

# Similarities in Postsurgical vs Nonsurgical Patients With Hypoparathyroidism: Post Hoc Analysis From Recombinant Human Parathyroid Hormone (rhPTH[1-84], Parathyroid Hormone rDNA) REPLACE Study

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## BACKGROUND

- Hypoparathyroidism, a rare disorder characterized by absent or low levels of parathyroid hormone (PTH), is most commonly caused by thyroid surgery.<sup>1</sup>
- Data from Denmark indicate that the prevalence of postsurgical hypoparathyroidism (20.6/100,000 inhabitants) is 9 times greater than the prevalence of hypoparathyroidism due to nonsurgical causes (2.3/100,000 inhabitants).<sup>2,3</sup>
- Both causes are associated with significant morbidity.<sup>2,3</sup>
- Little is known about characteristics and treatment responses of patients with hypoparathyroidism due to postsurgical versus nonsurgical etiologies.
- The full-length recombinant human parathyroid hormone rhPTH(1-84) is approved in the United States as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.<sup>4</sup>
  - The REPLACE study (NCT00732615, EudraCT2008-005063-34) was a phase III, double-blind, placebo-controlled study of patients with hypoparathyroidism from 33 centers in North America and Europe who received once-daily rhPTH(1-84) (50 µg initially, increased to 75 µg, then 100 µg if needed) or placebo. In the rhPTH(1-84) group, 52% of patients completed the study on a dose of 100 µg/day; 27% and 21% completed the study on a dose of 75 and 50 µg/day, respectively.<sup>5</sup>
  - The primary endpoint (≥50% reduction in oral calcium and active vitamin D while maintaining albumin-adjusted serum calcium levels) was achieved in 53% of rhPTH(1-84)-treated vs 2% of placebo-treated patients ( $P<0.001$ ).<sup>5</sup>

## OBJECTIVE

- To determine the baseline characteristics and responses of rhPTH(1-84) in patients with postsurgical or nonsurgical hypoparathyroidism

## METHODS

- This was a post hoc analysis of the REPLACE study.<sup>5</sup>
- Demographic and baseline characteristics were compared between patients with postsurgical and patients with nonsurgical hypoparathyroidism.
  - Chi-square tests for categorical variables
  - One-way analysis of variance with effect for continuous variables
- Definition of responder was similar to that in the REPLACE study:
  - Patients whose need for conventional treatment with oral calcium and active vitamin D was reduced by ≥50% from baseline while maintaining albumin-adjusted total serum calcium at 1.87–2.64 mmol/L.

## RESULTS

### Patient Disposition and Baseline Characteristics

- Of 124 patients randomized in REPLACE, 89 (72%) had postsurgical and 35 (28%) had nonsurgical hypoparathyroidism.
- Demographic and baseline characteristics are shown in **Table 1**.
- Significant differences between the groups were
  - Gender distribution
  - Age at study screening
  - Time since diagnosis (ie, duration of hypoparathyroidism)

## RESULTS CONTINUED

- Baseline calcium and active vitamin D doses were not different between the 2 groups.
- Per criteria that are now available in the 2015 ESE guidelines,<sup>6</sup> ≥80% of patients within each subgroup were not well controlled before treatment with rhPTH(1-84), even after optimization with conventional treatment.

**Table 1. Demographic and Baseline Characteristics of Patients With Postsurgical and Nonsurgical Hypoparathyroidism**

Parameter	Postsurgical n=89	Nonsurgical n=35	P Value
Age at study screening, y			
Mean ± SD	49.1±12.4	42.9±12.6	0.014
Gender, n (%)			
Men	9 (10)	17 (49)	
Women	80 (90)	18 (51)	<0.0001
Race, n (%)			
White	85 (96)	34 (97)	0.400
Other*	4 (4)	1 (3)	
Weight, kg			
Mean ± SD	80.1±16.9	83.5±20.2	0.343
Body mass index, kg/m <sup>2</sup>			
Mean ± SD	29.3±6.1	28.9±6.2	0.794
Geographic region, <sup>†</sup> n (%)			
North America	45 (51)	19 (54)	0.169
Western Europe	24 (27)	13 (37)	
Central and Eastern Europe	20 (22)	3 (9)	
Duration of hypoparathyroidism, y			
Mean ± SD	12.1±8.8	17.5±12.9	0.008
Active vitamin D dose, µg <sup>‡</sup>			
Mean ± SD	1.1±0.8	1.2±0.8	0.398
Calcium dose, mg			
Mean ± SD	2057.9±1398.7	2236.4±1109.41	0.500

\*Other includes Black, Asian, Native Hawaiian/Pacific Islander, and not specified.  
<sup>†</sup>North America includes Canada and the United States; Western Europe includes France, Italy, Belgium, Denmark, and the United Kingdom; Central and Eastern Europe include Hungary only.  
<sup>‡</sup>Includes both analogs of vitamin D, calcitriol and alfacalcidol; a converted active vitamin D value was used in which 2 doses of alfacalcidol were equated to 1 dose of calcitriol.

