

# Patient Experiences of Hunger in POMC or LEPR Deficiency

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## Summary

- Proopiomelanocortin (POMC) and leptin receptor (LEPR) deficiencies are rare genetic diseases of obesity that are associated with insatiable hunger, which places huge burdens on patients and caretakers
- We conducted in-depth interviews in a cohort of patients with POMC and LEPR deficiencies who received treatment with setmelanotide and found a decrease in the daily burdens of insatiable hunger that had meaningful impacts on the patients' quality of life (QOL)

## Introduction

- Many rare genetic diseases of obesity are associated with mutations in the melanocortin-4 receptor pathway, a hypothalamic pathway that regulates hunger and energy balance<sup>1-3</sup>
  - Variants in key genes including POMC and LEPR can disrupt melanocortin-4 receptor signaling, resulting in hyperphagia and early-onset obesity<sup>1-3</sup>
- In patients with POMC or LEPR deficiency, managing hyperphagia and obesity can be a daily struggle, and these burdens are not well characterized<sup>4</sup>
- In this study, we describe the experience of the daily impacts of insatiable hunger on patients with POMC or LEPR deficiency treated with setmelanotide as it relates to health-related QOL

## Methods

- In-depth qualitative interviews were conducted via video conference with patients who were aged  $\geq 15$  years, had previous diagnosis of POMC or LEPR deficiency, and were participating in an ongoing open-label extension of Phase 3 clinical trials with setmelanotide (NCT03651765)
- Using a semistructured interview guide, patients were asked to describe
  - Experiences of hunger, as well as the impacts of hunger on their lives prior to setmelanotide treatment
  - Changes in hunger, weight, and functioning after initiating setmelanotide treatment, including the perceived meaningfulness of the changes
  - Treatment satisfaction and feelings if setmelanotide were to be discontinued
- Interviews were conducted in German, recorded, transcribed, and translated into English for analysis

## Results

### Patient Characteristics

- We interviewed 5 patients with POMC (n=3) or LEPR (n=2) deficiency
- The average age was 23.8 years (range, 15–33 years), and 4 of the 5 patients were male
- One participant was hearing impaired; the interview was facilitated by the mother, who also responded to interview questions

### Patient Experience Prior to Setmelanotide Treatment

- Before setmelanotide treatment, all 5 patients described an abnormal sensation of hunger (2 described a strong psychological desire, much like addiction), with none indicating they felt full after meals (Table 1; Figure)
- All 5 patients reported insatiable hunger negatively impacted their families, emotions, and work and/or school functioning (Table 1; Figure)

Table 1. Patient-Reported Experiences of Hunger, Eating Habits, and Impact of Hyperphagia Prior to Clinical Trials With Setmelanotide

