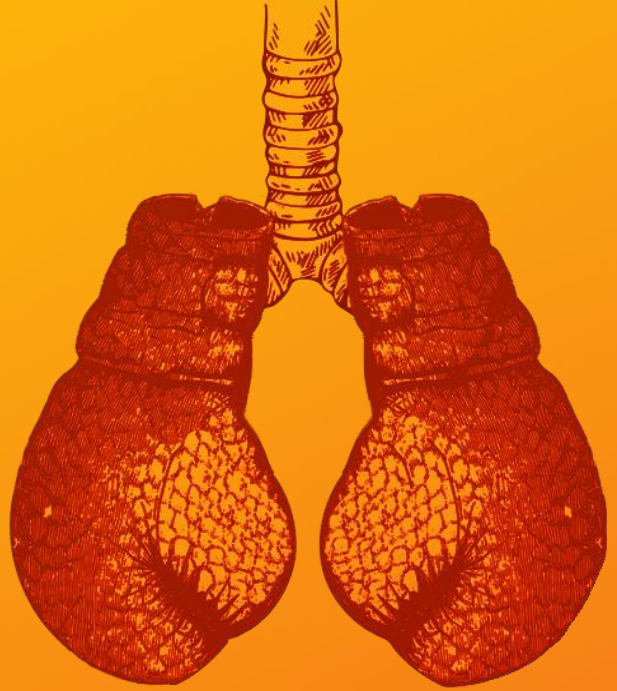
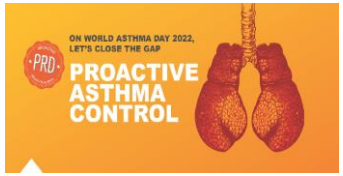


ON WORLD ASTHMA DAY 2022,
LET'S CLOSE THE GAP

PROACTIVE ASTHMA CONTROL

WORLD ASTHMA DAY 2022

CL Code: PM-KW-FPS-PPTX-220003
Date of preparation: May 2022



Closing the Gap in Asthma Management with Practicality

Helping Asthma Patients Enjoy a Future of Flourishing Health

PROACTIVE PRD REGULAR DOSING

Speaker

Dr. Sana Almutairi

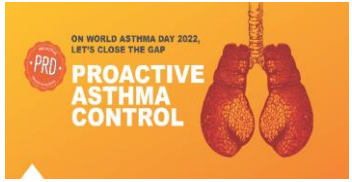
Consultant Chest Physician
Al Amiri Hospital, Kuwait
Associate Professor- Faculty of Medicine-Kuwait University

- Head of Respiratory unit Amiri Hospital since July 1996 till now.
- Chairperson of the Medical department Research committee –Faculty of Medicine since 2011.
- Many Publications in the field of respiratory and pulmonary disorders.
- Fellow of the Royal College of Physicians (FRCP) London UK 2005
- Member of British (BTS) Thoracic Society since 1995 till now.
- Member of American Thoracic Society (ATS)/ American lung association (ALA) since 1997 till now.
- Member of Kuwait Thoracic society.
- Member Saudi Thoracic Society.

Disclosure;

- I am a full time health care professional .
- I have received honorarium for this activity.

Agenda



- ❑ Asthma symptoms are the tip of the iceberg.
- ❑ Goal of Asthma Management.
- ❑ The Role of Proactive Regular dosing (PRD) in Asthma management.
- ❑ APPaRENT Study (Asthma Patients And Physicians Perspective on the Burden and management of Asthma)
- ❑ Appropriate use of SABA.
- ❑ The Role of an easy to use device in achieving asthma control .

PROACTIVE PRD REGULAR DOSING

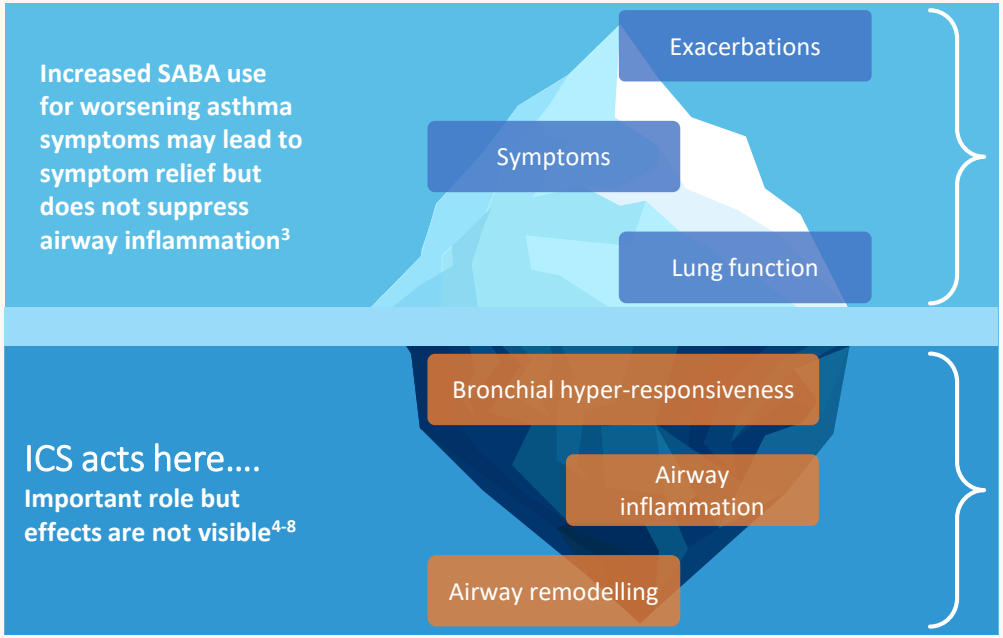
Asthma symptoms are the tip of the iceberg[1]

Achieving asthma control means controlling the underlying inflammation

Regular ICS-based treatment + SABA prn is proven to:[9-12]

- Control symptoms
- Reduce inflammation
- Reduce airway remodelling
- Reduce exacerbations and asthma-related hospitalisations

The anti-inflammatory protective effect of ICS treatment builds up over time; therefore, to get the most benefit, it should be taken regularly[8]

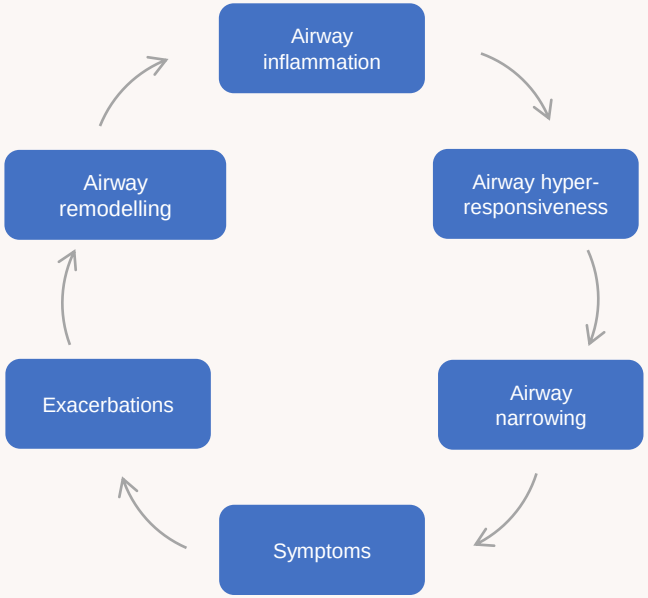


ICS, inhaled corticosteroid; prn, as needed; SABA, short-acting ß2-agonist.
1. Palomares O, et al. Int J Mol Sci 2017;18:1328; 2. GINA 2021. Available from: https://ginasthma.org/gina-reports/. Accessed 08 June 2021; 3. Martin MJ, Harrison T. Eur Respir J 2019;53:1802223; 4. Bousquet J, et al. Am J Respir Crit Care Med 2000;161:1720–1745; 5. Busse W. Chest 2010;138(2 Suppl):4S–10S; 6. Ozier A, et al. J Allergy 2011;742710; 7. Sont JK, et al. Am J Respir Crit Care Med 1999;159:1043–1051; 8. Ward C, et al. Thorax 2002:57:309–316; 9. Boushey H, et al. N Engl J Med 2005;352:1519-28; 10. Chauhan BF, et al. Cochrane Database Syst Rev 2013;28(2):CD009611; 11. Rodrigo GJ, et al. Respir Med 2013;107:1133-40; 12. Turpeinen M, et al. Arch Dis Child 2008;93:654–659.

PROACTIVE PRD REGULAR DOSING

Underlying asthma pathophysiology is driven by airway inflammation

- Airway inflammation has been demonstrated in all severities of asthma
- Untreated airway inflammation is implicated in the development of structural changes in airways
- Structural changes underpin a cycle of airway hyperresponsiveness and narrowing, symptom worsening and exacerbations



Bousquet J, et al. Am J Respir Crit Care Med 2000;161:1720–45.

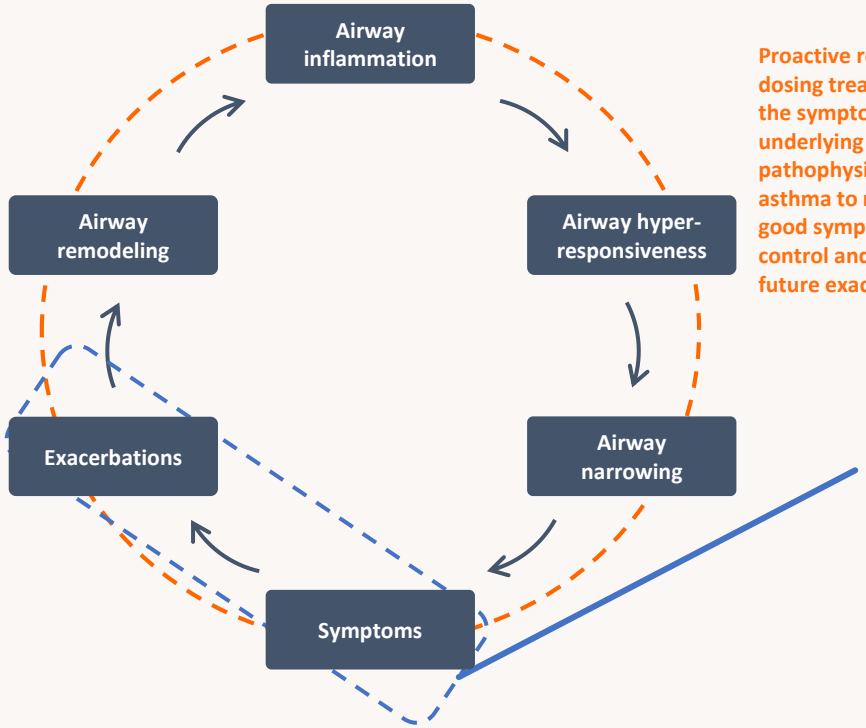
PROACTIVE PRD REGULAR DOSING

Underlying airway inflammation is managed with proactive early and regular treatment

Regular dosing ensures a consistent sufficient exposure to ICS-containing therapies to treat airway inflammation[1]

By treating the underlying pathophysiology, the risk of asthma-related airway impairment worsening is reduced[2]

Alternative dosing regimens designed to reduce ICS exposure may leave periods when patients receive little or no ICS resulting in undertreatment of inflammation and increased risk of irreversible airway impairment[3]



