REAL-TIME POLLING

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#ChaseTSAAI

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TSAAI 2023

REMISSION IN ASTHMA

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EMPLOYMENT/AFFILIATIONS

Employment

- Partner, St. Paul Allergy & Asthma
- Adjunct Assistant Professor, University of Minnesota
- Staff Physician, Minneapolis VA

Consultant/Speaker

- Amgen
- ARS
- AstraZeneca
- Blueprint
- Bryn
- Genentech
- GSK
- Hikma
- Incyte
- Kenota Health
- Novartis
- Regeneron
- Sanofi

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OBJECTIVES

Understand the various interpretations of asthma remission

Identify positive, negative predictors of remission

Describe various ways to achieve remission

Consider challenges, data gaps that remain

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QUESTION 1

What word do you think of when you hear “remission”?

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What word do you think of when you hear "remission"?

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REMISSION IN MEDICINE

Cancer

- Acute lymphocytic leukemia (pediatric)
- Acoustic neuroma
- Glioblastoma multiforme

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WHY DO WE STRIVE FOR REMISSION?

To prevent relapse

To reduce symptoms

To halt disease progression

To learn best practices

To stop medication?

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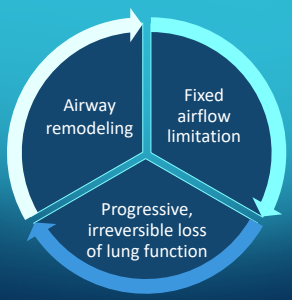
ASTHMA IN A SLIDE



Recurrent/persistent inflammation

Airway hyperresponsiveness

Mucus hypersecretion

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QUESTION 2

What is a necessary condition for remission in asthma?

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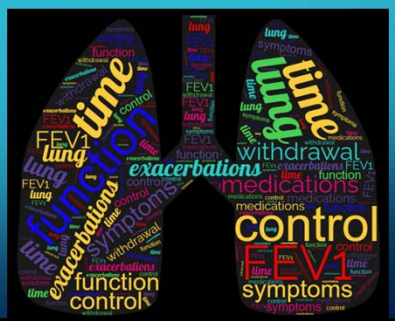
REMISSION IN ASTHMA?



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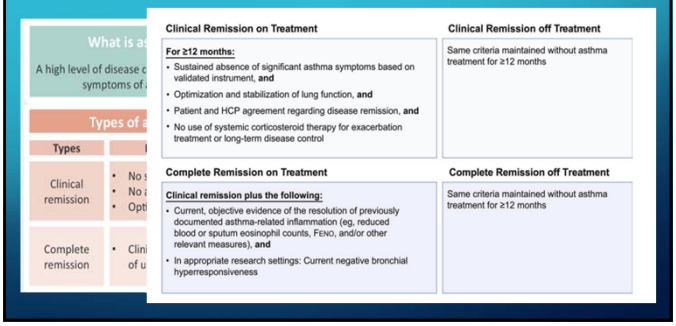
VARIATIONS ON A THEME



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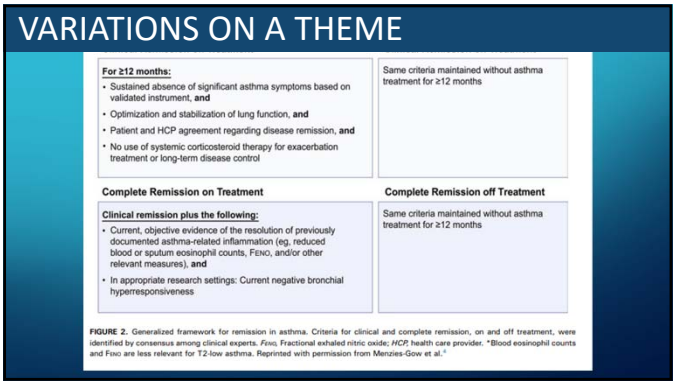
VARIATIONS ON A THEME



