Transcript Details
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Encaleret in Autosomal Dominant Hypocalcemia Type 1: Clinical Implications From the Phase 3 CALIBRATE Trial

Announcer:
You're listening to GLC on ReachMD. This DataPulse, titled *Encaleret in Autosomal Dominant Hypocalcemia Type 1: Clinical Implications From the Phase 3 CALIBRATE Trial*, is provided by Global Learning Collaborative.

Dr. Michael Levine:
Hello from ENDO 2026 here in beautiful downtown Chicago. I'm Dr. Michael Levine, and today I'm breaking down the clinical implications of newly presented phase 3 CALIBRATE data evaluating encaleret in patients with autosomal dominant hypocalcemia type 1. These data build on a presentation given just several weeks ago in Europe at the European Congress of Endocrinology, where a primary analysis of the CALIBRATE data were given.

Now, let me explain the sort of breakdown of what CALIBRATE was. CALIBRATE consisted of several periods of study. Patients with genetically confirmed diagnoses of ADH1 due to an activating mutation of the calcium-sensing receptor were enrolled in CALIBRATE, and for 4 weeks they had optimization of standard of care.

At the end of these 4 weeks, patients were randomized 2:1 to be either in the encaleret or standard of care groups. And in those patients who were randomized to encaleret, standard of care, which consisted of an activated form of vitamin D and oral calcium supplements, was discontinued, and patients underwent a 20-week period of time during which the dose of encaleret was titrated to achieve normal serum levels of calcium and normal urinary calcium excretion.

At the end of these 20 weeks, patients then went into a 4-week maintenance phase. And then at the end of that, so we call this week 24, the results, the biochemical results in these patients, were compared both within group to the data at the conclusion of standard of care, so week 4, and between groups, the patients who had encaleret versus standard of care. The patients who were randomized to encaleret had an increase in serum calcium levels in as few as 3 days, and by the end of the third week, urinary calcium levels had normalized in most of those patients.

So how do the overall data look? Well, serum calcium levels in the patients who were receiving encaleret normalized in 88.9% of patients. Urinary calcium levels normalized in 80% of patients. And by normal, I mean less than 300 mg/day in men, less than 250 mg/day in women. And the primary composite endpoint, which was a normal serum calcium level and a normal urinary calcium level, was achieved in 75.6% of patients in encaleret and in only 19% of patients on standard of care.

Now importantly, because the mechanism of action of encaleret is to correct the activation of the calcium-sensing receptor and restore it to a more physiologic biochemical behavior, in over 91% of patients taking encaleret, levels of PTH were at least 15 pg/mL or greater. This occurred in 0% of patients on standard of care.

And lastly, because serum phosphate levels is another very important indicator of overall mineral homeostasis, levels of serum phosphate were normalized in 91% of patients taking encaleret, whereas those patients who were randomized to encaleret at the end of week 4, the standard of care optimization period, serum phosphate levels were normal in only about 55% of patients.

So remarkable improvements in circulating levels of PTH, which led to normalization of serum calcium levels in the vast majority of patients, led to reduction in urinary calcium levels, so that, as I said, nearly 76% of patients taking encaleret had normalization of both serum and urinary calcium measurements, leading to achievement of that composite endpoint.

So where do we go from here? I think this is a real game changer for patients with ADH1. Treating them with conventional therapy leads to continued hypercalciuria and worsening renal complications. Using a negative allosteric modulator, such as encaleret, can normalize levels of PTH, normalize serum calcium levels, and normalize urinary calcium levels, so a real game changer using precision medicine to address the underlying metabolic defect in ADH1.

Thank you for your attention. This is Dr. Michael Levine reporting to you from the Endocrine Society meeting in Chicago. Take care.

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