New treatments for ~~poorly~~ uncontrolled asthma GenPaed Update 2022

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Huge health care burden

50% of asthmatics are poorly controlled

436
Australians died from asthma in 2019

157 males ■ 279 females

Total Deaths (Persons)
State/Territory[4]

1 IN 9
AUSTRALIANS ARE AFFECTED BY ASTHMA
2.7 million people

ASTHMA MORTALITY

Mortality rates are higher for:
- People living in remote areas
- People living in areas of lower socio-economic status
- Indigenous Australians

QUALITY OF LIFE

People with asthma are less likely to report excellent health, and more likely to report fair or poor health, than people without the condition.

ASTHMA AUSTRALIA

HOSPITALISATIONS

In 2017-18
38,792
Australians were hospitalised[3]

Approximately **80%** of asthma hospitalisations are preventable

Almost **half** (44%) of the hospitalisations for asthma in Australia are for children aged 0–14.

ASTHMA ACTION PLANS[e]

28.4% of people with asthma have an Asthma Action Plan.

- 0–14 years: 53.7%
- 15 years and over: 21.3%

Asthma Uncontrolled

Red Flags

- Poor adherence to preventer
- SABA overuse
- Poor understanding of asthma medications
- No asthma education to carers
- Adolescent male
- Vulnerable social background
- Poor health care engagement
- ICU admission

Dr Louisa Owens Head Resp SCH

SABAs

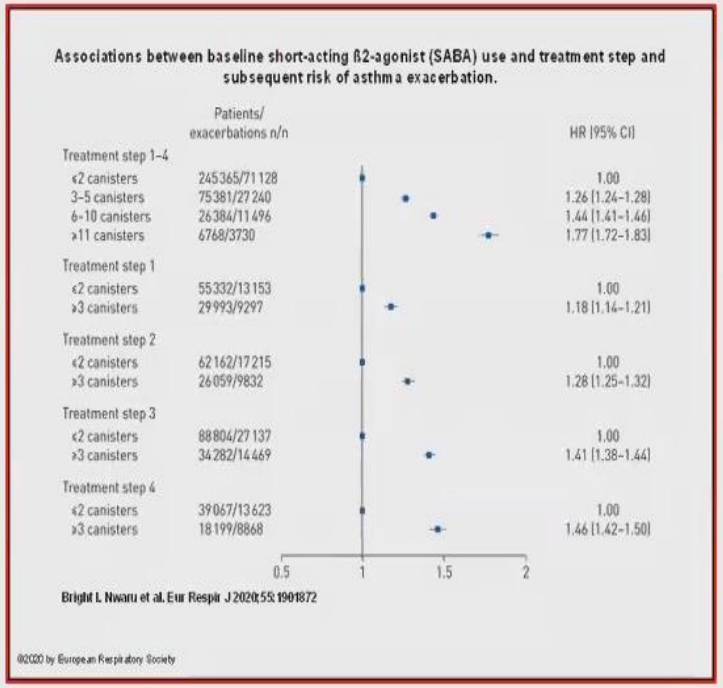
Benefits

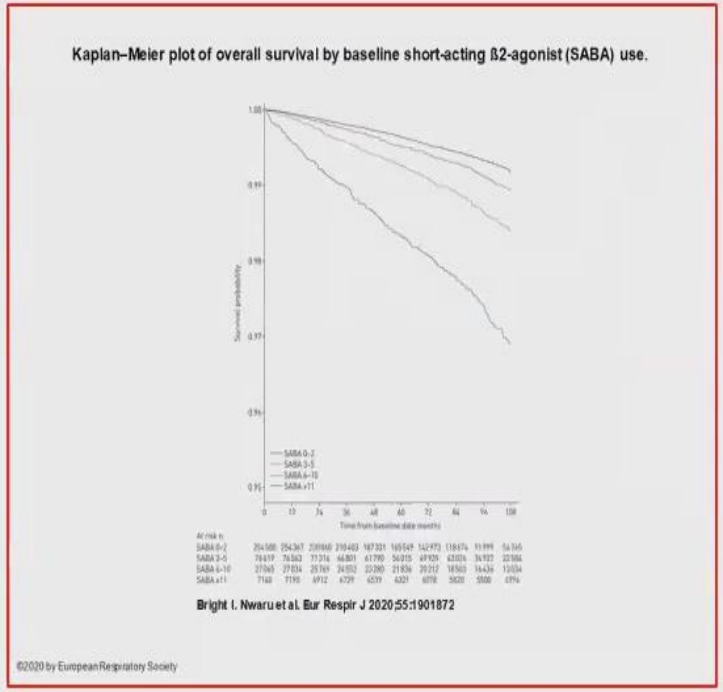
- ✓ Symptom relief
- ✓ Immediate action
- ✓ Cheap
- ✓ Pre-exercise: bronchoconstriction prevention
- ✓ Over the counter
- ✓ Same inhaler for all ages

