

# Carcinoid Syndrome Symptoms in Pancreatic Neuroendocrine Tumors (PNET) and Impact on Healthcare Utilization

Michael S. Broder, MD, MSHS<sup>1</sup>; Eunice Chang, PhD<sup>1</sup>; Sheila R. Reddy, PhD, RPH<sup>1</sup>; Maureen P. Neary, PhD<sup>2</sup>

<sup>1</sup> Partnership for Health Analytic Research, LLC, Beverly Hills, CA 90212 <sup>2</sup> Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936

## BACKGROUND

- PNET, rare neuroendocrine tumors from pancreatic origin, may lead to hormonal syndromes such as carcinoid syndrome (CS).<sup>1</sup>
- Progressive PNET may be treated with somatostatin analogues (SSAs), targeted therapy (i.e., everolimus and sunitinib), and cytotoxic chemotherapy.
- Symptoms associated with CS may occur in PNET and can be alleviated by SSAs.<sup>1,2,3</sup>
  - CS symptoms may include: flushing, diarrhea, nausea/vomiting, asthma, wheezing, cardiac palpitations, fatigue, hypotension, or dizziness.<sup>1,2,3</sup>
- Information is limited about the impact of CS symptoms on health resource utilization in patients with PNET.

## OBJECTIVES

Among PNET patients newly treated with targeted therapy or cytotoxic chemotherapy:

- To assess baseline demographic and clinical characteristics between those with and without CS symptoms.
- To examine descriptively the healthcare resource use between those with and without CS symptoms.

## METHODS

### Study Design and Data Source

- Retrospective cohort study using combined Truven Health MarketScan and IMS PharMetrics administrative claims data from 1/1/2008 – 12/31/2013.

### Patient Population

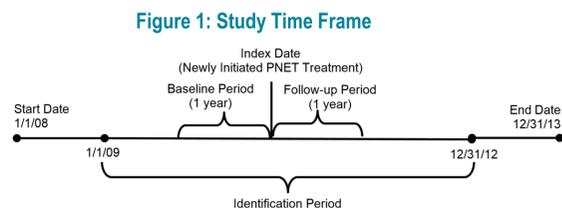
- Patients diagnosed with PNET who initiated treatment with targeted therapy or cytotoxic chemotherapy during identification (ID) period (2009-2012) (i.e., “newly treated” for PNET in this time period):

#### Inclusion Criteria:

- ≥ 1 medical claim with a diagnosis of PNET (ICD-9: 157.4) and receipt of targeted therapy or cytotoxic chemo-therapy during ID period. First date of treatment was defined as the index date.
- We required a fixed 1-year baseline and 1-year follow-up period for all patients. Continuous enrollment was required throughout the baseline and follow-up periods (Figure 1).

#### Exclusion Criteria:

- Receipt of targeted therapy or cytotoxic chemotherapy during the baseline period.



### Comparison Group

- Patients were stratified by the presence of a CS symptom during the follow up period. Indication of a CS symptom was measured by ≥1 claim with an ICD-9 code for one of the following symptoms: flushing (ICD-9: 782.62), diarrhea (non-infectious; ICD-9: 564.5, 787.91), nausea/vomiting (ICD-9: 787.0x), asthma (ICD-9: 493.x), dyspnea/wheezing (ICD-9: 786.0x), cardiac palpitations (ICD-9: 785.1), asthenia/fatigue (ICD-9: 728.87, 780.71, 780.79), hypotension (ICD-9: 458.x), or dizziness (ICD-9: 780.4).

### Study Measures

- Primary outcome was the rate of healthcare use in the follow-up period, measured by: proportion of patients with a hospitalization, proportion of patients with an emergency department (ED) visit, and mean number of physician office visits (any kind) per patient.
- Other baseline measures reported were age, gender, region, Charlson Comorbidity Index (CCI), number of chronic conditions (counted using the Healthcare Cost and Utilization Project Chronic Condition Indicator<sup>4,5</sup>), type of index treatment, and prior SSA use.

