Improving outcomes in severe paediatric asthma: New treatments, new possibilities

touch™ IMMUNOLOGY

Disclaimer

- *Unapproved products or unapproved uses of approved products may be discussed by the faculty; these situations may reflect the approval status in one or more jurisdictions*
- *The presenting faculty have been advised by USF Health and touchIME to ensure that they disclose any such references made to unlabelled or unapproved use*
- *No endorsement by USF Health and touchIME of any unapproved products or unapproved uses is either made or implied by mention of these products or uses in USF Health and touchIME activities*
- *USF Health and touchIME accept no responsibility for errors or omissions*

touch™ IMMUNOLOGY

A conversation between:

Dr Leonard Bacharier
Vanderbilt University Medical Center
Nashville, TN, USA

Dr Dermot Ryan
University of Edinburgh
Scotland, UK

touch™ IMMUNOLOGY

Diagnosing severe paediatric asthma

Dr Dermot Ryan
University of Edinburgh
Scotland, UK

Asthma presentation in children and adolescents

Asthma presentation can vary with age

Early childhood (0–6 years)[1]

- Dry or productive cough, wheeze, shortness of breath, troubled breathing
- Often virally triggered

Late childhood (7–11 years)[1]

- Allergy-triggered symptoms
- Symptoms may be precipitated by exercise
- Some may have few day-to-day symptoms with exacerbations due to environmental triggers

Adolescence (12–18 years)[1]

- Shortness of breath, wheeze in response to triggers, chest pain or tightness, cough

Allergic rhinitis in early childhood is often the first stage towards asthma development[1]

Symptoms that are worse at night or early morning or that vary over time are characteristic of asthma[2]

Symptoms can also be precipitated by triggers[3]

- Exercise
- Airborne allergens
- Viral infections
- Second-hand smoke
- Air temperature changes

1. Trivedi M, Denton E. *Front Pediatr*. 2019;7:256; 2. Global Initiative for Asthma. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf (accessed 14 November 2022); 3. Martin J, et al. *BMJ Paediatr Open.* 2022;6:e001277.

Diagnosing severe paediatric asthma

Diagnosis is based on symptoms and variable expiratory airflow limitation

Patient presents with symptoms

Wheeze, shortness of breath, chest tightness, cough

↓

Detailed history/examination for asthma

↓

Measurement of reversibility and/or variability:

Variability in lung function (≥1 of following):

- Positive bronchodilator responsiveness
- Positive exercise challenge
- Excessive variation in lung function
- Excess variability in twice daily PEF over 2 weeks
- Significant increase in lung function after 4 weeks of anti-inflammatory treatment

AND

Expiratory airflow limitation:

FEV_1/FVC reduced compared to lower limit of normal (>0.90 in children)

Asthma severity is defined by patient response to ICS-LABA therapy

If bronchodilator response is negative, repeat spirometry may be performed after withholding bronchodilators or when symptomatic

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroid; LABA, long-acting $beta_2$-agonist; PEF, peak expiratory flow.

Global Initiative for Asthma. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf (accessed 14 November 2022).

touch™ IMMUNOLOGY

Defining difficult-to-treat and severe asthma

Initial asthma treatment is based on ICS with or without LABA

Severity based on assessment after 2–3 months of treatment[1]

Difficult-to-treat asthma[1]

- Uncontrolled despite medium- or high-dose ICS plus a second controller (usually a LABA) or with maintenance OCS

OR

- Requires high-dose treatment to reduce the risk of exacerbation

Severe asthma

- Uncontrolled despite adherence to maximal high-dose ICS-LABA and management of contributory factors[1]
- Requires frequent OCS bursts or daily OCS[2]
- Associated with overuse of SABA[3]

Modifiable contributory factors may influence severity and must be excluded before diagnosis[1]

- Incorrect diagnosis
- Poor inhaler technique
- Poor treatment adherence
- Multimorbidity, e.g. rhinosinusitis, GORD, obesity, obstructive sleep apnoea
- Ongoing allergen/irritant exposure

GORD, gastro-oeosophageal reflux disease; ICS, inhaled corticosteroids; LABA, long-acting beta$_2$-agonist; OCS, oral corticosteroids; SABA, short-acting beta$_2$-agonist.

1. Global Initiative for Asthma. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf (accessed 14 November 2022); 2. Bourdin A, et al. *Eur Respir Rev*. 2020;29:190085; 3. Noorduyn S, et al. *ERJ Open Res*. 2022;8:00140-2022.

