

Real-world BMI outcomes in adult patients with acquired hypothalamic obesity treated with setmelanotide for up to 12 months in France

Pauline Faucher¹, Sarah Chalopin¹, Emilie Montastier², Héléna Mosbah³, Vincent Clotilde⁴, Claire Carette⁵, Anne-Laure Borel⁶, Karine Decaux⁷, Frédérique Albarel⁸, Elsa Fasciglione⁹, Thibault Bahougne⁹, Agnès Aubourg⁷, Benjamin Moreau¹⁰, Lucie Meillet¹¹, Vianney Demeocq¹², Arnaud De Luca¹³, Justine Cristante⁶, Nicolas Farigon¹⁴, Marie Michelet¹⁵, Véronique Savey¹⁶, Bérénice Ségrestin¹⁷, Géraldine Vitellius¹⁸, Karine Clément¹, Blandine Gatta-Cherifi¹⁵, Christine Poitou¹

¹Nutrition Department, La Pitié-Salpêtrière Hospital APHP, Sorbonne University, Paris, France; ²Nutrition Department, University Hospital of Toulouse, Toulouse, France; ³Endocrinology Department, University Hospital of Poitiers, Poitiers, France; ⁴Nutrition Department, University Hospital of Lille, Lille, France; ⁵Nutrition Department, Hôpital Européen Georges Pompidou APHP, Paris, France; ⁶University Hospital of Grenoble, Nutrition and Endocrinology Department, Grenoble, France; ⁷Nutrition Department, University Hospital of Rouen, Rouen, France; ⁸Endocrinology Department, Conception Hospital, AP-HM, Marseille, France; ⁹University Hospital of Strasbourg, Department of Endocrinology, Diabetology and Nutrition, Strasbourg, France; ¹⁰Department of Endocrinology, Diabetology and Nutrition, University Hospital Rennes, Rennes, France; ¹¹Minjotz University Hospital of Besançon, Endocrinology and Diabetology Department, Besançon, France; ¹²Endocrinology and Metabolism Department, University Hospital of Brest, France; ¹³Nutrition Department, University Hospital of Tours, Tours, France; ¹⁴University Hospital of Clermont-Ferrand, Clinical Nutrition Department, Clermont-Ferrand, France; ¹⁵Department of Endocrinology, Diabetology and Nutrition, University Hospital of Bordeaux, Bordeaux, France; ¹⁶Hepato-Gastroenterology and Nutrition Department, Caen-Normandy Hospital, Caen, France; ¹⁷Endocrinology Department, Lyon Sud Hospital, HCL, Lyon, France; ¹⁸Robert-Debré University Hospital of Reims, Endocrinology, Diabetology and Nutrition Department, Reims, France

Introduction

- Acquired hypothalamic obesity (aHO) is characterised by accelerated and sustained weight gain due to disrupted melanocortin-4 receptor (MC4R) signalling. This may result from physical injury to the hypothalamus, such as trauma, tumours, treatment-related damage, or inflammation, or from structural abnormalities^{1,2}
- In a 52-week placebo-controlled phase 3 trial of the MC4R agonist setmelanotide in patients with aHO aged ≥4 years, body mass index (BMI) was reduced by 16.5% in the setmelanotide group compared with a 3.3% increase in the placebo group³
- In France, setmelanotide treatment for patients with aHO was initiated through a pre-marketing early access program following the positive clinical trial study results

Objectives

- To report real-world data from adult patients with aHO treated with setmelanotide for up to 12 months in a French pre-marketing early access program

