French study confirms the safety and effectiveness of varenicline for HIV-positive smokers

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- People living with HIV are known to be at increased risk for smoking-related illnesses.
- Researchers find varenicline safe and effective at helping people with HIV quit smoking.
- Cessation counsellors who are infectious disease specialists have higher quit rates.

The widespread use of potent HIV treatment (ART) has led to improved measures of health and near-normal life expectancy for many people with HIV in Canada and other high-income countries. However, studies have found that ART users who smoke tobacco are at heightened risk for smoking-related illnesses, including cardiovascular disease and some cancers. As a result, their life expectancy will likely be shortened. Giving ART users who smoke the support and help they need to quit should therefore be a part of routine efforts to improve their health and longevity.

Researchers in France conducted a well-designed study of the smoking cessation medicine varenicline (Champix, Chantix) vs. placebo. They found that varenicline was significantly better than placebo at helping people quit, however, overall, its effects were modest. Furthermore, they judged varenicline to be generally safe.

Based on these results and the many health benefits of smoking cessation, the researchers encourage healthcare providers to offer smoking cessation assistance to their HIV-positive patients.

Study details

Researchers recruited participants who were motivated to quit smoking (as assessed by a questionnaire). Having any other addictions, suffering from depression and having previously used varenicline disqualified people from participating in this study.

Participants who received varenicline were given gradually increased doses so as to minimize the risk of developing nausea.

All participants received individualized face-to-face counselling sessions. The counsellors had been trained in encouraging behavioural change in smokers. During the first session, counsellors initially explored participants’ motivations and fears about quitting. Participants could have up to 15 counselling sessions over the course of the study.

The study had a complex design, as follows:

- For the first 12 weeks participants took either varenicline or placebo pills and underwent counselling.
- This was followed by a period of 13 consecutive weeks of no pills; counselling continued.
- At the 26th week, participants who had initially quit and who relapsed during the study were offered a 12-week course of varenicline. Those who accepted this offer were monitored up to the 48th week of the study after they completed the 12-week course of varenicline.

The average profile of participants upon entering the study was as follows:

- age ~ 45 years
- 83% men, 17% women
- duration of HIV diagnosis – 13 years
- taking ART – 94%
- having a viral load less than 50 copies/mL – 76%
- years of smoking – 26
- history of trying to quit smoking at least once – 82%

Participants had regular study appointments for assessments, including measurement of carbon monoxide levels in exhaled air (to confirm abstinence from smoking).

**A note about placebo**

The placebo was designed to have a similar “presentation, colour, taste and smell” to varenicline. According to the researchers, the placebo was designed to be “biologically inactive”; that is, it would not cause any effect on participants. As the trial was double-blind, the participants and researchers (except for one) did not know who received varenicline or placebo until after the end of the study. This blinding was important, as during the study researchers were asked to assess any perceived problems (symptoms, complications) that participants reported and decide if they were caused by the study medication.

A total of 123 participants were randomized to receive varenicline and 124 participants received placebo for the first 12 weeks of the study.

**Results—Short term**

Researchers initially focused on quit rates that occurred starting at week nine to the end of week 12 on varenicline or placebo. During this period quit rates were as follows:

- varenicline – 29% of participants were able to quit
- placebo – 11% of participants were able to quit

This difference was statistically significant; that is, not likely due to chance alone.

**Results—Long term**

When researchers took all of their data into account from weeks nine to 48, the proportions of participants who were able to remain free from smoking were distributed as follows:

- varenicline – 15% of participants were able to quit
- placebo – 6% of participants were able to quit

Although more people who used varenicline compared to placebo quit smoking, the proportion of varenicline users who quit is modest.

**Impact of the counsellor on quitting**

There were two types of counsellors deployed during the study, which took place at hospital clinics. One was a smoking cessation counsellor, called a tobaccologist, who specialized in helping mostly HIV-negative people quit smoking. The other counsellor was an infectious disease specialist who also had experience and training in helping patients quit smoking. When researchers analysed quit rates by the type of counsellor, they found the following results at week 48:

**Varenicline**

- infectious disease specialist counsellor – 20% were not smoking
- regular smoking cessation counsellor – 11% were not smoking

**Placebo**

- infectious disease specialist counsellor – 13% were not smoking
- regular smoking cessation counsellor – 3% were not smoking
These differences in quit rates by the type of counsellor were statistically significant. The researchers suspected that these differences “might reflect the use of a more tailored intervention by the infectious disease specialist because, for example, they might be able to understand specific barriers faced by people living with HIV, which might be less prevalent in the general population that a tobacccologist is familiar with.”

