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Treatment of chronic hypoparathyroidism by Eneboparatide, a novel PTH Receptor-1 Agonist: results from a phase 2a study

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CONFLICT OF INTEREST

Istvan TAKACS, MD, PhD

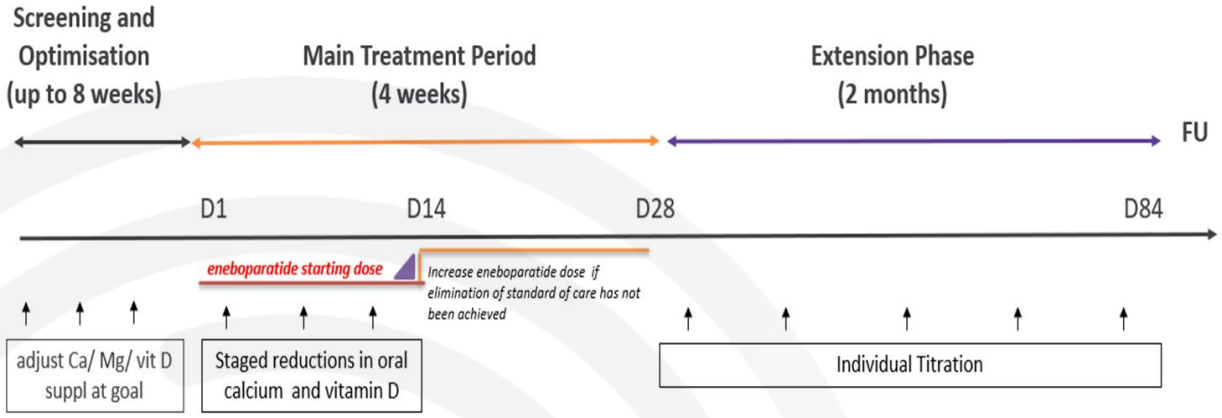
x I declare that I have no potential conflict of interest.

OPEN-LABEL, MULTICENTER, PHASE 2 STUDY

Mechanism of action / Properties

Eneboparatide is a 36-AA peptide specifically designed to have high affinity for activate the R° conformation of the PTH1 receptor
Eneboparatide has short half life (<1hr) and sustained pharmacodynamic effects

Study protocol design in hypoparathyroidism patients



- Target range of 7.8 to 9.0mg/dL (1,95 to 2,25 mmol/L) for albumin-adjusted serum calcium
- Starting dose of eneboparatide:
  - Cohort 1 (n=12): 20µg/day up to 60µg/day
  - Cohort 2 (n=16): 10µg/day up to 80µg/day

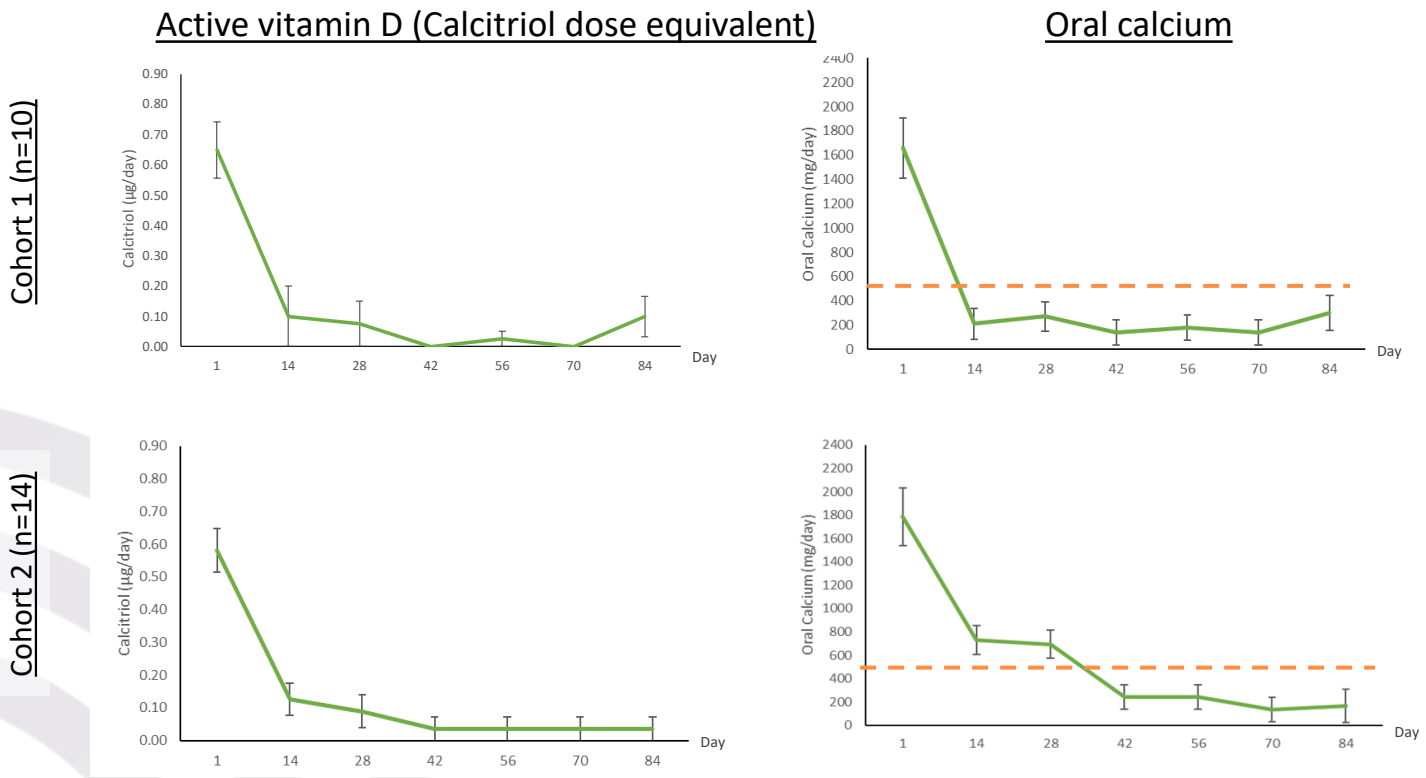
Study population main baseline characteristics

