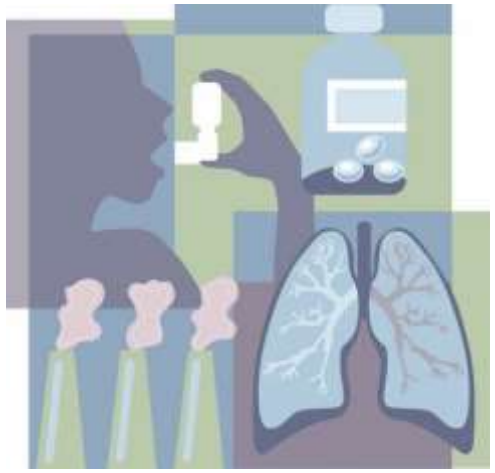
MAHIDOL UNIVERSITY
Wisdom of the Land

Airway Pharmacology for Asthma & COPD

Review & Update



รศ.ดร.ภกญ. วริสรา ปาริชาติกานนท์

ภาควิชาเภสัชวิทยา คณะเภสัชศาสตร์ ม.มหิดล

E-mail: warisara.par@mahidol.ac.th

Warisara PARICHATIKANOND

Dr.Scient.Med., Ph.D.
From Medical University of Graz, Austria (2016)

Assoc.Prof. in Pharmacology
Department of Pharmacology,
Faculty of Pharmacy, Mahidol University

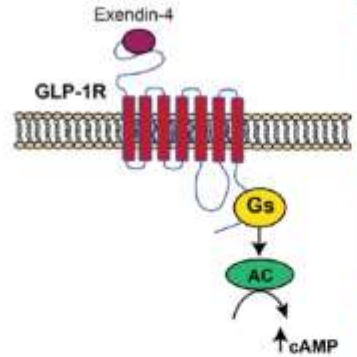
Email:
warisara.par@mahidol.ac.th

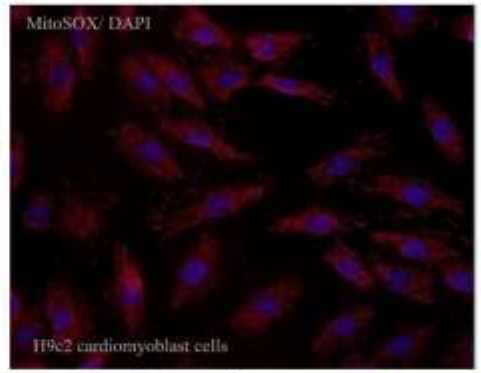
h-index: 20
Citations: 1,206
(Last update: Jan 2025)

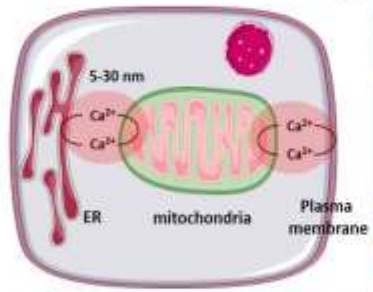
Cardiovascular Pharmacology

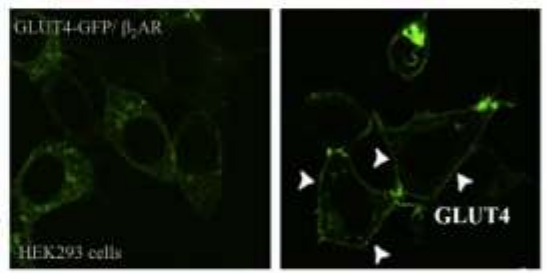
Research Interest:

- G protein-coupled receptors linked to mitochondrial dysfunction in insulin resistance and cardiovascular diseases
- Mitochondrial function in aging and aging-related diseases
- Mitochondrial calcium signaling and uptake machinery
- Pharmacological activities of herbal medicine and chemical compounds









Output in Top Journals

Textbook

Asthma & COPD

- Asthma & COPD are heterogeneous disease, usually characterized by chronic airway inflammation, over time, causing "airway remodeling" (permanent damage)
- Asthma & COPD are both obstructive & inflammatory lung disease
  - Obstructive component: Bronchoconstriction
  - Inflammatory component: Airway edema, goblet cell hyperplasia, mucus secretion, and cytokine release by immune cells
- Medications used to treat asthma act in one of two ways:
  - By relaxing bronchial smooth muscle: Bronchodilators
  - By treating inflammation: Anti-inflammatory agents

Common drugs for asthma & COPD

Bronchodilators

β_2-agonist (BA)

SABA: Short-acting BA

- **4-6 hr**
- Salbutamol, Terbutaline

LABA: Long-acting BA

- **12 hr (twice-daily)**
- Salmeterol, Formoterol

Ultra-LABA: Ultra-long-acting BA

- **24 hr (once-daily)**
- Indacaterol, Vilanterol, Olodaterol, Abediterol, Carmoterol

Muscarinic M_3 antagonist (MA)

SAMA: Short-acting MA

- **4-6 hr**
- Ipratropium

LAMA: Long-acting MA

- **12 hr (twice-daily)**
- Aclidinium

Ultra-LAMA: Ultra-long-acting MA

- **24 hr (once-daily)**
- Tiotropium, Glycopyrronium, Umeclidinium, Revefenacin

Anti-inflammatory agents

Anti-inflammatory agent

Inhaled corticosteroid (ICS)

- Budesonide, fluticasone, beclomethasone, mometasone

Anti-leukotrienes

- Montelukast, Zafirlukast

Biological products

Anti-IgE: Omalizumab

Anti-IL5: Mepolizumab (anti-IL5), Reslizumab (anti-IL5), Benralizumab (anti-IL5Ra)

