Tumor response was measured by CT or MR at baseline and every 6 months, and was assessed using the Response Evaluation Criteria in Solid Tumors (RECIST). Seven CgA and urinary 5-HIAA were obtained at baseline and monthly thereafter.

Safety and tolerability assessment consisted of reporting all adverse events and serious adverse events, with severity graded according to CTCAE (v4.0). Safety and tolerability were monitored throughout the study.

Response samples were collected for PK assessments after 4 weeks of treatment with pasireotide and blood samples were taken at time 0 (pre-dose), 0.5, 1, 2, 3, and 6 hours after morning administration of pasireotide.

### Statistical Methods

The primary response was a minimum of 30 patients. The sample size was chosen based on the assumption of a proportion of success of 0.3 and an adjustment of 0.05 for non-inferiority comparisons. The formal statistical comparisons were performed for the study.

### RESULTS

#### Study Population

Of the 44 patients included in the efficacy analyzable population, 12 (27%) had complete or partial symptom control over >1 year of treatment with pasireotide.

#### Study Design

The primary efficacy outcome was symptom control change, flushing over 15 consecutive days which was defined as the number of patients with at least a one-step reduction in median flushing per day for at least 2 weeks during the 28-day period following the last dose of octreotide LAR.

#### Safety and Tolerability

- Weight loss occurred in 19 patients (42%) during the study, with nine of the cases (20%) considered related to the combination of pasireotide and octreotide treatment. Three of four patients who experienced an adverse event of worsening diabetic symptoms had a medical history of type 2 diabetes.
- A randomized Phase III study to compare the efficacy of pasireotide LAR versus octreotide LAR is ongoing.

#### DISCUSSION AND CONCLUSIONS

- Pasireotide may offer an alternative treatment option for patients with the symptoms of carcinoid syndrome who are resistant or refractory to octreotide LAR. It is currently being evaluated in a randomized Phase III trial.
- The results of this study suggest that pasireotide may be a promising treatment option for patients with metastatic NET and carcinoid syndrome who are resistant or refractory to octreotide LAR.