Is it time to escalate to Triple Therapy and Trelegy 200 for your asthma patients?

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Moderator: 陳崇裕 醫師

September 17th 2023

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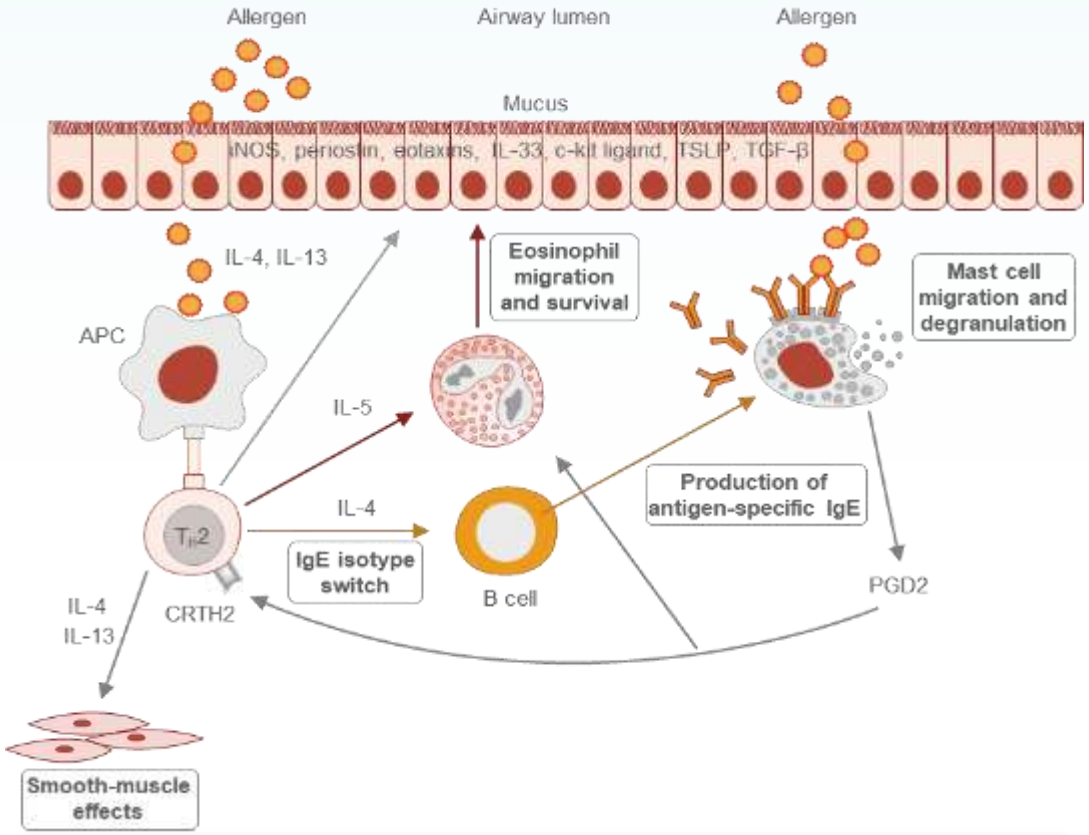
- For full prescribing information, refer to the package inserts approved by TFDA.

GSK

Outline

1. Overview of asthma
2. Clinical unmet need in asthma care
3. The role of LAMA in asthma treatment
4. Summary

Asthma Is Characterized by Chronic Inflammation & Variable Airway Obstruction



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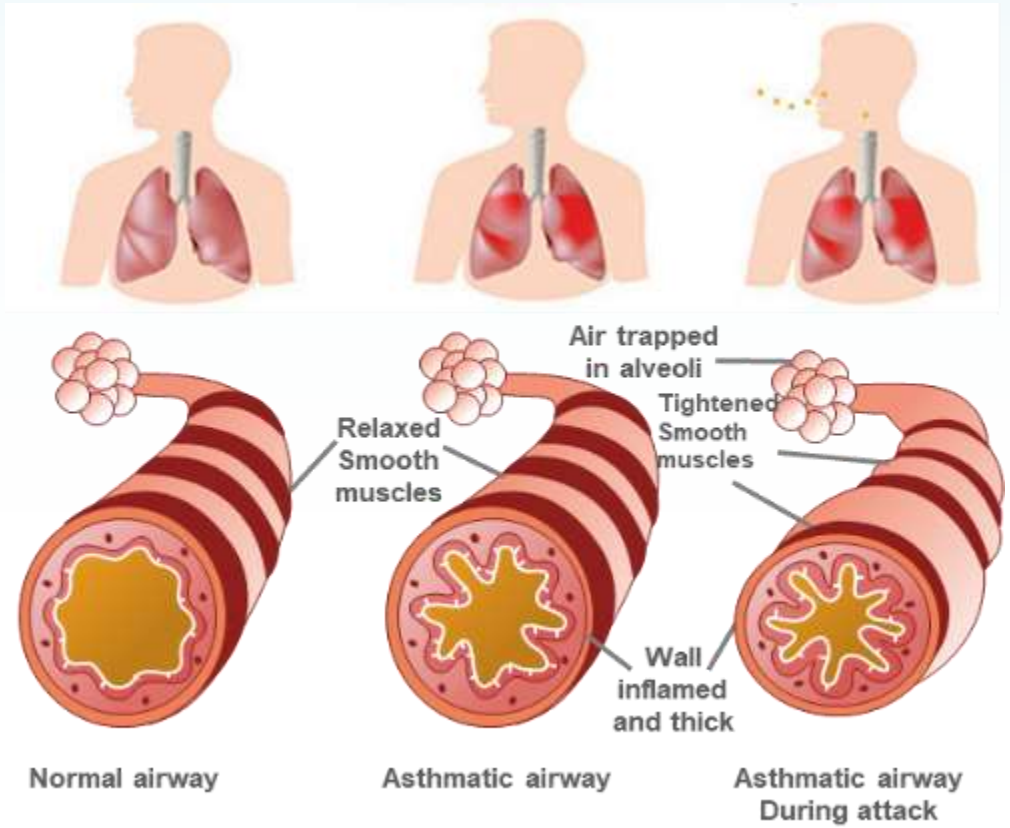


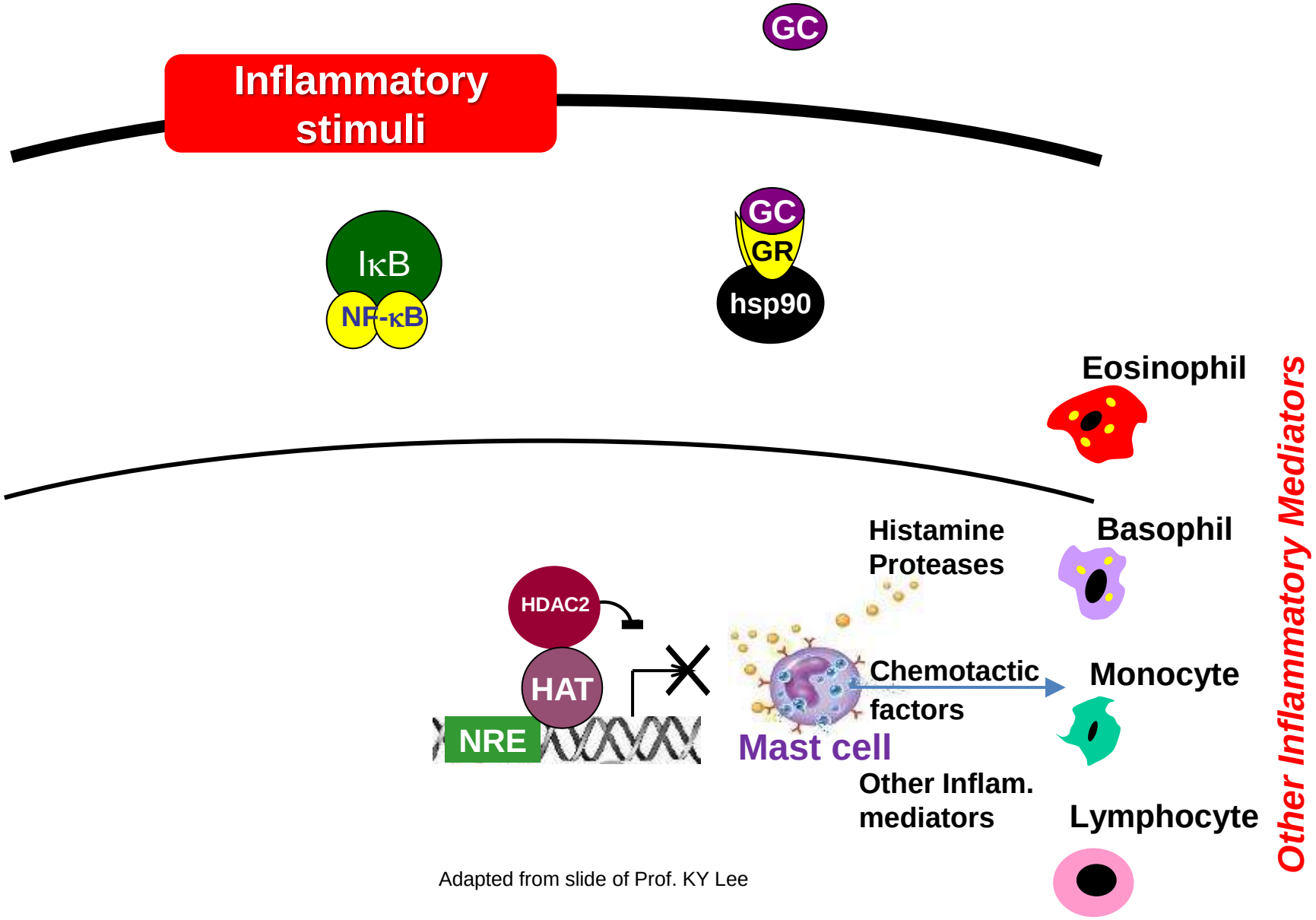
Due to the chronic inflammation, ICS is the cornerstone in the management of asthma

Bronchodilation in asthma can be achieved by the use of LABA and LAMA

DC, dendritic cell; IgE, immunoglobulin E; IL, interleukin; Th2, T helper 2; TSLP, thymic stromal lymphopoietin

1. Wenzel S. Nat Med 2012;18:716–725
2. Palomares O & Akdis CA. 2015. ISBN:978-0-323-29875-9
3. Palomares O, et al. Immunol Rev 2017;278:219–236

Mechanism of Glucocorticoid-mediated Anti-inflammation

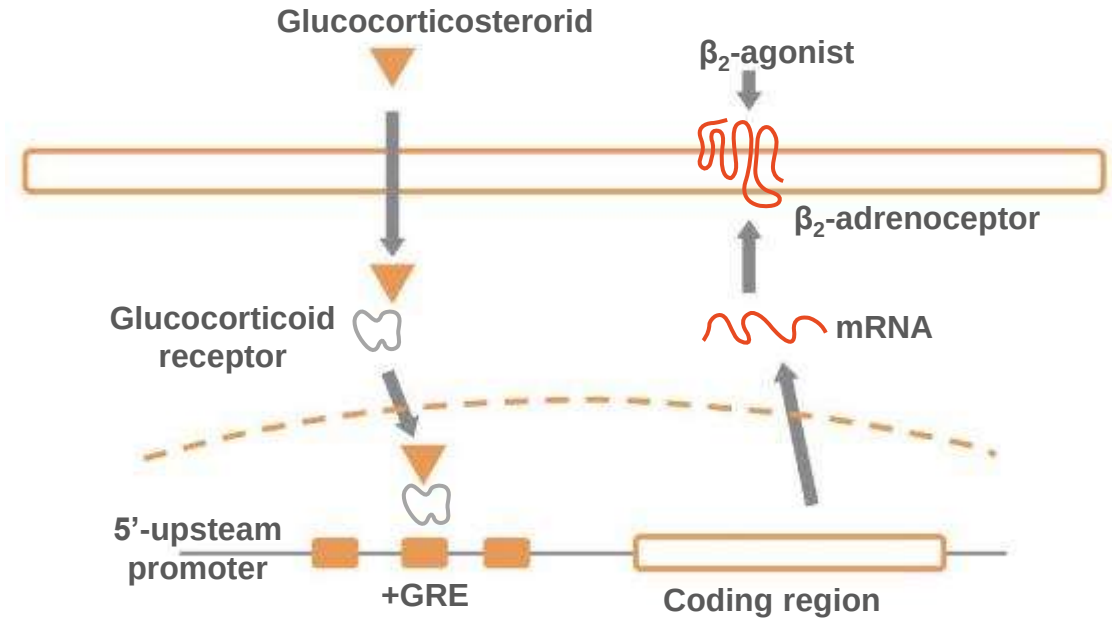


Adapted from slide of Prof. KY Lee

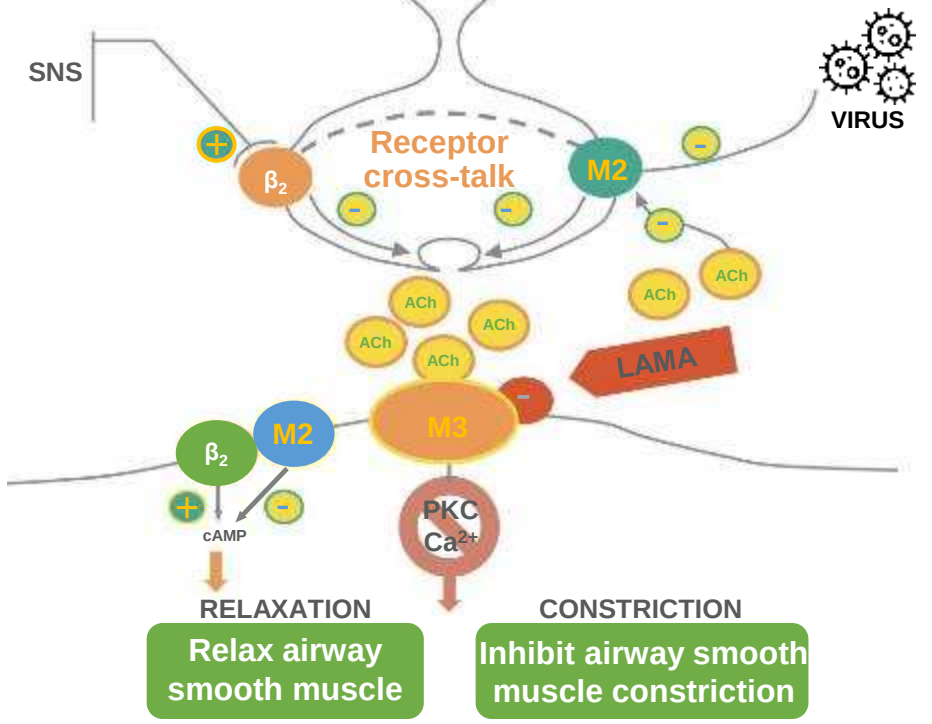
The Complementary Mechanisms of Action of LABA, LAMA & ICS

- **Synergic effects between ICS and β_2-agonists[1]**
  - β_2-agonists enhance the action of corticosteroids, with an increase in nuclear translocation of glucocorticoid receptors.
  - Corticosteroids increase the expression of β_2-adrenergic receptors in the lungs and prevent their downregulation and uncoupling in response to β_2-agonist activation
- **Muscarinic antagonists provide bronchodilation in a way that is both complementary and different to β_2-agonists.[1]**

ICS & LABA[1]



LAMA[2]



GRE, glucocorticoid-responsive elements; SNS, sympathetic nervous system

1. Barnes PJ, Adcock IM. *Ann Intern Med* 2003;139:359–370
2, Lipworth BJ. *Br J Clin Pharmacol*. 2014;77(1):55–62 4.

Asthma Is A Heterogeneous Disease With Several Phenotypes

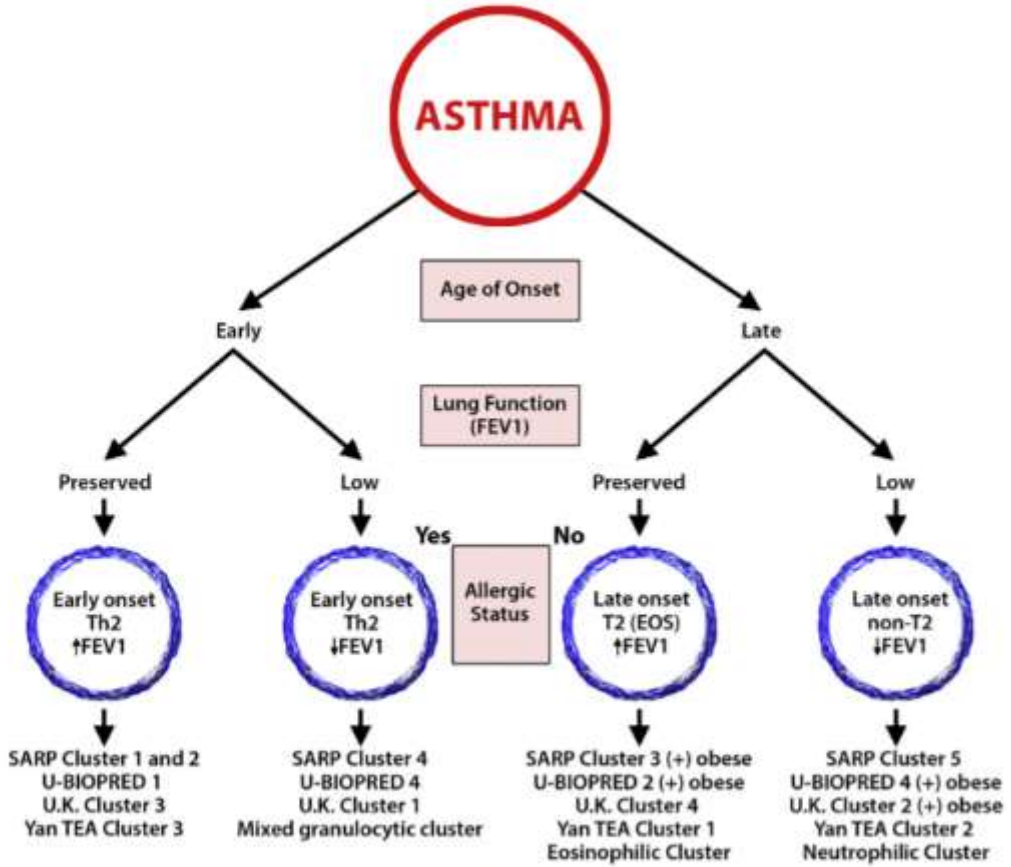


FIG 1. Diagram showing similarities between asthma phenotypes in cluster analysis studies using age of onset and lung function. Inflammatory subtypes: T_H2, positive IgE level, positive SPT response, elevated F_{ENO} value, elevated eosinophil count; eosinophilic *(T2)*, elevated eosinophil count, negative IgE level/SPT response, and elevated F_{ENO} value; *non-T2*, normal eosinophil count, negative IgE level/SPT response, and normal F_{ENO} value. Disease modifier includes obesity, which is present in both eosinophilic and noneosinophilic late-onset asthma. *EOS*, Eosinophils.

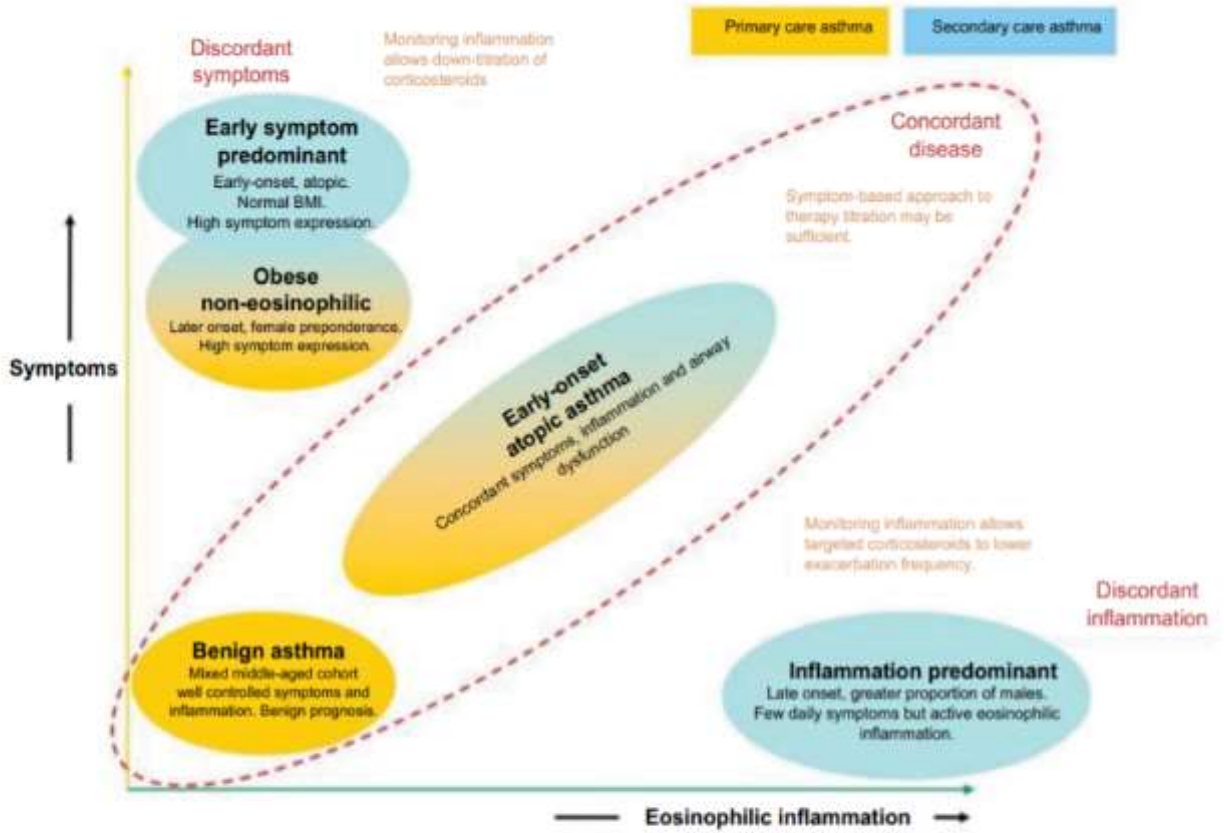


Figure 1 Asthma phenotypes, based on cluster analysis.

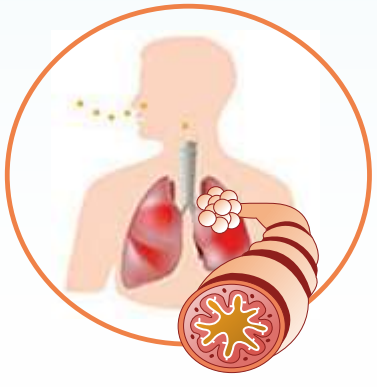
Notes: Reprinted with permission of the American Thoracic Society. Copyright© 2018 American Thoracic Society. Haldar P, Pavord ID, Shaw DE, Berry MA, Thomas M, Brightling CE, Wardlaw AJ, Green RH. Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med*. 2008;178(3):218–24.[7] The American Journal of Respiratory and Critical Care Medicine is an official journal of the American Thoracic Society.