Anti-IL4Rα: Dupilumab

Anti-TSLP: Tezepelumab

PDE inhibitors

Methylxanthine: Theophylline SR, aminophylline

PDE4 inhibitor: Roflumilast

PDE3/PDE4 inhibitor: Ensifentrine

Warisara Parichatikanond

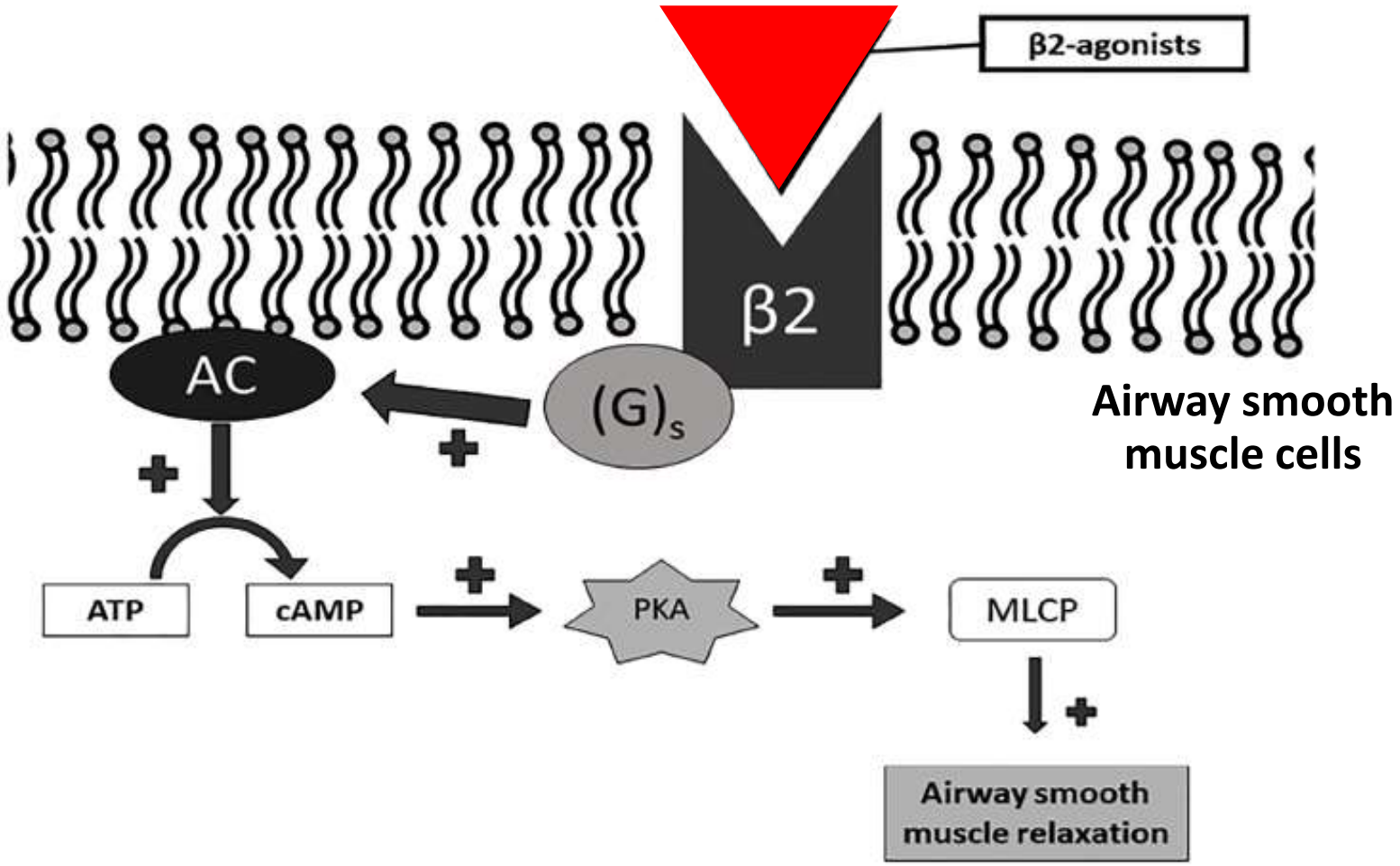
Inhaled Bronchodilators

- **Inhaled long-acting bronchodilators** are most often given on a regular basis to prevent or reduce symptoms in asthma & COPD
- **Aim:**
  - ☑ Reduce symptoms (bronchial obstruction & airflow limitation)
  - ☑ Reduce frequency & severity of exacerbations
  - ☑ Improve exercise tolerance
  - ☑ Improve health status

- Main: β_2-agonist & Muscarinic M_3 antagonist
- To date, there is no clinical trial evidence that any medications modify long-term rate of decline in lung function

β_2-agonist (BA)

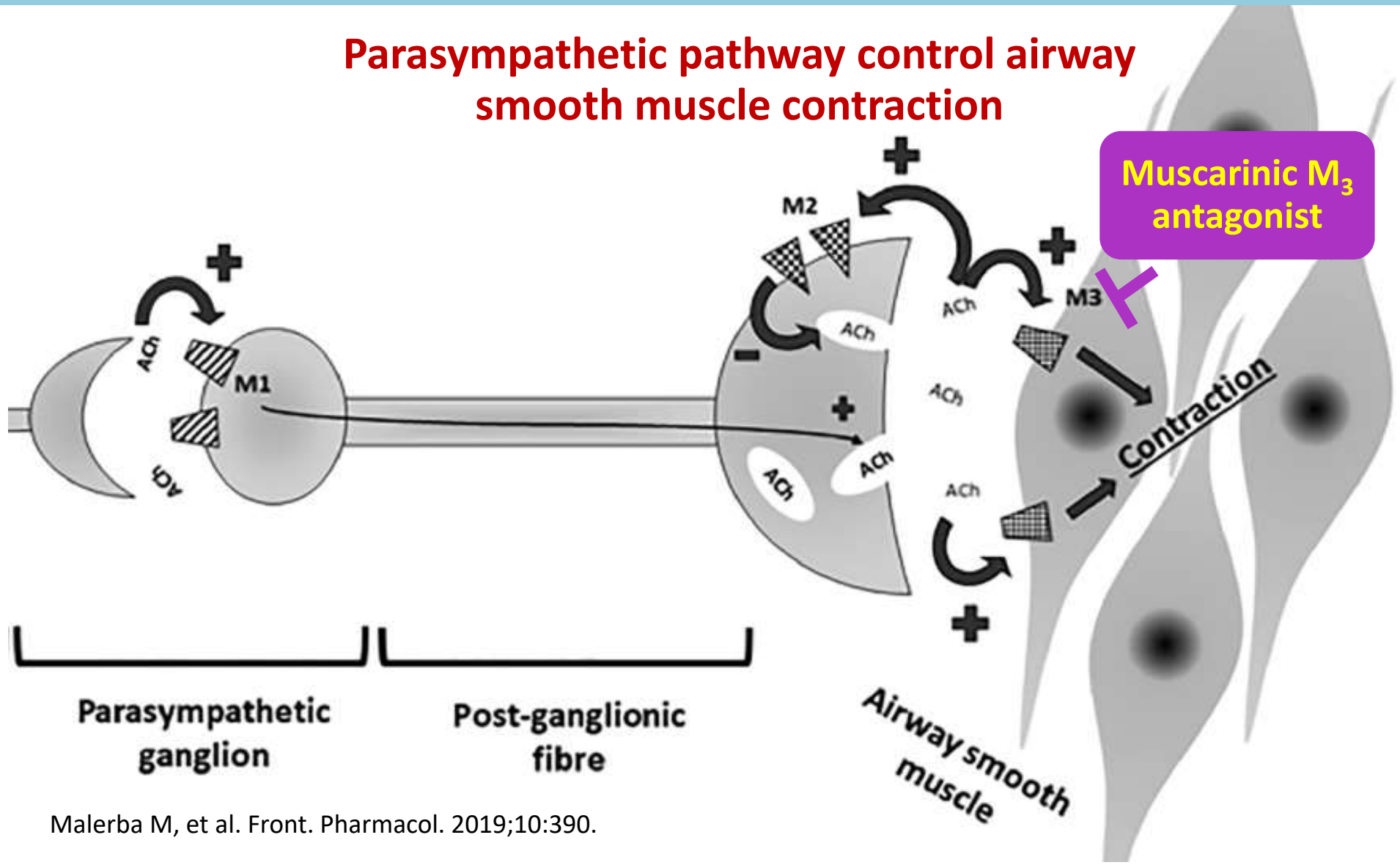
Signaling pathway of β_2-receptor activation



Malerba M, et al. Front. Pharmacol. 2019;10:390.

Muscarinic M_3 antagonist (MA)

Parasympathetic pathway control airway smooth muscle contraction



Malerba M, et al. Front. Pharmacol. 2019;10:390.

