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Real-World Treatment Patterns for Lung Neuroendocrine Tumors: A Claims Database Analysis

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Keywords
Chemotherapy · Somatostatin analogue · Neuroendocrine tumor · Insurance claims

Abstract
Objective: The aim of this study was to describe real-world lung neuroendocrine tumor (NET) treatment patterns. ***Methods:*** This study examined cytotoxic chemotherapy (CC), somatostatin analogues (SSA), targeted therapy (TT), interferon, and liver-directed therapies in 2 US claims databases. Patients ≥18 years with ≥1 inpatient or ≥2 outpatient claims for lung NET, initiating pharmacologic treatment between July 1, 2009, and June 30, 2014, were identified and followed until the end of enrollment or study end, whichever occurred first. ***Results:*** A total of 785 newly pharmacologically treated lung NET patients were identified: mean (SD) age was 58.6 (9.1) years; 54.0% were female; 78.2% started first-line therapy with CC, 18.1% with SSA, and 1.1% with TT. Mean duration of first-line treatment was 397 days for SSA, 142 days for CC, and 135 days for TT. 74.1% of patients received no pharmacological treatment beyond first-line. The most common second-line treatment was SSA. ***Conclusions:*** Most patients received CC as first-line treatment, with SSA being less common. SSA-treated patients remained on therapy for >1 year, compared to <5 months for CC. The high proportion of patients using chemotherapy and the low proportion receiving second-line treatment seems consistent with treatment guidelines for small cell lung cancer rather than for NET. Future studies are warranted to describe reasons for treatment choice, discontinuation, and switching.

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Introduction

Neuroendocrine tumors (NETs) comprise a broad family of rare and often slow-growing malignancies. NETs can develop anywhere in the body and arise from neuroendocrine cells throughout the endocrine system [1, 2]. Approximately one-quarter of NETs occur in the lungs [3]. Based on the US Surveillance Epidemiology and End Results (SEER) database, approximately 10% of lung NETs are found in the bronchi [4]. While they remain rare, the incidence and prevalence of NETs appear to be increasing worldwide [5–9]. The incidence of NETs in the US increased from 10.9 cases per million person-years (PMPY) in 1973 to 69.8 PMPY in 2012. Lung NET

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incidence rose from 3.0 to 16.0 cases PMPY during the same time frame [10].

Lung NETs are classified on a spectrum from low-grade typical carcinoid to intermediate-grade atypical carcinoid, to high-grade large-cell neuroendocrine carcinoma and small-cell carcinoma [11]. About 5% of lung NETs secrete peptides and neuroamines that cause distinct syndromes (e.g., carcinoid syndrome), in which case they are referred to as "functional" tumors [4]. Clinical presentation depends on the site of the primary tumor and whether they are functional. Surgery may be curative in the early low-grade stages, but delayed diagnosis is typical as functional presentation with hormonally active tumor products is rare [4, 11]. For patients with metastatic disease, treatment varies depending on the location. If confined to the liver (the most frequent site), metastases may potentially be treated by surgical resection or liver-directed therapies. In other circumstances, usual treatment includes pharmacologic therapy with agents typically used in other NETs (e.g., everolimus, sunitinib, and somatostatin analogues [SSA]) or in small cell lung cancer (SCLC) (e.g., cisplatin/etoposide).

Although multiple pharmacotherapy options exist, the evidence for the choice of one over another is suboptimal, and it is unclear how physicians in practice choose treatments in this rare disease. We aimed to describe the current real-world treatment patterns of lung NETs in a large sample of patients.

Materials and Methods

We conducted a longitudinal, retrospective cohort analysis of newly pharmacologically treated lung NET patients using 2 large US commercial claims databases. Data from the Truven Health Analytics MarketScan® Database and the IMS PharMetrics Database were combined to increase the sample size. Both databases are Health Insurance Portability and Accountability Act compliant administrative claims databases that contain de-identified adjudicated medical claims (e.g., inpatient and outpatient services) and pharmacy claims (e.g., outpatient prescriptions) submitted for payment by providers, health-care facilities, and pharmacies. For both data sources, claims include information on each physician visit, medical procedure, hospitalization, drug dispensed, date of service, number of days of medication supplied, test performed, and complete payment information. Each medical claim has a principal diagnosis and secondary diagnoses codes associated with it. Available patient demographic information includes age, gender, and geographic region. Dates of enrollment and disenrollment are also recorded. As the data were fully de-identified, this study was considered exempt from approval by the institutional review board.

