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An 8-Year Interim Report of the B2412 Study, an Open-Label, Multicenter Pasireotide Rollover Study for Patients Who Continued to Receive Benefit From Pasireotide at Completion of an Earlier Trial

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*Potential conflict of interest may exist. Refer to the Meeting App; †Deceased (November 25, 2022); ‡AMP was an employee of Recordati at time of abstract/poster development

Plain language summary

Why was this analysis carried out?

- Pasireotide is an approved medicine for treating endocrine disorders such as acromegaly and Cushing's disease. We wanted to assess the side effects of pasireotide in people who take the medicine for long periods of time

How was this analysis carried out?

- People who had completed an earlier clinical trial of pasireotide, and who were benefiting from treatment, could take part in a follow-up study (B2412) that gives patients continued access to treatment for up to 10 years
- Throughout treatment, people were monitored for side effects and clinical benefit
- The B2412 study is ongoing. This interim analysis was carried out 8 years after the first person entered the study

What were the overall results?

- All the side effects reported were as expected based on pasireotide's mechanism of action
- Only a small number of people stopped treatment because of side effects
- High blood sugar (hyperglycemia), an expected side effect of pasireotide, was one of the most common side effects and was reported at a lower frequency during long-term treatment than in earlier clinical trials
- Hyperglycemia was manageable with additional medicines, and few people stopped pasireotide treatment because of hyperglycemia

What do the results mean?

- Long-term treatment with pasireotide causes few new side effects, and these can be well managed; this means that few people need to stop treatment, and most people can continue to receive benefit over long periods of time

Where can I access more information?

- Details of the ongoing B2412 study can be found via the following link: https://www.clinicaltrials.gov/ct2/show/NCT01794793

Conclusions

- Hyperglycemia is an expected AE during pasireotide treatment[9,10] and often occurs in the first 3 months of therapy. These data show that patients who continue with pasireotide treatment long-term have a low incidence of new hyperglycemic events
  - Hyperglycemic events that may have occurred during the parent study have been well managed since, which may partly explain the low incidence of new events during long-term treatment
- Hyperglycemia is manageable and rarely leads to pasireotide discontinuation; the low rate of treatment discontinuation over 8 years suggests continued long-term clinical benefit outside a clinical trial setting
- These data support pasireotide as a well-tolerated long-term treatment in patients with acromegaly, CD or other endocrine disorders and affirm that patients receive long-term benefit

Acknowledgments

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Disclosures

The parent studies were sponsored by Novartis Pharma AG. The rollover study was initially sponsored by Novartis Pharma AG; however, as of July 12, 2019, osilodrostat is an asset of Recordati AG.

Abbreviations

AE, adverse event; CD, Cushing's disease; LAR, long-acting release; pas, pasireotide; SAE, serious adverse event; sc, subcutaneous

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Introduction

- Patients with acromegaly, Cushing's disease and other rare endocrine disorders have significant morbidity and reduced quality of life. If inadequately treated, patients with endocrine disorders have a higher mortality risk than the general population[1–4]
- A robust clinical program of 14 trials demonstrated pasireotide, a pituitary-targeted second-generation somatostatin receptor ligand, to be an effective treatment, achieving and maintaining biochemical control in patients with rare endocrine disorders, including acromegaly[5,6] and Cushing's disease[7,8]
- The B2412 rollover study assessed the long-term safety and clinical benefit of pasireotide in patients who had completed one of the 14 previous trials and continued to receive benefit
- This 8-year interim analysis evaluated long-term safety in patients with acromegaly, Cushing's disease or other endocrine disorders who had successfully completed a previous pasireotide parent trial and continued treatment in the B2412 rollover study

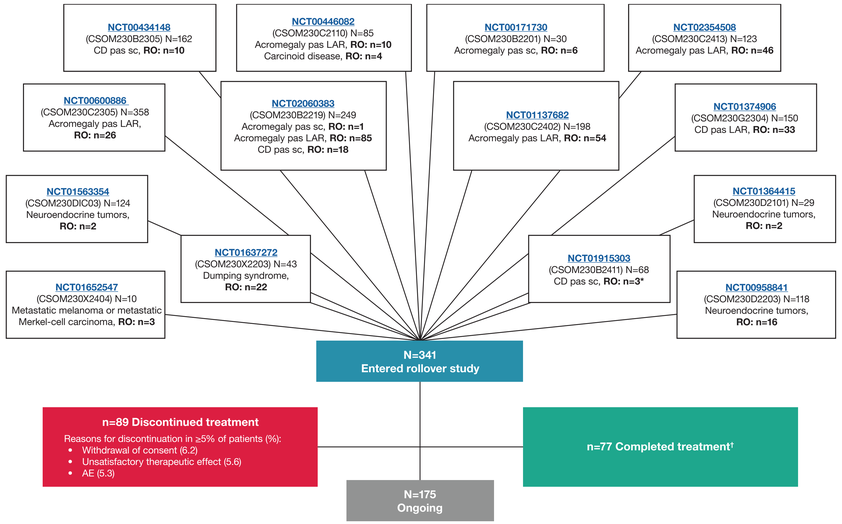
Methods

- B2412 is an ongoing, open-label, multicenter study that allows continued pasireotide treatment for patients who completed a previous parent trial (NCT01794793). This interim analysis was performed 8 years after the first patient first visit
  - Patients were enrolled from 14 parent studies of varying study designs and diverse patient populations (scan QR code for links to each parent study)
  - Patients who continued receiving clinical benefit according to the parent study investigator, and who were unable to access the drug outside of a clinical trial, entered the rollover study and remained on pasireotide at the same dose given in the parent study
  - Depending on the administration route in the parent study, patients received pasireotide LAR (n=303) or sc (n=38) as monotherapy (n=36), or sc combined with cabergoline (n=2)
  - If pasireotide became commercially available and reimbursed in a patient's location, they would be reported as having completed the study
  - The primary objective was to evaluate long-term safety over a period of approximately 10 years, determined by the frequency of AEs/SAEs

