Original Report: Patient-Oriented, Translational Research

American Journal of Nephrology

Am J Nephrol 2016;44:316–325
DOI: 10.1159/000450766

Received: August 15, 2016
Accepted: September 10, 2016
Published online: September 28, 2016

Use of Extended-Release Calcifediol to Treat Secondary Hyperparathyroidism in Stages 3 and 4 Chronic Kidney Disease

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Key Words
Chronic kidney disease · Secondary hyperparathyroidism · Vitamin D · Vitamin D insufficiency · Calcifediol (25-hydroxyvitamin D_3) · Parathyroid hormone

Abstract
Background/Aims: Vitamin D insufficiency and secondary hyperparathyroidism (SHPT) are associated with increased morbidity and mortality in chronic kidney disease (CKD) and are poorly addressed by current treatments. The present clinical studies evaluated extended-release (ER) calcifediol, a novel vitamin D prohormone repletion therapy designed to gradually correct low serum total 25-hydroxyvitamin D, improve SHPT control and minimize the induction of CYP24A1 and FGF23. ***Methods:*** Two identical multicenter, randomized, double-blind, placebo-controlled studies enrolled subjects from 89 US sites. A total of 429 subjects, balanced between studies, with stage 3 or 4 CKD, SHPT and vitamin D insufficiency were randomized 2:1 to receive oral ER calcifediol (30 or 60 µg) or placebo once daily at bedtime for 26 weeks. Most subjects (354 or 83%) completed dosing, and 298 (69%) entered a subsequent open-label extension study wherein ER calcifediol was administered without interruption for another 26 weeks. ***Results:*** ER calcifediol normalized serum total 25-hydroxyvitamin D concentrations (>30 ng/ml) in >95% of per-protocol subjects and reduced plasma intact parathyroid hormone (iPTH) by at least 10% in 72%. The proportion of subjects receiving ER calcifediol who achieved iPTH reductions of ≥30% increased progressively with treatment duration, reaching 22, 40 and 50% at 12, 26 and 52 weeks, respectively. iPTH lowering with ER calcifediol was independent of CKD stage and significantly greater than with placebo. ER calcifediol had inconsequential impact on serum calcium, phosphorus, FGF23 and adverse events. ***Conclusion:*** Oral ER calcifediol is safe and effective in treating SHPT and vitamin D insufficiency in CKD.

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