Drug Update

FEVIPIPRANT: GAME CHANGER FOR FUTURE TREATMENT OF ASTHMA

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Bronchial asthma is a clinical syndrome characterised by paroxysmal dyspnoea with wheeze due to increased resistance to air flow through narrowed bronchi. In the past, asthma was seen as a disease of bronchoconstriction due to the release of bronchoconstrictor mediators from mast cells and was treated predominantly with bronchodilators. Asthma etiology may be multifactorial like genetic, environmental, inflammatory and immunological. More recently it has been viewed as an inflammatory disease of the airways with a focus on anti-inflammatory treatments. Inhaled corticosteroids (ICSs) have revolutionized the management of asthma, leading to better control of symptoms, a marked reduction in hospitalization and reduced mortality. Current management of asthma is highly effective; most patients are well controlled if they take regular inhalational corticosteroids with or without long-acting β2-agonists in combination inhalers. Yet despite the availability of effective therapies over half of the patients with asthma appear to be poorly controlled largely due to poor adherence[1]. Current therapy for asthma with inhaled corticosteroids and long-acting inhaled β2-agonists is highly effective, safe, and relatively inexpensive, but many patients remain poorly controlled. Most advances have been through improving these drug classes and a major developmental hurdle is to improve existing drug classes. Major unmet needs include better treatment of severe asthma as well as curative therapies for mild to moderate asthma that do not result in the return of symptoms when the treatment is stopped. Several new treatments are in development, but many are specific, targeting a single mediator or receptor, and are unlikely to have a major clinical impact, although they may be effective in specific asthma phenotypes. Drugs with more widespread effects, such as kinase inhibitors, may be more effective but have a greater risk of side effects so inhaled delivery may be needed. Several new treatments target the underlying allergic/immune process and would treat concomitant allergic diseases. Improved

immunotherapy approaches have the potential for disease modification, although prospects for a cure are currently remote.

Eosinophilic airway inflammation is often present in asthma, and reduction of such inflammation results in improved clinical outcomes. Recently researchers have found a new drug that is fevipiprant, an antagonist of prostaglandin D2 receptor 2, might reduce eosinophilic airway inflammation in patients with moderate-to-severe eosinophilic asthma[2]. A single-centre, randomised, double-blind, parallel-group, placebo-controlled trial conducted at Glenfield Hospital (Leicester, UK). They recruited patients with persistent, moderate-to-severe asthma and an elevated sputum eosinophil count (≥2%). Patients were randomly assigned (1:1) by the trial pharmacist, using previously generated treatment allocation cards, to receive fevipiprant (225 mg twice per day orally) or placebo. The 12-week treatment period was followed by a 6-week single-blind placebo washout period[3]. The primary outcome was the change in sputum eosinophil percentage from baseline to 12 weeks after treatment. All patients who received at least one dose of study drug were included in the safety analyses. Between Feb 10, 2012, and Jan 30, 2013, 61 patients were randomly assigned to receive fevipiprant (n=30) or placebo (n=31). Three patients in the fevipiprant group and four patients in the placebo group withdrew because of asthma exacerbations. Two patients in the fevipiprant group were incorrectly given placebo (one at the mid-treatment visit and one throughout the course of the study). They were both included in the fevipiprant group for the primary analysis, but the patient who was incorrectly given placebo throughout was included in the placebo group for the safety analyses. Between baseline and 12 weeks after treatment, sputum eosinophil percentage decreased from a geometric mean of 5•4% (95% CI 3•1–9•6) to 1•1% (0•7–1•9) in the fevipiprant group and from 4•6% (2•5–8•7) to 3•9% (CI 2•3–6•7) in the placebo group. Compared with baseline, mean sputum eosinophil percentage was reduced by 4•5 times in the fevipiprant group and by 1•3 times in the placebo group (difference between groups 3•5 times, 95% CI 1•7–7•0; p=0•0014). Fevipiprant had a favourable safety profile, with no deaths or serious adverse events reported. No patient withdrawals were judged by the investigator to be

related to the study drug. Fevipiprant reduces eosinophilic airway inflammation and is well tolerated in patients with persistent moderate-to-severe asthma and raised sputum eosinophil counts despite inhaled corticosteroid treatment.

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