1. J Allergy Clin Immunol. 2019 Jul;144(1):1-12.
2. 2. J Asthma Allergy. 2019; 12: 7–19.

GINA-defined Asthma Treatment Goals Can Be Summarized as:

To achieve good **control of symptoms** and maintain **normal activity levels**

+

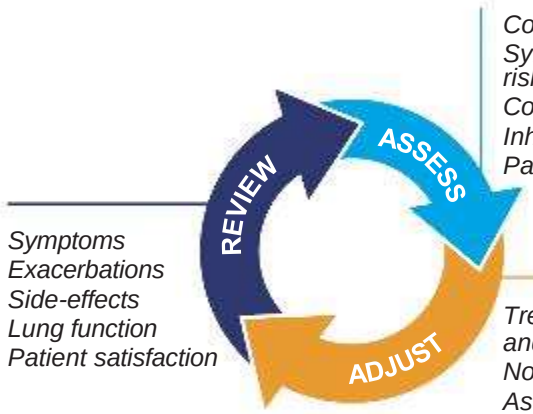


To **minimize** future risk of **exacerbations, fixed airflow limitation** and **side effects**

GINA 2022. www.ginasthma.org

Adults & adolescents 12+ years

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



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2B)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed low-dose ICS-formoterol			

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP
RELIEVER: As-needed short-acting beta$_2$-agonist				

Other controller options for either track (limited indications, or less evidence for efficacy or safety)

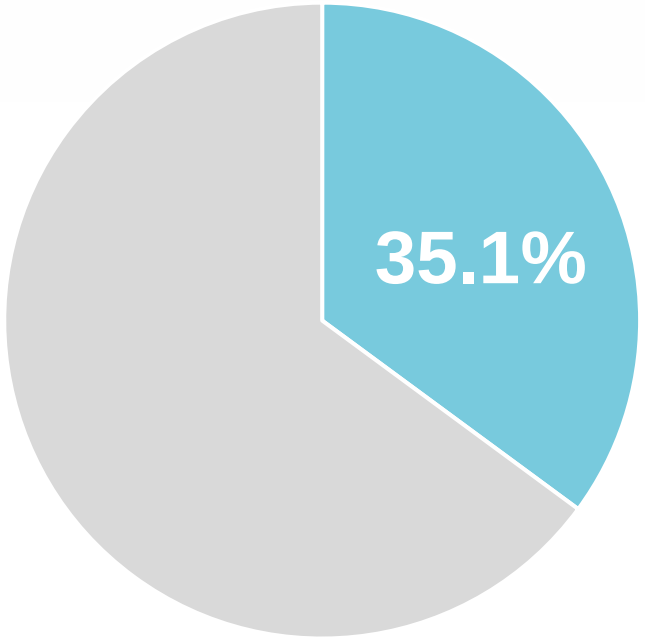
	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

More than One in Three Patients Remain Uncontrolled Despite Using Inhaled Treatments

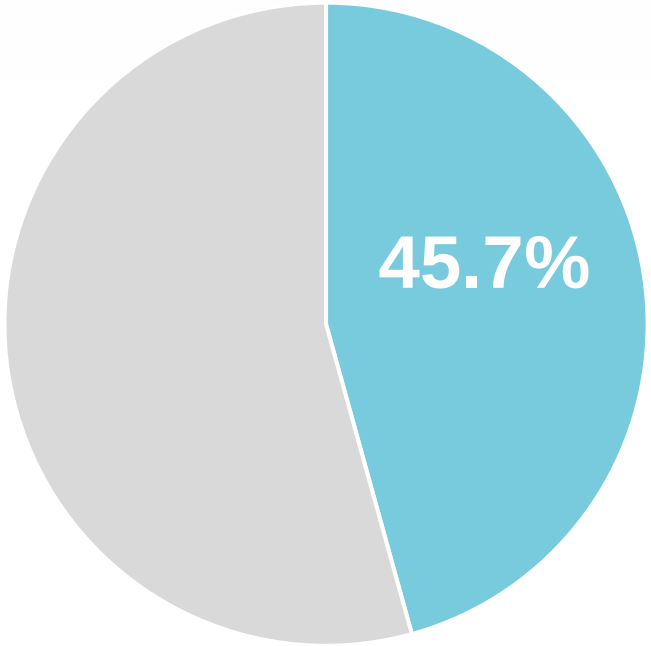
Proportion of patients with uncontrolled asthma despite receiving LABA/ICS

One year follow up in UK primary care settings

Medium-dose LABA/ICS
(n=29,229)



High-dose LABA/ICS
(n=16,575)



ICS, inhaled corticosteroid; LABA, long-acting beta agonist

Buhl R et al., *Respir Med.* 2020 Feb;162:105859.

Retrospective cohort study in patients with asthma newly initiated with medium- or high-dose ICS-LABA, followed up for a minimum of 12 months. Data from the United Kingdom Clinical Practice Research Datalink analysed between 01 January 2006 and 28 February 2016. Plotted data is patients who were uncontrolled during the post-index period.

Many Patients with Asthma Continue to Experience Symptoms Despite Treatment with ICS/LABA

Patients may continue to experience symptoms on ICS/LABA therapy:[1]

~50% Suffer from one or more night-time awakenings a week

~50% Suffer from 3 or more days with symptoms a week

~25% Have normal activities affected by symptoms 3 or more days a week

30%

of whom continue to experience symptoms despite good adherence and inhaler technique[2]

ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist.

1. Price D, et al. *NPJ Prim Care Respir Med* 2014;24;14009; 2. Bateman ED, et al. *Am J Respir Crit Care Med* 2004;170;836–44.

Poor asthma symptom control may be a result of overlooked and undertreated bronchoconstriction

13–26% of patients underperceive bronchoconstriction due to asthma

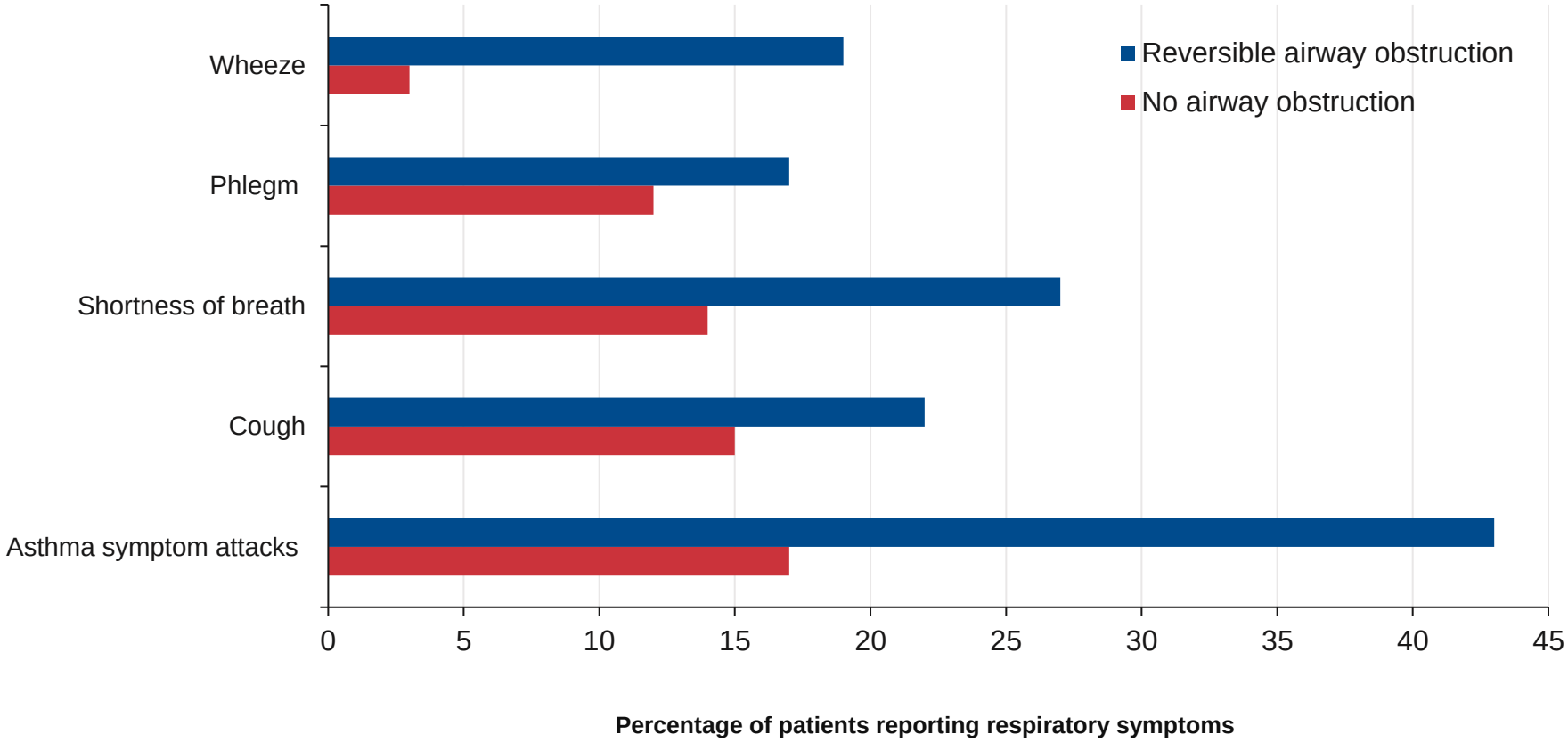
Bronchoconstriction is often overlooked by patients[1–3]

Undertreated bronchoconstriction due to asthma

contributes to **poor asthma symptom control**[4,5]

. Barnes PJ, et al. *J Allergy Clin Immunol* 2019;144;1180–6; 2. van Schayck CP, et al. *Thorax* 2000;55;562–5; 3. GINA: Global Strategy for Asthma Management and revention 2022. http://www.ginasthma.org [Accessed July 2023]; 4. Thamrin C, et al. *Thorax* 2011;66;1036–42; 5. Heffler E, et al. *Respir Med* 2016;112;45–50.

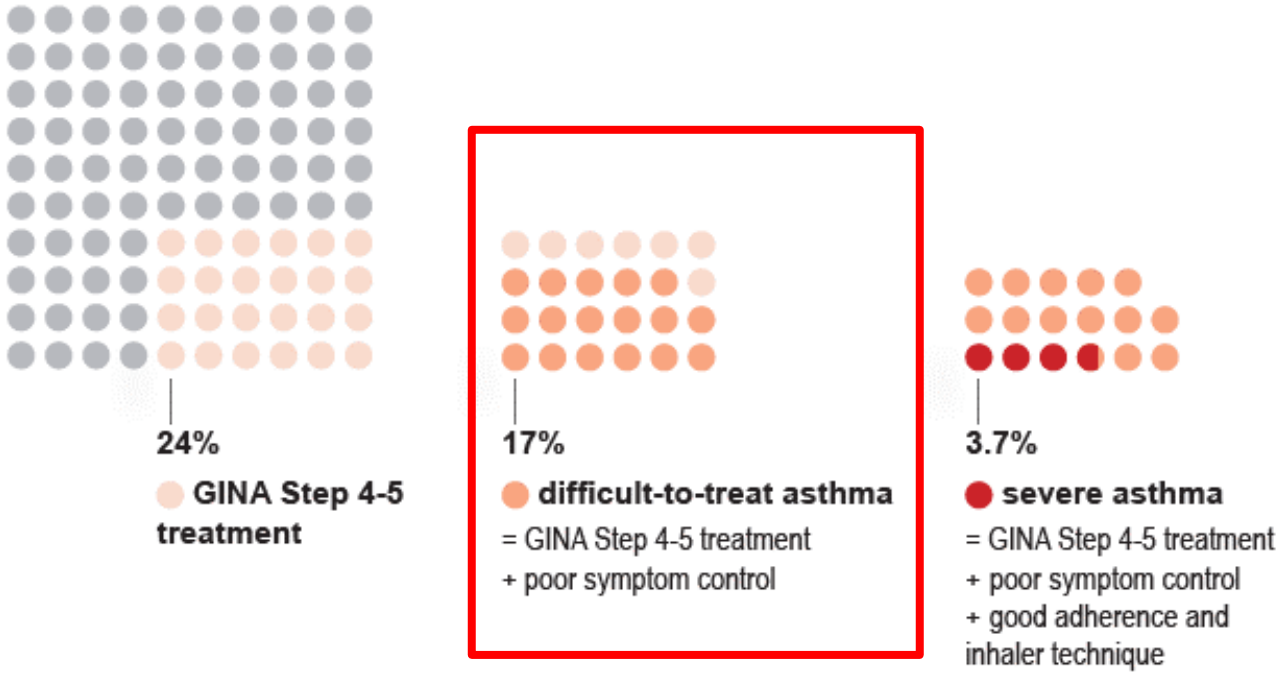
Symptoms are reported more in patients with asthma with airflow obstruction than without and could be due to undertreated bronchoconstriction



Vonk JM, et al. Thorax 2003;58:322–7.

Difficult-to-treat asthma (17% of total asthma patients) remain high unmet needs in clinical practice

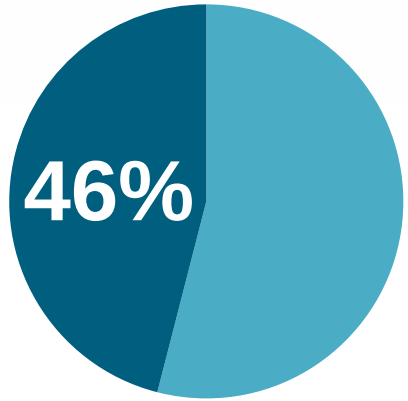
Box 1. What proportion of adults have difficult-to-treat or severe asthma?



These data are from a Dutch population survey of people ≥18 years with asthma[2]

Proportion of patients with uncontrolled asthma despite receiving high-dose LABA/ICS

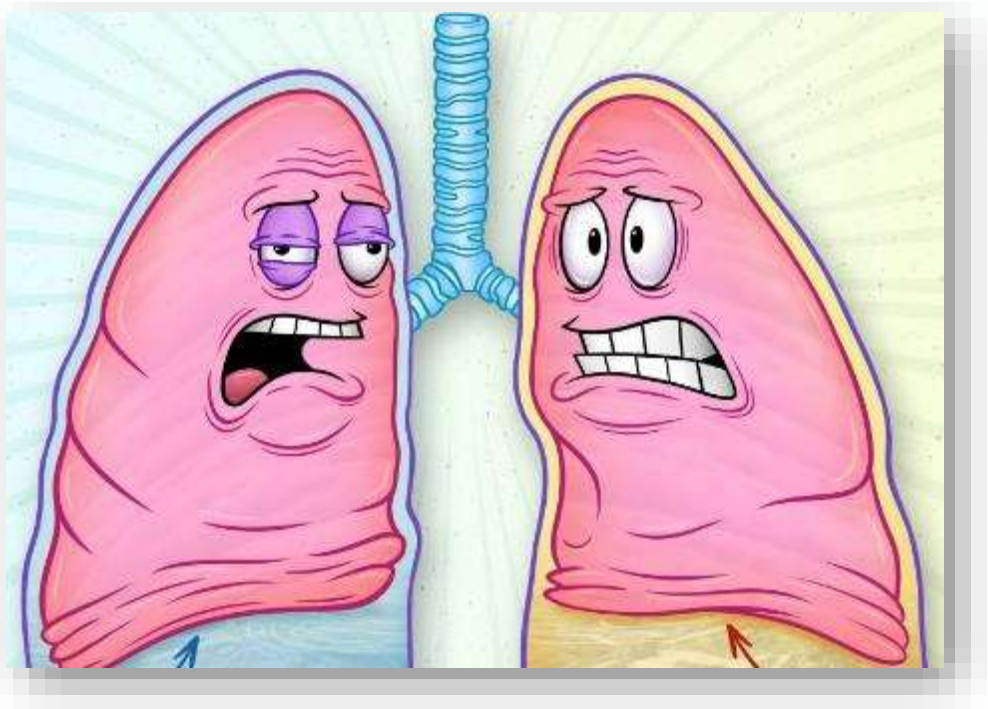
(n=16,575)



ICS = inhaled corticosteroid; LABA = long-acting beta agonist
Retrospective cohort study in patients with asthma newly initiated with medium- or high-dose ICS-LABA, followed up for a minimum of 12 months. Data from the United Kingdom Clinical Practice Research Datalink analysed between 01 January 2006 and 28 February 2016. Plotted data is patients who were uncontrolled during the post-index period.

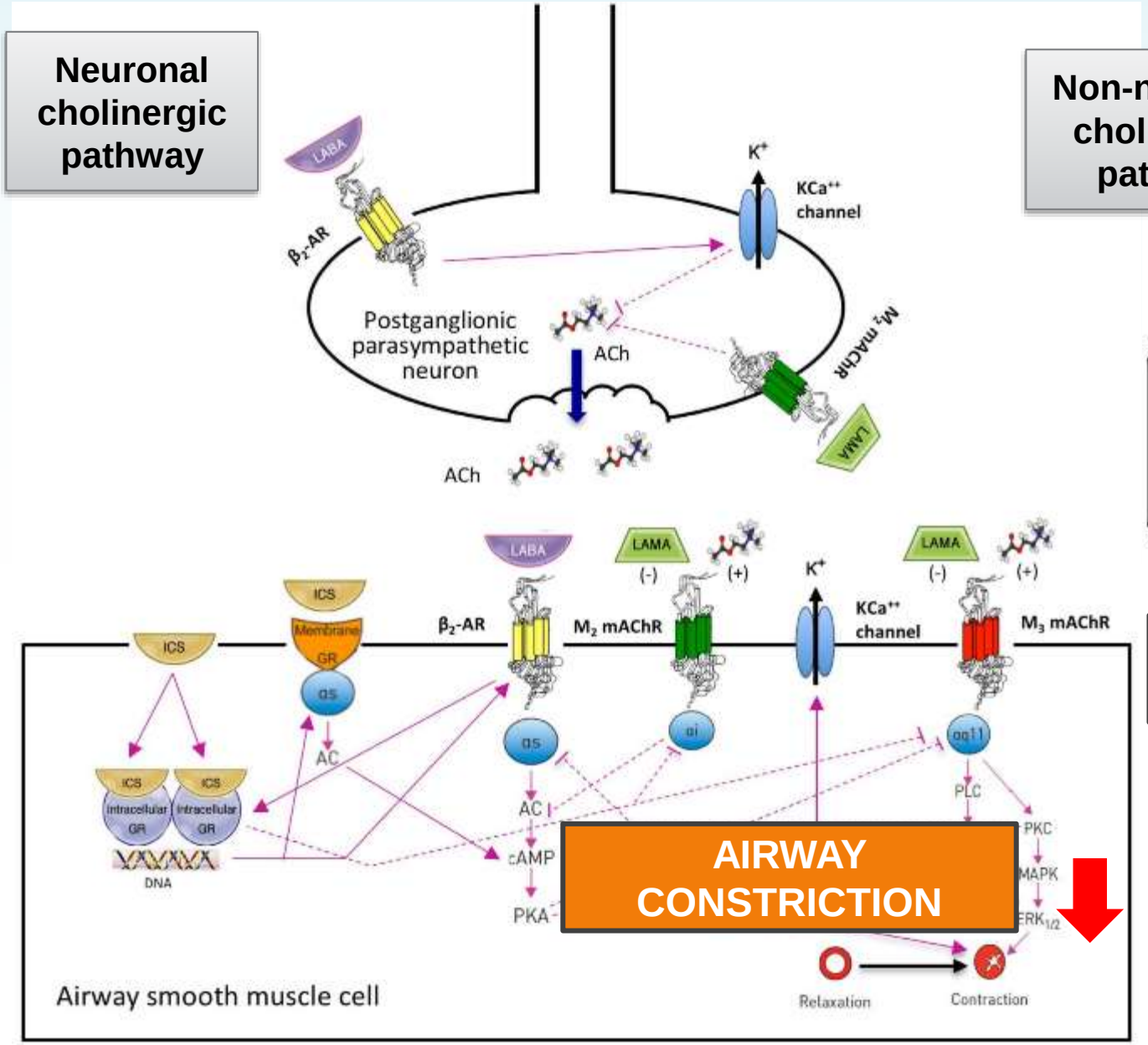
Hekking et al, JACI 2015 *Buhl R, et al. Resp Med 2020;105859.*

Benefit of LAMA in Asthma Treatment



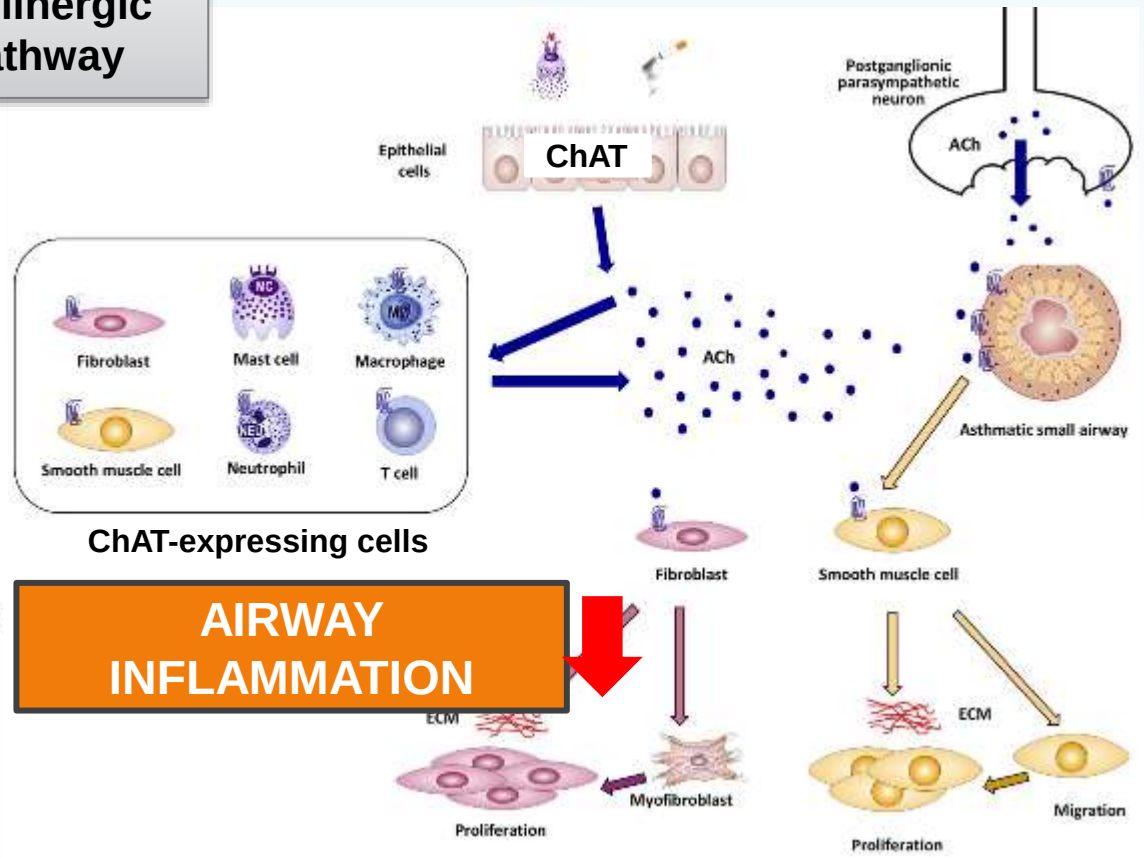
Allergy

Neuronal cholinergic pathway



AIRWAY CONSTRICTION

Non-neuronal cholinergic pathway



ChAT-expressing cells

AIRWAY INFLAMMATION

AIRWAY REMODELING

LAMA

ChAT: Choline acetyl transferase

Allergy. 2021;00:1–12

LAMA, long-acting muscarinic antagonist; M3, muscarinic acetylcholine subtype 3; SAMA, short-acting muscarinic antagonist.
Figure from Expert Opin Investig Drugs 2017;26;761–6. figure 1.
1. Ferrando M, et al. *Expert Opin Investig Drugs* 2017;26;761–6; 2. Gosens R, et al. *Eur Respir J* 2018;52;1701247; 3. Bulkhi A, et al. *Drugs* 2016;76;999–1013

