

Economic Burden of Illness of Malignant Gastrointestinal Neuroendocrine Tumors (NET)

Beilei Cai, PhD¹; Maureen P. Neary, PhD¹; Michael S. Broder, MD, MSHS²; Eunice Chang, PhD²; Elya Papoyan, MPH²; Al B. Benson III, MD³

¹Novartis Pharmaceuticals Corporation, East Hanover, NJ 07936; ²Partnership for Health Analytic Research, LLC, Beverly Hills, CA 90212; ³Northwestern University, Chicago, IL

BACKGROUND

- Neuroendocrine tumors (NET) comprise a broad set of tumors that are rare and slow-growing.
- Almost two-thirds of NETs arise in the gastrointestinal (GI) tract.
- U.S. incidence of all NET has increased from 10.9 cases per million person-years (PMPY) in 1973 to 52.5 PMPY in 2004.¹
- With the incidence of GI NET tumors increasing, it is important to understand the burden of the disease.

METHODS

- Retrospective, cross-sectional study using 2014 data from 2 U.S. commercial claims databases: Truven Health Analytics MarketScan and IMS PharMetrics.

Inclusion Criteria:

- Age ≥ 18, AND
- ≥ 1 inpatient or ≥ 2 outpatient claims for GI NET in 2014, AND
- ≥ 1 claim (inpatient or outpatient) with malignant GI NET or secondary (2°) malignant neoplasm of liver (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 197.7) in 2014, AND
- continuously enrolled in 2014.

Study Measures:

- Demographics and comorbidities
 - Charlson comorbidity index, which includes a total of 22 conditions and can predict 10-year mortality risks, was used to evaluate the patient's prognosis.²
 - Number of chronic conditions based on a validated index which captures chronic conditions that last at least one year, and place limitations on self-care or require ongoing medical care.³
- Presence of carcinoid syndrome (ICD-9-CM 259.2) in any claim.
- Systemic therapies: somatostatin analogues, targeted therapy, cytotoxic chemotherapy, and interferon.
- GI resection.
- Liver directed therapies: liver surgery excluding transplant, liver transplant, liver lesion ablation (includes radio, cryo, microwave, and thermal; laparoscopic, open, and percutaneous), embolization (includes bland, radio, and chemo) and radiation therapy (includes typical source plus LINAC).
- All-cause and GI NET-specific utilization (claims with primary diagnosis of GI NET).
- All-cause and GI NET-specific healthcare, pharmacy, inpatient, ED, and outpatient costs.
- Descriptive statistics, including mean, median, standard deviation, and percentage are reported for all study measures.
- Analyses were repeated for 2009-2013. Results were similar and are not presented.

RESULTS

Demographic and Clinical Characteristics

- 2,968 GI-NET patients were identified (Table 1).
 - Mean (SD) age was 52.7 (9.1).
 - 55.0% were female.
 - 25.8% had a claim with secondary malignant neoplasm of liver.
 - 25.2% had a claim with diagnosis codes for carcinoid syndrome.
- 33.0% (n=978) of patients received systemic therapy (e.g., surgery, embolization) and 8.0% (n=237) liver directed therapy (Table 2).
 - Among the 978 patients who received systemic therapies, 82.4% (n=806) used somatostatin analogues, 23.5% (n=230) cytotoxic chemotherapies, and 8.8% (n=86) targeted therapies.

Table 2. GI NET Therapies

All Patients, No.	2,968
Systemic Therapies, no. (%)	978 (33.0)
Somatostatin analogues	806 (27.2)
Octreotide LAR	764 (25.7)
Octreotide SA	145 (4.9)
Targeted therapies	86 (2.9)
Everolimus	66 (2.2)
Sunitinib	24 (0.8)
Lanreotide	14 (0.5)
Cytotoxic chemotherapies^a	230 (7.7)
Fluorouracil or 5-FU	127 (4.3)
Capecitabine	92 (3.1)
Oxaliplatin	92 (3.1)
Temozolomide	67 (2.3)
Doxorubicin	9 (0.3)
Streptozocin	8 (0.3)
Dacarbazine	2 (0.1)
Thalidomide	1 (0.0)
Interferon	4 (0.1)
Non-systemic therapies, no. (%)	769 (25.9)
GI resection	594 (20.0)
Liver Directed Therapies	237 (8.0)
Embolization	96 (3.2)
Liver surgery	89 (3.0)
Liver lesion ablation	52 (1.8)
Radiation therapy	55 (1.9)
Liver transplant	3 (0.1)

^aLiposomal doxorubicin was included in cytotoxic chemotherapy; however, the search did not yield any results for these patients.

