EDITORIAL

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Time to Prescribe Dual instead of Mono

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Chronic obstructive pulmonary disease (COPD) is one of the most common diseases with profound morbidity and mortality[1]. Inhaled long-acting bronchodilators are the cornerstones of treatment; these not only control symptoms but also prevent exacerbation events and attenuate the decline in lung function[2]. Historically, tiotropium (TIO) was the first approved long-acting muscarinic antagonist (LAMA), and was one of the most commonly used inhalers in COPD patients, past decades[3]. Recent reports revealed that newly developed long-acting β2-agonist (LABA)/LAMA combinations showed superior outcomes compared with monobronchodilators and inhaled corticosteroid/LABA combination in terms of symptom control, attenuation of lung function decline and exacerbation[3]. Regarding these results, analyses of clinical outcomes in switching from a monobronchodilator to dual bronchodilators may give us some clues in treating COPD patients who have formerly used monobronchodilators.

Lee et al.[4] performed a 12-week, randomized, parallel group trial on patients with mild to moderate COPD who formerly used TIO. After randomization to indacaterol/glycopyrronium (IND/GLY) and TIO groups, the former group immediately changed their medication and the TIO group did not. After 12 weeks of their challenge, the clinical outcomes (including the pre-dose trough forced expiratory volume in 1 second [FEV_1], the transition dyspnea index [TDI] focal score, the COPD assessment test [CAT] total score and rescue medication use) were analyzed. The change in pre-dose trough FEV_1 (the primary outcome) showed significantly superior in the IND/GLY group compared to TIO group (least square mean treatment difference [Δ] 50 mL; p=0.01). The changes in the TDI focal scores, CAT total scores, and rescue medication use did not differ between the groups but tended to be better in IND/GLY group. Safety index showed comparable between the two groups.

The Canadian real-world POWER study was similar to that of Lee et al.[4,5]. The trough FEV_1 improved by 176 mL by week 16 after switching from TIO to IND/GLY (70 mL, in Lee et al.[4]), and the mean TDI total scores and CAT scores also significantly improved. The safety profiles of the two groups were comparable. The CRYSTAL study, which was a multicenter randomized controlled study that investigate efficacy of direct switching to IND/GLY in moderate COPD patients, revealed more favorable outcomes in an IND/GLY group than in a monobronchodilator continuation group in terms of the trough FEV_1 (Δ, 101 mL) and TDI score (Δ, 1.26)[6]. Moreover, recent pooled analyses of the SHINE[7], SPARK[8], and ARISE[9] trial data enrolling long-acting bronchodilator-naïve moderate-to-very severe COPD patients presented greater improvement in trough FEV_1 in an IND/GLY compared to a TIO group (Δ, 86 mL), in line with study of Lee et al.[4,10].

These diverse studies of different study designs correspondingly support use of IND/GLY rather than TIO in previous TIO users and bronchodilator-naïve patients in COPD patients. However, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2020 guideline recommends initial use of monobronchodilator for groups B and C, and permits such usage in group D patients[11]. As the study of Lee et al.[4] also includes mild COPD patients, the results may imply necessity of dual bronchodilators in their earlier course of the disease. The pharmacological effects of switching from TIO to IND/GLY in various GOLD subgroups have not been investigated; subgroup analyses may be important when choosing an optimal initial therapy.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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