LAMAs prevent bronchoconstriction and reduce mucus secretion

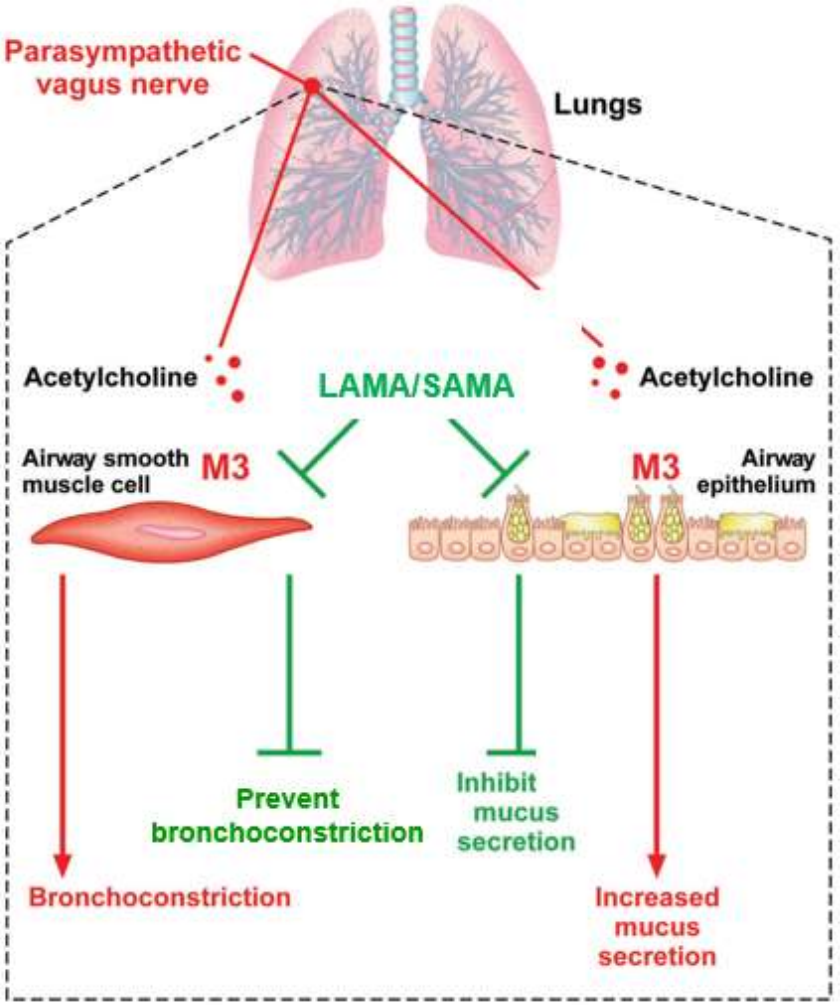
Role of acetylcholine in asthma

Acetylcholine plays a key role in the pathophysiology of obstructive airway diseases such as asthma, through binding to muscarinic receptors inducing bronchial smooth muscle constriction[1–3]

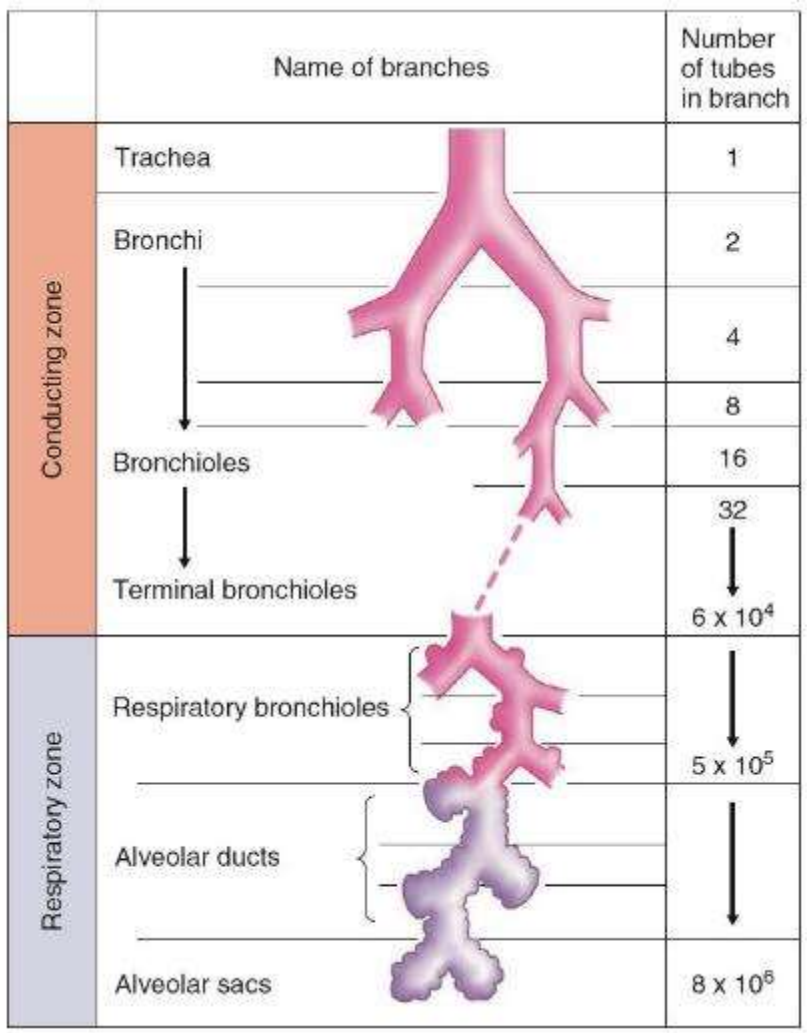
Role of LAMA in asthma

LAMAs bind to and inhibit activation of M3 receptors by acetylcholine, blocking smooth muscle contraction and preventing bronchoconstriction[3]

LAMAs also inhibit a key feature of asthma
– Acetylcholine-induced mucus[2]



Respective Advantages of LAMA and LABA



LAMA:
predominantly inhibits **tonic** contraction of **large** airways

LABA:
predominantly inhibits **phasic** contraction of **small** airways

Symptoms / Signs

Chest tightness
Breathlessness at rest
(tonic contraction)

Breathlessness on rapid breathing
(airflow turbulence)

Upper wheezes

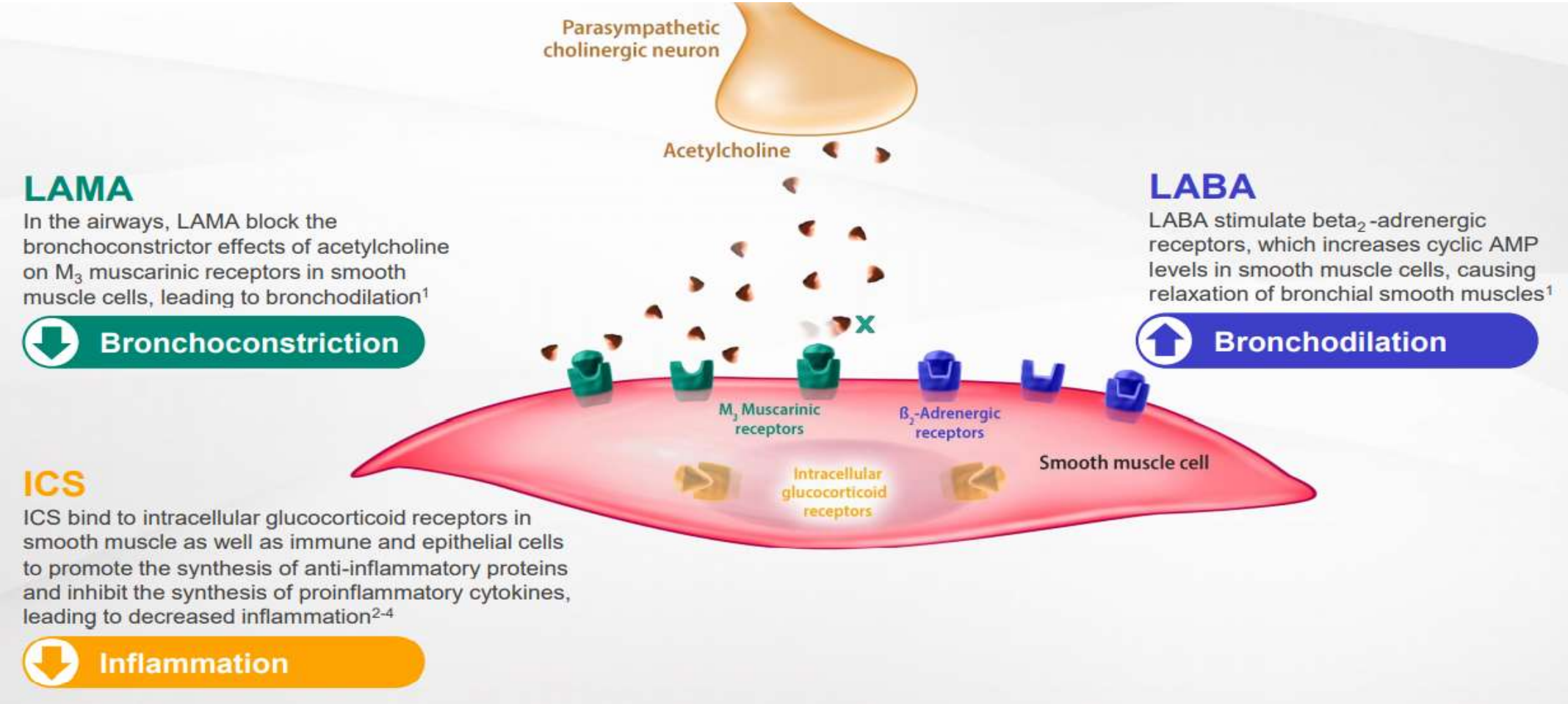
Exertional dyspnea and exercise incapability
(dynamic air-trapping)

Vulnerability to environmental stimulation
(phasic contraction)

End-expiratory wheezes

1. http://biosiva.50webs.org/respiration.html (last accessed 2023.07);
2. Allergy Asthma Immunol Res. 2017 September;9(5):386-393;
3. Nature reviews. Disease primers;2015;1;15076

LAMA Work Through a Distinct, Complementary Pathway to Support Bronchodilation

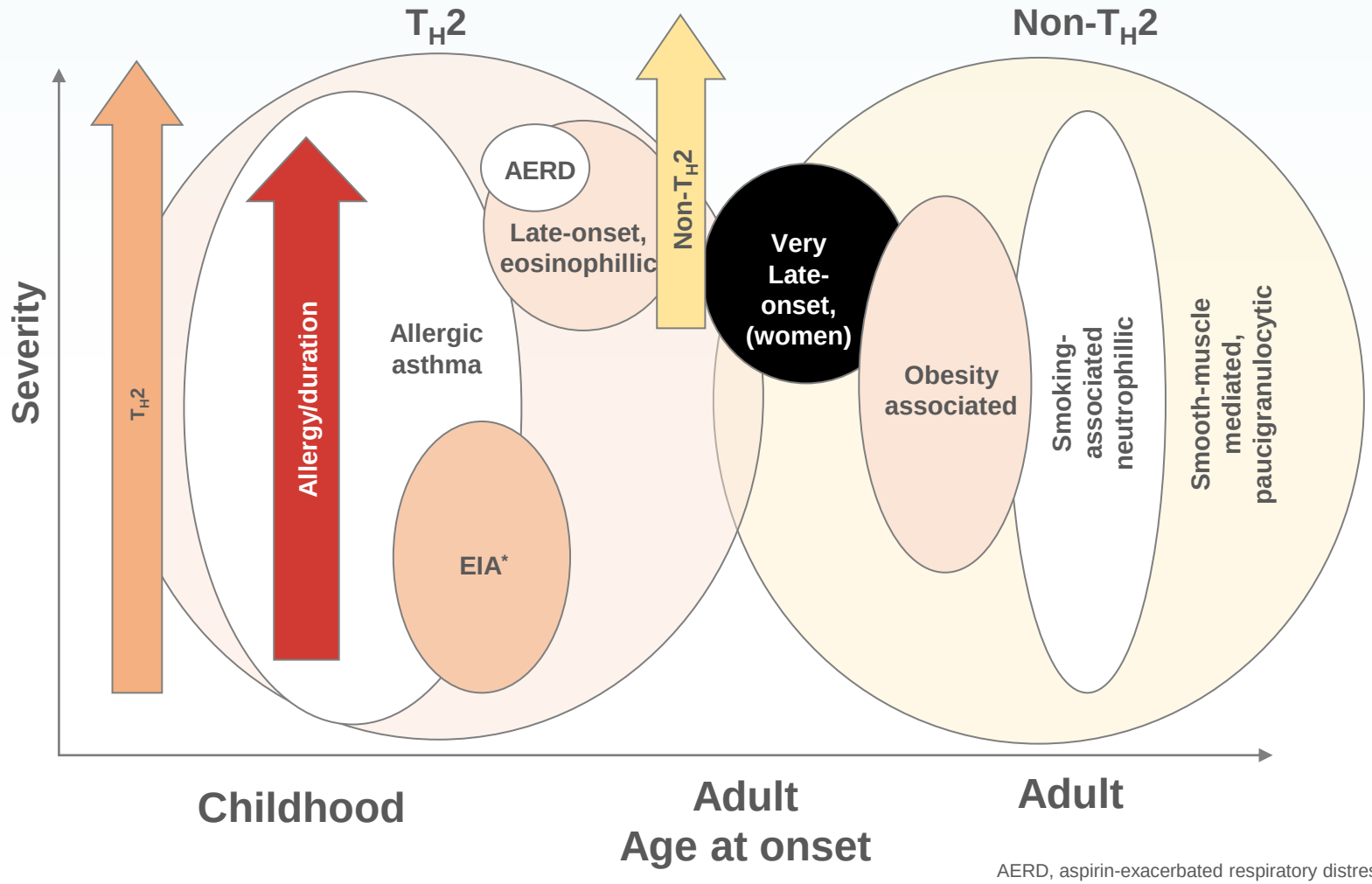


LAMA=long-acting muscarinic antagonist.

References: 1. Cazzola M, et al. Pulm Pharmacol Ther. 2010;23:257-267. 2. Suissa S, et al. Proc Am Thorac Soc. 2007;4:535-542. 3. Raissy HH, et al. Am J Respir Crit Care Med. 2013;187(8):798-803. 4. Barnes PJ. Pharmaceuticals (Basel). 2010;3(3):514-540.

Endotyping Asthma: T_H2-high asthma & non-T_H2 asthma

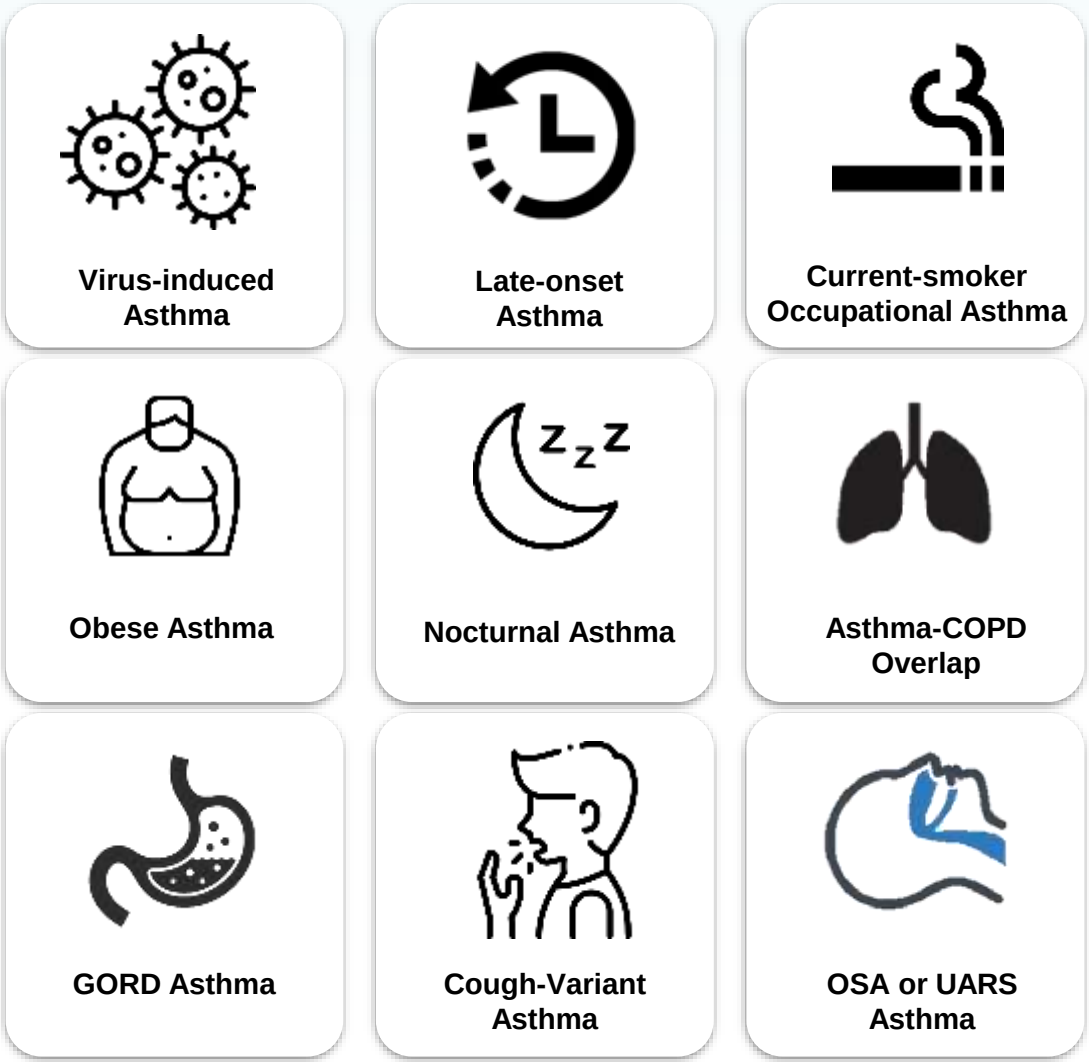
- T_H2 high most recognized phenotypes are allergic and eosinophilic asthma



AERD, aspirin-exacerbated respiratory distress; EIA, exercise-induced asthma; Th2, T helper 2

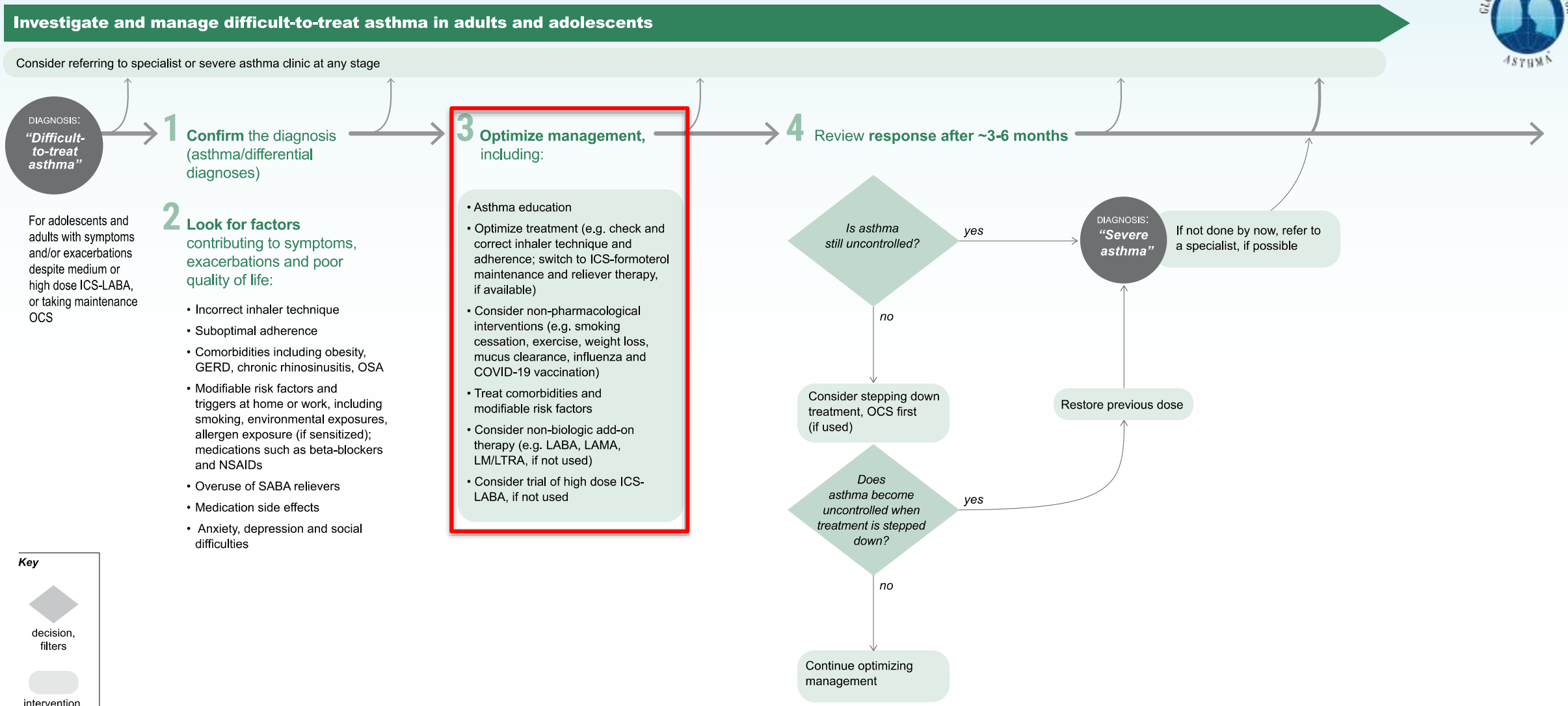
1. Wenzel S. Nat Med. 2012;18:716–725
2. Woodruff PG, et al. Am J Respir Crit Care Med. 2009;180:388–395
3. Fahy JV. Nat Rev Immunol. 2015;15:57–65

