EOSINOPHILIC (AND NON-EOSINOPHILIC) ASTHMA

JAMES FINGLETON

WHO AM I AND COI

- Respiratory SMO at Wellington Hospital
- Deputy Director of the Medical Research Institute of New Zealand
- Specialist interest in asthma and obstructive airways disease



WHO AM I AND COI

• I have received support to attend educational meetings from AstraZeneca, Boerhinger-Ingelheim, GSK and Novartis and presented independent medical education at symposia funded by AstraZeneca, Boerhinger-Ingleheim, and Novartis

Research funders:

Health Research Council AstraZeneca

Wellington Medical Research GSK

Foundation Fisher & Paykel

Asthma Foundation New Zealand Genentech / Roche



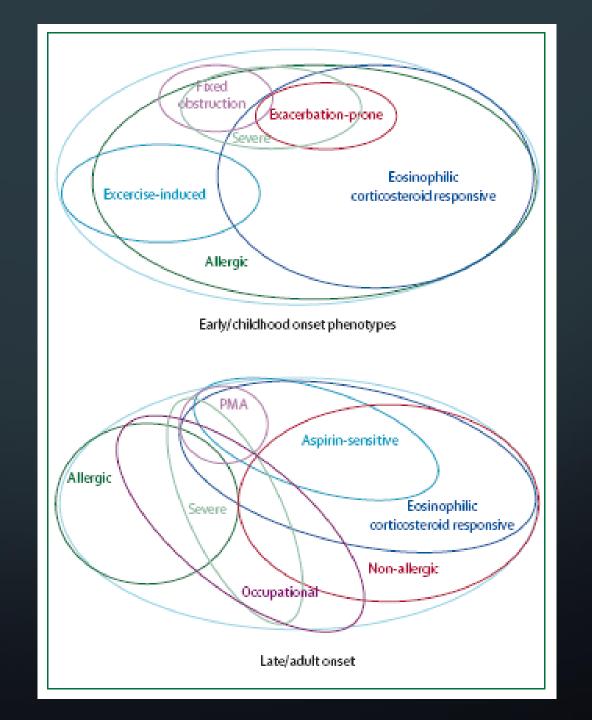
WHAT I'M NOT GOING TO ATTEMPT



AIMS

- What is eosinophilic asthma?
- How is it diagnosed?
- Why should we care?
- What about non-eosinophilic / treatable traits?

ISN'T ALL ASTHMA THE SAME?

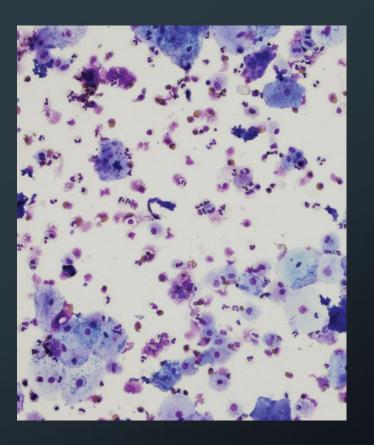


HOW IS EOSINOPHILIC ASTHMA DIAGNOSED?

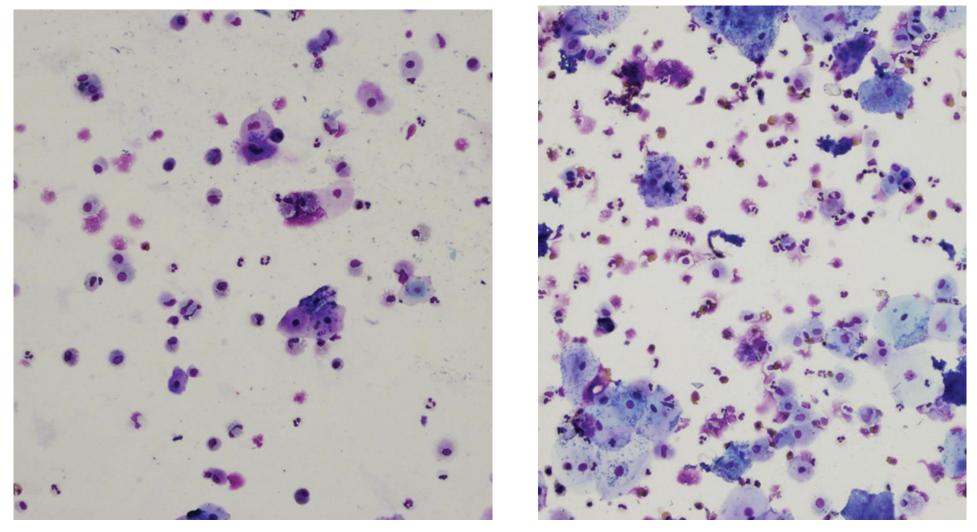
- Induced sputum
- Blood eosinophils
- Exhaled nitric oxide







