Respiratory Review of 2026

Asthma

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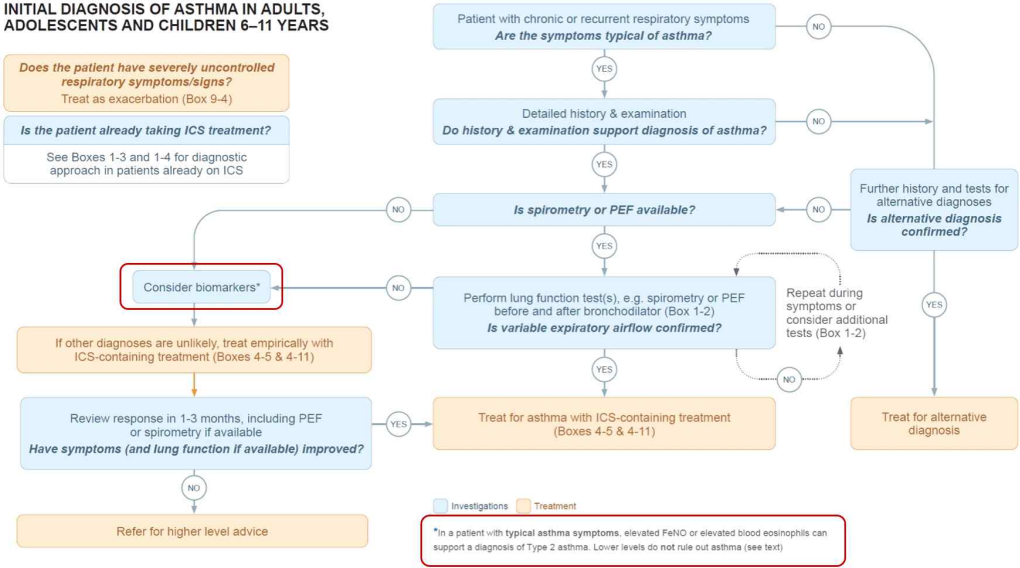
Contents

- Guideline: GINA 2025
- Risk factors & phenotype
- Clinical remission
- Treatment
  - Biologics
  - Inhaler



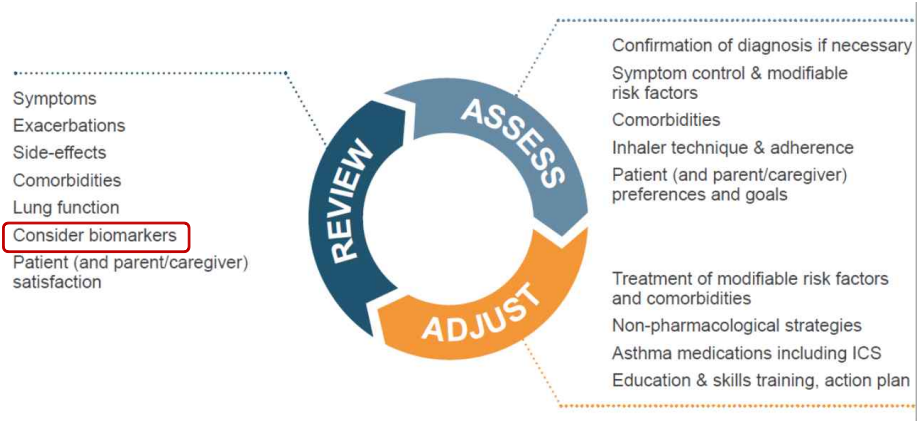
FeNO: fractional exhaled nitric oxide; ICS: inhaled corticosteroids; PEF: peak expiratory flow

Type 2 biomarkers in asthma

Box 1-2. Criteria for initial diagnosis of asthma in adults (≥18 years) and children (6–17 years)

ROLE OF TYPE 2 BIOMARKERS IN DIAGNOSIS OF ASTHMA
In patients with typical asthma symptoms, if spirometry or PEF is not available or testing is negative, elevated FeNO (adults/adolescents: >50 ppb; children: >35 ppb) or blood eosinophils above national/regional reference range can support the diagnosis of Type 2 asthma, but can also be due to non-asthma conditions. Lower levels of FeNO or blood eosinophils do **not** rule out asthma. FeNO and blood eosinophils vary substantially by sex, age and (for FeNO) device and site. Both vary by time of day: blood eosinophil count is higher in the early morning than in the afternoon, but FeNO is lower in the early morning. See Appendix A for more details about blood eosinophils and FeNO (p.216).

The asthma management cycle for personalized asthma care



GINA 2025
Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs

Symptoms
Exacerbations
Side-effects
Comorbidities
Lung function
Consider biomarkers
Patient (and parent/caregiver) satisfaction

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Patient (and parent/caregiver) preferences and goals

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications including ICS

AIR: anti-inflammatory reliever
AIR only: as-needed only ICS-formoterol
MART: maintenance-and-reliever therapy

MART with ICS-formoterol

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2
AIR-only*: low-dose ICS-formoterol as needed

STEP 3
MART* with low-dose maintenance ICS-formoterol

STEP 4
MART* with medium-dose maintenance ICS-formoterol

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider trial of high-dose maintenance ICS-formoterol. Consider anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol* **AIR**

See GINA severe asthma guide

Medium/high dose ICS-LABA

TRACK 2: Alternative CONTROLLER and RELIEVER
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1
Reliever only; if SABA, take ICS with each dose

STEP 2
Low dose maintenance ICS

STEP 3
Low dose maintenance ICS-LABA

STEP 4
Medium dose maintenance ICS-LABA

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider trial of high-dose maintenance ICS-LABA. Consider anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: as-needed ICS-SABA*, or as-needed SABA

Non-pharmacologic strategies include smoking cessation, physical activity, pulmonary rehabilitation, weight reduction, vaccinations (see text for more)
Allergen immunotherapy, e.g. HDM SLIT: consider for patients with clinically relevant sensitization and not well-controlled (but stable) asthma See text for further information and safety advice
Additional controller options (e.g., add-on LAMA at Step 4, add-on LTRA) have less evidence for efficacy or for safety than Tracks 1 or 2 (see text). Maintenance OCS should only ever be used as last resort.

AIR: anti-inflammatory reliever; HDM: house dust mite; ICS: inhaled corticosteroid; Ig: immunoglobulin; IL: interleukin; LABA: long-acting beta$_2$-agonist; LAMA: long-acting muscarinic antagonist; LTRA: leukotriene receptor antagonist; MART: maintenance-and-reliever therapy with ICS-formoterol; OCS: oral corticosteroid; SABA: short-acting beta$_2$-agonist; SLIT: subcutaneous immunotherapy; TSLP: thymic stromal lymphopoietin

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- **Risk factors & phenotype**
  - ✓ **Small airway dysfunction (SAD)**
  - ✓ **Mucus plugs**
- Clinical remission
- Treatment
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  - Inhaler

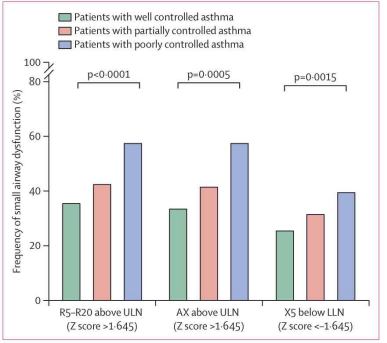
Assessment of the role of small airway dysfunction in relation to exacerbation risk in patients with well controlled asthma (ATLANTIS): an observational study

Stanley P Galant, Pauline J M Kuks*, Tessa M Kole, Monica Kraft, Salman Siddiqui, Leonardo M Fabbri, Bianca Beghé, Klaus F Rabe, Alberto Papi, Christopher E Brightling, Dave Singh, Janwillem W H Kocks, Laura Franzini, Judith M Vonk, Huib A M Kerstjens, Irene H Heijink, Simon D Pouwels, Dirk-Jan Slebos, Maarten van den Berge*

- Small airways in asthma
  - Major sites of airway inflammation and obstruction
- Impulse Oscillometry (IOS)
  - Non-invasive tool to assess small airway function
  - R5–R20, AX, X5
- Multinational, prospective observational cohort (ATLANTIS)
- Study aim
  - To determine whether small airway dysfunction predicts future exacerbations in well-controlled asthma.

Lancet Respir Med. 2025 Nov;13(11):990-1000.

Small airway dysfunction across different asthma control levels



	Patients with well controlled asthma (n=384)	Patients with partially controlled asthma (n=210)	Patients with poorly controlled asthma (n=178)	p value
(Continued from previous page)				
Number of patients with small airway dysfunction				
Defined by R5–20¶	108/304 (36%)*	76/177 (43%)*	75/130 (58%)†‡	<0·0001
Defined by AX‖	89/261(34%)*	63/150 (42%)*	65/113 (58%)†‡	0·0005
Defined by X5**	79/303 (26%)*	54/170 (32%)*	49/122 (40%)†‡	0·0015

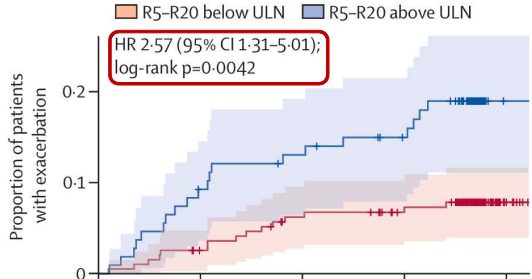
Lancet Respir Med. 2025 Nov;13(11):990-1000.

