Hipoparatiroidismo crónico postquirúrgico, ¿cómo tratar?

Post-surgical chronic hypoparathyroidism, how to treat?

Isabel Huguet Moreno

Hospital Universitario Infanta Leonor, Madrid

I have participated as an advisor for Ascendis Pharma

Agenda

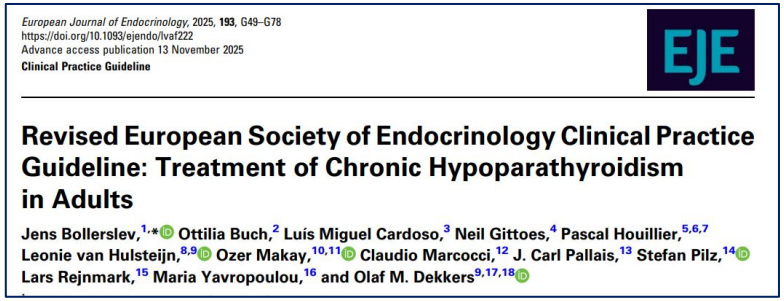
Introduction: Definition. Two main ideas. Who to treat

Conventional treatment

Optimized conventional treatment

PTH replacement therapy

Introduction. Definition



European Journal of Endocrinology, 2025, **193**, G49–G78
https://doi.org/10.1093/ejendo/lvaf222
Advance access publication 13 November 2025
Clinical Practice Guideline

Revised European Society of Endocrinology Clinical Practice Guideline: Treatment of Chronic Hypoparathyroidism in Adults

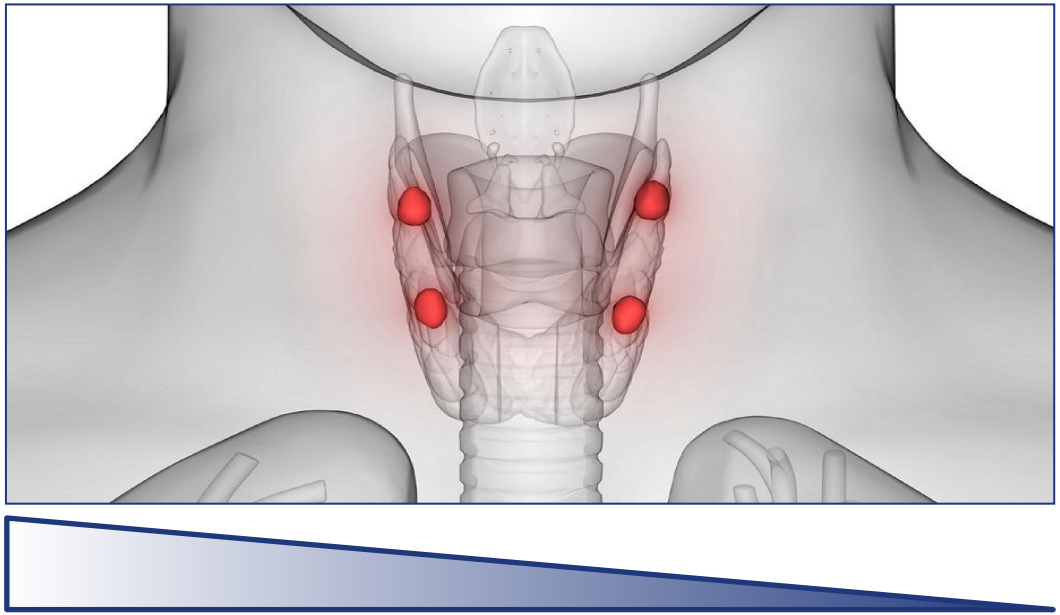
Jens Bollerslev,[1,*] Ottilia Buch,[2] Luís Miguel Cardoso,[3] Neil Gittoes,[4] Pascal Houillier,[5,6,7] Leonie van Hulsteijn,[8,9] Ozer Makay,[10,11] Claudio Marcocci,[12] J. Carl Pallais,[13] Stefan Pilz,[14] Lars Rejnmark,[15] Maria Yavropoulou,[16] and Olaf M. Dekkers[9,17,18]

- ✔ **Persistent hypocalcemia** and inappropriately **low or inappropriately normal** PTH levels
- ✔ More than **12 months** duration following neck surgery

Bollerslev J, et al. Eur J Endocrinol. 2025;193(5):G49-G78.

