

Prospective Asthma Treatments; Future Perspectives

PM O'BYRNE

Firestone Institute for Respiratory Diseases,
Department of Medicine, McMaster University,
Hamilton, Ontario, Canada.

Most asthma patients can be well controlled on medications that are currently available, and which are both effective and safe (1). However, 5-10% of asthma patients have severe refractory asthma, and do not achieved asthma control, even with high doses of inhaled corticosteroids (ICS), usually in combination with long-acting inhaled β_2 -agonists (LABAs), and other maintenance treatments (2).

A variety of approaches have been used to attempt to improve outcomes in patients with severe refractory asthma. These have included optimizing bronchodilation; reducing airway smooth muscle; reducing airway inflammatory cell number and/or activity; and targeting specific airway effector mediators.

The most promising treatment approaches currently under investigation are those which reduce airway eosinophils in patients with severe refractory asthma and a persisting airway eosinophilia. Monoclonal antibodies (hMab) against IL-5 have been shown to improve lung function, improve asthma control, reduce exacerbation risk and allow reduction or elimination of maintenance oral corticosteroids in this subset of patients (3;4).

Bronchial thermoplasty may provide benefit in improving control and reducing exacerbations in selected patients (5). Bronchial thermoplasty is a bronchoscopic

therapeutic procedure where the airways are heated using radiofrequency energy to 65°C. The procedure is done using a catheter passed through the bronchoscope, and can only treat the larger airways (6). A complete period of treatment requires three bronchoscopies, spaced several weeks apart. There is convincing evidence that the procedure reduced the volume of airway smooth muscle in the treated airways (7).

The addition of the muscarinic antagonist, tiotropium also improves airflow obstruction (8;9). One issue that the studies did not address, however, is whether tiotropium plus ICS has a beneficial effect in reducing the risks of severe asthma exacerbations that is an important benefit of the combination of ICS plus LABA (10).

Other developments being evaluated in severe refractory asthma are CXCR2 (the IL-8 receptor) antagonists in patients with a persisting neutrophilic airway inflammation (11), and CRTh2 antagonists (12), both of which are small molecule antagonists, and hMabs against IL4 and IL-13 (13;14). Finally, another approach to reduce receptor numbers, using inhaled anti-sense, has shown to reduce allergen-induced airway eosinophilia (15), and combining different anti-sense against different targets may become a feasible treatment option.

A variety of new treatment options are being investigated to help improve overall asthma control in patients with severe refractory asthma. These include medications to optimize lung function; bronchial thermoplasty to reduce airway smooth muscle in central airways; and those which target specific inflammatory cells or receptors of inflammatory mediators.

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Ref Type: Abstract
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