Add on LAMA Treatment Could Be Started With A Specific Phenotype of Asthma Subjects



Courtesy of Prof. Lin in CGMH-LK

GP OR SPECIALIST CARE



Severe Asthma Managements Proposed by GINA

Could patient have Type 2 airway inflammation?

no

No evidence of Type 2 airway inflammation

- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
- Avoid exposures (tobacco smoke, allergens, irritants)
- Consider investigations (if available and not done)
  - Sputum induction
  - High resolution chest CT
  - Bronchoscopy for alternative/additional diagnoses
- Consider trial of add-on treatments (if available and not already tried)
  - LAMA
  - Low dose azithromycin
  - Anti-IL4R* if taking maintenance OCS
  - Anti-TSLP* (but insufficient evidence in patients on maintenance OCS)
  - As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
- Consider bronchial thermoplasty (+ registry)
- Stop ineffective add-on therapies

Go to section **10**

7 Consider *other* treatments

Could patient have Type 2 airway inflammation?

yes

Type 2 airway inflammation

- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
- Consider add-on non-biologic treatment for specific Type 2 clinical phenotypes, e.g. AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis

Is add-on Type 2 biologic therapy available/ affordable?

yes

no

If add-on Type 2-targeted biologic therapy is NOT available/affordable

- Consider higher dose ICS, if not used
- Consider other add-on therapy (e.g. LAMA, LM/LTRA, low dose azithromycin)
- As last resort, consider add-on low dose OCS, but implement strategies to minimize side-effects
- Stop ineffective add-on therapies

Go to section 10

LAMAs Approved for Treatment of Asthma

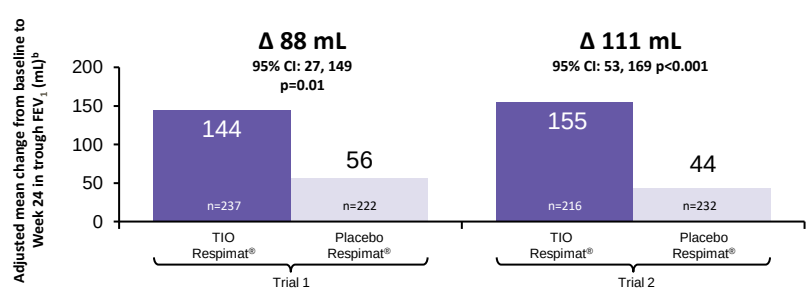
LAMA	THERAPY	TRIPLE THERAPY (ICS/LAMA/LABA)	STUDY	NAME	FIRST GLOBAL APPROVAL	SPONSOR
Tiotropium (TIO)	Add-on to ICS/LABA	–	PrimoTinA[1]	Spiriva Respimat	2014[2]	Boehringer Ingelheim and Pfizer
Umeclidinium (UMEC)	**Triple therapy (ICS/LAMA/LABA)**	**Fluticasone furoate/Umeclidinium/ Vilanterol**	**CAPTAIN[3]**	**Trelegy Ellipta**	**2020[4]**	**GSK**
Glycopyrronium bromide (GLY)	Triple therapy (ICS/LAMA/LABA)	Mometasone furoate/Glycopyrronium bromide/Indacaterol acetate	IRIDIUM[5]	Enerzair Breezhaler	2020[6]	Novartis
Glycopyrronium bromide (GLY)	Triple therapy (ICS/LAMA/LABA)	Beclometasone dipropionate/Glycopyrronium bromide/Formoterol fumarate	TRIMARAN and TRIGGER[7]	Trimbow pMDI	2021[8]	Chiesi Farmaceutici SpA

ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; pMDI, pressurised metered dose inhaler.

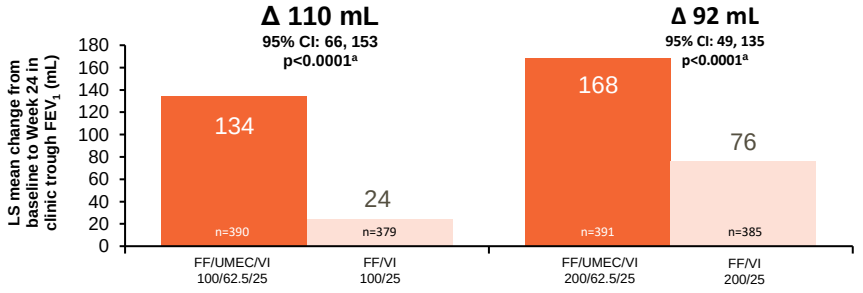
1. Kerstjens HAM, et al. *N Engl J Med* 2012;367;1198–207; 2. Boehringer Ingelheim Spiriva Respimat press release 16 September 2015 [Accessed July 2023]; 3. Lee LA, et al. *Lancet Respir Med* 2021;9; 69–84; 4. GSK Trelegy Ellipta press release 9 September 2020 [Accessed July 2023]; 5. Kerstjens HAM, et al. *Lancet Respir Med* 2020;8;1000–12; 6. Novartis Enerzair Breezhaler press release 7 July 2020 [Accessed July 2023]; 7. Virchow JC, et al. *Lancet* 2019;394;1737–49; 8. Chiesi Trimbow press release 1 February 2021 [Accessed July 2023].

Lung function improvements were observed with ICS/LAMA/LABA triple therapy compared with ICS/LABA in several clinical trials

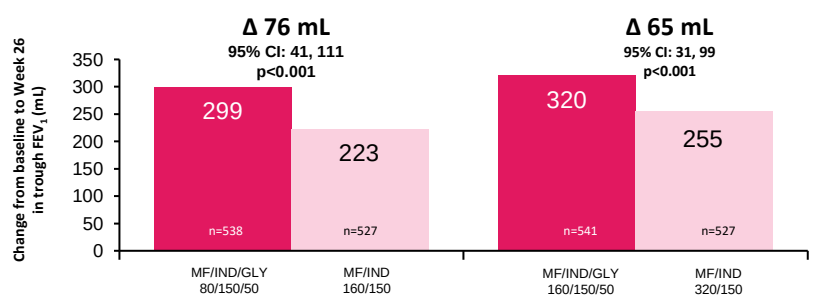
PrimoTinA[1–3]



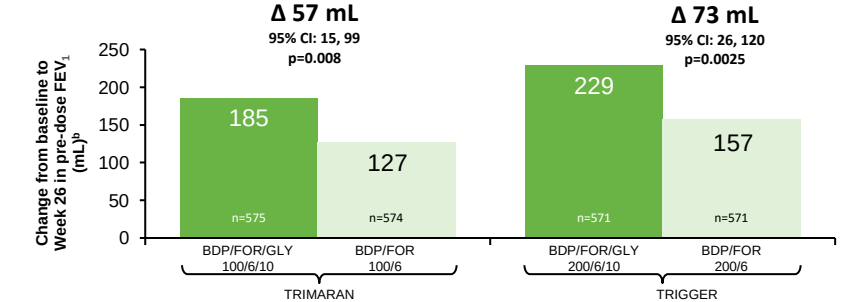
CAPTAIN[4]



IRIDIUM[5]



TRIMARAN & TRIGGER[6]



It is inappropriate to draw any comparisons and /or make any conclusions as the study design, demographics and other criteria may be different.

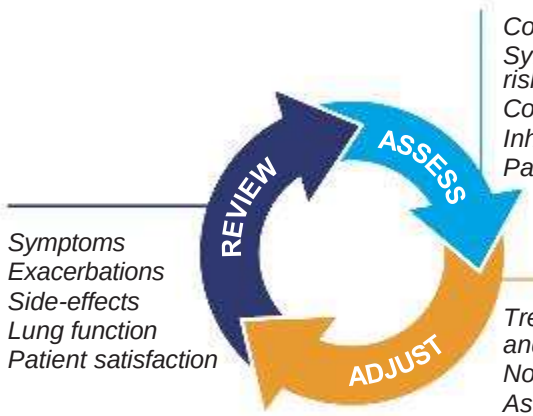
All doses are presented in µg. [A]p-value adjusted for multiplicity; [b]co-primary endpoint.

BDP, beclometasone dipropionate; CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; FOR, formoterol fumarate; GLY, glycopyrronium bromide; ICS, inhaled corticosteroid; IND, indacaterol acetate; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; LS, least squares; MF, mometasone furoate; TIO, tiotropium; UMEC, umeclidinium; VI, vilanterol.

1. Kerstjens HAM, et al. *N Engl J Med* 2012;367;1198–207; 2. ClinicalTrials.gov NCT00772538. [Accessed July 2023]; 3. ClinicalTrials.gov NCT00776984. [Accessed July 2023]; 4. Lee LA, et al. *Lancet Respir Med* 2021;9;69–84; 5. Kerstjens HA, et al. *Lancet Respir Med* 2020;8;1000–12; 6. Virchow JC, et al. *Lancet* 2019;394;1737–49.

Adults & adolescents 12+ years

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



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2B)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

CONTROLLER and **PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2
As-needed low dose ICS-formoterol

STEP 3
Low dose maintenance ICS-formoterol

STEP 4
Medium dose maintenance ICS-formoterol

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER**
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1
Take ICS whenever SABA taken

STEP 2
Low dose maintenance ICS

STEP 3
Low dose maintenance ICS-LABA

STEP 4
Medium/high dose maintenance ICS-LABA

STEP 5
Add-on LAMA
Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4R, anti-TSLP

RELIEVER: As-needed short-acting $beta_2$-agonist

Other controller options for either track (limited indications, or less evidence for efficacy or safety)

Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT

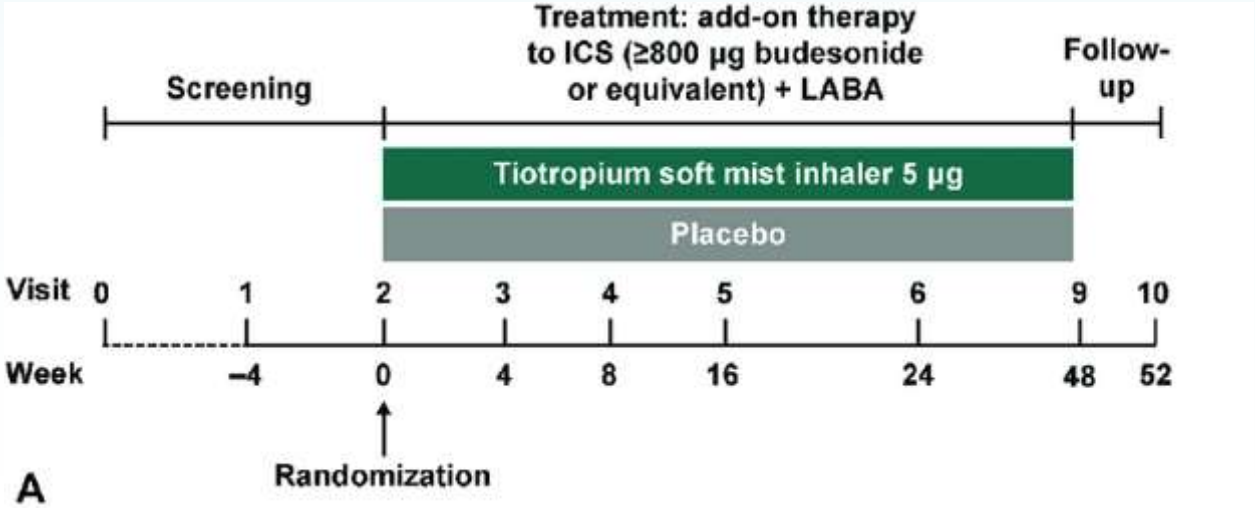
Medium dose ICS, or add LTRA, or add HDM SLIT

Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS

Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects

Tiotropium in Asthma Poorly Controlled with Standard Combination Therapy

Primo-TinA



- 5-year or longer history of asthma
- Diagnosed before the age of 40 years.
- ACQ-7 ≥ 1.5
- Persistent airflow limitation
- Daily therapy with inhaled glucocorticoids (≥800 µg of budesonide or the equivalent) and LABAs
- At least one exacerbation that was treated with systemic glucocorticoids in the previous year
- Nonsmokers or to have a smoking history of fewer than 10 pack-years, with no smoking in the year before enrollment.

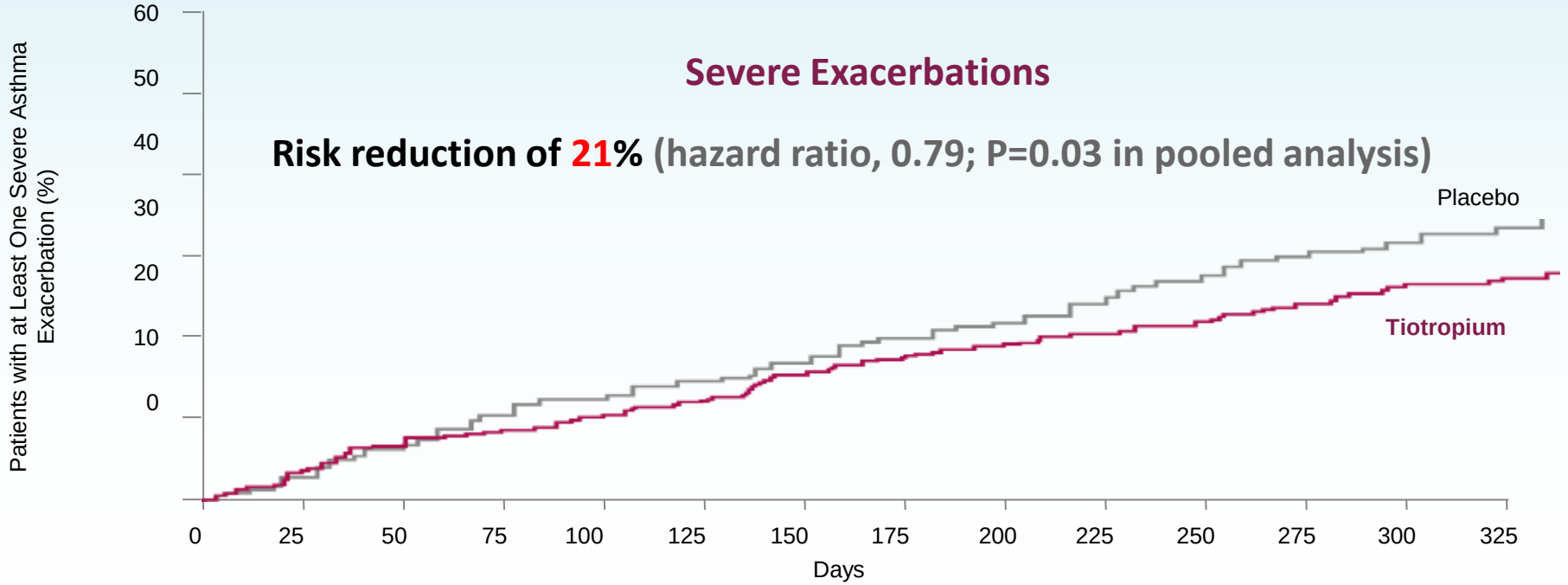
Table 1. Baseline Characteristics of the Patients.*

Characteristic	All Patients (N=912)	Trial 1		Trial 2	
		Tiotropium (N=237)	Placebo (N=222)	Tiotropium (N=219)	Placebo (N=234)
Female sex — no. (%)	551 (60.4)	146 (61.6)	143 (64.4)	127 (58.0)	135 (57.7)
Age — yr	53.0±12.4	52.9±12.4	53.9±12.8	51.4±12.5†	53.6±11.7
Body-mass index‡	28.2±6.0	28.2±5.8	28.1±6.4	28.2±5.9	28.2±5.9
Race — no. (%)§					
White	759 (83.2)	200 (84.4)	187 (84.2)	176 (80.4)	196 (83.8)
Other	153 (16.8)	37 (15.6)	35 (15.8)	43 (19.6)	38 (16.2)
Never smoked cigarettes — no. (%)	692 (75.9)	182 (76.8)	174 (78.4)	158 (72.1)	178 (76.1)
Median age of asthma onset — yr (range)	26 (0–44)	23 (0–40)	26 (0–39)	29 (0–44)	27 (0–39)
Median duration of asthma — yr (range)	28 (5–72)	31 (6–70)	28 (6–68)	26 (5–72)¶	28 (5–69)
Severe exacerbations in past year — no. (%)‖					
<3	738 (80.9)	201 (84.8)	185 (83.3)	179 (81.7)	173 (73.9)
3–5	128 (14.0)	27 (11.4)	27 (12.2)	30 (13.7)	44 (18.8)
>5	46 (5.0)	9 (3.8)	10 (4.5)	10 (4.6)	17 (7.3)
Use of maintenance oral glucocorticoids — %**	5.3	6.8	5.0	3.7	5.6
Use of omalizumab — %	3.9	2.5	4.5	2.7	6.0
Mean daily no. of puffs of short-acting beta-agonists††	3.2	2.8	3.3	3.4	3.3
Use of theophyllines — %	16.7	18.6	21.2	14.2	12.8
Use of leukotriene modifiers — %	22.3	25.3	27.5	16.4	19.7
Use of antihistamines — %	14.7	20.3	16.2	14.2‖	8.1
ACQ-7 score**‡‡	2.6±0.7	2.7±0.7	2.7±0.7	2.6±0.7	2.6±0.7
AQLQ score**§§	4.6±1.1	4.6±1.1	4.6±1.1	4.6±1.0	4.7±1.1
Forced expiratory volume in 1 sec					
Value before bronchodilation — liters**	1.603±0.540	1.596±0.546	1.558±0.537	1.659±0.569	1.598±0.506
Percent of predicted value before bronchodilation	54.8±12.4	54.6±12.2	54.6±12.2	55.1±12.8	55.0±12.6
Percent of predicted value after bronchodilation	62.2±12.7	61.5±12.5	62.7±12.6	62.6±12.5	62.3±13.0
Reversibility — ml	217±217	201±211	230±223	228±206	209±229
Forced vital capacity — liters**	2.744±0.900	2.715±0.923	2.704±0.912	2.894±0.909	2.788±0.851

N Engl J Med 2012; 367:1198-1207

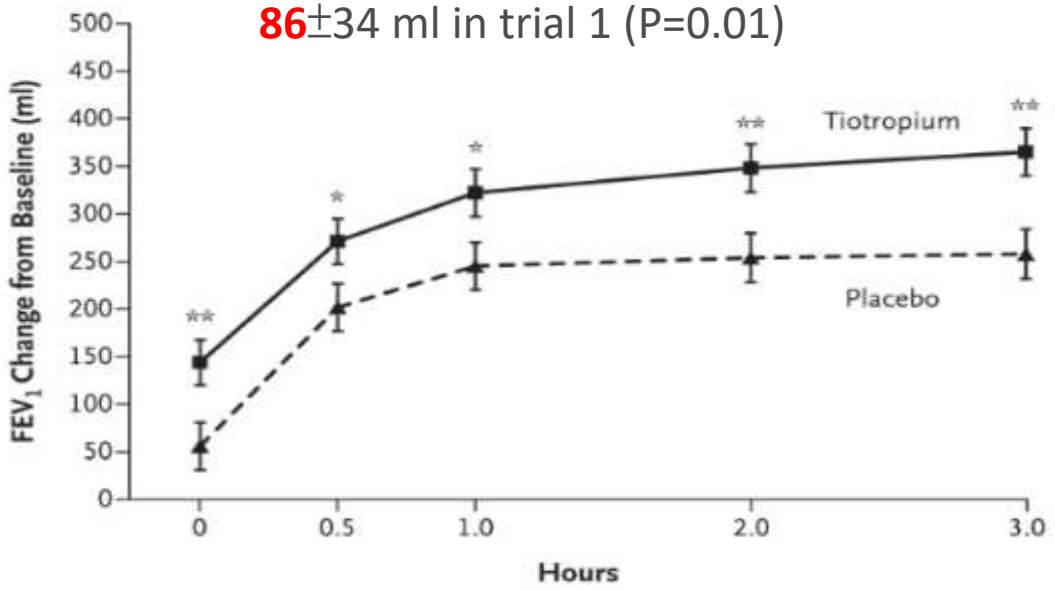
Severe Exacerbations

Risk reduction of 21% (hazard ratio, 0.79; P=0.03 in pooled analysis)

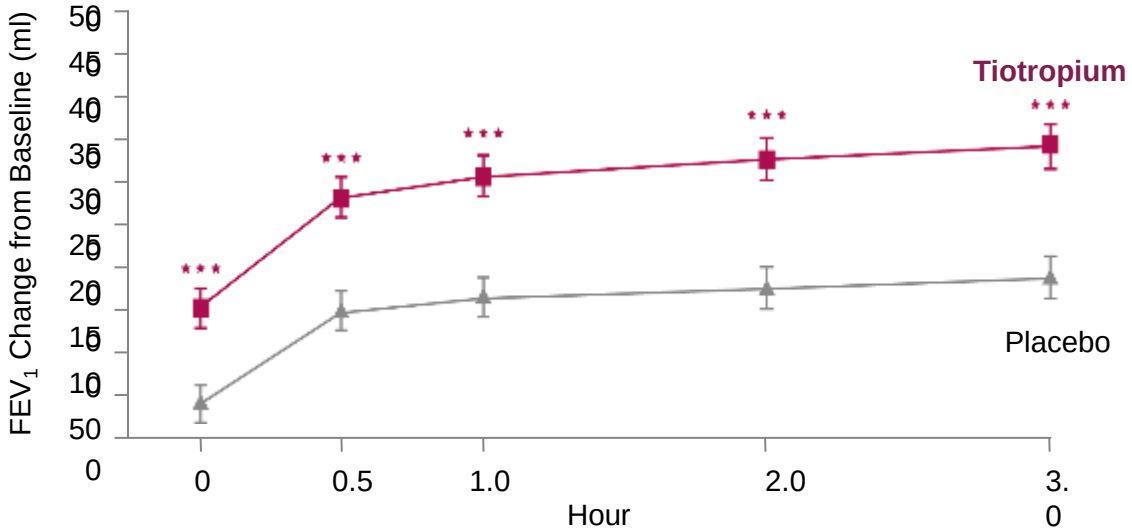


FEV_1 Improvements

86±34 ml in trial 1 (P=0.01)

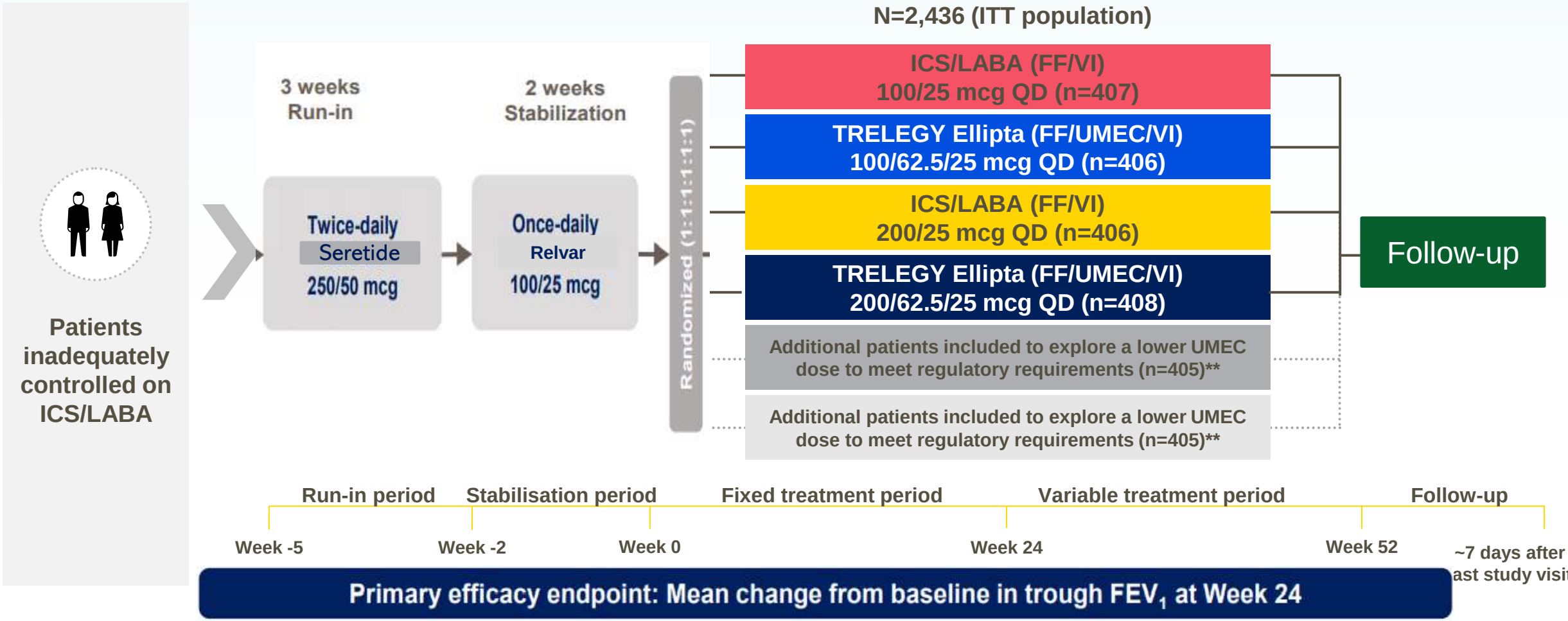


154±32 ml in trial 2 (P<0.001)



N Engl J Med 2012; 367:1198-1207

CAPTAIN trial: Designed to support personalised therapy for patients with asthma



*Randomisation stratified by pre-study ICS treatment strength (medium vs high); Two UMEC doses (31.25mcg) were included in this study for regulatory authorities. The licensed UMEC dose in TRELEGY Ellipta is 62.5 mcg, which reflects the data included in this presentation; FF, fluticasone furoate; ICS, inhaled corticosteroid; ITT, intention-to-treat; LABA, long-acting β_2-agonist; QD, once daily; R, randomisation; UMEC, umeclidinium; VI, vilanterol.