Univariable and multivariable Cox regression analysis of the association between small airway disease and exacerbations

	Univariable analysis		Multivariable analysis*	
	HR (95% CI)	p value	HR (95% CI)	p value
Small airway dysfunction				
Defined by R5–R20†	2·57 (1·31–5·01)	0·0042	2·26 (1·05–4·85)	0·038
Defined by AX‡	1·75 (0·85–3·59)	0·12	2·07 (0·91–4·70)	0·082
Defined by X5§	0·78 (0·34–1·81)	0·56	0·86 (0·33–2·21)	0·75
Severe small airway dysfunction				
Defined by R5–R20¶	2·47 (1·24–4·90)	0·0076	2·80 (1·26–6·26)	0·012
Defined by AX‖	1·96 (0·94–4·07)	0·065	2·51 (1·04–6·04)	0·041
Defined by X5**	0·96 (0·34–2·75)	0·95	0·99 (0·29–3·32)	0·98

Lancet Respir Med. 2025 Nov;13(11):990-1000.

Asthma exacerbations during 1 year of follow-up among patients with well controlled asthma



Number at risk (censored)					
R5–R20 below ULN	196	187	177	169	11
	(0)	(4)	(7)	(14)	(171)
R5–R20 above ULN	108	96	91	85	2
	(0)	(2)	(3)	(7)	(86)

◆ **R5–R20 defined SAD independently predicted future exacerbations.**

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- Small airway dysfunction is common even in well-controlled asthma.
- R5–R20 is a strong predictor of future exacerbation risk.
- Oscillometry may complement spirometry in asthma evaluation.

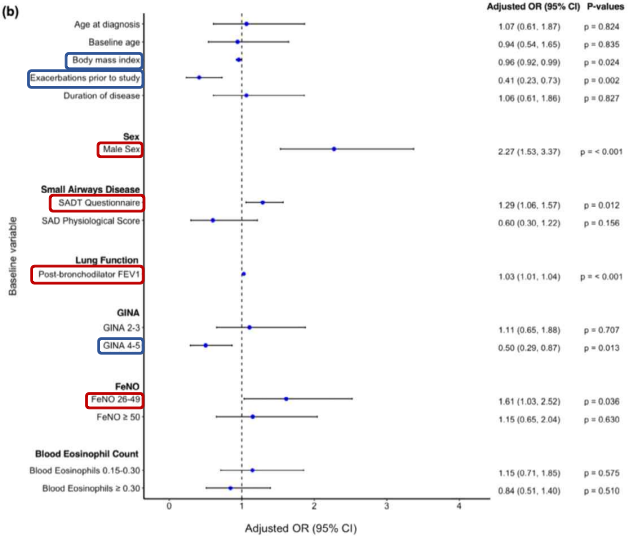
Lancet Respir Med. 2025 Nov;13(11):990-1000.

Small Airways Dysfunction and Remission in Adults With Asthma: A Longitudinal Exploratory Analysis of the AssessmenT of smalL Airways involvemeNT In aSthma (ATLANTIS) Study

Akshi Kumar[1] | Rory Chan[2] | Nazanin Zounemat-Kermani[1,3] | Eleanor Quek[1] | Ian M. Adcock[1] | Bianca Beghe[4] | Christopher Brightling[5] | Dave Singh[6] | Janwillem Kocks[7] | Alberto Papi[8] | Klaus F. Rabe[9,10,11] | Ulrica Scaffidi-Argentina[12] | Maarten van den Berge[13] | Monica Kraft[14] | Salman Siddiqui[1]

- Small airways involvement is common across all asthma severities and is associated with exacerbations, poor control, and disease severity.
- Study aim
  - To evaluate whether small airways dysfunction predicts clinical remission in asthma.
- Study design
  - Post-hoc analysis of the ATLANTIS cohort
  - Multinational prospective study
  - 684 adult asthma patients

Allergy. 2026 Feb 18.



◆ **↑ Likelihood of remission**

- Male sex
- **Higher SADT score**
  - **Fewer small airway sx. (less SAD)**
- Better baseline lung function
- Moderate FeNO levels

◆ **↓ Likelihood of remission**

- Frequent prior exacerbations
- Severe asthma
- Higher BMI

Allergy. 2026 Feb 18.

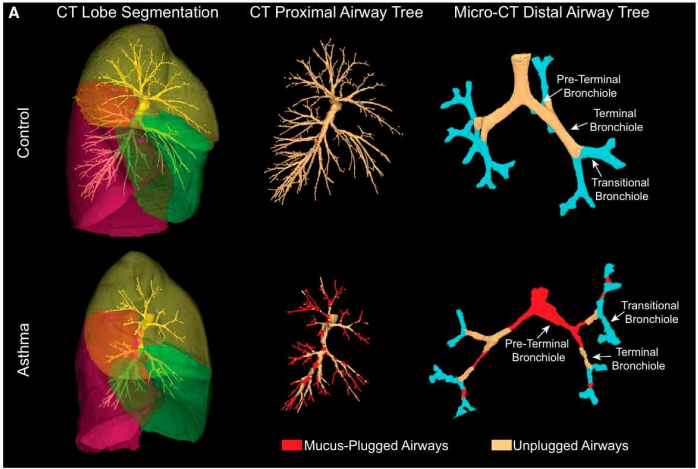
Mucus Plugs Correlate with Small Airway Remodeling in Asthma

A Case–Control Study

Aileen Hsieh[1,2], Dragoş M. Vasilescu[1,2], Jenna Barker-Mulleder[1,2], May Fouadi[1,2], Stacey Ledoux[1,2], David J. Erle[3], Maude A. Liegeois[4], John V. Fahy[4,5], and Tillie-Louise Hackett[1,2]

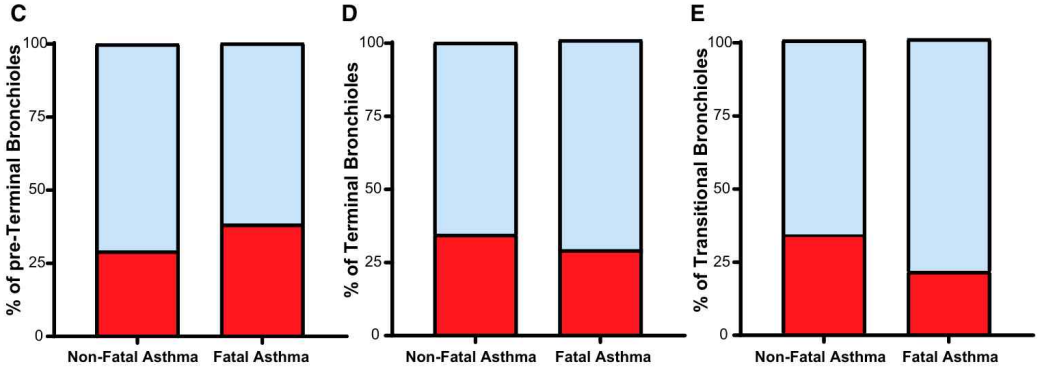
- Mucus plugs visible on HRCT in large airways are associated with asthma severity, airflow limitation, and worse clinical outcomes.
- Distal small airways (<2 mm) cannot be visualized by conventional CT.
- It remains unclear whether mucus plugs are also present in small airways, which are a major site of airflow resistance in asthma.
- Study aim
  - To determine the prevalence of mucus plugs in distal small airways & their association with airway remodeling in asthma.
- Study design
  - Case–control study using micro-CT (7 µm resolution)
  - 239 Lung tissue samples: Controls (n = 12), Non-fatal asthma (n = 5), Fatal asthma (n = 11)

Am J Respir Crit Care Med. 2025 Aug 22.



Mucus plugs are present in large and small airways in the asthmatic lung.

Am J Respir Crit Care Med. 2025 Aug 22.