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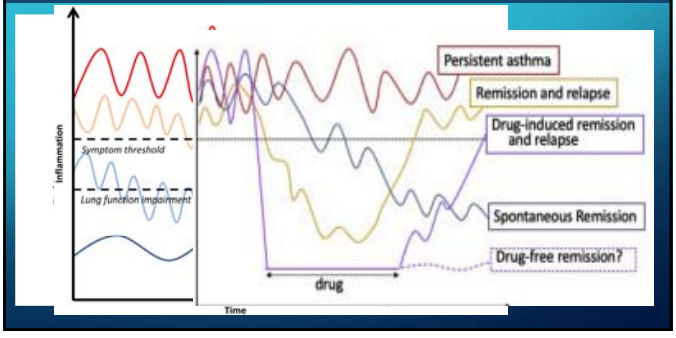
HISTORICAL PERSPECTIVE



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GINA 2023: REMISSION IN ASTHMA

GLOBAL INITIATIVE FOR ASTHMA 1993-2023

Global Strategy for Asthma Management and Prevention

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NAEPP 2020: REMISSION IN ASTHMA

2020 FOCUSED UPDATES TO THE **Asthma Management Guidelines**

A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

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GINA 2023 VS NAEPP 2020

Is absence of symptoms enough?

Should we require an absence of controller medications?

Will patients in remission achieve normal lung function?

Is remission fixed and achievable OR transient?

What about biologics/other treatments?

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QUESTION 3

When did clinicians start studying remission in asthma?

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PEER-REVIEWED CRITERIA

Table 1
Various criteria employed in the literature for defining clinical asthma remission.

Study	Criteria for asthma remission	Time frame
Bronnimann & Burrows, 1986	No asthma attacks, symptoms or medications	1 year
Boulet et al., 1994	No symptoms or medication requirement	2 years
Ronmark et al., 1999	No wheeze, dyspnoea or medications	1 year
Horak et al., 2003	No wheeze	3 years
Sears et al., 2003	No wheeze	1 year
Vonk et al., 2004	No active symptoms, no inhaled steroids	3 years
de Marco et al., 2006	No asthma attack	2 years
	No asthma medications	1 year
Holm et al., 2007	No asthma symptoms, no medications	2 years

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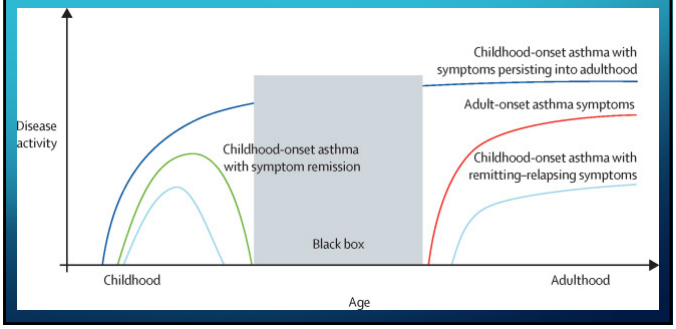
DOES REMISSION OCCUR IN ASTHMA?



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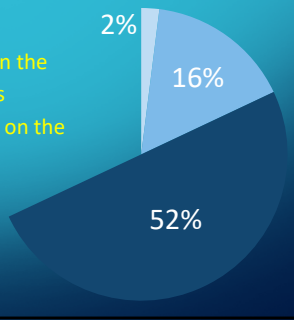
REMISSION IN ASTHMA: PREVALENCE

"The prevalence of remission in the adult asthma population varies between 2% - 52%, depending on the definition and criteria used."



