Ezetimibe Gets LDL to Goal in High-Risk Patients

**BY BRUCE JANCIN**  Denver Bureau

**Barcelona** — Adding 10 mg/day of ezetimibe to maximum dose rosuvastatin in a high-risk population enabled 94% of patients to achieve an LDL level below 100 mg/dL and 80% to get below 70 mg/dL, Dr. Christie M. Ballantyne reported at the joint meeting of the European Society of Cardiology and the World Heart Federation.

The combination also tripled the success rate in achieving both an LDL-cholesterol level below 70 mg/dL and a high-sensitivity C-reactive protein level (CRP) under 2.0 mg/L, compared with the results with 40 mg/day of rosuvastatin alone, added Dr. Ballantyne, professor of medicine at Baylor College of Medicine, Houston.

The National Cholesterol Education Program recommends the 70 mg/dL LDL target as an optional, more aggressive goal in very high-risk patients. Getting the CRP below 2.0 mg/L is not recommended in any major guidelines; however, a secondary analysis of the PROVE-IT trial concluded that rates of recurrent MI or cardiovascular death were lower in patients who achieved their LDL target.

To target LDLs of 190 mg/dL by 35%, and it reduced events by 35% with a 42% decrease in CHD mortality. So to me it’s amazing that here we are 12 years later and we’re still doing a study where we’re not reducing them by 70%, down to a mean of 57 mg/dL, and with an LDL-to-HDL ratio of just about 1,” the physician said.

Both treatments were well tolerated. The price paid in terms of side effects for combination therapy’s greater efficacy was limited to an increased incidence of abnormal liver function tests, rising from 0.4% with rosuvastatin alone to 2.5%.

“Dr. Ballantyne has received research support and consulting fees from AstraZeneca, which sponsored the EXPLORER trial. Dr. Ballantyne has received research support and consulting fees from AstraZeneca and from Merck Schering Plough, which markets ezetimibe.

Eating Nuts Tied to Highly Significant Drop in CHD Death Risk

**BY BRUCE JANCIN**  Denver Bureau

**Barcelona** — Consuming nuts, especially tree nuts, showed a powerful dose-response protective effect against coronary heart disease mortality in the largest-ever prospective cohort study focusing on the relationship between diet, cancer, and cardiovascular disease.

New results from the European Prospective Investigation Into Cancer and Nutrition (EPIC) indicate that participants who consumed two servings of nuts per week had an adjusted highly significant 16% reduction in risk of death from coronary heart disease (CHD), compared with those who rarely or never ate nuts, Dr. Joan Sabate said at the joint congress of the European Society of Cardiology and the World Heart Federation.

“Not a lot of nuts. Roughly 20 almonds, for example, constitute a serving. Two servings per week translate into 56 g, or an average of 8 g/day. And since EPIC also showed nearly half of Europeans rarely consume nuts, the potential exists for a major cardiovascular public health impact through a quite modest dietary change,” said Dr. Sabate, professor of medicine and chairman of the department of nutrition at Loma Linda (Calif.) University.

EPIC enrolled more than a half-million adults in 10 European countries during the 1990s. Dr. Sabate reported on 399,633 of those subjects, of whom 1,157 experienced a fatal coronary event during prospective follow-up.

Detailed dietary assessments backed by rigorous 24-hour diet recall validation studies in a subset of 37,000 subjects permitted categorization of EPIC participants into four quartiles based on nut consumption: those who rarely ate nuts, averaging less than 1 g/day, low consumers, defined as individuals who consumed at least 1 g but less than 4 g/day; subjects eating more than 4 g but less than 13 g/day, and high consumers, who averaged at least 13 g/day. Dr. Sabate and his coinvestigators found the risk of CHD death was 12% less in minimal consumers of nuts, compared with rare or never nut eaters; 10% less in midrange consumers; and 24% less in the highest quartile for nut consumption. These risk reductions were calculated after adjusting for conventional cardiovascular risk factors, consumption of fish and other healthy foods, smoking status, systolic blood pressure, diabetes, and other potential confounders.

The new EPIC findings are consistent with the results of the Adventist Health Study, the Iowa Women’s Health Study, the Nurses Health Study, and the Physicians Health Study.

Why then, do another study? The first four were conducted in Americans, whose pattern of nutrient consumption is quite different from that of many Europeans. Americans get much of their nut intake from peanut butter.

Many Europeans eat mainly tree nuts, such as walnuts, almonds, and hazelnuts. The French often eat nuts with wine as an appetizer, for example, while in Barcelona nuts often go into sauces. So there was a question about the generalizability of the earlier findings in studies conducted in the United States, Dr. Sabate explained.

In EPIC, the cardioprotective effect of nuts was strongest in countries where consumption of tree nuts predominates: Denmark, France, Germany, Greece, Italy, and Spain. In the Netherlands, Sweden, and the United Kingdom, where peanuts predominate, the dose-response benefit was weaker.

Mechanisms of nuts’ cardioprotective benefit backed by supporting research include a cholesterol-lowering effect derived from plant protein and fiber, as well as the anti-inflammatory effect of rich vitamin E content. Nuts also stimulate release of arginine, a precursor of nitric oxide, which plays a key role in improving endothelial function, the physician continued.

Audience members expressed concern that encouraging consumption of nuts, a calorie-dense food, could promote weight gain at a time when obesity is epidemic. Dr. Sabate replied that this hasn’t been seen in controlled dietary intervention trials, perhaps because eating nuts promotes satiety. One such recently published intervention trial (Am. J. Clin. Nutr. 2006;83:582) described how at the congress by its principal investigator, Dr. David J.A. Jenkins. He placed 66 hyperlipidemic patients for 1 year on a diet he developed called the Portfolio Eating Plan. It is a vegetarian, dairy-free, eggless diet utilizing plant sterol margarine, soy protein, viscous fibers from oatmeal and other sources, and 23 g of whole almonds daily.

At the end of 1 year, subjects had a mean 13% reduction in LDL cholesterol level, comparable to what might be seen with starting-dose statin therapy. Thirty-two percent of participants—those most adherent—had an LDL-cholesterol reduction in excess of 20%, added Dr. Jenkins, professor of medicine and holder of the Canada Research Chair in Nutrition and Metabolism at the University of Toronto.

The EPIC study was partially funded by the International Nut and Dried Fruit Council.