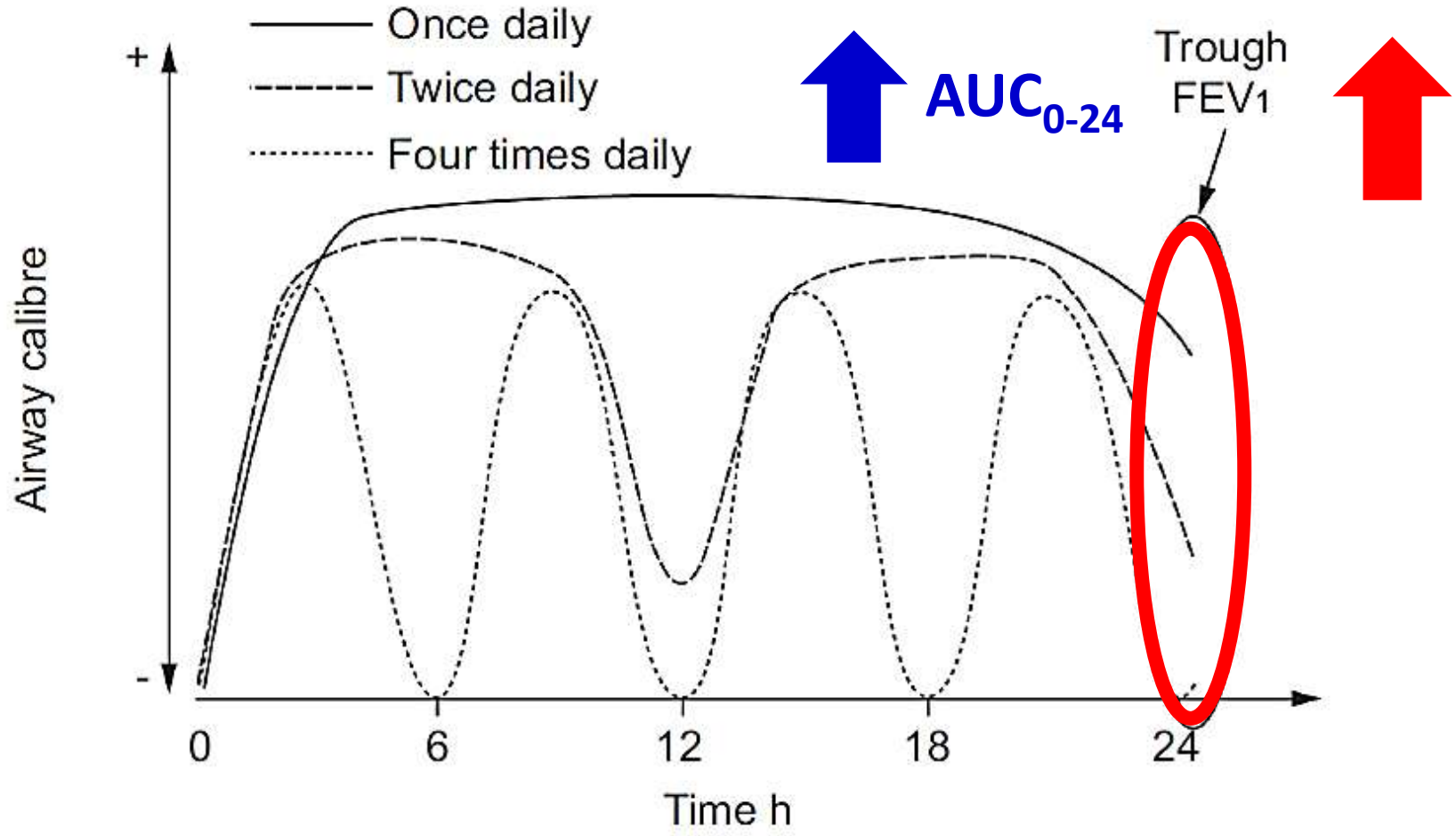
Long-acting bronchodilators

- **Long-acting bronchodilators** improve clinical outcomes including lung function, symptoms, quality of life and exacerbations
- Combination **LABA/ICS** and **LABA/LAMA** as **once a day formulation** are the norm for maintenance of **asthma** & **COPD**, respectively
- **"New generation long-acting bronchodilators":**

  Once-daily -> "ULTRA"

  - ☑ **Longer duration of action (>24 h)**
  - ☑ **Fast onset of action**
  - ☑ **Favorable safety profile**
  - ☑ **Efficient & convenient device**

Effects of long-acting vs. short-acting bronchodilators on 24-h airway tone



With extended duration, the net area under time/airflow curve (AUC) increases, persistent bronchorelaxant effects (less variable) and increased trough FEV1

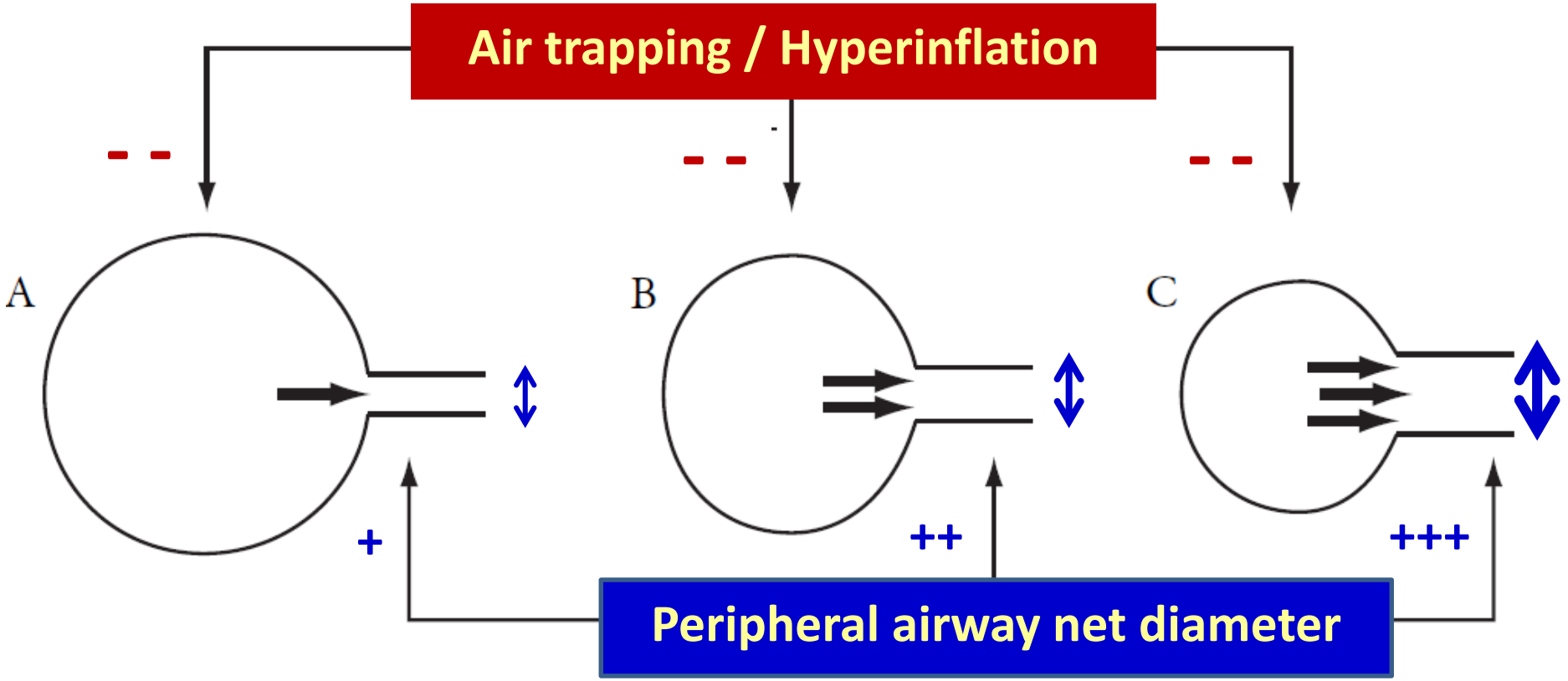
Wedzicha JA, et al. Eur Respir J 2012; 40: 1545–54