Before Setmelanotide Treatment			
Feelings of hunger	Eating habits	Impacts of hyperphagia	
			<p>"It sometimes felt as if I were an animal that was super hungry and could only think about food, and when I wanted to eat something, I searched until I found it."</p> <p>– Patient with POMC deficiency</p>
			<p>"What I recall very strongly is this addiction-like desire for food, and this constant preoccupation with it. It's more than the physical feeling of hunger. It also plays on a mental level."</p> <p>– Patient with POMC deficiency</p>
			<p>"I really had to struggle with myself... sometimes I could control myself, but most of the time I couldn't."</p> <p>– Patient with POMC deficiency</p>
			<p>"When I would start eating something, I'd eat the whole thing. No matter what sort of package it was, or whatever, I'd always eat the whole thing. I also ate it at an enormous tempo... it was really terrible."</p> <p>– Patient with LEPR deficiency</p>
			<p>"I would eat my way through everything crosswise, and very quickly, too. I would always do this in a certain feeling of stress so that my parents wouldn't see it, because they had set up certain rules about food so that I wouldn't gain weight. So, my eating was very hectic when I'd eat in secret."</p> <p>– Patient with POMC deficiency</p>
			<p>"It was like, if there were chips somewhere, I always kept eating, kept eating, kept eating, kept eating. Until someone complained and said I should stop. Then I had to struggle with myself, but since everyone was there and was watching, I somehow managed it."</p> <p>– Patient with POMC deficiency</p>
			<p>"It was as if I did not try to find work, but after 1 or 2 months something always occurred, so that I ended up back in the hospital, or I had to call in sick and couldn't work. Of course, I was always fired during my trial period, and I never arrived at a long-term employment situation."</p> <p>– Patient with LEPR deficiency</p>
			<p>"They took me away when I was 4 years old, claiming that my mother was feeding me to make me fat, and they took me to some sort of psychosomatic facility, for over a year, or a year and a half, where I was supposed to lose weight. That did not work either."</p> <p>– Patient with LEPR deficiency</p>
			<p>"It was not as if I did not try to find work, but after 1 or 2 months something always occurred, so that I ended up back in the hospital, or I had to call in sick and couldn't work. Of course, I was always fired during my trial period, and I never arrived at a long-term employment situation."</p> <p>– Patient with LEPR deficiency</p>
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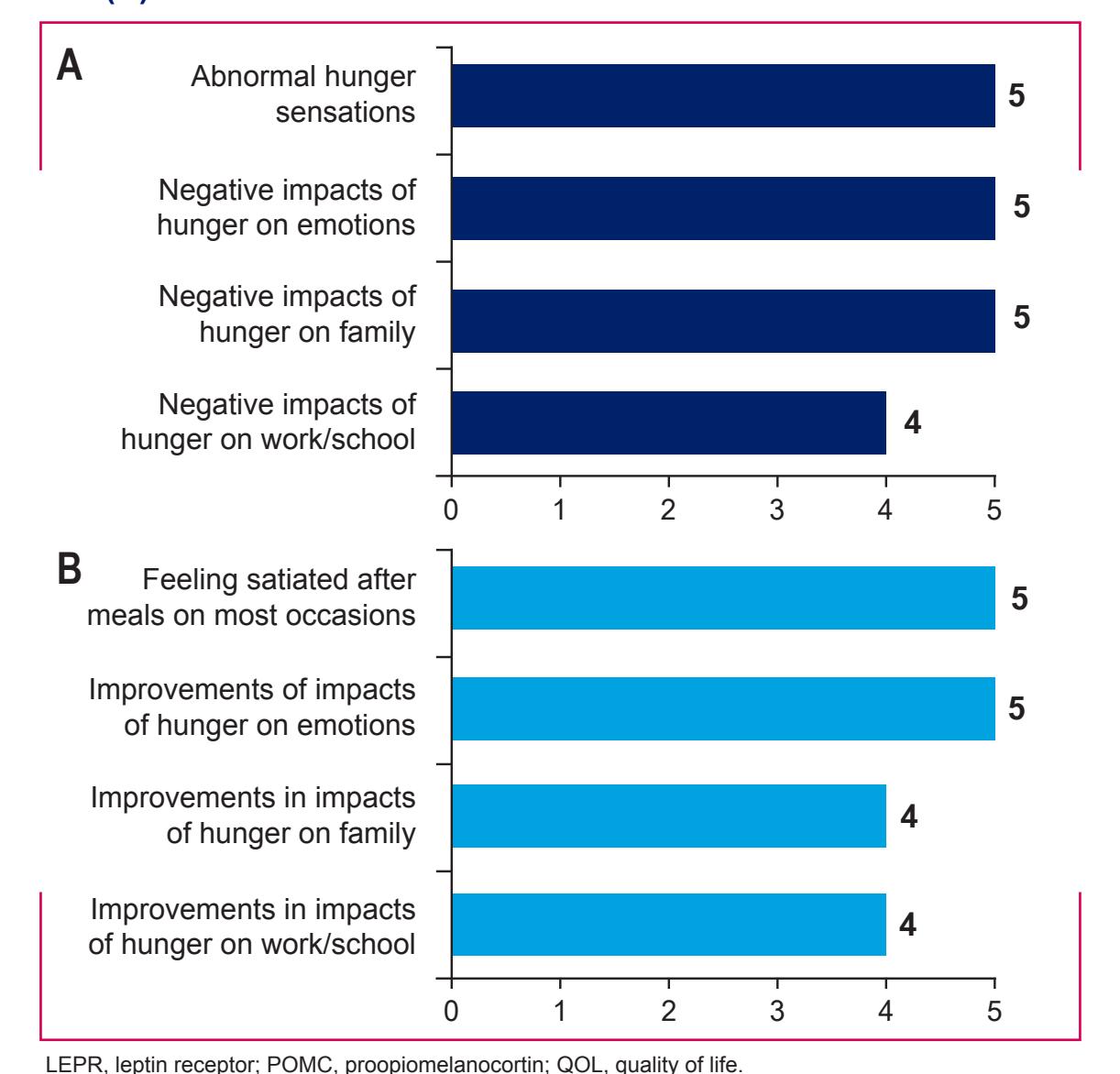
Changes With Setmelanotide Treatment Experienced by Patients