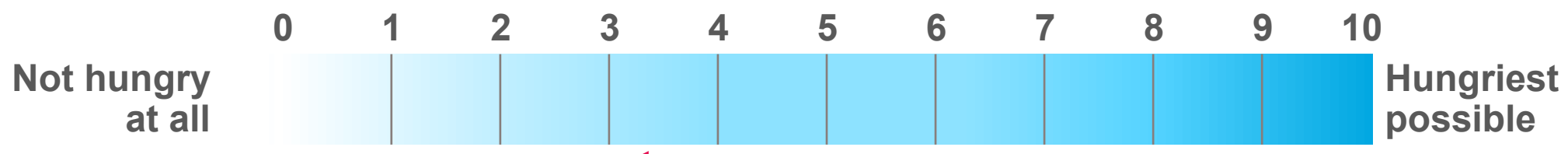
Methods

- Patients with aHO initiated setmelanotide treatment at doses of 0.25 to 2 mg/day and were up-titrated to 1–3 mg/day at the last included visit
- Weight and hunger outcomes were analysed at 6, 9, and 12 months as separate analysis groups. For each timepoint, patients with available data were included and compared with their baseline values. Consequently, the analysis groups differ across timepoints with patients contributing data at one or more timepoints, depending on data availability
- All outcomes are reported for patients aged ≥18 years, except the hunger scores, which were reported for patients aged ≥12 years

Hunger was assessed using the following questions

- Over the past 24 hours, on average, how hungry have you felt?
- Over the past 24 hours, how hungry did you feel when you were most hungry?
- Over the past 24 hours, how hungry did you feel when you were least hungry?
- This morning, when you woke up early in the day, how hungry did you feel?

Answers were scored from 0 to 10



A meaningful within-person change in hunger has been defined as a reduction of at least 1 point in hunger score^{4,5}

Results

- Of the 62 adult patients who started treatment with setmelanotide, 39, 26, and 25 patients had data available at baseline and at 6, 9, or 12 months, respectively