Patients at least 18 years of age were identified from each dataset if they had at least 1 inpatient or 2 outpatient claims with an International Statistical Classification of Disease-9-Clinical Modification (ICD-9-CM) for lung NET (209.21, 209.61) during the study identification period (July 1, 2009, to June 30, 2014). The claim for a pharmacologic treatment of interest after the appearance of the lung NET diagnosis code was considered the index date. Patients were required to be enrolled for a baseline period of at least 6 months before the index date. To ensure that the study included newly pharmacologically treated patients, those with any evidence of pharmacologic treatment during the baseline period were excluded. Patients were followed for a variable length of time: until the end of enrollment or the study end date (December 31, 2014), whichever was first. In order to avoid including the same patient twice, we searched for any patients with the same age, gender, region, and date of lung NET diagnosis who could be found in both databases, but we found none.

The primary outcome measure was the use of pharmacologic or liver-directed therapy. Pharmacotherapy was divided into 4 groups: SSA, targeted therapies (TT), cytotoxic chemotherapies (CC), and interferon. SSA included octreotide and lanreotide, TT included everolimus and sunitinib, and CC included carboplatin, cisplatin, etoposide, temozolomide, streptozotocin, doxorubicin, liposomal doxorubicin, fluorouracil, capecitabine, dacarbazine, oxaliplatin, and thalidomide. Pharmacologic therapy was identified in claims using both the Healthcare Common Procedure Coding System (HCPCS) and National Drug Codes. Liver-directed therapies comprised liver surgery (including transplant), liver lesion ablation (using radiotherapy, cryotherapy, microwave and thermal energy and including laparoscopic, open, and percutaneous routes), embolization (including bland, radioisotope, and chemotherapy), and radiation therapy. Liver-directed therapies were identified in claims using HCPCS, ICD-9-CM, and Current Procedural Terminology codes. Chemotherapy was observed only once and on the same date, as embolization was considered chemoembolization and not part of a pharmacologic regimen.

First-line therapy was defined as the pharmacologic treatment regimen (e.g., monotherapy or combination) observed on, or within 3 months of, the index date. Second-line therapy was defined as beginning when treatment was switched from one category of pharmacotherapy to another (e.g., from SSA alone to CC alone), or when a new category of treatment was added (e.g., from SSA alone to SSA plus CC). Changes from one cytotoxic agent to another, or one SSA to another, were not considered a switch. The first day of treatment switch or addition was defined as the initiation date of second-line therapy.

Means and proportions were presented in tabular analyses. An inverse Kaplan-Meier curve was used to show duration of first-line therapy. All data transformations and statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC, USA). Graphical analyses were conducted using GRAPHx™, which uses multi-colored line segments to represent various treatments, plotted over time.

Results

There were 731 patients in the MarketScan Database and 1,037 in the PharMetrics Database meeting the definition of lung NET who also had a claim for pharmacologic treatment between July 1, 2009, and June 30, 2014.

