New hope for smokers who decide to quit

Smoking cessation remains a major problem for the numerous tobacco-dependent smokers willing to quit. The aim of this study was to investigate the efficacy and safety of a new cytosine-derived product, varenicline (Champix®), which combines a moderate stimulation of dopamine release (with “rewarding” effects relieving nicotine-withdrawal symptoms) with a blockade of the nicotine receptors (reducing the rewarding effect of smoke nicotine in the event of a “lapse” after quitting).

Methods
In a multicentre double-blind placebo-controlled study with a 12-week treatment period, 1,027 smokers who smoked ≥10 cigarettes per day during the previous year were randomised to varenicline 1 mg b.i.d. or bupropion SR 150 mg b.i.d. (both with an initial dose titration to full strength during the 1st week) or placebo, given for a full week before the target quit date. Frequent psychological support was provided during the treatment period, but also during the follow-up until week 52, at each visit and by intermediate telephone calls.

Results
Demographic and smoking characteristics were similar in the three groups, with a mean smoking history of ~25 years, mean number of cigarettes smoked >20 per day and a rather high mean Fagerström 6-item test of nicotine dependence (>5).

Subjects were considered as abstinent participants whose nonsmoking status was known when they had an exhaled carbon monoxide measurement ≤10 ppm at every visit; for the missed visits, a self-report of no tobacco or nicotine use during the preceding period was accepted.

During weeks 9–12 and 9–52, varenicline was superior to placebo and bupropion in terms of continuous abstinence (OR 1.77 at end of study in comparison with bupropion).

Withdrawal symptoms and cravings (weeks 1–7) decreased as well as smoking reinforcement both after varenicline and bupropion, significantly more than after placebo. Nausea was the most commonly reported adverse event for varenicline (29.4%), but induced treatment discontinuation in 2.3% only. Insomnia (14.3%) and abnormal dreams (13.1%) were also observed with varenicline.

Altogether, discontinuation of the study medication due to adverse events occurred in 10.5% of the varenicline group, 12.6% of the bupropion group and 7.3% of the placebo group. A total of 35% of the participants did not complete the follow-up period.

Editorial comments
Varenicline appears to be a potent pharmacological product for cessation when supported with a frequent and long-lasting, albeit moderate, psychological intervention in smokers after the exclusion of former bupropion use and comorbidities. The validity of this study is confirmed by another multicentre evaluation of 1,025 smokers who were motivated to quit with similar results [1]. An additional 12-week varenicline therapy among those who succeeded in quitting after an open-label varenicline therapy of 12 weeks’ duration obtained a 13–52 week significantly greater albeit limited continuous cessation rate compared with placebo (43.6 versus 36.9%) [2].

These excellent results from clinical trials will probably become less satisfactory in normal everyday practice, where psychological support is less regular and where other types of smokers (including dis-eased people) are treated.

Long-term safety also needs to be confirmed by pharmacovigilance, which could show rare collateral effects. However, this product evidently enlarges our cessation armamentarium.

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References

Message
Varenicline is more efficacious than placebo, nicotine-replacement therapy and bupropion for smoking cessation.