

Early US Real-World Treatment Patterns and Outcomes in Palopegteriparatide Treatment for Patients with Hypoparathyroidism

Premise¹

Due to Natpara [rhPTH (1-84)] discontinuation and a lack of other approved treatment options for hypoparathyroidism, an Early Access Program (EAP) was enacted in January of 2023 for palopegteriparatide in the US.^{a,1}

Short-lived PTH therapies

- **rhPTH (1-84)**, approved as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism, was recalled in the US in 2019 (world-wide discontinuation at end of 2024)²
- **Teriparatide [rhPTH (1-34)]** and **abaloparatide** are approved for people with severe osteoporosis at high fracture risk, with reports of off-label use for hypoparathyroidism³⁻⁹

Palopegteriparatide (TransCon® PTH)

- **Palopegteriparatide** is a prodrug of PTH (1-34), subcutaneously once daily, designed to provide active PTH within the physiological range for 24 hours/day^{10,11}
- Phase 3 PaTHway demonstrated independence from conventional therapy and improved HRQoL, skeletal dynamics, and renal function in hypoparathyroidism¹²

The EAP enrolled patients directly switching from short-lived PTH therapy to palopegteriparatide¹

Design¹

Expanded Access Program

Starting dose 18 µg/day palopegteriparatide, co-administered with conventional therapy and titrated according to a protocol-specified algorithm

Assessments (analysis up to 12 months)

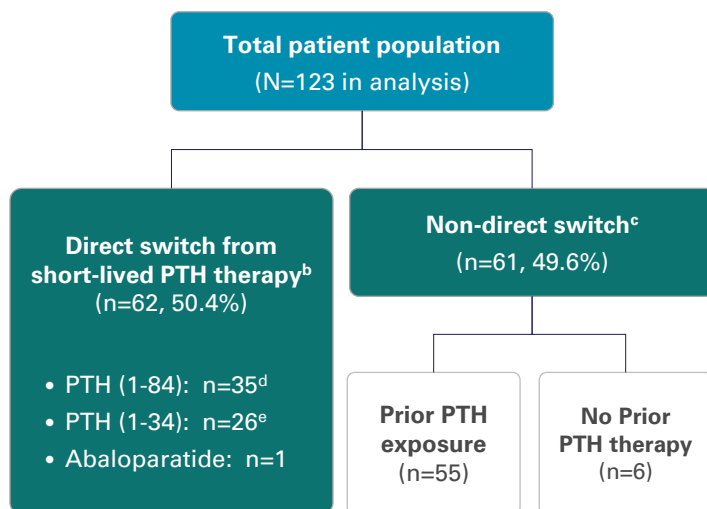
- Independence from conventional therapy (no calcitriol and ≤600 mg/day of elemental calcium)
- Serum calcium
- TEAEs

Key enrollment criteria (Mar 2023–Oct 2024, N=135)

- **Inclusion:** age ≥18 years, diagnosis of hypoparathyroidism, prior PTH treatment (with exemption), serum albumin-adjusted calcium ≥7.8 mg/dL, 25(OH) vitamin D in local reference range
- **Exclusion:** pseudohypoparathyroidism or severe renal impairment (eGFR < 30 mL/min/1.73m²)

Sites: 60 locations across the United States

Cohorts¹



^b**Direct switch:** stopped short-lived PTH therapy ≤ 1 day prior to palopegteriparatide initiation, including overlapping therapy

^c**Non-direct switch:** (1) stopped short-lived PTH therapy ≥ 2 days prior to palopegteriparatide initiation, or (2) no prior PTH exposure

^dIncludes 2 infusion pump patients

^eIncludes 4 infusion pump patients

- Previous use of short-lived PTH therapy was reported for 95.1% (117/123) of patients
- Intermittent rhPTH (1-84) was the most reported prior short-lived PTH therapy used in 69.1% (85/123) of patients

^aPalopegteriparatide received US regulatory approval in August of 2024 for treatment of hypoparathyroidism in adults.¹³

Abbreviations: 25(OH) vitamin D, calcifediol; eGFR, estimated glomerular filtration rate; HRQoL, health-related quality of life; PTH, parathyroid hormone; PTHrP, PTH-related protein; rhPTH, recombinant human PTH; TEAEs, treatment emergent adverse events

References: 1. Graham T, et al. *Endocr Pract.* 2025. 2. About the Discontinuation of NATPARA. October 3, 2022. [Link](#). 3. FORTEO® [Package insert]. Eli Lilly and Company; revised 2020. 4. FORSTEO® [SmPC]: Eli Lilly and Company; 2003. 5. TYMLOS® (abaloparatide) [package insert]. Radius Health, Inc.; 2017. 6. Eladynos® (abaloparatide) [SmPC]. Theramex; 2022. 7. Aouchiche K, et al. *Endocrine.* 2022. 8. Saraiva M, et al. *Am J Case Rep.* 2021. 9. Chamseddin R, et al. Abstract #1407986. *Endocrine Practice.* 2023. 10. Karpf DB, et al. *J Bone Miner Res.* 2020. 11. Holten-Andersen L, et al. *J Bone Miner Res.* 2019. 12. Khan AA, et al. *J Bone Miner Res.* 2023. 13. YORVIPATH® [package insert]. Ascendis Pharma Endocrinology, Inc. 2024.

