



# GLP-1 RAs: CARDIOVASCULAR OUTCOME TRIALS

|                                 | LEADER<br>2016  | PIONEER 6<br>2019  | REWIND<br>2019  | SUSTAIN-6<br>2016   |
|---------------------------------|---|--|---|---|
| <b>DRUG</b>                     | Liraglutide 1.8 mg SUBQ daily   | Semaglutide 14 mg PO daily   | Dulaglutide 1.5 mg SUBQ weekly  | Semaglutide 1 mg SUBQ weekly  |
| <b># RANDOMIZED</b>             | 9340<br>(active, n=4668; placebo, n=4672)   | 3183<br>(active, n=1591; placebo, n=1592)  | 9901<br>(active, n=4949; placebo, n=4952)   | 3297<br>(active, n=1648; placebo, n=1649)   |
| <b>INCLUSION CRITERIA</b>       | <ul style="list-style-type: none"> <li>Type 2 diabetes; HgA1c <math>\geq</math>7%</li> <li>Established ASCVD or CKD, or <math>\geq</math>1 cardiovascular risk factors</li> </ul> | <ul style="list-style-type: none"> <li>Type 2 diabetes</li> <li>Established ASCVD or CKD, or multiple cardiovascular risk factors</li> </ul> | <ul style="list-style-type: none"> <li>Type 2 diabetes; HgA1c <math>\leq</math>9.5%</li> <li>Established ASCVD or CKD, or multiple cardiovascular risk factors</li> </ul> | <ul style="list-style-type: none"> <li>Type 2 diabetes; HgA1c <math>\geq</math>7%</li> <li>Established ASCVD or CKD, or <math>\geq</math>1 cardiovascular risk factors</li> </ul> |
| <b>BASELINE CHARACTERISTICS</b> | <ul style="list-style-type: none"> <li>Age ~64 years; male ~64%</li> <li>HgA1c ~8.7%</li> <li>Established ASCVD ~81%</li> </ul>   | <ul style="list-style-type: none"> <li>Age ~66 years; male ~69%</li> <li>HgA1c ~8.2%</li> <li>Established ASCVD/CKD ~85%</li> </ul>          | <ul style="list-style-type: none"> <li>Age ~66 years; male ~53%</li> <li>HgA1c ~7.3%</li> <li>Established ASCVD ~31%</li> </ul>   | <ul style="list-style-type: none"> <li>Age ~65 years; male ~61%</li> <li>HgA1c ~8.7%</li> <li>Established ASCVD ~59%</li> </ul>   |
| <b>DURATION</b>                 | Median follow-up period 3.8 years   | Median follow-up period 15.9 months  | Median follow-up period 5.4 years   | Mean follow-up period of 2.1 years  |
| <b>PRIMARY OUTCOME</b>          | Composite of cardiovascular death, non-fatal MI and non-fatal stroke  | Composite of cardiovascular death, non-fatal MI and non-fatal stroke   | Composite of cardiovascular death, myocardial infarction and stroke   | Composite of cardiovascular death, non-fatal MI and non-fatal stroke  |
| <b>RESULTS</b>                  | <b>Primary Composite Outcome:</b><br>608 (13.0%) vs 694 (14.9%)<br>HR 0.87 (95% CI 0.78-0.97)<br>p=0.01; ARR 1.83%; NNT ~55   | <b>Primary Composite Outcome:</b> NSD<br>61 (3.83%) vs 76 (4.77%)<br>HR 0.79 (95% CI 0.57-1.11); p=0.17                                      | <b>Primary Composite Outcome:</b><br>594 (12.0%) vs 663 (13.4%)<br>HR 0.88 (95% CI 0.79-0.99)<br>p=0.026; ARR 1.37%; NNT ~73  | <b>Primary Composite Outcome: **</b><br>108 (6.55%) vs 146 (8.85%)<br>HR 0.74 (95% CI 0.58-0.95)<br>p=0.02; ARR 2.30%; NNT ~44  |
| <b>MORBIDITY OUTCOMES</b>       | Non-Fatal MI: NSD<br>Non-Fatal Stroke: NSD  | Non-Fatal MI: NSD<br>Non-Fatal Stroke: NSD   | Non-Fatal MI: NSD<br><u>Non-Fatal Stroke:</u><br>135 (2.73%) vs 175 (3.53%)<br>HR 0.76 (95% CI 0.61-0.95)<br>p=0.017; ARR 0.81%; NNT ~125                                 | Non-Fatal MI: NSD<br><u>Non-Fatal Stroke: **</u><br>27 (1.64%) vs 44 (2.67%)<br>HR 0.61 (95% CI 0.38-0.99)<br>p=0.04; ARR 1.03%; NNT ~98  |
| <b>MORTALITY OUTCOMES</b>       | <u>Cardiovascular Death:</u><br>219 (4.69%) vs 278 (5.95%)<br>HR 0.78 (95% CI 0.66-0.93)<br>p=0.007; ARR 1.26%; NNT ~80   | <u>Cardiovascular Death:*</u><br>15 (0.94%) vs 30 (1.88%)<br>HR 0.49 (95% HR 0.27-0.92)  | Cardiovascular Death: NSD   | Cardiovascular Death: NSD   |

These trials demonstrate the cardiovascular safety of GLP-1 RAs in patients with type 2 diabetes.

\* Cannot make claims about individual components of the primary composite outcome due to failure to demonstrate superiority for the composite as a whole (results must be considered exploratory).

\*\* Trial not powered for superiority - interpret results with caution.