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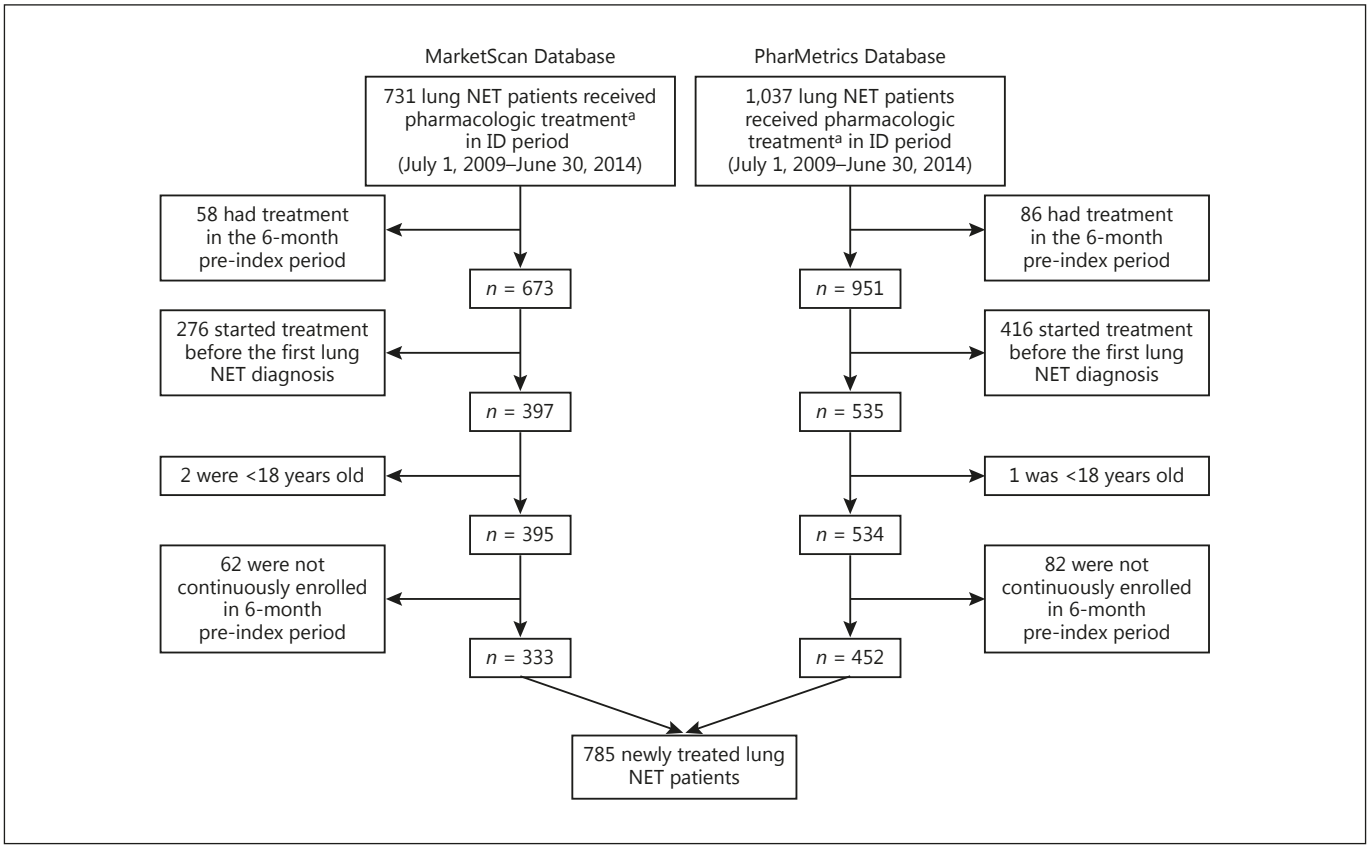

Fig. 1. Patient identification. There were 731 and 1,037 lung NET patients who also had a claim for pharmacologic treatment between July 1, 2009, and June 30, 2014, in the MarketScan and PharMetrics Databases, respectively. After excluding patients who had treatment during a 6-month pre-index period (and who therefore were considered to be continuing, rather than initiating, treatment); received treatment before receiving a diagnosis of lung NET; were <18 years old; or were not continuously enrolled in the 6-month pre-index period, there remained 785 newly treated lung NET patients who were included in the study. NET, neuroendocrine tumor. [a] Somatostatin analogues, targeted therapy, cytotoxic chemotherapy, or interferon.

After excluding patients who received treatment during a 6-month pre-index period (and who therefore were considered to be continuing, rather than initiating, treatment); patients who had received treatment before receiving a diagnosis of lung NET; those who were <18 years old; and those not continuously enrolled in the 6-month pre-index period, there were 785 newly treated lung NET patients who were included in the study (Fig. 1).

There were more females (n = 424, 54.0%) than males (n = 361, 46.0%) in the study group. The average age (SD) was 58.6 (9.1) years, and 52.5% of the patients were between 55 and 64 years old. All regions of the US were represented (Table 1). Of the 785 patients, 614 (78.2%) were treated with CC as first-line therapy. An additional 12 patients (1.5%) received CC in combination with SSA or TT. The second largest group (n = 142, 18.1%) was treated with SSA monotherapy, and 9 (1.1%) received TT monotherapy. Follow-up was variable, with a mean (SD, median) of 460 (401.1, 330) days (Table 1). Mean (SD) duration of first-line therapy was 192 (237.7) days for all newly treated patients. The mean (SD) observed duration of treatment for first-line SSA monotherapy users was 397 (390.7) days. Treatment duration (SD) was 142 (150.1) days for first-line CC monotherapy and 135 (104.4) days for first-line TT monotherapy (Table 2). By 460 days of treatment (1.26 years), half of SSA initiators had discontinued treatment, compared to 102 days (0.28 years) for half of CC users to discontinue treatment (Fig. 2).

