

Clinical Trial Design Considerations in Assessing Long-Term Functional Impacts of Tiotropium in COPD: The Uplift Trial [1](#)

Authors: Marc Decramer ^a; Bartolome Celli ^b; Donald P. Tashkin ^c; Romain A. Pauwels ^d; Deborah Burkhardt ^e; Cara Cassino ^e; Steven Kesten ^e

Affiliations:

^a Respiratory Division, University Hospitals, Leuven, Belgium

^b Saint Elizabeth's Medical Center, Boston, Massachusetts, USA

^c David Geffen School of Medicine at UCLA, Los Angeles, California, USA

^d University Hospital, Ghent, Belgium

^e Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, USA

Abstract

An accelerated loss of lung function is one of the defining characteristics of chronic obstructive pulmonary disease (COPD). To date, the only successful intervention shown to conclusively attenuate the loss of lung function over time is smoking cessation. Pharmacological interventions including inhaled corticosteroids and ipratropium bromide have not altered the rate of decline of lung function. Tiotropium is an inhaled anticholinergic that provides 24-hour bronchodilation with once-daily dosing due to prolonged muscarinic M3 receptor blockade. Controlled clinical trials have suggested sustained efficacy for periods of up to one year. We therefore initiated a four-year, controlled clinical trial (UPLIFT, Understanding the Potential Long-Term Impacts on Function with Tiotropium) in patients with COPD to evaluate the long-term effects of tiotropium on the rate of decline in lung function and health status as well as the frequency of exacerbations. The design of such large, long-term clinical trials presents unique methodological challenges including the definition of endpoints, the quality and variability of spirometric measurements and premature patient discontinuations from the trial. The present manuscript outlines the rationale for the UPLIFT study, and reviews the study design and the steps taken to address methodological challenges experienced in other long term studies. Careful design and implementation of the UPLIFT trial is anticipated to yield high quality results that will help in increasing our understanding of the long term natural history of COPD in a global population as well as to elucidate the role that tiotropium can play in affecting the course of this debilitating disease.

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