Introduction. Two main ideas

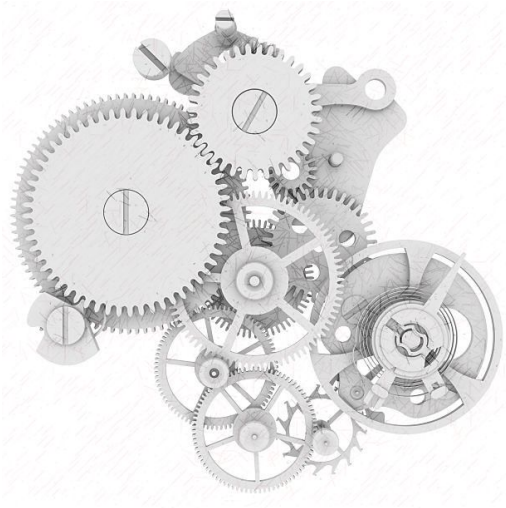
Rethinking Hypoparathyroidism: From Dichotomy to Continuum



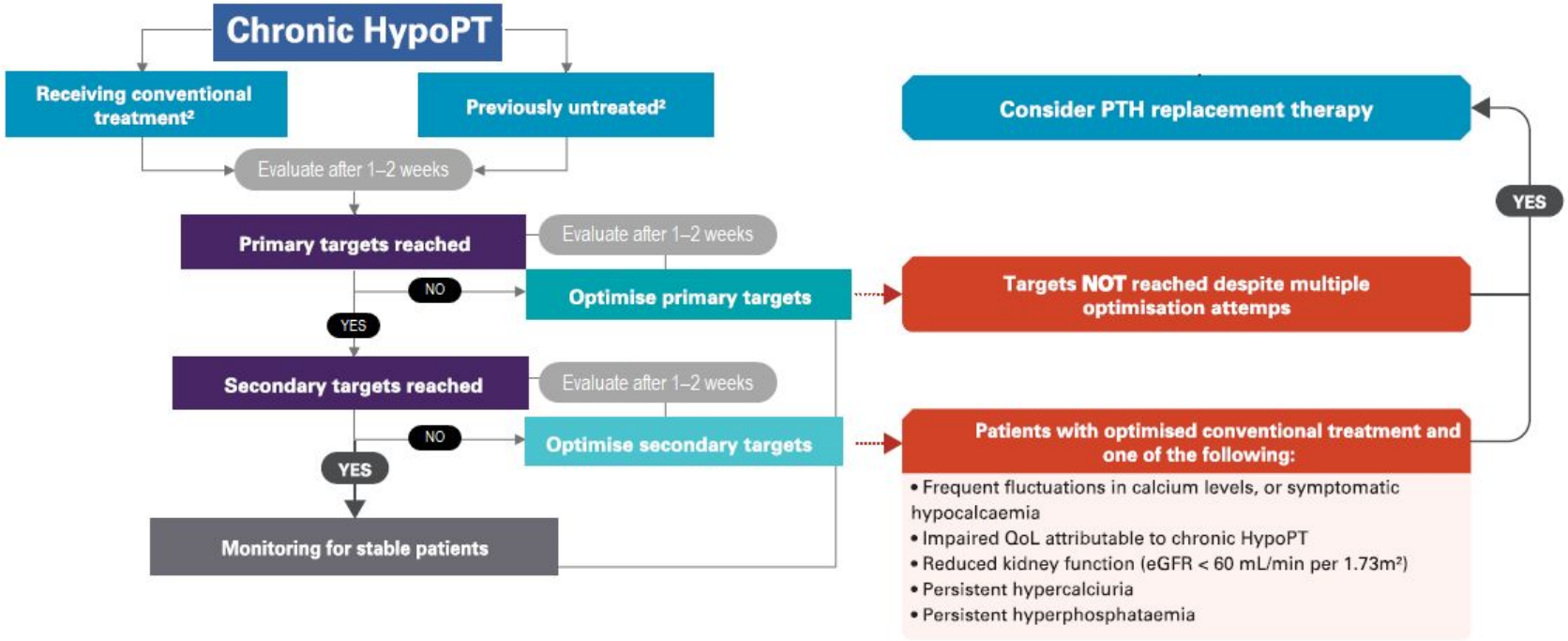
Introduction. Two main ideas.

Functionally, *HypoPTH represents a* ***dual hormonal deficiency***, *as level of activated vitamin D are reduced due to absent PTH stimulation of renal 1-alpha-hydroxylase.*

Rigid dosing schedule on a highly fluid, homeostatic system.



Brandi et al. Trends in Endocrinology & Metabolism, April, 2026.