Concerns

- ❖ Does not treat the underlying inflammation
- ❖ Does not prevent further bronchospasm
- ❖ Short acting
- ❖ Does not reduce severity of exacerbation
- ❖ Does not improve asthma control
- ❖ Patient misunderstanding of role
- ❖ Over the counter
- ❖ Side effects:
  - ❖ β receptor downregulation
  - ❖ Rebound hyperresponsiveness
  - ❖ Reduced bronchodilator response
  - ❖ Tachycardia and adrenergic effects
  - ❖ Hypokalaemia

SABA OVERUSE





- SABA canister = 200 doses
- 3 canisters / year = 12 puffs / week:
  ↑ risk of severe exacerbation
- 8 canisters / year = 4 puffs / day:
  ↑ risk of asthma mortality

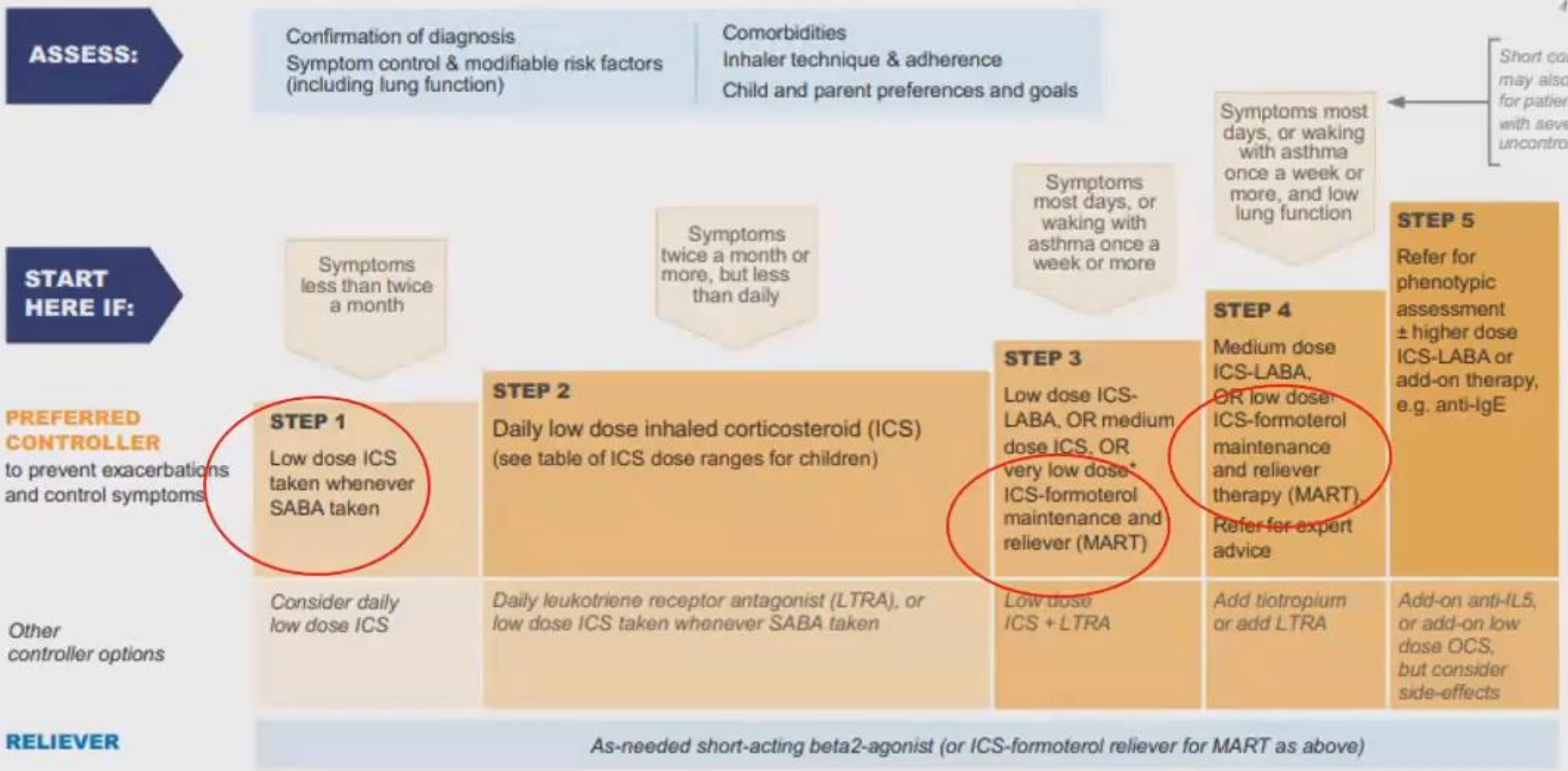
- *European Respiratory Journal 2020 55: 1901872*

