

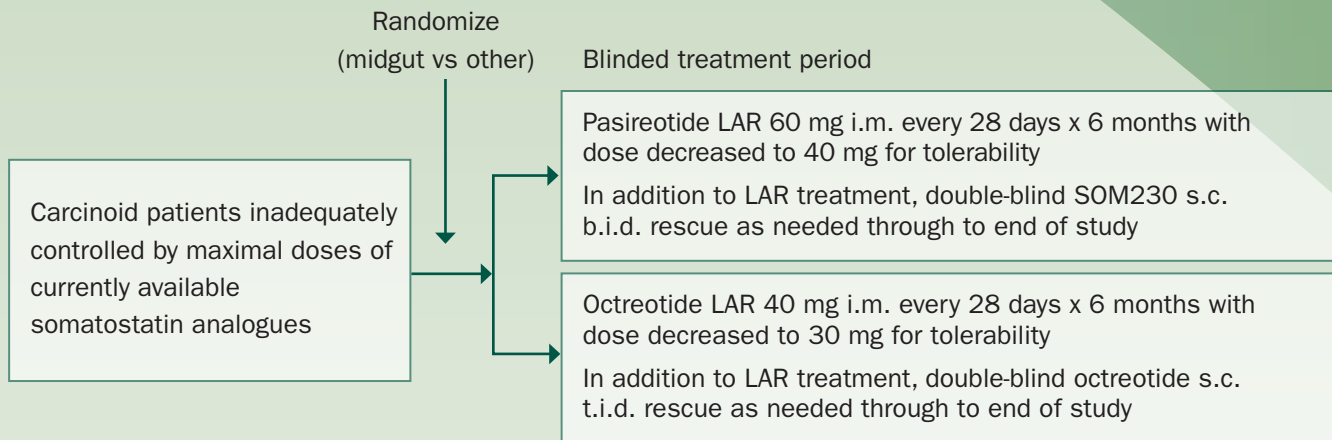
SIG-NET Clinical Study Summary

Protocol No. CSOM230C2303

Study Title:

A multicenter, randomized, blinded efficacy and safety study of SOM230 (pasireotide LAR) vs octreotide LAR in patients with metastatic carcinoid tumors whose disease-related symptoms are inadequately controlled by somatostatin analogues

Study Design



Endpoints:

- The primary endpoint is defined as a combination of the mean number of bowel movements and total number of flushing episodes*
- The key secondary endpoint is defined as a combination of the mean number of bowel movements and total number of flushing episodes using stricter response criteria for the percent reduction in daily mean number of bowel movements
- Other secondary endpoints include:
 - Mean change from baseline in bowel movements alone at month 6
 - Change from baseline in total flushing episodes alone at month 6
 - Time to symptom response
 - Duration of symptom response
 - Time to symptom progression
 - Objective tumor response
 - Change from baseline in Quality of Life scores
 - Safety

*See protocol for complete criteria.

Abbreviations: LAR, long-acting release; i.m., intramuscular; s.c., subcutaneous; b.i.d., twice a day; t.i.d., 3 times a day.

SOM230 is an investigational new drug. Efficacy and safety have not been established. There is no guarantee that SOM230 will become commercially available.

Inclusion/Key Exclusion Criteria

Key Inclusion Criteria:

1. Male or female patients ≥ 18 years old
2. Histopathologically confirmed (from primary or metastatic lesion biopsy) metastatic carcinoid tumors of the digestive system with extent of disease determined by computed tomography (CT) scan or magnetic resonance imaging (MRI)
3. Symptoms of carcinoid disease, diarrhea and flushing, must be inadequately controlled*
4. Patients must observe the following intervals between the last injection of their previous treatment and the first injection of study drug:
 - Octreotide LAR = 28 days (4 weeks)
 - Octreotide SC = 8 hours
 - Lanreotide Autogel = 28 days (4 weeks)
 - Lanreotide SR = 14 days (2 weeks)
5. Measurable or evaluable disease per RECIST criteria
6. Karnofsky Performance Status ≥ 60
7. Known history of impaired fasting blood glucose or diabetes mellitus may be included, however, blood glucose and antidiabetic treatment must be monitored closely throughout the study and be adjusted as necessary
8. Female patients of childbearing potential must have a negative pregnancy test at baseline
9. Patients for whom written informed consent to participate in the study has been obtained

Key Exclusion Criteria†:

1. Received radiolabeled somatostatin analogue therapy within the 6 months or any cytotoxic chemotherapy or interferon therapy within the 2 months prior to recording baseline symptoms
2. Undergone major surgery/surgical therapy for any cause within 1 month or surgical therapy of loco-regional metastases within the last 3 months before recording baseline symptoms
3. Hepatic artery embolization within the last 6 months (1 month if there are other sites of measurable disease), or undergone cryoablation or radiofrequency ablation of hepatic metastasis within the last 2 months before recording baseline symptoms
4. Received radiotherapy for any reason within the last 4 weeks or have not recovered from any side effects of radiotherapy before recording baseline symptoms
5. Unwilling to follow dietary restrictions within 3 days of urinary 5-HIAA sample collection or require medications that would interfere with urinary 5-HIAA measurement
6. Known malabsorption syndrome, short-bowel or chologenic diarrhea not controlled by specific therapeutic means
7. Not biochemically euthyroid
8. Diabetic patients on antidiabetic medications whose fasting blood glucose is poorly controlled as indicated by HbA1C $> 8\%$
9. Have received any formulation of SOM230 (pasireotide)

Abbreviations: SR, slow release; RECIST, Response Evaluation Criteria in Solid Tumors; HbA1C, glycosylated hemoglobin.

*Inadequate control: a daily mean of 4 or more bowel movements over a 2-week period and a total of 5 or more flushing episodes during this period, while receiving at least the highest recommended dose of 1 of the following somatostatin analogues for at least a 3-month period prior to study entry:

Octreotide LAR (= 30 mg q 28 days)
Octreotide SC (= 600 μg total daily dose)
Lanreotide Autogel (= 120 mg q 28 days)
Lanreotide SR (= 30 mg q 14 days)

†See protocol for complete exclusion criteria.



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