Bollerslev J, et al. Eur J Endocrinol. 2025;193(5):G49-G78

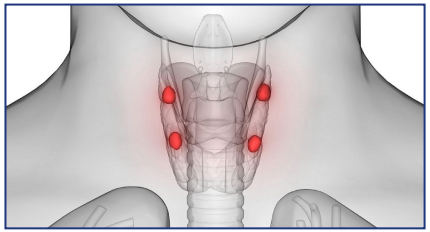
Conventional treatment

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R.3.3 We recommend treatment with vitamin D.

- R.3.3.1 We recommend treatment with activated vitamin D analogue
- R.3.3.2 If not available, we suggest treatment with supraphysiological doses of calciferol
- R.3.3.3 We recommend titration of vitamin D analogue doses aiming at calcium levels within the target range with patients being free of symptomatic hypocalcaemia and biomarkers within the target range.



Bollerslev J, et al. Eur J Endocrinol. 2025;193(5):G49-G78

Conventional treatment

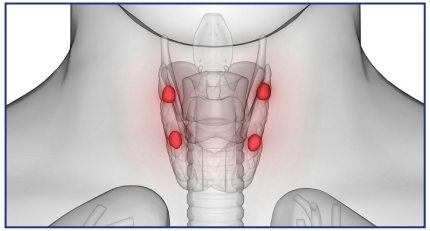
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EJE

Revised European Society of Endocrinology Clinical Practice Guideline: Treatment of Chronic Hypoparathyroidism in Adults

R.3.4 We recommend assuring an adequate calcium intake.

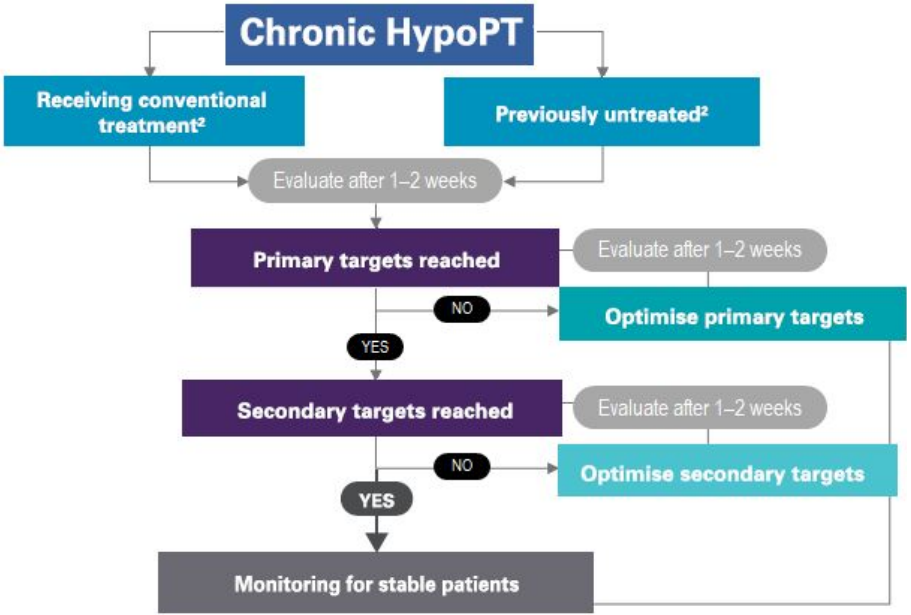
- R.3.4.1 We suggest a dietary calcium intake of 800-1000 mg/day
- R.3.4.2 We suggest calcium supplements if calcium levels in the target range cannot be achieved with activated vitamin D + dietary calcium intake.
- R.3.4.3 We recommend that elemental calcium supplementation >500 mg daily should be taken in smaller doses + spread throughout the day.



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Conventional treatment

Active vitamin D + dietary elemental calcium intake +/- calcium supplements



Primary targets

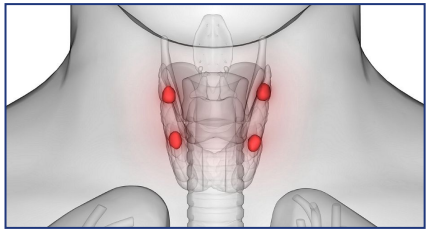
- ✔ No symptoms of hypocalcaemia
- ✔ Ca_c or iCa in the lower half of the reference range or slightly below

Secondary targets

- ✔ No impairment in QoL.
- ✔ No hypercalciuria.
- ✔ No hyperphosphataemia.
- ✔ No hypomagnesaemia.
- ✔ Stable eGFR.
- ✔ 25(OH)D over 75 nmol/L (30 ng/mL)

Optimization of conventional therapy

- **R.3.6 In the presence of hypercalciuria*,** we suggest:
  - Decreased dose of oral calcium and/or activated vitamin D
  - A low sodium chloride intake (< 6 g NaCl or < 2.4 g Na/day)
  - Addition of treatment with a thiazide diuretic.



