

GLP1 agonists (including LEADER, SUSTAIN 6)

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Diabetes is a well-known risk factor of cardiovascular morbidity and mortality, and the beneficial effect of improved glycemic control on cardiovascular complications has been well established. However, the rosiglitazone experience aroused awareness of potential cardiovascular risk associated with diabetes drugs and prompted the U.S. Food and Drug Administration to issue new guidelines about cardiovascular risk. Through postmarketing cardiovascular safety trials, some drugs demonstrated cardiovascular benefits, while some antidiabetic drugs raised concern about a possible increased cardiovascular risk associated with drug use. With the development of new classes of drugs, treatment options became wider and the complexity of glycemic management in type 2 diabetes has increased.

The LEADER study is a trial performed to demonstrate the cardiovascular safety of the glucagon-like peptide (GLP-1) receptor agonist liraglutide. The study was performed on patients with type 2 diabetes and high cardiovascular risk, mostly with prior cardiovascular events. Although the primary goal was the demonstration of non-inferiority versus placebo, the LEADER study revealed a significant reduction of the overall incidence of major cardiovascular events, as well as a reduction of all cause and cardiovascular mortality. Even though it was designed for safety purposes, the LEADER study provided a demonstration that liraglutide treatment is associated with a relevant reduction of cardiovascular risk. these results support the use of the drug as one of the treatment of choice in patients with diabetes and prior cardiovascular events. Recently, similar results have been observed with another GLP-1 receptor agonist, semaglutide, whereas another component of the class, lixisenatide, failed to show any differences in comparison with placebo. Overall, these results raise interesting questions on similarities and differences across GLP-1 receptor agonist, as well as on potential mechanisms responsible for cardiovascular protection.

I will talk about the cardiovascular considerations for using these novel anti-diabetic medications in the clinical setting along with related up-to-date topics.