	Cohort 1 N=12	Cohort 2 N=16
Mean age, yrs (SD), min-max	63 (10), 44-72	54 (11), 26-72
Female, n (%)	9 (75%)	12 (75%)
Post-menopausal women, n (%)	7 (58%)	7 (44%)
Etiology of hypoparathyroidism **Post-surgery, n (%)** **Idiopathic, n (%)** **Genetic, n (%)**	 10 (83.3%) 2 (16.7%) -	 13 (81.3%) 2 (12.5%) 1 (6.3%) (HRD)
Mean oral vitamin D dose, ug/day, min-max	0.67, 0.25-1	0.60, 0.25-1
Mean oral calcium dose, mg/day, min-max	1,625 (1,000-3,500)	1,688 (1,000-7,800)

In C1, the majority of patients remained at dose 20µg, only a few had their dose titrated up to 60µg.
In C2, the majority of patients were rapidly titrated to 20µg and then up to 80µg.

AMOLYT PHARMA

WITHDRAWAL OF CONVENTIONAL THERAPY

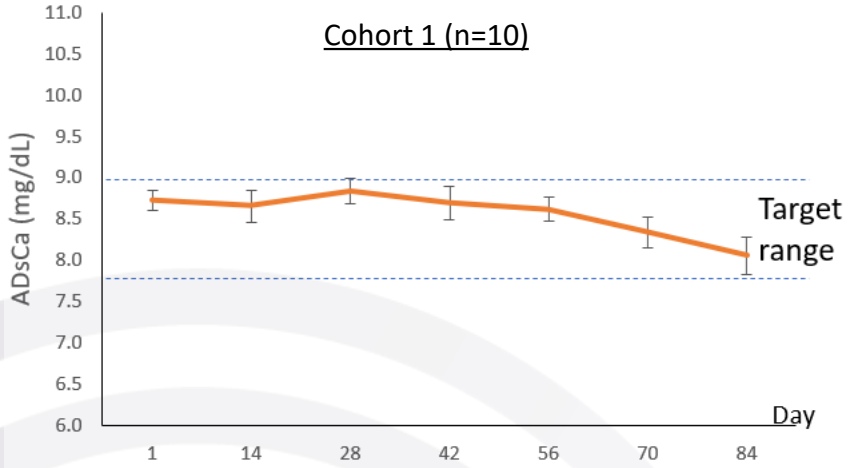


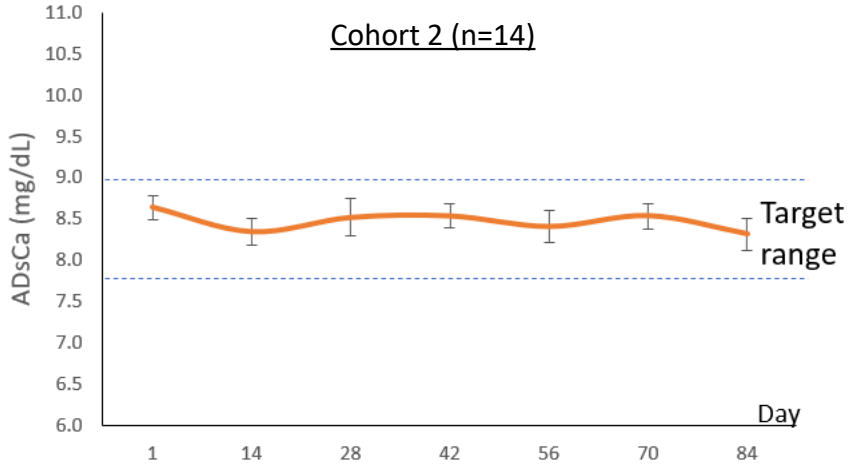
In both cohorts:

- active vitamin D was rapidly discontinued (8/10 and 13/14 patients were off at Day 84 in C1 and C2, respectively)
- oral calcium supplementation was brought below 500mg/day (8/10 and 13/14 patients in C1 and C2, respectively)

EFFECT ON SERUM CALCIUM LEVELS

Albumin-adjusted serum calcium





In both cohorts:

- mean albumin-adjusted serum calcium was within the target range of 7.8 to 9.0mg/dL (1,95 to 2,25 mmol/L)
- the positive effect of eneboparatide on urinary excretion of calcium will be reported in details in the next oral presentation (#2634)

Eneboparatide treatment was well tolerated with no safety concerns. No serious events were reported.
All adverse events were of mild or moderate intensity

AMOLYT PHARMA

RELEASE OF BONE BIOMARKERS

In the two cohorts, eneboparatide induced an increase in the blood levels of s-CTX and P1NP, that remained within the mid-normal range, consistent with a progressive resumption of a physiologic bone turnover

SUMMARY

Eneboparatide allowed in most patients:

- The withdrawal of active vitamin D and oral calcium supplements
- The maintenance of stable serum calcium levels
- A physiological resumption of bone turnover

A multicenter, randomized, placebo-controlled, double-blind phase 3 study is underway

CALYPSO STUDY

AMOLYT PHARMA