## RESULTS

### Patient Cohort

- 338 patients had a diagnosis of PNET and initiated pharmacologic treatment for this cancer, with 212 (62.7%) having CS symptoms and 126 (37.3%) not having these symptoms (Figure 2 & Table 1).
- Patients either with or without CS symptoms had similar age, gender, geographic region, CCI, current targeted therapy or chemotherapy, and prior SSA therapy use.
  - Mean age among treated PNET patients was 54.5 years and 45.6% of patients were female.
  - Patients had a CCI of 10.1 (SD 2.9). However, patients with CS symptoms had on average 1 additional chronic condition (5.4, SD 2.0) compared to patients without (4.4, SD 2.0).
- 101 (29.9%) patients received targeted therapy as current treatment vs. cytotoxic chemotherapy (n=237, 70.1%). One-third of patients had prior SSA use before initiating current treatment.

Figure 2: Patient Identification

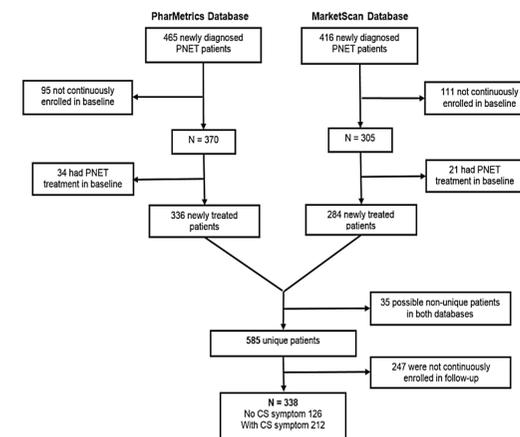


Table 1: Characteristics of treated PNET patients, with or without carcinoid syndrome symptoms

	All N = 338	Carcinoid Syndrome Symptoms		P-Value
		No N = 126	Yes N = 212	
Age, mean (SD)	54.5 (10)	54.7 (9.6)	54.4 (10.1)	0.752
Female, n (%)	154 (45.6)	56 (44.4)	98 (46.2)	0.750
Region				0.322
Northeast, n (%)	62 (18.3)	23 (18.3)	39 (18.4)	
Midwest, n (%)	102 (30.2)	33 (26.2)	69 (32.5)	
South, n (%)	130 (38.5)	56 (44.4)	74 (34.9)	
West, n (%)	44 (13.0)	14 (11.1)	30 (34.9)	
Charlson Comorbidity Index, mean (SD)	10.1 (2.9)	9.7 (2.9)	10.3 (2.9)	0.060
Number of chronic conditions, mean (SD) <sup>a</sup>	5.0 (2.0)	4.4 (1.9)	5.4 (2.0)	<.001
Index treatment				0.740
Targeted therapy, n (%)	101 (29.9)	39 (31.0)	62 (29.2)	
Cytotoxic chemotherapy, n (%)	237 (70.1)	87 (69.0)	150 (70.8)	
Prior SSA use, n (%)	113 (33.4)	41 (32.5)	72 (34.0)	0.789

<sup>a</sup>Chronic Condition Indicator developed by the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project.

### Presence of Carcinoid Syndrome Symptoms

- 212 (62.7%) of treated patients had CS symptoms, with fatigue (51.9%), dyspnea (36.3%), and diarrhea (25.9%) being most prevalent (Figure 3).

### Rates of Healthcare Use

- PNET patients with CS symptoms had considerably higher rates of healthcare use during the 1-year follow-up period compared to those without symptoms (Table 2 & Figure 4):
  - 57.5% vs. 19.8% were hospitalized (P<0.001)
  - 64.2% vs. 23.0% had an ED visit (P<0.001)
  - 29.2 vs. 19.3 mean number of physician office visits per patient (P<0.001)

Figure 3: Patients with carcinoid syndrome symptoms (N=212)