Induced sputum samples

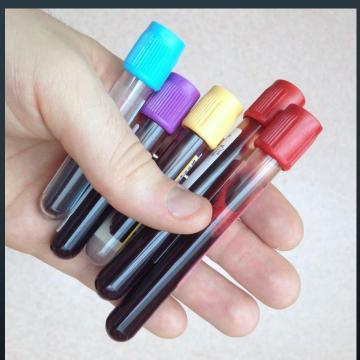


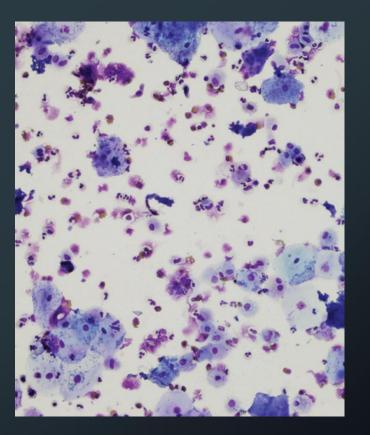
Zsoka Weiszhar, and Ildiko Horvath Breathe 2013;9:300-306

HOW IS IT DIAGNOSED?

- Induced sputum
- Blood eosinophils
- Exhaled nitric oxide

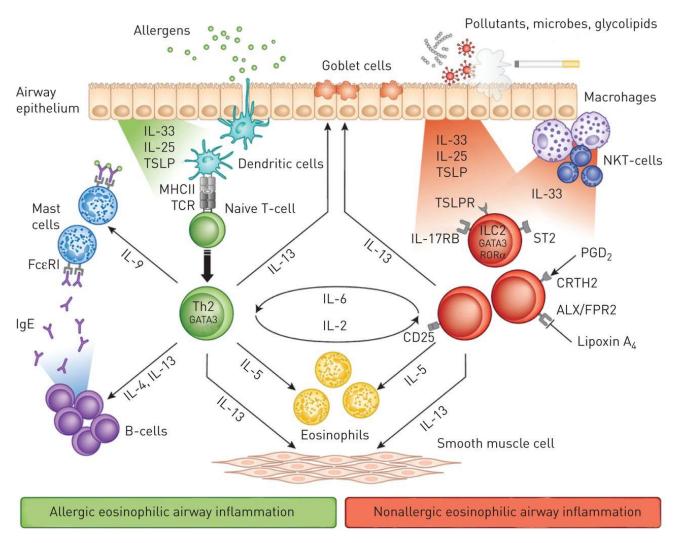






WHAT CAUSES IT?

Two different pathways lead to eosinophilic airway inflammation in asthma.



Jantina C. de Groot et al. ERJ Open Res 2015;1:00024-2015

WHY SHOULD I CARE?

- Diagnosis of asthma
- Management of asthma

DIAGNOSIS OF ASTHMA

PRESENTATION WITH SUSPECTED ASTHMA CLINICAL ASSESSMENT · History and examination · Measurement of PEF or FEV,, including brochodilator responsiveness **ASTHMA LIKELY** YES Poor response NO START ASTHMA TREATMENT AND Consider alternative diagnoses **REVIEW RESPONSE** Good response Alternative diagnoses confirmed NO YES Continue to monitor Consider further investigations Treat accordingly and treat and/or specialist referral

