

## EZETIMIBE (ZETIA)

The next drug used in lipid modulation we will talk about is Zetia. I will not talk about the results of the ENHANCE study other than to say that the official stance of the National Lipid Association is that on the basis of that study, zetia achieved the expected response in regard to LDL-C lowering and there were absolutely no safety issues. I know that there was an article in the New York Times recently that zetia was linked to cancer. This is totally false. I will admit to you that no outcome data on zetia will be available until 2011. A special article was published in the September 25, 2008 edition of the New England Journal of Medicine. The results from the SEAS, SHARP, and IMPROVE-IT trials were analyzed by Peto et al. There were over 20,000 patients included in these studies. The conclusion was that “the available results from these three trials do not provide credible evidence of any adverse effect of ezetimibe on rates of cancer.”

Zetia is a new class of drugs known as cholesterol absorption inhibitors. It inhibits the absorption of dietary and biliary cholesterol without affecting the absorption of Triglycerides or fat soluble vitamins. It also up regulates the number of LDL receptors in the liver. It works in the small intestine and inhibits cholesterol uptake and absorption. It has a half-life of 22 hours and this allows once daily dosing and it is not affected by food intake.

Zetia has been shown to reduce LDL-C in patients with hypercholesterolemia. Although some physicians use it as monotherapy, most lipidologists use it as an add on drug when cholesterol goals are not met on statin therapy. There is a low potential for drug interactions and zetia does not interact with statins.

Several randomized clinical trials with Zetia 10 mg have demonstrated decreases of LDL-C of 17-18.2%, decreases in total cholesterol of 12%, and increases of HDL of 1.3%. Zetia combined with statins has been studied in 4 randomized clinical trials and the efficacy of the combination in lowering LDL-C was superior to the statin alone. For example, in one study, zetia 10mg/Lipitor 10mg was as effective as Lipitor 80mg. One must remember that as the statin dose is increased the side effects are also increased so it is much better to use a lower statin dose combined with Zetia.

In terms of safety, Zetia is a very safe drug. The incidence of elevations in liver enzymes greater than three times normal ranges from 0-0.8% with statin monotherapy compared with 0-2.2% with Zetia plus statin co-administration.