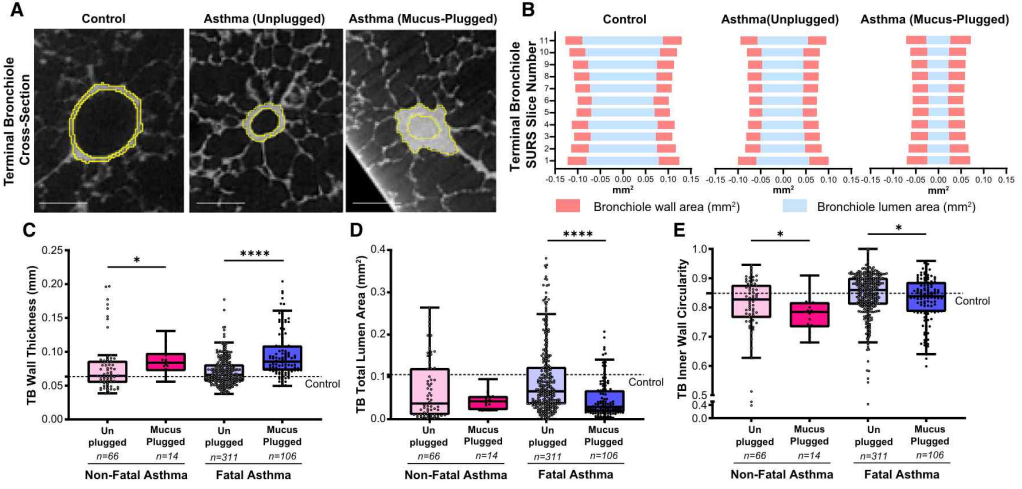


◆ **Mucus plugs are common in distal small airways**

- Prevalence in asthma lungs
  - Preterminal bronchioles: 30–38%
  - Terminal bronchioles: 29–34%
  - Transitional bronchioles: 21–33%

Am J Respir Crit Care Med. 2025 Aug 22.

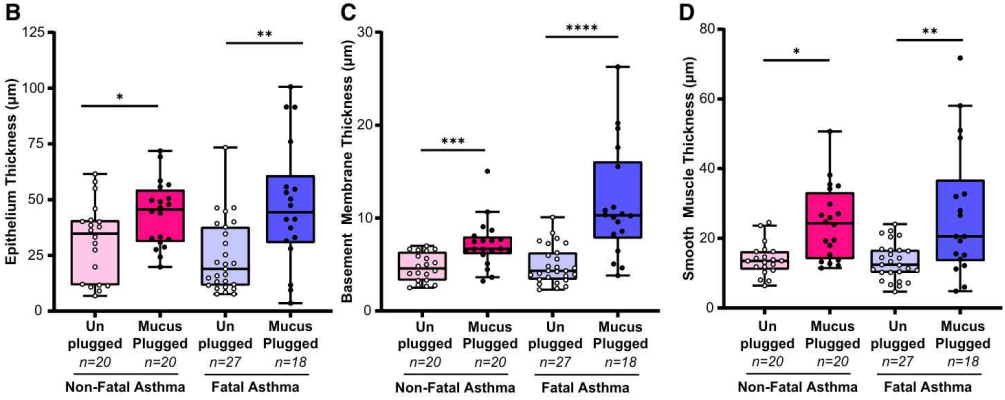
Mucus plugging correlates with terminal bronchiole (TB) wall remodeling in nonfatal and fatal asthma.



◆ **Mucus-plugged TB: ↑ Wall thickness, ↓ Luminal area, ↓ Circularity (irregular shape)**

Am J Respir Crit Care Med. 2025 Aug 22.

Mucus-plugged small airways are associated with a thickened airway epithelium, basement membrane, and smooth muscle.



◆ **Mucus-plugged small airway: ↑ Epithelium thickness, ↑ Basement membrane thickness, ↑ Smooth muscle thickness**

Am J Respir Crit Care Med. 2025 Aug 22.

Mucus Plugs Correlate with Small Airway Remodeling in Asthma

A Case–Control Study

Aileen Hsieh[1,2], Dragoş M. Vasilescu[1,2], Jenna Barker-Mulleder[1,2], May Fouadi[1,2], Stacey Ledoux[1,2], David J. Erle[3], Maude A. Liegeois[4], John V. Fahy[4,5], and Tillie-Louise Hackett[1,2]

- Mucus-plugged airways
  - ↑ epithelial thickness
  - ↑ basement membrane thickness
  - ↑ smooth muscle thickness
  - ↓ airway lumen area

  ➞ Indicating significant airway remodeling

Am J Respir Crit Care Med. 2025 Aug 22.

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Pro: Clinical remission in asthma – implications for asthma management

Stefania Principe[1] and Nizar N. Jarjour[2]

- Clinical remission in asthma: a new treatment goal
  - The introduction of biologic therapies has made clinical remission an achievable target in severe asthma.
  - Remission reflects sustained disease stability, including:
    - High asthma control
    - No exacerbations
    - Stable or normal lung function

- Shifting the goal from reactive symptom management → proactive long-term disease control.

Eur Respir Rev. 2025 Apr 2;34(176):240181.

Definition of asthma remission

- Most proposed definitions include:
  - Absence of asthma symptoms
  - No exacerbations
  - Stable or normalized lung function
  - No systemic corticosteroid use
  - Maintained for ≥12 months

- Additional components sometimes included:
  - Reduced airway inflammation (e.g., FeNO, eosinophils)
  - Minimal reliever use
  - Agreement between patient and clinician on remission status

- However, a universal definition of remission has not yet been established.

Eur Respir Rev. 2025 Apr 2;34(176):240181.

TABLE 1 Summary of the current statements (English language available)

First author [ref.]	Outcomes	Main results	Limitations
Menzies-Gow [5]	ACT score ⩾20, ACQ score ⩽0.75, lung function optimisation/stabilisation, patient/provider agreement, no systemic corticosteroids	Provided a definition of asthma remission Identified potential components of remission as a target in asthma	Framework should be tested in prospective studies Small group of experts
Blaiss [11] **ACAAI**	No exacerbations, no absenteeism from work/school, stable pulmonary function, continued low-to-medium dose ICS, symptom control (ACT score >20, AirQ score <2, ACQ score <0.75), minimal reliever use	Identified key criteria of asthma clinical remission on treatment	Lack of consensus on some criteria Limited data
Canonica [12] **SANI**	Absence of symptoms, absence of exacerbations, stable lung function, no OCS, partial clinical remission (no need for OCS, two of three primary criteria)	Defined clinical and partial remission in severe asthma	No consensus on reduction of ICS Specific value for lung function improvement
Álvarez-Gutiérrez [14] **SEPAR**	ACT score ⩾20, no rescue medication, normal lung function for ⩾12 months, F_{ENO} <40 ppb, sputum eosinophils <2%, no nasal symptoms (SNOT-22 score <30), normal nasal endoscopy for CRSwNP	Established consensus on clinical, complete remission and remission in asthma with CRSwNP	Potential bias due to respiratory specialists Geographical constraint as Spain-specific

ACT: Asthma Control Test; ACQ: Asthma Control Questionnaire; CRSwNP: chronic rhinosinusitis with nasal polyps; F_{ENO}: fraction exhaled nitric oxide; ICS: inhaled corticosteroids; OCS: oral corticosteroids; SNOT: Sinonasal Outcome Test.

Biologics and the potential for remission

- Real-world studies and clinical trial analyses
  - Approximately 20–40% of severe asthma patients may achieve clinical remission with biologic therapy.
- Predictors of remission
  - Shorter asthma duration
  - Higher baseline eosinophils
  - Better baseline lung function
  - Lower BMI
- Asthma remission is emerging as a realistic and meaningful treatment goal in the biologic era.

Eur Respir Rev. 2025 Apr 2;34(176):240181.

Current data on biologics: Evaluating clinical remission in asthma

Ian Pavord, MA, DM, FRCP, FERS, FMedSci,[a] Rohit K. Katial, MD,[b] David J. Jackson, FRCP, MSc, PhD,[c] Linda Rogers, MD,[d] Flavia Cecilia Lega Hoyte, MD,[b] Josef Smolen, MD,[e] Michael E. Wechsler, MD, MMSc,[b] Praveen Akuthota, MD,[f] and Daniel J. Jackson, MD[g]

Denver, Colo; La Jolla, Calif; London and Oxford, United Kingdom; Madison, Wis; New York, NY; and Vienna, Austria

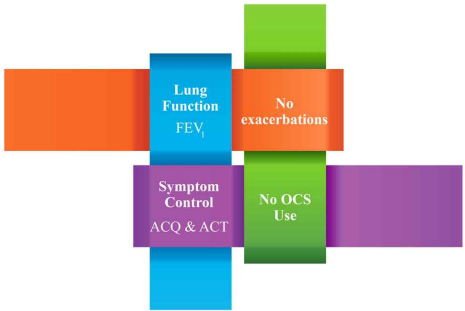

FIG 1. Four-component definition of clinical remission used in most studies of biologic therapy in severe asthma. *ACT*, Asthma Control Test.

Current studies use heterogeneous definitions of remission, which complicates comparison across trials.

J Allergy Clin Immunol. 2025 Sep;156(3S):S15-S19.

Real-world studies

TABLE I. Remission criteria and prevalence in real-world studies of biologic therapy for severe asthma

Biologic: Study	Remission criteria: Lung function	Remission criteria: Symptom control	Remission criteria: No exacerbations	Remission criteria: No OCS	Time point (receiving biologic therapy)	Prevalence of clinical remission
Any biologic: Danish Severe Asthma Register[6]	$FEV_1 > 80\%$	ACQ-6 ≤ 1.5	X	X	12 months	19% (97/501)
Mepolizumab: REDES[7]	—	ACT ≥ 20	X	X	12 months	37% (96/260)
	Post-BD $FEV_1 > 80\%$	ACT ≥ 20	X	X	12 months	30% (43/144)
Mepolizumab: REALITI-A[8]	—	ACQ-5 < 1.5	X	X	12 months 24 months	29% (61/214) 33% (60/184)
Any biologic: UK Severe Asthma Registry[9]	FEV_1 > LLN or no more than 100 mL less than baseline	ACQ-5 < 1.5		X	1.1 years (median)	18.3% (152/830)
Benralizumab: XALOC-1[10]	—	ACT ≥ 16 ACQ-6 < 1.5	X	X	12 months	43% (133/307)
Any biologic: German Asthma Net Severe Asthma Registry Cohort[11]	—	ACT ≥ 20	X	X	12 months	37.6% (79/210)
	FEV_1 increase ≥ 100 mL	ACT ≥ 20	X	X	12 months	32.1% (68/210)

- Rates of clinical asthma remission in patients treated with a biologic have ranged from **19% to 43%** in retrospective real-world studies.

