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Dulaglutide reduces cardiovascular disease in Type-2 diabetic people

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This international, double-blind randomized controlled trial enrolled 9,901 people, age 50 and older with T2D from24 countries at 371 care centers.

The Researching Cardiovascular Events With a Weekly Incretin in Diabetes (REWIND) trial has found dulaglutide, an injectable, glucagon-like peptide-1 (GLP-1) receptor agonist, demonstrates superiority in the reduction of cardiovascular events for a broad range of people living with type 2 diabetes (T2D), according to research at a symposium at the American Diabetes Association's (ADA's) 79th Scientific Sessions at the Moscone Convention Center in San Francisco. The REWIND trial is the first study to include a majority of participants (69%) with no history of cardiovascular disease (CVD) at enrollment. Additionally, the REWIND trial had a median follow-up period of more than five years, the longest for a cardiovascular (CV) outcome trial of a GLP-1 receptor agonist.

This international, double-blind randomized controlled trial enrolled 9,901 people, age 50 and older with T2D from 24 countries at 371 care centers. The study evaluated whether weekly subcutaneous injections of 1.5 mg dulaglutide could reduce major adverse cardiovascular events (MACE) compared to placebo. A wide spectrum of participants similar to those seen in a community practice were studied, including many without previous cardiovascular disease and many with guideline-recommended glucose levels. Participants had a mean A1C level of 7.3% (with half having a level below 7.2%) at the beginning of the study, 46% were women, and 69% of participants did not have prior cardiovascular disease. Researchers randomly assigned participants to receive either the placebo or dulaglutide for up to eight years, and the average follow-up duration was 5.4 years.

GLP-1 therapies work by affecting glucose control in the body via several mechanisms, including enhancement of glucose-dependent insulin secretion, slowed emptying of the stomach, and reduction of postprandial glucagon and food intake. They may also have other cardiovascular effects. The REWIND trial aimed to assess whether dulaglutide could reduce major cardiovascular events and other serious outcomes in people with T2D, when added to their anti-hyperglycemic regimen.

REWIND's primary CV outcome was the first occurrence of MACE, the composite of CV death or non-fatal myocardial

infarction or non-fatal stroke. The secondary outcomes included each component of the primary composite CV outcome, a composite clinical microvascular outcome comprising retinal or renal disease, hospitalization for unstable angina, heart failure requiring hospitalization or an urgent heart failure visit, and all-cause mortality. Established CVD at baseline within REWIND was defined as prior myocardial infarction, prior ischemic stroke, prior unstable angina with electrocardiogram changes, prior myocardial ischemia on imaging or stress test, or prior coronary, carotid, or peripheral revascularization.

"The REWIND trial was an ambitious study that conclusively assessed the effects of dulaglutide on people with type 2 diabetes both with and without prior cardiovascular disease," says Hertzel Gerstein, MD, MSc, FRCPC, professor of medicine, director of the division of endocrinology and metabolism, and deputy director of the Population Health Institute at **McMaster University and Hamilton Health Sciences**, in Ontario, Canada, and principal investigator of the REWIND trial. "The reduction in cardiovascular events observed in a wide range of people with diabetes regardless of sex, baseline cardiovascular disease, age or A1c level is compelling."

The study confirmed a cardiovascular benefit, without unexpected side effects or an increase in hypoglycemia. Moreover, it modestly reduced A1C by about 0.6%, weight by about 1.5 kg, and systolic blood pressure by 1.7 mm Hg.

"Both healthcare providers and patients who are looking for ways to reduce cardiovascular risks while also lowering glucose levels, blood pressure and weight will welcome the findings of this trial," says Matthew C. Riddle, MD, one of the lead investigators in REWIND and professor of medicine in the division of endocrinology, diabetes and clinical nutrition at Oregon Health and Science University in Portland, Oregon, and editor-in-chief of *Diabetes Care*, which is the highest-ranked diabetes research journal in the world and published by the ADA.

The American Diabetes Association's 79th Scientific Sessions, the world's largest scientific meeting focused on diabetes research, prevention and care, will be held June 7-11, 2019, at the Moscone Center in San Francisco, California. Nearly 15,000 leading physicians, scientists, health care professionals and industry representatives from around the world are expected to convene at the Scientific Sessions to unveil cutting-edge research, treatment recommendations and advances toward a cure for diabetes. During the five-day meeting, attendees will receive exclusive access to more than 850 presentations and 2,000 original research presentations, participate in provocative and engaging exchanges with leading diabetes experts, and can earn Continuing Medical Education (CME) or Continuing Education (CE) credits for educational sessions.