MART

What are the new treatments for uncontrolled Asthma?

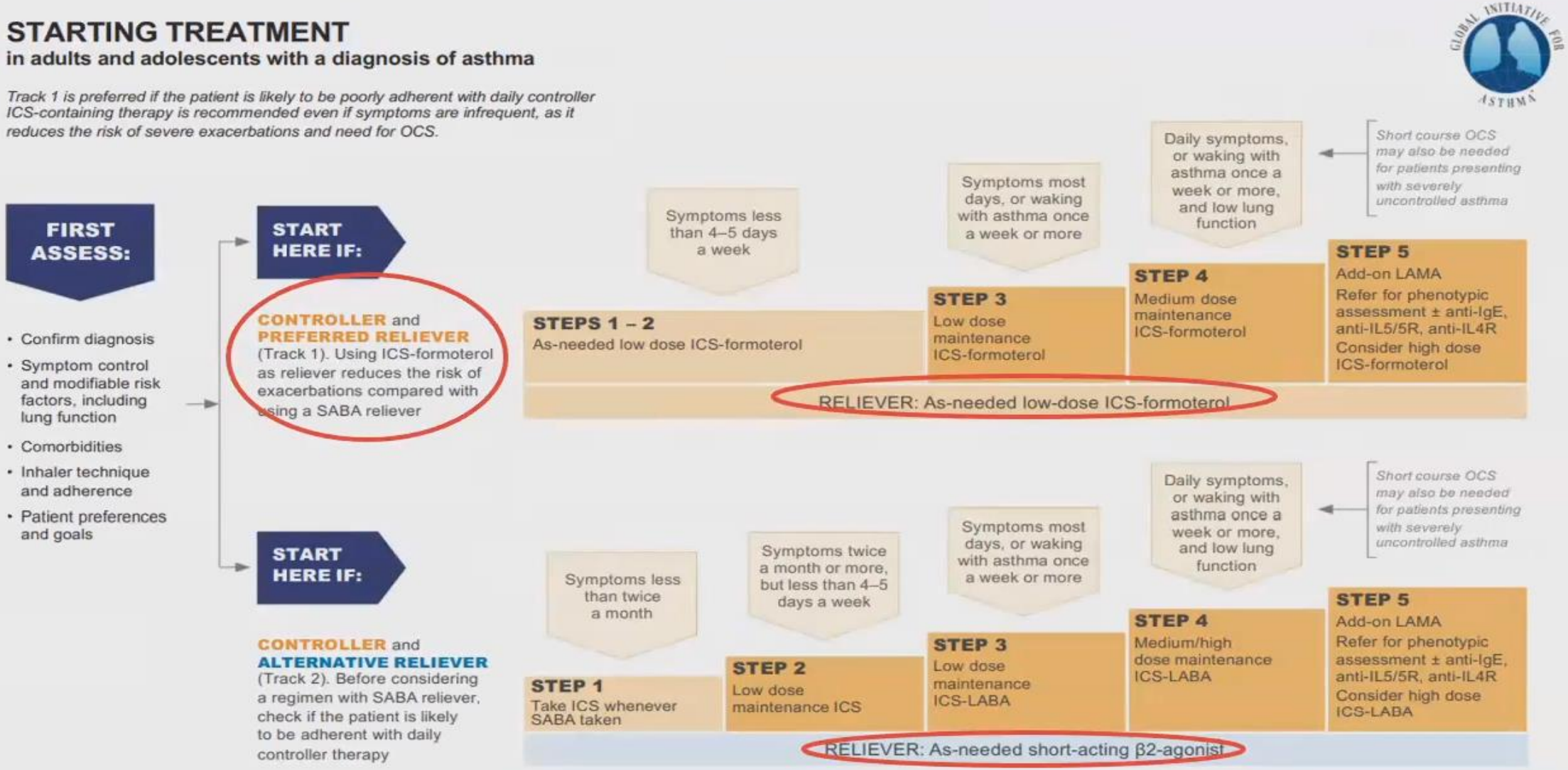
STARTING TREATMENT

Children 6–11 years with a diagnosis of asthma



*Very low dose: BUD-FORM 100/6 mcg
†Low dose: BUD-FORM 200/6 mcg (metered doses).