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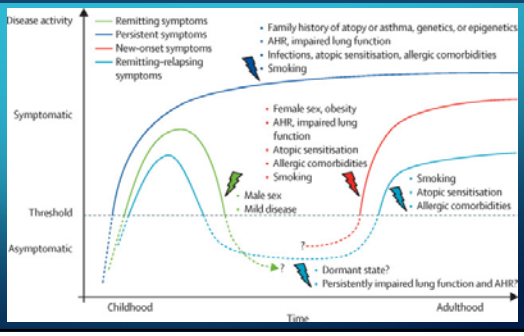
FACTORS IN ASTHMA REMISSION



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POSITIVE PREDICTORS OF REMISSION

Mild AHR

Younger age

Better control

Better lung function

Early-onset of disease

Shorter duration of asthma

Fewer comorbidities (atopic/other)

Never smoking or hx smoking cessation

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NEGATIVE PREDICTORS OF REMISSION

Smoking: initiation or continuation
Comorbidities (atopic/other)
Longer duration of asthma
Late-onset of disease
Worse lung function
More severe AHR
Severe asthma
Poor control
Older age

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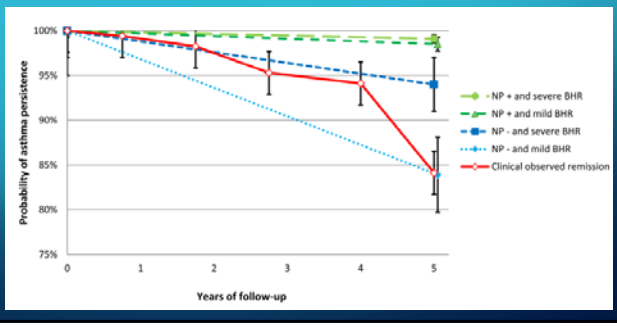
PREDICTORS IN ADULTS



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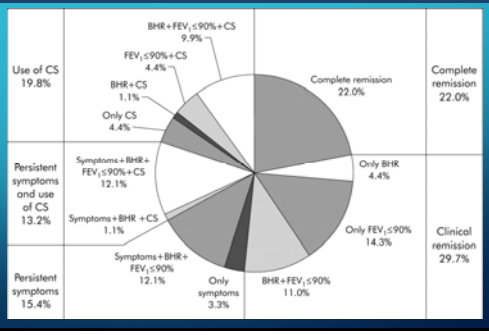
PREDICTORS IN CHILDREN



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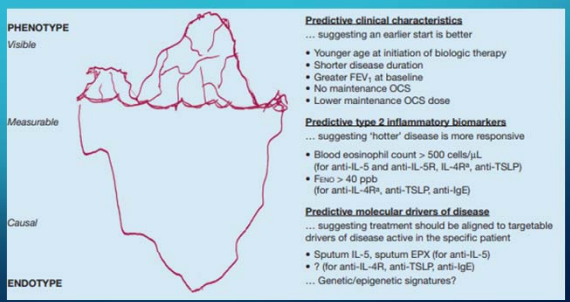
BIOLOGICS AND REMISSION



Predictive clinical characteristics
... suggesting an earlier start is better

- Younger age at initiation of biologic therapy
- Shorter disease duration
- Greater FEV_1 at baseline
- No maintenance OCS
- Lower maintenance OCS dose

Predictive type 2 inflammatory biomarkers
... suggesting 'hotter' disease is more responsive

- Blood eosinophil count > 500 cells/μL (for anti-IL-5 and anti-IL-5R, IL-4Rα, anti-TSLP)
- F_{ENO} > 40 ppb (for anti-IL-4Rα, anti-TSLP, anti-IgE)

Predictive molecular drivers of disease
... suggesting treatment should be aligned to targetable drivers of disease active in the specific patient

- Sputum IL-5, sputum EPX (for anti-IL-5)
- ? (for anti-IL-4R, anti-TSLP, anti-IgE)

... Genetic/epigenetic signatures?

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OMALIZUMAB

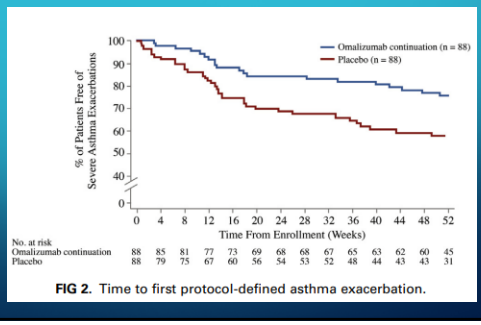

FIG 2. Time to first protocol-defined asthma exacerbation.