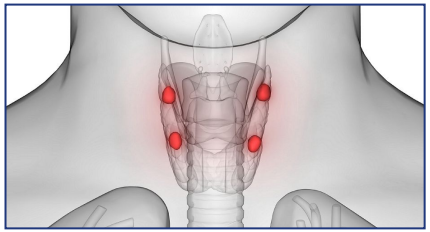
- **R.3.7 In the presence of hyperphosphataemia,** we suggest
  - Dietary interventions
  - Adjustment of treatment with calcium supplements and vitamin D. Calcium supplements (together with a meal)
  - Following changes, 24-hour urinary calcium should be measured.

* >7.5 mmol/24h [300 mg/24h] in men, > 6.25 mmol/24h in women [250 mg/24h] or > 0.1 mmol/kg/24h [4 mg/kg/24h] in both sexes

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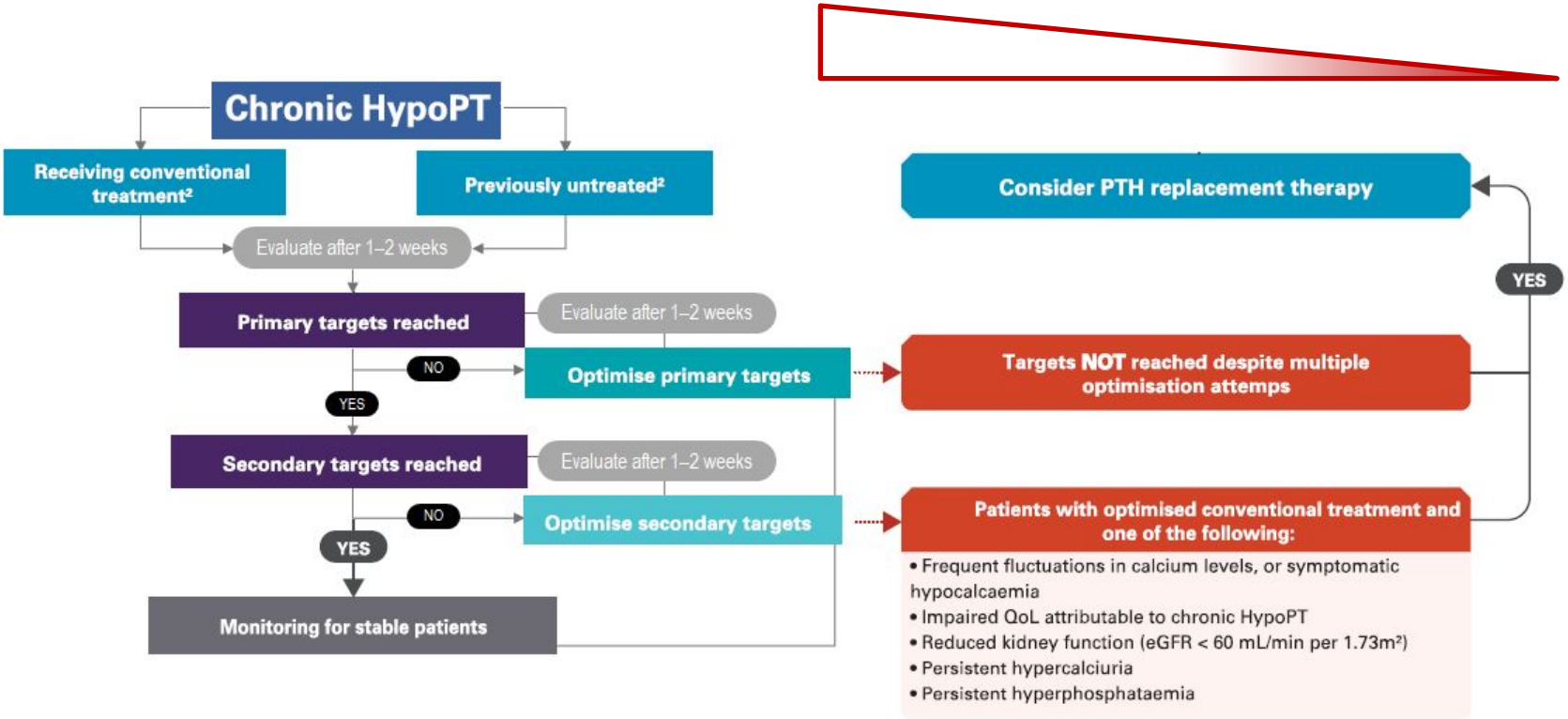
Optimization of conventional therapy