- **Track 1:** **Using ICS /formoterol combination as reliever +/- maintenance**
- **Track 2:** **Using ICS and SABA PRN**

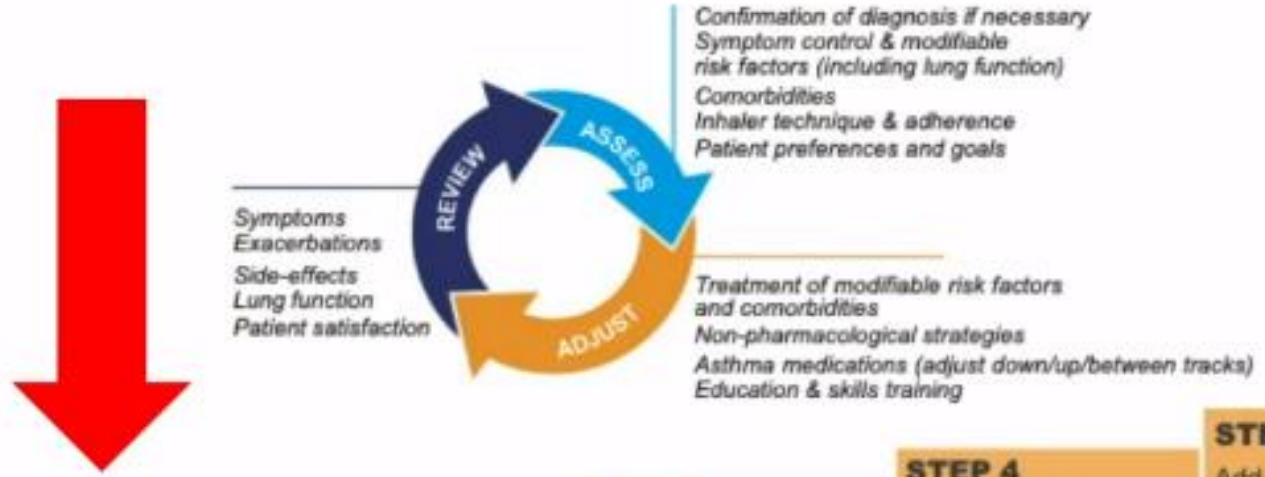


GINA 2021, Box 3-4Bi

MART -> SMART (Single Maintenance And Reliever Therapy)

Adults & adolescents 12+ years

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



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 phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol
RELIEVER: As-needed low-dose ICS-formoterol			