By the end of follow-up, 74.1% (n = 582) of the patients had stopped pharmacologic therapy completely. These patients continued to be enrolled in 1 of the databases but

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Table 1. Patient demographics and follow-up, stratified by first-line pharmacologic treatment

	First-line treatment								All newly treated patients
	CC	SSA[a]	TT	SSA + CC	SSA + TT	TT + CC	SSA + interferon	SSA + TT + CC	
Subjects	614 (78.2)	142 (18.1)	9 (1.1)	9 (1.1)	6 (0.8)	2 (0.3)	2 (0.3)	1 (0.1)	785 (100.0)
Age, years	58.8±8.8	58.0±10.3	60.0±7.8	58.4±7.4	54.2±8.7	67.5±7.8	43.0±8.5	53.0±0	58.6±9.1
25–34 years	5 (0.8)	1 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (0.8)
35–44 years	32 (5.2)	12 (8.5)	0 (0)	0 (0)	1 (16.7)	0 (0)	1 (50.0)	0 (0)	46 (5.9)
45–54 years	128 (20.8)	36 (25.4)	2 (22.2)	3 (33.3)	0 (0)	0 (0)	1 (50.0)	1 (100.0)	171 (21.8)
55–64 years	330 (53.7)	66 (46.5)	5 (55.6)	5 (55.6)	5 (83.3)	1 (50.0)	0 (0)	0 (0)	412 (52.5)
≥65 years	119 (19.4)	27 (19.0)	2 (22.2)	1 (11.1)	0 (0)	1 (50.0)	0 (0)	0 (0)	150 (19.1)
Female	323 (52.6)	88 (62.0)	1 (11.1)	5 (55.6)	4 (66.7)	1 (50.0)	1 (50.0)	1 (100.0)	424 (54.0)
Region									
Midwest	136 (22.1)	41 (28.9)	3 (33.3)	2 (22.2)	0 (0)	0 (0)	0 (0)	0 (0)	182 (23.2)
Northeast	158 (25.7)	28 (19.7)	4 (44.4)	1 (11.1)	2 (33.3)	0 (0)	0 (0)	0 (0)	193 (24.6)
South	263 (42.8)	48 (33.8)	1 (11.1)	4 (44.4)	3 (50.0)	2 (100.0)	1 (50.0)	1 (100.0)	323 (41.1)
West	57 (9.3)	25 (17.6)	1 (11.1)	2 (22.2)	1 (16.7)	0 (0)	1 (50.0)	0 (0)	87 (11.1)
Year of treatment initiation									
2009	41 (6.7)	9 (6.3)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	0 (0)	51 (6.5)
2010	89 (14.5)	30 (21.1)	2 (22.2)	1 (11.1)	2 (33.3)	1 (50.0)	2 (100.0)	1 (100.0)	128 (16.3)
2011	126 (20.5)	28 (19.7)	3 (33.3)	1 (11.1)	1 (16.7)	0 (0)	0 (0)	0 (0)	159 (20.3)
2012	156 (25.4)	28 (19.7)	2 (22.2)	4 (44.4)	0 (0)	1 (50.0)	0 (0)	0 (0)	191 (24.3)
2013	133 (21.7)	34 (23.9)	2 (22.2)	1 (11.1)	2 (33.3)	0 (0)	0 (0)	0 (0)	172 (21.9)
2014	69 (11.2)	13 (9.2)	0 (0)	1 (11.1)	1 (16.7)	0 (0)	0 (0)	0 (0)	84 (10.7)
Follow-up[b]	428±381.5	602±452.2	290±243.4	733±586.2	387±259.0	369±167.6	437±116.0	297±n/a	460±401.1
[median], days	[302]	[490]	[219]	[504]	[376]	[369]	[437]	[297]	[330]

Values are *n* (%) or means ± SD unless otherwise indicated. CC, cytotoxic chemotherapy; SSA, somatostatin analogues; TT, targeted therapy; n/a, not applicable. [a] Ninety-seven patients were treated with octreotide LAR, 45 with octreotide SA, and 0 with lanreotide. [b] From index date until study end or end of enrollment (whichever occurred first) regardless of treatment continuation; treatment duration is shown in Table 2.

Table 2. Use of first-line treatment, stratified by first-line pharmacologic treatment