Algorithm C Objective tests for asthma in adults aged 17 and over

Order of tests Interpretation of test results for adults aged 17 and over with symptoms suggestive of asthma Does spirometry show an Measure FeNO first obstruction? followed by spirometry in adults with symptoms of asthma Is there reversible airflow Carry out BDR test if obstruction? spirometry shows an obstruction Are FeNO levels 40 ppb Are FeNO levels 40 ppb Are FeNO levels 40 ppb Yes or more? or more? or more? No No No If diagnostic uncertainty remains after FeNO, spirometry and BDR, monitor Is there variability in peak Is there variability in peak Are FeNO levels between Is there variability in peak peak flow variability for Yes 🍆 25 and 39 ppb? flow readings? flow readings? flow readings? 2 to 4 weeks Yes No No Yes Yes Yes Nο No If diagnostic uncertainty Are FeNO levels between Is there variability in peak Yes > remains after measuring 25 and 39 ppb? flow readings? peak flow variability, refer for a histamine or No methacholine direct bronchial challenge test Is there airway Is there airway Yes hyperreactivity? hyperreactivity? If histamine or methacholine direct bronchial challenge test is unavailable: No Yes Yes suspect asthma and Consider Consider Suspect Suspect Consider review diagnosis after alternative alternative asthma and asthma and alternative treatment or diagnoses or diagnoses or review review diagnoses or refer to a centre with referral for a referral for a diagnosis diagnosis Diagnose referral for a Diagnose Diagnose with access to histamine or second second after after second with asthma with asthma asthma methacholine challenge opinion treatment opinion treatment opinion testing

Abbreviations:

FeNO, fractional exhaled nitric oxide BDR, bronchodilator reversibility

This algorithm is based on recommendations from NICE's guideline on asthma: diagnosis, monitoring and chronic asthma management (2017)

Positive test thresholds

Obstructive spirometry: FEV1/FVC ratio less than 70% (or below the lower limit of normal if available) FeNO: 40 ppb or more

BDR: improvement in FEV1 of 12% or more and increase in volume of 200 ml or more Peak flow variability: variability over 20%

Direct bronchial challenge test with histamine or methacholine: PC20 of 8 mg/ml or less



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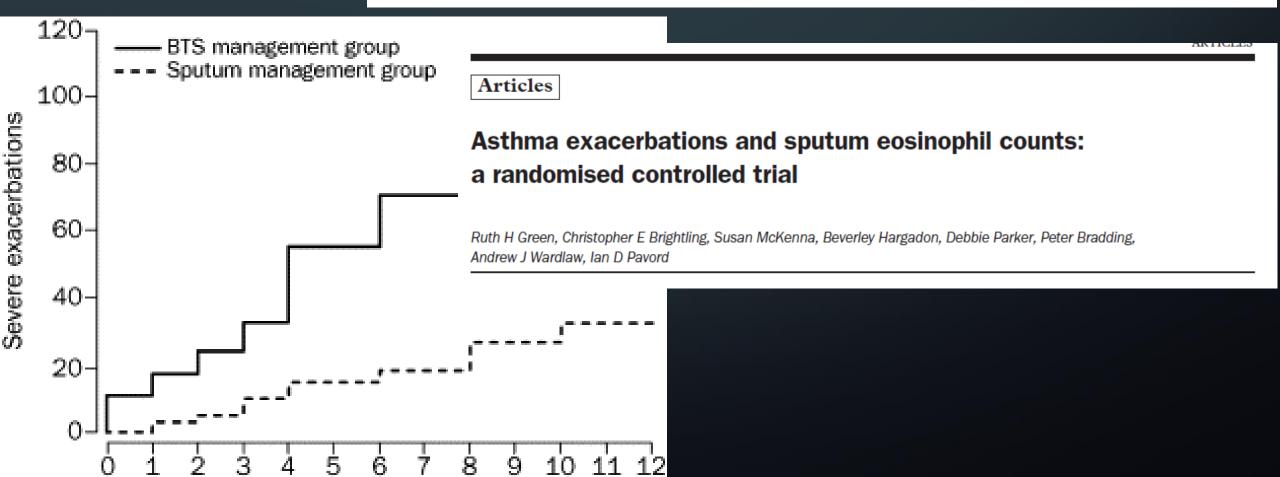
ASTHMA MANAGEMENT



Pathological features and inhaled corticosteroid response of eosinophilic and non-eosinophilic asthma

