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POSTER NO. **SAT-071**

Long-Term Effect of Subcutaneous Pasireotide on Clinical and Quality-of-Life Endpoints in Patients With Cushing's Disease: Results From a Non-interventional Study

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INTRODUCTION

- Cushing's disease causes chronic hypercortisolism associated with impaired QoL, long-term morbidity and increased risk of mortality[1]
- The efficacy and safety of pasireotide sc, a second-generation somatostatin receptor ligand, were demonstrated in patients with Cushing's disease in a 12-month Phase III trial (NCT00434148)[2]
- In addition to randomized clinical trials, observational studies are valuable for assessing drug efficacy and safety in more diverse populations when used in accordance with routine clinical practice[3]
- Here we report data from a non-interventional, multinational study (NCT02310269) evaluating the long-term safety of pasireotide sc and its effects on the clinical and physical manifestations of hypercortisolism and QoL in patients with Cushing's disease

CONCLUSIONS

- **Over 3 years of follow-up, many patients achieved and sustained mUFC ≤ULN during treatment with pasireotide sc**
- **There was a trend for a decrease in SBP and DBP in new users during 3 years of treatment with pasireotide sc, while SBP and DBP generally remained stable in prior users**
- **For the other clinical manifestations of hypercortisolism (body weight, waist circumference, and BMI), there was a trend for a decrease during pasireotide sc treatment**
- **QoL improved in both new and prior users during pasireotide sc treatment**
- **The data should be interpreted with caution as few patients were followed up to 3 years; however, trends were present at year 1, when data were available for a greater number of patients**
- **These data indicate that pasireotide sc is an effective long-term therapy option for adults with Cushing's disease for whom surgery has failed or is not feasible**

METHODS

- Non-interventional, multicenter, post-marketing study of pasireotide sc administered in routine clinical practice
  - Duration of follow-up: 3 years
- Adults with Cushing's disease for whom surgery had failed or was not an option were included in the study
- Patients were treated and monitored according to usual clinical practice at each center
- The primary endpoint was the incidence of pasireotide-related AEs and SAEs
- Secondary endpoints include changes from baseline in the clinical and physical manifestations associated with hypercortisolism and patient-reported QoL outcomes
- Data were analyzed according to when patients started pasireotide sc (at study entry: 'new users'; before study entry: 'prior users')
- The focus of this presentation is the effect of pasireotide sc on clinical and physical manifestations of hypercortisolism and patient QoL

RESULTS

Patient population

Full analysis set: 152 patients (45 new users, 107 prior users)

Safety set: 148 patients (43 new users, 105 prior users)

- Overall, 123/152 patients (81%) discontinued study treatment before study end: 41/45 (91%) new users and 82/107 (77%) prior users
- The most common reasons for discontinuation (≥20%) were AEs (38/152 patients, 25%), unsatisfactory therapeutic effect (31/152, 20%) and administrative issues (31/152, 20%)
  - Corresponding values in the new and prior users, respectively, were 17/45 (38%) and 21/107 (20%) for AEs and 10/45 (22%) and 21/107 (20%) for both unsatisfactory therapeutic effect and administrative issues
- The most frequent (>2.5%) AEs related to pasireotide sc that led to study drug discontinuation were drug ineffective, hyperglycemia and nausea

1. Baseline patient demographics, including age and race, were similar between new and prior users

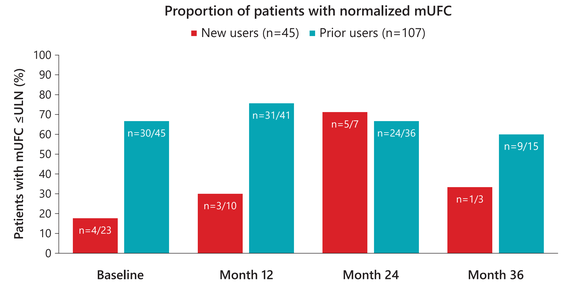
	New users (n=45)	Prior users (n=107)
Mean (SD) age, years	48.8 (12.7)	49.6 (14.1)
Female, n (%)	32 (71.1)	90 (84.1)
Race, n (%)		
Caucasian	34 (75.6)	84 (78.5)
Black	0 (0.0)	1 (0.9)
Other	11 (24.4)	22 (20.6)
Cushing's disease status, n (%)		
De novo	17 (37.8)	12 (11.2)
Persistent/recurrent	28 (62.2)	91 (85.0)
Missing	0 (0.0)	4 (3.7)
Mean (SD) time since diagnosis, months	44.5 (66.8)	87.2 (81.0)
Previous pituitary surgery, n (%)		
Yes	28 (62.2)	82 (76.6)
No	0 (0.0)	9 (8.4)
Missing	17 (37.8)	16 (15.0)
Previous pituitary radiotherapy, n (%)		
Yes	6 (13.3)	29 (27.1)
No	22 (48.9)	62 (57.9)
Missing	17 (37.8)	16 (15.0)