	First-line treatment								All newly treated patients
	CC	SSA	TT	SSA + CC	SSA + TT	TT + CC	SSA+ interferon	SSA + TT + CC	
Subjects	614 (78.2)	142 (18.1)	9 (1.1)	9 (1.1)	6 (0.8)	2 (0.3)	2 (0.3)	1 (0.1)	785 (100.0)
First-line treatment duration, days	142±150.1	397±390.7	135±104.4	354±295.8	301±224.0	215±50.2	324±43.8	280±n/a	192±237.7
First-line ending status									
Stop[a]	505 (82.2)	64 (45.1)	7 (77.8)	3 (33.3)	1 (16.7)	1 (50.0)	0 (0)	1 (100.0)	582 (74.1)
Switch[b]	31 (5.0)	23 (16.2)	1 (11.1)	3 (33.3)	1 (16.7)	0 (0)	1 (50.0)	0 (0)	60 (7.6)
End of enrollment[c]	78 (12.7)	55 (38.7)	1 (11.1)	3 (33.3)	4 (66.7)	1 (50.0)	1 (50.0)	0 (0)	143 (18.2)
Use of liver-directed therapy									
During first-line therapy	177 (28.8)	17 (12.0)	2 (22.2)	3 (33.3)	1 (16.7)	1 (50.0)	1 (50.0)	0 (0.0)	202 (25.7)
After first-line therapy	133 (21.7)	6 (4.2)	1 (11.1)	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	141 (18.0)

Values are *n* (%) or means ± SD. CC, cytotoxic chemotherapy; SSA, somatostatin analogues; TT, targeted therapy; n/a, not applicable. [a] Stop indicates first-line treatment termination observed during the follow-up period; no second-line pharmacologic therapy was observed. [b] Switch indicates first-line treatment termination observed during the follow-up period; second-line pharmacologic therapy (switch or addition) observed. [c] End of enrollment indicates that at the end of enrollment, first-line treatment was still ongoing.

no longer had claims for pharmacologic treatment. Almost 20% (*n* = 143, 18.2%) continued their initial therapy until the end of their enrollment; these patients were still receiving their first-line therapy at the time they disenrolled or at the end of study. The remaining 7.6% (*n* = 60) were observed to change pharmacologic treatment during the follow-up period (Table 2). In Figure 3, patients continuing enrollment but without further treatment are

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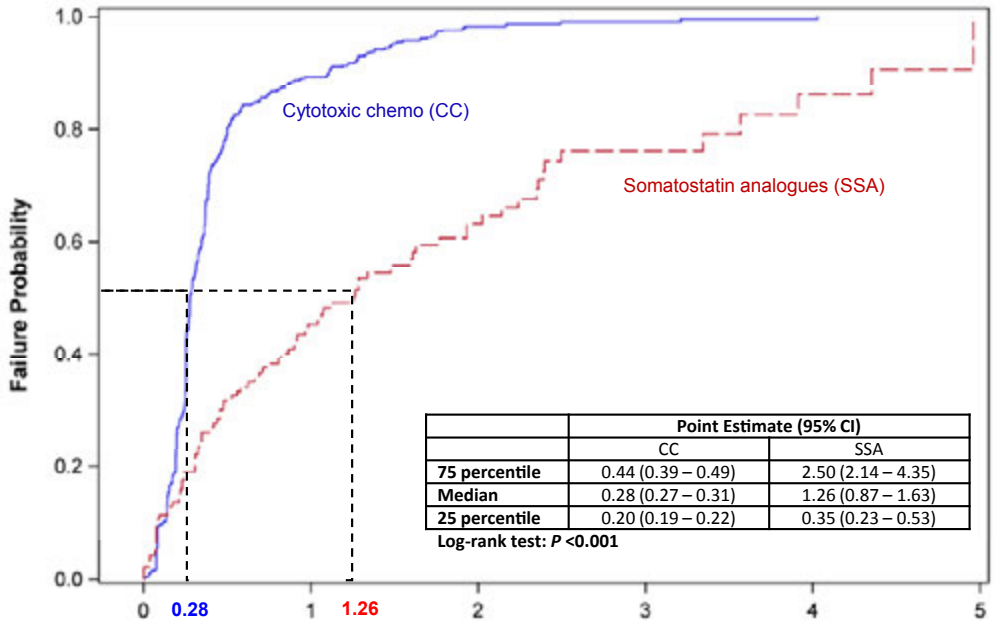

	Point Estimate (95% CI)	
	CC	SSA
75 percentile	0.44 (0.39 – 0.49)	2.50 (2.14 – 4.35)
Median	0.28 (0.27 – 0.31)	1.26 (0.87 – 1.63)
25 percentile	0.20 (0.19 – 0.22)	0.35 (0.23 – 0.53)

Log-rank test: *P* <0.001

	No. of Patients at Risk										
	Index Date	0.5Y	1Y	1.5Y	2Y	2.5Y	3Y	3.5Y	4Y	4.5Y	5Y
CC	614	104	48	18	5	2	3	1	1	0	0
SSA	142	84	59	36	27	13	9	6	4	2	0