J Allergy Clin Immunol. 2025 Sep;156(3S):S15-S19.

Clinical trials

TABLE II. Remission criteria and prevalence in clinical trials of biologic therapy for severe asthma

Biologic: Study	Remission criteria				Time point (receiving biologic therapy)	Prevalence of clinical remission	
	Lung function	Symptom control	No exacerbations	OCS receipt		Placebo	Biologic
Benralizumab: SIROCCO/CALIMA[12]	Pre-BD FEV_1 increase ≥ 100 mL	ACQ-6 ≤ 0.75	X	No	6 months	11% (71/643)	14.8% (90/609)
					12 months	7.7% (48/620)	14.5% (85/586)
	Pre-BD FEV_1 increase ≥ 100 mL	ACQ-6 < 1.5	X	No	6 months	19% (122/643)	26.3% (160/609)
					12 months	14.8% (92/620)	23.9% (140/586)
Dupilumab: QUEST and TRAVERSE[13]	Post-BD FEV_1 ≥ 80% or pre-BD FEV_1 increase ≥ 100 mL	ACQ-5 < 1.5	X	No	12 months	20.4% (111/544)	35.0% (462/1279)
					24 months	NA	36.1% (462/1279)
Tezepelumab: NAVIGATOR[14]	Pre-BD FEV_1 > 80% or pre-BD FEV_1 > 20% from BL ● Much or very much improved (CGI-C score) ● No or minimal symptoms (PGI-S score)	ACQ-6 ≤ 0.75	X	No	12 months	4.4% (17/386)	12.7% (53/417)
Tezepelumab: DESTINATION[15]	FEV_1 > 95% of BL at year's end	ACQ-6 ≤ 1.5	X	No	12 months	21.9% (41/187)	28.5% (108/379)
					24 months	26.7% (50/187)	33.5% (127/379)

- Rates of clinical asthma remission in patients treated with a biologic have ranged from **13% to 35%** in post hoc analyses of randomized controlled studies.

J Allergy Clin Immunol. 2025 Sep;156(3S):S15-S19.

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Biologic Management in Severe Asthma for Adults

An American College of Chest Physicians Clinical Practice Guideline

Amber J. Oberle, MD; Farrukh Abbas, MD; Muhammad Adrish, MD, MBA, FCCM, FCCP; Ioana Agache, MD, PhD; Megan Conroy, MD, MAEd, FCCP; Angel O. Coz Yataco, MD; Frederic F. Little, MD; Manoj J. Mammen, MD; Mahesh Padukudru Anand, MBBS, DTCD, DNB, FRCP; Raju Reddy, MD; Neha Solanki, MD; and Fernando Holguin, MD, MPH

- Severe asthma represents a high-burden phenotype with frequent exacerbations and OCS use.
- Multiple biologics are available, but direct comparative data are limited.
- This guideline provides PICO-based recommendations for biologic selection and switching (after 4–6 months).
- Key considerations: OCS dependency, exacerbation risk, lung function, biomarkers (eosinophils, FeNO), and comorbidities.
- Recommendations are conditional and emphasize individualized, shared decision-making.

Chest. 2026 Feb;169(2):336-348.

Pathophysiology of asthma, biologics, and associated therapeutic targets

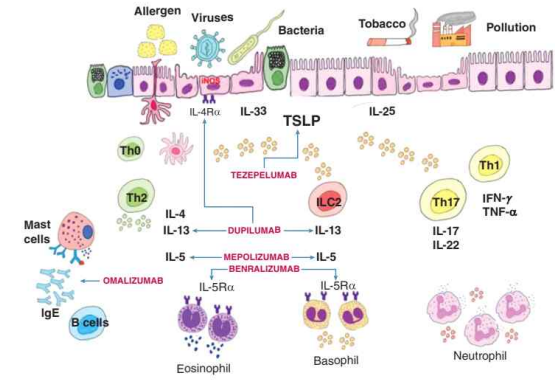
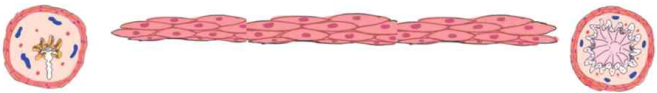


TABLE 1] List of Biologics in Asthma

Drug Target	Drug Name(s)
Anti-IgE	Omalizumab
Anti-IL5/5Rα	Mepolizumab, reslizumab, benralizumab (anti-IL5Rα)
Anti-IL4Rα/13	Dupilumab
Anti-TSLP	Tezepelumab

TSLP = thymic stromal lymphopoietin.

- **Anti-IgE:** Allergic asthma phenotype
- **Anti-IL5/5Rα:** Eosinophilic asthma, OCS-dependent asthma
- **Anti-IL4Rα/13:** Broad T2 inflammation, OCS-dependent asthma, FeNO-responsive
- **Anti-TSLP:** Effective in both T2-high & T2-low asthma



Chest. 2026 Feb;169(2):336-348.

TABLE 2] Summary of PICO Questions and Recommendations

PICO	Question	Recommendation	Strength of Recommendation	Supporting Evidence
1	Should adult patients aged ≥ 18 y with moderate to severe allergic asthma and history of ≥ 1 exacerbation per year requiring oral corticosteroids be treated with dupilumab or omalizumab?	In adult patients with moderate to severe allergic asthma and history of ≥ 1 exacerbation per year requiring oral corticosteroids, the panel suggests either omalizumab or dupilumab. A. For patients with frequent exacerbations (≥ 2 per year) or any severe exacerbation requiring hospitalization, the panel suggests dupilumab over omalizumab. B. For patients with more severe impairments in quality of life, (and < 2 exacerbations per year), the panel suggests omalizumab over dupilumab. C. For patients with a greater impairment in lung function (FEV_1 < 70% predicted), the panel suggests dupilumab over omalizumab.	Conditional	Very low certainty
2	Should adult patients with steroid dependent asthma be treated with anti-IL5/5Rα or dupilumab?	In adult patients with severe asthma who are steroid dependent, the panel suggests either anti-IL5/5Rα therapy or dupilumab.	Conditional	Very low certainty
3	Should adult patients with steroid dependent asthma be treated with dupilumab or tezepelumab?	In adult patients with severe asthma who are steroid dependent, the panel suggests dupilumab over tezepelumab.	Conditional	Very low certainty
4	Should adult patients with moderate to severe asthma who have not demonstrated a clinical response to omalizumab after 4-6 mo be treated with anti-IL5/5Rα or dupilumab?	In adult patients with moderate to severe asthma who have not demonstrated a clinical response to omalizumab after 4-6 mo, the panel suggests either anti-IL5/5Rα therapy or dupilumab.	Conditional	Very low certainty
5	Should adult patients with severe asthma who have not demonstrated a clinical response to anti-IL5/5Rα after 4-6 mo be treated with dupilumab or tezepelumab?	In adult patients with severe asthma who have not demonstrated a clinical response to anti-IL5/5Rα therapy after 4-6 mo, the panel suggests either dupilumab or tezepelumab. A. For patients who are steroid dependent, the panel suggests dupilumab over tezepelumab.	Conditional	Very low certainty
6	Should adult patients with severe asthma who have not demonstrated a clinical response to dupilumab after 4-6 mo be treated with anti IL5/5Rα or tezepelumab?	In adult patients with severe asthma who have not demonstrated a clinical response to dupilumab after 4-6 mo, the panels suggests either anti-IL5/5Rα or tezepelumab. A. For patients who are steroid dependent, the panel suggests anti-IL5/5Rα.	Conditional	Very low certainty
7	Should F_{ENO} be used for guiding changes in therapy to dupilumab in adult patients with severe asthma on anti-IL5/5R who have not demonstrated a clinical response by 4-6 mo?	In adult patients with severe asthma on anti-IL5/5Rα who have not demonstrated a clinical response by 4-6 mo, the panel suggests the use of post treatment F_{ENO} ≥ 25 ppb for advising changes in therapy to dupilumab.	Conditional	Very low

Chest. 2026 Feb;169(2):336-348.