- **R.3.8 In a patient with hypomagnesaemia,** we suggest
  - Consider other causes of hypomagnesaemia (diuretics and PPIs)
  - A diet rich in magnesium
  - Consider treatment with magnesium supplements or amiloride.



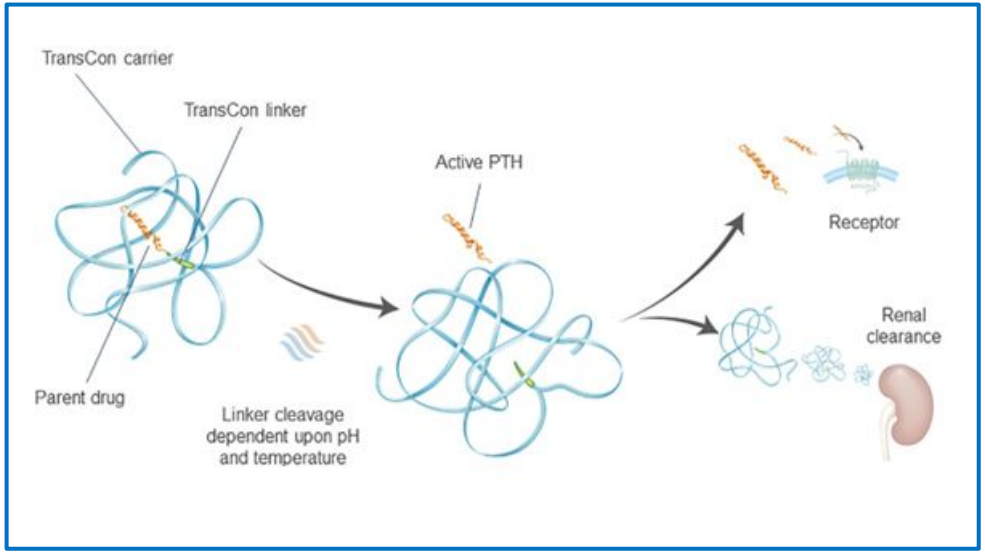
- **R.3.9 Ensure replete levels of vitamin D by using a daily supplement (cholecalciferol/ergocalciferol) 800-2000 IU**
  - Consider circulating 25(OH)D level ≥ 75 nmol/L (30 ng/mL)

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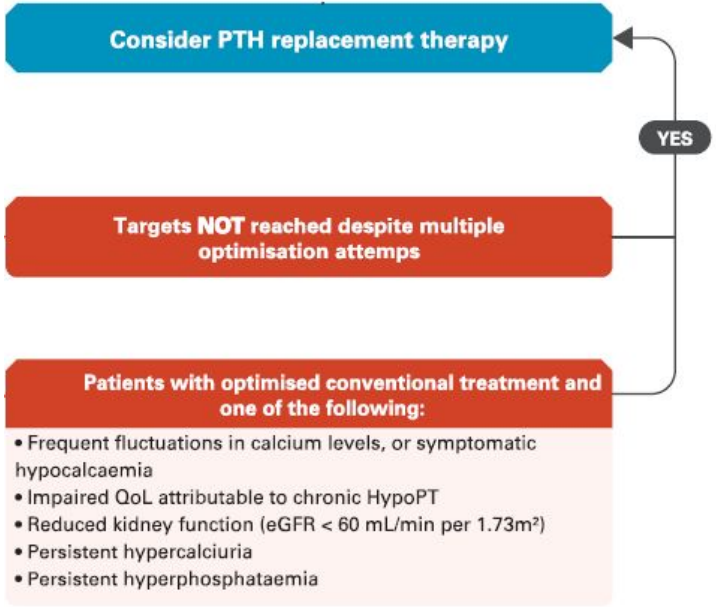


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PTH replacement therapy



From Karpf DB et al. A Randomized Double-Blind Placebo-Controlled First-In-Human Phase 1 Trial of TransCon PTH in Healthy Adults. J Bone Miner Res. 2020 Aug;35(8):1430-1440