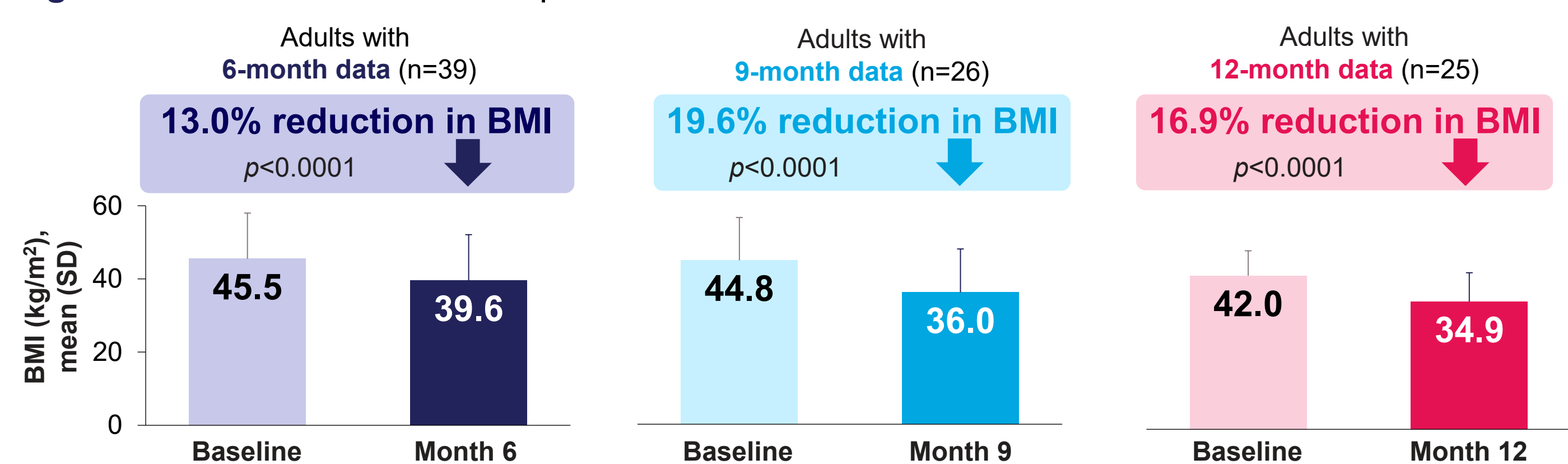
Table 1: Patient characteristics

	Patients aged ≥18 years N=62
Age at inclusion, mean (SD), years	34.4 (12.4)
Female, n (%)	39 (62.9)
BMI at baseline, mean (SD), kg/m ²	44.5 (11.2)
aHO aetiology, n (%)	
Craniopharyngioma	48 (77.4)
Astrocystoma	5 (8.1)
Langerhans cell histiocytosis	2 (3.2)
Hamartoma	2 (3.2)
Germinoma	1 (1.6)
Histiocytosis	1 (1.6)
Neuroglial tumour	1 (1.6)
Rathke's pouch cyst	1 (1.6)
Macroprolactinoma	1 (1.6)

aHO, acquired hypothalamic obesity; BMI, body mass index; SD, standard deviation.

- In all analysis groups, adult patients treated with setmelanotide had significant reductions in BMI

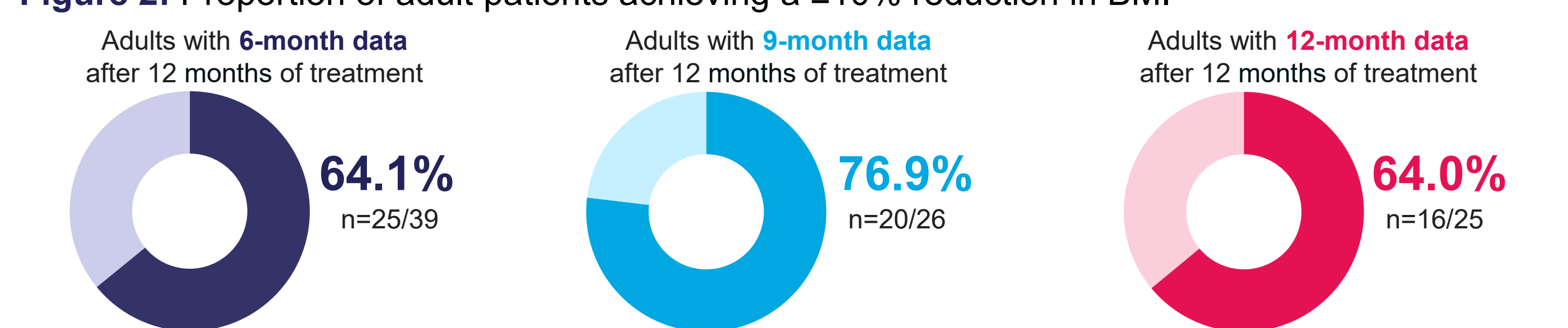
Figure 1: BMI outcomes in adult patients with aHO treated with setmelanotide



n = number of patients with data for respective month (6, 9, or 12 months)
aHO, acquired hypothalamic obesity; BMI, body mass index; SD, standard deviation.