Model of lung deflation with increased airway calibre

Asthma & COPD: Inflammation & airflow limitation

➡ ↓FEV1 + Air trapping ➡ Hyperinflation

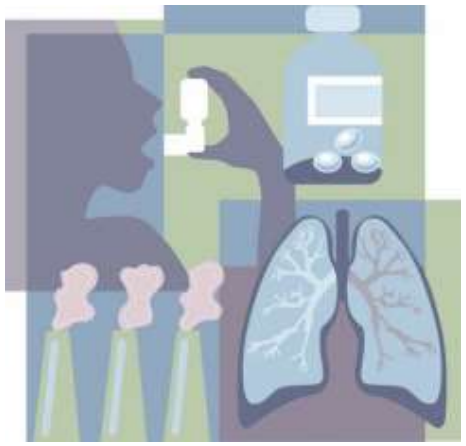
Short-acting	Twice daily	Once daily



Beeh KM, Beier J. Adv Ther 2010;27:150-9

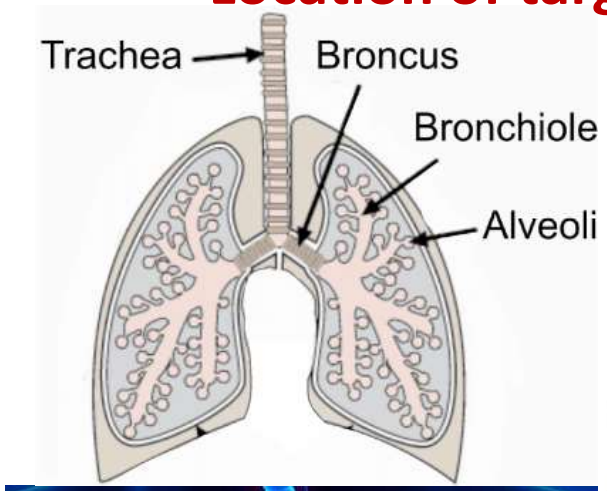
Combination: Dual / Triple therapy
LABA / LAMA & LABA / ICS & LABA / LAMA / ICS

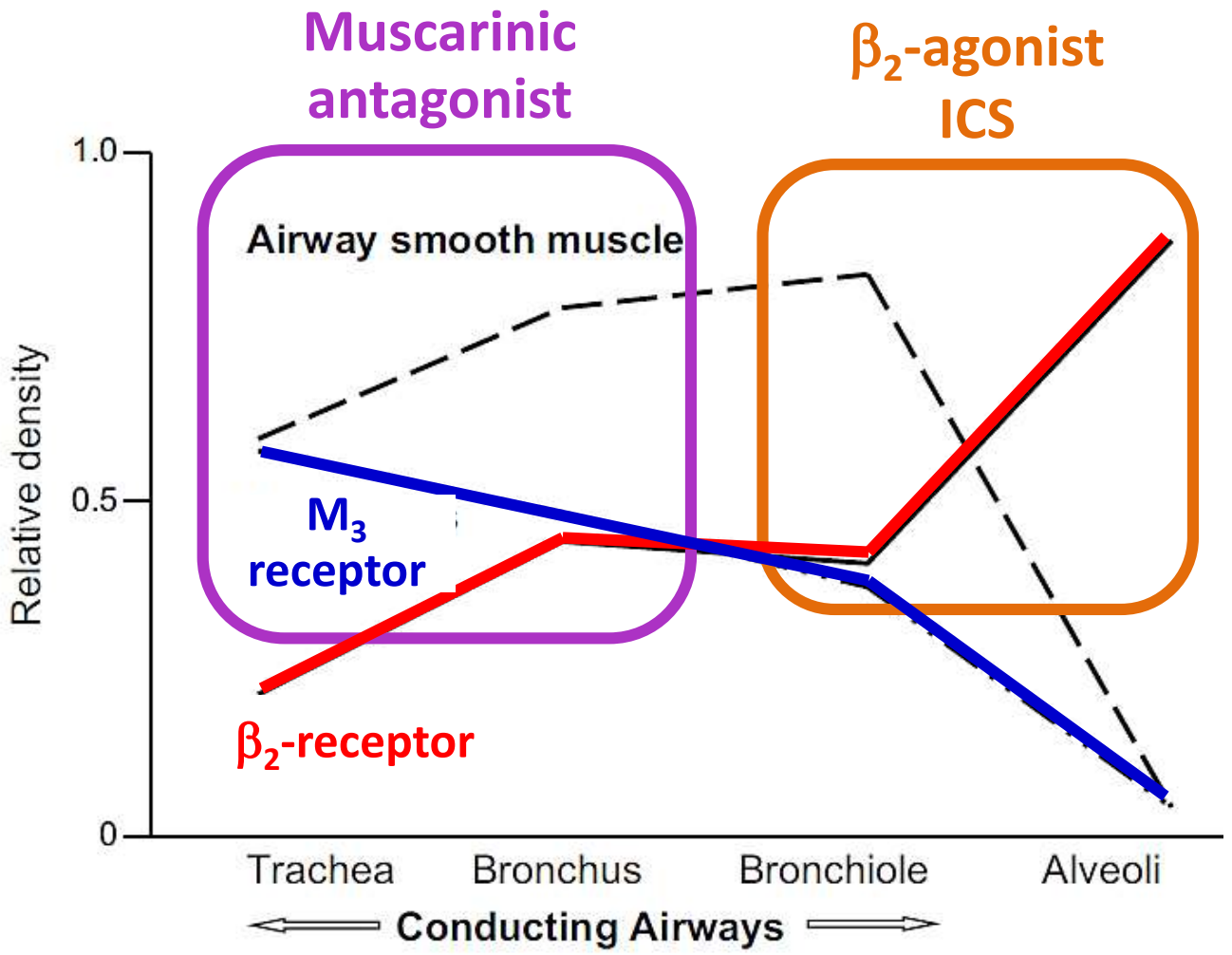
- **Combining bronchodilators with <u>different</u> mechanisms & durations of action is more effective than either component alone**
  - ☑ **Increase degree of bronchodilation**
  - ☑ **Lower risk of side-effects (compared to increase dose of a single bronchodilator)**
  - ☑ **Improve outcome: Symptoms, lung function (FEV1), exacerbation, quality of life**
  - ☑ **Better adherence (Single inhaler)**
  - ☑ **? Mortality rate**



Improved lung function with combination treatment

Location of targets for bronchodilators in human airways





Warisara Parichatikanond

Haughney J, et al. Respiratory Medicine 2010; 125-31

National Asthma Council AUSTRALIA

ASTHMA & COPD MEDICATIONS

BIOLOGIC THERAPIES FOR SEVERE ASTHMA

Fasenra*
benralizumab 30mg/mL

Dupixent*
dupilumab
200mg/1.14mL • 300mg/2mL

Nucala*
mepolizumab 100mg/mL

Xolair*
omalizumab
150mg • 75mg/0.5mL • 150mg/mL

* Section 100 (Highly Specialised Drugs)