- Time since diagnosis was longer in the prior users than in the new users, and the proportion of patients with previous pituitary surgery and/or radiotherapy was also higher

Pasireotide sc dose and exposure

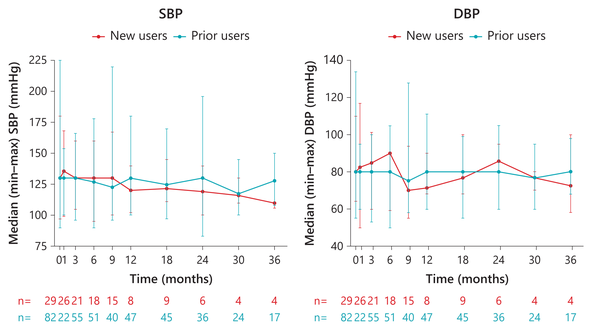
- Median (min–max) pasireotide sc exposure was 7.0 (0.1–36.6) months in new users (n=43) and 33.7 (0.1–131.8) months in prior users (n=105)
  - Duration of exposure in prior users included the period of pasireotide sc treatment before study entry
- 9.3% (n=4/43) and 47.6% (n=50/105) of new and prior users, respectively, received pasireotide sc for >36 months
- Median (min–max) pasireotide sc dose on study in all patients (n=148) was 1200 (300–1800) µg/day

2. Many patients achieved and maintained mUFC normalization over 36 months of treatment with pasireotide sc

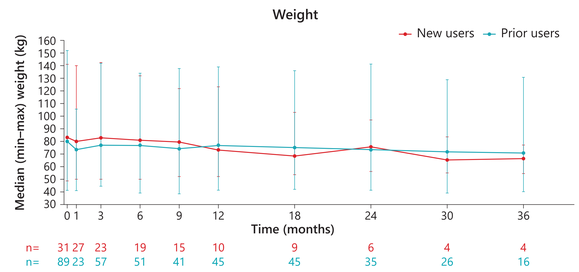


Data from full analysis set. Normalization is defined as mUFC ≤ULN (50 µg/24 h; 138 nmol/24 h)

3. There was a trend towards a decrease in median SBP and DBP in new users during 36 months of treatment with pasireotide sc, while SBP and DBP remained stable in prior users

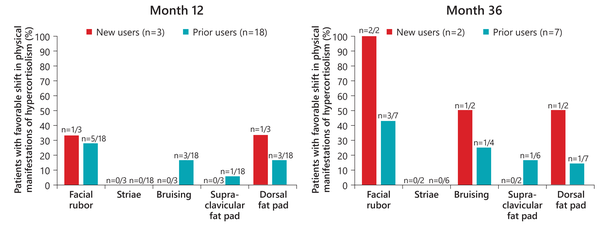


4. There was a trend towards a decrease in median weight in both new users and prior users during 36 months of treatment with pasireotide sc

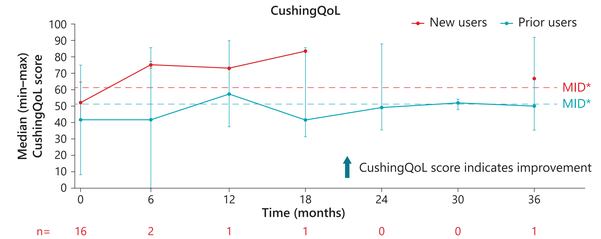


- A trend towards decrease in median waist circumference and BMI was also observed (scan QR code)

5. Although most patients had no or mild physical manifestations of hypercortisolism at baseline (scan QR code), some new users and prior users had improvements in facial rubor, bruising and fat pads during treatment with pasireotide sc



6. CushingQoL scores improved in new users and prior users during treatment with pasireotide sc



*MID corresponds to a 10.1-point change from baseline[4]

ACKNOWLEDGMENTS

We thank Natasha Daoud, Mudskipper Business Limited (funded by Recordati AG), for providing medical editorial assistance, as well as the site investigators, study coordinators and patients who participated in the trials.