Table 1. Demographics and Comorbidities

All Patients, No.	2,968
Age (years), mean (SD)	52.7 (9.1)
Female, no. (%)	1,632 (55.0)
Region, no. (%)	
South	1,367 (46.1)
Midwest	687 (23.1)
Northeast	592 (19.9)
West	322 (10.8)
Charlson comorbidity index, mean (SD)	5.5 (4.3)
No. of chronic conditions, mean (SD)	5.2 (2.2)
2° malignant neoplasm of liver, no. (%)	766 (25.8)
Carcinoid Syndrome, no. (%)	747 (25.2)

Healthcare Utilization and Costs (Table 3; Figure 1)

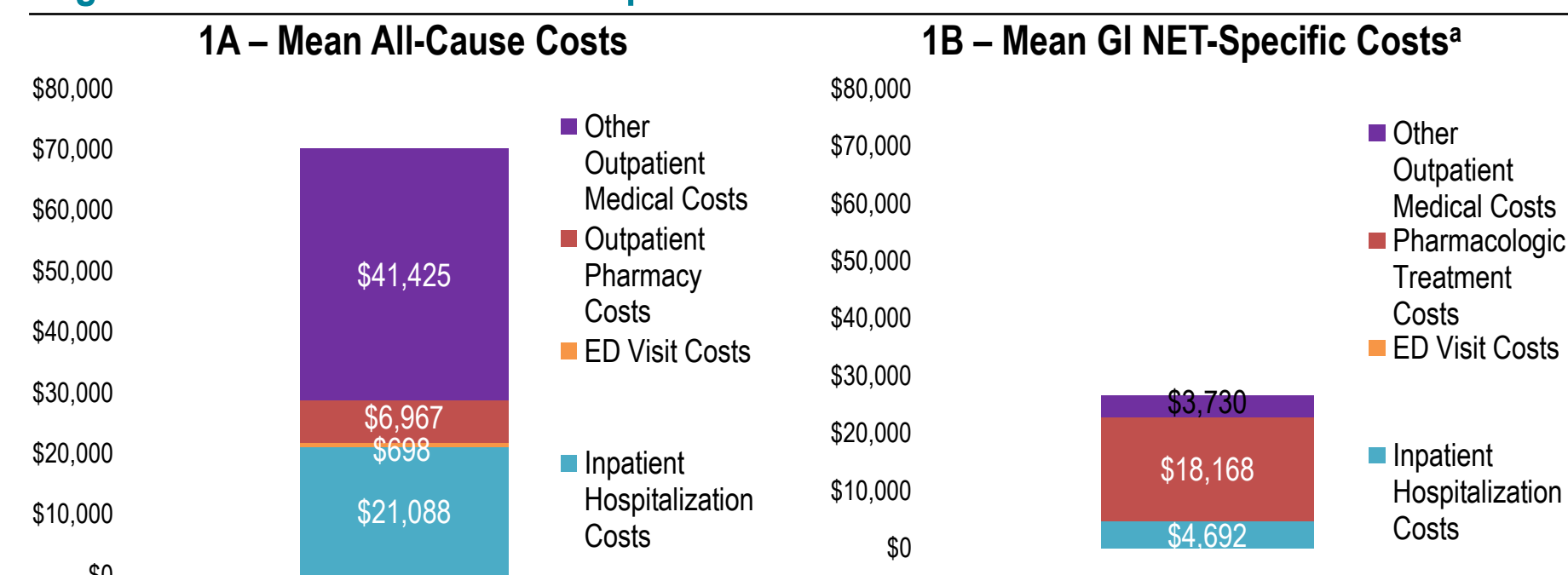
- Overall, patients had mean (SD) 16.6 (14.2) office visits, 33.5% had ≥1 ED visit, and 40.5% ≥1 hospitalization.
- Mean (SD) length of stay was 10.7 (17.4) days among hospitalized patients for any cause.
- Annual all-cause costs were \$70,179, comprising \$6,967 outpatient pharmacy and \$63,212 medical (\$41,425 outpatient, \$21,088 inpatient, and \$698 ED).
- GI NET-specific utilization and costs were a fraction of the overall however it should be taken into consideration that only claims with GI NET as the primary diagnosis code were considered GI NET-specific. ICD-9-CM codes for disease related complications were not included.
 - Less than one percent of patients had a GI NET-specific ED visit and 14.1% experienced a GI-net specific inpatient hospitalization.
 - Mean (SD) length of stay was 6.5 (9.1) days for GI NET-specific hospitalizations.
 - Annual GI NET-specific costs were \$26,612, 68.3% of which comprised GI-NET specific pharmacologic therapy costs.