ClinicalTrials.gov. NCT02924688. Available at: www.clinicaltrials.gov/ct2/show/NCT02924688 [accessed August 2021];
30 Lee LA, at al. *Lancet Respir Med* 2020. ePub September 2020 https://doi.org/10.1016/S2213-2600(20)30389-1 [accessed August 2021].

CAPTAIN Trial: Characters of Study Subjects

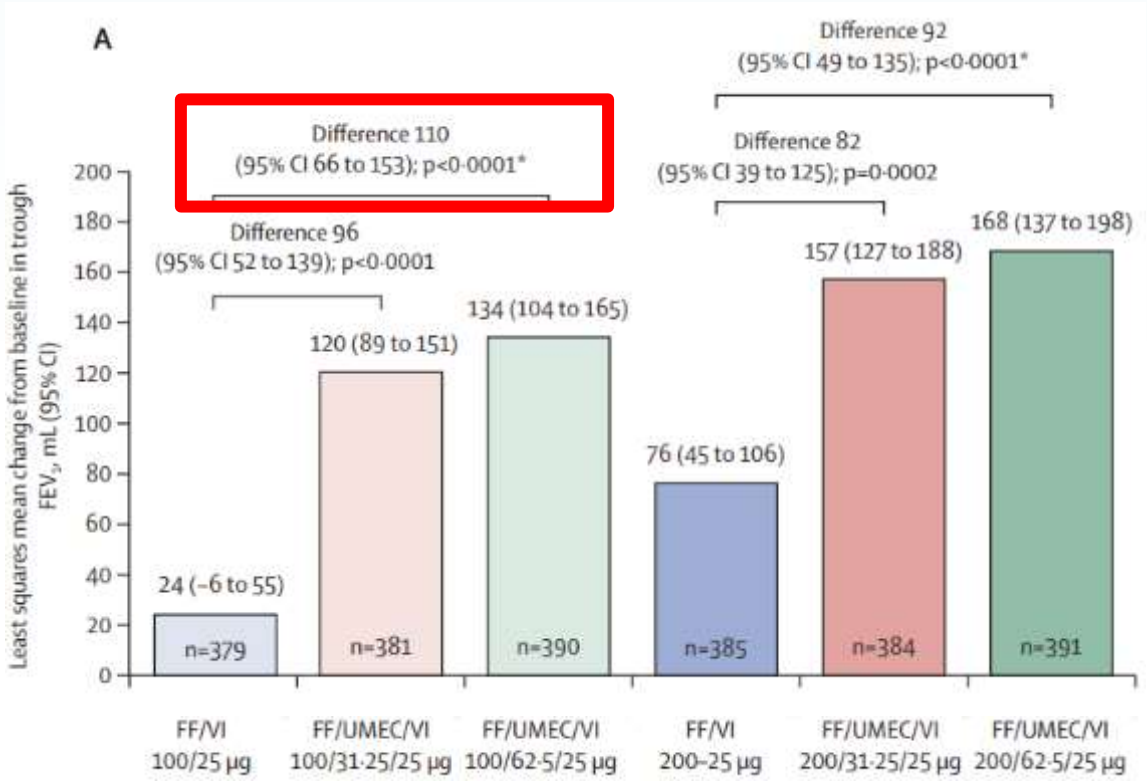
Mean (SD) / n (%)	Total (N=2436)
Age (years)	53.2 (13.11)
Female	1514 (62%)
BMI (kg/m^2)	29.35 (6.642)
Pre-study ICS dose at Screening - mid	1621 (67%)
CV history/risk factor	1181 (48%)
Duration of asthma (years)	21.2 (15.31)
Smoking status	
Never smoked	1966 (81%)
Former smoker	470 (19%)
Current smoker	0
Number of exacerbations requiring oral/systemic corticosteroids and/or hospitalisation in previous 12 months	
0	892 (37%)
1	1166 (48%)
≥2	378 (16%)

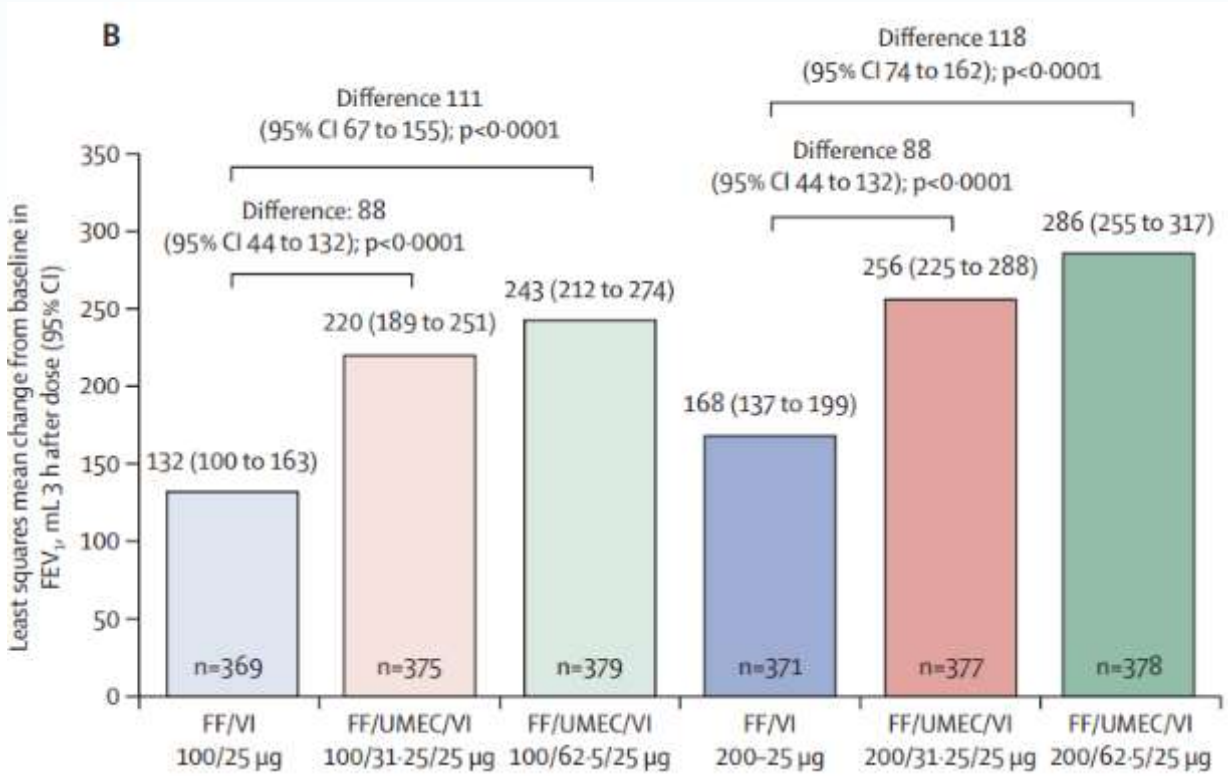
ITT population

BMI, body mass index; CV, cardiovascular; ICS, inhaled corticosteroid; ITT, intent-to-treat; SD, standard deviation.

Pavord I, et al. American Academy of Allergy Asthma & Immunology [AAAAI] 2020 AB241 # REF-78203; GSK DOF #REF-47001.

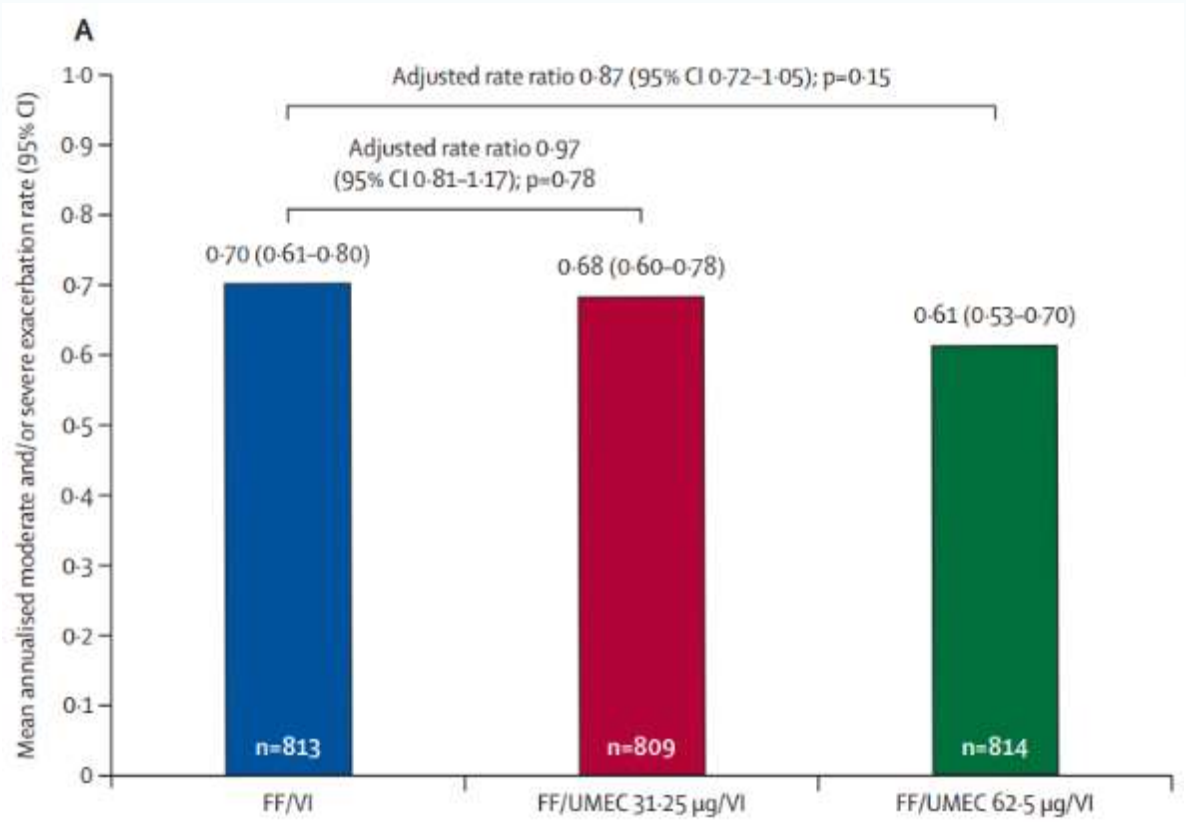
CAPTAIN Trial: Efficacy of LAMA Addition in Trough FEV1



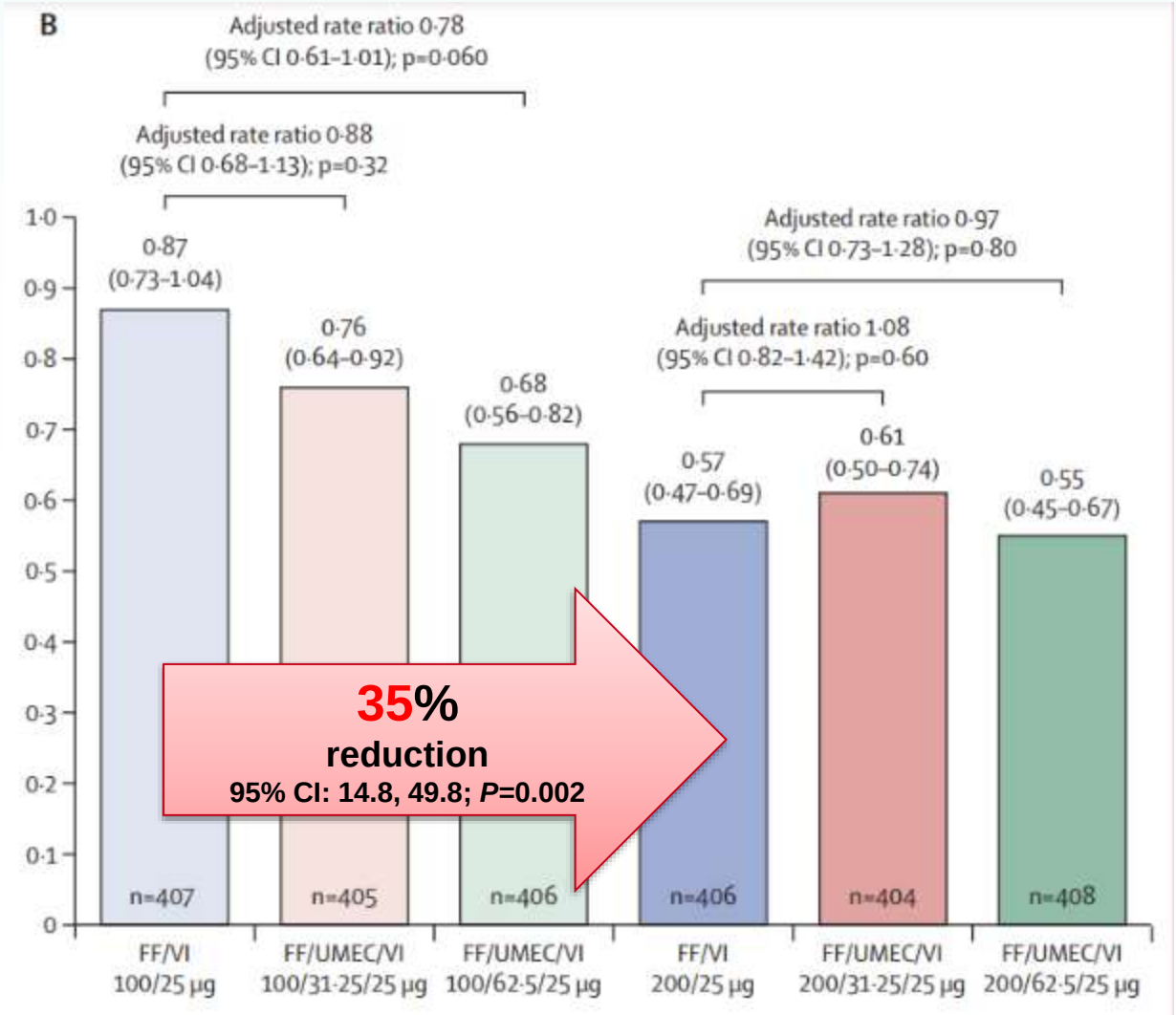


Lee LA, at al. *Lancet Respir Med* 2020. ePub September 2020

CAPTAIN Trial: ICS Titration Decreased Asthma Exacerbation

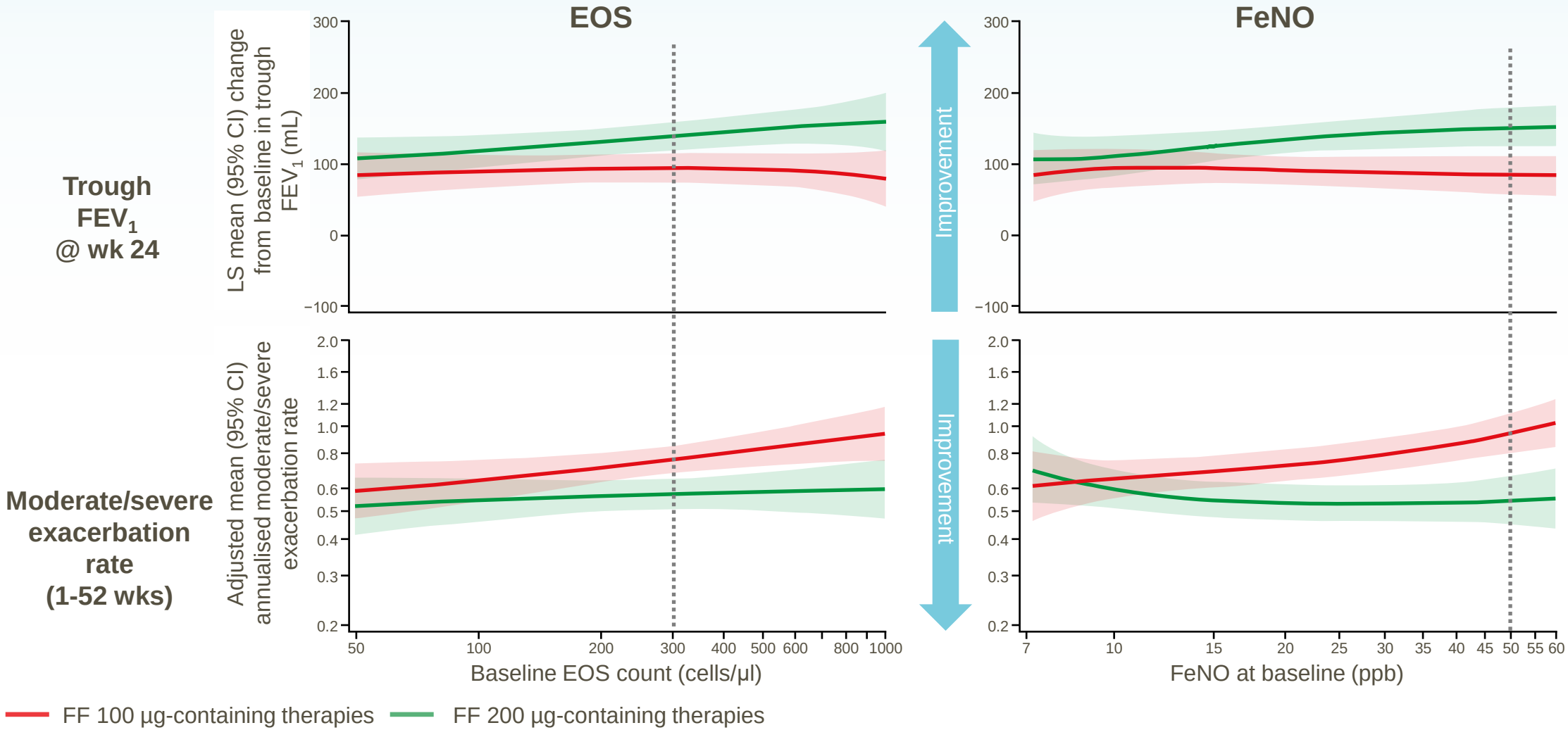


All comers of CAPTAIN study



Lee LA, at al. *Lancet Respir Med* 2020.

