OVERVIEW OF RECENT ADVANCEMENTS IN ASTHMA

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Inhaled corticosteroid (ICS) are the backbone of asthma management and should be initiated as soon as possible after a diagnosis of asthma

Pharmacotherapy for asthma can be divided into three categories:

1. P*reventer medication*, which controls symptoms, reduces risk of exacerbation and prevents the sequelae of chronic inflammation.

1.Reliever medication, which is taken as required for symptoms.

2.Add-on therapies, including biologic agents, for severe disease.

Add-on pharmacotherapies

In patients whose asthma is not controlled on moderate- to high-dose ICS-LABA (Inhaled corticosteroid–long-acting β_2-agonist), phenotypic and endotypic assessment for consideration of biologic drugs should occur. Additional therapies (see Table) can be considered at this step -

Add-on therapy	Comment
Increased ICS dose	Increasing the ICS dose provides little additional benefit at this step but is associated with an increased side-effect profile.
Long-acting muscarinic antagonists	Tiotropium is shown to improve moderately lung function and increase the time to severe exacerbation. Tiotropium inhibits muscarinic M3 receptors preferentially and reduces AHR in asthma patients and may act by targeting mast cells
Macrolides	Macrolides possess antimicrobial as well as immunomodulatory properties. Azithromycin taken three times weekly is shown to reduce exacerbations and improve asthma-related quality of life
Leukotriene receptor antagonists	Montelukast improves asthma control when added to ICS monotherapy, but ICS-montelukast was inferior to ICS-LABA. It may have some use in exercise-induced asthma

Low-dose oral corticosteroids: In patients with severe, uncontrolled disease despite appropriate stepwise management, regular OCS or frequent bursts of OCS may be required. Continuous OCS should be used at the lowest possible dose and be considered a temporary therapy only until specialist referral, where transitioning to steroid-sparing agents (such as biologics), should be considered. This is separate from management of asthma exacerbations where a short (3- to 5-day) course of OCS is routinely recommended. Corticosteroid use is associated with a significant adverse-effect profile including osteoporosis and bone fractures, weight gain, mood disorders and hyperglycaemia. It should also be noted that repeated short courses of OCS reach a cumulative toxic dose that can result in the above adverse effects

Table - Biologic drugs

Immunological target	Biologic Agent	Mechanism of action	Outcomes	Administration
IgE	Omalizumab	Monoclonal antibody that binds Fc portion of IgE, inhibiting binding to masts cells and instead forming omalizumab-IgE complexes.	In patients with severe allergic asthma, omalizumab reduced exacerbations by 25% at 12 months. Symptomatic onset of efficacy of omalizumab is at 12–16 weeks with stabilisation of peak flow and symptoms	2–4 weekly
IL-5	Mepolizumab	Monoclonal antibody that blocks binding of IL-5 to the α chain of IL-5 receptor, inhibiting eosinophilic inflammation.	In patients with severe eosinophilic asthma, mepolizumab reduced exacerbation rate by 53% at 12 months, and a clinically significant reduction in symptoms.	4 weekly
IL-5R	Benralizumab	Fucosylated monoclonal antibody that acts on IL-5Rα on eosinophils and basophils, inducing antibody mediated cytotoxicity and rapid eosinophil depletion	In patients with severe eosinophilic asthma, benralizumab reduced exacerbations by 51% at 12 months, reduced serum eosinophil counts and improved symptom control	4 weekly for first 3 doses, then 8 weekly dosing interval recommended .