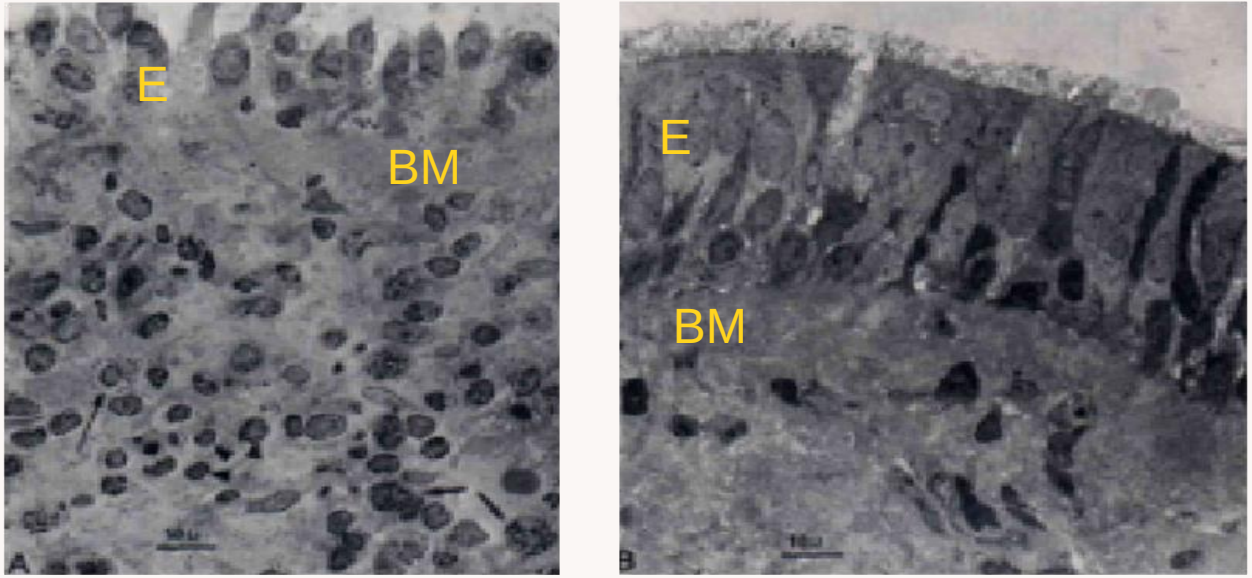
Proactive regular dosing treats both the symptoms and underlying pathophysiology of asthma to maintain good symptom control and prevent future exacerbations

Intermittent dosing regimens that reduce overall ICS exposure reactively treat symptoms and exacerbations as they occur but does not affect the underlying pathophysiology

ICS, inhaled corticosteroid.

1. Daley-Yates P, et al. Br J Clin Pharmacol 2021;87:483–93; 2. Bousquet J, et al. Am J Respir Crit Care Med 2000;161:1720–45; 3. Chapman KR, et al. Thorax 2010;65:747–52

Regular ICS reduces airway inflammation and remodelling



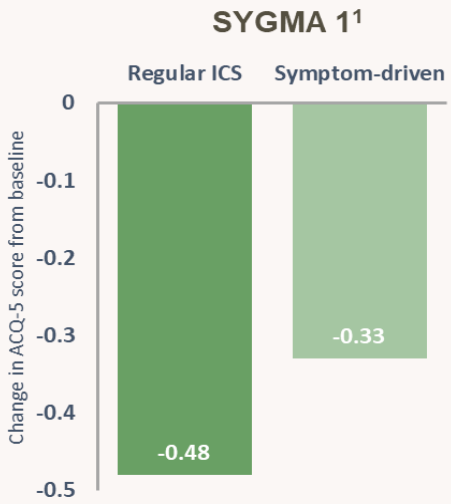
Pre and post 3-month treatment with regular ICS therapy

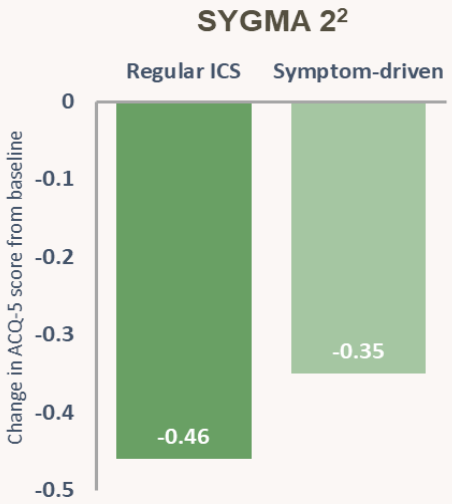
E, epithelium; BM, basement membrane; ICS, inhaled corticosteroid.

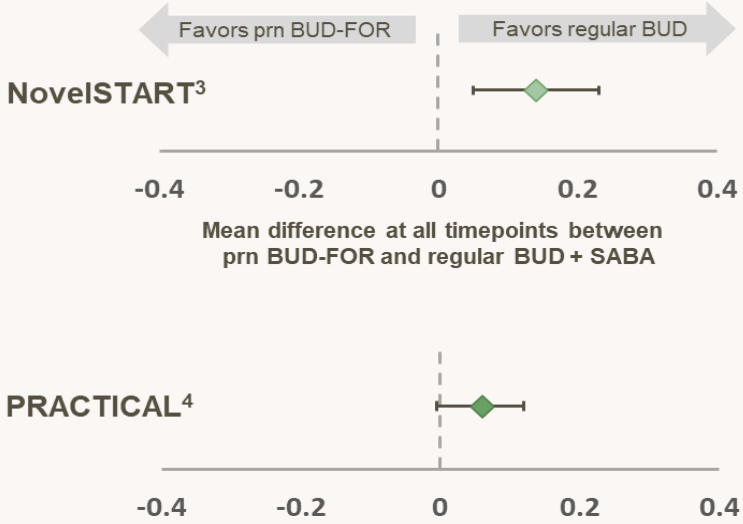
Laitinen LA, et al. J Allergy Clin Immunol 1992;90:32–42.

Regular ICS outperforms symptom-driven dosing in symptom control

Regular ICS outperforms symptom-driven dosing in symptom control







ACQ, Asthma Control Questionnaire; BUD, budesonide; FOR, formoterol; ICS, inhaled corticosteroid; prn, as needed; SABA, short-acting β_2-agonist.

SYGMA 1 was a double-blind, randomized, parallel group, 52-week, phase 3 trial that evaluated the efficacy and safety of bud/for (200/6 mcg prn; n=1277), vs terbutaline (0.5 mg prn; n=1277) or twice-daily budesonide (200 µg bid; n=1282) +terbutaline (0.5 mg prn) in patients aged ≥ 12 years with GINA Step 2 asthma.

SYGMA 2 was a double-blind, randomized, international, parallel-group, 52-week, phase 3 trial that evaluated the efficacy and safety of bud/for (200/6 mcg prn; n=2089) vs twice-daily budesonide (200 µg bid; n=2087) + terbutaline (0.5 mg prn) in patients aged ≥ 12 years with GINA Step 2 asthma.

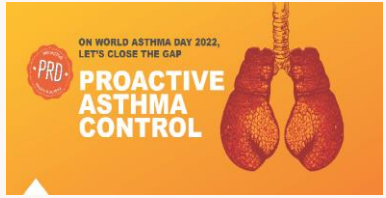
NovelStart was a 52-week, randomized, open-label, parallel group, controlled trial that evaluated the safety and efficacy of albuterol prn (n=223), budesonide + albuterol prn (n=225) or budesonide–formoterol prn (n=220) in patients aged ≥ 12 years with GINA Step 2 asthma.

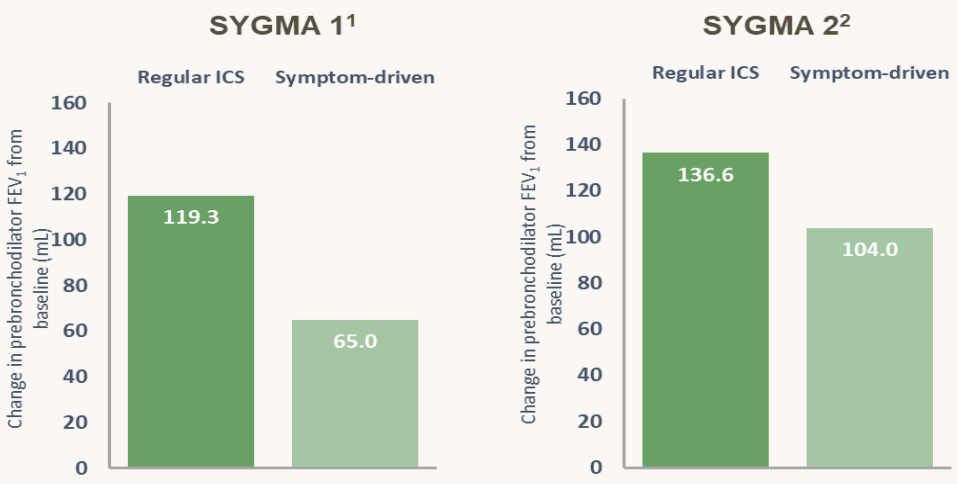
PRACTICAL was an investigator-led, pragmatic, 52 week, open-label, parallel-group, multicentre, superiority, randomised controlled trial that assessed the real-world safety and efficacy of bud/for group (200/6 mcg prn) or bud (200 mcg bid) + terbutaline prn in asthma patients aged 18-75 years who use SABA prn alone of low-dose daily ICS/LABA + SABA prn.

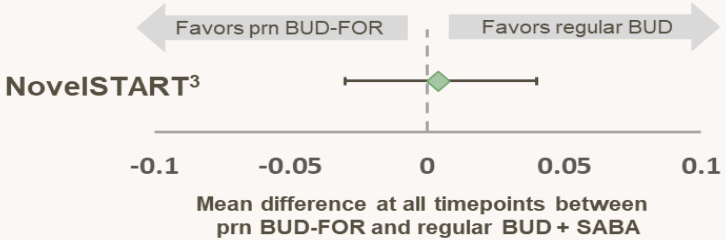
This graph has been independently created by GSK from the original data pubilshed in the source references

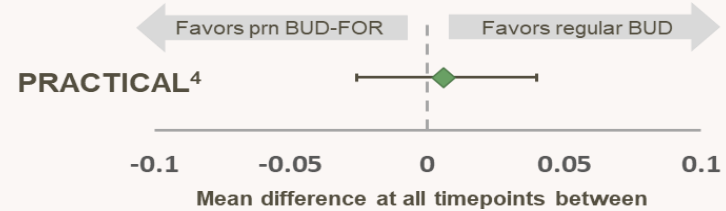
1. O'Byrne PM, et al. N Engl J Med 2018;378:1865–76; 2. Bateman ED, et al. N Engl J Med 2018;378:1877–87; 3. Beasley R, et al. N Engl J Med 2019;380:2020–30; 4. Hardy J, et al. Lancet 2019;394:919–28.

