Paediatric patients with acquired hypothalamic obesity treated with setmelanotide: real-world BMI and hunger data for up to 18 months in France

P1180

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Ahlam Azar-Kolakez,[1] Iva Gueorguieva,[2] Alcine Mailys,[3] Pascal Barat,[4] Natacha Bouhours-Nouet,[5] Marie Bournez,[6] Jean-Claude Carel,[1] Régis Coutant,[5] Tommaso De Giorgis,[7] Marine Delagrange,[4] Claire-Lise Gay,[8] Marion Gérard,[9] Marie-Aline Guitteny,[7] Marie Hoflack,[10] Dunlanjalee Kariyawasam,[11] Muriel Laurans,[9] Laetitia Martinerie,[1] Patricia Pigeon Kherchiche,[12] Rachel Reynaud,[13] Caroline Storey-London,[1] Gwenaelle Diene,[14] Béatrice Dubern[15]

[1]Pediatric Endocrinology-Diabetology Department, Robert-Debré Hospital APHP, Paris, France; [2]Pediatric Endocrinology Department, Jeanne de Flandre Hospital, Lille, France; [3]Pediatric Department, Saint Pierre Hospital, La Réunion, France; [4]Pediatric Endocrinology, Diabetology, Gynecology and Obesity Unit, University Hospital of Bordeaux, Bordeaux, France; [5]Pediatric Endocrinology and Diabetology Unit, University Hospital of Angers, Angers, France; [6]Department of Genetics, University Hospital of Dijon, Dijon, France; [7]Paediatric Endocrinology Department, Rennes University Hospital, Rennes, France; [8]Pediatric Endocrinology Department, Institut Saint-Pierre, Palavas-Les-Flots, France; [9]Pediatric Department, Caen-Normandy Hospital, Caen, France; [10]Pediatric Endocrinology Department, Paediatric Hospital of Nice CHU Lenval, Nice, France; [11]Pediatric Endocrinology, Diabetology and Gynecology Department, Necker-Enfants Malades Hospital APHP, Paris, France; [12]Pediatric Department, Felix Guyon Hospital, Saint-Denis, La Réunion, France; [13]Multidisciplinary Pediatric Department, Timone Hopital, AP-HM, Marseille, France; [14]Division of Endocrinology, Genetics, Gynecology and Bone Diseases, Children's Hospital, University Hospital Center of Toulouse, Toulouse, France; [15]Pediatric Nutrition and Gastroenterology Department, Trousseau Hospital APHP, Paris, France

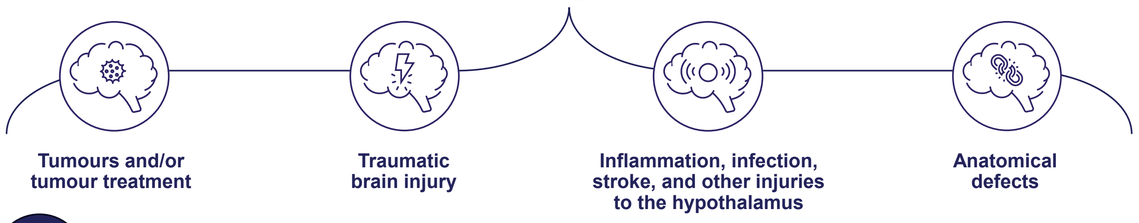
Conclusions

- This real-world data from paediatric patients with aHO who were treated with setmelanotide for up to 18 months showed improvements in BMI and hunger
- Safety outcomes were consistent with Phase 3 trial data
- These findings support the real-world therapeutic value of setmelanotide treatment for paediatric patients with aHO

Background

- Acquired hypothalamic obesity (aHO) is characterised by accelerated and sustained weight gain due to disrupted MC4R signalling.[1–3] This may result from physical injury to the hypothalamus or structural abnormalities of the hypothalamus
- In the pivotal, placebo-controlled, 52-week Phase 3 TRANSCEND trial in patients with aHO aged ≥4 years, treatment with the MC4R agonist setmelanotide reduced BMI by 16.5%, versus a 3.3% increase with placebo (placebo-adjusted difference: −19.8%)[4]
- In France, setmelanotide was made available to patients with aHO through a pre-marketing early access programme following positive Phase 2 clinical trial results

Identified aetiologies of aHO[1,5–8]



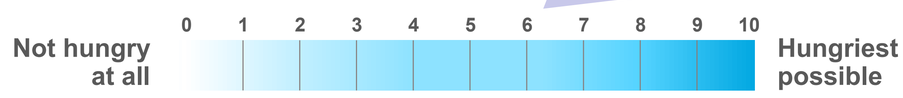
Objectives

- To report real-world data from paediatric patients (aged ≥6 to <18 years) with aHO treated with setmelanotide for up to 18 months in a pre-marketing early access programme in France

Methods

- BMI and hunger outcomes were reported for patients receiving setmelanotide treatment for up to 18 months (please see supplementary materials for more detailed information on the methods)
  - Outcomes were analysed at 6, 9, 12, and 18 months versus baseline using separate paired analysis groups
  - Hunger was reported for patients aged ≥12 to <18 years using the following question:

Over the past 24 hours, how hungry did you feel when you were **most hungry**?