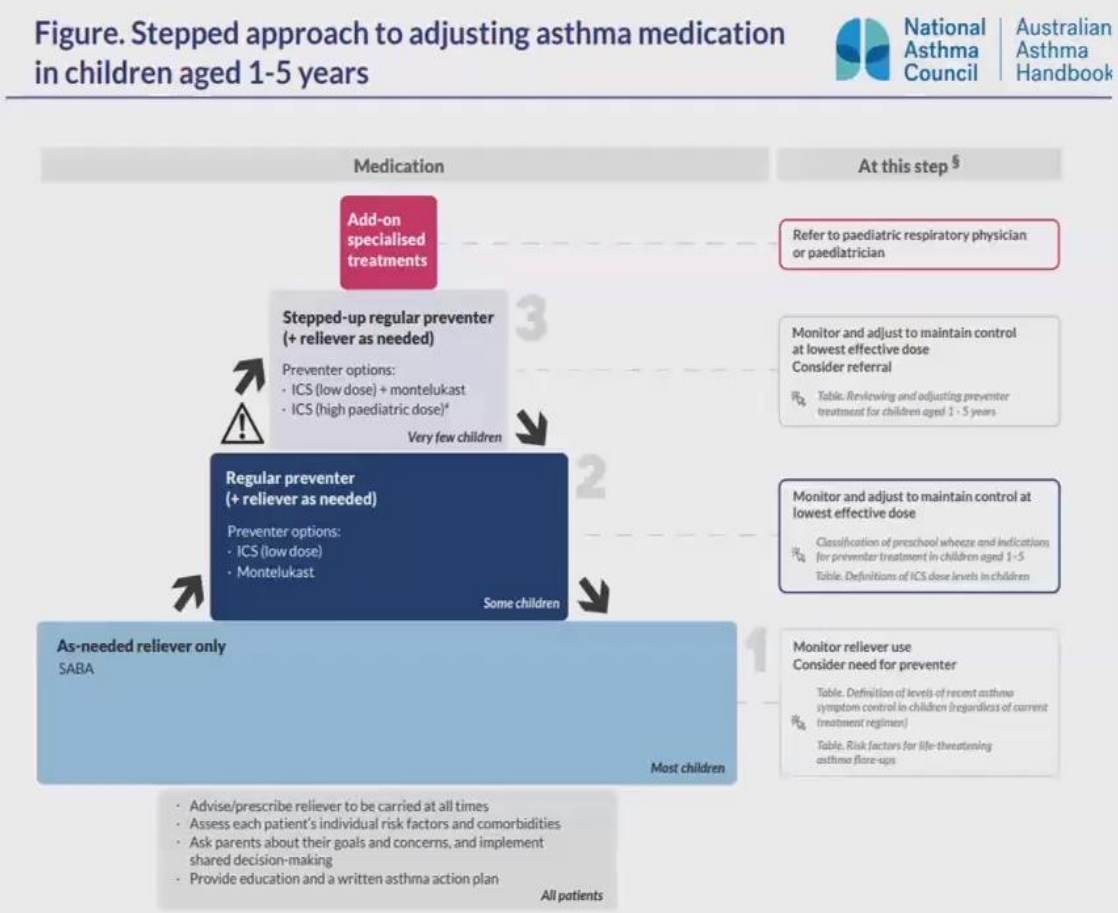
CONTROLLER and ALTERNATIVE RELIEVER
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

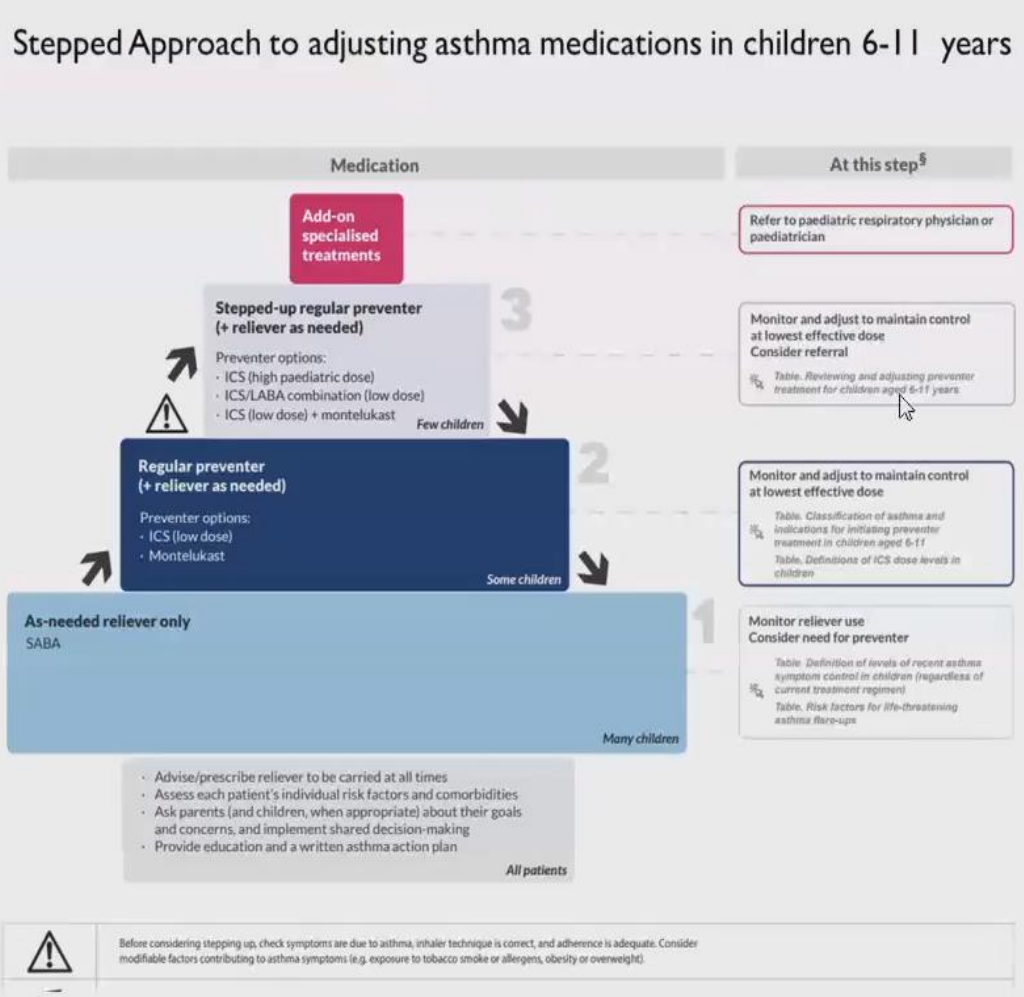
STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA
RELIEVER: As-needed short-acting β2-agonist				