Regular ICS outperforms symptom-driven dosing in lung function









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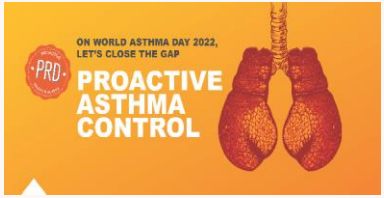
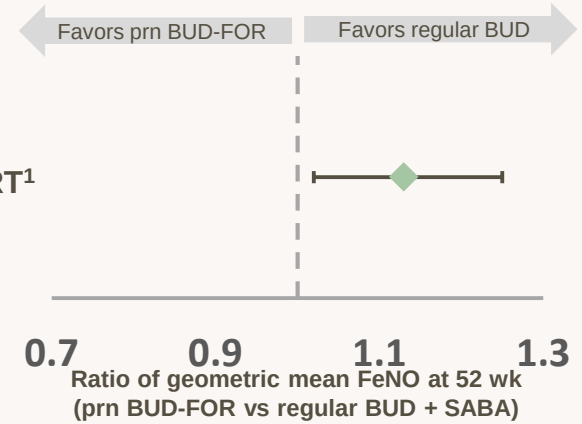
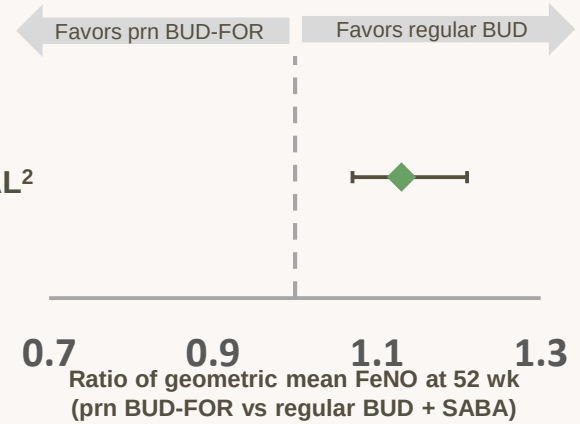
FeNO is reduced with regular ICS versus symptom-driven ICS/LABA







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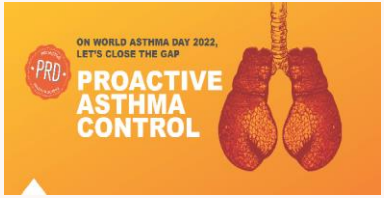
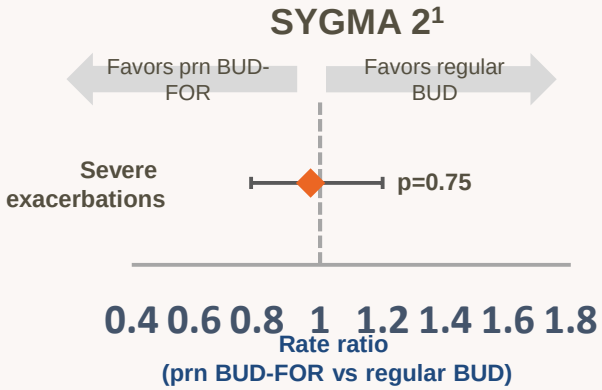
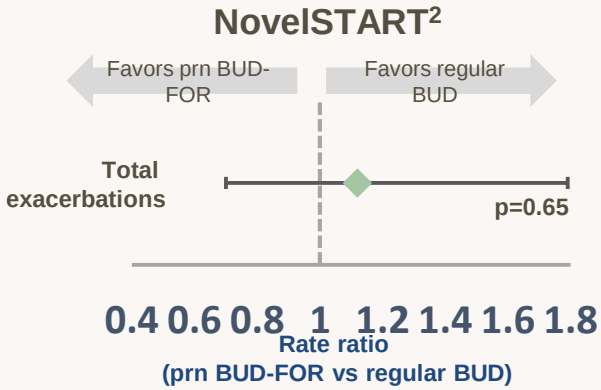
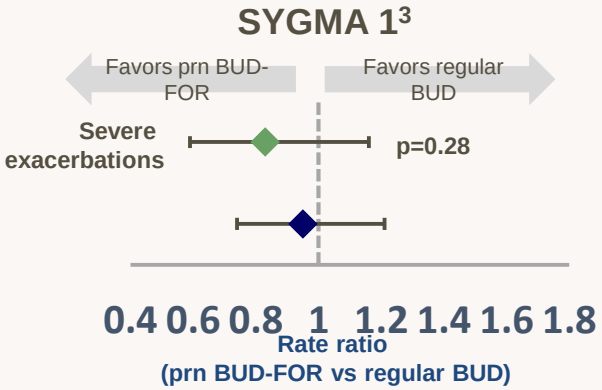
PROACTIVE PRD REGULAR DOSING

Regular ICS is non-inferior to symptom-driven dosing in reducing the rate of exacerbations









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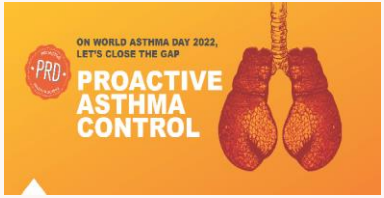
PROACTIVE PRD REGULAR DOSING

Optimal asthma management involves the management of pulmonary and extrapulmonary factors



Goals of optimal asthma treatment[1]

- To achieve good control of asthma symptoms and maintain activity levels
- To minimise the risk of asthma-related death, exacerbations, persistent airflow limitation and side effects

Pulmonary factors

- LABA/SABA → Airflow limitation
- ICS → T2 (eosinophilic) inflammation

Optimal asthma management[2]

Extrapulmonary factors

- Disease awareness/ literacy
- Adherence
- Persistence
- Symptom recognition
- Inhaler technique
- Self-titration of dose

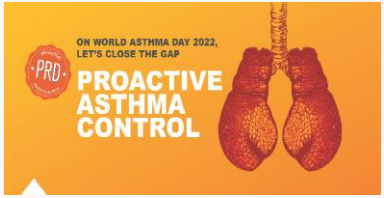
Patient/HCP management and patient self-awareness

ICS, inhaled corticosteroid; HCP, health care professional; LABA, long-acting β-agonist; SABA, short-acting β-agonist; T2, Type-2

1. GINA 2021. Available from: https://ginasthma.org/gina-reports/. Accessed 08 June 2021; 2. Agusti A, et al. Eur Respir J 2016;47:410–419

PROACTIVE PRD REGULAR DOSING

Poor perception of asthma symptoms may lead to over or under treatment for many patients



Approximately 25% of all stable asthma patients underperceive their asthma symptoms

- Underuse of as-needed medications
- Delays in initiating medication / seeking medical assistance

→ Progressive and irreversible disease worsening

→ Progressively poorer asthma control

Approximately 15% of all stable asthma patients overperceive their asthma symptoms

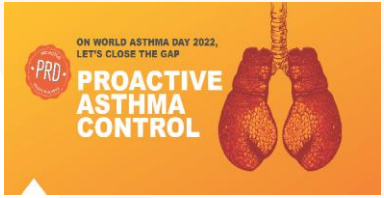
→ Leads to overuse of as-needed medications

→ Overexposure to ICSs / Increased risk of adverse events

ICS, Inhaled corticosteroids

Barnes et al. J Allergy Clin Immunol 2019;144:1180–6.


?
ONE SIZE FITS ALL
Store



Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPaRENT)

Chapman KE et al. Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPaRENT). Poster presented at ATS 2021. https://www.atsjournals.org/doi/pdf/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1453 (accessed 20 May 2021).

PROACTIVE PRD REGULAR DOSING

Rationale

The APPaRENT study aims to understand patient and physician attitudes to regular versus maintenance and reliever therapy (MART) dosing, and assess global relevance of GINA[1] recommendations in developed and developing nations.

- The 2021 Global Initiative for Asthma (GINA) report[1] recommends a stepwise approach to asthma management.
- This includes as-needed ICS/formoterol irrespective of GINA step classification and as MART for GINA Step 3.

GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; MART, maintenance and reliever therapy

1. Global Initiative for Asthma - Global strategy for asthma management and prevention. https://ginasthma.org/2021 (accessed 11 May 2021).

Methods

Multinational, cross-sectional online survey of patients and physicians between July and August 2020*

Included countries:

Australia
Canada
China
Philippines

Patients

Patients ≥18 years of age with self-reported history of a past/current physician-diagnosed asthma

- **13,203–23,024 patients invited**
- **300–308 surveys completed**

Physicians

Primary care physicians† with ≥3 years in clinical practice and responsible for care of ≥4 patients with asthma monthly

- **1131–3117 physicians invited**
- **200–202 surveys completed**

Per country

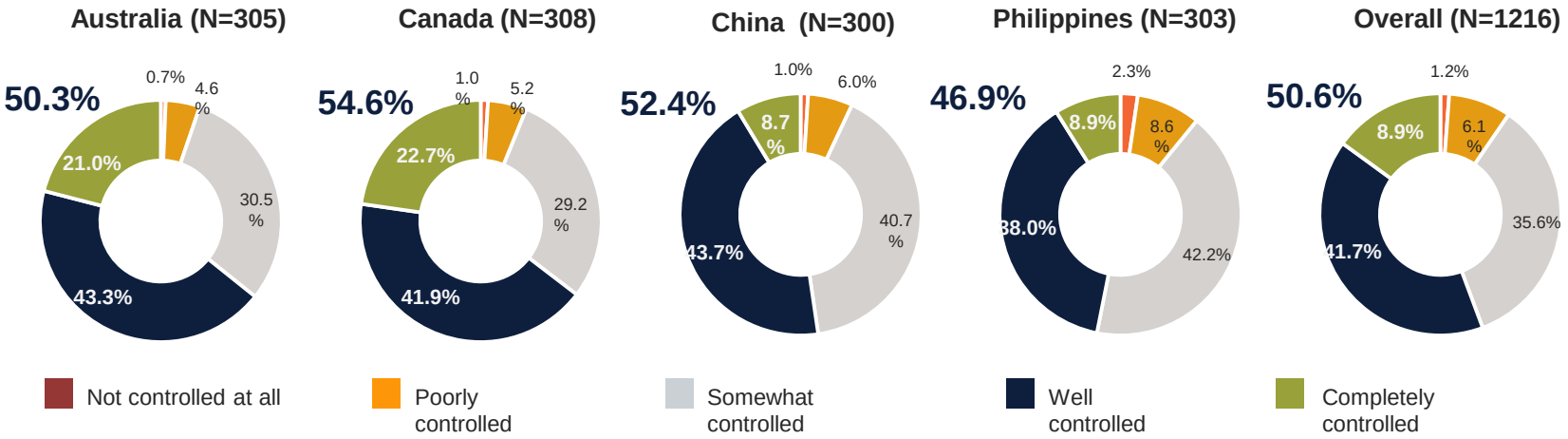
*Patients and physicians were sampled and recruited from high-quality, non-probability panels; †general practice, family medicine, and/or internal medicine physicians. Canada also included respirologists/respiratory therapists

Chapman KE et al. *Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPaRENT).* Poster presented at ATS 2021. https://www.atsjournals.org/doi/pdf/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1453 (accessed 20 May 2021).

Most Commonly, Patients Regarded Their Asthma to Be Well-Controlled or Somewhat Controlled

APPaRENT
ASTHMA PATIENTS' AND PHYSICIANS' PERSPECTIVES ON THE BURDEN AND MANAGEMENT OF ASTHMA

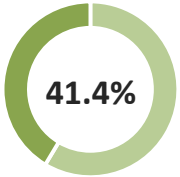
Patients Data



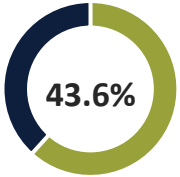
Patient survey question: How would you rate your asthma control during the past 4 weeks?
For all data reported here, *p*-values (determined by ANOVA test) indicated significant variation between countries ($p<0.05$).
ANOVA, analysis of variance; GINA, global initiative for asthma.
Chapman et al. *Resp. Med.* 2021 ePub before print.

