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Risk of Chronic Kidney Disease in Adult Patients With Chronic Hypoparathyroidism Treated With rhPTH(1-84) Compared With a Historical Control Cohort

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BACKGROUND

- Patients with chronic hypoparathyroidism (HypoPT) are at increased risk of renal complications, including nephrocalcinosis, nephrolithiasis, and renal insufficiency[1-3]
- In long-term clinical trials, recombinant human parathyroid hormone (1-84), rhPTH(1-84), improved biochemical parameters and normalised urinary calcium excretion for patients with chronic HypoPT[4,5]
- In a previous study, estimated glomerular filtration rate (eGFR) was preserved among patients with chronic HypoPT treated with rhPTH(1-84) compared with patients not treated with rhPTH(1-84);[6] however, further evidence is required to establish whether treatment with rhPTH(1-84) reduces risk of renal complications in these patients

OBJECTIVE

- Evaluate chronic kidney disease (CKD) outcomes over a period of up to 5 years in adult patients with chronic HypoPT treated with rhPTH(1-84) in clinical trials compared with a historical control cohort of patients who did not receive rhPTH(1-84)

METHODS

- rhPTH(1-84)-treated patient cohort: derived from the REPLACE (NCT00732615), RELAY (NCT01268098), RACE (NCT01297309), and HEXT (NCT01199614) clinical trials (**Figure 1**)
- Historical control cohort: adult patients with chronic HypoPT selected from the large, nationally representative US Explorys electronic medical record database (Jan 2007–Aug 2019) using criteria similar to the trial enrolment criteria (**Figure 1**)
- Patients with CKD at baseline were excluded
- Analyses: Kaplan-Meier analysis and Cox proportional hazards models (see table and figure footnotes for additional analytic details)

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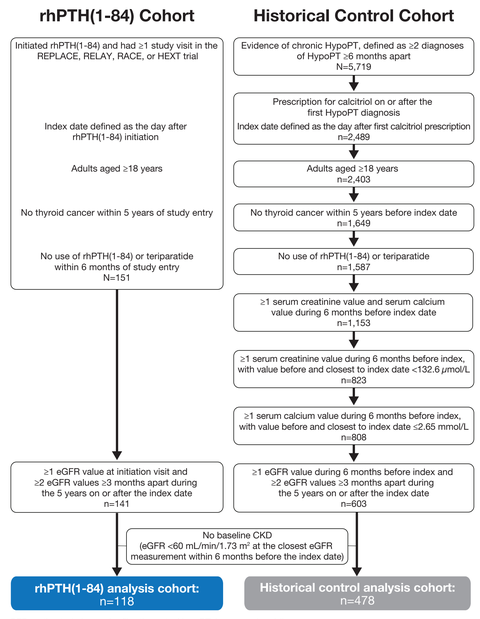
RESULTS

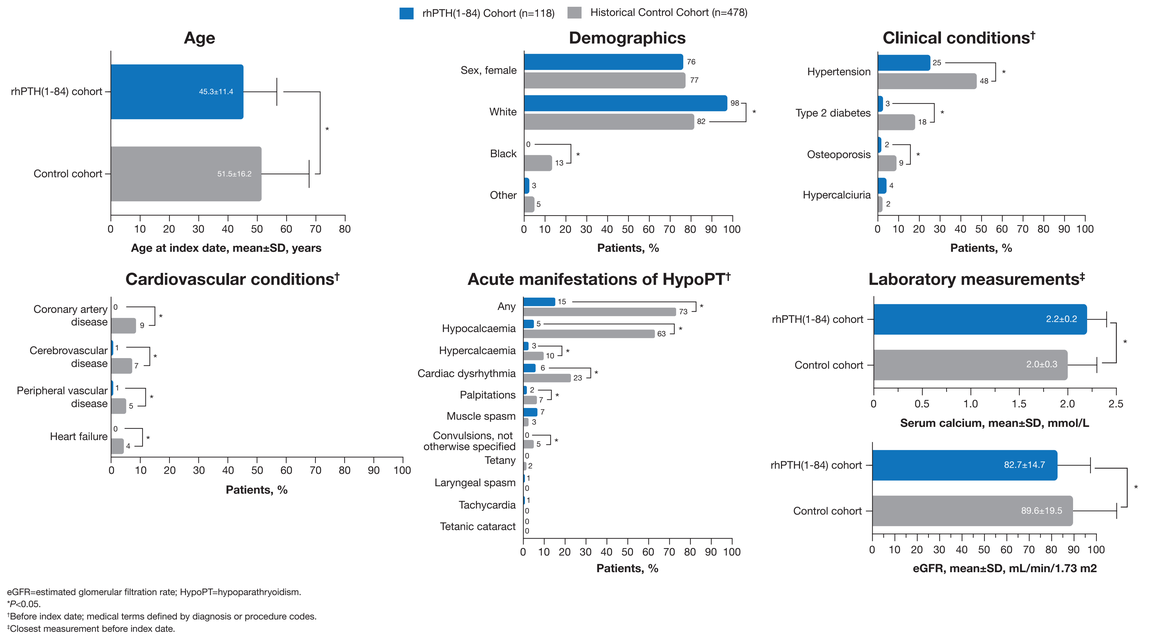
- Study cohorts: rhPTH(1-84), n=118; historical control cohort, n=478 (**Figure 2**)
- Kaplan-Meier analysis: rhPTH(1-84)-treated patients had a significantly reduced risk of developing CKD during follow-up compared with patients in the control cohort not treated with rhPTH(1-84) (P<0.01; **Figure 3**)
- Multivariable adjusted Cox proportional hazards model: hazard ratio for developing CKD associated with rhPTH(1-84) compared with no rhPTH(1-84) treatment was 0.47 (95% CI: 0.25–0.88; P<0.05; **Table 1**)

Figure 1. Patient Selection Flow Diagram



eGFR=estimated glomerular filtration rate; HypoPT=hypoparathyroidism.

