Re-analysis of diabetes drug finds no higher heart attack risk

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A re-analysis of the data from a pivotal study of rosiglitazone found no increased risk of cardiovascular events associated with the controversial diabetes drug, according to researchers at the Duke Clinical Research Institute (DCRI).

The DCRI study of the drug, marketed in the United States as Avandia, reassessed the original findings of a clinical trial called RECORD, which drew criticism during an advisory committee meeting of the U.S. Food and Drug Administration in July 2010.

Findings from the DCRI re-adjudication study appear June 6, 2013, in *American Heart Journal*, and were presented June 5-6 at an advisory committee hearing of the FDA.

Rosiglitazone has not been widely marketed in the United States since 2010, when the FDA restricted its use after studies showed it was associated with a higher risk of heart attacks; it is no longer marketed in Europe. The FDA required the new analysis, which was funded by the drug's manufacturer, GlaxoSmithKline.

"We were pleased to be chosen to perform this re-evaluation and we look forward to presenting our findings and being part of the FDA advisory committee discussion," said Kenneth W. Mahaffey, M.D., associate director of the DCRI and lead author of the study.

Mahaffey and colleagues conducted a broad examination of the

RECORD study, using the original data and applying the study's definition of deaths, suspected heart attacks and strokes.

The researchers also expanded the analysis. First, they worked to identify participants who had not been counted in the original study after dropping out or declining to seek follow-up care. The effort was hampered by logistical challenges, but the DCRI analysis included 328 more patients than the original study.

Additionally, the DCRI team conducted a fresh examination of the data using typical procedures and a systematic, unbiased and blinded approach to identify all potential deaths, myocardial infarction and stroke events and processed them for judgment by a team of physicians.

"I am proud of the dedicated and professional way that the DCRI team approached this effort," Mahaffey said.

In their analysis using the original RECORD definitions of cardiovascular events, the DRCI investigators confirmed no meaningful difference between rosiglitazone and the comparison drug, metformin/sulfonylurea, reflecting results in the original RECORD study.

When comparing the results between treatment groups using a contemporary set of cardiovascular endpoint definitions being developed by the FDA, the DCRI analysis also found little difference between the two drugs.

These findings, along with the additional sensitivity analyses performed by DCRI, support the original RECORD results, suggesting that when using essentially the same raw data, the observations were not affected by different end points and other factors.

"These analyses using the original RECORD or new FDA endpoint definitions show similar treatment effects of rosiglitazone compared with the original RECORD results," the study authors conclude.

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