RESOURCES

TREATMENT GUIDELINES

Australian Asthma Handbook:
asthmahandbook.org.au

COPD-X Plan:
copdx.org.au

COPD Inhaler Device Chart Poster:
lungfoundation.com.au/resources/copd-inhaler-device-chart-poster/

INHALER TECHNIQUE

How-to videos, patient and practitioner information
nationalasthma.org.au

pMDIs should be used with a spacer (and face mask if needed)

HOW-TO VIDEOS

SCAN ME

SABA RELIEVERS

Ventolin Inhaler † ^
salbutamol 100mcg
Additional brands: Asmol, Zempreon

Airomir Autohaler ‡ #
salbutamol 100mcg

Bricanyl Turbuhaler [a] [c]
terbutaline 500mcg

SAMA MEDICATION

Atrovent Metered Aerosol † ^
ipratropium 21mcg

NON STEROIDAL PREVENTER

Montelukast Tablet
montelukast
4mg [a] • 5mg [a] • 10mg
Multiple generic brands

ICS PREVENTERS

Flixotide Inhaler †
fluticasone propionate
50mcg* • 125mcg • 250mcg
**Flixotide Junior* [a]*

Flixotide Accuhaler †
fluticasone propionate
100mcg* • 250mcg • 500mcg
**Flixotide Junior*

Fluticasone Cipla Inhaler †
fluticasone propionate
125mcg • 250mcg

Pulmicort Turbuhaler †
budesonide
100mcg • 200mcg • 400mcg

QVAR Inhaler †
beclometasone
50mcg • 100mcg

QVAR Autohaler ‡
beclometasone
50mcg • 100mcg

Alvesco Inhaler †
ciclesonide
80mcg • 160mcg

Arnuity Ellipta †
fluticasone furoate
100mcg • 200mcg

Axotide Inhaler †
fluticasone propionate
50mcg* • 125mcg • 250mcg
**Axotide Junior* [a]*

Axotide Accuhaler †
fluticasone propionate
100mcg* • 250mcg
**Axotide Junior*

LAMA MEDICATIONS

Spiriva Respimat # ‡/a
tiotropium 2.5mcg

Spiriva Handihaler #
tiotropium 18mcg

Braltus Zonda #
tiotropium 13mcg

Bretaris Genuair #
aclidinium 322mcg

Seebri Breezhaler #
glycopyrronium 50mcg

Incruse Ellipta #
umeclidinium 62.5mcg

LAMA/LABA COMBINATIONS

Spiolto Respimat [c]
tiotropium/olodaterol
2.5/2.5mcg

Brimica Genuair [c]
aclidinium/formoterol
340/12mcg

Ultibro Breezhaler [c]
indacaterol/glycopyrronium
110/50mcg

Anoro Ellipta [c]
umeclidinium/vilanterol
62.5/25mcg

ICS/LABA COMBINATIONS

Seretide Inhaler [a]
fluticasone propionate/salmeterol
50/25 • 125/25 • 250/25 [c]
Additional brands: Pavtide, Fluticasone + Salmeterol Cipla, SalplusF, Evocair

Symbicort Turbuhaler [a]
budesonide/formoterol
100/6 • 200/6 • 400/12 [c]
Additional brand: Rilast Turbuhaler

Seretide Accuhaler [a]
fluticasone propionate/salmeterol
100/50 • 250/50 • 500/50 [c]
Additional brands: Pavtide, Fluticasone + Salmeterol Cipla

DuoResp Spiromax [a]
budesonide/formoterol
200/6 • 400/12 [c]
Additional brand: BiResp Spiromax

Salflumix Easyhaler [a]
fluticasone propionate/salmeterol
250/50 • 500/50 [c]

Flutiform Inhaler [a]
fluticasone propionate/formoterol
50/5 • 125/5 • 250/10

Bufomix Easyhaler [a]
budesonide/formoterol
200/6 • 400/12 [c]

Fostair Inhaler [a]
beclometasone/formoterol
100/6 • 200/6

Symbicort Rapihaler [a]
budesonide/formoterol
100/3 • 200/6 [c]
Additional brand: Rilast Rapihaler

Breo Ellipta [a]
fluticasone furoate/vilanterol
100/25 [c] • 200/25

Atectura Breezhaler [a]
mometasone/indacaterol
62.5/125 • 127.5/125 • 260/125
all units in mcg

LABA MEDICATIONS

Oxis Turbuhaler ‡
formoterol 6mcg • 12mcg

Serevent Accuhaler ‡
salmeterol 50mcg

Onbrez Breezhaler #
indacaterol 150mcg • 300mcg

ICS/LAMA/LABA COMBINATIONS

Trelegy Ellipta
fluticasone furoate/umeclidinium/vilanterol
100/62.5/25 [c] • 200/62.5/25 [a]

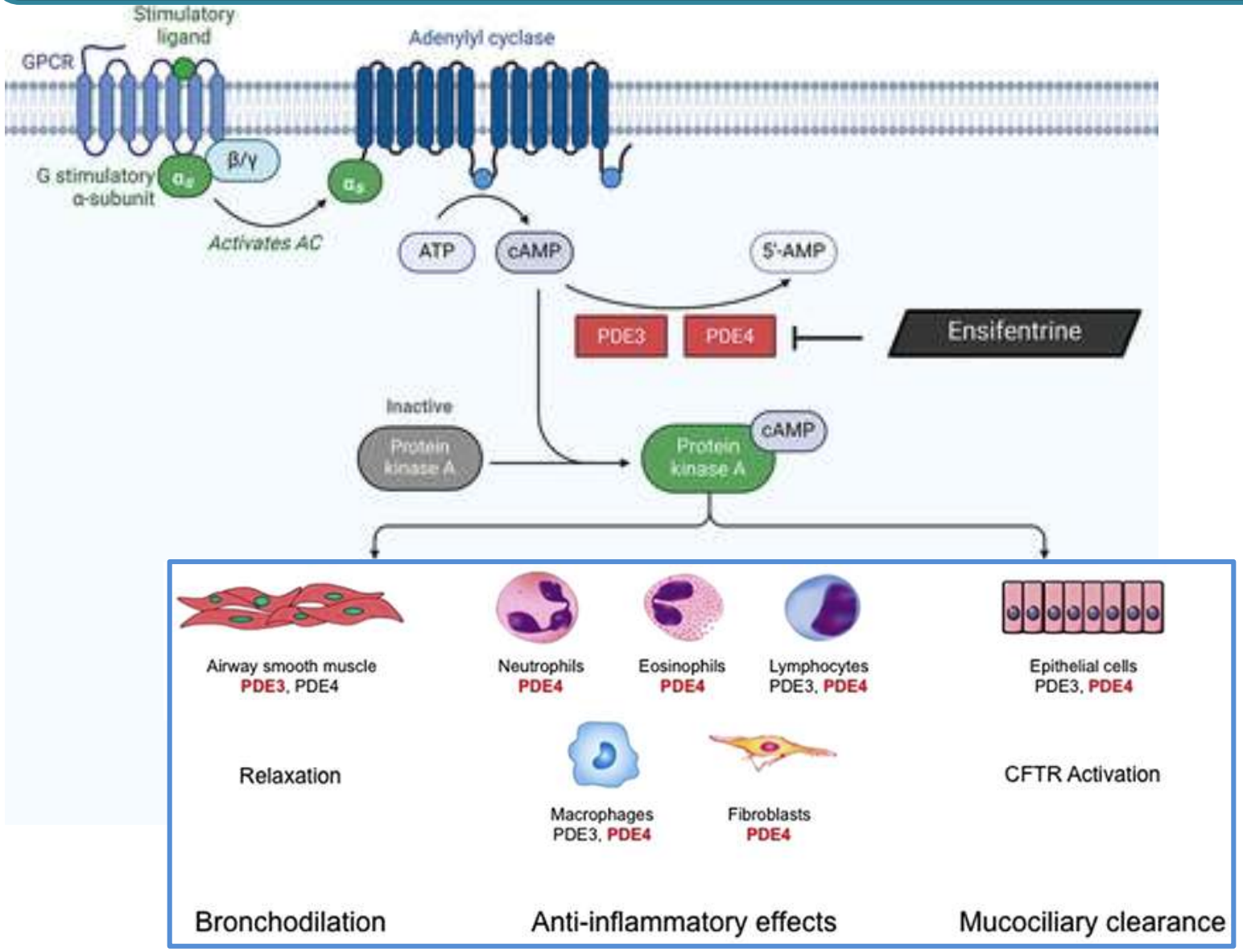
Enerzair Breezhaler [a]
mometasone/glycopyrronium/indacaterol
68/46/114 • 136/46/114