Results

1. 341 patients from 29 countries entered the study from 14 parent trials

- 228 patients had acromegaly, 64 had Cushing's disease, and 49 had other endocrine disorders, including dumping syndrome (n=22; 45%), neuroendocrine tumors (n=20; 41%), carcinoid disease (n=4; 8%), and metastatic melanoma or metastatic Merkel-cell carcinoma (n=3; 6%)



RO refers to the number of patients entering the rollover from each parent study. *Two patients received cabergoline at a dose of 1 mg in combination with pasireotide; †Patients completed the study when pasireotide became commercially available and reimbursed in their location

2. Baseline characteristics were typical for patient populations with acromegaly, Cushing's disease or other endocrine disorders

Baseline characteristics at start of rollover	Acromegaly Pasireotide LAR n=221	Acromegaly Pasireotide sc n=7	CD Pasireotide LAR n=33	CD Pasireotide sc n=29	CD Pasireotide sc + combination treatment n=2	Other disorders Pasireotide LAR n=49	All subjects N=341
Median age, years (min–max)	45.0 (23.0—77.0)	45.0 (32.0—74.0)	51.0 (20.0—70.0)	43.0 (22.0—72.0)	41.5 (33.0—50.0)	48.0 (28.0—81.0)	46.0 (20.0—81.0)
Female, n (%)	107 (48.4)	3 (42.9)	25 (75.8)	22 (75.9)	2 (100)	34 (69.4)	193 (56.6)

3. Median pasireotide exposure from rollover start to interim data cut-off varied across formulations and patient groups. Median pasireotide LAR monthly dose varied across patient groups

Pasireotide LAR exposure and dose in patients with acromegaly (n=221)
- 46.7 months — median pasireotide LAR exposure (min–max, 0.9–99.6)
- 54.4 mg/month — median pasireotide LAR dose (min–max, 17.7–77.3)

Pasireotide sc exposure and dose in patients with acromegaly (n=7)
- 80.9 months — median pasireotide sc exposure (min–max, 23.5–100.8)
- 1201.2 µg/day — median pasireotide sc dose (min–max, 900.0–1800.0)

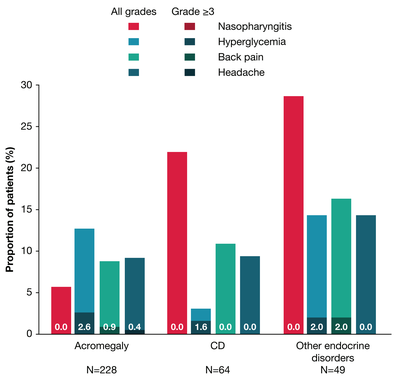
Pasireotide LAR exposure and dose in patients with other disorders (n=49)
- 53.9 months — median pasireotide LAR exposure (min–max, 0.9–95.5)
- 60.5 mg/month — median pasireotide sc dose (min–max, 9.0–128.3)

Pasireotide LAR exposure and dose in patients with CD (n=33)
- 40.0 months — median pasireotide LAR exposure (min–max, 3.7–66.9)
- 39.5 mg/month — median pasireotide LAR dose (min–max, 5.3–59.2)

Pasireotide sc exposure and dose in patients with CD (n=29)
- 14.9 months — median pasireotide sc exposure (min–max, 3.0–97.3)
- 1200.0 µg/day — median pasireotide sc dose (min–max, 300.0–1800.0)

Pasireotide sc exposure and dose in patients with CD who received combination treatment (n=2)
- 27.0 months — median pasireotide sc exposure (min–max, 27.0–27.0)
- 1500.0 µg/day — median pasireotide sc dose (min–max, 1200.0–1800.0)

4. The most common AEs during rollover (≥10% of patients across all indications) were nasopharyngitis, hyperglycemia, back pain and headache



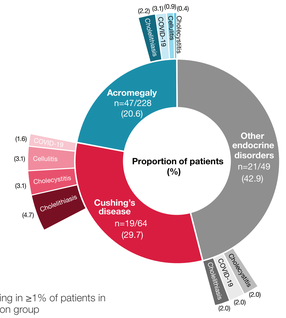
A patient with multiple severity for an AE is counted under the maximum grade

11% (n=38/341) Incidence of **new hyperglycemia-related AEs** across all indications during the rollover study was **low**

5. Few patients discontinued pasireotide during the rollover because of an AE. Concomitant medications were initiated in 65.4% of patients to manage AEs

- 5.3% (n=18/341) **discontinued treatment** because of an AE
- 1.5% (n=5/341) **discontinued treatment** because of **hyperglycemia**
- 65.4% (n=223/341) initiated **concomitant medications** because of an AE

6. SAEs were reported in 87 (25.5%) patients and were most commonly cholelithiasis and COVID-19 in all patient groups (both n=9, 2.6%)



SAEs occurring in ≥1% of patients in each indication group