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Fig. 2. Inverse Kaplan-Meier survival curve: time to first-line treatment discontinuation. By 460 days of treatment (1.26 years), half of SSA initiators had discontinued treatment, compared to 102 days (0.28 years) for half of CC users to discontinue treatment. Nine patients with targeted therapies in the first line are not shown. SSA, somatostatin analogues; CC, cytotoxic chemotherapy; Y, years.

represented by colored line segments that terminate in gray segments of variable length, with the color representing the specific pharmacotherapy used and the gray representing the period of no treatment. A colored segment terminating in white indicates the patient was observed to continue treatment until the end of enrollment, whereas a colored segment terminating in a different colored segment indicates a treatment switch. Liver-directed therapy (represented as red line segments) was interspersed throughout periods of both pharmacologic treatment (colored segments) and periods of no pharmacologic treatment (gray segments) (Fig. 3). There were 60 patients observed to begin second-line therapy. Of these, 31 (51.7%) had initially been treated with CC. Among these 31 first-line CC users, for 15 (48.4%) patients the second-line therapy was SSA. In patients whose first-line therapy was not CC, most received SSA monotherapy or SSA combination therapy as second line (Table 3).

Discussion

This study combined 2 very large, nationally representative claims databases, which together represent up to 100 million covered lives, to develop a sample size adequate to describe real-world treatment patterns for an uncommon cancer. Three findings were of particular interest. First, 78% of patients began therapy with CC, compared to just over 18% with SSA monotherapy and 1% with TT. Second, the median duration of first-line treatment varied considerably, depending on the treatment selected: half of patients treated with chemotherapy remained on treatment for about 3.4 months, whereas half of patients treated with SSA remained on treatment for more than 1 year. Third, despite the many available treatment options, nearly 6 in 7 patients were not observed to receive treatment with second-line pharmacotherapy of any type.

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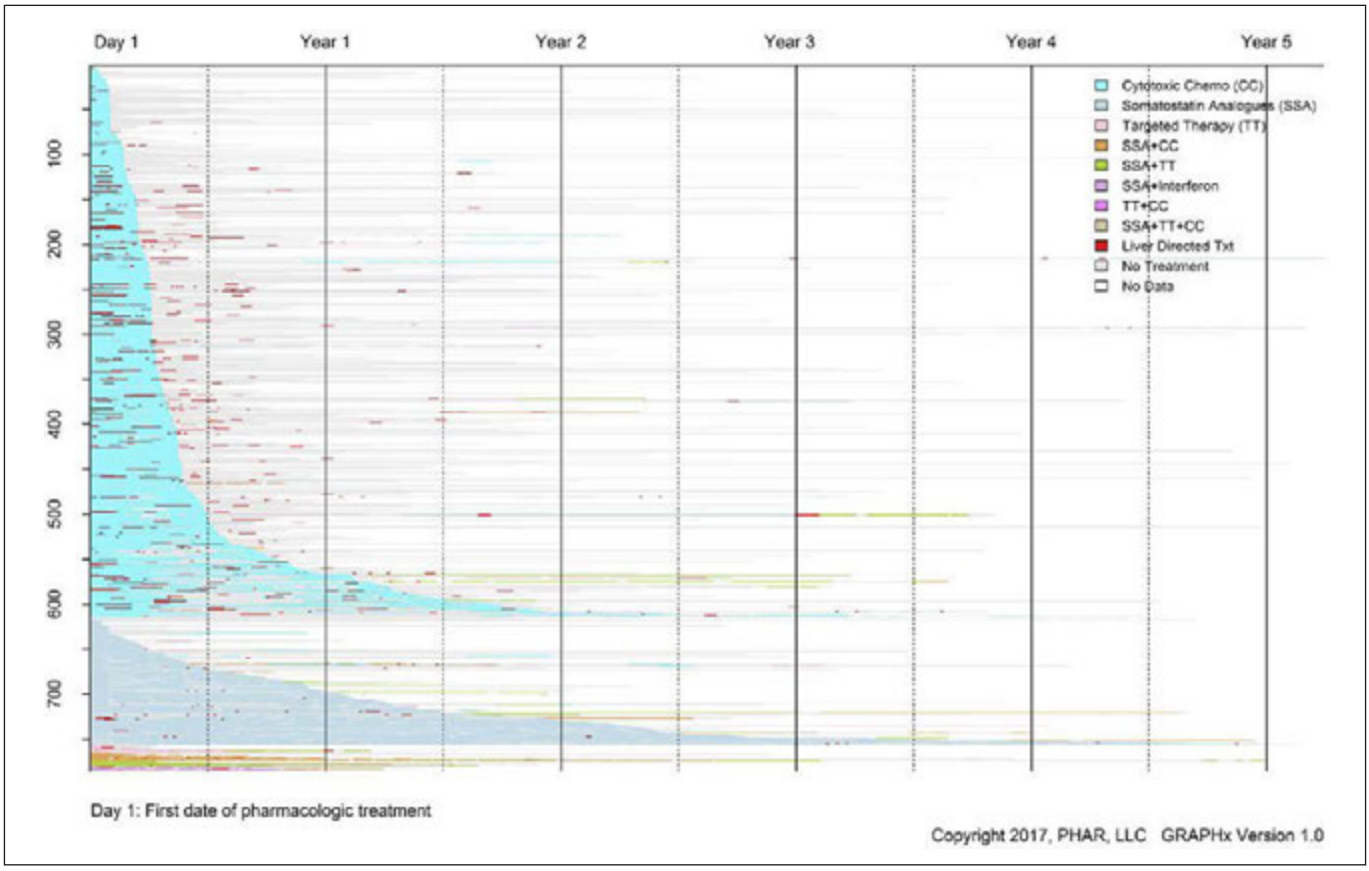