Table 3. Annual Healthcare Utilization and Costs

All Patients, No.	2,968
No. of office visits, mean (SD)	16.6 (14.2)
No. of ED visits, mean (SD)	0.62 (1.4)
0, no. (%)	1,973 (66.5)
1	599 (20.2)
2	226 (7.6)
3+	170 (5.7)
No. of inpatient hospitalizations, mean (SD)	0.72 (1.3)
0, no. (%)	1,767 (59.5)
1	748 (25.2)
2	255 (8.6)
3+	198 (6.7)
Length of stay (days), mean (SD)	10.7 (17.4)
No. of GI NET-specific office visits, mean (SD)	2.2 (3.9)
No. of GI NET-specific ED visits, mean (SD)	0.01 (0.1)
0, no. (%)	2,947 (99.3)
1+	21 (0.7)
No. of GI NET-specific inpatient hospitalizations, mean (SD)	0.15 (0.4)
0, no. (%)	2,550 (85.9)
1+	418 (14.1)
Length of stay (days), mean (SD)	6.5 (9.1)
All-cause costs, mean (SD)	\$70,179 (93,363)
All-cause outpatient pharmacy costs ^a	\$6,967 (19,762)
All-cause medical costs (excludes outpatient pharmacy)	\$63,212 (87,931)
GI NET-specific^b costs, mean (SD)	\$26,612 (45,245)
GI NET-specific pharmacologic treatments costs ^c	\$18,168 (41,603)
GI NET-specific medical costs (excludes pharmacologic treatments)	\$8,443 (18,929)

^aPharmacy cost calculations only reflect outpatient pharmacy claims; ^bGI NET-specific costs were calculated by summing the claims with GI NET as the primary diagnosis; ^cPharmacologic treatment costs include all inpatient, outpatient and pharmacy claims that include one of the therapies specified in the methods section.

Figure 1: All-Cause and GI NET-Specific Costs



^aGI NET-specific costs reflect costs of claims with GI NET as the primary diagnosis code and do not include any claims with diagnosis codes for disease related complications; pharmacy costs only reflect outpatient pharmacy claims while pharmacologic treatment costs include all inpatient, outpatient and pharmacy claims that include one of the therapies specified in the methods section; GI NET-specific ED visit costs were \$22 on average (not labeled in Figure 1B).

CONCLUSIONS

- Resource use and costs for treatment of malignant GI NET patients were high. Mean annual cost was >\$70,000 compared to a national average of ~\$38,000 among all cancers in the first year.⁴
- While 40% of patients were admitted to the hospital, the majority of costs were from the outpatient setting.
- One-third of patients received systemic therapies, most commonly somatostatin analogues, and GI NET-specific pharmacology costs represented ~26% of the total.
- Despite evidence in the literature regarding the suboptimal response rates in GI NET patients who receive chemotherapy compared to other treatments, approximately 24% of patients in this study were treated with cytotoxic chemotherapy.
- The development of more therapies is needed. Additional effective therapies may lead to better outcomes for patients and may mitigate healthcare resource and cost utilization.

LIMITATIONS

- GI NET-specific health care utilization and costs are likely to be significantly underestimated as they exclude hospitalizations with a primary diagnosis of disease related complications (e.g., bowel obstruction as the primary diagnosis).
- These results only reflect patients with commercial insurance and do not include those with Medicaid, Medicare, or uninsured individuals. Results may not be nationally representative.
- Costs were calculated based on patients with GI NET diagnosis code in year 2014, as it is possible patients were newly diagnosed during the year, the costs calculated here may be an underestimation.
- GI NET patients were identified using ICD-9-CM codes; neither pathologic diagnosis nor stage could be confirmed in this administrative database.

REFERENCES

- Yao JC, Hassan M, Phan A, Dagohoy C, Leary C, Mares JE, Abdalla EK, Fleming JB, Vauthey JN, Rashid A, Evans DB. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *Journal of Clinical Oncology*. 2008 Jun 20;26(18):3063-72.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373-383
- Chronic Condition Indicator (CCI) for ICD-9-CM. Rockville, MD: Agency for Health Care Policy and Research, 2009. Available from: URL: <http://www.hcup-us.ahrq.gov/toolsoftware/chronic/chronic.jsp>
- Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010–2020. *Journal of the National Cancer Institute*. 2011 Jan 12;103(2):117-128.