Increasing ICS Is Effective in Asthma With Higher EOS and FeNO Levels for Trough FEV_1 & Exacerbation Reduction

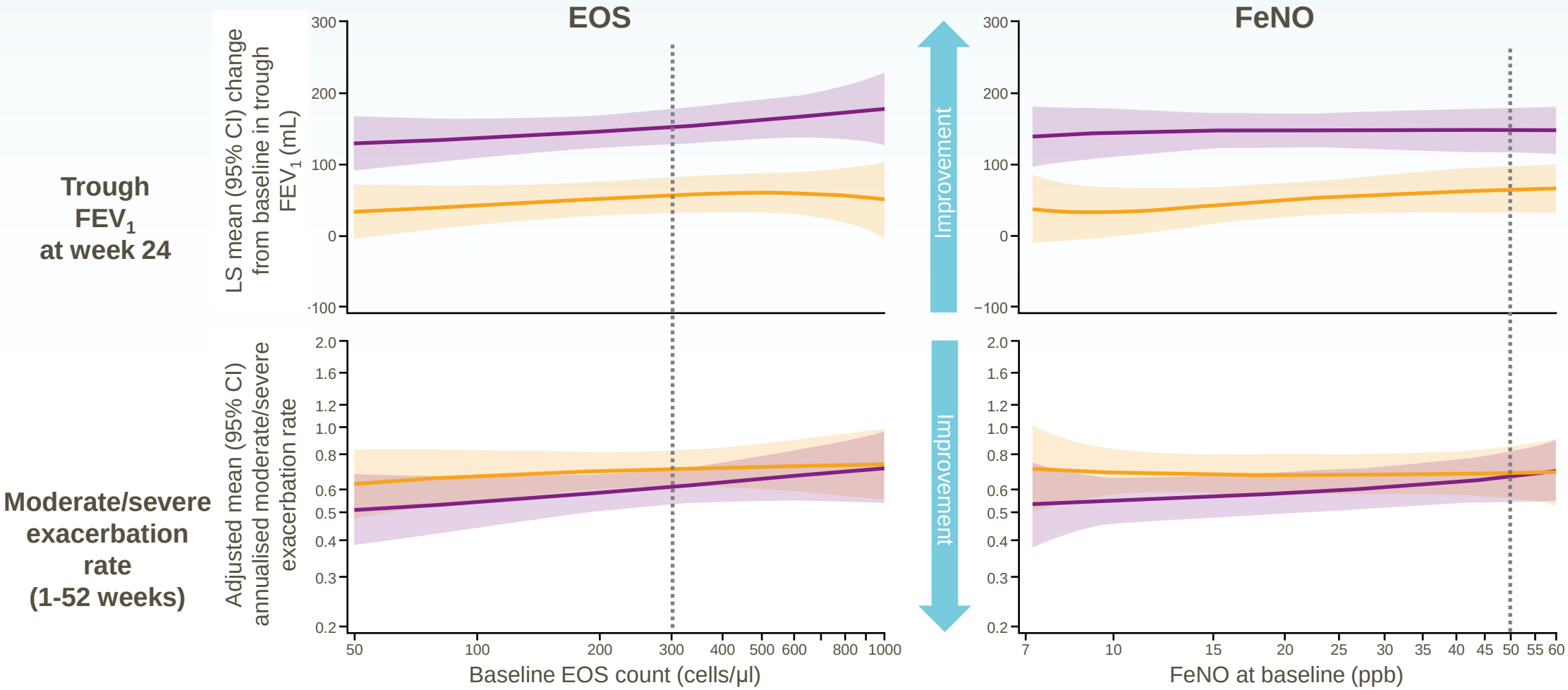


Pooled analysis

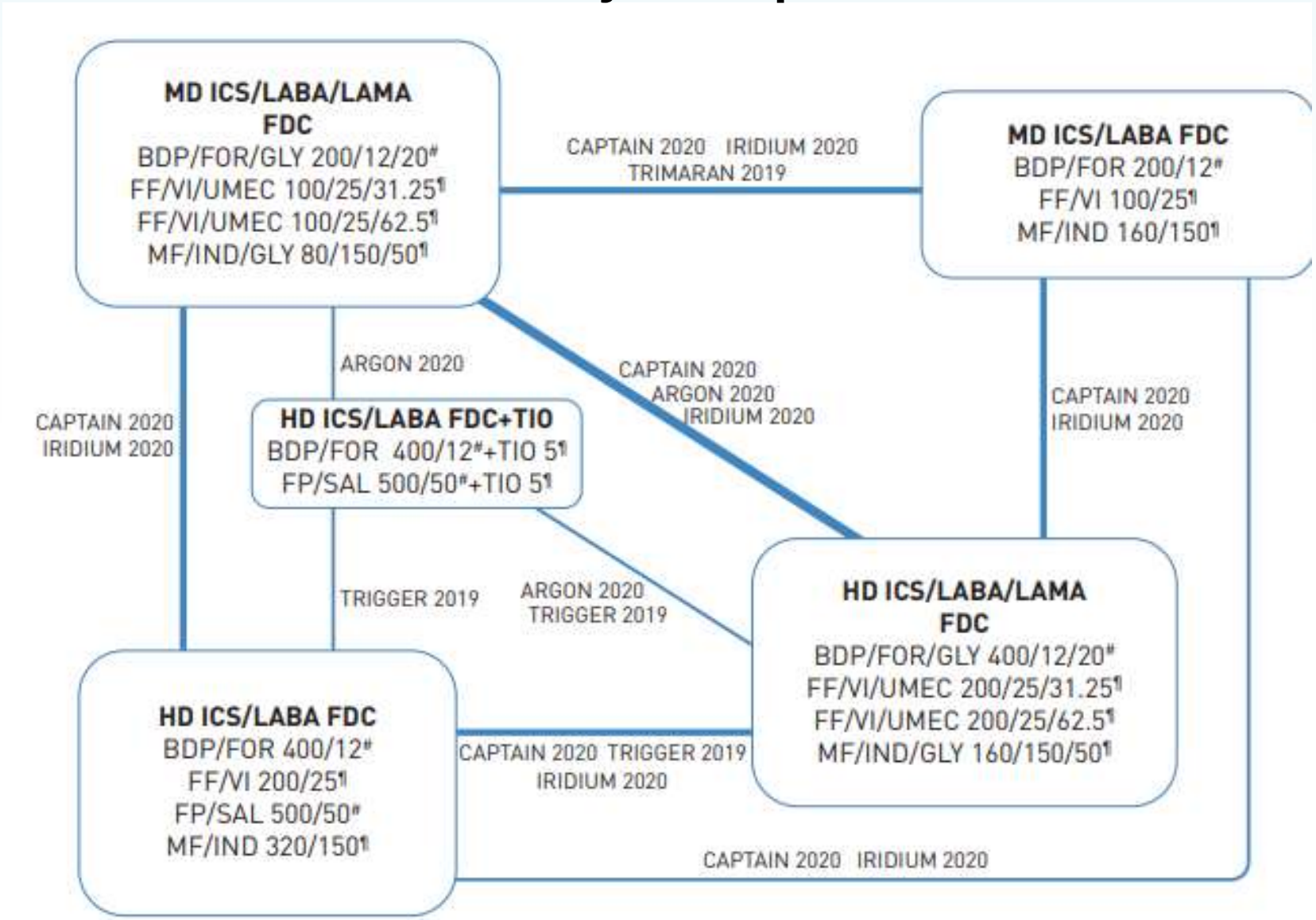
Unpooled analyses show similar trends for clinic trough FEV_1 and moderate/severe exacerbation rate. Pooled analyses were performed post hoc. Best-fitting fractional polynomial models from 36 pre-defined models are presented.

EOS, eosinophil; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FF, fluticasone furoate; ppb, parts per billion.

Adding Umeclidium 62.5 µg leads to numerically greater improvements in trough FEV_1 regardless of EOS/FeNO status

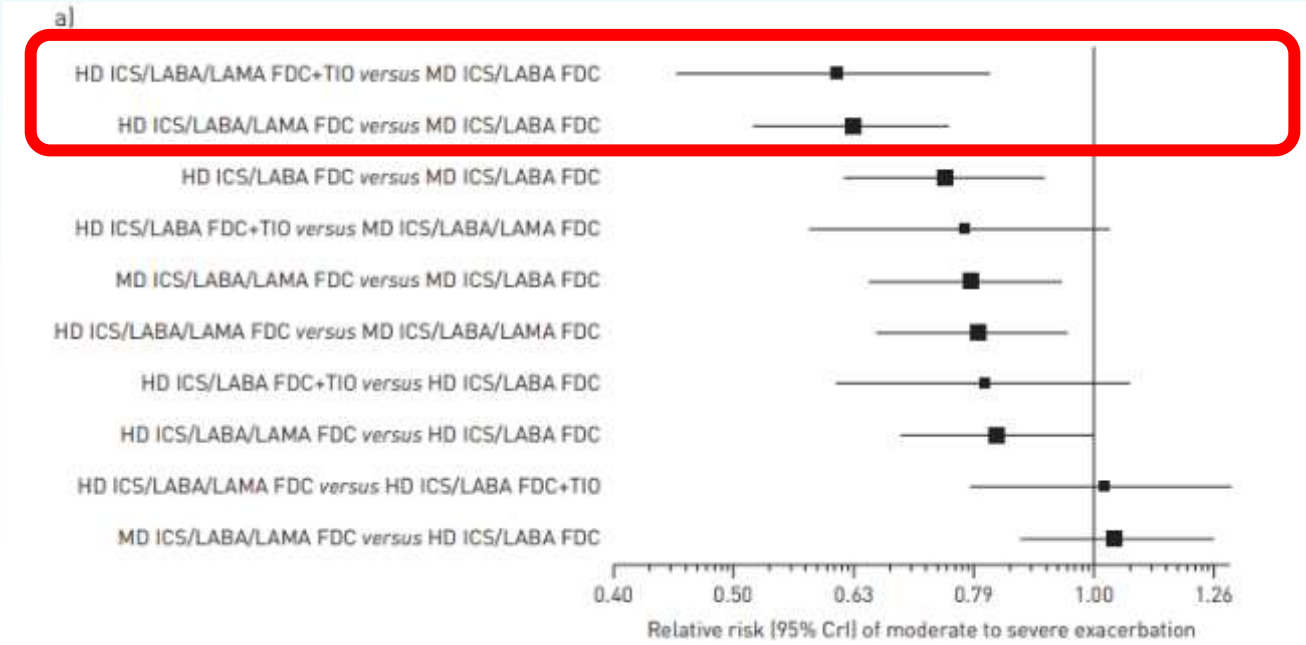


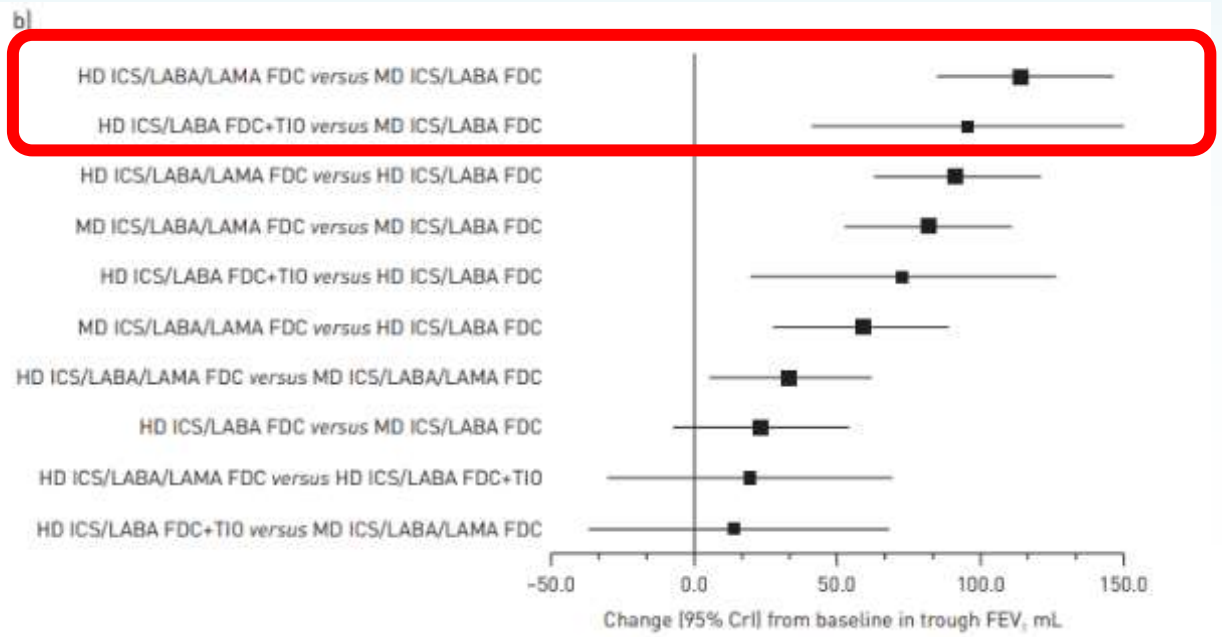
Triple therapy in uncontrolled asthma: a network meta-analysis of phase III studies

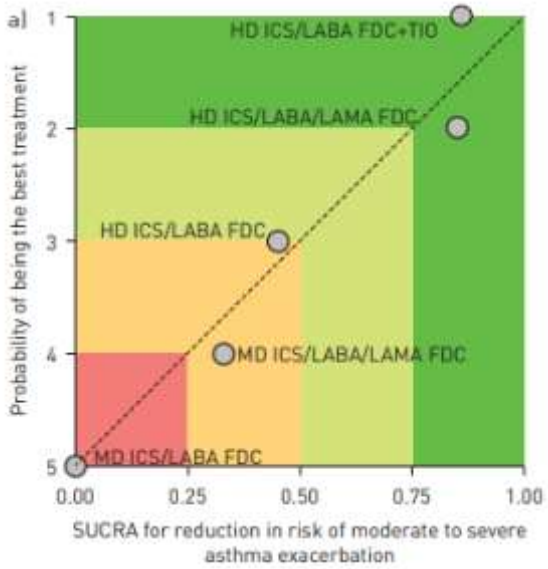


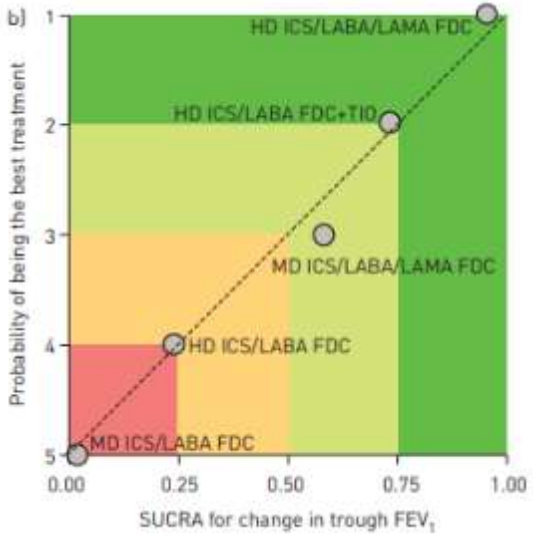
Eur Respir J 2021; 58: 2004233

Triple therapy in Uncontrolled Asthma: A Network Meta-analysis of Phase III Studies







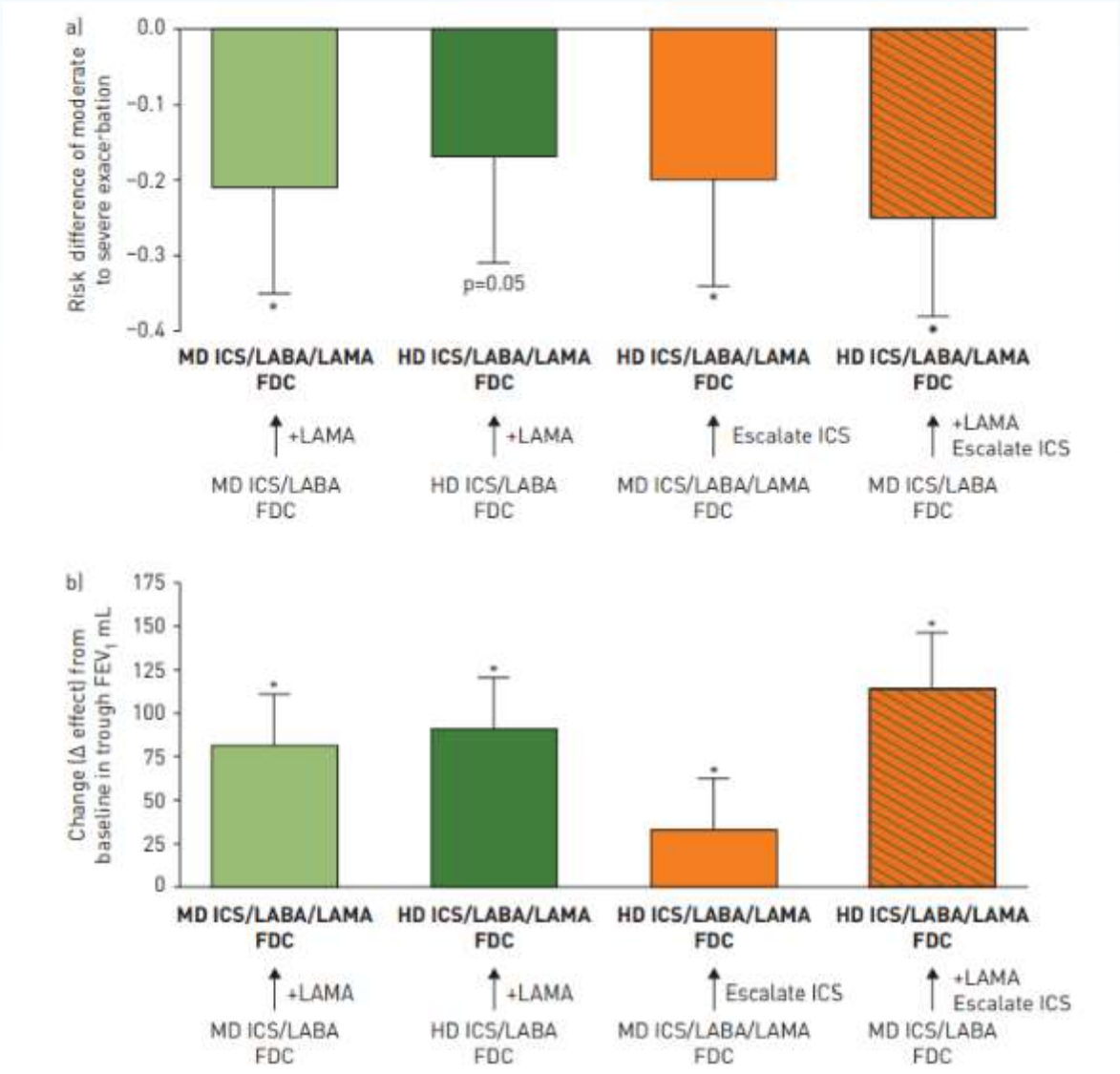


Eur Respir J 2021; 58: 2004233

Triple therapy in uncontrolled asthma: a network meta-analysis of phase III studies

TABLE 3 Relative effects with 95% credible interval resulting from the subset network meta-analysis with respect to the moderate or severe asthma exacerbations

Comparisons	Moderate asthma exacerbation relative risk	Severe asthma exacerbation relative risk
HD ICS/LABA/LAMA FDC *versus*		
HD ICS/LABA FDC+TIO	0.87 (0.65–1.15)	1.41 (0.92–2.21)
MD ICS/LABA/LAMA FDC	0.91 (0.75–1.10)	0.65 (0.49–0.87)#
HD ICS/LABA FDC	0.88 (0.73–1.06)	0.75 (0.57–1.00)¶
MD ICS/LABA FDC	0.67 (0.55–0.82)#	0.57 (0.42–0.78)#
HD ICS/LABA FDC+TIO *versus*		
MD ICS/LABA/LAMA FDC	1.04 (0.78–1.44)	0.46 (0.29–0.72)#
HD ICS/LABA FDC	1.00 (0.76–1.39)	0.53 (0.33–0.85)#
MD ICS/LABA FDC	0.77 (0.56–1.07)	0.40 (0.24–0.66)#
MD ICS/LABA/LAMA FDC *versus*		
HD ICS/LABA FDC	0.96 (0.79–1.18)	1.16 (0.87–1.58)
MD ICS/LABA FDC	0.74 (0.61–0.89)#	0.88 (0.66–1.16)
HD ICS/LABA FDC *versus*		
MD ICS/LABA FDC	0.76 (0.62–0.94)#	0.76 (0.55–1.02)



Eur Respir J 2021; 58: 2004233

Ellipta用藥步驟

1. 打開

扳開要聽到「喀」一聲，才有成功上藥

2. 吸入

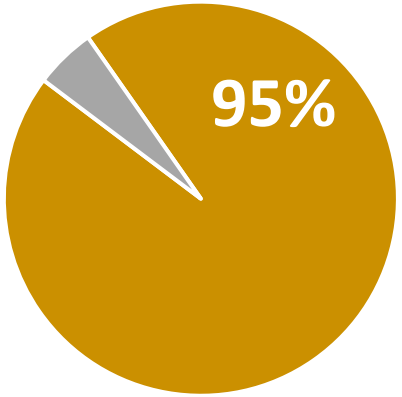
A. 先向外吐一口氣，勿朝吸嘴吐氣
B. 將吸嘴放入嘴唇內，緩而長的吸一口氣 (long, steady, deep breath)
C. 吸氣完畢後自口中移去吸入器，緊閉雙唇，接著盡可能地閉氣。(至少閉氣 3~4 秒)

3. 關上

使用完畢切記將吸入器蓋子關上

Trelegy Ellipta 92/55/22 mcg 乾粉吸入劑中文仿單

95% of patients can use Ellipta correctly after just one demonstration



of patients can use Ellipta correctly after just one demonstration
(n=1,000/1,049)*

100% of patients maintained correct inhaler technique at 2- and 4-week follow-up

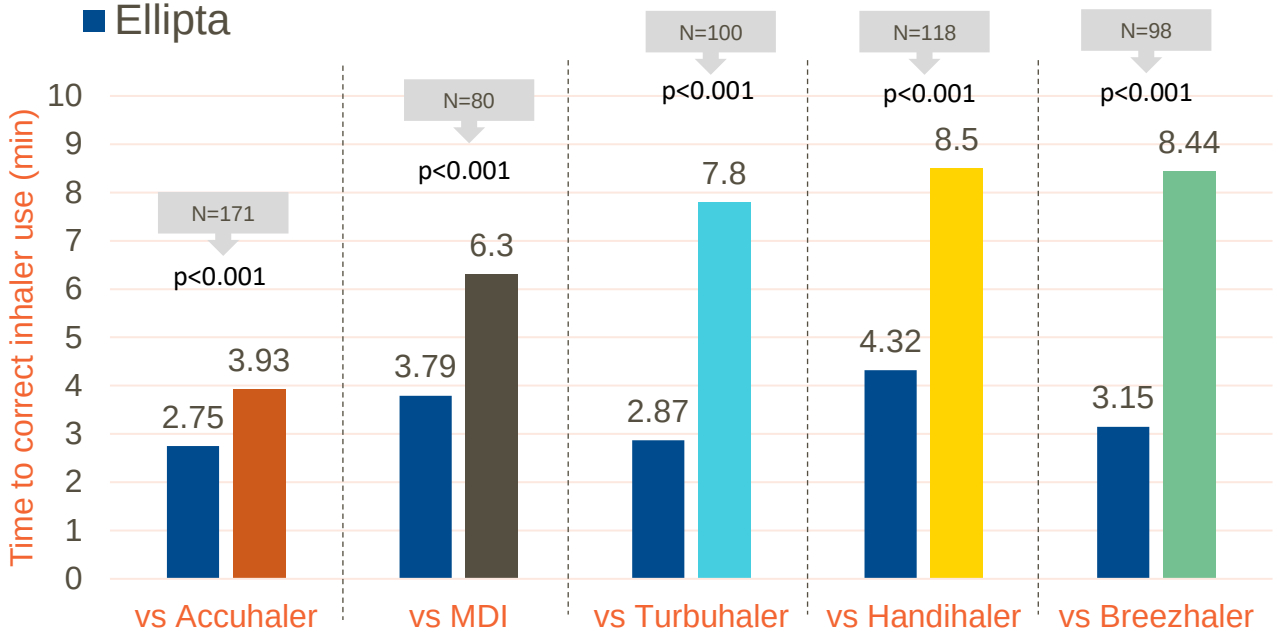
Ellipta - Patient preferred & has less critical errors[1,2]

*Pooled data from 3 randomised, double-blind studies in which Relvar 100/25mcg OD or FF 100mcg OD was delivered via the Ellipta inhaler
FF:Fluticasone Furoate; OD: Once Daily

Svedsater H et al. NPJ Prim Care Respir Med; 2014; 24; 14019; 1-3

Device Training: ELLIPTA is associated with less inhaler teaching time compared to other commonly used inhalers

每組都是同一個病人對於試驗的吸入劑都是naïve情況下，自行閱讀仿單操作。



57-70% of patients made no errors using the ELLIPTA inhaler, after reading PIL.

