Evaluation of New Drugs for Asthma and COPD: Endpoints, Biomarkers and Clinical Trial Designs

P. J. Barnes · E. M. Erin · T. T. Hansel · S. Kharitonov · A. J. Tan · R. C. Tennant

NHLI Clinical Studies Unit, Royal Brompton Hospital, Fulham Rd., London, SW3 6HP, UK
e-mail: t.hansel@ic.ac.uk

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Abstract The incidence of both asthma and chronic obstructive pulmonary disease (COPD) is increasing throughout the world, and acts as a major incentive for the development of new and improved drug therapy. For the large range of bronchodilator and anti-inflammatory agents in current clinical development, reliable decision-making is imperative in phase II, before entering large-scale phase III clinical studies. With anti-inflammatory therapies for asthma, many studies have been performed utilising the inhaled allergen challenge as a proof of concept study, effects on airway hyper-reactivity (AHR) can be assessed, and it is also possible to directly study limited numbers of symptomatic asthma patients. Additional clinical trial designs in asthma include studies to assess bronchodilation, bronchoprotection against a variety of inhaled constrictor agents, exercise tolerance, add-on and titration studies with inhaled and oral corticosteroids, and prevention and treatment of exacerbations. In contrast, it is a major issue for the development of new anti-inflammatory drugs for COPD that large-scale phase II studies are generally required in this disease in order to detect clinical efficacy. In COPD, clinical trial designs range from studies on lung function, symptoms and exercise performance, inflammatory biomarkers, natural history of chronic stable disease, prevention and treatment of exacerbations, and effects on cachexia and muscle function. Compared with asthma, inclusion criteria, monitoring parameters, comparator therapies and trial design are less well established for COPD. The large variety of potential clinical endpoints includes lung function, symptoms, walking tests, hyperinflation, health-related quality of life (HR-QOL), airway reactivity, and frequency and severity of exacerbations. In addition, surrogate biomarkers may be assessed in blood, exhaled breath, induced sputum, bronchial mucosal biopsy and bronchoalveolar lavage (BAL), and advanced radiographic imaging employed. Of particular utility is ex vivo whole blood stimulation to enable pharmacokinetic/pharmacodynamic modelling in establishing an optimal dosage regimen relatively early in human clinical studies. There have been considerable recent advances in the development of non-invasive biomarkers and novel clinical trial designs, as well as clarification of regulatory requirements, that will facilitate the development of new therapies for patients with asthma and COPD.

Keywords Asthma · COPD · Clinical trial designs · New drugs · Endpoints · Biomarkers