

## **VYTORIN & VASCULAR DISEASE** by *Ann Gerhardt, MD* (02/2008)

**Bottom Line at the Top: The verdict is still out on whether ezetimibe adds anything to simvastatin, when it comes to preventing vascular disease.**

**Vytorin** is a combination of ezetimibe and simvastatin. The ENHANCE trial (**E**zetimibe and **S**imvastatin in **H**ypercholesterolemia **E**nhances **A**therosclerosis **R**egression- a falsely hopeful acronym) compared the ability of Vytorin vs. simvastatin to reduce carotid artery wall thickening in people with genetically high cholesterol. The carotids are the major arteries to the brain. Carotid artery walls thickened by cholesterol and clot can eventually lead to the artery closing off, causing a stroke.

Though Vytorin lowers cholesterol more than does simvastatin, that did not translate into healthier carotid arteries. In fact, the carotids of people taking Vytorin had slightly thicker walls. ENHANCE's design did not allow statistical comparison of death and stroke rates in the two groups.

Ezetimibe lowers cholesterol by blocking the body's absorption of cholesterol from food and bile. Cholestyramine, one of the first cholesterol-lowering drugs, has the same mechanism of action and was proven long ago to reduce heart attacks. We don't use it much, because it is a grainy powder, tastes atrocious and has to be taken with each meal. Efforts to produce a cholesterol absorption blocker in a once-a-day-pill form ultimately resulted in ezetimibe. It reliably lowers cholesterol, though not as much as statins (lovastatin, Lipitor, Zocor, Pravachol, Crestor). So far we lack proof that it, like cholestyramine, reduces vascular disease risk or death.

Ezetimibe only lowers cholesterol, unlike many other drugs which reduce blood vessel clogging by mechanisms over and above cholesterol reduction alone. It is possible that ENHANCE's subjects, with genetically high cholesterol, needed more to improve carotid artery walls than ezetimibe's incremental cholesterol-lowering effect. A study comparing Vytorin and simvastatin's effects real outcomes, like death and heart attack, is underway.

Simvastatin's brand name is Zocor. Merck/Schering-Plough makes both Vytorin and Zocor. Zocor's patent has run out so the much cheaper generic simvastatin might cut into Merck/Schering-Plough's sales. The company stands to lose a lot of money if it can't prove that Vytorin is any better than simvastatin when it comes to saving lives.