PROACTIVE PRD REGULAR DOSING

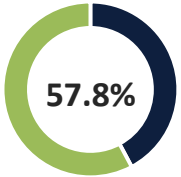
Despite Perceptions of Asthma Control, Patients Reported Frequent Symptoms and Rescue Inhaler Use



of patients reported **shortness of breath ≥3 times per week**



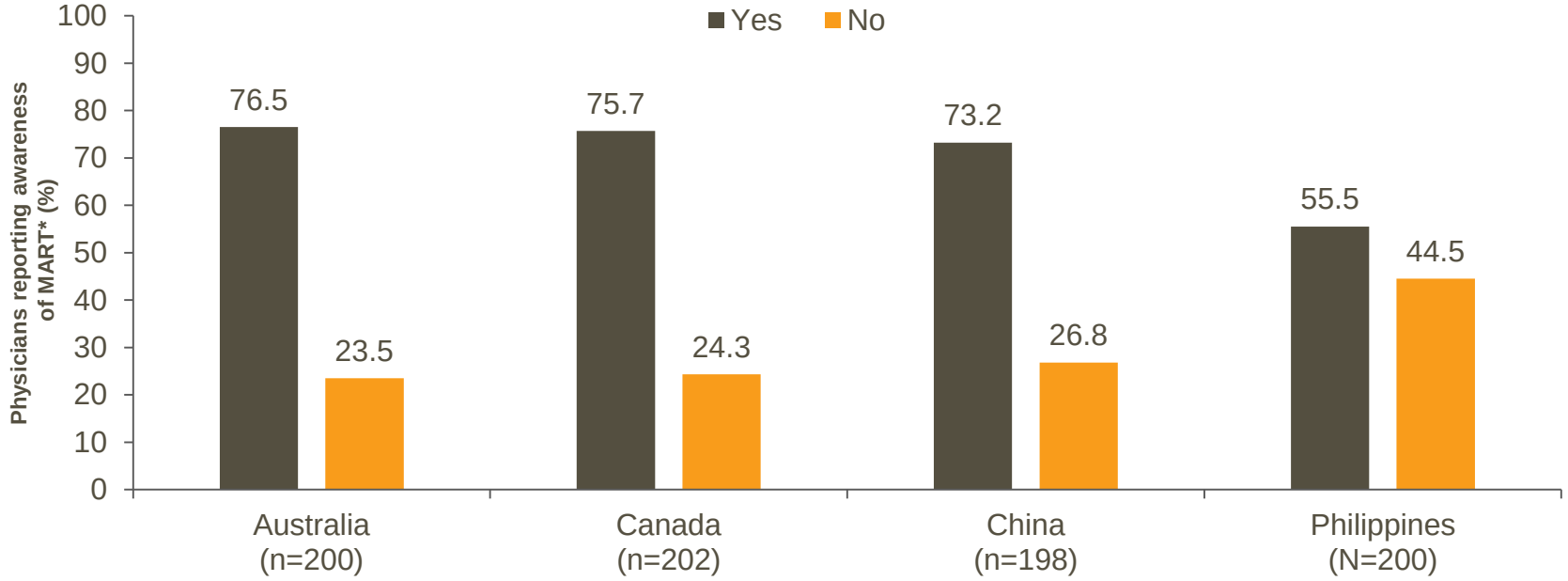
of patients reported **night-time awakenings due to symptoms ≥1 time per week**



of patients reported **using their rescue inhaler ≥2 times per week**

n=1215 for all questions. For all data reported here, *p*-values (determined by ANOVA test) indicated significant variation between countries ($p<0.05$).
Chapman et al. *Resp. Med.* 2021 ePub before print.

MART awareness was generally high among physicians but low among patients*



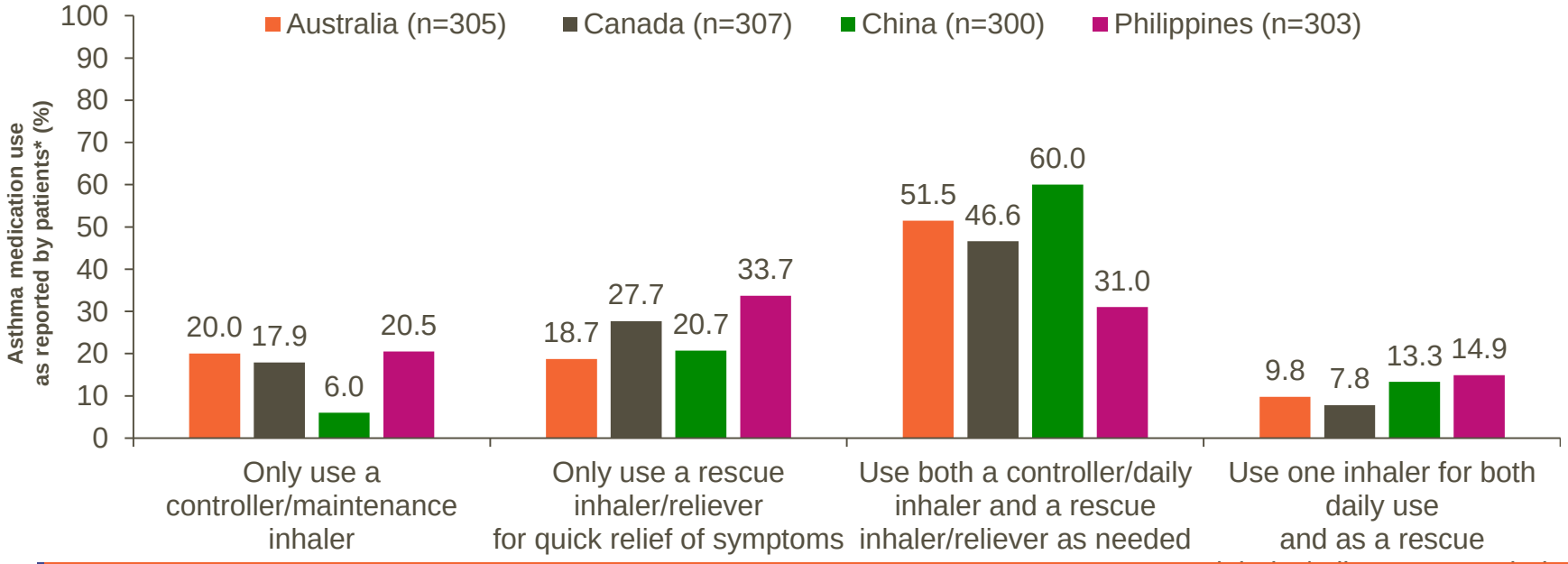
Only **~20–50% of patients** were aware of the MART dosing approach.

*Physician question: are you aware of the MART dosing approach for asthma?
*Patient question: Some inhalers can be used as a combination asthma controller/maintenance inhaler and as a rescue inhaler/reliever as needed, in one inhaler. This approach is called MART dosing... Are you aware of this approach for treating asthma?

For all data reported here, P-values (determined by Chi-square test) indicated significant variation between countries (P<0.05). n=number of patients who responded to the question.
MART, maintenance and reliever therapy

Chapman KE et al. *Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPaRENT).* Poster presented at ATS 2021. https://www.atsjournals.org/doi/pdf/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1453 (accessed 20 May 2021).

Most patients used regular maintenance therapy with or without as-needed reliever therapy*



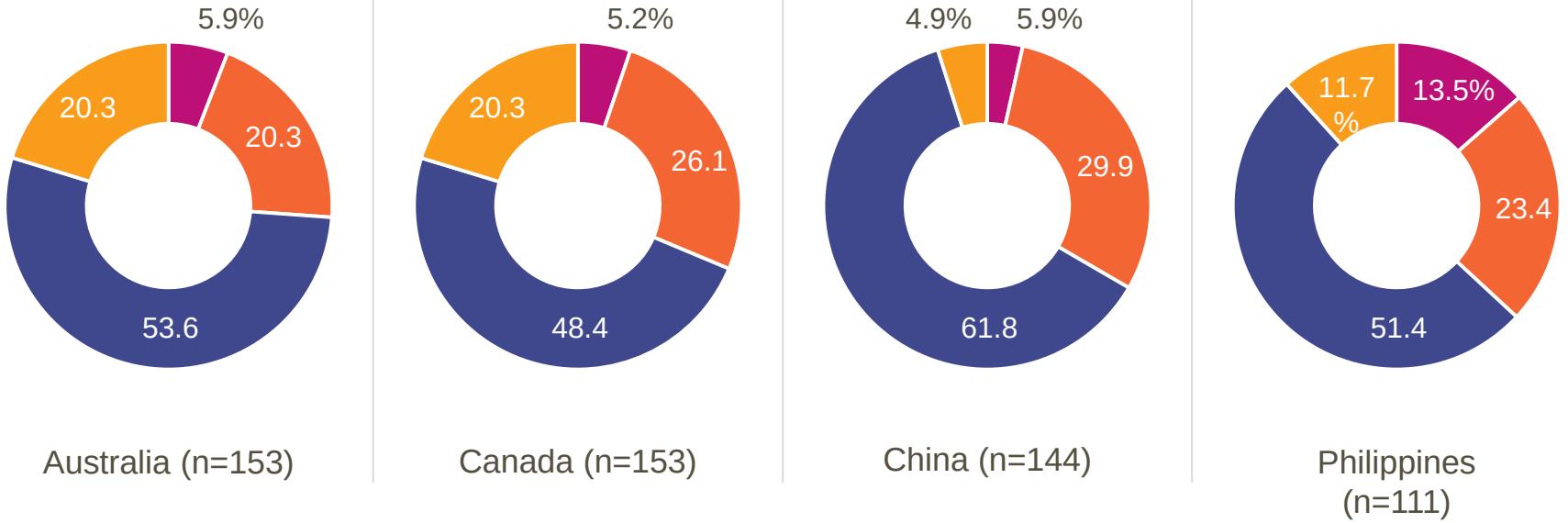
Overall, 66.3–81.3% of patients reported using regular maintenance therapy with or without as-needed reliever therapy; of these, 7.8–14.9% were using MART.

*Patient question: Thinking about your asthma medication, do you use a controller/maintenance inhaler, a rescue inhaler/reliever, both a controller/maintenance inhaler and rescue inhaler/reliever, or one inhaler that is for both control and rescue?

For all data reported here, P-values (determined by Chi-square test) indicated significant variation between countries (P<0.05).
n=number of patients who responded to the question. MART, maintenance and reliever therapy

Chapman KE et al. *Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPaRENT).* Poster presented at ATS 2021. https://www.atsjournals.org/doi/pdf/10.1164/ajr conference.2021.203.1_MeetingAbstracts.A1453 (accessed 20 May 2021).

Most physicians indicated that they prescribe a short-acting β_2-agonist (SABA) in addition to a MART regimen at least some of the time*

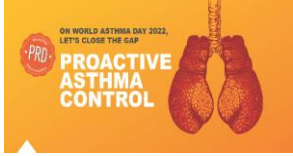


*Physician question: when you prescribe ICS/LABA as MART for asthma, how often do you also prescribe a short-acting β_2-agonist or a short-acting bronchodilator as a reliever?

For all data reported here, P-values (determined by Chi-square test) indicated significant variation between countries (P<0.05). n=number of patients who responded to the question.
MART, maintenance and reliever therapy; SABA, short-acting β_2-agonist

Chapman KE et al. *Asthma Patients' and Physicians' Perspectives on the Burden and Management of Asthma (APPaRENT).* Poster presented at ATS 2021. https://www.atsjournals.org/doi/pdf/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1453 (accessed 20 May 2021).