PICO Questions and Recommendations

- **PICO 1**
  - Question 1: Should adult patients aged ≥ 18 years with **moderate to severe allergic asthma and history of ≥ 1 exacerbation per year requiring oral corticosteroids** be treated with **dupilumab or omalizumab**?
  - CHEST Recommendation: In adult patients with moderate to severe allergic asthma and history of ≥ 1 exacerbation per year requiring oral corticosteroids, the panel suggests **either omalizumab or dupilumab** (Conditional Recommendation, Very Low Certainty of Evidence).
    - A. For patients with **frequent exacerbations (≥ 2 per year) or any severe exacerbation requiring hospitalization**, the panel suggests **dupilumab** over omalizumab (Conditional Recommendation, Very Low Certainty of Evidence).
    - B. For patients with **more severe impairments in quality of life** (and < 2 exacerbations per year), the panel suggests **omalizumab** over dupilumab (Conditional Recommendation, Very Low Certainty of Evidence).
    - C. For patients with a **greater impairment in lung function (FEV 1 < 70% predicted)**, the panel suggests **dupilumab** over omalizumab (Conditional Recommendation, Very Low Certainty of Evidence).

Chest. 2026 Feb;169(2):336-348.

PICO Questions and Recommendations

- **PICO 2**
  - Queston 2: Should adult patients with **steroid dependent asthma** be treated with **anti-IL5/5Rα or dupilumab?**
  - CHEST Recommendation: In adult patients with severe asthma who are steroid dependent, the panel suggests **either anti-IL5/5Ra therapy or dupilumab** (Conditional Recommendation, Very Low Certainty of Evidence).

- **PICO 3**
  - Question 3: Should adult patients with **steroid dependent asthma** be treated with **dupilumab or tezepelumab?**
  - CHEST Recommendation: In adult patients with severe asthma who are steroid dependent, the panel suggests **dupilumab** over tezepelumab (Conditional Recommendation, Very Low Certainty of Evidence).
  - ✓ Dupilumab results in a greater reduction in OCS dosing (28% reduction when compared to the control group) as opposed to no effect in OCS dosing for tezepelumab (SOURCE study).

Chest. 2026 Feb;169(2):336-348.

PICO Questions and Recommendations

- **PICO 4**
  - Question 4: Should adult patients with moderate to severe asthma who have **not demonstrated a clinical response to omalizumab after 4-6 months** be treated with **anti-IL5/5Rα or dupilumab?**
  - CHEST Recommendation: In adult patients with moderate to severe asthma who have not demonstrated a clinical response to omalizumab after 4-6 months, the panel suggests **either anti-IL5/5Ra therapy or dupilumab** (Conditional Recommendation, Very Low Certainty of Evidence).

- **PICO 5**
  - Question 5: Should adult patients with severe asthma who have **not demonstrated a clinical response to anti- IL5/5Rα after 4-6 months** be treated with **dupilumab or tezepelumab?**
  - CHEST Recommendation: In adult patients with severe asthma who have not demonstrated a clinical response to anti-IL5/5Ra therapy after 4-6 months, the panel suggests either **dupilumab or tezepelumab** (Conditional Recommendation, Very Low Certainty of Evidence).
    - A. For patients who are **steroid dependent**, the panel suggests **dupilumab** over tezepelumab (Conditional Recommendation, Very Low Certainty of Evidence).

Chest. 2026 Feb;169(2):336-348.

PICO Questions and Recommendations

- **PICO 6**
  - Question 6: Should adult patients with severe asthma who have **not demonstrated a clinical response to dupilumab after 4-6 months** be treated with **anti-IL5/ 5Rα or tezepelumab?**
  - CHEST Recommendation: In adult patients with severe asthma who have not demonstrated a clinical response to dupilumab after 4-6 months, the panels suggests either **anti-IL5/5Ra or tezepelumab** (Conditional Recommendation, Very Low Certainty of Evidence).
    - A. For patients who are **steroid dependent**, the panel suggests **anti-IL5/5Ra** (Conditional Recommenda tion, Very Low Certainty of Evidence).

- **PICO 7**
  - Question 7: Should **FeNO be used for guiding changes in therapy to dupilumab** in adult patients with severe asthma on **anti-IL5/5Rα have not demonstrated a clinical response by 4-6 months**?
  - CHEST Recommendation: In adult patients with severe asthma on anti-IL5/5Ra who have not demonstrated a clinical response by 4-6 months, the panel suggests the **use of posttreatment FeNO ≥ 25 ppb for advising changes in therapy to dupilumab** (Conditional Recommendation, Very Low Certainty of Evidence).

Chest. 2026 Feb;169(2):336-348.

TABLE 3] Biologics for Use in Moderate to Severe Asthma

	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab	Tezepelumab
Mechanism of action	Anti-IgE	Anti-IL5	Anti-IL5	Anti-IL5Rα	Anti-IL4Rα/13	Anti-TSLP
Criteria for initiation[a]	Uncontrolled symptoms of allergic asthma with sensitization to perennial aeroallergen despite ICS use	Eosinophilic asthma (AEC ≥ 150 cells/μL) with exacerbation (≥ 2 per year) despite use of ICS-LABA	Eosinophilic asthma (AEC ≥ 400) with exacerbation despite use of at least medium dose ICS	Eosinophilic asthma (AEC ≥ 300) with exacerbation (≥ 2 per year) despite use of medium to high dose ICS-LABA	Eosinophilic asthma (AEC ≥ 150) with steroid dependency or with exacerbation despite use of medium to high dose ICS-LABA	Uncontrolled asthma with exacerbation despite use of medium to high dose ICS-LABA, T2 high or low asthma
Mode of administration	Subcutaneous	Subcutaneous	IV	Subcutaneous	Subcutaneous	Subcutaneous
Dosing and dosing interval	Every 2 or 4 wks, based upon pre-dosing IgE level and body weight	100 mg every 4 wks	Weight based every 4 wks	30 mg every 4 wks × 3, then every 8 wks thereafter	200 mg or 300 mg every 2 wks (consider loading dose)	210 mg every 4 wks
Co-morbid conditions with FDA approval	CRSwNP; chronic spontaneous urticaria; IgE mediated food allergies	CRSwNP; EGPA/HES (300 mg monthly dosing regimen)	N/A	EGPA (monthly dosing regimen)	Atopic dermatitis; CRSwNP; eosinophilic esophagitis (300 mg weekly dosing for > 40 kg), COPD (AEC ≥ 300 cells/μL)	CRSwNP (FDA approval pending)

AEC = absolute eosinophil count; CRSwNP = chronic rhinosinusitis with nasal polyposis; EGPA = eosinophilic granulomatosis with polyangiitis; FDA = US Food and Drug Administration; HES = hyper-eosinophilic syndrome; ICS = inhaled corticosteroid; IL-4Ra = IL-4 receptor alpha subunit; LABA = long-acting beta-agonist; N/A = not applicable; TSLP = thymic stromal lymphopoietin.
[a]Based upon US FDA criteria.

Chest. 2026 Feb;169(2):336-348.

Oral corticosteroid reduction and discontinuation in adults with corticosteroid-dependent, severe, uncontrolled asthma treated with tezepelumab (WAYFINDER): a multicentre, single-arm, phase 3b trial

David J Jackson, Njira L Lugogo, Mark Gurnell, Liam G Heaney, Stephanie Korn, Guy Brusselle, Pascal Chanez, Ricardo del Olmo, Jean-Pierre Llanos, Nanna Keeling, Kinga Sałapa, Bill Cook, Amit D Parulekar, Konstantinos Kostikas, Robert Fogel, Neil Martin, Shradha N Chandarana

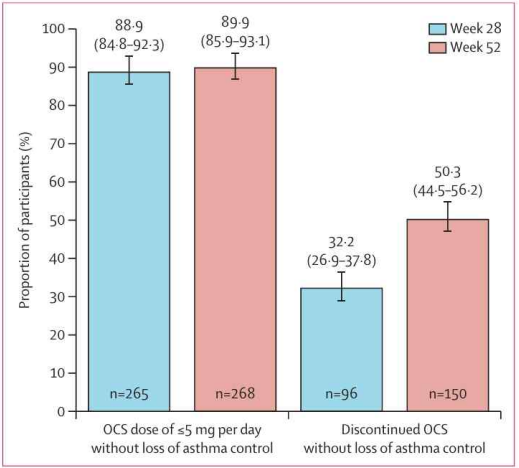
- Severe asthma accounts for 3–10% of asthma patients.
  - Many patients require long-term oral corticosteroids (OCS) for disease control.
  - Goal of modern asthma management: reduce or eliminate OCS use
- Tezepelumab
  - Human monoclonal antibody targeting TSLP (thymic stromal lymphopoietin)
  - Effective across multiple asthma phenotypes
  - SOURCE study: The primary endpoint of reduction in daily OCS dose at week 48 was not met.
- Study aim
  - To evaluate the ability of tezepelumab to reduce or discontinue OCS use in a larger cohort of patients with OCS-dependent severe, uncontrolled asthma.

Lancet Respir Med. 2026 Feb;14(2):129-140.