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MEPOLIZUMAB

Two definitions of on-treatment clinical remission used in this analysis

- **Three-component definition:** exacerbation-free + OCS-free + ACT score ≥20
- **Four-component definition:** exacerbation-free + OCS free + ACT score ≥20 + predicted post-bronchodilator FEV$_1$ ≥80%

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BENRALIZUMAB

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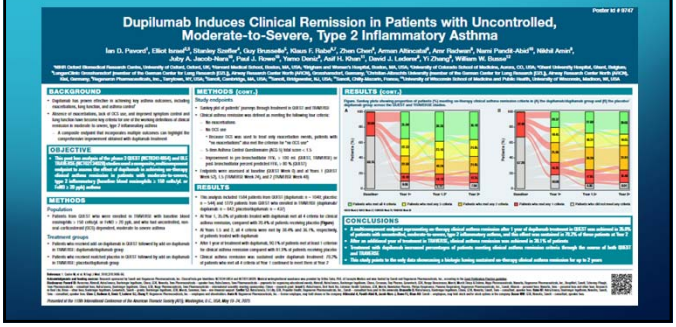
DUPILUMAB



Dupilumab Induces Clinical Remission in Patients with Uncontrolled, Moderate-to-Severe, Type 2 Inflammatory Asthma

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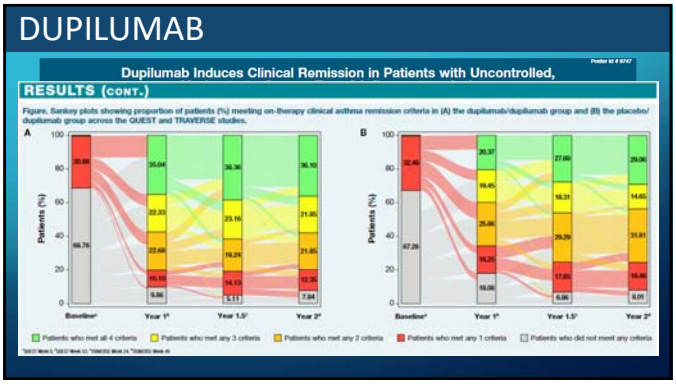
DUPILUMAB



Dupilumab Induces Clinical Remission in Patients with Uncontrolled,

RESULTS (CONT.)

Figure. Sankey plots showing proportion of patients (%) meeting on-therapy clinical asthma remission criteria in (A) the dupilumab/dupilumab group and (B) the placebo/dupilumab group across the QUEST and TRAVERSE studies.

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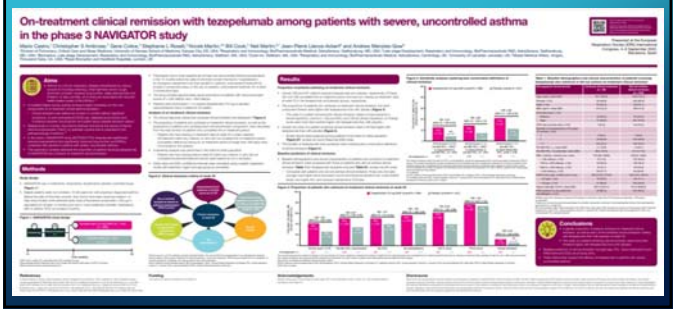
TEZEPELUMAB



On-treatment clinical remission with tezepelumab among patients with severe, uncontrolled asthma in the phase 3 NAVIGATOR study

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TEZEPELUMAB

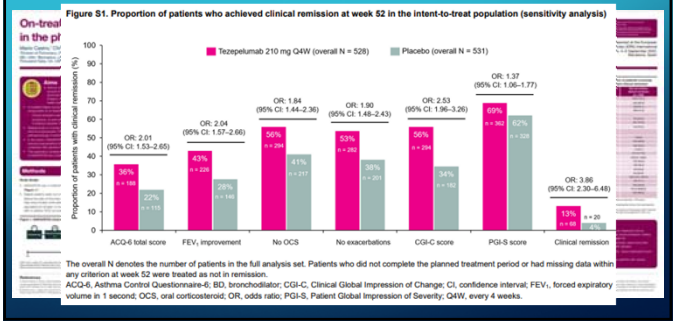

Figure S1. Proportion of patients who achieved clinical remission at week 52 in the intent-to-treat population (sensitivity analysis)