Other controller options for either track

	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; add low dose OCS but consider side-effects*

AUSTRALIAN GUIDELINES





Asthma Treatment Updates

- SABA overuse is bad
- ICS treats underlying inflammation
- ICS / formoterol does both, but not recommended < 12 years
- Cost implications
- Growth considerations
- Minimal evidence in this age group

My Symbicort (budesonide/formoterol) Turbuhaler 200/6 Asthma Action Plan

Anti-inflammatory Reliever
With or without Maintenance

Name: _____

Date: _____

Plan discussed with: (name of health care professional)

_____

My usual best peak flow (if used): _____ l/min

National Asthma Council AUSTRALIA

Usual Medical Contact: Name and telephone number

_____

NORMAL MODE

MY SYMBICORT ASTHMA TREATMENT IS:

☐ Symbicort Turbuhaler 200/6 mcg

RELIEVER

I should take 1 inhalation of my Symbicort whenever needed for relief of my asthma symptoms

I should always carry my Symbicort with me to use as a reliever when needed

MY REGULAR MAINTENANCE TREATMENT EVERY DAY IS : *(enter number of inhalations or 0 if no regular daily treatment prescribed)*

_____ Inhalation(s) in the morning (0, 1, 2)

_____ Inhalation(s) in the evening (0, 1, 2)

MY ASTHMA IS STABLE IF:

- I do not wake up at night or in the morning because of asthma
- My asthma has not interfered with my usual activities (e.g housework, school, exercise)

OTHER INSTRUCTIONS
(e.g. what to do before exercise, when to see my doctor)

ASTHMA FLARE UP

IF OVER A PERIOD OF 2–3 DAYS:

- My asthma symptoms are getting worse or not improving

  OR
- I am using more than 6 Symbicort reliever inhalations a day

  OR
- Peak flow below: _____ (delete if not used)

I SHOULD:

☑ **Continue to use my Symbicort to relieve my symptoms and my regular daily Symbicort if prescribed (up to a maximum total of 12 inhalations in a day)**

☐ Contact my doctor

☐ Start a course of prednisolone

COURSE OF PREDNISOLONE TABLETS:

Take _____ mg prednisolone tablets each morning for _____ days; OR

IF I NEED MORE THAN 12 SYMBICORT INHALATIONS (TOTAL) IN ANY DAY,

- I must see my doctor or go to hospital the same day

ASTHMA EMERGENCY

SIGNS OF AN ASTHMA EMERGENCY

- My asthma symptoms are getting worse quickly
- I am finding it very hard to breathe or speak
- My Symbicort is not helping

IF I HAVE ANY OF THE ABOVE DANGER SIGNS, I SHOULD DIAL 000 FOR AN AMBULANCE AND SAY I AM HAVING A SEVERE ASTHMA ATTACK.