Safety

The term adverse events is used to describe a range of unfortunate incidents that can occur in a clinical trial. Only some of these events are caused by the study medicine(s). As this was a placebo-controlled study, researchers have a good idea of which side effects were caused by varenicline.

According to the researchers, “most adverse events were [mild-to-moderate intensity] and were mainly gastrointestinal or [neuropsychiatric].”

The proportions of participants with an adverse event that was judged to be related to the study medicines (for this report we include placebo as a medicine) were distributed as follows:

- varenicline – 48% (49 people)
- placebo – 39% (43 people)

The proportions of participants with an adverse event that was judged to be related to the study medicines (for this report we include placebo as a medicine) and that was judged to be serious were distributed as follows:

- varenicline – 7% (seven people)
- placebo – 6% (seven people)

The difference in distribution rates was not statistically significant.

These serious adverse events were distributed as follows (some participants reported more than one adverse event):

Sleeping problems
- varenicline – two people
- placebo – two people

Depression
- varenicline – one person
- placebo – one person

Behavioural disorders (details were not provided)
- varenicline – two people
- placebo – one person

Drowsiness
- varenicline – one person
- placebo – zero

Headache
- varenicline – one person
- placebo – zero

Digestive disorders
- varenicline – zero
- placebo – two people
Ringing in the ears
- varenicline – zero
- placebo – one person

Feeling weak
- varenicline – one person
- placebo – one person

No one died as a result of the study medicines. One person died from wounds sustained from a physical assault unrelated to the study.

**Focus on depression**

Some studies suggest that people with mental health issues may be more likely to smoke tobacco. Other clinical trials and analyses have assessed the safety of varenicline (including its potential risk for depression). In the present study, the proportions of people who developed depression during the study were as follows:
- varenicline – 2%
- placebo – 10%

Thus, exposure to varenicline likely did not increase the risk for depression in this study. Also, there was no significantly increased risk of cardiovascular complications (heart attack, stroke) among varenicline users.

**Lab test results**

The proportions of participants with very abnormal lab test results during the study were as follows (note that none of these were judged to be caused by the study medicines):
- varenicline – 3%
- placebo – 8%

There was no pattern to these abnormal lab tests, as different organ-systems were affected.

There was no impact of varenicline or placebo on CD4+ cell counts or viral load.

**Bear in mind**

This well-designed study showed that varenicline resulted in modest recovery in a group of longtime smokers. Varenicline (combined with counselling) can clearly help some HIV-positive people to quit smoking. Smoking cessation is difficult but necessary and it is possible that HIV-positive people have additional barriers that make smoking cessation more difficult than it is for HIV-negative people. Researchers in the United States who reviewed the results of the French study stated in a commentary in the journal *Lancet HIV* that “the characteristics associated with high smoking prevalence in [HIV-negative people] ...are probably also important barriers to smoking cessation in people living with HIV.” These barriers include the following:
- alcohol and/or other substance use
- co-existing mental health conditions
- low socio-economic status
- low levels of education

The U.S. reviewers said that one important result from the French study is that serious side effects from varenicline were uncommon and this should reassure potential prescribers. A smaller study done in Ontario several years ago also found that varenicline was safe and it helped some HIV-positive people quit smoking.

Both the reviewers and the study researchers encourage healthcare practitioners to offer smoking cessation to their patients who smoke.

**Resources**
How to Say “I Quit”—and Mean It - The Positive Side

Break it off – Health Canada

Tobacco and your health - Santé et services sociaux Québec

Get help to quit smoking - Canadian Cancer Society

How to quit smoking - The Lung Association

Understanding tobacco addiction - CATIE News

Varenicline—An Ontario study assesses safety in HIV-positive people - CATIE News

Smoking cessation: Innovative group therapy–centered support found to double quit rate - CATIE News

Danish study underscores link between heart attacks and smoking - CATIE News

—Sean R. Hosein

REFERENCES:


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