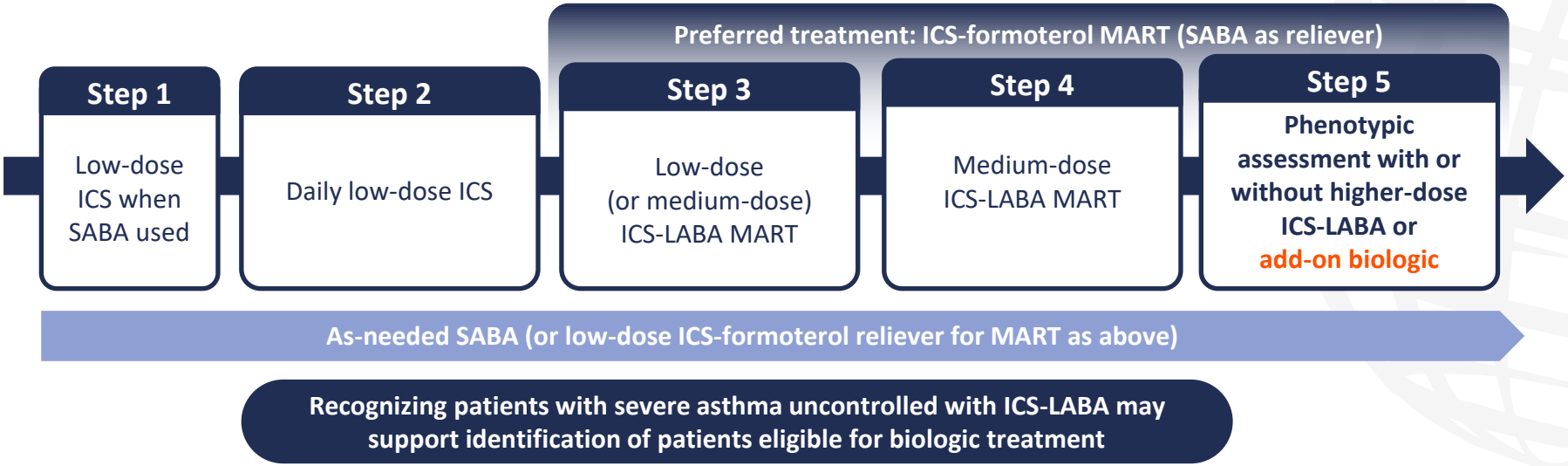
touch™ IMMUNOLOGY

Biologics for severe paediatric asthma

Dr Dermot Ryan
University of Edinburgh
Scotland, UK

Stepwise approach to initiating asthma therapy

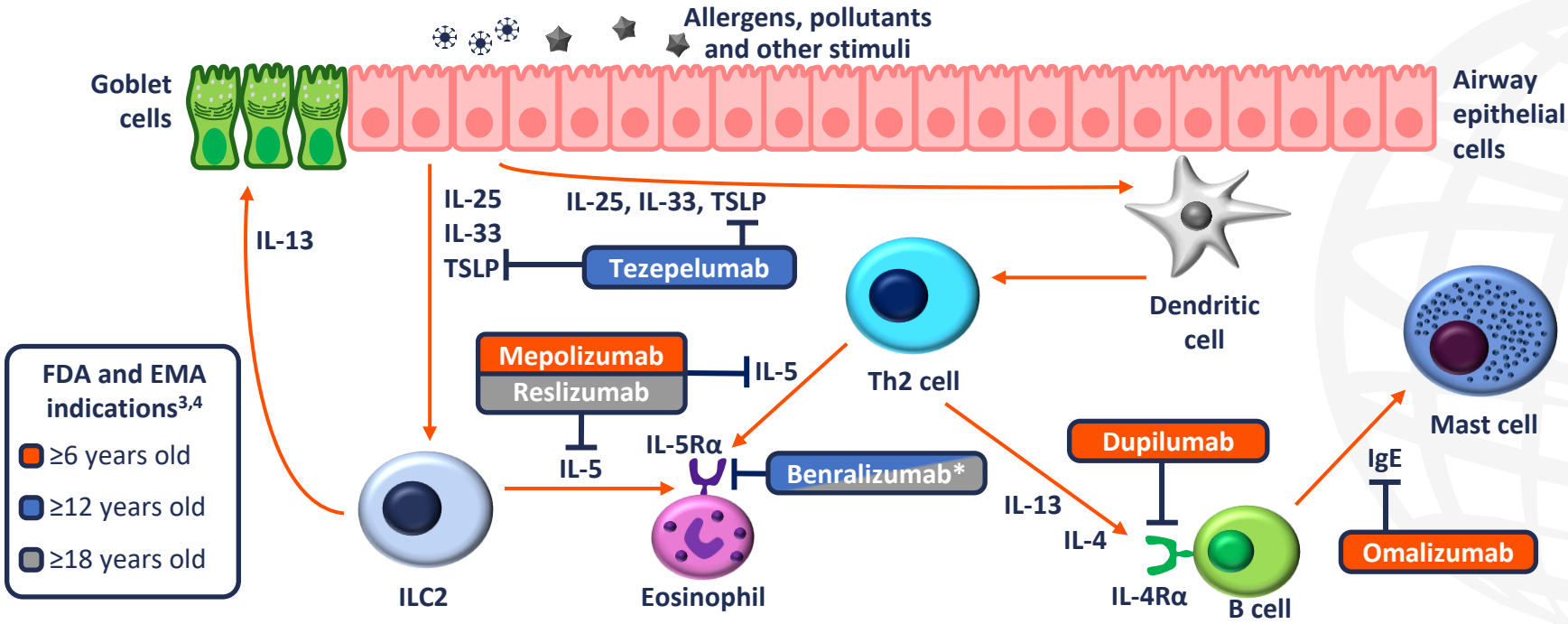
In children aged 6–11 years, biologics are recommended when ICS or LABA therapy is not sufficient to control symptoms



ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; MART, maintenance and reliever therapy; SABA, short-acting beta$_2$-agonist.
Global Initiative for Asthma. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf (accessed 14 November 2022).

touch™ IMMUNOLOGY

Biologic treatment targets in severe asthma[1,2]



* Benralizumab is indicated for adult patients by the EMA, and for patients aged 12 years or older by the FDA.

EMA, European Medicines Agency; FDA, US Food and Drug Administration; IgE, immunoglobulin E; IL, interleukin; IL-4Rα, IL-4 receptor alpha; IL-5Rα, IL-5 receptor alpha; ILC2, group 2 innate lymphoid cell; Th2, T helper 2; TSLP, thymic stromal lymphopoietin.

1. Brusselle G, et al. *N Engl J* Med. 2022;386:157–71; 2. Pelaia C, et al. *Front Immunol.* 2020;11:6033123; 3. EMA. Summary of product characteristics. Available at: www.ema.europa.eu/en/medicines/ (accessed 14 November 2022); 4. FDA. Prescribing information. Available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 14 November 2022).

touch™ IMMUNOLOGY

Optimal management of severe paediatric asthma

Dr Dermot Ryan
University of Edinburgh
Scotland, UK

Managing modifiable risk factors

Medication
- SABA overuse is associated with an increased rate of exacerbations and increased risk of mortality[1,2]

Comorbidity control
- Allergic rhinitis is associated with exacerbation,[3] which can be managed with effective treatment[4]

Poor treatment adherence
- Improved adherence can reduce severe exacerbations[5]
- Inhaler technique and adherence should be monitored[6]

Environmental exposures[7,8]
- Second-hand smoke
- Allergen exposure (in early childhood)
- Air pollution
- Mould in the home
- Physical inactivity

The GINA Global Strategy recommends avoiding risk factors, such as smoke or household mould, where possible,[6] which may help reduce asthma symptoms[7]

GINA, Global Initiative for Asthma; SABA, short-acting beta$_2$-agonist.
1. Noorduyn S, et al. *ERJ Open Res*. 2022;8:00140-2022; 2. Nwaru B, et al. *Eur Respir J.* 2020;55:1901872; 3. Kang H-R, et al. *BMJ Open*. 2018;8:e020825;
4. Yu C-L, et al. *J Microbiol Immunol Infect*. 2019;52:991–9; 5. Averell C, et al. *Ther Adv Respir Dis.* 2022;16:17534666221116997; 6. Global Initiative for Asthma. Available at: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf (accessed 14 November 2022);
7. Azalim S, et al. *Ann Agric Environ Med*. 2014;21:59–63; 8. Abreo A, et al. *Clin Trans Med.* 2018;7:15.

touch™ IMMUNOLOGY