Drug Monitor

ONLINE EDITION

The Economics of High Dose Statin Therapy

It is well established that moderate statin therapy is clinically beneficial and economically attractive. And a few large trials have suggested that intensive, high dose therapy can result in further prevention of major cardiac events. But do these extra benefits justify the additional expense of the higher doses? That's the question investigators from the Treating to New Targets (TNT) trial—a multicenter, double-blind, randomized, controlled trial that compared high and low dose atorvastatin therapy—set out to answer through a prospective, economic substudy.

The TNT trial involved 10,001 patients with stable coronary artery disease (CAD) from 14 countries. Results from the main trial, which were published in 2005, showed that, over a median of five years of follow-up, a regimen of atorvastatin 80 mg/day reduced the risk of death from CAD, nonfatal myocardial infarction (MI), resuscitation from cardiac arrest, and stroke by 22%, compared with a regimen of 10 mg/day. There was no significant difference in all-cause mortality between the two groups.

The economic substudy was designed to compare the medical resource use and costs over the follow-up period for all 5,308 of the U.S. participants in the TNT trial and to analyze the cost-effectiveness of the high dose therapy. Although the researchers originally intended to collect cost data for all-cause hospitalization, administrative challenges limited their analysis to hospitalizations for potential endpoint events (such as death, nonfatal MI, decompensated heart failure, angina, coronary revascularization, stroke or transient ischemic attack, new peripheral vascular disease events or procedures, or resuscitated cardiac arrest) and selected outpatient cardiovascular procedures (such as percutaneous coronary interventions). They also did not collect resource and cost data on encounters they deemed unlikely to result in treatment-related differences (such as routine outpatient care costs, productivity costs, nonmedical costs, or data on outpatient medications other than the study drug).

At a cost of $1 more per day than the low dose regimen, the high dose regimen resulted in significantly fewer potential endpoint cardiovascular hospitalizations (35% versus 41%) and significantly fewer revascularization procedures (16% versus 22%) for the U.S. participants. Patients in the high dose group also spent fewer days in the hospital.

Based on an absolute reduction in the primary endpoint of 2.8 events per 100 treated patients, the cost of preventing one additional primary endpoint event with high dose therapy was $8,964. According to the researchers, this cost is similar to those associated with the use of drug-eluting stents in place of bare metal stents in patients with stable CAD and the use of early invasive therapy in place of conservative therapy in patients with acute coronary syndromes.

The researchers say that, while the lack of reliable cost and length of stay data on hospitalizations unrelated to potential primary endpoint events could have biased their results, they found no evidence of differences in distribution of these hospitalizations that would have favored the high dose group. Although they used the average wholesale price of atorvastatin discounted by 15% to calculate drug costs, they determined through a sensitivity analysis that using a discounted retail price would not have altered the study results. They did find that substituting generic simvastatin (40 mg/day) for the low dose atorvastatin regimen would have increased the cost of preventing a primary endpoint event with high dose atorvastatin to more than $80,000. They point out, however, that atorvastatin is projected to go off patent in the United States around 2011, at which time high dose atorvastatin therapy could become "economically dominant over generic simvastatin therapy."

Source: *Am Heart J.* 2008;156(4):698–705. doi:10.1016/j.ahj.2008.05.032.

Higher Risk of Venous Thromboembolism with Bevacizumab

Patients with cancer who receive bevacizumab may have a higher risk of venous thromboembolism (VTE) than those not receiving the drug, according to a meta-analysis by researchers from Stony Brook University, Stony Brook, NY and Kidney Doctor PLLC, Port Jefferson Station, NY. The antiangiogenic drug is used widely in treating many types of cancer.

Examining data from 7,956 patients with a variety of advanced solid tumors (including breast, colorectal, renal cell, and non–small cell lung cancers and mesotheliomas), the researchers found that those patients treated with bevacizumab and concurrent standard therapy had a significantly higher risk of both all-grade and high-grade VTE compared with control patients who received standard therapy alone. The

risk was increased for patients taking either a low dose (defined by the researchers as 2.5 mg/kg/week) or a high dose (defined by the researchers as 5 mg/kg/week) of the drug.

The summary incidence of all-grade VTE was 12% and the summary relative risk (using a fixed-effects model) was 1.33 (95% CI, 1.13–1.56). Among the different cancer types, colorectal cancer was associated with the highest incidence of all-grade VTE (19.1%; 95% CI, 16.1%–22.6%) and renal cell cancer was associated with the lowest (3%; 95% CI, 1.6%–5.5%).

VTE is a major complication of cancer, one of the leading causes of death in patients with cancer, and an emerging problem with many angiogenesis inhibitors, the researchers say. They add that identifying the risks associated with a drug such as bevacizumab is a challenge because many randomized, controlled trials may not be big enough to reveal the relationship; their meta-analysis included 15 studies.

Source: *JAMA.* 2008;300(19):2277–2285. doi:10.1001/jama.2008.656.