Kiran Dubey, Madridge J Pharm Res. 2018
http://dx.doi.org/10.18689/2638-1591.a2.002

madridge CONFERENCES
International
Pharma Conference and Expo
May 2-4, 2018 Rome, Italy

Glitazones to Gliptins and Gliflozins: Quest for Cardio-Friendly Antidiabetics

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The well-characterized associations between type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) are twofold. First, CVD is the underlying cause of more than 60% deaths in diabetic patients. Second, the hyperglycaemia of T2DM, as measured by the percentage of glycosylated haemoglobin, is believed to increase the risk of coronary artery disease and myocardial infarction (MI). Given this relationship, physicians managing T2DM must remain aware of the cardiovascular effects of their therapeutic choices. Unfortunately, most oral antidiabetic therapies made available to date have not resulted in reduced incidences of MI, stroke or cardiovascular death in diabetic subjects. While metformin appears to be safe, it may lead to lethal lactic acid acidosis, especially in patients of recent MI or heart failure. An increased risk of all-cause mortality and cardiovascular related mortality has been associated with sulfonylureas and their combination with metformin. Meglitinides effects are similar to those of sulfonylureas, due to their analogous mechanism of action. Glitazones are unsafe in NYHA class III or IV due to weight gain and oedema. The cardiovascular safety outcome trials conducted with dipeptidyl peptidase-4 (DPP-4) inhibitors, saxagliptin and alogliptin showed an increase in hospitalization due to heart failure, while sitagliptin demonstrated no such effect. Evidence for cardiovascular benefits of glucagon-like peptide-1 (GLP-1) receptor agonists has been similarly heterogeneous, with liraglutide and semaglutide reducing the risk of composite cardiovascular outcomes, but lixisenatide having no reduction or increase in cardiovascular risk. The trial conducted with sodium-glucose co-transporter-2 (SGLT2) inhibitor, empagliflozin found it to be superior in reducing major cardiac events. However, there was a non-significant increase in silent MI with empagliflozin. While the FDA regulatory mandate to demonstrate the cardiovascular safety in order to approve new antidiabetic drugs, the quest for cardio friendly antidiabetics continues.

Biography:

Dr. Kiran Dubey (*M. Pharm, Ph.D. PGDMM*) is currently associated with Jamia Hamdard as Assistant Professor in the Department of Pharmacology, School of Pharmaceutical Education and Research, New Delhi. She has also served in the Medical Information Department of Ranbaxy Laboratories, Systopic Laboratories, Dee Pharma Ltd and Skin Institute and School of Dermatology. Her areas of research include cardiovascular safety profile of NSAIDs, diabetes and related complications. She has guided twenty four post graduate students and three Ph.D. students in the field of Pharmacology and Pharmacy Practice, published articles and has been reviewer for International and National journals of repute.