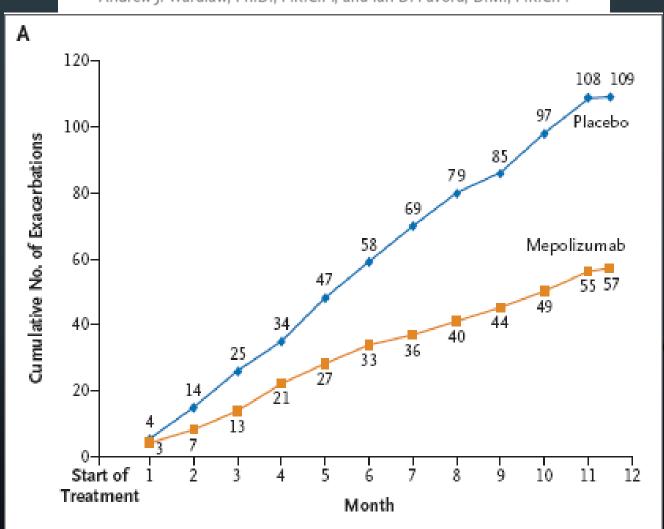
Mike Berry, Angela Morgan, Dominick E Shaw, Deborah Parker, Ruth Green, Christopher Brightling, Peter Bradding, Andrew J Wardlaw, Ian D Pavord

Thorax 2007;62:1043-1049. doi: 10.1136/thx.2006.073429



Mepolizumab and Exacerbations of Refractory Eosinophilic Asthma

Pranabashis Haldar, M.R.C.P., Christopher E. Brightling, Ph.D., F.R.C.P., Beverley Hargadon, R.G.N., Sumit Gupta, M.R.C.P., William Monteiro, M.Sc., Ana Sousa, Ph.D., Richard P. Marshall, Ph.D., M.R.C.P., Peter Bradding, D.M., F.R.C.P., Ruth H. Green, M.D., F.R.C.P., Andrew J. Wardlaw, Ph.D., F.R.C.P., and Ian D. Pavord, D.M., F.R.C.P.

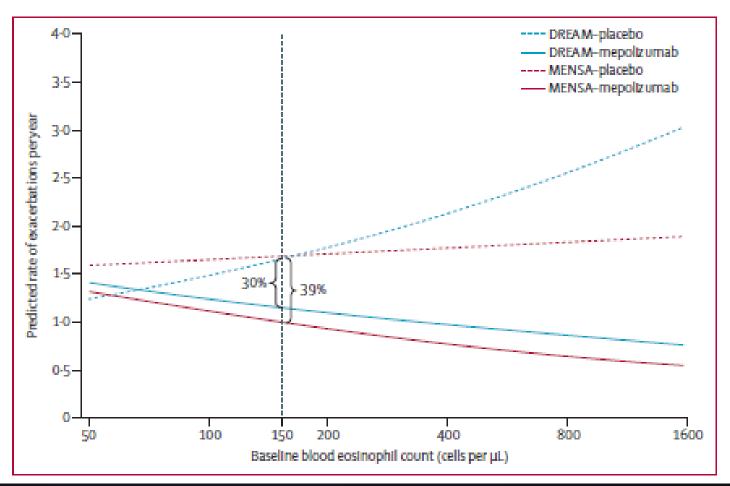


/1 2009]



Severe eosinophilic asthma treated with mepolizumab stratified by baseline eosinophil thresholds: a secondary analysis of the DREAM and MENSA studies

Hector G Ortega, Steven W Yancey, Bhabita Mayer, Necdet B Gunsoy, Oliver N Keene, Eugene R Bleecker, Christopher E Brightling, Ian D Pavord



spir 2016

ASTHMA MANAGEMENT

- Blood eosinophils >0.4 is a marker of increased risk of exacerbations
- Presence of eosinophilia predicts response to inhaled steroids
- Adjusting steroid dosing based on sputum eosinophils can improve outcomes
- Persistent eosinophilia despite treatment may indicate steroid insensitive disease OR poor adherence / technique
- Eosinophilia predicts response to anti- IL5 therapies

WHAT ABOUT NON-EOSINOPHILIC ASTHMA?

- Look for other treatable traits
- Try to avoid excessive steroids
- If frequent infective exacerbations and nothing else to optimise consider azithromycin

PERSPECTIVE
PRECISION MEDICINE FOR AIRWAY DISEASES



Treatable traits: toward precision medicine of chronic airway diseases



Alvar Agusti¹, Elisabeth Bel², Mike Thomas³, Claus Vogelmeier⁴, Guy Brusselle^{5,6}, Stephen Holgate⁷, Marc Humbert⁸, Paul Jones⁹, Peter G. Gibson¹⁰, Jørgen Vestbo¹¹, Richard Beasley¹² and Ian D. Pavord¹³

TREATABLE TRAITS

TREATABLE TRAITS

Specific characteristics of patients including phenotypes of airways disease, overlapping disorders, comorbidities, environmental and lifestyle factors, that potentially contribute to respiratory health, that are potentially amenable to specific treatments.