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Fig. 3. Comprehensive graphical representation of pharmacologic treatment for 785 patients with lung NETs. In this graphical representation, each patient is represented by a single row. The *y*-axis is labeled to indicate the number of patients. Time is shown on the *x*-axis. For each patient, their complete treatment history can be followed by observing the initial color and changes to different colors which indicate treatment changes. Changes to gray indicate that no treatment was observed with continued enrollment, and changes to white indicate that the patient has disenrolled and no further observation was possible. The vertical organization of the segment is arbitrary. Lines are organized in the current figure by first-line therapy (e.g., all segments beginning in dark blue are grouped together), then by length of initial treatment. NET, neuroendocrine tumor; CC, cytotoxic chemotherapy; SSA, somatostatin analogues; TT, targeted therapy.

Table 3. Second-line treatment, stratified by first-line pharmacologic treatment

	First-line treatment						Patients with second-line treatment
	CC	SSA	TT	SSA + CC	SSA + TT	SSA + interferon	
Subjects	31 (51.7)	23 (38.3)	1 (1.7)	3 (5.0)	1 (1.7)	1 (1.7)	60 (100.0)
Second-line treatment							
SSA	15 (48.4)		0 (0)	0 (0)	0 (0)	0 (0)	15 (25.0)
SSA + TT	3 (9.7)	7 (30.4)	1 (100.0)	2 (66.7)		0 (0)	13 (21.7)
SSA + CC	5 (16.1)	6 (26.1)	0 (0)		1 (100.0)	1 (100.0)	13 (21.7)
TT	8 (25.8)	2 (8.7)		1 (33.3)	0 (0)	0 (0)	11 (18.3)
CC		7 (30.4)	0 (0)	0 (0)	0 (0)	0 (0)	7 (11.7)
SSA + interferon	0 (0)	1 (4.3)	0 (0)	0 (0)	0 (0)		1 (1.7)

Values are *n* (%). CC, cytotoxic chemotherapy; SSA, somatostatin analogues; TT, targeted therapy.

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Treating NET is a complex process. Treatments are individualized based on tumor size, location, and pathology, as well as whether the tumor is functional, type and extent of the symptoms, and speed of the progression. Until 2017, the National Comprehensive Cancer Network (NCCN) covered the treatment of lung NET in 2 separate guidelines: NET and SCLC; since the 2017 update, the algorithm is now only presented in the NET guidelines. The NCCN NET guidelines generally recommend SSA as first-line treatment for unresectable and/or metastatic disease [12–14]. For typical lung NET, the NET guidelines mention chemotherapy as a Category 3 recommendation (major NCCN disagreement that the intervention is appropriate) only if other treatment options are not feasible; although for atypical disease and low-grade NETs with high tumor burden, chemotherapy may initially be used [3, 12–14]. The NCCN SCLC guidelines in place during the time of this study (e.g., all prior to 2017) recommended TT or CC for most patients with lung NETs, reserving SSA for patients with positive octreotide scans or carcinoid syndrome [15, 16]. Thus, it may be that physicians treating lung NETs more often followed the NCCN SCLC guidelines than the NCCN NET guidelines. Alternatively, the group in our study who was treated with CC may have included more atypical carcinoids, poorly differentiated or high-grade lung cancers, or small cell cancers, for example, than those treated with SSA. This cannot be confirmed as our administrative claims dataset did not contain such information, and privacy restrictions prohibit trying to contact patients or physicians to obtain it. Although we did not examine particular chemotherapeutic agents in this study, in a prior (unpublished) analysis using a similar population we found carboplatin, cisplatin, etoposide, and temozolomide were the most commonly used agents.