Trimbow Inhaler
beclometasone/glycopyrronium/formoterol
100/10/6 [c] • 200/10/6 [a]

Breztri Aerosphere [c]
budesonide/glycopyrronium/formoterol
160/7.2/5
all units in mcg

ICS, inhaled corticosteroid | LABA, long-acting beta$_2$ agonist | LAMA, long-acting muscarinic antagonist | SABA, short-acting beta$_2$ agonist | SAMA, short-acting muscarinic antagonist

Phosphodiesterase (PDE) inhibitors



Roflumilast

- Selective PDE4 inhibitor
- Anti-inflammatory effects
- Oral tablet
- Systemic side effects
- FDA (Feb, 2011): Reduce risk of exacerbations in severe COPD

Ensifentrine

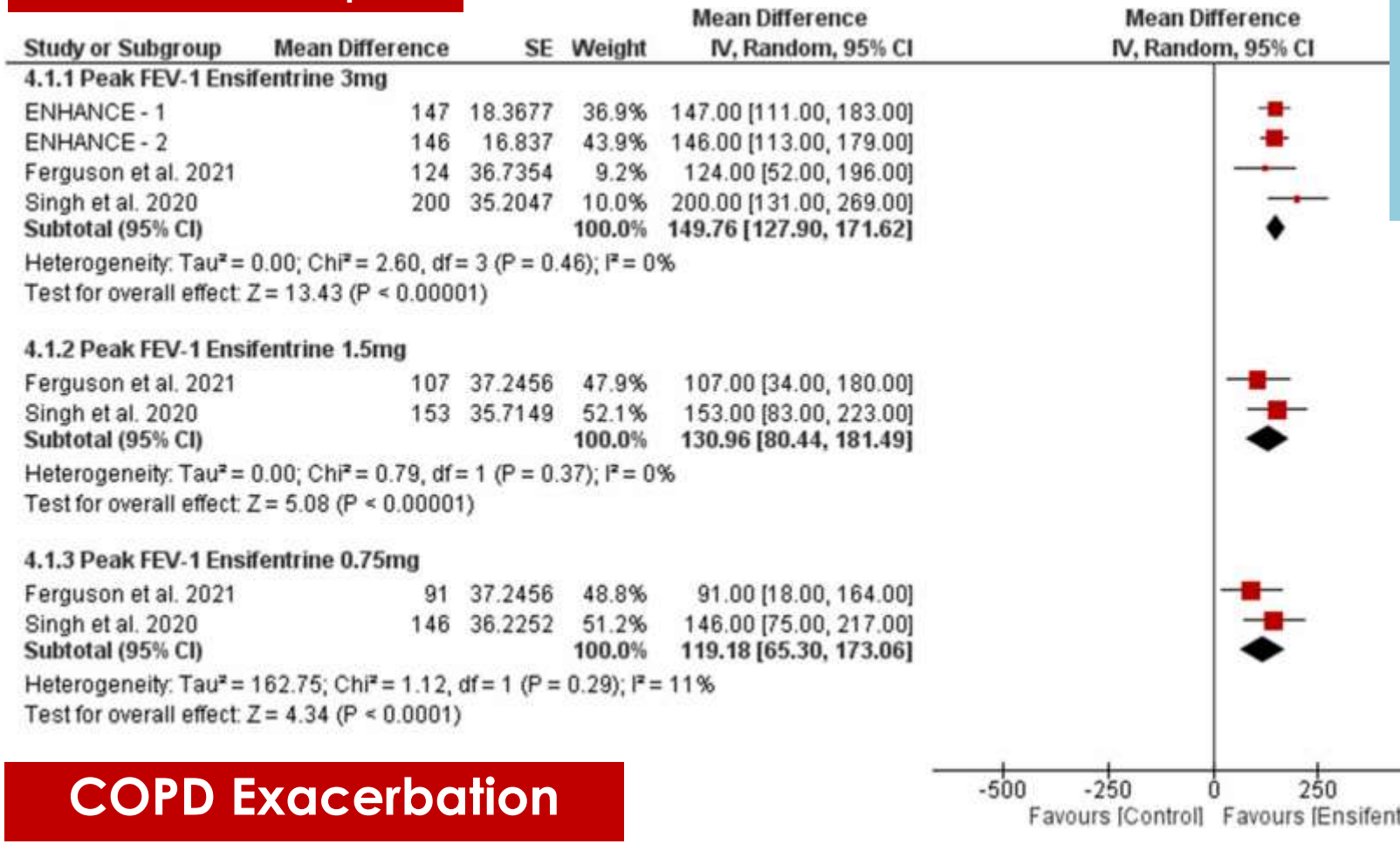
- Dual PDE3/PDE4 inhibitor
- Both bronchodilation & anti-inflammatory effects
- Inhaled via a nebulizer
- Acts directly in lungs -> faster relief & fewer systemic side effects
- FDA (Jun, 2024): COPD maintenance treatment in adults

Sciurba FC. Expert Opin Pharmacother. 2025;26(7):809-820.

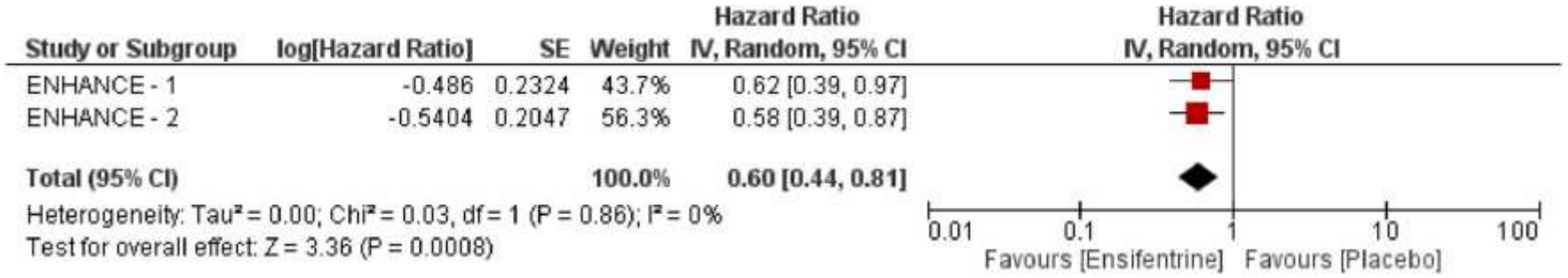
Meta-analysis: Ensifentrine in COPD

Fatima E. Respir Investig. 2025;63(1):146-155.