WAYFINDER Study design and participants

- WAYFINDER Trial
  - Phase 3b, multicentre, single-arm, open-label study
  - 68 centers, 11 countries
- Population
  - Adults 18–80 years
  - Severe uncontrolled asthma
  - Receiving maintenance OCS 5–40 mg/day
  - On high-dose ICS + LABA
- Intervention
  - Tezepelumab 210 mg SC every 4 weeks
  - Treatment duration: 52 weeks
- Key protocol feature
  - Personalized OCS tapering strategy
  - Adrenal function monitoring
    - morning cortisol
    - ACTH stimulation test
- Participants
  - 298 patients included in efficacy analysis

Lancet Respir Med. 2026 Feb;14(2):129-140.

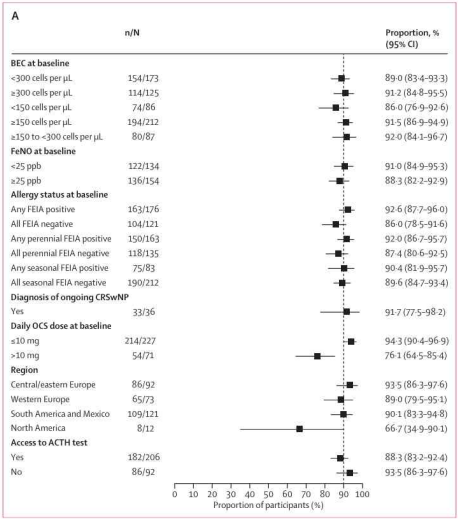


◆ **Co-Primary Endpoints**

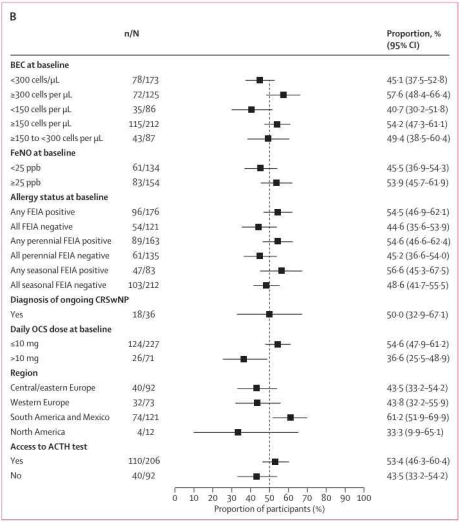
- OCS ≤5 mg/day without loss of asthma control
- Discontinued OCS without loss of asthma control

Lancet Respir Med. 2026 Feb;14(2):129-140.

OCS ≤5 mg/day



Discontinued OCS



- Benefits observed regardless of phenotype.

Lancet Respir Med. 2026 Feb;14(2):129-140.

Rademikibart Treatment for Moderate-to-Severe Uncontrolled Asthma

A Phase 2B Randomized Clinical Trial

Edward Kerwin[1], Ting Yang[2], Nan Su[2], Jiawang Guo[3], Radha Adivikolanu[4], Malinda Longphre[4], Junying Wang[2], Jili Yun[3], Wuban Pan[3], Zheng Wei[4], and Raúl Collazo[4]

- Rademikibart (CBP-201)
  - Anti-IL-4Rα monoclonal antibody
  - Potential alternative to existing biologics targeting T2 inflammation
- Study aim
  - To evaluate rademikibart in adults with moderate-to-severe, persistent, uncontrolled asthma
- Study Design
  - Phase 2b, randomized, double-blind, placebo-controlled trial
  - 322 adults with moderate-to-severe uncontrolled asthma

Am J Respir Crit Care Med. 2025 May;211(5):749-758.

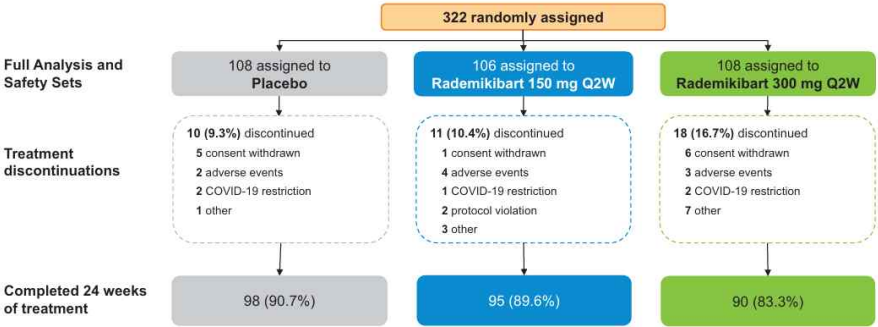
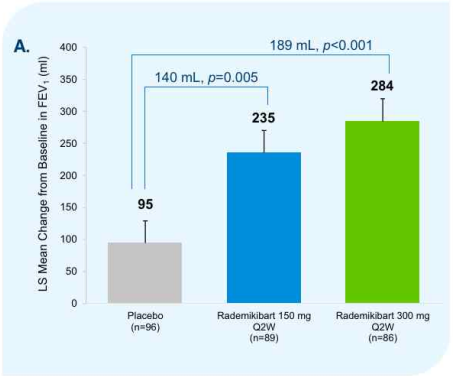


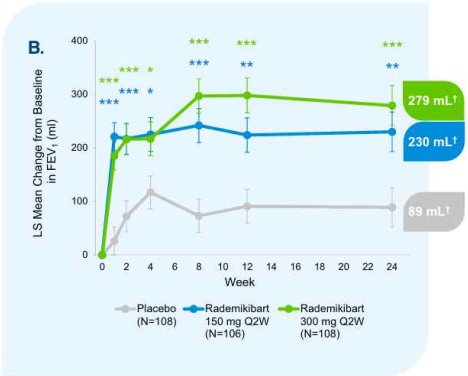
Figure 1. Patient disposition. All patients received at least one dose of study treatment. Q2W = every 2 weeks.

Am J Respir Crit Care Med. 2025 May;211(5):749-758.

Prebronchodilator FEV1 across 24 weeks of Rademikibart therapy

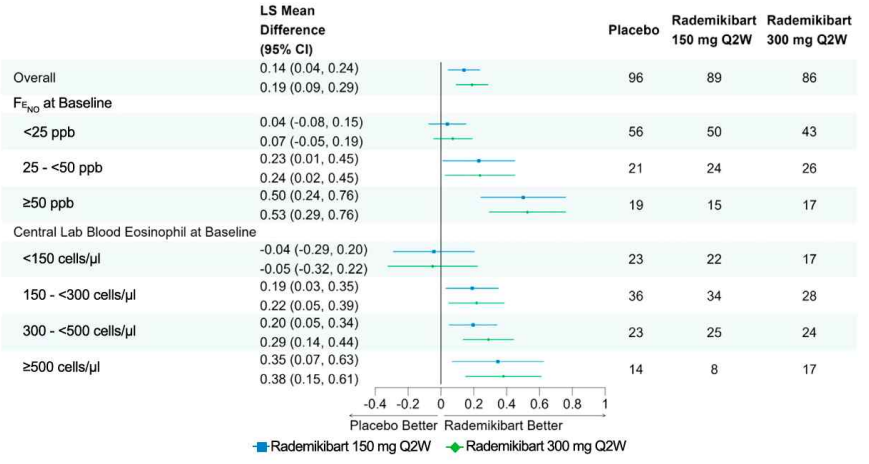


At Week 12



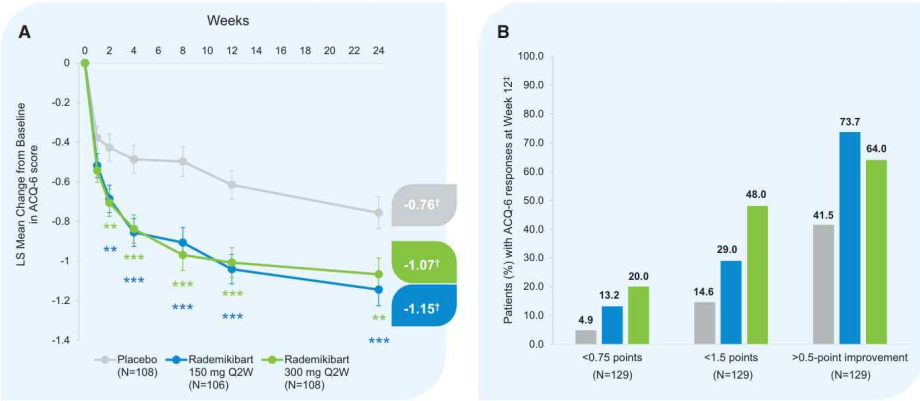
Across 24 weeks

Am J Respir Crit Care Med. 2025 May;211(5):749-758.



Am J Respir Crit Care Med. 2025 May;211(5):749-758.

Asthma control across 24 weeks of Rademikibart therapy



- **Rademikibart significantly improved lung function and asthma control.**
- **Effects were rapid and sustained over 24 weeks.**

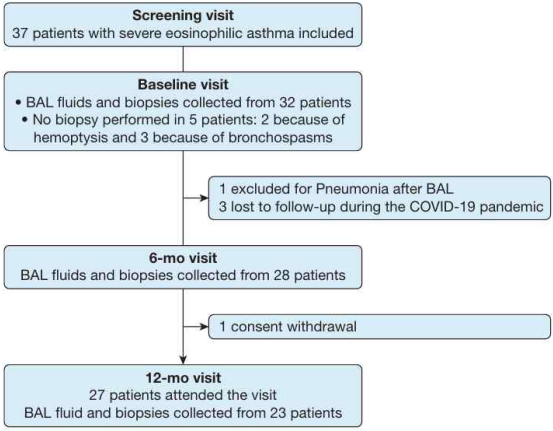
Am J Respir Crit Care Med. 2025 May;211(5):749-758.