The second observation is consistent with the clinical finding that patients continue SSA therapy for a sustained amount of time. Patients initiating treatment with SSA in our study remained on first-line therapy longer than patients initiating CC or TT. The third observation, that only a small proportion of patients were observed to receive second-line treatment, was surprising. The 5-year survival of patients with low- and intermediate-grade lung NETs ranges from 61 to 100%, and from 15 to 57% for higher-grade large cell neuroendocrine cancer [10, 11]. Most surviving patients would be expected to receive continued treatment, whether in the form of liver-directed treatment or pharmacotherapy. Although definitive conclusions are difficult to make because of loss to follow-up, nearly 60% of the patients were observed to continue enrollment but stop therapy. That is, they survived and remained in the dataset, but no second-line pharmacotherapy use could be identified.

We investigated the possibility that these patients received some liver-directed treatment that alleviated their symptoms or controlled their disease, obviating the need for second-line treatment. However, we found no evidence of this: liver-directed treatment was not more common in patients who stopped therapy. The majority of patients stopped treatment while still enrolled in the health plan, although if patients had secondary insurance that was used to cover their NET treatment we might have missed further treatment. Just over 14% of patients were 65 years old and older and would have been eligible for Medicare, and patients 64 years old at the time of our study would have become eligible for Medicare during the course of follow-up. Payment rules regarding patients with both commercial coverage and Medicare are complex [17] but generally require the commercial payer (for which we did have data) to be primarily responsible for payment. In cases where Medicare had primary responsibility, we would have missed claims for pharmacologic or liver-directed therapy and thus underestimated treatment. The magnitude of this problem is impossible to estimate using our current data source. A study using Medicare data and examining only patients over 65 years might be less likely to suffer from this bias. Finally, it may indeed be the case that some patients stop therapy after first-line treatment. Patients may be terminal and choose not to undergo further treatment, or they may be relatively asymptomatic and decline to be treated. To verify the study findings and understand reasons for discontinuation of treatment after first-line, a study using more detailed clinical information (e.g., medical charts or physician surveys) is warranted.

Our study had other limitations, and these may partially explain some of our findings. First, we could not confirm the diagnosis of lung NET clinically and relied on insurance claims. Tumor grade, stage, and histopathology are not recorded in insurance claims. It may be that some patients had a clinical or laboratory finding suggesting that chemotherapy would be beneficial, or they had SCLC incorrectly coded as NET. Second, patients observed to initiate cytotoxic treatment may have been treated in the past with other agents and may either have progressed or were intolerant to those agents. We reviewed data for 6 months before the first pharmacologic treatment, but treatments more than 6 months in the past would have been missed. Third, although median follow-up was more than 13 months, loss to follow-up

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was high. When (or if) individuals who were lost to follow-up progressed to second-line treatment cannot be determined. A majority of patients stopped treatment while still enrolled in the health plan. However, if patients had secondary insurance, we might have missed further treatment. Fourth, neither death nor the reason for treatment discontinuation are reported in commercial claims. So, although therapy may be stopped when patients are terminally ill, this cannot be confirmed. Finally, the database only included individuals with commercial and Medicare supplemental insurance. The majority of US individuals ≥65 years old have Medicare as their primary source of insurance. Our sample may not be representative of Medicare patients in general or of the uninsured.

To our best knowledge, this is the first study examining lung NET treatment patterns in the US. In this retrospective study of real-world pharmacologic treatment patterns, we found that 78% of patients began therapy with chemotherapy and 18% with SSA monotherapy. Mean treatment duration with CC was about 4.7 months. Lung NET patients were treated with SSAs for over 1 year, but this treatment duration was likely underestimated by the short duration of follow-up found in insurance claims databases. The high proportion of patients using chemotherapy and the low proportion receiving second-line pharmacotherapy seems consistent with established treatment guidelines for SCLC rather than for NET. With additional pharmacological treatment options for NET, future studies are warranted to further describe detailed treatment sequences for lung NET, including underlying reasons for treatment discontinuations and switching, along with associated clinical outcomes through the use of clinical information (e.g., medical charts, registries, and/or physician surveys).

Disclosure Statement

B.C. and M.P.N. are employees of Novartis. A.B.B. is an employee of Northwestern University and was paid by Novartis to consult as a subject matter expert. M.S.B., E.C., and E.P. are employees of Partnership for Health Analytic Research, LLC, a health services research company paid by Novartis to conduct this research.

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