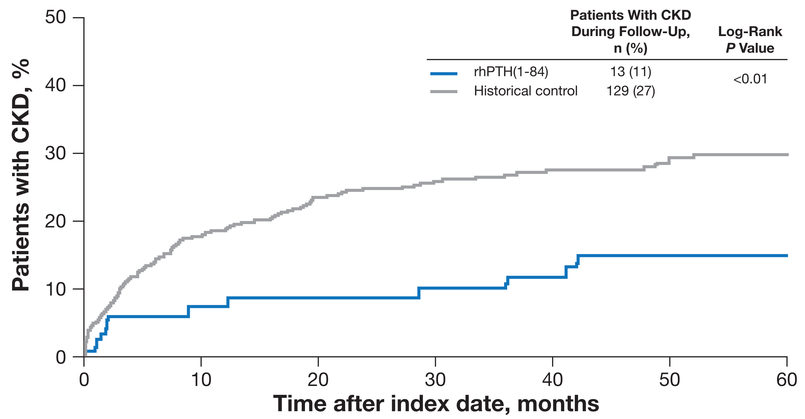
Figure 2. Baseline Patient Demographic and Clinical Characteristics



eGFR=estimated glomerular filtration rate; HypoPT=hypoparathyroidism.
*P<0.05.
†Before index date; medical terms defined by diagnosis or procedure codes.
‡Closest measurement before index date.

CKD outcome: First occurrence of eGFR <60 mL/min/1.73 m² on or after the index date, confirmed by a second measurement ≥3 months later

Figure 3. Kaplan-Meier Analysis of Time to First Instance of CKD Among Patients With HypoPT Without CKD at Baseline



Number of patients with CKD							
rhPTH(1-84) patients	0	8	9	10	11	13	13
Historical control patients	0	85	110	119	124	128	129
Number of patients at risk							
rhPTH(1-84) patients	118	66	63	59	56	53	48
Historical control patients	478	381	307	259	202	151	121

CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; HypoPT=hypoparathyroidism.

Table 1. Risk of Developing CKD

Cox Proportional Hazards Model of Time to First Instance of CKD Among Patients With Chronic HypoPT and Without CKD at Baseline

Estimated effect of rhPTH(1-84) vs historical control cohort

	HR	95% CI	*P* Value
Unadjusted	0.43	0.24–0.76	<0.01
Adjusted†	0.47	0.25–0.88	<0.05

CI=confidence interval; CKD=chronic kidney disease; CV=cardiovascular; eGFR=estimated glomerular filtration rate; HR=hazard ratio; HypoPT=hypoparathyroidism.
†Cox models were adjusted for demographics (age, sex, race), clinical conditions (hypercalciuria, hypertension, type 2 diabetes, CV conditions, and acute manifestations of HypoPT), and laboratory values (eGFR and serum calcium) at baseline.
CV conditions were defined as ≥1 diagnosis of cerebrovascular disease, coronary artery disease, heart failure, or peripheral vascular disease; medical terms defined by diagnosis or procedure codes.
Acute manifestations of HypoPT were defined as ≥1 diagnosis of hypercalcaemia, hypocalcaemia, laryngeal spasm, muscle spasm, convulsions (not otherwise specified), tetanic cataract, tetany, cardiac dysrhythmia, tachycardia, or palpitations; medical terms defined by diagnosis or procedure codes.

Patients with chronic HypoPT treated with **rhPTH(1-84)** had reduced risk of developing CKD over 5 years compared with **control** patients not treated with rhPTH(1-84)

LIMITATIONS

- Differences in patient management between the studied cohorts (ie, predefined clinical trial protocols for the rhPTH(1-84) cohort vs real-world practice for the control cohort)
- Potential for miscoding of diagnoses and misreporting of laboratory test measurements in the administrative claims database

CONCLUSIONS

- **After adjusting for baseline differences, patients with chronic HypoPT treated with rhPTH(1-84) in clinical trials had a significantly reduced risk of developing CKD compared with patients in a control cohort who did not receive rhPTH(1-84)**
- **Further research is warranted to better understand the mechanisms underlying these findings**

REFERENCES

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DISCLOSURES

EOG has served as a consultant for Shire, a Takeda company. OA and NS are employees of Shire Human Genetic Therapies, Inc., a Takeda company, Lexington, MA, USA. FM, AB, and ES are employees of Analysis Group, Inc., which was contracted by Shire Human Genetic Therapies, Inc., a Takeda company, to conduct this research. LR has served as an advisory board member, speaker, and research investigator for Shire, a Takeda company. This study was funded by Shire Human Genetic Therapies, Inc., a Takeda company, Lexington, MA, USA. Editorial support was provided by ICON, North Wales, PA, USA, and was funded by Shire Human Genetic Therapies, Inc., a Takeda company, Lexington, MA, USA.

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This poster is intended for healthcare providers