1,600)	1,600 (800-2,000)	.53
mOCS[a]	122 (41)	24 (25)	.01
Symptom control			
ACQ-6 score	2.67 ± 1.17	2.01 ± 1.26	< .001
ACQ-6 score ≤ 1.5[a]	39 (17)	36 (48)	< .001
Lung function			
FEV_1, L	2.10 (0.81)	2.78 (0.85)	< .001
FEV_1, percent predicted[a]	66 ± 21	83 ± 19	< .001
FEV_1/FVC	0.65 ± 0.16	0.68 ± 0.12	.03
Inflammatory markers			
Blood eosinophils, cells × 10^9/L	0.32 (0.13-0.58)	0.50 (0.25-0.75)	.01
Blood eosinophils ≥ 0.3 10^9/L	154 (55)	68 (72)	.001

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Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	SWIFT-1		SWIFT-2	
	Depemokimab (N=250)	Placebo (N=132)	Depemokimab (N=252)	Placebo (N=128)
Peripheral-blood eosinophil count — no. (%)				
≥150 cells/μl at screening	224 (90)	123 (93)	219 (87)	118 (92)
≥300 cells/μl in 12 mo before screening	127 (51)	61 (46)	151 (60)	66 (52)
Blood eosinophil count — cells/μl	298	310	339	330
No. of asthma exacerbations				
Leading to use of oral or systemic glucocorticoids in ≤12 mo — no.(%)				
0	1 (<1)	0	0	0
1	0	0	0	0
2	210 (84)	118 (89)	188 (75)	90 (70)
3	32 (13)	9 (7)	36 (14)	17 (13)
4	2 (1)	3 (2)	14 (6)	7 (5)
>4	5 (2)	2 (2)	14 (6)	14 (11)