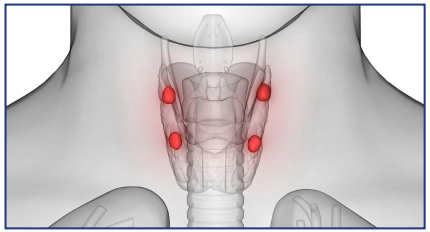


Bollerslev J, et al. Eur J Endocrinol. 2025;193(5):G49-G78

PTH replacement therapy

- **R.3.5** We recommend PTH replacement therapy in patients who **continue to have signs or symptoms of HypoPT** despite treatment with activated vitaminD + adequate calcium intake**.**

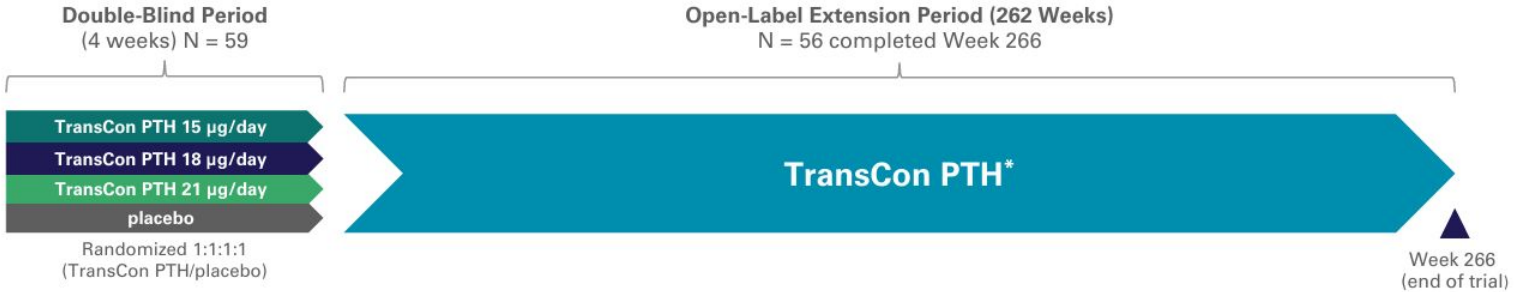
- R.3.5.2 We suggest to consider PTH replacement therapy in patients with one of the following despite optimized treatment.
  - **Frequent fluctuations in calcium, or symptomatic hypocalcaemia**
  - **Impaired quality of life attributable to chronic HypoPT**
  - **Reduced kidney function (eGFR < 60 mL/min per 1.73m²)**
  - **Hypercalciuria**
  - **Hyperphosphataemia**



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Phase 2 PaTH Forward Trial Design

Randomized, double-blind, placebo-controlled trial followed by an open-label extension period in adults with chronic hypoparathyroidism



Select Open-Label Extension Endpoints

- Levels of serum calcium (normocalcemia)
- Independence from conventional therapy (defined as taking no active vitamin D and ≤ 600 mg/day elemental calcium)
- Levels of 24-hour urinary calcium
- Incidence of AEs, SAEs, TEAEs

Skeletal Remodeling, Renal, and PRO Endpoints

- Bone turnover markers (P1NP and CTx)
- Bone mineral density by DXA of the lumbar spine L1-L4, femoral neck, total hip, and distal 1/3 radius
- Renal function as assessed by eGFR
- Hypoparathyroidism Patient Experience Scales (HPES) assessments evaluating symptoms and functional impacts

AE = adverse event; SAE = serious adverse event; TEAE = treatment-emergent adverse event; P1NP = procollagen type 1 N-terminal propeptide; CTx = C-terminal telopeptide of type 1 collagen; DXA = dual X-ray absorptiometry; eGFR = estimated glomerular filtration rate; PRO = patient-reported outcomes.* TransCon PTH (palopegteriparatide) 6-60 ug/day and conventional therapy titrated per algorithm to maintain normocalcemia.

For investor communication only. Not for use in product promotion. Not for further distribution.