Peak FEV_1



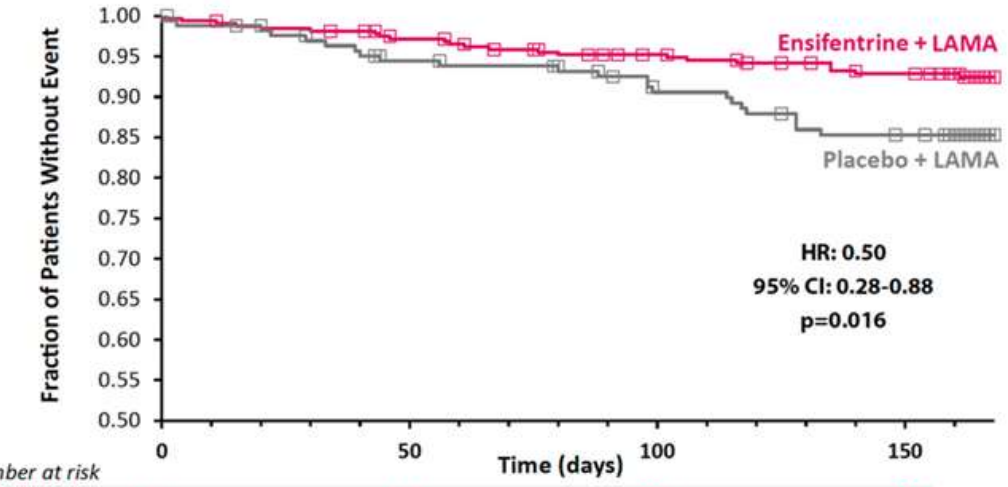
COPD Exacerbation



A post-hoc analysis of ENHANCE-1/2: Ensifentrine in COPD taking LABA & LABA/ICS

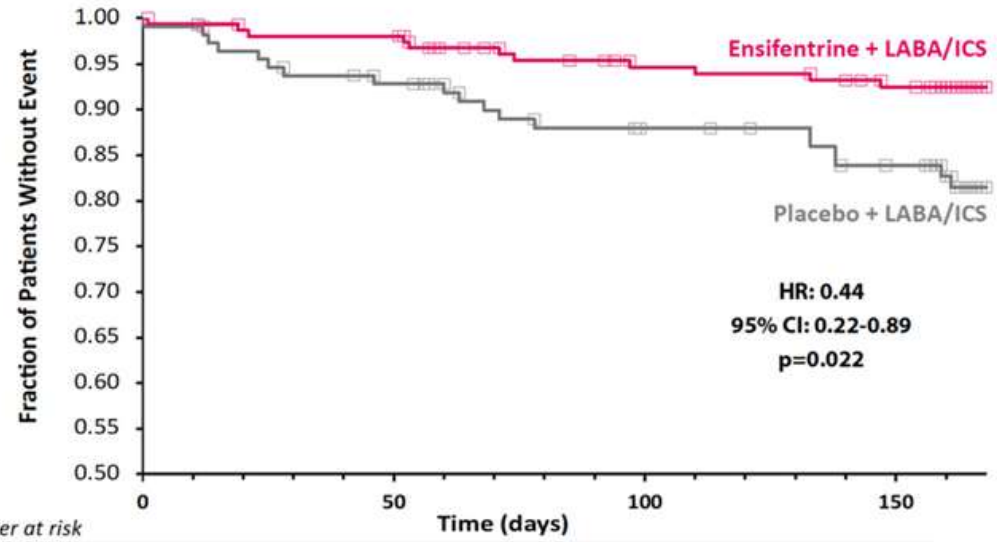
Without exacerbations over 24 wk

A.



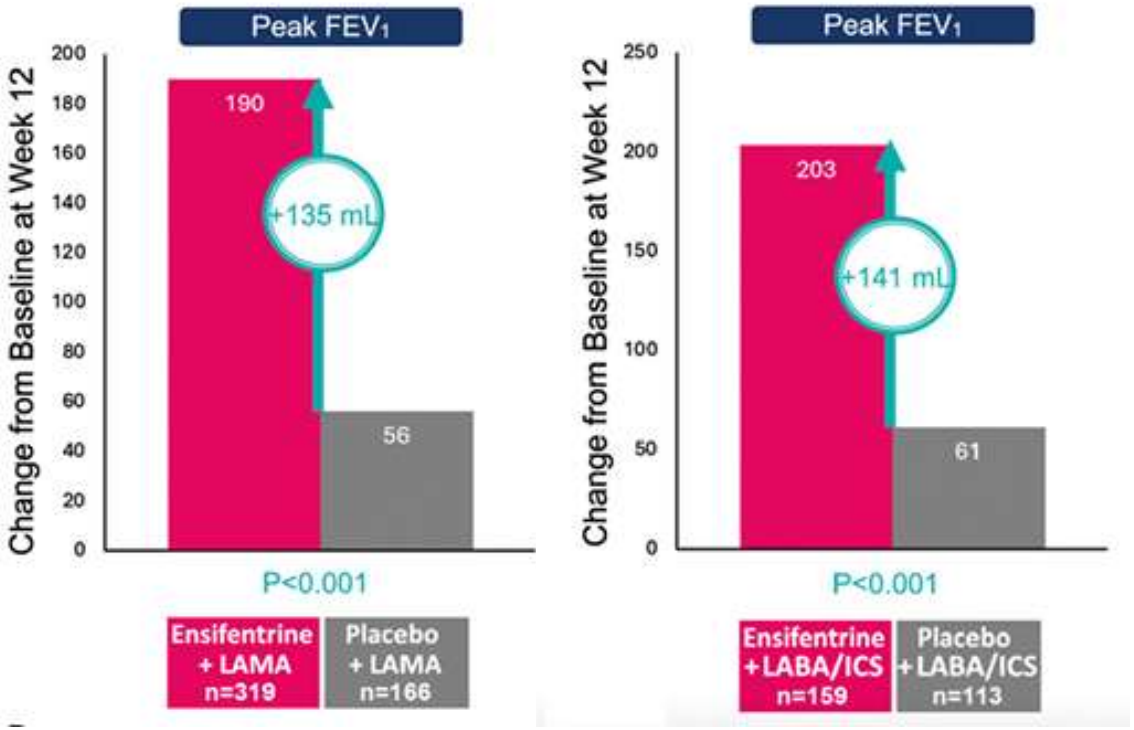
Number at risk				
Ensifentrine	319	302	286	273
Placebo	166	150	139	126

B.