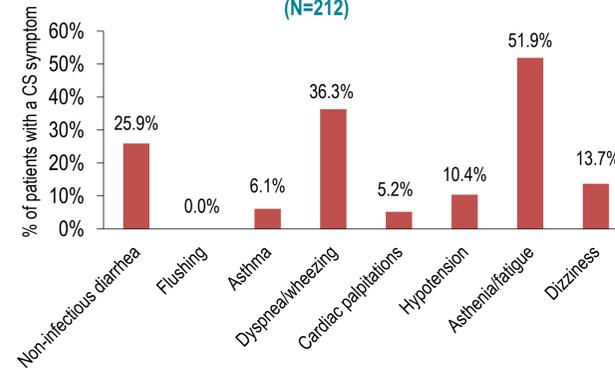
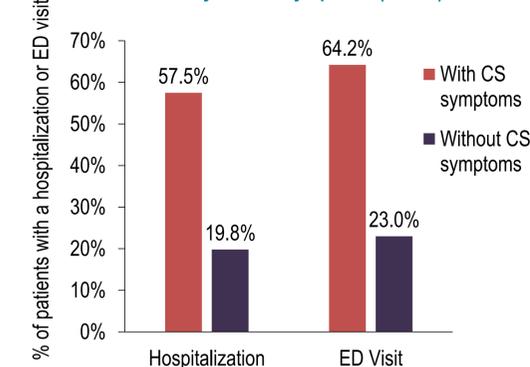


Table 2: Rates of healthcare use among newly treated PNET patients, with or without carcinoid syndrome symptoms

	All N = 338	Carcinoid Syndrome Symptoms		P-Value
		No N = 126	Yes N = 212	
Number of hospitalizations				<.001
0, n (%)	191 (56.5)	101 (80.2)	90 (42.5)	
1, n (%)	78 (23.1)	17 (13.5)	61 (28.8)	
≥ 2, n (%)	69 (20.4)	8 (6.3)	61 (28.8)	
Number of ED visits				<.001
0, n (%)	173 (51.2)	97 (77.0)	76 (35.8)	
1, n (%)	80 (23.7)	18 (14.3)	62 (29.2)	
≥ 2, n (%)	85 (25.1)	11 (8.7)	74 (34.9)	
Number of physician office visits, mean (SD)	25.5 (24.8)	19.3 (14.5)	29.2 (28.6)	<.001

Figure 4: Hospitalization and ED visits among newly treated PNET patients, with or without carcinoid syndrome symptoms (N=338)



## DISCUSSION

- Descriptive analysis showed nearly two-thirds of newly treated PNET patients (with either targeted therapy or chemotherapy) had symptoms related to CS, with fatigue, dyspnea or wheezing, and diarrhea being most common. This result appears consistent with prior research indicating a prevalence of CS symptoms of 62% among NET patients treated with a standard dose of SSA.<sup>1</sup>
- In addition, PNET patients with CS symptoms used significantly more healthcare resources than those without symptoms; 57.5% were admitted as inpatients and 64.2% sought ED care. This increased use may result from a high burden of symptoms and comorbid conditions.

## LIMITATIONS

- A limitation of this study of privately-insured patients is that the results may not be generalizable to uninsured individuals or to those with other types of insurance not included in this database.
- This analysis did not adjust for factors such as age, comorbidities, and disease severity, which may account for some of the observed differences in healthcare use by CS symptom status. However, we examined basic characteristics between the two groups and found them to be similar.
- Finally, both the overreporting of cases that were unrelated to CS (e.g. diarrhea from causes other than CS) and underreporting of cases that did not result in the adjudication of a medical claim may have impacted the CS symptom status of some PNET patients.

## CONCLUSION

- Findings provide information using a claims database analyses about real-world burden of CS symptoms in newly treated PNET patients (initially treated with either targeted therapy or chemotherapy) based on healthcare use. To our knowledge, this is the first claims database study in the US to provide these assessments for CS in PNET.
- PNET patients with CS symptoms had much higher rates of hospitalization, ED visits, and physician office visits than those without CS symptoms.
- Further research is needed to better understand the complete burden of CS symptoms in PNET, to include also healthcare costs associated with this observed excess resource use and costs associated with quality of life or functional status burden.

### References

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