PTH replacement therapy

Consider PTH replacement therapy

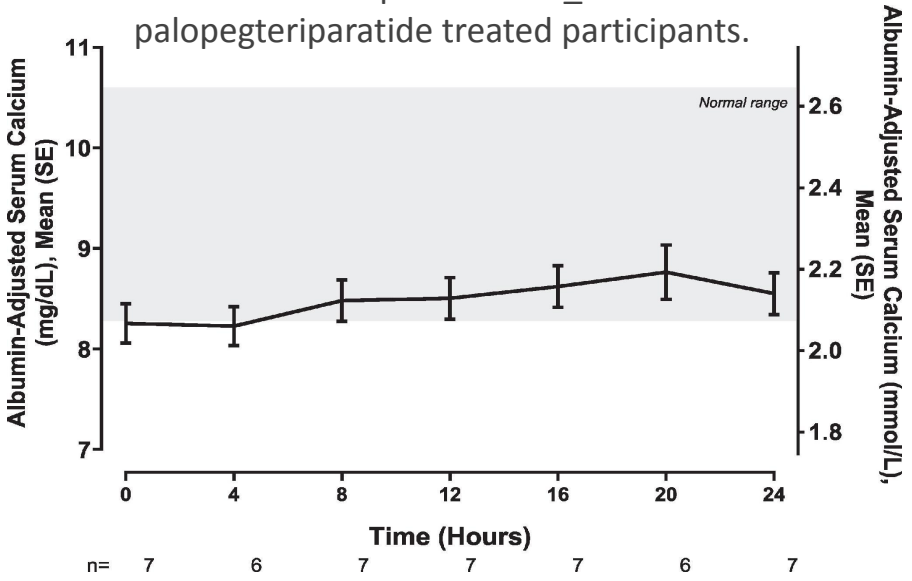
YES

Targets NOT reached despite multiple optimisation attemps

Patients with optimised conventional treatment and one of the following:

- Frequent fluctuations in calcium levels, or symptomatic hypocalcaemia
- Impaired QoL attributable to chronic HypoPT
- Reduced kidney function (eGFR < 60 mL/min per 1.73m²)
- Persistent hypercalciuria
- Persistent hyperphosphataemia

24-hour profile of Ca_c in palopegteriparatide treated participants.



J. Endocr. Soc., Volume 10, Issue 7, July 2026, bvag098.

PTH replacement therapy

Consider PTH replacement therapy

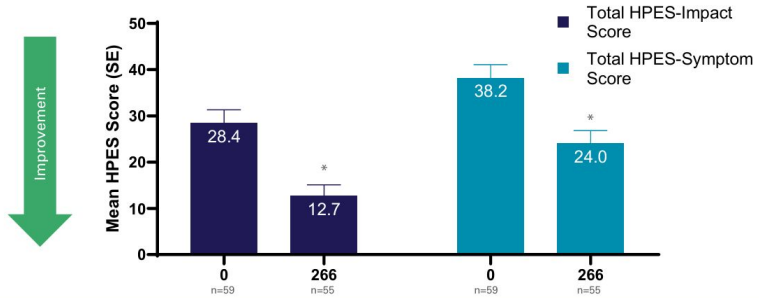
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Improvement in PROs with TransCon PTH Treatment Sustained Through Week 266



Hypoparathyroidism-related physical and cognitive symptoms and impacts on physical functioning and daily life improved with TransCon PTH treatment and were maintained through Week 266

* P value < 0.0001 when compared versus baseline
PRO = patient-reported outcome; HPES = Hypoparathyroidism Patient Experience Scales.

J. Endocr. Soc., Volume 10, Issue 7, July 2026, bvag098.

PTH replacement therapy

Consider PTH replacement therapy

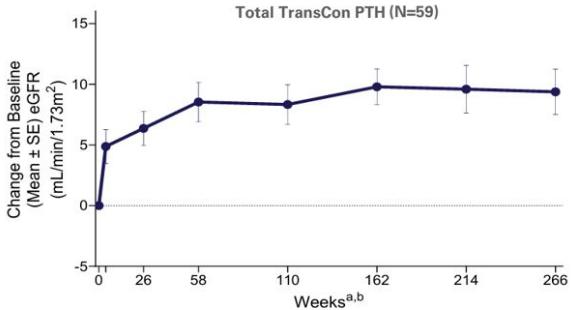
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Durable Increase in eGFR Through 5 Years with TransCon PTH Treatment



The increase in eGFR from baseline was sustained through Week 266, with mean (SE) increase in eGFR of 9.4 (1.9) mL/min/1.73m² for the total population[c]