Physicians and patients both considered symptom control to be very important



Physicians generally rated symptom control over exacerbation reduction as their main treatment goal for patients at GINA Steps 1–2 (29.3–45.1% vs 9.3–15.4%) and GINA Steps 3–4 (24.2–43.6% vs 20.9–30.2%)*

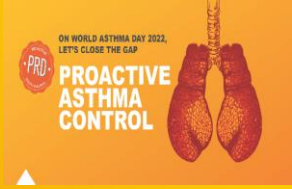
Physicians also prioritized symptom severity (29.4–44.1%) over exacerbation risk (18.0–29.2%) when prescribing daily maintenance medication†

Across all countries, approximately 50–90% of patients indicated that it was ‘very important’ that their inhaler treats symptoms such as chest tightness, coughing, and shortness of breath‡

*Physician question: What are the goals that you aim to attain in your patients with mild asthma (GINA Steps 1 and 2) / moderate asthma (GINA steps 3 and 4)?; †physician question: What is THE MOST important factor to you when prescribing controller/maintenance medications?; ‡patient question: How important is it that your inhaler treats chest tightness/shortness of breath/coughing?

GINA, Global Initiative for Asthma

Chapman KE et al. *Asthma Patients’ and Physicians’ Perspectives on the Burden and Management of Asthma (APPaRENT).* Poster presented at ATS 2021. https://www.atsjournals.org/doi/pdf/10.1164/ajrccm-conference.2021.203.1_MeetingAbstracts.A1453 (accessed 20 May 2021).

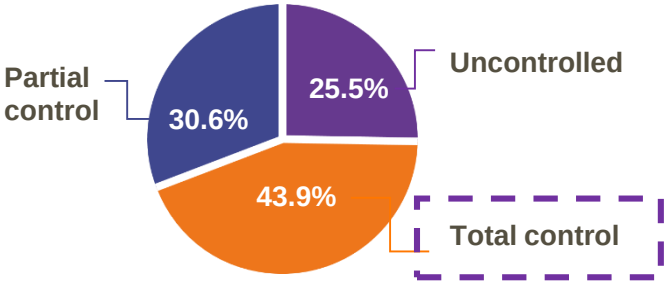


Proactive regular dosing showed better control levels vs reactive maintenance and reliever dosing

Seretide with proactive regular dosing showed better control levels vs reactive maintenance and reliever dosing

Seretide
Proactive Regular Dosing[2-4]

GOAL
Gaining Optimal Asthma control

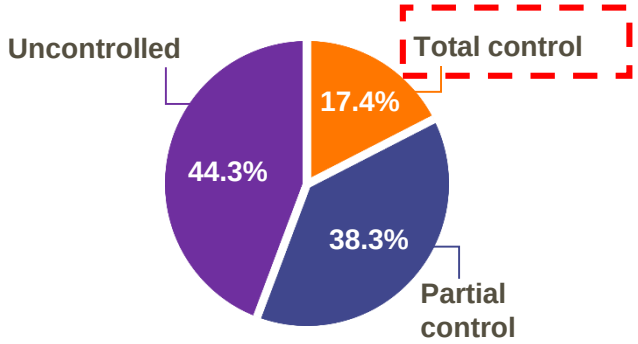


1-year, randomized, stratified, double-blind, parallel-group study (n>3,000) in patients with uncontrolled asthma. Fluticasone propionate vs. salmeterol/fluticasone in achieving totally and well-controlled asthma. Treatment was stepped-up until total control was achieved (or maximum 500 µg corticosteroid twice a day)

The same results were first published in Bateman E *et al. Eur Respir* J 2007;29(1):56–63 and 2. Bateman E *et al. Am J Respir Crit* Care Med 2004;170:836–44. This graph has been independently created by GSK from the original.

Maintenance and Reliver dosing [1, 2]

Level of control achieved with variable dosing regimen may not be optimal

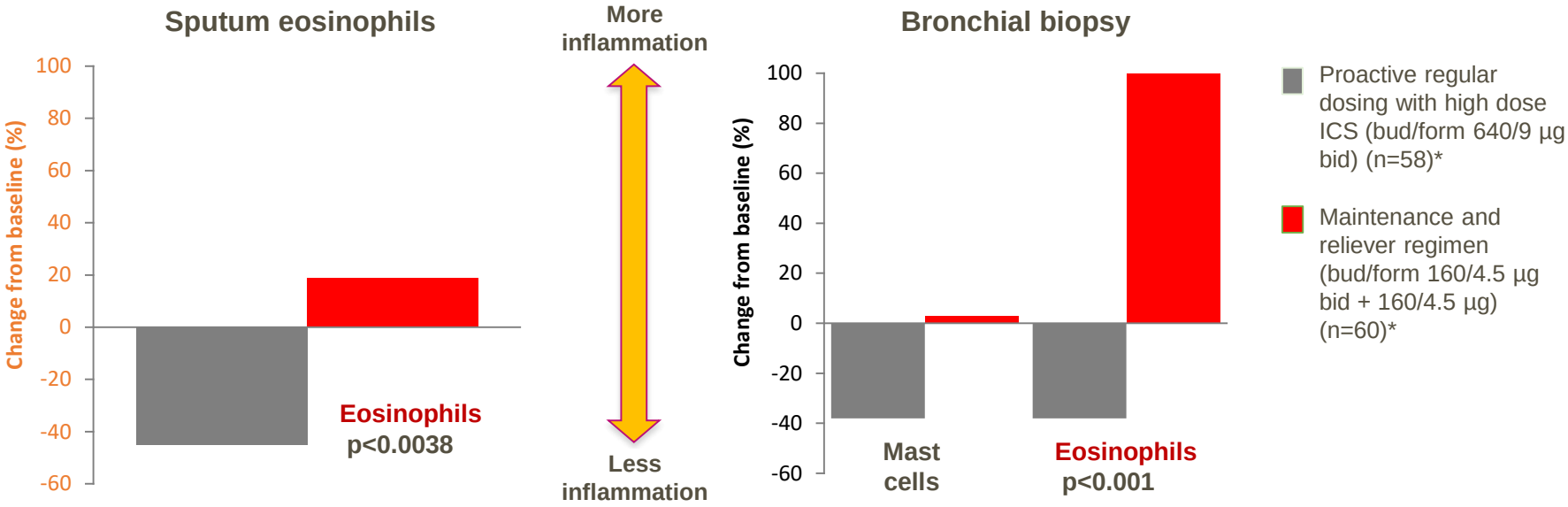


Post hoc analysis comparing BUD/FORM MART with fixed dose therapy; n>12,000. Asthma control from 5 studies defined by GINA classification or ACQ-5. Controlled week: all 5 diary card subcriteria controlled and no severe exacerbation. Partial control: any 1 or 2 subcriteria were uncontrolled and no exacerbation recorded. Uncontrolled: ≥3 uncontrolled subcriteria or an exacerbation.

The same results were first published in Bateman E et al. J Allergy Clin Immunol 2010;125:600–608. This chart has been independently created by GSK from the original

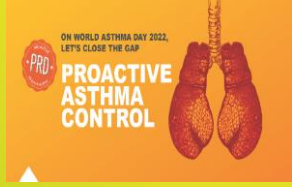
PROACTIVE PRD REGULAR DOSING

Proactive regular dosing leads to improvement of airway inflammation vs. maintenance and reliever, with the same ICS/LABA



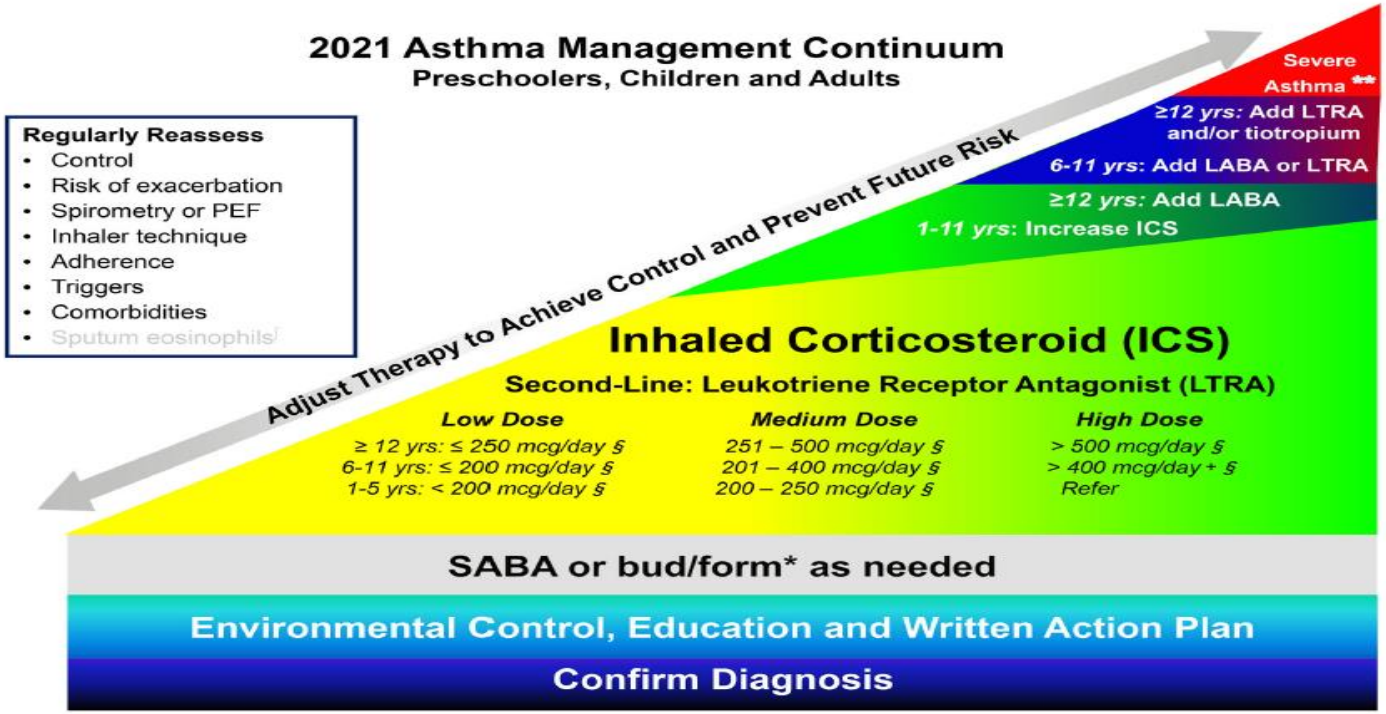
- 52-week, parallel-group, randomized, double-blind study (n with asthma=127; age18-65 years) designed to compare the effects of bud/form 200/6 µg bid plus as-needed (n=64) with bud/form 800/12 µg bid (n=63) on airway eosinophils and remodelling. Both treatments were well tolerated.
- *Delivered dose.
- bud/form, budesonide/formoterol; bid, twice-daily

The same results were first published in Pavord I, et al. J Allergy Clin Immunol 2009;123(5):1083–1089.
These graphs have been independently created by GSK from the original.



