

Efficacy and safety of varenicline for smoking cessation in patients with mild to moderate
Chronic Obstructive Pulmonary Disease (COPD)

Donald Tashkin, MD; Stephen Rennard, MD; J. Taylor Hays, MD; Wendy Ma, MS; Theodore C.
Lee, MD

Word limit: 330 words (without the title)

Current word count: 324

Purpose: Smoking is the most important cause of Chronic Obstructive Pulmonary Disease (COPD) and accelerates its progression. Finding effective smoking cessation interventions for this population is paramount. The primary objective of this randomized clinical trial was to compare the efficacy and safety of varenicline versus placebo in smokers with mild–moderate COPD.

Methodology: In a 27 center, double-blind, multinational study, patients with mild–moderate COPD (post-bronchodilator FEV₁/FEV <70% and FEV₁ % predicted normal value ≥50%) were randomized to receive varenicline (titrated to 1 mg BID) or placebo for 12 weeks, with a 40-week non-treatment follow-up. The primary endpoint was carbon monoxide (CO)-confirmed continuous abstinence rate (CAR) for Weeks 9–12. A secondary endpoint was CAR for Weeks 9–52. Adverse events (AEs) and safety parameters were monitored.

Results: Mean (± SD) baseline characteristics for all subjects were: age 57.1 (9.1) yrs; FEV₁ 2.28 (0.66) Liters; post-bronchodilator FEV₁ 69.9 (16.9) % pred; number cigs/day over past month 24 (11); smoking duration 41 (9) yrs; age commenced smoking 16 (4) yrs; Fagerström Test for Nicotine Dependence score 6.1 (2.2). 62.3% of participants were male and 83.0% Caucasian. Randomized and treated patients were included in the

efficacy and safety analysis (varenicline, n=248; placebo, n=251). Week 9–12 CAR was significantly higher for varenicline (42.3%) versus placebo (8.8%; $p<0.0001$; OR=8.40; 95% CI, 4.99, 14.14). Greater varenicline efficacy was maintained during Weeks 9–52 (varenicline CAR 18.6% vs placebo CAR 5.6%; $p<0.0001$; OR=4.04; 95% CI, 2.13, 7.67). Nausea, abnormal dreams, and insomnia were the most commonly reported AEs for varenicline. Serious AEs occurred in 2.8% varenicline participants and 4.4% placebo participants. Two varenicline patients and one placebo patient died during the study. One suicidal ideation event was reported for placebo; no such event was reported for varenicline. Reports of depression, depressed mood, and depressive symptoms were similar for both treatment groups.

Implications: Varenicline is an efficacious and safe pharmacologic treatment for smoking cessation among patients with mild–moderate COPD.