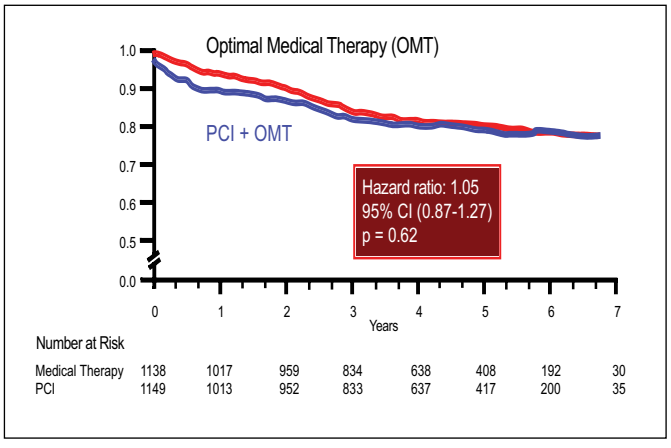
The study was conducted from 1999 to 2004 at 50 sites in the United States and Canada. Patients with myocardial ischemia and significant CAD were randomly assigned to either PCI with OMT (n=1,149) or OMT alone (n=1,138). OMT was defined as the best pharmacological treatment possible including medications such as aspirin, beta-blockers, statins (target LDL-C of 60 to 85 mg/dL), HDL-C raising therapies if required, and ACE inhibitors plus therapeutic lifestyle changes such as weight loss, improved diet, exercise, and smoking cessation. PCI was attempted in 1,007 patients; 1,006 received at least one stent. It is important to note that this study evaluated bare metal stents, as drug-coated stents were not yet available.

During follow-up, no differences were observed in the primary endpoint (HR=1.05; 95% CI, 0.87 to 1.27). Results were virtually identical for the secondary endpoint death, MI, and stroke (HR=1.05; 95% CI, 0.87 to 1.27; Figure 1). Additional analyses also indicated no differences in acute coronary syndrome hospitalizations (hazard ratio=1.07; 95% CI, 0.84 to 1.37) or MI (HR=1.13; 95% CI, 0.89 to 1.43). A similar number of patients required subsequent coronary artery bypass grafts (77 in the PCI group; 81 in the OMT group). Subgroup analyses did not reveal any interactions between the treatment effect and defined variables such as age, sex, or diabetes.

Figure 1. Survival Free of Death from Any Cause and Myocardial Infarction.



William S. Weintraub, MD, of the Christiana Healthcare System, Wilmington, Delaware gave a brief overview of the health status and economic outcomes data from the COURAGE study. Quality of life data was gathered by administering surveys including the Seattle Angina Questionnaire, the Rand 36, and the Utility by Gamble, at baseline, 1, 3, 6, and 12 months after randomization, and annually thereafter. The investigators found that angina improved in both treatment arms although the PCI group had a slight but significant incremental benefit compared to OMT. However, PCI was a more expensive choice for patients with stable CAD.

The authors concluded that the results of this study confirm the current American College of Cardiology/ American Heart Association clinical practice guidelines that state that PCI may be deferred in stable patients as long as OMT is initiated.

Succinobucol Treatment Leads to Mixed Signals

Succinobucol (AGI-1067) is a novel compound believed to reduce inflammation in blood vessel walls. Jean-Claude Tardif, MD, of the Montreal Heart Institute gave an overview of the findings from the Phase 3 randomized, double-blind Aggressive Reduction of Inflammation Stops Events (ARISE) study. This study, conducted at 261 sites in the United States, Canada, South Africa, and the United Kingdom, compared succinobucol to placebo in 6,144 patients with acute coronary syndrome (ACS). Eligible patients had been hospitalized 14 to 365 days prior to study entry with an acute myocardial infarction (MI) or unstable angina. The primary endpoint of the study was a composite of cardiovascular (CV) death, resuscitated cardiac arrest, MI, stroke, unstable angina, or coronary revascularization.