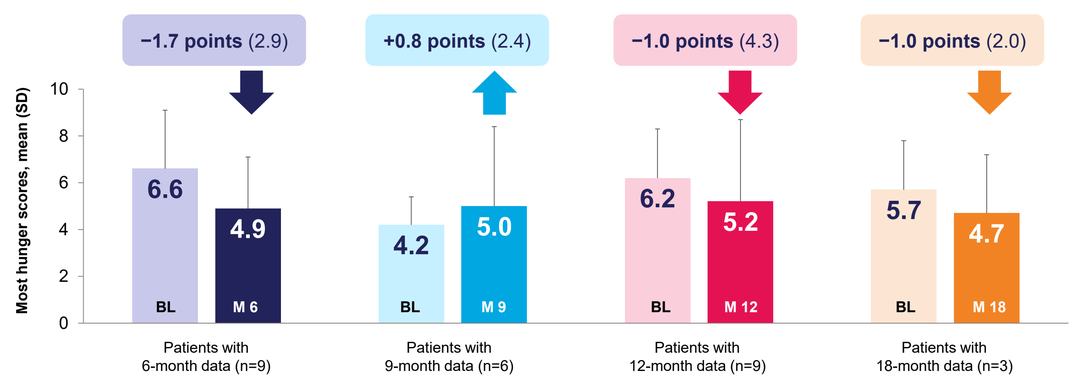


Results

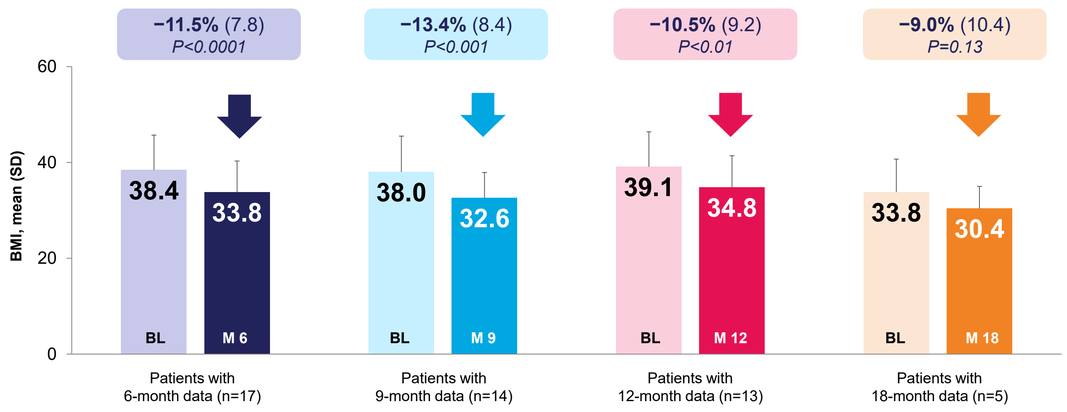
Overall, 40% of paediatric patients (n=12) had aHO due to craniopharyngioma

	Paediatric patients N=30
Age, mean (SD), years	13.5 (3.3)
Sex, male, n (%)	17 (56.7)
BMI z-score at initiation, mean (SD)	5.5 (2.1)
aHO aetiology, n (%)	0
Craniopharyngioma	12 (40.0)
Astrocytoma	6 (20.0)
Germinoma	1 (3.3)
Ganglioma	1 (3.3)
Septo-optic dysplasia	4 (13.3)
ROHHAD syndrome	2 (6.7)
Inflammatory "viral" involvement, thickening of the stalk	1 (3.3)
AQP4 antibody encephalitis with hypothalamic involvement	1 (3.3)
Midline thalamic syndrome	1 (3.3)
Non-tumoural pituitary abnormality	1 (3.3)