International Asthma Guidelines recommendations

Canadian Thoracic Society Guideline



* Or an alternative ICS/form preparation if another is approved for use as a reliever in the future. Bud/form is approved as a reliever for ≥12 years of age and should only be used as a reliever in individuals using it as monotherapy or in conjunction with bud/form maintenance therapy

§ HFA Fluticasone propionate or equivalent

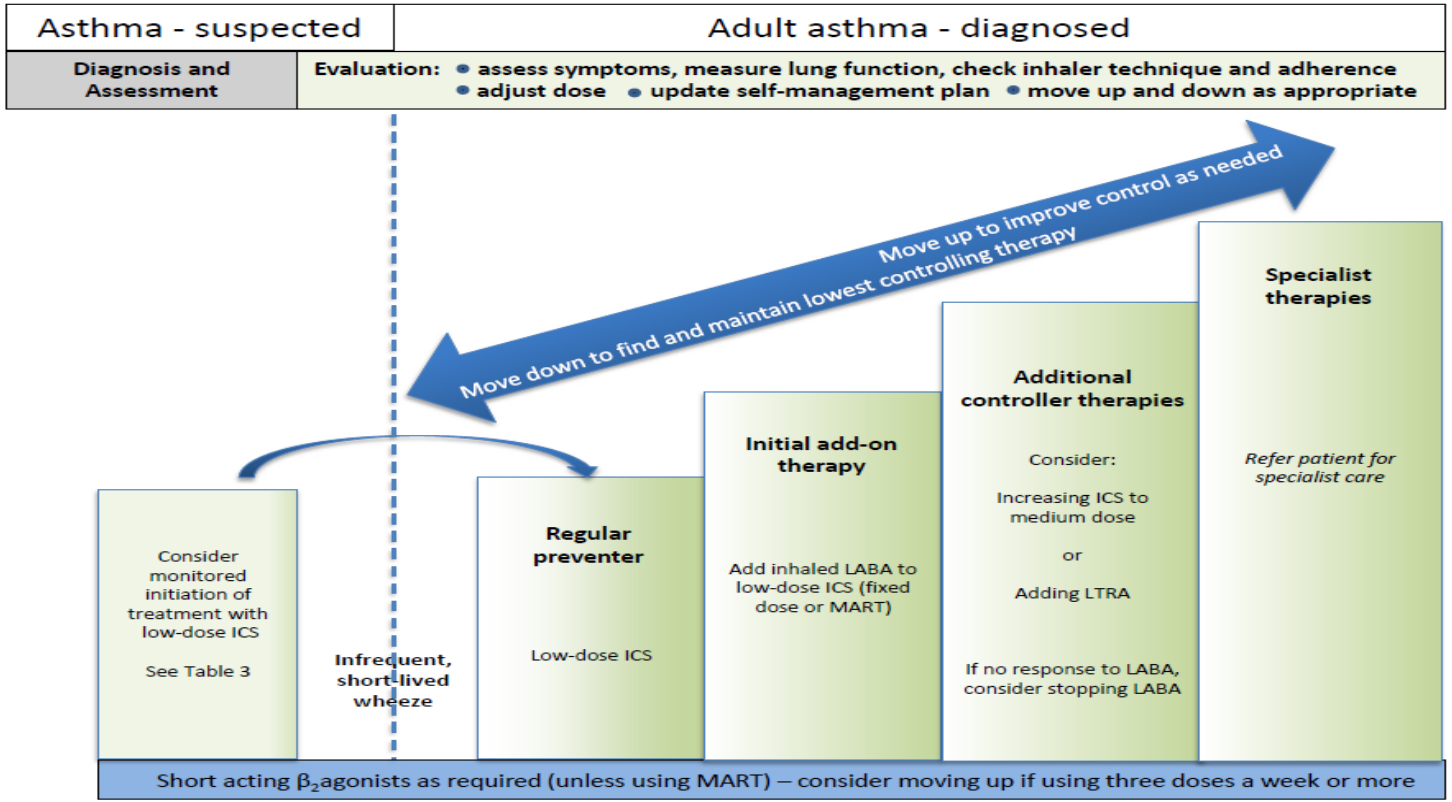
+ Not approved for use in Canada

∫ In adults, 18 years of age and over with moderate to severe asthma assessed in specialist centres

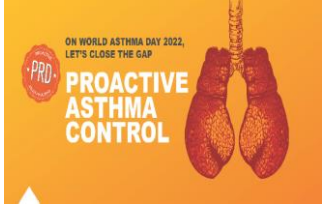
** For severe asthma refer to CTS 2017 Recognition and Management of Severe Asthma Position Statement

Yang CL, et al. Can J Respir Crit Care Sleep Med; DOI: 10.1080/24745332.2021.1877043

British Guideline on Asthma Management



1. BTS-SIGN. Available from: https://www.brit-thoracic.org.uk/quality-improvement/guidelines/asthma/. Accessed 08 May 21



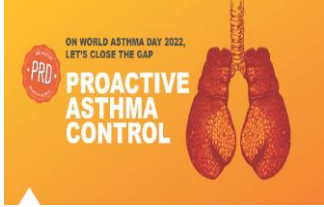
Effect of regular ICS on SABA use

Regular ICS supports appropriate SABA use

SABA use can be used to monitor asthma control

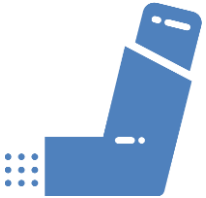
PROACTIVE PRD REGULAR DOSING

Adherence to regular maintenance therapy can promote appropriate SABA use



Patients often treat asthma as a short-term/ acute condition, rather than chronic:[1,2]

Relying on SABAs to **immediately** relieve symptoms instead of managing the underlying disease/inflammation



People who over-use SABA may have fundamentally different perceptions of asthma:[2]

over-users: more likely to focus on mechanical effects of bronchoconstriction & quick relief provided by SABA rather than on the underlying inflammatory process and the prevention provided by controller therapy

Many patients have an intense emotional attachment to their SABA inhaler, created by its ability to quickly alleviate asthma symptoms – a feeling they do not experience with maintenance ICS therapy[3]

As a result, patients may not understand that the frequent use of SABAs indicates poor asthma control[3,4]

Patients also often have a misperception of ICS, which can lead to a delay in escalation and poor adherence to treatment[3]

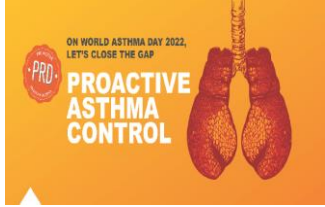
The overall consequence of these beliefs is a suboptimal behaviour that results in SABA reliance at the expense of appropriate use of ICS-based maintenance therapy to address underlying inflammation[3]

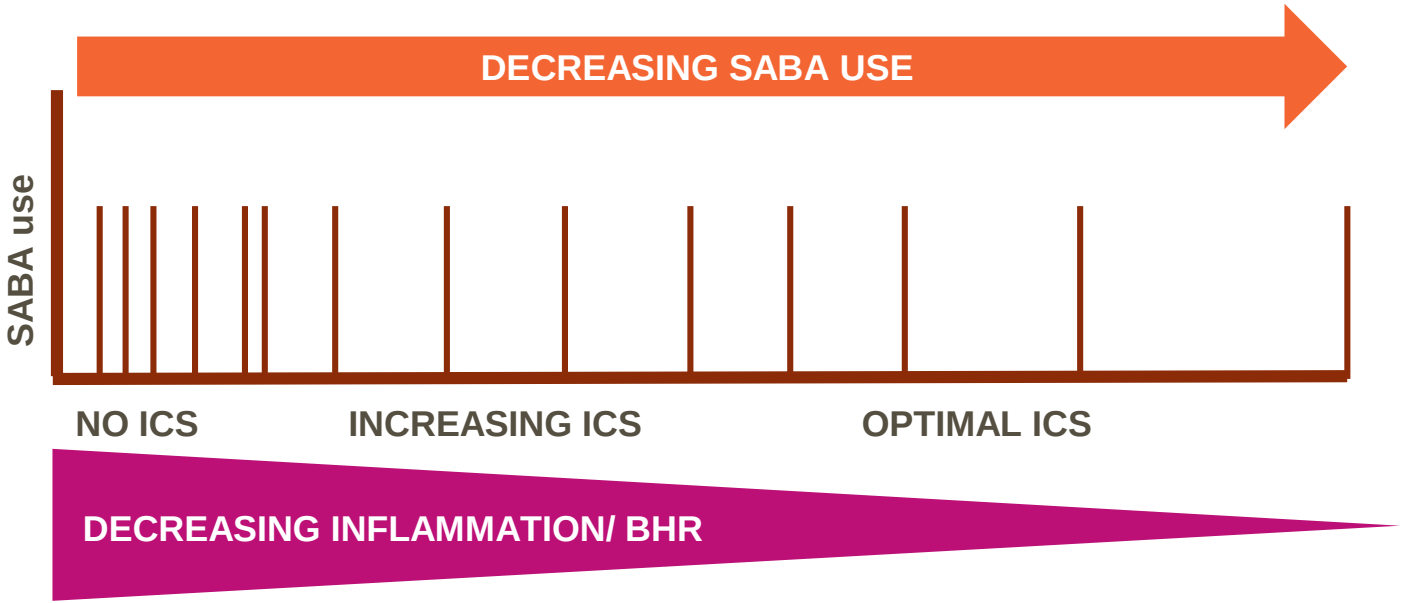
ICS, inhaled corticosteroid; SABA, short-acting β_2-agonist.

1. AIHW: Correll PK, Poulos LM, Ampon R, Reddel HK & Marks GB 2015. Respiratory medication use in Australia 2003–2013: treatment of asthma and COPD. Cat.no. ACM 31. Canberra: AIHW; 2. Cole S, et al. BMJ Open 2013;3:e002247; 3. Blakeston S, et al. J Asthma 2020; DOI:10.1080/02770903.2020.1761382; 4. GINA 2021. Available from: https://ginasthma.org/gina-reports/. Accessed 04 May 2021.

PROACTIVE PRD REGULAR DOSING

Regular maintenance therapy can promote appropriate SABA use and reduce inflammation





BHR, bronchial hyperreactivity; ICS, inhaled corticosteroid; SABA, short-acting β_2-agonist.

1. Sont JK, et al. Am J Respir Crit Care Med 1999;159:1043–51; 2. Bateman ED, et al. Am J Respir Crit Care Med 2004;170:836–44

Inhaled SABAs (prn) can be used for the rapid reversal of airflow obstruction during exacerbations and for the treatment of exercise-induced bronchoconstriction

Inhaled SABAs can be used prn for the initial treatment of acute asthma exacerbations and for exercise-induced bronchoconstriction[1-3]

Effect on lung function:[4,5]
- Rapid onset of bronchodilator action (within 5 minutes)
- Peak bronchodilation within 10 mins
- Short duration (4-6 hrs) of action

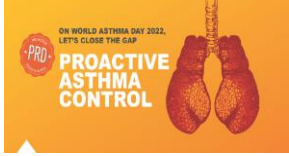
Available routes of administration: oral, inhalation, other formulations[4,5]

Well-tolerated safety profile[5]

Recommended by international guidelines[1-3]
- For all ages
- For acute exacerbations, acute bronchospasm and prevention/treatment of EIB

1. Global Initiative for Asthma. Global strategy for asthma management and prevention. 2021. Available at: www.ginasthma.org. Accessed September 2021;
2. NHLBI. EPR-3 Report. Guidelines for the diagnosis and management of asthma 2020 update. Available from https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines. Accessed September 2021; 3. Parsons J, et al. Am J Respir Crit Care Med 2013;187:1016-1027;
4. Salbutamol (inhaled formulations) Global Datasheet. GSK, Version 26; 29 April 2019; 5. Price AH, Clissold SP. Drugs 1989;38(1):77-122.