- After setmelanotide treatment, all 5 patients reported profound reductions in hunger and eating and substantial improvements in QOL (Table 2; Figure)
- Patients with POMC deficiency reported weight loss ranging from 40 to 97 kg following setmelanotide treatment, and those with LEPR deficiency reported weight loss ranging from 25 to 35 kg
- All 5 patients indicated they were very satisfied with the impact of setmelanotide treatment and would be upset if they had to discontinue (Table 3; Figure)

Table 2. Patient-Reported Experiences of Hunger, Eating Habits, and Impact of Hyperphagia During and After Clinical Trials With Setmelanotide

After Setmelanotide Treatment			
Feelings of hunger	Eating habits	Impacts of decreased hyperphagia	
			<p>"A lot has changed, and when I look at the hunger today, I'm assuming it's on the same level as other people. I don't have anything to compare it by, but I'm just assuming that."</p> <p>– Patient with POMC deficiency</p>
			<p>"Now, I do not feel huge hunger, but sometimes it's difficult to say. It's still like... You want to eat; you feel the urge. But the hunger itself is not that great."</p> <p>– Patient with POMC deficiency</p>
			<p>"Now, I really feel it. My stomach growls and I notice that I am hungry. It's a feeling I never had before. It is funny."</p> <p>– Patient with LEPR deficiency</p>
			<p>"I still give thought to food, and maybe I feel like eating this or that. But I can choose to eat something, and I can also set it aside, and in no way does it still hold this status."</p> <p>– Patient with POMC deficiency</p>
			<p>"Now, if I am hungry, I eat something, I am full right away and I stop, very simple. Previously, I wasn't able to manage that. It just didn't work."</p> <p>– Patient with LEPR deficiency</p>
			<p>"For me, not being able to work was the worst thing, to be honest. I simply could not, and this has changed with the study and with the weight loss... I've been working steadily for 2 years now, without interruptions and I'm doing well in my job. It's fun, no problems at all. It is really unbelievable."</p> <p>– Patient with POMC deficiency</p>
			<p>"Before, I tried for a long time to study, but I failed due to my physical and mental state. But now that I've been receiving the medication, I got into it very fast, and I'm beginning my final [undergraduate] semester, and it's working really super, I have to say. There's no comparison. Before, it just wouldn't have been possible, and now it's working wonderfully. That's also a big change."</p> <p>– Patient with POMC deficiency</p>

Figure. Number of patients with POMC (n=3) or LEPR (n=2) deficiency who experienced hyperphagia and related impacts on QOL (A) before and (B) after treatment with setmelanotide.



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## Conclusions

- Hyperphagia and the constant inability to feel satiety negatively impact QOL in patients with POMC or LEPR deficiency
- Reduced hunger and improved satiety resulting from setmelanotide treatment substantially and meaningfully change these patients' lives
- Results from this qualitative study are consistent with those reported in Phase 3 trials of setmelanotide and suggest that the impacts of setmelanotide treatment also include QOL improvements