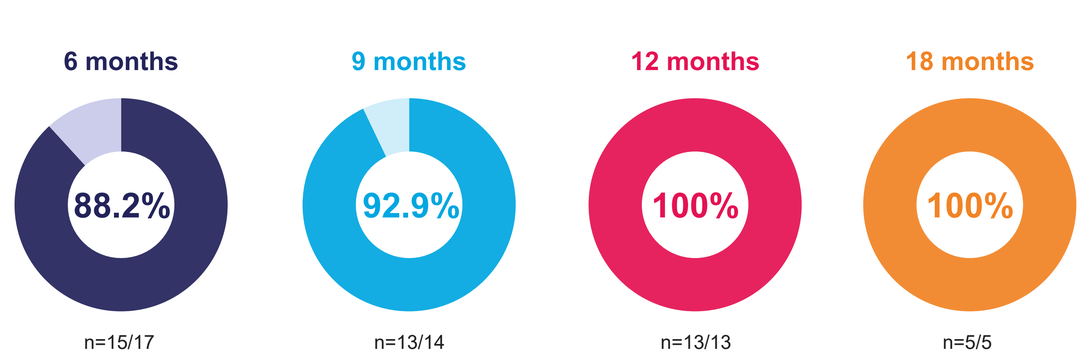
Patient-reported hunger decreased after 6, 12, and 18 months of treatment with setmelanotide in paediatric patients aged ≥12 to <18 years



After 6, 9, and 12 months of setmelanotide treatment, BMI was significantly reduced; the reduction was sustained after 18 months



After 6, 9, 12, and 18 months of setmelanotide treatment, most of the paediatric patients achieved ≥0.2-point reduction in BMI z-score



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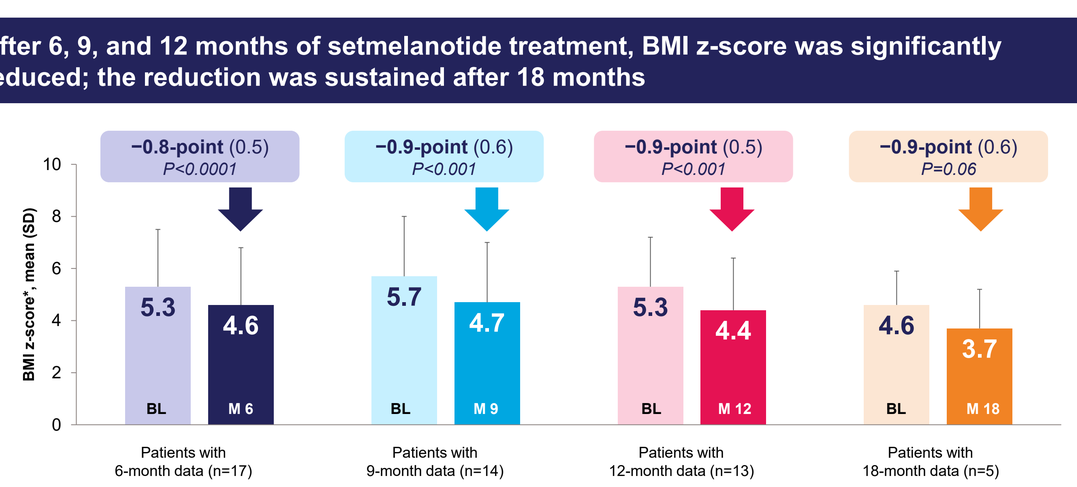

*BMI z-score based on the French reference

No new safety concerns were observed, and adverse events were generally consistent with Phase 3 trial data, with the most common adverse events being injection site reactions and skin hyperpigmentation

Adverse events reported by ≥3, n (%)	Paediatric patients n=24*
Injection site reaction	7 (29.2)
Hyperpigmentation	5 (20.8)
Nausea	3 (12.5)
Asthenia	3 (12.5)

*Adverse events reported for 24 patients, percentage based on n=24.

Limitations

The collection and analysis of real-world data may be affected by incomplete entries, missing values, or typographical errors and may rely on methods that are less robust for identifying adverse events (for more detailed information, please see **supplementary materials**)

Abbreviations: aHO, acquired hypothalamic obesity; AQP4, aquaporin-4; BL, baseline; BMI, body mass index; M, month; MC4R, melanocortin-4 receptor; ROHHAD, rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation; SD, standard deviation.

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References: 1. Roth CL, McCormack SE. *Diabetes Obes Metab*. 2024;26 Suppl 2:34–45. **2.** Müller HL, et al. *Nat Rev Dis Primers*. 2019;5(1):75. **3.** van Santen HM, et al. *Diabetes Obes Metab*. 2026;28(6):4437–4441. **4.** Miller JL, et al. *N Engl J Med*. 2026;395(2):138–150. **5.** Hochberg Z. *Obes Rev.* 2010;11(10):709–721. **6.** Cerbone M, et al. *E Clinical Medicin.* 2020:19:100224. **7.** Nannette G, et al. *J Clin Endocrinol Metab.* 2023;108(2):323–330. **8.** Roth CL, et al. *Obesity (Silver Spring).* 2015;23(6):1226–1233.

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