

Fenofibrate Can Reduce MI, Interventions in Type 2 Patients

World's largest intervention study among type 2 diabetic patients showed mixed results.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

Fenofibrate reduced myocardial infarctions (MI) and coronary interventions among type 2 diabetic patients in the world's largest type 2 diabetes interventional trial. Researchers presented the mixed results of the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) Study at the American Heart Association's (AHA) Scientific Sessions 2005 in Dallas.

Principal investigator Anthony Keech, FRACP, MScEpid, said: "FIELD was a large and scientifically rigorous study. It showed that, in patients with type 2 diabetes, treatment with fenofibrate does reduce the risk of coronary events such as [MI] and the need for coronary procedures, especially in those without known cardiovascular disease [CVD]." Professor Keech is from the National Health and Medical Research Council Clinical Trials Centre at the University of Sydney, Australia.

DID NOT MEET PRIMARY OUTCOME

Fenofibrate, a well-established agent for lipid improvement, was not associated with a significant reduction in the study's primary outcome, major coronary events. The double-blind, randomized, placebo-controlled trial was conducted at 63 sites in Australia, New Zealand and Finland, and included 9,795 patients who were studied for an average of 5 years. In the United States fenofibrate is marketed as TriCor (Abbott, Abbott Park, Ill).

Patients included in FIELD were aged 50 to 75 years and were recruited from usual practice; 6,139 men and 3,656 women with type 2 diabetes were included. More than three-quarters of the primary prevention group was free of previous CVD and the rest had at least one manifestation of CVD, according to a University of Sydney news release.

All patients were given AHA Step 1 dietary advice and then randomized to receive either daily comiconised

fenofibrate 200 mg or matching placebo for at least 5 years. Fenofibrate was associated with overall 11% fewer major coronary events, however this reduction was not statistically significant ($P=.16$). Fenofibrate significantly reduced the risk of CVD (cardiovascular death, MI, stroke and coronary and carotid revascularization) by 11%. This outcome was driven mainly by a 24% reduction in the risk of nonfatal MI and a 21% reduction in the need for coronary angioplasty or coronary artery bypass graft surgery (P values of .01 and .003, respectively).

EFFECTS SEEN IN PRIMARY PREVENTION

According to the news release, the effects of treatment were seen mainly among patients in the primary prevention group, with a 19% risk reduction in total cardiovascular events ($P=.004$).

In keeping with trial protocol, physicians were able to give patients nonstudy lipid-lowering therapy, mainly statins, during the study. Among patients assigned placebo, there was a higher rate of statin therapy initiation than among those assigned to fenofibrate. Researchers hypothesized that this may have masked a moderately larger benefit of fenofibrate.

In an AHA news conference, Lawrence Appel, MD, professor of medicine at Johns Hopkins Medical School and vice chairman of the AHA's nutrition committee, agreed with the statement that the FIELD results were mixed. "Diabetic [patients] often take a lot of medications. This could be at the least the sixth or the 10th. We need more convincing evidence."

MICROVASCULAR BENEFITS SEEN

FIELD is the first study to suggest that fenofibrate reduces nephropathy and retinopathy. Table 1 lists the complete results of the study. There were beneficial

TABLE 1. FIELD (THE FENOFIBRATE INTERVENTION AND EVENT LOWERING IN DIABETES) STUDY RESULTS

Analysis	Results fenofibrate vs placebo	P-value
Primary endpoint		
total coronary events	11% reduction	P=.16
Secondary Endpoints		
total cardiovascular events	11% reduction	P=.035
coronary revascularization	21% reduction	P=.003
total stroke	10% reduction	P=.36
Tertiary endpoints		
progression to albuminuria	9.5% vs 11%	P<.002
laser treatment for retinopathy	3.6% vs 5.2%	P=.0003
Mortality		
CHD	2.2% vs 1.9%	P=.22
total cardiovascular	2.9% vs 2.6%	P=.41
overall mortality	7.3% vs 6.6%	P=.18
Other observations		
average use of additional lipid-lowering agents, primarily statins	8.4% vs 17.4%	P<.0001
use of additional lipid-lowering agents at study close	19% vs 36%	P<.0001
ACE inhibitors	44.9% vs 47.9%	P=.003
beta-blockers	24.1% vs 26.3%	P=.011
diuretics	21.3% vs 23.6%	P=.006
digoxin	4.9% vs 4.1%	P=.045
Subgroup analyses		
total cardiovascular events:		
no prior CVD	19% reduction	P=.004
prior CVD	1.6% reduction	P=.85
Post-hoc analyses		
total cardiovascular events:		
no prior CVD	25% reduction	P=.14
prior CVD	8% reduction	P=.55

Source: Abbott Health Care Worldwide Media Fact Sheet

effects on urinary albumin excretion rate ($P<.002$) and the need for laser treatment of diabetic retinopathy was reduced by 30% ($P=.0003$)

While the overall results were mixed, Prof. Keech said that they would guide clinicians on the use of fenofibrate in patients with type 2 diabetes. "In the context of the well-established benefits of statin therapy in this patient group, the main use of fenofibrate will probably be in combination therapy. This question needs to be considered in future studies."

He concluded that, "Fenofibrate was well tolerated alone and in combination, it achieved reductions in non-

fatal macrovascular events, especially in primary prevention, and reduced microvascular complications." ■

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Keech A. The effect of fenofibrate on major CHD events in people with type 2 diabetes: FIELD. Presented at the American Heart Association's Scientific Sessions 2005. Nov. 13-16, 2005. Dallas.