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Effect of Etelcalcetide vs Placebo on Serum Parathyroid Hormone in Patients Receiving Hemodialysis With Secondary Hyperparathyroidism
Two Randomized Clinical Trials

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IMPORTANCE Secondary hyperparathyroidism contributes to extraskeletal complications in chronic kidney disease.

OBJECTIVE To evaluate the effect of the intravenous calcimimetic etelcalcetide on serum parathyroid hormone (PTH) concentrations in patients receiving hemodialysis.

DESIGN, SETTING, AND PARTICIPANTS Two parallel, phase 3, randomized, placebo-controlled treatment trials were conducted in 1023 patients receiving hemodialysis with moderate to severe secondary hyperparathyroidism. Trial A was conducted in 508 patients at 111 sites in the United States, Canada, Europe, Israel, Russia, and Australia from March 12, 2013, to June 12, 2014; trial B was conducted in 515 patients at 97 sites in the same countries from March 12, 2013, to May 12, 2014.

INTERVENTIONS Intravenous administration of etelcalcetide (n = 503) or placebo (n = 513) after each hemodialysis session for 26 weeks.

MAIN OUTCOMES AND MEASURES The primary efficacy end point was the proportion of patients achieving greater than 30% reduction from baseline in mean PTH during weeks 20-27. A secondary efficacy end point was the proportion of patients achieving mean PTH of 300 pg/mL or lower.

RESULTS The mean age of the 1023 patients was 58.2 (SD, 14.4) years and 60.4% were men. Mean PTH concentrations at baseline and during weeks 20-27 were 849 and 384 pg/mL vs 820 and 897 pg/mL in the etelcalcetide and placebo groups, respectively, in trial A; corresponding values were 845 and 363 pg/mL vs 852 and 960 pg/mL in trial B. Patients randomized to etelcalcetide were significantly more likely to achieve the primary efficacy end point: in trial A, 188 of 254 (74.0%) vs 21 of 254 (8.3%; $P < .001$), for a difference in proportions of 65.7% (95% CI, 59.4%-72.1%) and in trial B, 192 of 255 (75.3%) vs 25 of 260 (9.6%; $P < .001$), for a difference in proportions of 65.7% (95% CI, 59.3%-72.1%). Patients randomized to etelcalcetide were significantly more likely to achieve a PTH level of 300 pg/mL or lower: in trial A, 126 of 254 (49.6%) vs 13 of 254 (5.1%; $P < .001$), for a difference in proportions of 44.5% (95% CI, 37.8%-51.2%) and in trial B, 136 of 255 (53.3%) vs 12 of 260 (4.6%; $P < .001$), for a difference in proportions of 48.7% (95% CI, 42.1%-55.4%). In trials A and B, respectively, patients receiving etelcalcetide had more muscle spasms (12.0% and 11.1% vs 7.1% and 6.2% with placebo), nausea (12.4% and 9.1% vs 5.1% and 7.3%), and vomiting (10.4% and 7.5% vs 7.1% and 3.1%).

CONCLUSIONS AND RELEVANCE Among patients receiving hemodialysis with moderate to severe secondary hyperparathyroidism, use of etelcalcetide compared with placebo resulted in greater reduction in serum PTH over 26 weeks. Further studies are needed to assess clinical outcomes as well as longer-term efficacy and safety.

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