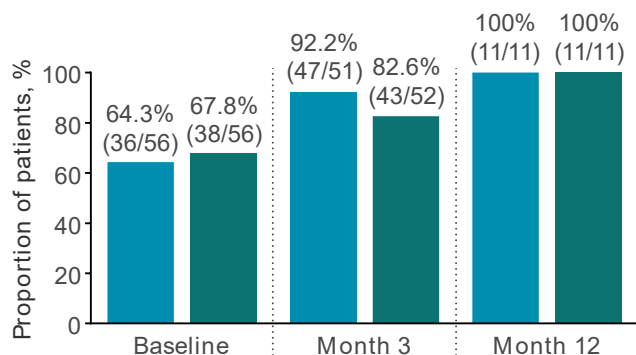
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Conventional therapy

Decreased after palopegteriparatide initiation

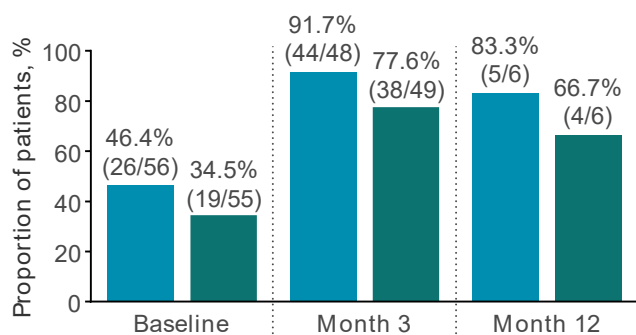
- Independence from calcitriol^a
- Independence from elemental calcium^b

Direct switch from short-lived PTH therapy



Independence from conventional therapy^{c,d}:
Month 3: 80.4% (41/51); Month 12: all patients (11/11)

Non-direct switch

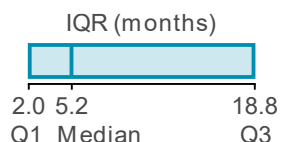


Independence from conventional therapy^c:
Month 3: 75.0% (36/48); Month 12: 66.7% (4/6)

Palopegteriparatide exposure

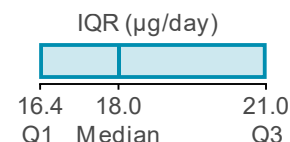
Duration

Median 5.2 months



Dose

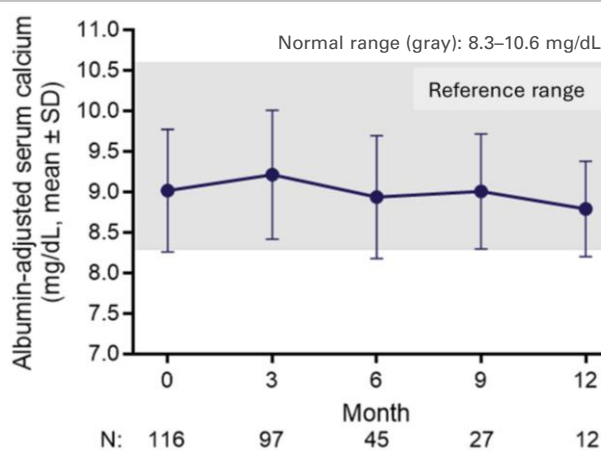
Median 18.0 µg/day
at month 3 (n=94)



At month 12 (n=18):
Median 21.0 µg/day

Serum calcium

Mean levels remained in the normal range at each timepoint



Safety

- Most common TEAEs were hypocalcemia (13.0%), hypercalcemia (8.9%), and paresthesia (7.3%), largely occurring in the first 90 days
- Most TEAEs were Grade 1 or 2 (mild to moderate)
- Grade 3 (severe) TEAEs reported in 7.3% of patients
- No Grade 4 (life-threatening) or 5 (fatal) events reported
- 2.4% of patients discontinued therapy due AEs^e

Safety and effectiveness summary

- Conventional therapy use was successfully reduced while maintaining normocalcemia in the real-world setting
- No new safety signals were identified with up to 12 months of palopegteriparatide treatment

Palopegteriparatide initiation summary

- Analysis suggests that initiation and subsequent dose titration of palopegteriparatide can be successfully conducted following the standard titration algorithm regardless of prior treatments

Real-world analysis of palopegteriparatide provides insights into outcomes associated with different treatment transition practices and reaffirms its efficacy and safety profile consistent with the pivotal phase 3 PaTHway trial

^aTaking no calcitriol. ^bTaking ≤ 600 mg/day elemental calcium. ^cTaking no calcitriol and ≤600 mg/day elemental calcium.

^dOf direct switch patients with available data, 51.8% (29/56) were taking calcitriol and/or therapeutic doses of calcium at baseline.

^eagitation (n=1), anaphylactic reaction (n=1), bone pain (n=1)

Abbreviations: IQR, interquartile range (Q1, first quartile; Q3, third quartile); PTH, parathyroid hormone; SD, standard deviation; TEAEs, treatment emergent adverse events

Reference: Graham T, et al. *Endocr Pract.* 2025.10.1016/j.eprac.2025.08.008