WHILE I AM WAITING FOR THE AMBULANCE:

- Sit upright and keep calm
- I should keep taking my Symbicort as needed
- If only Ventolin® is available, take 4 puffs as often as needed until help arrives
- Even if my symptoms appear to settle quickly I should seek medical advice right away
- ☐ Use my adrenaline autoinjector

OTHER INSTRUCTIONS

Monoclonal antibody therapy

- Four monoclonal antibody therapies
- Benralizumab, Mepolizumab, Dupilumab and Omalizumab need specialist prescribing PBS
- Treatment of severe asthma in patients whose asthma is uncontrolled despite optimised standard treatment
- Add-on treatment option for reducing severe flare-ups and improving symptom control in severe allergic or eosinophilic asthma which is uncontrolled despite treatment with high-dose inhaled corticosteroids and long-acting beta$_2$ agonists
- Target inflammatory pathways - activate type 2 immune responses -> airway inflammation
- Patients must keep taking ICS preventers

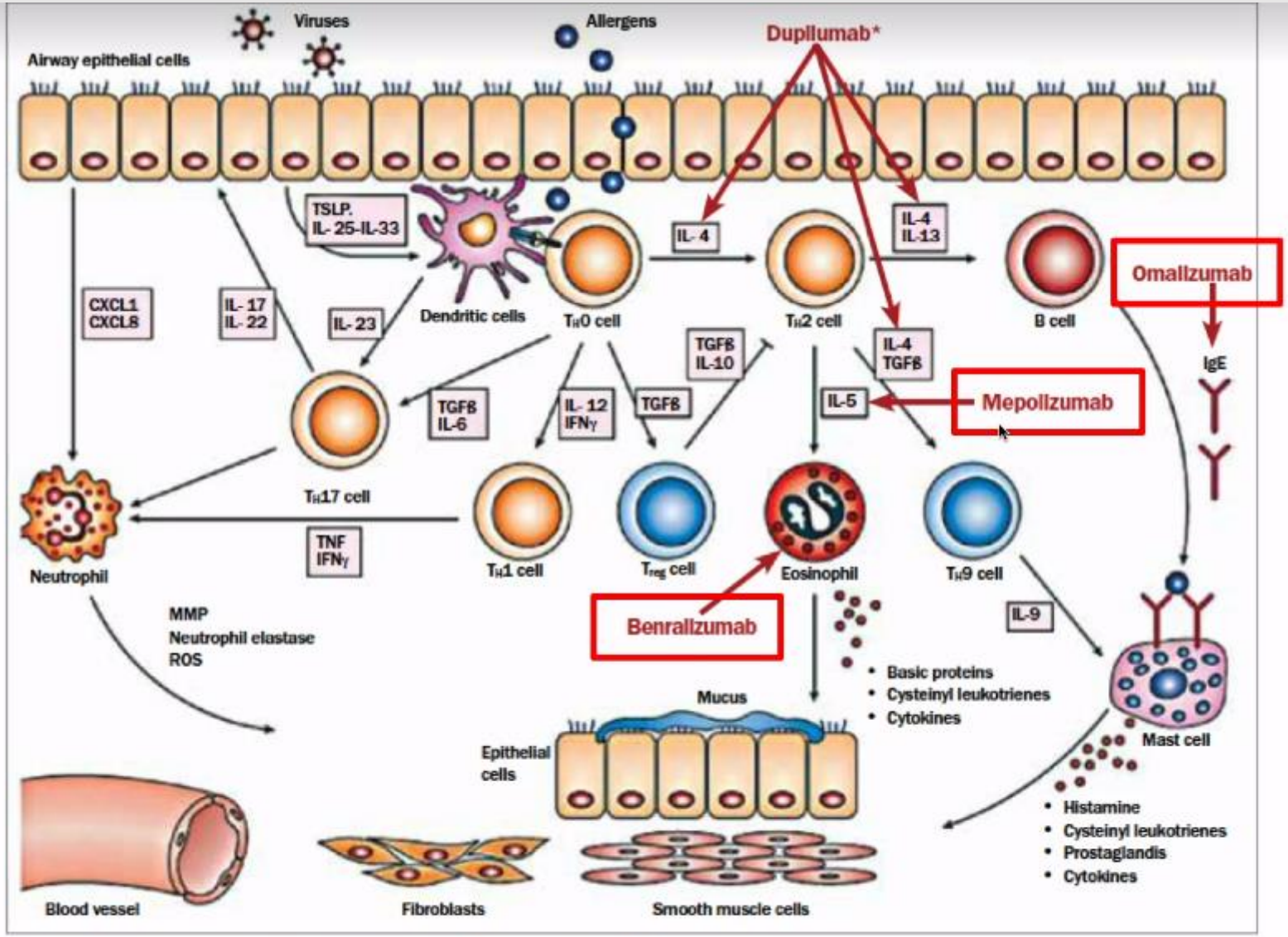


Figure 4. The pathobiology of asthma and targets for biologic medications to treat asthma.