PTH replacement therapy

Consider PTH replacement therapy

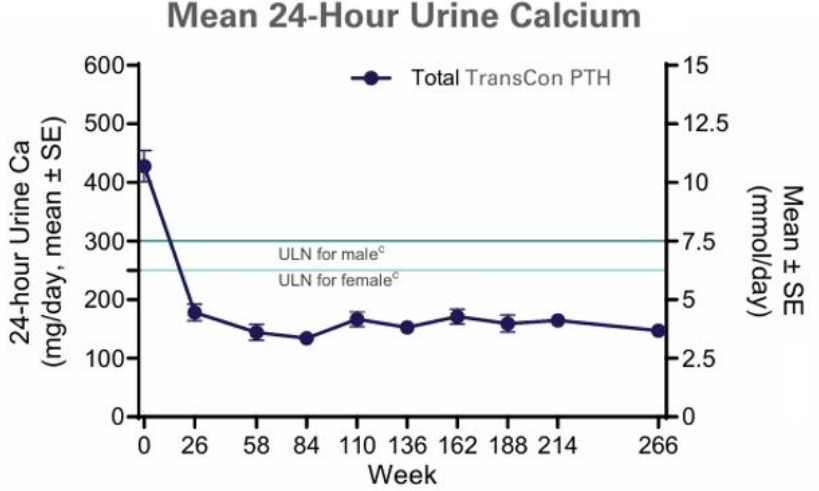
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Consistency of Mean Urine Calcium Values Observed Over 5 Years of Treatment



Mean serum calcium values remained within the normal range throughout the trial
24-hour urine calcium normalized within 26 weeks and remained normal through Week 266

PTH replacement therapy

Consider PTH replacement therapy

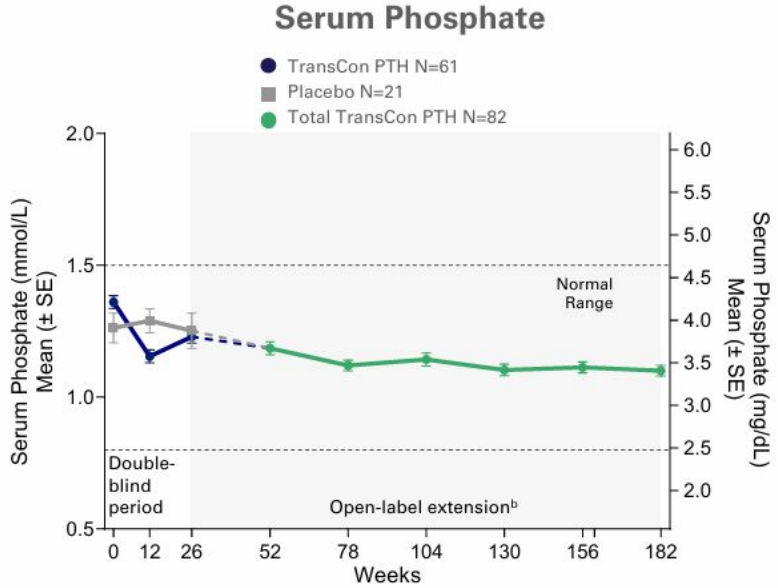
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Week 182 Data from the Phase 3 PaTHway Trial



Agenda

Introduction: Definition. Two main ideas. Who to treat

Conventional treatment

Optimized conventional treatment

PTH replacement therapy

What is next?

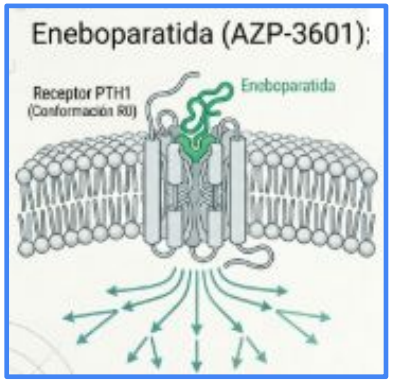
What is next?

Journal of Endocrinological Investigation (2026) 49:725–746
https://doi.org/10.1007/s40618-025-02760-9

REVIEW

Unveiling the complexities of hypoparathyroidism: a comprehensive review of clinical manifestations, diagnosis, and novel therapies

Filomena Cetani[1] · Francesco Bertoldo[2] · Marco Bononi[3] · Mariarita Tarallo[3] · Valentina Camozzi[4] · Cristiana Cipriani[5] · Andrea Palermo[6,7] · Daniela Pasquali[8] · Guido Zavatta[9,10]





1037 - The Oral Calcilytic Encaleret Reduced Urinary Calcium While Maintaining Blood Calcium in Individuals with Post-Surgical Hypoparathyroidism

Saturday, September 6, 2025
11:30 AM - 11:45 AM
General Session Room, 6BC (6th Floor, Seattle Convention Center)

ASBMR Annual Meeting 2025

Thank you for your attention