Frequency of SABA use is one of the indicators of worsening symptom control



- Monitoring of daytime symptoms, night wakening, SABA frequency and activity limitation can help assess the possibility of worsening asthma control
- GINA 2021 recommends that the frequency of ICS-formoterol use should not be included in symptom control assessment, particularly in patients not taking maintenance ICS

Box 2-2. GINA assessment of asthma control in adults, adolescents and children 6-11 years

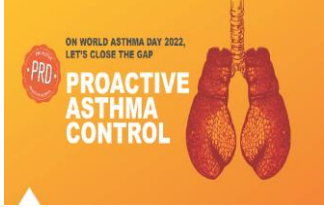
A. Asthma symptom control			**Level of asthma symptom control**		
In the past 4 weeks, has the patient had:			**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes ☐	No ☐	None of these	1-2 of these	3-4 of these
• Any night waking due to asthma?	Yes ☐	No ☐			
• Reliever (SABA) for symptoms more than twice/week?*	Yes ☐	No ☐			
• Any activity limitation due to asthma?	Yes ☐	No ☐			

GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; SABA, short-acting β_2-agonist

Global Initiative for Asthma. Global strategy for asthma management and prevention. 2021. Available from: www.ginasthma.org. Accessed 08 June 2021

PROACTIVE PRD REGULAR DOSING

SABA reliever therapy – what do other regulatory/ guideline updates recommend?



BTS SIGN guidelines[1]

All patients with symptomatic asthma should be prescribed a SABA to relieve symptoms

Regular ICS are the recommended preventer for adults/children for achieving overall treatment goals[1]

ICS/formoterol prn treatment approach in asthma is not recommended.

Japanese guidelines for adult asthma[2]

SABAs should be used as reliever therapy across all asthma severities

The use of a SABA as a reliever 5 or more times daily indicates controller agents need to be increased

ICS/formoterol prn are not recommended for any of the treatment steps in asthma

Regular ICS are the recommended preventer for achieving asthma control

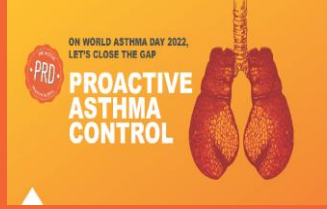
Spanish guidelines for asthma management[3]

SABA should be used in mild patients as required

For the vast majority of patients the treatment indicated for rapid symptom relief is an inhaled SABA

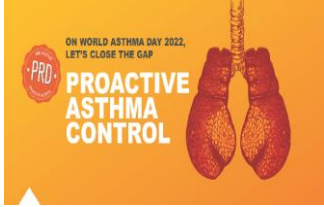
Regular ICS are considered the most effective treatment for persistent asthma

1. BTS/SIGN 158. British guideline on the management of asthma. Revised July 2019. Available from: www.brit- thoracic.org.uk/quality-improvement/guidelines/asthma/. Accessed September 2020.
2. Nakamura Y, et al. *Allergol Int.* 2020; https://doi.org/10.1016/j.alit.2020.08.001.
3. Spanish guidelines for the management of asthma. Available at www.gemasma.com. Accessed September 2020

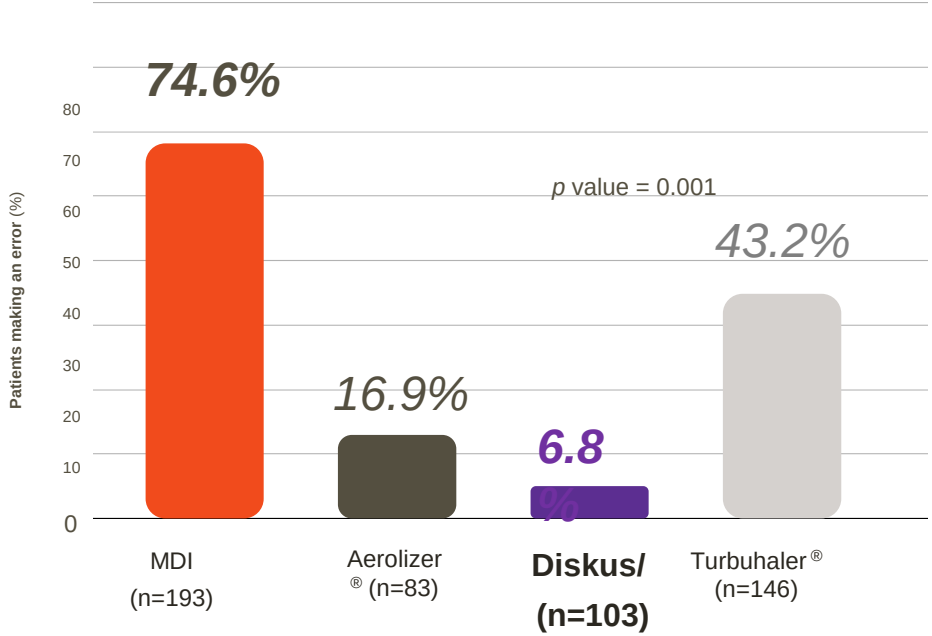


Importance of inhaler technique

The role of an easy to use device in achieving asthma control



Handling errors were lower in patients using **Diskus vs other devices**



Prospective, cross-sectional, observational study to assess handling errors in 300 patients using MDI or different DPIs

Khassawneh BY, et al. *Respir Care*. 2008; **53** (324)
Fluticasone propionate (inhaled formulations) Global Datasheet, Version 33; 18 April 2018.

The science of PRD in brief

PROACTIVE

A broad evidence base has demonstrated that regular dosing with ICS (GINA STEP2) and ICS-LABA (GINA Step 3) treats the underlying pathophysiology and symptomatology of asthma so that the disease is **proactively** and effectively managed[1-11]

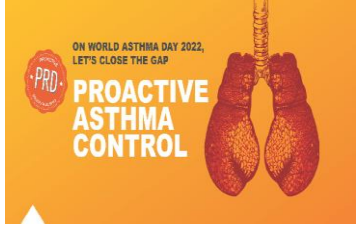
REGULAR DOSING

With consistent and **regular dosing**,[1-4] reliance on self-driven symptom tracking is reduced thus minimizing the risk of over-or under-treatment[12]

A guideline recommended treatment strategy in asthma aiming to proactively achieve asthma treatment goals of symptom control and exacerbation risk reduction through regular dosing with ICS–based medicines across all severities of asthma.[1-10]

GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist.

1. Flixotide SmPC. Available from: https://www.medicines.org.uk/. Accessed 07 April 2021; 2. Ventolin SmPC. Available from: https://www.medicines.org.uk/. Accessed 07 April 2021; 3. Seretide SmPC. Available from: https://www.medicines.org.uk/. Accessed 07 April 2021; 4. Relvar SmPC. Available from: https://www.medicines.org.uk/. Accessed 07 April 2021. 5. Bateman ED, et al. Am J Respir Crit Care Med 2004;170:836–44; 6. Stempel DA, et al. N Engl J Med 2016;374:1822–30; 7. Stempel DA, et al. N Engl J Med 2016;375:840–9; 8. Bateman ED, et al. Thorax 2014;69:312-319; 9. O'Byrne PM, et al. Eur Respir J 2014;43:773–82; 10. Woodcock A, et al. Lancet 2017;390:2247–55; 11. GINA 2021. Available from: https://ginasthma.org/gina-reports/. Accessed 18 May 2021; 12. Barnes PJ, et al. J Allergy Clin Immunol 2019;144:1180–6



Take Home messages

- Our aim is to **enable individuals with asthma to lead normal lives**, free from symptoms and with no long-term consequences of their disease or therapy

- **Real asthma control** means controlling visible symptoms and non-visible inflammation.

- Proactive regular dosing with **SAL/FP + SABA** reliever as needed results in good asthma control and reduction of exacerbations through effective reduction of airway inflammation.
- **SAL/FP** is proven to achieve and maintain guideline-defined asthma control in mild-to-moderate asthma in a randomised controlled trial **(GOAL).** With FP/Sal 43.9% patients achieved total control of asthma.

- **Engaging** patients **in shared decision-making** and **choosing a simplified treatment regimen** improves adherence and outcomes.[1-2]

- Device handling errors were lower in patients using **Diskus** vs. other inhalers.[6,7]

PROACTIVE PRD REGULAR DOSING

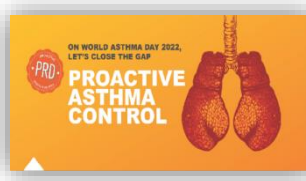

Personalisation?
Will this do for all of you?
No - that won't fit ME
1 SIZE FITS ALL
We are ALL unique with individual needs and requirements
© ogilviedesign.co.uk

THANK YOU

Q & A

PROACTIVE PRD REGULAR DOSING

Disclaimers



- For more information, please refer to the Fluticasone Propionate /Salmeterol Combination prescribing information or contact GlaxoSmithKline **via gcc.medinfo@gsk.com**

- To report Adverse Event/s associated with the use of GSK product/s, please contact us **via gulf.safety@gsk.com**

- All Quality complaints should be reported to the LOC Quality department mailbox **Gulf-KSA.Product-Complaints@gsk.com.**

PROACTIVE PRD REGULAR DOSING

Appreciated Prescribing Information
Seretide Qatar/Bahrain/Oman/Kuwait
CL Code: PI-6664

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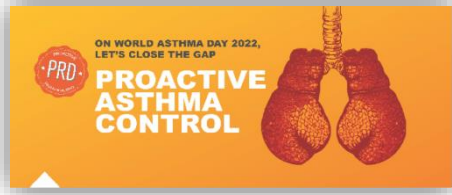