The overall N denotes the number of patients in the full analysis set. Patients who did not complete the planned treatment period or had missing data within any criterion at week 52 were treated as not in remission.
ACQ-6, Asthma Control Questionnaire-6; BD, bronchodilator; CGI-C, Clinical Global Impression of Change; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; OCS, oral corticosteroid; OR, odds ratio; PGI-S, Patient Global Impression of Severity; Q4W, every 4 weeks.

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TEZEPELUMAB

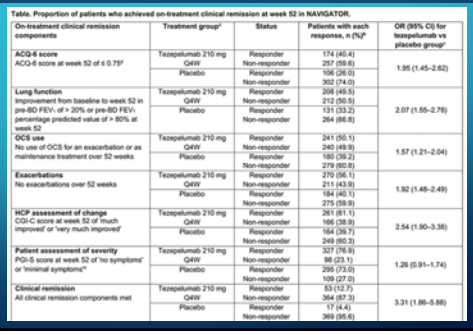

Table. Proportion of patients who achieved on-treatment clinical remission at week 52 in NAVIGATOR.

On-treatment clinical remission components	Treatment group[1]	Status	Patients with each response, n (%)[2]	OR (95% CI) for tezepelumab vs placebo group[3]
ACQ-6 score ACQ-6 score at week 52 of ≤ 0.75[4]	Tezepelumab 210 mg Q4W	Responder	174 (40.4)	1.95 (1.45–2.62)
		Non-responder	257 (59.6)	
	Placebo	Responder	106 (26.0)	
		Non-responder	302 (74.0)	
Lung function Improvement from baseline to week 52 in pre-BD FEV_1 of: • > 20% or pre-BD FEV_1 percentage predicted value of > 80% at week 52	Tezepelumab 210 mg Q4W	Responder	206 (49.5)	2.07 (1.55–2.78)
		Non-responder	212 (50.5)	
	Placebo	Responder	131 (33.2)	
		Non-responder	264 (66.8)	
OCS use No use of OCS for an exacerbation or as maintenance treatment over 52 weeks	Tezepelumab 210 mg Q4W	Responder	241 (50.1)	1.57 (1.21–2.04)
		Non-responder	240 (49.9)	
	Placebo	Responder	180 (39.2)	
		Non-responder	279 (60.8)	
Exacerbations No exacerbations over 52 weeks	Tezepelumab 210 mg Q4W	Responder	270 (56.1)	1.92 (1.48–2.49)
		Non-responder	211 (43.9)	
	Placebo	Responder	184 (40.1)	
		Non-responder	275 (59.9)	
HCP assessment of change CGI-C score at week 52 of 'much improved' or 'very much improved'	Tezepelumab 210 mg Q4W	Responder	261 (61.1)	2.54 (1.90–3.38)
		Non-responder	166 (38.9)	
	Placebo	Responder	164 (39.7)	
		Non-responder	249 (60.3)	
Patient assessment of severity PGI-S score at week 52 of 'no symptoms' or 'minimal symptoms'[5]	Tezepelumab 210 mg Q4W	Responder	327 (76.9)	1.26 (0.91–1.74)
		Non-responder	98 (23.1)	
	Placebo	Responder	295 (73.0)	
		Non-responder	109 (27.0)	
Clinical remission All clinical remission components met	Tezepelumab 210 mg Q4W	Responder	53 (12.7)	3.31 (1.86–5.88)
		Non-responder	364 (87.3)	
	Placebo	Responder	17 (4.4)	
		Non-responder	369 (95.6)	

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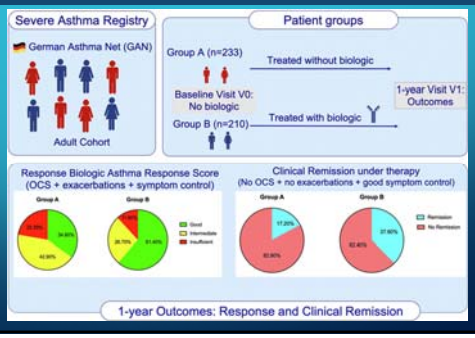
DO BIOLOGICS INDUCE REMISSION?



