Understanding cardiovascular outcomes trials in type 2 diabetes

What is a cardiovascular outcomes trial (CVOT)?

- A robust method to evaluate the safety of drugs, focusing on cardiovascular (CV) outcomes
- In 2008, the United States Food and Drug Administration (FDA) stated that all new antidiabetic therapies in type 2 diabetes (T2D) should demonstrate no unacceptable increase in CV risk
  - The guidance was introduced due to reported increased CV risk with the use of certain anti-diabetic therapies in T2D
  - Diabetes CVOTs are therefore conducted to rule out an unacceptable increase in CV risk for new T2D treatments
  - As such, they are primarily designed to assess non-inferiority vs placebo in addition to standard of care, to provide conclusive evidence of no increased CV risk

What is LEADER®?

- LEADER®: Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results
- LEADER® is a multicentre, international, randomised, double-blind, placebo-controlled trial examining the long-term effects of liraglutide on CV outcomes and other clinically important events in adults with T2D and high CV risk
- LEADER® trial facts
  - Start date (first patient first visit): 1 September 2010
  - 9,340 patients with T2D
  - Followed for 3.5–5 years

Patient demographics

- 64.3% men, 35.7% women
- Mean age: 64.3 ± 7.2 years
- Mean BMI: 32.5 ± 6.3 kg/m²
- Mean HbA₁c: 8.7 ± 1.5%
- CV disease (CVD): 81.3% with prior CVD, 18.7% high risk but without prior CVD

Trial design

- Liraglutide 0.6–1.8 mg Once-Daily (OD) + standard of care
- Placebo* + standard of care
- Randomisation (1:1)
- Duration 3.5–5 years
- End of treatment

Primary endpoint

- The time from randomisation to a composite outcome of the first occurrence of CV death, non-fatal myocardial infarction, or non-fatal stroke. These endpoint definitions follow FDA guidance for major adverse events (MACE)

Selected secondary endpoints

- First occurrence of an expanded composite CV outcome of CV death, non-fatal MI, non-fatal stroke, revascularisation, unstable angina or hospitalisation for chronic heart failure
- Time from randomisation to all-cause death
- Time from randomisation to each individual component of the expanded composite CV outcome
- Time from randomisation to individual and composite microvascular outcomes (eye, kidney, eye and kidney)
- Serious adverse events and medical events of special interest

References


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