DISCLOSURES

This study was sponsored by Novartis Pharma AG; however, as of July 12, 2019, pasireotide is an asset of Recordati AG.

ABBREVIATIONS

AE, adverse event; BMI, body mass index; CushingQoL, Cushing's Quality of Life Questionnaire; DBP, diastolic blood pressure; max, maximum; MID, minimal important difference; min, minimum; mUFC, mean urinary free cortisol; QoL, quality of life; SAE, serious adverse event; SBP, systolic blood pressure; sc, subcutaneous; SD, standard deviation; ULN, upper limit of normal

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PRESENTED AT: **The Endocrine Society Annual Meeting (ENDO), June 1–4, 2024**

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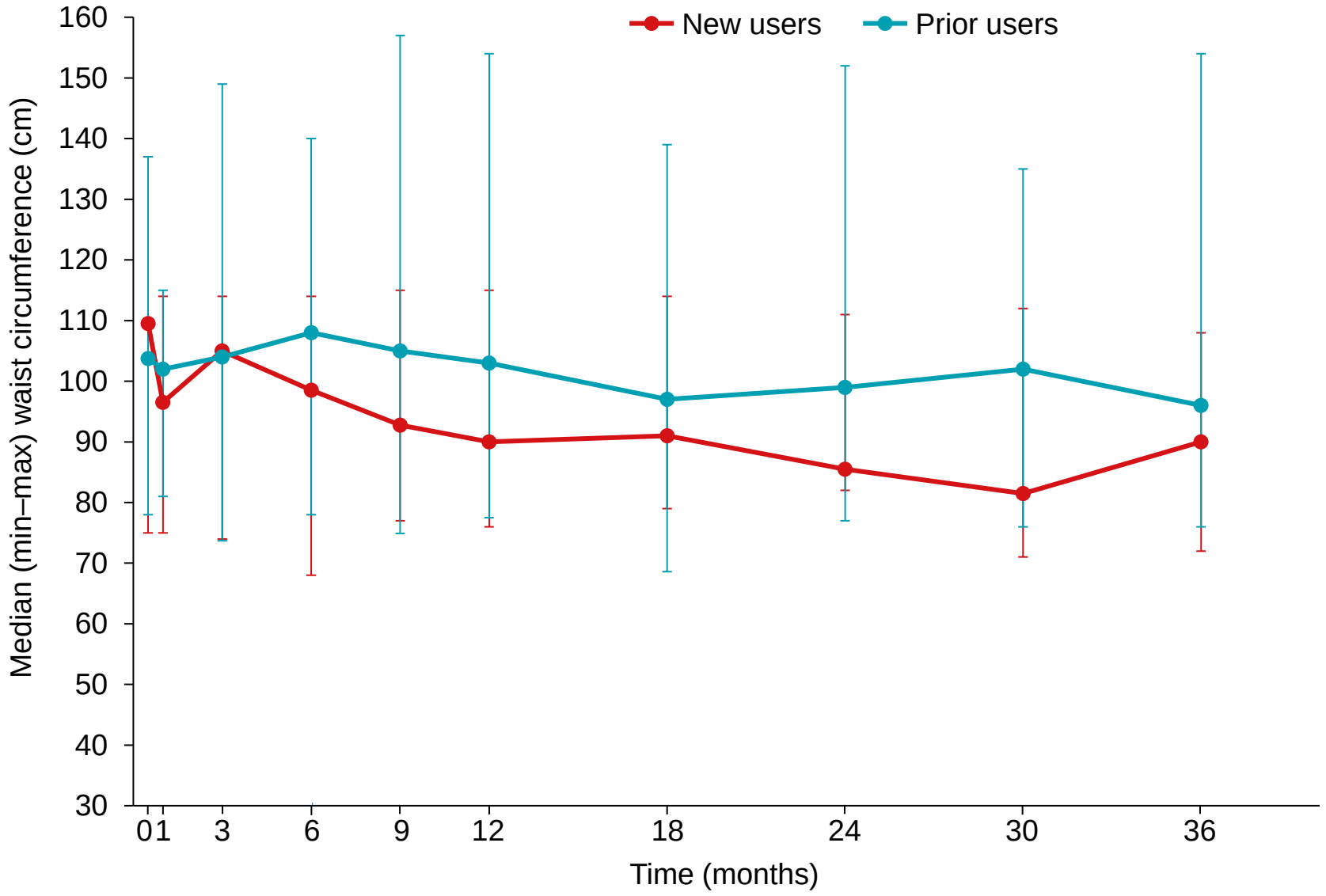
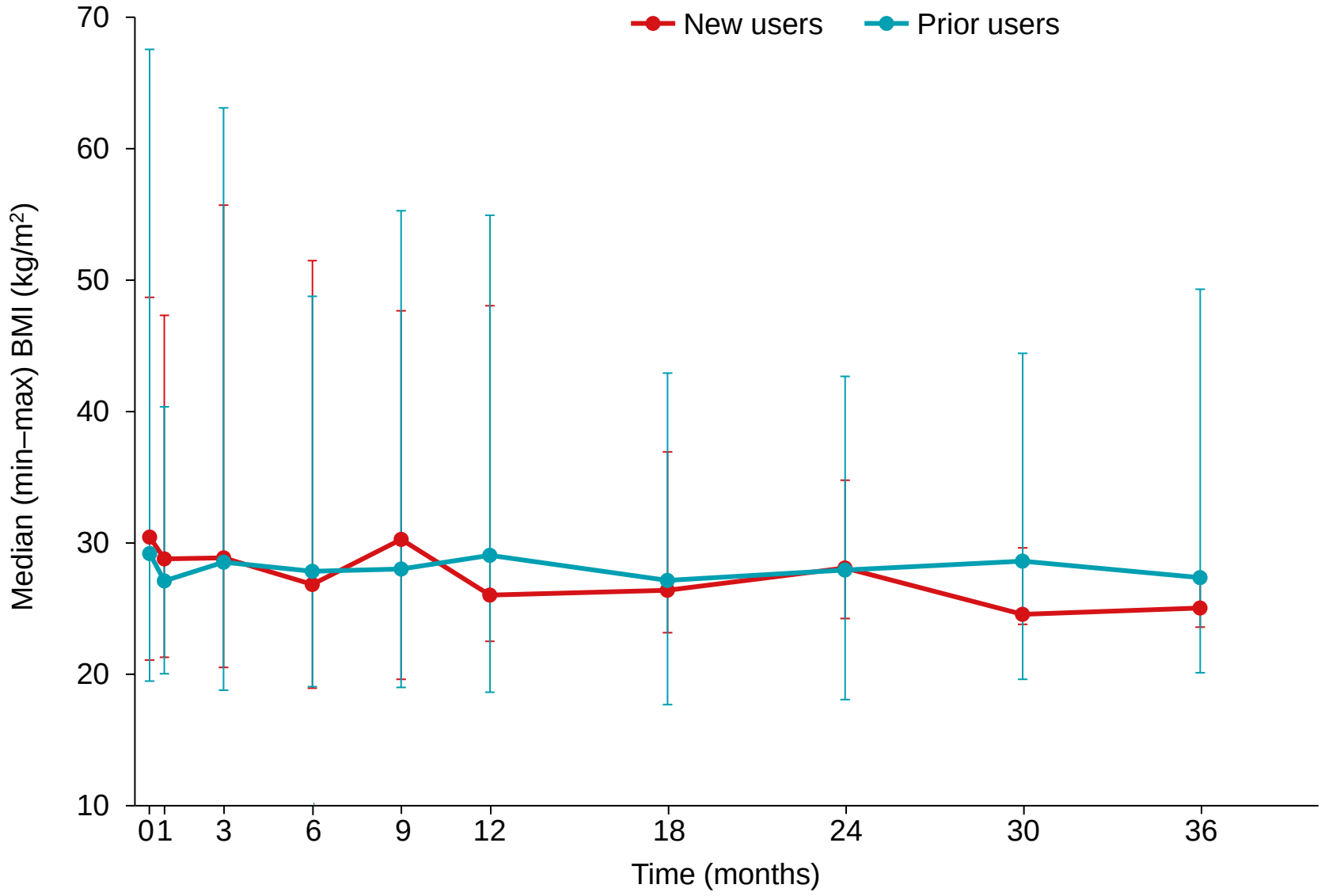
QR code content

Median change in waist circumference during pasireotide sc treatment over time



Median change in body mass index (BMI) during pasireotide sc treatment over time



n=	31	24	20	18	12	9	8	6	4	4
n=	87	20	41	40	32	39	35	27	19	16

Severity of physical manifestations of hypercortisolism at baseline