
P-03 New glucose-lowering drugs were favoured to prove non-inferior to placebo. An analysis of the nine mega-trials

Masayuki Ikeda ^a [*Member, Other Doctors*]

^a Department of Medical Informatics, Kagawa University

Background and aim: Since rosiglitazone was reported to increase cardiovascular risks, concerns about the cardiovascular safety of new antidiabetic agents have been raised. To evaluate the safety of a new antidiabetic agent to treat type 2 diabetes, the FDA has asked sponsors to demonstrate that the drug will not result in an unacceptable increase in cardiovascular risk. The aim of the present study was to investigate glycaemic controls in these trials.

Study Design: Descriptive study

Trials Studied: Trials of nine drugs (alogliptin, canagliflozin, empagliflozin, exenatide, liraglutide, lixisenatide, saxagliptin, semaglutide, and sitagliptin), all of which were performed in accordance with the FDA guidance and published as of 3 October 2017.

Measurements and analyses: Trial design, glucose control, and safety data.

Results: In all of the nine trials, use of open-label antihyperglycaemic agents was encouraged as required to achieve individually appropriate glycohaemoglobin (HbA1c) targets in all patients. This approach was taken to assess possible test drug-specific effects by minimizing potential confounding effects of differential glucose control. However, we have found that HbA1c was higher in the placebo group than in the test medicine group throughout the trial in all of the nine studies, even though the placebo group patients received more antihyperglycaemic agents than those in the test medicine group. Heart failure was significantly increased in the test drug group in the alogliptin and the saxagliptin trial. Amputation was significantly increased in the canagliflozin group compared with the placebo group.

Conclusion: The less-well-controlled HbA1c and more antihyperglycaemic agents used in the placebo group confound the treatment comparison and distort the interpretation of the results, misleading healthcare professionals.