Haggie S, Robinson PD. Respir Medicine Today 2020

Monoclonal antibody therapy for severe asthma

Information paper for primary care health professionals

National Asthma Council AUSTRALIA

Executive summary

Key points

- Monoclonal antibody therapy is an **add-on treatment** option for reducing severe flare-ups and improving symptom control in patients with severe allergic or eosinophilic asthma whose asthma is uncontrolled despite treatment with high-dose inhaled corticosteroids and long-acting beta$_2$ agonists.
- These therapies target inflammatory pathways that activate type 2 immune responses leading to airway inflammation.
- Patients using these treatments must keep taking their inhaled corticosteroid-containing preventers.
- Four agents are available in Australia: benralizumab, mepolizumab, dupilumab and omalizumab.
- These monoclonal antibody therapies are subsidised by the Pharmaceutical Benefits Scheme (PBS) for patients in specialist care who meet strict criteria.
- After treatment has been initiated by a specialist, ongoing maintenance doses can be administered in primary care, or by the patient or carer, under specialist supervision.
- Monoclonal antibody therapies currently available in Australia for severe asthma are generally well tolerated. Injection site reactions are among the most common adverse events. Systemic reactions, including anaphylaxis, are rare but can occur.
- Like all patients with asthma, those using monoclonal antibody therapies need an up-to-date written asthma action plan.

Recommendations

When asthma is poorly controlled, first check for common causes (e.g. incorrect inhaler technique and suboptimal adherence, comorbidities, self-management difficulties) and correct these.

For patients with uncontrolled asthma who might benefit from monoclonal antibody therapy, refer for specialist assessment as soon as possible to expedite access through PBS. Unless the diagnosis of severe asthma was made by a multidisciplinary severe asthma clinic team, the patient must be under the care of the same specialist for at least 6 months before becoming eligible for PBS subsidy.

Arrange specialist referral if any of the following apply, despite treatment with a moderate or high dose of inhaled corticosteroid and long-acting beta$_2$ agonist combination therapy: poor symptom control persists, the patient has been prescribed two or more short courses of oral corticosteroids for flare-ups in the past year, or you are considering long-term maintenance oral corticosteroids for asthma.

Advise patients who have been prescribed a monoclonal antibody therapy that they should keep taking their inhaled corticosteroid-containing preventer. Continue to check adherence and inhaler technique regularly and at every opportunity.

Ensure that patients understand that they must attend all scheduled specialist visits to remain eligible for access to monoclonal antibody therapy through the PBS.

When administering monoclonal antibody therapies, carefully follow instructions for storing, preparing and administering doses.

Ensure that each patient has an up-to-date written asthma action plan: review it at least yearly or whenever the medication regimen is changed. Remind patients taking monoclonal antibody therapy to follow their written asthma action plan when symptoms worsen.

- Preschool Children presenting to ED aged 1-6 years
- Capsule or placebo for 10 days of Month for 12months
- OM-85 capsule contains 3.5 mg of lyophilized bacterial lysates *Haemophilus influenzae, Streptococcus (Diplococcus) pneumoniae, Klebsiella pneumoniae and K. ozaenae, Staphylococcus aureus, Streptococcus pyogenes* and S. *viridans (S. sanguinis), Moraxella* (*Branhamella/Neisseria) catarrhalis.*

Summary
New therapies for uncontrolled asthma

- Outlined those at risk
- SMART therapy >12 year olds
- New Monoclonal antibody therapies (despite optimal therapy)
- Aware Local Study on way - ARROW Trial OM-85 oral medication

Session 4 – Wheezy Teens
Relevant HealthPathways

- Central Coast HealthPathways website – https://centralcoast.communityhealthpathways.org/
  Username: centralcoast Password: 1connect
- Asthma in Children section
  - Acute Asthma in Children pathway
  - Non-acute Asthma in Children pathway
  - Inhalers and Techniques pathway
- Allergic Rhinitis and Nasal Obstruction in Children pathway
- Urgent Paediatric Assessment referral page
- Non-urgent Paediatric Assessment referral page
- Paediatric Medical Advice referral page
- Non-urgent Immunology and Allergy Assessment referral page
- Asthma in Adults section
- Asthma in Adults – Acute pathway
- Non-acute Asthma in Adults pathway
  - Asthma Cycle of Care pathway
  - Inhaled Corticosteroids (ICS) pathway
  - Combination ICS / LABA Therapy pathway
  - Inhalers and Techniques pathway