Table 5: Treatable traits in asthma.

Overlapping disorders:

- COPD
- Bronchiectasis
- Allergic bronchopulmonary aspergillosis
- Dysfunctional breathing including vocal cord dysfunction.

Comorbidities:

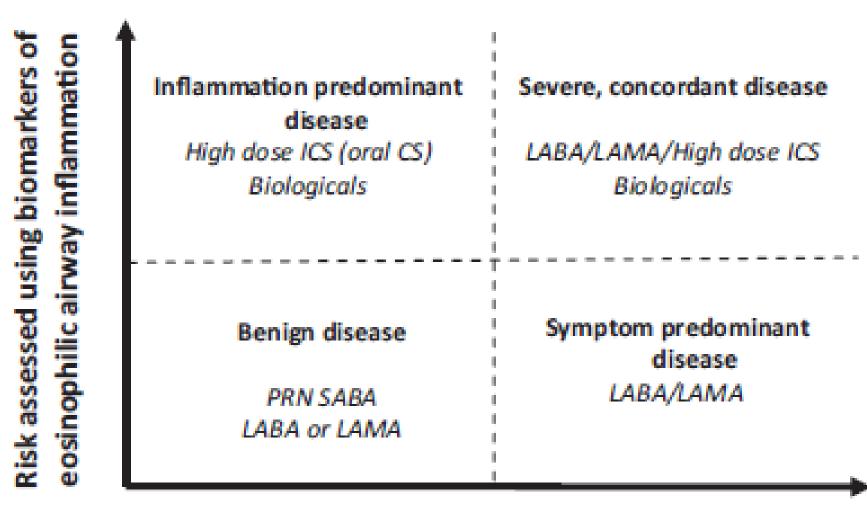
- Obesity
- Gastro-oesophageal reflux disease
- Rhinitis
- Sinusitis
- Depression/anxiety.

Environmental:

- Smoking
- Occupational exposures
- Provoking factors including aspirin, other NSAIDs and beta blockers.

Behavioural:

- Adherence
- Inhaler technique.



Symptoms due to airflow limitation

SUMMARY

- Not all asthma is the same
- Around 50% of patients with astahma have evidence of eosinophilic inflammation
- Assessment of eosinophils in asthma:
 - Can help confirm the diagnosis of asthma
 - Can hint at poor adherence
 - Can help guide the use of steroids in asthma
 - In the (?near) future will be essential to determine eligibility for biological therapies
- Considering treatable traits may help you personalise treatment for your patient

ANY QUESTIONS?

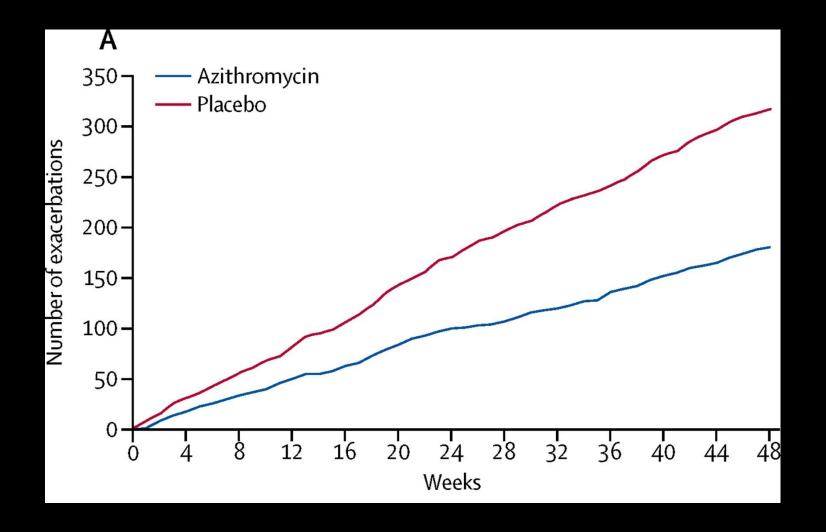
Effect of azithromycin on asthma exacerbations and quality of life in adults with persistent uncontrolled asthma (AMAZES): a randomised, double-blind, placebo-controlled trial

