Clinical Trial Highlights

IDEAL—Lowering CHD Risk with High-Dose Statins

The IDEAL (Incremental Decrease in Clinical Endpoints Through Aggressive Lipid Lowering) Trial compared high and low doses of statins over a five-year time period. The primary endpoint was a composite of heart attack, coronary heart disease death, or cardiac arrest with resuscitation. Secondary endpoints included the primary events plus unstable angina that required hospitalization, coronary artery bypass graft (CABG), or percutaneous coronary intervention (PCI).

IDEAL "begins where 4S left off," according to lead investigator Torje Pedersen, MD, professor of medicine at Ulleval University Hospital and director of the Center for Preventive Medicine in Oslo, Norway. Pedersen was also lead investigator on the Scandinavian Simvastatin Survival Study (4S), the 1994 study that demonstrated statin efficacy and launched the statin era. "One of our persistent questions at the end of 4S," Pedersen said, "was about statin dose—is the lipid-lowering effect of statins dose-related?"

The Pfizer-sponsored trial studied 8,888 patients, average age 62 and 19 percent female. Participants received either 80 mg of atorvastatin vs. 20 mg of simvastatin. In those patients whose total cholesterol exceeded 193 mg/dL and/or LDL remained above 115 mg/dL after six months, the simvastatin dose was raised to 40 mg.

High-dose statins reduced the risk of cardiovascular events by 16% compared to low-dose statins at the end of the study's 4.8 years of follow-up. In terms of the primary endpoint, high-dose statins produced an 11% decrease in events (P=0.07), not statistically significant in comparison with low-dose statins. "The overall benefits apparent in this trial were more modest than we expected," Pedersen said, but he noted that after a post-hoc analysis adjusting for risk factors in the primary endpoint, findings did reach statistical significance.

IDEAL: Baseline and follow-up levels of LDL cholesterol

Study arm	Baseline (mg/dL)	1 year (mg/dL)	5 years (mg/dL)
Simvastatin 20 mg	121.4	102.0	99.8
Atorvastatin 80 mg	121.6	79.1	80.0

Overall, high-dose statins reduced secondary endpoints by 16% and nonfatal heart attacks by 17%. The high-dose group saw average LDL reductions to 81 mg/dL, compared with 104 mg/dL in the low-dose simvastatin group. Pedersen said researchers observed a marked reduction in revascularization procedures among high-dose study participants, and this group also saw no increase in risk of non-cardiac deaths compared to patients in the low-dose group—an observation that should "calm concerns that high-dose statins contribute to excess non-cardiac deaths such as cancer," according to Pedersen.

Pedersen also noted the relatively high number (24%) of study participants between the ages of 70 and 80. "Going back 20 years, the average age of a patient with a heart attack might have been 50," Pedersen said. "Now it is closer to 70." With an aging population living longer thanks in part to advances in medical technology and treatment, Pedersen recommended that clinical research consistently include older patients in study designs.

In general, Pedersen said that "our results were in line with other recent studies on the same question that also found that high doses of statins improve outcomes."