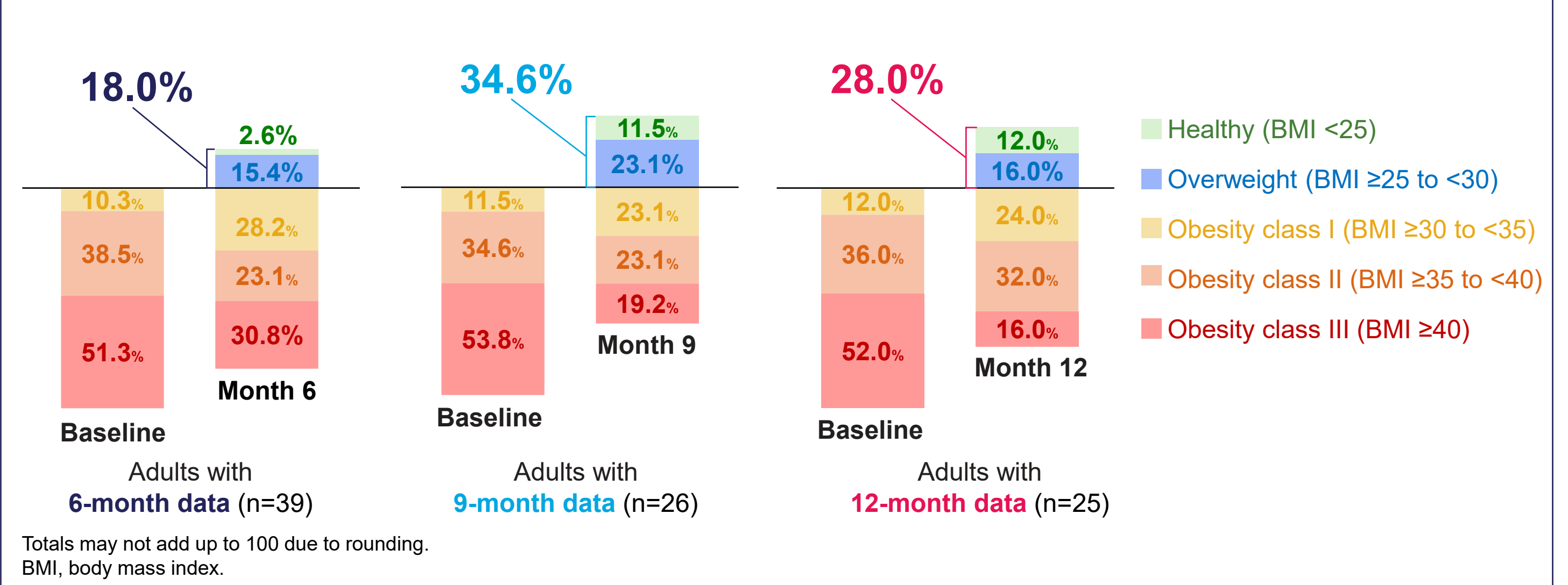
- The majority of patients had a BMI reduction of ≥10% after 6, 9, or 12 months of treatment

