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Effect of Etelcalcetide vs Cinacalcet on Serum Parathyroid Hormone in Patients Receiving Hemodialysis With Secondary Hyperparathyroidism
A Randomized Clinical Trial

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IMPORTANCE Secondary hyperparathyroidism contributes to extraskeletal calcification and is associated with all-cause and cardiovascular mortality. Control is suboptimal in the majority of patients receiving hemodialysis. An intravenously (IV) administered calcimimetic could improve adherence and reduce adverse gastrointestinal effects.

OBJECTIVE To evaluate the relative efficacy and safety of the IV calcimimetic etelcalcetide and the oral calcimimetic cinacalcet.

DESIGN, SETTING, AND PARTICIPANTS A randomized, double-blind, double-dummy active clinical trial was conducted comparing IV etelcalcetide vs oral placebo and oral cinacalcet vs IV placebo in 683 patients receiving hemodialysis with serum parathyroid hormone (PTH) concentrations higher than 500 pg/mL on active therapy at 164 sites in the United States, Canada, Europe, Russia, and New Zealand. Patients were enrolled from August 2013 to May 2014, with end of follow-up in January 2015.

INTERVENTIONS Etelcalcetide intravenously and oral placebo (n = 340) or oral cinacalcet and IV placebo (n = 343) for 26 weeks. The IV study drug was administered 3 times weekly with hemodialysis; the oral study drug was administered daily.

MAIN OUTCOMES AND MEASURES The primary efficacy end point was noninferiority of etelcalcetide at achieving more than a 30% reduction from baseline in mean predialysis PTH concentrations during weeks 20-27 (noninferiority margin, 12.0%). Secondary end points included superiority in achieving biochemical end points (>50% and >30% reduction in PTH) and self-reported nausea or vomiting.

RESULTS The mean (SD) age of the trial participants was 54.7 (14.1) years and 56.2% were men. Etelcalcetide was noninferior to cinacalcet on the primary end point. The estimated difference in proportions of patients achieving reduction in PTH concentrations of more than 30% between the 198 of 343 patients (57.7%) randomized to receive cinacalcet and the 232 of 340 patients (68.2%) randomized to receive etelcalcetide was −10.5% (95% CI, −17.5% to −3.5%, *P* for noninferiority, <.001; *P* for superiority, .004). One hundred seventy-eight patients (52.4%) to randomized etelcalcetide achieved more than 50% reduction in PTH concentrations compared with 138 patients (40.2%) randomized to cinacalcet (*P* = .001; difference in proportions, 12.2%; 95% CI, 4.7% to 19.5%). The most common adverse effect was decreased blood calcium (68.9% vs 59.8%).

CONCLUSIONS AND RELEVANCE Among patients receiving hemodialysis with moderate to severe secondary hyperparathyroidism, the use of etelcalcetide was not inferior to cinacalcet in reducing serum PTH concentrations over 26 weeks; it also met superiority criteria. Further studies are needed to assess clinical outcomes as well as longer-term efficacy and safety.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT1896232

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