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Bone-drug study finds heart benefit

'Designer estrogen' may lower risks

By Rita Rubin
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A drug used to fight osteoporosis in postmenopausal women might also reduce the chance of a heart attack in those most at risk, suggests a study out today.

Raloxifene, sold as Evista, is the first so-called "designer estrogen." The goal of such drugs is to mimic estrogen's positive effects – such as improving bone mineral density – but not its adverse effects.

Like estrogen, raloxifene appears to have a favorable effect on some risk factors for heart attacks, such as reducing blood levels of artery-clogging LDL cholesterol. But it's not clear whether that necessarily translates into fewer heart attacks and strokes. It doesn't appear to be the case with estrogen which, in some women at least, actually may even raise the risk of heart attacks and strokes.

In this week's *Journal of the American Medical Association*, scientists compared the risk of heart problems in 7,705 women randomly assigned to get either a placebo or raloxifene for four years. The study was funded by Eli Lilly of Indianapolis, which sells Evista.

Overall, there was no significant difference between the placebo and raloxifene groups as far as heart attacks, chest pain at rest or decreased oxygen to the heart because of narrowed arteries. But among the 1,035 women who started out at increased risk for such problems, those on raloxifene were 40% less likely to have them during the study.

"It's just very promising that this medication has a positive effect and not a harmful effect on the heart," says lead author Elizabeth Barrett-Connor of the University of California-San Diego.

Barrett-Connor cautions that the study was originally designed to test raloxifene's effect on bone, not the heart, so all the women had osteoporosis, and relatively few were at risk for heart problems. Another study of raloxifene in 10,101 postmenopausal women with heart disease or at high risk for it is underway.

For now, says Vanderbilt University cardiologist Rose Marie Robertson, "I think raloxifene would be a reasonable alternative" to estrogen for postmenopausal heart disease patients worried about osteoporosis.

REFERENCE: Barrett-Connor, E., Grady, D., Sashegyi, A., Anderson, P. W., Cox, D. A., Hoszowski, K., Rautaharju, P. and Harper, K. D. for the MORE Investigators. Raloxifene and Cardiovascular Events in Osteoporotic Postmenopausal Women. Four-Year Results From the MORE (Multiple Outcomes of Raloxifene Evaluations) Randomized Trial. *JAMA* **287**(#7): 847-857 (2002). [DC Library electronic journal]

It is of interest to compare the newspaper article to the *abstract* given in the journal article, which is:

Context: Raloxifene, a selective estrogen receptor modulator, improves cardiovascular risk factors, but its effect on cardiovascular events is unknown.

Objective: To determine the effect of raloxifene on cardiovascular events in osteoporotic postmenopausal women.

Design: Secondary analysis of data from the Multiple Outcomes of Raloxifene Evaluation trial, a randomized, double-blind, placebo-controlled trial conducted between November 1994 and September 1999.

Setting: Outpatient and community settings at 180 sites in 25 countries.

Participants: A total of 7705 osteoporotic postmenopausal women (average age, 67 years).

Intervention: Patients were randomly assigned to receive raloxifene, 60 mg/d (n = 2557), or 120 mg/d (n = 2572), or placebo (n = 2576) for 4 years.

Main Outcome Measures: Cardiovascular events, including coronary events (myocardial infarction, unstable angina, or coronary ischemia) and cerebrovascular events (stroke or transient ischemic attack), collected as safety end points and subsequently adjudicated by a cardiologist blinded to therapy. Cardiovascular risk at study entry was determined by the presence of multiple cardiovascular risk factors or prior coronary events or revascularization procedure.

Results: In the overall cohort, there were no significant differences between treatment groups in the number of combined coronary and cerebrovascular events: 96 (3.7%) with placebo, 82 (3.2%) with 60 mg/d of raloxifene, and 94 (3.7%) with 120 mg/d of raloxifene. Relative risks (RRs) were 0.86 (95% confidence interval [CI], 0.64-1.15) and 0.98 (95% CI, 0.74-1.30) for 60 mg/d and 120 mg/d of raloxifene, respectively. Similar results were obtained when coronary and cerebrovascular events were analyzed separately. Among the subset set of 1035 women with increased cardiovascular risk at baseline, those assigned to raloxifene had a significantly lower risk of cardiovascular events compared with placebo (RR, 0.60; 95% CI, 0.38-0.95 for both raloxifene groups). The number of cardiovascular events during the first year was not significantly different across groups in the overall cohort (P = .94), or among women at increased cardiovascular risk (P = .86) or with evidence of established coronary heart disease (P = .60).

Conclusions: Raloxifene therapy for 4 years did not significantly affect the risk of cardiovascular events in the overall cohort but did significantly reduce the risk of cardiovascular events in the subset of women with increased cardiovascular risk. There was no evidence that raloxifene caused an early increase in risk of cardiovascular events. Before raloxifene is used for prevention of cardiovascular events, these findings require confirmation in trials with evaluation of cardiovascular outcomes as the primary objective.

The presentation of the abstract in *sections*, similar to stages of our PPDAC cycle, is noteworthy.