Figure 2: Proportion of adult patients achieving a ≥10% reduction in BMI



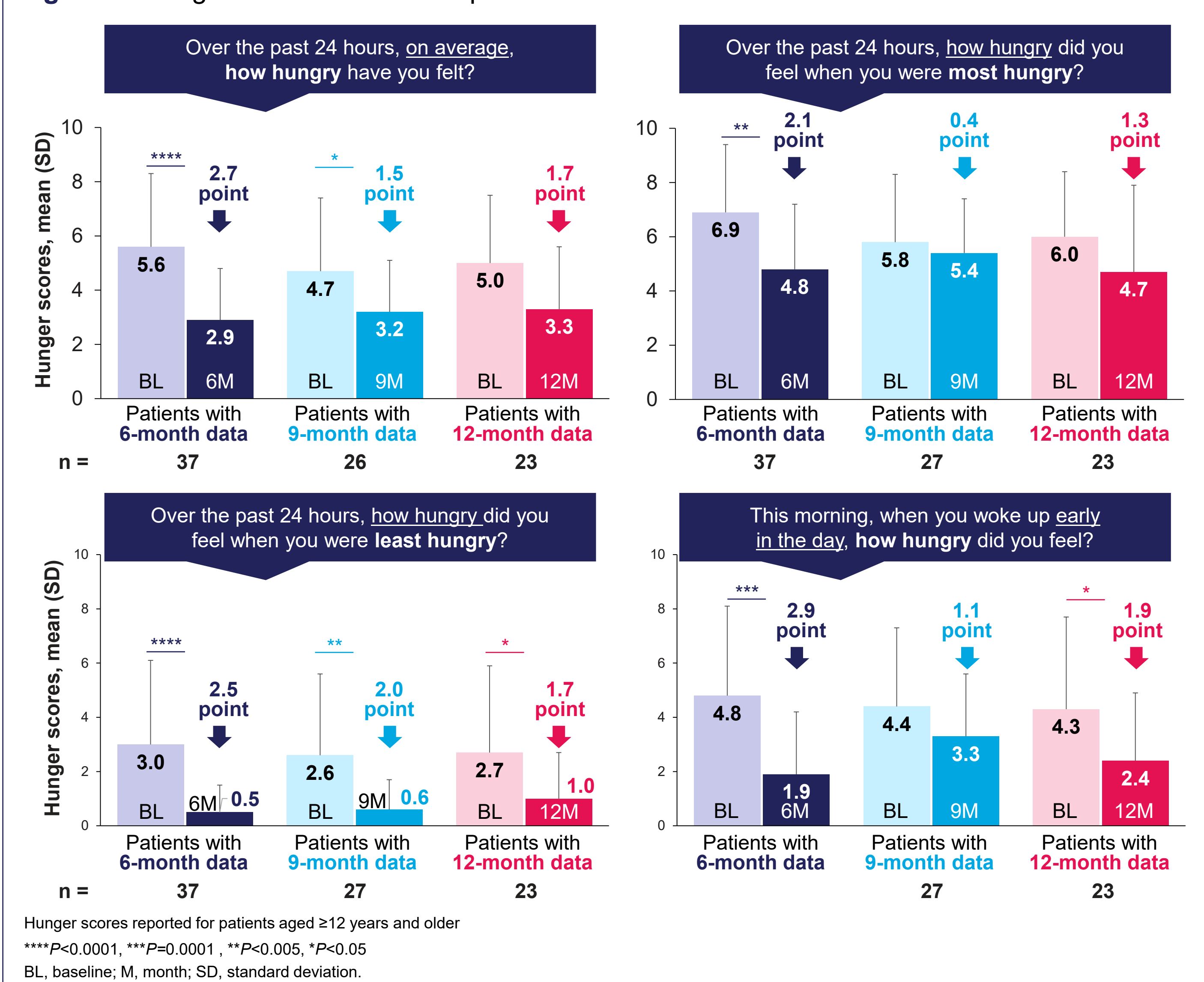
- Weight classes improved, with 18.0%, 34.6%, and 28.0% of patients no longer living with obesity after 6, 9, and 12 months, respectively

Figure 3: Proportion of patients by weight class before and after treatment with setmelanotide



- Patients aged ≥12 years reported improvements in all four hunger questions after 6, 9, and 12 months of treatment with setmelanotide

Figure 4: Hunger score outcomes in patients with aHO treated with setmelanotide



- No new safety concerns were observed and reported adverse events were consistent with phase 3 trial data

Table 2: Safety outcomes

	Adult patients* N=59
Adverse events reported by ≥10 patients, n (%)	
Hyperpigmentation	15 (25.4)
Nausea	13 (22.0)
Asthenia	11 (18.6)
Headache	11 (18.6)
Injection site reaction	10 (17.0)
Diarrhoea	10 (17.0)
Death, n (%)†	2 (3.4)
Treatment discontinuation, n (%)‡	10 (17.0)

*Adverse events reported for 59 patients, percentage based on N. †Death deemed unrelated to setmelanotide treatment. ‡Reasons for discontinuations have not been captured; may also include temporary discontinuation.

Limitations

- Collection and analyses of real-world data may be affected by incomplete entries, missing values, or typographical errors and may rely on methods that are less adequate for identifying all possible adverse events. This real-world analysis was not designed to accurately capture hunger scores

Conclusions

- Real-world evidence of 62 adult patients with aHO who received up to 12 months of setmelanotide under French pre-marketing early access authorisation showed significant reduction in BMI and meaningful decrease in hunger scores
- Efficacy and safety outcomes are consistent with phase 3 trial data, and contribute to the understanding of the real-world therapeutic value of setmelanotide as a targeted treatment for patients with aHO

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For more information, please contact EU_Medinfo@rhythmtx.com.