There were no significant differences between the succinobucol 300 mg/day group (n=3,078) and the placebo group (n=3,066) in terms of baseline demographic variables. The study failed to meet its primary endpoint and the survival curves of the two treatment groups were virtually identical.

"The two Kaplan-Meier curves are almost super-imposed and in fact there was an almost identical

number of primary events in both study groups. Basically the primary endpoint could not be more neutral than this," commented Dr. Tardif. Heart failure hospitalizations were higher in the succinobucol group. Succinobucol also caused a significant rise in low density lipoprotein-cholesterol (LDL-C; p<0.0001) and a significant decrease in high density lipoprotein-cholesterol (HDL-C; p<0.0001).

In a secondary measure of combined athero-thrombotic endpoints including CV death, cardiac arrest, MI, and stroke, a significant decrease was observed with succinobucol therapy (hazard ratio=0.81; 95% CI, 0.68 to 0.98; p=0.028). Other secondary analyses indicated that the time to new onset of diabetes was significantly reduced in the succinobucol arm, a finding that was further supported by improvement in glycated hemoglobin A1c and glucose (all p<0.001 vs placebo).

Serious adverse event rates were similar between the two groups. The most common adverse event associated with succinobucol was diarrhea (23% vs 8% for placebo). Although the study did not meet its primary endpoint, the investigators remain optimistic about the future of the drug.

Hawthorn Extract in CHF Patients: Results of a Controlled Study

Millions of patients worldwide purchase herbal supplements for their health and trust the manufacturers' claims. This burgeoning market, however, is often unregulated and a paucity of controlled data exist that support claims of safety and effectiveness. For this reason, the results of the randomized, double-blind, placebo-controlled multicenter Survival and Prognosis: Investigation of Crataegus Extract (SPICE) trial were greatly anticipated. Craetaegus extract in the form of the compound WS 1442 was studied versus placebo in patients with congestive heart failure (CHF). Crataegus extract (more commonly known as hawthorn extract) is available as an over the counter medication for the treatment of mild CHF (NYHA class 1 and class 2). Its purported mechanisms of action include vasodilation, positive inotropic effect, antioxidative properties, anti-ischemic effects, and anti-arrhythmic effects.

Dr. Christian Holubarsch, Median Kliniken Hospitals, Bad Krozingen, Germany presented the results of the study. The objectives of SPICE were to determine 1) if it was safe for patients to take WS 1442 concomitantly with existing medications and 2) what effects WS 1442 would have on measures of mortality and morbidity. The study was conducted at 156 centers in 13 European countries in patients with NYHA Class 3 CHF with a left ventricular ejection fraction of ≤35%. Patients received either WS 1442 900 mg/day or placebo and were followed for 24 months. The primary efficacy endpoint was a composite of cardiac mortality, non-fatal myocardial infarction, or hospitalization due to exacerbation of heart failure.

A total of 1,338 patients were randomly assigned to WS 1442 treatment; 1,343 received placebo. The study did not demonstrate significant differences between the two treatment groups in the composite primary endpoint. In a subanalysis, treatment with WS 1442 showed a significant effect in reduction of sudden cardiac death in patients with an LVEF ≥25% (p=0.025 at 24 months). In terms of safety, adverse event rates were similar between the two groups.

In conclusion WS 1442 is safe when patients take it in addition to their regular therapies, but did not reduce the composite of cardiac mortality, MI, or hospitalization for CHF. WS 1442 may reduce sudden cardiac death in a subpopulation of patients. The investigators were congratulated for undertaking a large controlled study of an herbal treatment, as well designed clinical trials in alternative and complementary medicine are sparse.

Reconstituted HDL Infusions Look Promising

Higher levels of high density lipoprotein cholesterol (HDL-C) have been associated with a reduction in risk of cardiovascular disease, largely through its reverse transport of cholesterol, anti-inflammatory and anti-oxidative properties. CSL-111 is a reconstituted HDL that is similar to native HDL. It is isolated from human plasma, with appropriate donor screening and purification steps to minimize the risk of disease transmission. The findings from the Effect of Reconstituted High-Density Lipoprotein