ABBREVIATED PRESCRIBING INFORMATION SERETIDE QATAR – Bahrain – Oman - Kuwait

Qualitative and quantitative composition each dose of Seretide provides: Salmeterol xinafoate equivalent to 50 micrograms of salmeterol and 100, 250 or 500 micrograms of fluticasone propionate. **Pharmaceutical form** Inhalation powder, pre-dispensed. **Indications** Seretide is indicated in the regular treatment of asthma where use of a combination product (long-acting beta-2-agonist and inhaled corticosteroid) is appropriate: patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta-2-agonist or patients already adequately controlled on both inhaled corticosteroid and long-acting beta-2-agonist.Seretide 50/100 microgram strength is not appropriate in adults and children with severe asthma. Seretide is indicated for the symptomatic treatment of patients with severe COPD (FEV_1 <60% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy. **Posology and Method of Administration** Seretide Diskus is for inhalation only. Patients should be made aware that SERETIDE Diskus must be used regularly for optimum benefit, even when asymptomatic. Patients should be regularly reassessed by a doctor, so that the strength of Seretide they are receiving remains optimal and is only changed on medical advice. The dose should be titrated to the lowest dose at which effective control of symptoms is maintained. Patients should be given the strength of Seretide containing the appropriate fluticasone propionate dosage for the severity of their disease. **Recommended Doses for Asthma**, Adults and adolescents 12 years and older, One inhalation of 50 micrograms salmeterol and 100 micrograms fluticasone propionate twice daily. Or one inhalation of 50 micrograms salmeterol and 250 micrograms fluticasone propionate twice daily. Or one inhalation of 50 micrograms salmeterol and 500 micrograms fluticasone propionate twice daily. Children 4 years and older: One inhalation of 50 micrograms salmeterol and 100 micrograms fluticasone propionate twice daily. The maximum licensed dose of fluticasone propionate delivered by Seretide Diskus in children is 100mcg twice daily. There are no data available for use of Seretide in children aged under 4 years. **For COPD,** Adults: One inhalation of 50 micrograms salmeterol and 500 micrograms fluticasone propionate twice daily. **Contraindications** Seretide is contraindicated in patients with hypersensitivity (allergy) to any of the active substances or to the excipient. **Warnings and Precautions** Seretide Diskus should not be used to treat acute asthma symptoms for which a fast and short acting bronchodilator (e.g. salbutamol) is required. Patients should be advised to have their relief medication available at all times. Increasing use of short-acting bronchodilators to relieve symptoms indicates deterioration of control and patients should be reviewed by a physician. Sudden and progressive deterioration in control of asthma is potentially life-threatening and the patient should undergo urgent medical assessment. Consideration should be given to increasing corticosteroid therapy. Also, where the current dosage of Seretide has failed to give adequate control of asthma, the patient should be reviewed by a physician. Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract and glaucoma. It is important, therefore, for asthma patients, that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control is maintained. The possibility of impaired adrenal response should always be borne in mind in emergency and elective situations likely to produce stress and appropriate corticosteroid treatment considered. Because of the possibility of impaired adrenal response, patients transferring from oral steroid therapy to inhaled fluticasone propionate therapy should be treated with special care, and adrenocortical function regularly monitored. Following introduction of inhaled fluticasone propionate, withdrawal of systemic therapy should be gradual and patients encouraged to carry a steroid warning card indicating the possible need for additional therapy in times of stress. **Interaction** Both non-selective and selective beta-blockers should be avoided unless there are compelling reasons for their use. Under normal circumstances, low plasma concentrations of fluticasone propionate are achieved after inhaled dosing, due to extensive first pass metabolism and high systemic clearance mediated by cytochrome P450 3A4 in the gut and liver. Hence, clinically significant drug interactions mediated by fluticasone propionate are unlikely. During post-marketing use, there have been reports of clinically significant drug interactions in patients receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects including Cushing's syndrome and adrenal suppression. Therefore, concomitant use of fluticasone propionate and ritonavir should be avoided, unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side-effects. **Pregnancy and Lactation** Administration of Seretide to pregnant and lactating women should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus or child. **Undesirable effects:** Candidiasis of mouth and throat, pneumonia (in COPD patients), Hypersensitivity reactions with the following manifestations have been reported: Cutaneous hypersensitivity reactions, dyspnoea.reactions, Anaphylactic reactions and Angioedema (mainly facial and oropharyngeal oedema) and bronchospasm, Possible systemic effects include: Cataract, Glaucoma and Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decreased bone mineral density, Hyperglycaemia, Anxiety, Sleeping disorder, Behavioural changes, including hyperactivity and irritability (predominantly in children), Hoarseness/dysphonia, Throat irritation, Paradoxical bronchospasm, Headache, Tremor, Palpitations, tachycardia, atrial fibrillations, Cardiac arrhythmias including supraventricular tachycardia and extrasystoles, Contusions, Muscle cramps, arthralgia. **Overdose:** The expected symptoms and signs of salmeterol overdosage are those typical of excessive $beta_2$– adrenergic stimulation, including tremor, headache, tachycardia, increases in systolic blood pressure and hypokalaemia. If higher than approved doses of SERETIDE are continued over prolonged periods, significant adrenocortical suppression is possible. **Pharmaceutical particulars List of Excipients** Lactose monohydrate (which contains milk proteins). **Special Precautions for Storage** Do not store above 30°C. GDS Version Number: 31 Version Date: 25 April 2013. **Manufactured by** Glaxo Wellcome Production*, Evreux, France * Member of the GlaxoSmithKline group of companies.* Member of GlaxoSmithKline Group of Companies SERETIDE and DISKUS are trademarks of the GlaxoSmithKline group of companies SERETIDE DISKUS Detailed information on this medicinal product can be requested Via: gcc.medinfo@gsk.com To report Adverse Event/s associated with the use of GSK product/s, please contact us via: gulf.safety@gsk.com. All Quality complaints should be reported to the LOC Quality department mail box Gulf-KSA.Product-Complaints@gsk.com. To report Adverse events in Oman **Department of Pharmacovigilance & Drug Information Directorate General of Pharmaceutical Affairs & Drug Control Ministry of Health, Sultanate of Oman Phone Nos. 0096822357687 / 0096822357686 Fax: 0096822358489 Email: pharma-vigil@moh.gov.om Website: www.moh.gov.om.**

Asthma Syndrome Phenotype , Endotype, Biomarkers

- phenotypes : observable characterestics in an individual that results from interaction of a genotype with the environment :

  -clinical phenotype: early onset
  - Exercise induced asthma
  - AERD
  - late eosinophilc asthma
  - obesity associated
  - smoking associated neutrophilic asthma

  -Inflammatory phenotype : Allergic
  - Eosinophilic
  - Non-eosinophilic

- endotypes: specific biologic mechanism that explain an observable characterestics of an organism

Lotvall,et al J Allergy Immunol 2011; 127: 355-360

Type 2 vs Non- type 2

- **Type 2 (High T2)**

More severe

Elevated FeNO

Blood Eosinophilia

Tissue Eosinophilia

Elevated serum IgE

Variable response to CS

Target type 2 inflammation

Coexisting type2 inflammatory diseases

Most Common cytokines : IL4, Il-5, IL-13

- **Non type 2 (Low T2)**

Less severe

Airways neutrophilia

Paucigranulocytes

poor response to CS

Obesity associated

Lacks response to target type2 inflammation

Allergic vs Eosinophilic Phenotypes:

EleftheriosZervas. An Algorithmic approach for the treatment of severe uncontrolled asthma ERJ 2018;4: 00125-2017

Clinical features and biomarkers that can be used to differentiate between allergic and eosinophilic T2-high severe asthma

	A: allergic-predominant asthma	B: eosinophilic-predominant asthma
1	Early onset	Late onset
2	SPT/RAST+ with clinically significant allergies#	SPT/RAST– or + with no clinically significant allergies
3	IgE >100 IU·mL^{-1}	IgE <100 IU·mL^{-1}
4	Allergic rhinitis	Nasal polyps
5	High F_{ENO} (30–50 ppb)	Very high F_{ENO} (>50 ppb)
6	Blood eosinophils <300 cells·μL^{-1}	Blood eosinophils >300 cells·μL^{-1}#

SPT: skin prick test; RAST: radioallergosorbent test; F_{ENO}: exhaled nitric oxide fraction. Check the number of relevant patient characteristics per column. If a patient has more features from column A or B it is more likely that he/she has allergic- or eosinophilic-predominant asthma, respectively. If the patient shares features from both columns, it is more likely that he/she suffers from eosinophilic/allergic overlap asthma. #: obligatory characteristics for allergic and/or eosinophilic asthma.

GINA Guidelines 2021 panel of Biomarkers for patients wit Type 2 inflammations

- *Assess the severe asthma phenotype during high dose ICS treatment (or lowest possible dose of OCS)*

Type 2 inflammation	
Could patient have Type 2 airway inflammation?	• Blood eosinophils ≥150/µl and/or • FeNO ≥20 ppb and/or • Sputum eosinophils ≥2%, and/or • Asthma is clinically allergen-driven and/or • Need for maintenance OCS (Repeat blood eosinophils and FeNO up to 3x, on lowest possible OCS dose)
Note: these are not the criteria for add-on biologic therapy (see **6b***)*	

- *Investigate for comorbidities/differential diagnoses and treat/refer as appropriate*
  - Consider: CBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO
  - Skin prick testing or specific IgE for relevant allergens, if not already done
  - Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion
- *Consider need for social/psychological support*
- *Involve multidisciplinary team care (if available)*
- *Invite patient to enroll in registry (if available) or clinical trial (if appropriate)*

Key changes to GINA severe asthma guide in 2022

- Additional investigations
  - Consider screening for adrenal insufficiency if patient is on maintenance OCS or high dose ICS-LABA
  - For patients with eosinophils ≥300/µl, investigate for non-asthma causes including *Strongyloides* (often asymptomatic), before considering biologic therapy
  - For patients with hypereosinophilia, e.g. ≥1500/µl, investigate for conditions such as EGPA
- Assessment of inflammatory phenotype
  - If blood eosinophils or FeNO not elevated, repeat up to 3 times, at least 1–2 weeks after stopping OCS, or on lowest possible OCS dose
- Treatment options for patients with no evidence of Type 2 inflammation on repeated testing
  - Consider add-on treatment with LAMA or low-dose azithromycin if not already tried
  - Can also consider anti-IL4R* (if on maintenance OCS) or anti-TSLP* (but insufficient evidence with maintenance OCS)
- Consider maintenance OCS only as last resort, because of serious cumulative adverse effects
- **Check local eligibility criteria for specific biologic therapies*

Key changes to GINA severe asthma guide in 2022 (continued)

- Anti-IL4R* (dupilumab) for severe eosinophilic/Type 2 asthma
  - Not suggested if blood eosinophils (current or historic) >1500/µl
  - Dupilumab now also approved for children ≥6 years with severe eosinophilic/Type 2 asthma, not on maintenance OCS *(Bacharier, NEJMed 2021)*
- Anti-TSLP* (tezepelumab) now approved for severe asthma (age ≥12 years)
  - Greater clinical benefit with higher blood eosinophils and/or higher FeNO

Class	Name	Age*	Asthma indication*	Other indications*
Anti-IgE	Omalizumab (SC)	≥6 years	Severe allergic asthma	Nasal polyposis, chronic spontaneous urticaria
Anti-IL5 Anti-IL5R	Mepolizumab (SC) Reslizumab (IV) Benralizumab (SC)	≥6 years ≥18 years ≥12 years	Severe eosinophilic/Type 2 asthma	Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome
Anti-IL4R	Dupilumab (SC)	≥6 years	Severe eosinophilic/Type 2 asthma, or maintenance OCS	Moderate-severe atopic dermatitis, CRSwNP
Anti-TSLP	Tezepelumab (SC)	≥12 years	Severe asthma	

**Check local eligibility criteria for specific biologic therapies; TSLP: thymic stromal lymphopoietin*

Interim advice about asthma severity descriptors

1. Severe asthma: GINA continues to support the current definitions of severe asthma, and difficult-to-treat asthma
2. 'Mild asthma': GINA suggests that this term should generally be avoided in clinical practice if possible, because it is used and interpreted in different ways
   - If used, emphasize importance of ICS-containing treatment to reduce risk of severe or fatal exacerbations
3. For population-level observational studies: report the controller and reliever treatment not the 'Step', and don't impute severity
   - e.g. 'patients prescribed low dose ICS-LABA with as-needed SABA', not 'Step 3 patients' and not 'moderate asthma'
4. For clinical trials: describe the included patients by their asthma control and treatment (controller and reliever), and don't impute severity
5. GINA proposes holding a stakeholder discussion about the definition of mild asthma, to obtain agreement about the implications for clinical practice and clinical research of the changes in knowledge about asthma pathophysiology and treatment since the current definition of asthma severity was published

Other changes or clarifications in GINA 2022

- "Written" asthma action plans
  - Handwritten, printed, digital or pictorial instructions about what to do when asthma gets worse
  - Not just verbal instructions!
- Acute asthma in healthcare settings
  - At present, salbutamol (albuterol) is the usual bronchodilator in acute asthma management
  - Formoterol has similar efficacy and safety in ED studies *(Rodrigo, Ann Allerg Asthma Immunol, 2010)*
  - One study showed high dose budesonide-formoterol had similar efficacy and safety as SABA *(Balanag, Pulm Pharmacol Ther 2006)*
  - Patients admitted to hospital for an asthma exacerbation should continue, or commence, ICS-containing therapy
- Air filters can reduce fine particle exposure, but no consistent effect on asthma outcomes *(Park, Allergy Asthma Immunol Res 2021)*
- Use of e-cigarettes is associated with increased risk of respiratory symptoms and asthma exacerbations *(Cho, PLoSOne 2016; Wills, ERJ 2021)*