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WATCH FOR "SUPER RESPONDERS"?

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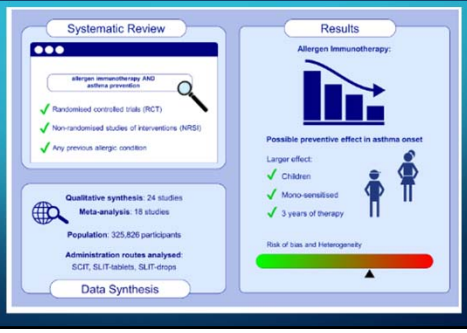
IMMUNOTHERAPY FOR REMISSION?



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SMALL MOLECULES FOR REMISSION?

Upadacitinib-induced remission of allergic asthma: A case report

TABLE I. Clinical characteristic of patient before and after treatment with upadacitinib

Patient's clinical characteristic	Before upadacitinib	2 y after upadacitinib
Atopic dermatitis		
EASI	21	7
SCORAD	58	29
IGA	4	1
Asthma/allergic rhinitis		
Frequency of respiratory symptoms	2-3 episodes per week of nocturnal wheezing and chest tightness; moderate rhinitis symptoms	Asymptomatic
Peripheral blood eosinophil count (cells/μL)	600	500
FeNO	251.3 ppb	54.1 ppb
Spirometry	FEV_1 95%; FEV_1/FVC 66%	FEV_1 109%; FEV_1/FVC 74.31
Methacholine challenge	Mild (3.93 mg/mL PC_{20})	Negative (>16 mg/mL PC_{20})
Adenosine challenge	Not done	Negative (<520 mg/mL PC_{15})

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STAKEHOLDERS IN ASTHMA

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GAPS & CHALLENGES IN REMISSION

Definition	
1	Does the definition of remission require measurement of inflammation?
2	How do asthma control and severity relate to asthma remission?
Treatment-induced remission	
3	Is treatment-induced remission possible?
4	How does treatment-induced remission compare with spontaneous asthma remission, based on prevalence, predictors and risk of relapse?
5	Is it possible to increase the proportion of people achieving remission with treatment?
6	Is it possible to prolong the remission period with treatment?
7	What are the rates of remission with MART and step therapy?
8	Does prolonging asthma treatment after control is achieved increase the chance of asthma remission?
Trajectory of remission	
9	How long should the treatment be continued to achieve remission? When to move from one stage to another?
Pathophysiology	
10	What are the molecular events leading to airway remodelling?
11	Can airway remodelling be treated?
12	Does treating airway remodelling induce remission?
Relapse	
13	How does ongoing airway inflammation and remodelling affect relapse?
14	How can inflammation/remodelling be effectively treated to prevent relapse in those who are in clinical remission?
Biologics and asthma remission	
15	What is the prevalence of remission after biologics therapy for asthma?
16	Are biologics more effective than inhaled preventers at achieving asthma remission?
17	Does the early introduction of biologics modify the trajectory of asthma and halt the disease progression?
18	Does continuing the treatment with biologics prolong remission and prevent relapse?
19	Is it possible to stop all asthma treatments except biologics in a patient who has achieved remission with biological therapies?

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FINAL QUESTION:

SHOULD
REMISSION
BE OUR GOAL?

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REFERENCES

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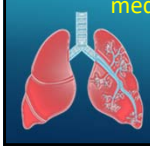
ARTIFICIAL INTELLIGENCE

"… you are a board-certified Allergist tasked with giving a presentation called 'Remission in Asthma'. Draft an outline… evaluate data from various FDA-approved medications… consider pitfalls and data gaps…"



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