Real-World Weight and Healthcare Utilization Outcomes with Setmelanotide in US Patients with Bardet-Biedl Syndrome

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Background

- Early-onset obesity is a hallmark feature of Bardet-Biedl syndrome (BBS), a rare ciliopathy, and confers a multi-faceted burden for affected patients and their families[1,2]
  - BBS is associated with impairment of the melanocortin-4 receptor (MC4R) pathway, which is responsible for energy balance and satiety[3]
- Setmelanotide, an MC4R agonist, has demonstrated efficacy in weight-related outcomes for patients with BBS by correcting disruption in the pathway[4]

Objectives

- *Primary*: To evaluate the real-world effectiveness of setmelanotide on weight-related outcomes and healthcare resource utilization among US patients with obesity due to BBS
- *Secondary*: To assess the impact of delayed setmelanotide initiation

Methods

Data Source: A retrospective observational study was conducted using de-identified specialty pharmacy data linked at the tokenized patient level with Komodo's Healthcare Map© claims data (2022–2025)

Cohort Selection: Patients aged ≥6 years with BBS who were prescribed setmelanotide and met the following inclusion criteria were included:

- ≥6 months enrollment prior to setmelanotide initiation
- No prior evidence of setmelanotide use
- *Primary objective only:* ≥12 prescription fills in a 12-month follow-up period (compliant use)
- *Secondary objective only:* aged ≥6 years on June 16, 2022 (setmelanotide approval date)

Descriptive Analyses were conducted

- *Secondary objective only:* patients were stratified by quartiles of time to setmelanotide initiation since June 16, 2022

Outcomes Assessed:

- Baseline clinical and demographic characteristics
- Weight, body mass index (BMI) in adults ≥18 years of age, and percentage of patients achieving ≥10% weight loss
- All-cause and obesity-specific healthcare resource utilization (inpatient, outpatient, and prescription)

Results

Study Population (Primary Analysis)

- A total of 286 patients met the inclusion criteria and were included in the primary analysis (n=653 for the secondary analysis)
- The mean age (standard deviation [SD]) was 27.83 (16.45) years; most were male (66%; **Table 1**)
- The most prevalent BBS manifestations were vision disorders (35%), developmental delays (27%), and chronic kidney disease (20%)
- There was a high burden of obesity-related comorbidities
- Mean baseline BMI in adults (n=167) was 45.75 (12.49) kg/m^2 and corresponded to Class 3 severe obesity[5]

Table 1: Baseline Patient Characteristics

	Cohort (N=286)
Age, mean (SD)	27.83 (16.54)
Male, n (%)	190 (66.4)
BMI in adults, mean (SD)	45.75 (12.49)
Top BBS manifestations, n (%)	
Vision disorders*	100 (35.0)
Developmental delay	78 (27.3)
Chronic kidney disease	56 (19.6)
Other comorbidities, n (%)	
Sleep disorders	187 (65.4)
Sleep apnea	155 (54.2)
Dyslipidemia	123 (43.0)
Hypertension	122 (42.7)

*Vision disorders included retinal dystrophy, retinitis pigmentosa, strabismus, and cataracts.
BBS, Bardet-Biedl syndrome; SD, Standard deviation.

Weight-Related Outcomes

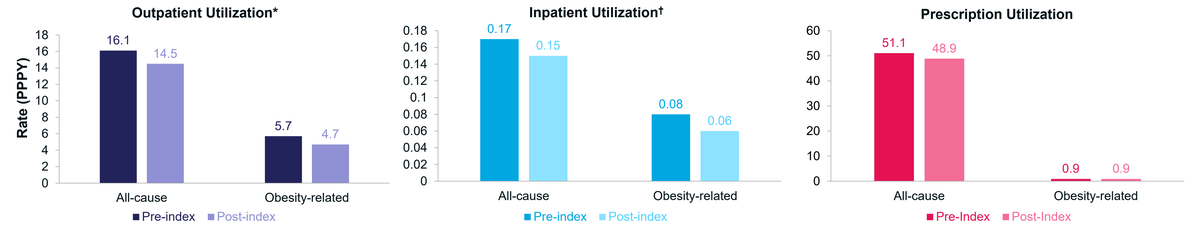
- After 12 months of setmelanotide treatment, 61.7% of adult patients achieved ≥10% body weight loss (52.1% of all patients)
- Mean percentage weight loss in adult patients was −9.8% (−7.8% in all patients)
  - Mean BMI reduction was statistically significant in adults (p<0.05)

Results (continued)

Healthcare Resource Utilization

- After 12 months of setmelanotide treatment, all healthcare utilization decreased (**Figure 1**)
- This reduction was largely driven by obesity-related utilization
  - Outpatient obesity-related visits were significantly reduced (rate difference: 1.03; p<0.05)

Figure 1: Subject Healthcare Resource Utilization Pre- and Post-Setmelanotide Initiation

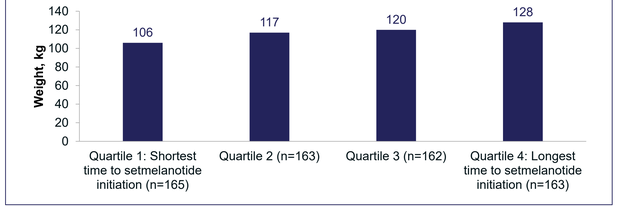


*Outpatient utilization included office, emergency room, laboratory, and bariatric surgery; †Inpatient utilization included hospitalization.
PPPY, per-patient-per-year.

Impacts of Delayed Setmelanotide Initiation

- There were no significant differences in time to setmelanotide initiation by demographic characteristics
  - However, patients with obesity-related comorbidities initiated treatment significantly sooner (p<0.05)
- Patients who took the longest time to initiate setmelanotide weighed 20.8% more at treatment initiation (**Figure 2**) and had 13.4% higher BMI versus earlier initiators
- Higher obesity-related outpatient visits were also observed in patients who took the longest to initiate treatment

Figure 2: Weight at Time of Setmelanotide Initiation



Conclusions

- **Sustained setmelanotide treatment in real-world clinical settings was associated with significant improvements in weight-related outcomes and healthcare resource utilization in patients with severe, progressive obesity due to BBS**

Disclosures: CH and **ML** are employees of Rhythm Pharmaceuticals, Inc. and receive stock or stock options with Rhythm Pharmaceuticals, Inc; **AN** and **SA** are employees of Precision AQ, which received funding from Rhythm Pharmaceuticals to support this research; **SK** is a clinical trials investigator and consultant for Rhythm Pharmaceuticals.
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