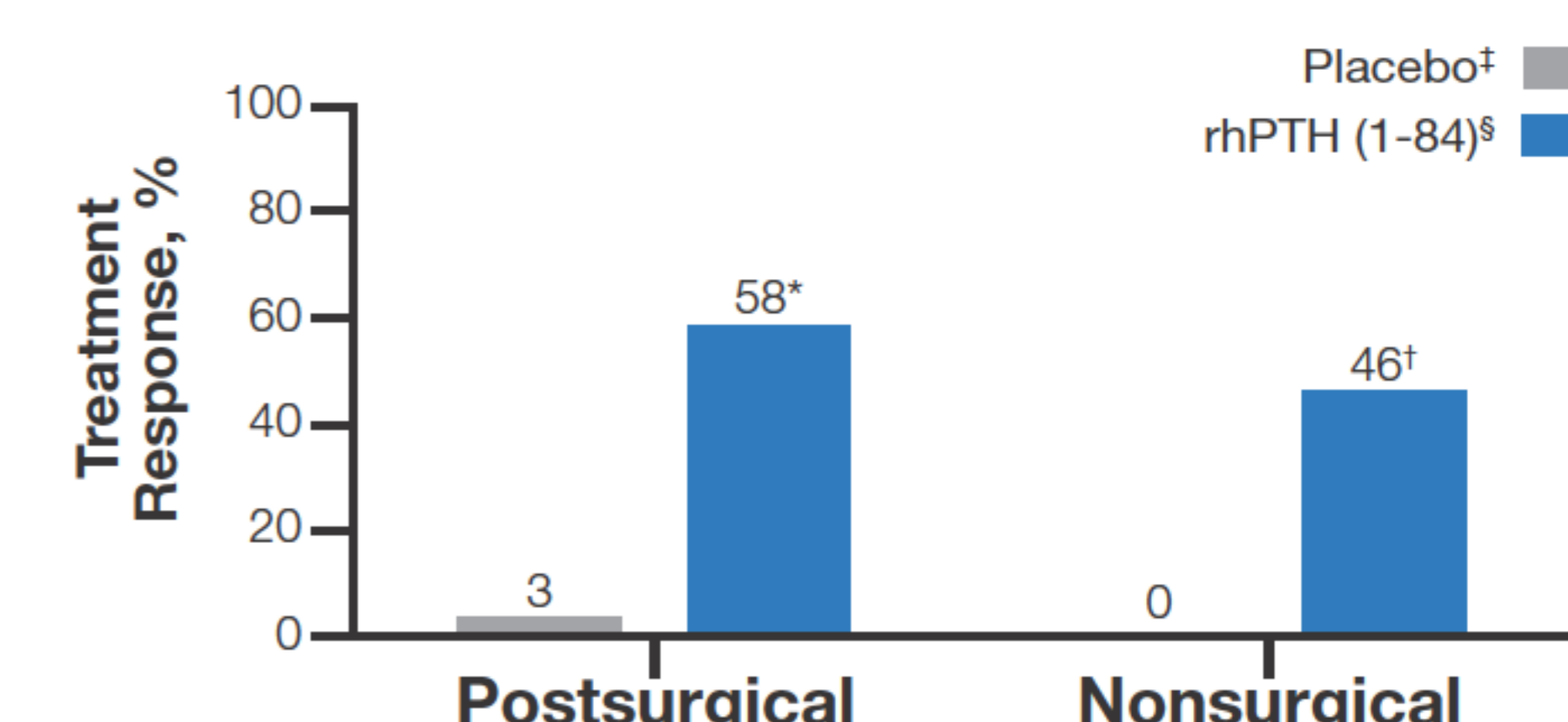
### Baseline key lab values

- At baseline, mean (SD) serum intact PTH levels were
  - 0.79 (0.94) pmol/L in the postsurgical group
  - 0.37 (0.48) pmol/L in the nonsurgical group
  - 1.48–7.63 pmol/L in the healthy adult reference range (ACM Global Lab)
- At baseline, mean (SD) albumin-adjusted serum calcium levels were
  - 2.13 (0.16) mmol/L in the postsurgical group
  - 2.16 (0.26) mmol/L in the nonsurgical group
  - 2.10–2.64 mmol/L in the healthy adult reference range (ACM Global Lab)
- At baseline, mean (SD) serum phosphate levels were
  - 1.47 (0.22) mmol/L in the postsurgical group
  - 1.41 (0.18) mmol/L in the nonsurgical group
  - 0.80–1.60 mmol/L in the healthy adult reference range (ACM Global Lab)

### Treatment response

- A significantly greater percentage of patients receiving rhPTH(1-84) versus placebo were deemed responders in relation to the primary endpoint regardless of cause (**Figure 1**).
  - Postsurgical group responder rate was 58% with rhPTH(1-84) (35/60) vs 3% with placebo (1/29;  $P<0.001$ )
  - Nonsurgical group responder rate was 46% with rhPTH(1-84) (11/24) vs 0% with placebo (0/11;  $P=0.007$ )

**Figure 1. Treatment Response in Postsurgical and Nonsurgical Groups**



\* $P<0.001$  vs placebo.  
<sup>†</sup> $P=0.007$  vs placebo.  
<sup>‡</sup>Postsurgical, n=29; Nonsurgical, n=11.  
<sup>§</sup>Postsurgical, n=60; Nonsurgical, n=24.

## CONCLUSIONS

- Patient demographics and baseline characteristics were similar between those with postsurgical and nonsurgical hypoparathyroidism.
  - A notable difference is gender distribution with women accounting for 90% of the postsurgical group, whereas men were evenly divided between the 2 groups.
- Treatment response was significantly greater for patients receiving rhPTH(1-84) versus placebo in both groups.
- Findings from this post hoc analysis show no differences in response, as defined by the primary endpoint, to rhPTH(1-84) treatment based on etiology of hypoparathyroidism.

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## DISCLOSURES

MLB has received institutional research grants from and served on the speakers bureau for NPS Pharmaceuticals, Inc.

JPB, BLC, LR, and DMS have received institutional research grants from and served as advisory group members for NPS Pharmaceuticals, Inc.

MM and TJV have served as advisory group members for NPS Pharmaceuticals, Inc.

AK is an employee of Shire plc.

HL and BL were employees of NPS Pharmaceuticals, Inc., at the time of the analysis.

WDF has served as an advisory group member and on the speakers bureau for NPS Pharmaceuticals, Inc. and Shire plc.

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