Impact of Mepolizumab on Airway Remodeling and Inflammation in Severe Eosinophilic Asthma

Camille Taillé, MD, PhD; Fatima Hamidi, MSa; Nicolas Heddebaut, MS; Nicolas Poté, MD, PhD; Pierre Le Guen, MD; Mathilde Le Brun, MD; Carine Roy, MS; Axelle Dupont, MD, PhD; and Séverine Létuvé, PhD

- Airway remodeling is a key pathological feature of severe asthma and contributes to persistent airflow limitation and disease progression.
- Eosinophils and IL-5–mediated inflammation play a central role in airway remodeling in severe eosinophilic asthma (SEA).
- Study aim
  - To evaluate whether mepolizumab modifies airway remodeling and inflammation in adults with SEA.

Chest. 2025 Dec 5:S0012-3692(25)05814-3.



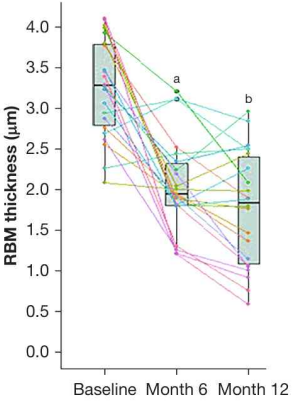
- REMOMEPO Study
  - Prospective interventional study
- Population
  - 37 adults with severe eosinophilic asthma
- Intervention
  - Mepolizumab 100 mg SC every 4 weeks
  - Treatment duration: 12 months
- Assessments
  - At baseline, 6 months, and 12 months
  - Bronchial biopsy
  - Bronchoalveolar lavage (BAL)
  - Blood biomarkers
  - Clinical outcomes (ACT, exacerbations)

Chest. 2025 Dec 5:S0012-3692(25)05814-3.

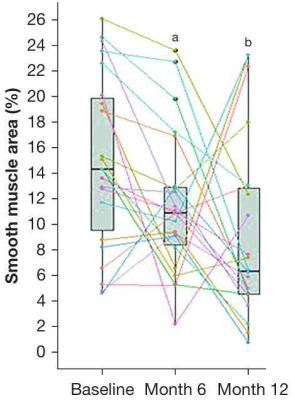
TABLE 2] Comparison of Clinical and Functional Parameters Between Baseline and 12 Months After Mepolizumab Therapy Initiation

Variable	Baseline	12 Months	*P* Value
ACT score	15.0 (12.0-18.5)	20.0 (18.0-23.5)	**< .0001**
FEV_1 before bronchodilation, mL	2,465.0 (1,840.0-3,010.0)	2,490.0 (2,170.0-3260.0)	.0851
FVC before bronchodilation, mL	3,514.0 (2,960.0-4,830.0)	3,730.0 (3,140.0-5,070.0)	**.0005**
FEV_1 to FVC ratio before bronchodilation, %	65.0 (59.0-72.0)	65.0 (63.0-71.0)	.8519
Most recent BEC, G/L	0.31 (0.20-0.66)	0.06 (0.02-0.11)	**< .0001**
No. of hospitalizations in the last 12 mo	0.0 (0.0-1.0)	0.0 (0.0-0.0)	**.0313**
No. of asthma exacerbations in the last 12 mo	4.0 (2.0-7.0)	1.0 (0.0-3.0)	**.0041**
No. of OCS courses in the last 12 mo	4.0 (2.0-7.0)	1.0 (0.0-4.0)	**.0115**

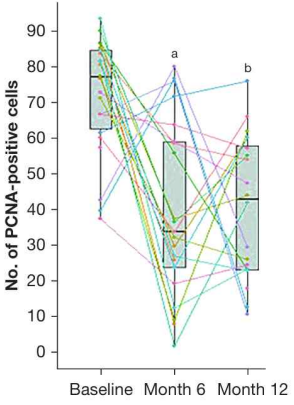
Effect of Mepolizumab on Airway Remodelling



3.3µm → 2.0µm →1.9 µm



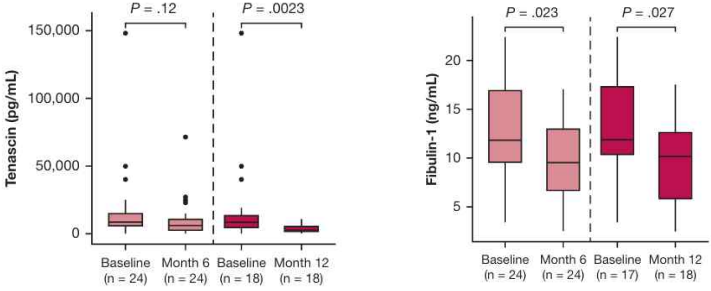
14.6% → 10.6% → 6.4%



80.4 → 30.9 → 41.9

Chest. 2025 Dec 5:S0012-3692(25)05814-3.

Effect of mepolizumab on BAL fluid extracellular matrix proteins



- **Mepolizumab improves clinical outcomes and reduces airway remodeling in SEA.**
- **Targeting Type-2 inflammation may modify disease progression.**

Chest. 2025 Dec 5:S0012-3692(25)05814-3.

Airway mucus and ^{129}Xe MRI ventilation after single inhaler triple therapy in asthma

Ali Mozaffaripour[1,2,6], Sam Tcherner[1,3,6], Eveline Durom[1,3], Harkiran K. Kooner[1], Marrissa J. McIntosh[1], Malcolm Sherwood[4], Narinder Paul[5], Hana Serajeddini[4], Anurag Bhalla[4], Cory Yamashita[4] and Grace Parraga[1,2,3,4,5]

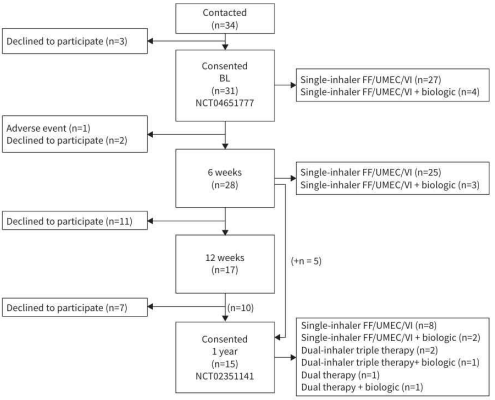
- 30–50% of patients remain poorly controlled despite ICS/LABA therapy.
- Single-inhaler ICS/LABA/LAMA triple therapy improves lung function and asthma control.
- However, the mechanisms at the small-airway level remain unclear.

- Study aim
  - To evaluate whether FF/UMEC/VI (fluticasone furoate/umeclidinium/vilanterol) improves
    - Airway structure and function
    - Ventilation defects
    - Airway mucus and remodeling

2025 Oct 13;11(5):01333-2024.

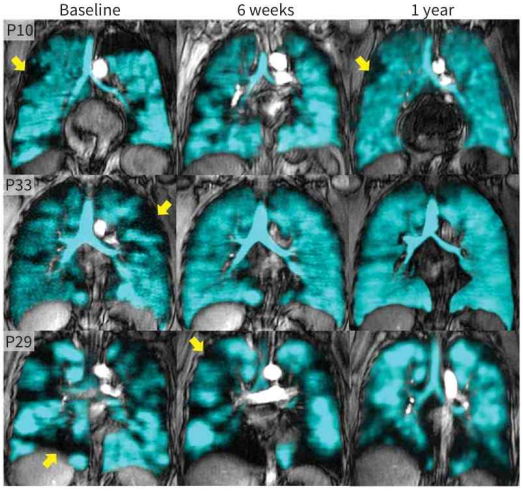
Study design

- Population
  - Adults with GINA Step 4–5 asthma
  - Poorly controlled on ICS/LABA
- Intervention
  - Single-inhaler triple therapy: Fluticasone furoate / umeclidinium / vilanterol (200/62.5/25 µg)
- Follow-up
  - Baseline → 6 weeks → 12 weeks → 1 year
- Assessments
  - ^{129}Xe MRI ventilation defect percentage (VDP)
  - CT airway morphology and mucus score
  - Spirometry and oscillometry
  - Asthma control and quality-of-life questionnaires



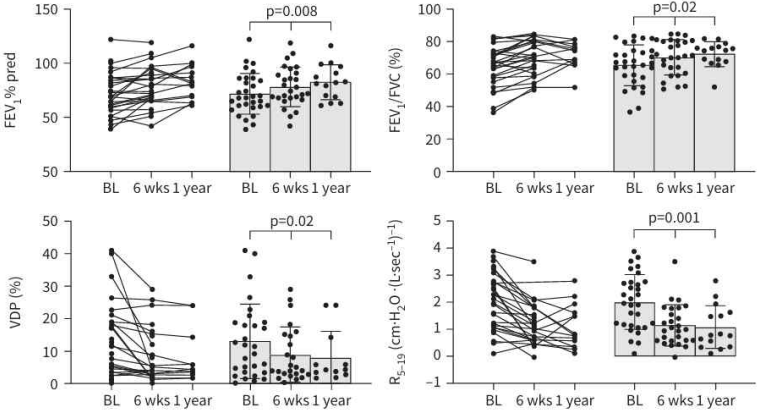
2025 Oct 13;11(5):01333-2024.

