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Cardiovascular Effects of GLP-1 Agonits

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Abstract

• The GLP-1 receptor agonists are antihyperglycemic agents that lower glucose levels as well as if not superior to most other antihyperglycemic agents including basal insulin. They are given subcutaneously (although oral GLP-1 agonists are being developed) and have low rates of hypoglycemia, are associated with significant weight loss and lower systolic blood pressure. In 2008 the Food and Drug Administration mandated that all new antihyperglycemic agents undergo cardiovascular safety studies and it is from these studies that many of the cardiovascular outcomes have been gleamed. These studies are powered for safety and not superiority and the populations studied are different and therefore head-to-head comparisons should not be made. If safety has been proven statistically in these cardiovascular safety outcome trials then superiority can be assessed.

Of the eight GLP-1 cardiovascular safety trials reported at least initially, all have been shown to demonstrate cardiovascular safety. However, a number of trials showed cardiovascular benefit. The LEADER study comparing liraglutide to placebo demonstrated a statistically significant reduction in 3-point MACE (Major Adverse Cardiac Events) which was the primary endpoint. Secondary analysis also demonstrated a reduction in CV death and all-cause mortality. SUSTAIN-6 which assessed semaglutide compared to placebo revealed a significant reduction in 3-point MACE. Albiglutide as well showed a significant reduction in 3-point MACE. Dulaglutide will report this year and an initial press release has stated there is a clinical benefit. Therefore now GLP-1 agonists should not only be thought of as antihyperglycemic agents but as medications that can prevent important cardiovascular events.

Keywords

GLP-1 agonist, cardiovascular, liraglutide, semaglutide, dulaglutide, albigltide, safety