For the other inhalers, more than half of the patients could not perform correct use after reading the PIL only.

*Critical error: defined as errors that are likely to result in no, or minimal, medication being delivered to the lungs. patients were naive to Ellipta and at least one other inhaler device (patients naive to Breezhaler and Handihaler must also have been naive to all other inhaler devices that required a capsule)
COPD, chronic obstructive pulmonary disease; MDI, metered-dose inhaler, PIL: Patient Information Leaflet

GSK created image, van der Palen J, et al. *NPJ Prim Care Respir Med*. 2016;26:16079;1-8.

Summary

- **Increasing ICS may reduce exacerbation and improve lung function in uncontrolled asthma, either T2 or non T2, but more benefit in T2 high patients**
- **Add on LAMA to HD/MD ICS + LABA may improve lung function, and modestly decrease exacerbation.**
- **We could use blood eosinophil or FeNO to predict response of escalating ICS or adding LAMA for AE prevention.**

Case 2: Addition of LAMA in Difficult To Treat Asthma

Identification

- Mr. C
- Age: 62 years old [2023]
- Gender: male
- First visit to my clinic: 2021/01/27
- Chief complaint: referred by cardiologist due to refractory wheezing
- BH: 165 cm, Bwt: 78 kgw, BMI = 28.65

Past & Social History of Mr. C

- Previous medical illness:
  - CRS s/p FESS in 2016, followed at ENT OPD
  - HTN/DM under regular OPD follow up at CV OPD

- Occupation:
  - Construction site worker
- **Active smoker**: hesitated about smoking cessation, more than 25 pack-year
- Residency: urban area of Kaohsiung City

Findings of Echocardiography & ENT Fiberscopy

心臟超音波檢查報告

1.Chamber and function
- LA dilatation
- Concentric LVH
- Adequate global LV systolic function
- Impaired myocardial relaxation , borderline LA (LV filling) pressure, average, E/E' =8.6
- Normal RV function
- Normal RA pressure
- Mild pulmonary hypertension, PA systolic pressure=45mmHg

2.Valves
- Mild MR
- Moderate TR

纖維內視鏡檢查報告

(2020/05/06) Fiberoscopy:

Nasal cavity: patent nasal cavity, no ulcer, no obvious tumor; no obvious nasal polyps; mucopus arising from left middle meatus (+)

Nasopharynx: smooth mucosa, bilateral Rosenmullar fossa patent, no obvious tumor; PND (+)

Oropharynx: smooth mucosa, no obvious tumor; tongue base lymphoid hyperplasia (+)

Hypopharynx: smooth mucosa, no ulcer, no obvious tumor

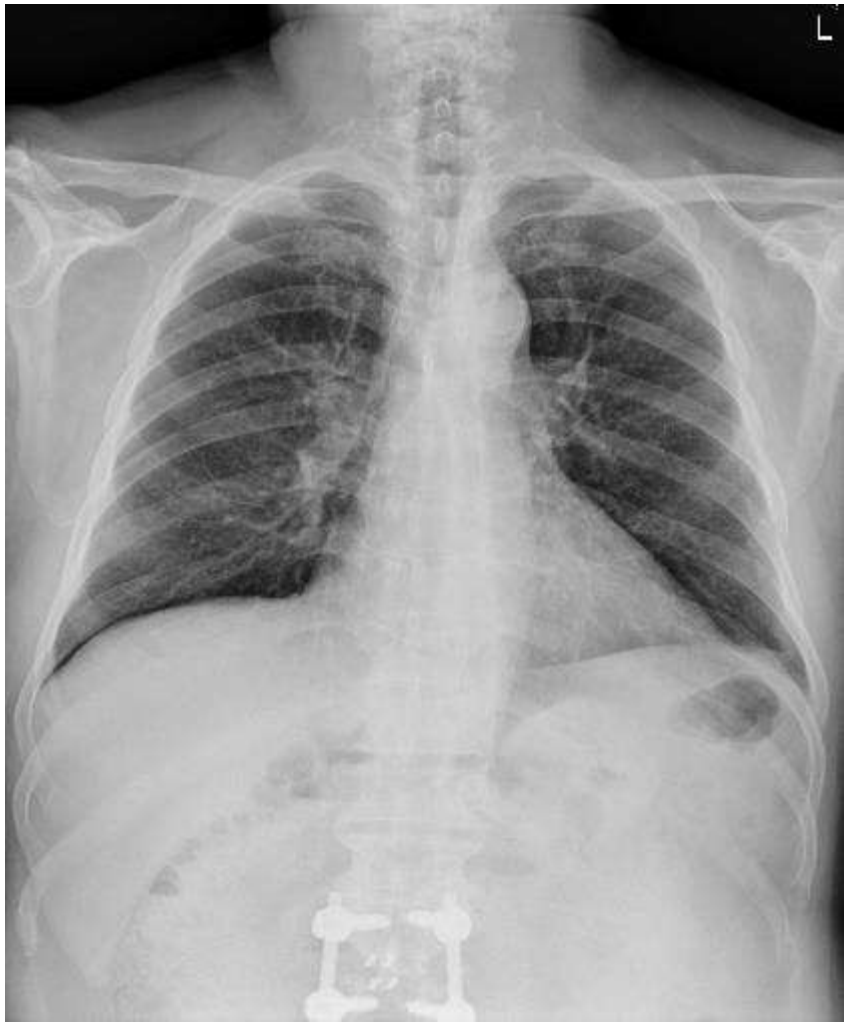
Larynx: freely bilateral vocal movement, no obvious tumor

Keep intra-nasal steroids + anti-histamine

About Mr. C Asthma

- Diagnosed at the age during his thirties. Family Hx: (-)
- He received ICS/LABA as controller for about 2 decades, but limited adherence to inhalation therapy by self-statements.
- Moved back to Kaohsiung City 2 years ago since retirement, but still under regular clinic visit in Tai-Tung for asthma medication.
- Frequent LMD visit for steroids injection due to SOB/wheezing → every one or two months.

Diagnostic Examinations At My Clinics



2022/01/27

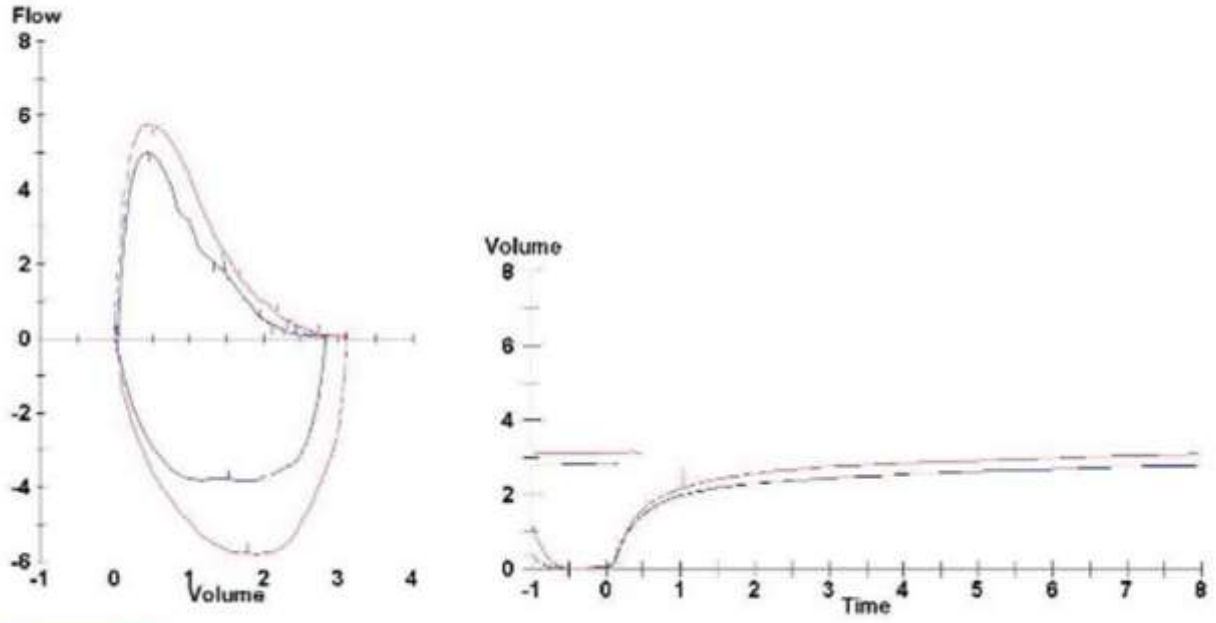
Chest PA view shows:
>Bilateral lung markings increased.
>No pleural effusion.
>No obvious mediastinal mass like lesion.
>The heart shadow is borderline enlarged.
>Status after fixation of the spine.
[redacted]醫師-放診專醫字 第[redacted]號

Lung Function Test Was Performed in Dec 2021

Spirometry

		PRED	PRE-RX BEST	PRE-RX %PRED	POST-RX BEST	POST-RX %PRED	% Chg
FVC	Liters	3.28	2.83	86	3.13	96	11
FEV1	Liters	2.42	1.99	82	2.21	91	11
FEV1/FVC	%		70		70		
FEF25-75%	L/sec	3.37	1.22	36	1.39	41	14
FEF50%	L/sec	4.61	1.92	42	2.20	48	15
PEF	L/sec	7.65	5.00	65	6.91	90	38
MVV	L/min	102					

PRE___ POST___



Comments:

T2 Inflammatory Potency Was Not Obvious

註	檢驗名稱	結果	單位	參考區間
	WBC	7.9	10^3/μL	3.4-9.1
	Seg	48.6	%	43.0-64.0
	Eos	2.0	%	0.0-6.0
	Baso	0.4	%	0.0-1.0
	Mono	9.1	%	3.0-9.0
	Lymph	39.9	%	27.0-47.0

Absolute eosinophil count = 158

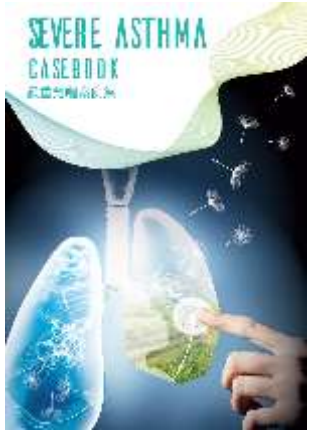
註	檢驗名稱	結果	單位	參考區間
	IgE	40.5	IU/mL	0-100

MAST/ immunoCAP were not performed
FeNO was NOT available then

Question 4: For patients with difficult-to-treat asthma, how to evaluate and correct their comorbidities and other modifiable risk factors?

Recommendation

We recommend using a check list to comprehensively evaluate the modifiable risk factors, including smoking status, exposures to environmental tobacco, allergens, and indoor and outdoor air pollutants. We also recommend using a check list to evaluate comorbidities, including chronic rhinosinusitis, COPD, bronchiectasis, OSA, cardiac diseases, GERD, anxiety and depression, and obesity.



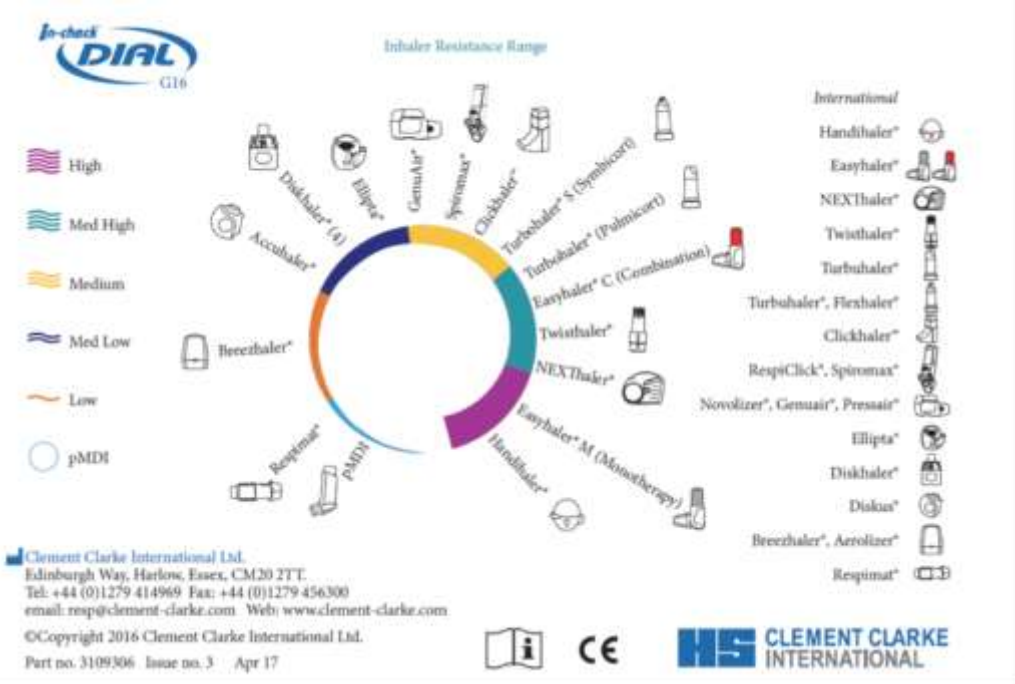
TSPCCM 2020

The Modifiable Risk Factors Check List		
	Patient has this factor?	Could be further modified?
Active smoking	☐ Yes ☐ No	☐ Yes ☐ No
Significant environmental exposures, including indoor/ outdoor allergens and pollutants	☐ Yes ☐ No	☐ Yes ☐ No
Chronic rhinosinusitis	☐ Yes ☐ No	☐ Yes ☐ No
Chronic obstructive pulmonary disease	☐ Yes ☐ No	☐ Yes ☐ No
Bronchiectasis	☐ Yes ☐ No	☐ Yes ☐ No
Obstructive sleep apnea	☐ Yes ☐ No	☐ Yes ☐ No
Cardiac diseases	☐ Yes ☐ No	☐ Yes ☐ No
Gastroesophageal reflux disease	☐ Yes ☐ No	☐ Yes ☐ No
Anxiety and/or depression	☐ Yes ☐ No	☐ Yes ☐ No
Obesity	☐ Yes ☐ No	☐ Yes ☐ No

Active Problems & Plans

- Active smoker, hesitating for smoking cessation.
- The adherence to inhalation therapy is quite doubtful!
- Overweight
- CRS & CV comorbidities → under surveillance and treatment!
- Refer to specialist for quitting smoking!
- Choose an ICS/LABA inhaler that may enhance his adherence.
- Suggest BW reduction → time consuming

Choosing An Inhaler for Mr. C



1 puff once daily

1. Start with step 3/4 treatment by GINA guideline
2. We choose "**once daily administration** with **dose counter**'' ICS/LABA in the hope of **enhancing his adherence** to inhalation therapy!

Response After Regular ICS-LABA Administration

	Jan 2022	Feb 2022	Mar 2022	Apr 2022	May 2022
ICS/LABA (medium)					
Anti-histamine Intra-nasal steroids					
SABA prescription					
OCS [20mg/day x 7 days]					
ACT	13	17	15	15	16
Smoking cessation program		join	**Drop out**	Re-join	join

Hydro-cortisone

LAMA Was Added Due To SAE in July

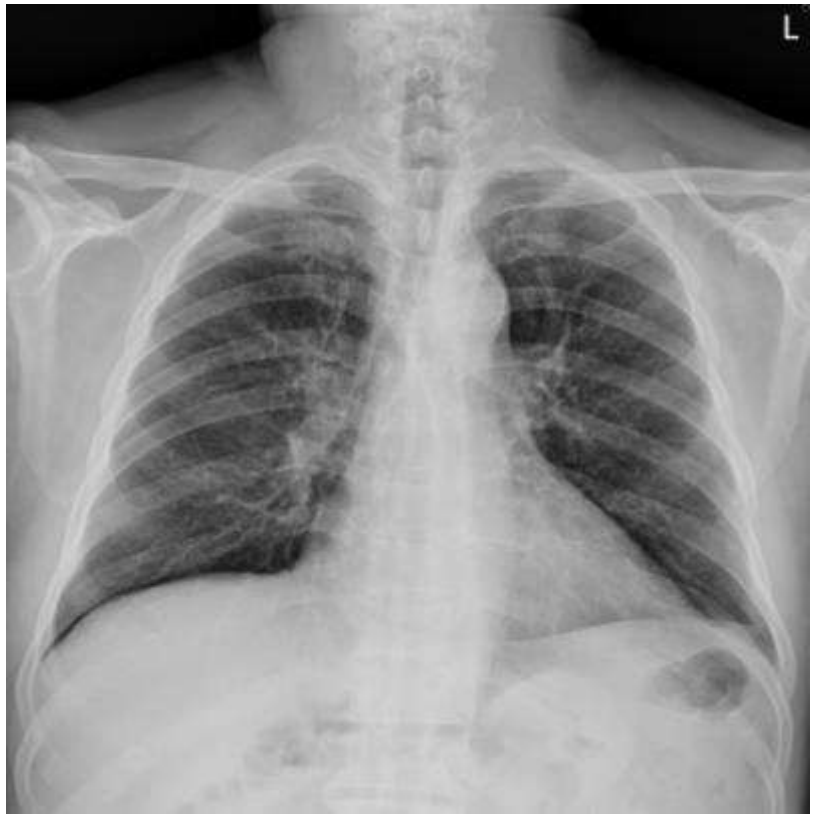
	Jun 2022	Jul 2022	Aug 2022	Sep 2022	Oct 2022
ICS/LABA (medium) LAMA					
Anti-histamine Intra-nasal steroids					
SABA prescription					
OCS [20mg/day x 7 days]					
ACT	16	14	17	19	19
Smoking cessation program	join	join	join	join	join

Hydro-cortisone

Biomarker Profiles & Chest Radiography At ER

註	檢驗名稱	結果	單位	參考區間	備註
	WBC	6.9	10^3/μL	3.4-9.5	
	Seg	52.6	%	40.8-76.6	
	Eos	2.8	%	0.4-7.5	
	Baso	0.4	%	0.2-1.7	
	Mono	8.5	%	4.4-11.8	
	Lymph	35.7	%	15.4-47.0	

Absolute eosinophil count = 193



2022/07/12

After SDM, Single Inhaler Triple Therapy Was Prescribed in July 2023

	Apr 2023	Jun 2023	Jul 2023	Aug 2023	Sep 2023
ICS/LABA (medium) LAMA					
Anti-histamine Intra-nasal steroids					
SABA prescription					
OCS [20mg/day x 7 days]					
ACT	18	20	20	21	
Smoking cessation program	join	**Finished!**			

Hydro-cortisone

PDC > 80%

Brief Summary of Case

- Clinical benefit post LAMA addition was observed in terms of ACT score and AE frequency!
- Better adherence to inhaled therapy after the introduction of Ellipta device!
- The follow up lung function test is pending due to PCR-screening concern [self-paid]
- The clinical efficacy from quitting smoking!


Thank
you

Safety information

Trelegy 92/55/22 mcg	Trelegy 184/55/22 mcg	Relvar	Seretide Accuhaler
禁忌症: 作為重積性氣喘(status asthmaticus)或其他急性COPD或氣喘發作且必須採取強效治療措施的第一線療法；有嚴重乳蛋白過敏問題，或已證實對fluticasone furoate、umeclidinium、vilanterol或任何賦形劑過敏 警語及注意事項:嚴重氣喘相關事件－住院、插管、死亡；病情惡化與急性發作－對病情正在快速惡化或發生可能危及生命之發作事件的COPD或氣喘病人，不可開始使用TRELEGY ELLIPTA；避免過度使用TRELEGY ELLIPTA及避免與其他長效型β2作用劑併用；口咽念珠菌病；肺炎；免疫抑制與感染風險 - 正在使用皮質類固醇的兒童或成人如果感染水痘和麻疹，其病程可能會更為嚴重甚或致命；對從全身性皮質類固醇轉換成ICS的病人必須特別小心，因為在從全身性皮質類固醇轉換成全身吸收量較低之ICS的病人中，曾有於轉換期間及轉換之後因腎上腺功能不全而死亡的病例；腎上腺皮質功能亢進與腎上腺抑制-超過建議劑量或與強效的細胞色素P450 3A4 (CYP3A4)抑制劑併用，可能會導致HPA功能障礙、藥物交互作用；反常性支氣管痙攣；過敏反應，包括全身性過敏；心血管影響 - 和其他的β2作用劑一樣，vilanterol對某些病人可能會產生具臨床意義的心血管影響；骨質密度降低；曾有COPD或氣喘病人在長期使用ICS或併用吸入性抗膽鹼激性藥物之後發生青光眼、眼內壓升高、白內障及中心性漿液性脈絡膜視網膜病變的報告；尿滯留惡化；和所有含有擬交感神經胺成分的療法一樣，對患有痙攣性疾病或甲狀腺毒症的病人或對擬交感神經胺異常敏感的病人，使用TRELEGY ELLIPTA時應謹慎。曾有報告指出，靜脈投予相關的β2腎上腺素接受體作用劑albuterol會使既有的糖尿病及酮酸中毒更加惡化；低血鉀與高血糖；對兒童與青少年投予經口吸入性皮質類固醇可能會導致生長速度減慢	禁忌症: TRELEGY ELLIPTA 並不適用於緩解急性支氣管痙攣，並禁用於作為重積性氣喘 (status asthaticus) 或其他氣喘急性發作且必須採取強效治療措施的第一級療法；有嚴重乳蛋白過敏問題，或已證實對fluticasone furoate、umeclidinium、vilanterol或任何賦形劑過敏。 警語及注意事項: 嚴重氣喘相關事件—住院、插管、死亡；病情惡化與急性發作；過度使用TRELEGY ELLIPTA及與其他長效型β2作用劑併用；口咽念珠菌病；肺炎；免疫抑制與感染風險；從全身性皮質類固醇轉換治療的病人；腎上腺皮質功能亢進與腎上腺抑制；與強效細胞色素P450 3A4抑制劑的藥物交互作用；反常性支氣管痙攣；過敏反應，包括全身性過敏；心血管影響；骨質密度降低；在長期使用ICS 或併用吸入性抗膽鹼激性藥物；尿滯留惡化；患有痙攣性疾病或甲狀腺毒症的病人或對擬交感神經胺異常敏感的病人；低血鉀與高血糖；生長速度減慢	禁忌症: 作為重積性氣喘(status asthmaticus)或其他急性COPD或氣喘發作且必須採取強效治療措施的第一線療法; 有嚴重乳蛋白過敏問題，或已證實對fluticasone furoate、vilanterol或本品之任何賦形劑過敏 警語及注意事項: 使用LABA做為氣喘的單一治療藥物(未併用ICS)會導致發生氣喘相關死亡的風險升高。從對照性臨床試驗中獲得的資料也顯示，在兒童與青少年患者中，使用LABA做為單一治療藥物會升高氣喘相關住院的風險。這些發現被視為是LABA單一療法的類別作用。大型臨床試驗的資料顯示，合併使用固定劑量的LABA與ICS時，和單獨使用ICS相比，並未明顯增加發生嚴重氣喘相關事件(住院、插管、死亡)的風險	禁忌症：禁止使用於對本劑任何一種成分有過敏史之病人；以及於對乳蛋白嚴重過敏的患者。 警語及注意事項：可逆性呼吸道阻塞疾病的處理應該遵循正規的階梯式治療程序，並監測病人的控制狀況。SERETIDE 並非供緩解急性症狀之用，此種情況必須以作用快速且短效之吸入型支氣管擴張劑 (salbutamol) 來治療。應告知病人隨時必備急性氣喘發作之緩解藥物。若需增加短效性支氣管擴張劑的使用，以緩解症狀，表示控制惡化，病人亦應接受醫師的詳細檢查。氣喘控制突然或逐漸惡化可能會有生命危險，這種病人應接受醫師的詳細檢查，也必須考慮增加皮質類固醇療法。此外，如果目前的 SERETIDE 劑量無法充分控制氣喘，則病人亦應接受醫師的詳細檢查。因為有氣喘惡化的危險，病人不可驟然停止 SERETIDE 的治療，應在醫師監督下逐步減量。