MRI Ventilation Defect Percentage (VDP) following ICS/LABA/LAMA treatment



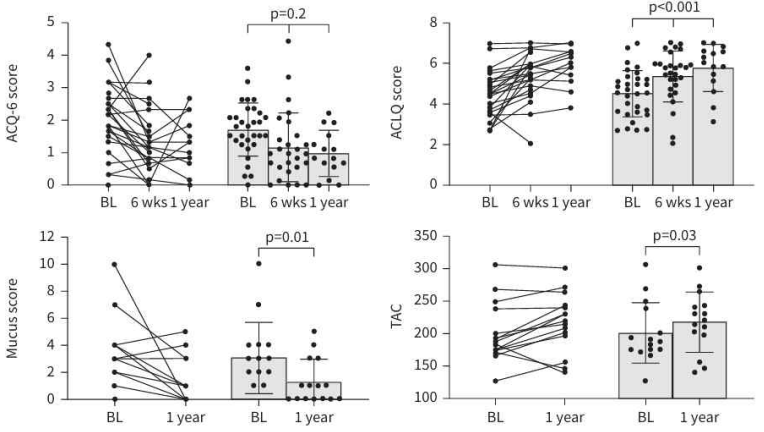
2025 Oct 13;11(5):01333-2024.

Measurement differences at 6 weeks and 1 year



2025 Oct 13;11(5):01333-2024.

Measurement differences at 6 weeks and 1 year



2025 Oct 13;11(5):01333-2024.

Airway mucus and ^{129}Xe MRI ventilation after single inhaler triple therapy in asthma

Ali Mozaffaripour[1,2,6], Sam Tcherner[1,3,6], Eveline Durom[1,3], Harkiran K. Kooner[1], Marrissa J. McIntosh[1], Malcolm Sherwood[4], Narinder Paul[5], Hana Serajeddini[4], Anurag Bhalla[4], Cory Yamashita[4] and Grace Parraga[1,2,3,4,5]

- Single-inhaler triple therapy improves both airway function and structure.
- Benefits occur rapidly (6 weeks) and persist up to 1 year.
- Imaging findings support mucus clearance and airway remodeling reversal.

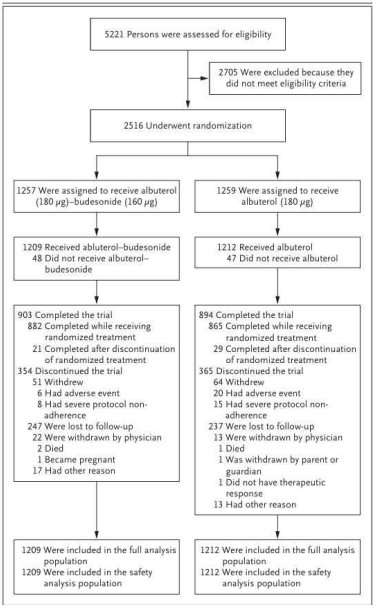
2025 Oct 13;11(5):01333-2024.

As-Needed Albuterol–Budesonide in Mild Asthma

C. LaForce,[1] F. Albers,[2] A. Danilewicz,[3] A. Jeynes-Ellis,[3] M. Kraft,[4] R.A. Panettieri, Jr.,[5] R. Rees,[3] S. Bardsley,[6] L. Dunsire,[6] T. Harrison,[7] O. Sobande,[8] R. Surujbally,[6] F. Trudo,[9] C. Cappelletti,[10] A. Papi,[11] R. Beasley,[12] B.E. Chipps,[13] E. Israel,[14,15] H. Pandya,[6] M. Clancy,[16] and L.B. Bacharier,[17] for the BATURA Investigators*

- Mild asthma accounts for 50–70% of asthma cases, but severe exacerbations still occur.
- Many patients rely on SABA-only rescue therapy, which does not treat airway inflammation.
- Current Guideline shift
  - GINA recommends ICS-containing reliever therapy.
  - Need evidence for ICS + SABA rescue strategy in mild asthma.
- MANDALA study: as-needed albuterol–budesonide reduced severe exacerbation in moderate to severe asthma
- Study aim
  - To evaluate whether as-needed albuterol–budesonide reduces severe asthma exacerbations compared with as-needed albuterol alone in patients with uncontrolled mild asthma.

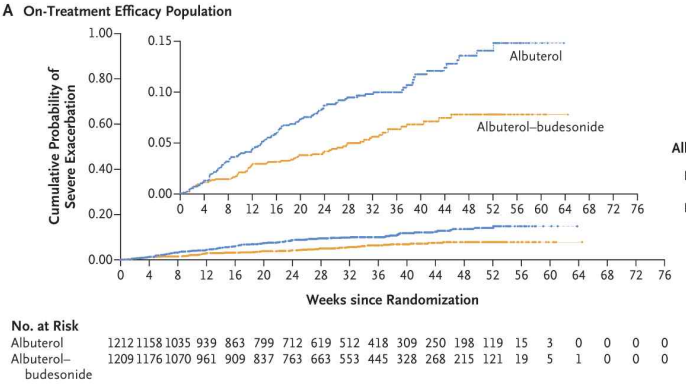
N Engl J Med. 2025 Jul 10;393(2):113-124.



- Design
  - Phase 3b randomized controlled trial
  - Multicenter, double-blind
  - Fully decentralized virtual trial
- Population
  - Age ≥12 years
  - Mild asthma uncontrolled on Step 1–2 therapy
- Participants
  - N = 2516 randomized
  - Follow-up 12–52 weeks
- Treatment
  - Intervention: As-needed Albuterol 180 µg + Budesonide 160 µg
  - Control: As-needed Albuterol 180 µg

N Engl J Med. 2025 Jul 10;393(2):113-124.

First severe asthma exacerbation



No. of Participants with Event (%)

Albuterol	110 (9.1)
Albuterol–Budesonide	62 (5.1)

Hazard ratio with albuterol–budesonide, 0.53 (95% CI, 0.39–0.73)
P<0.001

The risk of a severe exacerbation was 47% lower with albuterol–budesonide than with albuterol.

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Table 2. Annualized Rate of Severe Asthma Exacerbations and Annualized Total Exposure to Systemic Glucocorticoids.*

Variable	Full Analysis Population, ≥12 Yr of Age		Full Analysis Population, ≥18 Yr of Age	
	Albuterol–Budesonide (N=1209)	Albuterol (N=1212)	Albuterol–Budesonide (N=1180)	Albuterol (N=1173)
Annualized rate of severe exacerbations				
No. of participants evaluated	1209	1212	1180	1173
No. of first severe exacerbations	83	160	82	159
Time at risk — participant-yr	845.8	823.8	825.7	797.4
Estimated annualized rate (95% CI)	0.15 (0.11 to 0.20)	0.32 (0.25 to 0.41)	0.15 (0.12 to 0.20)	0.33 (0.26 to 0.43)
Rate ratio (95% CI)	0.47 (0.34 to 0.64)	—	0.46 (0.33 to 0.63)	—
P value	<0.001	—	<0.001	—
Annualized total exposure to systemic glucocorticoids†				
No. of participants evaluated	1204	1203	1175	1164
Mean total amount per participant of exposure to systemic glucocorticoids — mg/yr	23.2±142.9	61.9±662.1	23.0±142.4	63.0±672.3
Difference in arithmetic means — mg/yr	−38.7	—	−40.0	—
Percent difference in arithmetic means	−62.5	—	−63.5	—
P value‡	<0.001	—	<0.001	—

↓ 53%

↓ 63%

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As-Needed Albuterol–Budesonide in Mild Asthma

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- ICS+SABA rescue therapy significantly reduces severe exacerbations in mild asthma.
- Supports moving away from SABA-only treatment.
- As-needed albuterol–budesonide may be an effective anti-inflammatory reliever strategy.

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Summary

- **Small airway dysfunction**
  - R5-R20: predictor of future exacerbation risk
  - Associated with reduced asthma remission
- **Mucus plugs**: Associated with airway remodeling
- **Clinical remission**: New treatment goal
  - Definition: Absence of asthma symptom, No exacerbations, Lung function, No OCS use
- **Biologic selection & switching**
  - OCS dependency, exacerbation risk, lung function, biomarkers (eosinophils, FeNO), and comorbidities
- **Tezepelumab**: OCS reduction in severe asthma
- **Rademikibart**: improved lung function and asthma control, greater efficacy in T2-high asthma
- **Mepolizumab**: reduces airway remodeling in severe eosinophilic asthma
- **SITT(FF/UMEC/VI)**: improves both airway function and structure
- **As-needed albuterol–budesonide**: reduces severe exacerbations in mild asthma

Thank you for your attention