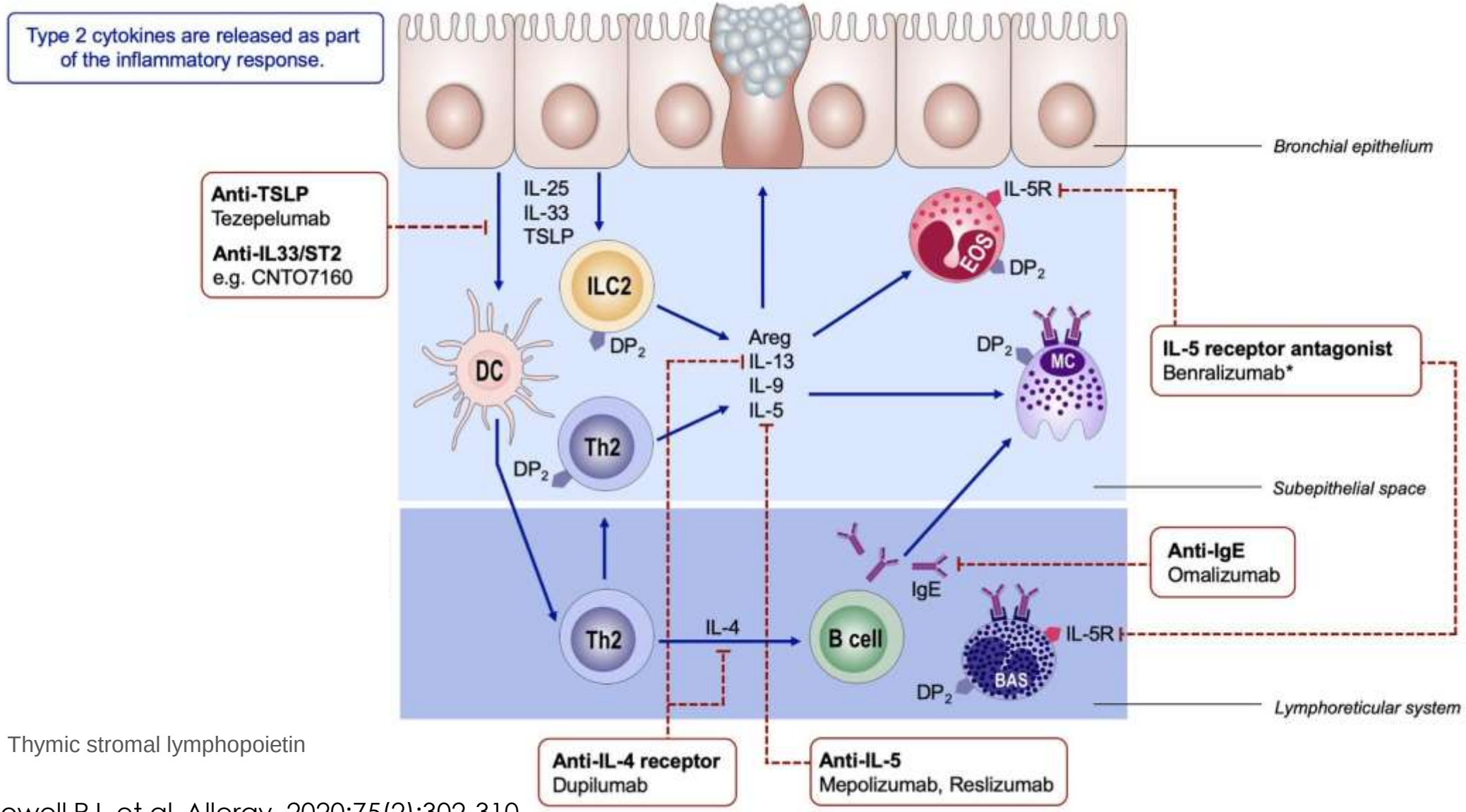
Number at risk				
Ensifentrine	159	154	133	126
Placebo	113	102	88	80

Peak FEV_1 change (at wk-12)



Dransfield M. Chron Respir Dis. 2025 ;22:14799731251314874.

Biological products for severe asthma

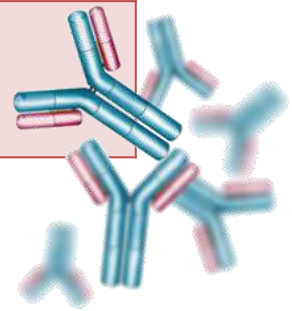


TSLP: Thymic stromal lymphopoietin

McDowell PJ, et al. Allergy. 2020;75(2):302-310.

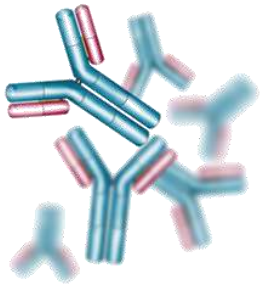
Biological products for severe asthma

Class	Name	Regimen	Age (Years)	Asthma indication
Anti-IgE	Omalizumab	SC, q 4 wk	≥6	Severe allergic asthma
Anti-IL5	Mepolizumab Reslizumab	SC, q 4 wk IV, q 4 wk	≥6 ≥18	Severe eosinophilic/ Type 2 asthma
Anti-IL5R	Benralizumab	SC, q 4/8 wk	≥6	
Anti-IL4Rα	Dupilumab	SC, q 2 wk	≥6	Severe eosinophilic/ Type 2 asthma, or maintenance OCS
Anti-TSLP **(*GINA 2022)**	Tezepelumab	SC, q 4 wk	≥12	Severe asthma

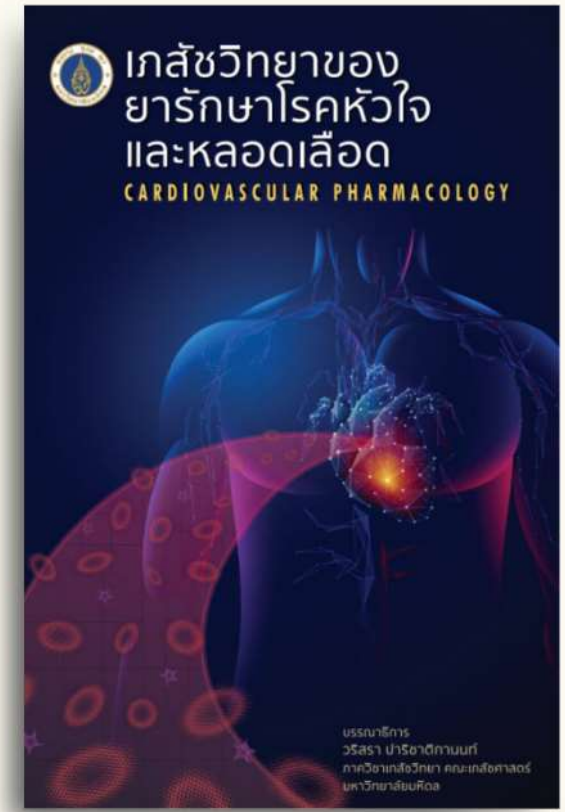


Summary

- LABAs & LAMAs improve lung function, dyspnea, health status and reduce exacerbation rate (are preferred over short-acting agents)
- Combination treatment with a LABA/LAMA reduces symptoms and exacerbation rate compared to monotherapy
- Patients may be started on single long-acting therapy or dual long-acting therapy depend on each individual
- Biological therapies against IgE, IL-5, IL-4 and TSLP are safe and promising in short- and medium-term treatment of patients with uncontrolled asthma
- The cost-effectiveness and adverse events associated with the use of each monoclonal antibody should be considered (clinical trials)



เภสัชวิทยาของยารักษาโรคหัวใจและหลอดเลือด



โดย รศ.ดร.ภญ. อริสรา ปาริชาติกานนท์
ภาควิชาเภสัชวิทยา คณะเภสัชศาสตร์
มหาวิทยาลัยมหิดล

SCAN สั่งซื้อ E-BOOK

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