Trelegy 92/55/22 mcg 簡易仿單

許可證字號	**衛部藥輸字第027395號**
中文產品名稱	肺樂喜易利達92/55/22 mcg乾粉吸入劑
活性成份學名	Fluticasone furoate 100 mcg、Umeclidinium 62.5 mcg及 Vilanterol 25 mcg (1劑TRELEGY ELLIPTA 92/55/22 mcg)
適應症或用途	**-慢性阻塞性肺病維持治療-** 適用於已接受吸入性皮質類固醇與長效β2作用劑合併治療，或已定期使用兩種吸入型長效支氣管擴張劑合併治療，而仍控制不佳的慢性阻塞性肺病(COPD)病人，以治療氣道阻塞。也適用於降低有惡化病史病人之COPD惡化。 **-氣喘維持治療-** 適用於併用吸入性長效型β2-腎上腺受體作用劑和吸入性皮質類固醇治療氣喘仍控制不佳的成年病人，做為氣喘維持治療。 **-使用限制-** TRELEGY ELLIPTA並不適用於緩解急性支氣管痙攣。
劑量與用法	• 應每天一次以經口吸入的方式投予1劑TRELEGY ELLIPTA 92/55/22 mcg。吸入之後，應用水漱口，且不可吞下，這是為了幫助降低發生口咽念珠菌病的風險。 • TRELEGY ELLIPTA 應每天於相同時間投藥。每24小時不可使用TRELEGY ELLIPTA超過1次。對老年病人、腎功能不全病人或中度肝功能不全病人，都不須調整劑量。 **-慢性阻塞性肺病維持治療-** TRELEGY ELLIPTA 92/55/22 mcg是唯一適用於治療COPD的劑量。如果在兩劑之間出現呼吸短促的現象，應使用吸入性短效型β2作用劑來達到立即緩解的效果。 **-氣喘維持治療-**選擇TRELEGY ELLIPTA的起始劑量時，應考慮病人的病情嚴重程度；先前的氣喘療法，包括吸入性皮質類固醇(ICS)的劑量；以及病人目前的氣喘症狀控制情形與未來更加惡化的風險。如果在兩劑之間出現氣喘症狀，應使用吸入性短效型β2作用劑來達到立即緩解的效果。
禁忌症	TRELEGY ELLIPTA禁用於下列狀況： •作為重積性氣喘(status asthmaticus)或其他急性COPD或氣喘發作且必須採取強效治療措施的第一線療法。 •嚴重乳蛋白過敏，或已證實對fluticasone furoate、umeclidinium、vilanterol或任何賦形劑過敏。
警語及注意事項	• 使用長效型β2腎上腺素作用劑(LABA)做為氣喘的單一治療藥物(未併用ICS)會導致發生氣喘相關死亡的風險升高。大型臨床試驗的資料顯示，合併使用固定劑量的LABA與ICS時，和單獨使用ICS相比，並未明顯增加發生嚴重氣喘相關事件(住院、插管、死亡)的風險。 • 對病情正在快速惡化或發生可能危及生命之發作事件的COPD或氣喘病人，不可開始使用TRELEGY ELLIPTA • TRELEGY ELLIPTA不可用於緩解急性症狀，亦即用於做為急性支氣管痙攣發作的救援治療藥物。 • 避免過度使用TRELEGY ELLIPTA及避免與其他長效型β2作用劑併用。 • 口咽念珠菌病 • 肺炎 • 正在使用皮質類固醇的兒童或成人如果感染水痘和麻疹，其病程可能會更為嚴重甚或致命。 • 對從全身性皮質類固醇轉換成ICS的病人必須特別小心，因為在從全身性皮質類固醇轉換成全身吸收量較低之ICS的病人中，曾有於轉換期間及轉換之後因腎上腺功能不全而死亡的病例。在停用全身性皮質類固醇之後，下視丘-腦下垂體-腎上腺(HPA)功能需經過數月才能恢復。 • 腎上腺皮質功能亢進與腎上腺抑制 - 超過建議劑量或與強效的細胞色素P450 3A4 (CYP3A4)抑制劑併用，可能會導致HPA功能障礙、藥物交互作用。 • 考慮將TRELEGY ELLIPTA與ketoconazole及其他已知的強效CYP3A4抑制劑合併投予時應謹慎，因為可能會發生全身性皮質類固醇增加及心血管不良作用增強的現象。 • 反常性支氣管痙攣 • 過敏反應，包括全身性過敏 • 心血管影響 - 和其他的β2作用劑一樣，vilanterol對某些病人可能會產生具臨床意義的心血管影響。 • 骨質密度降低 • 曾有COPD或氣喘病人在長期使用ICS或併用吸入性抗膽鹼激性藥物之後發生青光眼、眼內壓升高、白內障及中心性漿液性脈絡膜視網膜病變的報告。 • 尿滯留惡化

	• 和所有含有擬交感神經胺成分的療法一樣，對患有痙攣性疾病或甲狀腺毒症的病人或對擬交感神經胺異常敏感的病人，使用TRELEGY ELLIPTA時應謹慎。曾有報告指出，靜脈投予相關的β2腎上腺素接受體作用劑albuterol會使既有的糖尿病及酮酸中毒更加惡化。 • 低血鉀與高血糖 • 對兒童與青少年投予經口吸入性皮質類固醇可能會導致生長速度減慢。
(藥物)交互作用	•Fluticasone furoate與vilanterol皆為CYP3A4的作用受質。與強效的CYP3A4抑制劑ketoconazole合併投予會升高fluticasone furoate與vilanterol的全身暴露量。考慮將TRELEGY ELLIPTA與ketoconazole及其他已知的強效CYP3A4抑制劑合併投予時應謹慎。 •和其他的β2作用劑一樣，對正在使用單胺氧化酶抑制劑、三環抗憂鬱劑或已知會延長QTc間期之藥物治療的病人，或停用這類藥物未達2週的病人，投予vilanterol時應特別謹慎。 •β阻斷劑不僅會阻斷β作用劑(如vilanterol)的肺部作用，也可能會促使COPD或氣喘病人發生嚴重的支氣管痙攣。因此，COPD或氣喘病人通常不可使用β阻斷劑治療。 •非保鉀利尿劑(如loop類或thiazide類利尿劑)所可能造成的心電圖變化及/或低血鉀現象可能會因β作用劑而出現急性惡化的現象，尤其是在超過該β作用劑之建議劑量的情況下。 •與抗膽鹼激性藥物併用可能會產生加成性的交互作用。
不良反應	•嚴重氣喘相關事件– 住院、插管、死亡 •白色念珠菌感染 •COPD病人發生肺炎的風險升高 •免疫抑制與感染風險 •腎上腺皮質功能亢進與腎上腺抑制 •反常性支氣管痙攣 •心血管影響 •骨質密度降低 •眼部疾患 •尿滯留惡化 •Umeclidinium+Fluticasone Furoate/Vilanterol組中之發生率≥1%且高於安慰劑+Fluticasone Furoate/Vilanterol組的不良反應(COPD受試者)：頭痛、味覺障礙、背痛、咳嗽、口咽疼痛、腹瀉、胃腸炎、上呼吸道感染、肺炎、支氣管炎、口腔念珠菌感染、關節痛、流感、鼻竇炎、咽炎、鼻炎、便祕、尿道感染與發音困難。 •在氣喘受試者中，使用TRELEGY ELLIPTA治療時之發生率≥1%的不良反應：咽炎/鼻咽癌、上呼吸道感染/病毒性上呼吸道感染、支氣管炎、呼吸道感染/病毒性呼吸道感染、竇炎/急性竇炎、尿道感染、鼻炎、流行性感冒、肺炎、頭痛、背痛、發音困難、口咽疼痛、咳嗽、味覺障礙。
不良事件通報程序	若有不良事件可通報至葛蘭素史克藥廠; 通報電話: (02) 23126836, 通報網址: oax40892@gsk.com
公司名稱	荷商葛蘭素史克藥廠股份有限公司台灣分公司
公司地址	台北市忠孝西路一段66號23樓
(聲明)	詳細處方資訊備索
參考仿單版本編號	TW05 (USPI 05/2022) 版本日期：2022年5月

Trelegy 184/55/22 mcg 簡易仿單

許可證字號	**衛部藥輸字第028240號**
中文產品名稱	肺樂喜易利達184/55/22 mcg乾粉吸入劑
活性成份學名	Fluticasone furoate 200 mcg、Umeclidinium 62.5 mcg及 Vilanterol 25 mcg (1劑TRELEGY ELLIPTA 184/55/22 mcg)
適應症或用途	**-氣喘維持治療-** 適用於併用吸入性長效型β2-腎上腺受體作用劑和吸入性皮質類固醇治療氣喘仍控制不佳的成年病人，做為氣喘維持治療。 **-使用限制-** TRELEGY ELLIPTA並不適用於緩解急性支氣管痙攣。
劑量與用法	• 應每天一次以經口吸入的方式投予1劑TRELEGY ELLIPTA。吸入之後，應用水漱口，且不可吞下，這是為了幫助降低發生口咽念珠菌病的風險。 • TRELEGY ELLIPTA 應每天於相同時間投藥。每24小時不可使用TRELEGY ELLIPTA超過1次。對老年病人、腎功能不全病人或中度肝功能不全病人，都不須調整劑量。 **-氣喘維持治療-** • TRELEGY ELLIPTA用於氣喘維持治療的建議起始劑量為每日一次經口吸入1劑TRELEGY ELLIPTA 92/55/22 mcg)，或1劑TRELEGY ELLIPTA 184/55/22 mcg。 • 選擇TRELEGY ELLIPTA的起始劑量時，應考慮病人的病情嚴重程度；先前的氣喘療法，包括吸入性皮質類固醇(ICS)的劑量；以及病人目前的氣喘症狀控制情形與未來更加惡化的風險。 • 最高建議劑量為每天吸入1次TRELEGY ELLIPTA 184/55/22 mcg。 • 對TRELEGY ELLIPTA 92/55/22 mcg每日1次無法產生適當療效反應的病人，將劑量提高至TRELEGY ELLIPTA 184/55/22 mcg每日1次或可提供額外的氣喘控制改善效果。對TRELEGY ELLIPTA 184/55/22 mcg每日1次無法產生適當療效反應的病人，應重新評估，並考慮採取其他療法和額外的治療選擇。 • 如果在兩劑之間出現氣喘症狀，應使用吸入性短效型β2作用劑來達到立即緩解的效果。
禁忌症	TRELEGY ELLIPTA禁用於下列狀況： •作為重積性氣喘(status asthmaticus)或其他氣喘發作且必須採取強效治療措施的第一線療法。 •嚴重乳蛋白過敏，或已證實對fluticasone furoate、umeclidinium、vilanterol或任何賦形劑過敏。
警語及注意事項	• 使用長效型β2腎上腺素作用劑(LABA)做為氣喘的單□治療藥物(未併用ICS)會導致發生氣喘相關死亡的風險升高。大型臨床試驗的資料顯示，合併使用固定劑量的LABA與ICS時，和單獨使用ICS相比，並未明顯增加發生嚴重氣喘相關事件(住院、插管、死亡)的風險。 • 對病情正在快速惡化或發生可能危及生命之發作事件的氣喘病人，不可開始使用TRELEGY ELLIPTA。 • TRELEGY ELLIPTA不可用於緩解急性症狀，亦即用於做為急性支氣管痙攣發作的救援治療藥物。 • 避免過度使用TRELEGY ELLIPTA及避免與其他長效型β2作用劑併用。 • 口咽念珠菌病 • 肺炎 • 正在使用皮質類固醇的兒童或成人如果感染水痘和麻疹，其病程可能會更為嚴重甚或致命。 • 對從全身性皮質類固醇轉換成ICS的病人必須特別小心，因為在從全身性皮質類固醇轉換成全身吸收量較低之ICS的病人中，曾有於轉換期間及轉換之後因腎上腺功能不全而死亡的病例。在停用全身性皮質類固醇之後，下視丘-腦下垂體-腎上腺(HPA)功能需經過數月才能恢復。 • 腎上腺皮質功能亢進與腎上腺抑制 - 超過建議劑量或與強效的細胞色素P450 3A4 (CYP3A4)抑制劑併用，可能會導致HPA功能障礙、藥物交互作用。 • 考慮將TRELEGY ELLIPTA與ketoconazole及其他已知的強效CYP3A4抑制劑合併投予時應謹慎，因為可能會發生全身性皮質類固醇增加及心血管不良作用增強的現象。

	•反常性支氣管痙攣 •過敏反應，包括全身性過敏 •心血管影響 - 和其他的β2作用劑一樣，vilanterol對某些病人可能會產生具臨床意義的心血管影響。 •骨質密度降低 •曾有氣喘病人在長期使用ICS或併用吸入性抗膽鹼激性藥物之後發生青光眼、眼內壓升高、白內障及中心性漿液性脈絡膜視網膜病變的報告。 •尿滯留惡化 •和所有含有擬交感神經胺成分的療法一樣，對患有痙攣性疾病或甲狀腺毒症的病人或對擬交感神經胺異常敏感的病人，使用TRELEGY ELLIPTA時應謹慎。曾有報告指出，靜脈投予相關的β2腎上腺素接受體作用劑albuterol會使既有的糖尿病及酮酸中毒更加惡化。 •低血鉀與高血糖 •對兒童與青少年投予經口吸入性皮質類固醇可能會導致生長速度減慢。
(藥物)交互作用	•Fluticasone furoate與vilanterol皆為CYP3A4的作用受質。與強效的CYP3A4抑制劑ketoconazole合併投予會升高fluticasone furoate與vilanterol的全身暴露量。考慮將TRELEGY ELLIPTA與ketoconazole及其他已知的強效CYP3A4抑制劑合併投予時應謹慎。 •和其他的β2作用劑□樣，對正在使用單胺氧化酶抑制劑、三環抗憂鬱劑或已知會延□QTc間期之藥物治療的病□，或停用這類藥物未達2週的病人，投予vilanterol時應特別謹慎。 •β阻斷劑不僅會阻斷β作用劑(如vilanterol)的肺部作□，也可能會促使氣喘病人發生嚴重的支氣管痙攣。因此，氣喘病人通常不可使用β阻斷劑治療。 •非保鉀利尿劑(如loop類或thiazide類利尿劑)所可能造成的□電圖變化及/或低血鉀現象可能會因β作用劑而出現急性惡化的現象，尤其是在超過該β作用劑之建議劑量的情況下。 •與抗膽鹼激性藥物併用可能會產□加成性的交互作□。
不良反應	•嚴重氣喘相關事件– 住院、插管、死亡 •白色念珠菌感染 •病人發生肺炎的風險升高 •免疫抑制與感染風險 •腎上腺皮質功能亢進與腎上腺抑制 •反常性支氣管痙攣 •心血管影響 •骨質密度降低 •眼部疾患 •尿滯留惡化 •氣喘受試者中，使用TRELEGY ELLIPTA治療時之發生率≥1%的不良反應為：咽炎/鼻咽癌、上呼吸道感染/病毒性上呼吸道感染、支氣管炎、呼吸道感染/病毒性呼吸道感染、竇炎/急性竇炎、尿道感染、鼻炎、流行性感冒、肺炎、頭痛、背痛、發音困難、口咽疼痛、咳嗽、味覺障礙。
不良事件通報程序	若有不良事件可通報至葛蘭素史克藥廠; 通報電話: (02) 23126836, 通報網址: oax40892@gsk.com
公司名稱	荷商葛蘭素史克藥廠股份有限公司台灣分公司
公司地址	台北市忠孝西路一段66號23樓
(聲明)	詳細處方資訊備索
參考仿單版本編號	TW02 (USPI 05/2022) 版本日期：2022年5月

Relvar簡易仿單

許可證字號	衛部藥輸字第026318號; 衛部藥輸字第027034號
中文產品名稱	潤娃易利達92/22 mcg乾粉吸入劑 潤娃易利達184/22 mcg乾粉吸入劑
活性成份學名	Vilanterol trifenatate / Fluticasone furoate
適應症或用途	• RELVAR ELLIPTA 92/22 是一種吸入性的皮質類固醇/長效型β2腎上腺素作用劑 (ICS/LABA) 複方製劑，適用於慢性阻塞性肺病(COPD)患者之氣道阻塞症狀的維持治療。 •RELVAR ELLIPTA 92/22 也適用於降低有惡化病史患者之 COPD 惡化。 •RELVAR ELLIPTA是一種ICS/LABA複方製劑，適用於治療適合使用吸入型皮質類固醇及長效β2作用劑合併治療的18歲及以上氣喘患者。
劑量與用法	RELVAR ELLIPTA應以每天吸入一次的方式投藥，且僅可經口吸入。
禁忌症	RELVAR ELLIPTA禁用於下列狀況： • 作為重積性氣喘 (status asthmaticus) 或其他急性COPD或氣喘發作且必須採取強效治療措施的第一線療法. • 有嚴重乳蛋白過敏問題，或已證實對fluticasone furoate、vilanterol或本品之任何賦形劑過敏.
警語及注意事項	• 嚴重氣喘相關事件—住院、插管、死亡 • 病情惡化與急性發作 • 過度使用RELVAR ELLIPTA及與其他長效型β2作用劑併用 • 與吸入性皮質類固醇的局部影響 • 肺炎 • 免疫抑制 • 從全身性皮質類固醇轉換治療的患者 • 腎上腺皮質功能亢進與腎上腺抑制 • 與強效細胞色素 P450 3A4 抑制劑的藥物交互作用 • 反常性支氣管痙攣 • 過敏反應 (包括全身性過敏) • 心血管影響 • 骨質密度降低 • 青光眼與白內障

	• 合併症 •高血糖與低血鉀 •對生長的影響
不良反應	使用LABA可能會導致： • 嚴重氣喘相關事件– 住院、插管、死亡 • 心血管影響 使用全身性與局部性皮質類固醇可能會導致： • 白色念珠菌感染 • COPD患者發生肺炎的風險升高 • 免疫抑制 • 腎上腺皮質功能亢進與腎上腺抑制 • 骨質密度降低
不良事件通報程序	若有不良事件可通報至葛蘭素史克藥廠; 通報電話: (02) 23126836, 通報網址: oax40892@gsk.com
公司名稱	荷商葛蘭素史克藥廠(股)台灣分公司
公司地址	台北市忠孝西路一段66號23樓
(聲明)	詳細處方資訊備索
參考仿單版本編號	TW04 (USPI 01/2019) 版本日期： 2019 年 2 月

Seretide 250 Accuhaler 簡易仿單

許可證字號	衛署藥輸字第 023203 號
中文產品名稱	使肺泰 250 準納 乾粉吸入劑
活性成份學名	50 mcg salmeterol (as xinafoate) 及 250 mcg fluticasone propionate。
適應症或用途	SERETIDE 適用於可逆性呼吸道阻塞疾病 (ROAD) 之常規治療，包括適合使用 支氣管擴張劑及皮質類固醇組合療法之患有氣喘的兒童與成人。
劑量與用法	僅供口腔吸入使用。 患者必須明白，即使沒有症狀，仍須常規使用，才能得到最佳臨床效益。 • 成人及十二歲以上之青少年：每日兩次，每次吸一單位劑量。 • 四歲以上之兒童：每日兩次，每次吸一下。 • COPD患者：成人每日兩次，每次吸一單位劑量 • 特殊患者群：老年患者，以及肝功能或腎功能不全之患者，使用時不需要調整劑量。
禁忌症	禁止使用於對本劑任何一種成分有過敏史之患者；以及於對乳蛋白嚴重過敏的患者。
警語及注意事項	可逆性呼吸道阻塞疾病的處理應該遵循正規的階梯式治療程序，並監測病人的控制狀況。SERETIDE 並非供緩解急性症狀之用，此種情況必須以作用快速且短效之吸入型支氣管擴張劑 (salbutamol) 來治療。應告知病人隨時必備急性氣喘發作之緩解藥物。若需增加短效性支氣管擴張劑的使用，以緩解症狀，表示控制惡化，病人亦應接受醫師的詳細檢查。氣喘控制突然或逐漸惡化可能會有生命危險，這種病人應接受醫師的詳細檢查，也必須考慮增加皮質類固醇療法。此外，如果目前的 SERETIDE 劑量無法充分控制氣喘，則病人亦應接受醫師的詳細檢查。因為有氣喘惡化的危險，病人不可驟然停止 SERETIDE 的治療，應在醫師監督下逐步減量。
不良反應	極常見：頭痛 常見：口腔與喉嚨的念珠菌病、肺炎(COPD患者)、聲音嘶啞/發聲障礙、肌肉痙攣、關節痛 少見：皮膚過敏反應、呼吸困難、白內障、高血糖、焦慮、睡眠障礙、顫抖、心悸、心搏過速、心房纖維顫動、喉嚨發炎、挫傷 罕見：食道念珠菌病、嚴重過敏反應、青光眼、行為改變，包括過動與易怒(主要見於兒童)、心律不整，包括上心室心搏過速與期外收縮、血管性水腫(主要為臉部與口咽水腫)與支氣管痙攣、庫欣氏症候群、類庫欣氏症表徵、腎上腺抑制、兒童與青少年生長遲緩、骨質密度降低、反常性支氣管痙攣。
不良事件通報程序	若有不良事件可通報至葛蘭素史克藥廠; 通報電話: (02) 23126836, 通報網址: oax40892@gsk.com
公司名稱	荷商葛蘭素史克藥廠(股)台灣分公司
公司地址	台北市忠孝西路一段66號23樓
(聲明)	詳細處方資訊備索
參考仿單版本編號	GDS37/IPI22 版本日期：15 Dec 2020