Prof Peter G Gibson, MBBS, Prof Ian A Yang, MBBS, Prof John W Upham, MBBS, Prof Paul N Reynolds, MD, Prof Sandra Hodge, PhD, Prof Alan L James, FRACP, Prof Christine Jenkins, MD, Prof Matthew J Peters, MBBS, Prof Guy B Marks, PhD, Melissa Baraket, PhD, Heather Powell, MMedSc, Steven L Taylor, BSC, Lex E X Leong, PhD, Prof Geraint B Rogers, PhD, Prof Jodie L Simpson, PhD

The Lancet
Volume 390, Issue 10095, Pages 659-668 (August 2017)
DOI: 10.1016/S0140-6736(17)31281-3



Figure 2





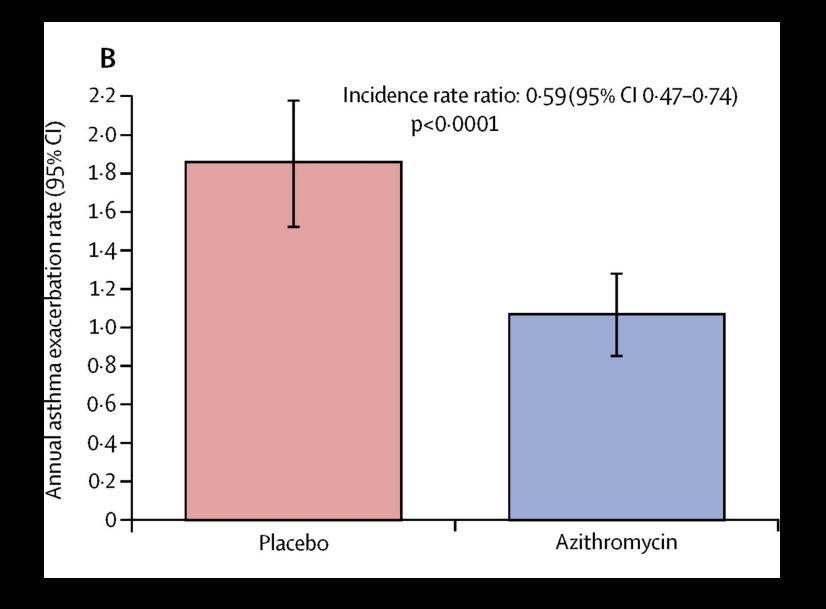


Figure 3

	Number	Exacerbations per person-year					Incidence rate ratio (95% CI)
		Placebo	Azithromyc	<u>in</u>			
Non-eosinophilic asthma	224	1.74	1.15				0.66 (0.47-0.93)
Eosinophilic asthma	196	1.98	0.96	•			0.52 (0.29-0.94)
Inhaled corticosteroid dose adjustment	420	1.86	1.07	-			0.58 (0.46–0.74)
Frequent exacerbators	140	2.79	1.47		<u> </u>		0.55 (0.41-0.73)
Cough and sputum VAS	48	1.72	0.79 -	•			0.49 (0.26-0.95)
Bacteria-negative	188	1.85	1.18		_		0.61 (0.52-0.72)*
Bacteria–positive	48	2.64	1.11 —		•		0.39 (0.22-0.69)
		Q	0.2	0.4 0.6	0.8	1·0 1	1·2 1·4
			Fa	← avours azithromyc	in		→ s placebo



CASE

45 year old female factory worker with atopic asthma

On 'Step 3' ICS/LABA treatment, Fluticasone/salmeterol 50/25 ii BD

Repeat courses of oral steroids for exacerbations

Background of anxiety/depression.

DEFAULT OPTION

The standard stepwise approach would be to either:

- Increase the ICS dose by stepping up to a higher dose FP/SM 100/25 2 bd. On the basis that this is likely to be ICS responsive eosinophilic asthma.
- Change to budesonide/formoterol 200/6 2 bd and one as required on the basis that a change to the SMART regimen reduces the risk of severe exacerbations.

POTENTIAL TREATABLE TRAITS IN THIS CASE

- Eosinophilic asthma
- Psychogenic vocal cord dysfunction
- Allergic bronchopulmonary aspergillosis
- Chronic rhinosinusitis
- Occupational asthma
- Adherence, inhaler technique